

# Basic Obstetrics series



Introduction to prenatal  
screening for anomalies

- Adegoke Adeniji MD FACOG



# Objectives:

Persuade you that pregnancy is a Disease

Most rampant and debilitating of all STDs.



# Objectives:

- Explain embryology of early development
- Genetics of aneuploidy and Chromosomal abnormalities
- Understand basis for preimplantation genetic diagnosis (PGD)
- Clinical correlatation of human embryology



# Birth defects and Prenatal Diagnosis:

- Congenital malformation, birth defect and congenital anomaly are synonymous terms used to describe structural, behavioral, functional and metabolic disorders present at birth.



# Congenital anomaly

- 2-3% of liveborn infants have a major structural anomaly.
- An additional 2-3% are recognised by the age of 5 years ( Hence total 4-6%)
- Birth defects are the leading cause of infant mortality
  - Cause approx 21% of infant deaths
- No discrimination in mortality caused by birth defects b/w races in US.



# Causes of birth defects:

- 40 – 60% cause unknown
- 15% Genetic factors
  - Chromosomal abnormalities
  - Mutant genes etc
- 10% Environmental factors
- 20% combination of Genetic and envirn.  
(multifactorial inheritance)
- 0.5 – 1% caused by twinning.



# Birth defects

- Minor anomalies occur in approx 15% of newborns. Findings such as microtia, pigmented spots, extra digits may be a flag as they may be associated with major defects.
- 1 minor anomaly– 3% chance of a major
- 2 minor – 10% chance
- 3 or more minor: 20 % chance of major



# Types of Abnormalities:

- Malformations

- Disruptions

- Deformations

- Syndrome



# Syndrome

- A group of anomalies occurring together that have a specific common cause.
- Contrast with ASSOCIATION:
  - This is a non random appearance of 2 or more anomalies that occur together more frequently than by chance alone, but whose cause has not been determined
    - Any examples?



# Syndrome:

- A group of anomalies occurring together that have a specific common cause.
  - Term indicates that a diagnosis has been made
  - The risk of recurrence is known.



# Malformations

- Occur during formation of structures – organogenesis
- Genetic factors, environmental factors, combination
- Complete or partial absence, alteration of normal configuration



# Disruptions

- Morphological alterations of already formed structures
  - Vascular accidents leading to bowel atresias, amniotic bands



# Deformations:

- Mechanical factors that mold a part of the fetus over a prolonged period.
  - Eg Clubfeet
- Deformations may be reversible post natally



# Prenatal Diagnosis

- History and Physical exam: ( ! )
- Ultrasound
- Biochemical screening
  - 1<sup>st</sup> trimester
  - 2<sup>nd</sup> trimester
- Preimplantation genetic screening
- Chorionic villous sampling
- Amniocentesis



# Let's talk about sex Baby:

- Developments begin with fertilization,
  - Male gamete, the sperm and female gamete the oocyte, to form a zygote.
- Gametes derive from primordial germ cells (PGCs).
  - Formed 2<sup>nd</sup> week in the epiblast
  - Migrate in the 4<sup>th</sup> week
  - Arrive developing gonad by end of 5<sup>th</sup> week.



## Clinical correlates:

- Teratomas are thought to develop from these pluripotent primordial germ cells
  - Can thus differentiate into any of the 3 germ layers or their derivatives.



# Gametogenesis:

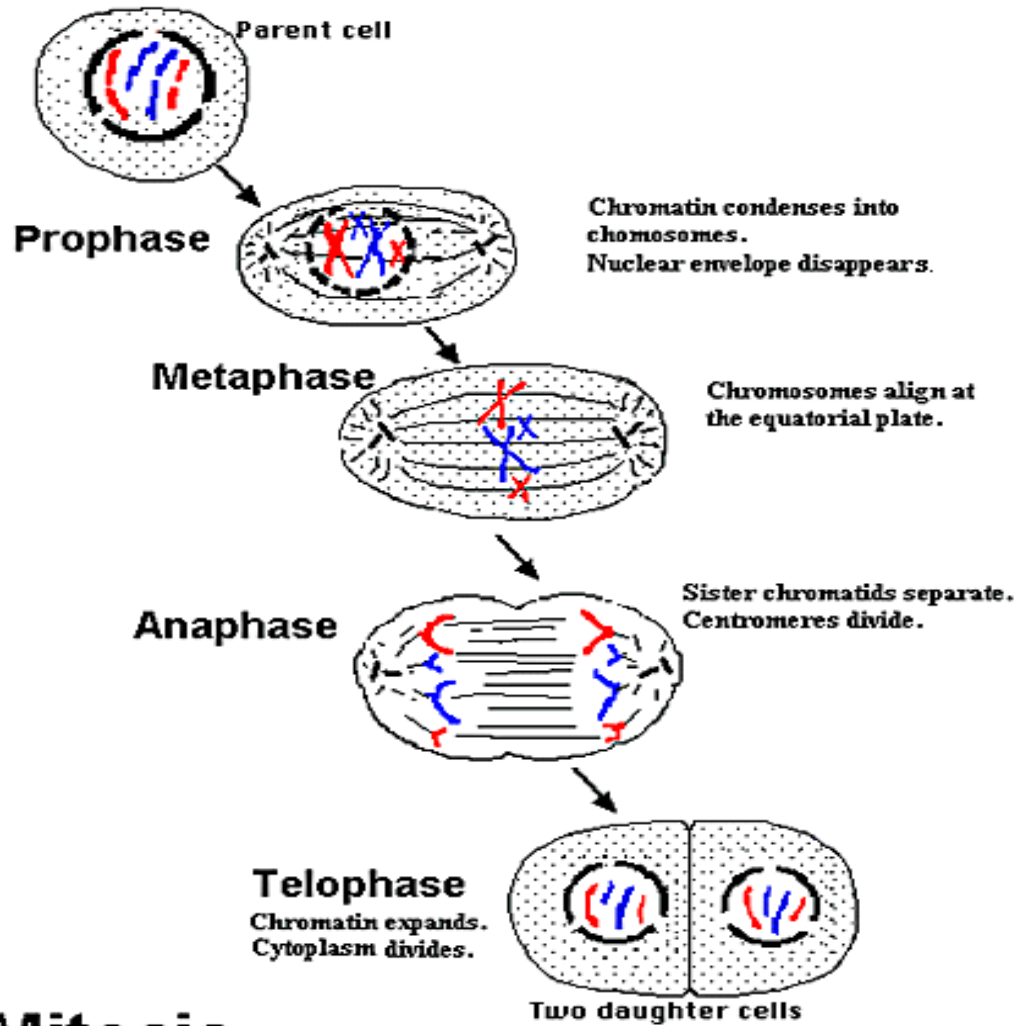
- These primordial germ cells in the ovary are called oogonia.
- They continue to multiply by:
  - -MITOSIS
- Some however transition into the gamete forming division called
  - -MEIOSIS



## Not so 'Trivia':

- The gamete forming division is called :
- Meiosis
- 2 stages of Meiosis I and II, which ultimately produce four Haploid daughter cells.
- In female: Oogonia go into meiosis I but remain suspended in the PROPHASE of meiosis I forming Primary oocytes.

# Stages of Cell Division:



**Mitosis**



## Clinical correlation:

- Reference cell cycle (on next slide) and chemotherapeutic agent activity
- Reference teratogens: Drugs, Physical agents such as Heat, Radiation
- Gametotoxicity, embryotoxicity

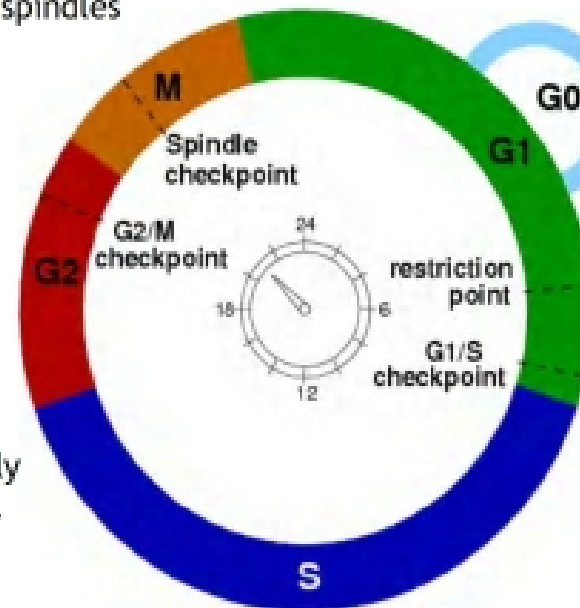


# Cell cycle

**M phase** - In mitosis chromosomes drawn apart by molecular motors, cell divides. Many cancer drugs like taxol act here freezing the process and causing apoptosis. There is a checkpoint to ensure chromosomes are correctly attached to the spindles before segregation.

G1 is entered when the cell senses growth signals or mitogens. These start the process of cell division.

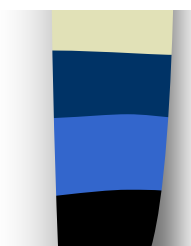
**G2/M** - cell arranges and checks chromosomes. There is a major checkpoint here to ascertain that DNA replication has successfully occurred. If not, a normal cell undergoes apoptosis.



Cell crosses a restriction point c 8-10 hours into G1 - This is a point of no return: the cell is committed to divide or die.

G1/S checkpoint -arrest here for cancer cells leads to apoptosis.

**S phase** - DNA is synthesised. Many cytotoxic anti-cancer drugs act here to disrupt DNA synthesis.





# Gametogenesis

- What is the most number of eggs a woman ever has ?
- 7 million !-By the 5<sup>th</sup> month of intrauterine life.

Many oogonia and primary oocytes become atretic

AT BIRTH: 1 MILLION 1<sup>0</sup> OOCYTES REMAIN



# Gametogenesis

- At Puberty: Approx 400K remain
  - Of which only approx 400 will be ovulated
- Each month 15 – 20 follicles are selected to begin maturation (recruitment)
- One (or two) dominate and ovulates Circa Day 14



# Clinical Correlates

- What is Clomiphene Citrate?
- How is it used?



# Twins and Zygosity/ Amnionicity

## ■ Twins:

- Dizygotic (10 / 1000 births)
- Monozygotic (3-4 per 1000)
- (Triplets 1/7500 pregs)

## ■ Monozygotic:

- Di/Di Split Day 1-3
- Diamniotic/Monochorionic Day 3-7
- Mono/Mono Day 7-12
- Conjoined Day 13

## ■ Twinning itself ‘anomalous’ higher anomaly risk in the fetuses