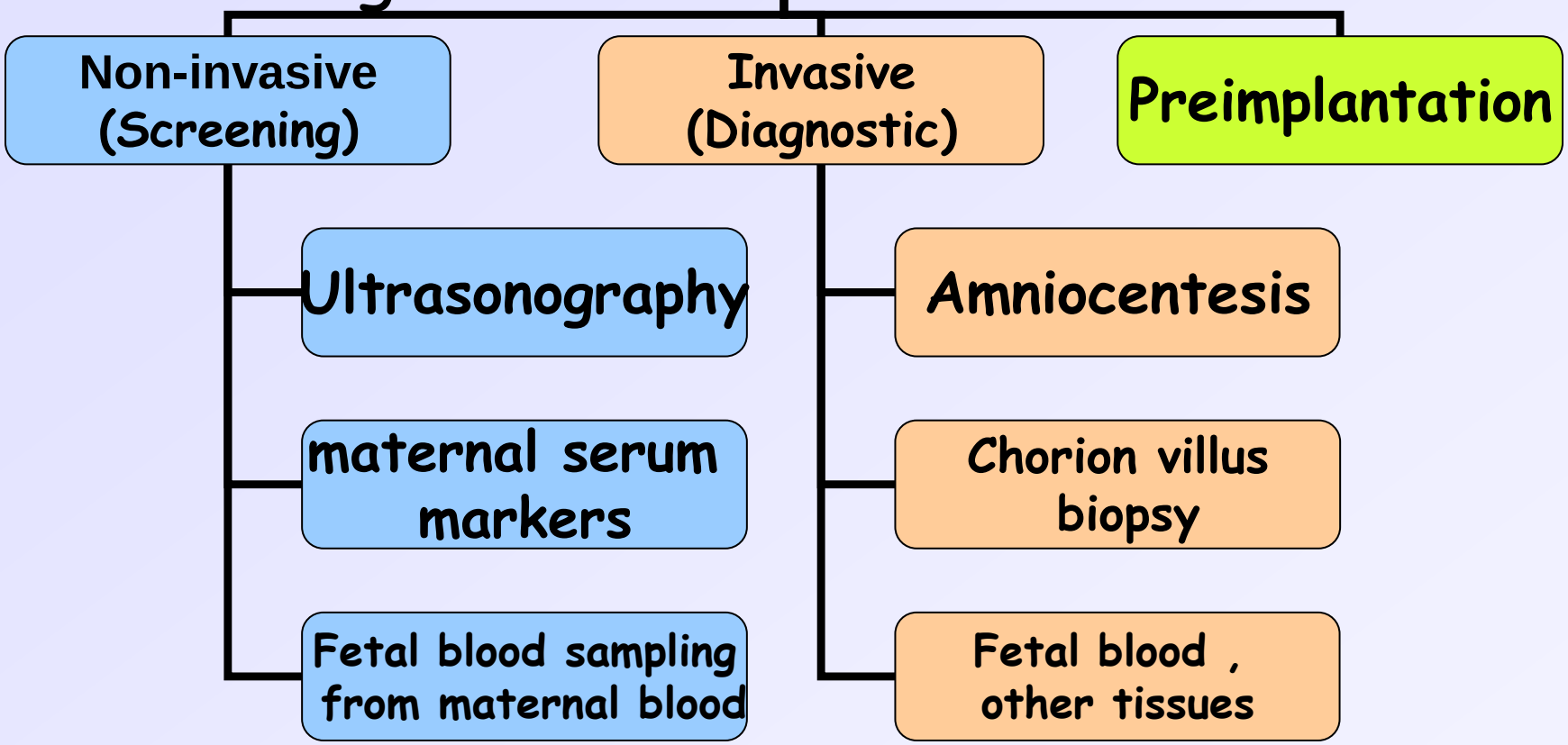
# Prenatal Genetic Diagnosis: Scope, Applications and Limitations in Arab countries

Professor Hanan Hamamy
GFMER
http://www.gfmer.ch/Medical_genetics_education_research/Hanan_Hamamy.htm

# Methods used for prenatal diagnosis of genetic fetal disorders

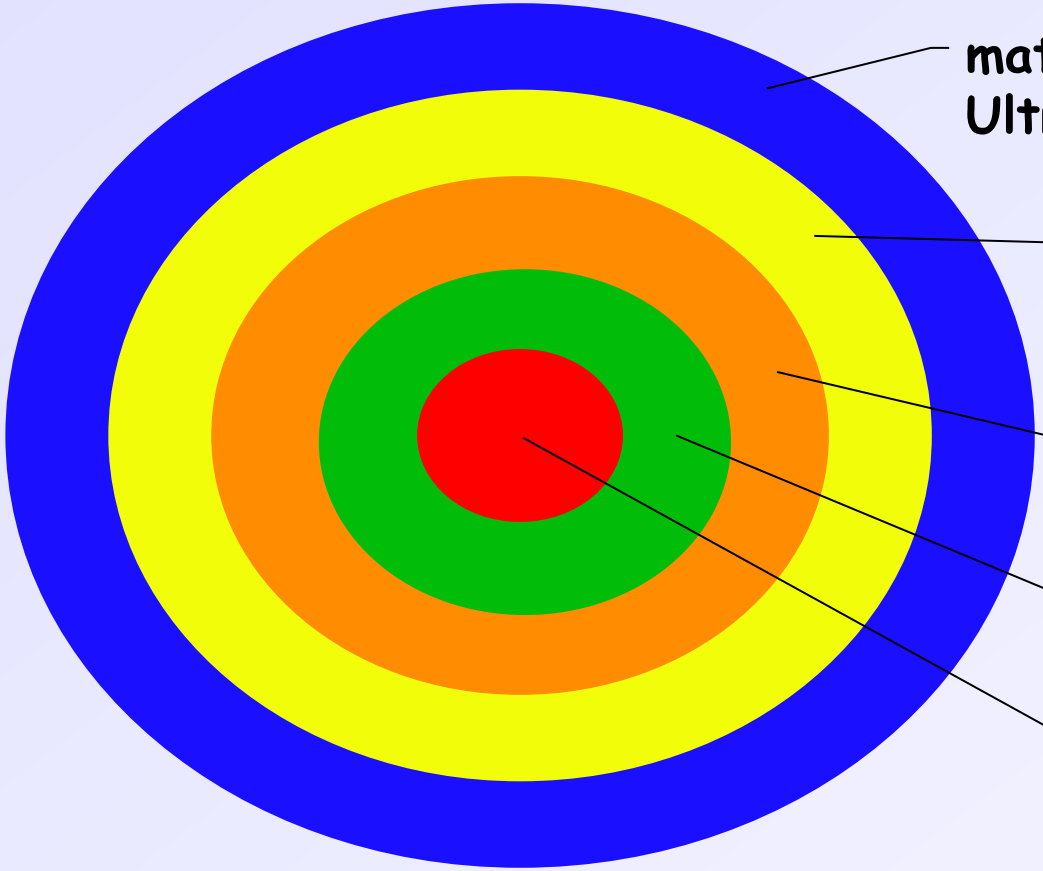


# Prenatal Screening facilities in Arab countries

- Ultrasound fetal scanning is routinely performed for any pregnant woman during her first antenatal visit. In most cases, no pretest information is provided to the couple on the possibility of finding an abnormality.
- Maternal serum markers' testing is another screening test that can diagnose certain congenital malformations and chromosome aberrations. This is offered by some obstetricians, but it is not mandatory.

- If the results of the test suggest an abnormality, then the couple will have to decide whether to take further invasive testing and be prepared to face the major decision of selective termination of an affected fetus.

# Progression of Prenatal screening



maternal serum markers
Ultrasound

Abnormal results

CVS
amniocentesis

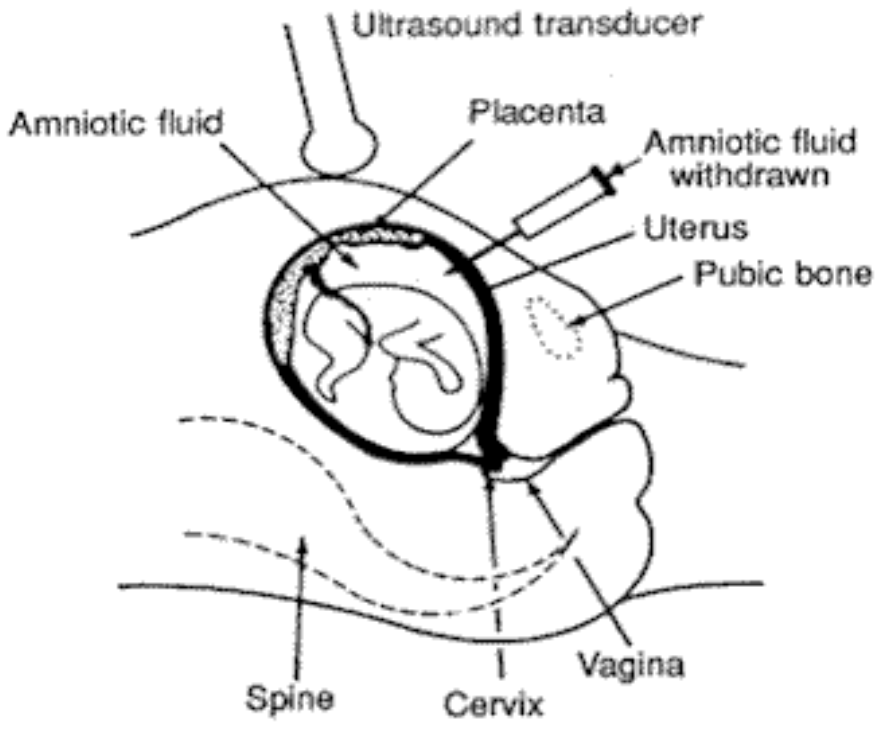
Abnormal results

Termination ???

# Indications for invasive prenatal diagnosis

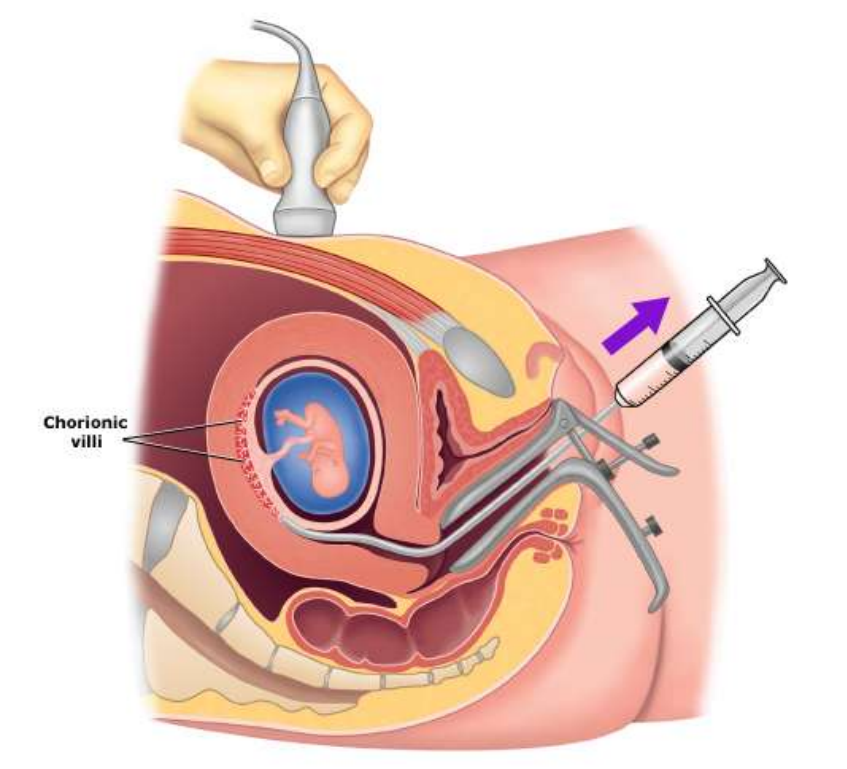
- Advanced maternal age; more than 35 years
- previous child with a chromosome abnormality ( probability of translocation carrier in parents)
- family history of a chromosome abnormality
- family history of single gene disorder
- family history of neural tube defect or other congenital abnormalities
- Suspicious US results and/or maternal serum markers

# Amniocentesis




- around the 14-16th week of gestation
- aspiration of 20 ml of amniotic fluid through the abdominal wall under ultrasound guidance
- 0.5-1% risk of miscarriage

# Chorion villus sampling




- Usually performed at 10-12 weeks gestation
- Transcervical aspiration of chorionic villi under ultrasound guidance
- About 1-2% risk of miscarriage

## Amniocentesis, chorionic villus sampling and genetic diagnosis in Arab countries

- Many cytogenetic laboratories are capable of diagnosing chromosome aberrations in fetal cell cultures whether obtained through amniocentesis or chorionic villus sampling.

- The diagnosis of single gene disorders in fetal cells is more difficult and requires specialized laboratories and advanced technology. For most common like thalassemia, the laboratory testing can be done in the country, for rare disorders, samples have to be sent specialised laboratories for testing.

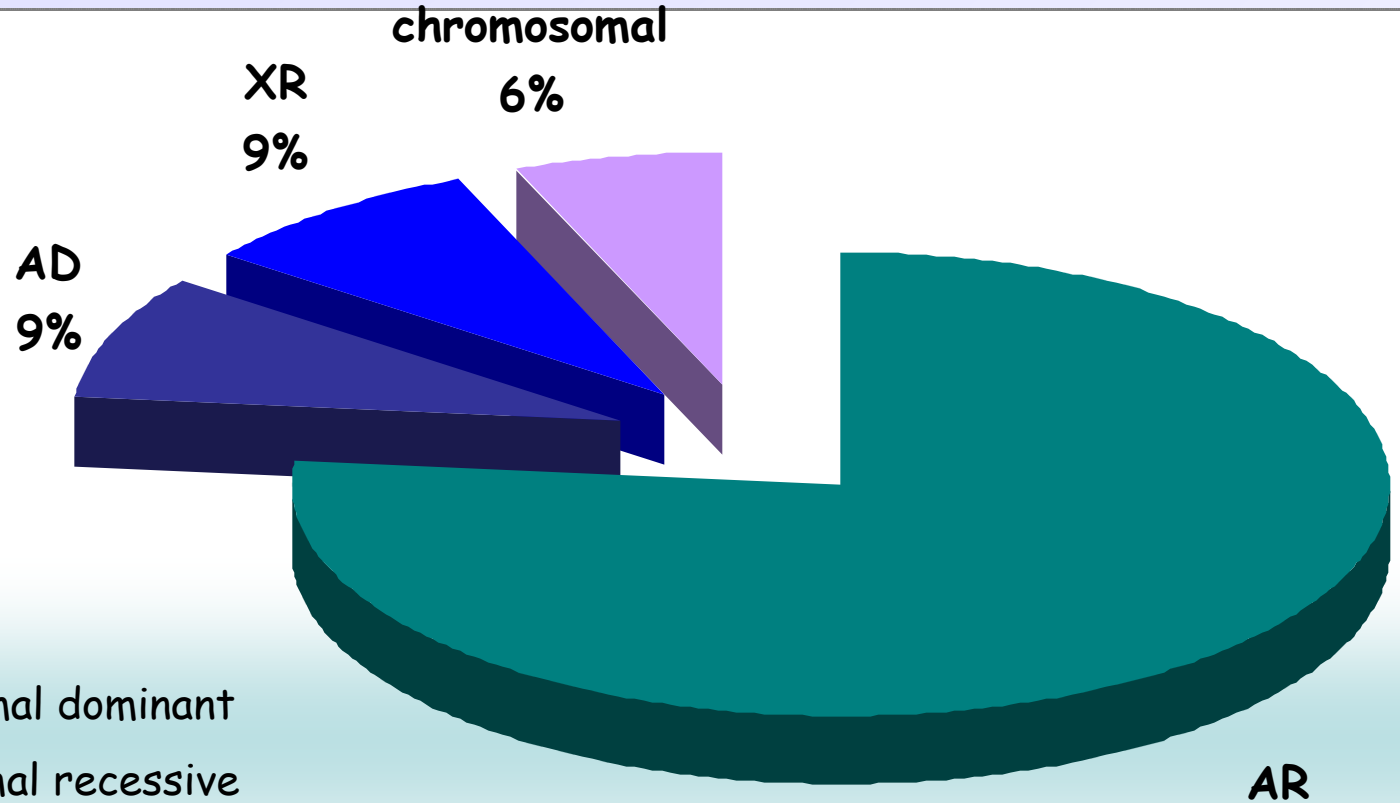
# Difficulties faced in prenatal diagnosis

- The main problem that is initially faced and has to be solved is to reach the diagnosis of the condition at the molecular level, when DNA analysis is the sole method for fetal diagnosis.

- A large percentage of requests for prenatal genetic diagnosis comes from families with autosomal recessive disorders.

- For molecular diagnosis ofless common and rare disorders, samples are usually sent to specialized laboratories in developed countries. This procedure requires a high cost, lengthy time and the availability of samples from the affected. Sometimes a molecular diagnosis is never reached because all affected offspring are dead.

# Categories of genetic diseases with request for prenatal testing among 81 families in a genetic center ( personal data)

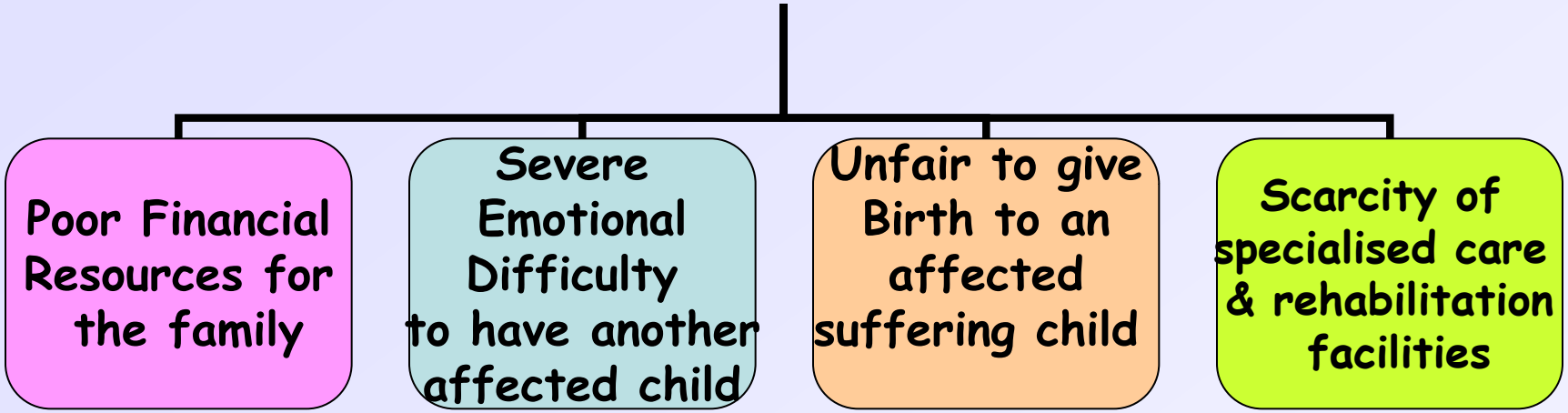



AD: autosomal dominant

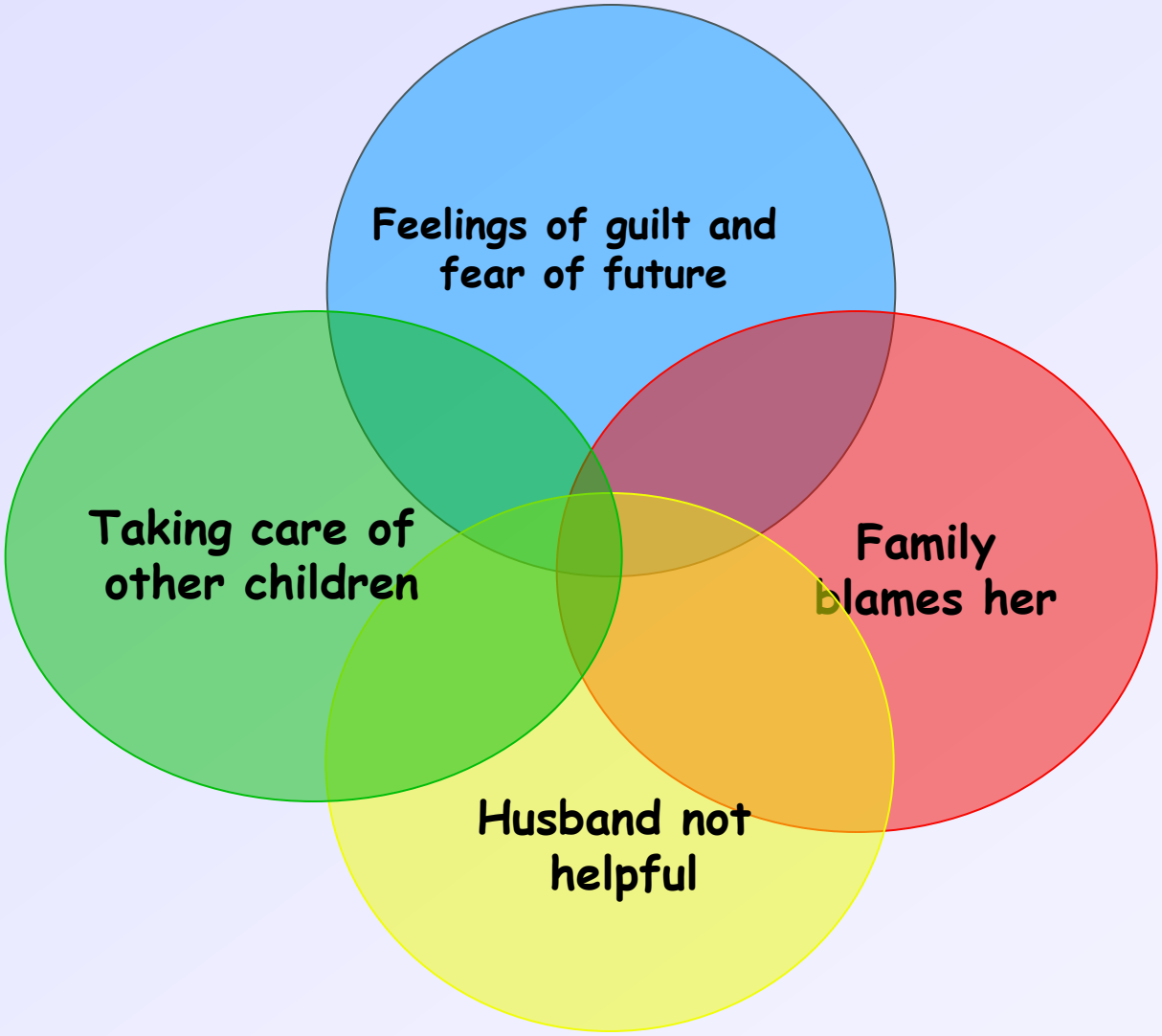
AR: autosomal recessive

XR: X-linked recessive

# Probable Reasons for requesting prenatal diagnosis



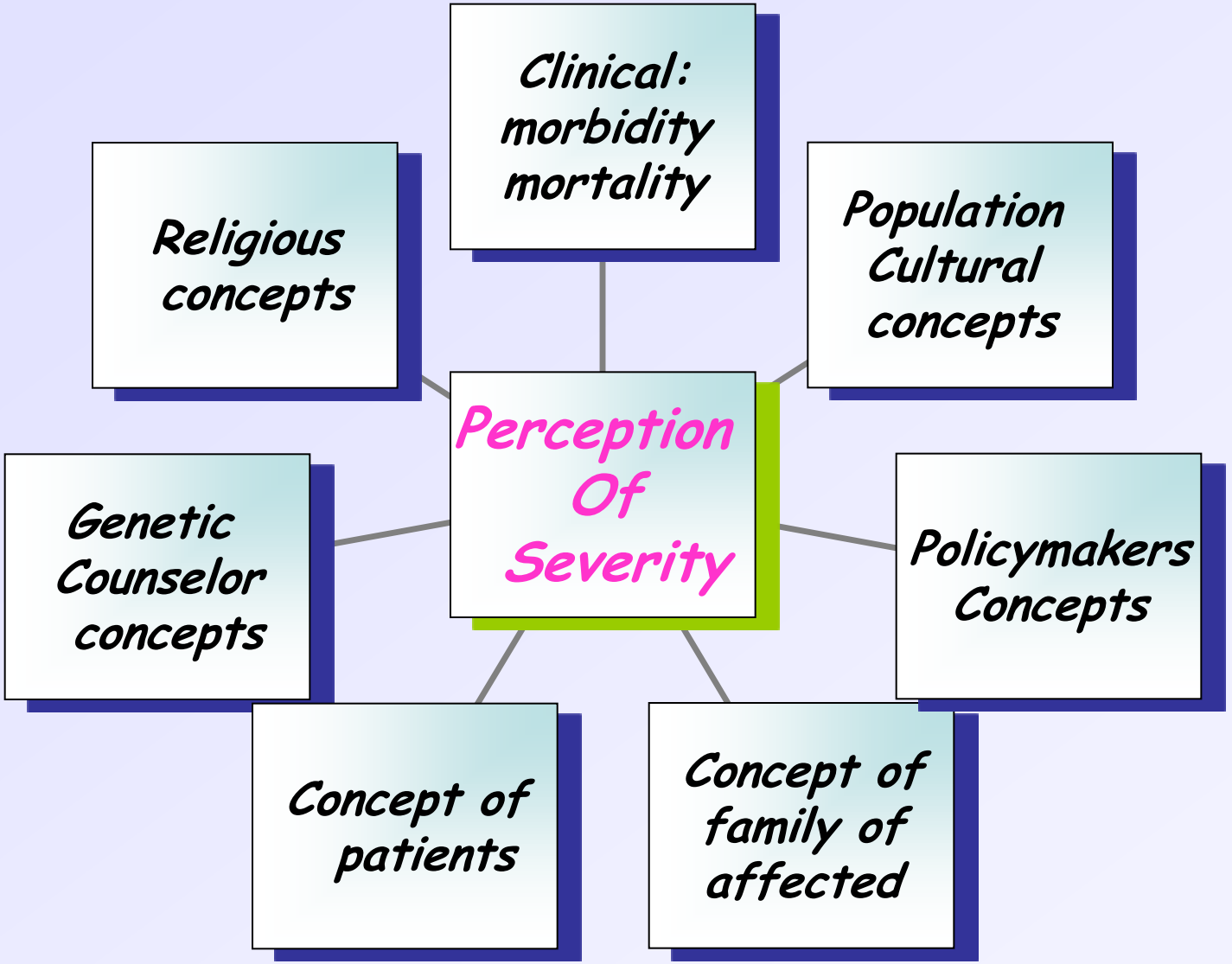
# Problems of the mother



# Selective termination of pregnancy when fetus is affected???

How can genetic and congenital disorders be categorized to ethically allow termination of an affected fetus???

1. Severity of disease?
2. Survival of affected?
3. Impact on family?
4. Impact on affected?
5. Impact on society and government?


Clinical: morbidity mortality
Religious concepts
Population Cultural concepts
Perception Of Severity
Genetic Counselor concepts
Policymakers Concepts
Concept of patients
Concept of family of affected

# Religion and therapeutic abortion

- There is a diversity of opinions among various Islamic institutions on the issue of pregnancy termination when the fetus is severely affected, which range from an absolute prohibition of abortion at any time post-conception to permission for termination before the 120$^{th}$ day of gestation under specific circumstances.
- All Arab countries permit abortion to save the life of a pregnant woman, but otherwise they differ quite widely in their legal indications.
- When the couple are in doubt of their religion limitations, they seek the opinion or the fatwa of an Islamic scholar to facilitate their decision-making regarding the early termination for a severely affected fetus.

# Preimplantation genetic diagnosis

- Preimplantation genetic diagnosis involves testing the early embryo after in vitro fertilisation. One or two cells (blastomeres) are removed at biopsy from the embryo at the 6-10 cell stage (day 3 of development), with implantation into the uterus of unaffected embryos

# Indications for Preimplantation Genetic Diagnosis

1. Detect chromosomal disorders by fluorescence in situ hybridization.
2. Determine the sex of the embryo for sex linked disorders where the specific genetic defect at a molecular level is unknown, highly variable, or unsuitable for testing on single cells.
3. Identify single gene defects such as cystic fibrosis, where the molecular abnormality is testable with molecular techniques after polymerase chain reaction (PCR) amplification of DNA extracted from single cells.

# Prospects for the role of prenatal diagnosis in the future

- Prenatal diagnosis can be followed by intrauterine or neonatal surgery for the correction of certain congenital anomalies such as cardiac and renal defects.
- In utero gene therapy could become a practical therapeutic option in the future for the treatment of serious monogenetic diseases.
- Prenatal diagnosis with in-utero transplantation offers the potential to treat a large number of diseases by transplantation of healthy cells into a fetus with a birth defect.

# Conclusions

- People differ in their beliefs and in their ability to endure stressful condition. There is a need for Arab and Islamic countries to develop clear strategies on prenatal diagnosis that is consistent with their social, ethical and religious beliefs and responsive to the needs of families with genetic disorders and the needs of the population in general when community genetic services are implemented.

# Conclusion

- Clear guidelines in Arab countries are needed to define the scope and limitations of prenatal genetic diagnosis and pregnancy termination when fetus is severely affected.