



# Fetal Development and Birth

ANAT2341: HUMAN EMBRYOLOGY

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# Aim:

To provide an overview the fetal period of development

## Learning Outcomes

1. Understanding of fetal growth - length and weight
2. Understanding of fetal systems development/changes
3. Understanding of fetal abnormalities
4. Understanding of gestation period
5. Understanding of maternal changes at birth
6. Understanding of fetal to neonatal transition
7. Understanding of system changes
8. Understanding of abnormalities and diagnostic testing

# Fetal Period

Weeks 9-36

- Rapid body growth
- Differentiation of tissues, organs and systems
- Rapid growth of body

# Gestational Period

## 1<sup>st</sup> trimester

Week 1-12

## 2<sup>nd</sup> trimester

Weeks 13-24

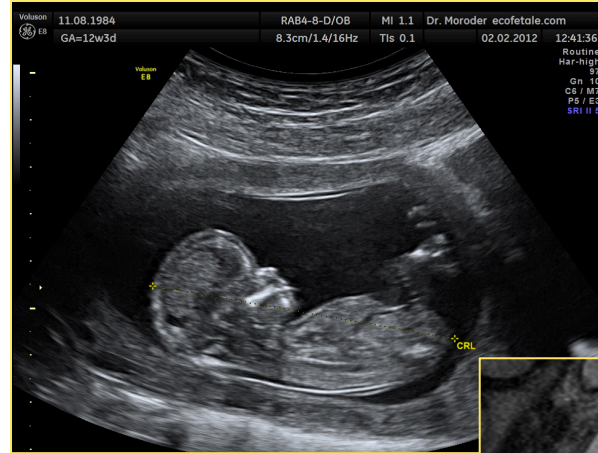
## 3<sup>rd</sup> trimester

Weeks 25~40

- Often determined from date of LNMP
- Need to clarify how the fetus is aged
  - LNMP
  - Date of fertilisation

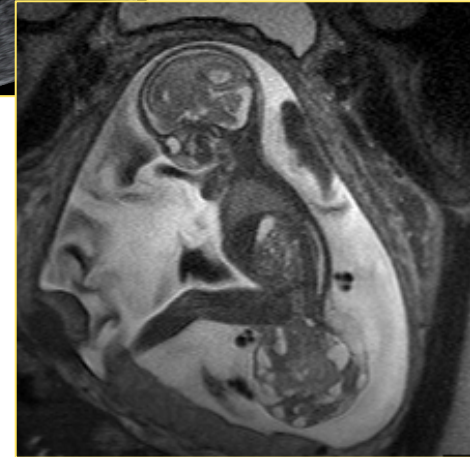
# Estimating fetal age

- Why?
  - Assess growth and development of organs and systems
  - Predict date of delivery
  - Detect anomalies and abnormalities
    - Most detected in 2<sup>nd</sup> trimester
- How?
  - Crown rump length
  - Femur length
  - Head circumference



## Ultrasound

- Placental & fetal size and position
- Multiple births
- Abnormalities
- growth



Fetal MRI



# Fetal Period – growth in size and weight

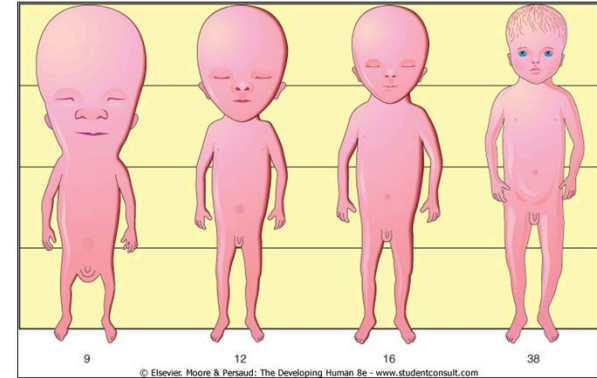
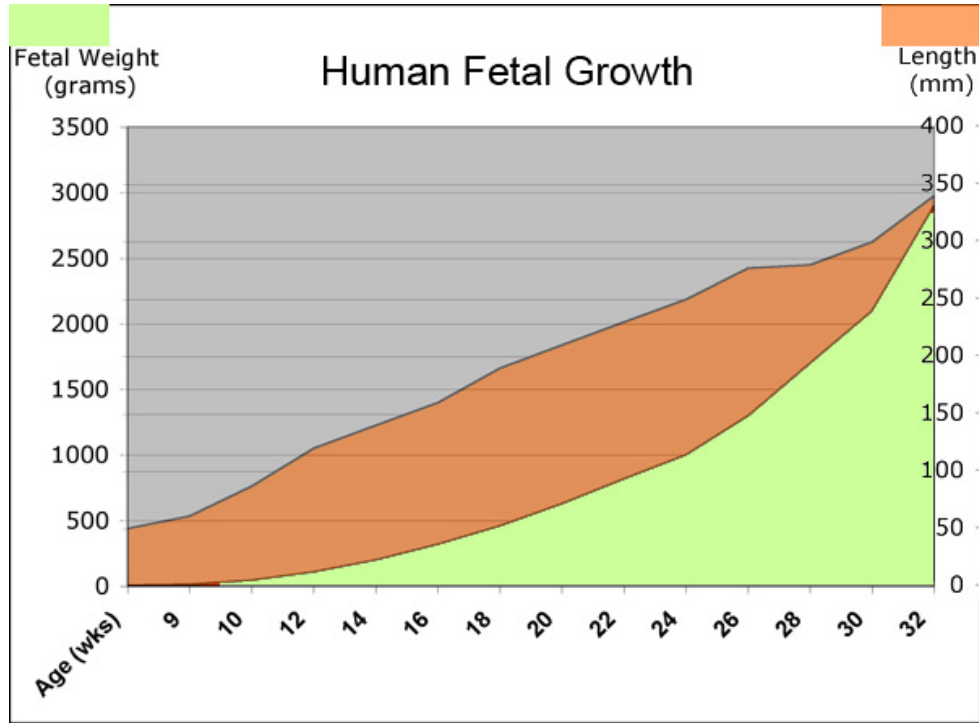


Figure 6-3 Diagram illustrating the changing proportions of the body during the fetal period. At 9 weeks, the head is approximately half the crown-heel length of the fetus. By 38 weeks, the circumferences of the head and the abdomen are approximately equal. After this (38 weeks), the circumference of the abdomen may be greater. All stages are drawn to the same total height.

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# Estimating developmental age

Age (weeks)		Crown-Rump Length (mm) <sup>a</sup>	Foot Length (mm) <sup>a</sup>	Fetal Weight (g) <sup>b</sup>	Main External Characteristics
Menstrual	Fertilization				
11	9	50	7	8	Eyes closing or closed. Head more rounded. External genitalia still not distinguishable as male or female. Intestines are in the umbilical cord.
12	10	61	9	14	Intestines in abdomen. Early fingernail development.
14	12	87	14	45	Sex distinguishable externally. Well-defined neck.
16	14	120	20	110	Head erect. Lower limbs well developed.
18	16	140	27	200	Ears stand out from head.
20	18	160	33	320	Vernix caseosa present. Early toenail development.
22	20	190	39	460	Head and body (lanugo) hair visible.
24	22	210	45	630	Skin wrinkled and red.
26	24	230	50	820	Fingernails present. Lean body.
28	26	250	55	1000	Eyes partially open. Eyelashes present.
30	28	270	59	1300	Eyes open. Good head of hair. Skin slightly wrinkled.
32	30	280	63	1700	Toenails present. Body filling out. Testes descending.
34	32	300	68	2100	Fingernails reach fingertips. Skin pink and smooth.
38	36	340	79	2900	Body usually plump. Lanugo hairs almost absent. Toenails reach toe tips.
40	38	360	83	3400	Prominent chest; breasts protrude. Testes in scrotum or palpable in inguinal canals. Fingernails extend beyond fingertips.

<sup>a</sup>These measurements are average and so may not apply to specific cases; dimensional variations increase with age.

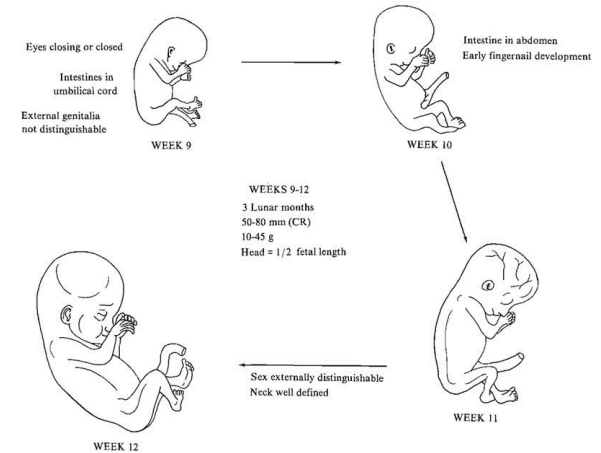
<sup>b</sup>These weights refer to fetuses that have been fixed for approximately 2 weeks in 10-percent formalin. Fresh specimens usually weigh approximately 5 percent less.

Modified from Moore, 2013.

Period:	Implantation		Embryonic Period (Organogenesis)						Fetal Period (Growth)									
	1	2	3	4	5	6	7	8	9	12	16	20	24	28	32	36	38	
Weeks																		
Crown-rump length (cm)										6-7	12	16	21	25	28	32		
Weight (g)										110	320	630	1100	1700	2500			
Brain			Neural tube			Hemispheres, cerebellum, ventricles, choroid plexus				Temporal lobe, sulci, gyri, cellular migration, myelination								
Face			Lips, tongue, palate, cavitation, fusion															
Eyes			Optic cups, lens, optic nerves, eyelids										Brows		Eyes open			
Ears									Canals, cochlea, inner ears, ossicles									
Pinnae												Pinnae						
Diaphragm			Transverse septum, diaphragm															
Lungs			Tracheoesophageal septum, bronchi, lobes							Canaliculi			Terminal sacs					
Heart			Primitive tube, great vessels, valves, chambers															
Intestines			Foregut, liver, pancreas, midgut			Abdominal wall, gut rotation												
Urinary tract			Mesonephric duct	Metanephric duct collecting system						Glomeruli								
Genitalia			Genital folds, phallus, labioscrotal swelling															
									♂ Penis, urethra, scrotum									
									♀ Clitoris, labia									
Axial skeleton			Vertebral cartilage, ossification centers															
Limbs			Buds, rays, webs, separate digits															
Skin									Fingernails		Vernix		Lanugo hair					

# Fetal stages: weeks 9-12

- Beginning week 9, head is large and round, but growth of the **body in CR length more than doubles** by the end of week 12
- Face is broad, eyes widely separated, ears low set, and eyelids fused
- Legs are short and thighs relatively small, but by the end of week 12, the **upper limbs reach relatively normal lengths**, but lower limbs are not well developed and are relatively shorter
- **External genitalia not differentiated until week 12**, urine formation begins
- Intestinal loops are clearly seen in the proximal end of the umbilical cord until the middle of week 10 when they return to the abdomen
- **Erythropoiesis – main site transitions from liver to spleen**
- By the end of week 12, the fetus will react to stimuli



# Fetal stages: weeks 17-20

- Growth slows, but fetal **CR length increases by ~50 mm**
- **Lower limbs reach final relative proportions**
- Fetal **movements (quickening)** are felt by mother
- Week 20:
  - Skin is covered by the **vernix caseosa** (greasy, cheeselike material) due to fetal sebaceous gland secretion and dead epithelial cells
    - Function: protects fetal skin
  - Fetus is covered by **lanugo**, a fine downy hair
  - eyebrows and head hair are visible
- **Brown fat forms** and is the site of heat production
  - specialized adipose tissue

FETAL GROWTH: ACTUAL SIZE  
WEEKS 9-20



WEEKS 13-16  
4 Lunar months  
90-140 mm (CR)  
60-200 g

Head erect  
Lower limbs  
well developed  
Ears stand out from head  
Generally rapid  
growth period  
Legs lengthen



WEEKS 17-20  
5 Lunar months  
150-180 mm (CR)  
250-450 g  
Head = 1/3 fetal length

Vernix caseosa seen  
Early toenails form  
Head and body  
hair (lanugo) visible  
Mother feels fetal movements (quickening)  
Brown fat forms

# Fetal stages – weeks 21 onwards

## Weeks 21- 25

- **weight gain**; the body is proportioned; the skin is wrinkled but is very translucent and is pink to red in colour due to vascularisation
- **Immature respiratory system, ?viable from 22 weeks**
- Week 24 – surfactant secreted

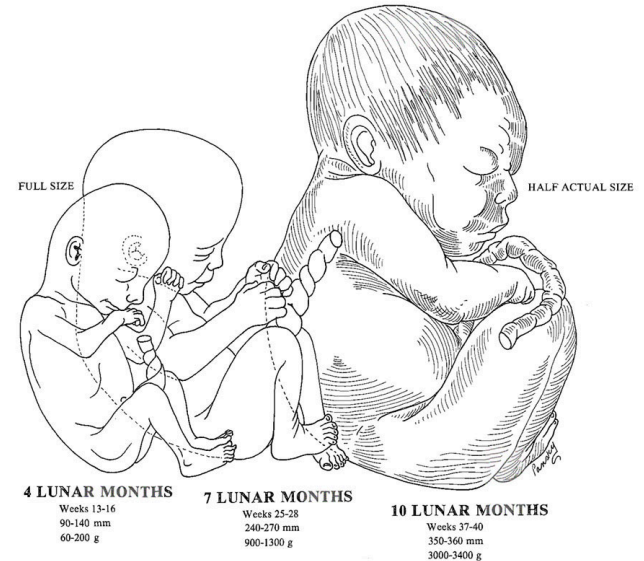
## Weeks 26 - 29

- fetal eyes reopen, head & lanugo hair well developed
- Increased subcutaneous fat, skin smooths out
- White fat increases to 5%
- **fetus is viable and can survive if born prematurely (mortality is high ->respiratory issues)**
- **CNS is mature and can control breathing & body temp**
- **28 weeks: 90% survival without impairment**

## Weeks 30-34

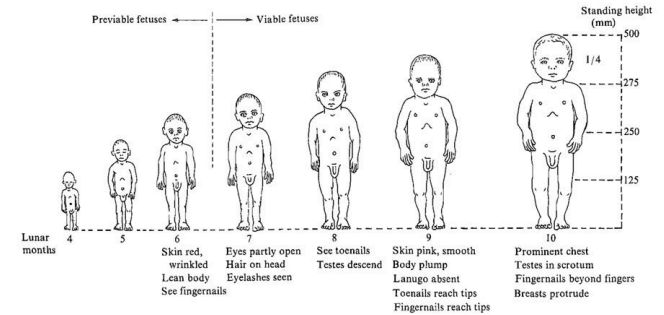
- Pupillary reflex present
- CRL @36weeks ~32cm
- Skin smooth and pink, and limbs proportionate
- White fat increases to 7-8%

## Weeks 35-38



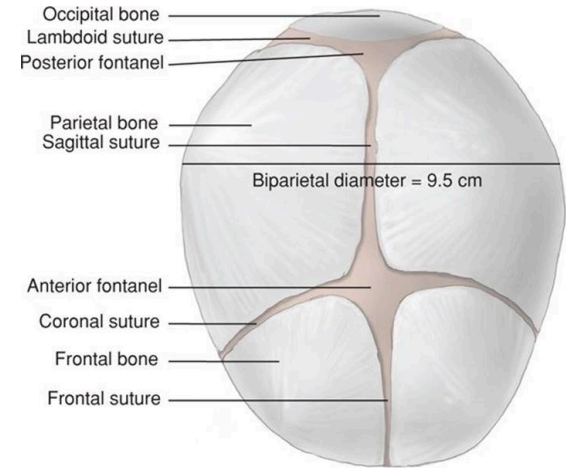
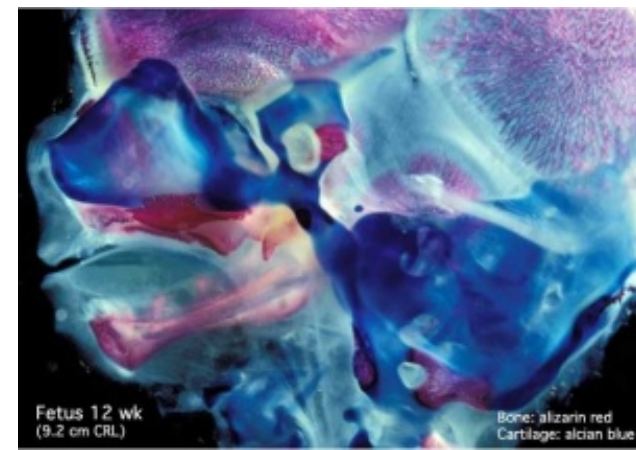
# Calculation of date of birth

- 266 days or 38 weeks after fertilization, or 280 days (about 40 weeks) from the onset of the last menstrua period (usually 10-15 days within this range)
- Variations are due to irregular menstrual periods and difficulty of counting
- *To calculation of birth date: in the typical 28-day menstrual cycle, count back 3 calendar months from the **first day of the last menstrual period** and then add 1 year and 1 week*
- Postmature infants are thin and have dry, parchentlike skin



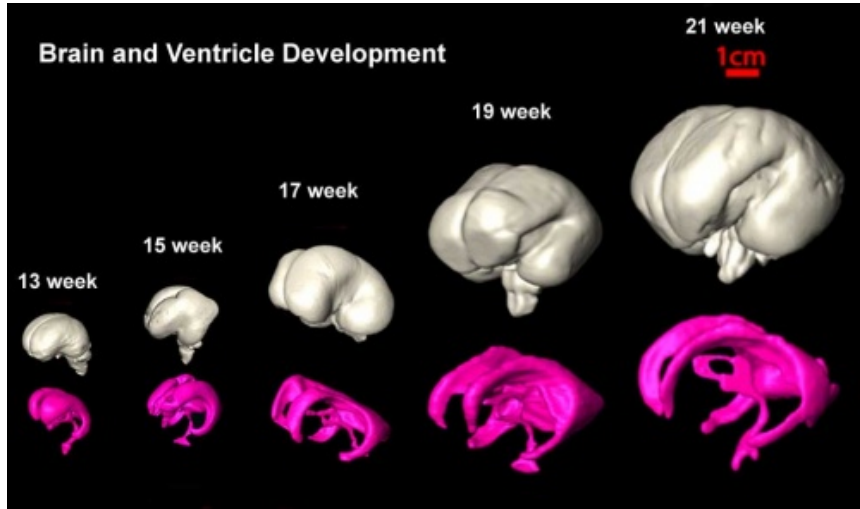
# Musculoskeletal

- **Primary ossification** centres appear at 12 weeks: endochondral and intramembranous
- Ossification of facial skeleton visible on US
- Long bones grow in length in fetal period and continues postnatally to ~25 years
- **Rapid growth periods** e.g. puberty
- **Relocation of haemopoietic stem cells** to bone marrow





# Neural Development

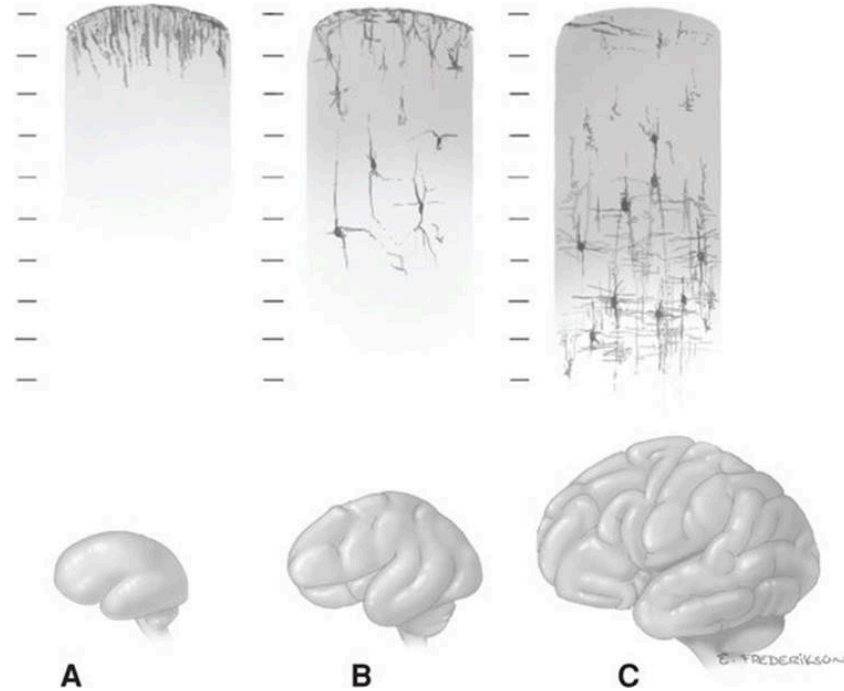


- Brain: **growth in size**, weight and surface area
- Microscopically there is ongoing: cell migration, extension of processes, cell death and glial cell development.
- Development of ventricular system
- **16 weeks:** eye movements begin weeks coinciding with midbrain maturation
- **22-25 weeks:** cochlear function begins and matures postnatally
- **26 weeks:** nociceptors are present over all the body, and the neural pain system is developed (Kadic, 2012)



# Nervous System

- **Cortical maturation** and vascularization of the lateral surface of the brain starts with the insular cortex (insula, insular cortex or insular lobe) region during the fetal period.
  - In adult: lies deep within the lateral sulcus
- **Sulcation and gyration** - in 2<sup>nd</sup> and 3<sup>rd</sup> trimesters, grooves or folds (sulci) visible on fetal brain surface as gyri grow (gyration)
  - Abnormality: smooth brain (lissencephaly)



# Cardiovascular

## Heart:

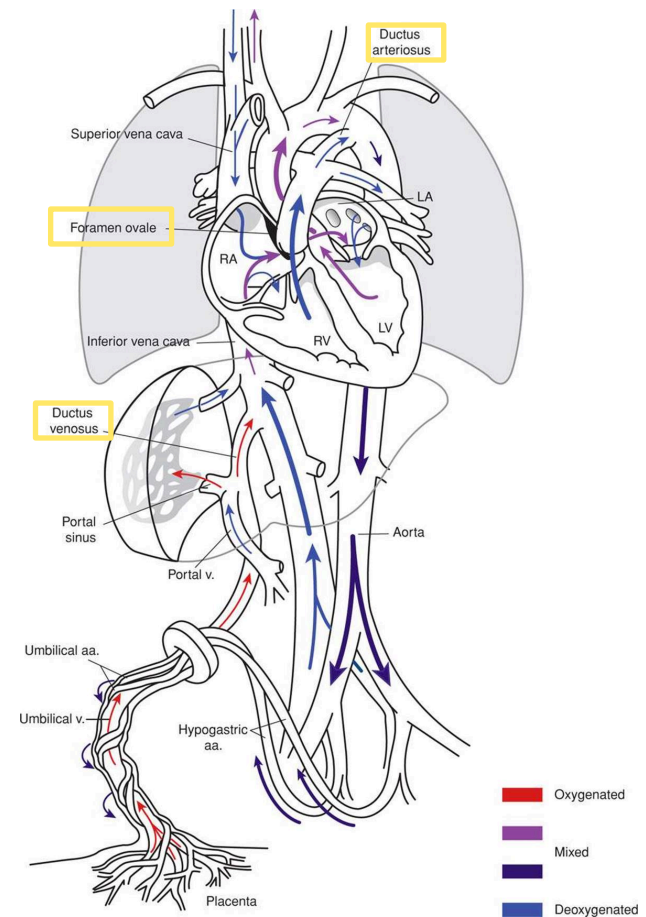
- At end of fetal period: **3 septation events** (atrial, ventricular and outflow tract) completed
- **3 vascular shunts** (foramen ovale, **ductus arteriosus**, ductus venosus) remain until after birth

## Blood Cells

- Fetal RBC- contain fetal haemoglobin (HbF) – needs to change to the form
- Fetal WBC- neutrophils, monocytes, and macrophages are produced. Neutrophils appear in clavicle marrow at 10-11 weeks
- Mononuclear phagocytes do not mature until after birth

## Circulation

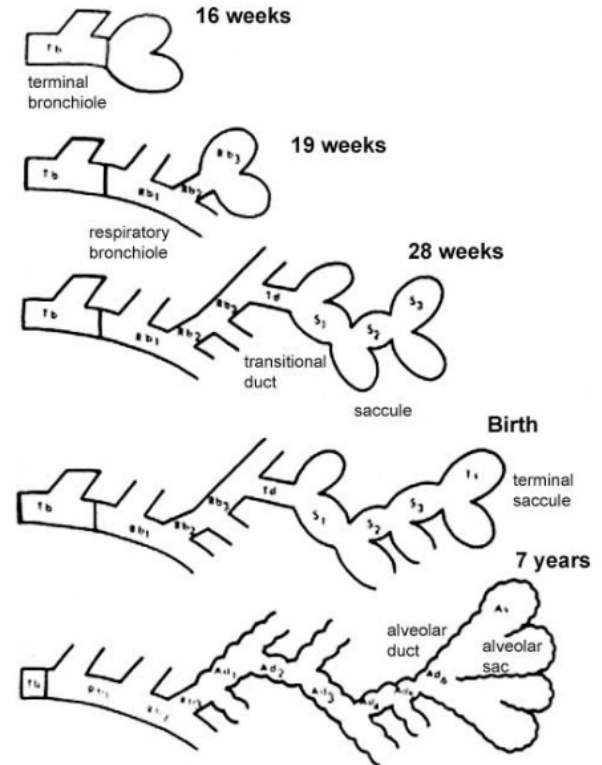
- Dramatic changes at birth



# Respiratory

## Lung Stages

- **week 4 - 5** embryonic
- **week 5 - 17** pseudoglandular – intersegmental bronchi
- **week 16 - 24** canalicular – bronchi cartilage, alveoli ducts appear
- **week 24 - 32** terminal sac – primitive alveoli
- **late fetal - 8 years** alveolar



Modified from Dilly SA. Thorax. 1984 Oct;39(10):733-42. PMID: 6495241

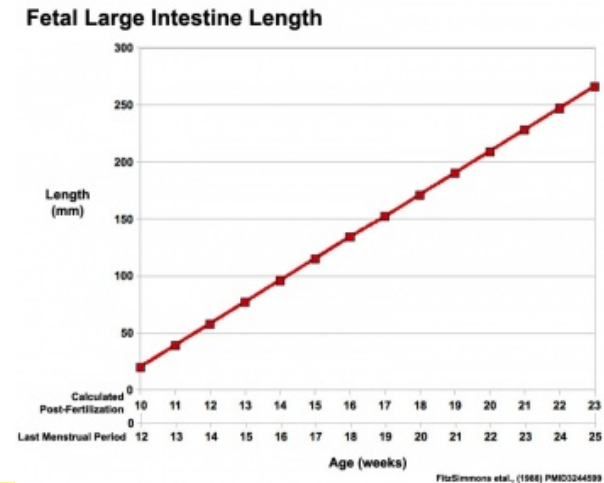
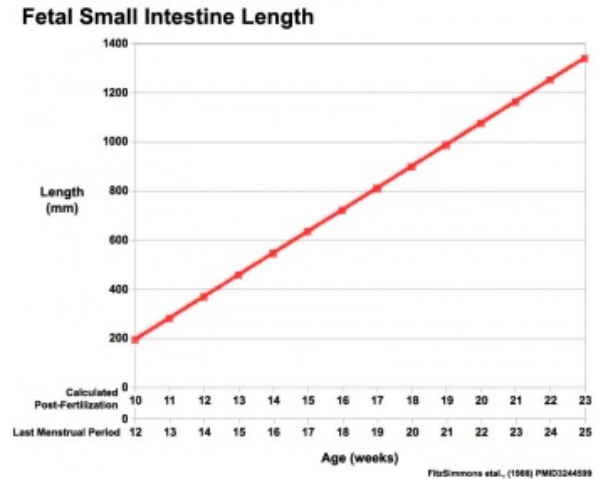
# Gastro-intestinal Tract

## Fetal development :

- initially herniated outside the ventral body wall
- growth and rotation of intestines mesentry
- change in mesenteries
- Differentiation of tract wall
- Vascularisation and innervation

## Initial functions:

- **Swallowing commences at 10-12 weeks:**
- **amionic fluid swallowing** - absorbed through the GIT and respiratory epithelium,. At term ~200-750ml
- **meconium** - accumulation of both secretions and swallowed components within the large intestine



# Birth Defects

# Congenital Malformations

Abnormalities present at birth



- Malformation
- Deformation
- Dysplasia
- Disruption

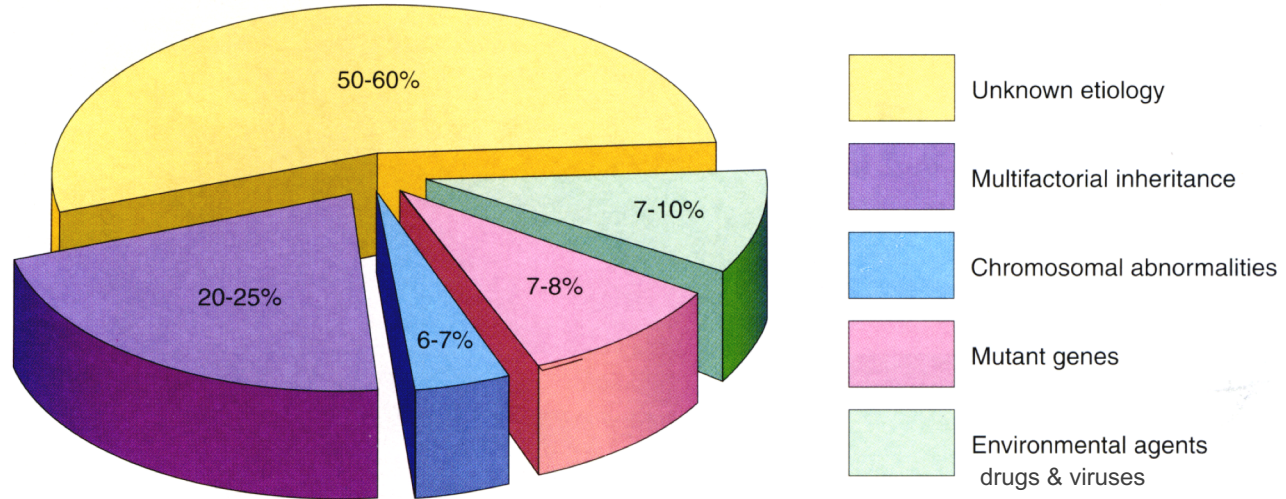
~20% neonatal deaths caused by malformations

~4% live births have one or more congenital abnormality

~6% one year olds have one or more congenital malformations

# What causes human birth defects?

Many causes are unknown



**Figure 9 - 1.** The causes of human birth defects. Note that the causes of most anomalies are unknown and that 20 to 25% of them are caused by a combination of genetic and environmental factors (multifactorial inheritance).

# Teratogens

**Teratogenesis: a process whereby an abnormality is induced in a developing organism during uterine life by foreign agents**

**Teratogenesis =  
To Produce a Monster**



© Disney/Pixar

Derived from the Greek words:  
*Gennan* = to produce  
*Terata* = monster



**UNSW**  
SYDNEY



# What is a teratogen?

Teratogenesis is commonly associated with chemicals/pollutants/radiation,

but there is more to it than this.....



## The Reality...

- Alcohol intake
  - Dietary intake
  - Virus exposure
  - Medication
- 
- Many substances could be teratogenic (dosage- and exposure-time-dependent)

# Common Teratogens

<b>Alcohol</b>	Fetal alcohol syndrome
<b>Vitamin A</b>	Cleft palate, mandibular hypoplasia, heart defects
<b>Rubella / HSV</b>	Deafness, cataracts, retinal dysplasia, microcephaly
<b>X-ray</b>	Microcephaly, spina bifida, cleft palate
<b>Valproate</b>	Neural tube defects, facial defects, limbs



# Teratogen Exposure

*'Pregnant women take on average 4 drugs excluding nutritional supplements per pregnancy. Around 40% of these are taken during the 'critical period'.*

Drugs used prior to knowledge of pregnancy

Drugs necessary for condition independent of pregnancy

Environmental agents that are impossible to avoid

Drugs necessary due to pregnancy specific condition



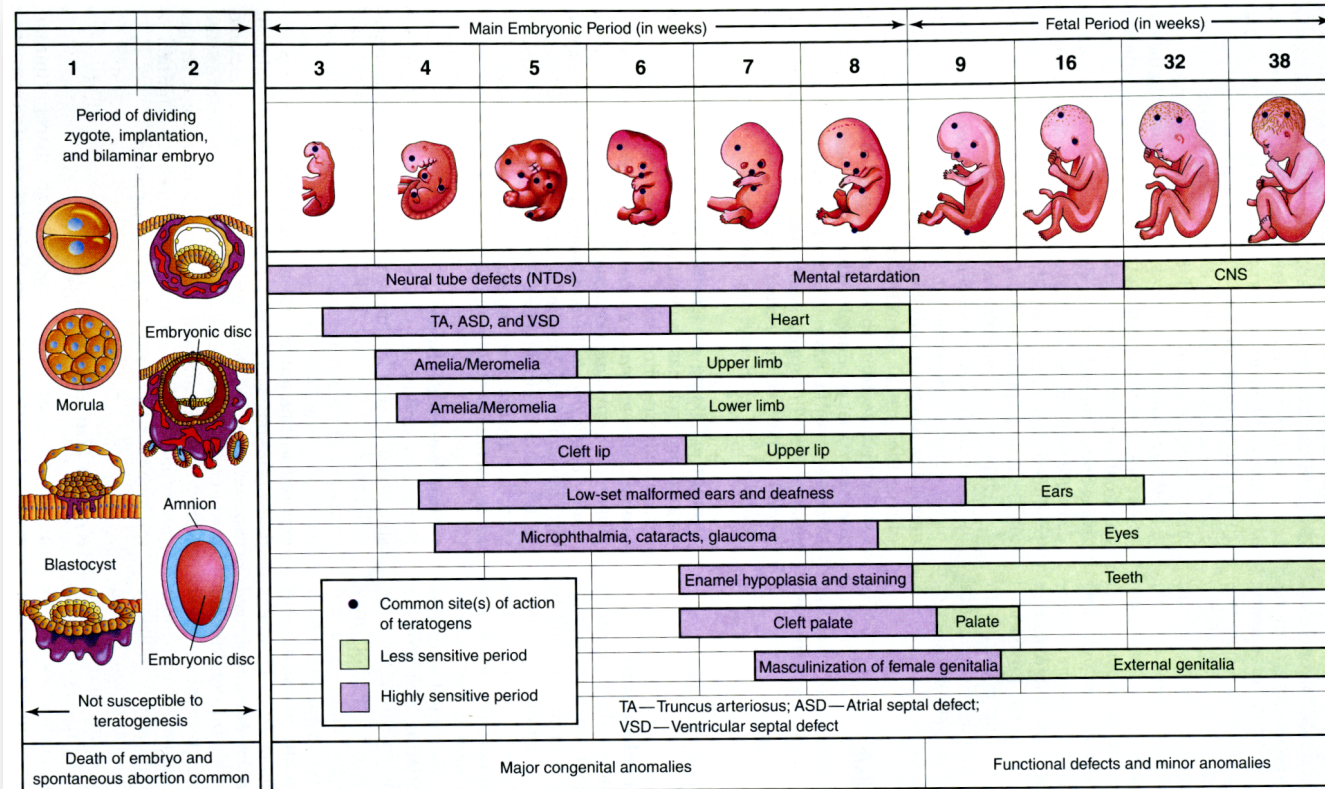
# Congenital Malformation: Nutritional Causes

Many birth defects could be prevented by appropriate avoidance or supplementation



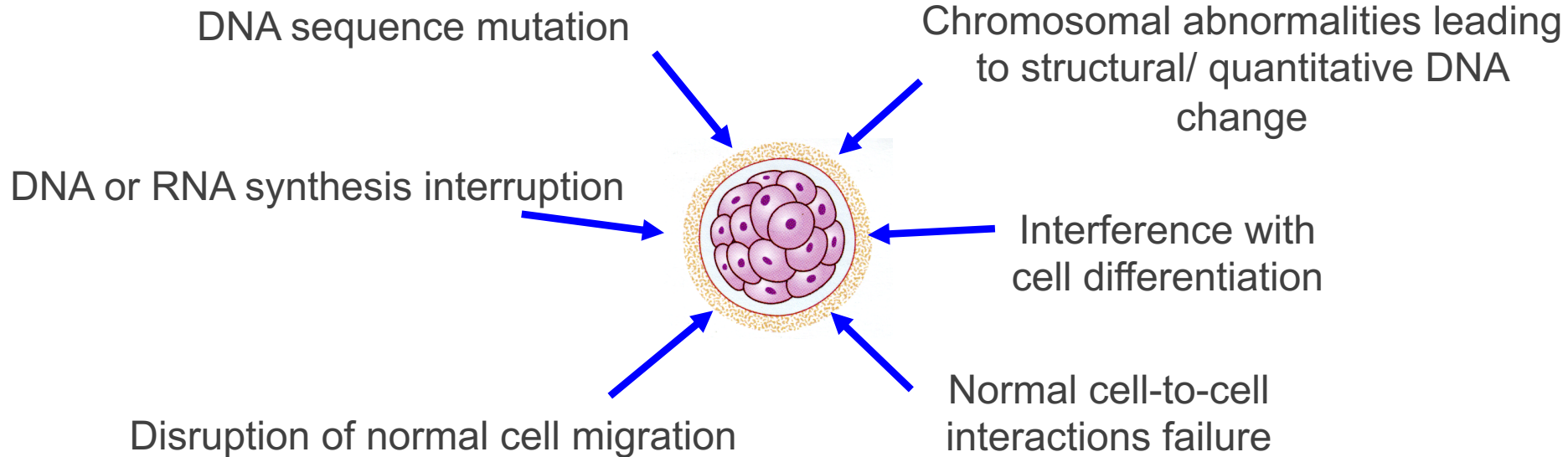
- Folate deficiency
- Zinc: too low or too high may cause problems
- Glucose & ketone bodies: diabetic conditions
- Retinoid excess

# Congenital Malformations



Taken from Moore & Persaud 'Before we are Born'

# Mechanisms of Teratogenesis

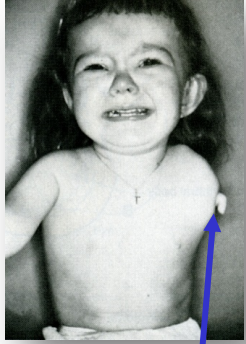


# Fetal Alcohol Syndrome

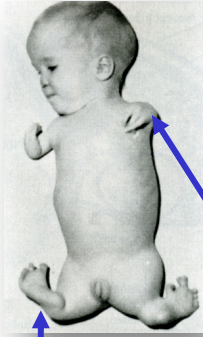


- Heart defects
- Short palpebral fissure
- Midline facial abnormalities (maxillary)
  - Lack of philtrum & thin top lip
  - Heavy epicanthic folds
  - Flattened nose
- Neural problems - behavioural & developmental

# Specific Abnormalities: limbs



Amelia



Meromelia

Phocomelia

- Teratogen or genetic mutation induced
- Thalidomide (anti-nauseant, sleeping pill)
- Retinoids (vitamin A derivatives)
- Mechanical *via* amniotic bands 'strangle' tissue



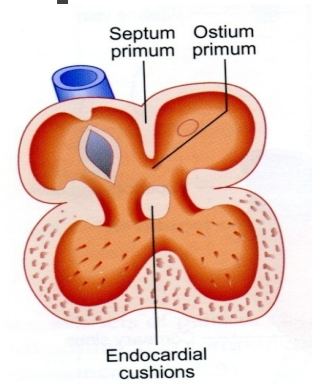
Polydactyly



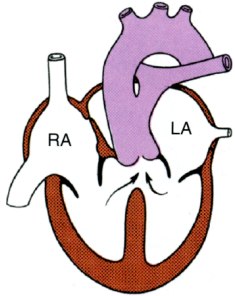
Syndactyly



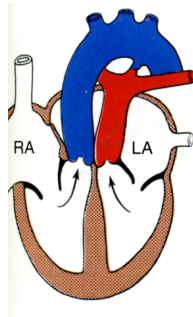
# Specific Abnormalities: cardiac



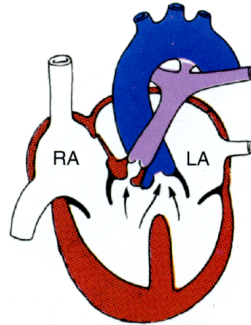
- Septal defects – can be neural crest cell associated
- Tetralogy of Fallot, transposition of great vessels
- Teratogens such as alcohol can cause cardiac defects



Ventricular-septal defect



Great vessel transposition



Tetralogy of Fallot

# Specific Abnormalities: spinal cord



Myelomelia



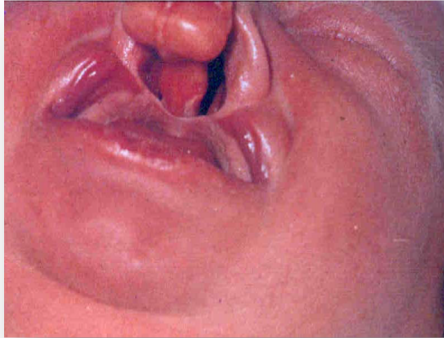
Meningocele



Anencephaly

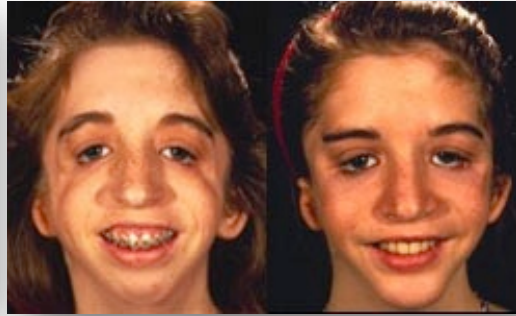
- Neural Tube Defects: meningocele, anencephaly
- Sensory system defects of the eye, ear
- Associated with multiple teratogens
- Associated with deficiency of folic acid

# Specific Abnormalities: face



- Associated with multiple teratogens e.g. Antiseizure drugs, retinoids, corticosteroids
- Cleft palate & lip
  - Cleft lip (1:1000 mainly male)
  - Cleft palate (1:2500 mainly female)
- Result from abnormal neural crest cell migration
- Tongue - macroglossia, microglossia

# Specific Abnormalities: face



Examples : Treacher-Collins or Pierre Robin Syndrome

- Autosomal dominant or teratogen-induced (alcohol, retinoids, maternal diabetes)
- Mandibulofacial maldevelopment/dysostosis (zygoma, mandible & maxilla)
- Downslanting palpebral fissure
- Malformed ears & possible conductive deafness

# Summary

- There are no absolutes in teratology
- Weeks 3-14 represent most susceptible period
- Advice pre-conception (Nutritional & Lifestyle)
- Avoid drugs where possible
- Choose the safest and prescribe minimal therapeutic doses

