NORMAL FETAL DEVELOPMENT & FETAL CIRCULATION

Fetal growth and development:

Is dependent on adequate transfer of nutrient and oxygen across the placenta, by itself is dependent on adequate maternal nutrition and placental perfusion. Fetal hormones have an important role in fetal development they affect the metabolic rate, growth of tissues and maturation of individual organs, For example: IGFs co-ordinate a precise and orderly increase in growth through late gestation.

Insulin and thyroxin are required through late gestation to ensure appropriate growth in normal and adverse nutritional circumstances (fetal hyperinsulinemia as in DM result in macrosomia due excessive fat deposition, while in growth restricted fetuses fetal insulin levels are low). Lack in thyroid hormone produces deficiency in skeletal and cerebral maturation (cretinism), also there is delayed surfactant production. Cortisol has a limited role in stimulating growth, but it is essential in:

1. Lung compliance and surfactant release, which ensure that spontaneous breathing can occur at birth.
2. In the fetal liver, it induces beta receptor and glycogen deposition to maintain a glucose supply to the neonate after delivery.
3. In the gut it is responsible for villus proliferation and induction of digestive enzymes, which enable the neonate to switch to enteral feeding after birth.

The average birth weight is about 3.5 kg at the end of normal pregnancy.

1/3 of the eventual birth weight is reached by 28 wk, ½ by 31 wk, 2/3 by 34 wk. Each baby has its own optimal growth potential, which is predictable from physiological characteristics known at the beginning of pregnancy; those factors are:

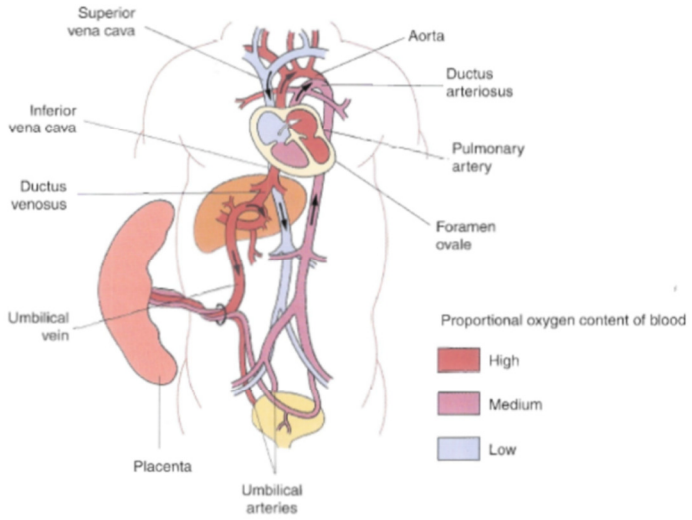
- Pre-pregnancy weight and maternal booking weight (increasing with maternal weight).
- Maternal height (increasing with maternal height)
- Maternal age and parity increased with mother > para2.
- Ethnic group (low in South Asian and Afro-Carbbean).
- Fetal sex (male >female).
- Paternal height.

Maternal smoking affect the birth weight significantly adversely, it is consistent and dose dependent. Growth restricted fetuses are those who have failed to achieve their growth potential, they have significantly higher perinatal mortality and morbidity rate.

Growth restricted fetuses/infants are more likely suffer from:

- Intrauterine hypoxia/asphyxia
- Stillborn
- Hypoxic ischemic encephalopathy (seizure)
- Multi organ failure
- Neonatal hypothermia, hypoglycemia, infection and necrotizing enterocolitis
- Cerebral palsy
- In adulthood they are at greater risk of hypertension, IHD, NIDDM

Cardiovascular system (fetal circulation):



Is quite different from that of the adult by the follows:

1. Oxygenation occurs in the placenta not in the lung.
2. The right and left ventricles wok in parallel rather than in series.
3. The heart, brain and the upper body receive blood from the left ventricle, while the placenta and lower body receive blood from both right and left ventricles.

There are modifications in fetal vascularity that ensure that the best, oxygenated blood from the placenta is delivered to the fetal brain, these are:

1. The ductus venosus that shunts blood away from the liver.
2. The foramen ovale, shunts blood from right to left atrium.
3. The ductus arteriosus that shunts blood from the pulmonary artery to the aorta.

Oxygenated blood from the placenta returns to the fetus through the umbilical vein, which is divided into two main branchs:

1. One supply the portal vein in the liver.
2. Another narrow vessel called ductus venosus which joins the inferior vena cava as it enters the right atrium.

50%of oxygenated blood will to the portal system and 50% will pass to the ductus venosus. The ductus is a narrow vessel and high blood velocities are generated within it. The streaming of ductus venosus blood , together with a membranous valve in the right atrium (the crista dividens), prevents mixing of the well- oxygenated blood from the ductus venosus with the desaturated blood of the inferior vena cava. The ductus venosus stream passes across the right atrium through a physiological defect in the atrial septum (foramen ovale) to the left atrium, then the blood will pass to the left ventricle through the mitral

valve and hence to the aorta. 50% of the left ventricle blood goes to the head and upper extremities, the remainder passes down to the aorta to mix with blood of reduced oxygen saturation from right ventricle. Blood from inferior vena cava and superior vena cava is directed across the tricuspid valve to the right venricle.Only a small portion of RT ventricle blood passes to the lungs as they are not functional. Most of the Rt ventricle blood is directed through a narrow vessel (ductus arteiosus) into the decending aorta below the origin of head and neck vessels from the aortic arch. The desaturated blood from the RT ventricle passes down the aorta to enter the umbilical arterial circulation and hence to the placenta. Prior to birth, the ductus remains patent due to production of the prostaglandin E2 and prostacyclin which act as local vasodilator, so administration of cyclo-oxygenase inhibitor will lead to premature closure of the ductus. At birth, the cessation of umbilical blood flow causes cessation of flow in the ductus venosus , a fall in the right atrium pressure and closure of the foramen ovale. Ventilation of the lungs opens the pulmonary circulation, with rapid fall in pulmonary vascular resistance. The ductus arteriosus closes functionally within a few days of birth.

Persistent fetal circulation: Occurs when there is delayed closure of the ductus arteriosus after birth because the pulmonary vascular resistance fails to fall despite adequate breathing. Results in left to right shunting of blood from the aorta through the ductus areriosus to the lung. The baby remains cyanosed and can suffer from life threatening hypoxia. This is mostly occurs in the premature infants. Result in congestion in the pulmonary circulation and reduction in the blood flow to the gastrointestinal tract and brain that lead to necrotizing enterocolitis and intraventricular haemorrahge.

Respiratory system (lung):

By 20 wk gestation full differentiation of capillary and canalicular elements of the fetal lung is apparent, but alveoli develop after 24wk. Fetal breathing movements occur in utero especially during rapid eye movement. Adequate amniotic fluid volume is necessary for lung maturation. The fetal lung is filled with fluid, the production of this fluid starts from early gestation and ends in the early stages of labour. At birth the production of this fluid must cease and the fluid present is absorbed, adrenaline plays a major role in this process. Lung alveoli are lined by a group of phospholipids known collectively as surfactant that prevents the collapse of small alveoli during expiration by lowering surface tension. The surfactant is continually produced from type 2 alveolar cell (10% of the lung parenchyma), maximum production will be after 28 wk. The predominant phospholipid (about 80% of total) is phosphotidylcholine (lecithin); and its production is enhanced by cortisol, growth retardation and prolonged rupture of membrane; and is delayed in diabetes. Phosphoatidylglycerol is another type of potent phospholipid that is present in the amniotic fluid, and it is more predictive of respiratory distress syndrome especially in diabetic preganat women. Oligohydramnios and reduced intrathoracic space (daiphragmatic hernia) or chest wall deformities can result in pulmonary hypoplasia, which lead to progressive respiratory failure from birth. Respiratory distress syndrome (RDS)is specific to babies born prematurely and is associated with surfactant deficiency. RDS may be complicated by hypoxia, intraventricular haemorraghe and necrotizing enterocolitis. The incidence and severity of RDS can be reduced by administrating steroids antenatally to mothers at risk of preterm delivery.

Fetal blood

The first fetal blood cells are formed on the surface of the yolk sac from 14 to 19 days after conception. Haemopoiesis from the yolk sac continues until the 3rd post-conceptional month. During the 5th wk of embryonic life extramedullary haemopoiesis begins in the liver and to a lesser extent in the spleen. The bone marrow starts to produce red blood cells at 7-8 wk and is the predominant source of red cell from 26 wk of gestation. Most haemoglobin in the fetus is the fetal haemoglobin (HbF) that has 2 gamma chains (2 alphas, 2 gammas). While the adult Hb is composed from HbA (2 alpha, 2 beta) chains and HbA2 (2 alpha, 2 delta) chains. 90% of fetal Hb is HbF from 10 to 28 wk. From 28-34 wk a switch to HbA occurs. At term the ratio of HbF to HbA is 80:20, by 6th month of age only 1% of the Hb is HbF. The HbF had high affinity for oxygen than HbA. This with association with a higher Hb concentration (at birth the mean capillary Hb is 18 g/dL) will enhance transfer of oxygen across the placenta. Abnormal Hb production results in thalassaemia. Beta major thalassaemia without treatment will results in severe anemia, fetal growth restiction, poor musculoskeletal development and skin pigmentation due to increased iron absorption. Severe alpha thalassaemia resuls in severe fetal anemia with cardiac failure, hepatoseplenomegaly & generalized odema, the infants are stillborn or shortly die after birth.

Immune system: The fetus reqiures an effective immune system to resist intrauterine and perinatal infections. Lymphocytes appear from 8 wk. By the middle of the second trimester all phagocytic cell, T and B cells and the complement are available to mount a response. Early infections with any of the TORCH organisms will affect the immune system. Immunoglobulin g (IgG) originates mostly from maternal circulation and crosses the placenta to provide passive immunity. The fetus normally produces a small amount of IgM and IgA, which don't cross the placenta. Detection of IgM& IgA in the newborn without IgG is indicative of fetal infection.

General immunological defences include:

-The amniotic fluid (lysosymes,IgG).

-The placenta (lymphoid cells, phagocytes, barrier).

-Granulocytes from liver and bone marrow.

-Interferon from lymphocytes.

Skin and homeostasis:

Fetal skin protects and facilitates homeostasis. The thickness of the skin increase progressively from the 1st month of gestation until birth. A stratum corneum forms in the 5th month and after 23 wks the appearance of the skin approaches that the adult epidermis. Vernix (consisting of desequemated skin cells, cholesterol and glycogen) is covering the skin of fetus in the last wks. Preterm infants have no vernix and thin skin, this allows a proportionately large amount of insensible water loss. Heat may be conserved by peripheral vasoconstriction and can be generated by brown fat catabolism which is deficient in preterm or growth restricted babies.

Alimentary system and energy stores

The primitive forgut and hindgut are present by the end of 4th wk as a straight tube suspended by the mesentery from the dorsal body wall. The midgut is herniated into the base of the umbilical cord during the 6th wk because the abdominal cavity is too small to accommodate the enlarging liver & intestine. By 12th wk the gut will re-enter the abdominal cavity but prior to that the gut undergoes rotation. Failure of the re-entre results in the development of omphalocele. The intestinal tract is patent from the time when the GIT is fully formed. The swallowing reflex develops and matures gradually. The fetus continually and increasingly swallows

amniotic fluid up to 20 ml/hr at term. A failure in the swallowing mechanism as in neurological abnormalities e.g. anencephaly and an obstruction gut e,g atresia of the esophagus will result in polyhydramnios. Peristalsis in the intestine occurs from the 2nd trimester. The large bowel is filled with the meconium, meconium stained liquor is a sing of post maturity and fetal hypoxia. Body water content gradually diminishes and the glycogen and fat stores increase about 5 fold in the last trimester. Preterm infants and growth restricted fetuses have reduced glycogen and fat stores.

Liver and gallbladder:

The primitive liver appears at about 18th day of embryonic life as a diverticulum arising from the duodenum. By the 25th day it has developed into a T shaped outgrowth which is invaded by blood vessels. The large portion of this diverticulum gives rise to the parenchymal cells and the hepatic ducts, while the small portion gives rise to the gallbladder. The liver plays an important in haemopoiesis starts from 6th wk and peaks at 12-16th wks and contiues untile 36th wk. Fetal liver differs from adult in that it has reduced ability to conjugate bilirubin because of relative deficiencies in necessary enzymes like glucuronyl transferase. The placenta is performing the normal metabolic function of liver. The glycogen store is small in the 1st trimester but it is maximal at term. The premature and growth restricted infants are more prone to jaundice and hypoglycemia.

Kidney and urinary tract:

The metanephros forms the renal collecting system (uerters,pelvis, calyces, and the collecting ducts). The mesenchyme of the nephrogenic cord forms the renal secretory system (glomeruli, convoluted tubes, loops of Henle). Nephrogenesis is complete by 36 wk. The maturation and the concenterating ability of the fetal kidneys is gradual, it is immature in preterm infant that may lead to abnormal water, glucose, sodium, or acid-base homeostasis. Fetal urine forms much of the amniotic fluid. Renal agenesis results in severe oligohydramnios.

Fetal behavior:

Fetal movement (quickening) can be 1st precieved by the mother by 18-

20 wk in primigravida, and several wks earlier in multigravida. Self-monitoring of fetal movement is an important method fetal well-being.

Diminished fetal movement may indicate chronic hypoxia and growth .restriction, this will need further investigation with maturation of the central nervous system, the fetus develops more complex and well defined behavioral states named 1F-4F.

-state 1F is similar to quit(non REM)sleep,absence of eye and body movements.

-state 2F periodic body and eye movement are present(REM sleep).

-state 3F is like quiet wakefulness when there are eye but no body movements.

-state 4F body in active ongoing body and eye movement.

> 80% of time the fetus will alternate between 1F and 2Fstate.

Amniotic fluid:

By 12 wk the amnion comes into contact to the inner surface of the chorion and obliterates the extra-embryonic space. The two membranes didn't contain blood vessels or nerves but do contain significant quantity of phospholipids and enzymes. Choriodicedual function play a pivotal role in initiation of labour through production of prostoglandin E2 and F2a. The amniotic fluid is initially secreted by the amnion. By 10th wk it is mainly a transudate of the fetal serum via the skin and umbilical cord. From 16 wks the skin become impermeable to water, so the increase in the amniotic fluid is through a contribution of kidney and lung fluids, and removed by fetal swallowing.

Amniotic fluid volume increases progressively: 10 wk: 30ml, 20 wk::300ml, 30 wk: 600ml and 38wk: 1000ml

From term there is rapid fall in the volume (40 wk :800ml, 42wk :350 ml). The function of amniotic fluid:

-protect the fetus from mechanical injury.

-permit fetal movement and preventing limbs contracture.

-prevent adhesions between the fetus and amnion.

-permit fetal lung development, if there is absence of the fluid especially in the 2nd trimester this will lead to pulmonary hypoplasia.