

SYSTEMATIC REVIEW PROTOCOL:



Interventions for the treatment of twin-twin transfusion syndrome

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IAMANEH Scholarship

- **Contributions:**

- Dr. Metin Gulmezoglu

- **Sources of support:**

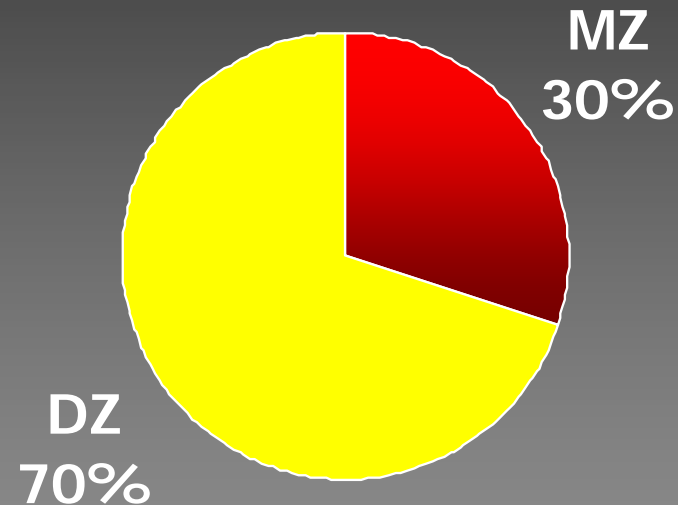
- The Geneva Foundation for Medical Education and Research
- The International Association for Maternal and Neonatal Health (IAMANEH)
- WHO, Department of Reproductive Health and Research (WHO/RHR)
- The Faculty of Medicine of the University of Geneva
- The Geneva Medical Association

Twin Pregnancies

Prevalence: 1,5-2%

- Zygosity

- **Monozygotic:** splitting of single fertilized ovum
- **Dizygotic:** fertilization and development from separate ovum



Monozygotic twins

- Monozygotic

- 0-3 days:

- Dichorionic/
Diamniotic (1/3)

- 4-8 days:

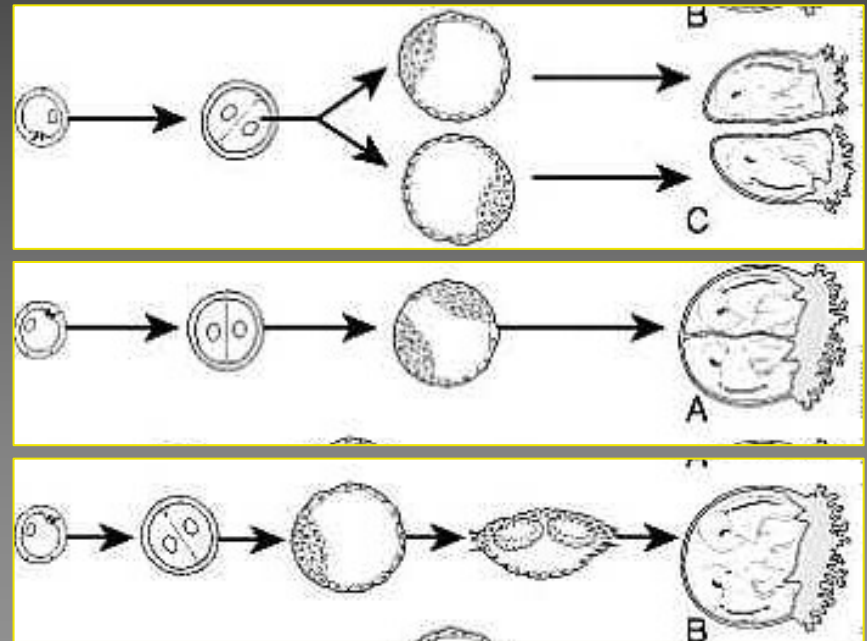
- Monochorionic/ Diamniotic

- 8-15 days:

- Monochorionic/
Monoamniotic (1%)

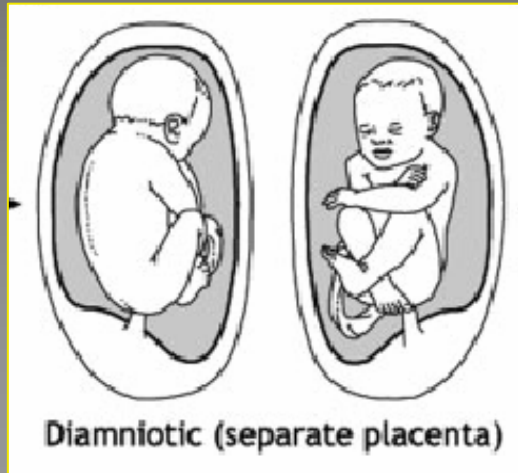
- >15 days:

- Conjoined

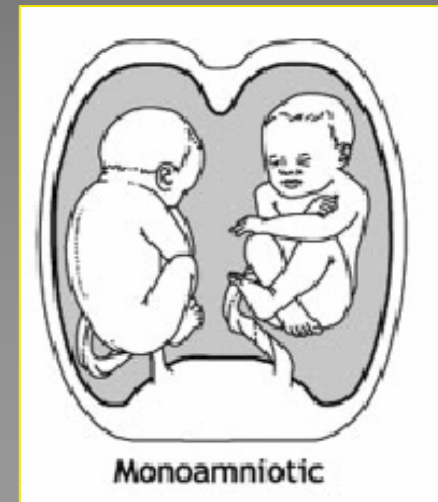
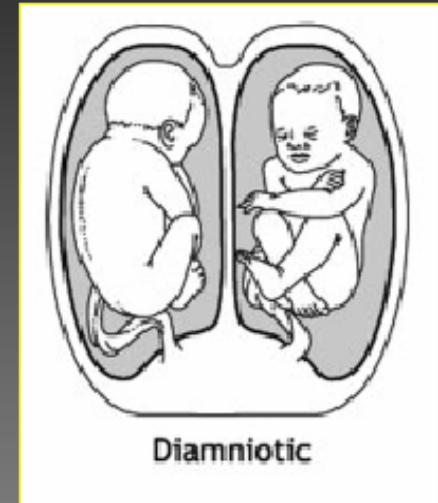


Chorionicity

- More important determinant of prognosis than zygosity
- Monozygotic, dichorionic prognosis similar to dizygotic, dichorionic



Dichorionic



Monochorionic

Complications of twin pregnancies

- Preterm Delivery
- Low Birth-weight
- Intrauterine Growth Restriction (IUGR)
- Preeclampsia
- Gestational Diabetes
- Placental Abruption
- Fetal Demise/Loss
- Cesarean rates

Perinatal Outcome of Twin Pregnancies

MISCARRIAGE	DC	MC
12-24 wks	1.8%	12.2%

MC

X 6

PERINATAL DEATH	DC	MC
>24 wks	1.6%	2.8%

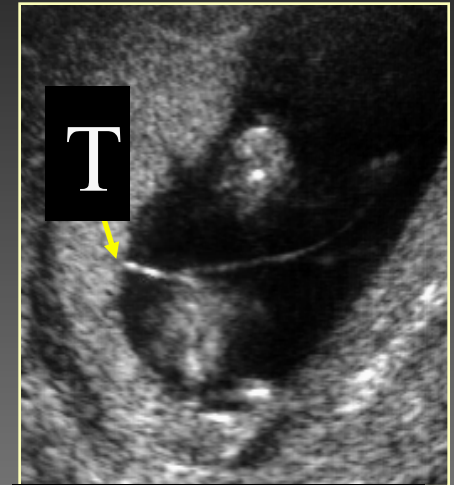
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GROWTH RESTRICTION	DC	MC
Total fetuses	12%	21%

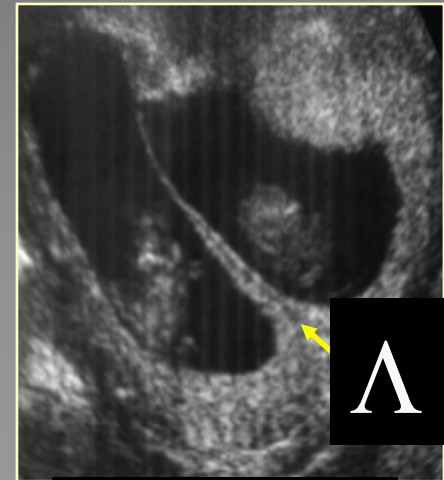
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PRETERM DELIVERY	DC	MC
Gestation <32 wks	5.5%	9.2%

X 2



Monochorionic 20%



Dichorionic 80%

Problems associated with chorionicty

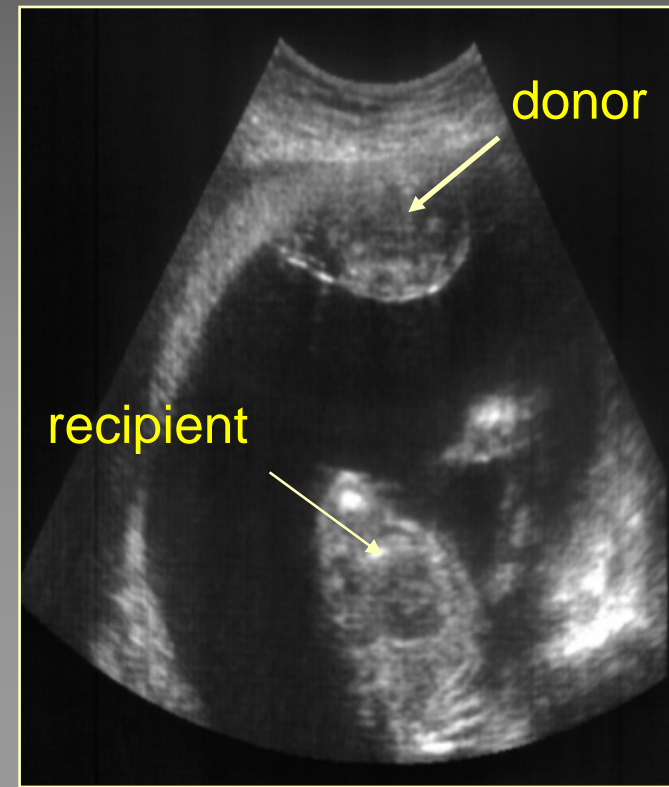
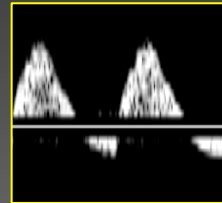
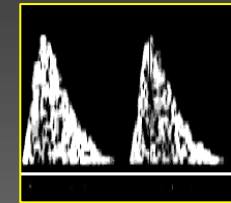
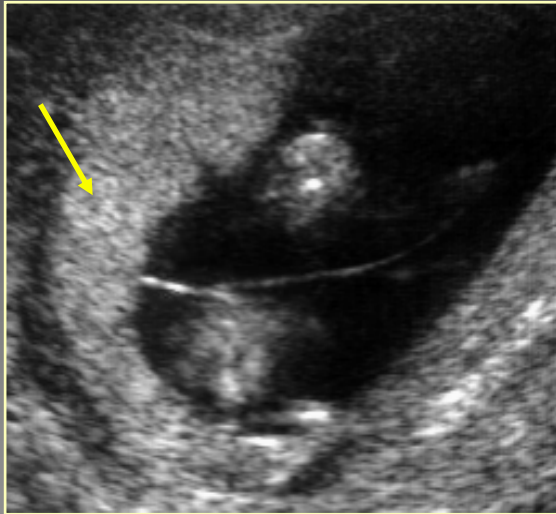
- Dichorionic:
 - Crowding problems
- Monochorionic:
 - Crowding:
 - talipes, congenital hip dislocation
 - Twinning:
 - conjoined twins, sirenomelia, NTD
 - Vascular exchange:
 - TTTS, acardia, embolization- microcephaly, limb amputation

Twin-Twin Transfusion Syndrome (TTTS)

- Unbalanced inter twin transfusions through placental anastomoses
 - Arterial- venous unidirectional anastomoses
- Donor twin
 - anemic, growth restricted
 - oligohydramnios, contractures, pulmonary hypoplasia
- Recipient twin
 - polycythemic, circulatory overload and hydrops
 - polyhydramnios, PPRROM, heart failure

Twin-Twin Transfusion Syndrome – Diagnosis:

- Monochorionic pregnancy
- Acute 2nd trimester polyhydramnios
- Normal fetal anatomy



Twin-Twin Transfusion Syndrome

- Occurs in 10% to 15% of identical twins
 - » Sebire 2000; Jain 2004
- The prognosis for both fetuses is extremely poor
 - mortality 60% - 100%
 - one third of survivors presenting with severe neurologic complications after birth
 - » Urig 1990; Skupski 1998; Cincotta 2000; Berghella 2001; Mari 2001

Treatment options

- Repeated serial amnioreduction
- Endoscopic laser ablation of anastomoses
- Amniotic septostomy
- Selective feticide

Amnioreduction

- Reduces uterine distension & PTL
- Correct hemodynamic inequalities in intra-amniotic pressure
- May lead to better uteroplacental perfusion
- May reverse TTTS
 - 60% survival, 20% neurological morbidity
 - » (Schneider 1985, Saunders 1991, Trespidi1997, Mari 2001)

Endoscopic laser ablation of anastomoses

Endoscopic laser

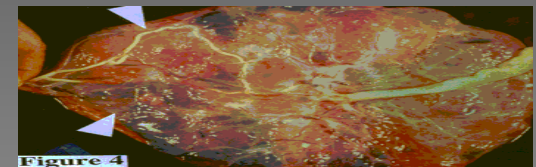
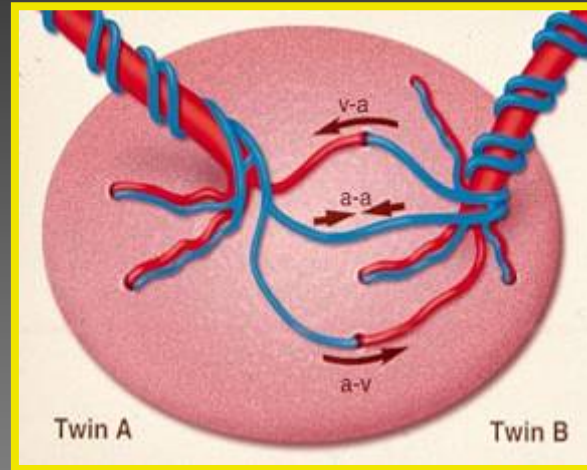
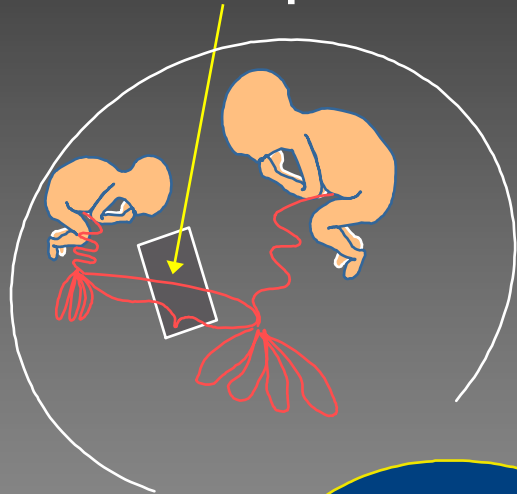
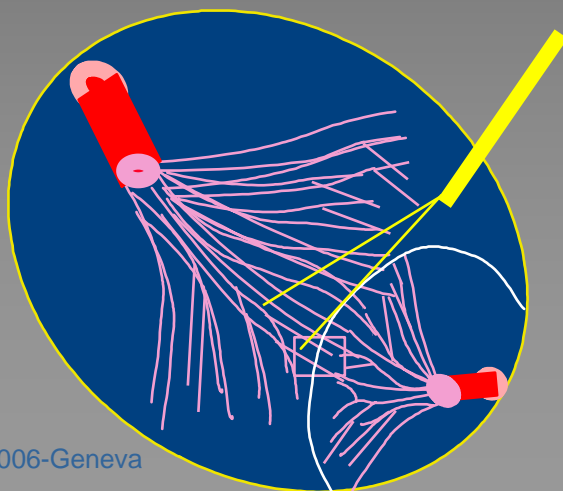


Figure 4



Figure 5



Survival 76%
periventricular leukomalacia 6%
Senat MV, 2004

Septostomy

- Equilibrates the fluid
- Donor can swallow some fluid
- TTTS rare in mono/mono twins
 - Survival rate 83%, but no figures for neurological outcome
 - » (Saade, Belfort et al. 1998; Moise, Dorman et al. 2005).
 - Cord entanglement
 - » (Gilbert, Davis et al. 1991).



Selective Feticide

- In the event of the death of one twin, approximately 25 to 50% of surviving twins will experience mortality or neurological handicap
 - » van Heteren 1998
- Techniques such as fetoscopic cord ligation and ultrasound guided vascular embolisation have been described
 - » Crombleholme 1996; Quintero 1996; Deprest 1998; Robyr 2005; Spadola 2005

Reason for this review

- The last systematic Cochrane review:
 - in 2001
 - found no evidence from randomized trials to influence practice
- There are some new studies

Quintero 2003; Senat 2004; Moise 2005

Criteria for selecting studies for this review

- **Types of studies:**
 - Randomised controlled trials
 - Quasi-randomised trials
 - Randomised studies

Comparisons of one treatment versus another will be considered.

Criteria for selecting studies for this review

- Types of participants:
 - Twin-twin transfusion syndrome diagnosed by ultrasound before 26 weeks:
 - confirmation of monochorionicity
 - oligohydramnios in one sac and hydramnios in the other
 - normal anatomy of both fetuses

Types of interventions:

- Any intervention performed as a therapy for twin-twin transfusion syndrome to improve
 - fetal, neonatal and childhood outcome
 - maternal symptoms
 - and prolonging pregnancy

will be reviewed

Types of outcome measures:

- Primary outcomes:
 - overall fetal survival
 - perinatal death
 - neuro-motor disorders
 - » intraventricular haemorrhage
 - » ventriculomegaly
 - » cystic periventricular leukomalacia
 - » seizures within 28 days of delivery/anticonvulsant therapy
 - » developmental delay at 2 years of age

Types of outcome measures:

- Secondary outcomes
 - Procedure related events
 - » number of interventions per pregnancy
 - » first intervention to delivery time
 - » need for a combination of therapies
 - » type of anaesthesia
 - Pregnancy outcome
 - » gestational age at birth
 - » preterm prelabour rupture of membranes (within 48 hours of procedure)
 - » preterm labour (within 48 hours of procedure)
 - » preterm labour/prelabour rupture of membranes prior to 32 weeks gestation.
 - » Neonatal outcome
 - » fetal haemoglobin discordance at birth
 - » need for blood transfusion within 48 hours of delivery
 - » use of mechanical ventilation
 - » admitted to neonatal intensive care unit
 - » length of stay on neonatal intensive care unit
 - Maternal outcome
 - » maternal death
 - » amniotic fluid embolism
 - » placental abruption
 - » chorioamnionitis
 - » intraperitoneal bleeding

Search strategy for identification of studies:

- The electronic sources of medical databases
- - MEDLINE/Pubmed
 - BioMed Central
 - ScienceDirect
 - Scitation
 - Pubmed Central
 - Cochrane Controlled Trials Register

will be used to identify relevant trials

Search terms used will be:

- Twin twin
- Fetofetal Transfusion
- Twin AND twin OR (transfusion) AND ("transfusion syndrome")
- OR Amnioreduction
- OR Amniodrainage
- OR Septostomy
- OR Laser coagulation
- OR Laser ablation
- OR Fetoscopic laser ablation

Methods of the review:

- Not blind: author's name, institution and the source of publication will be known by reviewer.
- Trials will be assessed for methodological quality and appropriateness for inclusion without consideration of results.
- The reason for excluding any trial will be stated.
- Data extraction will be performed by the contact reviewer and processed as described by Clarke in Cochrane Reviewers' Handbook, 1999.
- Statistical analysis will be performed using the Review Manager software (RevMan 1999).
- Relative risks and 95% confidence intervals will be calculated.

Date of last search: March 27, 2006

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Address <http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?CMD=meshlocation&DB=mesh>

Search PubMed for ("Fetofetal Transfusion/classification"[MeSH] OR "Fetofetal Transfusion/classification"[Text])

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Page 1 of 38 Next

- 1: [Kinnick V.](#) [Related Articles, Links](#)
Twin-to-twin transfusion syndrome.
AWHONN Lifelines. 2005 Dec-2006 Jan;9(6):512, 509-11. No abstract available.
PMID: 16480236 [PubMed - indexed for MEDLINE]
- 2: [Harkness UF, Crombleholme TM.](#) [Related Articles, Links](#)
Twin-twin transfusion syndrome: where do we go from here?
Semin Perinatol. 2005 Oct;29(5):296-304. Review.
PMID: 16360488 [PubMed - indexed for MEDLINE]
- 3: [Hayashi S, Sago H, Hayashi R, Nakagawa S, Kitagawa M, Miyasaka K, Chiba T, Natori M.](#) [Related Articles, Links](#)
Manifestation of mirror syndrome after fetoscopic laser photocoagulation in severe twin-twin

Eligible studies

- 1: Moise KJ Jr, Dorman K, Lamvu G, Saade GR, Fisk NM, Dickinson JE, Wilson RD, Gagnon A, Belfort MA, O'Shaughnessy RO, Chitkara U, Hassan SS, Johnson A, Sciscione A, Skupski D. **A randomized trial of amnioreduction versus septostomy in the treatment of twin-twin transfusion syndrome.** Am J Obstet Gynecol. 2005 Sep;193(3 Pt 1):701-7.
- 2: Senat MV, Deprest J, Boulvain M, Paupe A, Winer N, Ville Y. **Endoscopic laser surgery versus serial amnioreduction for severe twin-to-twin transfusion syndrome.** N Engl J Med. 2004 Jul 8;351(2):136-44.
- 3: Quintero RA, Dickinson JE, Morales WJ, Bornick PW, Bermudez C, Cincotta R, Chan FY, Allen MH. **Stage-based treatment of twin-twin transfusion syndrome.** Am J Obstet Gynecol. 2003 May;188(5):1333-40.
- 4: Ville Y, Hecher K, Gagnon A, Sebire N, Hyett J, Nicolaidis K. **Endoscopic laser coagulation in the management of severe twin-to-twin transfusion syndrome.** Br J Obstet Gynaecol. 1998 Apr;105(4):446-53.