

# **Complications of Early Pregnancy & Pregnancy Loss**

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# TOPICS

- **Spontaneous abortions** :pregnancy termination prior to 20 weeks' gestation or less than 500-g birthweight
- **Congenital abnormalities**
- **Chromosomal abnormalities**
- **Hyperemesis gravidarum**
- **Ectopic pregnancy: extra-uterine gestation**
- **Gestational trophoblastic disease**

# OBJECTIVES

- **To be aware of the different types and causes of abortions**
- **To understand the causes and risks factor of birth defects**
- **To obtain knowledge on types of abnormal early pregnancy**
- **To be aware of the effects of severe vomiting in early pregnancy**

# Threatened Abortion

- **Bleeding through a closed cervix in first half of pregnancy**
- **Bleeding of expected menses, decidual reaction, Cervical lesions**
- **No effective therapy**
- **Half will abort**
- **Increased risk for preterm delivery, low birthweight, & perinatal death**
- **Vaginal sonography, serial serum quantitative human chorionic gonadotropin (hCG) levels, serum progesterone values**
- **Anti-D immunoglobulin because up to 5 % of D-negative women become isoimmunized**

# Inevitable Abortion

- **Leaking amniotic fluid**
- **Cervical dilatation**
- **Heavy bleeding**
- **Severe pain**
- **Impending abortion**
- **Risk of incomplete abortion or sepsis**
- **Uterine evacuation**

# Incomplete Abortion

- **Partial expulsion with retained products of conception (POC)**
- **Open internal cervical os, bleeding,**
- **Ultrasound or pelvic exam shows POC**
- **Hemorrhage, Sepsis**
- **Uterine evacuation**
- **Complete Abortion**
- **Closed internal cervical os**
- **Ultrasound = Normal endometrial stripe**

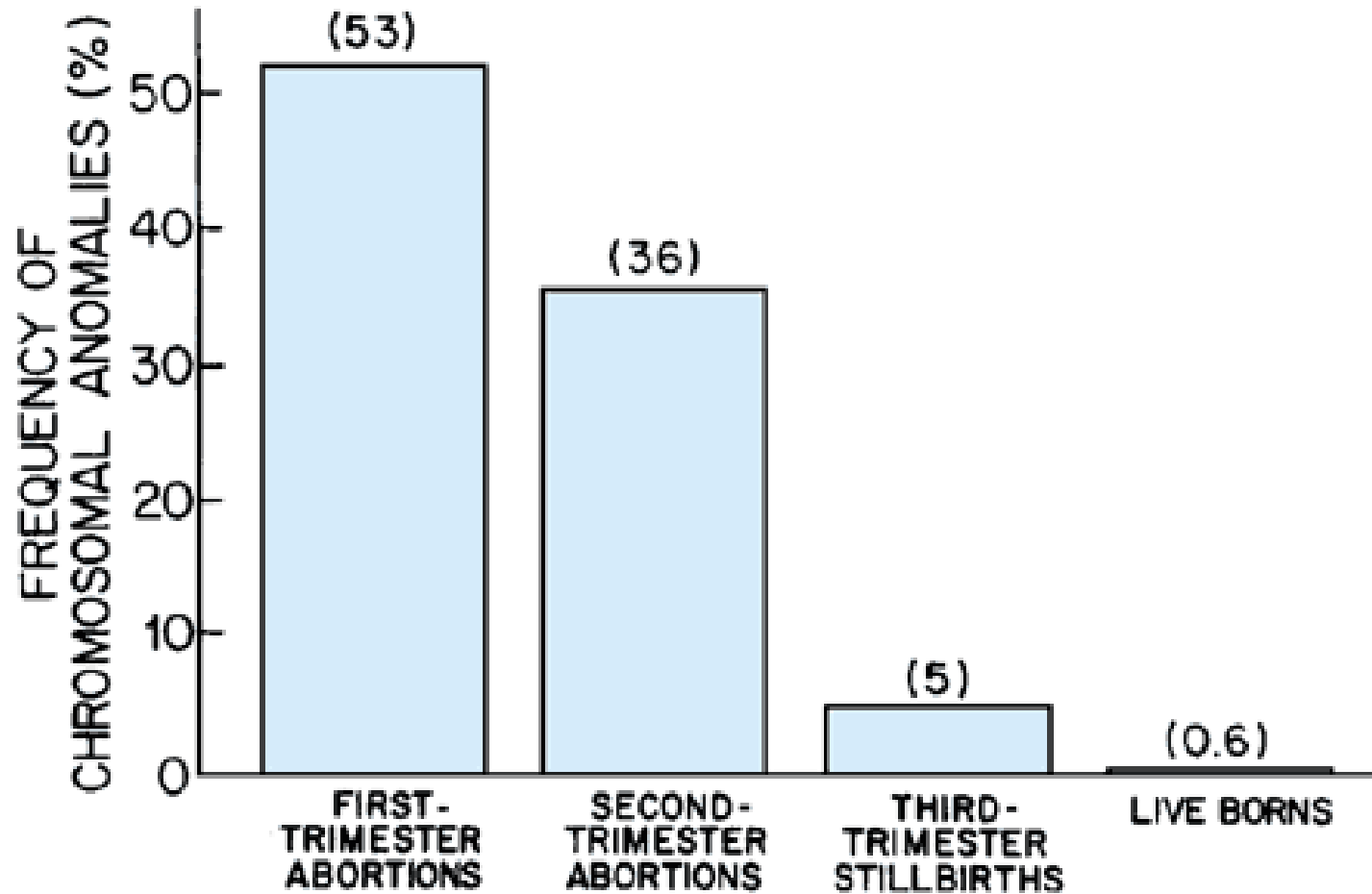
# Missed Abortion

- **Dead products of concept is retained inside uterus**
- **Maybe associated with coagulation defects**
- **Expectant, medical or surgical management**

# Recurrent Abortion

- **3 or more consecutive spontaneous abortions**
- **Risk of 1 loss = 10-15 %**,
- **Risk of 2 losses = 2.3 %**
- **Risk of 2 losses = 0.34 %**
- **Parental cytogenetic analysis**
- **Antiphospholipid antibodies**
- **If previous liveborn; risk for subsequent abortion was 30 %.**
- **If no liveborn, the risk of subsequent abortion was 46 %**

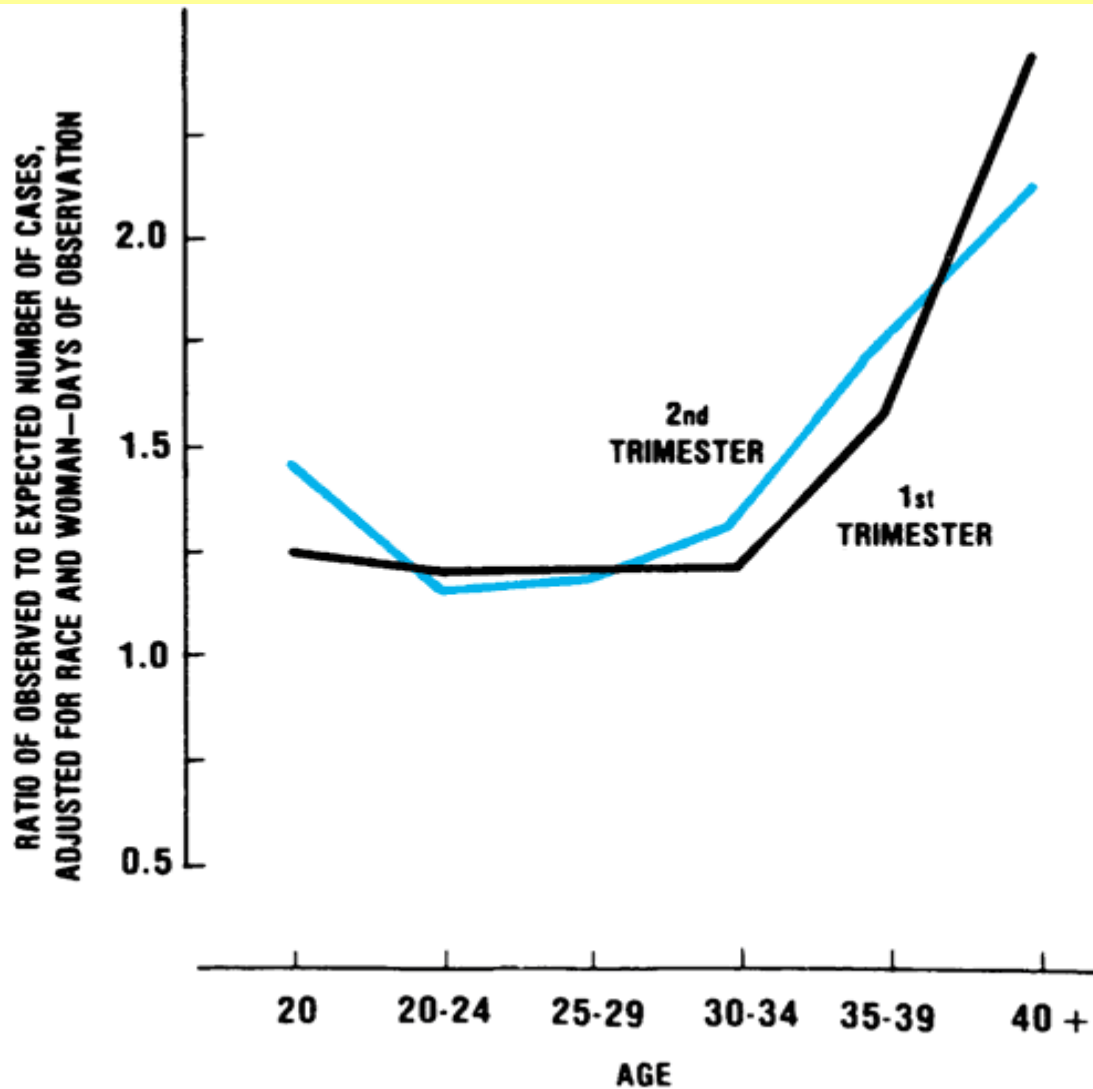
# Frequency of chromosomal anomalies in abortuses & stillbirths. (%) (Fantel, 1980; Warburton, 1980, et al.)



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# First- and second-trimester spontaneous abortions by maternal age.

(From [Harlap and colleagues, 1980](#))

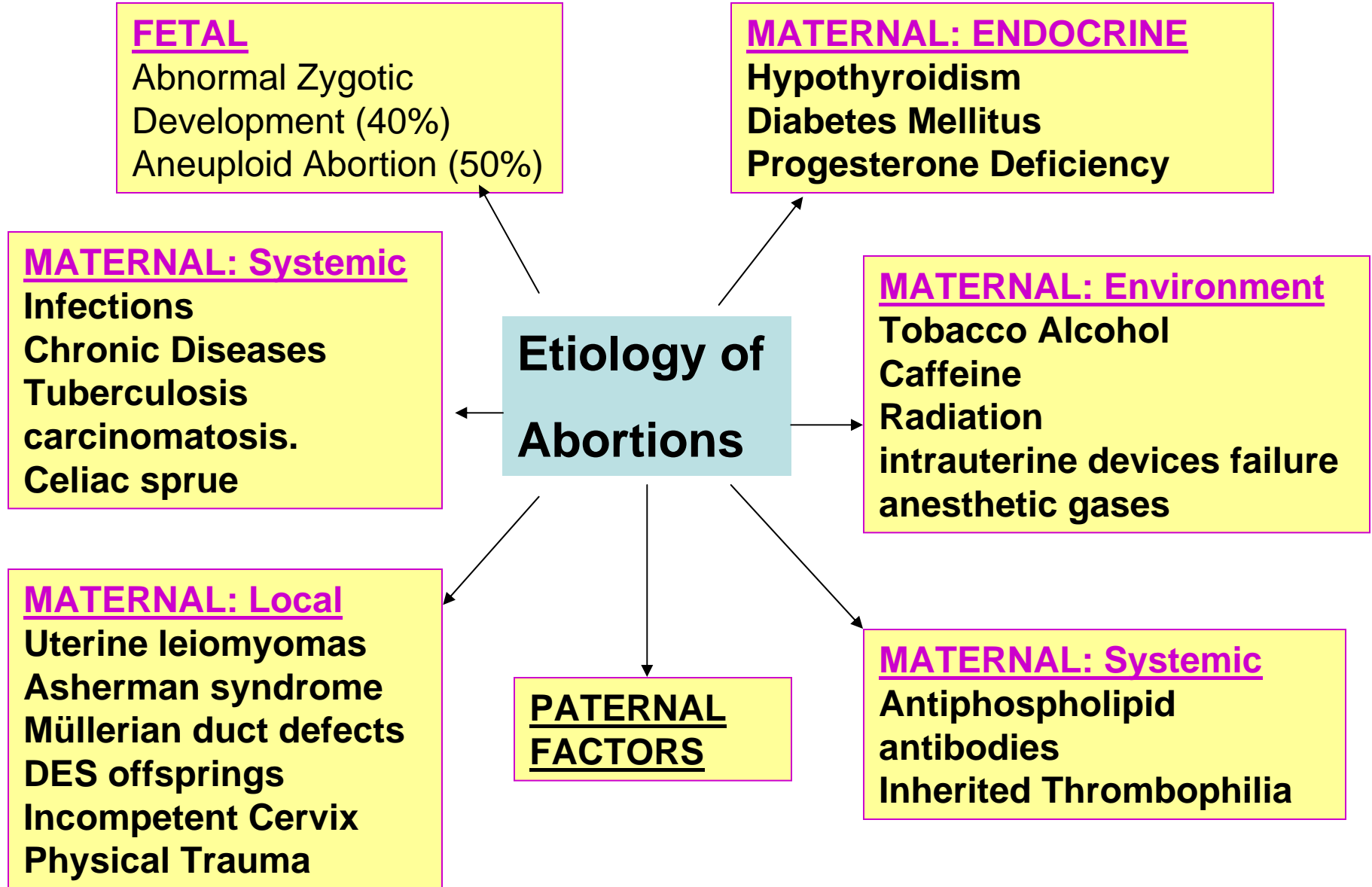


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## Chromosomal Findings in Abortuses

Incidence in Percent

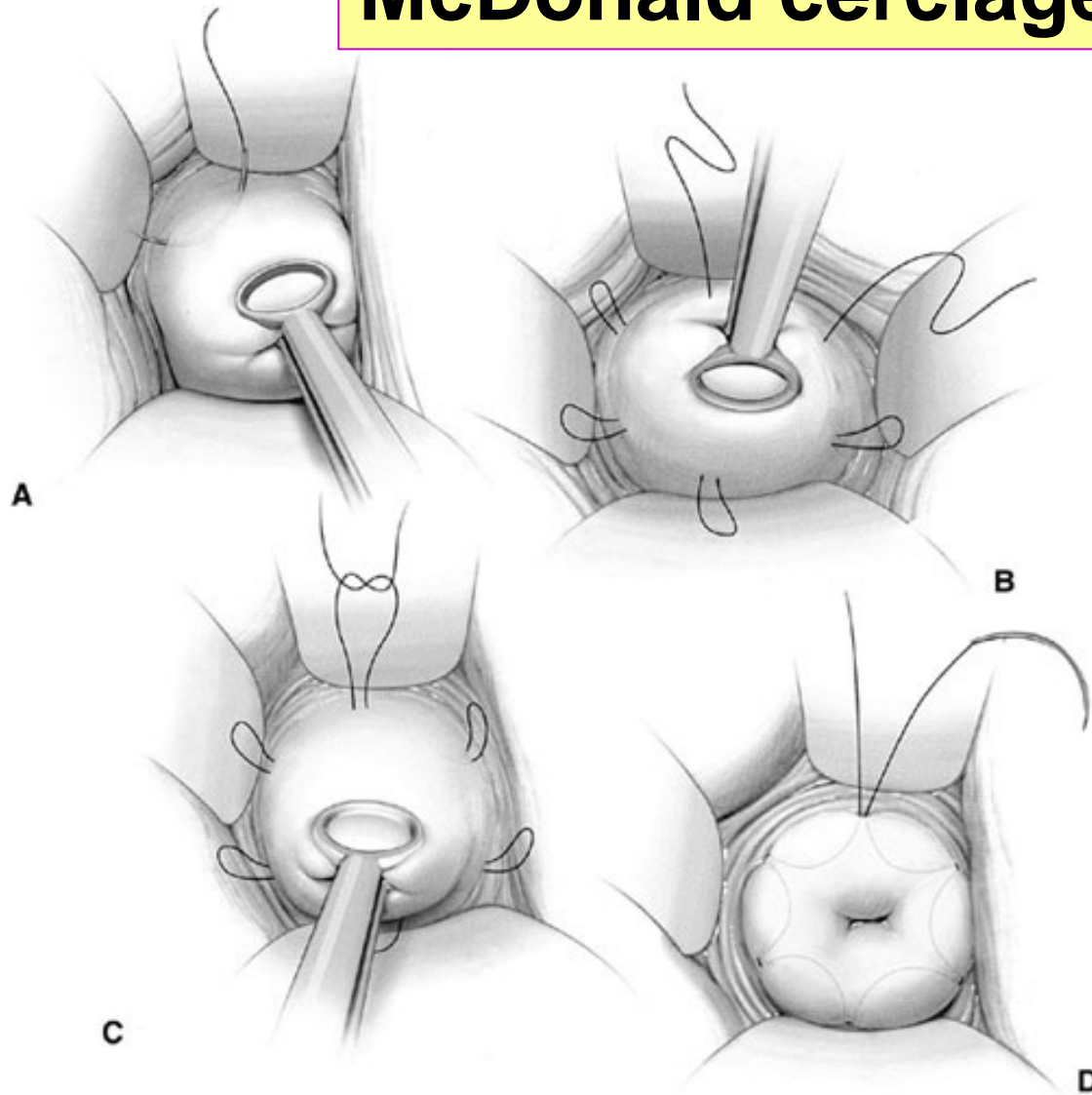
Chromosomal Studies	Kajii et al (1980)	Simpson (1980)
Normal (euploid), 46,XY & 46,XX	46	54
Abnormal (aneuploid)		
Autosomal trisomy	31	22
Monosomy X (45,X)	10	9
Triploidy	7	8
Tetraploidy	2	3
Structural anomaly	3	2
Double trisomy	2	0.7
Triple trisomy	0.4	NL
Others—XXY, monosomy 21	0.8	NL
Autosomal monosomy G	NL	0.1
Mosaic trisomy	NL	1.3
Sex chromosome polysomy	NL	0.2
Abnormality not specified	NL	0.9



# Cervical Incompetence

- **Painless cervical dilatation in 2nd trimester, with prolapse and ballooning of membranes into the vagina, followed by expulsion of an immature fetus.**
- **Transvaginal ultrasound cervical length & funneling**
- **Previous trauma to the cervix—dilatation and curettage, conization, cauterization, or amputation, delivery**
- **Abnormal cervical development, diethylstilbestrol**
- **McDonald cerclage or Shirodkar cerclage**

# McDonald cerclage



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# Abortion Techniques

## Surgical techniques

Cervical dilatation followed by uterine evacuation

Curettage

Vacuum aspiration (suction curettage)

Dilatation and evacuation (D & E)

Dilatation and extraction (D & X)

Menstrual aspiration

Laparotomy:

Hysterotomy

Hysterectomy

## Medical Techniques

Intravenous oxytocin

Intra-amnionic hyperosmotic fluid saline or urea

Prostaglandins

Intra-amnionic injection

Extraovular injection

Vaginal insertion

Parenteral injection

Oral ingestion

Antiprogesterones—RU 486 (mifepristone) & epostane

Methotrexate—intramuscular & oral

Various combinations

# Septic Abortion

- **Criminal abortion    Spontaneous abortion**
- **Legal elective abortion**
- **Anaerobic bacteria; coliforms, *Haemophilus influenzae*, *Campylobacter jejuni*, group A streptococcus**
- **COMPLICATIONS:**
- **Severe hemorrhage                      Bacterial shock**
- **Acute renal failure                      Uterine infection**
- **Parametritis                              Peritonitis**
- **Endocarditis                              Septicemia**
- **DIC    Infertility**
- **TREATMENT:**
- **supportive care; antimicrobials & evacuation**



# HEG: Risk Factors

- **Hyperthyroid disorders**
  - **Previous molar disease**
  - **Pre-gestational diabetes**
  - **Female fetuses**
  - **Occupational status**
  - **Increased body weight**
  - **Nausea & vomiting in a prior pregnancy**
  - **Prior intolerance to oral contraceptives.**
  - **Maternal smoking & older maternal age decreased risk.**
  - **DIAGNOSIS OF EXCLUSION.**
- **Psychiatric d**
  - **Gastrointestinal d.**
  - **Asthma**
  - **Multiple fetuses**
  - **Fetal anomalies**
  - **Infertility**

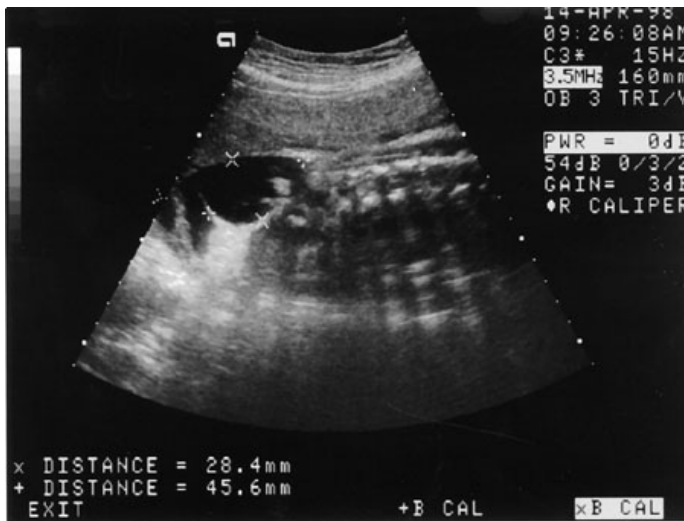
# HEG treatment & outcome

- Intravenous fluids
  - Anti-histamines
  - Anti-emetics
  - Pro motility agents
  - if low pregnancy weight gain, increased risks of:
    - Low birth weight,
    - Small for gestational age,
    - Preterm delivery
    - 5-minute Apgar <7.
- Diet
- Vitamin B6
- Ginger
- Parenteral Nutrition

# Congenital abnormalities

- **Malformation:** "programmed" to develop abnormally; thus intrinsically genetically abnormal.
- **Deformation:** a genetically normal structure develops an abnormal shape because of mechanical forces imposed by the uterine environment
- **Disruption:** severe change in form or function when genetically normal tissue is modified due to a specific insult
- **Phenocopies**

## Spina bifida



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## anencephaly

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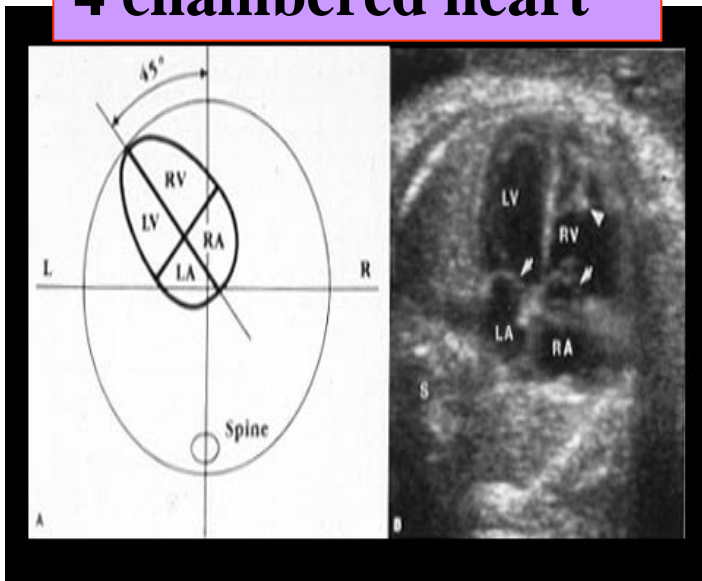


# omphalocele

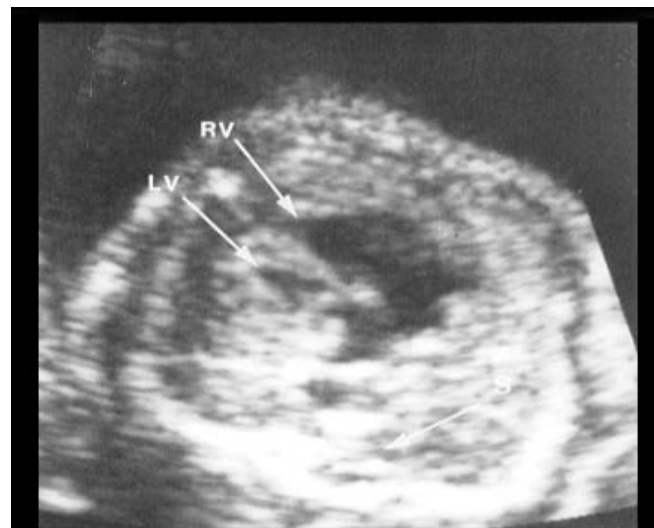
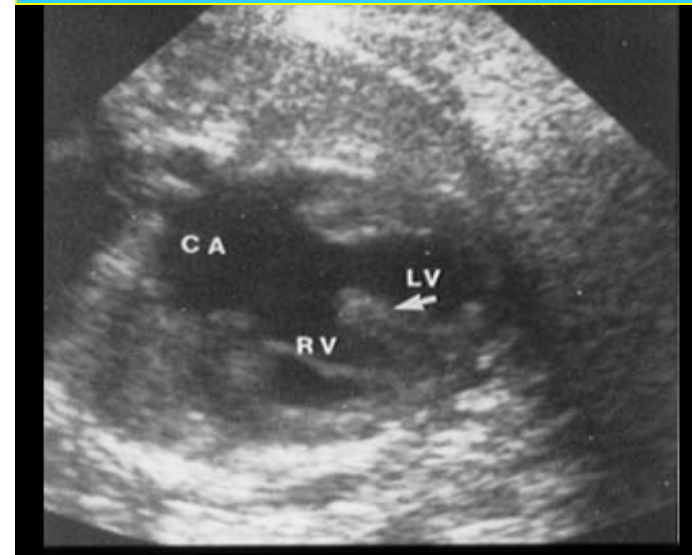


# gastroschisis

## 4 chambered heart



## Endocardial cushion defect



## Hypoplastic Left Heart

# Teratology

- **Dose:**
- **No effect at low dose,**
- **Organ effect at immediate dose**
- **Severe effect/abortion at high dose**
- **Timing:**
- **Up to 2 weeks gestation: all or none effect**
- **3-8 weeks gestation is period of organogenesis when can birth defects occur**
- **After 4<sup>th</sup> month usually decreased growth**

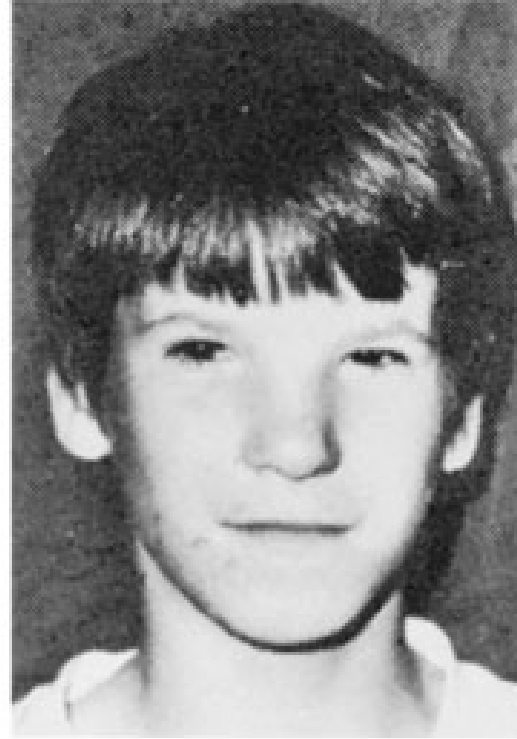
<b><u>Isoretinoin</u></b>	Ear defects, cardiac outflow tract defects , hydrocephaly system, & thymus aplasia
<b><u>Diethylstilbestrol (DES)</u></b> 25%	vaginal clear-cell adenocarcinoma,adenosis, cervix/vagina defects, hypospadias
<b><u>Antifungals</u></b>	CNS & skeleton defects.
<b><u>ACE Inhibitors</u></b> = renal ischemia,	Oligohydramnios, growth restriction, limb shortening, maldevelopment of calvarium
<b><u>Thalidomide</u></b> dysmorphogenesis/disruption	Phocomelia; Limb-reduction defects
<b><u>Tobacco:</u></b> vascular disruption	ileal atresia; hydrocephaly, hand defects, microcephaly, omphalocele, gastroschisis, cleft lip/ palate,
<b><u>Methyl Mercury:</u></b> neuronal & cell division migration	Microcephaly & severe brain damage
<b><u>Cocaine:</u></b> vascular disruption	skull defects, cutis aplasia, porencephaly, subependymal/periventricular cysts, ileal atresia, cardiac anomalies; visceral infarcts

<p><b><u>Alcohol</u></b></p>	<p><b><u>Fetal alcohol syndrome:</u> Craniofacial anomalies; Cardiac defects; Behavior disturbances, Failure to thrive, ADD</b></p>
<p><b><u>Anti-neoplastic drugs</u></b></p>	<p><b>IUGR, craniosynostosis , microcephaly, limb abnormalities</b></p>
<p><b><u>Coumarin:</u> 9% inhibiting posttranslational carboxylation of coagulation proteins.</b></p> <p>in 2<sup>nd</sup> &amp; 3<sup>rd</sup> hemorrhage leading to disharmonic growth and deformation from scarring</p>	<p><b>Fetal warfarin syndrome: nasal &amp; midface hypoplasia; stippled vertebral and femoral epiphyses.</b></p> <p><b>Dorsal CNS dysplasia, mental retardation</b></p>
<p><b><u>Phenytoin</u> 5–11%</b></p> <p>accumulation in fetal tissues of free oxide radicals, with toxic,carcinogenic, mutagenic effects.</p>	<p><b><u>Fetal hydantoin syndrome:</u> craniofacial anomalies, fingernail hypoplasia, growth deficiency, developmental delay, cardiac defects, facial clefts</b></p>
<p><b><u>Carbamazepine</u></b></p> <p><b><u>Valproate</u> 1–2%</b></p>	<p><b>Neural-tube defects</b></p>
<p><b><u>Phenobarbital</u> 10–20%</b></p>	<p><b>Clefts, cardiac anomalies, urinary tract malformations</b></p>

# Fetal alcohol syndrome



**A**



**B**



**C**

Fetal alcohol s.

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# Congenital Infections



**Toxoplasmosis**

**Syphilis**

**Rubella**

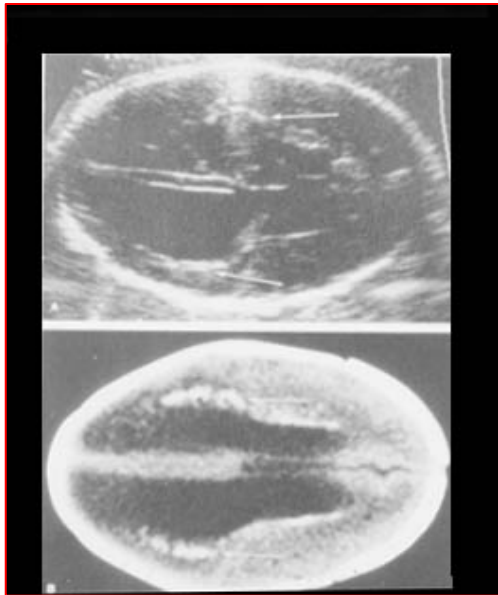
**CMV**

**HSV**

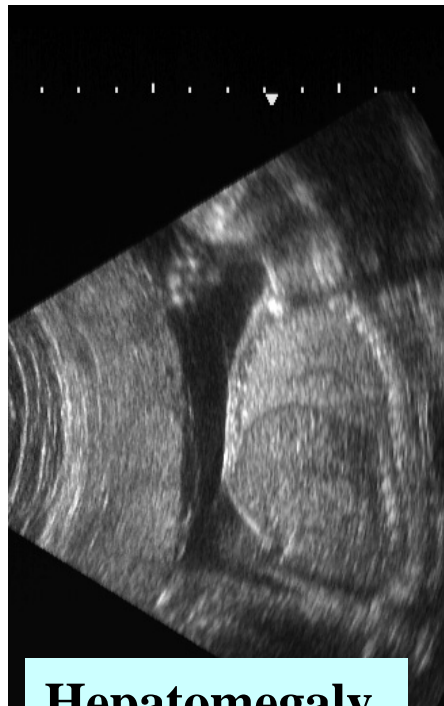
**Varicella**

# Congenital Infections

## Intracranial Infections



Dilated ventricles with bilateral periventricular calcifications (arrows)

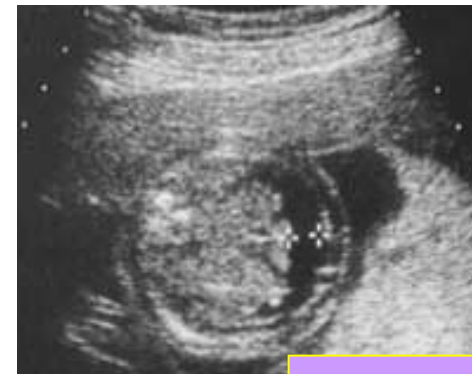


Hepatomegaly,  
Splenomegaly

## Hydrops: Features



Scalp edema



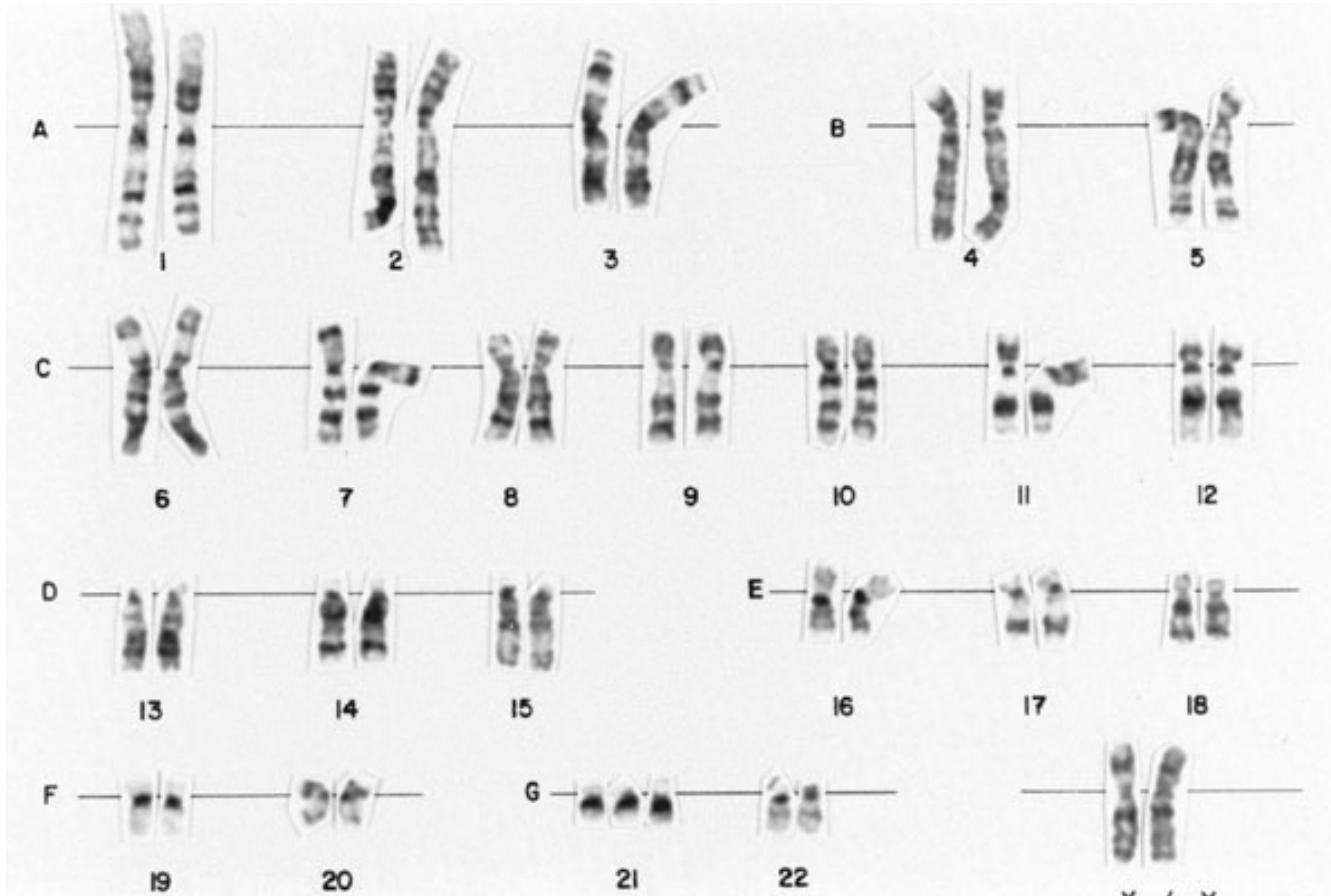
Ascites

# ANEUPLOIDY

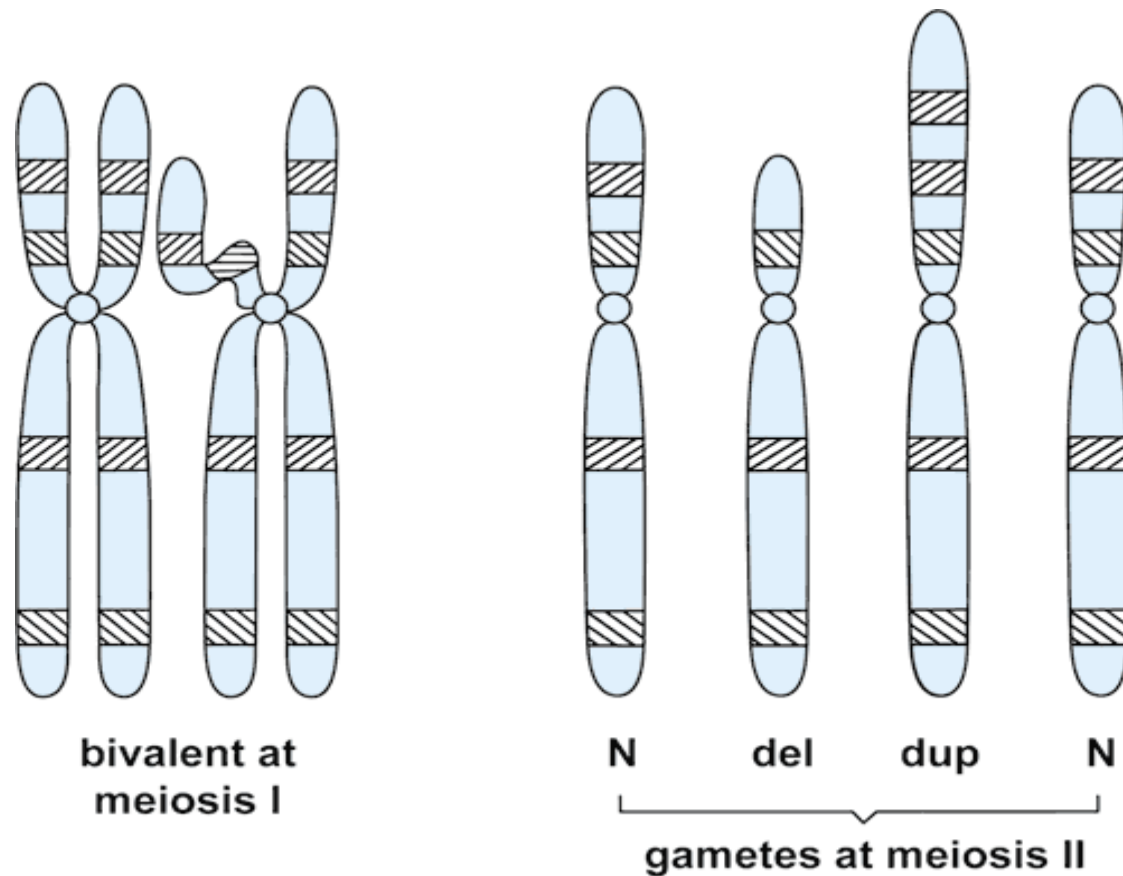
- **Trisomy: extra chromosome nondisjunction of meiosis I increases with maternal age**
- **Only autosomal trisomies 13, 18, and 21 result in viable term pregnancies**
- **Monosomy: missing a chromosome monosomy X,**
- **Polyploidy: number of haploid chromosomal complements hydatidiform mole fertilization of one egg by two sperm**

<b>Type</b>	<b>Cause</b>	<b>Karyotype</b>	<b>Syndrome</b>
<b><u>Trisomy</u> Extra chromosome</b>	nondisjunction of meiosis I Advanced maternal age	13 18 21 XXYXYY, XXX	Down, Edward, Patau, Klinefelter
<b><u>Monosomy; Lost chromosome</u></b>	nondisjunction of meiosis 1	45 XO,	Turners syndrome
<b><u>Triploidy</u> extra haploid chromosome</b>	fertilization of one egg by diploid or two sperms	69 xxx	Partial hydatidiform mole
<b><u>Deletions</u> during meiosis</b>	from mal-alignment/ mismatching at pairing chromosomes	del 5p 22q11.2 microdeletion	cri du chat Shprintzen & Digeorge
<b><u>Translocations</u> <u>Isochromosomes</u> <u>Inversions</u> <u>Ring</u></b>	Reciprocal; Robertsonian  Fused 2 q or 2p arms rearrangement may alter gene function	balanced Unbalanced Deletions	Trisomy Monosomy Infertility

# Trisomy 21



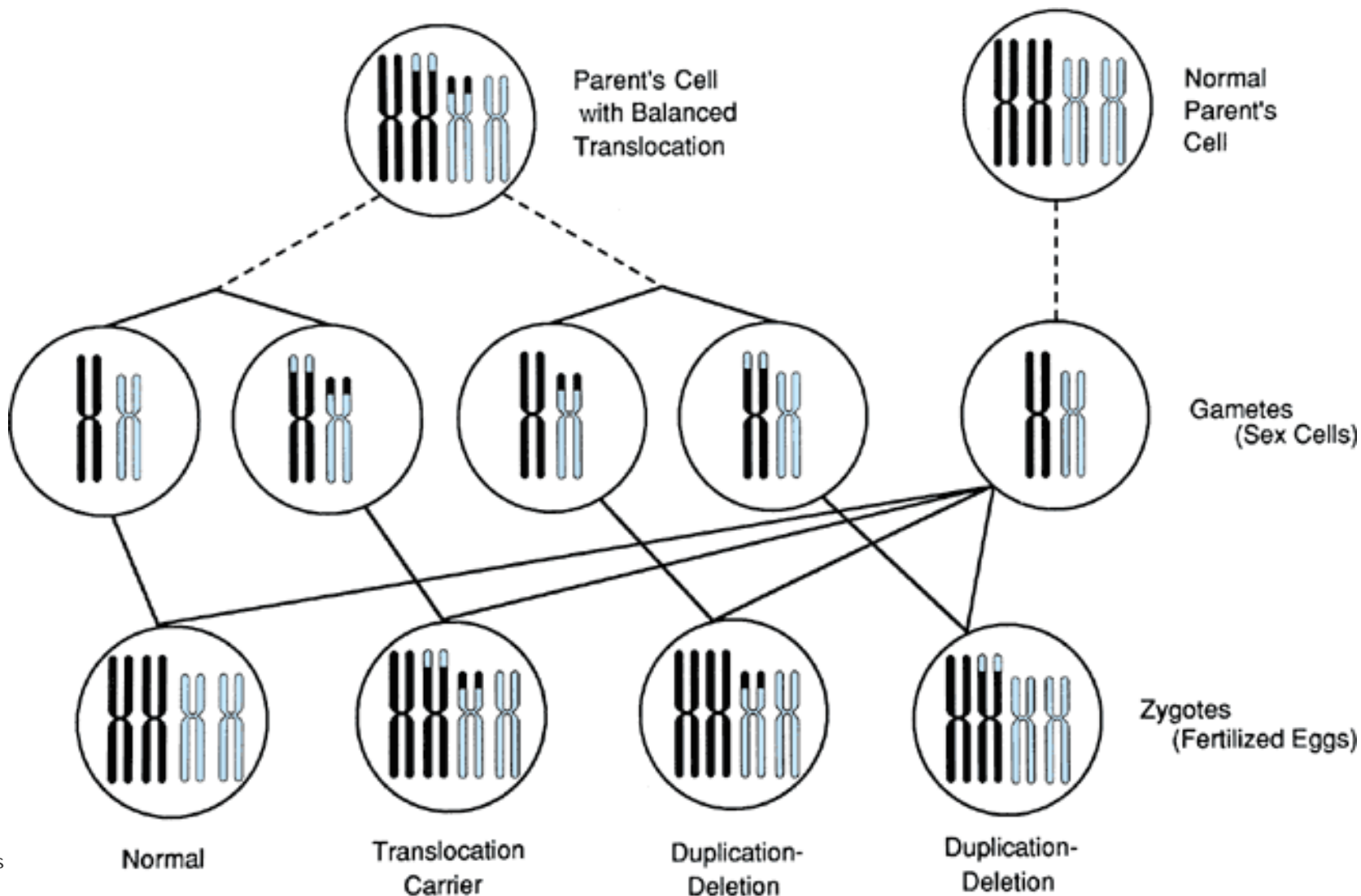
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**Mechanism of duplication & deletion. Similar sequences (crosshatched segments) exist at numerous places along the chromosome. Misalignment of two nonhomologous sequences, followed by illegitimate recombination within these two sequences (X), produces recombinant products that are reciprocally imbalanced: one with a duplication the other with a deficiency.**

# Reciprocal Translocations



Gametes

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# Autosomal Dominant

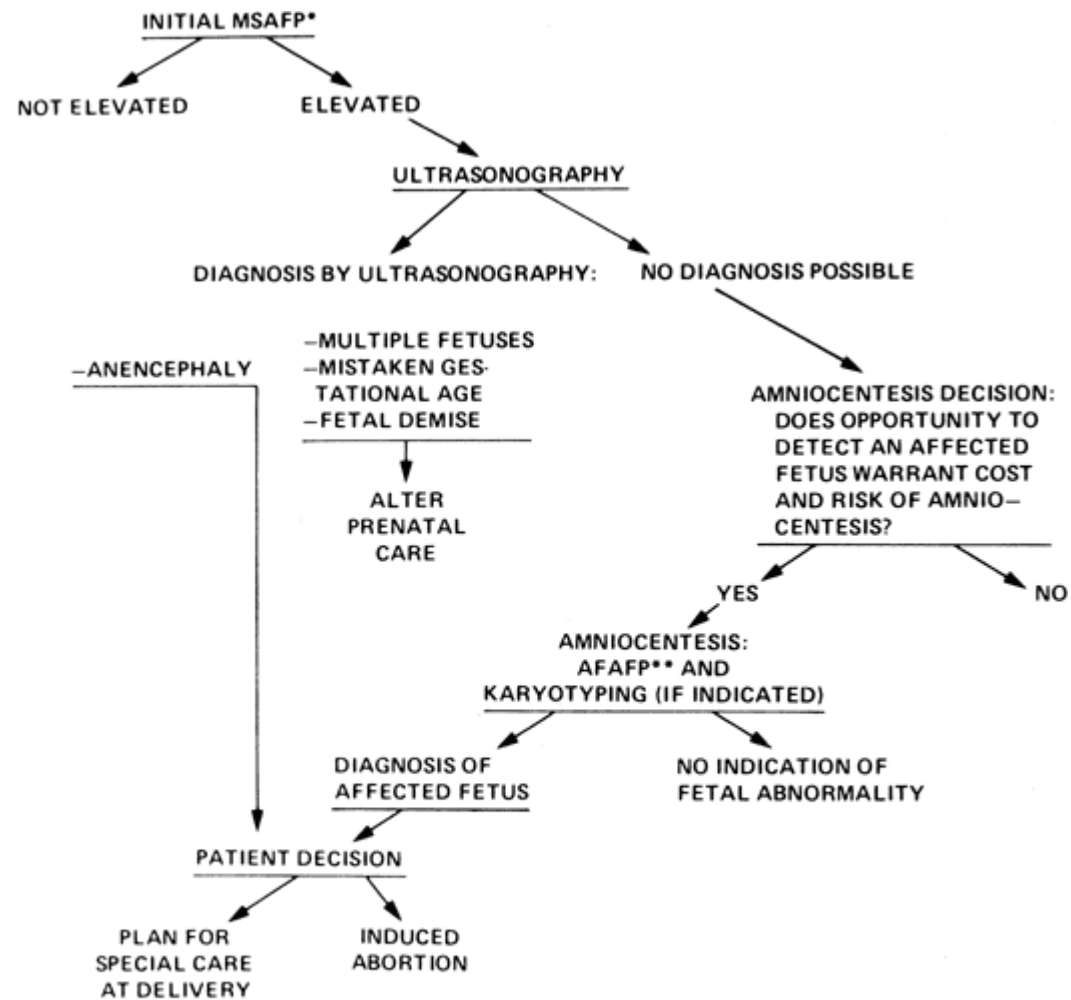
- One member of a gene pair determines the phenotype
- 50-percent chance of passing on the affected gene with each conception.
- Achondroplasia                      Marfan syndrome
- Huntington chorea                  Neurofibromatosis
- Factor V Leiden                      Von Willebrand D
- *BRCA1* and *BRCA2* breast cancer

# Autosomal Recessive

- Diseases develop when both gene copies are abnormal
- Carriers are asymptomatic
- If both parents are carriers:
  - 1/4 of offspring = homozygous normal
  - 2/4 = heterozygote carriers
  - 1/4 = homozygous abnormal
- Cystic fibrosis
- Thalassaemia
- Tay–Sachs disease
- Homocystinuria
- Sickle cell anemia
- Phenylketonuria
- Congenital adrenal hyperplasia
- Albinism

# X-Linked Genes

- **Women carriers are unaffected, unless unfavorable lyonization**
- **Son has a 50 % risk of being affected**
- **Daughter has a 50 % carrier risk**
- **Men carriers always affected**
- **Son has a 0 % risk of being affected**
- **Daughter has a 100 % carrier risk**
- **Duchenne muscular dystrophy      Hemophilia A**
- **Glucose-6-phosphate deficiency      Color blindness**
- **Androgen insensitivity syndrome      Fragile X**
- **X-linked dominant disorders affect mainly females & are usually lethal in males.**

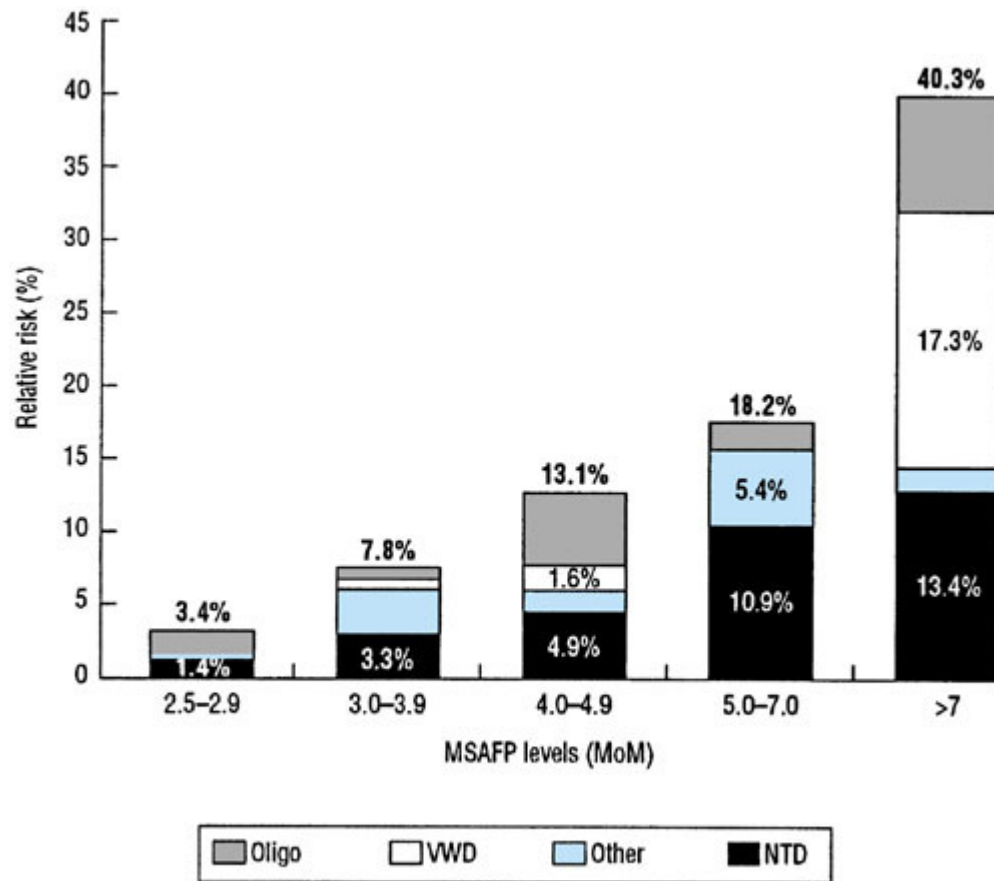


\*MSAFP = maternal serum alpha-fetoprotein

\*\*AFAFP = amniotic fluid alpha-fetoprotein

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Algorithm for evaluating an elevated maternal



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Distribution of the risk of anomalies and oligohydramnios as a function of elevated maternal serum alpha-fetoprotein levels (MSAFP). (MoM = multiples of median; NTD = neural-tube defect; Oligo = oligohydramnios; Other = subchorionic bleeding, intra-abdominal echogenicity, hydronephrosis, echogenic bowel, dilated kidney, heart defect; VWD = ventral wall defect.)

# Maternal Serum Marker Screening

- **FIRST TRIMESTER:**
- free B-hCG
- Pregnancy-associated plasma protein A (PAPP-A)
- Nuchal translucency (NT) measurement
- **SECOND TRIMESTER :**
- Trisomy 21: Low AFP, high HCG; low unconjugated estriol
- Trisomy 18: Low AFP, low HCG; low unconjugated estriol

# Amniocentesis for genetic diagnosis

## • PROCEDURE

- 14 - 20 weeks gestation.
- Ultrasonographic guidance is used to pass a 20- to 22-gauge spinal needle
- 20 mL of fluid is collected for fetal karyotype, AFP.
- Complications: Fetal loss 0.5%, transient vaginal spotting or amniotic fluid leakage in 1-2%; chorioamnionitis < 0.1 %.

## • INDICATIONS

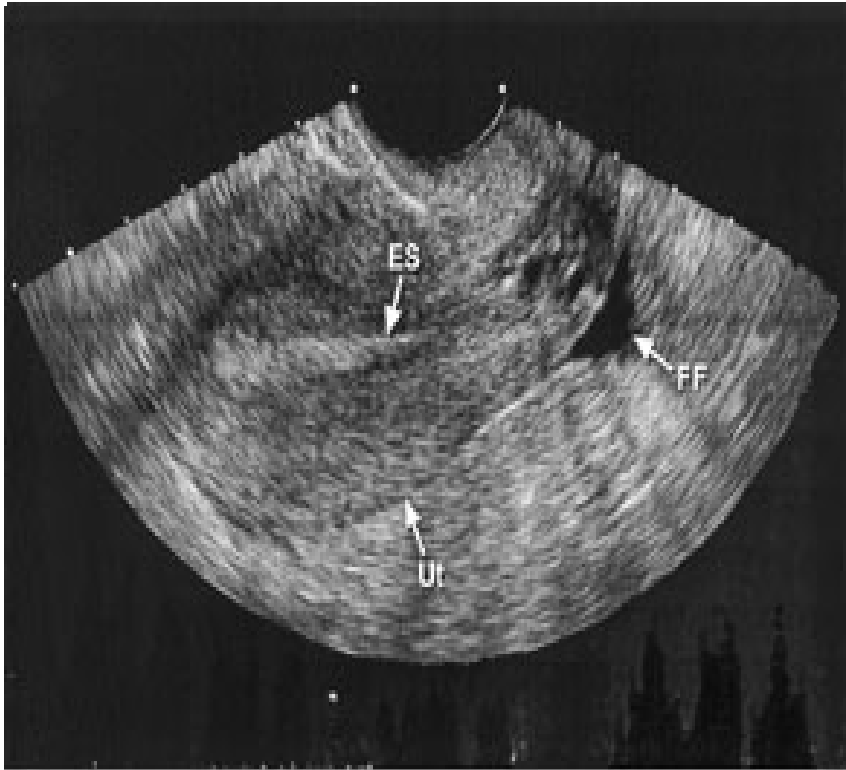
- Advanced maternal age
- Previous aneuploidy
- Couple with translocation
- Family history of
  - autosomal dominant d
  - X-linked disease  
Fragile X
  - Couple both carriers of autosomal recessive d  
Cystic fibrosis
- Abnormal serum screen
- Fetal defects noted

# Ectopic Pregnancy

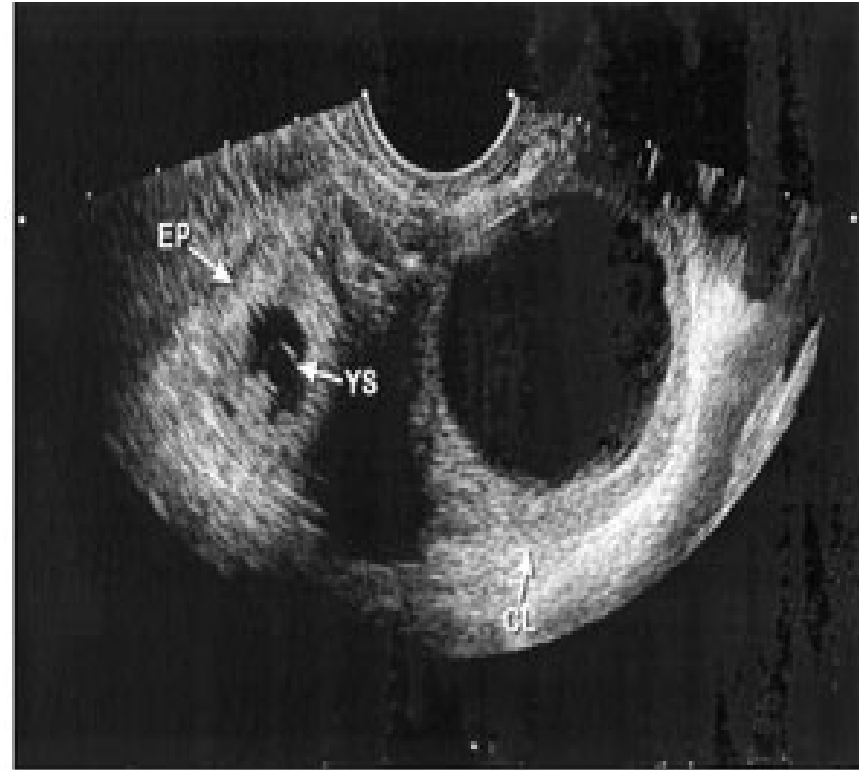
- Implantation outside endometrial cavity
- Mainly Fallopian tube
- **RISK FACTORS**
- PID
- Smoker
- Previous ectopic
- Tubal sterilization
- Tubal surgery
- IUD
- Infertility= tubal factor
- Assisted reproductive technology

- **PRESENTATION**
- Pain
- **Abnormal Menstruation**
- Abdominal and Pelvic Tenderness
- Vital signs
- Pelvic mass
- **COMPLICATIONS**
- Hemorrhagic shock
- Risk of death
- Decreased fertility

## Ultrasound of ectopic pregnancy.



**A**



**B**

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**A. The uterus (Ut) is seen with a normal endometrial stripe (ES). A small amount of free fluid (FF) is visible in the posterior cul-de-sac. B. The tubal ectopic pregnancy (EP) with its yolk sac (YS) is seen along with a corpus luteum (CL) cyst.**

## Features of Partial and Complete Hydatidiform Moles

Feature	<u>Partial Mole</u>	<u>Complete Mole</u>
<b><u>Karyotype</u></b>	Usually 69,XXX or 69,XXY	46,XX or 46,XY
<b><u>Pathology</u></b>		
Embryo-fetus	Often present	Absent
Amnion, fetal RBC's	Often present	Absent
Villous edema	Variable, focal	Diffuse
Trophoblastic	Variable, focal, slight to moderate	Variable, slight to severe
<b><u>Clinical presentation</u></b>		
Diagnosis	Missed abortion	Molar gestation
Uterine size	Small for dates	50% large for dates
Theca-lutein cysts	Rare	25–30%
Medical complications	Rare	Frequent
Gestational trophoblastic neoplasia	<5–10%	20%

# SUMMARY

- **Abortion occurs in about 10-20% of all pregnancies.**
- **Birth defects occur in about 3% of all pregnancies; teratogens can only cause defects between 3-8 weeks of gestation'**
- **Trisomy 21,13,18, monosomy XO are the commonest chromosomal disorders present in viable pregnancies and are associated with advanced maternal age.**
- **Morning sickness occur in a majority of pregnant women; a severe form called hyperemesis gravidarum is associated with weight loss and may be associated with adverse pregnancy outcome**
- **Ectopic pregnancy is extra-uterine pregnancy that is associated with intra-peritoneal bleeding and maternal morbidity and mortality**
- **Molar pregnancy is characterized histologically by abnormalities of the chorionic villi that consist of trophoblastic proliferation and edema of villous stroma**