Objectives

- At the end of lecture participants would be able to:
- Discuss system-wise basic fetal development
- Major anomalies associated with fetal development

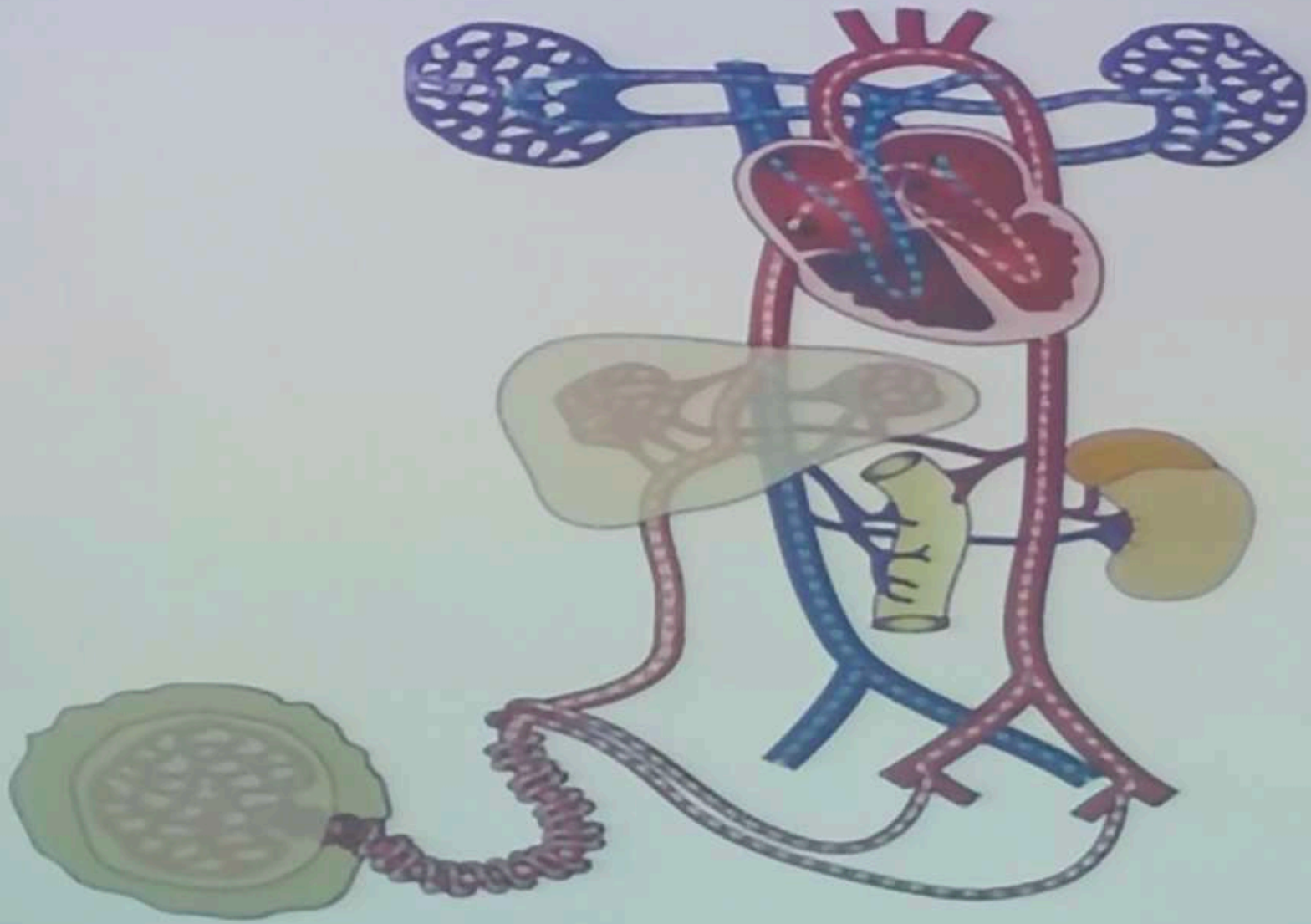
CARDIOVASCULAR SYSTEM & FETAL CIRCULATION

- The fetal circulation is characterized by **four shunts** that ensure that the oxygenated blood from the placenta is delivered to the fetal brain. These shunts are:
- **Umbilical circulation.**
- **Ductus venosus.**
- **Foramen ovale.**
- **Ductus arteriosus.**

UMBILICAL CIRCULATION

- The umbilical circulation carries fetal blood to and from the placenta for gas and nutrient exchange.
- Two umbilical arteries arise from the caudal end of the dorsal fetal aorta and carry deoxygenated blood from the fetus to the placenta.
- **Oxygenated blood** is returned to the fetus via the **umbilical vein** to the fetal liver.

before birth



- **Prostaglandin E2 and prostacyclin**, keep ductus arteriosus patent during fetal life.
- Premature closure of the ductus arteriosus has been reported with the administration of **cyclooxygenase inhibitors.**

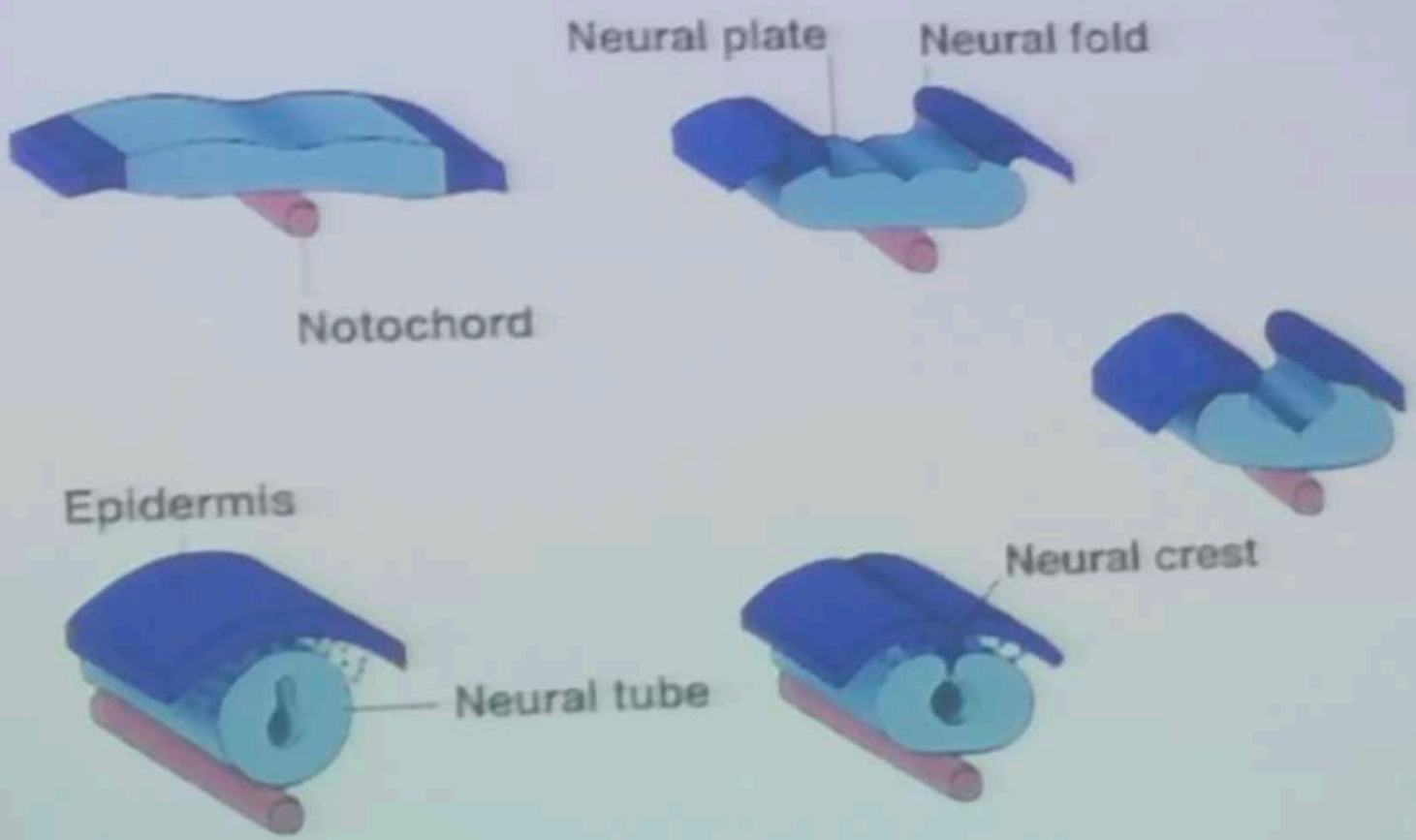
TRANSITION TO ADULT CIRCULATION

- At birth, **umbilical blood flow ceases causing cessation of flow in the ductus venosus**, leading to fall in pressure in the right atrium and **closure of the foramen ovale.**
- **Ventilation of the lungs opens** the pulmonary circulation, with a rapid fall in pulmonary vascular resistance, thus increasing the pulmonary circulation. The **ductus arteriosus closes** functionally within a few days of birth.

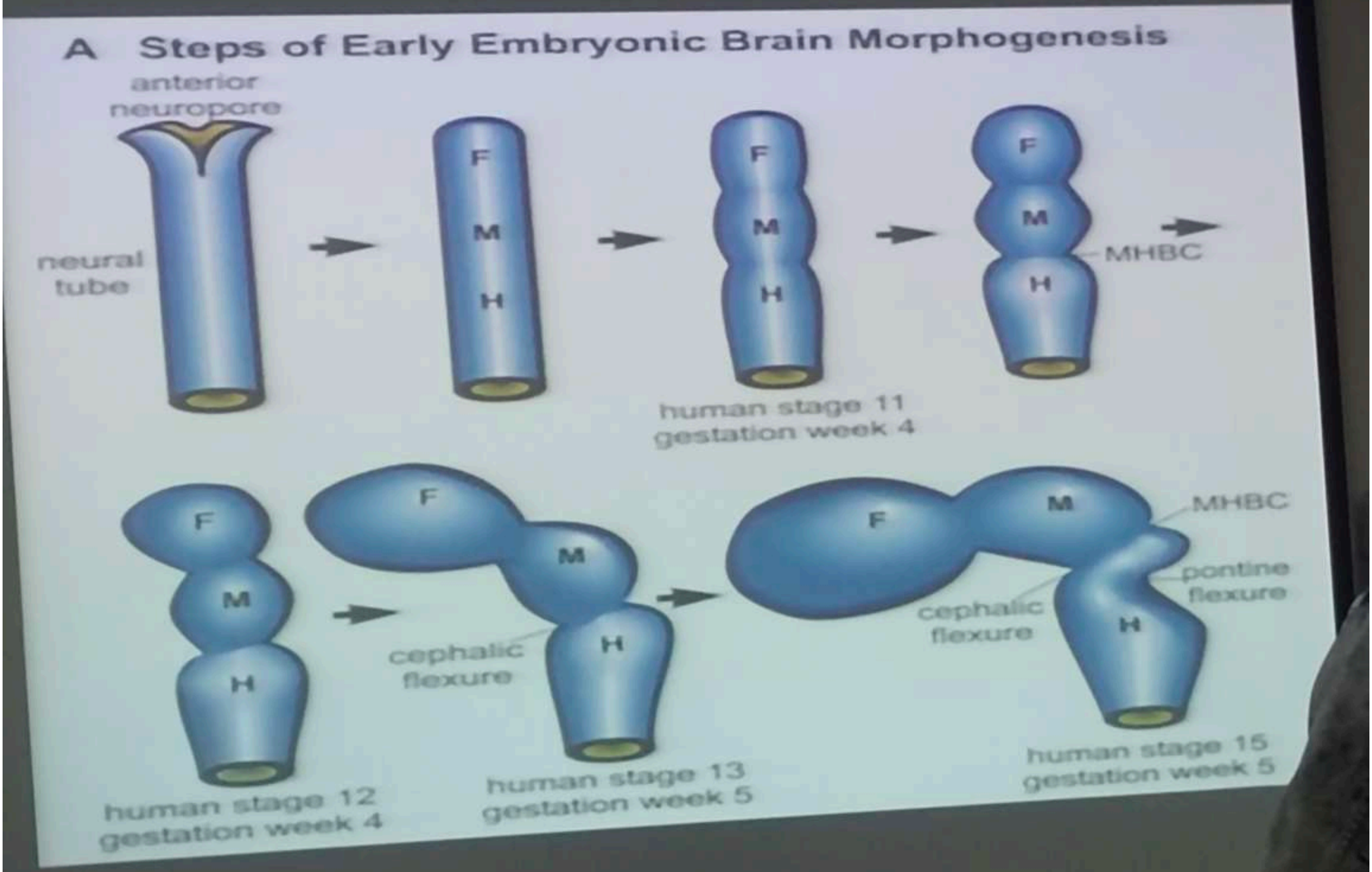
- The delay in closure of the ductus arteriosus is most commonly seen in **preterm infants** (<37 weeks' gestation).
- It results in left to right shunt leading to life threatening fetal hypoxia, congestion in the pulmonary circulation and a reduction in blood flow to the gastrointestinal tract and brain, causing necrotizing enterocolitis & intra ventricular hemorrhage.

CENTRAL NERVOUS SYSTEM

- The CNS appear at the beginning of 3rd **week** as a plate of **thickened ectoderm**, the neural plate.
- Its lateral edges elevate to form neural fold, which later on fuses to form neural tube.
- It is open initially from both ends, failure of closure of these opening can cause a major class of neural abnormalities called **neural tube defects (NTDs).**

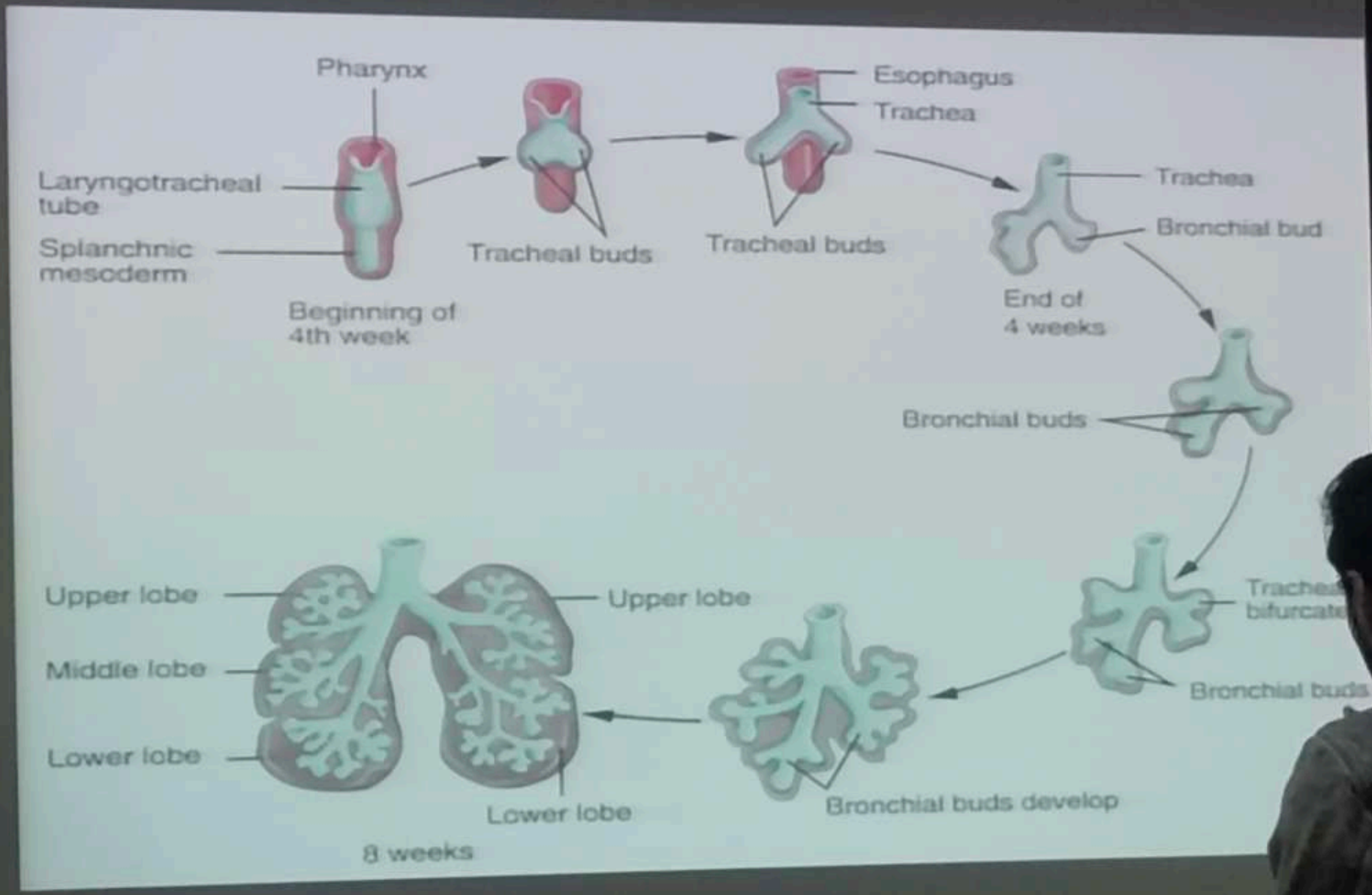

Neural plate
Neural fold
Notochord
Epidermis
Neural crest
Neural tube

- The cephalic end of the neural tube shows three dilatation, the primary brain vesicle
  - Prosencephalon
  - Mesencephalon
  - Rhombencephalon
- Simultaneously it forms two flexures
  - Cephalic flexure
  - Cervical flexure
- There is a rapid increase in total grey matter in the last trimester that is mainly due to a fourfold increase in cortical grey matter


A Steps of Early Embryonic Brain Morphogenesis
anterior neuropore
neural tube
F
M
H
human stage 11 gestation week 4
MHBC
human stage 12 gestation week 4
cephalic flexure
human stage 13 gestation week 5
pontine flexure
human stage 15 gestation week 5

REPIRATORY SYSTEM

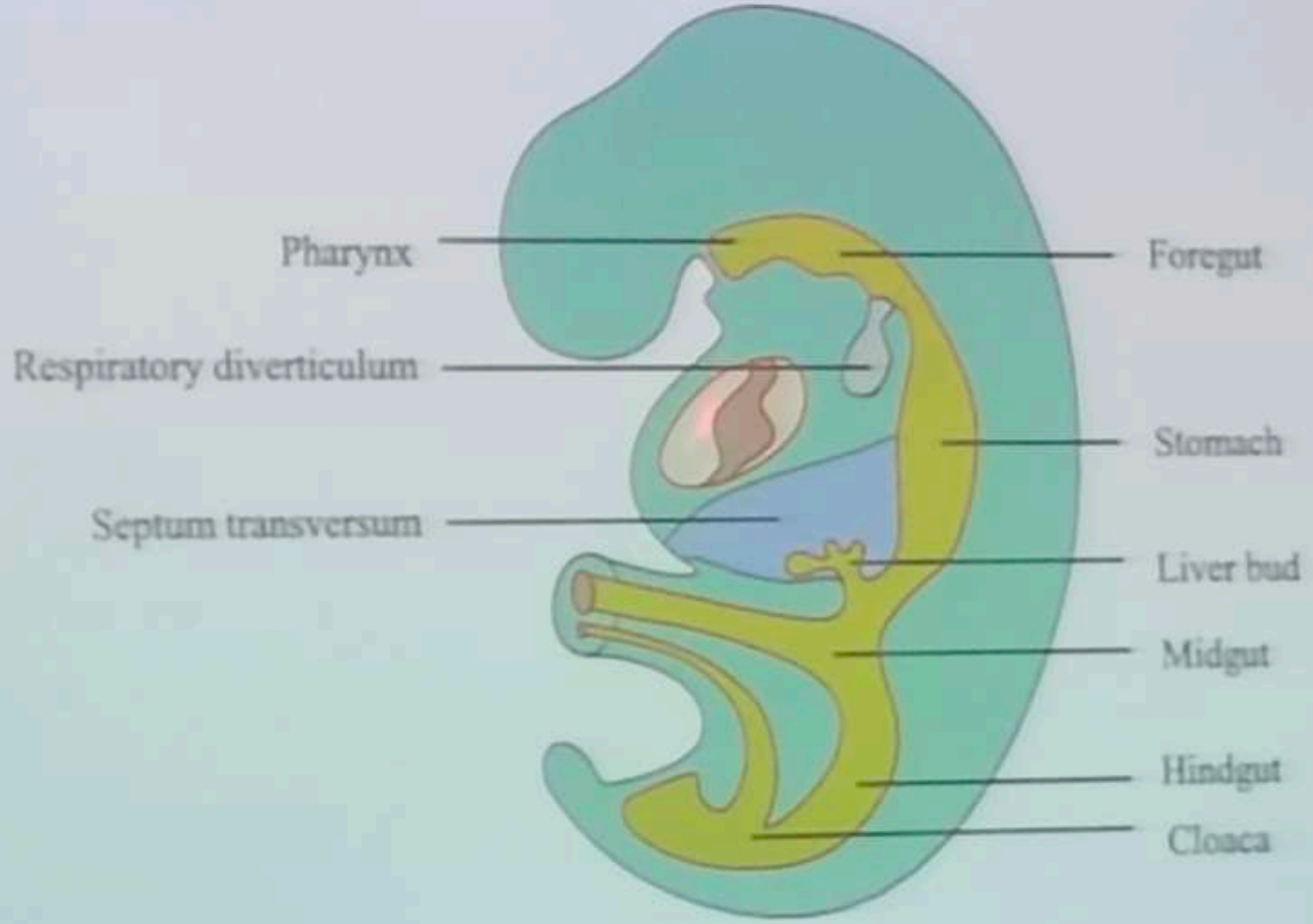
- The lung first appears as an **outgrowth from the primitive foregut.**
- By **4–7 weeks** epithelial tube branches and vascular connections starts forming
- By **20 weeks** the conductive airway and parallel vascular tree is well developed.
- By **26 weeks**, Type I and II epithelial cells are beginning to differentiate.
- Pulmonary surfactant, a complex mixture of phospholipids and proteins that reduces surface tension at the air–liquid interface of the alveolus, is produced by the type II cells starting from about **30 weeks**


Pharynx
Laryngotracheal tube
Splanchnic mesoderm
Beginning of 4th week
Tracheal buds
Esophagus
Trachea
Tracheal buds
Trachea
Bronchial bud
End of 4 weeks
Bronchial buds
Upper lobe
Middle lobe
Lower lobe
Upper lobe
Lower lobe
8 weeks
Bronchial buds develop
Bronchial buds

ALIMENTARY SYSTEM

- The primitive gut is present **by the end of the fourth week**, having been formed by folding of the embryo in both craniocaudal and lateral directions.

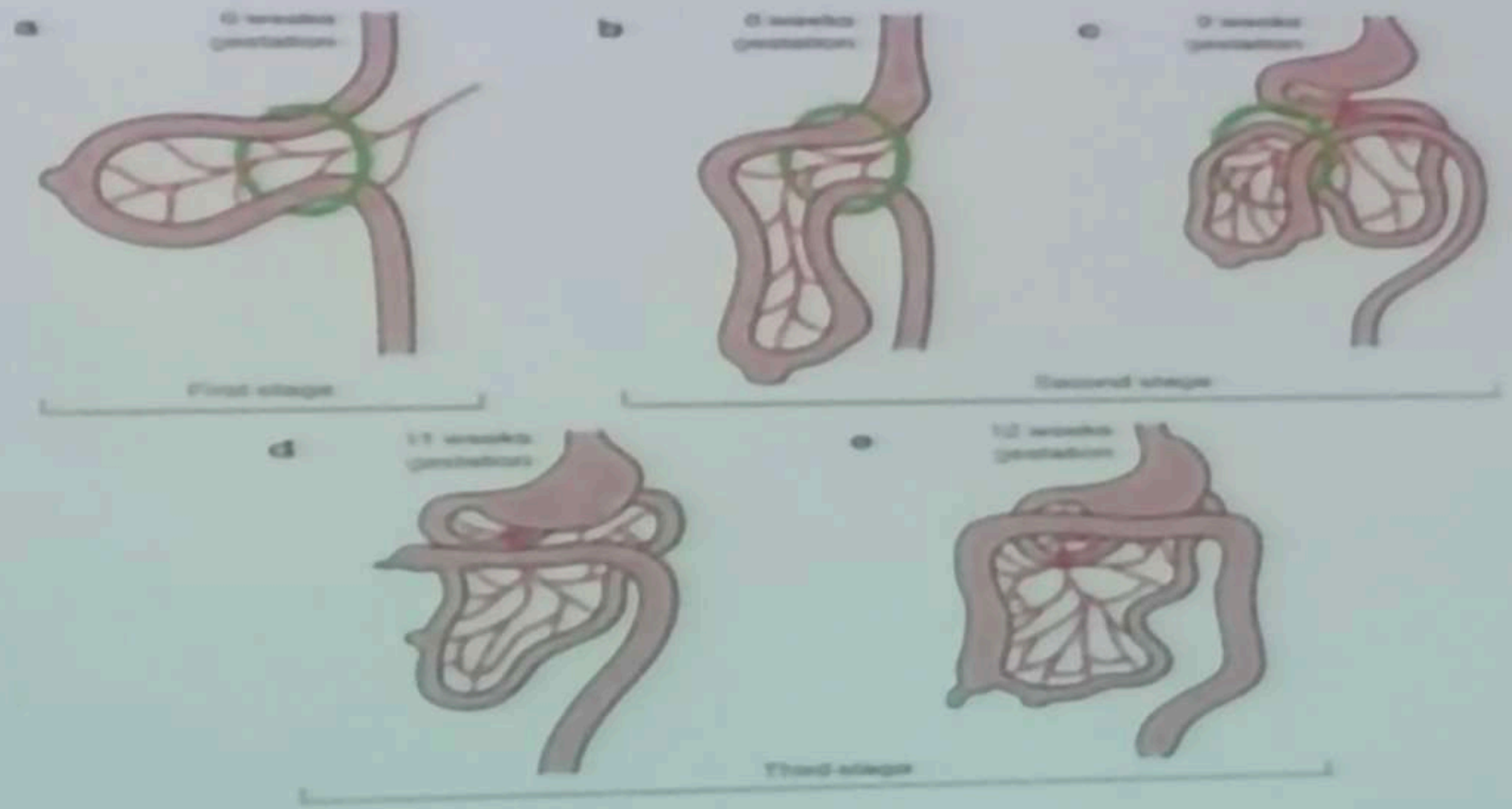
- The primitive gut consists of three parts, the **foregut, midgut and hindgut**, and is **suspended by a mesentery** through which the blood supply, lymphatics and nerves reach the gut parenchyma.


Pharynx
Respiratory diverticulum
Septum transversum
Foregut
Stomach
Liver bud
Midgut
Hindgut
Cloaca

- **The foregut endoderm** gives rise to the oesophagus, stomach, proximal half of the duodenum, liver and pancreas.

- **The midgut endoderm** gives rise to the distal half of the duodenum, jejunum, ileum, caecum, appendix, ascending colon and the transverse colon.

- The **hindgut endoderm** develops into the descending colon, sigmoid colon and the rectum.



- Between 5 and 6 weeks, due to the rapidly enlarging liver and intestine, the midgut is extruded into the umbilical cord as a physiological hernia.

- While herniated into the umbilical cord, the gut undergoes rotation prior to re-entering the abdominal cavity by 12 weeks of gestation.

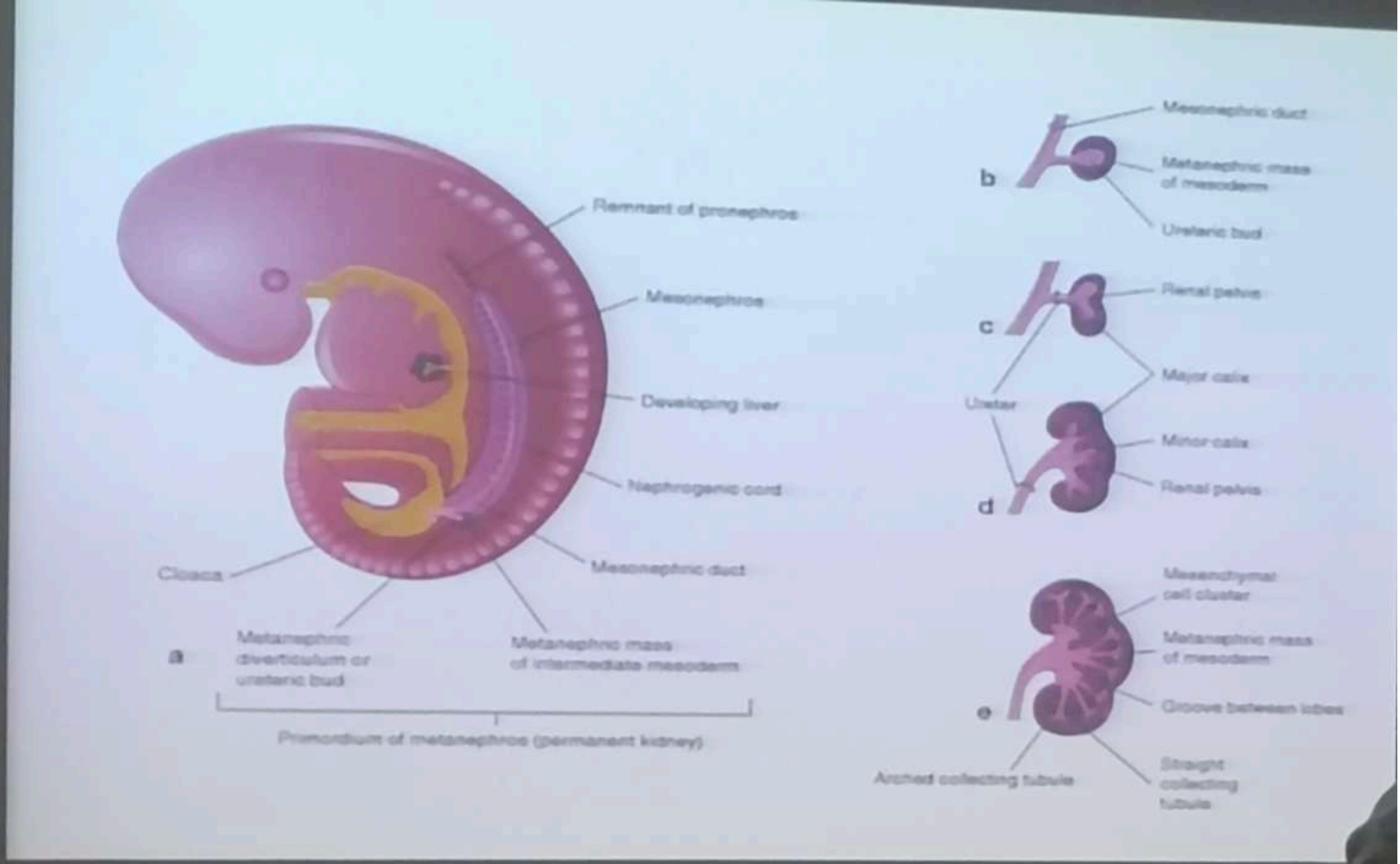
- Failure of the gut to re-enter the abdominal cavity results in the development of an omphalocele (otherwise called an exomphalos) and this condition is associated with chromosomal anomaly

DEVELOPMENTAL DEFECTS

- **Malrotation** can result in volvulus and bowel obstruction.
- **Atresias** exist when there is a segment of bowel in which the lumen is not patent and most commonly occur in the upper gastrointestinal tract (i.e. the oesophagus or duodenum).
- As the fetus continually swallows amniotic fluid, any **obstruction** that prevents fetal swallowing or passage of amniotic fluid along the gut will result in the development of polyhydramnios (excess amniotic fluid).
- Gastrointestinal **fistulae** can also occur, the most common being a tracheo-oesophageal fistula.

KIDNEYS & THE URINARY TRACT

- The development of the urinary tract begins with the formation of the nephrogenic cord in **week four**, along which the **pronephros, mesonephros** and **metanephros** form.
- Each pronephric duct grows towards the tail of the embryo, it induces intermediate mesoderm in the thoracolumbar area to become epithelial tubules called mesonephric tubules.
- The pronephros degenerates while the mesonephric (Wolffian) duct extends towards the most caudal end of the embryo, ultimately attaching to the cloaca.


Remnant of pronephros
Mesonephros
Developing liver
Nephrogenic cord
Mesonephric duct
Cloaca
Metanephric diverticulum or ureteric bud
Metanephric mass of intermediate mesoderm
a
Primordium of metanephros (permanent kidney)
b
Mesonephric duct
Metanephric mass of mesoderm
Ureteric bud
c
Renal pelvis
Major calix
Ureter
Minor calix
Renal pelvis
d
Mesenchymal cell cluster
Metanephric mass of mesoderm
Groove between lobes
e
Arched collecting tubule
Straight collecting tubule

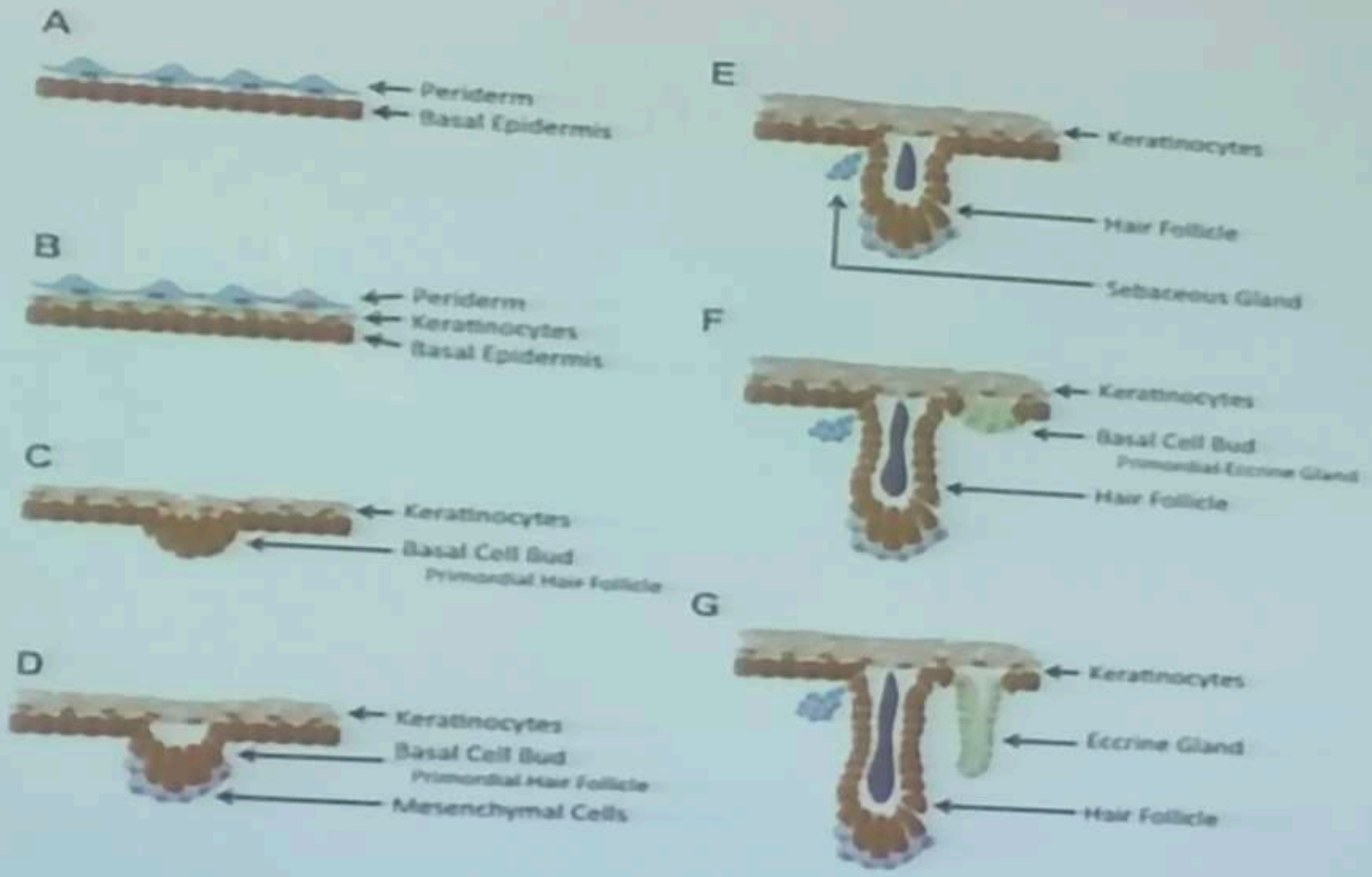
- **Failure of the normal migration** of the kidney upwards can result in a **pelvic kidney.**
- Abnormal development of the collecting duct system can result in duplications such as duplex kidneys.
- The most common sites of congenital urinary tract obstructive uropathies are at the pyeloureteric junction, the vesicoureteric junction or as a consequence of posterior urethral valves, an obstructing membrane in the posterior male urethra.

SKIN & HOMEOSTASIS

- The skin and its appendages (**nails, hair**) develop from the **ectodermal and mesodermal germ layers.**
- The **epidermis** develops from the **surface ectoderm**
- **Dermis and the hypodermis**, which attaches the dermis of the skin to underlying tissues, both develop from mesenchymal cells in the **mesoderm.**
- By the **fourth week** a single-cell layer of ectoderm surrounds the embryo
- **At about 6 weeks** this ectodermal layer differentiates into an outer periderm and an inner basal layer.
- The periderm eventually sloughs as the vernix.

SKIN & HOMEOSTASIS

- **The basal layer** produces the epidermis and the glands, nails and hair follicles.
- **By 16–20** weeks all layers of the epidermis are developed
- Hair follicles begin to develop as hair buds between **12 and 16 weeks** from the basal layer of the epidermis.
- **By 24 weeks** the hair follicles produce delicate fetal hair called lanugo, first on the head and then on other parts of the body. This lanugo is usually shed before birth.
- Fetal skin protects and facilitates homeostasis.


A
Periderm
Basal Epidermis
B
Periderm
Keratinocytes
Basal Epidermis
C
Keratinocytes
Basal Cell Bud
Primordial Hair Follicle
D
Keratinocytes
Basal Cell Bud
Primordial Hair Follicle
Mesenchymal Cells
E
Keratinocytes
Hair Follicle
Sebaceous Gland
F
Keratinocytes
Basal Cell Bud
Primordial Eccrine Gland
Hair Follicle
G
Keratinocytes
Eccrine Gland
Hair Follicle

ENDOCRINE SYSTEM

- Major components of the hypothalamic–pituitary axis are in place by **12 weeks** gestation.
- **Thyrotrophin Releasing Hormone** (TRH) and **Gonadotrophin Releasing Hormone (GnRH)** have been identified in the fetal hypothalamus by the **end of the first trimester.**
- Testosterone produced in the **first trimester** of pregnancy and increases to 17-21 weeks, which mirrors the differentiation of the male urogenital tract.
- **Growth hormone** is similarly present from early pregnancy and detectable in the circulation from **12 weeks.**
- **The thyroid gland** produces T4 from **10 to 12 weeks**

BLOOD & IMMUNE SYSTEM

- Red blood cells and immune effect cells are derived from **pluripotent haematopoietic cells**, first noted in the **blood islands of the yolk sac.**
- **By 8 weeks** the yolk sac is replaced by the liver as the source of these cells
- **By 20 weeks** almost all of these cells are produced by the **bone marrow.**
- At term the ratio of HbF to HbA is 80:20; by 6 months of age, only 1% of haemoglobin is HbF.
- Abnormal haemoglobin production results in thalassaemia

BEHAVIOURAL STATE

- From conception, the fetus follows a developmental path with milestones that continue into childhood.
- The first activity is the beating of the fetal heart followed by fetal movements at 7–8 weeks.
- By 12 weeks yawning, sucking and swallowing develops.

FOUR FETAL BEHAVIOURAL STATES

- **1F is quiescence**-1F is similar to quiet or non-REM sleep in the neonate
- **2F is frequent and periodic gross body movements with eye movements** -2F to REM sleep
- **3F no gross body movements but eye movements** -3F to quiet wakefulness
- **4F vigorous continual activity again with eye movements**- 4F active wakefulness
- An understanding of fetal behaviour can assist in assessing fetal condition and wellbeing.

AMNIOTIC FLUID

- The amniotic fluid is initially secreted by the amnion,
- **By the 10th week** it is mainly a transudate of the fetal serum via the **skin and umbilical cord.**
- **From 16 weeks' gestation, the fetal skin becomes impermeable to** water and the net increase in amniotic fluid is through a small imbalance between the contributions of fluid through **the kidneys** and lung fluids and removal by fetal swallowing.
- The amniotic fluid contains growth factors as well as multipotent stem cells

AMNIOTIC FLUID VOLUME

- Amniotic fluid volume increases progressively
- 10 weeks: 30 ml
- 20 weeks: 300 ml
- 30 weeks: 600 ml
- 38 weeks: 1,000 ml
- 40 weeks: 800 ml
- 42 weeks: 350 ml
- The amniotic fluid index is calculated as the total measurement of the deepest pool in the four quadrants of the uterus.