GENERAL INTRODUCTION
The process associated with development are maintenance, growth, differentiation and functional maturation. Each of these processes may individually or collectively influence the development. Specifically, by convention, growth implies an increase in size coupled typically with cell division, whereas development refers to increasing maturation and functional complexity along with growth. Such growth and development of human organisms proceed together from conception to maturity and during this period series of changes take place in overall enzymatic pattern which differ from organ to organ and are characteristics of those particular organs.

Heart is the major pumping station in the body. Therefore, the cardiovascular system attains functional importance relatively early in the life of the fetus and consequently the cardiovascular development is completed rapidly. In the human being, it takes about 8 weeks of gestational life for the heart to reach its definite four-chambered structure.

The origin of the human heart extend back in embryonic time when the cardiac tissue is morphologically or histologically recognizable. In mammal embryos which have been studied, regions of prospective heart material can be identified in the forming mesoderm layer during early gestation (stages 7 and 8) by the capacity of these fragments to differentiate into heart muscle when explanted from the embryo.
As the cardiogenic plate develops, the first histological evidence of distinguishable precardiac cells can be seen with the appearance of angioblasts in the region of the original amniocardiac vesicles (1).

Formation of the primary cardiac tube

In human embryo the early tubular heart has no epicardial layer. Epicardial cells migrate over the heart during stages 10-14 and gradually enveloping it. In the heart of 4 somite human embryo both the endocardium and premyocardium still give evidences of their bilateral origins. By 7-8 somites, the endothelial and myocardial tubes have fused.

'Conus cordis' which is situated caudal to the truncus arteriosus, forms the infundibulum of prospective right ventricle. The cephalic part of ventricular tube itself becomes the anatomic right ventricle. The paired halves of caudal ventricular region i.e. prospective left ventricle and primitive atrium are still widespread. Throughout stages 10 and 11, heart tubes elongates and fusion of premyocardial material occur. From this time, there is a progressive increase in the size of right and left side of right ventricle and left ventricle. The spaces between the endocardial tube become filled with cardiac gelly (2). The myocardial wall, which is single layered soon increase. The inner cells of this primary myocardium undergo rapid mitosis (3).
During stage 10, the human heart probably begins to beat (4). By stage 12 sufficient vascular specialization take place to permit, a simple circulatory system for the 1st time.

**Partitioning of the heart**

At the end of first month the primary heart tube has a pronounced curvature and shows local dialatations and constrictions. Yet it has not altered its primitive method of functioning. During the next three weeks of pregnancy, single tubular heart is converted into double pump system arranged in parallel, so that oxygenated blood from the lungs and systemic venous blood can later be handled separately. Further development establishes a one way passage for blood from the right atrium to the left.

After 8 weeks of gestation, the 4 chambered heart when fully formed, increases in size due to the thickening of the cellular wall and its functional development gradually predominates until the adult structure is attained.

The changes which may add their contribution range from the simple to the complex, there may be variations in the molecular properties of individual enzymes, differential synthesis or destruction of various enzymatically active protein, changes in their localization and attachment to,
the various components of the cells and finally, variations in their interaction with the general intracellular milieu (5-8).

**Cardiovascular energy metabolism**

The heart, as the result of its unique structure and function, has evolved an extraordinary complex metabolic system which is almost exclusively aerobic and provides a constant supply of high energy for mechanical and chemical work. As the heart is a constantly working organ therefore its energy use is high and important differences exist between the metabolism of cardiac and skeletal muscle. As there are more mitochondria in heart muscle (about 30% by volume) and it can utilize more substrates than skeletal muscle and under normal condition, the energy production in heart muscle is entirely by aerobic means (9). In fact, the cardiac muscle does not develop an appreciable 'oxygen debt' during each contraction, unlike the skeletal muscle.

The development of human fetal heart like many other organs are accompanied by several anabolic and catabolic events. It is now well established that these anabolic and catabolic processes are coordinated and integrated with great precision during morphogenesis of the organ.

In the post-absorptive state the heart obtains about two thirds of its energy from the oxidation of fatty acids. Though long
Chain fatty acids have been shown to be the principal metabolic fuel of the adult heart (10-12), it can also utilize lesser amounts of pyruvate and ketone bodies, but only very small amount of amino acids (13-15). Under ordinary conditions, amino acids do not contribute significantly to the energy production by the heart. By deamination, transamination and shortening of the carbon chain, amino acids are broken down to various members of the citric acid cycle for further oxidative metabolism. Human heart also utilizes significant amount of glucose and lactate for energy production. However for the heart tissues of mammalian fetus, carbohydrate rather than lipids appear to serve as the primary source of energy (16). This difference in energy metabolism related to maturation suggests that the heart of fetus and newborn, in contrast to that of adult, might be unable to utilize long chain fatty acids which may be due to low levels of carnitine and carnitine acyl transferase (17) required for the transfer of activated long chain fatty acyl group to the mitochondrial sites and must rely on glucose as the major substrate for energy production. Warshaw (18) have confirmed that the newborn and fetal heart have a greater capacity than the adult to oxidize glucose and therefore may be forced to rely upon carbohydrates as a primary source of energy. Several reports dealing with cardiac metabolism in newborn and fetal animals such as rat, rabbit, puppies etc. suggest that the immature heart is heavily dependent on glucose and glycogen metabolism (19-21) for their survival [Fetal
carbohydrate metabolism have been discussed in the next Chapter).

**Drugs in pregnancy**

Though it is advisable to stop all sort of medication during pregnancy yet it becomes unavoidable due to some risk to the mother and the conceptus. Until recently the usage of mild tranquiliser e.g., diazepam and analgesics were permitted in obstetrics. Not only that, sometimes it become necessary to use psychoactive drug to those psychic patients who are going to conceive. But each drug to be judged on its merit, the placental drug transfer, maternal and fetal drug metabolism and subsequently the harmful effect if any, it may exert on fetal development must be considered against its beneficial effect.

The use of the term 'placental barrier' typified a concept of the placenta as an organ where prime function is to protect the fetus against injury and infection and provides a physical barrier to the passage of noxious substances from mother to fetus. The substances essential for fetal development cross the placenta by a process of simple diffusion. The majority of other nutrients such as vitamins, amino acids and certain ions are transferred from mother to fetus against a concentration gradient. An adequate level of these essential nutrients are maintained on the fetal side of the barrier through the continued selective activity of the placental cells.
Various aspects of placental drug transfer have been reported by several authors (22, 23). The drugs and other exogenous compounds were reported to cross the placental barrier mainly by simple diffusion procedure depending on their lipid solubility (24). It is known that the young, both of animals and of human beings are more sensitive to certain drugs than the adults (25). The greater sensitivity could result from differences in the fate of drug - that is, with respect to absorption, excretion or metabolism. Numerous investigations in this area have created a massive, primarily descriptive literature tending to emphasize correlations between the morphologic rather than biochemical effects of teratogenic and embryopathic drugs. It seems desirable that the action of pharmacologic agents on developing biological system be viewed from a perspective which permits not only the analysis of drugs effects upon embryogenesis but also allows for an evaluation of how physiologic maturation basically influence the deposition and response to pharmacologically active molecules. Furthermore, in recent years studies on the interaction of the various psychotropic drugs and developing system have been carried out by various workers to correlate between various biochemical and physicochemical effects and their clinical effectiveness (26, 27).

Because of the minimum side effect with maximum beneficial pharmacologic effect (28, 29) antidepressent drugs are now-a-days widely used during pregnancy. Besides this, the
usage of different anesthetics and analgesic drug during pregnancy may have specific influence on neonatal adaptation to the new external environment (30) and those drug which can cross the placental barrier if applied during pregnancy can affect the structural and functional maturation of developing fetuses (31). Therefore a detailed knowledge of those drugs which are frequently used during pregnancy is necessary for proper management of pregnancy and postnatal management of the neonate.
REFERENCES


