

9th Postgraduate Course for Training in Reproductive Medicine and Reproductive Biology Scientific Reviews and Research Projects presented by the Participants



Geneva WHO Collaborating Center in Human Reproduction in collaboration with WHO Department of Reproductive Health and Research

Scientific reviews done by the participants of the 9th Postgraduate course

- <u>Apoptosis in the first-trimester decidua: the role in maintaining immune tolerance at the maternal-foetal interface (slide presentation)</u> M. Jerzak (Poland)
- Cervical assessment and other tests to predict preterm delivery (slide presentation) A. Fekih (Tunisia)
- <u>Cervical priming before surgical termination of first trimester pregnancy (slide presentation)</u> B. Gurguc (Turkey)
- <u>Chronic prostatitis</u> (<u>slide presentation</u>) R.A. Burnazyan (Armenia)
- Do fertility drugs increase the risk of ovarian cancer ? (slide presentation) M. Lamm (Argentina)
- Domestic violence in pregnancy (slide presentation) S. Parvez (Pakistan)
- Duration of treatment for asymptomatic bacteriuria in pregnant and non pregnant women (slide presentation) A. Roganti (Argentina)
- Ectopic pregnancy Diagnosis and treatment (slide presentation) A. Dadivanian (Armenia)
- Effect of micronutrients on pregnancy outcomes (slide presentation) R. Kabra (India)

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- Female genital mutilation M.A. El Imam (Sudan)
- Genetic analyses in the infertile couple (slide presentation) F. Florescu (Romania)
- <u>Global situation of STDs and future challenges</u> (slide presentation) M. Ahsan (Bangladesh)
- <u>H.T.A gravidique et mortalité maternelle</u> (slide presentation) F. Najah (Tunisia)
- Key points in the design of interventions to improve reproductive health among young people (slide presentation) L. Lombardi (Guatemala)
- Management of endometriosis associated infertility (slide presentation) R. Aniuliene (Lithuania)
- <u>Medical vs surgical termination of pregnancy (slide presentation</u>) L. Say (Turkey)
- Obstetric ultrasonography and maternal and perinatal mortality (slide presentation) J.D. Seffah (Ghana)
- Ovarian hyperstimulation syndrome in assisted reproduction (slide presentation) A. Peloggia (Brazil)
- Prevalence of sexually transmitted diseases in refugee population worldwide (slide presentation) B. Ahounou (Benin)
- Recombinant FSH : Options for ovarian stimulation (slide presentation) G. Kabili (Albania)
- <u>Semen quality in the male population</u> (slide presentation) B. Zilaitiene (Lithuania)
- Should genetic screening for Fragile X syndrome be recommended in Indonesian children with mental retardation ? (slide presentation) M. Mantik (Indonesia)
- Sperm chromatin structure : Implications on human fertility (slide presentation) G. Tofoski (Macedonia)
- The management of tubal obstruction (slide presentation) N. Nkele (Cameroon)
- The use of 10 mg Mifepristone as emergency contraception (slide presentation) G. Adriaansz (Indonesia)
- <u>Tubal infertility</u> (slide presentation) A.M. Tahir (Indonesia)
- Vitamin A supplementation during pregnancy (slide presentation) D.S. Nurdiati (Indonesia)

Reproductive health country profiles edited by the participants of the Postgraduate course

- Albania D. Islami, F. Kallajxhi, O. Gliozheni
- Armenia K. Martirosyan
- Cameroon S. Ako, S. Fokoua, M.Tchana Sinou, R. Leke
- Georgia L. Baramidze
- Hungary Z. Borthaiser, A. Kereszturi
- Indonesia S. Hadijono, N. Pramono, A. Soejoenoes, U. Praptohardjo
- Lithuania (slide presentation) L. Maleckiene
- <u>Russian Federation</u> (slide presentation) A. Ledina
- Tunisian Medical Web F. Anis, F. Najah

03.12.02

WATER NETWORK advancing reproductive health through research



Geneva WHO Collaborating Center in Human Reproduction

in collaboration with

UNDP/UNFPA/WHO/World Bank Special Programme of Research, Development & Research Training in Human Reproduction

Coordinator: Dr. Soerjo Hadijono

- <u>Matweb Network Initiative</u> S. Hadijono (Indonesia)
- <u>How to Get an Internet Connection and Join the Matweb Reproductive Health Network</u> S. Hadijono (Indonesia)

Scientific reviews done by the participants of the 8th Postgraduate course

- Antenatal Screening of Sickle Cell Disease M. Tchana Sinou (Cameroon)
- <u>Antenatal Screening of Sickle Cell Disease</u> (slide presentation) M. Tchana Sinou (Cameroon)
- Cytology as a Cervical Screening Test: How effective is it? S. Bomfim-Hyppolito (Brazil)
- <u>Cytology as a Cervical Screening Test: How effective is it?</u> (slide presentation) S. Bomfim-Hyppolito (Brazil)

MatWeb Network

- Efficacy of Emergency Contraception Regimens (slide presentation) C. Enciulescu (Romania)
- Emergency Contraception in Adolescents S. Cenameri (Albania)
- Emergency Contraception in Adolescents (slide presentation) S. Cenameri (Albania)
- <u>Mechanism of Action of Mifepristone and Levonorgestrel for Emergency Contraception</u> B. Krämer (Germany)
- <u>Mechanism of Action of Mifepristone and Levonorgestrel for Emergency Contraception</u> (slide presentation) B. Krämer (Germany)
- Preterm Premature Rupture of the Membranes M. Gjoni (Albania)
- Preterm Premature Rupture of the Membranes (slide presentation) M. Gjoni (Albania)
- <u>Recombinant Luteinizing Hormone. Is it necessary?</u> J.C. Pou (Argentina)
- <u>Recombinant Luteinizing Hormone. Is it necessary?</u> (slide presentation) J.C. Pou (Argentina)
- <u>Review of Two Rapid Screening Tests for Asymptomatic Bacteriuria during Pregnancy</u> E.J. Abalos (Argentina)
- <u>Review of Two Rapid Screening Tests for Asymptomatic Bacteriuria during Pregnancy</u> (slide presentation) E.J. Abalos (Argentina)
- <u>Second Trimester Maternal Serum Screening Programmes for the Detection of Down's Syndrome</u> A. Paralloi (Albania)
- <u>Second Trimester Maternal Serum Screening Programmes for the Detection of Down's Syndrome</u> (slide presentation) - A. Paralloi (Albania)
- <u>Semen Analysis</u> L. Rrumbullaku (Albania)
- <u>Single-dose Antibacterial Treatment for Asymptomatic Bacteriuria in Pregnancy</u> C. Diculescu (Romania)
- <u>Single-dose Antibacterial Treatment for Asymptomatic Bacteriuria in Pregnancy</u> (slide presentation) C. Diculescu (Romania)
- South Asian Perspective on Fertility Regulation Samina Shaheen Ali (Pakistan)
- The Importance of Sperm Morphology in the Evaluation of Male Infertility S. Parastie (Romania)
- <u>The Importance of Sperm Morphology in the Evaluation of Male Infertility</u> (slide presentation) S. Parastie (Romania)
- <u>The Recombinant Follicle Stimulating Hormone : A New Alternative for Induction of Ovulation and</u> <u>Treatment of Polycystic Ovary Syndrome</u> - D. Prasmusinto (Indonesia)
- <u>The Recombinant Follicle Stimulating Hormone : A New Alternative for Induction of Ovulation and</u> <u>Treatment of Polycystic Ovary Syndrome</u> (slide presentation) - D. Prasmusinto (Indonesia)

Reproductive health country profiles edited by the participants of the Postgraduate course

- Albania D. Islami, F. Kallajxhi, O. Gliozheni
- <u>Armenia</u> K. Martirosyan
- <u>Cameroon</u> S. Ako, S. Fokoua, M.Tchana Sinou, R. Leke
- <u>Georgia</u> L. Baramidze
- <u>Georgia</u> (slide presentation) L. Baramidze

MatWeb Network

- Hungary Z. Borthaiser, A. Kereszturi
- Indonesia S. Hadijono, N. Pramono, A. Soejoenoes, U. Praptohardjo

Scientific projects proposed by the participants of the 8th Postgraduate course

- <u>A Demonstration Project for Cervical Cancer screening using the « see and treat » approach</u> S. Bomfim-Hyppolito (Brazil)
- Evaluation of the Effectiveness of Screening Asymptomatic Pregnant Women for Bacteriuria by a <u>Combined Reagent Strip</u> - E.J. Abalos (Argentina)
- <u>Health Service Quality Improvement after Normal Delivery Competency-Based Training Package</u> S. Hadijono (Indonesia)
- <u>Health Service Quality Improvement after Normal Delivery Competency-Based Training Package</u> (slide presentation) - S. Hadijono (Indonesia)
- Prevalence of Cervical and Vaginal Infections in Pregnant Women J.C. Vásquez Nieblas (Cuba)
- <u>Prevalence of Cervical and Vaginal Infections in Pregnant Women</u> (slide presentation) J.C. Vásquez Nieblas (Cuba)
- Preterm Premature Rupture of the Fetal Membranes (Pprom) in Albania M. Gjoni (Albania)
- <u>The Acceptability of Contraceptives by Women in Pakistan. A Proposal for a Research Project</u> -Samina Shaheen Ali (Pakistan)

Training manual

• <u>Maternidade Escola Assis Chateaubriand Universidade Federal do Ceara: Manual for training</u> <u>Traditional Birth Attendants (TBAs) and Community Health Workers in Reproductive Health</u> - S. Bomfim-Hyppolito (Brazil)

03.12.02

Postgraduate Course in Reproductive Medicine and Reproductive Biology 1999 - List of Participants

Postgraduate Course in Reproductive Medicine and Reproductive Biology

1999



LIST OF PARTICIPANTS

NAME	FIRST NAME	COUNTRY	SPONSOR
ADRIAANSZ	George	Indonesia	IAMANEH
AHOUNOU	Brice	Benin	
AHSAN	Mohammad Ali	Bangladesh	IAMANEH
ANIULIENE	Rosita	Lithuania	UNFPA
BOURNAZIAN	Rouben	Armenia	UNFPA
DADIVANIAN	Ara	Armenia	UNFPA
EL-IMAM	Mohamed Ahmed	Sudan	IAMANEH
FEKIH	Anis	Tunisia	Ousseimi Foundation
FLORESCU	Fulga	Romania	IAMANEH
GURGUC	Banu	Turkey	WHO/part
JERZAK	Malgorzata	Poland	UNFPA
KABRA	Rita	India	
KABILI	Genc	Albania	SNSF1998
KATI	Kreston	Albania	IAMANEH
LAMM	Marina	Argentina	IAMANEH
LEDINA	Antonina	Russia	WHO
LOMBARDI GARCIA	Luis	Guatemala	IAMANEH
MALECKIENE	Laima	Lithuania	UNFPA
MANTIK	Max	Indonesia	IAMANEH

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Postgraduate Course in Reproductive Medicine and Reproductive Biology 1999 - List of Participants

NAJAH	Farah	Tunisia	Ousseimi Foundation
NKLE	Ndeki	Cameroon	Geneva-Yaounde Cooperation
NURDIATI	Detty	Indonesia	IAMANEH
PARVEZ	Sahar	Pakistan	IAMANEH
PELOGGIA	Alessandra	Brazil	IAMANEH
ROGANTI	Ariel	Argentina	WHO/part
SAY	Lale	Turkey	IAMANEH
SEFFAH	Darkwa	Ghana	WHO/part
TOFOSKI	Gligor	Macedonia	Ministry of Health of Macedonia
TAHIR	Andi Mardiah	Indonesia	IAMANEH
ZILAITIENE	Birute	Lithuania	WHO

26.11.02

9th POSTGRADUATE COURSE FOR TRAINING IN REPRODUCTIVE MEDICINE AND REPRODUCTIVE BIOLOGY

9th POSTGRADUATE COURSE FOR TRAINING IN REPRODUCTIVE MEDICINE AND REPRODUCTIVE BIOLOGY

WHO Collaborating Center in Human Reproduction Infertility and Gynecologic Endocrinology Clinic Department of Obstetrics and Gynecology Geneva University Hospital

in collaboration with

WHO Department of Reproductive Health and Research

Individual or all lectures listed here are public and can be attended by anyone interested in the field.

Lectures will be held in the Pavillon de l'Ecole de la Roseraie rue Barthélémy-Menn, 2nd floor or at WHO in Room M 505 when indicated by * or in Room M 605 when indicated by **

LECTURE PLAN 1999

Sept. 1	09.00h	Get together, formalities	
	09.30h	A. Campana (Geneva) G. Benagiano (Geneva) P. Rowe (WHO) F. Santschi (Geneva)	Introduction
	10.00h	E. Diczfalusy (Rönninge)	« Voyage into the 21 st century ; new realities and new challenges »
	14.00h	Presentation of the course and discussion	
	16.00h	Visit of the CMU library	
	17.30h	Get-together party (Cité Universitaire)	
Sept. 2	09.00h	J. Kasonde (Geneva)	Reproductive health in developing countries
	10.00h	J. Cottingham (WHO)	Gender issues in reproductive health research
Sept. 3	09.00h	F. Urner (Geneva)	Gametogenesis

	10.00h	F. Urner (Geneva)	Fertilization
	11.00h	E. Tribolet (Geneva)	Oxytocin in reproductive biology
Sept. 6	09.00h	J.M. Dubuis (Geneva)	Puberty: Physiology
	10.00h	J.M. Dubuis (Geneva)	Puberty: Pathology
	11.00h	A. Mauron (Geneva)	Ethical aspects of gene therapy
	14.00h	A. Mauron (Geneva)	Ethical aspects of reproductive health
Sept. 7	09.00h	P. Bischof (Geneva)	Implantation
	10.00h	P. Bischof (Geneva)	Implantation
	11.00h	P. Bischof (Geneva)	Hormone receptors
Sept. 8	09.00h	P. Herrera (Geneva)	Embryo development
	10.00h	P. Herrera (Geneva)	Experimental embryology
	11.00h	F. Pralong (Lausanne)	Leptin and reproduction
Sept. 9	09.00h	R. Gaillard (Lausanne)	The hypothalamo-pituitary-gonadal axis
	10.00h	P. Bischof (Geneva)	Menstrual cycle
	11.00h	M. Aubert (Geneva)	Regulation of GnRH secretion
Sept. 10	09.00h	C. DeLozier (Geneva)	The genetics consultation in Obstetrics/Gynaecology: who, why, how
	10.00h	S. Dahoun (Geneva)	Chromosomal pathology
	11.00h	S.E. Antonarakis (Geneva)	Principles of molecular genetic diagnosis
	14.00h	G. de Candolle (Geneva)	Surgical treatment of female infertility
	15.00h	G. Santschi (Geneva)	IAMANEH
Sept. 13	09.00h	A. Bottani (Geneva)	Genetic counseling : principles and practical examples
	10.00h	M. Neerman (Geneva)	Genes implicated in sexual determination
	11.00h	S.E. Antonarakis(Geneva)	The human Genome Project and its implication for genetics in the 21 st century
	14.00h	C. DeLozier	Visit of the Division of Medical Genetics
Sept. 14 *	09.00h	J. Villar (WHO)	Type of epidemiologic clinical studies
*	10.00h	J. Villar (WHO)	Unbiased estimation of effectiveness of preventive interventions and treatments in reproductive health

*	11.00h	M. Gülmezoglu (WHO)	Randomized controlled trials : study design
*	14.00h	Visit of the WHO Library	·
Sept. 15 *	09.00h	J. Villar (WHO)	Clinical epidemiology/screening in reproductive health
*	10.00h	R. Kulier (Geneva)	Case-control studies
*	11.00h	M. Gülmezoglu (WHO)	Cohort studies
*	14.00h	E. Ezcurra (WHO)	Reproductive health in Latin America and the Caribbean
Sept. 16 *	09.00h	G. Piaggio (WHO)	Strategies for data analysis: I. Observational studies
*	10.00h	G. Piaggio (WHO)	Strategies for data analysis: II. Randomized controlled trials
*	11.00h	O. Frank (WHO)	Fertility and infertility: Developing country patterns
*	14.00h	M. Boulvain (Geneva)	Protocol development
Sept. 17 *	09.00h	M. Gülmezoglu (WHO)	Summarizing evidence of effectiveness of reproductive health care activities (systematic reviews)
*	10.00h	R. Kulier (Geneva), M. Gülmezoglu (WHO)	The Cochrane Library / The Reproductive Health Library
*	11.00h	J. Villar (WHO)	Expressing study results
*	14.00h	H. Bathija (WHO)	Reproductive health in Africa and Eastern Mediterranean
Sept. 20 **	09.00h	K. Yount (WHO)	Contraceptive prevalence trends globally
**	10.00h	K. Yount (WHO)	Maternal mortality measurements
**	11.00h	F. Lüdicke (Geneva)	Medical eligibility criteria for contraceptive methods
Sept. 21 **	09.00h	E. Ezcurra (WHO)	Oral contraceptives
**	10.30h	E. Ezcurra (WHO)	Risks and benefits and metabolic effects of oral contraceptives
Sept. 22 **	09.00h	C. d'Arcangues (WHO)	Long-acting hormonal methods for women
**	10.00h	C. d'Arcangues (WHO)	Natural methods

11.00h	P. Rowe (WHO)	Intrauterine devices and barrier methods
14.00h	Y.F. Wang (WHO)	Reproductive health in Asia and the Pacific
09.00h	H. Von Hertzen (WHO)	Induced abortion
10.00h	H. Von Hertzen (WHO)	Emergency contraception
11.00h	D. Griffin (WHO)	Immunocontraception
09.00h	H. Bathija (WHO)	Female sterilization
10.00h	H. Bathija (WHO)	Control of fertility in adolescence and premenopause
11.00h	M. Mbizvo (WHO)	Male contraception
14.00h	P. van Look (WHO)	Reproductive health research at WHO
09.00h	A. Campana (Geneva)	Definition, prevalence and etiology of infertility
10.00h	A. Campana (Geneva)	Evaluation of the infertile couple
11.00h	A. Campana (Geneva)	Spontaneous abortion
09.00h	D. El-Mowafi (Geneva)	Diagnostic methods in female infertility
10.00h	JPh. Bonjour (Geneva)	Osteoporosis
11.00h	D. El-Mowafi (Geneva)	Diagnosis and treatment of abnormal uterine bleeding
14.00h	A. Campana (Geneva)	Internet and Medline
09.00h	R. Martin-du-Pan (Geneva)	Diagnostic methods in male infertility
10.00h	H. Lucas (Geneva)	Semen analysis
11.00h	G. de Boccard (Geneva)	Treatment of male infertility
09.00h	A. Stalberg (Geneva)	Assisted reproductive technologies
10.00h	H. Lucas (Geneva)	Embryo development in vitro
11.00h	D. Rouiller (Geneva)	Diabetes and reproduction
14.00h	M. Rice (WHO)	Communication techniques in training
09.00h	D. de Ziegler (Geneva)	The menopause
10.00h	D. de Ziegler (Geneva)	Hormone replacement therapy
	 11.00h 14.00h 09.00h 11.00h 09.00h 11.00h 14.00h 09.00h 10.00h 11.00h 10.00h 10.00h 10.00h 10.00h 10.00h 10.00h 10.00h 10.00h 10.00h 	11.00h P. Rowe (WHO) 14.00h Y.F. Wang (WHO) 14.00h H. Von Hertzen (WHO) 09.00h H. Von Hertzen (WHO) 11.00h D. Griffin (WHO) 09.00h H. Bathija (WHO) 09.00h H. Bathija (WHO) 11.00h M. Mbizvo (WHO) 11.00h P. van Look (WHO) 14.00h P. van Look (WHO) 09.00h A. Campana (Geneva) 10.00h A. Campana (Geneva) 11.00h D. El-Mowafi (Geneva) 11.00h JPh. Bonjour (Geneva) 11.00h D. El-Mowafi (Geneva) 11.00h JPh. Bonjour (Geneva) 11.00h A. Campana (Geneva) 11.00h JPh. Bonjour (Geneva) 11.00h A. Campana (Geneva) 10.00h H. Lucas (Geneva) 11.00h G. de Boccard (Geneva) 10.00h H. Lucas (Geneva)

	11.00h	D. Chardonnens (Geneva)	Hormonal treatment of female infertility	
	14.00h	G. Benagiano (Geneva)	Reproductive health : a new dimension	
Oct. 4	09.00h	E. Megevand (Geneva), S. Nazeer (Geneva), P. Vassilakos (Geneva)	Cancer screening programmes/Colposcopy & Management of cervical dysplasia	
	11.00h	S. Nazeer (Geneva)	Reproductive Tract Infections (Classification - Diagnostics and Treatment - Syndromic Management)	
	14.00h	B. Held (Geneva)	Sequelae of RTIs - Ectopic pregnancy	
Oct. 5	09.00h	P. Huppi (Geneva)	Brain development in the newborn	
	10.00h	O. Irion (Geneva)	Prevention of vertical transmission of HIV infection	
	11.00h	M. Boulvain (Geneva)	Anaemia in pregnancy	
	14.00h	J.C. Schellenberg (Geneva)	Maternal obstetric emergencies	
Oct. 6	09.00h	E. Roset (Geneva)	Operative delivery	
	10.00h	Ph. Extermann (Geneva)	Fetal medicine	
	11.00h	R. Pfister (Geneva)	Neonatal examination and resuscitation in the delivery room	
	14.00h	M. Pfizenmaier (Geneva)	Visit of the delivery room	
Oct. 7		Lectures will be held at WHO - Room M 505		
*	09.00h	M. Usher-Patel (WHO)	Safe Motherhood Initiative	
*	10.00h	(WHO)	Introduction to country case work	
*	14.00h	(WHO)	Group work on country case work	
Oct. 8 *	09.00h	(WHO)	Group work on country case work	
	14.00h	(WHO)	Group presentation and discussion	

26.11.02

Apoptosis in the first-trimester decidua: the role in maintaining immune tolerance at the maternal-foetal interface

Malgorzata Jerzak^{1, 2}, Tutor: Paul Bischof³

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²Department of Gynaecology, University School of Medicine, Wroclaw, Poland

³Department of Obstetrics and Gynaecology, Geneva University Hospital, Switzerland

Malgorzata Jerzak is the recipient of Polish Science Award in 1999.

ABSTRACT

INTRODUCTION: Apoptosis has been proposed as a mechanism for maintaining tolerance in the immune system. Expression of Fas ligand (FasL) by the human trophoblast has been recently accepted as a mechanism providing protection against the lytic action of decidual immune cells.

OBJECTIVES: Therefore, the purpose of the review was to determine the role of apoptosis in pregnancy maintenance according to the latest literature.

METHODS: We used Medline literature search.

RESULTS: These data suggest that apoptosis may serve as a previously unsuspected mechanism to induce tolerance of the foetal allograft against maternal immune system.

CONCLUSION: Trophoblast cells usually fail to stimulate alloantigen-specific T cells, but they may express non-classical MHC alloantigens to which mothers can produce immunoglobulin G alloantibody, which require T helper cell activation. An apoptosis of activated maternal immune cells in the human decidua through Fas- FasL signalling may be a defence mechanism against rejection of the foetal allograft by maternal immune system. Therefore, in this review contribution of programmed cell death to placental remodelling during gestation and protection against maternal activated lymphocytes influx are strongly emphasised.

KEY WORDS: Apoptosis, Fas receptor, natural killer cell, T cell, placenta, pregnancy.

INTRODUCTION

The actual rate of the first-trimester pregnancy loss after implantation may exceed the number of clinically recognised pregnancies. In a course of clinically established pregnancies abortion occurs at the frequency of 15 %.¹ Recurrent spontaneous abortion affects 2 to 5 % of couples attempting to reproduce.² Recent data support a hypothesis that maternal immunologic assault against the placental cells could lead to foetal loss at an early stage of pregnancy.^{1, 3, 4} However, the mechanisms regulating the survival of human foetal allograft still remain a mystery of reproductive and developmental biology. Therefore, unravelling the mechanisms regulating placentogenesis is critical to understanding the pathogenesis of early pregnancy loss.

Apoptosis of T cells has been proposed as a mechanism for maintaining tolerance in the immune system.⁵ The induction of the apoptotic cell death can also be a possible factor that limits lymphocyte proliferation following activation.⁶ Characteristic features of apoptosis are: cell shrinking, reorganisation of the cell nucleus, active membrane blebbing, and fragmentation into membrane-bound vesicles known as apoptotic bodies, which are then phagocytosed by macrophages without an inflammatory response (in contrast to necrosis). Apoptosis is associated with oligonucleosomal DNA fragmentation resulting in a «ladder» on agarose electrophoresis.^{7, 8} Regulation of apoptosis. Bcl-2 family proteins interact with each other through the formation of homodimers and heterodimers and susceptibility to apoptosis is controlled through the interaction of bcl-2 related inhibitors and apoptosis.^{7, 9, 10} Recent data suggest that Fas (CD95), a cell surface receptor belonging to tumour necrosis factor receptor (TNFR) family, is a mediator of apoptosis through cross-linking with FasL.^{5, 6, 11} Fas is highly expressed on activated T cells and natural killer cells (NK cells).¹¹

APOPTOSIS AND PLACENTAL REMODELLING

There is some evidence that regulation of apoptosis may be important during implantation and early embryo development. It has been recently demonstrated that apoptosis in the endometrial glands can serve as a marker of receptive endometrium for implantation. Von Rango et al detected apoptosis in the glandular epithelium of the basalis at the beginning of the implantation window which extended to the functionalis in the luteal phase.¹² Proliferation and bcl-2 expression, which are predominant in the glandular compartment during the proliferative phase, are limited to the stromal compartment during the luteal phase of the menstrual cycle.^{12, 13} As during the first trimester of pregnancy lymphoid aggregates of large granular lymphocytes- CD56⁺ NK cells are found in the basal layer of the decidua, authors conclude that apoptosis of these lymphocytes may be the first observation of an immunological preparation of endometrium for the successful implantation. Moreover, apoptosis may be related to the loss of protective effect of bcl-2 which is accompanied by increased expression of bax protein (Fig 1).^{12, 14} However, decreased expression of bcl-2 and increased expression of bax in the decidua characterises failing first-trimester pregnancies.¹⁵ Data of Yui et al suggest that a physiological role of tumour necrosis factor alfa (TNF-a) and of interferon gamma (INF-g) expression in the placental villi may be to induce the apoptotic death of cytotrophoblast cells (CTB).^{16, 17} Both TNF-a receptors localise to the villous trophoblast, however the apoptotic death of primary CTB is mediated almost by TNF-a receptor p55 (TNFR-1) and TNF-a receptor p75 (TNFR-2) appears to have a little effect on this process.¹⁶ Epidermal growth factor (EGF) inhibits cytokine (TNF-a or INF-g)induced apoptosis of primary human trophoblast.¹⁷ The apoptotic cascade seems to be initiated in the villous CTB which in turn promotes syncytial fusion.¹⁸ Moreover, data of Ho et al show that TNF-a and INF-g stimulate CTB apoptosis within those placental villi expressing low levels of bcl-2 protein.¹⁹ It has been recently demonstrated that bcl-2 is present on CD56+NK cells in the decidual stroma, the decidual glandular epithelium, and in the syncytiotrophoblast (STB) of the chorionic villi.¹⁰ Chan et al. show apoptosis in clusters mainly confined to the non-dividing STBs whereas proliferative activity is limited to CTBs and to the stromal cells.²⁰Apoptotic DNA-fragmentation has been demonstrated in CTBs, being most abundant in early placenta. In contrast, bcl-2 protein

expression has been found in STBs, being less abundant in early placenta. These data indicate that early placenta is characterised by the highly proliferative activity of CTB cells associated with increased occurrence of apoptosis.²¹ Therefore, bcl-2 may prevent apoptosis in STB.^{22, 23} In contrast to normal pregnancy, apoptotic cells are predominant in the STB layer in cases of spontaneous abortion.²⁴ Moreover, bcl-2 expression is consistently lower in STB from women undergoing sporadic or recurrent spontaneous abortions.¹⁰ Placental apoptosis increases as pregnancy progresses what suggest that is a normal physiological phenomenon throughout gestation.²⁵ These findings provide a potential explanation for villous remodelling during placentogenesis. Therefore, apoptosis seems to participate in the regulation of the extravillous trophoblast invasion.

FAS-FASL SIGNALLING IN PLACENTA

Several studies indicate that inner CTB and outer STB layers of anchoring and floating villi of the first trimester express FasL.^{26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37} The expression of FasL by human trophoblast has been proposed as a mechanism for providing protection against the lytic action of decidual immune cells.^{26, 27, 28} FasL is positioned to prevent the exchange of activated immune cells between the mother and the foetus during pregnancy in mice.²⁶ FasL is appropriately positioned first in the uterus and then in the placenta to deter trafficking of activated Fas⁺ immune cells at the materno-foetal interface.²⁶ Kauma et al determined that Fas is expressed on CD45⁺ (leukocyte common antigen) cells, found in maternal decidua. Phytohemagglutinin and interleukin-2 activated peripheral blood lymphocytes co-cultured with trophoblast undergo apoptosis.²⁹ According to Coumans et al the frequency of cell death in the peripheral blood CD3⁺ cell population is higher when the lymphoid cells were co-cultured with trophoblast expressing FasL then when they were cultured alone.³⁰ Our data show Fas expression on decidual CD3⁺ T cells at the maternal-foetal interface in the first-trimester human pregnancy.³¹ According to Hammer et al. Fas is expressed on CD45⁺ maternal leukocytes in the first-trimester human placenta.³² It has been recently shown that Fas expressed by human placental CTB does not mediate apoptosis. These data suggest that the Fas response is inactivated by unknown mechanism to avoid killing by FasL constitutively expressed on neighbouring CTB or STB. Therefore, FasL at the maternal- foetal interface protects the placenta against a maternal leukocyte influx that may reduce fertility. Taken together, these findings suggest that FasL expressed by foetal trophoblast cells can induce apoptosis in activated lymphocytes and provides a mechanism for maternal immune tolerance to the foetus. In this sense, reduction of Fas or FasL function may be associated with pregnancy loss.

MOLECULAR MECHANISMS OF APOPTOSIS IN HUMAN PLACENTA

Our knowledge of the molecular mechanisms of the apoptotic pathway in the placenta has been recently updated. The role of molecules recruited to the Fas/Fas L signalling system including caspases seems to be important in the development of human placenta. Caspases are a family of intracellular cysteine proteases that cleave their specific substrates at aspartic acid residues.^{38, 39} These proteases are involved in cytokine processing and apoptosis regulation. The caspase-1- like

family (caspase-1, caspase-4, caspase-5) function is most relevant to cytokine processing and the caspase-3- like family members (caspase-2, caspase-3, caspase-6, caspase-8, caspase-9, caspase-10) are executors of apoptosis. Caspase activation by TNFR family is shown in figure 2 and figure3. TNFrelated apoptosis- inducing ligand (TRAIL), like FasL, is a member of TNFR family which through binding of their receptors (TRAIL-R) control apoptotic signal transduction pathways. TRAIL-R activate TRAIL signal pathway, e.g. DR4 (TRAIL-R1) and DR5 (TRAIL-R2) or may act as decoys, e.g. DcR1/TRID and DcR2/TRUNDD.³⁸ Phillips et al demonstrated the presence of mRNAs encoding TRAIL as well as the four TRAIL receptors (DR4, DR5, DcR1, DcR2) in human placenta.⁴⁰ TRAIL protein is prominent in STB, which is in closed contact with maternal blood containing immune cells, and TRAIL-R expression is enhanced by INF-g. It is now well recognised that TRAIL co-operates with FasL in limiting lymphocyte proliferation in the process termed activated cell death.^{41, 42} This provide a potential mechanism responsible for killing activated lymphocytes to establish immune privilege in the placenta. A new death domain-containing TNFR, termed death receptor-6 (DR6), which interacts with TNFR1- associated death domain (TRADD), has been also recently identified in the placenta.⁴³ Another novel cytokine that belongs to the TNF family termed THANK (a TNF homologue that activates apoptosis) seems to activate apoptosis in the placenta, however it is expressed in this site at low levels.⁴⁴ Shirashi et al. examined expression of cytolytic granules (granzyme B, perforins) originated from cytotoxic T cells that induce programmed cell death. Expression of granzyme B mRNA is increased while expression of perforin mRNA is not changed in placenta after interleukin-2 administration to pregnant mice.45

CONCLUSIONS

It is evident that balance between cell death and proliferation plays a pivotal role in the maintenance of normal tissue homeostasis. This can be particularly important for the successful development of human pregnancy. Some data suggest that T cells may regulate the maternal immune response to the foetal allograft. Activated (during pregnancy) T cells may produce Th2 cytokines (interleukin-3, interleukin-4, interleukin-5, interleukin-6, interleukin-10, interleukin-13, transforming growth factor b 2,3-related factors and other related cytokines) at the maternal- foetal interface during successful pregnancy. They also may produce broadly cytotoxic Th1 cytokines (interleukin-2, TNF-a, INF-g), which indicate that the conceptus may be regarded as an allograft that is recognised by the maternal immune system.^{46, 47, 48} Thus, it is clear that the maternal immune system during pregnancy can enhance or inhibit development of the foetus and the placenta.

A tissue-specific expression of human leukocyte antigen (HLA)-G, a non-classical class I major histocompatibility complex molecule, was detected on extravillus CTB. HLA-G is capable of inhibiting the natural killer activity of decidual large granular leukocytes and cytotoxic action of decidual T cells against HLA-G⁺ trophoblasts in the first trimester pregnancy.^{49, 50} However, it remained unclear how the STB is protected. Therefore, expression of FasL has been proposed as an alternative mechanism of protection for both CTB and STB.^{26, 27, 28}

Recent data support a hypothesis that apoptosis of activated T cell at the maternal- foetal interface can be a regulatory mechanism during pregnancy. Disturbances in the programmed cell death of activated T cells in the human decidua can be responsible for pregnancy loss. Therefore, the apoptosis of activated Th1 cells might be an interesting possible explanation of successful pregnancy outcome.

Trophoblast cells usually fail to stimulate alloantigen-specific T cells, but they may express non-classical major histocompatibility complex alloantigens to which the mother may produce immunoglobulin G alloantibody, which require T helper cell activation. Therefore, apoptosis of activated maternal immune cells in the human decidua, through Fas- FasL signalling, may be a defence mechanism against rejection of the foetal allograft by maternal immune system. However, studies of deficient in Fas/FasL interactions transgenic mice indicate that this defect has no adverse effect on pregnancy outcome.^{51, 52} Accumulating data suggest that apoptosis may serve as a very important mechanism to induce tolerance of the human foetal allograft against maternal immune system. There are still a lot of controversies about diagnosis and management of recurrent spontaneous abortion because the pathogenesis pregnancy loss remains still unclear.⁵³ The challenge for the future would be to introduce new treatment modalities influencing the placental apoptotic pathways.

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Figure 1. The relative ratios of bcl-2 and bax heterodimers to homodimers determine the susceptibility to programmed cell death (PCD) in syncytiotrophoblast thus influence pregnancy outcome.



Figure 2. Caspase activation by tumour necrosis factor receptor (TNFR) family.

In human placenta six members of the TNFR family have been identified to contain cytosolic death domains. On ligand- induced clustering, these cytosolic domains recruit the adaptor protein: TNFR1-associated death domain (TRADD) and/ or Fas-associated death domain protein (FADD) and probably others that have not been discovered yet. FADD then binds to death effector domain (DED)-containing procaspases, particularly procaspase-8 and perhaps procaspase-10, what results in activation of caspases and triggers the apoptotic cascade. Downstream protease within this pathway can cleave and activate procaspase-3. Caspase-3 is a key protease that becomes activated during the early stages of the programmed cell death, so it is a marker of cells undergoing apoptosis.



Figure 3. Molecules involved in the apoptotic cascade of the trophoblast cells.

Part of the extracellular domain of FasL is cleaved to bind the Fas receptor thus activating caspase-1 family, which initiates apoptotic cascade. Activation of these caspases lead to upstream of phosphatidylserine flip and finally in the sequence of the apoptotic pathway is activation of caspase-3, which is the executor of apoptosis. Bcl-2 codes for proteins of the outer mitochondrial membrane and can inhibit caspase-3 activation. Caspase-3 cleaves cytoplasmic and nuclear proteins and initiates the irreversible stages of the apoptotic cascade.

02.12.02

APOPTOSIS IN THE FIRST-TRIMESTER DECIDUA: THE ROLE IN MAINTAINING IMMUNE TOLERANCE AT THE MATERNAL-FOETAL INTERFACE.

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From Gill, 1997





APOPTOSIS CASCADE



From Huppertz, 1999



The aim of the review was to determine the role of apoptosis in pregnancy maintenance according to the latest literature



 APOPTOSIS AND PLACENTAL REMODELLING
 FAS-FASL SIGNALLING IN PLACENTA
 MOLECULAR MECHANISMS OF APOPTOSIS IN HUMAN PLACENTA The relative ratios of BCL-2 and BAX heterodimers to homodimers determine the susceptibility to programmed cell death (PCD) in syncytiotrophoblast (STB) thus influence pregnancy outcome.



From Lea, 1999 From Akcali, 1996



CD56+ LGL in decidual stroma
decidual glandular epithelium
syncytiotrophoblast of the chorionic villi

From Lea, 1997

The possible outcome of interaction between uterine NK cells and extravillous cytotrophoblast at the implantation site.



The possible outcome of interaction between uterine T cells and syncytio- and cytotrophoblast at the implantation site





From Van Parijs, 1999

Molecules involved in the apoptotic cascade of the trophoblast cells



From Huppertz, 1998



 Placental apoptosis increases as pregnancy progresses suggesting that it is a normal physiological phenomenon throughout gestation. Moreover, apoptosis seems to participate in the regulation of the extravillous trophoblast invasion and villous remodelling during placentogenesis.


In contrast to normal pregnancy, apoptotic cells are predominant in the STB layer in cases of spontaneous abortion. Moreover, bcl-2 expression is consistantly lower in STB from women undergoing sporadic or recurrent spontaneous abortions.



Trophoblast cells usually fail to stimulate alloantigen-specific T cells, but they may express non-classical MHC alloantigens to which mothers produce IgG alloantibody and that requires T helper cell activation. An apoptosis of activated maternal immune cells in the human decidua through Fas- FasL signalling may be a defence mechanism against rejection of the foetal allograft by maternal immune system.

The challenge for the future would be to introduce new treatment modalities influencing the placental apoptotic pathways.

Cervical Assessment And Other Tests To Predict Preterm Delivery

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ABSTRACT

Preterm delivery is the leading cause of neonatal mortality. Thus predicting a preterm delivery is a major obstetrical problem. Endovaginal ultrasonography is a highly reliable and reproducible method of cervical examination. Unlike with a digital cervical examination the entire length of the endocervical canal can be measured.

Using these tools, measuring the dilatation of the internal os does not require the examining finger to be placed inside the endocervical canal. Therefore, the internal os can be measured even if the external os is closed. While a digital examination assesses the <<dilatability>> of the internal os, an ultrasonography assesses the <<true degree of dilatation>>.

In a low-risk population endovaginal ultrasonography helps rule out a preterm delivery if cervical length is long enough. It can also detect cervical incompetence. In a high-risk population, women whose cervix is longer than 30 mm can be identified. These women have over 80% chance to deliver on or after 36 weeks of pregnancy. Preliminary studies suggest that performing an endovaginal ultrasonography could decrease the number of false positive clinical diagnosis of modified cervix and thus, save long, expensive and inefficient hospital stays.

I- INTRODUCTION:

Preterm labour is defined as labour occurring prior to the completion of 37 weeks of gestation (less than 259 days from the last menstrual period). It is a major cause of preterm delivery, a complication that affects approximately 10% of pregnancies¹.

Preterm birth is the cause of at least 75% of neonatal deaths that are not due to congenital malformations¹. In about one-third of cases, preterm delivery is iatrogenic and in the other two-thirds it is spontaneous. Survival of preterm infants is mainly dependent on gestational age at delivery and survival increases from less than 5% for those born at 23 weeks to more than 95% by 32 weeks^{2,3}. The risk of severe handicap in survivors decreases from more than 60% for those born at 23 weeks to less than 5% by 32 weeks. Consequently, prediction of the high-risk group for preterm delivery, and intervention to prevent this complication of pregnancy constitutes a major challenge in obstetrics⁴.

Several methods have been developed to evaluate the risk of preterm delivery: fibronectin assay from the cervical secretion⁶, amniocentesis for searching latent infection⁷, cytokins assay from the cervical secretion⁸. These techniques are complex, costly and have a limited positive predictive value of 50%⁹. The risk of preterm delivery is well correlated with the effacement and premature ripening of the cervix⁵

The accurate diagnosis of preterm labour with a reduction in the high false positive rate is an important goal. It is sometimes difficult to determine which patients are in true preterm labour when

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they present with uterine contractions. In such patients, transvaginal ultrasound assessment of cervical length allows a more objective evaluation compared with the digital examination⁹. By correctly identifying patients with cervical change in the form of a shortened cervical length, one may be able to decrease the numbers of patients falsely diagnosed with preterm labour. As a result, one may more appropriately hospitalize, treat, and closely follow patients with cervical changes and avoid prolonged hospitalization and treatment of those patients without such changes.

Although preterm birth has been one of the most pressing and important problems in obstetrics, the rate of preterm births has not changed over the past 40 years. Despite a great deal of research and the introduction of new diagnostic and therapeutic technologies, there has been little or no improvement in the outcome. Although there are many different treatments available, there is great controversy over their effectiveness in the prevention of prematurity and the management of patients in preterm labour. Lack of consensus on criteria for diagnosing preterm labour, variations in the choice, the route of administration and dosage of tocolytic agents, and differences in interpretation of success with therapy add to this dilemma. In addition, a clinician's personal experience with successful inhibition of preterm labour in individual patients may differ from the findings of published controlled studies¹⁰.

The aim of this study is to establish the relation between cervical length in an unselected population of pregnant women and the risk of spontaneous preterm delivery.

II- RISK FACTORS FOR PRETERM DELIVERIES:

II-1- Induced preterm delivery:

Among preterm deliveries, about 20% are the consequence of a medical decision to induce a preterm delivery.

Fetal and or maternal conditions are the causes of these medical decisions. They depend on the severity of the disease and the balance between the risk of intra-uterine death and neonatal mortality and morbidity.

The most frequent conditions indicating induced preterm delivery is: hypertension, intrauterine growth retardation, severe diabetes, rhesus iso-immunisation, abruptio placenta, and hemorrhagic placenta preavia...

II-2- Spontaneous preterm delivery:

Spontaneous preterm delivery represents 80% of all preterm deliveries. History of three or more first-trimester miscarriage or one second-trimester miscarriage is associated with preterm delivery. Women with uterine malformation, cervical incompetence or overdistended uterus (multiple gestation, hydramnios...) are at high risk of preterm delivery, because of either preterm labour or a decrease of cervical resistance. Infections, especially urinary tract infection may trigger the onset of contractions. Chorioamnionitis and or chronic cervical infections may represent a frequent but a difficult cause to diagnose of preterm labour. Finally, all these causes may lead to premature rupture of membranes or to preterm labour with intact membranes.

Preterm delivery is a frequent condition; therefore prevention of the consequences of preterm delivery for the neonates is essential which involves: screening, a correct treatment of underlying factors, early diagnosis, treatment of preterm labour, prevention of consequences in the neonates and delivery in optimal conditions.

III- MARKERS OF PRETERM LABOUR AND DELIVERY:

A number of studies have attempted to identify clinical and biochemical markers of preterm labour and delivery. Overall, these studies have shown that these markers have a low predictive value (Tables 1 and 2)¹². The most promising of these markers is the presence of fetal fibronectin in cervicovaginal secretions, which, if positive (defined as greater than 50ng per ml) after 20 weeks of gestation, indicates decidual disruption¹⁴.

In 1995, the U.S. Food and Drug Administration labelled fetal fibronectin enzymatic immunoassay for use as a screening test for preterm labour. In symptomatic women, fetal fibronectin has an excellent sensitivity (69 to 93%) ^{6,12} and a negative predictive value as high as 99.7% (or, in other words, a one in 333 chance of delivery within one week of a negative test result) ¹¹. The positive predictive value (PPV), that is, the ability to predict that a patient with a positive test result will have a preterm delivery, is as high as 83% in symptomatic women. However, it is not proven that fetal fibronectin is an useful screening test in unselected populations (PPV: 13 to 36%) ¹³.

At the present time, general use of the test cannot be recommended because of its cost (approximately USD 215), a lack of accessible laboratories performing the test and insufficient data to justify a clinical benefit¹⁴.

Markers	Test	Sensitivity	Specificity	PPV (%)	NPV (%)
		(%)	(%)		
FIBRONECTIN	CERVICAL OU	69 TO 93	72 TO 86	13 TO 83	81 TO 99
	VAGINAL				
IL6	SERUM	50	73 TO 85	47 TO 57	67 TO 86
	AMNIOTIC FLUID	52	100	100	79
ESTRADIOL-17b	SERUM	12	71 TO76	12 TO 14	
ESTRIOL	SALIVARY	71	77	27	77
PROGESTERONE	SERUM	6 TO 35	67 TO 69	7 TO 32	

Table.1: Ability of Biochemical markers to predict Preterm Labour¹⁴

Table.2: Ability of Clinical markers to Predict Preterm Labour¹⁴

Markers	Sensitivity	Specificity	PPV(%)	NPV (%)
	(%)	(%)		
Risk scoring system	88 to 92	23 to 30	94 to98	41 to 76
clinical	8 to 64	68 to 96	7 to 32	89 to 94
examination	76 to 100	55 to 59	55 to 75	93 to 100
ultrasonography				
Monitoring of	18 to 58	45 to 94	7 to 20	82 to 94
uterine activity				
Vaginal bleeding	8 to 36	89 to 95	21 to 82	82 to 97

Figure 1 (fig.1) lists a number of markers that have been proposed to identify women at risk of

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preterm delivery. These markers can be expected to appear early enough in the pathways such that their presence in elevated concentrations indicates the initiation of one of the specific pathways.

These markers are currently the subjects of much research. However, given that most cases of preterm delivery appear to involve multiple pathological pathways, no single marker is likely to be unmasked as the 'magic bullet' for identifying women at risk for preterm delivery¹⁵.

Cervical length was proposed as a marker of the risk of premature delivery, with a shorter cervix predicting a higher risk. Given the substantial intra- and inter-observer variations that occur with digital examinations, it has been hypothesised that transvaginal ultrasonography would provide a more reliable testing method. Transvaginal ultrasonography is a reproducible method of examination during pregnancy^{29,30}. Cervical dilatation has been demonstrated with some accuracy up to 4 cm. Cervical effacement and lower uterine segment changes may predate cervical dilatation. The unaffected cervix in the third trimester usually measures between 3.5 and 4.8 cm in length. Fifty-percent effacement corresponds to a cervical length of 1.5 cm, and 75-percent effacement corresponds to a length of 1.0 cm.

IV- TECHNIQUES FOR CERVICAL ASSESSMENT:

IV-1- Clinical examination:

Several risk-scoring systems have been developed to identify women likely at risk of preterm delivery. Of these, the system devised by Papiernik and modified by Creasy has been applied most extensively¹⁶. It was validated prospectively in New Zealand, although only 30% of women classified as high risk actually delivered prior to term. When used in the United States, results are controversial. The best results have been found in upper socio-economic populations¹⁶; these scores have been poorly predictive of preterm labour and delivery in inner-city populations¹⁷. Overall, the sensitivity (the likelihood that a women with preterm delivery will be correctly identified) of such systems is less than 50%, and the positive predictive value has been less than 20%. These scoring systems are more accurate for multigravid women because of the importance of prior pregnancy complications as a predictor.

There is a controversy as to whether routine cervical examinations in late second and early third trimesters are a useful screening technique for women with uncomplicated pregnancies. Cervical dilatation of at least 2 cm at 28 weeks of gestation was associated with an increased risk of prematurity in one study on unselected women¹⁸, and other study demonstrated increased risk with internal os dilatation of 1 cm or more in the early third trimester¹⁹. In two earlier series, however, cervical dilatation was present in at least 7% of patients at 28 weeks of gestation, increasing to 32% or more at 32 weeks of gestation, and was not associated with a greater likelihood of preterm delivery^{20,21}. A multinational randomized trial compared a policy of performing a cervical examination at each prenatal visit (2,803 women, mean six exams) to a policy of avoiding a cervical examination if possible (2,797 women mean one exam). There were no significant differences between the experimental and control groups with respect to preterm delivery (6.7% versus 6.4%). This large study suggests that there is no benefit to perform routine cervical examinations in pregnant women ²².

IV-2- Transabdominal ultrasonography:

With transabdominal ultrasonography, the distance separating the probe from the cervix involves the use of low frequency probe, which limitates the image resolution. To avoid this disadvantage, transabdominal ultrasonography requires a full bladder for accurate imaging of the lower uterine

segment. The full bladder, however, may cause distortion and falsely reassure the clinician of normal cervix (increases the cervical length²³ and closes the internal os). The reproducibility of the measures can't be realised without a constant degree of vesical repletion²⁴, which causes discomfort for both pregnant women and physician. Moreover, after 33 weeks of gestation, the shadowing of fetal parts prevent cervical examination²⁴ and reduces its feasibility^{23, 26}.

Despite of the possible inaccuracies, abdominal ultrasonography laid the basis for later and more accurate transvaginal ultrasonography studies. Because of its physical properties, high resolution, and ease of operation (feasibility > 97%) 23,25,27,28 , transvaginal ultrasonography became the preferred tool for cervical examination.

IV-3- Ultrasonography protocol:

Transvaginal ultrasonography is performed after emptying the bladder. The cervical length is measured with the probe placed in the anterior fornix of the vagina (fig.2). The appropriate sagittal view of the cervix is obtained by simultaneous imaging of its external and internal os. The cervical canal length is seen as a sonolucent line connecting these two points (fig.3).

Pressure on the cervix that might artificially increase its length is avoided by first obtaining a satisfactory image, then withdrawing the probe until the image is blurred, and reapplying only enough pressure to restore the image³⁴. Markers are placed at the furthest points at which the cervical canal walls are juxtaposed and the cervical length is measured.

The following parameters can also be obtained:

• Presence or absence of funnelling (fig.5): funnelling is defined as a protrusion of the amniotic membranes 3mm or more into the cervical canal³⁵.

Funnelling width (fig.4): the width of the internal os is measured in a longitudinal sagittal section and values of 5 mm or greater are recorded as significant dilatation³⁶.

• Funnelling length

The measurement of cervical length has a mean interobserver variation of 4-10%³⁶ and a mean intraobserver variation of 5%³⁶. At present, cervical changes after transfundal pressure testing the cervical competence are less reproducible³⁷.

IV-4- Equipment:

The probe must have an ultrasonic-frequency comprised between 5 and 7.5 MHz and a transducer having an angle comprised between 90° and 240° ³⁷.

V- NORMAL BIOMETRIC VALUES OF THE CERVIX:

V-1- Cervical length: (Table. 3)

The study of this parameter leads at two comments:

For the same gestationnel age, there is a large scattering of normal values. Cervical competence is more a continuous variable than a categorical variable³⁵. Indeed, this can explain how the same uterine activity can cause premature delivery in woman with short cervix (incompetent) and doesn't have any effect in woman with long cervix (competent)⁹.

Many authors³⁸ have observed that there is a decrease in cervical length among pregnant woman,

which begins between 17 and 28 weeks of gestation²⁶. Thus, we must take in account the gestational age at which ultrasonography is made to say that the cervical length is short compared to the cervical length threshold at that time.

Most of the authors concluded that parity has no significant effect in cervical length. Anderson²⁶ observed significant long cervical length in multiparous.

Lastly, small variations were observed between the populations: the mean cervical length is higher in Caucasian²⁸ than in Asiatic women²³.

Table.3: Cervical lengths: PROM: premature rupture of membrane, T: twin, HP: history of prematurity, RFP: risk factors of prematurity, CI: cervical incompetence

Authors	Number	CL 1 st	CL 2 nd	CL 3rd	Exclusion criteria
		trimester	trimester	trimester	
Andersen ³¹	178	39.8+/-8.5	41.6+/-10.2	32.2+/-11.6	T, no HP, RFP, CI
Okitsu ²³	129	41+/-2.7	40+/-6.3	31+/-7.2	PROM, HP
Smith ³⁸	109	37.8+/-6.6	38+/-7.7	37+/-7.7	PROM, metrorrhagy, T, HP, RFP
Murakawa ⁴⁷	177	-	35.3+/-	31.2+/-4.4	-

V-2- Internal os width: (fig. 4)

Okitsu²³ described the physiologic opening of the internal os after 30 weeks of gestation. Before this date the length of the internal os is less than 5mm.

V-3- Funneling: (fig. 4,5)

Some authors propose to classify funneling as:

- 1. Cervical nippeling: when the membrane protrusion is less or equal to 6 mm.
- 2. funneling: when the membrane protrusion is superior to 6 mm.

We must remember that funneling is always an abnormal condition

VI-COMPARISON BETWEEN ULTRASONOGRAPHIC AND CLINICAL EXAMINATION:

Digital examination of the cervix in a pregnant women provides the clinician with important information that can be used in the management of pregnancy. Regarding patient care, the shape, orientation, length, dilatation and effacement of the cervix are important in the decision-making process. However, digital exams are subjective and do not provide information about the upper half of the cervix, and the internal os area³⁹.

Transvaginal sonography of the cervix provides the clinician with an extremely valuable picture of the anatomy, beginning with the external os and ending with the internal os. A 5-7.5 MHz transvaginal transducer probes and evaluates the anatomy in the median (sagittal) plane .Transvaginal sonographic evaluation of the cervix provides information in the following areas³⁹:

1. In early pregnancy it depicts the normal and the abnormal cervix with associated pathologies such as subchorionic bleeding, low placenta, cervical pregnancy, etc.

2. Predicting preterm labour and delivery. The shape of the internal os, as well as the length of the cervix, are important variables in this case. A wedged or U-shaped internal os is highly indicative of

preterm labour.

3. Providing information about the inducibility of labour in patients considered for a planned delivery. In predicting preterm labour, the shape of the internal os is informative and indicative of whether or not there will be a long or short (successful) induction of labour associated with successful induction of labour.

4. Imaging the relationship between the placenta and the internal os in case of a suspected placenta previa or in the detection of low laying placenta accreta.

In conclusion, transvaginal sonographic evaluation of the cervix is a new, easily learned, and informative tool that enables faster and goal-oriented obstetrical patient management.

VI-1- Cervical length:

All authors agree that in both population at risk⁴⁰ and general population²⁶, clinical examination underestimates the cervical length by about 10 to 23 mm^{25,26,40}. The clinical examination of cervical effacement is less reliable than measurement by ultrasonography. Since for the same cervical effacement of 50%, the cervical length varies from 6 to 34 mm by vaginal ultrasonography²⁹; and an effacement of 30% corresponds at a cervical variation of 8 to 60 mm^{23,25,41}.

These results are not surprising since the digital examination can measure only the intravaginal portion of the cervix. The interobservater variability is about 52% for clinical examination against 14% for ultrasonography⁹.

VI-2- Internal os width:

The clinical examination of the internal os (IO) comes up against three problems:

To evaluate the IO, the clinician's finger must probe the cervical canal; which carries significant risk infection⁹. This risk is negligible with ultrasonography.

When the external os (EO) is closed, the IO cannot be examined, but always the IO dilatation precedes EO dilatation. The ultrasonography is able to detect 61.5% of funnelling which aren't detectable by clinical examination²³.

The transfundal pressure is subjective when done by examining the cervix. Manual examination appreciates the cervix "dilatability", thus a cervix whose dilatability is about 3cm is seen closed with the ultrasonography ⁹.

In conclusion, the ultrasonography is more accurate when measuring the cervical length than the clinical examination. Therefore these two methods are complementary: ultrasonography assesses the true cervical dilatation and the manual examination evaluates the cervical "dilatability".

VII- OBJECTIVE:

Our objective was to evaluate routine measurement of the cervical length in uncomplicated single pregnancies during the second trimester of gestation, by ultrasound cervical measurements in order to predict the risk of spontaneous preterm delivery.

A second objective was to evaluate ultrasonographic cervical measurement to predict spontaneous preterm delivery in symptomatic women.

VIII- DATA SOURCES:

A computerised search in the medline database was conducted to identify relevant studies published in French or English or Italian languages between the years 1966 and 1998. Key words used: (cervix or cervical) and (ultrasonography) and (preterm or pregnancy).

This search was supplemented by a manual search of bibliographies of articles and textbooks.

IX- STUDY SELECTION:

To be included, studies had to fulfil the following criteria: prospective cohort study, women tested during the second trimester of gestation; single uncomplicated pregnancies, cut-off level for a cervical length yielding positive results set between 15 and 30 mm.

X- RESULTS:

We selected fourteen studies. All studies excluded multiple pregnancy, and women lost to follow up were not included in the analysis. Generally, studies excluded women with previous cerclage, with clinically evident cervical dilatation and premature rupture of membranes.

X-1- The Role of Ultrasonography to predict preterm delivery:

X-1-1- In general population (asymptomatic women, Table.4,5,6):

All studies show that cervical length is inversely proportional to preterm delivery frequency (Table 5). The shortening of the cervix is a risk factor for preterm delivery (likelihood ratio=3-3.5). Nevertheless, the positive predictive value (PPV) is low (many women with short cervix deliver at term). Indeed, a shortening of the cervix alone is not sufficient to predict preterm delivery, but the negative predictive value (NPV) is satisfactory. The longer the cervix, the lower is the risk of preterm delivery (absence of uterine activity, no cervical incompetence, before 30 weeks of gestation without considering funneling), then we shouldn't conclude about these high NPV.

Funneling is also a risk factor of preterm delivery (relative risk=5 between 24 and 28 weeks of gestation). The criterion of funneling is not sufficient to predict preterm delivery either. In fact, 83-91% of pregnant women with funneling deliver at term³³. On the other hand, NPV is between 97 and 98%^{32,33}.

Study	Number	Year	Term	Preterm delivery (n,%)	Definition of preterm delivery
low risk					
Taipale ³⁶	3694	95/96	18-22	88 (2.4)	< 35
Heath ⁴	2505	97/98	24-32	63 (2.5)	< 37
Iams ³³	2531	92/94	23-33	126 (5)	< 35
Tongsong ²⁷	730	91/93	24-34	91 (12.5)	< 37
Andersen ²⁶	113	88/89	24-34	22 (19.5)	< 37
high risk					
Goffinet ⁴⁵	108	94/96	28-30	24 (22.2)	< 37
Rosenberg ⁴³	76	94/95	<30	20 (26.3)	< 37
Timor-trish ⁴⁴	70	93/95	20-35	19 (27.1)	< 37
Du bose ⁴⁶	136	97	24-28	37 (27.2)	< 37

Table. 4: Characteristics of included studies

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Murakawa ⁴⁷	32	91/92	23-33	11 (34.3)	< 37
Gomez ³⁴	59	92/93	20-35	22 (37.3)	< 37
Rizzo ⁴⁸	108	93/95	23	47 (43.5)	< 37
Crane ⁴³	136	94/95	<30	65 (47.8)	< 35

Table. 5:Prediction of delivery before 37 weeks of gestation by measuring cervical length with vaginal ultrasonography

Study	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Cutoff in cm
Tsongtong ²⁷	65.9	62.4	45.2	93.2	=35
Taipale ³⁶	35	37	3	-	<u><</u> 35
Crane ⁴³	81	65	46	64	<30
Goffinet ⁴⁵	91.8	66.6	40.4	91.8	<26
Rozenberg42	75	73.2	50	89.1	<u><</u> 26
Taipale ³⁶	6	100	39	-	<u><25</u>
Rizzo ⁴⁸	68.8	78.69	71.11	74.5	<20
Gomez ³⁴	76	78	67	83	=18
De Bose ⁴⁶	81	65	46	90	=15
Timor-trish ⁴⁴	100	74.5	59.4	100	funnelling +

 Table.6: Prediction of delivery before 35 weeks of gestation by measuring cervical length with ultrasound

Study	Sensitivity %	Specificity %	PPV %	NPV %	Cutoff in cm
Taipale ³⁶	7	100	15	RR=15	<u><25</u>
	45	73	1.4	RR=2.2	<u><</u> 35
Iams ³³	23	97	25.7	96.5	<u><</u> 20
at 24 weeks of gestation	54	76.3	9.3	97.4	≤30
9	25.4	94.5	17	96.6	funnelling +
	27.6	99.4	38.5	96.5	Bishop>4
Iams ³³	31	94.7	16.7	97.6	<u><</u> 20
at 28 weeks of gestation	69.6	68.5	7	98.5	≤30
0	32.5	91.6	11.6	97.6	funnelling +
	42.5	82.5	9.9	96.9	Bishop≥4
Crane ⁴³	83	56	15	97	<30

X-1-2- In population at risk of preterm delivery (Table.7):

Like in general population, all the studies have shown that cervical length is inversely proportional to preterm delivery risk (Table.7). The shortening of the cervix is a risk factor for preterm delivery, for all authors ^{23,29,34,42} except Okitsu ²³.

Even if the PPV is higher compared to those found in general population, they remain lower than 70%. The PPV is higher because of the increase of preterm delivery prevalence in this population.

The NPV is satisfactory (women with uterine activity, even with long cervix have a minimum risk to deliver prematurely).

Funneling is a risk factor of preterm delivery (relative risk =4)²³. In this condition PPV is also low (33-59%) and high NPV (92-100%)^{23,40,44}.

Authors	number	ultrasound	Definition of risk	threshold	Se	Sp	PPV	NPV	Prevalence	Definition
					(%)	(%)			(%)	of
										prematurity
Murakawa	32	25-35wks	>1	<30mm	100	71	65	100	34	<37
47			contraction/10mn							
Okitsu ²³	130	24-28	Uterine activity or	<1.5SD	61	54	13	92	11	<37
			cervical dilatation							
Gomez ³⁴	59	20-35 wk.	Uterine activity or	<18mm	73	78	67	83	37	<36
			cervical dilatation							
Iams ³³	60	1 time	>4	<30mm	100	44	55	100	40	<36
			contractions/20mn							
			or 8/60mn							
Berghella	96	26-35 wk.	> voluntary	<25p	59	85	45	91	18	<35
40			abortion, history							
			of prematurity							
			exposition to DES							
Crane ⁴³	136	23-33 wk.	Uterine activity or	<30mm	81	65	46	90	27	<37
			cervical dilatation							

Table.7: prediction in population at risk of preterm delivery

X-2- Transvaginal Ultrasound Examination:

Several published studies^{26,32} have demonstrated an inverse relationship between cervix length and frequency of preterm delivery. One study³² showed that when the mean cervical length minus one standard deviation at each gestational age was chosen as a cut-off value, the group with a shortened cervix showed a significantly higher preterm delivery rate exclusively in the primigravida population (odds ratio: 4.86). In contrast, internal os dilatation was a more useful predictor in multiparous women³². The authors concluded that the length of the cervix was possibly an indirect indicator of cervical competence and that cervical length should be seen as a continuous rather than a dichotomous variable. Traditionally, it has been taught that the cervix is either fully functional or incompetent.

Another recent study³³ demonstrated that women with cervical lengths at or below the 25th, 50th and 75th percentiles (less than 3 cm) had a significantly greater risk of preterm delivery at each quartile (relative risk at 24 weeks of gestation: 3.79, 2.35 and 1.98, respectively; relative risk at 28 weeks of gestation: 5.39, 3.52 and 2.80, respectively) than did women whose cervical lengths were above the 75th percentile (more than 4 cm). Although the predictive value of ultrasonography was low in this low-risk population, it is postulated that the predictive value will rise as the risk of prematurity in the study population increases.

Currently, transvaginal ultrasonography is not indicated in the routine evaluation of the patient with a

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history of current risk factors for preterm delivery.

X-3- Comparison between the ultrasonography and manual exam

Digital examination³⁴:

1. cannot provide information about severity of funnelling

^{2.} may increase the risk of preterm delivery by mechanical stretching the cervix. that increases the prostaglandin secretion and thus induces uterine contractions⁴⁶

3. assesses the dilatation of the internal os. It requires the placement of the examining finger close proximity to the fetal membranes and thus, may increase the risk of infection. When membranes are ruptured, clinical examination may transport germs from the vagina into the amniotic cavity, leading then to chorioamnionitis

Therefore ultrasonography provides³⁴:

1. an objective and non invasive method for assessment of cervical status

2. information about cervical biometry, as well as other meaningful information about cervical anatomy such as changes in status of the internal os, endocervical dilatation with herniation of membranes, and dynamic changes in cervical morphologic features in response to uterine contraction or transfundal pressure

In fourteen studies that have calculated predictive value of ultrasonography, four had compared ultrasonography to clinical examination performances^{26,29,40,43}. All these studies suggest that the ultrasonography is more accurate compared to clinical examination with sensitivity > 3-18%, specificity > 5-22%, PPV > 7-17% and NPV > 5-22%⁹.

The major benefit of vaginal ultrasonography is its excellent NPV. When measuring the cervical length. Regath⁴⁹ in 1997 has shown that, it is possible to avoid false positive (pregnant women with uterine activity and long cervix) and thus, it will save costly hospitalisation for women who will be admitted for deliver post-term. Therefore, ultrasonography cannot predict preterm delivery in every kind of population. Even if it is used in a population at high-risk of preterm delivery (40%), the PPV remains 70% for thirty percent of women. Ultrasonography is necessary to assess certain risk factors (funneling, reduced cervical length) which increase the risk of preterm delivery by 3 to 5.

XI- DISCUSSION:

Cervical assessment can be evaluated by vaginal ultrasonography. The proximity of the probe to the cervix and optimal focal length allow close identification of the cervix and inspection of the canal and the internal os: it gives information about cervical biometry, as well as other information about cervical anatomy such as changes in the internal os, endocervical dilatation with membranes herniation, and dynamic changes in cervical morphologic features in response to uterine contraction or transfundal pressure. Vaginal ultrasonography allows to perform the examination when the pregnant woman's bladder is empty, which improves the quality of the assessment of cervical length compared to abdominal ultrasonography with full bladder.

This technique is more reproducible than clinical examination to measure the cervical length. It allows the examination of the cervix without the need to introduce the finger in the cervical canal, thus reducing the risk of infection or stretching.

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Whatever the threshold of the cervical length is and whatever the prevalence of the preterm delivery is in the population, all the studies have shown that not all women with short cervices deliver prematurely. The multifactorial character of preterm delivery can explain this fact (premature rupture of membranes, amniotitis, vaginal bleeding, uterus activity, and genito-urinary infection, among others, in addition to cervical length). According to the term of pregnancy, each factor has its own influence. It can explain why the predictive value is low when each of these factors is taken alone. In ultrasonography, the likelihood ratio derived from sensitivity and specificity (=sensitivity/1–specificity) is a better index for evaluating the prediction of preterm delivery than sensitivity or specificity alone²⁷. The likelihood ratio value is more constant than sensitivity, which was more likely to change between studies²⁷. However, both false positive and false negative rates are still rather high, and thus the cost-effectiveness of this method should be evaluated further.

Therefore, it may be useful to perform a vaginal ultrasonography in the second trimester to identify the pregnant women at risk of preterm delivery. When it is performed in the general population of pregnant women, it may allow a reduction in the number of unnecessary and potentially dangerous tocolytic treatments and unnecessary or prolonged hospitalization. And when it is realised among the population of pregnant women at high risk of preterm delivery it may help to predict preterm delivery, and consequently help to prevent severe complications.

In developing countries, the other tests like tumor necrosis factor, fibronectin, estriol in saliva... are expensive and not available. Using the combination of vaginal ultrasonography and clinical examination may help in predicting preterm delivery.

These observational studies have shown the need of randomised trials studies to confirm or invalidate the benefit of ultrasonography.

XII- **REFERENCES**:

04.12.02

CERVICAL ASSESSEMENT AND OTHER TESTS TO PREDICT PRETERM DELIVERY

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« The human foctus is expelled both in the seventh and tenth months, and at any period of pregnancy between these; moreover, when birth takes place in the eighth month it is possible for the infant to live »

ARISTOTLE

INTRODUCTION

- L'accouchement prématuré: < 37 semaine d'aménorrhée
- Fréquence: 8 à 12%. Dans mon hôpital elle atteint 15%
- Responsable de 80% de la mortalité néonatale
- La survie: 5% à 23 semaines, 95% à 32 semaines
- le risque de prématurité: l'effacement et à la maturation prématurée du col
- Malgré les progrès réalisés en néonatalogie pour diminuer le taux de mortalité néonatale, la fréquence de la prématurité reste élevée

Types d'accouchements prématurés

Accouchements prématurés induits (20%)

- HTA
- RCIU
- Diabète sévère
- Iso-Immunisation Rh
- HRP
- PP hémorragique
- etc.

Accouchements prématurés spontanés (80%)

• Infections urinaires

• RPM

- Utérus sur distendu
- Incompétence du col
- Atcd d'accouchements prématurés
- Facteurs Socio-Econo
- etc.

Différents types de marqueurs

Marqueurs	Sensibilité	Spécificité	VPP	VPN	
Fibronectine	69-93	72-86	13-83	81-99	-
116	50-52	73-100	47-100	67-86	
17 B-Estradiol	12	71-76	12-14	-	
Estriol	71	77	27	77	
Progestérone	6-35	67-69	7-32	-	
Scoring des facteurs de risques	88-92	23-30	94-98	41-76	
Tocodynamométrie	18-58	45-94	7-20	82-94	

L'examen échographique comporte quatre temps

- Repérage du col utérin
- Mobilisation de la sonde afin de visualiser la canal cervical dans sa totalité en coupe longitudinale
- Relâchement de la pression permettant de mesurer le col et d'étudier sa morphologie.
- Pression abdominale fundique pouvant révéler une ouverture de l'orifice interne du col utérin

Mesure du col



• chaque curseur est placé au niveau des orifices cervicaux, le canal médullaire est visible sur toute sa longueur.

cCNGOF - 1996

Résultats normaux

 Début de grossesse: le col mesure 40 à 50 mm. Cette longueur va physiologiquement diminuée tout au long de la grossesse

 A 24 SA et à 28 SA, la longueur du col est de 35.4 ± 8.3 mm, et 33.7 ± 8.5 mm, respectivement)

Les anomalies de l'orifice interne du col

- l'ouverture ou la dilatation en entonnoir de l'orifice interne, forme mineure de la béance cervicoisthmique
- la protrusion des membranes amniotiques dans le col, forme majeure ou évoluée de la béance cervico-isthmique

Orifice interne du col: dilatation



Orifice interne du col: dilatation en entonnoir



Orifice interne du col: protrusion des membranes



Résultats à 37 SA

auteurs	Nbre des femmes	Nbre d'Acc premature et %	Cutoff	Sensibilité	VPP	VPN	Likelihood ratio
Crane ⁴³	136	65(47.8)	<u>≥</u> 30mm	81	46	64	2.32[1.65-3.24]
Rizzo ⁴⁸	108	47(43.5)	10-20mm	68.8	71.11	74.5	3.19[1.9-5.38]
Gomez ³⁴	59	22(37.3)	<u>≥</u> 30mm	76	67	83	3.57[1.86-6.87]
Goffinet ⁴⁵	108	24(22.2)	10-20mm	91.8	40.4	91.8	2.75[1.99-3.8]
Taipale ³⁶	3694	88(2.4)	<u>></u> 30mm	35	3	95	1.32[0.99-1.76]
Tongsong ²⁷	730	91(12.5)	<u>></u> 30mm	65.9	45.2	93.2	1.76[1.47-2.1]

Commentaires

- Examen non invasif, faisable, reproductible, et peut être combiner avec d'autres examens
- Fournit des informations sur la biométrie du col
- Autres informations: anatomie du col, dilatation de l'orifice interne, protrusion des membranes, Changements dynamiques du col

Commentaires

- Identifier les femmes à haut risque d'accouchement prématuré
- Une bonne VPN qui permet d'éviter les faux positifs permettant d'éviter:
 - des hospitalisations coûteuses
 - des interventions qui ne sont pas dénuées de risques

remarquons que la sensibilité de l'échographie est basse chez les femmes à bas risque d'accouchement prématuré

Conclusion

- Les études récemment publiées ouvrent la voie à des études contrôlées, prospectives et randomisées qui seules pourront confirmer l'intérêt de cet examen
- Est-ce-que l'échographie justifierais une intervention chez les femmes enceintes avec col court?

CERVICAL PRIMING BEFORE SURGICAL TERMINATION OF FIRST TRIMESTER PREGNANCY

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ABSTRACT

OBJECTIVES: To review different methods for first trimester pregnancy termination and compare their effects, side effects and safety.

METHODS: Randomised controlled trials comparing different methods for cervical priming with placebo/no treatment before surgical termination in the first trimester are included. Women who were referred for surgical termination of pregnancy in the first trimester are included. Studies which compare cervical priming methods with each other or with placebo/no treatment are included. Onset of new symptoms following drug administration, cervical diameter, complications are considered as the main outcome measures. An electronic literature search of Medline and Cochrane library has been made.

RESULTS: Misoprostol seems to be effective at 400mg dose given 3 hours before operation. It is inexpensive, both orally and vaginally active, stable at room temperature and has few side effects which can be tolerated without medication. Gemeprost is effective in dilating the cervix at 1mg given 3 hours before operation but it is expensive and not stable at room temperature. Mifepristone is an orally active agent which is shown to have minimal side effects with the successful results to dilate and soften the cervix. However, it is expensive, not available in many countries and requires a long pre-treatment period. Nitric oxide donors seem to have very few side effects but a less favourable cervical dilatation. Tents are shown to be effective with more abdominal discomfort.

CONCLUSION: Many studies have been conducted comparing different methods of cervical priming. Systematic analysis is necessary to confirm methods, doses, routes and timing, to assess women's preferences, side effects, complications, effectiveness.

KEY WORDS: Cervical dilatation, mifepristone, misoprostol, gemeprost, nitric oxide donors, tents, first trimester.

INTRODUCTION

The physician requiring access to the uterine cavity often needs to first dilate the cervix. This guardian

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of the uterine cavity may be opened medically, surgically or by a combination of both.(1) Surgical/mechanical dilatation is an old procedure (Hippocrates,460-360 BC) and carries a significant complication rate which is largely dependent upon operator experience and force applied.(2) If the cervix is not sufficiently opened, uterine exploration might be inadequate resulting in increased risk of haemorrhage and incomplete uterine evacuation. The cervix is usually dilated up to 8mm. Beyond that if the cervix is not prepared, tears appear more frequently and it has been discussed that this may represent actual tearing of the internal os rather than true dilatation. As 12mm is exceeded the fibrous matrix of the cervix risks irreversible damage resulting in long term consequences such as cervical incompetence, mid- trimester abortion in future pregnancies, premature delivery, low-birth weight baby and fetal loss.(1,2,3,4,5,6)

For most people it is obvious that women have a right to terminate their pregnancy with effective, safe and careful methods. The unmet need for safe pregnancy interruption in many countries makes it highly desirable to find simple methods for effective and safe uterine evacuation.(6,7)

Globally an estimated 30 million abortions are performed yearly.(8) About 1.6 million elective abortions are performed annually in the United States and more than 90% are performed during the first trimester of pregnancy.(9,10) The safety of the operation is therefore a global public health issue.

Vacuum aspiration is the most commonly performed procedure for termination of first trimester pregnancy and became established as the standard method in early 1960s . (1,11,12,13,14,15) It is well known that termination of pregnancy by vacuum aspiration can be associated with complications such as excessive haemorrhage, uterine perforation, cervical laceration, cervical rupture and incomplete abortion.(3,4,5,6,11,12,13,16,17,18) Some of the complications can be attributed to the initial procedure of cervical dilatation which is a critical step in vacuum aspiration(3,6,12). Cervical priming before evacuation of the uterus reduces the risks of cervical injury and uterine perforation by making the cervix softer and easier to dilate.(4,8,14,16,19)

Dilatation and vacuum aspiration became established as the standard method for pregnancy termination in the first trimester. The procedure can be carried out in most cases with local anaesthesia or general anaesthesia and does not require an over night stay in hospital. The procedure is done by inserting a mechanical dilator through cervical canal into the uterine cavity. The degree of dilatation required and the diameter of the suction canal used increases with gestation. Up to 63 days, usually 8mm dilatation, at 10 weeks of gestation 8-10mm dilatation, at 12 weeks of gestation 10-12mm and at 14 weeks 12-14mm dilatation is adequate.(16)

Many techniques for cervical dilatation are available such as Intracervical tents, antiprogesterons, prostaglandin analogues and nitric oxide donors.

There are 3 types of intracervical tents. Laminaria are osmotic dilators made of seaweed sticks. Intracervical dilators are inserted into the cervix and they swell due to absorbing fluid. They dilate the cervix by slow application of force on the cervical canal. Sepsis, cervical tears, uterine rupture are rare complications. However, migration of the tent into the cavity, tent expulsion, fracture and fragmentation of the tents are seen more frequently.

Dilapan is a synthetic tent derived from hydrophilic polymerised, polyacylonitrate hydrogel. It expands rapidly but tends to fragment and fracture.

Lamicel is a synthetic polyvinyl sponge impregnated with magnesium sulphate (MgSO4),450mg.It expands to form a soft sponge. The true mechanism is not clear. There are no reports of fragmentation, fracture, tent associated sepsis, expulsion and migration into the uterine cavity.

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An inconveniently long duration of action, discomfort on insertion, pain and an increased number of patient-physician contacts have all led to a decline in popularity of tents.(1)

Gemeprost is a prostaglandin E1(PGE1) analogue. It is used only as a vaginal pessary. Gastrointestinal side-effects, mainly diarrhoea and nausea effect a significant minority of users. It is expensive, unstable and requires refrigeration for storage.

Misoprostol is also a synthetic PGE1 analogue, originally used for prophylaxis of peptic ulcer. It is stable at room temperature, inexpensive and active when given orally. It has relatively mild gastrointestinal side effects .

Mifepristone is a 19-norsteroid that specifically blocks the receptors for progesterone and glucocorticoids. It is active when given by mouth .The incidence of side effects is low. However, a long pre-treatment period (36 hours) is required. Due to its antiprogesterone action it is used together with misoprostol for medical termination in some countries. It is an expensive drug.

Nitric oxide donors are smooth muscle relaxants, which also induce cervical ripening. They are cheap and have few side effects.

OBJECTIVES

To review the effects of cervical dilatation in the first trimester before surgical termination and to identify the different kinds of methods used for the procedure and to compare their effects, side effects, and safety.

METHODS

TYPES OF STUDIES: Randomised controlled trials comparing different methods for cervical priming with placebo/no treatment before surgical termination in the first trimester are included.

TYPES OF PARTICIPANTS: Women undergoing first trimester surgical termination of pregnancy.

TYPES OF INTERVENTION: Studies which compare cervical priming methods with each other or with placebo/no treatment and different routes of application were considered.

TYPES OF OUTCOME MEASURES: Onset of new symptoms following drug administration (abdominal pain, nausea, vomiting, diarrhoea, vaginal bleeding, fever), cervical diameter measured objectively, duration of operation, interval between the drug administration and operation complications.

SEARCH STRATEGY FOR IDENTIFICATION OF STUDIES: Electronic literature search of MEDLINE (1985-1999), and THE COCHRANE LIBRARY databases with the following terms: Cervix AND (Dilatation OR Priming OR Ripening) AND First Trimester

RESULTS (see tables)

DISCUSSION

Prostaglandin analogues like misoprostol and gemeprost are effective in softening the cervix and in initiating dilatation prior to abortion. Misoprostol is inexpensive, stable at room temperature and it seems that cervical dilatation with misoprostol is dose dependent having fixed evacuation time.(3,11,12,13,16,17,20,22) Prolonged time can result in complications like incomplete abortions before vacuum aspirations.(3,19,21) 400mg misoprostol applied 3 hours before surgery has been shown to enable sufficient dilatation with few side effects. There is only one study comparing oral and vaginal route of application. Gemeprost is expensive and unstable at room temperature, but 1mg is shown to dilate the cervix in 2-4 hours time. In studies comparing these two agents misoprostol seems to have less side effects with a more favourable dilatation at the same time interval.(3,7,11,12,16,20)

Mifepristone is an antiprogesterone, effective in initiating dilatation and softening of the cervix seems not to be dose related (16,24). It is orally active, with minimal side effects. However, it is expensive and requires a long pre-treatment period (24-36 hours). In the studies which compare mifepristone with either gemeprost or misoprostol, it is concluded that there is no difference in cervical dilatation between mifepristone-gemeprost and mifepristone-misoprostol. However, prostaglandin analogues are related to more abdominal pain.(5,7,11,16)

Nitric oxide donors as concluded in the studies seem to have very few side effects but with less favourable cervical dilatation.(18,26)

Lamicel tents are also shown to be effective in cervical dilatation but they seem to cause more abdominal discomfort. Difficulty may be encountered if the cervical os is very tight.(1,2,27,28)

CONCLUSION

The technical report by the WHO Scientific Group on Medical Methods for Termination of Pregnancy recommends that dilatation and vacuum aspiration is the method of choice for abortion at 9-14 weeks of gestation. Cervical preparation before abortion by vacuum aspiration in the first trimester seems to reduce the risk of complications and could be considered in nulliparous women with gestations of 9 weeks or more and in all women with gestations of 12 weeks or more.

Cervical dilatation prior to surgical termination of pregnancy in the first trimester has been described to reduce the force needed for mechanical dilatation, to reduce the occurrence of incomplete uterine evacuation, cervical incompetence followed by mid-trimester abortion in future pregnancies and premature delivery and fetal loss.

A systematic search and analysis of the literature is necessary to confirm the methods, doses, routes, timing and also women's preferences as well as side effects and complications.

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03.12.02

CERVICAL PRIMING BEFORE SURGICAL TERMINATION OF FIRST TRIMESTER PREGNANCY

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- Inadequate uterine exploration
- Haemorrhage
- Incomplete uterine evacuation



- 30 million abortions yearly
- 1.6 million elective abortions performed annually in USA
- More than 90% are performed during the first trimester of pregnancy

Vacuum aspiration (1960s)

- Excessive haemorrhage
- Uterine perforation
- Cervical laceration
- Cervical rupture
- Incomplete abortion



Intra cervical Tents:

Laminaria Dilapan Lamicel

Prostaglandin Analogues: Misoprostol Gemeprost

Antiprogesterons:

Mifepristone

Nitric Oxide Donors:

Isosorbide dinitrate Glyceryl trinitrate



Misoprostol vs. Placebo

Intervention	Time	Cervical dilatation	Side effects
		up to Hegar 8	

- •200µg vaginally 5 hr 72.5% vs (10%) 85% pelvic pain
- •200µg vaginally 6 hr 74% vs (8%)
- •400 μ g orally 12 hr 7.4 \pm 2 mm (4.1 \pm 1.4)

Misoprostol (different doses, dose intervals)				
Intervention	Time	Cervical dilat	tation Side effects	
		≥8 mm		
•400µg vaginally	2 hr.	93.3%	-	
600µg vaginally	3 hr	16.7%	53.3%pelvic pain	
•200µg vaginally	3-4 hr	0	_	
400µg vaginally	3-4 hr	93.3%	36.7% pelvic pain	
•200µg vaginally	3-4 hr	23.3%	6.7% pelvic pain	
400µg vaginally	3-4 hr	96.7%	36.7%pelvic pain	
600µg vaginally	3-4 hr	100 %	73.7%pelvic pain	
800µg vaginally	3-4hr	100 %	100%pelvic pain	
			& 43% fever	
• 200µg vaginally				
water	3-4 hr	20.0%	-	
acetic acid	3-4 hr	23.3%	_	

Gemeprost vs	Placebo
Intervention	Time
•1mg	3 hr

Cervical DilatationSide effects6.35mm(vs 4.82mm)-

Mifepristone vs Placebo

•25mg, 50mg, 24 and 12 hr 100mg orally.

• 200mg orally 36 hr

100mg orally 48 and 36 hr100mg orally 36 and 24 hr

6.6mm	-
6.3mm	-
6.6mm	-
(vs5.4mm)	
7mm	-
(vs6mm)	
4.8mm	-
4.2mm	-
(vs3.4mm)	

Misoprostol vs Gemeprost				
Intervention	Time	Cervical Dilatation	Side Effects	
•400µg misoprostol orally	12 hr	8.1±1.7 mm	Asymptomatic patients were	
1 mg gemeprost vaginally	3 hr	7.0±1.7 mm	more in misoprostol group (87.5% vs 53%)	
•600µg misoprostol vaginally	2-4 hr	8 mm	-	
1 mg gemeprost vaginally	2-4 hr	8 mm	-	
•200µg misoprostol vaginally	3-4 hr	6.7-7.1 mm	nausea	
1 mg gemeprost	3-4 hr	6.7-7.1 mm	diarrhoea	

200mg mifepristone 36 and 12 hr orally

7.7 mm

48.9%vaginal spotting,46.7% abdominal pain. 25% vaginal spotting,22.9% abdominal pain.

Gemeprost vs Mifepristone

•200 mg mifepristone	36 hr	6.8 mm	
orally			7
1mg gemeprost	3-4hr	6.5 mm	2
vaginally			(

10% pelvic pain77%asymptomatic43% pelvic pain0 asymptomatic

Nitric Oxide Donors vs Prostaglandins

Intervention	Time	Cervical Dilatation	Side Effect
•Isosorbide mononitrate		5mm	-
40mg (vaginally)	3 hr		
Glyceryl trinitrate500mg		5mm	-
(vaginally)			
gemeprost 1mg,		6mm	-
no treatment		4.5mm	-

Intracervical Tents vs Other Methods

1 mg gemeprost
(vaginally)3-4hr.9mmlamicel tent3-4hr8mm

74% abdominal discomfort,68%vagi nal bleeding 50% abdominal discomfort,7.5% vaginal bleeding.

Intervention	Time	Cervical Dilatation	Side Effects
•Lamicel with MgSO4	3-4hr	4.4mm	-
Lamicel without MgSO4	3-4hr	4.1mm	_

Prostaglandin-Tents-Progesterone Antagonist Lamicel

•Lamicel	3-4hr	Cervical dilatation	88%pelvic pain
		in treatment group	
Gemeprost 1mg	3-4hr	5-6.7mm,largest	71%pelvic pain
vaginal		in lamicel group.	
Mifepristone	42-53hr		33%pelvic pain
600mg oral.			

No treatment

3 mm

DISCUSSION

Misoprostol:.Dose dependent, having fixed evacuation time.

• Complications with prolonged time

• 400µg received 3hr before surgery is shown to be sufficient with few side efects. Gemeprost: 1mg is shown to dilate the cervix in 2-4hr. time. Misoprostol seems to have less side effects with a more favourable dilatation at the same interval of time.

Mifepristone: The effect is not dose related. Minimal side effects. Expensive, long pre-treatment period. No difference between mifepristone, misoprostol and gemeprost in cervical dilatation. However PGE1 analogues are related with more abdominal pain.

Nitric oxide donors: Few side effects.

Less favourable dilatation.

Lamicel Tents:

Effective cervical dilatation.

More abdominal discomfort.

CONCLUSION

- •Vacuum aspiration is the method of choice for abortion at 9-14 weeks.
- Cervical preparation before abortion by vacuum aspiration in the first trimester reduces the force needed for mechanical dilatation, reduces the occurrence of incomplete uterine evacuation, cervical incompetence, mid trimester abortion, premature delivery, fetal loss.
 Systematic analysis is necessary to evaluate the different methods.

CHRONIC PROSTATITIS

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Abstract

Prostatitis is a condition that causes substantial morbidity in men. The clinical features are often non-specific while the aetiology and pathogenesis can be diverse and includes inflammatory, obstructive causes and/or related to calculi. Four categories of prostatitis are recognised: acute bacterial prostatitis, chronic bacterial prostatitis, chronic nonbacterial prostatitis and asymptomatic inflammatory prostatitis. The diagnosis of prostatitis was advanced substantially by the introduction of sequential sampling of urine aliquots following prostatic massage. Bacterial prostatitis is largely associated with Escherichia coli, Pseudomonas spp., Enterococci, Staphylococcus aureus, Klebsiella pneumonie etc. In chronic bacterial prostatitis a variety of streptococci and anaerobic bacteria can be isolated. Cytokines, soluble proteins secreted by cells of the immune system, have an important role in the pathogenesis of prostatitis. Nonbacterial prostatitis is the most common type of prostatitis and is associated with Chlamydia trachomatis, Ureaplasma urealyticum and Trichomonas vaginalis. Doppler and transrectal prostatic ultrasonographic imaging of the prostate have a potential value in the diagnosis of inflammatory disorders. Treatment of chronic prostatitis is difficult largely because of the limited range of agents able to achieve therapeutic concentrations within prostatic fluid. Trimetoprim/sulfamethxazole and fluoroquinolones: ofloxacin, ciprofloxacin and temafloxacin have produced the highest concentrations in prostatic fluid. Antibiotic treatment requires prolonged high dosage and careful monitoring to ensure that bacterial eradication has occurred.

Introduction, background

Prostatitis is an infection and /or inflammation of the prostatic gland with varying clinical features: urinary symptoms, sexual dysfunction, pelvic pain etc [1]. Prostatitis rarely occurs in males less than 30 years of age; however, it is a common problem in older males. Epidemiological data, which are very scarce, reveal that up to 50% of all males will develop an episode of prostatitis [2,3]. Available studies suggest that this condition is common [4,5,6,7]. For the disorders involving inflammation of the prostatic gland and its surrounding tissue the following classifications were approved by the working group of chairs of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) [8] and will be the standard reference for research studies on these diseases and disorders.

1. Acute bacterial prostatitis is an acute infection of the prostate.

2. Chronic bacterial prostatitis is a recurrent infection of the prostate.

3.Chronic nonbacterial prostatitis/chronic pelvic pain syndrome (CPPS), where there is no demonstrable infection. Subgroups of this class are:

3.1.Inflamatory chronic pelvic pain syndrome, where white cells are found in the semen, expressed prostatic secretions (EPS), or voided bladder urine-3(VB-3).

3.2.Non-inflammatory chronic pelvic pain syndrome, where white cells are NOT found in semen, EPS, and VB-3.

4.Asymptomatic inflammatory prostatitis (AIP), where there are no subjective symptoms but white blood cells are found in prostate secretions or in prostate tissue during an evaluation for other disorders.

Patients with acute and chronic bacterial prostatitis have documented bacterial infections of the prostate. Those with nonbacterial prostatitis have signs of prostatic inflammation but no signs of bacterial infection. Chronic nonbacterial prostatitis/CPPS is the most common symptomatic type of prostatitis, and it may be the most prevalent of all prostatic diseases, including benign prostatic hyperplasia. Chronic nonbacterial prostatitis/CPPS has not been scientifically demonstrated to be primarily either a disease of the prostate or the result of an inflammatory process.

Objectives

Since the prostate is a privileged site (an area in which antimicrobial penetration is generally poor), the efficacy of antimicrobial agents is limited, a long duration of treatment is required, and failure rates are as high as 30-40% [9]. Furthermore, the diagnosis of prostatitis is controversial. As a result, the diagnosis and therapy of chronic prostatitis remains a challenge. In this review we will discuss the pathophysiology, diagnosis and treatment of chronic prostatitis.

Methods

An English-language literature search in computerised general and specialised databases, employing

Medline, Matweb, Cochrane Library, Cochrane Prostate Group database and bibliographic review of the references obtained, was performed (key terms : prostatitis, cytokines, leukocytospermia, ultrasonography, antibiotic therapy.)

Results and discussion

Various physiological factors contribute to the development of prostatitis. Prostatic antibacterial factor (PAF) is a bactericidal fluid secreted from the normal prostate. PAF's antibacterial activity is dependent on adequate prostatic zinc concentrations. PAF is diminished in patients with prostatitis [10]. Normal prostatic secretions generally maintain a pH of approximately 6.6 to 7.6. With increasing age the pH of prostatic secretions tends to rise. Patients with prostatitis have alkaline prostatic secretions ranging in pH from 7-9 [11]. Whether these physiological factors are a cause or effect of prostatitis is unknown. The introduction of bacteria into the prostatic ducts which empty into the posterior urethra, invasion of rectal bacteria by direct extension into the prostate or by lymphatic spread and hematogenous spread. It is postulated that intraprostatic urinary reflux, either with infected urine or sterile urine, may be the primary aetiology of most bacterial and nonbacterial prostatitis cases [12,13]. One novel etiologic theory is that reflux of urine into prostatic ducts causes prostatic inflammation via high concentrations of purine and pyrimidine base-containing metabolites in prostatic secretions [14].

Some data represent direct evidence that some men with chronic prostatitis have an autoimmune component to their disease. The CD4 T cell proliferative response to seminal plasma was statistically significant when compared with medium alone in men with a history of chronic prostatitis [15]. There are also data indicating presence of IgG and IgA antibodies against common Gram negative microorganisms in post prostatic massage urine [16]. Liu S. et al. [17] reported 3 patients with histologically proven eosinophilic prostatitis and high levels of prostatic specific antigen. So, immunology and autoimmunity are potential etiological factors for chronic prostatitis.

Prostatitis is characterised by the presence of acute inflammatory cells in the glandular epithelium and lumens of the prostate, with chronic inflammatory cells in the periglandular tissue. However, the presence and quantity of inflammatory cells in the urine or prostatic secretions does not correlate with the severity of physical symptoms.

Principal regulators of inflammatory and immune responses are cytokines, soluble proteins secreted by cells of the immune system. In patients with chronic prostatitis were found elevated levels of TNF-alpha and Interleukin -1beta, Interleukin-6 in the semen [18,19,20,21]. These findings suggested that the cytokines have an important role in the pathogenesis of prostatitis and that the level of the cytokines are useful indicators in patients with prostatitis. These factors also may be involved in the regulation of sperm cell functions and thus may affect male fertility [19,20].

Serial collection of the urine(VB1,VB2,EPS,VB3) is used to define and identify the organisms involved. The Stamy-Meares test is a collection of segmented urine samples from the urethra, bladder, and prostate; it is considered the gold standard for diagnosis.

Chronic bacterial prostatitis (CBP) occurs when acute bacterial prostatitis is treated inadequately due to resistance, relapse, short-course therapy or because the ductal anatomy of the peripheral zone of the prostate may have blocked drainage of secretions from the prostate [12]. Among patients with chronic prostatitis almost all had a previous bout of acute prostatitis. The most common clinical feature of CBP is recurrent urinary tract infections. Subsequently, patients will complain of obstructive and irritative urinary symptoms (Table 1). Physical exam reveals a palpable, tender prostate [22,23]. However, patients often present asymptomatic, with a normal prostate gland exam.

The potential value of ultrasound methods in the diagnosis of inflammatory disorders of the prostate is largely unexplored. In several studies, specific ultrasonographic characteristics in patients with prostatitis have been described. Also non-specific echogenic qualities in prostatities have been pointed out. To evaluate ultrasound of the prostate in patients with nonbacterial prostatitis ultrasonographic images of these patients were compared with those of a healthy control group. Constant dilatation of the periprostatic venous plexus was seen more pronounced in the control group as well as elongation of the seminal vesicles. Finally, prostatic calcifications were frequently encountered in both groups [24]. The leading ultrasonic diagnostic symptoms of chronic prostatitis are capsular thickening and prostatic calculi, hypoechoic halo in the periurethral region, heterogeneous echo pattern, and also enlargement and thickening of the septa of the seminal vesicles [24,25]. The severity of the disease was determined primarily by the presence in the prostate of "true microabscesses" (microcavity of the irregular form) and pseudomicroabscesses(drop-shaped microspaces) which can be successfully drained irrespective of their number, size, location and characteristics of the content [25,26]. By colour Doppler ultrasonographic scanning was shown a marked increase in colour in the cervico-urethral site and/or around the ejaculatory ducts and close to the seminal vesicles [27]. A statistically significant accumulation of prostatic calcifications and unilateral seminal gland alterations was demonstrated in patients with chronic prostatitis. Transrectal prostatic sonography was recommended for differential diagnosis in cases of chronic prostatitis and prostatodynia [28]. In patients with pyospermia, caused by chronic prostatitis heterogeneous echo pattern of the prostate and capsular irregularity was shown also [29]. By power Doppler ultrasonography capsular and parenchchymal arteries in normal prostate were seen in radial and symmetrical fashion on coronal scans, in chronic prostatitis just an isolated capsular vessels was sometime present [30].

Localising bacteria from the prostate is paramount in order to diagnose CBP. The Gram-negative pathogens implicated in acute bacterial prostatitis have also been implicated in chronic bacterial prostatitis. Most clinicians discount Gram-positive bacteria as causative pathogens in CBP [22,31,32]. Bacterial prostatitis, caused mainly by Escherichia coli, Pseudomonas spp., Enterococcus, Staphylococcus aureus, Klebsiella pneumoniae, Enterobacter cloacae, and Staphylococcus saprophiticus [33,34,35,36,37,38]. There are also data in literature indicating the role of anaerobic bacteria in development of chronic bacterial prostatitis. Szoke I [39] had found in parallel specimens from 24 patients with chronic prostatitis high colony counts of Gram-positive and Gram-negative anaerobic bacteria, either alone (18 cases) or in combination with aerobic bacteria (6 cases). After treatment with amoxicillin/ clavulanic acid or clindamycin for 3-6 weeks samples revealed a decrease

or total elimination of the symptoms, and no anaerobic bacteria was detected. The molecular studies have been published reporting the presence of 16S rRNA bacterial sequences in prostate biopsy tissue that was negative for ordinary bacteria by routine culture in men with chronic prostatitis. Additionally special culture methods have indicated that difficult-to-culture genera Corynebacterium, Staphylococcus, Streptococcus and Escherichia were present in expressed prostatic secretions found to be negative by routine culture techniques [36,40,41,42].

Nonbacterial prostatitis (NBP) is the most common type of prostatitis, and occurs eight times more frequently than bacterial prostatitis [43]. NBP presents with the same signs as bacterial prostatitis; however, prostatic fluid cultures are negative for presence of bacteria. Inflammation is evident upon prostatic fluid analysis, and can be identified by a minimum of 10 to 15 white blood cells per high power field on microscopic examination [23]. Although controversial, implicated pathogens include Chlamydia trachomatis, Ureaplasma urealyticum, and Trichomonas vaginalis [23,44]. Minocycline 100 mg twice daily, doxycycline 100 mg twice daily, or erythromycin 500 mg four times daily have been utilised in order to eradicate the suspected pathogens .Erythromycin's antimicrobial activity is significantly enhanced in the presence of the alkaline pH in prostatic fluid, thus, it achieves high cure rates of prostatic infection [44]. Treatment duration is approximately 2 to 4 weeks. Prolonged therapy after treatment failure is not indicated, since nonbacterial prostatitis is generally self-limiting.

Fluoroquinolones and trimethoprim/ sulfamethoxazole (TMP/SMX) (Table 2) are first- and second-line therapy in the management of CBP, respectively [22,45] due to their broad-spectrum activity against the most prevalent isolated pathogens [13,46]. Trimetoprim inhibits bacterial dihydrofolate reductase; it works synergistically with sulfamethoxazole to interfere with microbial folic acid synthesis. Trimethoprim concentrations in prostatic fluid are two to three times that in serum, thus achieving adequate concentrations at the site of infection [44]. The usual dose is 160 mg of trimethoprim and 800 mg of sulfamethoxazole, which is equivalent to one double-strength tablet taken twice a day. TMP/SMX has a good safety profile, with most of the adverse effects limited to hypersensitivity reactions and gastrointestinal disturbances including nausea, vomiting, diarrhoea, and anorexia. The fluoroquinolone inhibit bacterial replication and transcription by blocking bacterial DNA gyrase and subsequent protein synthesis. Prostatic fluid contains lower Fluoroquinolones concentrations than does serum; nevertheless, appreciable concentrations are achieved in prostatic tissues to eradicate the most common causative pathogens. From Fluoroquinolones ofloxacin and ciprofloxacin are recommended because of their favourable antibacterial spectrum and pharmacokinetic profile [47]. Other antimicrobials include doxycycline, Minocycline, carbenicillin indanyl sodium, and erythromycin [48] however, these agents have shown variable results. The penicillins inhibit cell wall synthesis, and the aminoglycosides bind to bacterial ribosomes, inhibiting protein synthesis. The aminoglycosides and penicillins often yield a synergistic bactericidal effect. Chronic prostatitis warrants at least 6 to 12 weeks of therapy [49]. Usually, the bacteria remain susceptible to commonly used antimicrobials despite frequent, long term use.

However, poor clinical outcomes have been observed due to poor diffusion of antimicrobials into the prostate and difficulties in achieving therapeutic concentrations within prostatic fluid [22,50,51]. As a result, long-term suppressive therapy may be initiated with TMP-SMX given as a single-strength tablet daily, Trimetoprim 100 mg daily, or sulfamethoxazole 500 mg daily [52]. Surgery may be an alternative in recurrent cases that are caused by infected calculi [22].Alpha-1-selective blocking

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agents may relieve symptomatology of chronic pelvis pain syndrome [53].

The theory of high concentrations of purine and pyrimidine base- containing metabolites in prostatic secretions, as the causative factors of prostatic inflammation has led to the use of allopurinol for treatment of chronic prostatitis in hopes of lowering prostatic levels of uric acid and improving symptoms. However, the adoption of this treatment has been criticised as premature [54,55].

Adjunctive recommendations may include sit baths, normal sexual activity, and analgesics for painful urinary symptoms. Spicy foods, caffeine, and alcohol should be avoided ; they may cause bladder irritation and spasms culminating in reflux of urine into prostatic ducts, thus exacerbating nonbacterial prostatitis symptoms [23]. If symptomatology persists patients should be referred to a urologist for evaluation of serious conditions such as urinary bladder carcinoma and interstitial cystitis.

Conclusions

The chronic prostatitis is an inflammatory disease of prostatic gland. The diagnosis of it is difficult due to the absence of typical clinical symptoms, specific ultrasonographic signs and the sometimes difficult interpretations of culture results. Treatment of prostatitis is associated with high failure rates; the use of Fluoroquinolones and Trimetoprim/sulfamethoxazole due to their broad-spectrum antimicrobial activity and high local concentrations in prostatic tissue allows to treat patients more successfully.

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CHRONIC PROSTATITIS R.A.Burnazyan REPUBLIC OF ARMENIA

• Prostatitis is an infection and /or inflammation of the prostate gland which presents with several syndromes with varying clinical features: urinary symptoms, sexual dysfunction, pelvic pain etc (Krieger 1996).

Objectives

- <u>The prostate</u> is a privileged site an area in which antimicrobial penetration is generally poor.
- <u>The diagnosis</u> of prostatitis is controversial. As a result, the diagnosis and therapy of chronic prostatitis remains a challenge.
- <u>The efficacy</u> of antimicrobial agents is limited, a long duration of treatment of prostatitis is required, and failure rates are high (30-40%)[Patel KB et al 1997].
- <u>In this review</u> we will discuss classification, pathophysiology, diagnosis and treatment of chronic prostatitis.

<u>Classification of NIDDK(1995).</u>

- 1. Acute bacterial prostatitis is an acute infection of the prostate.
- 2.*Chronic bacterial prostatitis* is a recurrent infection of the prostate.
- 3.*Chronic non-bacterial prostatitis/chronic pelvic pain syndrome* (CPPS), exists where there is no demonstrable infection. Subgroups of this class are:
- 3.1.*Inflammatory chronic pelvic pain syndrome,* where white blood cells are found in the semen, expressed prostatic secretions (EPS), or voided bladder urine-3(VB-3).
- 3.2.*Non-inflammatory chronic pelvic pain syndrome*, where white blood cells are NOT found in semen, EPS, and VB-3.
- 4.*Asymptomatic inflammatory prostatitis* (AIP), where there are no symptoms, but white blood cells are found in prostate secretions or in prostate tissue during an evaluation for other disorders
- National Institutes of Diabetes and Digestive and Kidney Diseases (1995)

Pathophysiology

- <u>**1. Prostatic</u>** antibacterial factor PAF , a bactericidal fluid is diminished in patients with prostatitis [Fair W et al 1976].</u>
- <u>2. Patients</u> with prostatitis have alkaline prostatic secretions ranging in pH from 7-9 [Pfau A 1978].
- **<u>3. The introduction</u>** of bacteria into the prostate by:
- ascending urethral way,
- reflux of infected urine into prostatic ducts, which empty into the posterior urethra,
- invasion of rectal bacteria by direct extension into the prostate or by lymphatic spread,
- and hematogenous spread. This all can be the primary aetiology of most bacterial and nonbacterial prostatitis [Drach G 1986].
- <u>4.The reflux</u> of urine into prostatic ducts may cause prostatic inflammation via high concentrations of purine and pyrimidine base-containing metabolites in prostatic secretions [Persson B 1996].
Immunological evidences

- The CD4 T cell proliferative response to seminal plasma was statistically significant higher in patients with chronic prostatitis [Alexander R 1997].
- The presence of IgG and IgA antibodies against common Gram negative microorganisms in post prostatic massage urine [Shortliffe L 1989].
- Histologically proven eosinophilic prostatitis [Liu S 1992].



- In the semen of patients with chronic prostatitis elevated levels of cytokines, soluble proteins secreted by cells of the immune system were found. They are:
- TNF-alpha,
- Interleukin -1beta,
- Interleukin-6 [Alexander R 1998].
- These findings suggest that cytokines have an important role in the pathogenesis of prostatitis and that cytokine levels are useful indicators in patients with prostatitis

Bacterial prostatitis

- <u>Bacterial prostatitis is caused mainly by aerobes [Dominigue GJ, 1998]</u>:
- Escherichia coli,
- Pseudomonas spp.,
- Entercoccus faecalis,
- Staphilococcus aureus,
- Klebsiella pneumoniae,
- Enterobacter cloacae,
- Staphylococcus saprophiticus.
- And anaerobes [Szoke I, 1998].
- Additionally special culture methods have indicated that difficultto-culture Corynebacterium, Staphylococcus, Peptostreptococcus, Streptococcus and Escherichia were present in expressed prostatic secretions found to be negative by routine culture techniques [Tanner MA 1999].

Nonbacterial prostatitis

- Nonbacterial prostatitis (NBP) is the most common type of prostatitis, and occurs eight times more frequently than bacterial prostatitis [Crawford ED 1987].
- Causative factors are:
- Chlamydia trachomatis,
- Ureaplasma urealyticum,
- Trichomonas vaginalis [Moul JW1993, Kim ED 1994].

Diagnostic procedures

- Laboratory studies:
- Stamey-Meares test: serial collection of the urine and prostatic juice (VB1; VB2; EPS, VB3),
- Urine analysis and culture
- Sperm culture
- Imaging studies:
- Transrectal Ultrasound
- Color Doppler Ultrasound
- For the evaluation of prostatic abscesses and suspected neoplasms computed tomography, cystoscopy and iv urography may be useful.

Transrectal and Colour Doppler Ultrasound

- <u>The leading ultrasonographic diagnostic</u> <u>symptoms of chronic prostatitis are:</u>
- capsular thickening
- prostatic calculi
- hypoechoic halo in the periurethral region
- heterogenous echo pattern
- enlargement and thickening of the septa of the seminal vesicles [De la Rosette 1992, Gus'kov 1997]
- <u>Colour Doppler Ultrasound</u> shows isolated capsular vessels [Sauvain 1997].

Treatment

- Fluoroquinolones :
- **OFLOXACIN** 200mg 400mg
- Norfloxacin 400mg
- **Ciprofloxacin -** 250mg 500mg
- Nonsteroidal Antiinflammatory Drugs:
- Voltarene

2 weeks

3 weeks

3 weeks

3 weeks

- In case of non-bacterial prostatitis:
- **Doxycycline** 100mg
- Flagyl 500mg

3 weeks

2-3 weeks

Conclusions

- Prostatitis is a disease that causes men substantial morbidity
- In chronic bacterial prostatitis a variety of aerobic and anaerobic bacteria can be isolated. Nonbacterial prostatitis is the most common type of prostatitis and is associated with C. trachomatis, U. urealiticum and T. vaginalis
- Cytokines have an important role in the pathogenesis of prostatitis
- Doppler and transrectal prostatic ultrasonographic imaging a potential value in the diagnosis of prostatitis.
- Treatment is difficult and requires prolonged high dosage antibiotics and careful monitoring. Fluoroquinolones are most effective.

DO FERTILITY DRUGS INCREASE THE RISK OF OVARIAN CANCER?

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ABSTRACT

The relationship between the use of ovarian induction drugs and the risk of ovarian cancer has been reported since the late eighty's. Due to the large number of women that are nowadays under infertility treatment and the discouraging fact the there are no ways to decrease the mortality of ovarian cancer since there are no efficient screening methods, the ability to answer the question about the relation between infertility drugs and the risk of ovarian cancer is of striking importance.

Analysis of 4 cohort studies and 8 case-reports published until 1999 has been done in relation to the use of infertility drugs and the risk of ovarian cancer.

Although some studies have shown an increased risk of ovarian cancer with the use of infertility drugs, no conclusion can be drawn from the available published evidence, because of methodological problems making them neither comparable nor reproducible.

Key words: Ovarian neoplasm; infertility; infertility drugs, female

INTRODUCTION

The question whether fertility drugs could increase the risk for ovarian cancer started in 1993 with the report of Whittmore et al (1) who associated the use of ovarian stimulation drugs with an increased risk for developing ovarian cancer.

Drug induced ovarian stimulation became available in the mid sixties, with the introduction of clomiphene citrate (CC), and human corionic gonadotropin (hCG) (2). In the beginning, those drugs where only used in women with ovulation disorders. The trends have changed with the years.

In 1995 it was estimated the number of women aged 15-44 with impaired fertility was 6.1 million(3). According to the 1996 Assisted Reproductive Technology Success Rates National summary from the US, based on the report of 300 assisted reproductive technology (ART) clinics, only 14 % of women who underwent ART had ovulation disorder(4). The number of cycles induced for that year was 49.584, whereas the total number of cycles for the year 1992 was 37.995(5). This means an increase of more than 30% for a period of 4 years. 70 % of the women where between 30 and 39 years old.

Ovarian cancer is the principal cause for mortality among gynecological cancers(6). This is because most of the cases are diagnosed at late stage, due the lack of a screening methods for early diagnosis. The incidence for ovarian cancer varies with ageing (7). (table 1)

Why, theoretically, could ovulation stimulation drugs increase the risk for ovarian cancer? On one side, there is the theory of «incessant ovulation», described by Fatallah in 1971 (8). He states that ovulation left a mechanical sequel, like a mitotic stimuli to the ovarian epithelium. This theory has been supported by the fact that the only two well recognized protective factors for ovarian carcinoma are pregnancy and the use of oral contraceptives (1, 9-12), both related to the anovulation they produce.

The other theory is the «gonadotropin hypothesis». Stadel (13) hypothesized that the permanent exposure to persistently circulating levels of gonadotropins had a carcinogenic effect on the ovarian epithelium. This theory is also supported by the protective effect of pregnancy and the use of oral contraceptives, because of the inhibition of the secretion of pituitary gonadotropins, and also by experimental models that have shown that in animal models, ovarian tumor growth can be induced by gonadotropins and inhibited with the administration of gonadotropin-releasing hormone agonist. (14,15).

To be able to answer whether ovulation induction drugs can increase the risk of ovarian cancer is therefore of striking importance, considering the potential impact it could have on the future of women under infertility treatment.

OBJECTIVES

The objective is to review the available evidence about the use of infertility drugs and the risk of ovarian cancer, and delineate what an analytic study must have to be able to prove or not this important issue.

METHODS

Bibliographic search in MEDLINE and a review of the references obtained.

Analysis has been made from the evidence published until now, especially the analytical studies, in reference to the use of ovulation induction drugs for the treatment of infertility and the risk of ovarian cancer. There is a description of each study, their results, and their strength and limitations.

RESULTS

There are 59 cases of ovarian cancer in relation to the use of infertility drugs in form of case reports until today (16-36), the first of them described in 1982. All of them have reported the use of ovarian induction drugs before the diagnosis of ovarian cancer was done, but some of them lack the time between the exposure and the time of diagnosis (17,22,24), while in others the diagnosis was made during treatment or less than 1 year after the treatment (18,21-23,25,27,29-33). The age range at the time of diagnosis was from 21 to 41 years. The different histologic types reported where adenocarcinoma 42%, borderline 27%, granulosa-cell 29% and malignant melanoma 2%. The fact that more than 50 % of the tumors reported where low potential is possibly in relation to the reported ages of those women

There might also be a detection bias, since the women under infertility treatment are very closely followed, what increases the chances of diagnosis for otherwise asymptomatic tumors. There are in these case reports a inconsistency in the data reported, like type of infertility, or familiar history of ovarian or breast cancer.

Therefore, a relation cause-effect can not be drawn from these case-reports. They may be simple hypothesis generators.

ANALYTICAL STUDIES

Cohort studies (<u>Table 2</u>)

Rossing et al (37) examined a cohort of 3837 women evaluated for infertility between 1974 and 1985. The diagnosis of infertility was being unable to conceive after one year. 64% of the cohort were exposed to ovulation induction drugs. The cases where compared to the general population from the same area (Seattle, US) and to a sub-cohort of randomly chosen 135 women from the cohort. Eleven cases of invasive epithelial carcinoma or borderline or granulosa-cell from the ovary were detected (four, five and two respectively).

The SIR for invasive ovarian carcinoma, in comparison to the general population, was 1.5 (95% CI 0.4-3.7), and for borderline tumors, the SIR was 3.3 (95% CI 1.1-7.8) When comparing the type of infertility, the presence of ovulatory abnormalities doubled the risk for ovarian carcinoma, SIR 3.7 (95% CI 1.4-8.1). When the type of drug used was compared, only the use of CC for more than 12 cycles was statistically significant, for ever users the RR was 2.3 (0.5-11.4), less then 12 month users, RR 0.8 (0.1-5.7), more than 12 months, RR 11.1 (1.5-82.3), and it was observed in both the nulliparous and parous women. When eliminating the granulosa-cell tumors from their analysis (38), the risk was attenuated but still elevated for those women with more than 12 cycles of CC RR 6.7 (0.8-58.8). The increased risk was observed in both women with ovulatory abnormalities (RR =7.4 95% CI 1.0-53.1) and women without them (RR= 9.1, 95% CI 1.0-86.5) (2).

The strengths of this study are 1) information about type of infertility, 2) type and number of cycles for each induction drug, 3) the location at the end of the study of 96% of the women.

The limitations of this study are 1) the short time of follow up for ovarian cancer, with a median of 11 years, 2) the lack of registry of oophorectomy in the cohort and 3) no register of familiar history for ovarian or breast cancer.

The largest cohort carried among infertile women was published in 1995, conducted by Venn et al. (39). Their cohort was 10.358 women registered for IVF program between 1978 and 1992. Of them, 5564 were exposed to induced ovulation for at least one cycle. The median length of follow up was 5.2 years for the exposed group and 7.6 years for the unexposed, with only 51% of the women followed up for at least 5 years.

They found three invasive ovarian cancers in each group. Compared to general population, the SIR was of 1.7 (95% CI 0.55-5.27) for the exposed women and the SIR for unexposed women was 1.62 (95% CI 0.52-5.02). The risk remained similar after including only the women with more than five years of follow up.

When comparing the type of infertility, ovarian disorders vs. unexplained, the SIR was 6.89 (95% CI 2.9-16.8). The relative risk after adjustment to exposure to IVF, of unexplained infertility , was significant RR 19.19 (95% CI 2.23-165).

Although the large sample size, the study limitations are 1) no register of the type of infertility drugs to women were exposed, 2) the short median follow and only 51% follow up for 5 years, 3) more than 35% of the women in the unexposed group could not be located, 4) no information about parity or use of oral contraceptives, 5) no information about oophorectomy, 6) the inclusion of women with only one cycle were included in the analysis, and 7) no register of familiar history for ovarian or breast cancer.

Modan et al (40), evaluated a cohort of 2496 infertile women treated between 1964 and 1974, with a mean follow up of 21.4 years, and a mean age at the end of the follow up of 50.0 years. 1309 received treatment with ovulation induction drugs. They divided infertility in hormonal and non-hormonal.

There were 12 cases of ovarian carcinoma identified vs. 7.2 cases expected, SIR 1.6 (95% CI 0.8-2.9) when compared to general population, half of them in the exposed group. For the much higher prevalence of nulliparity and family history in the cohort compared to the reference population, sensitivity analysis was done, with an expected SIR for nulliparity of 2.4 and 4.9 for familiar history. In relation to the use of infertility drugs, there were no differences between users and no users (SIR 1.7 versus 1.6 respectively). When the use of ovulation induction drugs was analyzed only clomiphene citrate showed an increase in the risk for ovarian cancer, with a SIR 2.7 (95% CI 0.97-5.8). There were no cases within the users of the other infertility drugs. When comparing type of infertility, the non-hormonal showed an increase in the risk for ovarian cancer SIR 2.7 (95% CI 1.0-6.0).

The strength of the study are 1) the long follow up, 2) the information about confounding variables such as parity, use of oral contraceptive and family history, of cancer

The limitations are 1) the limited power, since a relatively small number of ovulation-treated women were included, 2) after identifying the confounding variables, they were not analyzed further, 3) the mean age of 50 years at the end of follow up, 4) the information about type of infertility.

The cohort reported by Potashnik et al. (41) evaluated 1197 infertile women attending a fertility clinic from 1960 to 1984. Fertility was defined as the failure to achieve pregnancy for more than 1 year. 780 of them were exposed to ovulation induction drugs. The mean duration of follow up was 17.9, with a median age at the end of the diagnosis of 44 years. Only two cases of invasive ovarian carcinoma were found, one in the exposed group. This results in a SIR of 0.68 (95% CI 0.01-3.80) for the exposed group and for the unexposed a SIR of 1.35 (95% CI 0.02-7.49). The single case found in the exposed group had received two courses of clomiphene citrate, with a SIR 1.9 (95% CI 0.02-10.5).

The strengths of the study are 1) long latency time, and 2) accurate data on type of drug, number of cycles and total dose.

The limitations are 1) the cohort size, 2) lack of information about confounding variables such as parity, use of oral contraceptive and family history of cancer, and 3) the median age at the end of follow up, so the population did not enter into the period of life with more risk for ovarian cancer.

Case control studies (Table 3)

Whittemore et al. (1), in 1992 presented an analysis from 12 case control studies of ovarian cancer in the US. Only three of them included data on infertility, use of infertility drugs and invasive ovarian cancer on 622 cases and 1101 controls. Infertility was defined as the difficulty in conceiving or in carrying a pregnancy to term. Among these, 96 cases and 135 controls were infertile, and only 20 women in the cases and 11 in the controls were exposed to ovulation induction drugs. The information about specific type of infertility drugs used was incomplete. Data were collected between 1977 and 1981. The risks were evaluated after adjusting for age, parity, contraceptive use and breast feeding.

The odds ratio for epithelial ovarian cancer according to the use of fertility drugs was OR 2.8 (95% CI 1.3-6.1) and for the non users the OR was 0.91 (95% CI 0.66-1.3) when compared to women with no clinical history of infertility. When comparing nulligravid to gravid women between the ever users, the risk was greater among the nulligravid, OR 27.0 (95% CI 2.3-315.6) vs. OR 1.4 (95% CI 0.52-3.6).

The strengths of this study are primary the magnitude of the observed odds ratio especially for the nulligravid women.

The limitations are 1) the small number of women exposed to fertility drugs, 2) lack of information about familiar history of cancer and type of infertility, 3) a maybe to broad definition of infertility, with no specification of time interval, 4) lack of information about type of infertility drug and doses, and 5) not having restricted the analysis to women diagnosed as infertile, since they are more comparable. Glud et al. (2) reanalyzed the risk estimates, using infertile women that were not exposed to infertility drugs as a reference group. The crude RR related to fertility drug use, (comparing only infertile women) and related to the parity state showed an increase for the nulligravid ever users RR 12.0 (95% CI 2.0-71) and for the gravid ever users a RR 1.5 (95% CI 0.6-4.0). Kaufman et al. (42) did the same calculations with similar findings, but they used the raw data, not adjusting for age and breast feeding.

Harris et al. (43), from the same collaborative case control trial, analyzed the data regarding the risk for borderline ovarian tumors with the use of ovulation induction drugs, using the same trials that included data about infertility and use of infertility drugs. The cases were 88 borderline tumors and the controls were 752, for the same period of time and only 4 women in the cases and 9 in the controls were exposed to ovulation induction drugs. The relative risks were adjusted for age, use of oral contraceptives, parity, breast feeding and study.

Relative to women who did not report infertility, the OR associated with the use of infertility drugs was 4.0 (95% CI 1.1-13.9) vs. never users that had a OR of 1.6 (95% CI 0.8-3.1). When the analysis was restricted to only women with an history of infertility (2), the crude estimate relative risk for the ever users was 2.5 (95% CI 0.7-9.0).

Franceschi et al. (44), evaluated 195 epithelial ovarian cancers with 1339 controls, between 1992-1993. Infertility was defined as an unsuccessful effort to achieve pregnancy for more then two years. No data were collected about the type of infertility, the type of drug used, nor the doses, since the study was not designed to evaluate infertility. Only 4 women among cases (2%) and 34 among controls (2.6%) reported a history of infertility. Fertility drugs were used only in 1.9% of the cases and in 1.5 % of the controls. The relative risks were adjusted for age, use of oral contraceptive, parity, breastfeeding and study.

No difference was found between users and non-users RR 0.7 (95% CI 0.2-3.3). When the analysis was restricted to only women with a history of infertility (2), the crude estimate risk was 1.3 (95% CI 0.7-2.4).

The limitations of the study are 1) not being designed to evaluate ovulation induction drugs, 2) lack of information about type of infertility drug and doses and type of infertility, 3) definition of infertility, and 4) low prevalence of infertility.

Shushan et al. (45) evaluated 200 women with epithelial invasive or borderline ovarian cancer (164 and 36 respectively) and 408 controls, between 1990 and 1993. Women had to be born after 1929, to being able to have being exposed to fertility drugs. The analysis were performed for all the cases together (invasive and borderline) and for the borderline alone. Infertility was not defined. Infertility prevalence was 17% in cases and 11.3% in controls, and use of infertility drugs was 12% in cases and 7.1% in controls.

The adjusted odds ratio for women with epithelial ovarian cancer ever exposed to any fertility drug was 1.31 (95% CI 0.63-2.74) and for borderline ovarian tumors it was 3.52 (95% CI 1.23-10.09). The adjusted OR when comparing the different drugs used with the non-users, showed for the epithelial ovarian cancer and the use of HMG 3.19 (95% CI 0.86-11.82) and for borderline tumors 9.38 (95% CI 1.66-52.08). When the analysis was restricted to only women with an history of infertility (2), the ever users had a slightly increased crude risk, RR 1.4 (95% CI 0.5-3.6), whereas comparing only in the borderlines, the ever users had a risk of RR 9.4 (95% CI 1.7-52.1). No association with the use of CC was found.

The strength of the study are 1) a proper statistical design, 2) information about type and dose of the fertility drugs, 3) information about parity, familiar history of cancer, use of oral contraceptives.

The limitations are 1) data collected by telephone (recall bias), 2) 25 % of the patients died before contacted, 3) lack of data about specific type of infertility, 4) combining for the analysis both the epithelial and borderline tumors, 5) no calculation of the risk separately for nulliparous and parous women.

In the case control study by Mosgaard et al. (46) 684 cases of invasive ovarian cancer (from a total of 1372 cases identified and verified) were analyzed. Women less than 60 years, diagnosed with ovarian cancer during 1989 and 1994 and 1721 controls were included. Infertility was defined as difficulty for more than 1 year to achieve pregnancy. Twenty-two percent of the cases reported infertility, from which only 20% received drugs for infertility treatment, and 15 % of the controls were infertile.

After adjustment for confounders, the OR for ovarian cancer was 2.26 (95% CI 0.92-5.58) among treated nulliparous women and 0.73 (95% CI 0.29-1.82) among treated parous women, as compared to nulliparous without infertility. The risk of ovarian cancer among treated infertile vs. non treated infertile women was 0.83 (95% CI 0.35-2.01) for nulliparous and 0.56 (95% CI 0.24-1.29) for the parous. No changes were seen after stratification for the different types of drugs. There were no differences when different types of invasive cancers were analyzed.

The strengths of the study are 1) the identification and verification of the tumors, 2) high proportion of the controls included (81%), 3) stratification according to parity and also only for the infertile population.

The limitations are 1) 50% of the identified cases could not be analyzed either due to they were dead (36 %) or refused to participate, 2) data collected by questionnaire (recall bias), 3) lack of information about specific type of infertility and accurate data for the specific drugs used.

Parazzini et al. (47) analyzed 971 cases of epithelial invasive ovarian cancer and 2758 controls, with a overall participation of > 95% for both cases and controls. Women were less than 75 years old. They were interviewed less than 1 year after the diagnosis was made. Infertility was diagnosed as active efforts to achieve pregnancy for more than 2 years. Only 14 cases (1.4%) and 45 controls (1.6%) reported infertility as defined above, and only five cases (0.5%) and eleven controls (0.4%) reported having ever used fertility drugs.

When compared to never users, the multivariate OR for ever users was 1.1 (95% CI 0.4-3.3), and no differences were found when the duration of use was calculated.

The strengths of the study are 1) high participation from both cases and controls.

The limitations are 1) the low statistical power due to the low prevalence of use reported (most of the fertility problems were identified before efficacious treatment was available), 2) lack of information about specific type of infertility and accurate data for the specific drugs used.

The same Italian group (48) published a case control study for the risk of borderline ovarian tumors (not included in the previous report) and the use of infertility drugs. Ninety-three cases of borderline tumors were compared to 273 controls. Patients were interviewed less than 1 year after the diagnosis was made. Infertility was diagnosed as unsuccessful active efforts to achieve pregnancy for more than 2 years. Only three cases and no control reported infertility, and four cases (4.3%) reported ever used fertility drugs vs. no controls. The difference was of statistical significance, the Fisher exact test P value was 0.004 (not included in table 3).

The limitations of the study are 1) the low prevalence of infertility and use of ovulation drug reported, 2) lack of information about specific type of infertility and accurate data for the specific drugs used.

In the study published by Mosgaard et al. (49) 231 cases of borderline ovarian cancer (from 263 identified) were compared to the same control group previously reported (45) (1721 women). Infertility was defined as difficulty for more than 1 year to achieve pregnancy. Twenty-two percent of the cases reported infertility, from witch only 20% received drugs for infertility treatment. In the case group, 53 (22.9%) reported infertility, and 245 (14.2%) in the control group.

Among infertile women 32% of the cases and 24% of the controls had used fertility drugs, corresponding to an OR of 2.19 (95% CI 1.24-3.85), after adjustment for age. In the multivariate analysis, infertile nulliparous women ever users did not have an increased risk compared with never users OR 1.5 (95% CI 0.51-4.39). For the users of CC and hCG, the OR was 3.01 (95% CI 0.73-12.33) and was 0.91 (95% CI 0.14-6.13) for women treated with hMG and hCG. There

were no differences among parous infertile women.

The strengths of the study are 1) stratification according to parity, 2) the high identification and validation of the tumors.

The limitations are 1) lack of information about the time of diagnosis (surveillance bias), 2) data collected by questionnaire (recall bias), 3) lack of information about specific type of infertility.

DISCUSSION

The possibility that fertility drugs may increase the risk of ovarian cancer is of vital interest to many women and their physicians. There are women being exposed to infertility treatment and ovulation induction drugs, without ovulation disorders and there are no satisfactory means of detecting ovarian cancer early enough so that the clinical course of this disease could be affected. On the other side, infertility by itself might be a risk for ovarian cancer(2,19, 39).

The awareness of the women about ovarian cancer is also important. On a report by Rosen et al.(50), the maximum risk that a group of infertile women was able to tolerate was measured and they awareness of ovarian cancer. Almost 80% accepted an increased risk of ovarian cancer, but only 24% had the idea that until today there was no cure for most of the ovarian carcinomas. Ten percent of these women stated that they would not accept an increased risk of ovarian cancer.

The published data available until now shows neither a striking increase in the risk nor an absence of the risk of invasive ovarian cancer with the use of ovulation induction drugs.

In general, most of the epidemiological studies described above are hampered by methodological problems, that affect their study power, like small sample size and lack of sample size calculations, short follow up time, low prevalence of infertility and fertility drug use, and also lack of information about important confounding variables, which could have underestimate the real effect.

When considering the studies that have full information on the specific use of ovulation induction drugs (37,39-41,45), three of them (37,39,44) showed that there was an increased risk among infertile women who had ever used infertility drugs, and an even higher risk was found when comparing them with other infertile women that had never used such drugs.

Higher risks were also found with specific types of drugs like for CC in the study by Rossing et al.(38), or hMG in the study by Sushan (45), but not in the others.

In the case of borderline tumors, four studies (37,43,45,46) have showed a statistical significant increase of the risk for the users of infertility drugs. Rossing (37) related it to the use of CC for more than 12 cycles and Shushan (45) to the use of hGM.

A very important question has been raised, but the data currently available are basically not adequate, for the reasons stated above, for drawing a conclusion in either direction especially in the case of the invasive epithelial ovarian tumors.

What would be necessary in future studies to avoid all the methodological bias that have been previously described? The complete data about infertility and separation according voluntary nulliparity and infertility, the exact causes of infertility, the treatment received with doses and number of cycles, if these women achieved pregnancy after the infertility treatment, the family history of cancer, previous exposure to other kind of hormonal treatment. Also the studies will have to follow these women (in case of cohorts) for al least 30 years, so they reach women's peak incidence of ovarian cancer. Such studies have been reported to have started in the US, conducted by the National Cancer Institute; in Denmark, conducted by the Danish Cancer Society and in the Netherlands(2,42). They reported on cohorts of 10.000-20.000 women diagnosed infertile.

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Table 1 Risk of ovarian cancer according to age (7)

Age group

	Rates per 100000
15-44	3.1
45-54	14.94
55-64	22.45
+65	28.47
All ages	6.3

Table 2 Cohort studies of infertility drug use and the risk of ovarian cancer

Study	Type of	Composition of cohort	Mean length of follow up	No of cases	Risk of ovarian cancer †
	cohort				
Rossing et al. (37), 1987	Women referred for infertility	Subcohort of 135	12.3 years	11 cases (4 invasive, 5 borderline, 2 granulosa-cell	Compared with general population
	1974-85	64% ever users of ovulation induction drugs			Invasive SIR 1.5 (0.4-3.7)
		Total 3837			Borderline SIR 3.3 (1.1-7.8)
					Compared with infertile women*
					Ever CC use RR 2.3 (0.5-11.4)
					1-11 months CC RR 0.8 (0.1-5.7)
					12+ months CC RR 11.1 (1.5-
					82.3)
					after excluding granulosa cell
Venn et al. (39), 1995	Infertile women referred to IVF program 1978-1992	Total 10358 5564 exposed	5.2 yearsforexposed7.6 yearsforunexposed	6 cases(3 in the exposed and 3 in the unexposed (all invasive)	RR 6.7 (0.8-58.8) Compared with general population
					Exposed SIR 1.7 (0.55-5.27)
					Unexposed SIR 1.62 (0.52-5.02)
					Compared with infertile women
					Unexplained infertility + exposure
Modan et al (40), 1998	Women diagnosed for infertility between 1964-1974	Total 2496	21.4 years		RR 19.19 (2.23-165) Compared with general population
		1507 exposed			SIR 1.6 (0.8-2.9)
					Compared with infertile women
				12 cases (6 in the exposed and 6 in the unexposed)	Exposed SIR 1.7 (0.6-3.8)
					Unexposed SIR 1.6 (0.6-3.5)
					When fertility drug was

compared

CC users SIR 2.7 (0.97-5.8)

Potashnik et alInfertile women Total 1197 (41), 1999 attending fertility clinic 1960-1984) 780 exposed 17.9 years 2 cases (one in When comparing the exposed exposure to drug group) exposed SIR 0.68 (0.01-3.8)

> unexposed SIR 1.35 (0.02-7.49)

When comparing type of drug,

CC users SIR 1.9 (0.02-10.5)

SIR standardized incidence ratio; RR relative risk; CC clomiphene citrate

† all SIR and RR expressed with 95 % confidence interval; * adjusted

Table 3 Case control studies of infertility drug use and the risk of ovarian cancer

Study	Type of case control	Type and No of cases and controls	f Data collection period	Data collection method	Prevalence infertility	Risk of ovarian cancer †
Whittemore et al. (1),	Pooled analysis	622 invasive epithelial	1977-1981	Personal interview	15% cases ; 12% controls	When comparing women without infertility
1992 from three case control studies	ovarian cancers : 1101 hospital and population controls				exposed OR 2.8 (1.3-6.1)	
					unexposed OR 0.91 (0.66-1.3)	
	stadios	controls				When comparing parity in the exposed group
						nulliparous OR 27.0 (2.3-315.6)
						parous OR 1.4 (0.52-3.6)
						When comparing users to infertile women
						nulliparous RR12.0 (2.0-71)
						parous RR 1.5 (0.6-4.0)

,	0					
Harris et al. (43), 1992	Pooled analysis	88 borderline tumors ; 752	1977-1981	Personal interview	19% cases, ; 12% controls	When comparing to women without infertility
	from three case	population controls				exposed OR 4.0 (1.1-13.6)
	control					unexposed OR 1.6 (0.7-9.0)
	studies					When comparing users to infertile women
						RR 2.5 (0.7-9.0
Franceschi et al (44) ; 1994	Hospital based case	195 invasive epithelial	1992-1993	Personal interview	2% cases ; 2.6% controls	When comparing women without infertility
	control	ovarian cancers ; 1339 controls	;			exposed RR 0.7 (0.2-3.3)
						When comparing users to infertile women
						RR 1.3 (0.7-2.4)
Shushan et al.	. Population based case control	164 invasive epithelial and 36 borderline ; 408 controls	1990-1993	Personal interview	17% cases ; 11.3% controls	When comparing users
(45); 1996						s all tumors OR 1.31 (0.63-2.74)
						borderline OR 3.52(1.23-
						10.09)
						When comparing different drug to non users
						all tumors/hMG OR 3.19 (0.86-11.82)
						borderline/hMG OR 9.38 (1.66-52.08)
						When comparing only infertile women
						all tumors/users RR 1.4 (0.5-3.6)
						borderline/users RR 9.4 (1.7-52.1)

OR odds ratio; RR relative risk; CC clomiphene citrate ; hMG human menopausal gonadotropin

† all OR and RR expressed with 95 % confidence interval

Table 3 Case control studies of infertility drug use and the risk of ovarian cancer (cont.)

Study	Type of case Type and No of		Data	Data	Prevalence	Risk of ovarian cancer \dagger
	control	cases and	collection	collection	infertility	
		controls	period	method		

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Mosgaard e al (46) ;	tPopulation based case	684 invasive epithelial	1989-1994	Posted questionnaire	20% cases ; 15% control	When compared to nulliparous swithout infertility
1997	control	ovarian cancers 1721 controls	•			users/nulliparous OR 2.26 (0.29-1.82)
						users/parous OR 0.73 (0.29-
						1.82)
						When compared to nonusers infertile women
						users/nulliparous OR 0.83 (0.35-2.01)
						users/parous OR 0.56 (0.24-1.29)
Parazzini et Hospital al. (47) ; based case 1997 control	Hospital based case	ital 971 epithelial l case ovarian cancers ol 2758 controls	1983-1991 ;	Personal interview	1.4% cases ; 1.6% controls	When compared to infertile women
	control					users/ OR 1.1 (0.4-3.3)
Mosgaard e al. (49) ;	tPopulation based case	231 borderline tumors ; 1721	1989-1994	Posted questionnaire		When compared to infertile women
1998	control	controls				users/ OR 2.19 (1.24-3.85)
					22% cases ; 22.9% controls	When comparing infertile women
						users/nulliparous OR 1.5 (0.51-4.39)

OR odds ratio; RR relative risk; CC clomiphene citrate ; hMG human menopausal gonadotropin

 \dagger all OR and RR expressed with 95 % confidence interval

27.11.02

DO FERTILITY DRUGS INCREASE THE RISK OF OVARIAN CANCER?

M. Lamm (Argentina)

Why is this possible in theory?

INCESSANT OVULATION GONADOTROPIN HYPOTHESIS

PREGNANCY ORAL CONTRACEPTIVES

Why is it important?

- Change in trends for infertility treatment
- Constant increase in the number of procedures

OVARIAN CANCER

A BIG PROBLEM

Whittemore et al. (1992)

- 622cases, 1101controls
 (15% and 12% infertile)
- When comparing women without infertility exposed OR 2.8 (1.3-6.1) unexposed OR 0.91 (0.66-1.3)
- When comparing parity in the exposed group nulliparous OR 27.0 (2.3-315.6) parous OR 1.4 (0.52-3.6)
- When comparing users to infertile women nulliparous RR 12.0 (2.0-71) parous RR 1.5 (0.6-4.0)

3837 infertile women11 cases

CC USERS
 <12 m RR 0.8 (0.1-5.7)
 >12 m RR 11.1 (1.5-82.3)

Gral. population SIR 1.5 (95% CI 0.4-3.7)

•With ovulatory anomalies RR7.4 (1.0-53.1)

•Without ovulatory anomalies RR 9.1 (1.0-86.5)

Parazzini et al. (1998)

- 971 cases, 2758 controls (1.4 % and 1.6 % infertile)
- •When compared to infertile women users/ OR 2.19 (1.24-3.85)

 When comparing infertile women users/nulliparous OR 1.5 (0.51-4.39)

OTHER

- MODAN et al, 1998
- POTASHNIK et al, 1999
- VENN et al, 1995
- FRANCHESCHI et al, 1994
- MOSGAARD et al, 1997

Harris et al. (1992)

- Borderline tumors
 88 cases, 752 controls
- When comparing to women without infertility exposed OR 4.0 (1.1-13.6) unexposed OR 1.6 (0.7-9.0)
- When comparing users to infertile women
 RR 2.5 (0.7-9.0)

Shushan et al. (1996)

200 cases, 408 controls
(17 % and 11.3% infertile)
164 invasive, 36 borderline

- When comparing users all tumors OR 1.31 (0.63-2.74) borderline OR 3.52(1.23-10.09)
- When comparing drug to non users
 borderline/hMG OR
 9.38 (1.66-52.08)

• When comparing only infertile women borderline/users RR 9.4 (1.7-52.1)

Mosgaard et al. (1998)

- Borderline tumors
 231 cases, 1721 controls

 (22 % and 15 % infertile)
- When compared to infertile women users OR 2.19 (1.24-3.85)
- When comparing infertile women users/nulliparous OR 1.5 (0.51-4.39)

FERTILITY DRUGS

BORDERLINE OVARIAN TUMORS



FERTILITY DRUGS

INVASIVE OVARIAN CANCER





DOMESTIC VIOLENCE IN PREGNANCY

Sahar Parvez

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Supervisor: M. Usher-Patel, WHO, Geneva, Switzerland

Abstract

This literature review addresses the issue of violence against women in pregnancy. The data reviewed suggests that it is responsible for negative health consequences for a significant proportion of the female population. It has also a direct negative impact upon other health-related issues such as family planning, safe motherhood, and prevention of sexually transmitted diseases. Unwanted and mistimed pregnancies for adolescents and young adults would appear a major contributing factor to violence in pregnancy and both factors are associated with known negative health outcomes for the mother, fetus and newborn infant.

Pregnancy is a time for most women, which offers the opportunity to interact routinely with the health care system. For many who have been abused, health workers are the main and only means of contact with public services which are able to offer support and information. Health professionals, especially obstetricians and family doctors, nurses and midwifes have a fundamental role in this with chances of preventing serious physical, psychological and social consequences.

Keywords: Violence, domestic violence, abuse, pregnancy

Introduction

Objectives

Methodology

Results: Annexes I & II
Domestic violence in pregnancy - S. Parvez

Discussion

Conclusions and Recommendations

Objectives

To undertake a review of current literature to determine the extent of domestic violence in pregnancy, identify key factors that may increase the probability of violence occurring during pregnancy, determine the affect this has on the health of the mother and outcome of pregnancy and make recommendations on the action health care providers can take to recognise and manage domestic violence in pregnancy.

Methodology

Method of Search Strategy

A computerized literature search to verify all studies on domestic violence in pregnancy was undertaken using the WHO Reproductive Health Database, WHO Bibliographic Data-base on violence against women, Medline, and BMJ Database. The methods used for verifying relevant studies were as follows:

- 1. domestic violence (1985 1998)
- 2. women (1985 1998)
- 3. **#1 and #2**
- 4. pregnant or pregnancy (1985 1998)
- 5. domestic violence (pregnant or pregnancy) (1986 1998)

Searched were the reference of articles between 1996 and 1999 in order to obtain references not included in the WHO databases.

122 articles were reviewed for relevance to this literature review and 53 were selected, based on the following criteria:

- articles that focused on prevalence, risk factors and health consequences of domestic abuse in pregnancy
- articles which used standard measurement tools for analysis of date collected by

structured or semi-structured questionnaires

- articles in which the sample size was considered sufficiently large enough to estimate the prevalence of abuse with high precision (minimum sample of 544 women is required to estimate the prevalence of abuse with high precision *95% confidence intervals (CI) extending 3% above or below the point estimate (Muhajarine N, 1999).
- articles that address the problems of domestic violence in pregnancy in less-developed settings.
- WHO publications on violence against women.
- articles that used standard measurement tools for the analysis of data and concluded with recommendations on actions that can be taken to reduce domestic violence in pregnancy.

40 articles related to studies undertaken in developed countries and only 13 articles were identified from less developed countries.

Of the fifty-three articles and four WHO publications reviewed only nineteen articles and two WHO publications met either one or more of the criteria and provided either qualitative or quantitative information that:

- determined to what extent domestic violence occurs in pregnancy;
- identified what factors if any, increase the probability of domestic violence occurring;
- identified what adverse affects this may have on the health of the woman and the outcome of pregnancy;
- made specific recommendations on the action health care providers can take to recognise and manage domestic violence in pregnancy.

Characteristics of the studies

Annexe 1 provides a table summarising each of the articles that has been reviewed. The studies have been arranged in chronological order and analysed according to:

Type of study - Whether the study was quantitative or qualitative, retrospective or prospective.

Participants - Sampling process and populations selected.

Setting - Location of study.

Interventions- Methodologies used to analyse the data.

Outcome - Summary of key outcomes and conclusions reached by the authors of the study. Remarks - Assessment of the quality of the study.

Description of the studies

The majority of studies on issues related to violence in pregnancy have been undertaken either in the United States of America or Europe. Out of 122 studies maintained on the WHO Reproductive Health Data-base related to domestic violence in pregnancy only 43 were undertaken in resource poor settings and out of these 13 had been published in peer reviewed journals.

It would appear that information on violence from scientifically sound studies is rather scanty. In fact, according to the World Health Organization (WHO) there is little accurate and comparable data available on domestic violence in pregnancy since the majority of the research is population based and the lack of consistent methods and definitions makes comparison difficult. This is mainly because definitions tend to be subjective. Survey questions often ask whether women experience specific acts of violence, during a fixed time period and some studies only examine physical abuse while others may consider physical, sexual and psychological abuse. In family, violence research may focus on only those currently married while others report on single and married populations and the severity of violence reported may vary between studies. In addition, the true prevalence has proven to be a difficult and complex task to measure since it is often under-estimated due to under-reporting.

Therefore this paper will not attempt to make comparisons between studies but focus on the outcome of the studies selected for review.

02.12.02

Domestic violence in pregnancy

OBJECTIVES

Review of current literature to

determine extent of domestic violence in pregnancy

identify key factors increasing probability of violence in pregnancy

determine the health consequences for the mother and infant

<u>Make</u> recommendations to recognise and manage domestic violence in pregnancy

Domestic Violence

Physical, Psychological and Sexual coercive acts by intimate partner

WHO estimate: globally 20% -50% physically abused by intimate partner

1 in 5 women

Domestic violence Emerging as a public health issue

Issue of human rights Women's rights International forums

There are many forms of violence

Sex-selective abortion Female infanticide child marriage female genital mutilation incest pornography dating and



Supervisor:

M. Usher-Patel



5 Oct 1999

Sahar Parvez

domestic violence in pregnancy- S Parvez

courtship violence rape sexual harassment dowry abuse and murders physical, sexual and psychological abuse partner homicide

Domestic violence

ignored/condoned by society

gender discrimination

impact upon future generations as well as victims

pregnancy perspective turns it into maternal and infant health issue

What is the extent of domestic violence in pregnancy

Extent of problem

Estimated prevalence rate ranges between 1% and 20%

Hidden, difficult to study, accepted as a cultural norm

Perpetrator - close relationship husband, boyfriend, ex-husband

Little accurate and comparable data

Lack of consistence in methods and definitions

Under-reporting of problem

Scanty statistics available

Need for scientifically sound studies

Key factors

Young age (teenagers and less than 25

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domestic violence in pregnancy- S Parvez

years) particularly in unstable relationship

Unwanted and mistimed pregnancies

Abuse before pregnancy

Alcohol abuse by partner

Other factors

Less socially advantage

Woman better educated than partner

stress and negative live events

divorce, separated and living alone

financial problems

Affect on mother, affect on the outcome of pregnancy

Consequences in the pregnant woman

In the mother

direct physical injury

mental illnesses and psychiatric disorders

adoption of health risk behaviours

STD,miscarriage and preterm labour

In the fetus/neonate

direct physical injuries

disturbances in physical development

<u>death</u>

child that grows up with abuse learns to be abusive domestic violence in pregnancy- S Parvez

Conclusions and recommandations

Conclusions

Gender based violence affects significant proportion of women globally

Unwanted /mistimed pregnancy major catalyst for violence in pregnancy

Pregnancy related violence is health concern for both mother and child

<u>More</u>

sophisticated means needed to measure extent of violence

Recommendations

health care providers must become:

Trained Aware Sympathetic Competent to screen Proactive management Accurate recording

Educate and sensitise communities

Education

Media attention

Legal rights

Programs of support

Effective measurement

What can we all do?

Be aware and supportive

Provide access to quality family planning service

Prevent unwanted pregnancies

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Hospital Nacional A. Posadas

Argentina



DURATION OF TREATMENT FOR ASYMPTOMATIC BACTERIURIA IN PREGNANT AND NON PREGNANT WOMEN

ARIEL ROGANTI

DEFINITION

 THE PRESENCE OF GREATER THAN OR EQUAL TO 100,000 cf./ml. OF ONE OR MORE ORGANISMS ON TWO CONSECUTIVE URINE SPECIMENS AND THE ABSENCE OF SYMPTOMS ATTRIBUTABLE TO URINARY INFECTION.

WHO SHOULD BE TREATED?



PREVALENCE OF ASYMPTOMATIC BACTERIURIA

- 2 to 10% Pregnant women
- 5 to 10% Women age 60
- 20 to 30% Women older than 60

Antibiotic vs. no treatment for asymptomatic bacteriuria in pregnancy Smaill F. 1997



Duration of treatment for asymptomatic bacteriuria in pregnancy Villar J. et al. 1997

SINGLE DOSE VS. SHORT COURSE (4-7 DAYS)

Preterm delivery Low birth weight Preterm delivery or low birth weight Pyelonephritis Side effects No cure

Recurrent asymptomatic bacteriuria



Study	Patient Population	Study Numbers and Duration	Outcomes
Boscia et al 20	Women, geriatric apartment, mean age 85.8 years.	Treated: 63 No Treated: 61 Duration: 6 month	With treatment of bacteriuria, prevalend decreased at 6 month (64% not treated, 35% treated p<0.05, symptoms during 6 months 16% treated, not treated p=0.15)
Nicolle et al (22)	Women, long term care, mean age 83.5 years.	Treated: 26 No Treated: 24 Duration: 12 months	Genitourinary morbi- and mortality similar both groups; therapy group had increased adverse drug reaction (p=0.03) and increas- antimicrobial resistan (p=0.05)
Abrutyn et al 1	Women, ambulatory apartment and nursing home, mean age 82 years.	Treated: 166 No Treated: 192 Duration: 8 years	Mortality: 13.8 and 1 100000 resident days (RR: 0.92) in treated non treated, respectively.
Ouslander et al 26	Women, nursing home, mean age 85 years.	Treated: 33 Non Treated: 38 Duration: 4 weeks	Eradicating bacteriur had no short term eff on presence or degre urinary incontinence

Table 4. Prospective, Randomised Studies of Therapy for Asymptomatic Bacteriuria

Population	Number Enrolled	Regimens	Follow up	Cure and Reinfected
Women, geriatric apartment 9	63	Single dose TMP. Or Cefaclor	2 weeks	68% - 5%
Elderly women, mean age 82 years, some symptomatic 13	53	Single dose amoxicillin, TMP., Ciprofloxacin (N=31) 7 to 10 days ampicillin, TMP., Ciprofloxacyn Amoxicillin/Clavula nate of (N=22)	1 week 6 weeks 1week 6 weeks	52% - 19% 38% - 25% 59% - 23% 52% - 23%
Women , home, for aged , mean age 84 years. 38	54	Cefadroxil or T/S, or Norfloxacyn x 3 days	1 week 4 weeks	70% - 13% 46% - 23%
Elderly women, nursing home. 23	47	Single dose T/S, ampicillin, Tobramyicin or Amikacyn.	4 weeks 8 weeks	35% - 17% 11% - 32%

Table 5. Outcome Following Treatment for Asymptomatic Bacteriuria in ElderlyPopulation.

Conclusion

Pregnant Women

Non Pregnant Women

- Drug treatment decreases the risk of pyelonephritis, occurrence of low birth weight and preterm delivery
- Therapy compliance is virtually guaranteed and drug cost is reduced considerably.
- Permanent eradication of bacteriuria is difficult, time consuming, costly and potentially hazardous.
- In the absence of urologic obstruction or other urologic abnormalities it does not recommend treatment.

•Single dose therapy in inapropriated circumstances and in the poorly selected patient may place the patient at major risk.

•Practitioners should follow their current preferred practice until search evidence becomes available

We are doctors, we represent one of the minorities in this crazy world but we have a kind of power. If we do not change, we will never use it as well as we can.

ECTOPIC PREGNANCY—Diagnosis and Treatment Ara Dadivanian Armenia

Tutor— Berel Held Professor and Chief Division of Gynecology The University of Texas Medical Branch at Galveston

The most common sites for an ectopic pregnancy

Tubal-97,7% of all cases, which divide into -interstitial - 1.3% -ampullary - 90% -fimbrial - 5% Abdominal - 1.4% Ovarian - 0.2% Cervical - 0.2%

The rate of ectopic pregnancy





The fatality rate



RISK FACTORS

- Pelvic inflammatory disease
- A history of previous ectopic gestation
- Failed tubal sterilization and tubal reanastomosis
- Scarring of the uterine cavity secondary to multiple previous induced abortions and other surgical intervention
- Uterine myomas and adnexal mass
- Smoking

DIAGNOSIS

• <u>Symptoms</u>

- Pain-the most frequent symptom(90-100%)
- History of amenorrhea (60-80%)
- Vaginal spotting or bleeding (60-80%)

• <u>Signs</u>

- Abdominal tenderness
 (91%)
- Pelvic mass (20-50%)
- Uterine changes (25%)

DIAGNOSIS

- Laboratory studies
- Sensitive blood hCG assays
- The rate of rise of hCG
- Progesterone measurement
- Serum estradiol

- <u>Other diagnostic tests</u>
- Transvaginal ultrasonography
- Culdocentesis

TREATMENT

surgical management
medical management
expectant management

SURGERY

- <u>Laparotomy</u>
- hysterectomy
- salpingectomy
- salpingostomy
- salpingotomy

- Laparoscopy
- salpingectomy
- salpingostomy
- salpingotomy

Subsequent intra-uterine pregnancy rate after surgical treatment (both laparotomy and laparoscopy) of a previous E.P. is 49-80%

Subsequent ectopic pregnancy rate is 10-20%

MEDICAL MANAGEMENT

Unruptured tubal ectopic pregnancy in woman who elect conservative management may be able to be treated with methotrexate. Methotrexate is a folic acid antagonist and consequently interferes with DNA synthesis and cell reproduction.

METHOTREXATE THERAPY

- single IM injection of 50mg/m2 of body surface area
- orally in a dose of 0.3 mg/kg daily for 4 days
- intraamniotic injection under ultrasound guidance

- Bone marrow suppression
- Both acute and chronic hepatotoxity
- Rapidly progressive pulmonary toxity
- Dermatologic effects

CONCLUSIONS

- Many basic questions regarding E.P. still remain unsolved theand important one is how to discern an E.P. at an early stage. The incidence of E.P. has dramatically increased during the last two decades and now it has a character of a pandemic. It still remains one of the greatest problems connected with female health.
- Existing tests for early pregnancy diagnosis can not distinguish between intrauterine and ectopic pregnancies. Creation and introduction in clinical practice of a specific test for early diagnosis E.P. will radically improve the management
- Another hopeful development is the further wider use of laparoscopy worldwide in the treatment of E.P. and improvement of laparoscopic surgery techniques, which will decrease morbidity and mortality and preserve fertility .
- Medical treatment will also be more widely used in the management certain groups of patients with E.P. Newer therapeutic agents, more effective than methotrexate and with less side effects may be introduced into clinical practice.
- The current literature shows that scientific thoughts moves in these directions.

Effect of micronutrients on pregnancy outcomes

Rita Kabra Tutor: Dr Metin Gulmezoglu

Micronutrients and pregnancy outcomes

Micronutrient deficiencies associated with adverse pregnancy outcomes

Iron Folic Acid Iodine Calcium Vitamin D Vitamin K anaemia, haemorrhage neural tube defects cretinism hypertension, pre-eclampsia neonatal hypocalcaemia haemorrhage

Micronutrients and pregnancy outcomes

Micronutrient deficiencies associated with adverse pregnancy outcomes

Zinc

Copper Selenium

Magnesium

anaemia, neural tube defects, low birth weight, anencephaly anaemia, anencephaly, low birth weight neural tube defect, dysfunction of brain, and cardiovascular system, abortion. increased blood coagulability, toxaemia preterm birth.

Micronutrients and pregnancy outcomes

Review of Evidence

Zinc

Copper

Selenium

Magnesium

300 enzymes, nucleoprotein, DNA and protein synthesis,cell division Cu-proenzymes,Cytochrome-coxidase,angiogenesis,connective tissue synthesis antioxidant, co-factor for enzyme glutathione peroxidase, prevents free radical formation, DNA changes anticonvulsant
Selection criteria Reviews Individual studies Outcomes: maternal and fetal Search strategy Medline, The Cochrane Library Key words: micronutrients, zinc, copper, selenium, magnesium, zinc levels, pregnancy outcome, birth weight, IUGR

Zinc and pregnancy outcomes

Twenty studies

Serum zinc levels

- Fall in 13 studies
- No change in 6 studies
- Rise in one study

Levels in pregnant women - 7-10 mol/l

Birth weight

- Positive correlation in 4 studies
- Negative correlation in 1 study
- No correlation in 7 studies

18 prospective / 2 retrospective

Zinc and pregnancy outcomes

Intra-uterine growth retardation

- Positive correlation in 2 studies
- No correlation in 4 studies
- Pre-term babies
 - Positive correlation in 2 studies

Congenital abnormalities

- Positive correlation in 1 study
- Positive correlation only with extreme deficiency in 1 study
- No correlation in 2 studies

Infection, atonic uterine bleeding, inefficient labour

Positive correlation in 1 study

Copper and pregnancy outcomes Six studies - All Prospective *Rise in serum copper during pregnancy in all studies.*

- Normal range varies 110 to 210 micro gm/dl
- Peak value 220-300 micro gm/dl
- Pattern of rise First/Second trimester
- Postpartum levels 2 / 4 / 8-12 weeks.

No correlation between maternal and fetal copper levels No correlation with abortion, weight, preterm delivery or other adverse pregnancy outcomes. Inverse relationship with birth weight

Selenium and pregnancy outcome

Four studies - prospective Fall in serum selenium during pregnancy Levels in pregnancy - 35-70 ng/ml Neural tube defects in one study First trimester miscarriage in one study Preterm delivery in one study Retinopathy and respiratory distress syndrome in one study



Magnesium and pregnancy outcome Three studies - prospective

Fall in serum magnesium in pregnancy in one study No changes during pregnancy in one study Levels in pregnant women - 1.55-4.92mg/dl Inverse correlation with birth weight in one study Intra uterine growth retardation in one study



Limitations of studies

Pregnancy outcomes

Physiology of micronutrients

Maternal micronutrient status



Limitations of studies

Pregnancy outcomes

- Not clearly defined
- Fetus intra uterine growth retardation, small for gestational age, low birth weight, preterm birth
- Maternal preterm delivery, ineffective labour, atonic uterine bleeding

Limitations of studies

Physiology of micronutrients discrepancies across studies normal range peak values pattern of rise/fall



Maternal micronutrient status Materials for assessment

Serum	8	studies
Plasma	7	studies
Hair	4	studies
Amniotic fluid/ Leucocytes	3	studies
Umbilical cord blood	2	studies
Muscle/ Erythrocytes	1	study
Dietary intake	1	study

Time of assessment during pregnancy

First trimeseter	4 studies
Second trimester	1 studies
Third trimester	3 studies
Birth-maternal/cord blood	6 studies

Frequency of assessment

Serial (>2) - 7 once or twice *riable and wide*

Range of normal was variable and wide



Conclusions

Insufficient evidence exists to support micronutrient deficiency during pregnancy

Insufficient evidence exists to associate micronutrient deficiency with adverse pregnancy outcomes

There is insufficient research on the physiology of micronutrients

Need for rigorous scientific research to assess maternal micrnutrient status and it's correlation with pregnancy outcomes

Need to identify the normal range of micronutrients during pregnancy

Need for standardised tests to assess maternal micronutrient status

FEMALE GENITAL MUTILATION

Mohamed Ahmed A/Gadir El imam

SUDAN

Tutor

Diaa El –Mowafi,MD.

who collaborating centre Department of obstetrics and gynaecology University of GenEva UNDP/UNFPA/WHO/ WORLD BANK DEPARTMENT OF REPRODUCTIVE HEALTH AND RESEARCH

ABSTRACT

This review aims to throw some light on the practice of female genital mutilation: history, definition, prevalence, justifications and complications.

Female genital mutilation is defined by WHO as all procedures involving partial or total removal of the external female genitalia or other injury to the female genital organs whether for cultural or other non therapeutic reasons.

The practice dates back to the 5th century BC. It is prevalent mainly in Africa (28 countries) with a prevalence rate between 5% to 98%. It is also practised in Asia. In western countries it is practised by the immigrants mainly .The estimated number world wide is more than 120 million women circumcised and there are 2 million of girls at risk every year. The justifications vary from custom and tradition and beliefs to religious reasons. The practice is usually performed at home by an old women with primitive and crude tools. Home made poultices are used to promote healing. The age group is between 5 to 9years.

WHO classified the mutilation in to 4 types :

- Type 1: Excision of the prepuce with or with out excision of part or all of the clitoris
- Type 2: Excision of the clitoris with partial or total excision of the labia minora
- Type 3: Excision of a part or all the external genitalia and stitching and or narrowing of the vaginal opening
- Type 4: Unclassified. Depending on the type, the mutilation may be followed by many ill health complications. These could be physical, social, psychological and psychosexual and financial .

A lot of efforts are needed to eliminate this practice.

OBJECTIVES:

The objectives of this review are :

1. to provide a historical background of the practice of female genital mutilation (FGM).

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2. Identify the justifications for its continuation

3. Describe the procedure and its consequences

4. Draw the attention of those who are concerned e.g. society leaders, non

governmental organizations and female unions to participate energetically in order to eliminate this practice.

METHODS:

Review of the literature through the Medline with search for the words female genital mutilation (FGM), female circumcision (F/C). The articles identified in this search and special articles, reports and review articles were selected.

INTRODUCTION

DEFINITION:

Female genital mutilation (FGM) is defined by the World Health Organization as comprising all procedures involving partial or total removal of the external female genitalia or other injury to the female genital organs whether for cultural or other non therapeutic reasons. The procedures are irreversible and their effects last a lifetime (WHO)(1).

The practice is known by many names e.g.: female genital cutting, female circumcision, clitoridectomy and infibulation (2).

HISTORICAL BACKGROUND:

There have been various reports on female circumcision through out history. The first historical reference to it can be found in the writing of Herodotus, who reported its existence in ancient Egypt in the 5th century BC. He held the opinion that the custom had originated in Ethiopia or Egypt, as it was being performed by Ethiopians as well as Phoenicians and Hittites. A Greek papyrus in the British Museum dated 163 BC mentions circumcision performed on girls at the age when they receive their dowries. Various authors have shown that female circumcision was practised as well by early Romans and Arabs. In some groups it has been a mark of distinction, in others a mark of enslavement and subjugation (3,4).

PREVALENCE:

Female circumcision is a deeply rooted traditional practice that adversely affects the health of girls and women. At present, it is estimated that over 120 million girls and women have undergone some form of genital mutilation and that 2 million girls per year are at risk. Most of the girls and women affected live in 28 African countries where the prevalence of female genital mutilation is estimated to range from 5 % to 98 % (5). Apart from Africa, female circumcision is known to be practised in other countries in the Middle East as well. Concern has recently been expressed that female genital mutilation is also being practised in USA, Europe and other western countries by immigrants from these societies (4).

WHY ?:

Female genital mutilation is a painful and dangerous practice (2). It is a dramatic example of how gender can affect health (6). There are many gaps in knowledge concerning female genital mutilation. In many countries, the underlying sociocultural, gender and economic factors that predict and influence the practice and the morbidity by type of female genital mutilation are not equally documented. All societies have norms of care and behaviour

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based on age, life stage, gender and social class. These norms, often called traditional practices, may be beneficial or harmless but sometimes may be harmful (1). The anthropologic, cultural and social rationale of this custom is complex and case specific. Attitudes regarding a women's role in the society have a strong impact on the acceptance and perpetration of this practice (7).

The reasons for practising circumcision vary in different areas are associated with perception of religious health moral and social acceptability. There are beliefs that FGM increases a girl's chance of marriage, protects her virginity, discourages promiscuity, improves fertility or prevents stillbirth! (8). Other reasons include a strong desire to continue ethnic tradition, altered sexual urge for women, increases sexual performance for men, protection of baby's health and gender reproductive and aesthetic considerations (9). In a study done by Dirie and Lindmark (1991) (10), it was found that most of the investigated women justified the practice with religious reasons (10).

WHEN, WHERE, HOW AND WHO:

The time of performing the circumcision varies a lot. It can be performed during the neonatal period as early as when the girl is just 7 days old, or delayed when she is at the age of 10 years, or sometimes even later during adult life. But it is mostly performed at the age between 5 to 9 years (11,12,13,14).

The operation is usually performed by a non medical practitioner in the home or other non clinical setting (15). The conditions are usually non sanitary. A midwife (most commonly; rarely a barber) uses unclean sharp instruments such as razor blades, scissors, kitchen knives, a piece of glass or even her teeth. These instruments are usually used in succession and are rarely cleaned causing transmission of a variety of viruses such as HIV and other infections (14,15,16) 17).

THE OPERATION AND ITS SEQULAE :

The mutilation varies from simple removal of the prepuce to excision of the whole female external genitalia and closure of the vagina leaving a small whole for the passage of urine and menstrual flow. As a result the morbidity could be categorised in broad terms into medical, social, psychological, psychosexual and financial.

RESULTS:

CLASSIFICATIONS:

WHO classified female genital mutilation in to four types:

- 1. Type 1: Excision of the prepuce, with or with out excision of part or all of the clitoris
- 2. Type two: Excision of the clitoris with partial or total excision of the labia minora .
- 3. Type three: Excision of part or all of the external genitalia and stitching and or narrowing of the vaginal opening (infibulation).
- 4. Type four: Unclassified :
- Including pricking, piercing or incising of the clitoris and or the labia,
- Stretching of the clitoris and or the labia,
- Cauterisation by burning of the clitoris and surrounding tissue,
- Scraping of the tissue surrounding the vaginal orifice or cutting of the vagina,
- Introduction of corrosive substances or herbs in to the vagina to cause bleeding or for the purpose of tightening or narrowing it,
- And any other procedure that falls under the definition of female genital mutilation as defined earlier (1).

COMPLICATIONS (14, 15, 20-42)

1. MEDICAL COMPLICATIONS :

A. Immediate :

- 1. Injury to adjacent tissue e.g. urethra, vagina, perineum and rectum.
- 2. Fracture of the clavicle, femur or humerous, or dislocation of the hip joint.
- 3. Failure to heal.
- 4. Pain.
- 5. Haemorrhage.
- 6. Shock .
- 7. Infection: bacterial, viruses e.g. HIV
- 8. Death.
- B. Late :
- 1.Chronic back pain.
- 2. Anaemia.
- 3. Decreased growth.
- 4. Disability.
- 2 Gynaecological complications:
- A. Early :
- 1. Labial adhesion.
- 2. Labial occlusion.
- 3. Vulval abscess.
- B. Late :
- 1. Inclusion cyst.
- 2. Chronic infection
- 3. Haematocolpos.
- 4. Chron pelvic inflammatory disease.
- 5. Keloid scar.

Female genital mutilation - M.A. El Imam 6. Dysmenorrhoea.

- 7. Vaginal stenosis.
- 8. Dysparunia.
- 9. Clitorial neuroma.
- 10. Aparunia.
- 11. Infertility.
- 12. Calculus formation in the vagina.
- 13. Development of a false vagina.
- 14. Difficulty in gynaecological examination.
- 15. Need to surgery to facilitate intercourse.

3. OBSTETRICAL COMPLICATIONS :

- 1. High maternal mortality rate (MMR).
- 2. Prolonged labour.
- 3. Obstructed labour.
- 4. Tears to the vagina and the perineum.
- 5. Double episiotomy.
- 6. Puerperal infection.
- 7. Postpartum haemorrhage.
- 8. Unnecessary caesarean section.
- 9. Increased fœtal loss

4. URINARY COMPLICATIONS :

- A. Early :
- 1. Acute urine retention.
- 2. Urinary tract infection.
- 3.Weak urine stream .
- 4. Dripling of urine.

B. Late :

- 1. Long term difficulty in passing urine.
- 2. Chronic urinary tract infection.

- 3. Stone formation.
- 4. Damage to kidneys .
- 5. Vesicovaginal fistula.
- 6. Rectovaginal fistula.

5. SOCIAL, PSYCHOLOGICAL, PSYCHOSEXUAL AND EDUCATIONAL :

- 1. Shame
- 2. (Sexual scars) from pain and fear lead to marital problems
- 3. Anxiety and depression .
- 4. Sexual dysfunction.
- 5. Increased drop out from school .

6. FINANCIAL:

Long period of occupancy of hospital beds

ESTIMATED PREVALE OF (FGM) IN AFRICA .Table(1) (18)

COUNTRY	ESTIMATED PREVALENCE %	NUMBER OF WOMEN (000S)
BENIN	50	1,370
BURKINA FASO	70	3,650
CAMEROON	20	1,330
CENTRAL AFRICA REPUBLIC		
	43	740
CHAD	60	I,930
COTE DEIVORE	43	3,020
DJIBOUTI	98	290
EGYPT	80	24,710
ERITREA	90	1,600
ETHIOPIA	85	23,420
GAMBIA	80	450
GHANA	30	2,640
GUINEA	50	1,670
GUINEA BISSAU	50	270
KENYA	50	7,050
LIBERIA	60	900
MALI	75	4,II0
MAURITANIA	25	290
NIGER	20	930

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NEGERIA	50	28,170
SENEGAL	20	830
SIERA LEONE	90	2,070
SOMALIA	98	4,580
SUDAN	89	12,450
TOGO	50	1,050
UGANDA	5	540
UNITED REPUBLIC OF TANZANIA	10	1,500
ZAIRE	5	1,110
TOTAL		132,490

COUNTRIES IN THE MIDDLE EAST AND ASIA (19)

Bahrain

Yemen

Oman

United Arab Emirates

Indonesia

Malaysia

OTHER CONTINENTS	AND COUNTRIES (IMMIGRANTS MAINLY)	(1,4)
		· · · · ·

Europe

Canada

Australia

USA

JUSTIFICATIONS FOR PRACTICING FEMALE GENITAL MUTILATION

1	Tradition
2	Personal hygiene
3	Discourage promiscuity
4	Preservation of virginity
5	Increases a girl's chance of marriage
6	Improves fertility
7	Prevents still birth .
8	Increases sexual performance for man



Table(2) Immediate complications. Adopted from El Dareer(30)

bleedir	ngshock	swelling	fever	Wound	Difficulty	Urine	total	Νο
				infection	in	retention		complication
					passing urine			•
168	31	51	133	151	172	84	790	2375
(21.2%)	3.9%)	(6.4%)	(16.8%)	(19.1%)	(21.7%)	(10.6%)		

Table(2): The number of immediate complications is 790 (23%) from all types of the circumcision. Bleeding, difficulty in passing urine and wound infection headed the list of complications.

Table(3) Delayed complications. Adopted from ElDareer (30).

Painful	Vulval	Recurrent	Chronic	Difficult	Pain	Difficulty in	Inclusion		No
scar	abscess	UTI	pelvic	penetration	during	menses	cyst	total	complication
or			infection		intercourse			ισιαι	
keloid									

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11	143	283	241	231	56	39	19	10232185
(1.07%)	(13.9%)	(27.6%)	(23.5%)	(22.5%)	(5.4%)	(3.8%)	(1.8%)	

Table (3): The total number of delayed complications is 1023 (32%). Recurrent urinary tract infection, chronic pelvic infection and difficult penetration are the most common complications encountered.

 Table (4). Complications in (41) children. Adopted from Egwautu and Agugua(35)

		Urinary	tetanus	Labial	Urine	Rectovaginal fistula	Dermoid	Interoital
Haemorrahge	septicaemia	tract		fusion	retention		cyst	swelling
		infection						
2	1	2	1	21	12	1	9	2
(4.8%)	(2.3%)	(4.8%)	(2.3%)	(51.2%)	(29.2%)	(2.3%)	(21.9%)	(4.8%)

Table (4):Labial fusion, urine retention and dermoid cyst are the commonest complications. Serious complications like septicaemia and rectovaginal fistula are encountered in this series.

Table(5). Presenting complications and clinical findings in (15) adults . Adopted from Egwautu and Agugua (35)

Dyspareunia + in adequate penetration	infertility	Vulval lump	Poor urine stream	Complete Iabial fusion	Implantation dermoid	Prolong Iabour	Partial vulval stenosis	Total
9	6	4	2	1	4	2	10	15
(60%)	(40%)	(26.7%)	(13.3%)	(6.7%)	(26.7%)	(13.3%)	(66.6%)	

Table (5): Presenting complications and clinical findings in (15) adults. Partial vulval stenosis, dyspareunia and infertility are the commonest complications.

Table (6). Genital tract infections. Adopted from De Silva(24)

	Circumcia	sed	Uncircumcised			
	108	3	398			
Candida albicans	28	25.9%	16	4%		
Mixed Infection	12	11.1%	25	6.3%		

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Table (6): shows that the incidence of candida albicans was the most common in the circumcised group, this was highly significant compared to the control group. Mixed infection occurred significantly more often in the study population as opposed to the controls.

Table(7). Urinary tract infections. Adopted from De Silva (24)

	Circumcised (135)		Uncircumcised (1691)	
E.COLI	No 35	% 22.9	No 78	% 4.8
Mixed infection	12	7.8	23	1.4

Table(7): E.coli occurred in (22.9%) of the circumcised and (4.6%) of the controls. This difference was highly significant. The occurrence of mixed growth was highly significant in the circumcised group compared to the controls.

Table(8). Complications in 118 females. Adopted from Dirie and Lindmark (36) Lindmark (3)

dermoid		Abso	ess	Vag ster	inal Iosis	Total
65	(55%)	10	9%	43	36%	118

Table (8): Shows the distribution of dermoid cyst ,vulval abscess and vaginal stenosis in 118 females admitted to the gynaecological ward. Dermoid cyst and vaginal stenosis headed the list. These patients occupied the beds for a period of 1967 days.

Table(9) : The performance of circumcised females during labour. Adopted from De Silva (24)

Labour	Circume	ised 167	Uncircumcised 1990		
Prolong 2nd stage	No 23	% 13.8	No 86	% 4.3	
Pim > 90 min					
Mul > 60 min PpH> 500 ml	9	5.4	31	1.6	

Table (9): These findings show that the second stage of labour in both primigravidae and multigravidae is prolonged significantly. Also the occurrence of postpartum haemorrhage is significant.

 Table (10) The performance of episiotomy. Adopted from De Silva (24)

	No of patient	episi	otomy	otomy Urethral te	
		No	%	No	%
Primigravidae circumcised	43	43	100	2	6.4
Primigravidae not circumcised	361	325	90	1	0.23
Multigravidae circumcised	124	49	39.5	4	3.2
Multigravidae not circumcised	1533	557	36.3	0	0

Table (10): This table shows the performance of episiotomy in (43) circumcised primigravidae females. The difference is found to be significant. Also the occurrence of urethral tears in both primigravidae and multigravidae shows a significant difference.

Table (11) Apgar score. Adopted from De Silva (24)

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Apgar score	Circumcised 167		Uncircumcised 1990	
<	9	5.4	48	2.4
-5 min				
6-10	158	94.6	1942	97.6

Table (11): Shows the immediate performance of new born babies born to 167 circumcised females. Apgar scores show a significant difference at 5 minutes.

DISCUSSION

Female genital mutilation has been called the three feminine sorrows, for it brings pain and sorrow when the women is mutilated, when she is wed and she gives birth (38). It has deep roots in the history and represents social, psychological and health problems with short and long term morbidity. It constitutes a challenge to the civilised societies in order to eliminate its practices. The circumcision has a particular strong cultural meaning because it is closely linked to the woman's sexuality and their reproductive role in life (39).

Historically it exists and has been practised since the 5th century BC. Table 1 shows the prevalence of FGM. It is apparent that Africa has a high prevalence rate. It is practised in 28 African countries. The prevalence rate estimated in some of these countries is low (5% in Zaire and Uganda) and is very high others, like Somalia and Djibouti (98%), Sierra Leone and Eritrea (90%), Sudan (89%), Gambia and Egypt (80%). The total number of women who are already mutilated is estimated to be more than 120 million and there are about 2 million of girls who are at risk yearly. This is a tremendous figure that necessitates a lot of efforts at all levels to abolish this practice. The prevalence rate is less in Asia. In the western countries, FG M is practised mainly by the immigrants. This practice puts these females at greater health risks and puts the health professionals at a real challenge, because health professionals there are not aware of the circumcision. This needs understanding of its important aspects including management of complications, cultural attitudes and sensitivities (42).

The reasons behind its existence still present are many. Some of these reasons do not sound logic when put to a real test. With regard to the pleasure for either the husband or the women, Hanny Lightfoot-Klein (1989) (44) conducted an extensive research in Sudan over a period of 5 years and interviewed 300 Sudanese women and 100 Sudanese men on the sexual experience of circumcised and infibulated women. She found that sexual desire and pleasure and orgasm are experienced by the majority of women who have been subjected to this extreme sexual mutilation. These findings, though seriously question the importance of the clitoris as an organ that must be stimulated in order to produce female orgasm, but can not justify mutilation because the orgasm is experienced by females who are not circumcised as well.

As for the religion and the study conducted by Derie and Lindmark (1991) (10), who found that the majority of their study group (290 Somalian women) justified the mutilation with religious reasons, this is in contradistinction to the study conducted by Myer's et al in Nigeria (1985) (9) and Sayed et al in Egypt (1996) (14). Both showed that tradition and custom headed all other reasons. This is besides the study of De Silva in Saudi Arabia (1989) (24), who found that those who are mutilated are outsiders, mainly Sudanese, and none of them is a Saudi Arabia female. It is known that Saudi Arabia is one of the biggest and influential Islamic countries. It is the place where Prophet Mohamed started his Mission. In Islam in particular there has been a lot of debates and opinions about this issue. Historically, it is well known that FGM predated both Islam and Christianity, so it is hardly difficult to accept that the mutilation is of a definite religious origin and that any religion encourages the practice.

Thus it is obvious that people practice the circumcision for custom and tradition reasons. Probably because tradition and beliefs have very strong deep roots in the cultural and social life of people. It is noticed that people occasionally believe in tradition more than religion itself because of illiteracy.

Various studies showed that the target group are the young girls (commonly below 10 years), but it is also clear that a new born girl in the first week of her life may be circumcised (11). These young girls are not mature yet so as to decide for themselves. If they escape the circumcision till adulthood, It may be unlikely that any of them would accept any sort of mutilation. The fact that some were circumcised when they are adults (13), throws strong lights again on the deep impact of the tradition on the practice of the mutilation. Sterilised equipments are rarely used. In one study conducted by Sayed et al in Egypt, medical instruments were used in only 0.7% (14). This factor, besides the non use of anaesthesia and antibiotics may lead to numerous ill health problems.

Besides WHO Classification for FGM, Nahid toubia (1994(39) described the mutilation into two broad categories and each category is divided in to two types. This classification is not accurate because it missed the severe forms of mutilation in which every part of the vulva is removed including the labia majora and leaving only a small pin hole opening for the passage of urine and the menstrual flow.

The classification is often simplified in to 3 types (30):

Type 1: Sunna circumcision.

Type 2: intermediate type

Type 3: pharoanic circumcision

This classification is not very descriptive. More than that, the word Sunna links the circumcision with the religion and gives a wrong understanding that the religion is in favour or encourages the practice.

The complications of the FGM are classified broadly into medical, social, psychological and psychosexual. Some of them have early and or late sequelae. According to El Dareer (1983)(10), bleeding, difficulty in passing urine and wound infection are the commonest early complications. Bleeding(14,22,23) is unavoidable. It results from the clitorial artery and other blood supply of the vulva or from sloughing after the first week. Severe bleeding may end in shock or even death (38,39). If the victim survives, anaemia is a probable result. Neurogenic shock can also result from severe pain and lead to death . Difficulty in passing urine is reported by others (20,23,35). It is due to pain and fear of passing urine on a raw wound, tissue swelling or inflammation or injury to the urethra. This may lead to urine retention and hydronephrosis. Surgical intervention may be crucial. Diejomaoh and Faal(1981)(23) reported a case complicated by hydronephrosis and was treated by suprapubic cystotomy. Wound infection (12,20) can complicate the circumcision due to various factors . The infecting organisms could be bacteria or virus like HIV. Tetanus, septicaemia and gas gangrene can result and lead to fatalities. Interestingly, Fahal and Sharfy (1998)(37) reported a rare case of vulval mycetoma which led to bladder outlet obstruction in a woman at the age of 20 years .

Labial adhesion and occlusion and dermoid cyst can occur (23,28,35,36). In Egwuatu and Agugua study(1981)(35), labial adhesion and inclusion cysts constitute a good number of their series. The cyst can reach an enormous size and get infected. One girl got tetanus which is a fatal condition. In Dirie and Linmark series (1991)(36), dermoid cysts and vulval abscess constitute 75 out of 118. In the same series of Egwuatu and Agugua (1981)(35), one girl developed a rectovaginal fistula and colostomy was performed. Such accidents to the adjacent structures to the vulva like the urethra, the vagina, the rectum and the perineum are likely to occur since the girl struggles during the circumcision because of the non use of the anaesthesia, and because of the pressure exerted by the females holding her, the clavicle and humerus bones are likely to be fractured. Dislocation to the hip joint could happen.

Many authors reported late complications (24,30,32,33,41). In El Dareer study (1983)(30), recurrent urinary tract infection, chronic pelvic inflammatory disease and difficult penetration during sexual intercourse are the commonest morbidities. The circumcision seems to lead to stagnation of urine which is an aetiological factor in urinary tract infection . Supporting this, De Silva(1989)(24) found a significant difference in the growth of E.coli and other mixed infectious agents in the urine of circumcised compare to the uncircumcised females. She also found that genital tract infections are common and a significant difference in the growth of monilial and other mixed infections was demonstrated. Chronic pelvic infection can lead to tubal blockage and infertility. Difficult penetration results from the pine hole opening of the introitus that is left for the passage of urine and menstrual flow.

Other complications like clitorial neuroma and dysmenorrhoea can complicate the circumcisions. Clitorial neuroma results from cutting and entrapment of the dorsal clitorial neuroma results from partial or complete occlusion of the vaginal opening. Rare cases of haematocolpos result from complete coalescence of the labia.

In obstetrics the circumcision causes many morbidities. Generally, it is associated with a high mortality rate (34). The prolongation of the second stage of labour, the performance of episiotomy, the occurrence of postpartum haemorrhage and urethral tear injuries, all showed a significant difference in the circumcised compared to the uncircumcised females(24). Some of these findings are supported by other authors (21,26). McSwiney and Saunders (1992)(21) reported a case of postpartum haemorrhage which lost 6 litres of blood from the tears. Berardi et al (1985)(26) found that the incidence of perineal tears are more in the circumcised females. These injuries result directly from the performance of episiotomy which is done to facilitate the delivery of the baby. Deinfibulaton (called decircumcision or anterior episiotomy) is mandatory at the time when the baby's head crowns. Its performance at that critical time can contribute to the injury of the urethra and or the vagina. Puerperal infection can result from these injuries. Ausen (1977)(42) reported maternal death of a women and her newborn from septicaemia that resulted from the circumcision which was performed to the mother one day prior to her presentation to the obstetric casualty in labour .

The low Apgar score at 5 minutes in the new born of the circumcised females (24) could be explained by the prolongation of the second stage of labour. This can be avoidable by timely deinfibulation, though , this can carry some risks of injuries to other organs as stated earlier .

Because of the above mentioned gynaecological complications e.g. difficult penetration or even in inability to practice intercourse at all, it is frequently noticed that many couples fail to achieve pregnancy for many years after marriage because of the very tight circumcision. Pregnancy is achievable once deinfibulation is performed. These complications can lead to many psychosexual and social problems. Sexual dysfunction can happen to both partners. Divorce may be the ultimate end .

Financially, all these complications of circumcision may have a lot of impact on the resources available. In the study of Dirie and Lindmark (1991) (36), 118 females were admitted to the gynaecological ward with diseases related to FGM (dermoid cyst, vulval abscess and vaginal stenosis). These females occupied the beds of the hospital for a period of 1967 days. This will definitely pose a significant constraint to the hospital resources.

CONCLUSION:

Female genital mutilation exists since the 5th century BC. It is prevalent in Africa where it is practised in 28 countries. The prevalence rate there is between 5% to 98%. In the world the estimated number of females who had undergone the mutilation is more than 120 million. There are 2 million girls at risk of the mutilation every year. The justifications for its practice are diverse. It is classified by WHO into 4 types. Depending on its severity, the practice has many ill health complications. These could be physical, social and psychological. A lot of efforts are needed to eliminate its practices.

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27.11.02

GENETIC ANALYSES IN THE INFERTILE COUPLE

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ABSTRACT

In the recent past, cytogenetic and molecular genetic methods have led to an enormous increase in knowledge of genetic information concerning infertility. Therefore, new starting points concerning the origin of this problem arise. Genetic analysis can be carried out on the following four established levels:

- phenotype level
- biochemical level
- chromosomal level
- molecular genetic level.

Genetic analysis in the infertile couple is used to test whether there is a significant genetic influence in the aetiology of the disease and to identify the mode of inheritance of these disorders. The main methods (parental karyotype, amniocentesis, chorionic villus sampling, fetal blood sampling for testing the karyotype of the fetus or for molecular genetics procedures) are discussed with their indications.

Genetic programs to detect individuals at risk, genetic counselling and prenatal diagnosis are some of the current applications of new genetic knowledge to medical practice.

Practicians must open their mind to these new possibilities and methods, knowing the increased possibility to predict the risk to develop a disease for descendants in certain couples and to diagnose it prenatal.

The diagnostic progress raises new ethical problems. The answers will have to be given by society as a whole. A protocol for workup of the infertile couple (implying genetic aspects) is suggested.

Key words:genetic analysis, infertile couple, karyotype, molecular genetics, prenatal diagnosis, genetic counselling.

INTRODUCTION

Human conception and pregnancy is both a vulnerable and a robust process. Vulnerable in that a remarkably large proportion of all pregnancies are chromosomally abnormal with the great majority of these aborting, robust in that more than 99% of time a term pregnancy results in a chromosomally normal baby [1].

The recognition of the role of genetic factors in the causation of human disease has made clinical genetics one of the most rapidly developing fields in medicine. With the marked reduction in nutritional and infectious diseases in the developed countries there has been an increasing awareness of the role of genetic determinants of human diseases. Much of this progress has been propelled by recent advances in the area of molecular genetics which in turn have been applied directly to a better understanding of the pathogenesis of disease and to improve diagnosis and management of patients [2].

Appropriately major contribution of these new developments in genetics has been in the area of prevention and/or avoidance of disease, the aspect of medicine that must become the focus of modern medicine. Genetic screening programs to detect individuals at risk and genetic counselling and prenatal diagnosis are some of these current applications of new genetic knowledge to medical practice[3].

°Causes of genetic disorders:

Genetically determined diseases are classified into three major categories:

-chromosomal: these diseases are the result of the addition or deletion of entire chromosomes or parts of chromosomes; most major chromosomal disorders are characterised by growth retardation, mental retardation and a variety of somatic abnormalities; the loss of whole chromosomes other than the sex chromosomes is generally incompatible with survival and such abnormalities are a major cause of spontaneous abortions or miscarriages; major chromosomal anomalies are found in almost half of spontaneous abortions and a quarter of conceptions may suffer from major chromosome problems [4].

- single gene defects: are due to single mutant gene with a large effect on the patient`s health; single gene disorders are inherited in a simple mendelian fashion(autosomal dominant, autosomal recessive, x-linked);ex: sickle cell anaemia, cystic fibrosis, haemophilia [4].

- polygenic diseases (multifactorial = predisposition + environment):result from the interaction of multiples genes, each of which may have a relatively minor effect; conceptually this group of diseases poses the challenge of sorting out the ways in which the additive or interactive effects of multiple genes create the predisposition for disease; ex: congenital heart diseases, cleft lip, cleft palate, diabetes, hypertension [4].

Formal genetic analysis of diseases are used to test whether there is a significant genetic influence in the aetiology of disease and to identify both the modes of inheritance of any responsible genes and their locations in the human genome. A genetic analysis usually involves two steps: first, different genetic hypotheses are proposed; second, the hypotheses are tested and are accepted or rejected by statistical criteria until one is identified that fits the data and cannot be rejected and that can make successful predictions relevant for disease

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Genetic disorders can produce:

- occult abortion
- miscarriage/multiple miscarriages
- hydatiform mole
- infant death
- congenital malformations
- mental retardation
- male and female infertility [5].

°Infertility

World-wide, between 2%.-7% of couples trying to have a child fail to conceive, the two partners in the relationship appearing to make an equal contribution [6].A special program of research found that the three largest categories of problems in men were varicocele(12.6%),accessory gland infection(6.9%),abnormal sperm analysis(80.5%)most commonly idiopathic [6].Owing to extensive screening of patients in attendance at infertility clinics, at both the chromosomal and DNA levels, it has become clear that a gene defect or chromosome anomaly can underlie impaired spermatogenesis leading to oligo-or azoospermia in men [7].A whole range of karyotypic anomalies are known to be associated with disturbance of spermatogenesis. Gametogenesis in men appears more sensitive to disturbance by genetic and chromosomal anomaly than does oogenesis in women. Nevertheless, oogenesis in female carriers of numeric or structural chromosomal anomalies can be impaired to a greater or lesser degree, giving rise to reductions in oocyte numbers [8].

The men can be karyotyped using peripheral blood lymphocytes and 2,2% showed a chromosome abnormality [4]. The phenomenon of spermatogenic impairment through chromosome anomaly has been described as chromosomally derived sterility, knowing that the control of spermatogenesis is dependent on the normal arrangement of the genome. Female carriers of chromosomal anomalies may be at risk for shortened reproductive span, leading to reductions in the oocyte pool [9].

OBJECTIVES

- 1. To asses the importance of genetic analysis in infertility and to stress the contribution of disturbed genetic information system to the development of diseases.
- 2. To establish when genetic analysis is indicated in an infertile couple and what are the current genetic possibilities in order to improve clinical practice (by determining the origin of the infertility and the syndromic causes).
- 3. To reveal the possibility of prediction of risk for recurrence of a large number of genetic disorders.

4. To show how inherited disorders become subject of prenatal detection.

METHODS

Two aspects of genetic evaluation are involved:

- 1. prior to pregnancy (for parents)
- 2. during pregnancy (for fetus)

The initial evaluation of an infertile couple must begin with a complete history and physical examination. A sexual history should be obtained and the couple instructed as to the optimum time for intercourse.

Collecting genetic information is the first and most important step in genetic analysis and is best achieved by drawing up a family tree or pedigree [10].

Family tree:

- enquires specifically about infant deaths, stillbirths and abortions
- consanguinity should be directly, but tactfully asked about and may be the clue that suggests autosomal recessive inheritance
- mistaken or unacknowledged paternity must be kept in mind, but definitive tests of paternity based on DNA can help to resolve these questions more easily
- take at least basic details about both sides of the family, even in a dominantly inherited disorder clearly originating from one side
- record names of women: this is significant for X-linked disorders, where the surname of affected members is likely to change with each generation [10].

Chromosomes analysis: peripheral blood, bone marrow, amniotic fluid and products of conception can be used [11].

Looking at chromosomes at a magnification of about 1000x, involves the following steps:

- tissue culture
- addition of a mitotic inhibitor(usually colchicine to stop in mitosis)
- harvest cells hypotonic solution
- fixative solution
- staining treatment(most common is G-banding with trypsin)
- interpretation(karyotyping)

Typically 15-20 cells are scanned and counted with at least 5 cells being full analysed and 2 cells karyotyped(to compare band for band with it`s homologue).

It is necessary to examine this many cells in order to detect clinically significant mosaicism.

Molecular genetics(looking at genes)involves:

- extraction of DNA
- denaturation and cutting with enzymes
- PCR amplification(for some analysis)
- hybridisation with probe(radioactive)
- gel electrophoresis
- developing(film radioactive)

Genetic analyses are very expensive procedures in order to establish a cost effective program for screening carriers of a genetic disease, several criterias should be met:

- 1. the disease is severe enough to warrant such a screening program
- 2. a high risk population can be identified in which to focus screening efforts
- 3. definitive tests are available for specific diagnosis in individuals identified as being at high risk
- 4. reproductive options are available to couples found to be at risk [12].

Once pregnancy is established, the genetic techniques mentioned before are similar, but the difference is how the samples can be obtained.

The main indications for prenatal cytogenetic diagnosis are:

- increased age of mother,
- parental heterozygoty for a chromosome re-arrangement, the birth of a previous child with a chromosome defect,
- abnormal maternal blood chemistry indicating risk for aneuploidy
- IUGR and/or fetal malformation detected on ultrasonography.
- couples who have experienced two or more pregnancy losses, spontaneous abortions, stillbirths, neonatal deaths)
- couples who are concerned about having an abnormal baby [1].

°Chorionic villus sampling(CVS)

The usual time for CVS procedure is at 10 to 11 weeks. CVS may be the procedure of choice for

couples with a medium to high genetic risk(>5%),particularly if DNA analysis is involved. The main disadvantages are a slightly higher risk to cause a miscarriage than with amniocentesis(1% compared to 0.5% over the background rate and a higher likelihood of equivocal diagnostic results.

Trophoblast cells are the source of the population studied at direct and short-term CVS culture.

°Early amniocentesis

Early amniocentesis(10-13 weeks) was introduced as an alternative to CVS [1].

°Standard amniocentesis

Transabdominal amniocentesis done at about 16 weeks of gestation has been the standard cytogenetic prenatal diagnostic procedure for over a quarter of a century. It has a very high degree of safety to both mother and infant; maternal complications or fetal injury due to direct trauma are practically unknown. The obvious disadvantage of 16 weeks amniocentesis is that the results are not at hand until 18 weeks [8]. If a result cannot be available by 20 weeks, another procedure (fetal blood sampling, placental biopsy) may be worth considering [1].

°Fetal blood sampling

Fetal blood is aspired by direct puncture of a blood vessel in the umbilical cord and a cytogenetic result is obtained in only a few days. Cordocentesis under ultrasound guidance is a considerable improvement. Fetal blood sampling is particularly applicable in the case of midtrimester diagnosis when structural defects have been identified at ultrasonography; it has a role in clarifying the issue of mosaicism on amniotic fluid culture [1].

°Placental biopsy

In principle this is the same as a direct culture CVS; it is usually performed in the late second or third trimester when rapid results is needed [1].

For most pregnancies, with no genetic family history usually invasive techniques are not indicated. Therefore, it is a common practice to follow these pregnancies by non- invasive techniques like:-ultrasounds
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-maternal serum screening (AFP,HCG,estriol)(which are looking for symptoms not causes)

Usually, karyotype is made by amniocentesis samples, which are better than CVS samples(less good for subtle structural changes).

DNA is better studied on CVS samples(technically easier for lab, when it exists an increased risk of genetic disease), also by amniocentesis samples(but results are late).

Prenatal diagnosis allows to convert a probability statement about the risk of a specific disease to a certainty. It does not address all possible birth defects or genetic diseases [13].

DISCUSSION

a)Chromosomal pathology

Genetic disorders make a greater or lesser contribution to human morbidity or mortality. Looking at prenatal existence, chromosomal mortality is very high and aneuploidy is the major cause of spontaneous abortion, followed by translocations. Perinatal and early infant death have a significant chromosomal component of which trisomies 18 and 21 are the major contributors. As for morbidity, chromosomal defects are the basis of a substantial fraction of all intellectual deficit and many of these retarded individuals will also have structural malformations that cause functional physical disability [14].

In table 1 we set out the birth incidence of the various categories of chromosomal abnormality. (table1)

Overall 1 in 120 liveborn babies has a chromosomal abnormality and about half of these are phenotypically abnormal due to the chromosome defect [2]. A parental chromosome rearrangement is found in fewer than 10% of couples with repeated abortions. In approximately 3.2% of such couples one or the other parent has a balanced translocation(4.8% for women and 2.4% for men) [15].

Characteristically, aneuploidy (autosomal imbalance)produce a phenotype of widespread dysmorphogenesis and there may be malformations of internal organs and limbs. It is often in the «facies» that the most specific physical abnormality is seen. The most complex organ of all, the brain, is the most vulnerable to a less than optimal constitution. Thus, the central concern of most people seeking genetic counselling for a chromosomal condition is the fear of having a physically and mentally handicapped child [15].

Sex chromosome imbalance has a much less deleterious effect on phenotype than does autosomal aneuploidy. Excess whole X-chromosomes are inactivated, abnormal X-chromosomes are selectively inactivated to leave the normal X as the active one. In X imbalance the reproductive tract and the brain are predominantly affected [16]. As for the Y chromosome excess, there is a limited phenotype consequence because this chromosome is composed largely of inactive material.

During the workup of the infertile couple, two main types of chromosomal anomalies can be found:

1)Gonosomal aneuploidy

- Klinefelter syndrome(47,XXY):men with sex chromosome complement are azoospermic with hyalinised testis; it has been suggested that a dosage effect underlies the germ cell atresia, two X chromosomes being lethal to a germ cell in a testicular environment [17].
- 47 XYY:the XYY condition can have a deleterious effect on spermatogenetic development, although the testis of others display a more histology picture; the cells with an XYY genotype can have difficulties completing spermatogenesis [18],resulting in lowered sperm production.
- Turner syndrome(45,XO): is characterised by primary amenorrhea, infantile genitalia and failure of secondary sexual development; studies on XO fetal ovaries shows severs reductions in oocyte numbers, with few oocytes progressing beyond the earliest prophase stages of meiosis [19,20].
- Triple X(47,XXX):triple X women are phenotypically unremarkable and usually fertile; most menstruate normally and many have children.

2)Structural rearrangements

Can be balanced(as in infertile couple) or unbalanced(as in foetuses from abortions), and can affect autosomal or sex-chromosomes [19,20].

° reciprocal autosomal translocations :have a correlation with low sperm count; also a number of robertsonian translocations have been reported with a range of testicular phenotypes ranging from near normal spermatogenesis to severe spermatogenetic disruption.

° X-autosome and Y-autosome translocations: reciprocal X-autosome translocations invariably cause male sterility(azoospermia);for men carrying Y-autosome reciprocal translocations there is also a risk of infertility, although histologic studies on testicular biopsies show a range of variation from near normality to severe germ-cell impairment [21,22].

It has been a tendency in the past to assume that oogenesis is unaffected by the presence of those chromosomes anomalies that cause disturbance to spermatogenesis. Fertility can be retained in female carriers of marker chromosomes, X-autosomal translocation carriers of purely autosomal rearrangements; female structural heterozygotes may be at risk for a shortened reproductive span and lower rate of oocytes [21,22].

b) Monogenic disorders

Infertility and/or hypogonadism in monogenic disorders

Infertility, hypogonadism or both may be a feature of more generalised syndromes.

° Testicular atrophy is recognised as a feature of myotonic dystrophy(autosomal dominant) [23].

° Congenital bilateral absence of ductus deferens is present in cystic fibrosis and may be the only manifestation in the CFTR gene(autosomal recessive) [24].

° Hypogonadism characterises Kallman and Noonan syndromes, as well as X-linked ichthyosis(sex-linked) [23].

c)Y-linked genes and spermatogenesis

In some cases a reduced sperm count might result from microdeletions in Y chromosome which could disrupt an important spermatogenic control region.

In 1989, a search for the AZF genes commenced in laboratories. The analysis included men from the oligo-and azoospermic categories, most of whom had small testis and raised levels of FSH in blood and whose Y chromosome appeared cytological normal. Initial screening with a DNA probe set revealed that some of this cases have microdeletions in interval 6 in which disruption or loss of the AZF gene might have occurred [25].

The main results of these genetic disorders in pregnancy can be (table 2):

- non-implantation and occult abortion (some genetic imbalances are so devastating than even the first few cell divisions are fatally compromised leaving the conceptus unable to implant)
- miscarriage/spontaneous abortion: (the great majority of chromosomal abnormal pregnancies abort at between 8 and 16 weeks of gestation; a few remain beyond this time and be lost as a later abortion, intrauterine fetal death, perinatal death)
- confined placental mosaicism (a chromosome abnormality may be present in a pregnancy but not involve the embryo/foetus trisomic placenta may be structurally and functionally leading to loss of the normal fetus. The presence of a normal cell line in the placenta, the fetes being abnormal may promote survival in some aneuploidies [26]. (table2)

PROTOCOL FOR WORKUP OF THE INFERTILE COUPLE (genetic aspects)

° In any case of infertile couple we should start by taking the family history:

- for the man: family history of a specific genetic disease----genetic analysis (karyotype, DNA)
- for the woman: positive family history of genetic disease-----genetic analysis (karyotype, DNA).

° Medical history and physical examination. We should ask specifically some key-questions for the man:

- pulmonary or digestive symptoms?-----ex: cystic fibrosis(autosomal recessive transmission)-----molecular genetics-----if positive, gene testing of wife [27].
- neuromuscular symptoms?-----ex: Steinert myotonic dystrophy (autosomal dominant transmission)-----molecular genetics

For the woman we should have the medical history and perform a physical and genital examination:

- unusual stature for the family: suggests an aneuploidy (triple X, Turner syndrome)-----genetic analysis (karyotype)
- hypogonadism (especially hypergonadotropic)that suggests a gonadal dysgenesis-----genetic analysis (karyotype)
- repeated miscarriages -----genetic analysis (karyotype)

People who have had one or two miscarriages must be advised by their physician to come to a genetic clinic. If a chromosomal rearrangement is identified, this could be the underlying cause. Most couples karyotype as 46,XX and 46,XY. In most centres cytogenetic analysis of abortus material is not able to be demonstrated. Some laboratories karyotype the products of conception. Wartburton and Morton (1992) conclude that a chromosomally abnormal abortion and the parents being chromosomally normal, implies minimal genetic risk for a future pregnancy.

° Spermiograme: abnormal spermiogram (oligospermia, asthenospermia, azoospermia, teratospermia) imply genetic analysis (karyotype) [16] or molecular genetics-particularly severe OAT or azoospermia (possible cystic fibrosis gene carrier).

Genetic diagnostic testing of infertile males should be strongly recommended where there is a significant risk of transmitting identifiable chromosomal abnormalities or genetic mutations to the conceptus that will severely impact its future health and well-being.

All couples in which a male has identified as having a chromosomal anomaly or a clinically significant genetic mutation should be referred to a certified genetics counsellor and/or a clinical or prenatal geneticist for preconception counselling (perhaps assisted reproductive technology – intracytoplasmic sperm injection [28], or artificial insemination by donor [28] will be recommended)

and possible prenatal diagnostic evaluation.

° Once pregnancy occurs, most of the couples who have had a problem of infertility have medical indications for invasive prenatal diagnostic techniques:-----chorionic villus sampling or amniocentesis

in addition to non-invasive techniques : ultrasounds, maternal serum levels of AFP,HCG estriol.

° It's important to have a general genetic workup of the couple and if fertility is idiopathic we should karyotype both parents.

Genetic counselling and ethical aspects

Genetic counselling after genetic analysis is an educational process that seeks to assist affected and/or at risk individuals to understand the nature of genetic disorder, its transmission and the options open to them in management and family planning.

Genetic counselling in these cases involves three aspects:

- the diagnosis (already done)
- the actual estimation of risks
- a communicative role ensuring that those given information actually benefit from it and from the various supportive and preventive measures that may be available [29].

One benefit of genetic counselling in the patient population is the identification of the couples who have a high risk for genetic diseases (table 3) and this aspect underscores the potential value of genetic counselling for all patients in an assisted reproductive technology setting. (table3)

An essential accompaniment to genetic counselling is that those being counselled should have full and accurate knowledge concerning their problem. Further «back-up» measures that may be required are contraception and sterilisation, as well as the exploration of other possible options such adoption, artificial insemination by donor or ovum donation [30].

Little is known about either the processes by which patients decide whether or not to undergo tests or medical interventions, or the outcomes of different ways of processing information in making decisions [30,31]. In the case of prenatal tests, there is some evidence that health professionals do not give information in a manner conducive to systematic decision making. An observational study showed that the information given about fetal anomaly scan in most antenatal clinics was minimal and the test was presented as routine, rather than one requiring a decision. We need to learn more about the presentation of these tests as tests involving the woman's decision-making and how to facilitate it [31,32].

The counsellor is required to respect the autonomy of the client and this translates into the principle

that counselling be nondirective.

Ingelfinger (1980)comments:»A physician who merely spreads an array of vendibles in front of the patient and then says: Go ahead and choose, it is your life-it's guilty of shirking his duty, if not of malpractice».

In other societies, the perceived good of the group may carry more weight than the professed wishes of the individual [32,33]. The degree to which one society can seek to influence practice in another is a matter of no little controversy.

CONCLUSIONS

° Genetic analyses in the infertile couple are used to test whether there is a significant genetic influence in the aetiology of the disease and to identify the mode of inheritance of these disorders.

° Genetic testing are strongly recommended when there is a family history or medical and physical examination suggestive for a genetic disease.

° In the infertile population, the most frequent genetic problems occurs in male, so ,when there is an abnormality of sperm (especially oligospermia, azoospermia, oligoasthenospermia) karyotype and/or DNA-analysis should be performed. Because infertile males have a higher risk than normal male population of carrying and thus transmitting to their offspring significant chromosomal abnormalities, karyotyping of peripheral blood should be performed, especially for those which need intracytoplasmic sperm injection.

° If the infertile couple is determined to have a carrier of a chromosomal abnormality by peripheral blood karyotype, then the couple should be counselled by a genetics counsellor and/or prenatal geneticist on the reproductive risks associated with the specific abnormality.

° Prenatal diagnosis of ongoing pregnancy should be offered to the couple who had an infertility problem. The type of prenatal diagnosis invasive or non-invasive should be discussed and the couple should be allowed to choose.

Psychological support should be offered to the couple during the process of genetic testing before, during and after a pregnancy.

° Most infertility remains idiopathic, inspite of genetic analyses. Our protocol should be reviewed and modified regularly in light of new genetic testing which will become available.

REFERENCES

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GENETIC ANALYSES IN THE INFERTILE COUPLE

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INTRODUCTION:

- <u>Cytogenetic and molecular genetic methods</u> have led to an enormous increase in knowledge of genetic information concerning <u>infertility</u>.
- -genetic programs
- -genetic counselling
- -prenatal diagnosis
- <u>Practicians must open their mind to these new</u> <u>possibilities and methods,</u> knowing the increased possibility to predict the risk for the offspring of developing a disease and to diagnose it <u>prenatal.</u>
- Human conception and pregnancy is both a vulnerable and a robust process.
- -vulnerable---chromosomally abnormal---abortus
- -robust----->99% of time ? chromosomally normal baby

INTRODUCTION:

- <u>Causes of genetic disorders:</u>
- <u>-chromosomal:</u> addition or deletion of entire chromosomes or parts of chromosomes (ex: translocations, aneuploidy)
- <u>-single gene defects:</u> a single mutant gene (ex:sickle cell anemia, cystic fibrosis, hemophilia)
- <u>-polygenic diseases</u> (multifactorial = predisposition and environment): interaction of multiples genes creats the predisposition for disease (ex: congenital heart diseases, cleft palate, cleft lip, diabetes, hypertension)
- Infertility: 2%-7% of couples fail to conceive
- the most frequent genetic problems occur in <u>male</u>?
 gametogenesis in men appears more sensitive to genetic disturbance than oogenesis in women---<u>females</u> carriers

OBJECTIVES:

- 1) To asses the importance of genetic analyses in infertility and to stress the contribution of disturbed genetic information system to the development of diseases.
- 3)To reveal the possibility of prediction of risk for recurrence of a large number of genetic disorders.

- 2) To establish when an infertile couple should have a genetic analysis and what are the current possibilities in order to improve clinical practice.
- 4) To show how inherited disorders become subject to prenatal detection.

METHODS:

- The initial evaluation of an **infertile couple** must begin with <u>a complete history and physical examination.</u>
- Collecting genetic information is best achieved by drawing up <u>a family tree</u> (consanguinity, infant deaths, stillbirths, abortions, inherited disorders known...).
- Chromosome analysis: peripheral blood, bone marrow, amniotic fluid and products of conception can be used. The following steps are involved: a) tissue culture; b) addition of a mitotic inhibitor; c) harvest cells hypotonic solution; d) fixative solution; e) staining; f) karyotyping
- Molecular genetics involves: 1) extraction of DNA; 2) denaturation and cutting with enzymes; 3) PCR amplification; 4) hybridisation with radioactive probe; 5)gel electrophoresis; 6) developing (film radioactive).

METHODS:

- Once pregnancy has occurred ? prenatal cytogenetic diagnosis
- The main indications are:
- 1) increased age of mother;
- 2) parental heterozygoty for a chromosome rearrangement, the birth of a previous child with a chromosome defect;
- 3) abnormal maternal blood chemistry indicating risk for aneuploidy;
- 4) IUGR and/or fetal malformation detected on ultrasonography;
- 5) couples with two or more pregnancy losses, spontaneous abortions, stillbirth, neonatal deaths;
- 6) couples who are concerned about having an abnormal baby.

METHODS:

- Prenatal diagnosis:
- Chorionic villus sampling : at 10 to 11 weeks; may be the procedure of choice for couples with a medium to high genetic risk (>5%), particularly if DNA analysis is involved.
- <u>Standard amniocentesis :</u> at about 16 weeks, has a high degree of safety to both mother and infant, but the results are not at hand until 18 weeks.
- **Early amniocentesis:** at about 10-13 weeks.
- Fetal blood sampling: cordocentesis under ultrasound guidance, especially when structural defects have been identified at ultrasonography.
- Placental biopsy: rapid results
- <u>Ultrasounds, maternal serum levels, embrioscopy</u>

DISCUSSIONS:

- A) During the workup of the infertile couple, two main types of <u>chromosomal</u> anomalies can be found:
- <u>1) gonosomal aneuploids:</u> Klinefelter syndrome (47,XXY), 47,XYY- syndrome, Turner -syndrome, triple X-syndrome
- <u>2) structural rearrangements:</u> balanced or unbalanced (reciprocal autosomal translocations, X-autosome and Y-autosome translocations)
- **B)** <u>monogenic disorders :</u> myotonic dystrophy, cystic fibrosis, Kallman syndrome, Noonan syndrome ...
- These genetic disorders can produce : male and female infertility, congenital malformations, mental retardation, miscarriage, hydatiform mole, infant death.

DISCUSSIONS:

- <u>The frequency of chromosome abnormality in new-</u> borns:
- autosomal trisomy (13,18,21)------1,4/1000
- sex chromosome aneuploidy (M)-----2,5/1000
- sex chromosome aneuploidy (F)------1,4/1000
- structural rearrangement, unbalanced------0,3/1000
- extrastructurally abnormal chromosome-----0,4/1000
- total unbalanced------4,0/1000
- structural rearrangement, balanced------4.3/1000
- total------8,3/1000

(1 in 120)

PROTOCOL FOR WORKUP OF THE INFERTILE COUPLE (GENETIC ASPECTS)

- 1) family history: if positive ??? genetic analyses
- 2)medical history and physical examination:
- -for the man: pulmonary or digestive symptoms? neuromuscular symptomes? ? ? ? molecular genetics
- -for the woman: <u>genital examination</u>
- unusual stature, hypogonadism, repeated miscarriages ? ? ? karyotype
- 3) spermogramme: abnormal spermogramme ??? karyotype and/or molecular genetics
- For the woman: predisposed <u>ethnic group</u> or the husband is <u>carrier</u> for a recessive disorder ? ?? molecular genetics
- If infertility is idiopathic ??? karyotype both parents

DISCUSSIONS:

- 1) **PRECONCEPTION COUNSELLING** (ART, ICSI, AID): all couples identified as having a genetic problem should be referred to a genetic counsellor .
- 2)PRENATAL DIAGNOSTIC EVALUATION(CVS, AMN, FBS): once pregnancy occurred there are medical indications for invasive prenatal diagnostic techniques
- 3)GENETIC COUNSELLING AND ETHICAL ASPECTS: the diagnosis,
- -the actual estimation of risks
- - a communicative role
- -to respect the autonomy of the patient ? counselling must be non-directive !

CONCLUSIONS:

- Genetic analysis in the infertile couple is used to test whether there is significant genetic influence in <u>the</u> <u>etiology</u> of the disease and to identify the <u>mode of</u> <u>inheritance</u> of these disorders.
- Genetic testing is strongly recommended when there is a <u>family history or medical and physical examination</u> suggestive for a genetic disease.
- In the infertile population, the most frequent genetic problem occurs in male partners, when there is <u>an</u> <u>abnormality of sperm</u> (oligospermia,

azoospermia,oligoasthenospermia) karyotype and/or DNAanalysis should be performed.

CONCLUSIONS:

- If the infertile couple is determined to be <u>a carrier of a</u> <u>chromosomal abnormality</u> by peripheral blood karyotype, then the couple should be counselled by a genetic counsellor and/or prenatal geneticist on the reproductive risks associated with the specific abnormality.
- **Prenatal diagnosis** of ongoing pregnancy should be offered to the couple who had an infertility problem.
- Psychological support for these couples: <u>before, during</u> <u>and after a pregnancy.</u>
- Most infertility remains idiopathic;our protocol should be modified regularly in light of <u>new genetic testing</u> which will become available.

1. GLOBAL SITUATION OF SEXUALLY TRANSMITTED DISEASES AND **FUTURE CHALLENGES**

2. "It is conservatively estimated that fully one-eighth of all human suffering comes from these sources"

PRINCE MORROW, 1912

• 3. FACTS

- 340 MILLION NEW CASES OF STDS EACH YEAR
- STDS ASYMPTOMATIC
- MORE IN FEMALES
- CONTROL STDS LOWER HIV
 TRANSMISSION

• 4. OBJECTIVES

1. TO TRY TO ESTABLISH THE TRUE PREVALENCE OF STDS

2. GLOBAL TRENDS OF STDS

3. FUTURE CHALLENGES

• 5. METHODS / SOURCE

OF SEARCH

- MEDLINE, COCHRANE LIBRARY, WHO WEB
 - KEY WORDS: Sexually transmitted diseases; prevalence and world

Period - 10 years

• 6. RESULTS

- STUDY PERIOD: 1985-1999
- STUDY TYPES not clear
- SAMPLE SIZES not mentioned
- STUDY AREAS global, developed countries

developing countries

• STUDY POPULATION:

gonorrhoea, syphilis, chlamydia, trichomoniasis

7. REGIONS STUDIED

North America Western Europe Australasia Latin America & the Caribbean Sub-Saharan Africa North Africa & the Middle East Eastern Europe & Central Asia East Asia & Pacific South and south-East Asia

Syp/Gon/Chl & Tri 14 million 16 million 1 million 36 million 65 million 10 million 18 million 23 million 150 million

8. MOST FREQUENTLY OCCURRING STDS

- SYPHILIS
- GONORRHOEA
- CHLAMYDIA
- TRICHOMONIASIS
- GENITAL HERPES

• 9. FUTURE CHALLENGES

- **1. True prevalence in general population**
- 2. Asymptotic STDs
- 3. STD linked HIV transmission
- 4. Sexual behaviour
- 5. Inadequate treatment and drug resistance
- 6. Disease burden

10. CONCLUSION

1. EDUCATION

2. PREVENTION

3. COMMITMENT

4. INTEGRATION

H.T.A gravidique et mortalité maternelle

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<u>Hypertension artérielle gravidique et mortalité</u> <u>maternelle</u>

DEFINITION

L'HTA gravidique :une hypertension se manifestant après 20 semaines de gestation chez une femme jusque là normotendue.

Korotkoff I bruit présent de 3/4: systole

Korotkoff IV disparition de 3/4: diastole

<u>Épidémiologie</u>

En Afrique: la létalité de l'éclampsie se situe entre 7 à 25% alors que elle n'est que de 1.4% en Suède .

<u>Physiopathologie</u>

TA=débit cardiaque x résistance périphérique

1-sténose vasculaire:

- hypoxie locale tissulaire ?hémorragie , nécrose et autres changement pathologiques.

-augmentation de l'acide urique plasmatique

2-coagulation:augmentation de la formation de la fibrine.

3-retentions hydrosodées.

Diagnostic

A/signes:

* HTA :TA >140/90 mmHg+augmentation de 30mmHg en systolique et 15mmHg en diastolique.
*Protéinurie: sup à 0.3mg/l/24h de collection

*Oedème:augmentation de poids de 1kg/semaine ou 2.25kg/mois.

Diagnostic

B/symptômes:
-maux de tête.
-troubles visuels.
-douleurs épigastrique
-nausées, vomissement
Types : *PreE légère : TA 140/90 + /- œdème *PreE sévère: TA= 140/90 + protéinurie +/œdème TA diast > 110Troubles visuels ou cérébraux *Éclampsie imminente *PreE fulminante

> Complications Foeto- maternelles

Investigations

examen complet des urines
tests de la fonction rénale
statut de la coagulation
fond d'œil

TESTS DE DEPISTAGE

A/Hypertension artérielle -détection des femmes à haut risque

B/Tests urinaires -HTA modérée sans protéinurie -HTA avec protéinurie

C/Clinique

TRAITEMENT

basse dose d'aspirine
rôle du repos
antihypertenseurs
anticonvulsivants
mesures obstétricales



PRéECLAMPSIE -ECLAMPSIE

Les questions qui doivent orienter les recherches :

Tableau no 1 :

Stade /état	Questions	Méthodes d'études
Prévention primaire	Quelle est actuellement l'incidence de l'HTA gravidique de la préeclampsie, de l'eclampsie et de la mortalité due aux TTG ?	Epidémiologie
	Quelles sont les tendences en matière d'incidence, de progression et de létalité ?	Epidémiologie
	Quels sont les déterminants des TTG que l'on peut modifier ? (p.ex. :facteurs diététiques, meilleure préscription de médicaments efficaces)	Epidémiologie
	Peut-on prévenir l'incidence ou la gravité des troubles par une supplémentation en Calcium, huile de poisson, d'autres précurseurs, des prostaglandines, des antiagrégants à faible dose, chez toutes les femmes ou les femmes à haut risque ?	EAC

Les questions qui doivent orienter les recherches

Dépistage et étude	Le dépistage précoce prévient-il la progression de la maladies et la mortalité ?	Epidémiologie EAC (surveillance très étroite/ normale)
	Quelle est la méthode de dépistage la pllus efficace au niveau primaire (meure de la tension artérielle, analyse d'urine, œdème, symptômes, associations) ?	Opérationnelle EAC
	Comment rendre la mesure de la TA possible universellement/ au niveau primaire ?	Développement des technologies Opérationnelle
	L'éducation sanitaire des femmes enceintes et de la communauté permet-elle d'améliorerla reconnaissance de la préE grrave, la recherche des soins adéquats et le résultat final ?	EAC
	A quels intervalles et à quel(s) moment(s) de la Gsse faut-il surveiller la TA ?	Epidémiologie EAC
	Quelle méthode est la plus efficace pour dépister une maladie grave	Epidémiologie EAC

Tableau no.2 : Recherche-questions sur interventions prénatales susceptibles de prévenir et de combattre les TTG

Stade /état	Questions	Méthodes d'études
Traîtement : préE légère à modérée	Dans l'HTA gravidique où la préE, le repos au lit (chez soi ou à l'hôpital) prévient-il la progression de la maladie ou en améliore-t-il l'issue pour la mère et le foetus	EAC
	Le traîtement par hypotenseurs de la préE légère ou modérée prévient-il la progression de la maladie ou en améliore-t-il l'issue pour la mère et le fœtus ?	EAC
	Certains hypotenseurs sont-ils supérieurs à d'autres (bêta – bloquants, diurétiques, méthyldopa, autres)	EAC
	Quel degré de TA ou autres signes de gravité doivent-ils faire envoyer les femmes au premier niveau de recours pour y être prises en charge ? Directives ?	EAC Et/ou épidémiologie Opérationnelle
	Que font les femmes à qui l'on conseille de se reposer chez elles et quel soutien peuvent- elles recevoir ?	Sociologie

Tableau no.2 : Recherche-questions sur interventions prénatales susceptibles de prévenir et de combattre les TTG

Traitement de la préE grave	A partir de quels chiffres de TA faut-il intervenir?	EAC
	Quels hypotenseurs sont les plus sûrs et les plus efficaces concernant l'issue pour la mère et le fœtus (bêta –bloquants, hydralazide, diazoxide, méthyldopa, autres)?	EAC
	Faut-il administrer les hypotenseurs et contrôler la TA à l'échelon primaire avant transfert au premier niveau de recours'	EAC Épidémiologie Opérationnelle
	L'administration prophylactique d'anticonvulsivants dans la préE grave prévient-elle les crises /la progression vers l'éclampsie ?	EAC

Tableau no 3 : Recherche-questions sur interventions prénatales susceptibles de prévenir et de combattre les TTG.

Stade /état	Questions	Méthodes d'études
Traîtement de la préeclampsie grave	Faut-il donner des anticonvulsivants à titre prophylactique à l'échelon primaire avant transfert au premier niveau de recours ?	EAC Epidémiologie Opérationnelle
	Quelles sont les meilleures directives concernant le transfert au premier niveau de recours ?	Epidémiologie Opérationnelle EAC
	Quelles sont les meilleures directives pour hâter l'accouchement ?	EAC Epidémiologie

Tableau no 3 : Recherche-questions sur interventions prénatales susceptibles de prévenir et de combattre les TTG.

Traîtement de l'eclampsie	Est-ce que, par l'éducation sanitaire et la formation des accoucheuses traditionnelles, on peut améliorer les premiers secours/ soins d'urgence au premier niveau de recours ?	Essai/ évaluation de l'éducation sanitaire (étude)
	A quelle rapidité un transfert au premier niveau de recours peut-il être organisé ?	Opérationnelle
	Faut-il administrer des hypotenseuers et/ou des anti convulsivants au niveau primaire avant le transfert ?	EAC Epidémiologie Opérationnelle
	Quel est meilleur hypotenseur du point de vue sécurité et résultat final pour la mère et le fœtus ? (bêta – bloquants, hydralazide, diazoxide, méthyldopa, autres)	EAC
	Quel anticonvulsivant est le plus sûr et le plus efficace sur le plan résultat final pur la mère et le fœtus (sulfate Mg, diazépam, phénitoïne) ?	EAC
	Le remplissage vasculaire améliore-t-il l'issue pour la mère et le fœtus ?	EAC

INTERVENTIONS TO IMPROVE REPRODUCTIVE HEALTH AMONG YOUNG PEOPLE

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ABSTRACT

The purpose of this literature review is to identify successful key issues in the implementation of educational activities to promote reproductive health among young people.

Two databases were searched and personal communication with professionals at the World Health Organization (WHO) took place to obtain information regarding interventions in young people, making emphasis on reproductive health. Nine reports were reviewed, for information related mainly to identify those features that proved to have an impact on subjects` behavior or knowledge to improve their reproductive health.

According to the findings, the following characteristics seems to have a pivotal role for successful outcomes.

The programs should have a strong concern about:

- Providing a safe and supportive environment.
 - Providing effective training for the people implementing the program.
 - Enhancing close relationships with family and society.
 - Promoting collaboration with other institutions linked with adolescents activities
 - Providing Information

• Topics: male/female reproductive function, adolescent development, human sexuality and responsible sexual behavior (delaying sexual activities or contraceptive practices), sexually transmitted diseases (STDs) / HIV.

Information should Focus on changing risk taking behavior.

 \cdot The involvement of parents, counselors, peers, teachers and mass media should be encouraged.

Provide activities to build on life skills in adolescents.

In small groups

• Using interactive teaching methods to help students to personalize information, to enhance decision making and to strengthen their ability to resist social pressures to engage in risk behaviors; and to obtain materials to adopt prevention practices as well as to assist them in communicating their thoughts and feelings.

- · Involve Health services
 - Build on competent and motivated health care providers.
 - In schools : according to their needs and available schedule.

 \cdot Giving adolescents greater access to health products like quality condoms and other contraceptives.

Providing prenatal care to teenage mothers.

The programs should be designed, implemented and evaluated by the active participation of young people, their parents, teachers, youth leaders, religious leaders and politicians, addressing gender and developmental stage of adolescents.

Key words : (Adolescen*, Health, Education*, Interventions)

INTRODUCTION.

Facing the year 2000, most developing countries are being challenged by the increase in population due to the increased reproductive age group. More than half of the world population is below 25 years of age with 4 out of 5 of them living in developing countries. Once a girl becomes pregnant, she is more likely to withdraw from school, resulting in lower expectations for her future, having larger families and being a single parent. In addition, babies of teenage mothers are more likely to become ill and have less supportive and stimulating home environments. This may lead to behavioral problems later in life. (1).

Fifty three percent of young women less than 20 years in developing countries have had at least one live birth, demonstrating the importance of addressing the problem of early sexual activity. In addition, sexually transmitted diseases, HIV and also precursor lesions of cervical carcinoma increase its unfortunate impact due to sexual risk taking behaviors. (1,2).

Young girls are more likely to experience sexual pressure or even abuse. They are more likely to use alcohol and drugs leading to engagement in other and unhealthy behaviors such as unprotected sex.

Adolescents change their sexual partners more frequently and are more likely to have more than one partner at the time and commonly have negative attitudes towards contraception mainly because their ignorance in these matters.(1).

Pregnancy in adolescence has shown to be a risk factor for maternal mortality, which even more in developing countries, remains a major concern for health systems.(3).

It seems that efforts to approach this group have been undertaken for the last 20 years. During this time researchers and educators have learned how to better approach young people with educational messages, with the intention to avoid their exposure to risky sexual behaviors. There have been great achievements, specially regarding the identification of features of interventions linked to better outcomes, in terms of delaying sexual activities or recognizing the need for protected sex.(4).

The focus of the review is on successful interventions to improve either knowledge or behavior among adolescents for the benefit of their reproductive health.

OBJECTIVES.

a. Review of the literature concerning the interventions to improve reproductive health among young people, with emphasis on detecting key issues that have been tested and the quality of outcomes in terms of comparative benefits with other or no intervention at all.

b. To assess the effectiveness of different interventions in raising reproductive health

status among adolescents.

METHODOLOGY

Two databases were searched, Medline and the Cochrane library. In addition experts in the field at the World Health Organization were consulted.

Nine reports were reviewed, all of them in English, dating from 1995. The key words used to allocate the information were: Adolescen*, Health, Education*, Interventions. The information collected included technical reports, experimental and non experimental studies regarding the field of interest. The focus of the review is on successful interventions to improve either knowledge or behavior among adolescents for the benefit of their reproductive health.

RESULTS (see tables)

DISCUSSION

There have been many approaches that have proved to be efficient in the promotion of reproductive health among young people.

The following statements summarize the key findings in this review, regarding successful features:

In the implementation of programs for reducing risk behaviors among young people, it has been stated that effective programs are those who take parents, teachers, youth leaders, religious leaders, political leaders, media, popular entertainers and even industry executives into consideration for the design, implementation and evaluation activities, depending on their influence in the corresponding field. (1).

First, the needs of the target population should be assessed, considering knowledge on different aspects as nutrition care, hygiene, what should a young person have to expect about physical and psychological adjustment during this period of changes, knowledge about sexual behavior, contraceptives and risky behaviors to develop sexually transmitted diseases or HIV, and to become drug addicted among others.(1).

Having established a baseline parameter, for the continuous monitoring of success or even to address difficulties, the following interventions have shown to be the most successful in terms of placing the young in a position " more likely to recognize the threats and to respond adequately to hostile environments ".

Successful interventions should focus on:

1. Promoting Safe and Supportive Environment :

a) Family and society:

In order to facilitate healthy choices, there should be a safe and supportive environment. Safe in terms to withdraw the adolescent from harmful situations and supportive to enhance positive close relationships with family and society. The family members play an important role due to their close relationship and their advice and guidance is often of great importance. The effective communication between family members should be emphasized. This responsibility can be shared with other institutions such as schools which focus on the well being of adolescents.(1,5,6,7).

b) Media:

This supportive environment should be extended to the mass media as well. They have a strong potential to ease the changes, by printing information on products used by the young and in this regard the manufacturer significantly contributes to promote health in the community making clear to the commercial sector the humanitarian and economic benefits of their actions.

This supportive environment should also assess that opportunities to reach the target population are being appropriately used to enhance positive information, counseling or whatever the context demands. It should also be careful in assessing that supplies and physical services are being able at times when required (1,8).

c) Policies:

Policy and legislation offers a great contribution to all of the above. Politicians should be sensitized to strengthen the access of information and reproductive health services to young people.

Politicians should promote legal submission for the people abusing adolescents` rights, prohibit the marriage at early ages and demand from the media to increase their coverage with issues on sexual behavior, contraceptive services and others(1).

2. Providing Information :

It can be defined as the provision of appropriate information, by whatever means, with the principal aim of increasing adolescents` knowledge and understanding of a particular health issue, and sometimes with the explicit intention of motivating them to adopt healthy behavior and to prevent hazards such as unwanted pregnancies, STDs, abuse of harmful substances, violent behavior and nutritional deficiencies.

The areas where information should focus on is as follows :

* Information about human development and the changes experienced physically, psychologically and socially during maturation (2,6,8,9).

* Information about the gender roles, in family relationships as well as in society (1).

* Information about specific areas of health : nutrition, dental care, physical activity, sexual and reproductive health and ways to express feelings without resorting to aggression toward others (1,6).

* Information about sexual risk taking behaviors (1,2,5,7,9).

* Information about availability of health services (1).

This provision of information can take place in two strategies :

a) Interpersonal Communication

b) Media

Interpersonal Communication :

Parents : Parents may be unwilling to approach their children with issues specially concerning sexual behavior and young people do not look for their parents as a source of information on this issue. But it seems that family members could provide not only adequate information, but they could have a follow up activity to monitor their achievements as well (1).

Counseling : A process of interpersonal communication within a supportive professional relation through which the counselor helps the counseled person to deal more effectively with problems by enabling him/her to understand the situation better and make sound decisions. There are two approaches in this modality: The directive and the non-directive approach. The former, advice is provided by the counselor while in the non-directive approach the advice comes from the client himself by the acquisition of judge elements to distinguish the more appropriate behavior. It is especially important to enable the adolescent to articulate feelings since this is often the most important and most neglected component motivating behavior. The intervention should deal with the issue in such a way as to strengthen the persons` capacity for self-understanding and build the confidence needed for positive and effective action to help prevent future problems (10).

Peers : This method is perhaps the most used even though friends tend to be equally uninformed. Nevertheless, using proper peer education can help to reduce misinformation. This method has been particularly useful with vulnerable groups such as street children and commercial sex workers. They could play a role for distributing supplies, like contraceptives, as well (1).

Teachers : Schools have the potential for addressing and reducing adolescent sexual risk-taking behavior. Virtually all adolescents attended before initiating sexual activity and the majority are still in school when they initiate intercourse. In general, schools are designed both to increase students` knowledge and to improve their skills. In addition schools have access to the peers of pupils and thus have the potential for influencing peer pressures and norms. And finally, if school programs are effective, their organizational structure, in theory, can implement these programs broadly and can institutionalize them (8). Teachers are in an outstanding position to run programs on health education and health promoting behavior. They should be trained, sensitized and have the ability to communicate in an interactive setting.

Youth Clubs : Are equally important partners not only to encourage their physical development but also to explore their strengths and weans to provide adequate guidance in the management of feelings and behaviors (1).

Mass Media :

Although mass media is often considered as a one way communication, there are many ways in which some form of interactivity can be achieved, for example, telephone talk ins, questionnaires in newspapers, debates on television and radio and nowadays the internet.

The provision of information through interactive methods is vital to influence attitudes and choices in sexual and reproductive health. Nevertheless, programs focusing on knowledge and attitudes alone had limited effect. Such programs often fail to address the psychological factors underlying an specific behavior or problem (1).

3. Building on Adolescents` life Skills:

This is the process of teaching competencies to influence behavior through a set of structured activities. Teaching of skills is practical and intended to equip the young person with new or improved abilities. They should be interactive, participatory approaches which fully involve the adolescents.

Life skills are defined by WHO as follows : " abilities for adaptive and positive behavior, that enable individuals to deal effectively with the demands and challenges of everyday life ". They need to develop skills in physical, psychological, social, moral and vocational areas, to promote healthy development and help to prevent particular health problems (1,2,5,6,7,8,9). The skills willing to be attained by young persons include : self awareness, empathy, interpersonal relationship skills, communication, critical thinking, creative thinking, decision making, problem solving and coping with stress and emotions (1).

The activities used to build skills include working in small groups and pairs, brainstorming, rehearsal, role playing, games and debates. To teach a new skill, it is useful to introduce the behavior or skill and provide information on its use, demonstrate the skill, give the participants the opportunity to try it out, ask for self assessment of performance and ways to improve it, provide feedback and then provide the opportunity to try out the skill again.

Researchers have found that programming "life skills "leads to the development of positive changes in self reporting of health behavior, positive health status, in particular, self-esteem and self-confidence, positive inter-personal communications and improved teacher-pupils relationships.

This supports the mounting evidence of the benefits of programs that combine various types of interventions in a range of settings.

4. Health Services and their availability.

Health workers could make valuable contributions both within and outside health facilities by helping to promote healthy behavior, to prevent health problems, and to respond to health problems as they arise. To be active in this strategy they are required to fully understand the problem and to be willing to become a partner of the team. They need to be technically competent, interested, concerned and

with high communication skills.

When adolescents have limited access to such services, this represents countless missed opportunities for the prevention of health problems. In order to reach adequate access to health services, the following steps are recommended, since they have proven its efficacy in developing countries :

a) School health services : Provided by local government bodies in conjunction with school authorities. They may include periodical monitoring of growth and development, routine checks for the detection of problems, administration of vaccines, diagnosis and treatment of common illnesses, arrangements to refer to health and social services when requested, and sexual and reproductive health services.

b) Social marketing : Give adolescents greater access to health products like quality condoms and other contraceptives.

Comprehensive prenatal care programs for pregnant adolescents : They have proved dramatic reductions in pregnancy complications among teenagers, as well as better neonatal outcomes, increased breastfeeding and postpartum contraception. Teenagers participating in these programs have also attained a better health status through treatment of STD's and decreased use of harmful drugs during pregnancy and subsequently.

All the mentioned above strategies should bear in mind a common denominator : The active participation of the young, their families and society. People are more likely to support health services when they fully understand their value in promoting and safeguarding health, and the consequences of not making them available to adolescents.

CONCLUSIONS

There are effective interventions to improve knowledge and sexual risk taking behaviors among young people. The interventions that have been suggested as successful are as follows:

The interventions should:

Provide a safe and supportive environment:

providing effective training for the people implementing the program

Enhancing close relationships with family and society.

Promoting collaboration with institutions linked with young activities.

Provide information:

Topics: male/female reproductive function, adolescent development, human sexuality, responsible sexual behavior, STD's including HIV.

Focusing on changing risk behaviors.

The information could be provided by parents, teachers, counselors, peers and mass media.

Build on life skills in adolescents:

In small groups.

Using interactive teaching methods to help students personalize the information, to enhance decision making and to strengthen their ability to resist social pressures to engage in risky behaviors and to obtain materials to adopt prevention practices as well as to assist them in communicating their thoughts and feelings.

Involve Health Services:

By competent and motivated health care providers.

In school basis: according to their schedule and needs.

Giving adolescents greater access to quality condoms and other contraceptives.

Providing prenatal care to teen mothers.

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03.12.02

KEY POINTS IN THE DESIGN OF INTERVENTIONS TO IMPROVE REPRODUCTIVE HEALTH AMONG YOUNG PEOPLE

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Objectives

- Review of the literature concerning interventions to improve reproductive health among young people
- To assess the effectiveness of different interventions in raising reproductive health in this population

METHODOLOGY

- Two Databases were searched:
 - MEDLINE
 - COCHRANE LIBRARY
 - Nine reports were reviewed from 1995
- Experts in the field were consulted:
 - World Health Organization

• STUDY:

 An impact evaluation of Proj. SNAPP: An AIDS and Pregnancy prevention middle school program. AIDS EDUCATION AND PREVENTION.1997.

• SAMPLE:

- 7th Grade. 102 classrooms randomly assigned.
- 1657 students. Follow up at 5 and 17 months
- Mean age: 12 yrs
- 46% males

• INTERVENTION:

- Theory based curriculum to delay the onset of intercourse and increase the use of condoms.
- 8 sessions, two week period..

• FINDINGS:

 Significantly improved knowledge but unable to significantly change sexual or contraceptive behaviours

• STUDY

 Impact of a school AIDS prevention program on young adolescents` self efficacy skills. HEALTH EDUCATION RESEARCH.1995

• SAMPLE

- 15 school districts were randomly assigned
- 2318: treatment
- 900: control

INTERVENTION

- Educational program to reduce risk behaviours by teaching behavioural skills to enhance adolescents' self-efficacy and to adopt prevention practices
- 15 sessions, 7th and 8th grades.

• FINDINGS

 Self efficacy to obtain and use contraceptives significantly increased in the intervention group

• STUDY

 Trends in reproductive health knowledge following a health education intervention among adolescents in Zimbabwe. THE CENTRAL AFRICAN JOURNAL OF MEDICINE.1997

• SAMPLE

- A randomized controlled study. Follow up at 5 and 9 months.
- Total participants: 1609
- Mean age: 13 years

INTERVENTION

 Program designed to improve knowledge, reproductive behaviour, sexual and reproductive health.

• FINDINGS

 Knowledge levels increased in all areas of reproductive health in the intervention group.

• STUDY

 No easy answers: Research findings on programs to reduce teen pregnancy. THE NATIONAL CAMPAIGN TO PREVENT TEEN PREGNANCY.1997

• SAMPLE:

Literature review on 80
 programs to reduce teenage
 pregnancy

INTERVENTIONS

 Research review: Effectiveness of five types of teen pregnancy prevention programs.

• FINDINGS

- Programs need to address both, postponing sex and using contraception in the context of a supportive environment.
- Educational programs focused upon sexuality do not increase any measure in sexual activity.
- Increase in community outreach
- Multicomponent rather than single programs

- Design, Implementation and Evaluation: Active participation.
- Baseline parameter.
- Promote safe and supportive environment
 - Safe: Withdraw harmful situations
 - Supportive: Enhance positive close relationships with family and society

- Provide information:
 - Growth and development
 - Specific areas of health.
 - Potential risks to their health
 - Available services
- Strategies
 - Interpersonal communication
 - Mass media

- BUILD UP ADOLESCENTS LIFE SKILLS:
 - WHO: Abilities for adaptive and positive behaviour that enables the individual to deal effectively with the demands and challenges of everyday life.
 - Benefits the programs that combine various types of interventions

• HEALTH SERVICES.

- Health workers technically competent, interested, concerned and with high communication skills
- School health services
- Comprehensive prenatal care programs for pregnant adolescents

THANK YOU

MANAGEMENT OF ENDOMETRIOSIS ASSOCIATED INFERTILITY

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Abstract. The treatment of endometriosis–associated fertility is still controversial. Formulating a treatment plan for infertility associated with endometriosis is difficult due to unknown exact aetiology for the disease and hence the subsequent proposed treatment. Several molecular and cellular mechanisms have been postulated to play a role in endometriosis-associated infertility.

Modern surgical techniques as laparoscopy, ultrapulse lasers were shown to be of value in the treatment of less extensive stages of endometriosis. GnRH analogues also showed no evidence of a treatment effect. The recurrence rate of the disease is impressively high after either medical or surgical therapy. A combined medical and surgical approach for the treatment of endometriosis-associated infertility confirms great clinical benefit. In the last 10 years, better data from numerous studies with improved design support laparoscopic ablation and/or resection of lesions as the most successful treatment for minimal and mild stages of endometriosis. Observation alone is sometimes indicated in young women with minimal/mild disease. IVF-ET therapy may be indicated in prolonged infertility, and/or multiple-factors infertility. The choice of medication should be individualised, as the side effects may not be readily tolerated by some women.

Key words : endometriosis, infertility, laparoscopic surgery, IVF-ET therapy, gonadotrophin releasing hormone (GnRH) therapy.

Introduction

Endometriosis is diagnosed in about 30%-40% of infertile women (1, 2, 3) in whom no other significant abnormalities are found. Infertility could be associated with any stage of endometriosis. ⁽⁴⁾.Infertility can be a sequel to endometriosis, but still it can be a cause for it. ⁽⁵⁾

The association between infertility and minimal to mild endometriosis when no anatomical defect is evident, may be explained by the following possible mechanisms :

1. Alterations in peritoneal fluid (macrophages, immunoglobulins, Interleukin 1, protease inhibitors, prostanoids)

- 2. Ovulatory dysfunctions (anovulation, LUF syndrome)
- 3.Luteal phase defect
- 4. Disturbed implantation
- 5. Spontaneous abortion

Management of endometriosis associated infertility - R. Aniuliene

The latest prospective controlled studies offer strong evidence that endometriosis per se is not a direct cause of infertility. Women with minimal to mild endometriosis only should be diagnosed as having unexplained infertility, which today may be treated by in vitro fertilisation.⁽⁶⁾

Some authors reported that there does not appear to be a single explanation for the association between endometriosis and infertility ⁽⁶⁾. The infertility specialist should always consider various possible contributions when deciding on the management. These links include (but are not limited to):

- · Pelvic adhesions and anatomic distortions
- · Implants near the site of fertilisation which may produce molecular messengers that impact on fertilisation
- · Abnormal ovarian follicular development

Endometriosis–associated infertility has been the subject of several trials of ovulation suppression therapy and cohort studies of laparoscopic ablation of endometriosis implants ⁽²⁾.

Objectives

To review studies that explore the effects of different endometriosis treatment options on infertility outcome.

Methods

Selection of literature by computerised Medline search.

Results

Mechanisms of endometriosis-associated infertility are:

• Disturbances in the ovum pickup mechanism

The pelvic surgeon is very familiar with the sequelae of endometriosis, including pelvic adhesive disease and scarring. These alterations undoubtedly contribute to the disruption of the ovum pickup and transport mechanisms, making it difficult, if not impossible, for ovum capture to occur. More severe cases might result in gross alterations in the configuration of the fallopian tube, perhaps predisposing the patient to ectopic pregnancy. These macrofactors can explain the infertility.

Alterations in peritoneal fluid parameters

The pelvic structures are continuously bathed in peritoneal fluid. For that reason it is reasonable to assume that examination of this fluid might provide insight into potential alterations in the extracellular milieu in women with endometriosis.

Several studies have suggested that women with endometriosis have alterations in peritoneal fluid volume and its leukocytes content (7,8,9,10,11).

Hormonal alterations

Examinations of peritoneal fluid for alterations in the levels of steroid hormones and prostanoids have yielded a variety of findings, ranging from elevations in prostaglandins^(12,13) to alterations in the ratio of luteal

progesterone (P) to estradiol(E2) $^{(14)}$. The altered P:E ratio might lead to luteolysis $^{(14)}$ and prostaglandins might affect tubal motility, perhaps explaining a higher incidence of luteal phase defects $^{(15,16)}$ and potentially, tubal dysfunction in women with endometriosis. Subsequent studies, unfortunately, have failed to confirm significant alterations in these hormones, $^{(9,17,18)}$ and we must await further studies to clarify their role in endometriosis-associated infertility.

• Protein factor alterations

The potential importance of proteins in modulating cellular processes in the pelvic milieu has stimulated considerable research, leading to the identification of several factors, including interleukins, ⁽¹⁹⁾ in peritoneal fluid from women with endometriosis. Again, subsequent studies have demonstrated no significant difference in the levels of IL-1 in women with endometriosis relative to controls ^(20,21,22).

Cellular alterations

Macrophages were found to be present in increased amounts, and the activation of these macrophages was increased, particularly toward phagocytosis of sperm ^(23,24,25). Again, subsequent research has demonstrated no significant differences relative to controls ⁽²⁰⁾.

• Systemic alterations

Elevated levels of circulating autoantibodies have been reported, ⁽²⁶⁾ leading to the hypothesis that a defective immune response might play a role in endometriosis, either in the development of the disease or in endometriosis-associated infertility.

The mechanisms by which this disease causes infertility are multiple, potentially involving several physiologic processes and according to those.

Treatment options

Medical therapy

The premise on which hormonal suppression is proposed to improve likelihood of pregnancy was that the peritoneal implants were, in some unexplained way, responsible for the infertility. A variety of hormonal regimens have been advocated (table 1).

Table 1. Agents used or proposed for medical suppression of endometriosis

Methyltestosterone	
Danazol	
Diethylstilbestrol	
Clomiphene citrate	
Tamoxifen	
Gestrinone	
Medroxyprogesterone acetate Gonadotrophin-releasing hormone agonists

In early uncontrolled clinical trials, hormonal suppression gave the impression of improving endometriosis-associated infertility. This had the unfortunate consequence of prolonging hormonal use in absence of demonstrated efficacy. The initial studies failed to include untreated control groups and treatment independent pregnancies were erroneously attributed to the hormonal suppression. Controlled studies were performed and failed to demonstrate any treatment-dependent improvement in fertility (28,29,30). This is true regardless of the specific agent used for hormonal suppression. Mettler et al.(1991) (31) treated eighty patients with different stages of endometriosis with Zoladex, injected subcutaneous every 4 weeks. The stages of endometriosis were classified according to the revised American Fertility Society recommendations via pelviscopy before and after 6 months of treatment. All 57 symptomatic patients showed a subjective response to Zoladex therapy with a significant decrease of the total pelvic symptom score. Thirty eight patients with infertility wished to become pregnant and 16 (40%) have conceived.

Utsunomiya et al (1988) ³³ treated 46 infertile women with Gestrinone 5 mg-10 mg/week and 25 patients were treated with Danazol 300-400 mg/day for 6 months. Cumulative pregnancy rate in the Gestrinone group was 23.8%.

Pruksananonda et al.(1999) ³⁴ treated 22 patients with pelvic endometriosis with Gestrinone 2.5 mg twice weekly. After 6 months of treatment, 81 % of patients had amenorrhoea. Return of fertility was observed in 25% (5 patients) after 30-254 days post treatment. The results suggest that gestrinone may be considered an option for the treatment of endometriosis related infertility.

Salat-Baroux et al.(1988) ³⁵ treated 33 patients with endometriosis (15of them were with infertility) with Danazol. Seven pregnancies were reported in infertile patients, but a relapse was noticed in 30% of the cases.

The study of Balasch et al (1997) ³⁶ is the first prospective randomised controlled trial of the effect of pentoxifylline on future fertility in infertile women with asymptomatic minimal or mild endometriosis. After completion of a basic infertility workup and laparoscopy, patients were included into the study. The 12 month overall pregnancy rates were 31% and 18.5% in the pentoxifylline and placebo groups respectively. In this pilot study, enrolling 60 women, the difference was not statistically significant. However, further studies are needed to evaluate the use of pentoxifylline for infertility treatment in women with minimal or mild endometriosis.

In a multicentre study in seven German centres, the efficacy, tolerance and safety of the GnRH agonist leuprolide acetate were tested. One hundred four women were treated: 33% of patients had minimal, 22% mild, 28% moderate and 8% severe endometriosis. The patients mean age was 30 ± 6 years and 66 of 104 patients had infertility problems. Treatment was started within the first 3 days of the menstrual cycle and consisted of a subcutaneous injection of leuprorelin acetate 3.75mg, repeated once monthly over 24 weeks. Treatment results were judged as good and satisfactory in 82% and 11% of cases, respectively. On the basis of this study, it can be concluded that leuprolide acetate treatment is safe, well tolerated and effective in the medical management of endometriosis and endometriosis-related complaints ⁽³⁷⁾.

Fedele et al (1992) $^{(38)}$ reported about the efficacy of superovulation with buserelin acetate, human chorionic gonadotrophin (hCG) and human menopausal gonadotrophins (HMG) in the treatment of infertility associated with minimal or mild endometriosis. Nine pregnancies were obtained in the superovulation-treated patients and 6 in the control group. The cycle fecundity rates and CPR were 0.15% and 37.4% after 3 superovulation cycles and 0.045% and 24% after 6 months of expectant management (p <0.05). One conception occurred during this period/cycle fecundity rate=0.020). One spontaneous abortion occurred in each group. Three treated patients had multiple pregnancies, and 4 had ovarian hyperstimulation syndrome. They concluded: superovulation seems to be associated with a better CPR cycle fecundity rate but not a better CPR than expectant management in infertile women with endometriosis stages I and II.

Clinical effectiveness of ovulation suppression therapy for endometriosis–associated infertility: the combined data from trials comparing danazol, gestrinone and medroxyprogesterone acetate with placebo show no evidence of a treatment effect.(see table 2).

 Table 2. Treatment of endometriosis-associated infertility by means of ovulation suppression, in placebo-controlled randomised clinical trials

Reference	Treated		Control		Odds ratio	95% CI
	Pregnant	Total	Pregnant	Total		
Thomas and	5	20	4	17	1.08	0.24-4.78
Cooke						
(1987)						
Bayer et	13	37	17	36	0.16	0.24-1.54
al.(1988)						
Telimaa et	6	18	6	14	0.67	0.16-2.79
al.(1988)						
Telimma et	7	17	6	14	0.67	0.23-3.83
al.(1988)						

p>0.005

The combined data from trials comparing gestrinone, GnRHa and danazol as an active control also show no evidence of a treatment effect.

Surgical treatment: laparoscopy and laser therapy

Surgical treatment for endometriosis has been shown to improve fertility in advanced stages of endometriosis. Modern surgical techniques such as those using ultrapulse lasers are just now being shown to be of value in the treatment of less extensive stages of endometriosis. The surgical approach to a

patient with endometriosis currently leans strongly toward ``minimally invasive procedures``. In the hands of an experienced laparoscopic surgeon, virtually any endometriosis associated problem that can be treated by laparotomy, can now be dealt with via laparoscopy.

The combined data from cohort studies comparing laparoscopic ablation therapy with ovulation suppression or no therapy showed significant evidence of a treatment effect. (table 3)

Reference	Laparoscopy		Control		Odds ratio	95% CI
	Pregnant	Total	Obs	Total		
Seiler et al.(1986)	20	45	16	41	1.25	0.53-2.92
Nowroosi et al.(1987)	42	69	10	54	5.59	2.73-11.46
Fayez et al. (1988)	60	82	20	76	6.44	3.46-12.00
Levinson (1989)	44	83	9	21	1.50	0.58-3.88
Chong et al. (1990)	37	83	23	47	0.84	0.41-1.72
Paulson et al.(1991)	236	315	76	157	3.26	2.17-4.88

The aggregate numbers of patients and pregnancy rates were 439/677 (65%) in the ablation group versus 154/396 (39%) in controls.

In the study of Sulewski et al.(1980) ⁽³⁹⁾ one hundred consecutive patients with mild/moderate endometriosis were treated by laparoscopy. Forty of these women achieved a pregnancy within 37 months postoperatively; 73 % of these pregnancies occurred within 6 months, and 88% within 12 months of operation. Although this pregnancy rate is similar to rates obtained after treatment by laparotomy and/or hormonal therapy, the pregnancies in this study population occurred significantly earlier than after laparotomy or combined therapy. They concluded: laparoscopy offers an alternative for the treatment of mild/moderate endometriosis in infertile women .

Marcoux et al.(1997) ⁽⁴⁰⁾ studied 341 infertile women 20 to 39 years of age with minimal or mild endometriosis. During diagnostic laparoscopy the women were randomly assigned to undergo resection or ablation of visible endometriosis or diagnostic laparoscopy only. Among the 172 women who had resection or ablation of endometriosis, 50 became pregnant and their pregnancies that continued for 20 weeks or longer, as compared with 29 of the 169 women in the diagnostic-laparoscopy group (p>0.005). The corresponding rates of fecundity were 4.7 and 2.4 per 100 person months . Their conclusions: laparoscopic resection or ablation of minimal and mild endometriosis enhances fecundity in infertile women.

Nezhat et al.(1989) ⁽⁴¹⁾ reported the results of 243 patients with endometriosis-associated infertility ranging in severity from mild to extensive who were treated by the same surgeon using CO2 laser laparoscopically and control. Of the 243 infertility patients, 168 (69.1%) achieved pregnancy. The pregnancy rates were 71.8% in 39

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patients with stage I disease, 69.8% in 86 patients with stage II disease, 67.2% of 67 patients with stage III disease, and 68.6% in 51 patients with stage IV. The results indicate that laparoscopic treatment of endometriosis-associated infertility, in surgical experienced hands, is at least as efficacious as other forms of therapy for mild and moderate cases of disease, but appears to be more successful than laparotomy for more severe and extensive stages of disease.

Murphy et al.(1991) ⁽⁴²⁾ estimated cumulative pregnancy rates for 72 patients with stage I and II disease (98.2% and 76.6%, respectively ; not significantly different).No significant difference was seen when anovulation complicated the endometriosis (68.6%). Patients with stage I disease had an average fecundity of 10.30% with decreasing values observed in stage II (7.59). They concluded that cauterisation is effective for the treatment of stage I and II endometriosis associated with infertility.

Starcewski. et al.(1992) ⁽⁴³⁾ reported that the efficiency of treating endometriosis by hormonal as well as combined methods, and employing the operative laparoscopy was evaluated. The study involved 89 infertile women with endometriosis being of various grade of advancement. Sixty women underwent combined treatment remaining 29 were given hormonal therapy with danazol and Orgametril .Only 8 women became pregnant after combined therapy. Complete recovery concerned mainly less advanced endometriosis, particularly following the combined treatment. Early laparoscopic diagnosis increases the chance of curing endometriosis and infertility associated with it.

Chapron et al.(1999) ⁽⁴⁴⁾ conclude that in case of infertility surgical treatment of choice is laparoscopic surgery, may be in conjunction with medical treatment and possibly followed-up by a second-look. When there is pelvic pain, the treatment relies on complete exeresis of the endometriotic lesions. In this context, laparoscopic surgery is efficient as laparotomy for dealing with ovarian endometriomas, deep endometriosis infiltrating the uterosacral ligaments, the rectovaginal septum and bladder. However, in the majority of cases bowel endometriosis is still an indication to operate by laparotomy.

Gordts et al.(1984) ⁽⁴⁵⁾ were treated with endometriosis 176 infertile women with atraumatic and microsurgical techniques. Nine of these patients received preoperative or postoperative antigonadotrophin therapy. After 2 years the cumulative pregnancy rate of the severe group (40%) was not different from that of the mild (43%) or moderate group (45%). It is therefore suggested that the use of microsurgical techniques can improve the pregnancy outcome in patients with severe endometriosis.

From the experience of Pouly et al.(1996) ⁽⁴⁶⁾ in cases of endometriosis-associated infertility, operative laparoscopy is the first line treatment and assisted reproductive technology (ART) the second one. GnRH analogues are only useful in cases of extensive endometriosis to render surgery easier, and for ART. The average pregnancy rate following laparoscopic treatment was approximately 50% (range 34-80%). However, duration of infertility, age and sperm quality have a direct influence on it. Therefore the authors proposed a scheme for management of endometriosis-associated infertility.

Rock et al.(1981) ⁽⁴⁷⁾ treated 214 infertile women with endometriosis received conservative surgery. Among this group, 115 patients (54%) conceived following surgery; of these conceptions, 109 resulted in live birth. Among 49 patients with secondary infertility, the spontaneous abortion rate was reduced from 49% to 20% after conservative surgery (p < 0.01).

Combined hormonal and surgical treatment

The treatment of infertility associated with endometriosis is controversial and usually consists of either medical therapy with hormonal manipulation designed to suppress the disease, surgical therapy designed to debulk the disease and repair anatomic distortion, or combination of both. Endometriosis does not respond to hormonal changes the same way that normal endometrium does and has been shown to persist despite extensive medical therapy. The recurrence rate of the disease is impressively high after either medical or surgical therapy.

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Interestingly, expectant management of minimal or mild disease is associated with pregnancy rates equal to those of any other type of therapy. Only when the disease is more extensive does aggressive treatment appear to show improvement in pregnancy rates. Whether combination therapy of endometriosis is better than single agent therapy remains open to debate. Some of the best-designed studies using combination therapy have shown no difference in pregnancy rates. Yet, when taken as a whole, it would appear that combination medical and surgical therapy is chosen, the medical therapy should be given preoperatively. The literature abounds with a wide variety of classification systems, methods of calculating pregnancy rates, and inclusion of control groups. Because of this disparity between studies, reliable conclusions cannot be drawn ⁽⁵⁰⁾.

Ruhlmann et al.(1996) ⁽⁴⁸⁾ conducted an observational prospective cohort study with a control group and 140 infertile women with the laparoscopic diagnosis of ovarian endometrioma over 1 cm diameter. The groups were comparable regarding age, duration of infertility and disease severity. The laparoscopic group (A) consisted of 46 woman, of whom 35 received suppressive treatment with danazol, gestrinone, or leuprolide acetate for 4 to 6 months. Twenty four pregnancies were achieved in group A (52%) and 58 in group B (control) (61%). Only 4 (36%) of the women in group A who did not receive suppressive treatment became pregnant. According to the revised American Fertility Society's classification of endometriosis, 18 (51%) of 35 pregnancies were achieved in women with moderate disease in group A and 41 (64%) of 64 in group B. In those with severe disease, 6 (55%) of 11 became pregnant in groups when comparing global results, ovarian endometrioma size, medical treatment, and severity of endometriosis. Given comparable surgical expertise, operative laparoscopy should be the procedure of choice in the treatment of infertility associated with ovarian endometrioma whenever possible, due to its recognised advantages.

Falcone et al.(1996) ⁽⁴⁹⁾ in their study suggested that pregnancy rates with endometriosis-associated infertility may be improved by laparoscopic surgery or laparotomy for moderate to severe disease. Surgery for minimal to mild disease does not increase pregnancy rates. Medical treatment has not been shown to increase fecundity for any stage of the disease. Pregnancy rates with assisted reproductive technology for endometriosis appear to be comparable with those for tubal disease that are also treated with assisted reproductive technology. Medical and surgical treatments for pelvic pain with endometriosis are both effective, but surgery avoids the side-effects associated with drugs and may result in lower recurrence rate.

Schindler et al.(1998) ⁽⁵¹⁾ analysed the data of 198 patients, most of them with recurrent endometriosis histologically confirmed during first-look laparoscopy. Patients were treated in a prospective, multicentre phase III study with 6 months GnRHa leuprorelin acetate depot (LAD) followed by a second-look laparoscopy for precise assessment of therapeutic effects. These results can be claimed as the prerequisites for long-term relief of endometriosis complaints and encouraging pregnancy rates in endometriosis related infertility. This confirms great clinical benefit of the combined medical-surgical approach for the treatment of this enigmatic disease.

In vitro fertilisation for the treatment of endometriosis-associated infertility

The objective of Kodama et al.(1996) ⁽⁵²⁾ study was to evaluate the effectiveness of IVF treatment in endometriosis-associated infertility (n=118 infertile patients in whom diagnosis of endometriosis was established by laparoscopic examination).The prognoses of 60 patients (IVF group) who started within 6 months after laparoscopy were compared with those of 58 patients who were managed expectantly without IVF treatment during the same period. The cumulative conception rates at 36 months after laparoscopy were 62% in the IVF group and 43% in the control group, and difference was not significant. For patients 32 and more years of age, the conception rates were significantly higher in the IVF group (59% versus 29%). A relatively large but non significant difference in the conception rate between the two groups was observed in patients with endometriosis at stages III or IV (52% versus 27%). They concluded that in vitro fertilisation treatment provides better prognosis in patients 32 and more and is recommended for such patients. The benefit of treatment appears to be greater in patients with more advanced stages of endometriosis.

Chillik et al.(1985) ⁽⁵³⁾ studied 39 cycles in patients with a history of endometriosis who went through in IVF. The pregnancy rates per cycle were 33%, 60%, and 70%, respectively (groups I and II, no significant difference; groups II and III, p < 0.01). There was also a significant difference in the number of pregnancies per transferred cycles. The reproductive potential, which seemed to be similar in groups I and II, was impaired in the group with severe endometriosis.

The objective of the study of Tummon et al.(1997) ⁽⁵⁵⁾ was to evaluate the efficacy of superovulation and IUI versus no treatment for infertility associated with minimal or mild endometriosis. Three hundred and eleven cycles in 103 couples in whom minimal or mild endometriosis was the sole identified subfertility factor. Interventions: superovulation with FSH and IUI. Results: Live birth followed 14 of 127 (11%) superovulation and IUI cycles and 4 of 184(2%) no-treatment cycles. OR was 5.6(95% CI=1.8-17.4) in favour of superovulation and IUI. They suggested that treatment with superovulation and IUI was associated with superior outcome both by crude live-birth rates and proportional hazard analysis.

Lopes et al.(1988) ⁽⁵⁴⁾ compared the results of IVF in patients with endometriosis after ovulation induction with clomiphene-human menopausal gonadotrophin (group 1) and GnRH analog's short administration using regimen and human menopausal gonadotrophin (group 2). Fourty cycles have been conducted for 18 patients. Mean duration of infertility was 6.9 years and mean age of patients was 34.8 years. The fertilisation and cleavage rates are not affected by the presence of endometriosis when compared to IVF patients without endometriosis. The number of recovered oocytes decreases with the severity of endometriosis, but the pregnancy rate was not affected. Overall 3rd trimester pregnancy rate was 12.5% per induction cycle and 21.7% per embryo transfer. They concluded that the presence of endometriosis does not affect the quality of the oocyte and is not a cause of exclusion in an IVF program.

Matson et al.(1986) $^{(56)}$ performed IVF and embryo transfer (IVF-ET) on women with tubal disease only (28 women, 40 cycles), endometriosis grade I (15 women, 24 cycles), grade II(25 women, 37 cycles), grade III(26 women, 36 cycles), or grade IV (31 women, 52 cycles9. Pregnancy rates per cycle were similar to that of the tubal group(18%) for women with grade I(13%) or grade II(14%) endometriosis, lower in women with grade III endometriosis (6%) and significantly reduced in women with grade IV (2%, p <0.05).

The objective of the study of Kodama et al.(1996) ⁽⁵⁷⁾ was to evaluate the effectiveness of IVF treatment in endometriosis-associated infertility. One hundred and eighteen infertile patients in whom diagnosis of endometriosis was established by laparoscopic examination. The prognoses of 60 patients (IVF group) who started IVF treatment within 6 months after laparoscopy were compared with those of 58 patients who were managed expectantly without IVF treatment during the same period. Results: the cumulative conception rates at 36 months after laparoscopy were 62% in the IVF group and 43% in the control group, and the difference was not significant . For patients 32 and less years of age, the conception rates were significantly higher in the IVF group (59% versus 29%). The authors concluded that IVF treatment provides better prognosis in patients 32 or less years of age and is recommended for such patients. The benefits of treatment appear to be greater in patients with more advanced stages of endometriosis.

The objective of Huang et al.(1997) ⁽⁵⁸⁾ was to compare the outcome of IVF and ET (IVF-ET) after laparoscopic surgery in women with endometriosis. It was a retrospective survey of hospital and office charts using a computerised worksheet. Charts of 67 women with minimal or moderate to severe endometriosis were reviewed. Seventy five consecutive cycles of IVF-ET were performed in these patients who failed to conceive after laparoscopic conservative surgery. The authors suggested that the outcome of IVF-ET in patients with endometriosis after laparoscopic surgery did not differ from that in the group with tubal factor infertility, but the former required more ampoules of gonadotrophin to achieve the same response. The advantages of laparoscopic surgery in women with endometriosis should be probably correlated with success of IVF-ET .

Pagidas et al.(1996) ⁽⁵⁹⁾ evaluated the efficacy of reoperation for stage III or IV endometriosis-related infertility versus IVF-ET. Twenty three couples with stage III or IV endometriosis-related infertility undergoing reoperation for stage III or IV disease, both groups undergoing treatment after failed initial surgery to restore fertility. They concluded: if initial surgery fails to restore fertility in patients with moderate (stage III) or severe

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(stage IV) endometriosis-related infertility, IVF-ET is an effective alternative; reoperation for asymptomatic patients offers little added benefit.

Agnani et al.(1991) ⁽⁶⁰⁾ investigated the results obtained by IVF in cases of pelvic endometriosis. 58 stimulation cycles have been analysed in function of previous curative treatment, which may have been a combined medico-surgical treatment or conventional surgical treatment. 6 pregnancies which progressed to full term were achieved in the 8 patients who had previously received medico-surgical treatment. Twenty punctures were performed. In patients who received initial medical treatment, there were no pregnancies carried to full term and 3 clinical terminations of pregnancy for a total of 20 punctures. A coelioscopy check-up revealed persistent endometriosis in 10 patients. No clinical pregnancy was observed following primary surgical treatment. In all cases, there were lesions affecting the ovary and the numbers of oocytes and embryos were significantly reduced.

Medical versus surgical therapy

Some studies ^(48,50) indicated that medical and surgical treatments sometimes have the same results in infertile patients. However, laparoscopic surgical treatment appropriately completed at the time of diagnosis has a distinct advantage over medical therapy ^(42,43,44). All medical therapy regimens require at least 6 months of therapy before the patient can even begin her attempts to conceive. On the other hand, patients fully treated at their initial laparoscopy can try to conceive within 3 weeks, a significant saving in time over medical management. In addition, patients undergoing medical therapy must tolerate the side effects of their treatment for at least 6 months. Surgically treated patients recover from their laparoscopic procedure in 1-2 weeks.

Laparoscopic treatment of endometriosis may sometimes be combined with medical therapy involving progesterone or GnRH agonists ⁽⁵⁰⁾. This combination is used in patients who are not currently attempting pregnancy, but plan to do so in the next 1 to 2 years. Medical therapy is used in these patients (after laparoscopic treatment) in the hope that it may inhibit growth of new endometriotic implants before the patient begins her attempts at pregnancy. Some patients will be placed on medical therapy preoperatively to suppress ovulatory function so that functional ovarian cysts will not be confused with endometriosis ⁽⁵⁰⁾. Potential disadvantages of preoperative medical treatment include the changed appearance of endometriosis, which might make it more difficult to diagnose; drug cost and side effects and delay in attempting pregnancy.

Conclusions

1.Laparoscopic surgery is superior to medical treatment for minimal and mild endometriosis-associated with infertility.

2. For moderate and severe disease, laparoscopic surgery is usually used and has the best correlation with pregnancy rate.

3. A comprehensive long-range treatment approach must be individualised for each patient.

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Management of endometriosis associated infertility

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Objectives:

Purpose of review: on the basis of literature to compare the different treatment modalities of endometriosis associated infertility.



2



Methods:

Selection of literature by computerised Medline search.



Endometriosis is diagnosed in about 30%-40% of women being studied for infertility in whom no other significant abnormalities are found.

All stages of endometriosis are associated with infertility. Some have suggested that it may in fact be that the infertility causes early stages of endometriosis.

A common assumption is that the endometriosis causes the infertility.



Mechanisms of endometriosis - associated infertility are:

- disturbances in the ovum pick-up mechanism,
- alterations in peritoneal fluid parameters,
- hormonal alterations,
- protein factor alterations,
- o cellular alterations,
- systematic alterations.



Treatment options:

1. Medical therapy

 Surgical treatment : Microsurgery, laparoscopy, laser therapy

3. Combined hormonal and surgical treatment

4. In vitro fertilization treatment for endometriosis-associated infertility

Medical therapy

7

A variety of hormonal regimens have been advocated: Methyltestosterone Danazol Diethylstilbestrol **Clomiphene citrate** Tamoxifen Gestrinone Medroxyprogesterone acetate Gonadotropin-releasing hormone agonists (Zoladex, Enanthoine)



Clinical effectiveness of ovulation suppression therapy for endometriosisassociated infertility: the combined data from trials (Thomas and Cooke 1987; Bayer et al 1988; Telimaa et al 1988;) comparing danazol, gestrinone and medroxyprogesterone acetate with placebo show no evidence of a treatment effect.

Surgery treatment:

Surgical-laparoscopicaltreatment^{*}for endometriosis has been shown to improve fertility in advanced stages of endometriosis.

Modern surgical techniques such as those using ultrapulse lasers are just now being shown to be of value in the treatment of minimal and mild endometriosis.



Laparoscopy is:

- Minimally invasive same day surgical approach.
- A telescope is entered through an incision about 1 cm long near the umbilicus and one to three smaller incisions are also usually made in the lower abdomen for the entry of additional instruments.
- Postoperative recovery usually only a few days with little time out from work.

The combined data from cohort studies (Levinson 1989; Paulson et al 1991; Nowroosi et al 1987; Fayez et al 1988: Chong et al 1990; Seiler et al 1986; Marcoux S. et al 1997; Nezhat C. et al 1989; Murphy et al 1991; Chapron et al 1999; Gordts S. et al 1984; Pouly JL et al 1996; Rock JA et al 1981;) comparing laparoscopic ablation therapy with ovulation suppression or no therapy showed significant evidence of a laparoscopic treatment effect.



Combined hormonal and surgical treatment

The treatment of infertility associated with endometriosis is controversial and usually consists of either medical therapy with hormonal manipulation designed to suppress the disease, surgical therapy designed to debulk the disease and repair anatomic distortion, or combination of both.

The studies of Ruhlmann et al 1996; Falcune et al 1996; Schindler et al 1998. analyzed the data of many patients confirms great clinical benefit of the combined medical-surgical approach for the treatment of this enigmatic disease.

In vitro fertilization treatment for endometriosis-associated infertility

It is the last method of treatment of endometriosis-associated infertility. Different authors get different results and different pregnancy rates. But general conclusion of most of authors was similar: IVF treatment provides better prognosis in patients of 32 years old or less and benefits of treatment appear to be greater in patients with more advanced stages of endometriosis.

Medical versus surgical treatment

In the infertile patients some studies indicated that medical and surgical treatments sometimes have the same results. However, laparoscopic surgical treatment appropriately completed at the time of diagnosis has distinct advantage over medical therapy.



All medical therapy regimens require at least 6 months before the patient can begin her attempts at pregnancy. Patients fully treated at their initial laparoscopy begin attempts at pregnancy within 3 weeks, a significant savings in time over medical management. In addition, patients undergoing medical therapy must tolerate the side effects of their treatment for at least 6 months. Surgically treated patients recover from their laparoscopic procedure in 1-2 weeks.





Laparoscopic treatment of endometriosis may sometimes be combined with medical therapy involving progesterone or GnRH agonists. This combination is most often used in the patient who is not currently attempting pregnancy, but plans to do so in the next 1 to 2 years. Medical therapy is used in these patients (after laparoscopic treatment) in the hope that it may inhibit growth of new endometriotic implants before the patient begins her attempts at pregnancy.



Some patients will be placed on medical therapy preoperatively to suppress ovulatory function so that functional ovarian cysts will not be confused with endometriosis.

Potential disadvantages of preoperative medical treatment include the changed appearance of endometriosis, which might make it more difficult to diagnose; drug cost and side effects; delay of diagnosis; and delay in attempting pregnancy.

Conclusions:

- Laparoscopic surgery is superior to medical treatment for minimal and mild endometriosisassociated infertility.
- For moderate and severe disease, laparoscopic surgery is usually used and has the best correlation with pregnancy rate.
- A comprehensive longterm treatment approach must be individualised for each patient.

MEDICAL VERSUS SURGICAL TERMINATION OF PREGNANCY

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Abstract

Objective: To provide the background literature for a systematic review of evaluation of medical methods in comparison to surgical methods for termination of pregnancy. Methods: A Medline search is performed. Review articles and studies of 100 or more women on first trimester pregnancy terminations were included. Results: Mifepristone with a prostaglandin and methotrexate with misoprostol are shown to be effective for termination of first trimester pregnancies. Various dose regimens have comparable efficacy. Side effects of medical methods are heavy bleeding, pain and gastrointestinal side effects. The amount of bleeding and pain is increased with the gestational age. The most common reasons for choosing medical methods include the less invasiveness, more naturalness and privacy of the medical procedure. Prolonged bleeding, pain, the inconvenience of several visits and the lack of immediate confirmation of success are among the most frequent complaints after the procedure. When compared to surgical methods, medical methods offer slightly lower efficacy, takes longer time, leaves the patient more conscious of bleeding and requires extra visits. Conclusion: Summarising the evidence from the studies comparing medical methods to surgical ones for pregnancy termination is a difficult process because of the important differences in study designs and the variety of both the medical and surgical methods. A systematic review comparing the medical approach to surgical approach will be valuable in evaluating the existing literature.

Key words: abortion, pregnancy termination, mifepristone, methotrexate, misoprostol

Background

Pregnancy terminations have been performed world-wide since ancient times. Millions of unwanted pregnancies occur each year. Some of them are carried to term, some of them end in miscarriages and others are terminated using different methods. It has been estimated that 42-50 million pregnancy terminations occur each year.1 One third of all pregnancy terminations are estimated to be performed under unsafe conditions leading to 13 % of all maternal deaths 2,3 and result in 135-275 deaths each day.4 The majority of these deaths are in developing countries where pregnancy terminations are either illegal or legal but not available and accessible. Data shows that the global case fatality rate associated with unsafe abortion is probably 700 times higher than the rate associated with the legal pregnancy termination in the United States.4

Unsafe abortion is defined as those abortions not being provided through approved facilities and/or persons. They are characterised by the lack or inadequacy of skills of the provider, hazardous techniques and unsanitary facilities and are among the great neglected problems of healthcare in developing countries.4 Ninety per cent of unsafe abortions take place in developing countries.2

Surgical termination of pregnancies can be performed legally in modern aseptic conditions and may be available to women in need but especially in developing countries, this is not always the case. Twenty-two percent of countries in the world have laws allowing pregnancy terminations on demand. Among developing countries, this ratio is 6 %.2 Legalisation of pregnancy terminations has reduced maternal mortality rates in certain countries.3 Nevertheless, there are many countries like India and Russia, where pregnancy termination is legal but access to adequate conditions is severely limited.2 Thus, women with limited access to safe services seek to terminate unwanted pregnancies with unsafe procedures.

Surgical pregnancy termination methods currently available are, vacuum aspiration with or without dilatation, and dilatation and curettage (D&C).

Vacuum aspiration is the evacuation of conception products using a vacuum source. The source can be either an electric pump or a hand-held plastic syringe (Manual Vacuum Aspiration, MVA). A cannula attached to the vacuum source is passed into the uterine cavity and products of conception are evacuated. Cervical dilatation is not usually necessary for pregnancies up to 63 days of amenorrhoea. When dilatation is necessary for pregnancies up to 63 days of amenorrhoea. When dilatation is necessary for pregnancies up to 63 days of amenorrhoea and for those with more than 63 days of amenorrhoea, dilatation and vacuum aspiration is used. Ripening of the cervix before dilatation may be useful in order to reduce the incidence of minor cervical tears and incomplete evacuation due to inadequate dilatation.5 Agents used for this purpose are; Laminaria, Lamicel and Dilapan which are hydrophilic dilators that absorb water from the cervical secretions thus, dilate the canal and also soften the cervix. Foley catheters can be used for mechanical preparation. Prostaglandins, when given 3 hours before vacuum aspiration lead to the dilatation of the cervix and sometimes even initiate abortion within 12 hours. Mifepristone is also used for cervical dilatation but has to be administered 24-48 hours before the procedure.

Vacuum aspiration is generally performed as an outpatient procedure under local anaesthesia. But some providers and users prefer general anaesthesia. When local

anaesthesia is used, the pain of dilating the cervix is blocked but the women still feel uterine pain or cramping due to the evacuation of products of conception.

D&C is still used routinely in many countries although it is replaced by vacuum aspiration in most developed countries.6 Conception products are removed with a sharp metal curette following dilatation of the cervix. The cervix is dilated with rigid dilators. D&C is usually performed under general anaesthesia although sometimes it can be carried out with local anaesthesia.6

Surgical pregnancy termination methods are found to be safe and effective if they are carried out under modern aseptic conditions.6 Mortality rate is under 1 per 100,000 and the major complication rate was found to be 0.7 per 100,000 surgical pregnancy termination procedure in developed countries.5,7 Under unsafe conditions, mortality rates are estimated to range from 100 to 1,000 in 100,000 procedures.4 The success rate of vacuum aspiration is around 98 %.8

Morbidity of surgical pregnancy terminations are affected by gestational age, the method of the termination, age and parity. The risk of pregnancy termination increases with the

gestational age. The lowest major complication rate is at 49-to-56 days of pregnancy. The major complication rate of dilatation and curettage is 2.3 times higher than vacuum aspiration.7 Serious complications are more frequent in parous women and with increasing age.5

Unrecognised failed pregnancy termination rate was found in 2.3 per 1,000 procedure in a case series of 33,090 women.9

The complications of surgical evacuation are, infection, cervical laceration, incomplete evacuation, uterine perforation, haemorrhage and complications due to anaesthesia. The medical literature on complications of surgical pregnancy termination procedures under unsafe conditions particularly in developing countries is scanty. Unsafe procedures may lead to further infertility, miscarriages and low birth weight in subsequent pregnancies in addition to the complications above.5,10

In the last decade, attempts to develop alternative pregnancy termination methods have largely focused on medical methods. Medical methods could increase the choice, eliminate the risks of surgical procedures performed under inadequate conditions and thus, contribute to improving reproductive health.5 They could be successfully provided by medical practitioners even if they are not gynaecologists, by trained nurses and even by supervised paramedical staff particularly in developing countries, which would increase the accessibility of women to pregnancy termination services.

Medical pregnancy termination methods evolved largely in the last ten years and they provide new options for women seeking to terminate their pregnancies. Some authors think they might provide good alternatives to unsafe procedures and would increase the access to services11,12 while others think they will not be a panacea for limited access to services.13

Currently, 20 % of pregnancy terminations in England, 30 % of those in France and 60 % of those in Scotland are carried out medically.14,15

Medical methods used for pregnancy terminations are prostaglandins, mifepristone alone,

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mifepristone with prostaglandins and methotrexate with prostaglandins.

Prostaglandins (gemeprost, metenoprost, misoprostol) have softening effect on the cervix and so facilitate dilatation. Gemeprost and metenoprost given vaginally have been shown to terminate pregnancies up to 49 days of amenorrhoea but are not routinely used because they require to be used in small doses at intervals of 3-6 hours and the process is slow.5 Misoprostol is an anti-ulcer drug widely found over-the-counter and is used for pregnancy terminations informally in some parts of the world.11,16

Mifepristone is an antiprogestin and blocks the progesterone receptors. This blockage results in the breakdown of maternal capillaries in the decidua, the synthesis of prostaglandins by the epithelium of decidual glands and inhibition of prostaglandin dehydrogenase.5 Pregnancy support is inhibited and increased prostaglandin induces uterine contractions. Mifepristone increases the sensitivity of the uterus to prostaglandins by a factor of five. This effect develops over 24-48 hours and this is the rationale for giving prostaglandins vaginally 36-48 hours after the administration of mifepristone. Mifepristone alone with divided doses up to a total of 1600 mg given over a period of 4-7 days was found to be successful in 60-65 % of cases for pregnancies up to 56 days of amenorrhea.5

Mifepristone has been licensed in France and China since 1988, in the United Kingdom since 1991 and in Sweden since 1992. The recommended dose regimen by the manufacturer is, 600 mg oral mifepristone followed by a vaginal prostaglandin (gemeprost 1g). But a variety of different regimens have been used.

Because of the commercial and political difficulties in producing and distributing mifepristone, other alternatives were searched.17 The clinical application of intramuscular methotrexate to treat early extrauterine pregnancies led to its use in intrauterine gestations.13

Methotrexate is a folic acid antagonist which inhibits purin and pyrimidine synthesis, thus halts cell division. The use of methotrexate with misoprostol was first introduced by Creinin in 1993.13

This review aims to look at review articles and clinical studies describing the various interventions, the mechanism of pregnancy termination methods and main medical, social and psychological issues surrounding pregnancy terminations.

Objective

Objective of this review is to provide the background literature for a systematic review of evaluation of medical methods in comparison to surgical methods for termination of pregnancy.

Methods

A MEDLINE search was performed back to 1966 using the key words «abortion» «pregnancy termination» «vacuum aspiration» «mifepristone» «misoprostol» and «methotrexate». World Health Organisation (WHO) resources have been consulted. The review was limited to documents in English.

This search strategy revealed a total of 112 articles. Only documents related to first trimester (pregnancies up to 84 days of amenorrhoea) pregnancy terminations were considered. Case series with 100 or more patients were selected. Mechanisms of pregnancy termination methods, medical, social, cultural aspects of pregnancy terminations and advantages, disadvantages of various methods from user and provider perspectives are discussed.

Results and Discussion

This search strategy yielded 12 review articles, 17 case series, two randomised controlled trials, four controlled clinical trials, one technical group report by WHO Scientific Group on Medical Methods for Termination of Pregnancy and one book and one monograph published by WHO.

Efficacy

The results of studies evaluating the effectiveness of various medical termination regimens with mifepristone are presented in <u>Table 1</u>.

In the first cohort study using methotrexate with misoprostol for pregnancy termination, Creinin used 800 µg misoprostol 3 days after 50 mg/m2 methotrexate for termination of pregnancies up to 56 days of gestation and in a later randomised trial, it was found that misoprostol was more effective when administered vaginally rather than taken orally and given 7 days instead of 3 days after the methotrexate. Drug cost is calculated as USD 413 per patient while the cost for mifepristone-gemeprost is around USD 100 and for mifepristone –misoprostol it is around USD 22.24

In a case series of 300 women, success rate was 91.3 % with 50 mg/m2 orally taken methotrexate followed 5-6 days later by vaginally administered 800 µg misoprostol.27

In a randomised trial from Cuba, three groups of randomly selected participants received 50 mg/m2 methotrexate intramuscularly and were instructed to self administer 800 µg misoprostol vaginally after three, four or five days. The success rates were found to be 93%, 92 % and 93 % in three groups.28

Wiebe compared methotrexate- misoprostol regimen to vacuum aspiration. The success rate was 91.8 % in the medical group.17

Blanchard reviewed eight studies on misoprostol alone for termination of pregnancies. Success rates were between 5-100 % and the review concluded that in spite of the difficulty on synthesising the data, misoprostol alone seemed to hold promise as it was inexpensive, stable and widely available.11

Side Effects

Side effects of medical methods are heavy bleeding, pain, nausea and vomiting and diarrhoea changing in severity due to the protocols and gestational age.8 They involve a longer duration of time from initiation until termination and more observed blood loss when compared to surgical procedures. Surgical procedure is a mechanical event done at a specific time and medical procedure is a process entailing a series of noticeable times; when the woman takes the various drugs, when she observes symptoms and when the expulsion occurs.29

In the multicentre trial conducted in China, Cuba and India, side effects with 600 mg mifepristone and 400 µg oral misoprostol were observed as abdominal cramping, nausea, vomiting and excessive bleeding. The per cent of women whose haemoglobin dropped >2g/dl was small and differed significantly between the medical and surgical method groups only in Cuba (medical 6.8 % vs surgical 0.8 %). The author interpreted that the reporting of more blood loss in the medical group could be due to their observing of all their blood loss.22

In a case series of 2121 women, the most serious side effect was observed as vaginal bleeding with 600 mg mifepristone and 400 µg oral misoprostol. The amount of bleeding increased with advancing pregnancy.23 The pain also is observed more with increasing gestational age.8

In another study comparing 0.5 mg vaginally given gemeprost to 600 µg orally taken misoprostol after 200 mg mifepristone, abdominal pain was greater in the gemeprost group while nausea and vomiting were higher in misoprostol group. The author claimed that nausea and vomiting could be related to a direct effect on the stomach and this could be reduced by administering misoprostol by the vaginal route.20

Grimes reviewed different studies with various regimens of mifepristone with either gemeprost or misoprostol given orally or vaginally. In most of the studies bleeding was found to be significantly greater with medical procedures than with suction curettage. Nevertheless, clinically important decreases in haemoglobin levels were rare. He concluded that women who are anaemic might not be appropriate candidates for medical pregnancy termination.13

In another review by Winikoff, prolonged bleeding and the long duration of treatment were the most common complaints in different studies with different regimens of mifepristone with prostaglandins.30

A study comparing vaginal prostaglandins to vacuum aspiration rated bleeding with medical method about twice as long with surgical method.30

Methotrexate with misoprostol has similar gastrointestinal side effects to the mifepristone-gemeprost regimen.14 With methotrexate-misoprostol regimens fewer than 2 % of women had a fall in haemoglobin levels of 20 % or greater.13 The mean total days of bleeding was 12.3 days in a study from Canada.17

Failed attempted expulsion is an infrequent but important complication of medical methods. Both methotrexate and misoprostol may lead foetal anomalies if the pregnancy persists.13

Misoprostol alone regimen is under interest with its potential efficacy especially in

developing countries considering the advantages of storage, cost and availability.17,31 Blanchard's review of misoprostol alone regimens emphasises that side effects are not different from those with the mifepristone-misoprostol regimen. Some of the studies been evaluated used a complex regimen with dose numbers ranging between two and six and this could be a disadvantage in integrating the method into health services.11

User Perspectives

Among the few studies which women were allowed to choose a method themselves, various results are obtained. In a study with 363 women, 20 % preferred mifepristone-gemeprost regimen and 26 % chose surgical method. 54 % of them had no choice. There were no significant difference in terms of age, parity, education and social status between the two groups. However, women who preferred surgical method lived a significant greater distance from the clinic.32 Probably they wished to avoid extra visits that medical methods require.

Another study from the United Kingdom (UK) compared 132 women having medical pregnancy termination to 143 having surgical procedure. Comparisons of demographic characteristics between the two groups indicated that those having the medical termination had obtained higher levels of educational qualifications and were more likely to be in a relationship which would be continuing after the termination. Other indicators showed no significant difference. Initial levels of anxiety or depressive symptoms were evaluated before the procedure and there was no significant difference between the two groups.33

Bachelot from France conducted a study involving 458 women comparing 600 mg mifepristone with 0.25 mg intramuscular sulprostone regimen to vacuum aspiration under local anaesthesia (VA-LA) and vacuum aspiration under general anaesthesia (VA-GA). 62% chose medical method. Women who preferred medical and VA-GA were younger. Medical group and VA-LA groups had higher education, and women who chose medical method were in a higher occupational status. 93 % of women in medical group and 95 % in VA-LA group had a «Western cultural background». 51 % of the medical group and 56 % of the VA-GA group were nulliparous.34

A study comparing methotrexate-misoprostol regimen to surgical method enrolled 405 women. 28.6 % chose medical method. It is considered as quite a high ratio as the medical method was offered only for research protocols in the US. Younger women were found to have tendency for a surgical procedure. As pregnancy termination with methotrexate-misoprostol regimen occur at women's homes the reason for this was considered to be the lack of necessary emotional support they would have at home. Wiebe did not find any significant difference among women having «non-Western» and «Western» background. The author emphasises that it was impossible to predict which women would choose medical methods on the basis of demographics.17

Married women with children often chose surgery because of the conflict between responsibilities at home and the extra visits required by medical methods.22
Younger, single or nulliparous women were more likely to select the medical method in a study from Hong Kong.35

In the study of Henshaw, of the women who chose surgery, 40 % said medical methods were «too slow», 39 % preferred to be unconscious and 23 % feared from adverse physical effects of a medical procedure. Those who preferred the medical method expressed fear of surgery or anaesthesia (59 %), felt medical procedure was «more natural» and believed surgery was «too fast».32

In the study from the UK, the most frequent reason for choosing the medical termination was to avoid some aspects of the operative process, particularly the anaesthetic (61 %). 32 % of women chose it for the process being simpler and natural. Those who chose the surgical procedure generally wanted to avoid the awareness and involvement in the process of

termination (49%) and were concerned about the pain (16%) or emotional impact (14%) of the medical termination. 11% of women who chose medical and 14% of those who chose surgical methods reported the impact of the other's advises. Women were able to access medical termination more rapidly than the surgical procedure and many women choosing to have a medical termination method indicated that this factor was important in their choice.33

Bachelot's study from France reported valued characteristics when choosing medical method as newness, less invasiveness, the possibility of verifying the expulsion and the naturalness of the method.34

In another study, the most common reasons for choosing medical procedure were fear of surgery (81 %), fear of general anaesthesia (11%), less injury to the body (21%) and convenience for work (41%). Those who chose surgery said they preferred it because it was quick and convenient (82%), they did not like the number of visits or the length of the medical procedure (69%) or they were worried about drug efficacy and side effects (11%).35

Wiebe evaluated the methotrexate-misoprostol regimen from users' perspectives and for women chosen medical procedure, expected pain (39.3 %), fear of surgery (44.7%) were very important. The timing of the procedure was also reported to be very important. In their written comments, many women mentioned that it felt better emotionally to terminate pregnancy as early as possible. This was one of the main reasons for choosing medical method.17

In a study from Sweden, 128 women were allocated according to their preferences to undergo vacuum aspiration, vacuum aspiration with dilatation or medical procedure. The great majority of women (88%) who had a vacuum aspiration, 72 % who had a dilatation and vacuum aspiration and 87 % of those who had a medical procedure evaluated the experiences positively. Those who had a medical procedure reported more pain and evaluated the bleeding heavier than did the women who had undergone surgical procedure. There were no significant differences between the three procedures in outcomes such as psychological difficulties, feeling of guilt or regret. However, women undergoing medical procedure reported significantly more feelings of shame.36

Another study has evaluated psychological responses following medical termination of pregnancy and they were not able to find evidence that medical procedure led to an increase in post abortion low self esteem when compared to vacuum aspiration.37

Henshaw's investigations after the procedure showed the high level of acceptability among

the women having medical and surgical procedures who had chosen their own methods. The two methods were rated equally on all factors except the higher rating of pain in the medical procedure. Women who had assigned to a method showed lower satisfaction rates. Seventy-four percent of those who had a medical procedure and 87 % of those who had a surgical procedure would choose the same method again. Of women who had assigned to the medical procedure and found it unacceptable, 95% had been in 50 or more days of gestation.32

The study of Slade, when asked about choices for a subsequent pregnancy termination, 92 % of the women having the surgical method would opt for this again while only 53 % of those having the medical process would make the same choice of method. The main reasons for changing to a surgical procedure under general anaesthesia were : the experienced medical termination was highly stressful (33 %), surgical method would involve less pain both at that time and after the termination (25 %), to avoid seeing the foetus (18 %). The main reasons for the one's who wish to change to a surgical procedure under local anaesthesia were : the expectation that it would take a shorter time (41 %), be less distressing (24%), involve less use of chemicals (18 %) and avoid seeing the foetus (18 %). Only 5 % of women having a surgical termination would opt in future for the medical method.33

The majority of women in three groups (mifepristone-intramuscular prostaglandin, vacuum aspiration with general anaesthesia and vacuum aspiration with local anaesthesia) expressed satisfaction with their method in a study conducted in France. Dissatisfaction rate was higher in medical group than in surgical groups (12% vs 4%). This entity was interpreted by the authors as women who heard their physician and media talking about the new method and saw it as a «magic» one. Once their procedure did not appear so easy and quickly; dissatisfaction occurred. The authors also pointed out the medical personals' strong influence on the selection of a pregnancy termination method.34

Women's perceptions after the medical procedure was evaluated by Tang. Eighty five per cent of women who tried medical process said they would use it again. Most common reactions after the process were relief (38%) and complaints that the procedure took too long (11%) or that there was too much bleeding (10%).35

It is hard to summarise the data from studies comparing medical methods to surgical ones because the drug regimens are different and service delivery is not uniform both for surgical and medical methods. Individuals in comparative studies are thus assessing various medical methods against an alternative that varies from study to study (Henshaw and Holmgren performed vacuum aspirations with general anaesthesia while Wiebe performed with local anaesthesia in their studies comparing the medical and surgical pregnancy termination methods). 8,17,36

However, regardless of the drugs or protocols used, there are some main characteristics of medical methods; When compared to surgical methods, medical methods offer slightly lower efficacy, takes longer time, leaves the woman more conscious of bleeding and expulsion of conception products and requires additional visits.

Advantages of medical methods include the ease of swallowing pills, privacy, naturalness and avoidance of surgery and anaesthesia. Disadvantages can be summarised as the longer process, gastrointestinal side effects, prolonged bleeding, higher failure rate, the inconvenience of several visits and for some women the lack of immediate confirmation of success.

There is few data on providers' attitudes towards medical methods of pregnancy terminations. A study with nurses in a clinic in Scotland found out that after the introduction of medical methods, 63 % of nurses reported no change in job satisfaction while 27% reported decreased satisfaction and 10% reported increased satisfaction. Those who found their work less rewarding cited distress at seeing the products of contraception.30 Healthcare providers are found to have a strong preference for early pregnancy termination.5 Pregnancy termination service providers who are target of the antiabortion activists particularly in the US may prefer to provide medical methods because they would be less visible than providing surgical methods.38

Conclusion

There are many studies on medical methods of pregnancy termination and comparisons of them with surgical methods. Various regimens with different drugs, doses, administration, and service delivery procedures of medical methods has been compared to different service delivery and methods of surgical procedures in these studies. Summarising the evidence is a difficult process for these reasons. A systematic review comparing the medical approach to surgical approach will be valuable in evaluating existing literature.

References

27.11.02



MEDICAL VS SURGICAL TERMINATION OF PREGNANCY

Lale Say Istanbul Medical Faculty

Demography of pregnancy termination

- 42-50 million pregnancy terminations occur each year (Henshaw 1999)
- 1/3 of all pregnancy terminations are performed under unsafe conditions (WHO 1999)
- 13% of all maternal deaths are due to unsafe abortions (Singh 1998)
- 135-275 women die from unsafe abortions each day (wно 1998)



Abortion that is not been provided through approved facilities and/or persons (WHO 1998)



- Vacuum aspiration without dilatation
- Vacuum aspiration with dilatation
- Dilatation and Curettage (D&C)

Mortality/Morbidity of surgical termination

Safe conditions

Unsafe conditions

Death rate

< 1 / 100,000

100-1000 / 100,000

Major complication rate

0.7 / 100,000





Infection Cervical laceration

Further infertility

Incomplete evacuation

Haemorrhage

Uterine perforation

Subsequent miscarriages

Low birth weight infant in future pregnancies

Anaesthesia complications



- Prostaglandins (gemeprost, metenoprost, misoprostol)
- Mifepristone (RU 486)
- Mifepristone with prostaglandins
- Methotrexate with misoprostol

Efficacy of medical methods (I)

<u>Protocol</u>

- Mifepristone 600 mg (oral)
 Gemeprost 1 g (vaginal) 48 hr later
- Mifepristone 200 mg (oral)
 Gemeprost 0.5/1 g (vaginal) 48 hr later
- Mifepristone 600 mg (oral)
 Misoprostol 400 ug (oral) 48 hr later

Success rate (range, %)

94-96.5

94-96.7

81.7-94.8

Efficacy of medical methods (II)

Protocol

- Success rate (range, %)
- Mifepristone 200 mg (oral)
 Misoprostol 800 ug (vaginal) 36-48 hr later
- Methotrexate 50 mg/m² (oral)
 Misoprostol 800 ug (vaginal) 3-7 days later
- Misoprostol alone up to 2400 ug with variable dose numbers orally or vaginally

84-97.6

91.3-93

5-100



 Various protocols of mifepristone with prostaglandins and methotrexate with misoprostol have comparable efficacy

Efficacy decreases with increasing gestational age



More bleeding Clinically important decreases in hemoglobin levels are rare (Grimes 1997)

Amount of bleeding increases with gestational age (Spitz 1998)

* when compared to surgical methods



More pain • Pain is more observed with increasing gestational age (Henshaw 1994)

Vaginal suppository users require more analgesia (Holmgren 1992, Baird 1995)

* when compared to surgical methods



Gastrointestinal side effects (nausea, vomiting, diarrhoea)

• Nausea and vomiting are more observed with oral misoprostol regimens (Baird 1995)



Reasons for choosing medical method

new less invasive simple natural fear of surgery

earlier than surgery

fear of anaesthesia

privacy

possibility of verifying the expulsion



Reasons for choosing surgical method

avoidance of involvement in the process

convenien

1

unsure about drug efficacy and side effects

quick

medical methods require more visits

less painful

avoidance of emotional impact of medical process



Post abortion attitudes of medical method users

painfulsafeprolonged bleedingsafeconvenientavoidance of surgery

time-consuming

not as quick as expected

stressful

54-85% would use again

Main characteristics of medical methods*

- Offer slightly lower efficacy
- Take longer time

 Leave the women more conscious of bleeding and expulsion of conception products

Require additional visits



 A variety of medical regimens and protocols with different service delivery procedures have been compared to different methods and service delivery requirements of surgical procedures

 A systematic review comparing the medical approach to surgical approach will be valuable in evaluating the existing literature OBSTETRIC ULTRASONOGRAPHY AND MATERNAL AND PERINATAL MORTALITY

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INTRODUCTION

Diagnostic ultrasound has become an imaging technique widely used in developing and developed countries. It has made possible new areas of diagnosis in obstetrics in particular. There have been controversies about the use of ultrasonography in developed countries. Routine scanning in low risk women has not been demonstrated to improve the perinatal outcome in most studies. It has rather increased the cost of medical care(1).

The situation in developing countries needs critical evaluation. Maternal and perinatal mortalities are very high. We are often dealing with a large percentage of high risk women at any antenatal or labour ward. These patients might benefit from routine scanning although the cost might be high in terms of training the personnel and maintaining the equipment.

GENERAL OBJECTIVE

To evaluate the implementation of ultrasonography in developing countries such as Ghana.

SPECIFIC OBJECTIVES

To evaluate the sensitivity and specificity of ultrasonography in the diagnosis of some specific pathologies which contribute to maternal and perinatal mortality (ectopic pregnancy, placenta praevia, trophoblastic diseases, pelvic abscess, oligohydramnios and macrosomia)

BACKGROUND

Ghana is a developing country in West Africa. It has a total population of about 18 million and the projected population in 2025 is 36.5 million. The annual growth rate is 2.87% and the average birth per woman is 5.7. The contraception rate is 10-20% and the literacy rate of the women is 54%. The GNP per capita is \$390(2)

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There are 2 teaching hospitals and at least a specialist hospital in each of the 10 adminstrative regions of the country. Each region is divided into districts. Each of the 120 districts has a hospital which supervises the other smaller hospitals, clinics, maternity homes and primary health care out-reach programmes. With a maternal mortality of 700/100,000 and a perinatal mortality of 75/1000 at the Korle Bu Teaching Hospital, a lot has to be done to improve the health care delivery system(3). During the past 3 years, the Ministry of Health has purchased some ultrasound machines to be used in the districts. Specialists at the Korle Bu Teaching hospital (two obstetricians, including the author, and two radiologists) have been running a training course for the senior medical officers in the districts.

There are anecdotal reports of improvement in maternal and perinatal outcomes in the centres where the ultrasound services are running. However, this has not been proven by research(3). This literature review of the work done in other countries will certainly help us in evaluating the role of obstetric ultrasonography in Ghana. The main causes of maternal and perinatal mortality in Ghana are : obstetric haemorrhage, sepsis , hypertensive disorders and dystocia. The main causes of perinatal mortality are: prematurity, infections, and birth asphyxia. The maternal and neonatal causes are not mutually exclusive and may occur together. The role of ultrasonography in managing these complications is the subject of this literature review.

- Haemorrhage: The principal subheadings are: ectopic pregnancy, abortion, trophoblastic diseases (in the first trimester), placenta praevia, abruptio placenta (mostly in the third trimester), ruptured uterus and postpartum haemorrhage (after labour and delivery)
- Infections : Puerperal infections.
- Prematurity : Iatrogenic causes, inadequate treatment of medical complications of pregnancy are important causes.
- Birth asphyxia : macrosomia, postmaturity and oligohydramnios are significant risk factors for birth asphyxia and trauma.

METHODS OF STUDY

My sources of the literature review are : the MEDLINE, the COCHRANE LIBRARY , and from PERSONAL COMMUNICATIONS. THE EFFICACY OF DIAGNOSING ECTOPIC PREGNANCY BY ULTRASONOGRAPHY

METHODS

The eligible studies for the review involved the use of sonography for the diagnosis of ectopic pregnancy. A comprehensive search for potentially eligible studies was conducted. Studies were identified in the Medline data base using the key words: ECTOPIC OR EXTRAUTERINE PREGNANCY, ULTRASONOGRAPHY, SENSITIVITY. The Cochrane Library was searched with the same keywords. References of the studies were identified by electronic search A form was designed to facilitate the process of data extraction. The true positive(TP), true negative(TN), sensitivity(ST), specificity(SP), positive predictive value(PPV), negative predictive value(NPV) were

calculated.

RESULTS (table 1, table 2)

A total of 11 studies were identified. All studies were cohorts with prospective or retrospective collection; 9 were done in developed countries while 2 were done in a developing countries.

All the studies involved patients who had been admitted to the hospitals during first trimester of pregnancy. It included women who reported to the hospitals with complications such as bleeding, and lower abdominal pain. They all had vaginal ultrasound.

The sensitivity reported in the various studies showed a range of 71% to 100%. The low sensitivity of 71% obtained in the centre in Nigeria might indicate that the cases were difficult or the sonographers needed more training. An alternative explanation might be that the centre could also have had a higher sensitivity if HCG was added to the screening procedure. The specificity ranged between 41% and 99% and the positive and negative predictive values ranged between 46%-100% and 65%-100% respectively. With the exception of one or two centres which showed low results all centres reported values more than 90%.

THE EFFICACY OF DIAGNOSING PLACENTA PRAEVIA BY ULTRASONOGRAPHY.

Placenta praevia is one of the major causes of obstetric haemorrhage. As the incidence of caesarean section continues to increase world-wide, the problem of placenta praevia/accreta is likely to be more common and obstetricians should be ready to face the late sequelae of their decision for caesarean section. The early diagnosis and treatment of placenta praevia is important to reduce mortality.

Ultrasonography has proved quite useful for the diagnosis and management of this condition. As a result, adequate preparation could be made before surgery. Some reports have indicated that it is useful to follow a mid-pregnancy diagnosis of placenta praevia with a confirmation of the diagnosis using the vaginal probe prior to delivery(15). Others have stated preventive measures a surgeon should adopt to reduce the morbidity and mortality associated with placenta praevia/accreta(16). The emphasis has been on early diagnosis with Doppler ultrasound. Other measures emphasised were the reduction of the massive blood loss averaging 3L with the administration of erythropoietin, acute normovolaemic haemodilution selective arterial embolisation, prophylactic uterine artery ligation and good surgical technique. It has also been found that the prior diagnosis with the Doppler ultrasound has reduced bladder injury during surgery for placenta accreta/praevia(17). In Ghana, the diagnosis of placenta praevia calls for an approach along the principles of expectant management until the fœtus has matured . Before any surgery is done adequate amount of blood and blood products as well as crystalloids and plasma expanders should be available.

THE EFFICACY OF ESTIMATING AMNIOTIC FLUID INDEX (AFI) FOR PREDICTING THE PERINATAL OUTCOME

Quite a number of our patients report to the antenatal clinic very late in pregnancy and for those whose scan reports show that they might be at term, it appears useful to estimate the AFI as a screening method to predict the perinatal outcome. A study of AFI of some 370 women who reported late in pregnancy (>37weeks gestation) for the first time at the antenatal clinic at the Korle Bu Teaching Hospital in Accra was done in 1998. It showed that the clinician could use an AFI score of <5cm to screen for adverse maternal and perinatal outcome such as fœtal distress, increased rate of induction of labour and high caesarean section rate. The sensitivity and specificity were about 70% each (18).

However, a case control study revealed that high risk pregnancies with AFI<5 appeared to carry intrapartum complication rates similar to those of similar high risk pregnancies with AFI>5 (19). Yet another study has shown that AFI<8 showed higher incidence of meconium staining, caesarean section for fœtal distress, abnormal fœtal heart rate monitoring and Apgar score of <7 at one minute(19). Further report from a longitudinal study concluded that irrespective of the rate of change in AFI, post-term pregnancies were associated with potential complications such as fœtal heart rate decelerations and meconium staining when the AFI<5. It was further found that prominent changes in the AFI of >50% increase or decrease had no association with adverse fœtal outcome provided the AFI remained >5(20). The AFI is therefore useful for predicting perinatal outcome.

THE EFFICACY OF USING ULTRASONOGRAPHY FOR DATING PREGNANCY

Preterm delivery of the baby can be caused by the obstetrician due to a mistake in estimating the gestational age. The accuracy of gestational age estimation is one of the important applications of ultrasound in developing countries where the low literacy rate makes recall of the last menstrual period(LMP) quite difficult. In addition, it has been shown that if LMP is used alone about 10% of the pregnancies are considered post-term. If ultrasonography is added the rate falls to 3-4%. Therefore the scan can help to prevent iatrogenic causes of preterm delivery. It has been emphasised that diagnostic scanning has contributed to the evaluation of fœtal condition in two ways—the detection of fœtal abnormality and the assessment of fœtal growth and development (21). Routine early scanning helps to detect structural abnormalities and provide accurate dating. Maternal alpha-fetoprotein levels complement ultrasonography in identifying abnormalities.

THE EFFICACY OF PREDICTING MACROSOMIA BY ULTRASONOGRAPHY

The definition of macrosomia varies among authors but the generally accepted definition is a

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foetal weight above 4 kg. The condition is more common with diabetes, rhesus incompatibility, postdate pregnancies and grandmultiparity. The assessment of fœtal weight can be made more accurately by ultrasound. Both, clinical and ultrasound assessment should be complimentary to each other. Complications associated with macrosomia include perinatal and maternal morbidity and mortality from traumatic deliveries.

Many authors have reported various methods for the use of ultrasound to measure the fœtal weight (e.g. the measurement of abdominal subcutaneous tissue thickness to predict macrosomia)(22). The mean tissue thickness differed significantly between normal and macrosomic foetuses (7.0mm versus 12.4mm,respectively ; p<0.0001. However, some have compared the clinical and sonographic models in an intrapartum setting and concluded that neither was superior to the other(23). Some authors in a cross-sectional study found that subcutaneous tissue/femur length ratio is a gestational age-independent parameter that has a greater sensitivity than the fœtal abdominal circumference or estimated fœtal weight formula for the intrapartum identification of large–for–gestational–age foetuses(24). For the fœtal weight estimation and prediction of fœtal macrosomia in non-diabetic pregnant women, it has been shown that increased incidence of macrosomia was observed with ultrasonic foetal weight estimation above 3400g and this level might be useful as a cut-off value for prediction of macrosomic foetuses in non-diabetic pregnant women when the Shepard's formula is used (25).

Ultrasonography is therefore useful for predicting macrosomia.

THE EFFICACY OF ULTRASONOGRAPHY IN DIAGNOSING TROPHOBLASTIC DISEASES

Trophoblastic diseases cause mortality through haemorrhage, infection or metastases. The diagnosis, often made clinically and biochemically, can be improved with the use of the ultrasound. The treatment should usually be prompt. Molar pregnancy should be evacuated. The post-evacuation follow -up should be thorough. Ultrasound can be used in the diagnosis and follow-up as the clinician combines the clinical picture, the serum HCG, and the scan report.

There are controversies about the use of the scan in the diagnosis of trophoblastic diseases. A study was carried out to evaluate the sonographic appearance of early complete molar pregnancy(26). The classical snowstorm appearance was found in all the molar pregnancies above the age of 13 weeks but only in 50% of the cases below 12 weeks. Another study indicated that the scan was good for the initial diagnosis (27) and yet another study showed that the first trimester scan picture was not specific(28). Bilateral lutein cysts were not found only in trophoblastic diseases but could also be found in normal pregnancies, and erythroblastosis foetalis(29). The sonographic pattern in trophoblastic diseases include cluster of high amplitude echoes within the myometrium and echo-free areas defining haemorrhage as well as theca lutein cysts(30).

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THE EFFECTIVENESS OF ULTRASONOGRAPHY IN DIAGNOSING PELVIC ABSCESS.

Pelvic abscesses in the reproductive age are usually attributed to complications of pelvic inflammatory disease (PID). These may follow sexually transmitted diseases(STDs) or post-abortion or post-delivery sepsis. The diagnosis is almost always clinical. However, in difficult cases the clinician may have to exclude important pathologies such as ectopic pregnancy, ovarian cysts and therefore ultrasound becomes useful. It is also useful in estimating the size and site of the abscess.

Following the diagnosis of pelvic abscess, laparotomy is usually performed once clinical improvement has not been obtained after conservative management with antibiotics. Drainage of the abscess and removal of the affected organ is undertaken. Failure to do this could result in complications such as peritonitis, septicaemia and mortality.

Modern management has changed this approach to the treatment of pelvic abscesses. Under sonographic guidance, pelvic abscesses can be drained successfully from the perineum (31), per vaginal (32) or per rectum (33) and (34). The success rates in all methods have been estimated to be more than 70%

THE EFFICACY OF ULTRASONOGRAPHY IN DIAGNOSING POST-PARTUM HEMORRHAGE(PPH)

PPH is associated with a high mortality if the treatment not started promptly. The diagnosis is often clinical. Primary PPH is mostly caused by retained placenta, atonic uterus, trauma to the genitalia and coagulopathy. There is hardly any role for ultrasound as the diagnosis is clinical.. Secondary PPH poses a different problem and the causes such as retained products of conception can be diagnosed with the aid of the scan. The possibility of scanning all women immediately post-partum in order to reduce the incidence of secondary PPH has been advocated (35) but this approach may not be cost effective in Ghana.

DISCUSSION

The important question is: Is ultrasonography effective, safe, and feasible, and is it an appropriate health technology for a developing country ? From the literature search, the sensitivity, specificity, positive and negative predictive values are high when ultrasound is used for the diagnosis of ectopic pregnancy. It can therefore be concluded that ultrasonography is a reliable tool for the detection of ectopic pregnancy. It should be emphasised that clinicians should always have a high a sense of suspicion for ectopic pregnancy when the patient presents at early pregnancy with lower abdominal pain and bleeding per vagina. The accuracy of the diagnosis can be increased with the determination of serum levels of HCG. In very difficult cases laparoscopy may be done to finally come to the diagnosis. Therefore, ultrasonography is an important tool used to diagnose ectopic pregnancy.

Some interventions performed during antenatal visits have been demonstrated to be effective in reducing the maternal and perinatal mortality and morbidity. These include routine iron and folic acid supplementation in areas of high prevalence of anaemia ; haemoglobin determination late in pregnancy; screening for asymptomatic bacteruria; screening for syphilis by serology; obtaining history of difficult labour in multiparous women; measurement of height in the nulliparous women and ECV are interventions of proven benefit to maternal outcomes. Routine measurement of fundal height, reduction of maternal physical strain, diagnosis and treatment of TB, malaria prophylaxis, adequate tetanus immunisation, antenatal and perinatal zidovudine in HIV positive mothers and one vaginal examination during pregnancy are interventions proven to benefit neonatal outcomes (37),(38). In contrast, the role of routine antenatal ultrasonography has been a controversial topic in developed countries. Therefore, before implementing this intervention in resource limited setting, careful assessment of the benefits and risks should be performed.

Nevertheless, the literature search has thrown light on the uses and limitations of obstetric ultrasonography in diagnosing difficult obstetric and gynaecologic conditions which have direct bearing on maternal and perinatal mortality. Maternal mortality and perinatal mortality are important issues addressed by international organisations such as WHO/Safe Motherhood Initiative and IAMANEH(39) focusing on the effort to reduce these human tragedies.

Certainly routine scanning has not been proven to be useful in low risk patients. But the majority of the patients we see at the hospitals in the developing countries are not low risk patients. Quite a large percentage are admitted in an emergency situation and the physicians need their clinical skills and any appropriate diagnostic tool available to initiate appropriate management for these patients. Thus the scan can be helpful in conditions such as ectopic pregnancy, placenta praevia, PPH, trophoblastic disease, pelvic abscess, and in diagnosing amniotic fluid changes and macrosomia.

RECOMMENDATIONS

The conclusions from the literature and my own clinical experience indicate that ultrasonography is a useful technique but it has its limitations.

<u>REFERENCES</u>

27.11.02

OBSTETRIC ULTRASONOGRAPHY AND MATERNAL AND PERINATAL MORTALITY **DR JD SEFFAH** DEPT OF OBS AND GYN **UNIV OF GHANA MEDICAL SCHOOL SUPERVISOR:** DR M. BOULVAIN DEPT OF OBS/GYN, HUG, GENEVA

INTRODUCTION

- A 23 YR OLD WOMAN, PARA 0+1,WITH A PREVIOUS HISTORY OF ECTOPIC PREGNANCY AND TUBAL SURGERY REPORTS WITH :
- 1 SEVERE LAP
- 2 MONTHS AMMENORHOEA
- 3 IRREGULAR BLEEDING
- 4 PREGNOSTICON TEST POSITIVE
- CAN USG HELP IN THE DIAGNOSIS?

GENERAL OBJECTIVE

- TO EVALUATE THE IMPLEMENTATION OF USG IN DEVELOPING COUNTRIES
- SPECIFIC OBJECTIVE
- TO EVALUATE THE SENSIVITY AND SPECIFICITY OF ULTRASONOGRAPHY IN THE DIAGNOSIS OF SOME SPECIFIC
 PATHOLOGIES WHICH CONTRIBUTED TO MATERNAL AND PERINATAL MORTALITY
- METHODS: SEARCH ON MEDLINE AND COCHRANE LIBRARY.

BACKGROUND

- POP. OF GHANA 18 MIL
- MMR 700/100,000
- PERINATAL MORTALITY 75/1000
- CAUSES OF MMR (HEMMORHAGE, SEPSIS, HYPERTENSIVE DISORDERS)
- CAUSES OF PERINATAL MORTALITY
- (PREMATURITY, ASPHYXIA, INFECTIONS)

TABLE 1: CHARACTERISTICS OF STUDIES INCLUDED INTHE META-ANALYSIS

STUDY	POPULATI	ION YEAR	COUNTRY	
ANKUM(4)	208	1993	NETHERLANDS	
NYBERG(5)	232	1991	USA	
ILOABACHIE	(6) 102	1991	NIGERIA	
PELLERITO(7	') <u>65</u>	1992	USA	
SADEK(8)	57	1995	NORWAY	
HOPP(9)	184	1995	GERMANY	
DUBISKY(10)	52	1997	USA	
SHALEV(11)	840	1998	ISRAEL	
PICAUD(12)	1234	1990	GABON	
TIMOR-T(13)	145	1989	USA	
BRAFFMAN(2	14) 269	1994	USA	

TABLE 2 SUMMARY OF EFFECTIVENESS IN DIAGNOSING ECTOPICPREGNANCY WITH ULTRASONOGRAPHY.

STUDY	TP	TN	FP	FN	ST	SP	PPV	NPV
ANKUM(4)	88	49	70	1	99	41	50	98
NYBERG(5)	68	83	78	3	94	50	46	97
ILOABACH(6)	52	28	6	16	71	81	83	65
PELLERITO(7	36	89	1	29	95	98	97	75
SADEK(8)	51	4	0	2	96	99	100	75
HOPP(9)	99	71	4	10	96	88	90	95
DUBISKY(10)	52	IO7	49	3	95	91	94	97
SHALEV(11)	331	553	27	49	87	94	92	90
PICAUD(12)	213	873	27	15	98	97	84	98
TIMOR-T(13)	39	16	1	0	100	98	99	100
BRAFFMAN(14)	102	139	27	1	99	84	100	100

USG AND PLACENTA PRAEVIA

- SCANNING EXCLUDES PLACENTA PRAEVIA AND HOSPITAL STAY IS SHORTER
- REPEAT SCAN AT TERM esp. FOR POSTERIOR PLACENTA
- MOST EUA AVOIDED
- GOOD PREPARATION FOR SURGERY RESULTS IN REDUCED BLOOD LOSS AND INJURY TO BLADDER AND URETER

AMNIOTIC FLUID INDEX(AFI) FOR PREDICTING PERINATAL OUTCOME

- AFI <5 CM USEFUL FOR SCREENING (SEFFAH AND ARMAH)
- SENSITIVITY INCREASED BY ADDING FŒTAL HEART RATE MONITORING
- USEFUL FOR PREGNANCIES WHICH REPORT LATE (>37WKS)
USG FOR PREDICTING MACROSOMIA

- DEF: ABOVE 90th PERCENTILE OR 4kg
- CAUSES: OBESE WOMEN, DIABETICS, RHESUS INCOMPATIBILITY, MULTIPARITY
- COMPLICATIONS: SHOULDER DYSTOCIA, MATERNAL INJURIES.

USG IN TROPHOBLASTIC DISEASES

- MM FROM HEMORRHAGE, INFECTIONS, METASTASES
- SNOW STORM APPEARANCE, THECA LUTEIN CYSTS CHARACTERISTICS
- USG FOR DIAGNOSIS AND FOLLOW-UP

USG AND PELVIC ABSCESS

- PELVIC ABSCESS USUALLY FROM PID AND POSTABORTAL SEPSIS
- SHOULD BE DIFFERENTIATED FROM ECTOPIC PREGNANCY, OVARIAN CYSTS AND OTHER TUMOURS.
- LAPAROTOMY INDICATED IF ANTIBIOTICS FAIL
- ASPIRATION CAN BE DONE UNDER USG GUIDANCE

CONCLUSION

- IS USG APPROPRIATE FOR DEVELOPING COUNTRIES ?
- CONTROVERSY ABOUT ROUTINE SCANNING ?
- MMR IMPROVED BY WHO, IAMANEH. CAN USG BE ADDED TO THE ROUTINE REQUIREMENTS IN OBSTETRICS?



Ovarian Hyperstimulation Syndrome in Assisted Reproduction

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ABSTRACT

Ovarian hyperstimulation syndrome (OHSS) is a serious complication that affects ovulation induction.

OHSS is a life threatening situation which can lead to hemoconcentration, acute renal failure and thromboembolism.

Although the pathogenesis of this syndrome has not been completely elucidated , it seems that there is an increase of the capillary permeability by the release of substances under administration of human chorionic gonadotrophin (HCG).

In the past, histamine, prostaglandins and estrogen were supposed to play a role in this syndrome. More recently, there are studies relating factors such as renin-angiotensin, interleukins and vascular endothelial growth factor (VEGF) to be involved. The risk is increased in patients with polycystic ovary disease, young women under 35 years old and excessive follicle development during stimulation.

It is not possible to establish a complete prevention, but there are some methods that help in reducing its occurrence. Some optional courses of action are: withholding HCG, cryopreservation of the embryos and continuation of gonadotrophin – releasing hormone analogues.

Since the pathogenesis is not complete understood, a large empirical treatment is needed trying to reduce complications and long term sequelae.

This review tries to summarize the published literature correlating the various factors with the clinic, treatment and prevention of this iatrogenic condition.

Key words : Ovarian hyperstimulation / pathophysiology / prevention and control / complications

INTRODUCTION

Ovulation induction is widely used for the management of anovulatory infertility as well as for controlled ovarian hyperstimulation in assisted reproductive techniques. However, it may occasionally lead to the development of the ovarian hyperstimulation syndrome (OHSS).

Ovarian hyperstimulation syndrome is an iatrogenic and life-threatening complication during ovulation induction treatment. OHSS is a syndrome in which the induction of ovulation results in a large variety of clinical and laboratory signs and symptoms.

OHSS is characterized by extreme ovarian enlargement with multiple follicles and corpora lutein cysts with estroma edema. Massive ascites, hydrothorax, hypovolemia, arterial hypotension, tachycardia, hemoconcentration and acute renal insufficiency can occur.

Ovarian hyperstimulation syndrome is thought to result from an increase in capillary permeability of the mesothelial surface, which leads to a depletion of intravascular volume and its secondary hemodynamic consequences (1, 2).

This increase in capillary permeability probably is mediated by vasoactive substances of ovarian origin (3) and these ovarian factors are secreted by corpora lutea in response to HCG stimulation.

There are lots of efforts to find the exact factors that lead to the increased vascular permeability. Recently there are some studies relating that several factors as cytokines such as interleukin -1 (IL-1), interleukin -6 (IL -6), interleukin -8 (IL -8), vascular endothelial growth factor (VEGF), endothelin -1 and renin may play a modulatory role on ovarian physiology (6, 7).

Several risks are reported to be associated with OHSS : young age (< 35 years), polycystic ovarylike patients, pregnancy, HCG luteal supplementation, high serum estradiol (E), multiples follicles (> 25) and ultrasonic ovarian necklace (4, 5).

CLASSIFICATION OF STAGES OF OHSS

As there are many differences in the severity of clinically apparent OHSS and its management, they induce the need of an useful and accurate classification.

The first classification was proposed by Rabau et al in 1967 in which OHSS was divided into three

categories and six grades. By the time that new knowledge of the disease was been discovered, many authors tried to improve this classification.

In 1978, Schenker et al proposed a classification based on clinical manifestations, laboratory and ultrasonographic findings: (5)

 \cdot Mild hyperstimulation : The ovary enlargement may be up to 6 cm in diameter and there is a sensation of abdominal heaviness, tension and pain.

 \cdot Moderate hyperstimulation : The ovary enlargement is up to 12 cm in diameter and the abdominal discomfort is more pronounced. There can be also gastrointestinal symptoms such as nausea and diarrhea.

• Severe hyperstimulation : pleural effusion, pericardial effusion, hypovolemia, failure of renal function, thromboembolic phenomena, tension ascites and adult respiratory distress syndrome (ARDS).

In 1992, Navot et al proposed another classification defining two degrees in the severe classification as critical or life threatening stage. The authors proposed the classification based more on clinical and laboratory parameters than on ovarian enlargement in controlled ovarian hyperstimulation. (<u>Table 1</u>)

OBJECTIVES

The aim of this study is to review critically the literature on pathogenesis, modern management and prevention of OHSS.

METHODS

DATA SOURCES

An English language review of the literature from 1979 to 1999, using Medline was performed.

RESULTS

DISCUSSION

Ovarian hyperstimulation syndrome remains a threat to the patients that undergo ovulation induction. With the great number of women receiving different kinds of ovarian stimulation protocols as part of different infertility treatments, the number of ovarian hyperstimulation syndrome is likely to increase.

The pathophysiology of this syndrome is still unclear at present. Various mechanisms are said to be related, but none of the studies could really prove anything.

The only thing that is known is that there is an ovarian enlargement and an increase in the capillary permeability, leading to fluid shifts out of the intravascular space and complications arising from this effusion.

Attempts have been made to identify women who may develop ovarian hyperstimulation syndrome so that alternate strategies may be employed to decrease this incidence. A relevant point is that women with PCOS are at high risk of developing OHSS.

When managing OHSS, one of the most important factors to consider is the anxiety of the couple, especially when concerning the possibility of pregnancy. The most useful parameters to assess the severity of this condition are the hematocrit, renal function and gradually accumulating ascites.

Since the pathogenesis has not been completely understood, a large empirical treatment is needed when the syndrome becomes severe. Correction of the reduced intravascular volume and hemo-concentration are the first priority in the management.

Although some authors see paracentesis as a contraindication, it is useful especially when there is tense ascites causing renal congestion.

Surgical treatment remains only for cases of intraperitoneal bleeding and torsion.

Monitoring of the induction of ovulation associated with clinical evaluation and serum estradiol are the first step to try to prevent this syndrome.

In this review we tried to show the factors that are probably responsible for this syndrome. The interaction between these factors needs more studies, but it seems that a combination of immune and non immune mechanisms may allow a better understanding of the disorder.

Until then, it is the responsibility of the clinician to impose rules and look for the prediction and

prevention of this iatrogenic disease.



27.11.02

Ovarian hyperstimulation Syndrome in Assisted Reproduction

> Peloggia, Alessandra Caism - UNICAMP, Brasil

INCIDENCE



Aboulghar et al 1,8 %



LIFE THREATENING COMPLICATION

PATHOGENESIS

?

PATHOGENESIS

Interleukins

Renin - Angiotensin system

Vascular Endothelial Growth Factor

Increased capillary permeability



NUMBER OF FOLLICULES



ESTRADIOL

RISK FACTORS





MANAGEMENT



DOPAMINE

PARACENTESIS ?

HEPARIN



SURGERY

PREVENTION

MONITORING



SERUM ESTRADIOL

PREVENTION

Stimulation protocol

Intravenous albumin







PREVENTION

Aspiration of follicles

Cryopreservation

Luteal phase

CONCLUSION



Non immune





Understanding of the disease





9 th post-graduate Course for Training in Reproductive Medecine and Reproductive Biology

GENEVA 99

Doctor Ahounou Brice

PREVALENCE OF SEXUALLY TRANSMITTED DISEASES IN REFUGEE POPULATION WORLDWIDE

PLAN

- INTRODUCTION
- **OBJECTIVES**
- SEARCH STRATEGY/ METHODOLOGY
- RESULTS
- CONCLUSION

PLAN

- INTRODUCTION
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- CONCLUSION

"Il n'existe pas de plus grande douleur au monde que la perte de sa terre natale."

-Euripide, 431 av. J.- C.



Refugees have rights like other Humans



PLAN

- INTRODUCTION
- **OBJECTIVES**
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- RESULTS
- CONCLUSION

SPECIFIC OBJECTIVE

To assess the STDs among the refugee population around the world

SPECIFIC OBJECTIVES

- To determine the different types of STDs amongst refugee population
- To determine the measures to prevent STDs amongst refugee population

PLAN

- INTRODUCTION
- **OBJECTIVES**
- SEARCH STRATEGY/ METHODOLOGY
- RESULTS
- CONCLUSION

SEARCH STRATEGY & METHODOLOGY

- <u>Period</u> : 1989 to 1999
- <u>Source</u> : a computerised Medline search, a manual literature search and discussions or meetings
- <u>Identify</u> :32 abstracts, review articles and manuals
- <u>Keywords</u>:Prevalence,STDs, RH, Refugees
- <u>Selection</u> : four (4) studies

PLAN

- INTRODUCTION
- **OBJECTIVES**
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- **RESULTS**
- CONCLUSION

MAYAUD and als 1994

- A rapid assessment in Rwandan refugees camps
- Prevalence of STDs among:
 - 100 antenatal clinic attenders (ANC)
 - 239 men from outpatient clinics (OPD)
 - 289 men from community in Ngara District of Tanzania (estimated population 300.000) (8 days in 1994)
- Examination, Laboratory, Interview

Table 1: General results

	Antenatal Women Clinic attenders	Men outpatient clinic	Community males
Gonorrhoea	3 %		
Syphilis	4 %	6,1 %	
Urethritis		2,6 %	2,9 %
Vaginitis (TV, BV, CA)	50 %		
MAYALID et als 1994	1		

Table 2 : Prevalence of STD and RTI pathogens amongRwanda refugees in Tanzania

PATHOGENS	Antenatal Women N = 100	M en O P D N = 233	M ale community N= 272
Genital specimens:			
N.gonorrhoea (NG)	3	3 (1,3%)	4 (1,5%)
NGU		3 (1,3%)	4 (1,5%)
C.albicans (CA)	27	ND	ND
T.Vaginalis (TV)	31	N D	N D
B.V. (clue cells)	16	N D	N D
Any RTI (NG/TV/BV/CA)	60	-	_

KING and als 1989

• A prospective study on STDs

 179 pregnant Vietnamese refugees in Hong Kong from Feb to May 1989

Table 4 : Prevalence of STDs amongst Vietnamesepregnant refugees in Hong Kong

		Results	Laboratory	
Syphilis	(N= 179)	3,4 %	VDRL 2 + F.T.A. abs	
Gonorrhoea	(N= 158)	0 %	ТММ	

FTAabs = Fluorescent treponemal antibody absorption TMM = Thayer Martin medium

WALKER and als 1995

- A retrospective analysis of data of all refugees and immigrants at their arrival to USA
- N =179096
- Period :1993 to 1995
Table 5 Refugee health assessment results (partial)US Public Health service

	Total tested	Total positive
Syphilis	17179 (16,5 %)	234 (1,4 %)
Hepatitis B HbsAg +	44299 (42,6 %)	2712 (6,1 %)

WALKER and als 1995

INTERNATIONAL FEDERATION OF IRANIAN REFUGEES AND IMMIGRANTS COUNCILS (IFIRIC)

- Focus group discussions
- A reproductive health needs assessment surveys conducted of 27 self identified refugee women
- Additional qualitative information through of another 15 refugee women and 12 refugee men in Kaysari Turkey 1996

FINDINGS of Kaysari refugees

- 70 % had no heard about HIV/AIDS
- 60 % stated that they had some form of vaginitis /infection
- Only 25 % received treatment for vaginitis and 75 % had not
- Many misconceptions about HIV/AIDS
 IFIRIC 1996

PLAN

- INTRODUCTION
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- SEARCH STRATEGY/ METHODOLOGY
- RESULTS
- CONCLUSION

CONCLUSION

- STDs are a reality in the refugee population
- Most important STDs found in the surveys were gonorrhoea, syphilis.
- This problem should be addressed in the global setting of the reproductive health, which must be implemented in an integrated health system
- Syndromic approach to STD case management allows effective care for symptomatic cases.
- Surveys must continue to evaluate the impact of the led interventions of prevention and control of the STDs

RECOMBINANT FSH : OPTIONS FOR OVARIAN STIMULATION

Genc KABILI

Albania

INTRODUCTION



Programming ovulation in the menstrual cycle (fig. 1)



•Objective : to optimize COH protocols (under GnRH-a use)

- •Allows assessement of the true follicualr-phase length
- •Important : a) synchronization of endogenous & exogenous FSH signals b) concept of FSH threshold / "FSH window"



- highly pure (99.9 %) rFSH
- avoided of LH activity
- exhibits a high specific bioactivity (>10'000 IU/mg protein)

- safety and tolerance OK!
- i.m. and s.c. administration OK!
- FSH levels were raised after 30 min
- no serum anti rFSH antibodies were detected but further studies are required)
- pharmacokinetics and pharmacodynamics (fig. 2)



• strong negative correlation between body weight and serum FSH levels after rFSH administration (fig. 3)



• Isoforms less acidic (ISO >4.8) vs more acidic (ISO=4.8)

RESULTS

In comparison with urinary gonadotropins rFSH ensures : high batch-to-batch consistency

the absence of any LH activity

the lack of contaminating urinary proteins of undetermined origin

the potential of being produced in limitless quantities

it can be self administered subcutaneously

META-ANALYSIS (Daya S, Gunby J Sept. 1999)



CONCLUSIONS

Potential benefits of rFSH versus uFSH (B. Fauser)

Characteristics of rFSH	Potential clinical implications
Absence of urinary	Allows for safe s.c.
contaminants	administration
contammants	administration
Not dependent on availability	Availability guaranteed
of uring	fittenteed
or unite	
Potential for improved batch-	More consistent treatment
to betch consistency	outcomo?
to-daten consistency	outcome?
Minor differences in	Improved treatment outcome?
is a hormon of distribution	improved treatment outcome:
isonormone distribution	
compared with urinary	
gonadotropins	Continue
	Continue

Potential benefits of rFSH versus uFSH (B. Fauser)

Characteristics of rFSH	Potential clinical implications
Totally devoid of LH	Ovulation InductionLH/hCG should be added in WHOclass I anovulationSatisfactory for WHO classII(improved treatment outcome inPCOS?)Ovarian hyperstimulation for IVFSatisfactory in cases of combinedstimulation with GnRH agonist orantagonist, although therelationship between serumoestradiol concentrations andfollicle numbers may change

Continue...

Potential benefits of rFSH versus uFSH (B. Fauser)

Characteristics of rFSH	Potential clinical implications
Modified rFSH	
selected rFSH isohormone	Improved treatment outcome?
fraction	
long-acting rFSH	Less frequent administration
	but increased chance for
	ovarian hyperstimulation
short-acting rFSH	Less chances for ovarian
	hyperstimulation if
	administered in the late
	follicular phase?
recFSH antagonists	Male or female contraception?

- rFSH is a new alternative for ovarian stimulation
- this substance seems to be in agreement with the rationale "to bring to clinics more consistent, better defined, safer, more user friendly monotherapeutic preparations" (Loumaye, et al. 95)
- it is demonstrated that COH with rFSH leads to statistically and clinically significantly higher ongoing PRs compared with urinary FSH and hMG
- but consider: cases which need LH and cost



SEMEN QUALITY IN MALE POPULATION: TRENDS AND EXPOSURES

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Abstract

Over the last six years research suggestive of declines in semen quality has generated substantial scientific debate. The landmark study of changes in semen quality over time was the meta-analysis of Carlsen et al which demonstrated semen quality decline between 1938 and 1990. The objectives of this systematic review are the following: to review studies that are based on a re-analysis of the data collected by Carlsen et al., to evaluate studies in sperm quality conducted since 1992 and to review studies that explore the effects of the environmental and other factors on semen quality. Some portion of the available evidence is consistent with the hypothesis that semen quality declines over time. This evidence includes multiple re-analyses of Carlsen et al's dataset as well as studies of discrete populations. The strongest supporting evidence is based on studies that have focused on more reliable measures of semen quality such as semen concentration, and that have attempted to control for various confounders at the stages of analysis. The degree to which environmental factors affect male reproductive function remains unclear. The available evidence on the risk factors of declining semen quality suggest that there are only a few toxicants, as dibromochloropropane (DBCP), high - level exposure to lead, that cause significant deterioration of semen quality. In the future, focused research on the determinants of semen quality decline in those regions where the phenomenon has been observed may provide useful insights. Prospective studies that measure hypothesised risk factors, potential confounders, and changes in semen quality would provide the most convincing evidence of the expected fate of this aspect of male reproductive function.

1. Introduction

Reproduction is a topic that attracts significant interest in the scientific community and in the public media. Over the last six years, research suggestive of declines in semen quality has generated substantial scientific debate. Assessment of semen quality is based on an evaluation of several parameters, including semen volume, sperm concentration, sperm motility, and sperm morphology (See Annex 1). Methods for estimating sperm concentration have not changed since 1929 and are based on manual counts using a haemocytometer [1], while the methodology for the motility and morphology estimation was changing over the time [2]. The standard use of sperm concentration from 1938 to the present.

The first reports that suggested declines over time in semen quality among humans appeared in the 1970s and early 1980s. These reports were generally ignored because they were based largely on data from infertility clinics or selected groups of fertile man [3,4,5]. However, a landmark study of changes in sperm quality over time was the meta-analysis of Carlsen et al. [6]. This meta analysis was based on sixty-one studies that were published between 1938 and 1990 and that included 14,947 men with proven or unknown fertility. Patients that were investigated for infertility were excluded from the analysis. Using linear regression, Carlsen et al. estimated an annual decline in sperm concentration of 0.93x106 /mL and an overall decrease in mean sperm count from 113x106 /mL in 1940 to 66x106 /mL in 1990. These results fuelled scientific debates about declining semen quality in men, and a series of publications followed that further explored both semen quality (particularly semen concentration) and trends in semen quality over time.

2. Objectives

The objectives of this systematic review are the following:

- 1. To review studies that are based on a re-analysis of the data collected by Carlsen et al. (1992)
- 2. To evaluate studies of trends in sperm quality conducted since 1992
- 3. To review studies that explore the effects of environmental and other factors on sperm quality

3. Methods

To complete this review, the author searched Medline systematically for peer-reviewed articles published since 1992 to identify studies focused on trends in sperm quality and their possible determinants. Please see Annex 2 for a summary of the search strategy employed.

4. Results

4.1. Statistical re-analysis of Carlsen et al.'s dataset

In addition to being a landmark article in the field of male reproduction, Carlsen et al.'s analysis also received substantial criticism. First, pooling data across different laboratories and failing to account for inter-laboratory variations in sperm concentration may have led to biased estimates of trends in semen quality. Second, researchers have questioned the statistical methods that were used to estimate trends in semen quality. Third, researchers have questioned the extent to which the various semen samples were representative of their respective populations. Unfortunately, information on sampling frames and response rates for each dataset that was included in the meta-analysis is not available. Fourth, relatively few observations are available before 1960. Finally, the data used by Carlsen et al. is derived from various laboratories, populations, and geographic regions. If systematic relationships exist between time and any of these variables, then failing to control for such confounders could yield biased estimates of trends [7].

Since 1992, several researchers have re-analysed the data of Carlsen et al. to explore the potential limitations of their findings. To address the question of modelling strategy, Olsen et al. (1995) used the same dataset and fit models that included quadratics, splines, and stairsteps [8]. Two models - the quadratic and spline fits - suggested some increase in sperm concentration after 1970. The stairstep model suggested a drop in sperm concentration after 1964 with mean sperm concentration constant before and after. Backward projections based on the three other model fits suggest that sperm counts may already have been declining substantially before 1940 [8]. Forward projections of estimated trends in semen quality would suggest that men's capacity to procreate would disappear by the middle

of the next century.

To explore the possible confounding effects of the geographic distribution of samples included in Carlsen et al.'s dataset, Fish and Goluboff (1996) selected a sub-sample of 20 studies, each of which included 100 or more men, and in total representing 91 percent of the original sample. Fish and Goluboff hypothesised that the decline in semen quality observed by Carlsen et al. could be explained by an uneven geographic distribution of studies included in the meta-analysis [9]. In particular, earlier studies involved men from the United States, where the sperm counts were higher, and later studies involved men from developing countries, where sperm counts were lower. However, mean sperm counts estimated for the year 1975 from a sample of 1300 men from New York and with known fertility [10] were significantly lower than mean sperm counts estimated for the period 1935 to 1951 and including men with known and unknown fertility from New York [6].

Bahadur et al., Becker and Berhane, and Swan et al. analysed Carlsen's dataset by geographic region [11,12,13]. Swan et al. observed a significant decline in sperm concentration from 1940 to 1990 in the United States, a finding that is consistent with that of Fish and Goluboff. Re-analysing data only for Europe, Swan et al. also found a significant decline in sperm concentration from 1971 to 1990 [13]. Bahadur et al. and Becker and Berhane [11,12] did not find a statistically significant decline in the European data collected by Carlsen (see Table 1). Becker and Berhane stated that their analysis lacked the power to detect a true decline in semen quality [12]; however, differences in the findings for Europe merit further exploration. One difference between the two analytic strategies was that Swan et al. included controls for potential confounders such as time of abstinence, age, percentage of men with known fertility, method of semen collection, study goal, and geographic location. In the analysis of Swan et al. (1997) studies from Carlsen et al. meta-analysis were grouped into three regions: US (27 studies, 1938-1988), Europe and Australia (16 studies, 1971-1990) and other (non-Western) countries. Multiple regression analyses were used to fit both linear and non-linear models. These multiple regression analyses considerably improved model fit. Using spline the authors noted that slopes before and after 1970 did not differ significantly so that this model reduces to the linear as did to quadratic model. Model fit was good: the linear multiple regression model explained 80% of variation of data. Data of non-Western countries did not fit any of these models well, perhaps reflecting the heterogeneity of the areas included, the small number of studies and the short time, during which the studies were published (12 years). To address criticism that the trend reported by Carlsen et al. was influenced by a few large studies with high sperm concentration early in the study period authors used multiple regression methods to model post 1970 studies separately. The significant decline after 1970 was estimated (p=0.04) as well as during the all study period (p<0,0001). Swan et al. examined population source and percent of men with proven fertility. Only the later variable remained significant in the final regression model. It is possible that the composition of one or more of these subpopulation changed over the time. For example, potential semen donors might reflect different geographic groups in historical and modern studies. However, it is not clear how such changes would affect the trends reported. Other factors related to sperm density such as age and abstinence time did change during the study period with later studies including older men and earlier studies controlling less strictly for abstinence time. When these variables were controlled in multiple regression models, the slope of the regression line increased and the fit of the model improved considerably [12]. However due to incomplete data of age, abstinence time and other confounders, it is possible that uncontrolled confounding remains. Anyway it is unlikely that they can account for the observed decline in sperm concentration.

Swan and Elkin reviewed post-1992 re-analyses of Carlsen et al.'s dataset and also conducted their own re-analysis based on their earlier publication (1997) results of which were discussed above [1] (<u>See Table 1</u>).

Their review shows surprising consistency in results across studies. Controlling for the possible confounding factors they demonstrated an even faster estimated decline in semen concentration

4.2. Temporal trends in semen quality

Recent research on trends in sperm quality has not been limited to re-analysis of Carlsen's et al.'s dataset. Rather, other researchers have explored changes in semen quality for specific populations. Table 2 summarises recent studies of temporal trends in semen quality by population.

Irvine reported a significant decline between 1984 and 1995 in sperm counts among 577 semen donors in the United Kingdom [14]. Sperm concentration levels were found to be associated with the year of donor's birth. This finding is consistent with the hypothesis that factors acting in fetal life (exposure to environmental xenoestrogens) could in part be responsible for decreased sperm production and increased incidence of abnormalities detected in male reproductive organs [14].

Auger et al. examined semen samples provided by 1351 sperm donors from the Paris area between 1973 and 1992. The donors were healthy, unpaid volunteers who had fathered at least one child. The authors observed a significant annual decline in sperm concentration of 2.1 percent. The percentage of morphologically normal and motile cells also declined over the study period. Consistent with the results of Irvine et al., Auger et al. observed that semen quality, as measured by sperm concentration, was associated with the year of the donor's birth [15].

Based on an analysis of 416 Belgian donor candidates, Van Waeleghem et al. observed declines in sperm concentration, motility and morphology between 1977 and 1995 [16]. Although the investigators state that the technique of semen analysis remained unchanged over time, observed declines in semen motility and morphology should be interpreted with caution given that no internal laboratory control was routinely performed. Previous reports indicate that temporal changes in the assessment of qualitative characteristics such as sperm motility and morphology may occur without observable changes in laboratory procedures [17]. (e.g., turnover in laboratory staff, lack of staff training, and irregular intra-laboratory control).

Ginsburg et al. analysed the semen of 260 men from London who had partners with ovulatory infertility. The researchers compared mean estimates of sperm concentration, motility, and morphology for the period 1978 to 1983 and 1984 to 1989 and observed significant declines in all three measures between the two periods [18].

Adamopolous et al. analysed semen samples from 2,385 Greek men from infertile couples and observed a decrease in total sperm count [19]. Finally, Younglai and colleagues analysed data on 48,968 men in Canada and observed a decline in sperm concentration from 1984 to 1996 [20]. However, subjects in the last three studies were selected among patients attending an infertility clinic; therefore, the selectivity of the samples of men limit the generalisability of observed trends.

Other researchers have either failed to detect declines in various measures of semen quality or have observed increases in measures of semen quality over time. These findings are largely based on studies conducted on men residing in the United States and Europe. For example, Vierula et al. examined semen quality of normal Finish men and found no significant trends in sperm concentration [21]. Bujan et al. analysed data from 302 candidate sperm donors from Toulouse, France who provided semen samples between 1977 and 1993 [22]. Donors in this study were recruited in the same manner as those in the study by Auger et al., and no changes in sperm concentration were detected. Unchanged or even increased sperm counts have been reported based on analyses of semen samples from male residents in the United States and Israel [23,24,25,26].

The most resent studies from Europe do not provide convincing evidence of declines in semen quality [27,28,29]. For example, analysis of semen samples collected between 1977 and 1995 from 1,927 donor candidates in Copenhagen showed a slight but significant increase in mean sperm concentration and total sperm count [27]. In two other studies, analysis of semen quality in partners of women with tubal infertility showed non significant changes of sperm concentration . First, Rasmussen et al. looked at sperm concentration among four cohorts of men according to their data of birth [28]. In this study, year of birth was not associated with any change in sperm concentration. Second, Zorn et al. analysed spermiograms of Slovenian men over 14 years and did not find any significant changes in either sperm concentration or percentage of semen samples with normal morphology [29].

Berling et al., Avdolz et al. and Tortorelo et al. studied semen samples of Swedish, Spanish and Venezuelan men coming from couples exhibiting infertility of unknown cause; therefore, the generalisability of this latter set of studies is questionable [30,31,32].

Overall, some portion of the available evidence is consistent with the hypothesis that semen quality has declined over time. This evidence includes multiple re-analyses of Carlsen et al.'s dataset as well as studies of discrete populations. The strongest supporting evidence is based on studies that have focused on more reliable measures of semen quality, such as semen concentration, and that have attempted to control for various confounders at the stages of analysis. Evidence to the contrary mostly comes from studies conducted in the United States and Europe.

4.3. Determinants of semen quality

Researchers have identified several possible determinants of observed declines in semen quality, including environmental estrogens, lifestyle exposures, and occupational exposures. Studies addressing these determinants are presented in the next sections.

4.3.1. Environmental xenoestrogens

The hypothesis that exposure to estrogens causes decline in semen quality as well as disorders of the male reproductive tract (e.g., testicular cancer, cryptorchidism, and hypospadia) was first published in 1992 by Sharpe and Skakkebaek [33]. The sources of these estrogens have been postulated to be both endogenous and exogenous (Figure 1). Endogenous increases in levels of oestrogen could result from changes in diet, which increase the enterohepatic circulation of estrogens. It means that women on a low fibre diet would be exposed to more of her endogenous oestrogen than a woman on a high-fibre diet. Increases in body fat may also increase levels of bio-available estrogens by converting other steroids into estrogens. Sources of exogenous estrogens are synthetic estrogens and environmental xenoestrogenes (e.g., xenoestrogenes - environmental chemicals with known estrogenic activity on male reproductive health). Levels of synthetic estrogens may increase through exposure to (women who use) oral contraceptives and to active anabolic steroids in livestock. [33,34]

Humans can be exposed to environmental estrogens orally (diet, drinking water, and air) and through the skin. Many food plants (e.g. soya), cow milk can contain oestrogens. Environmental «estrogenic» chemicals include pesticides, combustion products, polychlorinated biphenyls [33,34,35].

Different authors have reported increases in testicular cancer in different industrialised countries [36,37,38]. Adami et al. examined data from the cancer registers of countries of the Baltic region and observed some increase in the incidence of testicular cancer in all countries [36]. Other studies have

shown increased incidence of cryptorchidism and hypospadia [38,39]. Finally, decreased semen quality has been shown to occur in the sons of women treated between 1945 and 1971 with a synthetic oestrogen known as diethylstilbestrol [40,41]. Also these conditions can be induced in laboratory animals by brief exposure to exogenous oestrogen/DES during pregnancy [42].

4.3.2. Lifestyle exposures

The most investigated everyday exposures that may influence sperm quality are exposure to heat, smoking, and alcohol consumption (<u>Table 3</u>).

Possible routes of local increases in scrotal temperature include posture, types of clothing (tightly fitting underwear), sauna bathing, seasonal temperature variations, hours per day spent sitting or sleeping in night clothes or with an electric blanket, occupational heat exposure, and congenital factors such as varicocele and cryptorchidism. Mechanisms of testicular heating such as wearing tightly fitting clothes and sauna bathing are often labelled «lifestyle factors» in studies of the determinants of sperm quality. The data available on the influence of lifestyle factors that induce localised testicular heating (posture, clothing, or sauna bathing) on human spermatogenesis are controversial. For example, Oldereid et al.'s analysis of survey-based data from 312 infertile men showed no association between certain lifestyle factors and various sperm parameters [43]. Of course, retrospective design and small number of men included might bias the result of this study. A few earlier clinical studies [44,45] and a case-control study by Parazzini et al. (1995) [46] showed an influence of posture and clothing on semen quality. Sauna bathing is one of the most studied sources of potential testicular heating, and earlier studies have suggested its association with spermatogenesis [47].

The effect of smoking on sperm concentration was evaluated by Vine et al. in a meta-analysis [48]. The purpose of this meta-analysis was to explore the association between sperm concentration and cigarette smoking among studies published between 1966 and 1992. Findings from this study suggest that smoking is associated with lower sperm concentration.

Results from the most recent studies of the effects of smoking on sperm quality are inconsistent. Chia et al. investigated 184 men for infertility. Semen analysis and estimation of levels of cadmium and lead in blood and seminal plasma were conducted, and a heavy smoking was significantly associated with lower sperm concentration [49]. Goverde et al., in their study of data from 5000 men from infertile couples, did not find a significant association between smoking and semen quality. Rather, excessive alcohol consumption was observed to be associated with a lower number of morphologically normal spermatozoa [50]. Notably, the data for this study were based on medical reports, which may be subject to substantial selection biases. In conclusions, the available evidence suggests some association between smoking and reduced semen quality, but the effects of smoking are likely to be marginal.

4.3.3.Occupational exposures

The majority of epidemiological studies on male reproductive toxicology are addressed the workplace which offers the best opportunity to study effects of male reproductive toxicants.

Occupational heat effects were demonstrated in three case-control studies in which fertility status and/or semen analyses were compared between exposed and unexposed workers. In all studies, exposure to occupational sources of heat were associated with declines in semen quality. Specifically, Rachootin and Olsen reported a significantly increased odds of sperm abnormalities among men with occupational exposure to heat than among men without occupational exposure to heat [51]. In the well-known Italian ceramic industry, Figa-Zalamanca et al. observed that individuals exposed to high temperatures had a higher incidence of childlessness and of self-reported difficulty in conceiving than those who were not exposed to the same high temperatures; evaluation of semen parameters showed a higher prevalence of pathologic sperm profiles among heat-exposed workers [52]. [1] Finally, in a longitudinal study of 17 welders who were exposed to moderate radiant heat but not substantial levels of welding-fume toxicants, significant declines in the proportion of spermatozoa with normal forms were observed after six weeks of exposure. This proportion increased after a break from heat exposure (see Table 4) [53].

Besides physical exposures as heating some chemical occupational exposures were demonstrated to have a vulnerable effect on male reproductive system. A well-known toxicant is brominated organochlorine nematocite DBCP. This pesticide causes severe oligospermia after a few months of low level exposure [54]. The most recent multi-centre study to identify, characterise, and quantify selected widespread occupational risk factors for abnormalities of the male reproductive system was the Asclepios Project. The objective of this study was to explore whether occupational exposure to fungicides, styrene, and lead reduces semen quality. Results of this project and other recent studies on occupational exposures are summarised in <u>Table 4</u>.

The degree to which environmental factors affect male reproductive function remains unclear. Although strong evidence suggest that high-level exposure to lead causes deterioration of spermatogenesis there is still a need to establish the lowest effect level [55]. Other metals such as cadmium, aluminium and hexavalent chromium also have been implicated in male reproductive toxicity, but the evidence is very limited [56,57]. The recent studies failed to prove influence of pesticides on sperm quality [58]. Some evidence on organic solvent styrene deteriorating effect on semen quality was given in the study from Asclepios Study Group [59], however due to the small number these findings are only preliminary. So, the most recent studies in occupational medicine have not estimated the influence of widespread occupational exposures on semen quality.

5. Conclusion

During the last few years, factors related to male reproductive function have become major topics of discussion in the scientific literature and in the public media. This paper is a review the most recent data on temporal trends in semen quality and possible risk factors associated with semen quality decline. Re-analyses of the data compiled by Carlsen et al., as well as post-1992 studies of trends in semen quality by country do not widespread and universal declines in semen quality over the last several decades. Rather, declines in semen quality appear to have taken place in only certain parts of the world. Researchers have hypothesised that exposure to estrogens, exposure to toxins through smoking and alcohol consumption, and occupational exposures are the most likely determinants of declines in semen quality. However, the available evidence on the risk factors of declining semen quality suggest that only a few toxins as DBCP, high level exposure to lead can cause a significant deteriorating effect on semen quality.

In the future, focused research on the determinants of semen quality decline in those regions where the phenomenon has been observed may provide useful insights. Prospective studies that measure hypothesised risk factors, potential confounders, and changes in semen quality would provide the most convincing evidence of the expected fate of this aspect of male reproductive function.

References

Annex 1. Basic parameters of semen quality

According to WHO Laboratory Manual for the Examination of Human Semen and Semen-Cervical Mucus Interaction [60] basic semen analysis includes:

- 1. Determination of ejaculate volume.
- 2. Sperm concentration (number of spermatozoa per 1 ml) and total sperm count (number of spermatozoa in the ejaculate) evaluation.
- 3. Sperm motility investigation, classifying all spermatozoa as of rapid progressive, slow progressive, non-progressive motility and immotility
- 4. Sperm morphology evaluation counting normal and abnormal spermatozoa. Defects of abnormal spermatozoa must be scored as head, mid-piece tail defects and cytoplasm droplets.

Annex 2. Search strategy

- 1. A computerised Medline search for English-language publications using key words: semen quality decline and semen quality decline + risk factors or exposures or determinants. For the first strategy 66 articles were extracted, for the second 11 articles.
- 2. For each publication search of related articles was done in Medline database.
- 3. For each article manual search of it's references was performed.
- 4. Medline search according to authors: Giwercman A., Skakkebaek NE

Acknowledgement

Dr.Kathryn M. Yount

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SEMEN QUALITY IN THE MALE POPULATION: TRENDS AND EXPOSURES

BACKGROUND

OBJECTIVES

RESULTS

RESULTS 1. Statistical re-analysis of Carlsen 's dataset

RESULTS 2. Recent studies on temporal trends in semen quality

RESULTS 3. Determinants of semen quality in male population

Sources of estrogens and their effect on fertility

RESULTS 3.2. Determinants of semen quality Lifestyle exposures

RESULTS 3.3. DETERMINANTS IN SEMEN QUALITY. OCCUPATIONAL EXPOSURES

The human testis an organ at risk?

CONCLUSION (1)

CONCLUSION (2)

Conclusion (3)

Acknowledgements

SEMEN QUALITY IN THE MALE POPULATION: TRENDS AND EXPOSURES

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SHOULD GENETIC SCREENING FOR FRAGILE X SYNDROME BE RECOMMENDED IN INDONESIAN CHILDREN WITH MENTAL RETARDATION ?

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FRAGILE X SYNDROME

- The most common cause of inherited mental retardation
- The second most frequent chromosomal cause of mental handicap (*after Down Syndrome*)
- X linked mental retardation
- Mild emotional/learning disabilities ? mental retardation
- Distinctive features : prominent fore head, long thin face, prominent jaw, large protuberant and slightly dysmorphic ears, macro-orchidism

CONFIRMATION OF DIAGNOSIS

- Cytogenetic analysis
 Fragile site at X_q27.3 chromosome
- DNA testing
 Fragile X gene ? FMR₁ ? trinucleotide repeat expansion, CGG.
- FMRP test

Antibody test to detect the presence of FMRP

FMR1 mutation

- Trinucleotide repeat expansion, CGG
- Normal individual has 6 54 CGG repeats (average 29 - 30 repeats)
- Individuals who are carrier have 55 200 CGG repeats, so called permutation
- Individuals with greater than 230 CGG repeats usually have methylation of the gene, so called full mutation
- Punctuated by an AGG repeat at every 9 to 10 CGG repeats

Objective

To provide background information needed to set up a screening program for FXS



- Prevalence of FXS
- Pattern of screening
- Problems

Rapid antibody test to FMRP

Willemsen et al, Hum Genet (1997)99:308-11

- Mouse monoclonal antibody against FMRP http://www.eur.nl/FGG/ch1/fragx/
- Enables to discriminate normal from affected males
- Suitable for screening males in institutes or school for mentally handicapped or children with learning disabilities
- Screening male newborn babies
- Identified patient ? allow genetic counselling through the families ? Further DNA analysis for carrier detecting
- The value of FMRP expressed in males have higher discriminating power than those in women

Cytogenetic vs DNA testing

- In some patients, who were positive cytogenetically in 1980, no mutation in FMR1
- Fragile sites at X_q28, so called FRAXE (distal to the FMR1 mutation) and FRAXF (distal to FRAXE locus)



Table 2. Prevalence of mental retardation

WHO Region	Population	Prevalence (%)
Africa	585,000,000	0.62
America	770,000,000	0.51
Eastern	454,000,000	0.65
Mediterranean	866,000,000	0.47
Europe	1,425,000,000	0.56
South-East Asia	1,602,000,000	0.55
Western Pacific		

Source: WHO. <u>http://www.who.int/msa/mnh/ems/ratesolld/retard.htm</u>⁸ Last, update 30.09.96
Table 3. Clinical features and medical problems of fragile X males.

	%
Clinical features	
Long face	70
Prominent ears	70
High arched palate	52
Hyperextensible finger joints	67
Double jointed thumbs	53
Single palmar creases	25
Hand calluses	29
Flat feet	71
Heart murmur or click	18
Macro-orchidism	70
Medical problem	
Vomiting	31
Failure to thrive in infancy	15
Strabismus	36
Myopia or hyperopia	22
Hernia	15
Joint dislocation	3
Orthopaedic problem	21
Otitis media	85
Sinusitis	23
Seizures	22
Mitral valve prolapse	35
Apnoe	10
Autism	20
ADHD	80
Motor tics	19
Source: Adapted from de Vries et al. 1998. ³	

CHECKLIST ITEM

Physical Large ears Large testes Hyperextensible finger **101nt** Plantar crease Simian crease **Behavioral** Poor eye contact Hyperactivity and attention span Hand flapping Hand biting Loud voice Swearing Shv Perseverative speech Tactually defensive **Family history** Mentally retarded sibling Mentally retarded mother Second degree maternal relative with MR (*Arvio et al,1997*)

Mental retardation Family history Elongated face Large or prominent ears ADHD Austistic-like behaviour

(Giangreco et al, 1996)

Emotional/behavioral difficulties Taken medication **Received treatment** Attention difficulty Avoid eye contact Depressed mood Nervousness/anxiety **Injured** self **Repetitive movement** Repetitive word/phrase **Repetitive subject**

(Teisl et al, 1999)

<u>Table 5.</u> Risk that a premutation in a female will expand to full mutation

Maternal CGG repeat Size	Risk for expansion
<60	<1%
60 - 69	17%
70 – 79	71%
80 – 89	82%
>90	99%

Source: Fu et al. (1991). ⁴

Molecular screening of FXS in Indonesia Faraz et al, Am J Med Genet. 1999:83:350-1

- Male children with mild DD (IQ above 50) from C grade special schools
- Majority from ethnic Javanese
- Prevalence was 2.4% (5/206)
 - 4 had full mutation
 - 1 had permutation

SITUATION in INDONESIA

Population is 206,338,000 Prevalence MR in Southeast Asia is 0.47%

Prevalence. FXS
Indonesia 2.4% (Faraz et al, 1999)
Taiwan 0.6% (Pang et al, 1999)
China 3.8% (Li et al, 1988)
China 2.8 (Zhong et al, 1999)
Thailand 2.7% (Jinorose et al, 1997)

1,153,600 MR
Undiagnosed FXS?

Screening approach

- Case finding with cascade screening of relatives at risk in extended family
- Population screening most commonly suggested:
 - during pregnancy
 - all male newborns

Planning screening program

- The attitudes and reactions of (non) consenting parent/guardian
 - Well accepted

Turner et al. BMJ.1997:315:1223-6 de Vries et al. Am J Hum Genet. 1997:67:660-7

- Well-trained genetic counselor
- Multi-disciplinary approach
- Approriate technology
 - accurate
 - available
 - inexpensive

Conclusion

- Genetic screening is needed in a certain group of mental disabilities in Indonesia
- Rapid (less time consume), inexpensive and reliable screening
- Fullfill the simple category will improve cost effectivness
- Ethnic prevalence (ethic?)

Genetic screening should enable people to escape their fate by giving them the freedom to make an informed choice and adopt a chosen course of action which they regard as acceptable

> (Health Council of the Netherlands, Committee of Genetic Screening, 1994)

Sperm chromatin structure : implications on human infertility

<u>author : D-r Gligor Tofoski</u> tutor : D-r Patrizia Grace Bianchi

Objective : The purpose of this review is to present the most recent research data about the chromosomal aberrations and chromosomal packaging and its implications on infertility.
 We stress the need of genetic counselling and genetic screening in all patients before undertaking ICSI assisted reproduction.

Methods : The literature on sperm chromatin structure and chromosomal abnormalities associated with the treatment of male factor infertility was rewieved, especially in connection with assisted reproductive techniques like intracytoplasmic sperm injection. The most recent outcome data from surveys of ICSI derived offspring is presented. Studies related to this topic were identified through MEDLINE.

Assisted reproductive techniques - ART



- In-Vitro Fertilization IVF
- Partial Zona Dissection PZD
- Sub Zonal Insemination SUZI
- Intracytoplasmic Sperm Injection -ICSI
- Round Spermatid Nucleus Injection
 ROSNI
- Microsyrgical Sperm Aspiration -MESA
- Testicular Sperm Aspiration -TESA

ICSI bypasses natural selection



ICSI is an assisted reproductive technique that bypasses the effective biological mechanisms of sperm selection that were set in place during the evolution of the human reproductive process

spermatozoa oocyte needle pipette media

Research trials

- Palermo 1992
- The application of ICSI to human reproduction was not preceeded by an extensive research in other mammals

First concerns

- Encouraged by the first reported results, which presented high success rate in both, fertilization and pregnancy rates, regardless of the severity of sperm defect, medical professionals thought that they have found an ideal solution.
- Debate and concern were raised on if using ICSI for the treatment of male infertility has the potential of a negative impact on the genetic composition of the human population for the future generations.
- Cystic fibrosis carriers in infertile males
 - CBAVD

Results

Chromatine structure of spermatozoa

- Normal variations: intra- and inter-variability
- Damaged DNA consequences
- During fertilization the oocyte may:
- 1) reject the sperm and fail to be fertilized,
- 2) it could repair the DNA and complete fertilization,
- 3) attempt to repair the DNA and complete fertilization after only partially completing the repair process.

Chromosomal abnormalities



- Infertile Fertile
- Sperm chromosomal abnormalities
 - infertile
 - fertile

Chromatine structure of spermatozoa

- Sperm chromatin structure abnormalities are not infrequent in males undergoing infertility treatments especially intracytoplasmic sperm injection.
- The application of ICSI in these males may results in the transmission or de novo introduction of genetic mutations or chromosomal abnormalities in their offspring.

Sperm analysis

 Morphology light microscope - computer assisted sperm analysis-CASA – Transmission Electronic Microscopy- TEM

- DNA structure
- Sperm Chromatine Structure
 Assay -SCSA
- staining, using Chromomycin A₃ - CMA₃
- sperm microinjection in mouse oocytes- cytogenetic analysis of the hybrid zygote

To date, no single laboratory test can assess a man's total fertility.

Genetic disorders disturbances in spermatogenesis

- azospermic, oligozoospermic men

- » a) 9766 infertile men (Johnson MD. 1998) 5,8% chromosomal abnormalities (sex chromosomes -4,2%, autosomal -1,5%)
- » normal newborns (cytogenetic screening- 0,38%)
- » b) (Peschka et al. 1996)
- » azospermic 13,7% (Klinefelter Sy-10,8%,
- » sex chromosomes 1,8%, autosomal-1,1%)
- » <u>oligozoospermic</u>- 4,6% (autosomal -3%,
- » sex chromosomes 1,6%)

Genetic disorders- certain diseases

- Klinefelter Syndrome
- Reciprocal translocation
- Robertsonian translocation
- AZF locus deletion
- Cystic fibrosis
- Androgen receptor mutations (insensitivity)
 - Kennedy's disease (late onset)
 - Immotile cillia syndrome
 - Kartagener syndrome

Offspring-different data - potential concerns

- I) Bonduelle et al. 1996 slightly increased sex chromosomes aneuploidy
- II) Prenatal Dg-amniocenthesis -585 newborn (Wisanto et al.1996)
 - 2% abnormal karyotypes
 - (1% paternaly transmission, 1% de novo)
- III) Danish cohort (Loft et al) –730 newborns -
 - 2,7% major birth defects, 1,2% minor birth defects
- IV) same Belgian data (Bonduelle) 420 newborns (Kuriczuk et al. 1997, Australia) using British Pediatric Association ICD-9 system : (major birth defects -7,38%, minor birth defects 0,71%)
 (normal in Australia population major- 3,78%, minor-0,48%)
- V) extensive genetical and pediatric control (Silber et al. 1998), no increased risk of congenital malformation (2,6%), no increased risk of de novo autosomal abnormalities, 1% risk of sex chromosome abnormalities

IVF-ICSI

130 IVF –120 ICSI (Van Golde et al. 1999) congenital malformations 3,0% - 1,7%
145 IVF-145 ICSI (Govaerts et al. 1998) congenital malformations 2,2% - 2,8%
not significantly differrent





Discussion

- Reproduction in human beings is generally a risky process
 - major cause of embryonic or fetal death chromosomal abnormalities
- Currently, our knowledge of genetics, genome and the genetic basis of disease is expanding at an unprecedent rate and will continue to provide us with an improving ability to identify and screen for genetic abnormalities and to asses the genetic risks of procreation.



Discussion

- Genetic counselling and appropriate screening of couples with male factor infertility should be performed before undertaking ICSI-assisted reproduction.
- An effort must be made to institute protocols that will allow a careful assessment of the inherent genetic risks; they should include genetic counselling, prenatal karyotype analysis, and evaluation and extended follow up of all children born.
- Results of such protocols should be continuously updated with respect to ICSI.

Dr Nkele Ndeki Ngoh.

ABSTRACT

Tubal disease constitutes 30% of infertility problems world wide, and has persistently been the bugbear of surgeons. Surgical attempts to solve the problem have been many and results have varied according to the technique as well as the surgeon. Earlier reports were frustrating and led to almost abandonment. The birth of new techniques accompanied with technological advancement did not only improve upon the knowledge of tubal pathology but brought along with it more than ever before, more controversies, concerning the management. Newer techniques appear to yield better results but their cost precludes many from their advantages. Simplified techniques may prove to be of much value to some communities. However, a more global approach as to the classification of pathology, patient selection, operative technique and result reporting is necessary to evaluate the real benefits of each procedure. Key words: Tube; Obstruction; Treatment.

INTRODUCTION.

Fallopian tube disease is responsible for over 20 to 30% ⁽¹⁾ of female infertility world wide. The lesions range from intrinsic intraluminal malformation of cilia, mucosa, or muscularis to gross occlusion of the lumen. Tubal obstruction has preoccupied many gynaecologists for several years. Its importance as a major cause of infertility was recognised by Burns in 1809 ⁽²⁾.

Whereas tubal surgery has been criticised for lack of convincing evidence, untreated complete bilateral tubal obstruction offers no hope of pregnancy ⁽³⁾.

Earlier attempts on the surgical repair of the fallopian tube were met with very poor pregnancy out come. Greenhill quoted success rates of 1 in 20 in 1957 and 1 in 6 28 years later ^{(1).} Until recently many authors believed that low pregnancy rates were due to major invasive surgery, being the main treatment at that time^{(4).} However, traditional microsurgery had an almost 20% pregnancy rate (PR) ^{(5).}

Despite the development of endoscopy during the 1960-1970s, the idea that large problems require large incisions so deeply dominated surgical thinking that there was little room to appreciate the advances of 'Key hole' surgery. Effective surgical correction of diseased fallopian tube is a relatively new aspect of gynaecological surgery that came up with the 'laparoscopic evolution' in 1989-1990. Its sweeping success marked the end of the traditional open surgery and encouraged surgeons to consider new perspectives ⁽⁶⁾.

Currently, a 50% overall success rate in surgery on the fallopian tube has been claimed ⁽¹⁾. This improvement may be due to the recent development of tubal endoscopic and carbon dioxide laser, techniques that have lead to better assessment of tubal disease and less invasive tuboplasty or tubal recanalisation procedures. However, despite these innovations, the absence of a universally accepted classification of the location, type and severity of tubal disease^{(1),} combined with conflicting views of management distorts the appreciation of the true pregnancy outcome rates.

In this article we attempt to review all the pertinent articles on MEDLINE, about the management of the three main sites of obstruction which are, proximal, mid and distal.

PATHOGENESIS

Pelvic inflammatory disease, including salpingitis, is mostly caused by ascending gonorrhoeal, chlamydial and non-specific infections. Tuberculosis, probably through haematogenous spread, is also a major cause of salpingitis. These germs have been discovered in many cases of acute salpingitis and are associated with tubal obstruction ^(7,8,9).

The acute phase of salpingitis is characterised by oedema of the plicae. In severe cases there is leukocyte infiltration of the inner muscularis and necrosis of the tubal epithelium. This may extend to the serosa and to the ovary –causing acute oophoritis and perisalpingitis. With recurrent infection the tubal plicae adhere and form typical adenomatous spaces. Eventually the entire tubal wall becomes involved, with subsequent occlusion of the fimbriated end. Partial or complete sealing of the isthmus leads to subsequent retention of inflammatory fluid (hydrosalpinx) or pus (pyosalpinx) within the tubal lumen ⁽¹⁰⁾.

In tuberculous salpingitis small elevated tubercles may be identified on the serosal surface. When the disease is more advanced the tube is markedly thickened and firm and there are numerous adhesions to adjacent bowel and ovary. The lumen contains caseous material and the peritoneum of the pelvis is usually involved with small white tubercles varying in size from

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0.1 to 0.2 cm. The fimbriated part is usually patent and everted. Microscopically the tubal mucosa presents with characteristic tubercles. In addition, when the disease is extensive, areas of caseous necrosis are common. In chronic cases the fallopian tubes are straight, rigid and have the appearance of a pipe stem⁽¹⁰⁾. Tubal obstruction may occur from the occasional exuberant growth pattern of the epithelium.

Salpingitis isthmica nodosa is also a major cause of tubal obstruction. Wang, 1989 ⁽⁷⁾ in his series, observed that salpingitis isthmica nodosa was the cause in 33% of tubal obstruction. Gonorrhoea and non specific infections were the 1st and 2nd most common causes in the same series. Salpingitis isthmica nodosa is a disease process of unknown aetiology, characterised by nodular thickening in the intramural and isthmic portions of the fallopian tube. It is thought to be a sequelae of inflammation either of gonorrhoeal or tuberculous type ⁽¹⁰⁾.

Endometriosis may affect the fallopian tube in severe cases and lead to distal obstruction with hydrosalpinx formation. Tubal obstruction is more often caused by compression or stricture than by mucosal adhesions⁽²⁾. Tubal obstruction also results from voluntary tubal ligation and may also be a complication of pelvic surgery.

DIAGNOSIS

CLINICAL PRESENTATION

The fallopian tube is the most sensitive pelvic organ to pain (10). Patients with acute or chronic salpingitis may present with either a present or a past history of pelvic pain or dysmenorrhoea. Some who had undergone treatment may be asymptomatic but complain of either primary or unexplained secondary infertility. Others may or have had an abortion, a puerperal infection or had either undergone a voluntary surgical sterilisation or pelvic surgery for a gynaecological problem.

INVESTIGATION

BACTERIOLOGICAL :

It is generally accepted that before any assessment of tubal patency and structure the first line of investigation should be bacteriological investigation followed by treatment with appropriate antibiotics.

ASSESSMENT OF EXTENT OF TUBAL PATENCY

<u>Hysterosalpingography (HSG</u>). Hysterosalpingography is commonly accepted as the initial test of tubal function in the investigation of infertility $^{(2)}$. However it may give rise to false diagnosis of proximal obstruction because of tubal spasm. Tubal diverticulum too may be wrongly diagnosed as distal obstruction $^{(11)}$

The combined use of HSG with laparoscopy increases the diagnostic possibilities to include endometriosis (¹²). However, if investigation is limited to HSG and to laparoscopy, proximal tubal obstruction (PTO) may be over diagnosed and consequently overtreated ^{(2).}

Swart et al, 1995 ⁽¹³⁾ did a metanalysis of 20 studies comparing HSG and laparoscopy for tubal patency and peritubal adhesions. They observed that HSG was of limited use in tubal diagnosis because of its low sensitivity. However, its high specificity makes it a useful test for ruling out tubal obstruction. For the evaluation of peritubal adhesions, HSG is not reliable.

In order to circumvent the problem of tubal spasms and to distinguish organic tubal obstruction from functional obstructions, some authors have suggested the use of muscle relaxants such as terbutaline ⁽¹⁴⁾.

<u>Contrast sonography</u>, has the advantage over HSG of not using radiation $^{(2,15)}$ and the site of obstruction can be ascertained more accurately with colour Doppler depending on the contrast medium used. The proponents of this technique claim that, its high concordance of about 86% in diagnosing blocked tubes gives it an edge over laparoscopic chromopertubation $^{(16)}$.

<u>Laparoscopic chromopertubation</u>. With the use of intrauterine dye injection, tubal patency can be checked during laparoscopy. Under local anaesthesia, laparoscopic chromopertubation can be an office procedure ⁽¹⁷⁾. Laparoscopy has the added advantage of diagnosing fibroids, ovarian abnormalities, endometriosis and/or other congenital abnormalities ⁽¹⁸⁾.

Patency of the fallopian tube does not necessarily equate with normality of the mucosa and pathological lesions may be missed if more accurate methods of tubal assessment are not employed ^{(2).}

Fallopian tube endoscopy. Tubal endoscopy either by the transvaginal (Falloscopy) or transabdominal approach

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(Salpingoscopy) permits the direct visualisation of the tubal epithelium. *Falloscopy* is used in the investigation of the status of the proximal tube. Two types exits: The coaxial (guide wire) falloscope, introduced by Kerin, requires hysteroscopy for its introduction. The linear everting catheter (LEC) falloscope has a terminal everting balloon sheath which facilitates its introduction without hysteroscopy. Falloscopy may be employed with or without general anaesthesia. They are suitable for office use. Many authors have used falloscopes for both diagnostic and therapeutic purposes. In case of proximal tubal obstruction, the only alternative for assessing the state of the tubal mucosa is by performing transabdominal *salpingoscopy* during laparoscopy. It is most convenient in the evaluation of the distal segment of the tube ^(2,20,19).

TREATMENT OF TUBAL OBSTRUCTION

In the literature, there have been many techniques and technique combinations used in the treatment of tubal disease. These range from the old laparotomy, gaseous insuflation, hydrotubation, microsurgery to the more recent laparoscopic surgery, modern microsurgery using the CO2 laser and the micro endoscopic procedures. Irrespective of the type of surgical procedure, the general principles of infertility surgery include gentle manipulation, meticulous haemostasis, prevention of post operative infection and adhesion formation ⁽²⁾. These could be met by the use of good magnification instruments, continuous saline cleansing and pinpoint haemostasis.

The once commonly used gaseous insufflation became obsolete when its usefulness was questioned in1986 ^{(2).} On the contrary hydrotubation is used by some authors to maintain tubal patency while some feel it may predispose to infection. Grant (1971), ⁽²¹⁾ used hydrotubation and had a PR of 37% as against 16% pregnancies in treated controls. Recent reports especially from China reveal the importance of hydrotubation in the treatment of tubal disease ^{(22).} Those who use hydrotubation as an adjuvant to the post surgical management of tubal obstruction do it on day 3,6 and 14 ^{(1).}

Since 1987, following the approval of tubal endoscopic techniques on humans in the USA, there have been many reports of several techniques and technique combinations on the treatment of tubal obstruction ⁽²⁰⁾. Hereby we review some of the common techniques and technique combinations relative to the site of obstruction.

A: TREATMENT OF PROXIMAL TUBAL OBSTRUCTION

I) ENDOTUBOPLASTY TECHNIQUES

The first known attempt to pass instruments through the vagina and enter the tubal lumen by the uterotubal ostium (UTO), was attributed to Tyler Smith in 1849. In 1856, Gardner described a method for transvaginal passage of graduated probes. In 1970, a fibroscope 1mm in diameter was used to examine the tubal lumen but poor illumination and technical problems made it difficult to explore this adequately ⁽²⁰⁾. Intra-luminal tubal endoscopy may be performed by the transvaginal (falloscopy) or transabdominal (salpingoscopy) approach ⁽²⁾.

FALLOSCOPY

The coaxial technique of falloscope described by Kerin,1990 ⁽²⁰⁾ required hysteroscopically directed tubal cannulation with a flexible guide-wire having an outer diameter (OD) of 0.3-0.8 mm followed by serial passage of a Teflon cannula (OD up to 1,3) over the guide wire. The guide-wire was then removed and the falloscope passed down the lumen of the Teflon cannula ⁽²⁾. The falloscope has balloon catheters with a shaft OD of 1,0 mm and inflated balloon diameters ranging from 2 to 5 mm over lengths of 2 cm that were used for dilating tubal strictures breaking down intraluminal adhesions and mobilising intaluminal debris. This coaxial balloon catheter had its balloon mounted outside the catheter shaft ⁽²⁰⁾.

The second (more recent) type of falloscope is the Linear Eversion Catheter (LEC) system (Imagyn Medical Inc,San Clemente, California, USA). It utilises a pressurised tubular polyethylene balloon which can be unrolled from within a plastic polymer cannula after having the falloscope preloaded into its lumen. The balloon caries the endoscope into and along the tube, protecting the tube and endoscope from damaging one another and negotiating the curves and strictures without exerting sharing forces on the tubal wall ⁽²⁾. The LEC system may be used without hysteroscopic control ^(2,20).

Falloscopic descriptions of endotubal lesions, secondary to endotubal infection, tubal surgery, ectopic pregnancy, salpingitis isthmica nodosa (SIN), endotubal polyps and non-specific areas of devascularisation, epithelial flattening, atrophy and fibrosis, have been published ⁽²³⁾. From these falloscopic findings Kerin, (1992) ⁽²³⁾ developed a scoring system for tubal disease as shown in table I.

Table I: Falloscopic classification and localisation of tubal lumen disease (23).

5						
	Right tube				Left tube	
SITE OF DISEASE PATENCY	intramural isthmic	ampullaryfimbrial	intramural	isthmic	ampullary	fimbrial
Patency 1						
Stenosis2						
Obstruction3 EPITHELIUM						
Normal1						
Pale,Atrophic2						
Flat,Featureless3 VASCULARITY						
Normal1						
Intermediate2						
Poor pallor3						
ADHESIONS						
None1						
Thin, weblike2						
Thick3						
Hydrosalpinx3						
DILATATION						
None1						
Moderate2						
Hydrosalpinx3						
OTHER2-3 Cumulative score TOTAL SCORE	RIGHT TUBE=	(NORMAL=20)	LEFT 7	ГUBE=	(NORMA	L=20)

A cumulative score for each tube of: 20 = Normal Tubal lumen; > 20 but < 30 = Moderate Endotubal disease; > 30 = Severe Endotubal disease. Mucus Plugs or Tubal Debri, Endotubal Polyps, Salpingitis Isthmica Nodosa, Inflammatory, Infective; Neoplastic conditions and absent tubal segments are each assigned a score of 2 to 3 depending on the significance of the lesion.

Falloscopy may be combined with other procedures such as :

(1)Laparoscopy.

(2)Ultrasound.

(3)Fluoroscopy.

(4)Hysteroscopy and laparoscopy.

(5)Lavage under pressure.

The coaxial technique may be used to canalise the tubal lumen, and/or the balloon catheter may be used to dilate the lumen (Balloon tuboplasty) ⁽¹⁴⁾. Tables II to IX are summarise the various techniques described in the literature. Pregnancy rates (PR) are mentioned when possible.

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Table II:Fluroscopic guided transcervical catheter salpingoplasty with catheter and guide wire.

Reference	N°	Pat%	IUP%	EP%	Observation
Martensson et al (1993) ⁽²⁴⁾	10	61.5	50	10	4 months
Lang and Dunaway (1994) ⁽²⁵⁾					6 months
failed reversal surgery, 4 had fistulas	7	43			no fistula case was
failed tuboplasty	12	100			occurred after 3-36 months
total	19	79	16	0	

Table III: Fluroscopic guided transcervical balloon tuboplasty.

Reference	N°	Pat%	IUP%	EP%	Observation
	77	92	27.2	1.3	12 months follow-up
Confino et al (1990) $^{(14)}$					5 re occlusions
Lasry et al (1993) ⁽²⁶⁾	30	57	20	3.3	6 months follow-up. 2
					re-occlusions
Sueoka et al (1998) ⁽²⁷⁾	106	90	34.9	0	

Table IV: Laparoscopic guided transvaginal catheterisation followed by ultrasonographic guided hydrotubation to ascertain patency.

Reference	N°	Pat	IUP%	EP%	Observation
Lisa and Syowa (1999) ⁽²⁸⁾	19	84.2	26.3	0	

Table V: Hysteroscopic, laparoscopic and fluroscopic guide wire cannulation and direct balloon tuboplasty (DBT)

Reference	N°	Pat%	IUP%	EP%	Observation
Kerin et al (1990) ⁽²⁰⁾					The was partial perforation of
non obstructive cases	10	60			the tubal wall in one case of SIN and two complete isthmic
stenosis	15	40			perforations.
SIN	2	50			
fibrotic obstruction	5	0			
total	32	41			

Table VI: Laparoscopic guided falloscopy with LEC.

Reference	N°	Pat%	IUP%	EP%	Observation
Lee (1998) ⁽²⁹⁾					one case of perforation of the
interstitial occlusion	5	60			ampulla.

Table VII: Non hysteroscopic falloscopy.

Reference	N°	Pat%	IUP%	EP%	Observation
Sueoka et al (1998) ⁽²⁷⁾	50	85.3	22	0	2 months follow-up. 19.6% had
	50				re-occlusions within 3 months

Table VIII: Ultrasound guided transcervical tuboplasty.

Reference

N° Pat% IUP% EP% Observation

Stern et al (1993) ⁽³⁰⁾ 30 96 38 0 1 year follow-up						
	Stern et al (1993) ⁽³⁰⁾	30	96	38	0	1 year follow-up

Table IX: Ultrasound and fluroscopic guided transcervical balloon tuboplasty:

Reference	N°	Pat%	IUP%	EP%	Observation
Confino et al (1992) ⁽³¹⁾	4	100	25	0	1 month follow-up

NB: N° = Number. Pat = Patency. IUP= Intrauterine pregnancy. EP= Ectopic pregnancy.

With the different techniques, it is not possible to compare the various methods used. It is generally accepted that tubal endoscopic procedures provide a better assessment of the structure of the tubal mucosa thus facilitating patient selection. Falloscopic techniques are less invasive, have high patency rates (>80% in most studies) but appear to be limited to non-fibrotic tubal obstructions. Complications of perforation are possible in cases of applied force to bypass complete pathologic obstructions such as SIN ⁽²⁸⁾. Their use without general anaesthesia gives it a further advantage in daily office use.

II) HSYTEROSCOPIC TUBAL CATHETERIZTION AND HYDROTUBATION

This technique has been described by Su-Chong,1994 and others in the Chinese literature and success rates of 35,9%, and 40-60% have been reported ^(22,18). In Su-Chong's (1994) ⁽²²⁾ series 54 infertile women with previously diagnosed tubal disease underwent hysteroscopic catheterisation . Catheterisation was performed by the introduction at the utero-tubal ostium (UTO) of a plastic tube of 1.4 OD, up to 1-5 mm into the tubal lumen under hysteroscopic guidance. The procedure was followed by successive monthly selective hydrotubation over a period of 3 months. Patency was achieved in 62.5% of cases of intramural block and 38.8% of isthmic stenosis. Globally, complete patency was achieved in 54.1%. Thirteen women fell pregnant, 12 were intrauterine pregnancies and one was an ectopic pregnancy. Su-Chong (1994), however pointed out the possible complication of hydrosalpinx with this technique.

III) INTRAUTERINE INJECTION OF 'ANGELICAE' COMPLEX.

Lian et al, 1991 ^{(33),} after preliminary experimentation in rabbits, followed up 48 infertile women. Fallopian tubal obstruction had been previously proved by hysterosalpingography in all the women. These women were divided into two groups. Thirty patients were treated with intrauterine injection of 'Angelicae' complex. The control group of eighteen women were treated with transcervical intrauterine injection of gentamycin and 0,9% saline for 3 to 6 months. The effective rates were 94.6% and 56.6% (p < 0,01) and the subsequent pregnancy rates were 46.7% and 27.8% respectively in the different groups. Angelicae complex is a Chinese medication of the Kampo medicines which has an effect on the clearance of circulating immune complexes ^{(34).}

IV) MICROSURGICAL ANASTOMOSIS FACILITATED BY CO2 LASER MICRODISSECTION OF INTRAMURAL SEGMENT AND RESECTION OF SCARRED TISSUE.

Vilos,1991 ^{(5),} reported the use of CO2 laser technique in the microdissection of intramural segment and resection of scarred tissue prior to microsurgical anastomosis. Within a period of 5 years, 21 fallopian tubes in 14 patients had been anastomised using this technique. After re-anastomosis, tubal length was 4 to 8 cm in all tubes. All patients were followed for at least 1 year post surgery. In this study, 7 of the included women had proximal tubal occlusion after electrocautery for sterilisation. In this group, the tubal patency rate was 100%, whereas the intrauterine pregnancy rate was 71% (5 of 7 patients). One other patient had two successive ectopic pregnancies. The seventh patient was 40 years old and did not ovulate on 150 mg of clomiphene citrate. In the other group of seven women, proximal tubal obstruction was associated with other tubal diseases. In this group one patient with salpingitis isthmica nodosa conceived twice after bilateral intramural re-anastomosis.

B: TREATMENT OF MID-SEGMENT OCCLUSION

The most common surgical treatment of the mid segment is re-anastomosis for reversal of sterilisation $^{(1)}$. Other causes may be localised constriction from previous tubal repair following ectopic pregnancy, endometriosis, infection and congenital constrictions $^{(1,35)}$. Mid segment tubal occlusion as a complication of inguinal repair is rare $^{(35)}$.

In the selection of patients, preoperative HSG and laparoscopy to determine the length of the proximal tube and that of the remaining tube are important ⁽¹⁾. The PR after surgery in most studies has been associated with the length of the tube ^(36,37,38). The longer the tube is above the critical length of 3cm ⁽¹⁾ the better the PR outcome. However, in a large study by Kim et al,1997 ⁽³⁹⁾ there was no statistically significant difference in the lengths of tubes. However, he observed that the younger patients had longer tubes and became pregnant earlier than the older patients with shorter tubes.

The success rate also depends on the type of sterilisation that was carried out $^{(1)}$. It is higher with the Pomeroy and Uchida techniques as well as with the fallopian ring and the Hulka clip methods of ligation $^{(1,40)}$.

Re-anastomosis of the chronically ill tube is not helpful. Wang et al, 1998 ⁽⁷⁾ in a series of sixty cases of female infertility in which several operative procedures were used, re-anastomosis of the chronically ill tubes was not helpful. However neither unilateral nor bilateral re-anastomosis seems to affect the PR outcome.

The different possibilities of anastomosis are isthmic-isthmic, isthmic-ampullary and ampullary-ampullary ^{(1).} Re-anastomosis of tubal segments requires adequate proximal and distal lengths of normal tube. After excision of the occluded segment, the mesosalpinx is approximated, and an end to end , layer to layer anastomosis performed. Disparity between the calibre of the residual normal tube segments is compensated by angulation incision of the smaller diameter segment or by a smaller incision made in the potentially larger segment. The anastomosis may be performed over a nylon splint ^{(1).}

Theoretically, the procedure of re-anastomosis is better achieved by way of microsurgery under magnification ^{(1).} However, Jones and Rock, 1978 ⁽⁴¹⁾ found no difference between macro- and microsurgery. Winston and Gomel without using magnification in microsurgery had a success rate of 70% ^{(1).} Similarly Gupta et al, 1990 reported a higher PR of 88% with macroscopic tuboplasty in 57 cases with reversal of sterilisation ^{(42).} Despite these controversies many large studies reveal very high success rates following microsurgery. Liu et al,1997 out of 1029 cases, had 960 IUPs and only 12 EPs ^{(43).} Kim et al,1997⁽³⁹⁾ out of 922 cases had a global PR of 53% ^{(38).} Kim et al,1997 ⁽³⁷⁾ out of 387 cases had a PR of 91%. In a relatively smaller study of 23 patients, Fischer,1996 ⁽⁴⁴⁾ obtained an overall PR of 78.3% and an IUP of 68.6%.

Laparoscopic microsurgery though relatively new ⁽⁴⁶⁾ is gradually being considered an alternative to open microsurgery. The first laparoscopic microsurgical anastomosis was carried out in February 1992 and since then most cases of laparoscopic microsurgery had encouraging results. Yoon et al (1997) ⁽⁴⁰⁾ reported a PR of 77.7% (38/49). Lee et al,1995 ⁽⁴⁷⁾ reported a successful case in a woman of 33 years who had had a failed tubal anastomosis. Silva and Perlins,1995 ⁽⁴⁷⁾ used a combination of laparoscopic and minilaparotomy techniques in treating 11 patients of which five (45%) had an IUP and one had two successive ectopic pregnancies. Kartz and Donesky, 1994 ⁽⁴⁸⁾ out of 5 patients had a PR of 50%. Various stitch techniques to ease laparoscopic microsurgery have been developed. Dubuisson and Swolin, 1995 ⁽⁴⁵⁾ used a new one- stitch technique to treat 4 cases. The stitch was placed at the ``12 o`clock`` site of the antimesenteric border. Barjot et al ,(1999) ⁽⁴⁹⁾ used a three stitch technique in 16 patients and had a PR of 31.2% (5/16). However, Reich et al, 1993 ⁽⁵⁰⁾ in a retrospective review of 22 laparoscopic tubal anastomosis cases, in which the Swolin two-stitch technique was used, reported a low overall fertility rate.

C: TREATMENT OF DISTAL TUBAL OBSTRUCTION

The very frustrating PR results (0-5%) of tubal surgical repair in the pre-antibiotic era of the 1930s led almost 60% of the participants of the Chicago Gynaecologist Society to be ``definitely opposed`` to salpingostomies and tubal implantations ⁽⁵¹⁾. From that period until 1977, the combination of a thick walled ampulla and an intramural occlusion was considered irreparable, and the tube was left in-situ ⁽⁵²⁾. However, in case of thick-walled tubal end, a so called 'cuff neostomy' was performed. Palmer,1960 ⁽⁵²⁾ described a less radical technique of neostomy which consisted of stripping the fibrotic muscular layer under the microscope so that eversion of the mucosa was easier.

In addition to conventional and traditional microsurgery, other operative techniques on the distal tube include the use of laparoscopy and CO2 laser. All of these can be used in performing salpingostomies, fimbrioplasties and salpingectomies. As of now there is no consensus about which of the methods yields the best results in terms of intrauterine pregnancy out come.

CONVENTIONAL SURGERY AND TRADITIONAL MICROSURGERY.

Earlier PR results of conventional surgery ranged from 5.6% to 41% while those of traditional microsurgery range from 21% to 37% ⁽⁵³⁾. Term pregnancy rates in conventional surgery are quite variable and generally less than 20% whereas those of microsurgery are less variable and most are in 20% to 30% range ⁽⁵¹⁾. The success depends on the type of technique used. Verhoven in 1983 in a review of 167 cases reported a PR of 20.4% following microsurgery salpingostomy and 0% after cuff neostomy ⁽⁵²⁾.

Fimbrioplasty and Neosalpingostomy.

These terms have created a lot of controversy. In 1977 the 9th World Congress of Fertility and Sterility defined Fimbrioplasty as : a) deagglutination and/or dilatation of the fimbriae, b) by incision of the peritoneal ring, c) by incision of the tubal wall. Salpingo-neostomy (Salpingostomy) was defined as: a) terminal, b) mid-ampullary (medial), c) isthmic (including linear salpingostomy) ^{(51).} Authorities differed whether surgery on distal tubes found to have remnants of the fimbriae after incision of the tubal wall constituted a fimbrioplasty or salpingostomy ^{(51).} The modified definition of fimbrioplasty by the 10th World Congress (1980) of Fertility and Sterility as ``with serosal incision for completely occluded tube`` did not help ⁽⁵¹⁾. In reporting cases Verhoven (1983) and Bateman (1987) used the term ``Fimbrioplasty`` in cases of

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partial tubal obstruction with fimbriae present and salpingostomy as complete tubal obstruction, regardless of the findings after incision. In complete tubal obstruction there is no spillage, and if pin point openings were found the repairs were not considered as salpingostomy because these tubes usually had undergone less damage and offered the possibility of better results ⁽⁵²⁾. From earlier reports, fimbrioplasty has always yielded better PR than salpingostomies ⁽⁵²⁾ as shown in the table Xa and Xb.

Table Xa :Results of salpingostomy.

Reference	Number of Patients	Term Pregnancy(%)
Mulligan (1966) ⁽⁵⁴⁾	45	8
Garcia (1968) ⁽⁵⁵⁾	25	8
Rock et al (1978) ⁽⁵⁶⁾	18	6
Decherney and Kase (1981) ⁽⁵⁷⁾	9	0
Wallach et al (1983) ⁽⁵⁸⁾	24	8

Table X b: :Results of fimbrioplasty.

Reference	Number of Patients	Term Pregnancy(%)
Siegler and Kontopoulos(1979) ⁽⁵⁹⁾	20	35
Fayez and Suliman(1982) ⁽⁶⁰⁾	25	40
Frantzen and Schlosser(1983) ⁽⁶¹⁾	49	22
Patton(1982) (62)	35	60
Donnez and Casanas(1986) ⁽⁶³⁾	132	60

LAPAROSCOPY

Results of salpingoscopy and fimbrioplasty done by laparoscopic surgery also give an edge to fimbrioplasty in terms of IUPs. Lavergne ⁽⁶⁴⁾ in 1996 out of 46 cases of laparoscopic surgery in which salpingostomy and fimbrioplasty were performed, 75% of the 18 patients who were pregnant were as a result of fimbrioplasty. Table XI is a summary of three studies comparing fimbrioplasties and salpingostomies.

Table XI: Fimbrioplasty compared with salpingostomy.

Reference	Fimbric	oplasty	Salpingostomies		
	NumberIUP(%)		Number	IUP(%)	
Mettler at al (1979) ⁽⁶⁵⁾	51	31	38	26	
Fayez(1983)(66)	14	21	19	-	
Kasia (1997) ⁽⁶⁷⁾	108	33.3	86	10.5	

Tubal Score.

Many authors hold that, the outcome of tubal surgery depends on the extent of tubal damage. While IUPs are higher in tubal stages I and II, and fairly low in stage III, they are hopeless in stage IV as observed in table III. Dubuisson (1994),⁽⁶⁸⁾ Filipini (1996),⁽⁶⁹⁾ Kasia (1997),⁽⁶⁷⁾ and many others state that patients with tubal stage IV would benefit more from IVF-ET. Table XII is a summary of the various findings.

Table XII :Variation of IUP rates with tubal score.

Reference	Tubal Score							
	Ι	III	IV					
Dubuisson (1994) ⁽⁶⁸⁾	9/15(60)	15/29(51.7)	2/16(12.5)	0/21(0)				
Filipini (1996) ⁽⁶⁹⁾	12/21(51)	19/49(38.7)	3/22(13.6)	0/12(0)				
Kasia (1997) ⁽⁶⁷⁾	26/78(33.3)	15/46(32.6)	4/47(8.5)	0/23(0)				

NB :Values in parentheses are percentages.

CO2 Laser in laparoscopic and micro surgery.

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With the advent of CO2 laser the IUP outcome of laparoscopic surgery is almost equating that of modern microsurgery. CO2 laser has the advantage of performing adhesiolysis by vaporisation. For neostomy, the tube can be sectioned without any bleeding and the surgeon can work both, quickly and accurately ^{(5,70,71).} In 1991, Canis ⁽⁷²⁾ operated on 87 patients. He used a combination of laparoscopic surgery and CO2 laser. The IUP outcome per tubal stage, as observed in table XIII, was better than those described earlier. However, not all results were statistically significant.

Tubal score	Laparoscopic	surgery	Microsur	gery
	Number	NumberIUP(%)		IUP(%)
	07	22.2	76	20.2
	8/	33.3	/6	30.3
Ι	32	50	12	66.6
II	37	32.4	30	36.6
III	12	8.3	21	14.3
IV	6	0	13	7.7

Table XIII : CO2 laser laparoscopic surgery versus microsurgery.

SALPINGECTOMY OR CONSERVATIVE SURGERY.

Alboulgar et al,1998 ⁽⁷³⁾, were the first to mention how fluid in the uterine cavity before embryo transfer could be a possible hindrance for implantation. Hydrosalpinx fluid has pH values (8.45 to 8.65), significantly higher than the physiologic range and at either the 100% or 10% concentration it has a significant embryotoxic effect ⁽⁷⁴⁾. Anderson et al (1994) ⁽⁷⁵⁾ diagnosed hydrosalpinges by ultrasound and found that those patients with hydrosalpinges had decreased pregnancy rates and increased miscarriage rates. There is however a controversy as to the benefits and disadvantages of salpingectomy or conservative management. Aspiration of the hydrosalpinx fluid has been tried ⁽⁷⁶⁾ while others have proposed salpingectomy and or referring the patient for IVF-ET ⁽⁷⁷⁾.

Dechaud et al,1998 ^{(78),} in a pilot study of 60 women who underwent IVF-ET, reported an implantation rate of 13.4% in women with salpingectomy and only 8.6% in those without salpingectomy. Still in the same group the rate of ongoing pregnancies was higher (34%) in the salpingectomy group compared to the control group (8.7%). However, Bredjaer (1999) ^{(79),} in a case control study found no difference in the rates of implantation and ongoing pregnancies between the two groups. Table XIV is a summary of both studies.

Reference	Salpingectomy			No salpingectomy.		
	N°	Impl R.	On Pr.	N°	Impl R.	On Pr.
Dechaud(1998) (78)	30	13.4%	34.2%	30	8.6%	18.7%
Bredjaer(1999) ⁽⁷⁹⁾	139	19%	21.7%	139	21.%	21.6%

Table XIV: salpingectomy versus no salpingectomy before IVF-ET.

Nb : N°= number Impl R=Implantation rate. On Pr=Ongoing pregnancy.

VanVoorhis ⁽⁷⁶⁾ in 1998 carried out a study in which he assessed the differences in implantation rates between women with tubal disease with or without hydrosalpinges based on ultrasound diagnosis. He observed that implantation as well as clinical pregnancy rates were reduced in women with hydrosalpinges although these differences did not quite reach statistical significance. His results as well as those of similar studies are summarised in table XV.

In the summary that follows the ongoing pregnancy has been calculated as the percentage of the difference between the total number of pregnancies and the total number of pregnancy loss over the total number of pregnancies.

Table XV :	Hydrosalpinx	compared	with no 2	hydrosalpinx	in IVF-ET.
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Reference	Hydrosalpinx			No hydrosalpinx			
	N°	ImplR (%)	OnPr (%)	N°	ImplR (%)	OnPr(%)	
Anderson et al 1994 ⁽⁷⁵⁾	62	3	30	493	10	64	
Vandromme et al 1995 ⁽⁸⁰⁾	37	4	100	41	11	86	
Fleming and Hall 1996 ⁽⁸¹⁾	79	9	83	198	15	93	
Katz et al 1996 ⁽⁸²⁾	79	4	56	812	12	69	
Sharara et al 1996 ⁽⁸³⁾	63	10	89	60	13	91	
Van Voorhis 1998 ⁽⁷⁶⁾	34	18	15	124	37	34	

The negative effect of hydrosalpinges on implantation as observed in the above studies seems to be nullified when the hydrosalpinx is treated. It may be that surgical removal has an advantage over aspiration. In the summary that follows (Table XVI) van Voorhis,(1998)⁽⁷⁶⁾ used aspiration for treatment whereas Vandrome et al (1995) ⁽⁸⁰⁾ used surgical treatment. When these cases were compared to a control group with untreated hydrosalpinges, the implantation rate was still higher in the treated group than in the control group. However, both the implantation rate and the ongoing pregnancy rate were higher in the surgically treated group than in the aspirated group. More studies have to be carried out to show if this difference could be due to the incomplete removal of hydrosalpinx fluid by aspiration procedures.

Reference	Hydrosalpinx treated			Hydrosalpinx not treated		
	N°	PR.	ON Pr.	N°	PR.	ON Pr
By aspiration	16	31%	31%	18	5%	0%
(van Voorhis (1998) ⁽⁷⁶⁾						
Surgical treatment (Vandrome et al	22	73%	81%	37	19%	100%
(1995) (80)						

Table XVI : Hydrosalpinx treated versus untreated hydrosalpinges in IVF-ET.

The study carried out by Shelton et al (1996) ⁽⁸⁴⁾ falls in line with the above studies but peculiar because it was a retrospective study in which the same patients were followed up by the same team. When fresh and frozen embryo transfers were carried out in 15 patients who had hydrosalpinges there was only one pregnancy. This pregnancy ended in a miscarriage. However, after salpingectomy fresh and frozen embryo transfers resulted in 9/15 (60%) pregnancies, of which 3 ended in miscarriages and 6 (67%) were ongoing pregnancies ⁽⁸⁴⁾.

Discussion

Green Armytage (1959), sited by Bateman, (1987),⁽⁵¹⁾ as early as 1959 remarked that tubal disease was the still the greatest bugbear of infertility clinics. To date, Green-Amrytage's quotation is still quite appropriate ⁽⁵¹⁾. Its magnitude can be objectivated from the plethora of techniques and technique combinations that are employed today to treat this disease.

In the pre-antibiotic era of the 1930s the pregnancy rates were frustrating $(0-5\%)^{(51)}$. It gradually climbed to 20-30% with microsurgery and lately to 50-79% with the combined use of CO2 laser techniques in both laparoscopic and laparotomy microsurgery. With the invention of falloscope a good proportion of intraluminal pathology of tubal obstructions was found not to be of tubal origin ⁽¹⁴⁾. The tendency since then has been shifted towards endotubal surgery which of course has its own limits.

In the mid 1980s, when Platia and Kudy (1985) and Confino et al (1986) suggested the possibility of intraluminal interventions, DeCherney, 1987⁽⁸⁴⁾ was sceptical. Today, apart from tubal spasms, transcervical tubal catheterisation has been applied in dislodging intraluminal plugs, functional sphincterotomy and polypectomy ⁽¹⁴⁾. Its success can be seen from the many authors who have used various methods in applying this procedure.

This suggests that a transvaginal catheter approach towards proximal tubal occlusion can be successful in achieving patency in a good number of women and will allow pregnancy in many $^{(19)}$. The patency rates have reached high levels such as 90-97% $^{(19)}$. However the PR outcome which is the prime concern of the surgery has also climbed (50%) $^{(19)}$ but not as much. The various techniques have their merits and demerits:

Fluoroscopic guided catherisation has the advantage of being both diagnostic and therapeutic. The highly detailed image of the fallopian tube remains unsurpassed by sonography even when high resolution Doppler flow equipment is used (Stern et al 1991) ⁽³¹⁾. This method, however, exposes patients to radiation, the equipment is expensive and not easily available ⁽³¹⁾.

Sonographic guided intracervical catheterisation has the advantage over fluroscopic procedures in that it is less expensive, readily available (Lisse and Sydow,1991) ^{(31),} can be used on an out patient basis and for the deposition of spermatozoa and gametes. It is also minimally invasive, diagnostic and therapeutic. The human fallopian tube is a tortuous organ which renders ultrasonoghaphic imaging rather difficult. Frequent movements of the catheter tip call for continuos movement of the transducer. This requires a very skilful reproductive sonographer who is familiar with genital anatomy and sonographic appearance of the catheter ^{(31).} Visualisation of microbubbles through the fallopian tube and into the cul-de-sac `lighting up` is a less equivocal sign of tubal patency ^{(31).}
Balloon tuboplasty is equally minimal invasive and can be used on outpatient basis. It has the added advantage of achieving functional sphincterotomy. This is particularly useful because it delays the reformation of intraluminal plugs unlike other procedures which simply dislodge them^{(14).}

When transcervical tubal catheterisation is performed under laparoscopic guidance the structure of the uterine cavity is seen and any abnormalities noted.

Transcervical tuboplasty combined with laparosopy has the advantage of direct visualisation of pelvic structures and other related pathologies.

Though complications with the use of tubal catheterisation procedures are few cases of perforation of the ampulla have been noted especially when force is used to bypass fibrotic occlusions and salpingitis nodosa.

In China a less expensive method of tubal catheterisation under hysteroscopic control has been developed ^(18,22). In the place of catheters, flexible plastic tubes of 1.4 mm OD were introduced at the UTO up to 1-5 mm into the tubal lumen. This was followed by hydrotubation over a period of 3 months. A global patency rate of 54% and PR of 24% were achieved. These results were lower than the other more expensive methods of tubal catheterisation and almost equate with those of more invasive surgical techniques.

Many agents have been used in hydrotubation with the aim of maintaining tubal patency ^{(2).} Grants,1971⁽²¹⁾ used hydrotubation and had a PR of over 40% in his series. Lian et al (1991) used the `Angelica`complex in hydrotubating women with proximal tubal obstruction and achieved a patency rate of 94.6% as well as a PR of 46.7%. Unfortunately there are very few reports so far on the use of this complex in hydrotubation. Otherwise, if these results could be reproducible, hydrotubation, using the Ángelica`complex , as an adjuvant to transcervical tubal catheterisation may be beneficial.

Laparoscopic and laparotomy microsurgical techniques in combination with CO2 laser are used for the treatment of tubal implantations ⁽⁵⁾. However preference of this technique, except for a selected group of patients, should be reconsidered. Sulak et al,1987 demonstrated that crystallised tubal secretions can cause obstruction of the proximal tube ⁽¹⁴⁾. Similarly in a multicentre study, Confino et al (1990), observed that a significant proportion of their patients with proximal tubal had obstructions form intraluminal plugs. If tubal occlusion is caused in many by intraluminal plug formation, microsurgical tubal re-anastomosis would convert an apparently normal tube into a scarred tube ⁽¹⁴⁾.

In mid tubal occlusions, sterilisation reversal is the main surgical procedure^{(1).} Most of the operations used to be carried out through laparotomy with or without magnification but presently they are also carried out by microsurgical laparoscopy ^{(1,44).} Results of surgery seem to be associated with the tubal length above the critical 3 cm ^(36,37,38) and the previous method of surgical intervention ^(1,40) than to the type of reconstructive surgery opted for. The global PR outcome is fairly high and varies between 50 to almost 90% in both laparotomy with or without magnification and laparoscopic microsurgery ^{(1,37,40,44).} The Pomeroy, Uchida, Fallopian ring and the Hulka methods of ligation have the highest reversal success rate. The recently developed laparoscopic Mne` (Dubuisson,1995), `two` (Barjio et al,1999), and `three`(Reich,1993) stitch techniques have facilitated laparoscopic microsurgery ^{(46, 49,50).}

In the treatment of distal occlusion almost all the studies have shown that hydrosalpinx and/or the chronically ill tube are associated with low rates of implantation and high rates of pregnancy loss. Irrespective of the tubal score the pregnancy out come is better with: i) fimbrioplasty than with neo-salpingostomy ^{(51, 52,67),} ii) salpingectomy than with the chronically ill tube ^{(78, 79),} iii) diseased tube without hydrosalpinx than with a tube with hydrosalpinx ^{(75,76,80,81,82,83),} iv) aspirated hydrosalpinx than with a non-aspirated hydrosalpinx ^{(76),} v) surgically treated hydrosalpinx than with an aspirated hydrosalpinx ^{(80).} The above findings apply to both cases of normal pregnancy and to IVF-ET. In a prospective study carried out by Shelton et al (1996), fresh and frozen embryo transfers were carried out in 15 women who had hydrosalpinges. The only pregnancy that issued ended up in a miscarriage. However, after salpingectomy, fresh and frozen transfers resulted in 9 pregnancies (60%), of which there were 3 miscarriages and 6 (67%) ongoing pregnancies ^{(84).}

From the above observation it will be logical to go for the most profitable surgical procedures which to our opinion will be fimbrioplasty for the less damaged tubes and surgical removal of the more damaged tubes prior to IVF/ET. However, the fact that cases of intrauterine pregnancies have been reported following neo-salpingostomy in patients who have had several failed trials of IVF/ET ⁽⁷⁸⁾. Also the fact that surgical removal of diseased tubes may not be accompanied by positive IVF/ET result, preventive salpingectomy should not be routine. A better understanding of the actions of hydrosalpinx fluid may be the solution of this problem.

Aboulgar et al,1998 ⁽⁷³⁾ observed fluid accumulation in the uterine cavity during embryo transfer, and Anderson ⁽⁷⁵⁾ sonographic diagnosed hydrosalpinx and observed its association with low rates of implantation and high pregnancy loss. Following these findings many studies have confirmed this association. Mukeherjee ⁽⁷⁴⁾ demonstrated its significant embryotoxic nature. The real mechanism by which the fluid affects implantation is not known. It is however speculated that

the mechanism may be: i) reflux of fluid into the uterine cavity; ii) irreversible endometrial damage; iii) release of intrauterine cytokines, prostaglandins, leukotrienes and other inflammatory compounds directly into the endometrium, or via the circulatory or lymphatic system; iv) delayed hypersensitive response to increased production of a 57-kda heat shock protein leading to pregnancy loss or v) chronic endometritis caused by chlamydia trachomatis. All off the above mechanisms may potentially act by altering endometrial receptivity ⁽⁶⁾.

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The management of tubal obstruction - N. Nkele

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THE USE OF 10 mg MIFEPRISTONE AS EMERGENCY CONTRACEPTION

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9th Postgraduate Course for Training in Reproductive Medicine and Reproductive Biology

INTRODUCTION

Emergency Contraception

Administration of material^{*} or substance⁺ which exerts contraceptive effects after the unprotected sexual intercourse has occurred

* i.e., IUD

⁺ i.e, ethinylestradiol & levonorgestrel

UNFPA (1997)

Acclaimed at least 75 million unwanted pregnancies each year resulted in 45 million abortions and over 30 million live births. About 70,000 women die as a result of unsafe abortion, more than 585,000 women die from causes related to pregnancy, and only 7% of women hospitalized for abortion complication had ever used contraception.



Emergency Contraception ...

Unintended pregnancy, is not only a problem in many underdeveloped countries, it is also a major problem in developed countries.

It is not dependent on the GNP or illiteracy but on a variety of cultural and economic milieus.

For some, emergency contraception becomes the most useful method of preventing unwanted pregnancy.



- REDUCING THE NUMBER OF UNWANTED PREGNANCIES BY IDENTIFYING THE POPULATION AT NEED AND PROMOTING THE USE OF EMERGENCY CONTRACEPTION
- REVIEW OF THE LITERATURE THE MECHANISMS OF ACTION OF LOW DOSE MIFEPRISTONE THAT EXERTS CONTRACEPTIVE EFFECT

SELECTION OF LITERATURE

- Health Surveys and Clinical Trials
- Literature search from 1995-1999
- 48 of 2980 references were selected (8 related to the target population, 16 to emergency contraception and 24 to mifepristone studies

THE POPULATION AT RISK FOR UNWANTED PREGNANCY

- Adolescence
- Commercial sex practitioner
- Sexual assault victims
- Non-current user and unmet-need FP services group

EMERGENCY CONTRACEPTION

Yuzpe Regimen

Levonorgestrel

• Mifepristone



Substitution of 11 and 17 aromatic ring of norethindrone with a high affinity for progesterone and glucocorticoid receptors

Receptor binding is not followed by transcription of progesterone dependent gene

Rapid absorption and maximal serum concentration were reached rapidly within 0.5-2 hour/s

Half-life of 25-30 hours

EFFECTS ON HPG-AXIS

Pituitary

- Block of LH Surge by attenuating LHRH
- Reduction of NPY potentiating effect

Ovary

- Inhibition of ovulation
- Interference of rupture of the luteinized follicle

Endometrium

- Impairment of endometrial receptivity
- Prevention of implantation
- Binding on PR without transcription for mRNA



The mechanisms of action of mifepristone are not clearly understood yet. Most investigators support the theory of suppression of LH surge and ovulation, alteration of endometrial gland function, impaired endometrial receptivity and blockade of facilitating process and substances for implantation.

DISCUSSION

- Progesterone plays a key role in the establishment of pregnancy: follicular maturation and leading to ovulation
- Endometrial changes that are essential for successful implantation and continuation of pregnancy
- Antiprogestogen (mifepristone) antagonizes the role of progesterone through receptor binding

Studies of mifepristone effects revealed

- Inhibition of ovulation
- Alteration window period for fertilization
- Impaired endometrial receptivity



Mifepristone

The lowest single dose contraceptive effective is 10 mg

Superior than other EC

- **?** lowest pregnancy rate
- **?** more tolerable
- ? minimal side-effects
- ? simple administration



EFFECTIVENESS OF EMERGENCY CONTRACEPTION REGIMENS IN PREVENTING UNWANTED PREGNANCY



Side Effects of Emergency Contraception Regimens





Yuzpe : 3.2% Levonorgestrel : 1.1% Mifeperistone : 0.9%

Conclusion



- Effectiveness of 10 mg of mifepristone for emergency contraception is similar to Yuzpe and levonorgestrel regimens
- **?** Effective up to 120 hours after unprotected sexual intercourse
- **?** Proven minimal side effects according to the effective single low dose
- ? The main target is endometrial tissue and the dose is 60 fold less than abortifacient dose

TUBAL INFERTILITY

INTRODUCTION

INTRODUCTION

INCIDENCE

ETIOLOGY

DIAGNOSIS

MANAGEMENT

PREGNANCY OUTCOME

PREGNANCY OUTCOME

PREGNANCY OUTCOME

PREGNANCY OUTCOME

PREGNANCY OUTCOME Effect of hydrosalpinx on success rates^{37,41,51}

PREGNANCY OUTCOME IVF outcome by number of fresh embryos transferred (From Paulson,Thornton)³⁴

CONCLUSION

CONCLUSION

THANK YOU VERY MUCH

TUBAL INFERTILITY

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WHO-UNDP-UNFPA-HRP-WORDBANK-UNIVERSITY OF GENEVA

VITAMIN A SUPPLEMENTATION DURING PREGNANCY

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Abstract

Objectives: To determine whether there is sufficient evidenced based information to propose recommending vitamin A supplementation during pregnancy to improve the outcome of pregnancy for the mother and/or infant.

Search strategy: Systematic review was conducted following the Cochrane strategy. A computerised article search was conducted to identify suitable studies using the Cochrane library, Medline, PubMed and the WHO-Reproductive Health databases. Hand-searching was also done in addition to computerised searching.

Selection criteria: All randomised or quasi-randomised clinical trials evaluating the effect of vitamin A supplementation versus placebo, or versus selective supplementation during pregnancy.

Data collection and analysis: Trials were assessed for methodological quality of adequacy of allocation concealment, blinding of outcome assessment and lost to follow up. Data of the outcomes were extracted from each published report.

Main result: Four references reported the randomised clinical trials of the effect of vitamin A supplementation during pregnancy on maternal and/or infant morbidity and mortality were eligible for this review. The vitamin A and iron supplementation was sufficient to eliminate anaemia in 97% of those anaemic pregnant women in Indonesia, compared to only iron supplemented group (68%). The study on vitamin A and ß-carotene supplementation during pregnancy in Nepalese women found that vitamin A reduced anaemia during pregnancy. Vitamin A supplementation was found to reduce the incidence of night blindness during pregnancy from 10.7 among controls to 6.7% (RR 0.62, 95% CI: 0.45 – 0.85). While, ß-carotene supplementation had less effect (RR 0.83, 95% CI: 0.63 – 1.11). The relative risk of mortality related to pregnancy was 0.60 (95% CI: 0.37-0.97) and 0.51 (95% CI: 0.30-0.86) in the vitamin A and ß-carotene groups. Among infants of supplemented mothers, a slight reduction in the percentage of those with haemoglobin <11 g/dI was observed.

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Conclusion: The available data from controlled trials provide substantive evidence of possible improvement in haematological indices and clinical indices. Where there is evidence that vitamin A deficiency and anaemia is prevalent, vitamin A supplementation should be introduced in conjunction with iron supplementation programs. Further substantiation and randomised controlled trials focusing on these issues need to be undertaken in populations in which vitamin A deficiency is common to provide definitive evidence. Studies are needed to establish the most appropriate strategies for prevention of vitamin A deficiency among children and women in reproductive age.

Keywords: Vitamin A supplementation – pregnancy – maternal morbidity – maternal mortality – infant morbidity

Introduction

Stunting and chronic energy deficiency are the result of malnutrition during fetal growth, infancy and childhood, with low energy intakes continuing into adulthood for many women. Micronutrient deficiency including iron, folic acid, vitamin A, zinc, iodine and calcium can steam from deprivations in childhood, but is primarily related to current inadequate intakes.¹ Among women in developing countries, poor dietary quality is the major determinant of inadequate micronutrient status rather than dietary quantity.² Adequacy of diets for women is determined by comparing their average nutrient intake to recommended level of intake such as the Recommended Dietary Allowance (RDA). The RDAs are calculated as the mean requirement for a nutrient. It is known that the RDAs increase substantially during pregnancy and lactating.³⁻⁴ When women become deficient in any micronutrient, they exhibit low serum, red blood cell or tissue levels of the nutrient. As the deficiency worsens, clinical signs such as anaemia, night blindness can be observed. If the micronutrient deficiency occurs in conjunction with infection it further impair women's health; and can affect the outcome of pregnancy; fetal growth and development; and the health of breast-fed infants.¹

Iron deficiency is the world's most widespread nutritional disorder, affecting both industrialised and developing countries. The most vulnerable groups are children and women is reproductive age, particularly during pregnancy when it is often a contributory cause of maternal death.⁵ Women in reproductive age have a particularly high demand for haemotopoietic nutrients. WHO (1992) reported that in 1988 56% of women in developing countries had haemoglobin levels below 110 g/l, regardless of the cause of such deficiency.⁶ A varied array of intervention exist which are designed to prevent and correct iron deficiency anaemia (IDA) in pregnancy. These include dietary improvement, fortification of foods with iron, iron supplementation, and other public health measures, such as helminth control and improved obstetrical techniques. At present, WHO recommends supplementing all pregnant women's diet with iron and folic acid. Supplementation with folic acid around the time of conception significantly reduces the incidence of neural tube defects.⁷⁻⁹ Still, the prevalence of IDA

has been little declining.⁷ Behind the medical causes of anaemia, cultural and socio-economic factors contribute significantly to IDA. The poverty, hard-work, poor nutrition, water shortages, food taboos, inadequacies in food production and storage, absence of effective systems of social security all combine to undermine women's health and cause anaemia compounded at times by a host of other debilitating diseases, such as malaria.⁶

Anaemia has been found to be associated with vitamin A deficiency, especially in developing countries.¹⁰ A cross sectional study carried out in Indonesia showed that serum retinol was significantly positive associated with haemoglobin, haematocrit and serum iron concentration.¹¹

Vitamin A deficiency (VAD) is also a major public health problem, and again the most vulnerable group are children and pregnant women, especially in developing countries. Africa has the highest prevalence of clinical VAD, while the highest number of clinically affected are in South-East Asia.⁷ In children, VAD is leading to visual impairment and blindness. VAD increases the risk of severe illness and death from common childhood infectious disease, such as diarrhoea and measles.¹² Adequate supply of vitamin A, either through supplementation or adequate diet, has a major role in preventing morbidity and mortality of children in developing countries.¹³⁻¹⁵ In VAD prevalent countries, pregnant women often experience deficiency symptoms, such as night blindness, that continue into the early postpartum.⁷ In some countries of South-East Asia, the prevalence of night blindness has been reported to be as high as 10-20% in pregnant women.⁷ Recent randomised controlled trials in Nepal illustrated the benefits of vitamin A supplementation on maternal morbidity and mortality.¹⁶ It has been considered that in poorly nourished people low serum of concentration of vitamin A may increase the virulence of HIV infection. And it is still possible that treatment of this poorly nourished population with vitamin A or β-carotene may improve immunological status and slow the progression of HIV to AIDS.¹⁷

Therefore, the vitamin A status of target groups should be an important consideration when carrying out iron supplementation programs, especially in places where infections are highly prevalent.¹⁸ Some studies on adding vitamin A supplementation in pregnant women receiving iron supplementation showed a significant increase of haemoglobin level.¹⁸⁻²⁵ However, the mechanism of vitamin A is effective against anaemia is not yet clear.

In children vitamin A supplementation is well accepted practice, but it is only recently that the need to supplement the diet of pregnant women has become an issue of public health concern. This systematic review is undertaken to determine the effectiveness of vitamin A supplementation in improving the health of both mother and infant in general.

Objectives

To determine whether there is sufficient evidenced based information to propose recommending vitamin A supplementation during pregnancy to improve the outcome of pregnancy for the mother and/or infant.

Methods

Criteria for considering studies for this review

Types of studies

All randomised or quasi-randomised clinical trials evaluating the effect of vitamin A supplementation versus no vitamin A or placebo, or versus selective supplementation during pregnancy.

Types of participants

Pregnant women receiving vitamin A supplementation either in areas with endemic vitamin A deficiency or presumed adequate intake.

Types of intervention

Vitamin A supplementation, alone or in combination with other supplementation compared to control (placebo or nothing) or other supplementation (including iron).

Types of outcome measures

Maternal:

Haematological and biochemical parameters: haemoglobin, haematocrit, total iron binding capacity, serum iron, serum ferritin, serum vitamin A.

Clinical outcomes: night blindness, infection (chorioamnionitis, urinary tract, sepsis), blood transfusion, death.

Infant:

Haematological and biochemical parameters: haemoglobin, haematocrit, total iron binding capacity, serum iron, serum ferritin, serum vitamin A.

Clinical outcomes: impaired growth retardation, low birth weight (<2500g), 1 minute Apgar score <7, 5 minute Apgar score <7, preterm birth (<37 weeks), intensive care admission, infection (sepsis), death (intrauterine, neonatal).

Search strategy for identification of studies

This review followed the search strategy developed for the Cohrane Pregnancy and Childbirth Group. A computerised article search was conducted to identify all studies on vitamin A supplementation on pregnant women using the Cochrane Library, MedLine, PubMed and The WHO-Reproductive Health databases. The method for identifying relevant studies was as follows:

- 1. Vitamin A supplementation
- 2. Women
- 3. #1 and #2
- 4. Pregnan* (Pregnant or Pregnancy)
- 5. #3 and #4

Hand-searching of the references of each article identified was conducted in order to obtain possible references not included in the databases being used.

Eleven articles were identified concerning impact of vitamin A supplementation and women on haematological, biochemical status and clinical condition of mother and/or infant (2 articles reported the same study-West Java, Indonesia-the first publication was selected for the review).¹⁸⁻²⁸ Trials to

assess vitamin A supplementation for HIV positive pregnant women will not be considered in this review ad they are included already in another review.²⁹ Thus only 4 out of 11 remaining articles on impact of vitamin A supplementation on haematological, biochemical status and clinical condition of mother and infant were finally selected on the review (see the criteria for considering studies for this review).

Methods of review

Trials were assessed for methodological quality using the standard Cochrane criteria of adequacy of allocation concealment: adequate, unclear, or that allocation concealment was not used. Information on blinding of outcome assessment and lost to follow-up was collected.

The following data were extracted:

- ^o Number of randomised women
- ^o Setting (country, hospital or population based)
- [°] Exclusion after randomisation and lost to follow-up
- ^o Method of randomisation and allocation concealment
- [°] Supplementation dose
- [°] Supplementation frequency
- [°] Time of initiation of supplementation
- ^o Pre-randomisation laboratory parameters of supplemented and control groups if available
- [°] Primary and secondary outcomes as listed in types of outcome measures

Description of studies

<u>Table 1</u>. Characteristics of studies included in systematic reviews of vitamin A supplementation in pregnancy.

<u>Table 2</u>. Characteristics of studies excluded in systematic reviews of vitamin A supplementation in pregnancy)

All trials included vitamin A supplementation versus placebo or any other supplementation.

Methodological qualities of included studies

[°] Allocation of concealment was adequately performed in all studies (Suharno, Stoltzfus, Christian, West).^{18-19, 26-27} The 3 articles which are Stoltzfus, Christian, West were coming from the same randomised clinical trial with the same population.^{19, 26-27} The time period of the study and sample size of these three publications in somehow were different.

[°] Blinding on supplementation was conducted in all studies.

[°] Information on blinding of outcome assessment was reported in all studies, and so outcome assessment was good.

[°] Lost to follow-up was reported on 3 studies (Suharno, Christian, West).^{18, 26-27}

[°] Studies in which the outcome variable were in the form of mean values with standard deviation were included in the meta-analysis.

Results

In <u>Table 1</u> the characteristics of all RCTs included in the reviews reporting main maternal and infant outcomes are listed according to the intervention. Overall, the sytematic reviews considered in this paper had only four trials that reported selected maternal outcome. Six studies were excluded because of lack of clarity in the study design (<u>Table 2</u>). One of these studies was excluded because the high drop out rate, which made the sample size too small to be able to measure accurately the impact of the intervention.

In <u>Table 3</u> the results are presented according to the main clinical and laboratory outcomes.

Anaemia

Improvement in Vitamin A status may contribute to the anaemia control among pregnant women.

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Suharno et al. (1993) found that maximum haemoglobin was achieved in anaemic pregnant women supplemented by both vitamin A and iron, with one-third of the response attributable to vitamin A and two-thirds to Iron.¹⁸ The vitamin A and iron supplementation was sufficient to eliminate anaemia in 97% of those anaemic pregnant women, compared to women who only received iron supplementation (68%).

The study on vitamin A and β -carotene supplementation during pregnancy in Nepalese women found that vitamin A reduced anaemia during and after pregnancy.¹⁹ The risk ratio (RR) of anaemia in pregnant women in the vitamin A group with or without adjustment for malarial outcome was 0.94 (95% CI: 0.84 – 1.05). While the RR of iron deficiency anaemia was 0.85 (95% CI: 0.73 – 1.00) without adjustment to malaria and 0.86 (95% CI: 0.74-1.01) with adjustment for malaria. This study was done in the hookworm prevalent area (77%). Hookworm was found strongly associated with IDA and modified the effect of vitamin A on iron status.

Night blindness

Vitamin A supplementation was found reducing the incidence of night blindness during pregnancy from 10.7 among controls to 6.7% (RR 0.62, 95% CI: 0.45 - 0.85).²⁶ While, β -carotene supplementation had less effect (RR 0.83, 95% CI: 0.63 - 1.11). Interviewer-verified rates of night blindness were slightly lower but associated with stronger protective effect. There was a strong dose response relationship between compliance to the supplement and relative risk of developing night blindness during pregnancy.

Maternal mortality

Mortality related to pregnancy was 704, 426, 361 maternal deaths per 100.000 pregnancies in the placebo, vitamin A and \(\beta\)-carotene supplemented groups, respectively.²⁷ These yielded RR of 0.60 (95% CI: 0.37-0.97) and 0.51 (95% CI: 0.30-0.86) in the vitamin A and \(\beta\)-carotene groups. Mortality rate among women receiving vitamin A and \(\beta\)-carotene were not significantly different. Analyses of cause specific mortality based on interviews with relatives showed that there were no significant effects from supplementation against risk of death from obstetric causes and infection. It could, however, have contributed to reduce the level of infection.

Infant Outcome

Only one study reported the effect of vitamin A supplementation on infant outcome. Among infants of supplemented mothers, a slight reduction in the percentage of those with haemoglobin <11 g/dl was

Discussion

Systematic reviews are being recognised as the most objective available way to evaluate the effectiveness of health care interventions.³⁰ This paper is an overview of randomised clinical trials of vitamin A supplementation during pregnancy aimed at reducing both maternal and infant mortality and morbidity. There are only 10 published articles available on these issues and only 4 references were reviewed (Table 1 & 2). However, the 4 remaining articles were based on 2 randomised clinical trials, which were undertaken in Indonesia and Nepal. There are some methodological issues discussed in this review, including the type and source of data, sample size and study design which could influence the meaningfulness of conclusions.

Overall, as a first conclusion, there is a benefit effect of vitamin A supplementation during pregnancy on both maternal and infant health. Anaemia has long been recognised as one of the potential consequence of vitamin A deficiency.³¹⁻³² It has been shown that adding vitamin A onto iron supplementation could increase the haemoglobin level in children.³³⁻³⁹ In areas where vitamin A deficiency is endemic periodic massive vitamin A dose program can improve iron status of the child population.⁴⁰ Although supplementation with vitamin A increases haemoglobin in children, little attention been paid to pregnant women, particularly as nutritional anaemia is prevalent and is known to contribute to maternal morbidity and mortality in pregnancy.⁵ However, some clinical trials showed that haemoglobin was increased in pregnant women supplemented with iron plus vitamin A, even though the design of those studies were not clear.²⁰⁻²⁵

Suharno and colleagues (1992) in Indonesia reported that small daily vitamin A supplementation had an impact on increasing the level of haemoglobin and serum ferritin.¹⁸ It showed that the effectiveness of combined vitamin A and iron treatment in reduced the level of anaemia in 97% of pregnant women provided with the supplement. In this study women with clinical manifestation of chronic or infectious disease were excluded. These findings were confirmed by the study of Stoltzfus in Nepal, vitamin A supplementation reduced prevalence of anaemia during pregnancy.¹⁹ The impact was on IDA, but on mild and not severe anaemia. The RR could not be measured due to limited information in her published article. Hookworm infestation appeared to modify the effect of vitamin A on iron deficiency because of the blood loss due to the infestation. It was found that malaria prevalence was reduced in women receiving vitamin A, but malaria did not change the vitamin A effect on anaemia. Shankar and colleagues had similar finding that number of episodes of falcifarum malaria among young children in Papua New Guinea was 30% lower in those who received vitamin A than in placebo recipient.⁴¹ This finding would suggest the possibility that vitamin A supplementation may reduce the number of malaria episodes and have an impact on reducing low birth weight, which is indirectly caused by malaria.

Although much work is still to be done to elucidate the mechanism involved, a number of mechanisms have been found that might be involved, including a block in the transport of iron from liver to erythropoietic tissues, absorption and storage of iron. The vitamin A has an important role in differentiation and maturation of cells in the body; this could include those in the haematopoietic system too.^{12, 32, 42-43} Nevertheless those two findings by Suharno and colleagues and Stoltzfus could be considered, along with iron supplementation, as a need of involving vitamin A supplementation in preventing and controlling nutritional anaemia in pregnancy.¹⁸⁻¹⁹

The randomised clinical trials in Nepal also showed that vitamin A supplementation could significantly prevent the incidence of night blindness in pregnant women. Even though the effect of B-carotene supplementation was not significant, it still had a clinical impact on reducing night blindness.²⁶ In this study they found a degree of misclassification of night blindness collected from a weekly history taken by an untrained interviewer compared to the information which was verified a week later by a trained interviewer. However, they found that interviewer-verified rates of night blindness were slightly lower but associated with stronger protective effect both in vitamin A and β-carotene supplemented groups. There was a strong dose response relationship between compliance to the supplement and relative risk of developing night blindness during pregnancy. One critical discrepancy in the methodology that should be considered in this study was that the calculation of compliance was defined as the proportion of weekly doses a woman received from ~1 month before conception until the end of pregnancy. Some women included in the study actually started supplementation a long time before they became pregnant. In addition, it has been found that women who experience night blindness during pregnancy and have a low vitamin A status will also have several other risk factors which appear to cluster among these women. For example, women with night blindness are also more likely to be anaemic, ill and acutely undernourished. They seem to be consuming a nutritionally poorer diet during pregnancy than non-night blindness pregnant women.⁴⁴

West et al (1999) reported the tremendous effect of vitamin A and β-carotene supplementation on reducing maternal mortality.²⁷ The author used a hard end point by measuring all cause maternal mortality with in a strong study design. The main end point chosen was maternal deaths from any cause during pregnancy or within 12 weeks of delivery rather than conventional maternal mortality, which is limited to the first 42 days after delivery. This period was selected on the basis that mortality related to malnutrition could extend beyond the conventional postpartum period. This appears rather an arbitrary cut off point since there does not appear to be any evidence that supports this rationale.

The possible misclassification of cause of maternal mortality by interviewing with relatives of the mother was considered. However, the ascertainment of pregnancies and the cause of maternal death is difficult to know with certainty, unless it was conducted in a case specific study.⁴⁵ Surprisingly, the greatest risk reduction was found at maternal mortality caused by injuries, even though it was not significant. This finding in a way differed with the findings on impact of vitamin A supplementation in reducing child morbidity and mortality especially due to infectious diseases.¹³⁻¹⁴ Further research specifically focused on pregnancy outcome rather that maternal mortality may give a clearer indication of the mechanism of prevention of infection, such as puerperal sepsis.

One study on the impact of vitamin A and zinc supplementation on puerperal and neonatal infection and prematurity is still on going in rural area in Central Java, Indonesia.⁴⁶⁻⁴⁷ The study is randomised, double masked, clinical trials, involved 2173 pregnant women. Preliminary result of this study found that daily, low dose vitamin A of 8000 IU given during the 2nd & 3rd trimester of pregnancy substantially reduces risk of maternal postpartum infections in populations of vitamin A deficient women. Pregnant women who experienced night blindness have a low vitamin A status. Daily vitamin A supplementation markedly reduced the incidence of night blindness in pregnant women.

Micronutrient deficiency in pregnancy could lead to placental dysfunction, fetal loss and congenital malformation. Vitamin A deficiency would be expected to contribute to higher rates of neonatal and infant morbidity and mortality. The information of effect of maternal deficiency on fetus and infant are mostly available from animal studies.¹² Only one article showed the impact of vitamin A supplementation on anaemia during infancy.¹⁹ It showed that there was a slight reduction in the percentage of anaemia among infant of supplemented mothers with haemoglobin <11 g/dl. It appears that the Nepalese study has not given a great deal of attention on the impact on infant morbidity or mortality. This could however, be due to the unfinished nature of the data analysis. Communication with the investigators should be undertaken for further reviews.

The Nepal randomised clinical trials on vitamin A and β-carotene supplementation for women in reproductive age raise many questions. The main objective of this study was conducted to assess the effect of continuous, weekly, low dose supplementation of vitamin A and β-carotene on fetal, infant, or maternal health and survival. The study design was very strong, but the field trials must be reported more clearly in order to assist the reader to comprehend their findings. There are discrepancies in this study which are difficult to understand. For example, the period of the study reported by Christian and colleagues differed with the latest one by West and colleagues.²⁶⁻²⁷

From this review it is possible to conclude that positive benefits to public health can be expected by improving the vitamin A status of deficient populations through an appropriate mix of acceptable, affordable and available programs.¹² Inspite of the results from the two randomised clinical trials on maternal and infant health, the teratogenicity of vitamin A should be thought in conducting vitamin A supplementation during pregnancy. Vitamin A in retinoid compounds is an essential micronutrient for embryogenesis, growth and epitelial differentiation. A small number of case reports suggest an association between the use of high doses of vitamin A during pregnancy and birth defects. A cohort study in USA of more than 22,000 pregnant women showed that high dietary intake of performed vitamin A appears to be teratogenic.⁴⁸ The attributable risk of a malformation was about 1 in 57 infants born to women who took more than 10,000 IU of preformed vitamin A per day in the form of supplements. Nepalese study reported that vitamin A had a slight protective effect on birth defects, but there was no significant overall impact of maternal vitamin A or β-carotene supplementation on risk of defects, except for significant decrease in ocular abnormalities.¹⁶

WHO recommendations for mothers during pregnancy is maximum daily preformed vitamin A
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supplements of 10,000 IU ($3000\mu g$ RE).⁴⁹ Where VAD is endemic, health benefits are expected for the mother and her developing fetus with little risk of detriment to either from either a daily supplement not exceeding 10,000 IU ($3000\mu g$ RE) at any time of pregnancy, or a weekly supplement not exceeding 25,000 IU ($8500\mu g$ RE). In this regard, a single dose of >25,000 IU is not advisable, particularly between day 15 and day 60 following the conception day; but else beyond 60 days after conception the safety of a single dose of >25,000 IU is uncertain.

Vitamin A supplementation of lactating mother in the first month postpartum is recommended by the WHO for regions where vitamin A deficiency is common. It is recommended that supplementation of one dose of 200,000 IU (60.000 RE) vitamin A should be given as soon as possible after delivery in order to maximise the benefits on maternal vitamin A status, breast-milk vitamin A concentration and subsequent infant vitamin A status.⁴⁹ A randomised double blind trial conducted in Indonesia showed that high dose of vitamin A supplementation of lactating mothers is effective on vitamin A status improvement of both mother and infant.⁵⁰

The intervention program to improve vitamin A status may well suffer the same well documented problems that have failed to make iron supplementation programs effective intervention for the prevention of IDA. These interventions in low-income countries must include the promotion of local food rich in iron and vitamin A from infancy to adulthood.⁵¹ de Pee and colleagues found that effective vitamin A programs in poor countries will need to include a mix of supplementation, fortification, and dietary diversification.⁵²

Conclusion

Implications for practice

The available data from controlled trials provide substantive evidence of possible improvement in haematological indices (haemoglobin, serum ferritin) and clinical indices (night blindness, maternal mortality). No conclusions can be drawn in terms of any effects, beneficial or harmful, on outcomes for mother and baby as insufficient data is available.

Where there is evidence that vitamin A deficiency and anaemia is prevalent, vitamin A supplementation should be introduced in conjunction with iron supplementation programs. The WHO recommendation of vitamin A supplementation during pregnancy should be considered as guiding standard for such program.

However, many uncertainties remain about the value of routine vitamin A supplementation in terms of substantive measure of pregnancy outcome; neither is there is any evidence against a policy of routine vitamin A during pregnancy. This matter requires further research before a definitive conclusion can be reached.

Implications for research

The existing evidence suggests that vitamin A supplementation during pregnancy combined with iron supplementation may reduce the risk of anaemia, night blindness and maternal mortality. In addition, vitamin A supplementation may have more beneficial effect on other important outcomes of pregnancy particularly in malaria endemic areas or where the evidence of poor dietary intakes among women is common.

However, this requires further substantiation and randomised controlled trials focused on this issues need to be undertaken in populations in which vitamin A deficiency is common to provide definitive evidence. In addition, studies are needed to establish the most appropriate strategies for prevention of vitamin A deficiency among children and women in reproductive age.

Potential conflict of interest

Not known.

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VITAMIN A SUPPLEMENTATION DURING PREGNANCY

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Detty Siti Nurdiati



Objective



 To determine whether there is sufficient evidenced based information to propose recommending vitamin A supplementation during pregnancy to improve the outcome of pregnancy

Introduction

Malnutrition

- Stunting, CED
- Micronutrient Deficiency
- Iron Deficiency
 - Public Health Problem
 - Cause of iron deficiency
 - Prevention Program



Vitamin A Deficiency

• Public Health Problem

Children

- SA-1-C
- Morbidity 🗆 :
 - Impairment & Blindness
 - Infections
- Mortality 🗆
- Pregnant Women
 - Morbidity
 - Mortality



Methods

- Systematic Review
- Search Strategy
 - Computerised searching
 - Hand searching
- Selection Criteria
 - Randomised clinical trial
 - Vitamin A vs placebo and/or selective suppl.
- Data Collection and Analysis
 - Quality of study
 - Extracted outcomes









- 10 References
 4 Included
 6 Excluded
 Unclear of study design
 High drop-out
- Extraction of the study outcomes



Characteristics of studies included

- Suharno D, West CE, Muhilal, Karyadi D, Hauvast JGAJ. 1993
 - Double blind and placebo control
 - Anaemic pregnant women, rural villages, Bogor, Indonesia
 - April-September 1992
 - Supplementation: daily, 8 weeks
 - Vitamin A (2-4 mg retinol) and placebo iron;
 - Iron (60 mg elemental iron) and placebo vitamin A;
 - Vitamin A and iron
 - Placebos

Stoltzfus RJ. 1997

978 pregnant women, 766 postpartum mothers & 728 infants
 Christian P, West KP, Khatry SK et al. 1998
 9932 pregnant women

 West KP, Katz J, Khatry SK et al. 1999
 44 646 married women, of whom 20,119 became pregnant 22,189 times

- Randomised, double blind, placebo controlled trial
- Rural plains of Sarlahi, Nepal.
- March 1994 September 1997
- Supplementation: single dose weekly, for almost 3 years
 - Vitamin A (7000 µg RE)
 - β-carotene (7000 μg RE)
 - Placebo

Results

• Anaemia

- Anaemia \Box RR 0.04
- IDA [] RR 0.85 (Malaria & Hookworm)



• Night blindness

- Vitamin A

 RR 0.67
- → β-carotene □ RR 0.83

Results

Maternal Mortality
 Vitamin A
 RR 0.60

 \$-carotene
 RR 0.51



Infant Outcome
 Slight reduction of anaemia

- Anaemia in pregnancy
 - Other studies: cross sectional & clinical trials
 - Children Studies
 - Result findings
 □ □anaemia
 - Mechanism?
 - Malaria 🗆 LBW
- Anaemia in infancy





• Night blindness

- Vitamin A > ß-carotene
- Dose response
- NB [] [] morbidity
- Maternal mortality
 - Definition used
 - Misclassification of cause of mortality

On-going study



- RCT: Vit A, Zinc, Placebo
- Rural Central Java
 - Puerperal sepsis
 - □ Night blindness □

• Vitamin A supplementation

Teratogenicity Animal study

Cohort Study

- malformation: 1 in 57 infants
- Women who took >10.000 UI/day



Supplementation Recommendation



▶ Pregnancy
 □ ≤ 10,000 IU/daily
 □ ≤ 25,000 IU/weekly

Lactating Period
 Single dose of 200,000 IU

Conclusion



- Implication for practice
 - Substantive evidence of possible improvement on maternal and infant morbidity and decrease of maternal mortality
 - Vitamin A supplementation availability & feasibility
- Implication for research
 - RCT with specific outcome of pregnancy
 - Vitamin A Deficiency, malaria endemic areas



Thank You For Your Kind Attention







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in collaboration with the

Geneva WHO Collaborating Centre for Research in Human Reproduction

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ABBREVIATIONS / ACRONYMS

AIDS	Acquired immuno-deficiency syndrome	
AFPA	Albanian Family Planning Association	
ALB/91/PO3	Albania/91/Project Number 3	
ARI	Acute Respiratory Infection	
CPR	Contraceptive prevalence rate	
СҮР	Couple years of protection	

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FP	Family planning			
FUFARMA	Furnizim Farma (central store for pharmaceutical products in Albania)			
GP	General practitioner			
HMIS	Health Management Information System			
HIV	Human immuno-deficiency virus			
ICPD	International Conference on Population and Development			
IEC	Information, education and communication			
IMR	Infant mortality rate			
INSTAT	(National) Institute of Statistics			
IPPF	International Planned Parenthood Foundation			
IUD	Intrauterine device			
KAP(S)	Knowledge, attitude and practice (satisfaction)			
KfW	Kreditanstalt für Wiederaufbau (German Development Bank)			
МСН	Mother and Child Health			
MMR	Maternal mortality rate			
МоН	Ministry of Health and Environment			
MSI	Marie Stopes International			
NGO	Non-governmental organisation			
OC	Oral contraceptive			
Phare	Development Programme of the European Commission for East European countries			
РНС	Primary Health Care			
PSI	Population Service International			
RH	Reproductive health			
RTI	Reproductive tract infection			
SEATS	Family Planning Service Expansion & Technical Support			

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STD	Sexually transmitted diseases		
U5	Under-5 (years old)		
U5MR	Under-5-mortality rate		
UNDP	United Nations Development Programme		
UNFPA	United Nations Population Fund		
UNV	United Nations Volunteer		
WHO	World Health Organization		
WRA	Women in reproductive age (15 to 49 years of age)		

1. Introduction

1.1 Implications of recent changes in political and economic life in Albania

The transition from communism to a more plural form of government came later in Albania than in most other countries of central and Eastern Europe. The resignation of the last communist government in June 1992 plunged the country into political and economic chaos. Thereafter, following the election of a new government, attempts began to introduce comprehensive reform programmes. This process was interrupted in the early months of 1997 when the political and security situation became extremely volatile with the development of criminal activities, resulting in the evacuation of their staff by many of the donor organisations.

At the end of 1997, although the staff of the donor agencies has largely resumed their humanitarian activities, the security situation is still not entirely stabilised, and travel in certain areas presents a risk. There are very major infrastructure problems, giving rise to serious difficulties as regards water, electricity supplies and drainage. The arrangements for garbage collection have evidently broken down, and rotting rubbish in the streets would seem to pose a very real threat to public health. In these circumstances, the outbreak of epidemics, such as the cholera, which affected Albania in 1996, cannot be excluded.

Generally in Albania the roads are in bad condition, making transport very difficult even in urban areas, to say nothing of the more remote mountain regions which are almost impassable in winter. Postal services and telephones are unreliable. Assistance from the international community is critically needed in order to restart economic activity, but the fundamental changes which have marked the political and economic transition, combined with the uncertainty which characterises life in Albania, seem to have resulted in a certain level of inertia within the country.

2. Background and Demographic Data

After 45 years of Communist dictatorship it came to dramatic changes in Albania in the years 1991/92, which made possible first democratic elections, the introduction of first steps towards liberal market regulations and an opening of the society.

It is difficult to get a clear picture of the health situation in Albania. Data gathering is hampered by various factors, not least of which are the demographic movements and communications problems. In addition, the use of different definitions (for example, of infant, perinatal and neonatal mortality) and different methods of data gathering and recording, added to staffing problems and a lack of co-ordination results in a certain degree of inaccuracy in the field of Reproductive Health statistics.

In 1989 the total number of the Albanian resident population was reported to be 3.199.200 inhabitants (last official population census). The population was relatively young with about 33 per cent being younger than 15 years of age. The number of women in reproductive age (WRA: women 15-49 years of age) was about 800.000. It was estimated that 75 per cent of them were married. The gross reproduction rate was 1.46, the net reproduction rate 1.38 and the fertility rate 3.0 births per WRA (1990). With a female life expectancy at birth of 76.3 and male life expectancy at births of 70.0 years (1992), the rate of natural increase of the population was 1.9 in 1989 which predicted a population doubling time of about 40 years. In 1989 the Albanian population was in large majority a rural population. Only 36 per cent of the population (in absolute numbers 1.183.000) lived in an urban environment. Average population density was in 1993 : 110.2 inhabitants per square kilometre.

After the end of the Communist regime a huge wage of emigration flooded mainly to the neighbouring European countries (Greece and Italy). In 1992-93 during 1 1/2 years 165.000 people left the country (50 per 1.000 of the total population). During this time the emigration rate for the age group of 20-29 years old was even higher (20 per 1.000). In 1990 it was estimated that 300.000 people (or 90 per 1.000 of the population) and in 1994 nearly 400.000 people (120 per 1.000 of the population) had left the country.

Albania experienced a most difficult transition of its economy, still lacking a mature market economy. The massive trade imbalance is largely due to a precipitous decline in exports. The relative progress of development was and still is possible only because of foreign aid (US\$ 320 million, 1993) and the income received from Albanian emigrants working abroad and sending home money (US\$ 400 million, 1993).

Before, health care was purely public, centrally organised and controlled. The population policy was pro-natalist, modern Family Planning (FP) unknown and it was taboo to speak about sexuality and contraception in the public. Constitutional guarantees existed also regarding the participation of women in political, economic, social and cultural life. Despite this, Albanian society remains relatively paternalistic, and status of women and their participation in public life have not improved over the last few years. According to the Albanian Development Report 1995, there are more young women than young men in secondary and higher education, possibly because of the greater difficulty they experience in finding posts within the private sector.

It is very difficult to draw a clear picture of the health status of the Albanian population. Especially, statistical data of the years 1991/92 are little reliable, incomplete or were based on different definitions. Even mortality data were somewhat uncertain. In 1989 overall perinatal mortality was 13.5/1.000. It was recognised that the official infant mortality rate (IMR) of 28.3/1.000 in 1990 was underestimated by one third. Instead of the under-5-mortality, the mortality of the under-4-years old children was reported. Estimating the under-5-mortality in 1991 by adding 10 per cent to the under-4-mortality, results in 43.9 per 1.000 live births. In 1989 the maternal mortality ratio (as obstetric risk) was: 49.5 per 100.000 live births. The maternal mortality rate (MMR) in 1989 was 4.8 per 100.000 WRA.

Till 1988 modern FP methods were forbidden, their application, effectiveness and safety virtually unknown and their use claimed to cause cancer or permanent sterility. Through the "Order of the Minister of Health concerning the

performance of abortion" (April, 1991) and the "Decision of the Council of Ministers for the approval of activities of FP in Albania" (May, 1992) abortion became legalised and modern FP methods could be introduced in the public health services (*Annex 5*). In 1989, 300 abortions per 1.000 live births were performed. Premature birth rate was 6.55 per 100 live births (birth weight under 2.500 gr.). The life expectancy of women is increased through the years (*Graph 11*), while the total fertility rate (TFR) is decreased (*Graph 12*)

Of the sexually transmitted disease (STD), syphilis had been declared eradicated. AIDS or HIV-infections were unknown (the first HIV-infection was reported in May 1993).

2.1 Arguments to introduce Reproductive Health in Albania:

- Psychosocial aspects (rights of reproduction, economic situation, inclusion of social workers).
- Mothers and children's health status is not yet satisfactory (reduce maternal and infant mortality).
- Health of adolescents is threatened (changing social and cultural environment).
- Burden through STD's and other genital diseases may increase in the near future.
- Knowledge of the population in Reproductive Health is still not satisfactory.
- Health personnel are not yet sufficiently trained in Reproductive Health.
- Quality of the services related to Reproductive Health is not satisfactory.
- Health information system for Reproductive Health is weak and not satisfactory.
- Lack of co-ordination between the structure of primary and secondary health care.
- Integrated services have proved to be more cost-effective and more equitable.
- Reproductive and sexual health concerns of older women and men are inadequately addressed (<u>Annex 8a</u>, <u>Annex 8b</u>)

2.2 Strategy for Reproductive Health

- Human Rights, Ethics, Laws (in no case abortion should be promoted as a FP-method, rights of children to be protected against violence) and Regulations.
- RH in the context of socio-economic development of the country.
- Research in Reproductive Health (defavoured people, children; needs assessment for training, resources and infrastructure, etc.).
- Building institutional capacity (training, quality of service).
- RH will be introduced as a concept in all relevant services (facilities, resources, supervision, operational health management information system, IEC).
- Women-centred care (santé des femmes).
- IEC (multi-media approach).

- Introduction of the elements of RH at all levels of the concerning partners (training of health staff at different levels and with different specialisation, training of medical students, nurses, midwives and family doctors, job descriptions of Regional Inspectors of RH).
- Dialogue and coalition building (public/public and public/private mix, NGOs, international organisations).

2.3 Structure of Reproductive Health

- Reproductive Health is a concept and does not obligatoriously need an own structure (building, services, personnel). The concept must be introduced in several services and the concerned medical personnel trained to understand the concept and to perform the necessary services in an integrated manner.
- The type of vertical approaches to health problems has long been shown to be less cost-effective and less equitable than an integrated approach. Also the different elements of Reproductive Health are closely linked and patients are faced often to cumulating consequences of reproductive problems. Therefore, elements like STD/AIDS prevention, family planning, abortion, sterility, neonatal care, delivery and breast-feeding cannot been focused separately. Integration and an overall understanding of Reproductive Health are essential.
- Porte d'entrée (how to differentiate types of client enter the RH care? Central registration and orientation of client towards different parts of the service).

The services, which provide RH, are spread in the whole health institution network of the country. They involve:

1. First Level Care:

- Ambulances in rural zones;
- Public run health centres in rural zones;
- General Practitioner or Family Physician;
- Mother and child consulting centres in districts;

2. Second Level Care:

• District Maternities and Paediatric Hospitals.

3. Third Level Care:

- University Hospital of OB/GYN;
- University Hospital of Paediatrics;

The second and third level centres are in the same time referral services for the whole country.

• Who is concerned with RH elements?

<u>1. Public Health Institutions:</u>

- O PHC-directorate:
 - sector of reproductive health;
 - sector of hygiene and epidemiology;
- Hospital care directorate:
 - gynaecological and obstetrical services;
 - paediatric services (peri- and neonatal care);

- O Institute of Public Health:
 - STD/AIDS prevention and control programme;

2. Public Education Institutions:

- O Ministry of Education.
- O Medical Faculty of the University of Tirana, Department of OB/GYN.

3. Private Sector:

- gynaecologists;
- paediatricians;
- family physicians;
- druggists;
- different NGOs

2.4 Definition of Reproductive Health periods

There are three main periods of Reproductive Health:

- Period of pre-Reproductive Health, which corresponds to adolescent age;
- Period of Reproductive Health, which includes:
- Maternal period: prenatal, delivery, post-natal, post-partum and breast-feeding period;
- Intervals between deliveries;
- Period of post-Reproductive Health, which corresponds to menopause and andropause time;

2.5 Components of Reproductive Health

2.5.1. Adolescent care

- Improvement of RH education in school;
- Increased knowledge of STD and contraception;
- Prevention of pregnancies in early age;
- Prevention of STD;
- Prevention of inadequate sexual behaviours;
- Safe abortion;

2.5.2. Family Planning

- Pre-conception counselling;
- Prevention of abortion;
- Post-partum and post-abortion counselling;
- Safe abortion;
- Information, application and counselling on different contraceptive methods;
- Follow-up of contraceptive side-effects and complications;
- Providing of modern contraceptive methods;
- Sexuality;
- Infertility;

2.5.3. Mother care

- Pre-conception;
- Prenatal care;
- Reduction of pre-term and hypotrophic deliveries;
- Adequate vaccination of pregnant women;
- Labour care;
- Postnatal care;
- Promotion of breast-feeding;
- Reduction of perinatal mortality;
- Reduction of maternal mortality;
- Reduction of obstetrical and neonatal complications;

2.5.4. Care for woman nourishment

- Improving the knowledge and education on nourishment;
- Reduction of anaemia during pregnancy;
- Promotion of breast-feeding;

2.5.5. New-born care

- Reduction of neonatal mortality and morbidity;
- Reduction of neonatal infections after delivery;
- Improvement of early neonatal intensive care;
- Incitement of exclusive breast-feeding;
- Incitement of rooming-in in the maternities all over the country;

2.5.6. Care for 0-5 years old children

- Check up of psycho-motor development;
- Adequate vaccination;
- Improvement of education and knowledge on child feeding;
- Reduction of mortality and morbidity;

2.5.7. Care for sexual health

- Prevention, treatment and counselling on STD/AIDS;
- Reduction of other genital infections;
- Reduction of gynaecological disease complications;

2.5.8. Check up of genital and breast tumours

- Early screening of breast, cervical and prostate cancer;
- Counselling and referring;
- Reduction of HPV prevalence (human papilloma virus);

2.5.9. Care for post-reproductive health

• Prevention and treatment of menopause disorders;

3. Country Strategies for Albania

3.1 Governmental Policy

Within the framework of the national health policy, the government has defined a set of primary health care priorities. These include: maternal and infant mortality, antenatal and post-natal care, access to RH/FP/SH care and prevention of sexually transmitted diseases.

The Governing Council asked for \$3 million from UNFPA for a five-year programme starting in 1991. The programme aimed to strengthen Government capacity in the area of maternal and child health, by providing training and equipment; reduce maternal mortality and promote child spacing; increase the knowledge base in demographic statistics, analysis and research to help integrate population factors into development planning and further develop population policies; and improve the status of women and their participation in population and development.

With external technical assistance and in co-operation with the Phare Health Programme of the European Commission, the MoH developed a policy of Primary Health Care (PHC). In this policy it was stated that MCH will be a future priority for the public health services. Reproductive health (RH) was mentioned for the first time. It was further stated that equity and equality are important elements of the PHC-policy to allow the same access to health care services to every Albanian citizen.

A number of laws, Presidential decrees and orders of the Minister of Health related to FP and RH-issues have passed the Parliament or were published (<u>Annex 5</u>).

Amidst the current climate, it is hardly surprising that the advancement of Reproductive Health/Family Planning and Sexual Health rests always one among many on the list of priorities currently facing the Ministry of Health and Environment. Not least of these are the impending across-board budgetary cuts of 15% and staff cuts of 10% which are to be introduced as part of the structural adjustment conditions attached to the World Bank loan of US\$ 204 million in which 100 primary health care centres and 2 regional hospitals will be rehabilitated and equipped, health management improved and health personnel trained, drugs procurement and distribution improved, and health financing reviewed and reorganised.

4. Reproductive Health Situation in Albania

4.1 Reproductive Health of Adolescents

According to one study made in 1994 on the abortion situation, 3.6% of abortions were performed in girls of 13-19 years old, mostly living in the cities. 45.3% of adolescents undergoing an abortion had followed just the low school, and 48.2% the high school. Only 2.9% of them were students.

Another study on sexual education found that information provided by mass media and different sources was often inadequate and not professional. 92% of adolescents of 13-19 years old had at least once tried a sexual experience.

Sexual education in school is still in the first steps and thus, its level is quite low. Even teachers are not yet liberated from the ancient mentality and hardly speak freely or naturally on sex problems. To improve the quality of teaching skills, a number of seminars and workshops are organised in different cities by the Ministry of Health and the Ministry of Education in collaboration with UNFPA and diverse NGOs.

4.2 Mother Health and Safe Pregnancy

From 1991 to 1996 maternal mortality decreased by 25 per cent and reached the level of under 30 per 100.000 live births (28.5 in 1995, <u>Annex 1</u>, <u>Graph 1a</u>). The main causes of maternal mortality in recent years have been defined, as: 1) haemorrhage during and post-partum; 2) different previous pathologies; 3) pregnancy-induced hypertension.

It has been assumed, that the decrease of maternal mortality was primarily due to the legalisation and liberalisation of abortion in 1991. Abortions became more safe, but there is still no clear sign for a decrease of the abortion rate (*Annex* 2, *Graph 2a*). In Albania abortion was and still is one of the most important methods to reduce the number of births. Maternal deaths from abortion are considerably reduced, mainly occurring above 12 weeks of pregnancy, a fact that is also related to the old abortion techniques still in use. 28% of abortions are performed in 30-34 age group and 22.9% in 25-29 age group, thus in the most reproductive period. Regarding the parity, 23.7% of abortions come after two other pregnancies, while 17.1% of them are performed at the very first pregnancy. Data related to abortion complications are still missing, but several studies are undergoing for their evidence.

The assessment of pregnancy is mostly done in specialised centres, which means mother counselling centres and maternities. The number of hospital beds for ob/gyn service in 1994, was 60 for 100.000 inhabitants. The average number for prenatal control of a pregnant woman is 5.4, and about 72% of pregnancies are covered by a medical service (1995).

In 1990, about 2.370 general practitioners, 2.090 medical specialists (all together: 1 physician per 730 inhabitants) and 14.780 nurses/midwives (1 para-medic per 220 inhabitants) were employed by the MoH. At PHC-level were working: 1.500 general practitioners (GP), 240 medical specialists (mostly gynaecologists and paediatricians) and 4.250 nurses/midwives. On average 2-3 GPs and 4 nurses/midwives worked in one health centre (1993).

One of the main problems of maternal morbidity is ferriprive anaemia of pregnancy, which varies from 40 to 56% of all pregnant women.

4.3 Family Planning

Information about and availability of modern FP methods were introduced for the first time in Albania by 1992. Many gynaecologists, paediatricians and midwives participated in the fellowship programmes abroad and in training courses in Albania. But there was no ex-ante evaluation of knowledge, attitude and practice of the health staff, to quantify the changes after training and to measure the impact of the training activities.

In 1995, the first National Conference of Population and Development was organised by the MoH, the Academy of Science and UNFPA, as follow-up of the Cairo Programme of Action. This was a first opportunity to discuss in public and within a wider auditorium, population issues and FP. The conference documentation was published in August 1996.

FP facilities

First (PHC) level:

At PHC-level, there are about 1.973 ambulances operating at village level, staffed by a midwife-nurse. There are currently 731 functioning, publicly run health centres in Albania, 129 in cities and 602 in rural areas. 137 of the health centres (19 percent) have a mother and child consulting centre and provide FP services. At district level, 11 regional FP centres (4 of them are so called pilot FP centres) provide FP services.

Second level (District Maternity Hospitals):

28 district maternity hospitals offer FP services and provide contraceptives. These FP facilities at maternity hospital level do not play a reference role for the PHC-facilities but offer FP-services to the hospital patients (pre- and post-abortion counselling, post-partum counselling, counselling for FP, prescription and application of FP methods).

Third level (Maternity Hospital of the University, Tirana):

The Maternity Hospital in Tirana has two compounds at different places in town and is part of the University Hospital. Recently it was decided that both facilities (in former times separated in maternity and gynaecological hospital) shall have the same gynaeco-obstetrical services and function. In the Maternity Hospital 1, AFPA/IPPF has installed its main centre offering counselling (pre- and post-abortion, post-partum), contraceptives and abortion. Next door to the AFPA-centre and the maternity's abortion ward, a social service of the "pro life" initiative (Bethany Hospital) is offering counselling and help to pregnant women. In the Maternity Hospital 2, a UNFPA supported FP-centre is offering counselling and modern methods of contraception.

The main modern FP-methods have been made available all over Albania. In general, there were no major or longer interruptions in the availability of contraceptives at central level. Till the year 1995 the contraceptives were distributed to and sold through public pharmacies. When pharmacies became privatised in 1995, access to contraceptives decreased through higher retailer prices. By order of the Minister of Health, contraceptives were distributed free of charge through the FP-facilities themselves, starting in January 1996 (*Annex 5*). This had a positive influence on the utilisation of the FP-facilities and the access to modern contraceptives. On the other side, the distribution of contraceptives free of charge would limit the sustainability of the FP-services, especially when it came to future finance of FP activities and contraceptives. Gratis contraceptives provided through the public services decreased their valorisation through the users.

Data about the use of contraceptives are available since the beginning of 1996, assuming that contraceptives given to the acceptors are used. The estimated contraceptive prevalence rate of the first six months of 1996 (data from 28 of 36 districts), indicates that the use of contraceptives may not exceed 5 per cent. An additional difficulty in calculating the CPR was the unclear number of the target population per district or covered by FP-facility. In the years 1993 to 1995 the CPR was calculated out of the couple years of protection (CYP) and distribution of contraceptives to the district. A coverage of contraceptives of 4.96 per cent of WRA in 1993 was reported, 8.27 per cent WRA in 1994 and 10.9 per cent of WRA in 1995. Reasons for the differences are the uncertainty of both calculations, based on unclear numbers of target population, incomplete data about the number of acceptors and the number of distributed contraceptives.

An increase of OC and injectable method use in years 1995-1996 has been observed, while IUD-s were not any longer the most preferred method. The age group of 30-34 years old counts for 35% of total contraceptive users, followed by the age group of 25-29 with 24.9%, while the adolescents of 15-19 years old represent only 2% of contraceptive users.

From mid-1992 to 1995 contraceptives (except condoms) were imported nearly exclusively through UNFPA and IPPF, with UNFPA importing the main part of more than 95 per cent (<u>Annex 6</u>, <u>Graph 6a</u>, <u>Graph 6b</u>)

In the public FP-facilities the contraceptives are given free of charge to the client. The clients sign the register of the free reception of the contraceptives. There was and still is no effective monitoring or control system for storage, consumption, needs and demand of contraceptives, neither in the different districts nor at central level.

4.4 Newborn Care

The perinatal mortality rate has significantly increased during the period from 1991 to 1995, early postnatal mortality from 4.8% to 8.0% o and late postnatal mortality from 8.6% o to 11.3% o. Neonatal mortality accounted for 27.6% of infant mortality in 1991, and this was increased in 1997 to 46.5%. The actual rate of 13.2 per 1.000 live births is still above the target set of 12 per 1.000 live births. Data on perinatal mortality, especially for 1992/93, may not be reliable (*Annex 3*). It is important to note the fact that early postnatal mortality (0-6 days) in 1997 counted for 33.4% of infant mortality and late postnatal mortality (7-27 days) for 13.1% of it.

The causes of increased neonatal mortality

- 1. Increased medicalisation of deliveries.
- 2. The inadequate low technical level of medical personnel in rural maternities and of their equipment.
- 3. Lacking of prenatal assessment, especially in rural areas.

In 1991, 7.5% of deliveries took place at home, while in 1991 this rate was 9.1% and 0.3% of all deliveries were not medically assisted. Currently, 89% of all deliveries take place in maternity hospitals.

The premature birth rate has not obviously changed: 3.5 per 100 live births in 1995. But different definitions were used (birth weight under 2.500 gr. versus number of gestation weeks at birth) which makes interpretation difficult (*Annex 4*).

Breast-feeding

In Albania several programmes are already written for the training of personnel and mothers on breast-feeding. The initiative of a "baby friendly hospital" is also progressing fast. UNICEF and different NGOs have collaborated in preparing these programmes.

New-dorns led by breast-leeding, according to their monthly age

Year	1994	1995	1996
0 - 4 months	40.231 (55.7%)	40.769 (56.5%)	43.078 (63.4%)
4 - 6 months	7.231 (10%)	7.346 (10.1%)	7.209 (10.6%)
6 - 12 months	7.126 (9.8%)	8.447 (11.7%)	9.016 (13.2%)
Total	54.498 (75.5%)	56.562 (78.4%)	59.303 (87.3%)

4.5 Child Health and Development

Infant mortality is high in Albania, thus presenting one of the main health problems of the country. In 1990 this index was 45 for 1.000 live births, in 1997 it decreased to 22.5 for 1.000 live births and it is 4% higher in rural areas. 39% of infant (0 - 1 year old) deaths happen at home and in 1997 42.2% of them died before 28 days of life (*Annex 3*).

At the first level in 1997, 1.986 child-care units functioned in rural areas and 181 in towns and cities. At the second and third levels, 49 paediatric wards provide service in the whole country. The number of paediatric beds in 1994 was 55.7 for 100.000 inhabitants.

The childcare is improving in the following ways:

- priority of primary care;
- integration of service;
- training of medical personnel;

To achieve better results, projects of UNICEF in collaboration with MoH have started since July 1993. These projects involve:

- Check up and prevention of ARI;
- Immunisation;
- Nutrition;
- Check up for diarrhoeic diseases;
- Safe Motherhood;
- Breast-feeding and rooming-in;

4.6 Post-Reproductive Health

So far, the control of women in menopause has been almost spontaneous and not co-ordinated and the gynaecological services are provided at the first and second levels of the health care system.

4.7 Genital Cancers Care

The services that provide screening of genital cancers are placed in specialised polyclinics of some cities of the country, in gynaecological hospitals and in services of gynaecological oncology. The service for the prevention of genital cancers is not yet organised by first, second or third level services.

5. Family Planning / Reproductive Health Projects

5.1 Multilateral Organisation Assistance

5.1.1 United Nations Population Fund

As far as external assistance is concerned, co-operation between UNFPA and the Government of Albania started in 1983 and until 1990 was focused mainly on maternal and child health, family planning and data collection. The first Country Programme (1991 - 1995), which was extended into 1996, concentrated essentially on the training of medical personnel in all aspects of MCH/FP, on equipment and other structures of RH. The project aimed to decrease maternal and infant mortality and the incidence of premature birth, and to increase modern contraceptive prevalence.

5.1.1.1 Goals and objectives

The objectives of the project (signed on 28 July, 1992 by the MoH, WHO and UNFPA) were the following:

- the reduction of maternal and perinatal mortality rates by adequate birth spacing and prevention of induced abortion;
- the upgrading of services at the central level and in 26 districts by training of personnel (physicians and midwives) and upgrading of equipment;
- modern contraception was to be made available in 26 maternity hospitals by the end of 1992/3 and in all 137 women's consulting centres by the end of 1995.

The following immediate objectives are specified in the project document:

- to decrease maternal mortality by at least 50 per cent to 30 per 100.000 at the end of the project;
- to reduce perinatal mortality by 30 per cent at the end of the project to reach 12 per 1.000 live births;
- to reduce the number of premature births by 20 per cent from 8 per 100 to 6 per 100 live births at the end of the project (1995);
- to improve contraceptive coverage to at least 10 per cent of WRA through the implementation of FP-activities in all district maternity's, 137 women's consulting centres and 400 pharmacies.

5.1.1.2 Strategy and approach

In 1992, the main focus of the project on gynaecologists for training and performance of project activities was justified. Women were used to visit the gynaecologist for specific health reasons and the former reference system had foreseen this "entrance point" to the public health system. The gynaecologists were the first medical profession who had learned about FP and its scientific background. Furthermore, the project focus was not a pure FP project but included MCH as an equally important part. Whereas the MCH-component concentrated on fellowships and provision of some medical equipment, the FP-component focused on the installation of services, local training and provision of contraceptives.

It was therefore logic that at the start of the project, FP-services were delivered only by gynaecologists and project's activities (training, fellowships) focused on them. During project implementation it turned out that gynaecologists were more interested in performing "real medical interventions" such as performance of abortions or application of IUDs. The clinical-, service- and doctor-orientation approach of the project neglected somewhat the needs of the clients.

5.1.1.3 Outputs

Taking into account the very difficult political, economic and social circumstances in Albania during at least three
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years of implementation, the project can be considered to have been a success in certain areas. Within less than four years the political and health understanding changed tremendously. A centrally planned health care system became liberalised, legal preconditions for FP and abortion were created, knowledge of health personnel improved and modern FP was no longer banned. The presence of the project alone influenced positively these changes. FP and information structures have been built up and supply structures established. Even if these systems are still not fully operational, a dynamic process could be initiated which showed increasing commitment of the MoH.

5.1.1.4 Conformity to project design

The contraceptive needs (unmet and met needs) were estimated in May 1996. Assuming a 5 per cent coverage with contraception of married women in reproductive age in 1995, the unmet needs were calculated to be on average 40 per cent or about 250.000 women in reproductive age (*Annex 7a*, *Annex 7b*).

The five most important contraceptives were available at central level most of the duration of the project. Only brief shortages could be noticed, but never resulted in a longer absence of contraceptives in the pharmacies or FP services.

Some supplementary activities have been performed by the project, which were not foreseen in the project document: for the training of trainer and the training of the gynaecologists/midwives, a training module was elaborated and distributed to the participants. These modules were very well accepted by the trainees and are still in use and preferred to the later published FP book.

When contraceptives were distributed, receptively sold, in the time from 1992 to 1995 through the firstly public and later private pharmacies, it became evident, that better knowledge of the pharmacists was desirable. Therefore, in 1993, 248 pharmacists were trained to improve the quality of distribution of contraceptives.

Till now about 150 GPs were trained in FP and 4 GPs are now working in the pilot FP centres where they also have training obligations.

The newly established RH sector has elaborated a draft for the implementation of the RH-concept, an analysis of problems in the RH-sector and the definition of priorities.

(Annex 8a, Annex 8b)

5.1.1.5 Outcomes

The crude birth rates decreased slightly over the last years from 24.7 in 1989 to 22.7 live births per 1.000 population in 1995. The rate of natural increase of the population was in 1989: 1.9 per cent and in 1995: 1.74 per cent. Also the total fertility rate decreased from 1980 : 3.6 births per women to 2.3 births per women in 1995, independently from pro-natalist Government policies. But in the same time the abortion rates increased and contributed most to the decrease of the total fertility rates. The achieved contraceptive prevalence rate was still too low to have significant impact on the reduction of fertility. The decrease of the maternal mortality is an important health gain, which was due to the reduction of clandestine and self - induced abortion and its liberalisation.

Indeed, maternal mortality as an indirect measure of the health status decreased by 25 per cent, but in the same period perinatal mortality did not decrease and infant mortality increased slightly. However, influences on mortality are manifold, especially when dramatic changes characterised the transition period.

5.1.2 Other Multilateral and Bilateral Agencies

Although UNFPA is the only donor organisation present in Albania which has an overall Reproductive Health strategy, a number of other multilateral and bilateral organisations are also active within this field.

Among the international organisations, there are: UNDP, UNICEF, WHO, World Bank, the European Union and the International Red Cross. A WHO Programme which aimed the strengthening of Maternal and Child Health/Family Planning Services, was implemented in 1995, with a funding of \$ 114.464.

5.1.2.1 Bilateral Agency Assistance

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The main bilateral donor agencies in Reproductive Health are: United States Agency for International Development (USAID) and Kreditanstalt für Wiederaufbau (KfW). The Italian and Swiss Governments, Population Services International and Marie Stopes International have been involved in rehabilitating and upgrading health facilities, supplying equipment, providing training and supporting social-marketing.

The Project of German Federal Ministry for Economic Co-operation and Development aimed to rehabilitate and construct 60 MCH centres in six districts in the southern and northeastern region and would also include a contraceptive social marketing component. Executing agency was the Ministry of Health and the duration of Project was 1996-1998. The German contribution is DM 8 (5 + 3) million.

5.1.3 NGOs and the Private Sector

The following national and international NGOs are working in the field of FP/RH: AFPA, MSI, PSI, SEATS.

AFPA is actually running three FP centres in Albania (Tirana/maternity 1, Durres and Lezha / maternity hospital). The FP centre in Tirana offers the full range of FP services, including abortion while the centres in Durres and Lezha do not perform abortions. AFPA receives their funds from IPPF and provide services with own contraceptives. IPPF was asked to extend their activities to Shkodra. There are plans to install, together with the UNFPA-project, a joint youth counselling centre for reproductive and sexual health in Tirana. IPPF requested funding from UNFPA to install a computer based "client management information system" (CMIS).

MSI is most likely to implement the social marketing project, financed through a DM 3 million soft loans of the Kreditanstalt für Wiederaufbau (KfW, German Development Bank). The project started at the end of 1996 and includes the social marketing of 3 to 5 contraceptives. This project is executed by the MoH and is complementary to the UNFPA activities.

PSI has started the execution of a social marketing project for their own brand of condoms. They performed focus group discussions and some analysis for the marketing of their product. PSI imported 500.000 condoms in 1996.

USAID has performed focus groups discussions and training of personnel working in FP in the districts of Tirana and Durres. They held a first training course in FP in October 1996, with special focus on counselling and IEC. Seminars and training activities have often been co-ordinated by the MoH and UNFPA. A 3-year project (1995 - 1997) is already implemented on RH of US\$ 800.000, and the same funding is planned to be available for another 3 other years (1998 - 2000).

Currently, there are at least 3 wholesalers and about 630 private pharmacists operating in Albania (April 1996) who stock some contraceptives. Prices vary widely with a cycle of OC costing from US\$ 1.5 to US\$ 5 (and up to US\$ 10 in some cases). Since contraceptives are distributed free of charge through the public sector, most private pharmacies have only limited stocks and varieties of contraceptives available and often refer clients to the public FP-facilities. It was estimated by PO3 that in 1996 about 10 per cent of the contraceptives are provided by the private sector. Wholesalers with exclusive sales and distribution rights for specific brand products (e.g. MicrogynonO from Schering) have sometimes problems with illegally imported (mostly from Greece) or falsifications of their brand drug.

Private health care services are not yet widely spread. Approximately 10 per cent of physicians have shown interest in working privately. Till now the social security as a civil servant is preferred, the possibilities to earn money "under the table" and second jobs in the afternoon are compensating low public salaries. However, it is expected that the private sector will increasingly provide contraceptives. Social marketing projects and IEC will contribute to the increase of the private share of the public-private mix of supply of contraceptive and FP services in the next 5 to 10 years. Projections suggest that in the year 2005 about 65 per cent of contraceptives shall be provided by the private sector (*Annex 10*).

6. Perspectives for Future Projects Implementation

6.1 Objectives and Indicators of Reproductive Health till the year 2000

Goals:

- To offer good quality of Reproductive Health service in the relevant services to the Albanian population. Quality means to ensure good quality of information, of the services provided, availability of clinical and referral services, good quality of training and the application of different approaches for single women, female and male adolescents and men.
- To improve the health status of women during their reproductive age, especially during child bearing and delivery.
- To improve the health status of the foetus, newborn children, infants and children till 5 years of age.
- To improve the sexual health of adolescents and adults.
- To enable individuals and couples to make informed choices when and how many children they want to have. This will be achieved through adequate timing, spacing or limiting of pregnancies, the use of a wide range of methods, high quality counselling, IEC and efficient logistics of high quality contraceptives.
- To contribute to the development of Reproductive Rights, which promote gender equality, contraception, voluntary sterilisation and abortion as reproductive right, family planning as a human right and women's right to health.

Objectives (Indicators):

- 1. To reduce infant mortality (to under 25 per 1.000 live births).
- 2. To increase the vaccination coverage (to over 95%: with effective vaccines of a good working cold chain, complete and respected vaccination scheme, correct application, to eradicate neonatal tetanus, to eradicate new poliomyelitis infections).
- 3. To reduce the mortality of children under 5 years of age from diarrhoea (by 50% and to reduce incidence of diarrhoea infections (by 25%).
- 4. To reduce maternal mortality (to 25 per 100.000 live births).
- 5. To reduce the risks in fertility regulation (e. g. mortality of abortion).
- 6. To increase the coverage of antenatal care by medical professionals (to 90%).
- 7. To increase the percentage of deliveries through qualified medical personnel (to 95%).
- 8. To reduce the incidence of high-risk pregnancies (to reduce pregnancy anaemia, defined as Haemoglobin < 10 mg%).
- 9. To increase the contraceptive prevalence rate (from 10% to 20%).
- 10. To reduce the prevalence and incidence of STDs through IEC, early detection and early treatment and herewith reduce the risk for the foetus for STD infections (basic data should be required through studies).
- 11. To reduce mortality through ARI of children under 5 years of age (by 30%).

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12. To reduce under- and malnutrition of children under 5 years of age, to reduce the severe and moderate dystrophy in children under 5 years of age (by or to 50%, to eliminate the disorder caused by Vitamin A deficiency).

6.2 Population Development

Future project planning and implementation has to consider changes in demographic and epidemiological transition: projections of population growth (medium population growth: overall life expectancy at birth will increase over the next 15 years from 71.4 to 74.5 years and infant mortality rates are assumed to decrease from 43.2 to 26.8 per 1.000 live births) predict populations of 3.350.000 in the year 2000, of 3.550.000 in 2005 and of 3.750.000 inhabitants in 2010. The present demographic transition will not only change the distribution of urban and rural population, but the population will grow older in the next ten years. Epidemiological transition may appear especially in the rural areas, whereas in cities prevalence rates of infectious diseases will remain high.

6.3 Health Policy and Strategy

Increasingly, elements of decentralisation and privatisation will affect the public health system and also be introduced at the PHC-level. RH as a concept has to find ways to enable intra- and inter-sectoral co-operation between ministries and the different services of ministries which are still vertically organised. NGOs will be increasingly active in RH activities, especially women's groups and non-for-profit organisations, in order to reach special target groups (students, young women, "community women", minorities, etc.). The co-ordination and supervision of NGOs should be a major task of the MoH both, at central and district level.

At central level:

- Knowing of legislation on human reproduction rights and ethics, necessary improvement. (Women and children rights on RH).
- RH and its role on socio-economic development of the country. (Identification of problems and co-ordination with different organisations involved in these issues).
- Research on RH (unfavourable population, need for training and for infrastructure).
- Increasing the capacity of services (formation, quality of service).
- Integration of RH services.
- Focusing on woman health.
- Improving of IEC (using mass media, as well).
- Collaboration between institutions (public/public, public/private, NGO, international organisations).

At district level:

- Knowing the concepts and components of RH in general, and especially for respective districts.
- Creating a professional team, supervised by the second level care Director, which will provide the adequate information in different districts, regarding the:
 - re-evaluation of situation;
 - the priorities;
 - the level of IEC;

- necessary materials and equipment;
- Creating a specialised team, supervised by the first level care Director, which will aim at improving the quality of life of families in the rural areas:
 - family planning, related to mother health care;
 - adequate conditions for delivery;
 - vaccination, breast-feeding and adequate child nourishment;
 - spacing between deliveries;
 - preventing very early marriages and pregnancies;

6.4 Approach

Albania is a low FP-prevalence country and STD/AIDS-prevalence is still low. Therefore, the major orientations should be the introduction of innovative services, information education communication and operations research on consumers/clients, to influence the health-policy, and to improve the training of personnel.

6.4.1 Holistic approach of Reproductive Health

The exclusive focus on MCH and FP has to be widened in the future towards a holistic approach of RH as an integrated part of PHC. In order to orient RH/FP towards PHC, GPs, family physicians, midwives and nurses should be in the centre of training and delivery of services at first level. In the future special attention should be paid to improve the quality of training and refresher courses. To that end, separate training will be provided for those who work at maternity, at the primary health care level, in abortion services and in the regional centres.

MoH will be encouraged to create some form of recognition for its principal trainers and this should be evident in their title, status or by alternative incentive of the MoH. The appointment of future trainers should be by open competition within the profession and will be decided by an authoritative panel on which the MoH, the IPH, the MoE and the Faculty of Medicine and the School of Midwifery are represented. Trainers need to be made accountable after providing their training to this authority and their recommendations need to be considered in the ongoing development, review and emergence of the Reproductive Health/Family Planning and Sexual Health profession.

6.4.2 Client and Patient oriented

People should be put in the centre of concern. Therefore RH and FP-services should be more client/patient oriented (i.e. based on unmet needs of the client/patient, acceptance or rejection of contraception, etc.). RH should be concerned with women as women, with women's needs before, during and after the age of reproduction and not just as mothers. RH should respond to sexual and RH needs of women, of men and of adolescents and it should respond especially to the needs of the rural population, who still represents the majority of the population of Albania.

At present, men are hardly participating in any discussion concerning FP or RH. It seems that actually FP is a women's issue. Most FP-services are offered close to MCH-services and may therefore limit the accessibility for men. At present it may be difficult to involve men in RH and FP, but first measures should be taken to address men and to facilitate their access to condoms. For planning and evaluation purposes, needs assessments related to the population and health personnel are important to describe the baseline situation in RH. In order to be more client oriented, knowledge, attitude, practice surveys are needed to find out the position of women and men with regard to FP, contraception and other RH-issues.

6.4.3 De-medicalisation of Reproductive Health and Family Planning

In order to de-medicalise RH-services and to improve accessibility and availability of contraceptives, it should be considered to give trained midwives and nurses the right to distribute some of the contraceptives without the approval of a medical doctor. This should contribute to improve the information level of the population, especially of the rural population, to enable them to make free and informed choices in FP. RH and FP should be de-medicalised by introducing IEC, social marketing and improving counselling.

6.4.4 Information, education and communication

A wide range of leaflets covering a variety of key subject areas have been produced. However, in rural areas the services are poor and maternal and child morbidity is also the highest. Print runs have only been small and quantities are insufficient to meet need and guarantee distribution throughout the country. Distribution of existing materials has been confined mostly to the capital and main urban towns.

IEC should be one of the main components of the future programmes. The high rate of literate persons, the high number of TVs and radios will facilitate the transmission of FP/RH-messages. There will be heavy emphasis on the collaboration of the television and radio through regular spots and documentary broadcasting. Improved communication with the client during counselling and follow up of the client are urgently needed. IEC with service delivery at the same time should be considered as a standard quality of service.

Through public media and medical personnel the clients should be informed better about contraceptives, their use, effectiveness, their side-effects and their price (or free distribution). Especially the consequences of abortion, the risk of too early pregnancies, too frequent pregnancies and too late pregnancies are important information. The main concern of women not using modern contraceptives should be widely discussed. The Albanian women and even the medical specialists are not yet aware that OC contribute to reduce the risk for endometrial or ovarian cancer. Other main focuses of information and education should be the nutrition during pregnancy, RTI/STD and general education about human reproduction.

Special emphasis will also be placed on assisting the Ministry of Education to elaborate a multi-sector (Government and NGO) policy document on introducing and providing sex education into school, both using formal and informal teaching opportunities. NGO experience, especially among the young people, will be exploited in the informal learning aspects, while sociology and biology teachers will increase their comfort and skill in providing sex education to secondary school age children through formal learning.

Community, religious leaders and opinion leaders should be motivated to promote a positive public image of and esteem about FP and RH.

7. Necessary Inputs for the Future

7.1 Personnel

The MoH has expressed the need for technical support concerning the execution of the project and past experience has demonstrated that a short-term technical assistance is less efficient. Therefore the possibilities of a long-term technical assistance in project management for the RH-Sector should be considered, especially if baseline and consumer oriented research will be planned and co-ordination of different NGOs will become essential. Long term local staff for the implementation and supervision of activities should be contracted, to assist the MoH and the personally weak RH-Sector, especially in improving the inter- and intra-sectoral co-operation.

7.2 Training

Human resources development is needed at the MoH, at both the central and district level. Training in clinical as well as in management issues is still necessary. Training courses in Albania should be promoted and especially directed towards the para-medical personnel, especially of the level of ambulances. The quality of the training through the national and regional training teams should be evaluated and improved. Training in information and research techniques (use of data, concentrate on the important) and training in supervision techniques (more training than control and inspection) should be considered in the curriculum.

7.3 Material, facilities and contraceptives

Basic medical equipment should be provided to the mother consulting centres which have not yet been supplied and which are not included in other projects (e.g. partial rehabilitation of 60 health centres through KfW loans). Equipment, such as adequate midwife-kits should be provided to the midwife-nurses at the level of ambulances and to midwives and nurses at health centres.

An evaluation should be made to identify the necessary material resources to realise the holistic approach of RH at PHC level, for instance, the needs of basic laboratory equipment. The MoH needs to be supported in the purchase of contraceptives. Quantities and method mix should be planned in close co-ordination with the NGOs providing contraceptives, including condoms. Contraceptive supply should be planned on the base of the needs assessment and the expected changes of different variables such as population growths, unmet needs, increasing demand and contraceptive use, changes of the method mix, increasing involvement of the private sector, etc. Preliminary needs in contraceptives have been calculated by the project till the year 2005, based on different assumptions (*Annex 10, Graph 10a*)

8. Output Measures

To measure at least the outputs and some quality indicators of the RH-services (e.g. accessibility, availability, continuation rate) a newly designed health information system should be introduced and adapted to the overall health management information system. The new HMIS should include data which allow to calculate the contraceptive prevalence rate based on new acceptors and repeated cases. Simple methods to evaluate the needs and satisfaction of clients should be introduced to increase follow-up and communication between the service provider and client.

9. Primary Expected Effects and Outcomes

To evaluate changes in primary expected effects, the awareness of special population groups concerning RH should be evaluated as well as the acceptance of different contraceptives and the acceptance of condoms by men, the motives of different population groups to practice or to reject different FP methods, including natural methods.

Behaviour change, FP practice, the continuation in contraceptive use and consumer satisfaction should be evaluated at the beginning of the project and monitored throughout its implementation to allow the evaluation of the effectiveness,

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efficiency, relevance and sustainability of the interventions in RH. (Graph 9a, Graph 9b)

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Geneva WHO Collaborating Centre for Research in Human Reproduction

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1. Basic Information on Armenia

1.0 General

Armenia is a landlocked, mountainous country located in the southern part of the Caucasus region. The smallest republic of the former USSR, Armenia covers an area of 29,800 km2 and has a population of 3.7 million, over 96 percent of which is ethnic Armenian. Armenia shares a border with Turkey to the west, Georgia to the north, Azerbaijan to the east and southeast, and Iran to the south.

The new Constitution, adopted by referendum on June 5,1995, declares Armenia as a « sovereign, democratic state, based on social justice and the rule of law ».

Administratively, the country is divided into 11 provinces, called Marz, including the capital of Armenia, Yerevan, which has the status of province. Governors, who are appointed by the President of the Republic and represent the Central Government, rule provinces. Elected local councils and mayors exercise decentralised local governance in all the communities.

Armenia was the first nation, which adopted Christianity as the country's State religion in 301 AD the Holy See of the Catholics, the Supreme Patriarch of the Armenian Apostolic Church, is in Echmiatsin, a town 18 km west of Yerevan.

The official language of the country is Armenian. It is the only surviving member of the Thracian branch of the Indo-European group of languages. The Armenian alphabet was created in 405 AD and is remarkably well suited to the phonetic values of the language. From the earliest manuscripts to the latest computer fonts, the Armenian alphabet has undergone no alteration in form or structure.

1.1 Historical overview

The present-day Republic of Armenia occupies a small fraction of the territory of ancient Armenia, which extended from the lesser Caucasus Mountains south across the Armenian plateau to the Taurus Mountains. Archaeological studies trace back the history of Armenia to the 5th millennium BC.

Armenia is mentioned in the Bible as the Araratian Kingdom, historically known as Urartu. The geographic location played an essential role in the history and culture of Armenia. For many centuries, Armenians were in constant warfare with invaders and conquerors—Assyrians, Romans, Byzantines, Parathions, Arabs, and Turks—who ruled over their homeland, although not without meeting the most uncompromising resistance. Throughout these turbulent centuries, Armenians successfully asserted their historical identity and upheld their national heritage against great odds.

In the final part of this history, Armenia connected with USSR, and was one of the 15 Soviet Republics during more than 80 years.

The tumultuous changes throughout the Soviet Union from the late 1980's had inevitable repercussions in Armenia. In 1988, a movement of support began in Armenia for the constitutional struggle of Nagorno-Karabakh Armenians to exercise their right to self-determination. (This predominantly Armenian populated autonomous region had been placed under the jurisdiction of Azerbaijan in 1923). In the same year, Armenia was rocked by a severe earthquake that killed thousands, while the Azerbaijani Government fighting Armenians in Nagorno-Karabakh blocked supplies from both the Soviet Union and the West. These two issues have dominated Armenian politics since the first democratic elections in Armenia during the Soviet era. On September 21, 1991, the Armenian people voted overwhelmingly in favour of independence in a national referendum, and the independent Armenia came into being. The high level of public participation in these revolutionary events in Armenia can account for the stable political situation in the last years: people feel responsible towards society and the economy.

1.2 Diaspora

Armenia has a large Diaspora that is spread all over the world. The formation of the modern Armenian Diaspora is a result of the anti-Armenian policy of the Ottoman Empire that culminated in the first Genocide of the twentieth century. In 1915, about one million people were killed and more than 800,000 deported from their ancestral lands in Eastern Anatolia, Turkey. Currently, there are about 8 million Armenians living in the world, of which 60% live outside Armenia in more than sixty countries.

In recent years, the proportion of professionals, businessmen and civil servants in the Diaspora has grown more rapidly than other professional groups. Many Armenian organisations function in the Diaspora. They link communities of Armenians in the Diaspora.

The independence of Armenia created favourable conditions for the participation of Diaspora Armenians. They help solve the economic, technical, health, and social problems. They also contribute more generally in the creation of the new Armenian State. ``Armenia``, ``Aznavour for Armenia``, as well as other funds and organisations function successfully. The ties between Armenia and the Diaspora have evolved from the implementation of charitable projects and unilateral help, to the establishment of bilateral co-operation in different spheres.

1.3 Economic and social overview

Since declaring independence in 1991, Armenia has vigorously pursued free-market reforms within a democratic framework, facing acute political and economic difficulties that have beset the country in recent years. The major factors contributing to these difficulties are the devastating earthquake of 1988 that destroyed infrastructures and killed 25,000 persons, the economic blockade (the country has no access to the sea, which makes it economically

dependent on neighbouring countries) imposed upon Armenia as a result of armed conflict between the Republic of Azerbaijan and the enclave of Nagorno-Karabakh, the choking off of Armenia's major northern trade route due to civil conflict in Georgia, and the considerable economic dislocation associated with the disintegration of the Soviet Union. Economic decline has been reflected in sharp output reductions, falling incomes, reduced trade flows, severe energy shortages, and scarcity of food and other consumer goods.

The social situation in the country and the living conditions remain rather difficult. With respect to poverty, the World Bank estimates that in 1994, 28% of the population had incomes below 40% of average household expenditures, and is classified as either poor or very poor. The most vulnerable people—single/disabled pensioners, orphans, institutionalised children and the elderly, expectant/nursing women and destitute people needing regular social assistance—are identified through PAROS, a government-operated vulnerability assessment system. They constitute 12.5% of the population and can be considered to be living in extreme poverty. Pensioners and others living on fixed incomes account for 40% of the country's population. The main coping mechanism has been through emigration, humanitarian aid, and the high level of social solidarity, including remittances from the Armenian Diaspora. Elements of a poverty alleviation strategy have been identified in the World Bank's poverty assessment for Armenia as well as in the National Human Development Report 1996, promoted by UNDP.

2. Women's Activities in the New Situation

2.0 Legal status of women

Women around the world are seeking empowerment and human rights, including the right to reproductive health and self-determination.

In a country which was rarely independent, the Armenian people considered the family as the main factor for keeping the fabric of society together. The Armenian women played a crucial role in the survival of the nation.

The peculiarity of the social conditions of women in Armenia is in the fact that their constitutional rights are in no way inferior to those of men; legislation now as before recognises equal rights for all regardless of gender, age or ethnic origin. This sets Armenia and the other former socialist states aside from developing countries and even some Western nations. Moreover, the Armenian Constitution in some instances grants women certain advantages and privileges. This has led to women surpassing men in several social indices. Among these are educational level, social benefits, medical coverage, and preferential parenthood rights.

2.1. Real status of women

In social practice, women remain subordinate to men in a number of issues. The Armenian woman traditionally had an accessory role in the family and in society. The way of life, popular rites, social norms and common mentality have presumed a woman's subordinate role in the family and to her husband. These traditions have not lost their substance even today. For example, the possibilities for promotion are not the same for women as they are for men and women often remain economically dependent upon men. The overall average salary for women is less than two thirds of that of men because of the low involvement of women in high-paid activity. Social mobility for women is lower than for men. Women's representation in senior civil service positions is as low as 3 to 5%. And, women bear the burden of the so-called informal sector of the economy, which includes assuring the functioning of the family, educating and caring for the children, and the household.

2.2 Violence against women

There is little information about sexual, physical and psychological violence against children and women. In general, national mentality and moral prevent women and children from reporting about violence. There is a telephone counselling service «Trust » for children to report any kind of physical or mental abuse.

2.3 Women in the transition period (Table 1)

The predicament of the development of market relations during the transition period resulted in apparent changes in the condition of women. There seem to be two general tendencies. In 1993 women accounted for 49% of Armenia's labour force and unemployment among them the same year reached 64%, whereas the same index among men was 36%. Women's employment in the newly formed private sector was not high, only 45 out of every 1,000 working women were involved in registered small businesses, whereas for men this index was 75. Men take out the majority of bank loans. All sorts of deposits and bequests are also usually made in the name of men. As a result of the privatisation of land in 1991 and 1992, 304,000 individual farms emerged. These lots were registered to women only when there were no men in the family or when a woman was the elder of the family. By rough estimates, the GDI should have declined since 1993 because registered unemployment among women had reached 79% by 1994, thus affecting income levels.

On the other hand, compared with the past more and more Armenian women are attaining active economic positions as opposed to men, who are confused with loss of their jobs in the state sector because of low wages. Women have started to make serious contributions to family budgets, sometimes becoming the sole bread providers. Mostly their activity is in unregistered self-employment (cooking for sale, working as housekeepers, engaging in trade outside of Armenia, etc.). Their social and political activity has also increased: there are three political and 25 women's social organisations currently registered. A women's party was rated second by party ballots in recent parliamentary elections, increasing women's representation from 3.6 to 6.3% in the National Assembly. Women's educational attainment levels are continuing to increase. Their enrolment in higher education exceeds that of men (54% in 1995).

In 1995 women accounted for 85% of schoolteachers and there is similar evidence in respect to medical, journalistic, judicial and other professions. The overwhelming majority of NGO members are women. Of course, this increase is a partially passive process, because of men leaving these positions. Nevertheless, it gives women a lever for influencing current economic, social, and political processes.

Thus, the market is revealing the economic potential of women, so far unrecognised. Economic crisis and liberalisation processes create favourable conditions for many women to attain economic independence. This appears to be a gain that they will not give away easily.

Equality is the main principle of the international movement for women's rights. Equal opportunities require laws and opportunities to be gender sensitive. Armenia's Parliament has ratified most of the conventions protecting women's rights. The rights of women to vote and to run for office, the right to citizenship and participation in government are guaranteed in the draft constitution. An important objective is to eliminate gender discrimination in employment and compensation as well as to stipulate a number of privileges connected with maternity.

The Parliament of the Republic of Armenia ratified the International Convention on Women's Rights on 9 June 1993.

In October 1994 in Yerevan was conference « Armenian Women on the Verge of the 21st Century », where issues of equal rights for women, social security, health protection and family planning were discussed.

More that twenty *Women's Non-governmental Organisations* are registered in Armenia. Women's opportunities to participate in public activities has increased in the process of democratic reforms.

3. Lifestyles

Health and wellbeing are inextricably linked to the overall conditions of life. The prerequisites for both health and healthy living include feeling free from life's threats, and having meaningful roles and functions in society, proper education, a decent home, and the necessary earnings to meet basic needs.

The supremacy of health in the concept of human development is indisputable. In social policy there are four ways by which the government can contribute to the improvement of the health status of the population. These are medical and biological research, assuring the availability and quality of medical services, control over the quality of the environment and food along with regulation of hazardous impacts, and, finally, promotion of healthy lifestyles.

3.0 Nutrition

The issue of food has reached crucial dimensions for the 80% of the population of Armenia that lives in absolute or relative poverty or impoverishment. The quantitative and qualitative inadequacy of food negatively affects public health.

There is a programme financed by the Government of the United States and implemented through the Ministry of Health, for nutrition of pregnant and breastfeeding women, and 0-5 year-old children. All pregnant women receive iron and vitamin supplements.

Specialists from National Institute of Nutrition of Rome, Italy visited Armenia in 1998 at the invitation of UNICEF, to assist the Ministry of Health in developing a nutrition surveillance system and designing a national nutrition survey. The survey will focus on the nutritional status of children and women with a particular attention to micronutrient deficiencies.

Nutrition and health policy in women and children: <u>Report on a WHO workshop, Yerevan,</u> <u>Armenia, 2-3 July 1997</u>

A child's right to adequate nourishment, and the duty of society to ensure that a pregnant woman has access to good nutrition, have been matters of concern for over a century. Yet even in the 1990s, babies are still at risk of undernutrition before birth. Recent years have seen increasing evidence of the importance of nutrition for a satisfactory birth outcome. The Workshop was designed for health facility administrators, policy- makers and clinicians interested in nutrition and how food affects the health of women and infants, and was attended by gynaecologists/obstetricians, paediatricians and hygienists working in the saneped system. On the first day a short course for administrators and policy- makers on « Promoting breastfeeding in sanitary facilities » was held, and during the following three days the WHO/UNICEF training module on « Healthy eating in pregnancy and lactation » was pilot tested. Participants gained knowledge on providing health advice for women during pregnancy, birth and the postpartum period with a view to promoting WHO guidelines on healthy eating. The Workshop contributed to developing a national plan of action for Armenia to implement national dietary guidelines for pregnant and lactating women and their families.

Copenhagen WHO Regional Office for Europe 1998

3.1 Healthy behaviour

Armenia has a lowest number of registered cases of alcoholism among former Soviet Republics.

There is no significant data about the consumption of psychotropic drugs. However, cases of death caused by drug abuse increased from 3 in 1988 to 32 in 1994.

The tendency toward tobacco smoking among teenagers in urban areas is especially alarming.

Among adolescent girls (14 to 16 years old) 21% of girls questioned smoked and of these 98% smoked 1 to 5 cigarettes a day, 48% started smoking from the age of 16, 24% from the age of 15 and 20% from the age of 14.

4. Health Care Potential

During the Soviet time the public health care system in Armenia was based upon the principles of social justice and health-care was free of charge. The law on "Health Care and Services" which was signed by the President on April 1996 has started reforms in Health Care system. The health system is presently involved in the transition to a market economy.

The Ministry of Health has focused on decentralisation of the Health Care and introduction of Health Insurance. Also planned is decentralisation of the health care system and privatisation of premises, as well as design of a mechanism for providing low cost treatment to poor patients. However, Maternity, Child Health and some other services are free of charge.

There are 517 outpatient clinics, 182 hospitals with 30,068 hospital beds. Eleven sanatoriums for children and three orphanages are also operational. In 1993, the Health Ministry employed 13,578 physicians. The health-care network is sufficiently developed and there are an adequate number of professionals (Table 2).

There are innovative programmes for the effective use of human resources, including the computer information centre of the Ministry of Health (help programme management and decision- making) and Diagnostica (a private firm undertaking diagnostic studies and continuing medical education).

5. Obstetrical and Gynaecological Services

5.0 Obstetrical and gynaecological services

There are many Obstetrical and Gynaecological Services in Armenia:

- Armenian Research Centre for Maternal and Child Health Protection in Yerevan ;
- Republican Centre of Perinatology, Obstetrics and Gynaecology in Yerevan ;
- Centre for Family Planning and Sexual Health in Yerevan ;
- five independent maternity centres in Yerevan, five in other cities, and regional centres (Gumri, Vanadzor, Hrazdan, Kotaik, Armavir);
- eight obstetric/gynaecological departments in clinical and city hospitals ;
- 33 obstetric/gynaecological departments in central regional hospitals ;
- 22 rural district hospitals with obstetrical beds,
- 36 independent maternal consultations and 64 obstetrical and gynaecological consulting rooms ;
- 636 feldsher/obstetrical posts.

There is a specialised Centre on Women's Reproductive Health in Yerevan.

The country has 5019 hospital beds in the obstetric/gynaecological departments and institutions and 835 obstetricians and gynaecologists. There is roughly one gynaecologist for every 100 births.

5.0.1 External assistance in reproductive health and family planning

The Ministry of Health has developed the special national programme on human reproduction, which includes the development of a network of Family Planning/Health centres in all administrative districts of the country (<u>Table 3</u>, <u>Table 4</u>, <u>Table 5</u>).

5.0.2 Major institutions in maternal and child health/family planning

- National Institute of Reproductive Health
- Government MCH/FP services and women's polyclinics at all levels of health care

6. Health Status and Its Trends

6.0. Population general mortality and growth rate

The location of the total population has changed significantly. In 1960 the urban and rural populations were split evenly between urban and rural areas. In 1994 this gap widened, with 67.7% of the population living in urban areas and 32.3% in rural areas. In 1994 two thirds of the population lived in urban areas, and nearly one half the population lived in the capital of Yerevan (Table 13).

The natural growth rate of Armenia has steadily declined since 1940 from 27.4 per 1000 to 16.3 in 1990.Between 1991 and 1993 the natural growth rate dropped from 15.1 to 8.4%. This may be a consequence of the economic crisis (Table 7).

In the early sixties, women constituted 52.4% of the total population. Because of the considerable mobility of the population (60% of them being men), the distribution of sexes later became nearly equal. The early nineties reduced the proportion of women reduced to 51.5% (Table 8).

In the last few years, the population general mortality rate has increased from 6 per 1000 of population in 1990 to 7.36 in 1993 (Table 17, Table 18). The absolute number of deaths within these three years has increased by 5500 (from 22,000 to 27,500) or by 24%. Circulatory diseases are the leading cause of death (3.9 per 1000). Over the last five years, this indicator has significantly increased. It stood at 2.97 in 1989 and reached 3.9 in 1994. Malignant diseases are the second most frequent cause of death. That rate was 0.96 per 1000 in 1993. Deaths due to injuries and poisoning are in third place and equal 0.62 per 1000 (Table 9). The death rate due to respiratory diseases was 0.51 in 1993.

The available statistics on mortality do not classify the number of deaths according to the initial causes of death (cold, malnutrition, and stress). Furthermore, some causes of death may be related to the prevailing socio-economic situation in the country. In fact, according to some estimates, no less than half of the increase in the number of deaths may be attributed to this particular situation.

6.1 Life expectancy

At the beginning of the 1980s, life expectancy in Armenia was the highest of all the former Soviet republics and higher than the European average. Estimates in 1990 show that it is still one of the highest, but some three years below the European average (Table 9, Table10).

The dramatic decline in life expectancy in 1988 was attributable to the 1988 earthquake. Life expectancy reverted to its previous level in 1989. However, while all other republics show a slight improvement in life expectancy, Armenia is experiencing a decline: male life expectancy declined from 70.4 years in 1981 to 68.5 in 1990, while female life expectancy declined from 76.8 years to 75.4 years.

An incomplete account of the migration caused by the earthquake and conflicts with neighbouring countries may also give rise to some bias in mortality and life expectancy.

6.2 Marriage and divorce practices

A radical change in the reproductive behaviour of Armenia's population took place within the span of one generation. This was a natural transition from a traditional family type to one that was modern and urban.

Marriage practices have changed during last years. Marriage rates remained fairly constant from 1960 until 1988 when marriages per 1000 population fell below 10 and have not returned to that level. In 1993 the marriage rate was 5.8. The divorce rate was around 1 to 1.4 over the last 20 years, but has dipped to 0.8 in 1993. Low marriage rate may be also connected with the fact, that some couples may not officially register their marriage, to receive Government financial support for single mothers (Table 13).

Traditionally, the choice of spouse was highly dependent from parents. Now there is a tendency to premarital relations, choice of spouse is less dependent from parents.

In 1993, the average age of marriage was 21.7 for women and 25.8 for men. In 1989-94, the average age at the first marriage for women was 22.2 years.

6.3 Fertility

The fertility rate in Armenia declines. In 1959, it was 4.7; in 1969-70, it declined to 3.2 children per woman; and in 1979-80, it dropped to 2.4. For 1990, the total fertility rate (TFR) increased to 2.7. The projection for TFR for 2010 is 2.3 children per woman.

The rural fertility rate is higher. In 1993 it was 2.5 to the urban rate of 1.7; however, it is also steadily declining.

6.4 Perinatal care

As a result of socio-economical difficulties, the number of women attending prenatal clinics has dropped, especially in the rural areas, and the number of complications during pregnancy and birth has risen. The percentage of pregnant women under the supervision of prenatal clinics in 1993 was 17.6% lower than in 1992. As a result of the difficulty to organise preventive examinations of the « high risk groups » of pregnant women, the incidence of pre-eclampsia and eclampsia cases increased significantly from 2.3% in 1980 to 3.8% in 1990 and to 7.1% in 1993.

Low-iron and low-protein diets have increased the incidence of anaemia among pregnant women (Table 14).

The number of births at home and under the supervision of not trained personnel has increased. Due to difficulties with transportation, women often arrive very late at the maternity hospitals, in many cases in the placental period of labour.

6.5 Birth rate

After the legalisation of abortion and the introduction of contraception during the 1960s, the birth rate declined.

The 1990 birth rate of 24 has remained stable since 1980. The birth rates among the country's 37 districts vary from 19 (Yerevan) to 40 (Spitak, hit by the 1988 earthquake).

One of the main characteristics of the birth rate in Armenia, during the period of 1990-95, is the decline of the total number of births in about 39% of women. In multiparas, it declined in 41% and in primiparas in 35% (<u>Table 11</u>, <u>Table 12</u>). The recent decline of the birth rate may be explained by the current economic crisis in Armenia.

The most important structural factors of the traditional Armenian family model were the effective absence of births among women over the age of 40, the largest proportion of births (75%) occurs in the relatively narrow age-range of

20 to 29 years, the steady increase (45%) in the proportion of middle-sized families (families with two to three children make up 80% of the total).

The number of pregnancies in women under 19 have increased, while pregnancies those aged 20-29 have decreased. Fertility is especially high in those 15-19 (in 1990 there were 80 live birth per 1000).

During the period 1990-1995, there was a high rate of elderly primiparas (<u>Table 11</u>, <u>Table 12</u>). In the age group of primiparas 30 years and over, the birth rate increased from 3,64% in 1990 to 4,5% in 1995; and the rate of primiparas 45 years and over, increased twice, which is very uncommon for a traditional Armenian family.

6.6 Abortion

Abortion has been legally permitted in Armenia since 1955. It is available upon request up to 12 weeks of pregnancy. As modern contraceptive methods have not, and are yet not generally available, abortion rates are very high in Armenia. In 1990, the abortion rate was 29.6 per 1000 women of fertile age. In 1992, the abortion: live birth ratio was 1/2.5 (Table 15). A WHO survey in 1991 showed, that 63% of married women of reproductive age had at least one abortion and 6% had 10 or more.

6.7 Female mortality and cancer

The leading causes of female mortality are diseases of the circulatory system, malignant neoplasms (<u>Table 25</u>, <u>Table 29</u>), diseases of the respiratory system (1992).

Annually, females in Armenia lose a total of 28 902 years of potential life (YPLL) per 100 000 population due to various causes of death. Injuries are the most common, accounting for 15 334 YPLL; circulatory conditions account for 4 816 YPLL; respiratory conditions total 2 140 YPLL; neoplasms 2 744 YPLL; and residual causes account for 3 868 YPLL.

Armenia had a general screening programme for women. However, this programme was closed in 1991 as a result of the economic crisis. Consequently, the detection of malignant neoplasms has decreased and the mortality has increased (<u>Table 25</u>, <u>Table 29</u>).

6.8 Maternal mortality

The maternal mortality rate in Armenia is about three times higher than the WHO target for Europe (<u>Table 20</u>, <u>Table 21</u>). The primary causes of this high mortality ratio are haemorrhaging, abortions and hypertensive complications (<u>Table 22</u>). The high rate of post-abortion mortality in the country has been attributed to lack of sanitary supplies, short supply of drugs, and poor skills of health care personnel.

6.9 Infant mortality

Infant mortality is just below the former USSR average (Table 24). The main causes are conditions in the perinatal period (33%), respiratory diseases (26%) and infectious and parasitic diseases (20%). The actual rates may by underreported because the definition of infant mortality rate as used in Armenia (which is based on that used in the former USSR) differs from that which is recognised by the WHO.

There is a significant difference in infant mortality between urban and rural areas. The infant mortality rate is higher in the rural areas (Table 23), but 70% of all cases of infant mortality is in urban areas, because of the transfer of the

severe patients from the rural areas to the hospitals in urban areas.

6.10 Contraception

There are not many official studies on the contraceptive prevalence in Armenia. Available data is very controversial.

Data from the Ministry of Health for 1991 showed that the contraceptive prevalence rate in Armenia is 56%. In the document from WHO Regional Office for Europe, however, it is estimated to be under 10%. From hospital-based studies, data from 1992 showed that 1,6% of women used IUD and 0,06% used OC.

A study in 1991 on contraceptive prevalence and use pattern in Yerevan of 4349 married women, aged 15-44 years showed: 56% currently used contraception; 11% used contraception at some point in the past, but are not current users; 33% never used contraception.

The same study showed, that couples, who currently used contraception (56%), mainly used withdrawal (32%), traditional methods (23%), and condom (28%). The use of IUD was14% and pills 3%.

Modern oral and injectable contraceptives are available since a couple of years in special family planning services and have been received through humanitarian aid as external assistance in Reproductive Health and Family Planning or as free research samples.

Contraceptives are available in private pharmacies in Yerevan, but costs are very high. Outside Yerevan, contraceptives are generally not available.

6.11 Infertility

Data available for 1992 showed a high prevalence of infertility in Yerevan. 21.4% of the women in the study had secondary and 3.2% had experienced primary infertility.

During the last years, as a result of high prevalence of STDs, malnutrition, stress, cold and other causes, the incidence of infertility is very high.

6.12 Sexually transmitted diseases

The incidence of STDs has consistently increased in the early 1990s (Table 16) as a consequence of low socio-economic conditions, poor state of maintenance of basic water supply and sanitation infrastructure, malnutrition, the unavailability of drugs, frequent migration of the male part of the population to different countries for temporary job finding.

Many women, especially in rural areas, do not seek specialised medical care, because of financial problems and because of the shame to have a STD. There is a high practise of treatment without attending the clinic.

Armenia has a Republican Centre for Combating and Prevention of AIDS since 1984. In 1994, it became part of the Republican Centre for Population Health Observation.

AIDS tests are performed for pregnant women in maternity or prenatal clinics, for donors in the blood transfusion service, and for patients at the Infectious Disease Hospital No.1 in Yerevan, where there are specialists in HIV/AIDS treatment.

6.13 Breastfeeding

From 1988 to 1992, the rate of breastfeeding during the first four months decreased from 64% to 37%, the cause of which may be women's opinion, that mother's malnutrition can affect milk quality; and the abundance of child nutrition by humanitarian aid during the first years after the earthquake.

During 1995-97 the National Government, with external assistance, carried out a programme for early and continuous breastfeeding during the first four months of the baby's life.

In rural areas, 80%-90% of the women breastfeed their infants for the first six months.

7. News from Armenia

A ceremony for commemorating the opening of the Maternity Department took place in Goris hospital. The Department was renovated with the contribution of material and financial resources from UNHCR, UNICEF, ICU (Italian NGO) and the Armenian Research Centre for Maternal and Child Health Protection.

8. Tables

Table 1: Status of Women in Armenia

Secondary net enrolment ratio (%)	Upper-secondary graduates (as % of female of normal graduate age)	Tertiary full-time equivalent gross enrolment ratio (%)	Tertiary natural and applied science enrolment (as % of female tertiary)	Women in labour force (as % of total Labour * force)	Administrators and managers (% females)	Parliament (% of seats occupied bywomen)
1995	1989	1995	1995	1994	1995	1995
83	81.9	96	49	44	35.9	6.3

*Employed in the state sectors Source: UN DR 1996

Table 2: Basic Health Indicators, Service Capacity, 1990-1994

	1990	1991	1992	1993	1994
Physicians per 10 000 Population	40.5	40.8	39.3	36.8	34.0
Nurses per 10 000 Population	98.6	99.3	98.1	93.2	85.0
Hospital beds per 1000 Population	8.5	8.5	8.3	8.2	7.8
Number of outpatient facilities	176.0	179.0	183.0	182.0	181.0

Source: Department of Statistics

Table 3: Functional	Composition	of Health Spending	1992-1995 (in	i millions US\$ equivalent)
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Health Program	<u>1992</u>	<u>1993</u>	<u>1994</u>	<u>1995</u>
Public Health	1.32	3.20	0.73	4.24
Family Planning and nutrition	1.12	2.80	0.61	3.81
AIDS Prevention		0.02	0.00	0.02
Clinical Services	13.52	29.04	8.80	29.13
Pregnancy- related care	1.32	3.00	1.00	2.87
Family Planning services		0.02	0.01	0.02
Infectious diseases	0.61	1.24	0.41	1.29
Children's health	2.10	4.80	1.50	6.26
Oncology	0.31	0.58	0.15	0.84
TOTAL HEALTH EXPENDITURES	15.00	32.60	9.70	33.50

Source: Ministry of Health, Armenia Totals are approximate due to rounding.

Title	Duration	Country/donor (exec. agency)	Total commitment	Disbursements in 1996	Type/terms	Project objectives (beneficiary institution)
Maternal and Child Health Care Training	96-97	CAN/CIDA (CIDA)	20	0	FTC/GRANT	Training and symposium on neonatal and perinatal resuscitation and maternal health care.
Primary Health Care / Maternal and Child Health Care	95-97	UNICEF	495	132	FTC/GRANT	Improvement and extension of essential services as basic set of preventive interventions,promotional activities and clinicalservices, which have direct impact on reduction of childcare and maternal mortality and morbidity.
Breastfeeding	95-97	UNICEF	73	19	FTC/GRANT	Empowerment of 60% of women to breast-feed their children extensively for four months. ()

Emergency Health	95-96	SWE/SIDA	224	0	ERA/GRANT	Immunisation of Children :diphtheria
		EU	38	38	ERA/GRANT	control ; support to Safe
		UKM/ODA	69	0	ERA/GRANT	provision of basic
		USA/USG	660	0	ERA/GRANT	equipment; support to physically disabled
		EU	598	0	ERA/GRANT	children. ()
		SWE/SIDA	473	473	ERA/GRANT	
		NET/GNL	121	121	ERA/GRANT	
		EU (UNICEF)	73	73	ERA/GRANT	
Strengthening Reproductive Health Services	95-99	UNFPA	527	428	ETC/GRANT	Establish 75RH/FP service sites through training of services providers, supply of modern contraceptives and equipment information system at the MOH for evaluation of trends in RH/FP care; evaluate the project through pre- and post KAP survey. (Rep. Centre of Perinatology and Gynaecology)
Reproductive	96-96	UKM/ODA	15	15	ERA/GRANT	(-)
Health		UKM/OXFAM-UK	10	10	ERA/GRANT	(-)
		(OXFAM-UK)				
Women and Child Health : Strengthening Reproductive Health in Armenia/ Infant and Young Child Nutrition	96-97	WHO	7	1	ETC/GRANT	Strengthening Reproductive Health in Armenia. (Ministry of Health)
Safe Motherhood	95-97	UNICEF	30	0	ETC/GRANT	(-)
Strengthening Reproductive Health Services	95-98	UNFPA (WHO)	369	12	ETC/GRANT	Establish 75RH/FP service sites through training of service providers, supply of modern contraceptives and equipment; establish a management information system at the MOH for evaluation of trends in RH/FP care; evaluate the project through pre- and post KAP survey. (Ministry of Health)
Partnership Hospitals and Family Planning	96-97	USA/USG (USAID)	1,400	0	ETC/GRANT	Medical exchange to support the hospital partnership programme; family planning. (-)

Activities of the Fonds Armenien de France in the Health Sector	96-96	FRA/FAF (FAF)	69	69	ETC/GRANT	Assistance to the Maternity Hospitals of Baghramian. ()
Support to Mother and Child Care	96-97	EU (CHAD)	190	190	ERA/GRANT	Integrated support to mother and child care. ()

Table 5: UNDP Project Fact-Sheets (Status Report)

(1)

PROJECT NO.:	ARM/95/P01
PROJECT TITLE:	STRENGTHENING REPRODUCTIVE HEALTH SERVICE IN ARMENIA
EXECUTION:	WHO GOVT.
IMPLEMENTING COUNTERPART:	MINISTRY OF HEALTH BUDGET:US\$ 860,000 (UNFPA)
DATE OF SIGNATURE:	3 November 1995
ACTUAL START DATE:	January 1997

DEVELOPMENT OBJECTIVES:

Contribute to reduction of maternal mortality of 50% by year 2000 by assisting Government in implementation of National Reproductive Health Programme aiming to reduce high abortion rates and incidence of haemorrhage and infections among women of reproductive age.

IMMEDIATE OBJECTIVES:

- 1. Improve access to, and quality of RH/FP services available at 75 service delivery sites through training of service providers, supply of modern contraceptives and provision of essential medical equipment;
- 2. Develop capability of Ministry of Health to evaluate trends in RH/FP care through development and implementation of management information system (MIS);
- 3. Provide information on knowledge, attitudes, beliefs and practices of Armenian population towards reproductive health and family planning and to assess impact of project in these areas through design and administration of a pre-post KAP survey.

EXPECTED OUTPUTS:

75 RHP Centres fully equipped and in operation

RESULTS OBTAINED AS OF 30 MARCH:

All required contraceptives and medical equipment delivered to the Ministry of Health.

CONTACT PERSON:

Svetlana Topchyan, UNFPA Programme Officer

(2)

PROJECT NO.:	ARM/95/P02
PROJECT TITLE:	STUDIES ON MIGRATION AND REPRODUCTIVE BEHAVIOR
EXECUTION:	UNFPA
IMPLEMENTING COUNTERPART:	NOYAN TAPAN AGENCY AND ARMENIAN FAMILY HEALTH ASSOCIATIONS
BUDGET:	US\$18,000
DATE OF SIGNATURE:	October 1995
ACTUAL START DATE:	October 1995

DEVELOPMENT OBJECTIVES:

Assistance to the Government in developing policies and programmes that will respond to the reproductive health needs of the population, particularly those of teenagers, and adequately deal with the effects of migration.

IMMEDIATE OBJECTIVES:

To collect and analyse data relevant for policy makers on a) socio-cultural and other non-demographic determinants of reproductive behaviour; b) sexual attitudes and behaviours of Armenian youth; and c) the social and demographic aspects of migration patterns.

CURRENT STATUS:

The project was completed in May 1996.

EXPECTED OUTPUTS:

Report prepared, discussed and approved.

RESULTS OBTAINED:

Reports on:

- Migration of Armenian Population During the Transition Period (1990-1995);
- Reproductive Behaviour of Armenian Population During the Transition Period;
- Sexual and Reproductive Health of Adolescents.

CONTACT PERSON:

Christine Karapetian, Programme Assistant

Table 6: Demographic Indicators: 1998 and 2010

	1998	2010
Births per 1,000 population	14	18
Deaths per 1,000 population	9	11
Rate of natural increase (percent)	0.5	0.8
Annual rate of growth (percent)	0.4	<u>0.3</u>

Life expectancy at birth (years)	66.7	69.1
Infant deaths per 1,000 live births	41	35
Total fertility rate (per woman)	1.7	2.2

Source: U.S. Bureau of the Census, International DataBase.

<u>Table 7</u>: Midyear Population Estimates and Average Annual Period Growth Rates 1950 to 2050 (Population in thousands, rate in percent)

Year	Population	Year	Population	Period	Rate				
1950	1,355	1996	3,444	1950-1960	3.2				
1960	1,869	1997	3,434	1960-1970	3.0				
1970	2,520	1998	3,422	1970-1980	2.1				
1980	3,115	1999	3,409	1980-1990	0.8				
1990	3,366	2000	3,396	1990-2000	0.1				
1991	3,413	2010	3,369	2000-2010	-0.1				
1992	3,449	2020	3,416	2010-2020	0.1				
1993	3,463	2030	3,469	2020-2030	0.2				
1994	3,460	2040	3,504	2030-2040	0.1				
1995	3,454	2050	3,428	2040-2050	-0.2				

Growth

Source: U.S. Bureau of the Census, International DataBase.

Table 8. Mid	vear Population	hv Age an	d Sex• 1998 🤉	and 2010 (Por	nulation in 1	(shreemoth
Table 0. Milu	ycai i opulation	, by Age an	u ben 1770 e	inu 2010 (1 0 ₁	Julation III	mousanus

	1998	1998	1998	2010	2010	2010
AGE	TOTAL	MALE	FEMALE	TOTAL	MALE	FEMALE
TOTAL	3,422	1,672	1,749	3,369	1,632	1,737
00-04	228	116	112	274	140	134
05-09	322	164	158	217	110	107
10-14	352	180	172	192	97	95
15-19	311	159	152	249	125	124
20-24	273	140	134	320	162	158

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REPRODUCTIVE HEALTH IN ARMENIA

25-29	259	134	125	306	155	151
30-34	260	125	134	256	129	127
35-39	302	146	156	225	112	112
40-44	254	122	133	212	104	108
45-49	188	89	100	251	116	135
50-54	107	50	57	247	115	133
55-59	132	61	71	185	83	101
60-64	145	67	78	118	52	66
65-69	126	57	69	69	29	39
70-74	93	39	54	110	47	63
75-79	33	12	21	70	29	41
80-84	18	6	12	49	20	29
85+	18	6	12	20	7	13

Source: U.S. Bureau of the Census, International DataBase.

Table 9: Life expectancy, 1990-1994

	1990	1991	1992	1993	1994
Health Status					
Average life expectancy at birth					
Overall	70.7	72.4	71.2	71.2	
Male	67.4		68.7	67.9	
Female	73.3		75.5	74.4	
Average life expectancy at 30					
Overall	43.4	44.9	44.7	43.8	
Male	41.0		41.6	41.0	
Female	45.7		47.6	46.4	

Source: Department of Statistics

<u>Table 10</u>: Life expectancy at age 60, 1992-1994

Life expectancy at age 60 (years)				
Male 1992-94	Female 1992 -94			
15.9	18.4			

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Birth/years	1990	1991	1992	1993	1994	1995
Total	79882	77825	70581	59041	51143	48960
primiparas 30 years and over	2904	3093	2754	2327	2171	2183
	3.64%	4%	3.9%	3.95%	4.24%	4.5%
primiparas 30-34 years old	2065	2112	1817	1522	1352	1309
	2.6%	2.7%	2.6%	2.6%	2.64%	2.7%
primiparas 35- 39 years	669	797	764	632	654	714
old	0.84%	1.03%	1.1%	1.1%	1.3%	1.5%
primiparas 40 years and over	170	181	173	173	165	160
	0.21%	0.23%	0.25%	0.3%	0.32%	0.33%
primiparas 45 years and over	19	19	11	8	7	20
	0.024%	0.025 %	0.02%	0.02%	0.014%	0.04%

Table 11: Total number of birth and primipara rates in different age groups in Armenia (1990 - 1995)

Source: Department of Statistics

Primiparas /year	1990	1991	1992	1993	1994	1995
Total	29996	31546	30208	26370	21635	19409
primiparas 30 years and over	2904	3093	2754	2327	2171	2183
	9.7%	9.8%	9.12 %	7.7 %	0.03 %	11.3 %
primiparas 30-34 years old	2065	2112	1817	1522	1352	1309
	6.9 %	6.7 %	6%	5.8 %	6.2 %	6.8 %
primiparas 35- 39 years	669	797	764	632	654	714
old	2.23 %	2.53 %	2.53 %	2.4 %	3.2 %	3.7 %
primiparas 40 years and over	170	181	173	173	165	160
	0.6 %	0.6 %	0.6 %	0.7 %	0.76 %	.83 %
primiparas 45 years and over	19	19	11	8	7	20
	0.064%	0.06 %	0.04%	0.03%	0.032 %	0.1 %

Table 12: Total number and rate of the primiparas in different age groups in Armenia (1990-1995)

Source: Department of Statistics

Table 13: Population of the Republic of Armenia by Regions

	Population		Land	Population			Natural	Infant	Marriages	Divorces
Name of	(in	Population(by	area	density(per			increase	mortality		
the region	thousands)	%)	(km2)	km2)	Births**	Mortality	**	***	**	**

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		urban	rural								
	1995	1995	1995	1995	1995	1994	1994	1994	1994	1994	1994
Rep. of Armenia	3,759.8	67.5	32.5	29743*	126	13.7	6.6	7.1	14.7	4.6	0.9
Yerevan	1,248.7	98.9	1.1	210	3547	10.8	7.4	3.4	16.1	3.7	1.6
Aragatsotn	161.7	33	67.4	2755	59	17.7	6.1	11.6	13.7	5.5	0.4
Ararat	302.1	33.5	66.5	2104	144	14.7	6.0	8.7	16.4	4.4	0.5
Armavir	314.0	39.2	60.8	1241	253	15.7	5.7	10.0	13.6	5.1	0.5
Gegarkunik	255.8	39.4	60.6	4073	63	17.5	5.3	12.2	15.0	5.8	0.3
Lori	391.7	68.1	31.9	3791	103	12.7	6.2	6.5	11.9	4.2	0.7
Kotayk	327.1	60.1	39.9	2100	156	13.7	5.5	8.2	13.9	4.2	0.6
Shirak	357.6	68.8	31.2	2679	134	15.4	6.1	9.3	14.9	5.5	0.6
Syunik	161.4	70.7	29.3	4505	36	13.4	7.7	5.7	15.7	4.6	0.9
Vayots Dzor	69.7	42.0	58.0	2308	30	16.1	6.2	9.9	17.3	5.0	0.5
Tavush	170.0	40.6	59.4	2702	63	17.0	8.9	8.1	18.6	6.3	0.5

• including the area of lake Sevan 1,278 km

• ** per 1000 population

• *** per 1000 births

Source: UN DR 1996

Table 14: The prevalence of anaemia in pregnant Armenian women who attended clinics

Year	Anaemia(%)						
	I trimester	II trimester					
1980	1.1	8.4					
1985	1.3	9.5					
1990	2.6	13.8					
1991	3.4	20.0					
1992	4.5	24.6					
1993	6.5	44.6					

Source: Ministry of Health, Armenia

Table 15: Abortions per 1000 live births, 1975 - 1992

Year	Number of abortions
	per 1000 live births
1975	723
1980	464
1985	422

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1990	316
1991	349
1992	394

Source: Ministry of Health, Armenia

Table 16: The prevalence of Sexually Transmitted Diseases (STDs) in Armenia

Disease	Value per 100 000				
	1991	1992	1993		
Syphilis	6.9	7.1	8.7		
Women	4.9	6.3	7.2		
Men	8.9	8.1	10.3		
Acute gonorrhoea, total	21.6	12.0	24.9		
Women	12.8	9.0	17.6		
Men	30.8	15.2	32.7		
Chronic gonorrhoea, total	1.6	1.3	3.7		
Women	1.5	1.3	2.3		
Men	1.8	1.28	4.7		

Source: Women's Health Profile, Armenia

Table 17: Total mortality (per 100 000 population)

Mortality	1990	1991	1992	1993	1994
Total	620.4	650.9	700.7	736.9	658.0

Source: Department of Statistics, Armenia

Table 18: Crude Death Rate (per 1 000 population)

Death rate	1990	1991	1992	1993	1994
	6.2	6.5	7.0	7.4	6.5

Source: Department of Statistics, Armenia

Table 19: Mortality rates, by sex, from accidents at home, due to poisoning and other factors

Year	Deaths per 100 000				
	Total	Female			
1980	0.45	0.52	0.37		
1985	1.39	1.76	1.05		

1987	1.30	1.77	0.85
1988	0.95	1.18	0.74
1990	1.24	1.69	0.82
1991	1.42	1.92	0.09
1992	1.42	1.83	1.04
1993	1.36	1.99	0.78

Source: Women's Health Profile, Armenia

Table 20: Maternal mortality in Armenia, 1987-89 and 1990-92

Years	Live births	Maternal deaths	Maternal mortality rate
1987- 1989	227.401	91	40.0
1990-1992	228.625	88	38.5

Source: Ministry of Health, Armenia

Table 21: Maternal mortality ratio in Armenia (per 100 000 live births)

	1980	1989	1990	1991	1992	1993
Maternal mortality ratio	27	34.6	40.1	23.1*	14.2	27.1

Sources: Department of Statistics, Armenia Armenia: USAID Health Profile

* For 1991 MMR was 34.5 by the data from « Highlights on Women's health ».

Table 22: Cause-specific Maternal Mortality Rate (MMR) in Armenia, 1990-1992

Causes	MMR
Haemorrhage	10.1
Abortion*	7.0
Hypertensive disease	5.3
Infection	4.4
Ectopic pregnancy	1.3
Amniotic embolism	1.3
Ruptured uterus	0.4
Other direct causes	0.4
Total direct causes	34.1
Total deaths	38.5

* includes all causes of maternal deaths occurring until 28th week of pregnancy related to induced or spontaneous abortion

Source: Ministry of Health, Armenia

Area	1975	1980	1986
urban	30.1	25.5	21.6
rural	31.3	27.5	26.9

Table 23: Infant mortality rates (per 1000 live births) in Armenia (1975-1987)

Source: Highlights on Women's health: Armenia

Table 24: Infant mortality rates (per 1000 live births) in Armenia.

1970	1987	1990	1991	1992	1993	1994
25.6	22.6	18.5	17.9	18.5	17.1	18.0*

Sources: Armenia: USAID Health Profile Department of Statistics, Armenia

* 15.1 by the Department of Statistics

Table 25: Mortality rates, by sex, from malignant neoplasms (WHO classification, 2nd class, code 140-149).

Year	Deaths per 100 000		
	Total	Men	Women
1980	73.8	86.1	62.0
1985	81.6	92.3	71.0
1987	85.3	97.7	73.4
1988	87.4	102.7	72.6
1990	98.3	114.4	83.1
1991	97.8	116.95	79.7
1992	95.6	110.95	81.2
1993	93.8	112.7	76.1

Source: Women's Health Profile, Armenia

Table 26: Mortality rates from malignant neoplasms of the cervix

Year	Deaths per 100 000		
1980	2.30		
1985	2.58		
1987	1.59		
1988	2.75		
1990	2.59		

1991	3.12
1992	2.42
1993	2.70

Source: Health for all database, WHO Regional office for Europe.

Table 27: Mortality rates from malignant neoplasms of the cervix

Age	Deaths per 100 000	
	1990	1993
15-44 years	1.64	0.91
45-64 years	8.47	7.68
0-64 years	2.59	2.70

Source: Health for all database, WHO Regional office for Europe.

Table 28: Mortality rates from malignant neoplasms of female breast

Year	Deaths per 100 000	
1980	10.69	
1985	11.12	
1987	11.8	
1988	11.96	
1990	17.1	
1991	14.84	
1992	16.04	
1993	16.26	

Source: Women's Health Profile, Armenia

Table 29: Mortality rates from malignant neoplasms of female breast

Age	Deaths per 100 000		
	1990	1993	
1-14		0.19	
15-44 years	6.84	7.21	
45-64 years	51.9	46.3	
0-64 years	17.1	16.3	

Source: Women's Health Profile, Armenia

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REPRODUCTIVE HEALTH IN CAMEROON

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1. INTRODUCTION

1.1. History

Cameroon was initially colonised by the Germans. After the Second World War, they lost their mandate over Cameroon. The latter was then shared between the French and the English. The French ruled the East while the English ruled the West. Cameroon got her independence in 1960 and became the Federal Republic of Cameroon, made up of the former East and West Cameroon. She later became the Republic of Cameroon in 1972.

1.2. Geography

Cameroon is situated in the Golf of Guinea, extending from the Atlantic Ocean in the south to Lake Tchad in the north. She lies between the 2nd and 13th Latitudes and the 9th and 16th Longitudes. She has a surface area of 475 442 square kilometres.

She is bounded in the south by the Atlantic <u>Ocean (320 km of cost</u>), the Republics of Congo and Gabon, on the east by the Republic of Central Africa, on the north by the Republic of Tchad and on the west by the Federal Republic of Nigeria. She has both the <u>sahelian and equatorial</u> types of climate. Temperatures range between 15 and 40 degrees centigrade. The rainfall averages between 900 and 4 000mm.

One third of the country is covert by forest (the south region), savanah in the North

1.3. Economy

Cameroon is essentially an agricultural country producing mainly coffee, banana, cocoa, oil palms, wood, rubber and cotton. The currency is francs CFA. The gross national product per capita is 610 US dollars *

1.4. Government

Cameroon has the multiparty system of government with a Presidential politic system. The other power are Legislative with National Assembly and Judiciary.

The president appoints the Prime Minister and Head of Government who in consultation with the latter appoints the ministers. There about 30 ministries including the ministry of public health.

1.5. Culture

Cameroon is a bilingual country. The two officials languages are both French and English.

There are more than two hundred ethnic groups each with a dialect.

The main Religious bodies are Catholic, Protestant and Muslim. Those who can read and write are 75.1% and 52.1% for men and women respectively **

1.6. Education

Cameroon has 2 millions students in Primary and Secondary Schools; 35 000 in Universities and Higher Schools. 6 Universities exists in the country .

1.7. Demography

The population of Cameroon is projected to 14 323 000 of which 49% and 51% are men and women respectively ***. The population of women <u>of reproductive age (WRA)</u> is 23% or 4 000 000 in absolute terms. The annual population growth rate is 2.83%***. The mean fertility rate is 6.1 children per WRA ***. The crude birth rate is 42.5 per 1000 population while the crude mortality rate is 17.5 per 1000 population***.

1.8. Health ressources

- Ministry of Public Health Annual Budget 1998/1999 : 38 099 000 000 FCFA (US \$ 6,349,835)

SOURCES : Loi des Finances de la Republique du Cameroun adoptée par l'Assemblée Nationale - Session de Juin 1998

1.9. Organisation of the Health System in Cameroon

Reproductive Health is a component of public health which is managed by the Ministry of Public Health. There are health units which are divided into categories depending on their level of competence. These are in descending order:

i) category one: General Hospitals of which there are three including one University Teaching Hospital;

- ii) category two: Central hospitals of which there are three including one Parapublic;
- iii) category three; provincial Hospitals of which there are 10
- iv) category four: District Hospitals of which there are 136;
- v) category five: Sub-Divisional medical centres and
- vi) category six: Integrated Health Centres.

In addition to these are mission hospitals and private individual clinics and hospitals. The Ministry of Public Health is divided into directorates and divisions according to specialty as follows:

- I) Directorate of human resources
- ii) Directorate of finance and infrastructure

- iii) Directorate of pharmacy and drugs
- iv) Directorate of community health
- v) Directorate of hospital medicine
- vi) Division of cooperation
- vii) Division of studies, planning and communication.
- Viii) Division of maternal mental health

2. The evolution of Reproductive Health in Cameroon

Reproductive Health has evolved almost parallely with the health system in Cameroon. The primary health care (PHC) approach was adopted in 1982. It was redefined in 1987 after the Alma-Ata <u>conference</u> with the aim of achieving the main objective which is health for all by the year 2000. The District Health approach was also initiated. A Health District (HD) is a unit in which the community participates actively in the management of its health. It is semi-sufficient in the sense that it can carry out essential health services and only refer difficult cases to the provincial or central level. There are 360 HD in Cameroon.

*World Bank 1998, ** UNESCO 1995, *** United Nations 1998 (WHO Stastitics 1998)

2.1. Arguments for Reproductive Health in Cameroon

Reproductive Health is a concept which has been existing since. It was only reoriented following observations in the early 1970s. It was observed that :

i) maternal mortality was on the rise compared to developed countries;

ii) large family size despite limited resources;

iii) families delivered many children because they feared that some will die-thus they delivered many so that some will die and they will still have some;

iv) perinatal and infant mortality rates were on the increase;

v) children are highly valued in Cameroonian societies;

vi) women were dying from pregnancy-related causes that could be prevented (haemorrhage, sepsis, preeclampsia/eclampsia etc);

vii) a sizeable proportion of the society could not have children when they wanted (involuntary infertility);

viii) pregnancy and delivery were considered by their partners as the woman's issue only - men only decided on the number of children;

ix) there were few qualified personnel to take care of women during pregnancy and labour;

x) many births took place at home or were conducted by untrained traditional birth attendants (TBA);

xi) many young girls 14-19 years were bearing children.

These and many other issues prompted the few Gynaecologists at the time like Professor Nasah to reflect on RH which was then only concern with the mother and child. Professor Nasah even wrote a book titled " Care of the Mother in the Tropics".

2.2. Why RH became a necessity

RH services were aimed at the following:

i) reduce maternal mortality;

ii) reduce infant mortality rate;

iii) introduce the notion of high risk pregnancy and bring men to participate in taking decisions about pregnancy;

iv) introduce the notion of family planning;

v) train enough medical personnel to take care of women during pregnancy and delivery;

vi) train TBA to be able to recognise high risk pregnancies and or difficult labours and transfer the woman on time

2.3. Structure of RH

As stated above, RH is a concept and does not necessarily need separate structures (buildings, personnel, services etc) to put it in place. All that is needed is that health authorities become aware of the need and introduce it to all services and personnel concerned. The required personnel is trained or recycled accordingly to understand the concept and to perform the necessary services in an integrated manner.

Vertical approaches to health problems have long been shown to be less cost effective and less equitable than an integrated approach. Also, the different elements of RH are so closely linked and interrelated that one structure can handle many of them at the same time. Therefore, elements like STD/AIDS diagnoses, treatment and prevention, family planning, complications of illegal abortions, infertility, neonatal care (vaccinations, screening for malnutrition etc), pregnancy and post partum care ought to be treated together. This will not only save time and reduce the need for infrastructure and personnel but it will also be time saving for the clients and so increase compliance. In this system all that is needed is a good reception service to receive and orientate clients.

The referral system is from the health centres to the to the DH. From the DH to the Provincial hospitals (PH). From the PH to the Central Hospitals or the General Hospitals. The flow chart shows the patient movement.

INTEGRATED AND MEDICO-SOCIAL HEALTH CENTRES

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SUB-DIVISIONAL MEDICAL CENTRES



RH falls under the directorate of community medicine and the division of mother and mental health in the ministry of public health. RH services are offered at all the levels. In addition to the above structures are parallel or complementary services like:

i) medico-social centres which primarily take care of STD cases including AIDS (diagnosis, treatment and prevention);

ii) mother and child care centres (Protection Maternelle et Infantile (PMI)) which offer prenatal care, vaccination of infants and pregnant women, and family planning and

iii) high risk clinics which take of pregnant women with an increased risk for both the mother and child (grand multipares, elderly primis, adolescents, scarred uterus etc).

2.4. TRENDS

RH has moved from a stage where it used to be considered as concerning only the mother and child to a level where it involves both women and men. It has also moved from curative activities alone to include both curative and preventive activities. The scope of Rh has also widened. This has been partly due to the increasing demands for better health for women and also for the increase in life expectancy . The latter has increased from 52.9 years (1992) to 54.5 years (1997) for men and 57.4 years to 59 years for women ****. However, alternate sources estimate life expectancy within the period 1995-2000 at 45.5 and 48.4 years for men and women respectively***. A general consensus is that life expectancy is increasing and so will new RH problems like menopause come up and need to be taken care of .

SOURCES: **** MPH Cameroon annual report to WHO 1998, *** United Nations in WHO member country statistics 1998

Definition of RH periods and related problems

i) prepubertal period :

The period between 10 and 13 years. The problems here are those of transition from childhood to adolescence and eventually adulthood. these problems are often increased when a pregnancy occurs.

ii) adolescence:

The period between 10 and 19 years. The problems in this age group are those of transition from childhood to adulthood. They are characterised by ego development, experimentations and

explorations of the unknown.

iii) menarche:

This is the period of onset of menses and therefore the beginning of reproductive life proper. It is characterised by physiological and anatomic changes some of which are often embarrassing to the young girl who must of the times is not prepared for these changes.

iv) Reproductive age:

This is considered as the period between 15 and 49 years. It is the age when sexual activity and child bearing are maximised. It goes without saying that this is the age where most of the RH activities are concentrated. In our environment it is marked by ignorance, the desire for many children, poverty etc.

v) perimenopause:

The period around menopause (45- 50 years). It is characterised by irregular cycles and the occurrence of cancer especially what of the breast.

vi) postmenopause:

The period after menopause. This period that is characterised by the aging of the ovary is not yet posing problems in our environment. This explains why hormone replacement therapy is little known in our country. The changes are often very passive and so go unnoticed even by the woman.

2.5 The components of RH in Cameroon

RH was redefined to mean a state of wellbeing of the reproductive organs concerning their functions and functioning and not only the absence of disease. Taken in this sense the components are:

i) Adolescent care:

Adolescent reproductive health as an entity is not yet developed in Cameroon. It is only of recent (1996) that the ministry of Public Health created a sub-division for adolescent health. This is associated with maternal health. However, before this time and even now adolescents received health services in different units. For example pregnant adolescents were taken care of in high risk clinics, adolescents with STDs consulted at medico social centre etc.

Medical services exist in schools (dispensaries) but only in theory or are there only to establish that a student is ill and refer he or she to the hospital. Very often it is a student volunteer who shows interest in medicine who is sent to do a short training in a dispensary during holidays who manages the school dispensaries. These are often not equipped or contain only first aid drugs for dressing wounds before referring the student to the hospital. There are really no activities like health education or counselling in schools.

ii) Mother child care clinics (PMI):

These services have been existing for long. They are being renamed "maternal and infant health and family planning services" (in french "Santé Maternelle et infantile/Services en Planification Familiale (SMI / PF)". These centres offer services to pregnant women like prenatal caring, vaccinations of the women and also new born and infant care. This latter includes vaccinations, weighing and diagnosis and treatment of minor illnesses. They also offer family planning services. They also take care of high risk pregnancies in areas where high risk clinics are not existing and refer the patients to the doctor or hospital.

iii) High risk clinics:

These only exist in big cities like Yaounde. Women with increased risk for the mother or the foetus are followed up in these clinic more closely than those with apparently no risk.

iv) Family Planning clinics:

These clinics are located in the hospitals or PMIs. These clinics are taken care of by Nurses who have undergone training in family planning. They offer all the services with the exception of sterilisation in which case they refer the patient to a hospital.

iv) STD and dermatological clinics:

These clinics are called medico- social centres. They are located only in big cities. They were initially called venereal disease centres (centre vénérien). The name discouraged people from frequenting them. It is important to note that HIV screening is not done in these centres. They also carry out educational and preventive activities. This activity is also carried out at the PMIs. It is also important to note that men have not yet developed the attitude of using these centres.

The following services are also being offered in hospitals during routine consultations. They have no special clinics.

i) premarital counselling;

ii) infertility diagnosis and treatment for the couple;

iii) menopause complications;

iv) genital cancer screening, diagnosis and treatment;

v) care of men with sperm abnormalities (andrology) and

vi) counselling couples or individuals on the transmission of chronic conditions like sickle cell and or Rh negative problems.

It is important to note that psycho-social and sexology as well as genetic services are lacking in our settings.

3. Health Strategy for Cameroon

3.1. Introduction

The health policy for any government is aimed at having a healthy public. A healthy public policy is a concern for health and equity in all areas of policy. The goal of healthy public policy is to promote health. This is in line with the familiar WHO concept that health is determined by reference to "physical, mental and social wellbeing and not merely the absence of disease or infirmity" emphasises the significance of the social welfare of populations and not merely the medicalisation of disease. Even though medical science occupies a central position in health, the latter is the outcome of a combination of many factors: biological, genetic, environmental and socio-economic.

The elements that condition a population's health go beyond physiological factors to include gross national product, wealth distribution and access to income-earning capacity and opportunities,

availability of and access educational resources, the urban and rural living environment and physical infrastructure, and, for instance, political structures through which individuals and groups can influence distribution of resources that affect health status (Women's Health and Human Rights by R.J. Cook WHO)

3.2. Cameroon Government Policy

In 1982, Cameroon subscribed to the strategy of Primary Health Care (PHC). In 1985, she undertook a reformation process aimed at putting into place the PHC strategy which she called a Reorientation of PHC@. This was <u>reiterated in 1987 following</u> the <u>Alma-Ata conference. The main</u> aim was to achieve health for all by the year 2000. This reorientation aimed at reinforcing the District Health System (DHS) and the effective implication of the community in the management of their health in what could called a contract between the state and the community. Between 1989 and 1991, more reflections were made on the practical implementation of this system. Since 1992 some significant changes have occurred. These included among others the realisation of the DHS with eminent advantages like

i) a better rationalisation of the health coverage;

ii) an end was put to the further creation of health centres;

iii) existing health centres became integrated and more responsible, serving as intermediate between the population and the community;

iv) the notion of contract between the state and community in the management of health issues became clearer and

v) health programmes were integrated at the peripheral level.

An intersectorial collaboration approach concerning decision making at higher levels was also adopted. In 1976, the President signed a decree ordering the creation of a High Council of Health, Hygiene and Social Affaires (decree no 76/450 of 08/10/76). This interministerial collaboration unfortunately never worked. At the level of the ministry of Public Health, a coordination and follow up committee was created in 1992 in order to avoid incoordination of ministerial decisions. As a follow up of this a decree was passed in 1996 for the creation of the National Council for the civil protection (decree no 96/054 of 12/03/96). Still in the search for improvement of cooperation, another law had been passed

(law no 96/03 of 04/01/96) governing state action and other parties in the domain of health.

All these laws and actions actually improved the health status of Cameroonians. But unfortunately the economic crises became evident. The government under pressure from the World Bank instituted a structural readjustment programme. Among other measures was the slicing of workers salaries by more than 70%. This reflected on standard of living, health status and health projects with serious consequences as will be seen under the RH situation.

3.3. National Resources

The following is the national health resources situation:

Number of physicians	1007*(1996)
Number of midwives	69* (1996)

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Number of nurses	4998* (1996)
Number of pharmacists	59* (1989)
Number of dentists	55* (1996)
Number of other health care providers (including community health workers)	6968*(1996)
Total national health expenditure as % of GNP	4.3* (1989-90) / 1.4** (1990-95)
% of national health expenditure devoted to local health care	8.0* (1980-82)
Total government health expenditure as a % of GNP	0.6* (1995-96) / 1.0** (1990-95)
Total government health expenditure as per capita (PPP\$)	3.3*(1995-96) / 24** (1994)
% of recurrent government health expenditure as a % of total government health expenditure	81.6* (1995-96)
% of recurrent government health expenditure going to salaries	54.8 *(1995-96)

3.4. International assistance

Total international aid received as a % of public expenditure on health for the year 1996 was 66% ***.

The amount of external money for the budgetary session 1995/96 was 12797 million Fr CFA (600 Fr CFA=1US\$) for a total health budget of 18167 million Fr CFA giving the 66% above***

It is important to note that foreign aid to health has been increasing as shown below

Year	1990/91	1991/92	1992/93	1993/94	1994/95	1995/96
Amount (\$US million)	2185	5226	8157	7979	3828	12797

* MPH, ** World Bank, *** volet santé avril1996.

4. Reproductive Health situation

4.1. Genesis of RH

RH is a concept that has been existing parallely with the other medical disciplines. It is only undergoing modifications with new impetus being added to it as more knowledge is acquired on the subject through research. important changes at the level of organisation in Cameroon include;

i). Since 1994, PMI/FP have been progressively integrated into the health system at all levels with the support of international funding agents;

ii) The former Directorate of family and mental health was replaced by the Sub-Directorate of family health, placed under the Directorate of Community medicine in 1995. This was in order to integrate the activities of MCH/FP at both the national and operational levels among the PHC activities.

these changes are reflected in the activities of the components of RH.

4.2. Mother and Child health Care/ Family Planning (MCH/FP)

This is the component that takes care of pregnant women, infants and child-spacing or planned and responsible parenthood. The objectives of this component are:

i) reduce maternal mortality rate by proper surveillance of pregnancy to detect risk cases and refer early enough for proper management;

ii) educate women on the notion of high risk pregnancy, the importance of planned and responsible parenthood and thus promote family planning;

iii) offer routine cost-effective care to newborn and infants in order reduce malnutrition and infant deaths.

the following examples show how these objectives have been achieved or not.

i) the proportion of pregnant women whose pregnancy is supervised by a qualified personnel (nurse, midwife or medical doctor/gynaecologist increased from 605 in 1994 to 73% in 1997 (WHO 1998);

ii) similarly the proportion of women whose labour is attended to by qualified personnel increased from 54% in 1994 to 585 in 1996 (WHO 1998);

iii) the proportion of infants consulted by qualified personnel in 1994 was 50% (Ministry of public Health (MPH) (recent figures are not available);

iv) the level of contraceptive use increased from 3% in 1990 (Akam E. 1990) to 10.5% and 24.9 % in rural and urban areas respectively in 1991 (Leke 1993) the overall national level reported in DHS 1991 is 5%;

v) maternal mortality decreased from 220 per 100000 in to 130 per 100000 in the Central maternity (Leke), however, national maternal mortality rates have increased from 450 per 100 000 in 1995 to 547 per 100 000 in 1997 (UNICEF reported by WHO 1998);

vi) in 1993, the infant mortality rate was 84 per 1000 (United Nations 1993), in 1997 it was estimated at 58 per 1000 (UN), the probability of dying before the first birthday is 126 per 1000 (MPH 1995);

vii) one woman out four is anaemic (WHO 1991).

4.3. High Risk Clinics /Approach

This approach consists of identifying or targeting women with increased risk during pregnancy and following them more closely. This approach was introduced in the University Teaching Hospital and the Central Maternity Yaounde in the mid 1970s. Later evaluation showed that maternal mortality dropped from 220 to 130 per 100 000 live births in these centres. It has consequently been introduced throughout the country. Some high risk cases include:

i) grand multiparity (>5 deliveries): this constituted 18.5% of the total obstetric population in 1982, and accounted for 48.5% of maternal mortality (Leke 1984) It is attained in Cameroon at the age of 27 years.

ii) elderly primi (>30 years), older gravidas (.35 years) and teenagers (10-19 years) constitutes high risk groups.

iii) Natural child spacing is well practised in Cameroon (21 and 21 months breast-feeding respectively

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REPRODUCTIVE HEALTH IN CAMEROON
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for urban and rural areas but without any attempt at birth limitation (Leke).

4.4 Adolescent RH

This is unfortunately not yet a reality in Cameroon. It is only of recent that it is drawing the attention of the public. This is probably because of the high rate of adolescent sexuality and child bearing which posses an economic burden on the parents and the society. Whereas adolescents constitute a sizeable proportion of the population. A few examples of the consequences of their sexual activity will illustrate the problem: in 1984 38.6 % of the obstetric population in the central maternity was adolescents (Leke 1993); sixty-five percent are married by the age of 16 years (DHS 1991); thirty-two percent of the illegal abortion complications received in the central maternity are adolescents (maternity statistics 1992), the average age of menarche and semenarche is 13 1/2 and 15 years respectively; about 70% are sexually active by 16 years with 4 % delivering before 16 years, only 4% of the pregnant adolescents (married or not desired to be pregnant; knowledge on contraception is from the media in 53%, school mates - 21%, peers-16% and only 9% from parents.

However, adolescent RH is now on the national agenda. Ways are being explored to improve on the utilisation of existing health services by adolescents. Age that was once a barrier to contraceptive use (Paul Nkwi 1995) thus excluding adolescents from using pills is no longer.

4.5. Newborn / Infant Care

Cameroon has benefited only little from the technology of newborn care. Equipped newborn centres are only in the big cities like Yaounde and Douala. Children born with birthweights <2000g are very likely to die while those with birthweights ,2500 g have just a slightly increased chance of surviving. The mean birthweight is 3200g. About one out of four children of 0-5 years is anaemic (DHS 1991); infant mortality rate seems to have increased from 84%0 in 1992 to 93%0 in 1995 (MPH 1995); The main causes of infant mortality are: malaria-43%, diarrhoeal diseases-17.6%, measle-12.3% (DHS 1991); the proportion of infants correctly immunised against diphtheria, tetanus and whooping cough in 1996 was 46% (WHO 1998); the proportion of infants reaching their first birth day that have been correctly immunised against measles and tuberculosis is 46% and 54% respectively (WHO 1998). Breast feeding is almost 100% and more than 90% in rural and urban areas respectively. Women are highly motivated because breast feeding serves as a natural means of spacing birth. Also, the government encourages iit by giving a maternity leave of three months. The few women who work in offices practice mixed feeding. Another thing that encourages breast feeding is the high cost of artificial milk.

4.6. Child Health and Development

This is directly linked to the intrapartum and peripartum periods. Care during these critical periods is at the maternities. Although a good number of women especially in the rural areas still deliver at home or with traditional birth attendants (TBA). Further development is determined by so many factors. Even though Cameroon is food sufficient there are still some cases of malnutrition due to lack of balanced diets and parasites.

4.7. Post-Reproductive period (menopause)

The mean age for menopause is 49 ± 1 years (Shasha 1990). The majority of women have no clinically manifesting symptoms and so the period often passes unnoticed. Though occasionally we see women with pathological fractures resulting from osteoporosis. Traditionally, menopaused women can do certain things, go to certain places or even talk to notables which they could not do during their active periods. In some cultures the woman during her menses neither cooks nor shares the room with her husband. Because menopause does not really constitute a problem studies in this domain are scarce.

4.8. Genital cancer screening programme

The two most frequent female cancers are breast and cervical constituting more than 70 % diagnosed female genital cancers. These cancers are often diagnosed in the advanced stage and so the population believes that cancer is not curable, that when one has it, it is a curse and the one is bound to die. Data on these cancers at the national level is lacking. Other less frequent female genital cancers are in order of decreasing frequency, ovarian, endometrial and vulva. Because of the attitudes and beliefs of the population about cancer, a national cancer screening programme is organised periodically. Unfortunately this takes place only in Yaounde and Douala. The rural population that is most involved is not included.

5. Family planning / RH Projects

5.1. Evolution of FP in Cameroon

Contraceptive methods are etymologically the techniques used to prevent conception or pregnancy. These are also known as child spacing methods.

In the early days of independence (1960-1970) tribes were very powerful as far as decision making at the national level was concern. Each tribe therefore wanted to increase its population as fast as possible. Even though the problem of infertility had not been studied in any detail until Nasah in 1973 (Nasah and coll 1973), the concern of tribes was the fear of their eventual extinction. The tendency was thus to procreate as much as possible and so family planning was not known. however, families practised child spacing by prolonging breast feeding (21 and 20 months in rural and urban areas respectively (Leke 1993), it was not to limit the number of children.

Before 1980 Cameroon was pronatalistic and there was a law (Law no 29/69 of 20.5.69) prohibiting the sale of contraceptives or any form of anticonceptional publicity. Also certain legislations like the laws on family allowances, birth allowances, supplementary for underaged children and reduction of taxes as a function of the number of children were in favour of increased number of children.

But things did not remain the same . By 1976, the authorities started reflecting on the adverse effects of a high population increase on the economy and social life. In 1980 during one of the President's policy speech he officially made mention of the consequences of a rapid and uncontrolled population increase on employment, urbanisation , health etc. As follow up, in 1981 the government chose individual couple awareness to limit births under what was known as responsible parenthood in the 5th five year plan(1981-1986).

Consequently, a national commission was set up and the result was that contraceptives could be

prescribed. In Yaounde there was a child spacing clinic that was functioning officially since 1977 in the University Teaching Maternity Unit of the Central Hospital and the Teaching hospital (CHU). This was at the initiative of Prof. Nasah. Family planning thus gradually spread throughout the country.

In 1992, the MPH/Directorate of Family Planning and Mental Health (FPMH) with the assistance of the Programme for International Training in Health (INTRAH) listed potential barriers to FP and developed scientifically justifiable medical policies towards FP (Paul NKWI 1995). Still in an effort to improve both the quality and access to FP services the MPH/DFPMH and INTRAH created a set of national service delivery guidelines which were distributed to all service delivery units in the country. In 1993 the policy guidelines were standardised with the collaboration of SEATS Project of John Snow Inc. (JSI) and since then seminars and training sessions are being organised for Fp service deliverers.

5.2. Main actors:

The following bilaterals, multilaterals and NGO's international agencies collaborate with the government, national organisations, social groups and individuals in the field of research, interventions and evaluations of projects related to FP and other RH domains:

- 1. World Health Organisation (WHO)
- 2. United Nations Development programme (UNDP)
- 3. World Bank
- 4. United Nations International Children's Educational Fund (UNICEF
- 5. United States of America, Agency for International Development (USAID)
- 6. Johns Hopkins Program for International Education in Reproductive Health (JHPIEGO)
- 7. German Technical Assistance (GTZ)
- 8. International Training in Health (INTRAH)
- 9. Family Health International (FHI)
- 10. United Nations Population Fund (UNFPA)
- 11. The Program for Appropriate technology in Health (PATH)
- 12. International Children's Center (ICC)

and many other's.

6. Associations

6.1 The <u>"Association Camerounaise des Femmes Médecin"</u> (ACAFEM)

This was formed in the early 1990s. The objectives are to bring together female physicians, promote research activities among members and evaluate health activities. One research that they carried on the "Traditional Practices that affect RH of women in Cameroon showed that immediately after delivery women used hot water to massage their abdomen and episiotomy/perineal wounds in order to promote uterine involution and wound healing respectively, pregnant women were not allowed to eat certain foods leading to malnutrition and anaemia , women used douching regularly claiming that they were being more hygienic thus predisposing them to frequent vaginal infections.

6.2. The Society of Gynaecologists and Obstetricians of Cameroon (SOCOC)

This society was created in the early 1990s. It hosted the Society of African Gynaecologists and Obstetricians (SAGO) in 1994. It meets every three months to discuss RH issues and research projects and or results.

6.3. The Cameroon National Medical Conference

This is open to all doctors. It holds yearly at March. Each year it decides on a term. One of such terms was "How to decrease health cost" and the topics discussed included RH components like infertility management.

6.4. The National Committee for the Fight against Cancer***.

The main objective is to reduce the incidence and prevalence of clinical gynaecological cancers in Cameroon by the year 2000, by organising regular information, education and sensitisation campaign.

The incidence of clinical cervical cancers is estimated at 40/100 000 women aged 20 and above with a prevalence of 2750 cases.

Only 10 000 Pap's smear are carried out every year, (1 for 200 women) and concern particularly urban women. The majority of women (70%) lives in rural area and they don't have financial, geographical and educational accessibility to screening methods. It is estimated that 90% of patients with cervical cancer are from rural areas.

The Committee carry out mass campaigns twice yearly (April and December) in Douala and Yaounde with an attendance of 1000 women at each campaign. The main target of the Committee now are these majority of rural women.

Gynaecological cancer	%
Breast cancer	21,5
cervical cancer	21,5
Cancer of the Ovary	6
Endometrial cancer	less frequent
Lymphomas (Burkitt lymphoma)	frequent in young women (teenage)

The common gynaecological cancer in Cameroon are:

file:///D//Webs_On_David/gfmer/Endo/Reprod_health/Cameroon/Net_Reproduction_Cameroun.htm (17 sur 23) [19.12.2002 14:26:12]

Cervical cancer is the fourth more common cancer in general in Cameroon(11%). By the end of year 1997, the prevalence was 2750 cases. It is the first gynaecological cancer, with cancer of the breast with 21,5%. The main types are carcinomas (99,9% with a predominance of squamous carcinomas) Malignant lymphomas (Burkitt's lymphomas) are frequent in young women (teenage).

The patient's age distribution is the following* (1997):

AGE (years)	%
0 - 19	0
20 - 29	4
30 - 39	10
40 - 49	32
50 - 59	30
60 - 69	20
70 - 79	4
>80	0

Majority of cervical cancer patients are seen at advanced stages :

Clinical aspects	% of cases
Ulcerated cervix	50
Ulcerated and fungating	25
Fungated cervix	25

The main clinical stages found are :

Stages	%
Stages I	25
Stages II - III	70
Stages IV	5

Surgery, radiotherapy chemotherapy are available but very costly. Less than 10% of few who try the treatment have achieve it. The prognosis is generally bad, less than 10% five years survival for stage I cervical cancer.

***Sources :

1) MBAKOP A. & coll. : Cancers au Cameroun. Guide Pratique. Ed. Comité National de Lutte Contre le Cancer/Comité National d'Epidémiologie - SOPECAM 1997

2) MBAKOP A. : Present situation of Cervical Cancers in Cameroon. 1997

7. Research Activities/ National Organisations

The following organisations carry out research in various domains of RH, either national projects or in association with international organisations:

i) Ministry of Public Health (MPH)

ii) Ministry of Higher Education (Higher Teacher's Training College (ENS)

- iii) Ministry of Scientific Research
- iv) University of Yaounde -the Faculty of Medicine and Biomedical Sciences (FMBS)
- v) World Health Organisation Collaborating Centre -Human Reproduction Programme (HRP)
- vi) Network for research in RH (CRESAR)

Just to mention that the WHO collaborating Centre was opened 11 years ago. It carries research projects in human reproduction activities. During 1997 the centre had 23 ongoing research projects: 8 in the field of reproductive biology, 8 on maternal and infant health, 1 on abortion, 4 on contraception,1 on infertility and 1 on STDs. Five of these projects were funded by HRP, 12 were funded by national sources and the rest from international sources.

8.Some set backs (Not yet available)

- 8.1.Government Policy
- 8.2. Economy Crisis
- 8.3. Political situation
- 8.4. Communication difficulties
- 8.5. High illiteracy rate
- 8.6. Lack of publishing facilities for research results
- 8.7. Increasing population
- 8.8. Gender Issue

9. Perspectives for future projects implementation

9.1. Objectives and indicators of RH till the year 2003 (Development plans are made for every five years).

Goals:

i) Offer quantity and qualitative RH services to the population.

- <u>Quantitatively</u>, the number of pregnant women attended to by qualified personnel should increase from the current 80 % to 90% or more; the number of women attended to in labour by qualified personnel should increase from the current 64% to 70% or more; the number of women of child bearing age using modern method of contraceptives should increase from <u>the current 16% to about 20% or more;</u> ?

- <u>qualitatively</u>, quality services should be able to attract more users and thus and thus improve on the quality of life. We therefore expect more women to use the MCH services with a <u>reduction in the current maternal mortality rate to less than 420 per 100 000</u>; similarly quality services for adolescents would enable them to better utilise FP services so that the number of unwanted pregnancies and unsafe abortions which is currently responsible <u>for some 40% of the causes of maternal mortality to</u>

less; etc

In general, improving Rh means ensuring quality information to all, detecting high risk cases and referring early enough for specialised management, providing good roads so that referred cases can arrive the centres etc, offering quality training and recycling of personnel and providing good working conditions.

ii) improve the health status of women during the reproductive years so that they can enjoy quality RH. This means that more women should be allowed to take decisions on matters directly affecting their lives like the number and when to bear children, prevent STDs so that the 70% of the 30% of women with infertility with tubal pathology may decrease to 30% or less and the infertility rate decreased to 25% or less.

iii) improve prenatal care so that the proportion of children born with normal parameters as accepted by international standards may pass from the current 90% to 95% or more; offer immunisation to children so that the rate of correctly immunised children by one year passes from the current 50% to 70% or more ; the overall goal would be to reduce the current <u>infant mortality rate of 84.0 per 1000 to less</u>.

iv) improve the RH of adolescents so that they may enjoy RH in the real sense as defined by WHO.

v) The overall goal of RH will be to develop strategies which will enable individuals to enjoy RH right by promoting gender equality, contraception, abortion services (caring for those who have unsafe abortions without discrimination or judging) etc.

9.2. Objectives (Indicators of RH)

The following are the set indicators to be monitored (the list is not exhaustive)

i) maternal mortality (fall below the current 420 per 100 000)

ii) infant mortality (fall below the current 84.0 per 1000)

iii) women of reproductive age using modern contraceptive (increase above the current 16%)

iv) increase the rate of detecting complications of pregnancy, referral systems etc so as to reduce the deaths resulting from them which currently account for about 40% of maternal deaths.

v) increase the number of correctly immunised women and infants so as to reduce the deaths resulting from these illnesses.

vi) reduce the prevalence of anaemia in pregnancy from the current 26.3 % to 20% or less

vii) Increase the number of pregnancies and deliveries attended to by trained personnel.

9.3. Population and Development

The above objectives can only be achieved if future project planning and implementation takes into account the eventual socio-demographic changes (population growth, urbanisation, life expectancy, crude birth and death rates, schools, job availability and basic social amenities like water, electricity, health units etc.

The population is expected to increase in absolute terms by 400 000 each year taking into account the annual population growth rate of 2.8 and a current population of 14 000 000. Life expectancy is

expected to increase from the current 54.5 years and 59 years to 55 and 65 for men and women respectively; infant mortality is expected to decrease from the 126 per 1000 to about 100 or less.

All these demographic changes will affect urbanisation with its inherent problems. Therefore this needs to be taken into consideration when drawing up development plans.

9.4. Health Policy and Strategy

The government has undertaken by since 1976 the initiative by making a law governing the creation and organisation of a superior council for Health, Hygien and Social Affairs (Decree no 76/450 of 8/10/76) which had never been implemented. It is hoped that will become active. At the level of the MPH, the coordination committee that was created in 1992 to follow up projects in order to promot intersectorial cooperation and which held only for two years and stopped will resum. At peripheral and intermediate levels, intersectorial collaboration between administrative authorities, health personnel and the community will increase so that RH can advance.

All these collaborations needs that the government should increase the fraction of the state budget allocated to health to at least 10% as recommended by the UN.

9.5. Approach

Cameroon has a low prevalence of modern contraceptive use (16%), a low rate of utilisation and provision of antenatal services, with a high maternal mortality ; the population is increasing disproportionately to the resources and social amenities, the concept of RH is still new even to health personnel, government policy towards international organisations <u>interested in RH are not flexible etc</u>. A change in this approach is needed to advance RH.

9.5.1. Holistic Approach

RH is a concept . The definition and components require that the concept be integrated at all levels of the health care system. Treating components in isolation is not cost effective and has been shown to decrease compliance. Thus it is hoped that focus will not only be on MCH/FP as has been in the past, but will be widened to include all the components of RH. Also, Rh does not specialists at all levels. The scope of RH services and providers can widened to include all existing health structures and personnel. All that is required is creating awareness, motivation and cooperation.

9.5.2. Client and Patient Oriented

RH as defined does not require that one be physically ill before seeking it. Rh clients are not necessarily patients. If they are considered as clients, which they should, then research should be carried out regularly to discover what they need or lack. Services should then be orientated towards the unmet needs or services. Also health personnel need to know that they are selling their services to potential users and not the current practice where health personnel feel that RH is a disease state and who ever is ill has no choice.

9.5.3. In like manner,

RH should not be medicalised. Barriers to acquiring or offering RH should not exist. people with competence in RH should be allowed to offer the services. The current practice where only doctors insert Norplant and or carry out bilateral tubal ligation should be discouraged as it does not adapt in

our context with few doctors. Nurses can do it and even better because they have the time. Also, it has been shown that a pelvic examination is not necessary for prescribing oral contraceptives. This means that women can procure them from the pharmacy without a medical prescription.

9.5.4. The success of RH lies in education, information and counselling.

To this effect the government passed a law (Decree no 95/040 of 07/03/95 replacing the former department of Health Education in the MPH with the department of Education for Health, Government Communication and Public Relations. Accordingly, two trained journalists were posted to the MPH. They have as a mission, the transformation of mass educational messages for easy comprehension. This idea is good but apparently the more than 60% of rural residents, the majority of whom can neither read nor write, nor possess Radios / TV sets. In some places Cameroon Radio and TV does not even reach there. How do they get the health messages? The government or international agencies should explore ways of reaching this important fraction of the population which is also those who need RH most. May be posters with health messages placed at strategic places like palaces or church premises could serve more.

10. Necessary inputs for the future

10.1. personnel training, recycling and management

<u>Cameroon has relatively qualify human resources to manage RH services (see table on health</u> resources). The problem is that of role defining and assigning functions to the right (qualified) people. The problem of personnel management is crucial for RH advancement. However, this does not mean that she does not need to train and or recycle personnel. RH <u>technology is changing fast and</u> Cameroon needs to train or recycle her personnel in order to meet of with modern RH technology.

10.2. Infrastructure

The present infrastructure belonging to the MPH at levels is enough for offering RH services. Most of the structures are under utilised. All that is required is reorganisation of the structures to accommodate the different components of RH.

10.3. Research

Research is the key to development . So it is too for RH achievement. The government has taken measures to promote research as :

i) the creation of the department of studies, planning and health information in the MPH in order to promote operational research;

ii) the training of personnel at both the district and provincial levels in research in order to promote research at these levels.

iii) The system where each graduating student from the FMBS presents a research thesis is aimed at encouraging research at an early stage.

All these measure are good but they need to be backed by necessary funds and proper utilisation of

research results.

10.4.Government Policy (Not yet available)

11.Annex (Health Indicators/Resources)

- 1. Trends in socio-economic development
- 2. Health and Environment + Health resources
- 3. Health services
- 4. Trends in health status
- 5. Demographic distribution of population (not yet available)

Reproductive Health in Georgia

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Content

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1. Information about the country

Georgia is situated between Eastern Europe, Asia, the Black Sea and the Caspian Sea. The territory of the Republic of Georgia is spread from West to East-from the Black Sea to the Mingachauri water storage and covers 69.492 sq. km. Tbilisi is the capital of Georgia. The population is close to 5.5 million and the official language is Georgian. From the point of nationality the majority of the population are Georgians and they form about one third of the entire population. Some other nationalities reside in Georgia as well: Russians, Armenians, Azerbaijanians, Greeks and Jewish. Looking at the demographic characteristics, Georgia is similar to countries of European type, where low birth rate and a tendency towards increase of population ageing is typical. Orthodox Christianity is the main religion in Georgia. Other religions, amongst others, are Islam and Judaism.

During more than 70 years Georgia was one of the 15 Soviet Republics. In a national referendum in 1991, the people of Georgia voted overwhelmingly in favour for an independent country. During two years, 1992-1993, a civil war took place between Abkhasia and Osetia in the territory of Georgia. Only in 1994, the political situation was more or less stabilised. But Georgia had lost some territory and the economic situation was poor. There were major infrastructure problems giving rise to serious difficulties such as water and electricity supplies.

Roads in Georgia are still in bad conditions making transport very difficult even in urban areas, but especially the more remote mountain regions are almost impossible to access in winter. Since late 1996 the economic situation has improved but it is yet still far from the normal position. After the end of the communist regime, a huge wave of emigrants left for mainly the neighbouring Russia, Europe and the United States.

2. Health system characteristics

Nowadays, the health system of the Republic of Georgia undergoes a fundamental reorganisation from a general state system to a system shared between state, private and public. Currently, at the beginning of this process, it is rather difficult to determine their share and structure. But it seems that all of them are necessary like in the developed world, when their positions are defined by the principles of reasonable competition of market economy.

It is very difficult to draw a clear picture of the health status of Georgian population. Data collection is difficult because of various factors including the demographic movement and communication problems. In addition, the use of different definitions and methods of data collection and recording added to staffing problems and a lack of co-ordination results in inaccuracy in the field of reproductive health statistics.

Due to the present economic situation in Georgia, the data obtained is not sufficient, maybe due to underreporting. For example, the drastic increase in maternal mortality ratio to 128% over 5 years and the high abortion rate despite an apparent decrease over three years are not reflected in the data on maternal mortality from abortion.

There is minimal information about sexual, physical and psychological violence against children and women. In general, tradition and culture prevent women and children from violence reporting.

Georgia has one of the highest rates of doctors and nurses in the world. Midwives still play a central role in providing health care for pregnant women.

The government tries to reform the health care system but the economic situation and the threat of unemployment for medical staff makes it very difficult. Although maternity hospitals are relatively easy to access, many of them are under-equipped. Sanitary conditions in hospitals are poor and health risks resulting from abortion are high, especially in rural areas.

Maternal mortality is expected to further increase as a result of the rise of unprepared home deliveries (estimated to be approximately 10% of all deliveries), non-functional referral systems and a diminishing capacity of health services being able to deal with obstetric complication.

3. Formulation of the problem

Annually, the world population increases by 1.73%, i.e. 87 million. This fact causes the intensive increase of resource consumption (water, food, power and even, fresh air); thus mankind will face a catastrophe at the beginning of the 21th century. Therefore, voluntary family planning directed to the zero increase of the population (0-1%) is common to all populations and embraces the majority of population at fertile age.

According to data of WHO, about 525.000 women die because of pregnancy complications every year, 99% are from developing countries. Approximately 20 million illegal abortions cause thousands of women's deaths, about 120 million women wish to avoid unwanted pregnancy, but have no possibilities and 15 million girls at the age of 15-19 years have one delivery every year, which presents the main reason of mortality in this group.

Annually, 300 million people suffer from STDs, and 1 out of 20 being an adolescent.

HIV in Africa and Asia will infect about 40 million people by the year 2000.

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Reproductive Health in Georgia
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It has also been estimated to save about 20 million women by increasing the interval between pregnancies to 2-3 years.

Infertility affects about 10% of all marriages. Except for medical problems, low fertility rate is associated with higher personal welfare, while on the other hand, it negatively influences the demographic situation in Georgia.

In summary, the necessity of an established state policy in the field of voluntary family planning and infertility therapy is apparent and should be part of a general National Reproductive Health Programme.

4. Maternal mortality

Previously, Georgia had the second lowest ratio in maternal mortality in the present CCEE and CIS states. The number of registered cases for complications in pregnancy in general health care institutions was lower than in any other of the CCEE and CIS countries. The main causes of maternal mortality were haemorrhage (over 25%), sepsis, emboli, abortion and toxemia. Action is now being taken to analyse the causes of maternal death and what will be the implications for health services.

5. Infant mortality

Until 1992, Georgia underwent a steady decrease in infant mortality close to the European average (15.8 per 1.000). The major causes of infant death were diseases of the respiratory system (38%) followed by perinatal and diarrhoeic conditions. But recent data from 1995 show an increase in infant mortality (21.4 per 1000) indicating a risk of two thirds caused by perinatal abnormalities. There is a significant difference in infant mortality between urban and rural areas. The mortality rate is higher in rural areas, reflecting the more difficult conditions there.

The available statistics on mortality do not classify the number of deaths according to initial causes of death (cold, malnutrition, and stress). Furthermore, some causes of death may be related to the already existing poor socio-economic situation in the country. In fact, according to some estimation, at least 1/3 of the increasing number of deaths may be attributed to this situation.

6. Birth and fertility rates

In Georgia, fertility rates in rural areas are still higher than in urban areas. Although there is a tendency for the two rates to become similar. This is probably due to the migration of couples at reproductive age to cities. The crude birth rate declined in the nineties, probably because of the civil war. Different ethnic groups present different demographic behaviours. In 1995, only 53.587 deliveries were reported. It is estimated that 10-12% of married couples are infertile.

7. STD

The incidence of STDs consistently increased as a consequence of low socio-economic conditions, poor state maintenance and sanitation infrastructure, malnutrition, the unavailability of medicines and frequent migration of the population to different countries for temporary employment.

A large part of the population suffering from STD does not seek specialised medical care mostly because of financial problems and the fear of social consequences. There are different, well-practised treatments without having to attend the specialised clinics.

Georgia has a 'Republican Centre for Combating and the Prevention of AIDS'. According to its reports, 11 AIDS cases were detected in the whole country till the end of September 1996. This number is steadily increasing.

8. Breast feeding and safe motherhood

Several programs for the training and education on breast-feeding are already in place and mainly UNICEF sponsors them. The World Bank sponsors safe motherhood programmes.

9. Reproductive health of adolescents

According to data of one study on the abortion situation, around 4,5% of abortions are performed in girls 13-19 years old. 70% of 13-19 years old adolescents had sexual experience.

Sexual education in school has only started and is still very limited. Even teachers are not yet liberated from the ancient mentality and hardly speak freely or naturally about sexual problems.

10. The principles of development of reproductive health in Georgia

Issues regarding birth control and infertility have been neglected during the last 20-30 years. Because of their global social importance they have become a problem for the state. Therefore, the World Health Organisation (WHO) considers birth control as one of the main problems in a number of developed and developing countries. Besides being a medical problem it also includes other aspects such as sociology, demography, economics and physiology which need to be addressed.

Reproduction and human fertility regulation is of particular importance for Georgia, as the birth rate in a number of regions is very low and the present economic and political situation alongside with migration negatively influences the demographic situation of the Republic. On the other hand, it should be noted that modern contraceptives are the only way to fight the demand for abortions (both medical and illegal).

Despite the difficult political and economic situation created in the Republic, all the current situation requires the establishment of a national reproductive health service lead by the Zhordania Institute of Human Reproduction (ZIHR) with Reproductive health consultations (RC) for the regions. It is desirable to establish Departments in reproductive health (RD) in large cities, such as Kutaisi, Batumi and Rustavi. This kind of service should represent a general system with unified organisational and methodological management.

Investigation and treatment of a considerable part of diseases affecting reproductive health can be carried out in an outpatient way. The inpatient medical service is necessary for those patients, who need invasive methods of investigation and treatment (diagnostic and operative laparoscopy, surgery). In total, the rate of these patients does not exceed 20-25% of the total number of patients. Hence, in case of normal working conditions a great number of patients will be able to get the qualified service in RC according to their residence, which will significantly reduce the treatment costs. Those patients, who can not be treated in regional consultations due to the therapy difficulties and lack of appropriate personnel skills will be sent to the National Centre of Human Reproduction (NRC) where exist up- to date facilities exist. Results of the treatment and investigations obtained in the National Centre, with all necessary recommendations on further rehabilitation treatment and prophylactic medical examination will be forwarded to the regional consultation centre and so establishing a highly

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qualified reproductive health service system with affordable economic expenditures.

The consultation centres (RC) should introduce record cards and prophylactic medical examination, carrying out the primary investigation and treatment and sending patients for highly qualified investigations, treatment and follow-up if necessary to the NRC. Another important task will be to emphasise on the education on family planning issues and modern contraceptive methods.

It is desirable, that one RC serves for 1-3 regions (according to the size of the population) and is with a large medical institution. This will be important to carry out different investigations on the patients avoiding extra organisational expenses (including ultrasound and X-ray). The RC staff should consist of 1 gynaecologist, specially qualified in human reproduction, a part time urologist, qualified as andrologist, 1 nurse and 1 laboratory assistant (cytologist). In such case, the clinic will become the regional centre of birth control and infertility treatment. A good example of the importance of such a centre is the one in Batumi, where 528 primary patients were treated during the first year of its existence. The total number of visits was 4900, and 50% of the patients became pregnant. Highly specialised investigations and treatments, like echo-monitoring, hormonal, bacteriologic and immunologic investigations, diagnostic and operative laparoscopy, hysteroscopy, microsurgery, "in-vitro" fertilisation and determination of treatment tactics by skilled specialists should be carried out in every NRC.

Selection and training of personnel in reproductive health, development and introduction of methodological recommendations in the Republic, processing and generalisation of statistic data, working on a reproductive health strategy and its realisation are carried out in the National Centre. NRC should have a single leadership and act within the general medical principles.

The *Zhordania Institute of Human Reproduction* has elaborated the main directions for its activity, which will be in force in case of establishing the general national reproductive health service:

- Birth control (aspects of abortion and contraception)
- Social aspects of birth and demographic situation in Georgia
- Establishment of general reproductive health service in the Republic
- Clinical and experimental andrology
- Diagnosis and treatment of woman infertility due to endocrine and inflammatory causes
- STD and AIDS centres.

Besides the above mentioned issues, this service, as it is in the Institute, can solve the problems connected with adolescent gynaecology, gynaecological endocrinology and problems concerning the climacteric period (menopause) in the whole country.

Therefore, the number and qualification of staff engaged in practical medicine should be determined according to the number of patients using the service of the centre. Namely, if about 50 beds of the inpatient clinic are occupied, no more than 5 doctors and one senior specialist should be the staff of the department. Similar, for the outpatient service, 1 doctor for 15-20 outpatients will be required (with corresponding quantity of nursing staff).

Hence, the structure of the National Reproductive health Service cannot be determined once and forever. It should undergo annual assessment and correspond to the needs existing in the Republic based on the principles of market economy. As for medical and other personnel, an agreement (contract) should be made for a definite period (0,5-1-3-5 years), which will contribute to the flexibility of the reproductive health service structure and maintenance of a high level medical service.

To provide financial support for the reproductive health service is a rather difficult problem and of course, it can not come from only one source. Particularly, the directions we mentioned above: creation of general reproductive health service in the Republic, social aspects of birth rate and demographic situation in Georgia can be financed only in the framework of a national programme and the participation of central and local medical organisations. The only real source of financial support for these programmes is the government. The realisation of the programme - birth control by using modern methods of contraception should be implemented in cooperation with International programmes, especially with ZIHR being is a Collaborating Centre of WHO.

Another possibility to realise the programme would be based on financial support from the state and market economy principles. The increase of the latter depends on the establishment and development of medical insurances and the general economic situation of the Republic. The scientific work should also be developed in the framework of the national reproductive health service, which will be focused on:

- International cooperation
- Research priority
- Solving national (specific) issues

Financial support for research should be done on the basis of contracts for different projects, both, on the expenses of state (budget) and contract orders. The number of people engaged in research should not be permanent and should be defined by the need of current, financed subjects.

On the background of many years of experience in Western countries, in order to make medicine serving a greater number of people, it is important for the coexistence and cooperation state, insurance and private medicine. Therefore, it is absolutely important, that the state contributes to introduce and develop the insurance and, particularly private medicine in Georgia. As mentioned above, birth control is among high priority issues discussed even on political levels in developed and developing countries and besides being a medical problem, it is associated with sociology, demography, economics and psychology. This fact has been proven once more in September 1994, at the United Nations International Conference of Population and Development (ICPD).

11. Principles of family planning development in Georgia

The regulation of human reproduction has a particular importance for Georgia as in some regions of the Republic the birth rate is very low. The present political and economic situation, alongside with migration seems to negatively affect the demographic situation of the country. At the same time, modern methods of contraception are an important step to decrease abortion rates.

12. Programme management and executors

The realisation of a National Family Planning Programme should be carried out through the National Reproductive Service. The organisation and the principal of the programme should be the RNC and its branches in the region should be the RCs. As for the big cities, such as Kutaisi, Batumi, Telavi, RDs are to be established. This service should represent the joint system with common organisational and methodological management.

Primary consultations on family planning issues can be performed on an outpatient basis in the regional RCs. Only those patients, who need more complicated methods of contraception will be

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especially supervised. The total number of these patients should not exceed 20-25%. Hence, a great number of patients will be able to have qualified service in regional RCs according to their residence and this will considerably reduce the treatment costs. These patients who cannot be treated in a regional RC because they require more complicated treatment or investigations or the RC lacks highly skilled personnel will be immediately sent to the National Centre, where modern facilities exist. The results obtained from the referral centre with further recommendations on rehabilitation treatment will be sent back to the regional consultation centres and the joint, highly qualified reproductive service system will therefore be economically affordable.

The National Centre should select and carry out the training of gynaecologists, develop and introduce methodological recommendations in the Republic and process statistical data. The National Reproductive Service should have a single authority and act within the general medical principles.

As it is well known, family planning represents a global social, ecologic, demographic, medical and even political problem, considering of course the regional peculiarities. This was one of the aspects the participants of a conference in Cairo focused on and is the basic principle of the Programme of Action. Accordingly, the Family Planning Programme of Georgia should be founded on medical background, in the framework of reproductive health service development and reform.

The modern principles of family planning have been pursued in Georgia since 1987, when the number of abortions significantly reduced (from 100.000 to 41.000 by 1992). Though, the birth rate in the same period considerably reduced by 15%, but the decrease of abortions for more than 100% indicated the efficacy of the existing family planning programme. Taking into account that the above mentioned programme has been worked out in accordance with the main principles of WHO for years, when Georgia was still in the process of developing medical reforms.

As it is known, financial and economic support from international societies to reform Georgian medicine is based on the high efficiency of its results. Thus, the ignorance of achieved results, even if it embraces only the starting stage cannot be justified and state, church and our society should attract great importance to the support of working programs.

13. Family planning

After the efforts of UNFPA and its executive Director Dr. Nafis Sadik, the Programme GEO/96/P01 "Strengthening of Reproductive Health Service" was approved for the Republic of Georgia on May 21, 1995. This programme includes a number of significant activities, such as education of doctors and medical personnel, contraceptive distribution, local and abroad training, visits of foreign experts, working with mass media (population education) etc. The final result of the programme implementation should be the creation of so called "National Programme on Reproductive Health". Because of different reasons, the programme started its activities only in February 1996, but it is already implemented, and the whole project is scheduled to finalise in December 1999.

According to the decision of APR last April, the start of the National Programme implementation was recommended and its executors were also determined. The above mentioned activity has already started, though, at this stage the creation of the National Programme is not yet possible, because of the absence of epidemiological data on Reproductive Health in the Republic. For this reason, this Programme is preliminary and should be used only for orientation until the above mentioned international standards of epidemiological data will be available for Georgia.

14. Project GEO/96/PO1

Project title	Strengthening of reproductive health services in Georgia
Execution	WHO-EURO / ZIHR
Implementing counter	UNFPA
Budget	925000\$
Actual start date	01.01.1997

a) Development objectives

Contribute to the reduction of maternal mortality by 50% by year 2000 with government assistance in the implementation of a National Reproductive Health Programme, which aims to reduce the high abortion rate.

b) Immediate objectives

- To improve access to RH/FP services available at 55 service delivery sites through training of service providers, supply of modern contraceptives medical equipment.
- To develop capability of Ministry of Health to evaluate trends in RH/FP care through development and implementation of the management information system (MIS).
- To provide information of knowledge, attitudes, beliefs and practices of Georgian population towards RH/FP and to assess the impact of the project through design and administration of KAP survey.

c) Expected output

55 centres fully equipped and working.

d) Programme budget

Financial security of the national reproductive health and family planning programmes is a rather complicated issue and, of course, cannot be provided by only one source. Creation of a joint reproductive health service in the Republic may be financed only in the framework of the National Programme with the participation of central and local medical organisation. Correspondingly, governmental financing is the only source for the program's financial security.

Realisation of voluntary family planning and contraception should be implemented by participating in international programmes and with the assistance of these programmes, mainly with that of the Institute as a WHO Collaborating Centre.

Realisation of other directions is also possible through combined ways, based on the financial support of the state and economic principles. Increase of the latter totally depends on the development of medical insurances and on the general economic situation of the Republic.

e) Main tasks

Reproductive Health in Georgia

- Creation of a joint national service in reproductive health and infertility treatment
- Training of highly skilled personnel in RH/FP
- Establishment of health and education organisation service

f) Main strategy

- Foundation of a National Centre
- Creation of RDs in big cities
- Establishment of regional RCs
- To meet needs of the population by free or acceptable priced modern contraceptives
- Establishment of training centres in RH/FP
- Programme elaboration to up-to-date level
- Development of methodological recommendations
- Health and educational work among population

g) Material and technical basis

NRC will be located at ZIHR in Tbilisi, which is situated 43, Kostava str. The Institute has an in-patient clinic with a surgical department (80 beds), policlinic and clinical and experimental departments: clinical-diagnostic, biochemistry laboratories, laboratory of physiology and pathology of reproductive organs, experimental andrology, contraception, bacteriology and immunology, medical information and patent service, hormonal diagnostics and organisational sector.

The Institute is equipped with all modern techniques, such as: diagnostic and surgical laparoscopes, ultrasound machines, thermography, X-ray, sperm counter, radio-immunological and biochemical equipment and clinical laboratories.

All these services are more or less supplied with reagent and laboratory equipment, but the main equipment exploitation period is not longer than 6-8 years.

The Institute employees 392 people, including 12 head of the departments, 1 leading scientist, 10 senior scientific workers, 8 scientific workers, 40 junior scientists, 8 scientific workers, 1 academician, 8 scientific doctors, 29 scientific candidates, 3 professors.

h) Working Plan

- 1998-2003: organisational activities of the Ministry of Health and ZIHR for the establishment of a general reproductive health service
- 1998-2003: Ministry of Health and ZIHR organise training centres for preparinghigh skilled personnel in reproductive health
- 1996: Start to prepare personnel in RH/FP ZIHR
- 2000: Start to apply general National Reproductive Health System Programme, monitor and assess its progress,

15. Areas for action and policy changes

- Further evaluation of the actual situation is needed to identity specific action.
- Technical assistance in human reproduction is needed through the continuous support, supply of contraceptives by means of raising funds and thus strengthening FP promotion.

Reproductive Health in Georgia

- Strengthening MCH services and training health care staff, thus strengthening FP promotion.
- Future projects should include medical equipment and supplies for primary health care services, training in public health issues on healthy infants and mothers and issues on AIDS.
- Antenatal and perinatal care and the management of respiratory diseases should be examined in order to reduce the avoidable deaths in infants.
- Assistance to adolescent health projects is needed.

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Reproductive Health in Hungary

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Geneva WHO Collaborating Centre for Research in Human Reproduction

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Abbreviations

AIDS	Acquired immuno-deficiency syndrome
FP	Family planning
IUD	Intrauterine device
IUGR	Intrauterine growth retardation
LB	Number of the life births
LBW	Low birth weight
OC	Oral contraceptive
RH	Reproductive health
VNS	Visiting Nurse Service
WRA	Women in reproductive age / 15-49 years of age

1. Introduction

1.1 History

The mother and infant health care has an old tradition in Hungary. Igancz Semmelweis was the first well-known physician who strove to defeat puerperal sepsis. The first easy-to-survey obstetrical statistics were initiated by Vilmos Tauffer in 1892. This statistical methods have served as a basis for Hungarian obstetrical statistics for more than one hundred years.

1.2 Political and economical aspects

During the socialist government many laws and programs were created to increase the birth rate, but have only been partially successful. Most of these laws are still valid e.g. :maternity support, child welfare support etc. The unequal socio-economic status within the Hungarian population was more obvious after the break up of the socialist regime and this decreased its influence on reproductive health in Hungary. Nowadays, one part of the population is living in good social conditions, similar to western-Europeans. civil. The other part of Hungarian population lives in low social conditions, mostly in villages.

The women's workforce was very important after the second world war and was strongly supported by the socialist government. Several generations have lived these circumstances since that time. Many divorces and broken up families resulted by the overworked way of life. The educational and FP problems, which established during that time are characteristic for both parts of the population.

2. Background

2.1 Demographic data

The number of live births (LB) decreased significantly in the last few years in Hungary. This is probably due to the financial uncertainty of families who formed during the change of the regime. The extensive decrease of LB appears in the population belonging to a higher socioeconomic status. Families with one or two children are common in this group. Big families (6-8 children) are not rare in the lower socioeconomic population group. This is based on the ethnical traditions. This process has just weakened the financial position of these families and the state has been in charge for the up-bringing and education of some of these children.

Nowadays, the number of the Hungarian population is decreasing. In 1990, 10.374.823 inhabitants were reported, in 1997 this number decreased to 10.174.442 (Annex 1). The number of LB decreased in the population, this can be seen in the number of LB per 1.000 inhabitants (Annex1). The percentage of women at reproductive age (WRA: women 15-49 years old) is about 25% of the total population (Annex1). The increasing number of elderly people is one of the characteristics of Hungarian population.

2.2 Women's perspectives and life styles

In Hungary, the female life expectancy at birth was 74.7 yr. and male life expectancy at birth was 66.06 years in 1996 and women are already emancipated in legal, cultural and educational aspects.

The rather unhealthy nourishment and the insufficient physical exercise are important characteristics of Hungarian people. This is valid for the population of WRA as well.

The treatment of diseases which are due to the unhealthy life style (cardiovascular diseases, obesity, diabetes mellitus) are the most serious medical problems in Hungary.

3. Government strategies

The increase population size has been supported by the Hungarian government by introducing laws which tended to increase the population number and financially support families with children, mainly with children less than 14 years old. The place of a professional mother is established: mothers who have three or more children receive a salary. However, we can feel some discrepancy between these laws and the health service. The health establishments are financed from the fund of Health Insurance in Hungary. Only the treatment of diseases is covered by the Health Insurance which excludes pregnancy. Therefore, Hungarian women have to pay for interruption of pregnancy, for sterilisation, contraceptive pills and IUDs. It was discussed that the Health Insurance wants to stop financing prenatal care. This has to be considered a very dangerous process, taking into account that many pregnant women will not be able to cover the expenses for antenatal care and will therefore not attend the clinics.

4. Reproductive health services

4.1 Structure

First level care:

The services which provide RH are spread in the whole health institution network of the country.

Reproductive Health in Hungary

They involve:

- Prenatal care services
- Public run health centres in rural zones
- General practitioner or family physician
- Mother and child consulting centres in districts
- Private specialists (obstetricians/gynecologists)
- Outpatient clinics for menopausal women

Second level care

District hospitals with obstetric/gynecology and paediatric departments

Third level care

University hospital with obstetrics/gynecology and pediatric departments

4.2 Definition of reproductive health periods

There are three main periods of Reproductive Health:

- Period of the pre-reproductive health, which corresponds to adolescent age.
- Period of the reproductive health, which includes: maternal period: prenatal, delivery, postnatal, postpartum and breast feeding period. intervals between deliveries
- Period of post reproductive health, which corresponds to menopause and andropause.

4.3 Components of reproductive health

4.3.1. Adolescent care

- Improvement of RH education in school
- Increased knowledge of STD and contraception
- Prevention of inadequate sexual behaviours
- Safe abortion

4.3.2 Family planning

- Pre-conception counselling
- Prevention of abortion
- Post-partum and post-abortion counselling
- Safe abortion
- Information, application and counselling on different contraceptive methods
- Follow-up contraceptive side effects and complications
- Providing of modern contraceptive methods
- Sexuality
- Infertility

4.3.3 Mother care

• Pre-conception
Reproductive Health in Hungary

- Prenatal care
- Decrease of pre-term and low birth weight babies
- Care during labour
- Postnatal care
- Promotion of breast-feeding
- Reduced perinatal mortality
- Reduced maternal mortality
- Reduced obstetric and neonatal complications

4.3.4 Maternal nutrition

- Improving the knowledge and education on nourishment
- Reduced anaemia during pregnancy
- Promotion of breast-feeding

4.3.5 New-born care

- Reduction of neonatal mortality and morbidity
- Reduction of neonatal infections after delivery
- Improvement of early neonatal intensive care
- Promoting exclusive breast-feeding

4.3.6 Care for sexual health

- Prevention, treatment and counselling on STD/AIDS
- Reduction of gynaecological disease complications

4.3.7 Care for post-reproductive health

• Prevention and treatment of menopause disorders

5. Reproductive health situation in Hungary

5.1 Maternal health and safe pregnancy

More than 94% of the pregnant women in Hungary attend antenatal care services. The prenatal care services assessing pregnant women, are found in every big area with mobile services available in smaller villages. Attendency of prenatal care service is not compulsory, but financial support for the mother will be paid if she visits antenatal care clinic. Screening for gestational diabetes, FPH gestosis, IUGR and other risc factors are performed by the Perinatal Care Service and women will be treated by the second level of RH if necessary. Fetal monitoring is a routine task provided by the clinic.

There is close co-operation between this system and the Visiting Nurse Service (VNS) in Hungary. The VNS was founded in 1916. The nurses prepare the pregnant women for their delivery and they instruct the women on infant-care and child welfare.

Maternal mortality ratio, being one of the most sensitive indicators of women's health, is one of the lowest in Central and Eastern Europe (Annex 3). In 1996, 33% of all maternal deaths were due to abortions.

Reproductive Health in Hungary

5.2 Family planning

The modern FP methods are well known and accepted in Hungary. There exist only partial or estimated data because there are no national statistics about the use of contraceptive methods in Hungary. The OC is the most wide-spread method in the whole country. A increase in IUD use has been observed, because the women are often afraid of OC complications. The increased use of condoms is likely due to the AIDS-propaganda and recently the use of traditional or natural methods is more preferred. Oral contraceptives are only available in clinics and pharmacies. IUD insertion is only performed in hospitals, and sterilisation is strictly only permitted for men and women over 40 years of age, for those over 35 years with three children, or over 30 years with four children.

Interruption of pregnancy is legal and performed upon request up to 12 weeks of pregnancy, if there is a risk to the woman's life, a risk of having a disabled child and in case of an unwanted pregnancy. Abortion is performed up to 24 weeks of pregnancy if there is an acute risk for the woman's life or intrauterine death or suspected genetic defect. An abortion costs about US \$ 60. The law on legal abortion stipulates that abortion is not a family planning method.

77.000 abortions are officially induced during one year. 15 % of all abortions in Hungary are performed in adolescent girls (14-19 years) (Annex 2). The method of interruption of early pregnancies (less than 12 weeks) are dilatation and aspiration.

5.3 New-born care

99% of births are assessed by trained medical staff in Hungary. Recently, there was a claim to family delivery, mainly in big cities. The hospitals and other delivery rooms are prepared also for the presence of the father or other members of family during the birth process. Home-delivery is not widely practised.

The perinatal mortality rate is decreased in the last years (Annex 2). This result is due to a the work of the Prenatal Care Service and delivery rooms. The data of the perinatal mortality rates are not comparable with other countries statistics, because in Hungary the perinatal period was defined as starting from 28 weeks of gestation till the 7th day of life.

The number of new-borns with low birth weight (less than 2500 grams) also decreased in the last few years (Annex 2). The duration of hospital staying for healthy babies is usually 5 days. The babies usually stay inneonatal departments which are in close connection with the delivery rooms. Babies with different pathologies or congenital problems are transferred to the regional perinatal intensive centres.

5.4 Screening of genital cancer

Breast, colon and rectum cancer have the highest morbidity in women in Hungary. All women examined by gynaecologists are also screened for cervical cancer, as the gynaecologist is obliged to take a cytological smear. This has helped to diagnose this malignant pathology at an early stage, even in symptom-free patients. The services that provide screening of genital cancers are placed in specialised polyclinics of some cities of the country, in gynaecological hospitals and in services of gynaecological oncology.

5.5 Post-reproductive health

The care for women after menopause is performed in the outpatient clinics for menopausal women, at the first level of the health care system.

6. Perspectives for the future

- To reduce maternal and infant mortality and increase maternal and infant safety
- To introduce health education programmes with an emphasis on antenatal care services and to promote healthy lifestyles
- To strengthen the commitment to women's and infant's health by developing, improving and implementing health promoting policies and friendly health services to enhance sexual health and avoid unwanted pregnancies
- To support the integration of reproductive health programmes
- To assist the adolescent health projects

Annex 1.

Population	in	Hung	ary
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Year	Number of men	Number of women	Number of women (15-49 years old)	Number of the total population
1990	4.984.904	5.389.919	2.529.529	1.0374.823
1991	4.972.184	5.382.658	2.549.243	1.0354.842
1992	4.960.529	5.376.707	2.566.152	1.0337.236
1993	4.943.410	5.366.769	2.575.443	1.0310.179
1994	4.922.949	5.354.019	2.582.511	1.0276.968
1995	4.903.704	5.341.973	2.581.232	1.0245.677
1996	4.883.916	5.328.384	2.583.725	1.0212.300
1997	4.863.277	5.311.165	2.583.384	1.0174.442

Proportion of women in reproductive age (15-49 years)

Year	1990	1991	1992	1993	1994	1995	1996	1997
	24.38%	24.61%	24.82%	24.97%	25.13%	25.19%	25.30%	25.39%

Life expectancy at birth (in years)

Year	1990	1991	1992	1993	1994	1995	1996
Female	73.71	73.83	73.73	73.81	74.23	74.50	74.70
Male	65.13	65.02	64.55	64.53	64.84	65.25	66.06

Proportion of live births / 100.000 habitants

Year	1990	1991	1992	1993	1994	1995	1996
	12.12	12.28	11.77	11.35	11.25	10.09	10.03

Annex 2.

Pregnancy outcomes

Year	1990	1991	1992	1993	1994	1995	1996
Total number of pregnancies	228.530	229.116	219.398	202.324	199.657	197.891	190.243
Number of live births (LB)	125.679	127.207	121.724	117.033	115.598	112.054	105.272

Number of spontaneous abortion	10.661	10.255	9.136	8.834	8.485	7.866	7.424
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	Induced abortions in Hungary										
Year	1990	1991	1992	1993	1994	1995	1996				
Total number of induced abortions	90.394	89.931	87.065	75.258	74.491	76.957	76.600				
Induced abortions per 1.000 LB	719	707	715	643	644	686	727				
Percentage adolescents (15-19 years) per 100 abortion	13.29	14.95	16.24	17.70	18.06	16.93	15.22				

Perinatal mortality rate

Year	1990	1991	1993	1994	1995	1996	1997
Total number of perinatal deaths	1.796	1.723	1.473	1.199	1.083	1.014	947
Perinatal mortality rate (28wks-7d/per 1.000 LB)	12.12	12.28	11.77	11.35	11.25	10.09	10.03

Low birthweight infants in Hungary

Year	1990	1991	1992	1993	1994	1995	1996
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Reproductive Health in Hungary

Number of LBW (premature and IUGR)	11.652	11.800	10.975	10.061	9.962	9.192	8.773
Ratio of LBW per 100 LB	9.27	9.28	9.02	8.59	8.62	8.20	8.33

Annex 3

Maternal Mortality in Hungary

Maternal mortality rate = number of maternal deaths/100000 women 15-19

Maternal mortality ratio as obstetric risk = number of maternal deaths/100000 live births

Maternal mortality ratio as risk of pregnancy = number of maternal deaths/100000 pregnancies

Year	1990	1991	1992	1993	1994	1995	1996
Number of maternal deaths*	22	15	10	20	8	14	10
Maternal mortality ratio /per 100000 LB/	17.5	11.7	8.27	17.08	6.92	12.49	9.49
Maternal mortality ratio/per 100000 pregnancies/	9.6	6.5	4.56	9.89	4.0	7.07	5.25
Maternal mortality rate / per 100000 WRA/	0.86	0.58	0.38	0.77	0.30	0.54	0.38

* deaths caused by complications of pregnancy, abortion, delivery and puerperium.

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Indonesian Medical Association (Ikatan Dokter Indonesia - IDI)

Indonesian Society of Obstetrics & Gynecology (Perkumpulan Obstetri dan Ginekologi Indonesia – POGI/ISOG)

Indonesian Society for Perinatology (Perinasia)

Indonesian National Training Center Network to strengthen Clinical FP Training

National Coordination Board for Family Planning Program (Badan Koordinasi Keluarga Berencana Nasional – BKKBN)

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AVSC International Training Site Semarang

Indonesian Society for Cancer (Yayasan Kanker Indonesia – YKI)

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1. Introduction

1.1. History

Indonesia becomes independent when the Indonesian founding fathers Soekarno and Moh.Hatta on behalf of the people announce the proclamation at Pegangsaan Timur 56 Jakarta on August 17th, 1945. Soekarno and Hatta were then become the first President and Vice President.

Pancasila is the philosophical basis of the Indonesian State and the constitution is usually referred to as the 1945 Constitution. Pancasila itself, which means the five principles, is the name given to the foundation of the Indonesian Republic. The five principles of Pancasila are • Belief in the One and Only God, Just and Civilized Humanity, f the Unity of Indonesia, Democracy guided by the inner wisdom in the Unanimity arising out of deliberations amongst representatives and ... Social Justice for all the Indonesian people.

The national flag is called "Sang Saka Merah Putih" which is made up of two colors, red on top of white. The Indonesian coat of arms consists of a golden eagle and the motto "Bhinneka Tunggal Ika" (Unity in Diversity is enshrined on a banner in the eagle's talons. The national anthem is Indonesia Raya, which means the Great Indonesia.

1.2. Geography and climate

Republic of Indonesia is the largest archipelago in the world, consisting of five main and 17,508 small islands according to the Indonesian Naval Hydro-oceanographic office. It is situated across the Equator, between Indian and Pacific ocean, bridges two continents Asia and Australia, stretching 5,110 kilometers from West to East and 1,888 kilometers from North to South. The total area is 5,193,250 square kilometers with 39% land and 61% sea territory. With archipelago form, it maintains Territorial Waters and Exclusive Economic Zone (EEZ). The relief is filled with volcanoes, rivers and lakes. The geography is quite magnificent, supported by tropical climate and weather, and covered by thick tropical rain forest. Indonesia has a dry season influenced by the Australian continental air masses from June to September and rainy season resulted by the Asian and Pacific Ocean air masses from December to March.

The average temperature for coastal plains, inland and mountain are 27-28 $^{\circ}$ C, 25 $^{\circ}$ C and 22 $^{\circ}$ C respectively. Rainfall differs between the regions, with higher level of rainfall in highland areas.

Indonesia is also rich in tropical plants, including the most famous Rafflesia Arnoldi, the largest flower in the world and Amorphophallus Tatinum, the largest inflorescence of its kind.

1.3. Economy

Indonesia is enjoying a 25 years period of steady growth, resulting in almost fifteen folds increase in per capita Gross Domestic Product (GDP), from US\$ 70 in 1969 to US\$ 1023 in 1995. Since the 1970's, annual GDP growth has averaged 7.1% well above the average 4.5% for developing countries. More recently, its growing prominence in multi institutions, including the Asia Pacific Economic Cooperation (APEC), the Non-Aligned Movement (NAM) and the Association of South-East Asian Nation (ASEAN) has expanded it's sphere of international cooperation.

The trade sector will grow by an average of 8.3% per annum, the international trade networks are also expected to grow stronger to help increase Indonesia's non oil exports by an average of 16.8%. Indonesia's leading industrial products (based on export values) are: textile and garment, wood product, electronic, leather good and footwear, rubber product, palm and coconut oil product, pulp and paper, etc.

The currency is Indonesian Rupiah (IDR) and last reported Gross National Product per capita is US\$ 3,800 (World Bank, 1997)

1.4. Government

Republic of Indonesia has a President as the highest executive. Indonesia is divided into 27 Provinces each of them administered by a Governor, provinces are subdivided into 241 Regencies, 55 Municipalities, 3,625 Sub-districts and 67,033 Villages. Provinces, regencies are autonomous regions.

In a democratic life based on Pancasila, the People's Consultative Assembly (MPR), being the highest state institution, has a very important role to play. As an institution which fully exercises the sovereign rights of the Indonesian people MPR should always reflect the aspirations and the wishes of the people with all its decisions or decrees. And as the holder of the highest power in the state, the Assembly appoints the President and Vice-President and determines the Guidelines of State Policy for implementation by the President.

The House of Representatives (DPR), the members of which are from the people and are elected by the people, has the function of exercising control over the conduct of the administration by the President. The mechanism of this control by the House of Representatives constitutes a means to prevent constitutional deviation or deviations from the people's wish by the government.

1.5. Culture

The country consists of 27 provinces with about 500 tribes and correspondingly, it has about the same amount of different cultures, languages and dialects. The official language is Bahasa Indonesia.

The population has now reached the fourth most populated country in the world after China, India and the United States of America. The people are a mix between natives and new comers.

The main religion is Moslem, other religions are Catholic, Protestant, Buddhism, and Hinduism.

1.6. Education

Level of education Schools Population School services ratio

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Primary	174,414	26,321,400	151
Junior Secondary	28,089	13,484,400	480
Senior Secondary	14,792	12,977,000	877
High Education	1,570	15,629,100	9,955

Adult literacy rate in both male and female is 83.8% (UNESCO, 1995)

1.7. Demography

The total population of Indonesia in 1998 is 206.5 millions, projected population estimated in 2025 is 275.2 millions, with annual population growth rate of 1.5% (1995-2000) and Total Fertility Rate (TFR) is 2.63 (UN Population Division, 1998). The Crude Birth Rate (CBR) is 24.8 per 1000 population and the Crude Death Rate (CDR) is 8.4 per 1000 population (1990-1995)

1.8. Health resources and organization of the Health System in Indonesia

The Ministry of Health in Indonesia is part of the People's Welfare Sector, together with the Education and Culture, Religious Affairs and Social Affairs under the coordination of the Minister Coordinator for People's Welfare.

Health service facilities with the large coverage are hospitals and health centers. The health service units divided into five categories according to their level of competence and provided health services:

1) Category A: General Hospitals of which including University Teaching Hospitals

- 2) Category B: Central hospitals
- 3) Category C: Provincial Hospitals
- 4) Category D: District Hospitals
- 5) Primary Health Center

In addition to these are military, mission hospitals and private individual hospitals and clinics.

Each Sub-district in Indonesia has at least one Primary Health Center headed by a medical doctor, supported by two or three sub-health centers, which is in the majority headed by a nurse. Primary Health Center provide 16 basic health services, and most are equipped with four-wheel vehicles or motor-boats to serve mobile health centers and provide health services to under-served population in urban and remote rural areas.

At the village level, an Integrated Health Post (Posyandu) provides preventive and promotive health services. These Health Posts are establish and manage by the community with the assistance of Health Center staff. To improve maternal and child health service, midwives are being deployed to the villages.

2. Progress of Reproductive Health in Indonesia

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Reproductive Health has grown up after the health system in Indonesia. The primary health care (PHC) approach was redefined in 1987 after the Alma-Ata conference with the aim of achieving the main objective Health for All by the year 2000.

2.1. Orientation and progress of Reproductive Health in Indonesia

Reproductive Health is a concept that is being released following research and observations in the early 1970's summing up that:

- maternal and perinatal mortality was high in comparison with other South East Asian countries;
- high maternal morbidity and mortality due to pregnancy-related causes that can be prevented (haemorrhage, sepsis and preeclampsia/eclampsia);
- lack of qualified health service providers to take care of women during pregnancy and labour; many deliveries still took place at home or were conducted by untrained traditional birth attendants (TBA);
- large family size despite limited resources; wrong perception on "more children more prosperity"
- early-age marriage and adolescence child bearing period.

2.2. Requirement for Reproductive Health

The aim to provide RH services are to:

- Reduce maternal and infant mortality rate
- Introduce and promote early detection of high-risk pregnancy and delivery among community and health service providers
- Introduce and promote the sustainability of family planning services
- Provide health service provider for quality improvement in management of pregnancy and delivery
- Improve the delivery of RH services and identify actions outside the health sector which contribute to improvement in RH provided in the major health programs.

2.3. Structure of Reproductive Health

Reproductive Health in practice does not require separate structure or health system. The main action needed is that health authorities become acquainted to the need and introduce it to all concerning and related services/systems. System's sustainability should be expanded through continuous training and improving the main concept.

Integrated management approach among associated personnel and systems are more efficient and effective than any other approach available. Different elements of RH are closely linked and related each other. Therefore, maternal (ante and postnatal) and neonatal/perinatal care, family planning and infertility, complications of illegal abortions, STD/AIDS diagnosis, treatment and prevention must be treated simultaneously.

Quality improvement of the health services and referral system must also be properly authorize, adjust and applied appropriately. Actions being considered to renew the strategy for Health for All and RH in this area are to:

- Intensify efforts to expand management capabilities including sound policy decision making and focusing on priorities setting
- Manage all available resources while mobilizing additional resources
- Institutionalize the use of health research results for decision making in the health systems
- Implementation of the National of Health Research and Development Network (which has been established in 1994)
- Establishing health research committee and focal points located in MOH and in Provincial Health Office, i.e. under the Administrative Coordinator or the other available division.
- Develop a system for monitoring and evaluating the health research
- Networking between universities, other institutes of health research, training institutions and operational levels
- Developing the online access between National Information on Health Resource and Development and Central Health Data for easy information access.

2.4. Trends

General Guidelines of State Policy (GBHN, 1993) has indicated that health development was aimed to increase the quality of human resources. As well as the quality of life and life expectancy of human, improving welfare of the families and the community at large, and develop awareness about the importance of healthy life style.

In accordance to this policy, RH has moved from a stage where it used to be considered as concerning only the mother and child to a level where it involves both women and men. It has also moved from curative activities alone to include both curative and preventive activities. The scope of RH has widened due to the increasing demands for a better health for women and the increase of life expectancy. The latter has increased from 58.0 years (1986) to 63.3 years (1995) for male and 61.5 years to 67.0 years for female (UN Population Division, 1996). As life expectancy is increasing and so will new RH problems like menopause come up and need to be take care of.

2.5. Components of Reproductive Health in Indonesia

Reproductive Health means a state of wellbeing of the reproductive organs concerning their functions and functioning and not only the absence of disease. The components of RH are:

Planning and programming for reproductive health

The effort to improve the delivery of RH services and identify actions outside the health sector which contribute to improvement in RH has been partially provided in the major health programs. Some of them has been included in the interprogram and intersectoral linkage among the Ministry of Health, National Coordination Board for Family Planning, Ministry of Education and Culture, Religious Affairs and Social Affairs under the coordination of the Minister Coordinator for People's Welfare.

Sexual development, maturation and health

The aim to establish or strengthen (through research) the national capacity to develop, implement and evaluate policies and programmmes (including services), that support healthy sexual development and maturation, and sexual and reproductive behavior with special attention to adolescence, are provided and adapted through collaborating programmes with the national universities/teaching hospitals.

Fertility regulation and infertility management

The aim to help people plan pregnancy and prevent unwanted childbearing has been mostly included in the linkage programs among the Ministry of Health and National Coordination Board for Family Planning.

Maternal and neonatal/perinatal health

The Government of Indonesia is committed reduce maternal mortality rate by the year of 2000, by acceleration of different initiatives. These initiatives are revision of training programs for midwives and medical doctors, changes in the health service structure, policy and legislative changes and innovate interventions for reduction of maternal and neonatal/perinatal morbidity and mortality. An initiative to update the curriculum of medical students and midwives and the method of competency-based training have been introduced to improve clinical skills of emergency obstetrics and neonatal health workers since 1996. The primary health center provides health services for antenatal, mother and child vaccinations, weighing and diagnosis and treatment of minor illnesses. They also offer FP services which are taken care of by proficient medical professionals. They offer all the services with the exception of sterilization, in which case they refer the patient to the district hospital.

Unsafe abortion

Abortion practices are illegal by law in Indonesia. The aims to prevent unsafe abortion and to ensure the effective management of post abortion complications have been included in the health standards and guidelines for good clinical practices of the Ministry of Health and National Coordination Board for Family Planning.

Reproductive tract infections including cervical cancer

The aim to prevent reproductive tract infection including sexually transmitted disease and HIV infection have been mostly included in the competency-based training programs adapted and provided by the Ministry of Health and National Coordination Board for Family Planning. An initiative to update the curriculum of medical students and midwives have been introduced both in under and postgraduate medical education since the early 1998. HIV screening is provided only in authorized laboratories/central hospitals. They also carry out educational and preventive activities in collaboration with non-governmental organization and national working group on HIV/AIDS.

Female genital mutilation and other harmful practices

The aims to improve understanding of the physical, mental, sexual and reproductive health consequences of female genital mutilation in childhood and adulthood are not yet being included in the health programs and services. For other harmful practices, the aim is to review what is known about practices related to Caesarean section, episiotomy and histerectomy in order to develop standards and guidelines for good clinical practices has been introduced into obstetrics training packages for service providers. An initiative to update the curriculum of medical students and midwives have been introduced both in under and postgraduate medical education since 1998.

The following services are offered in hospitals during routine consultations, but have no special clinics: premarital counseling; infertility diagnosis and treatment, and menopause complications. Genetic services were not available in our settings.

3. Health Strategy for Indonesia

3.1. Government Policy

The directions of health development in Indonesia has been guided by the following principles:

- Enhancing the quality of human resources, the quality of life and life expectancy, family and community welfare and community awareness of the importance of pursuing a healthy life style
- Further developing integrated health management, including monitoring of appropriate medical technology, enhancing the quality of health services, expanding the capabilities of the health system and increasing the accessibility to services, particularly for the low-income population
- Improving the quality and developing health facilities with health personnel equitably distributed throughout the country, and
- Improving community health through prevention and infectious diseases control, creating a healthy improvement, improving nutritional status, and assuring clean water supply, health education and appropriate maternal and child health services.

All these actions actually should improved the health status of Indonesian population, when in May 1998, unfortunately the economic crisis became evident. The government has to establish a structural readjustment program and this could reflected on standard of living, health status and health projects with serious consequences as will be seen under the RH situation.

3.2. National Resource

	Best alternate source		
National resource	Value	Reference year	Source
Physicians per 10,000 population	1,404	1988	WHOSIS (1996)
Midwives per 10,000 population	0.370	1989	WHOSIS (1996)
Nurses per 10,000 population	3.544	1989	WHOSIS (1996)
Pharmacists per 10,000 population	0.098	1989	WHOSIS (1996)
Dentists per 10,000 population	0.215	1988	WHOSIS (1996)
Total national health expenditure as % of GNP	3.7	1991-1993	World Bank
% of national health expenditure devoted to local health care	24.6	1989-1990	
Total government health expenditure as a % of GNP	0.7	1990	World Bank

Source: WHOSIS. Cited from Internet. http://www.who.int/whosis/hfa/countries/ino1.htm Last update August 1996

The policy to recruit health personnel such as doctors, dentists, midwives and pharmacist, under a contract basis by the government has been enacted since 1990. Different incentives were applied for different remoteness of the work site. In support for the provision of adequate services at the district public hospital, compulsory assignments for specialists of six basic specialties were implemented. In the fulfillment of midwives, the strategy has been provided to one year of midwife training for nurses before a three-year assignment of the village midwife.

3.3. International assistance

Foreign aid played a very important role. Since 1983, 20-30% of expenditure for health were borne by foreign aid of which more than 70% had been used for the development of health services and human resources for health. Constraints in the development of international partnership is the limitation of skilled manpower. As supporters of certain health programmes is considerable, relationship with these NGOs will be intensified and strengthened.

4. Reproductive Health situation

4.1. Initiation of Reproductive Health

RH is a concept that has been existing equally with other medical disciplines. It is only undergoing modifications with new considerations added, as more knowledge is acquired on the subject through research. Reproductive health research as well as research training, are major national needs in nearly all of the developing countries in this region. In contrast, the opportunities and demands for continued institutional and human resource development are virtually limitless and certainly beyond the means of the RH programmes.

4.2. Mother and Child Health Care/ Family Planning (MCH/FP)

Some significant changes/trends in MCH that have influenced the overall health of the population:

- 1. Deployment of 54,120 community midwives who work at the village-level and provide MCH services. This policy is more supportive for improving reproductive health services.
- 2. Increasing coverage of deliveries by health personnel from 32% in 1992 to 50% in 1995, which predicted will reduce the MMR.
- 3. Mother Friendly Movement coordinated by Ministry of Women Affairs that deals with advocacy and social mobilization for Safe Motherhood.
- 4. Partnership and family approach become a trend in the area of reproductive health.
- 5. Increasing awareness for quality of care and improvement of MCH program management. This includes technical and managerial issues. Integrated planning, budgeting and program monitoring. The aim of this approach is improving budget allocation and inter-program coordination.

Some action have been taken to ensure that MCH will have continuing desirable influences on health:

- 1. Efforts on reducing MMR (by 50% by the year 2000), IMR and under-five mortality rate (to 50 and 66 per 1,000 live births) as the country priority enlarge MCH problem's contribution in public health. A health-strategy for accelerating the reduction of both MMR and IMR had also provided.
- 2. Involvement of related sector to overcome MCH problem.
- 3. The development of Mother Friendly Hospital.
- 4. Reduce maternal and perinatal mortality rate by proper surveillance for early detection of high-risk pregnancy and delivery cases and manage for appropriate level health service. Educate the community and health providers on high-risk early detection, the importance of planned and responsible parenthood and thus promote family planning;
- 5. Improve integrated program planning and budgeting at the district level.
- 6. Improve intersectoral coordination between Ministry of Interior, Ministry of Health, Ministry of Social Affair, Ministry of Education and Culture, Ministry of Religion and State Minister for Population and the National Family Planning Coordination Board.
- 7. Life Saving Skill Training for Community Midwives (Bidan Di Desa) on Obstetric and Neonatal Emergency care.

- 8. Provide health insurance privilege card for the low-income community.
- 9. Improve the quality care for sick children in health facilities by introducing an innovative approach of development of Integrated Management of Childhood Illnesses (IMCI)

4.3. High Risk Clinics/Approach

The approach consists of identifying or targeting women with increased risk during pregnancy and delivery. The approach was introduced to the PHC service throughout the country by using the KMS Ibu Hamil which include:

- 1. Hemoglobin level less than 11 g/dl
- 2. Grande multiparity (more than 5 deliveries)
- 3. Height less than 140 cm
- 4. Early age pregnancy (less than 17 year), elderly primipara (more than 35 year)
- 5. Short period child spacing (less than 2 years)

4.4. Adolescence Reproductive Health

This part of RH service is unfortunately not yet become a reality in Indonesia. This is probably because of the high rate of adolescence fertility and child bearing which posses an economic burden on their parents and the society.

However, adolescent RH is now on the national agenda. Efforts are being explored to improve on the utilization of existing health services by adolescents.

4.5. Newborn / Infant Care

Infant mortality rate 49/1000 live births (1997), Under-five mortality rate 59/1000 (1997) and Low Birth Weight Babies 14% (1990-1994). Full immunization during the age of 12-23 months was given to 50% infants. Upper respiratory tract infection 10%, fever 28% and diarrhea 12% (SDKI, 1994).

Management of Sick Neonates by Community Village Midwives in West and Central Java and South Sulawesi has developed by the Indonesian Society for Perinatology consist of a special module for newborns 0-28 days which did not exist in the current module of WHO. Mother's Perception and Acceptance of the Kangaroo Care for Low Birth Weight Babies in Rural Areas and Training for Neonate Resuscitation are found useful for increasing newborn survival.

Basic Maternal and Neonate Health Care, Obstetric and Neonate Emergency Training Packages for health service providers will ensure the quality for neonatal care instead of mother care.

4.6. Child Health and Development

Child health and development is directly linked to the intra and peripartum periods. Care during these critical periods was almost done at the birthing huts and at home after the home delivery. Almost all of women especially in the rural areas still deliver their babies at home, attended by trained Traditional Birth Attendants (TBA), only 36% of them were attended by health personnel (1983-1990). Further child development will be determined by many environmental factors. Although Indonesia has sufficient food, there are still some cases of malnutrition due to lack of balanced diets and parasite infestation.

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4.7. **Post-Reproductive period (Menopause)**

Age related alterations for menopause start at approximately 42-44 years in Indonesia. As life expectancy becomes higher in the past ten years of development, some post-reproductive period problems will be encountered.

The majority of women have no clinically manifesting symptoms of menopause due to cultural manner, so the period often passes unnoticed. Although occasionally some suffer pathological fractures resulting from osteoporosis. Traditionally, menopause women still do lot of things in their daily life without obstructed by the hormonal changes. Because menopause does not really constitute a problem, studies in this domain are rarely done among reproductive research.

4.8. Genital cancer screening program

Compared with 20 years ago, the problem of cancer is now on the increase in Indonesia. Cancer as the cause of death in various hospitals ranked number 7 after infectious diseases, accidents and cardiac diseases. Cancer of the cervix uteri and breast cancer were the most frequent cancer found in females throughout Indonesia.

In a 10-years period (1970-1979) 7,646 cases in females were registered. The female genital tract cancers occurred in 23.8% of all malignancies in the female. The relative frequency of the gynecological tumors was: cervix 60.3%, ovarium 25.5%, corpus uteri 6.9%, choriocarcinoma 5.1% and vulva/vagina 2.2%. (Mangunkusumo, 1985)

Some malignant neoplasms were diagnosed from 2102 women at the Department of Pathology of the Gadjah Mada University in Yogyakarta during 1970-1973. 25.7 % were cancer of the cervix uteri, 17.0% of breast cancer and 25.7% chorionepithelioma. (Soeripto, 1977) The highest frequency of cervical cancer was found in Bali (34.0%)

5. Family planning / RH Projects

5.1. Development of Family Planning in Indonesia

With an estimated population of 200 million, Indonesia is the fourth most populous nation on earth after China, India, and the United States. The key to controlling Indonesia's population was to address the problem with a comprehensive program that integrated education and health care delivery.

Indonesia's family planning program is a measurable success. The nation's fertility rate, which was as high as 5.6 children per woman in the late 1960s, dropped to about 2.9 children per woman in 1992. Fertility declined fastest in the 1980s when the National Family Planning Program expanded to cover the entire country. Indonesia's population is still concentrated in the younger ages, currently it is growing at 1.6 percent annually.

Indonesian Family Planning Program was launched in 1970 through the establishment of the National Family Planning Coordinating Board (BKKBN), the largest social service agency with more than 40,000 family planning staff and fieldworkers. It is supported by 1.5 million volunteers, made up overwhelmingly of community women, who have been mobilized and trained to provide general health, nutritional, and family planning counseling under the nationwide volunteer organization called the Family Welfare Movement (PKK) and other women's organizations.

With the support of the international donor community, the World Bank, United Nations Fund for Population Activities and United States Agency for International Development, Indonesia has successfully struck a balance among its peoples' religious, cultural and economic needs to establish a dynamic, flexible and pragmatic approach to population management.

Indonesia's approach to family planning reaches beyond mere birth control to include the overall improvement of family welfare and quality of life. Family planning becomes an individual and community responsibility and thus forms an integral part of "nation-building". Population and family planning education has introduced into in-school and post-school programs.

An overall strategy was defined and popularized through slogans. "A Small Family is a Healthy, Happy, Prosperous Family" came to be accepted over time as a watchword within villages across the nation. This integrated strategy called for making family planning more acceptable and effective at the grassroots level through a broad range of programs to improve the health and welfare of both mother and child. These programs provide a variety of services, including income generation, nutritional supplements, primary health care, agricultural assistance, help in forming cooperatives, and educational scholarships — are intended to encourage active individual participation and commitment to other development programs and community efforts.

As part of the strategy to reach as many families as possible, households are organized by PKK volunteers into groups of ten. The groups meet monthly to record the number of pregnant and lactating women, births, infant deaths, as well as the immunization status of children under 5-years of age. The group also target illiterate members of the community for informal learning groups; discuss ways of preventing and combating maternal and childhood illnesses, promote family planning and plan small income-generating activities.

In coordination with BKKBN and the Ministry of Health, the PKK has organized a nationwide network of Integrated Community Health Services Posts, called Posyandu, with at least one post in every village in Indonesia. Each Posyandu provides five basic services: immunization, nutritional counseling, family planning services, maternal and child health care and the control of diarrhea diseases (the leading cause of infant mortality). While each Posyandu is staffed by PKK-trained volunteers, technical support in the form of contraceptives, medication and medical personnel is provided by the Ministry of Health.

By 1990, 67,000 village posts and more than 190,000 posts in hamlets were operated by local family planning volunteers, mobilized by the PKK and coordinated by BKKBN fieldworkers. At least one out of every fifty villagers does some work without pay to promote family planning. The goals are: • avoid childbirth before age 20, , limit the number of children to two per family and f space children at least three years apart.

Along with prenatal care, pregnant women are offered advice on how to prevent their next pregnancy. Women with infants and small children are taught to avoid illnesses through nutrition and immunization. And are then shown that they can take better care of the children they already have by postponing future ones or refraining from having additional children altogether.

PKK volunteers have also established family planning clubs, made up of family planning acceptors in each community or village. These acceptor groups are directly involved in motivating non-users and counseling new acceptors, as well as in the resupply of consumable contraceptives such as oral contraceptives and condoms.

In a typical village on Java, a mother of three who has practiced family planning regularly since the birth of her last child receives a ten percent discount card which is redeemable indefinitely for all food at her local grocery. The card is also honored by most Indonesian cinemas, insurance companies and merchants.

Coconut seedlings are donated by the Government to family planning acceptors. The BKKBN, in cooperation with the Ministries of Agriculture and Home Affairs, organizes education and training sessions for the management and care of the seedlings and selects family planning acceptors who will receive the seedlings as a reward for their participation in the program.

The Activity for Increasing the Family Income of Acceptors (UPPKA) program aims to achieve four goals: • increase the economic skills and incomes of family planning participants, , provide economic opportunities which directly relate to a happier family life, f augment the status of Indonesian women by increasing their active involvement in economic decision making and , help the family join self-reliant family planning movements.

The Community Incentive Project (CIP) provides financial and technical assistance for the construction of physical facilities at the village level. Such projects include clean water sources, public roads, village markets and clinics. Loans are made to village family planning acceptor groups or individual group members for a period of one year, developing the ability among villagers to plan for themselves, according to their own needs.

The nationwide information campaign focuses on two main messages: "A Small Family Is a Happy, Healthy, and Prosperous Family," depicted by two smiling children bracketed by their parents; and the more straightforward and succinct Dua Anak Cukup, "Two Children Are Enough." The theme is repeated everywhere, in all manners and forums. On the back of a five-rupiah coin, the smallest denomination in circulation, is displayed a two-child family with the message "Family Planning: the Way to Prosperity." Everywhere, posters bearing this message greet people from billboards and storefront windows. Family planning subjects are written into soap opera and film scripts, as well as radio and television programs. Even Indonesia's ancient puppet theater programs, the wayang kulit and wayang golek, feature family planning storylines.

The wide availability of highly subsidized contraceptives has been an important ingredient in the success of Indonesia's family planning program. Indonesian contraceptive manufacturers currently meet approximately 90 percent of domestic demand.

During the past few years, much of Indonesia has been in a stage in which most people are in favor of family planning and have already internalized its importance.

In 1987 BKKBN launched an International Training Program (ITP). As part of the ITP, BKKBN offers both bilateral and multilateral courses. Spurred by the success of the International Training Program (ITP), Indonesia is pursuing additional international cooperation for family planning programs, including an expanded training program; contraceptive commodity exchange; and technical assistance.

5.2. Collaborating agencies

The following bilateral, multilateral and NGO's international agencies collaborate with the government, national organizations, social groups and individuals in the field of research, interventions and evaluations of projects related to FP and other RH domains:

- 1. World Health Organization (WHO)
- 2. United Nations Development Program (UNDP)
- 3. World Bank
- 4. United Nations International Children's Educational Fund (UNICEF)
- 5. United States of America, Agency for International Development (USAID)
- 6. John Hopkins Program for International Education in Gynecology and Obstetrics (JHPIEGO)
- 7. The Pathfinder International
- 8. International Association for Maternal and Neonatal Health (IAMANEH)
- 9. Asian Development Bank (ADB)
- 10. International Training in Health (INTRAH)
- 11. American Voluntary Sterilization Corporation (AVSC) International
- 12. Family Health International (FHI)
- 13. Population Council
- 14. United Nations Population Fund (UNFPA)
- 15. The Program for Appropriate technology in Health (PATH)

And many others.

6. Associations 6.1. Indonesian Medical Association (Ikatan Dokter Indonesia - IDI) The association was created on October 24th, 1950. The aim of the association is to bring together Indonesian physicians, promote research activities among members and improve health activities. 6.2. The Indonesian Society of Obstetrics and Gynecology (ISOG) The Indonesian Medical Association has only 476 members when it was created on October 24th, 1950. During that time, there was only less than 10 Obgyn specialists. The International Federation of Obstetrics and Gynecology was created during that period of time, and one of the advantage in joining such an international federation is the possibility to send junior obgyn's for a fellowship abroad. In order to join the federation, the Indonesian Society of Obstetrics and Gynecology was stated on July 5th, 1954 in Jakarta by Dr.Sarwono Prawirohardjo, Dr.Gulam, Dr.Imam Sujudi and Dr.Makaleuw.

The ISOG establish the Obstetrics and Gynecology Post-graduate Education Curriculum Catalog and counterpart the Ministry of Education and Cultural through its Board of Study.

6.3.	Indonesian Society for Perinatology
	The society have developed a model of Obstetrics and Perinatal Emeergency Service, Management of Sick Neonates by Community Village Midwives, Kangaroo Care for Low-Birth Weight Babies in Rural Areas and Neonatal Resuscitation Training Package.
	Correspondence: Perinasia, Jl.Tebet Utara 1A/22 Jakarta 12820 (-fax +62 21 828 1243 E-mail: perinasi@centrin.net.id
6.4.	National Training Center Network to strengthen Clinical FP Training
6.5.	National Coordination Board for Family Planning Program (Badan Koordinasi Keluarga Berencana Nasional – <u>BKKBN)</u>
6.6.	Biomedics and Human Reproduction Study Group, Faculty of Medicine, Diponegoro University Semarang (KSBRM-FK Undip)
	Correspondence: KSBRM FK Undip – RSUP Dr.Kariadi Semarang, Gedung Serba Guna Lt.II Jl.Dr.Soetomo 14 Semarang 50231 Indonesia (-fax +62 24 441175 E-mail: ceuundip@indosat.net.id
6.7.	<u>Indonesian Society for Pediatricians (Ikatan Dokter Anak Indonesia – IDAI)</u>
6.8.	AVSC International Training Site Semarang
	The main objective of the training site is to conduct international training on Tubectomy Minilaparotomy under Local Anestesia (TMLA), No-Scalpel Vasectomy (NSV) and Health Quality Improvement by using competency-based training packages, coordinated and provided by AVSC international master and local trainers.
	All correspondence to Dr.Soerjo Hadijono SpOG, Klinik Mantap PKMI Cabang Jawa Tengah, Jl.Lingkar Tanjung Mas A.15 Semarang Indonesia (+62 24 558775 Fax +62 24 317650 E-mail: srobgyn@indosat.net.id
6.9.	Indonesian Society for Cancer (Yayasan Kanker Indonesia – YKI)
	The main objective is to reduce the incidence and prevalence of clinical gynecological cancers in Indonesia by the year 2000, through organizing regular cancer information, education and sensitization campaign.
7. Resear	ch Activities / National Organizations
Actions h	ave been taken to ensure that health research and technology will have continuing desirable influence the health as follows:
7.1.	Consensus building include:
	1. Setting priority in research

Processing of research formulation priorities have been coordinated and discussed with related Directorate General (Echelon I). The forum is for example R & D workshop in 1988 and 1993.

Research implementation have been carried out by involving health program personnel. (e.g. House Hold Survey 1986, 1992, 1995)

2.

3.	The research results have been informed and disseminated to Health Program Officers using particular
	discussions or meetings.

- 7.2. Capacity building include:
 - 1. Development of carriers structure
 - 2. Training activities for researchers, research administrators and laboratory assistants (innocently and abroad)
 - 3. Fellowship in the field of health related science to get higher degree (innocently and abroad)
 - 4. Development of research laboratory facilities

Improving research communications

- 5. Development of Health Literature and Library Information Services (Hellos) Network (national and international)
- **7.3.** Consolidation include:
 - 1. Mobilizing resources
 - 2. Ensuring the utilization of research's results
 - 3. Marketing of the research and development products
 - 4. Receiving R & D function in the provincial health office

The following organizations carry out research in various domains of RH, neither national projects or in association with international organizations:

- 1. Ministry of Health (MOH)
- 2. Ministry of Education and Cultural
- 3. Ministry of Religious Affair
- 4. Ministry of Social Affairs
- 5. National Coordination Board of Family Planing (BKKBN)
- 6. National Clinical Training Network

8. Perspectives for future projects implementation

8.1. Objectives and indicators of RH until the year 2003 (5-Years Development Plan)

1.

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Quantitatively, the number of pregnant women attended to by qualified personnel should increase to 80 % or more; the number of attended labour by qualified personnel should increase to 70% or more; the number of women of child bearing age using modern method of contraceptives should increase to about 80% or more

Qualitatively, quality health services should be able to attract more users and thus improve on the quality of life. Therefor more women were expected to use the MCH services with a reduction in the current maternal mortality rate to less than 225 in the year 2000. Similar quality services for adolescence would enable them to utilize FP services, so the number of unwanted pregnancies and unsafe abortions will decrease.

In general, improving RH means ensuring quality information to all detected high-risk cases and referring early enough for a higher level management, providing good transportation system so that referred cases can arrive at the appropriate health centers, offering high quality training and recycling of personnel and providing good working conditions.

- 2. Improve the health status of women during their reproductive age, so that they can enjoy quality RH. This means that more women should be allowed to take decisions on matters directly affecting their lives like the number and when to bear children, prevention against STD and decrease the infertility rate to 15% or less.
- 3. Improve prenatal care in order to bear children with normal parameters as accepted by international standards and offer immunization prevention to mother and child. The overall goal would be to reduce the infant and under-five morbidity and mortality rate.
- 4. Improve the RH of adolescents so that they may enjoy RH in the real sense as defined by WHO.

The overall goal of RH will be develop strategies which will enable individuals to enjoy RH right by promoting gender equality, appropriate high quality health services, contraception, etc.

8.2. Objectives (Indicators of RH)

The following are the set indicators to be monitored (Under construction - the list is not exhaustive)

INDICATORS OF REPRODUCTIVE HEALTH	LAST REPORTED	PLAN TO REDUCE
Total Fertility Rate	2.9 (1992)	1.6 (2000)
Contraceptive Prevalence Rate	55.0 (1994)	
Maternal Mortality Ratio	391.0 (1997)	225 (2000)
Antenatal care coverage: Percentage of women attended, at least once during pregnancy, by skilled health personnel (excluding trained TBA's) for reasons relating to pregnancy		
Percentage of births attended by skilled health personnel (excluding trained or untrained TBA's)	36.0 (1994)	

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Number of facilities with functioning basic essential obstetric care per 500,000 population			
Number of facilities with functioning comprehensive essential obstetric care per 500,000 population			
Perinatal mortality rate	49.0 (1995)		
Low birth weight prevalence: percentage of live births that weight less than 2,500 g	14.0 (1994)		
Prevalence of positive syphilis serology in pregnant women	N/A		
Prevalence of anemia in women			
Prevalence of obstetric and gynecological admission owing to abortion	N/A		
Reported prevalence of women with female genital mutilation			
Prevalence of infertility in women: percentage of women of reproductive age (15-49 years of age) at risk of pregnancy (not pregnant, sexually active, non-contracepting and non-lactating) who report trying for a pregnancy for 2 years or more			
Reported incidence of urethritis in men (15-49 years of age)			
Source:HRP UNDP/UNFPA/WHO/World Bank Special Programme of Research, Development and Research Training in Human Reproduction. Annual Technical Report 1997. WHO. Geneva 1998; Wang YF, Rowe P. Visions and Strategies of Regional Cooperation in Reproductive Health Research Asia and Pacific. Bangkok. 1998; Departemen Kesehatan RI; Badan Koordinasi Keluarga Berencana Nasional RI			

8.3. Population and Development

Indonesia's State Policy Guidelines aim for "harmonious balance in the development of people and of the whole of society in all aspects of life". Before the end of the century, Indonesia will have reduced its population growth to 1.6%, giving it the lowest growth rate of any low- or middle-income developing nation. In contrast, the nation's explosive growth rate in the 1950s and 1960s caused its population to double in just two decades. Indonesia has achieved this significant reduction as a part of general improvement in the health and quality of life of its people, including a fertility rate which has fallen by more than 40%, lowered maternal and infant mortality, and longer life expectancy. The Center for Population and Family Health at Columbia University has ranked Indonesia among the top five of 94 countries for its efforts in controlling population growth.

But the real rewards of this successful program are the opportunities it has created for future generations of Indonesians and the dramatically improved quality of life for Indonesians today.

By taking a comprehensive, cooperative approach that balances the development of individuals as well as of society,

Indonesia will achieve its goal of controlling population growth and mapped a strategy for success that is an example for other nations. The above objectives can only be achieved if future project planning and implementation takes into account the eventual socio-demographic changes (population growth, urbanisation, life expectancy, crude birth and death rates, schools, job availability and basic social amenities like water, electricity, health units etc.)

All these demographic changes will affect urbanization with its inherent problems. Therefor this needs to be taken into consideration when drawing up development plans.

8.4. Health Policy and Strategy

Based on the principles of Health Development, the long-term health development should be carried out according to the following policies:

• Health endeavors should be comprehensive, integrated, evenly distributed, can be accepted and accessible to all the people, and carried out with active community participation

, Priority will be given to the low-income group, infants, children and mothers, and the labour force, based on the level of morbidity and mortality

f Health endeavors should apply science and appropriate technology with a cost that the government and community can afford

" Resources for carrying out health endeavours are to be used rationally, so that selected action for dealing with each problem give optimal result and health endeavours should be adjusted to demographic, socio-cultural and economic factors of each region.

8.5. Approach

Indonesia has a low rate of utilization and provision of antenatal services, with a high maternal mortality. The population is still have low access to RH services caused by low income and inappropriate service ability. The concept of RH is still new even to some health personnel, government policy towards international organizations interested in RH are not fully supported etc. A change in this approach is needed to advance RH.

1. Humanistic Approach to RH

The RH concept definition and components should widened to include in all existing health structures or personnel and require to be integrated at all levels of the health care system. Its focus will not only be on MCH/FP as in the elapsed time, but will be expanded to include all the components of RH. All the effort required is creating awareness, motivation and coordination.

Health care service providers including RH services must competently skilled to provide high quality care and less risk for clients by using humanistic competency-based training and anatomic models for quality and skill improvement.

2.

Client and Patient Orientation

RH does not require physically ill condition seeking for health service. RH "patients" are considered as clients, then examinations should be carried out regularly to discover what they need or lack. Services should orientated towards the unmet needs or services. Health personnel need to know that they are providing their services to potential users and not the current practice where health personnel feel that RH is a disease state.

3. Competency-based Training for Reproductive Health and Family Planning

Competency-based clinical skills training builds on each participant's past knowledge and takes advantage of his/her high motivation to accomplish the learning tasks in the minimum time. Training emphasizes doing, not just knowing, and uses competency-based evaluation of performance. Successful completion of the course is based on mastery of both the content (knowledge and attitudes) and skills component (i.e. satisfactory performance on mid-course questionnaire and competency-based performance evaluation by the trainer).

Courses should be based on:

- 1. A reference manual containing only "need-to-know" information
- 2. A course handbook containing a validated (field-tested) questionnaire and learning guides that break down each activity or procedure into its essential components
- 3. Well-designed slide sets, video tapes and other teaching aids linked to the learning guides and to the information in the reference manual
- 4. Questionnaire and checklists for use in evaluating performance

Effective training will use these four essential elements to facilitate the learning process and foster competence in the task or activity. Training in clinical skills should make as much use of teaching techniques that minimize risk to clients. For example, the use of well-designed visual aids and anatomical model rather than clients for training at the skill acquisition and skill competency levels should be encouraged. Effective training with models facilitates learning and shorten training time, and is therefore an important factor in improving the quality of clinical skills training and minimizing risk to the client.

4. Health Service Providers Training Quality Improvement

Under ISOG's leadership and working with external assistance as appropriate and needed, the following steps to begin technical strengthening of the proposed clinical practice training sites should be undertaken:

- a. The clinical skills of any faculty member who might participate as a MCH/FP clinical trainer and all of staff who provide clinical MCH/FP services at each training clinic should be standardized.
- b. The clinical training portion of the RH component of the curriculum taught in the corresponding medical school should be reviewed and revised, as necessary, to conform to the National Resource Document Guidelines

National MCH/FP clinical training quality improvement team should be integrated in the MOH system at all levels of health services

9. Necessary inputs for the future

c.

9.1. Overall assessment and strategic issues

The strategic issues identified were the following:

Health status – The slow decline of mortality rates particularly the maternal mortality rate (MMR), emerging and re-emerging diseases and malnutrition

Health policy, promotion and health protection – Efforts were made to reallocate some of the subsidies for public hospitals to support primary health care services, particularly for the under served by means of converting hospitals into self supporting service units

Development of health system – Some crucial issues in this respect are law enforcement and legislative actions, private health care, review of functions of MOH and pollution

Health services - Although availability of health care has been improved, attention needs to be paid to the quality of care

Socio-economic development – The impact of rapid socio-economic development has been mostly positive although several disadvantages have been identified such as environmental health problems, lifestyle changes etc.

International partnership – Developing partnership with other development sectors, private sector, NGO's, community organizations and international agencies

9.2. Infrastructure

Management of health resources – Some of the crucial issues in this area were the allocation of public funds to support interventions which are cost-effective. An example is the recruitment of new HRH (medical doctors, dentists, midwives and pharmacists) under a contract agreement in accordance with the national policy of zero growth for public servants. The present infrastructure belonging to the MOH at all levels is enough for offering RH services. Most of the structures are under-utilized. All that is required is reorganization of the structures to accommodate the different components of RH.

9.3. Research

The government has taken measures to promote research as: • the creation of the department of studies, planning and health information in the MOH in order to promote operational research, the training of personnel at both the district and provincial levels in research in order to promote research at these levels, f the system where each graduating student presents a research thesis is aimed at encouraging research at the early stage.

Efforts have been made to improve research capability, strengthening of researchers, institutional strengthening, coordinated planning of research projects and better utilization of research results. Main constraints are limited funding, poor utilization of research results and need for institutional strengthening.

9.4. Government Policy (Under-construction)

10.1. Trends in socioeconomic development	
10.2. Health and Environment, Health resources	
10.3. Health services	
10.4. Trends in health status	
10.5. Demographic distribution of population	

04.12.02

REPRODUCTIVE HEALTH IN LITHUANIA

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Maternal Health, Safe Motherhood

Since the beginning of the Safe Motherhood Initiative (Nairobi 1987) many efforts have been spent on the issue of reducing maternal mortality in Lithuania.

Antenatal and birth care services in Lithuania are available for all women who need them and referral systems function well enough to ensure that women with complications get essential treatment.

Maternal Health, Safe Motherhood

95% of women in Lithuania receive antenatal care during pregnancy,95% give birth under skilled health professional assistance.

Maternal Health, Safe Motherhood

Lifetime risk of maternal death is 1 woman in 1200.

Maternal mortality ratio in 1990 was 26.3, in 1997 - 15.87 per 100,000 live births
Maternal mortality ratio in Lithuania (per 100,000 live births)



Source: Health for all database, WHO Regional Office for Europe, 1998

Perinatal mortality, infant mortality

Since 1992 the Preventive Program of Perinatal, Neonatal and Congenital Abnormalities was implemented in Lithuania. Due to reorganisation of perinatal services, establishment of modern equipped NICU in Perinatal centres, organisation of the neonatal transportation system, the main indicators of perinatal mortality have decreased remarkably. Perinatal mortality, stillbirths and early (0 – 6 days) neonatal death rates in Lithuania (per 1,000 birth)



Source: Basys et al. LTH, 1999

Infant mortality rate (per 1,000 births) in Lithuania





Sexually transmitted diseases

Sexually transmitted diseases (STD's) are one of the major reproductive health problems at present time in Lithuania.

Since 1992 the dramatic increase in reported cases of STD's in Lithuania was registered.

Syphilis incidence in Lithuania (per 100,000 population)



Source: WHO/EURO, UNAIDS. Copenhagen, 1999

HIV infection and AIDS

A national AIDS prevention centre was created in 1989.

The incidence of diagnosed HIV/AIDS cases has increased during the last few years in Lithuania, but it is significantly lower than the EU average.

Considering the high incidence of STDs and recent outbreaks of HIV infection in neighbouring countries, it is easy to predict a rapid spread of HIV infection in Lithuania.

Family planning

Contraceptive use in Lithuania:

IUD –17% COCs - 4.1% Condoms –19.2% Withdrawal –19.4% Abstinence and rhythm –17% Other methods –2.6%



Until recently, abortions were the most frequent measure of birth control in Lithuania.

The number of abortions per 1000 live births in Lithuania was 599.81 (*latest available data*).

High incidence of STD's and their sequelae, high abortion rate, specific problems of female ageing, violence against them, etc. should be addressed by the reproductive health care system in Lithuania.

Improved education and access to safe contraceptives are required to reduce the number abortions carried out as a mean of 'family planning'.

Family planning counselling and services should be available to all individuals of reproductive age and adolescents as well.

National screening programme for cervical cancer should be established urgently in Lithuania.

• A shift in the allocation of resources and redirection in medical education is required for the challenge of introducing evidence-based medicine in Lithuania.



A. Ledina



Population of the Russian Federation

Total 1 47.7 million Female 78.1 million Women of fertile age 38.5 million

(Health Ministry of RF, 1998)



Russian Federation

- Territory- 17, 075.4 thousand square km
- 89 ADMINISTRATIVE AND TERRITORIAL UNITS:
 - **21 Republics**
 - Autonomous region (oblast)
 - **10 Autonomous areas (okrugs)**
 - **6** Territories (krays)
 - **49 Regions (oblasts)**
 - **2** Cities of Federal subordination

In the Russian Federation reside

70 nationalities and ethnic groups

Birth rate (per 1000 population)





Death rate (per 1.000 population) 1997

















Marriages and divorces in Russia (per 1.000 population)







Infertility

15-16.2 % infertile couples in Russia



Russian Federation 1998



1.259.943 abortion

(32,8 per 1.000 women fertile age)



Complications after abortion

• 15.2% women 1 year after abortion out of them

52.4% women after 3-5 years

Russian Federation 1997

- 633 cases of maternal mortality
- 24.3% deaths due to inducted abortion, from them
- 84.4% deaths due to illegal abortions



Pregnancy outcomes (per 1.000 deliveries)





Health state of pregnant women (per 1.000 deliveries)





Infant mortality rates by main groups of Cases (death at < 1 year of age per 10.000 birth)





Morbidity with syphilis (per 10.000 population)





Russian Federation

10.631 cases of HIV-infection

1.01.1999

Demographic and social situation in the Russian Federation

- decrease in birth-rates and increase in death-rates
- high rates of maternal and infant mortality and morbidity, poor indices characterising pregnant women and adolescents health
- high abortion rates
- Inadequate use of modern contraceptives, hormonal ones primarily





avec la collaboration de

Dr Fekih Anis; Dr Farah Najah

et

le Département de Gynécologie et d'Obstétrique de Genève (Pr Aldo Campana)	
Histoire de la Tunisie	Publications et Recherches Médicales
<u>Géographie</u>	LLes indications des césariennes
<u>Société</u>	2.Les priorités en matière de santé reproductive en Tunisie
<u>Culture</u>	
<u>Environnement</u>	3.Les meilleurs liens de recherche médicale
Vie politique	4. Cervical assessment and other tests to predict preterm delivery
Économie	
Tourisme	5. Hypertension gravidique et mortalité maternelle
Informations Générale	
Mosaïques	



POUR TOUTES VOS SUGGESTIONS CONTACTEZ NOUS PAR E-MAIL

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