CHAPTER - I

INTRODUCTION

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The first step in ontogenesis is the formation of the zygote which is formed by the union of two gametes, a male gamete or the sperm and a female gamete or the ovum. The mammalian embryo reaches varying degrees of development before it is finally expelled by the mother through an intricate process that protects its viability. The newborn infant continues to derive nourishment and protection from the mother till it can fend for itself.

The growing embryo and the fetus are well-protected in the intrauterine environment because of the preferential transport of many nutrients to the fetus across the placenta which on the other hand acts as a barrier against the free entry of nutrients that are harmful in excess, (e.g. fat soluble vitamins) and prevents the entry of other substances altogether (e.g. most proteins) so that fetus is protected even from the internal environment of the uterus.

In man, intra-uterine life lasts for about nine months and can be broadly divided into three stages.

1. The pre-embryonic period : During this period the growing zygote is implanted in the mucous membrane of the uterus (endometrium) and is differentiated into embryonic and non-embryonic portions. This period lasts for about less than 2 weeks (Figure 1).

2. The embryonic period : During this period the rudiments of all the main organs of adult are developed, although the embryo has not yet assumed a distinctly human form. This period extends to the end of second month. The rate of growth is most rapid during this period. From a minute globule of tissue, the body increases to about 10,000 times that size by the end of the first month of gestation. Along with this rapid growth, much differentiation of cell structure into tissues and organs occurs. Because of the release of genetic information, the dividing cells produce cells of differing structure and functional capacity. Three distinct layers of tissue, each with a specific function, emerge at the onset of the embryonic phase. The outermost layer, the ectoderm gives rise to the epidermis of the skin, hair, nails, skin glands, sensory cells, brain and the entire nervous system of the body. The middle layer, the mesoderm, produces the deeper skin layers, muscles, bone structure, kidneys, gonads and circulatory (including blood)

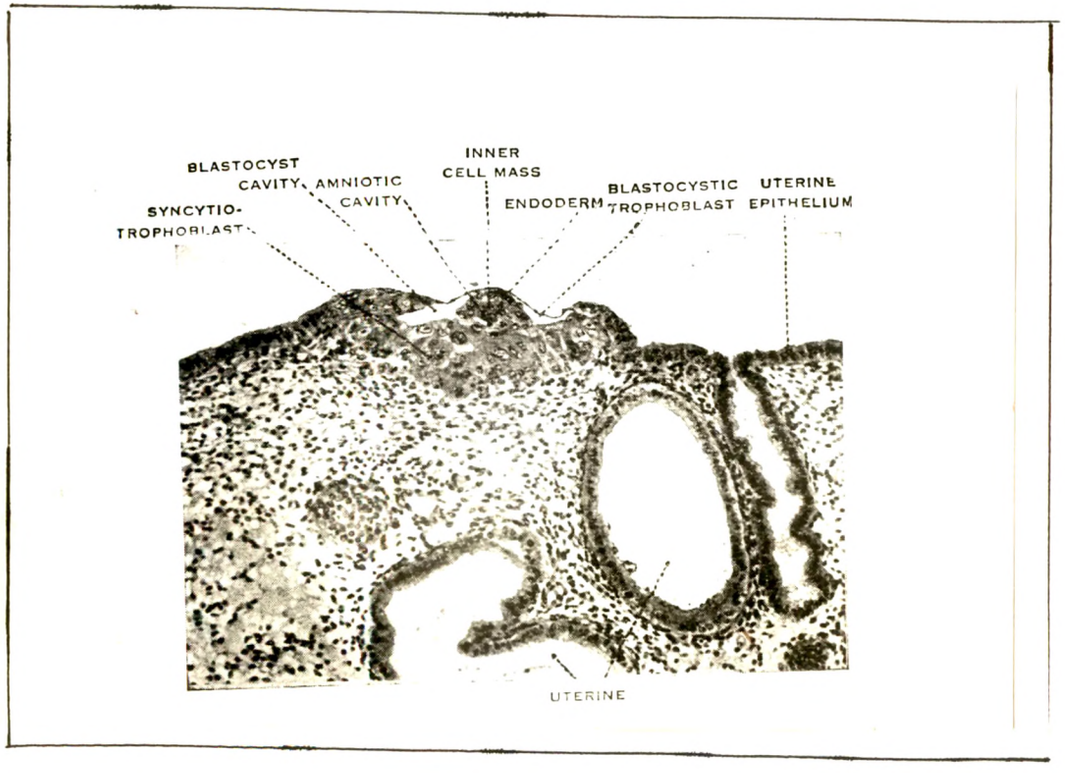


FIG.1 : Pre-embryonic stage.
Fertilized ovum at the age of one week.

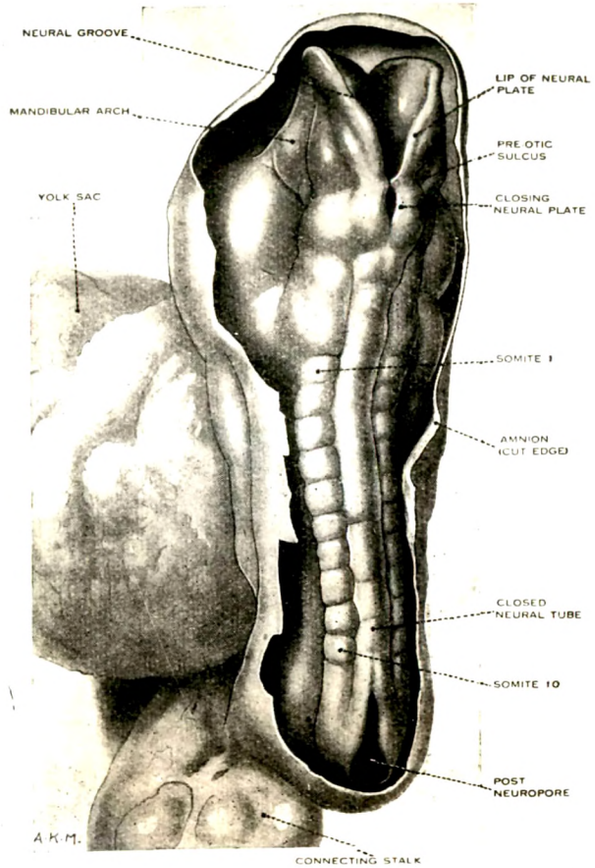
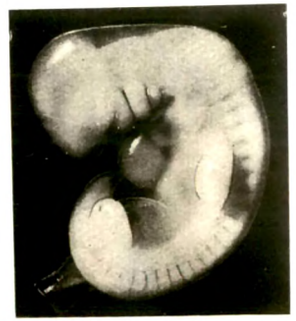


FIG.2 : Embryonic stage of development.
Embryo at the age of 3 weeks.

and excretory systems. The innermost layer, the endoderm, is the base from which are developed the digestive system, lungs, liver, pancreas and other internal organs. By the end of the second lunar month, about 95% of the physiological organs and features are already formed. The nervous system, including the brain, spinal cord and the specialized receptor organs are developed to a rudimentary stage by this time. The ears are just beginning their external formation. The EEG activity of the fetal brain reflects an individual pattern. The body proportions are greatly different from those of the newborn at this stage. The head is enormously large, the trunk is about as large as the head and the extremities are very small (Figures 2 & 3).

3. The fetal period : This starts from the end of the second month when the embryo begins to resemble a human being which can be recognized as male or female and is called a fetus. The fetal period largely ends at birth when the fetus becomes a child (Figures 4).

The fetal period is largely one of the structural refinement and proper organ positioning for most body systems. Cartilage is converted into bone mass. Primary centre of ossification, namely, protein matrices absorbing calcium and other minerals from the blood stream are set up in various areas of the body. During this period physiological



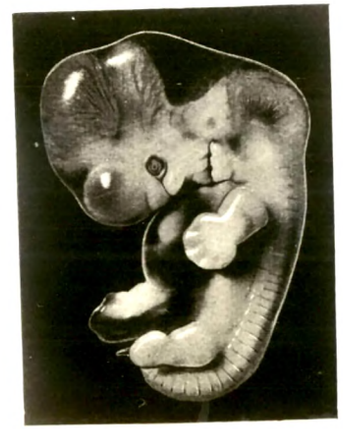
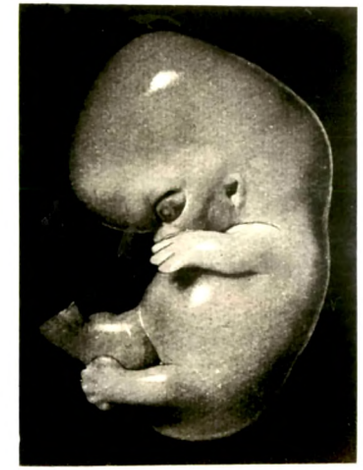


FIG.3 : Embryonic stage of development.
Embryo at the age of 5 weeks (3A)
and 6 weeks (3B).



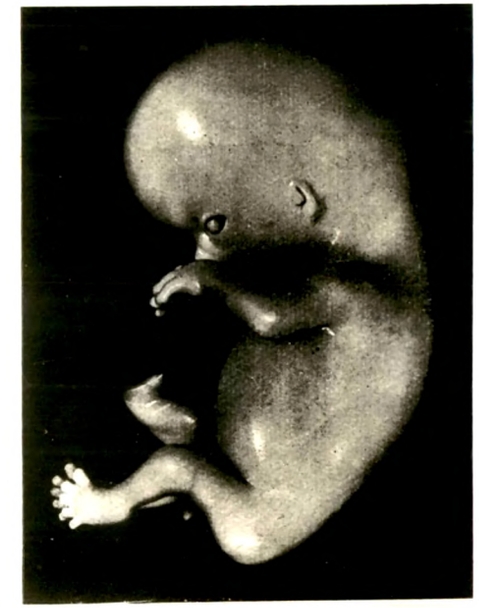


FIG.4 : Fetal stage of development.
Fetus at the age of 7 weeks (4A)
and 9 weeks (4B).

* Source: Hamilton et al. (1945)
"Human Embryology", Haffer, Cambridge.

growth occurs at a rapid rate. About 15 weeks after conception, the pituitary gland begins secretion of somatotrophin.

Fetal growth prepares the organism to sustain itself after birth. One by one the organs and systems become partially or fully functional and serve the organism. At this stage, the viability or the ability to survive premature birth, starts at about the end of the sixth month of gestation and by twenty-seven weeks of age neonate has a chance of surviving even if it is born prematurely (Hooker, 1969).

The systematic formation of the various organs and bodily systems is a notable fact in prenatal development. The development of each organ follows a specific temporal sequence. Metabolic activity is intensified in the area where a new organ undergoes rapid growth phases.

The morphological and functional development of the fetus are summarized in Table 1.

The quantitative requirements for embryonic growth are very small at the beginning but increase progressively for mid-pregnancy and in spite of the capacity of the placenta to transport critical nutrients

TABLE-1 : Morphological and functional development of the fetus.

Age (weeks) Menstural	Age (weeks) Fertilization	Crown-rump length (mm)	Foot length (mm)	Fetal wt. (g)	Main external characteristics
1	2	3	4	5	6
11	9	50	7	8	Eyes closing or closed. Head more round. External genitalia still not distinguishable as male or female, intestines are in the umbilical cord.
12	10	61	9	14	Intestine in abdomen; early development of finger nails.
14	12	87	14	45	Sex distinguishable externally; well defined neck.
16	14	120	20	110	Head errect; 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.
20	20	190	39	460	Hair in scalp and body hair visible.

TABLE-1 (Contd.)

1	2	3	4	5	6
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, eye lashes present.
30	28	270	59	1300	Eyes open, skin slightly wrinkled.
32	30	280	63	1700	Toenails present, body filing 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 grow fully.
40	38	360	83	3400	Prominent chest, breasts protrude. Testes in scrotum or palpable in inguinal canals, fingernails extend beyond finger tips.

Source : Moore (1977). The Developing Human, 2nd edition. Cf. Williams Obstetrics.

against a concentration gradient. However, adequate circulating levels of these nutrients in the maternal blood are important.

The supply of nutrients in the prenatal life is achieved in four stages (Figure 5):

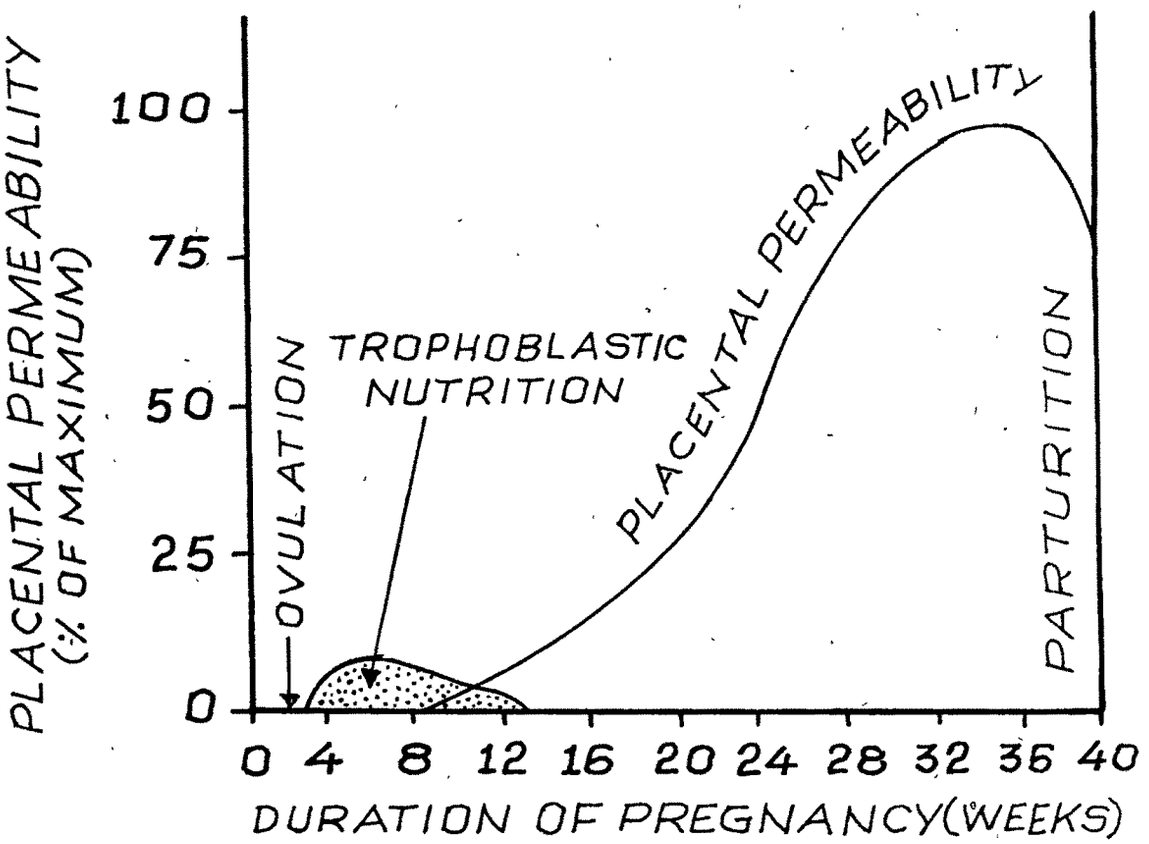
1. The egg-obtains its nutrients from its own duetoplasm (vitellus egg yolk).

2. Blastocyst - absorbs fluids and nutrients from the uterine luminal fluid. As the blastocyst increases in size, it can no longer absorb sufficient uterine fluids by diffusion.

3. Trophoblastic cells of blastocyst have a secretory action. These cells secrete proteolytic enzymes that digest and liquefy the cells of the endometrium. The released fluid and nutrients are actively absorbed into blastocyst as a result of phagocytosis by the trophoblastic cells. These provide the sustenance for the further growth of the blastocyst. At the same time, additional trophoblastic cells form cords of cells that extend into the deeper layers of the endometrium and attach to them.

Once implantation has taken place, the trophoblastic and sublying cells proliferate rapidly, and

FIGURE:5 - NUTRITION OF THE FETUS



Source : Guyton (1976). Text Book of Medical Physiology, 5th edition, W.B. Saunder Co., Philadelphia, U.S.A.

these along with cells from the mother's endometrium form the placenta.

4. Lastly, after the formation of the placenta, absorption of nutrients from the maternal circulation occurs across the placental membrane.

The critical nutrients whose deficits affect development at different stages vary. In the earlier stages, the quantitative requirements for micronutrients such as substrates for oxidation, proteins, calcium, etc. are small in relation to the requirements of maternal metabolism. On the other hand, deficiency of micronutrients such as iodine (Clements, 1960; Hurley, 1976; Benitez-Fierro et al, 1978), pantothenate (Nelson et al, 1957), folate (Fraser and Watt, 1964; Hibbard and Hibbard, 1966; Schorah et al, 1983),etc. which are critical for cell division and organogenesis may have more adverse consequences. Those in the former category acquire greater importance in latter stages (Mitchell, 1964; Rajalakshmi and Ramakrishnan, 1969; Widdowson, 1980). A supply of critical nutrients in the earlier stages is more likely to result in the fetal resorption, fetal abnormalities, (e.g. iodine and vitamin A) miscarriages and retarded fetal growth, whereas those critical for latter development seem to have a greater effect on fetal growth only. Fetal growth retardation represents a heterogenous

condition with more than one cause. Two main types of fetal growth retardation were first described by Gruenwald (1963) and confirmed by other investigators (Ounsted and Taylor, 1971; Dubowitz, 1971; Cook, 1977). In the first type, the infant has a normal crown-heel length for fetal age but is deficient in subcutaneous fat, and to some extent, in skeletal muscle. Such infants also have reduced weights of their liver, spleen, adrenals and thymus glands (Naeye, 1965). In the second type, the infant is symmetrically small at birth in external body dimensions for gestational age but not necessarily under-weight for height. Of course some fullterm infants in the latter category may also be lean and deficient in subcutaneous fat and thus have both types of fetal growth retardation. Gruenwald (1963) suggested that the first type of fetal growth retardation occurs late in pregnancy and that the second type has its origins much earlier in pregnancy. Further, the two types differ not only in their pathogenesis but also in their postnatal courses (Holmes et al, 1977). Infants who are long and lean at birth tend to have good appetites even if they are underweight and achieve catch up growth rapidly during 3-6 months after birth. On the other hand, infants who are symmetrically small for their gestational age at birth tend to have ordinary appetites and some of them remain short in stature.

Human fetal growth results from an interplay of maternal, fetal and placental factors. The nutritional supply to the fetus is provided by transport of substrate across the placenta, the fetal endocrine milieu and the expression of the fetal genome, all important in fetal ontogeny.

Winick (1970) has pointed out that fetal growth is a homogeneous process, in as much as accretion of net protein has been demonstrated to be linear in all organs in utero. Enesco and LeBlond (1962) assumed diploid constancy of each developing human cell and evaluated organ growth by determining the increase in cell number by the total content of DNA in the organ, and the increase in cell size, measured by the weight or protein content of the organ per unit of DNA. In the human diploid nucleus, the amount of DNA per cell is fixed at 6.0 picograms of DNA per cell nucleus (Mirsky and Ris, 1949). An increase in DNA thus represents growth by mitotic activity. An increase in protein content without an associated increase in DNA content of an organ represents growth by enlargement of already existing cells. Using this technique, Winick (1971) quantified growth in terms of cellular and organ growth in several species, including man and described three distinct phases of growth :

Phase-I - Hyperplasia : During this phase, there is a proportional increase in weight, protein and DNA content of tissues.

Phase-II - Hyperplasia and concomitant hypertrophy : Increase in DNA content is slower than increase in protein and weight of tissues during this phase.

Phase-III - Hypertrophy : During this phase, there is no further increase in DNA content but continued increase in weight and protein content of tissues is observed.

Winick and Noble (1966) demonstrated that undernutrition during hyperplastic growth curtailed the rate of cell division and that this could result in prolonged undernutrition and in organs with permanently reduced cell numbers. The same degree of undernutrition imposed during the hypertrophic phase retarded the expected increase in cell size and this could be generally reversed on the institution of proper nutrition (Winick and Rosso, 1969; Brasel and Winick, 1970; Winick et al, 1970).

Placental regulation

The placenta is a highly specialized organ designed to transmit a number of nutrients from maternal to fetal blood and diffusion of excretory products from the fetal blood into maternal circulation. In the early months of development, placental permeability is relatively slight for two reasons. First, the local surface area of the placental membrane is still small at that time, and second, the villar membranes have not yet been reduced to their minimum thickness. As the placenta becomes older, its permeability increases progressively until the last month or so of pregnancy when it begins to decrease again. This increase in permeability is caused by both progressive enlargement of the surface area of the membrane and thinning of the layers of the villi. On the other hand, the decrease shortly before birth results from deterioration of the placenta caused by its age and sometimes from destruction of whole segments due to infarction.

During the first few months of pregnancy, the placenta grows tremendously in size while the fetus remains relatively diminutive. During this time considerable amounts of metabolic substrates including proteins, calcium and iron are stored in the placenta to be used in the later months of pregnancy for growth by the fetus. In addition, the placenta forms large quantities of chorionic gonadotrophin,

estrogens, progesterone and human placental lactogen. The two peptide hormones, human chorionic gonadotrophin and human placental lactogen are secreted into the maternal circulation whereas steroids are released in both maternal and fetal circulation. The first three of these hormones are essential to the continuance of pregnancy whereas human placental lactogen has a prolactin like activity i.e. a weak growth promoting effect and it potentiates human growth hormone.

Transfer of nutrients across the placenta occurs mainly by diffusion, active transport and facilitated diffusion (Table-2). The transport mechanisms in both are stereospecific. For the efficient operation of these mechanisms, adequate size and normal structure of the placenta are very important. A summary of the factors affecting placental transfer is given in Table-3.

Most placental transport mechanisms are bi-directional. Fetal utilization of nutrients maintains the net transfer of these materials towards the fetus, while the accumulation of the end products of fetal metabolism (e.g. CO_2, urea, uric acid, creatinine) is prevented by transfer in the reverse direction. The factors that influence delivery of substances to the placenta on the maternal side are also

TABLE-2 : Mode of transfer of nutrients across the placenta.

Nutrient		Mode of transfer
Water		Diffusion
Oxygen and carbon dioxide		Diffusion
Electrolytes	Na, K	Diffusion
	Ca and inorganic phosphorus	Active transport
Iron		Active transport
Carbohydrate (Glucose)		Facilitated diffusion
Essential amino acids		Facilitated diffusion
Certain proteins such as albumin, immunoglobulins		Pinocytosis
EFA and other lipids		Limited transport by diffusion
B-vitamins and Ascorbic acid		Cleaved by enzymes in placental membrane and resynthesis after crossing.
Fat soluble vitamins		Diffusion
Steroid hormones		Diffusion
Peptide hormones		Impermeable.

Source : Masani and Parikh (1976)
A Textbook of Obstetrics, Popular Prakashan Pvt. Ltd., Bombay.

TABLE-3 : Major factors affecting the placental transfer of diffusible substances.

Maternal	Placental	Fetal
1. Amount delivered to the placenta.	1. Area of diffusing membrane.	1. Blood concentration.
a. Blood concentration, exogenous and endogenous supplies, homeostatic mechanisms.	2. Diffusion Pressure : difference in concentration in intervillous space and in villous capillary.	2. Hemodynamic factors : Systemic and local.
b. Flow rate in intervillous space, hemodynamic factors in the mother, local circulatory factors.	3. Diffusion resistance.	3. Flow Characteristics (Pool, cross, current etc.)
2. 'Shunting' and arterio-venous mixing in intervillous space.	a. Characteristics of transferred material : size, charge, polarity etc.	
	b. Characteristics of membrane : physio-chemical composition, thickness.	

Source : G.B. Avery (1975).
ed. Neonatology, patho-physiology and management of newborn.
J.B. Lippincott Company, Philadelphia.

operative in removing materials into the fetal circulation. As mentioned earlier, the placenta transmits a number of nutrients from the mother to the fetus against a concentration gradient. Nutrients such as calcium (Hytten, 1980), iron (Fletcher and Suter, 1969) and water soluble vitamins (Hytten, 1980) are preferentially transferred to the placenta even at the cost of maternal depletion. Thus, the infant at birth has high levels of calcium, most amino acids and water soluble vitamins than does its mother. In contrast to this, other nutrients such as fat soluble vitamins A and E are in lower concentrations in cord blood than in maternal blood. Teleologically, these relationships might be viewed as protective in the interests of the fetus since the substances that are present in high concentrations in the fetus tend to be those which are poorly stored by it and thus associated with a danger of deficiency (e.g. folate), whereas the nutrients in low concentration in the fetus tend to be those with risks of toxicity due to excessive storage (e.g. vitamin A).

Fetal growth in humans is affected by a number of factors including genetic factors (Polani, 1974; Metcoff et al., 1981), maternal parity (Achar and Yankauer, 1962; Basu and Puri, 1963; Banik et al, 1967; Garcia-Sicilia et al, 1978; Reinhardt et al, 1978; Dowding, 1981; Newcombe, 1981), height and weight of the mother (Thomson et al, 1968;

Eastman and Jackson, 1968; Niswander et al, 1969; Peckham and Christianson, 1971; Ademowore et al, 1972; Ounsted and Ounsted, 1973; Niswander and Jackson, 1974; Simpson et al, 1975; Newcombe, 1981; Raman, 1981), weight for height (Naeye, 1980; Ounsted and Scott, 1981), gestational age (Reinhardt et al, 1978; Woods, 1981) and sex of the infant (Hambrasus, 1980; Reinhardt, 1980). Other factors affecting fetal growth include abnormalities in the mother and the placenta or the infant. Some of these abnormalities are listed in Table-4.

About 10-15% of infants among the urban poor in this country are born with a weight of less than 2 kg. This proportion may be higher in the rural areas. Some consequences of fetal growth retardation and malnutrition include poor maturation of tissues which are critical for the survival and the development of the newborn such as the lung and respiratory capacity (Hallman and Gluck, 1977; Lafeber et al, 1979; Schulte, 1981), gastrointestinal tract (Brown, 1962; Koldovsky, 1982) and the nervous system (Drillien, 1970, 1972; Davies and Stewart, 1975; Lubchenco, 1976; Winick, 1976; Vohr et al, 1978; Commey and Fitzhardinge, 1979;,Rajalakshmi, 1980). Fetal growth retardation is also associated with poor stores in the liver of critical nutrients, such as vitamin A and iron (Dave, 1980).

TABLE-4 : Some factors associated with fetal growth retardation (FGR).

1. Maternal factors	- Dietary insufficiency
	- Abnormally low pre-pregnancy weight for height
	- Poor maternal weight gain during pregnancy
	- Failure to show expected biochemical changes
	- Lack of adequate prenatal care
	- Delivery before 17 years and after 35 years of age
	- Placental size
	- Placental protein content
	- Short inter-pregnancy interval
	- Excessive cigarette smoking, alcoholism, use of addiciting drugs.
2. Fetal factors	- Intrauterine infections
	- Chromosomal aberrations
	- Congenital malformations
	- Inborn errors of metabolism
	- Multiple births.
3. Medical complications of pregnancy.	- Acute or chronic hypertension.
	- Pre-eclampsia
	- Severe vaginal bleeding (third trimester)

Table-4 (Contd.)

	- Severe chronic diseases involving heart, liver, lungs, kidneys, gastrointestinal tract, thyroid or adrenal glands
	- Disseminated lupus erythematous sarcoidosis
	- Severe chronic infections
	- Anemia
	- Leukemia
	- Malignant solid tumors
	- Large ovarian cysts
	- Multiple large fibroids of uterus
	- Continuous medication with immunosuppressive, teratogenic or growth retarding drugs
	- Abnormalities of uterus, placenta or umbilical cord.
	- Polyhydramnios
	- Oligohydramnios
4. Environmental factors	- High altitute
	- Exposure to toxic substances
	- Thermal stress.

Source : Miller and Merritt (1979)
Fetal growth in humans, Year Book Medical Publishers Inc., Chicago.

Profiles of skeletal development during infancy derived from previous studies (Shah, 1983) suggest that at least some infants are born with retarded skeletal development and fail to catch up in early infancy, presumably because of maternal deficiencies with regard to calcium, vitamin D and other nutrients. Delayed epiphyseal and osseous development has been noted by other investigators (Stuart and Burke, 1945, 1948; Scott and Usher, 1964; Roord et al,, 1978).

Maternal nutrition

The inadequate availability of nutrients during gestation probably constitutes the single most important environmental factor influencing the outcome of the reproductive process. In poor areas, it appear to account for the majority of cases of fetal growth retardation and a substantial proportion of pregnancy and neonatal loss on the basis of differences found between poor and upper class women. For example, apart from low birth weights of live infants, the rates of miscarriages, still-births, prematurity and neonatal mortality are much higher in poorly nourished women than in well-nourished women. Poor gestation performance of the poor women has also been shown by a number of investigators (Banik et al, 1967; Gopalan and Raghavan, 1969; Rajalakshmi and Ramakrishnan, 1969; Aiyar, 1972;

Bhatt et al, 1972; Parekh et al, 1972; Banik and Saha, 1975; Godbole et al, 1976; Ghosh et al, 1977; Purohit, 1979 (Table-5). If the mother does not have an adequate supply of essential nutrients, the delicate balance between the needs of the maternal organisms and those of the fetus is upset, and, ultimately, the well-being of both organisms is at risk.

Thus, pregnancy involves the physiological imperatives of providing for optimal fetal growth and development and preservation of maternal homeostasis as pointed out by Barcroft (1946) and Polani (1974). The demands of the unborn young of 19 species made on the maternal body as compared to those made by the human fetus are given in Table-6 (Leitch, 1969-60).
In short, the larger the mother, the smaller the daily gain of the young in relation to her weight. The amount of weight gained by a single human fetus is 0.02% of the mother's weight per day and is only a tenth as much as a litter of the rat and one hundredth that of a litter of the mouse. The nutritional demands of the growing human fetus for major nutrients are shown in Table-7.
To meet these demands, a complex series of intricate physiological adjustments take place during pregnancy. These adjustments include a more efficient utilization of critical nutrients such as protein (Macy and Hunscher, 1934; Steinbock and Tarver, 1954; Hytten and Leitch, 1971;

TABLE-5 : Reproductive performance in low (LIG) and high (HIG) income groups women.

	LIG	HIG
	% incidence	
Normal delivery	77	76
Mis-carriages	7	3
Prematurity	1.3	1.3
Still-births	7	3
Caesarean births	3.7	6
Breech delivery	0.5	0
Use of forceps	2	5
Perinatal deaths	5.9	3.0
Birth weight of infant (kg):		
$\angle$ 2.0	10.0	Nil
2.0 - 2.5	29.0	20.0

Source : Rajalakshmi and Ramakrishnan (1969).

TABLE-6 : Demands on the mother of the unborn young in different species.

Species	Weight of mother (g)	Total weight of young (g) (No.of litter in bracket)	Length of gestation	Mean gain per day (g)	Mean gain per day % of mothers weight.
1	2	3	4	5	6
Mouse	25	10 (8)	20	0.5	2.0
Rat	205	50 (10)	22	2.3	1.11
G. Pig	560	380 (4)	68	5.6	1.00
Rabbit	1175	270 (6)	31	8.7	0.74
Red fox	4200	700 (7)	52	13.5	0.32
Cat	2750	452 (4)	63	7.2	0.26
Dog	9000	1100 (5)	63	17.5	0.19
	(kg)	(kg)			
Sheep	50	5 (1)	150	33.3	0.067
Goat	62	6.4 (2)	154	41.6	0.067
Rhesus monkey	5.3	0.47 (1)	167	2.8	0.053
Pig	200	12 (12)	115	104	0.051

TABLE-6 (Contd.)

1	2	3		4	5	6
Lion	114	4.4	(5)	110	44	0.039
Horse :						
Shetland	190	19.6	(1)	337	58.2	0.031
Shire	800	71	(1)	337	211	0.026
Cow	600	40	(1)	280	143	0.024
Woman	56	3.4	(1)	280	12.1	0.021
Chimpanzee	46	1.8	(1)	228	7.9	0.017
Polar Bear	258	0.59	(1)	244	2.4	0.00094
Elephant	2590	93	(1)	650	143	0.0055
Blue whale	79000	2000	(1)	365	540	0.00068

Source : Widdowson (1981). In 'Maternal nutrition in pregnancy - Eating for Two ?' Ed. Dobbing. Academic Press.

TABLE-7 : Nutritional demands of the growing fetus in relation to maternal diet, expressed in amounts per day†.

Nutrient	Amount in diet*	Amount transferred to the growing fetus**
Kcal	1500-1600	160-170
Protein (g)	35-40	1.4
Fat (g)	30	1.6
Calcium (mg)	400	100
Vitamin C (mg)	10-15	3-5
Vitamin A (ug)	125	10-15
Iron (mg)	20-25	0.75
Folate (mg)	0.5-0.7	0.0013
Vitamin B_{12} (ug)	0.5	0.045
Thiamin (mg)	1.0 - 1.5	-
Riboflavin (mg)	0.5	-
Niacin (mg)	5-6	-

* Based on intakes of poor women in urban Baroda.

** Based on amount in whole body at birth for protein, fat, calcium, iron and vitamin C for and on amounts in liver for the other nutrients (Apte and Iyengar, 1972).

† No allowances made for more efficient conservation of certain nutrients during pregnancy; quantitatively, the amounts needed are likely to increase with the progress of gestation, specially for the macro-nutrients.

Source : Rajalakshmi (1980).

King et al, 1973; Calloway, 1974; King et al, 1976), calcium and iron (Macy and Huncher, 1934; Duckworth and Warnock, 1942; Nicolaysen, 1943; Spray, 1950; Beaton, 1961; Kimberg et al, 1961; Hytten and Leitch, 1971; Finch, 1976) and this is achieved by increased absorption and decreased endogenous losses. Nevertheless, pregnancy can be presumed to involve some additional requirements of nutrients based on the approximate quantities transferred to the fetus. The additional nutrient requirements during pregnancy as given by NAS-NRC (1980) are shown in Table-8. The extent and the timing of the increased requirements vary considerably from nutrient to nutrient (Widdowson, 1980) (Table-9). This can be expressed in terms of the volume of serum required to supply the necessary quantities each day. The largest volumes of the mother's serum are needed to provide the fetus with its requirements of energy in the form of glucose, calcium and phosphorus. It has been reported that the diet of poor women is inadequate in food energy, protein, calcium, vitamin A and riboflavin (Rajalakshmi and Ramakrishnan, 1977) as shown in Table-10. These deficiency symptoms are in an appreciable proportion and are aggravated during pregnancy (Table-11). On the other hand, the diets are not improved either in quantity or quality to meet these demands. A poor weight gain and low placental weights among these poor women is noted by many investigators (Smith, 1947;

TABLE-8 : Additional nutrient requirements during pregnancy as given by NRC, 1980.

Nutrient	Per day
Kcalories	300
Protein (g)	30
Iron (mg)	30-60
Folacin (ug)	400-800
Calcium (g)	0.4
Vitamin C (mg)	20
Vitamin A R.E.	200
Vitamin B_{12} (ug)	1.0
Vitamin B_1 (mg)	0.4
Vitamin B_2 (mg)	0.3
Vitamin B_6 (mg)	0.6
Niacin (mg)	2.0
Vitamin E (mg)	2.0
Vitamin D (ug)	5.0
Phosphorus (mg)	400
Iodine (ug)	25
Magnesium (mg)	150
Zinc (mg)	5.0

Source : NRC (1980).

TABLE-9 : Increments of body constituents in fetal body per 24 hr.

Fetal age range (weeks)	12-16	16-20	20-24	24-28	28-32	32-36	36-40	Amount in 1 litre maternal serum	Volume serum required for daily increment in last 4 weeks (litres)
Weight range (kg)	0.02-0.1	0.1-0.3	0.3-0.75	0.75-1.35	1.35-2.0	2.0-2.7	2.7-3.4		
Fat† (g)	0.02	0.07	0.37	1.07	2.11	4.57	8.79	-	-
Protein† (g) (N x 6.25)	0.18	0.58	1.52	2.04	2.41	3.15	4.46	-	-
Na (mg)	7.1	17.5	31.4	39.6	39.6	37.1	23.9	3220	0.007
K (mg)	4.6	13.6	26.4	35.7	38.2	48.6	53.2	187	0.284
Cl (mg)	8.2	19.6	38.6	38.6	47.1	29.3	25.4	3620	0.007
Ca (mg)	11.8	36.4	109.0	158.0	173.0	229.0	286.0	100 total 50 ionised	5.7
Mg (mg)	0.6	1.0	2.9	4.6	5.4	6.1	6.4	20 total 15 ionised	0.43
P (mg)	7.9	23.2	60.4	98.2	111.0	143.0	139.0	40 inorganic	3.4
Fe (mg)	-	0.44	1.01	1.62	1.78	2.39	2.50	0.6*	-
Cu (mg)	-	-	0.02	0.09	0.10	0.10	0.11	2.5*	0.2
Zn (mg)	-	-	0.28	0.36	0.37	0.36	0.31	1.0*	-

TABLE-9 (Contd.)

* These are the total amounts.

† Protein is synthesized by the fetus from amino acids of maternal circulation and glucose provides it with most of its energy, for both general metabolism and for new body tissue in the form of fat. Total of 60-90 litres/24 hr of serum is required to meet the total energy requirement of fetus at the end of gestation.

Source : Widdowson (1980).

TABLE-10 : Nutrient intakes of pregnant and lacting women in comparison to non pregnant and non lactating women.

Nutrient	RDA	Pregnant & lactating		Non pregnant and non lactating	
		LIG	HIG	LIG	HIG
K Calories	2200	1520	2020	1500	1800
Protein (g)	55	38	49	36	42
Fat (g)	-	35	80	35	80
Calcium (mg)	1400	400-500	1290	400-500	900
Vitamin A (I.U)	3000	1300	2140	1200	1900
Riboflavin (mg)	1.02	0.50	0.98	0.48	0.78
Thiamine (mg)	1.02	1.28	1.25	1.21	1.14
Niacin (mg)	16.5	10.8	9.3	10.2	8.9
Vitamin C (mg)	50	43.5	84.9	41.0	65.5
Vitamin B_{12} (µg)	1.5	-	-	-	-
Iron (mg)	40	20-27	22-30	20-25	22-30

Source : Rajalakshmi (1980).

Recommended Dietary Allowances (1968).

TABLE-11 : Data on the incidence of clinical symptoms of nutritional deficiency during pregnancy and lactation.

Symptoms	Cross sectional study			Longitudinal study			
	Percentage incidence during			No. showing symptoms			
	Pregnancy	Lactation	Controls	Incidence during pregnancy	lactation	Control values at corresponding period	
No. of subjects studied	33	66	38	18	18	10	10
Xerosis of conjuctiva	48	23	18	9	3	3	3
Pigmentation of conjuctiva	55	38	33	12	5	3	4
Xerosis of cornea	33	3	5	6	1	2	2
Pale tongue	73	67	62	14	13	8	10
Fissured tongue	39	38	21	5	7	4	6
Adipose tissue deficient	36	11	26	11	2	1	1
Edema on dependent parts	3	2	0	-	-	-	-
Anorexia	24	2	26	3	1	1	1
Diarrhea	9	2	0	1	1	0	0

Source: Rajalakshmi and Ramakrishnan (1969)

Cawley et al, 1954; Hytten and Leitch, 1964; Eastman and Jackson, 1968; Sack, 1969; Bergner and Susser, 1970; Goujard et al, 1973; Naeye et al, 1973; Habitch et al, 1974; Smith, 1974; Lazar et al, 1975; Lechtig et al, 1975; Petterson and Melander, 1975; Rajalakshmi, 1980).

On an average, poor pregnant women gains about 6-7 kg weight during pregnancy, the gain being not uniform (Munro, 1973; Desai et al, 1974; Sen and Agarwal, 1975, 1976). The gain in the first trimester is quite small or nil and some women may even lose about 0.5-0.6 kg. But in the subsequent two trimesters, this loss is made up and the mean weight gain is of the order of 7 to 8 kg. (Rajalakshmi et al, 1978). A poor weight gain during the last trimester is associated with a relatively low birth weight. In the investigations carried out in this laboratory, gains of less than 2.5 kg, 2.5-3.0 kg and more than 3.5 kg. were associated with birth weights of 2.30 $\pm$ 0.21 (1.5 - 3.0), 2.84 $\pm$ 0.08 (2.0 - 3.9) and 2.60 $\pm$ 0.06 (2.0 - 3.5) kg. Further, placental weights of less than 300g, 300-400g, 400-500g and more than 500g were associated with mean birth weights of 2.17, 2.53, 2.57 and 2.62 kg (Rajalakshmi, 1980). A similar pattern is found in subsequent parities although both placental weights and birth weights tend to show an increase on an average.

The increased demands during pregnancy are met to a considerable extent by increased efficiency in absorption and decreased endogenous losses as in the case of protein (Macy and Hunscher, 1934; Steinbock and Tarver, 1954; Hytten and Leitch, 1971; King et al, 1973; Calloway, 1974; King et al, 1976), calcium and iron (Macy and Hunscher, 1934; Duckworth and Warnock, 1942; Nicolaysen, 1943; Spray, 1950; Beaton, 1961; Kimberg et al, 1961; Hytten and Leitch, 1971; Finch, 1976). In the case of iron, the cessation of menstruation during pregnancy and the postpartum amenorrhea which is prolonged among the poor also helps in the conservation of available stores. In studies in this laboratory nitrogen retention was estimated to be of the order of 1.4g per day in poor women living on their customary diets providing about 35 to 40g of protein (Rajalakshmi and Ramakrishnan, 1969). Balance studies for four consecutive days on a selected subject showed substantial retentions with regard to nitrogen (1.1g) and calcium (90 mg) per day as early as the fourth month of pregnancy (Rajalakshmi and Ramakrishnan, 1969). The capacity of poor women to adapt to a low plane of nutrition and the failure of this adaptation when nutrient supplies are below critical levels have been reported by Lechtig et al. (1975). The differences in gestation performance between

poorly nourished women and better nourished women have already been pointed out suggesting the role of nutritional status. This should lead us to expect better performance with nutritional improvement. Better gestation performance has been associated with better nutrition in several studies in this country and elsewhere (Gopalan, 1949; Toverud et al, 1950; Dean, 1951; Hamlin, 1952; Berry, 1955; Varkki et al, 1955; Woodhill et al, 1955; Arora et al, 1963; Nirmala et al, 1966; Monckeberg, 1968; Blackwell et al, 1973; Stein et al, 1975; Ankegowda and Sumitra Devi, 1976; Pitkin, 1977). A number of studies have reported striking beneficial effects on birth weight when the mothers were given supplementary foods (Iyengar, 1967; Srikantia and Iyengar, 1972; Habitch et al, 1973; Higgins, 1973; Qureshi et al, 1973; Chavez and Martinez, 1974; Habitch et al, 1974; Iyengar, 1975; Read, 1975; Brozek et al, 1977; Adams et al, 1978; Lechtig et al, 1979; Mora et al, 1979; Prentice, 1983; Adair et al, 1984) or a specific nutrient supplement for example iron, folate (Iyengar, 1971; NIN annual report, 1974; Gandy and Jacobson, 1977). However, the magnitude of the effect observed in terms of differences in birth weights varies widely and ranges from 40g to 298g. Moreover, many other studies have

failed to find a similar correlationship (Williams and Fralin, 1942; McGanity et al, 1954, 1955). These discrepancies may be due to deficiencies in the initial nutritional status of the subjects, the nature and duration of supplementation, sample size etc.

Most of these studies were carried out during the last trimester of pregnancy on the assumption that the effects would be maximum during this period since the demands are greatest and perhaps because the pregnant women are more accessible then. Benefits from supplementation initiated earlier in gestation appears to have been reported in only one study (Habitch et al, 1974b). The differences in birth weights of supplemented and unsupplemented women remained about the same no matter whether 75% of the supplement was ingested at the end of the pregnancy (third trimester only), or at the beginning of pregnancy (first and second trimester only). This implies that energy storage during early pregnancy and energy mobilization at the end of pregnancy are efficient. It also appears from other studies that some nutrients particularly vitamins and iodine are critical for embryonic and early fetal development. For instance in rats, the effects of pantothenate deficiency during gestation are greater during first,

second and third weeks in that order (Nelson et al, 1957). Iodine supplementation during early pregnancy or when initiated before pregnancy is found to be more effective in preventing cretinism and deaf mutism than in later pregnancy (Benitez-Fierro et al, 1978). Beneficial effects of folate supplementation during the last trimester on birth weights have also been well documented (Iyengar, 1971; NIN annual report, 1974; Gandy and Jacobson, 1977). Similarly the risk of neural tube defects in mothers with a previous history of this disorder is found to be reduced by supplementation with large doses of 'B' vitamins soon after conception (Smithells et al, 1980; Schorah et al, 1983). Such changes may be important in terms of resultant decreases in the proportion of low birth weight infants, reductions in perinatal and infant mortality, and their effects on subsequent child development.

Iron nutrition during pregnancy

Pregnancy imposes a substantial burden on the maternal hematopoietic system because of the need for augmented erythropoiesis in the face of an expanding plasma volume and obligatory placental transfer of iron. In normal pregnancy, total iron requirement averages to 800 mg (500 mg for maternal erythropoiesis and 300 mg

for transfer to the fetus and placenta) (USCFN, 1968). This amount is the sum of the endogenous losses, the requirement for cell mass enlargement and the supply to the fetus and placenta. The needs are unevenly distributed, rising exponentially with advancing gestational age (Table-12). To meet this demand, a pregnant women needs 1-1.5 mg/day which has to be derived from the diet and about 300 mg of iron which is stored in the reticuloendothelial cells of the bone marrow and can be utilized. These amounts are marginally adequate. Thus a supplementary dose of 30 to 60 mg of ferrous iron daily after mid-pregnancy through the early post-partum period is advised.

Anemia due to iron deficiency in pregnancy is a major cause of maternal morbidity, its incidence being of the order of 20-30% in the developed countries and 52-99% in developing countries. This has raised a world wide concern over last many years.

The human body is very economical in its handling of iron and is provided with mechanisms to facilitate the maintenance of the iron balance (Hallberg, 1975). Iron is continuously being reutilized in the body and is mainly depleted via the loss of cells from the body. The amounts lost in sweat and urine are relatively small. A considerable amount of iron is stored chiefly in liver for

TABLE-12 : Iron requirements (mg/day) during pregnancy.

	Gestational age		
	Ist trimester	2nd trimester	IIIrd trimester
Endogenous losses	0.5	0.5	0.5
Fetus	0.04	0.7	2.4
Placenta	0.04	0.3	0.5
Maternal red cell volume expansion	0.00	1.4	4.2
Total	0.58	2.9	7.6

Source : USCFN on iron deficiency (1966).

mobilization when dietary supplies are lower than the required amounts. For instance, in the mother during pregnancy and in an infant during the suckling period. The absorption of iron increases with increased needs. Radioactive isotopic studies suggest an increased absorption of iron with the progress of pregnancy, being 7% during the first trimester and about 20-30% during the second and third trimesters (Balfour et al, 1942; Hahn et al, 1951; Heinrich et al, 1968; NRL, 1968). Such increased absorption is made possibly by an increased concentration of transferrin which increases with progressive gestation (Beaton, 1960; Charley and Saltman, 1960; Gulyaev, 1974).

Pregnancy is also associated with a fall in blood hemoglobin levels. This is believed to be because of a physiological increase in blood volume (Singh et al, 1967; Goodhart and Shils, 1973). In spite of this, as the hemoglobin content of the red cell shows little change, and the number of circulating red cells increases, the actual amount of hemoglobin also increases. Further, during gestation, the cessation of menstruation represents an iron economy amounting to 200-300 mg of iron.

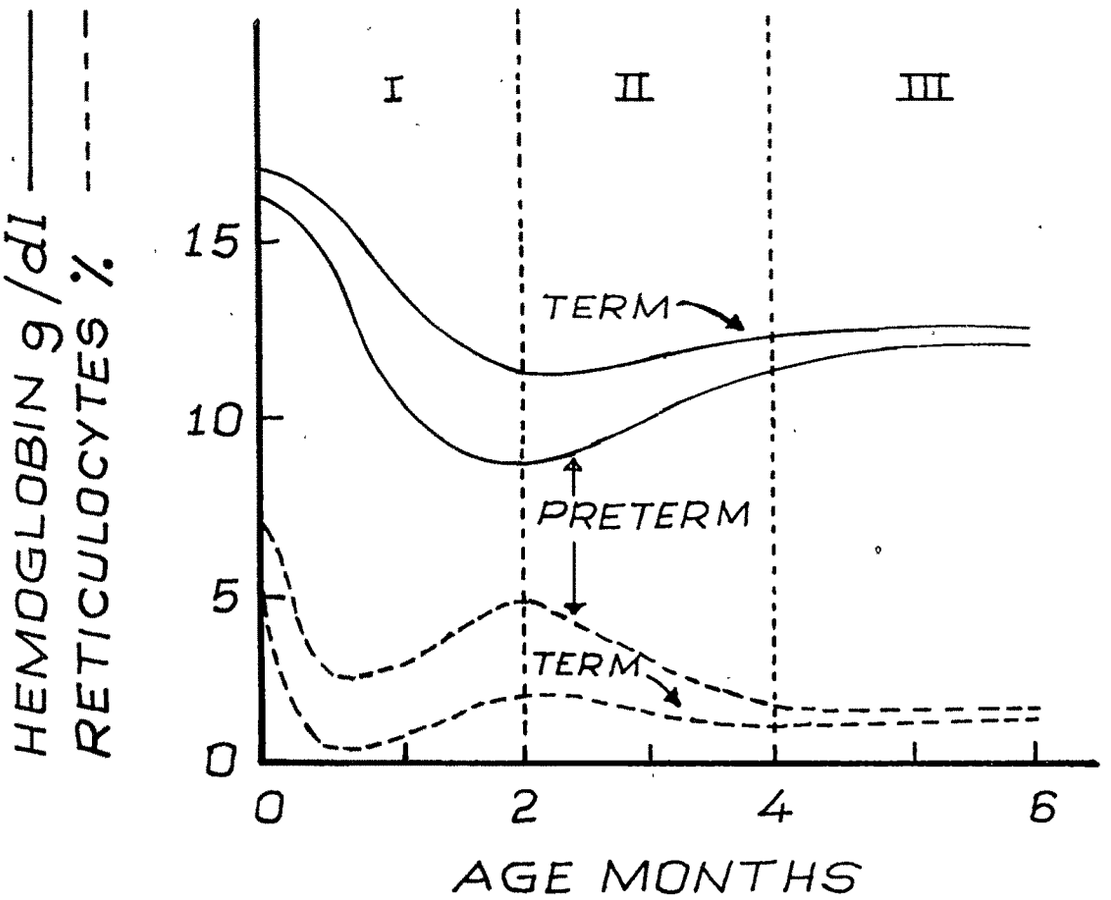
In spite of this impressive evidence in favour of more efficient utilization of iron during pregnancy, anemia is a major problem encountered in gynaecological practice, hemoglobin levels below 5 g/dl being by no means a rarity.

Iron transport across the placenta is a unidirectional active process. The amount of iron crossing the placenta is more than what is required for fetal growth and is utilized for augmenting fetal stores. As the human fetus grows, the amount of iron in it increases from 5.0 mg at 16 weeks to 278 mg at term (Iob and Swanson, 1934; Widdowson and Spray, 1951). A large proportion of fetal iron is stored in the liver (Widdowson and Spray, 1951). Liver iron concentration increases in a manner similar to whole body iron (Iob and Swanson, 1934) and this probably reflects the storage levels. Although the concentration of iron in the spleen is high, this concentration as compared to total iron is small because of its much smaller size. The concentration of iron both in the whole body and in the liver of newly born animals varies greatly amongst species and within the same species (Widdowson, 1950).

The ratio of iron to fetal body weight (about 75 mg/kg) is relatively constant throughout intrauterine life. But the amount increases with growth so that the newborn infant is well supplied with about 275 mg (Dallman et al, 1980) not only as storage iron in the liver but also in the form of hemoglobin whose concentration is very high at birth (Schulman and Smith, 1954; Sturgeon, 1954). Hemoglobin accounts for 80% of total body iron (Schulman, 1961), 14% being accounted for by storage iron in the liver and spleen (Widdowson, 1950; Schulman, 1961).

After birth, marked changes take place in iron metabolism and in rate of erythropoiesis. This occurs in three stages (Figure 6). The first stage, encompassing the first 6 to 8 weeks of life, is marked by a decline in the concentration of hemoglobin from the highest to the lowest levels observed during any period of development. This decline is attributable primarily to an abrupt decrease in erythropoiesis in response to increased postnatal delivery of oxygen to the tissues. The percentages of erythroid cell in the bone marrow declines from a mean of about 80% at birth (Shapiro and Bassen, 1941) to 10% between the first week and the first month of age (Rosse et al, 1977). Extramedullary erythropoiesis

FIG.6. THREE POSTNATAL STAGES OF IRON BALANCE AND ERYTHRO--POIESIS.



Source : Dallman, P.R. (1980).

comes to a halt during this period. In the peripheral blood, these changes are reflected in the disappearance of nucleated red blood cells and a precipitous fall in the reticulocyte count (Siimes et al, 1974). During this marked depression of erythropoesis, the concentration of hemoglobin decreases at a rate that is determined primarily by the life span of red blood cells produced before birth. Because a relatively small proportion of the iron from senescent red cells is re-utilized for erythropoiesis, the remaining iron temporarily augments iron stores (Seip and Halvorsen, 1957; Siimes et al, 1974; Lundstrom et al, 1977; Saarinen and Siimes, 1978). The percentage of dietary iron absorbed during this period is lower than in later infancy, probably due to the inhibitory effect of large iron stores on absorption (Gotze et al, 1970).

During the second stage, the normal decline observed in hemoglobin concentration is reversed. Erythropoiesis becomes more active to far above the normal adult levels due to an increase in the percentage of erythroid precursors in the bone marrow (Rosse et al, 1977) and by an elevation of the reticulocyte count (Melhorn and Gross, 1971). The concentration of hemoglobin rises from its lowest mean value of about 11 g/dl and is subsequently maintained at an average value of about 12.5 g/dl during

the remainder of the first year of life (Saarinen and Siimes, 1978; Dallman and Siimes, 1979).

A third stage is characterized by an increased dependence on dietary iron. A rapid rate of growth and the low iron content of either breast or unsupplemented cow milk products predispose to the depletion of iron stores. If iron stores are exhausted, then the rise in the concentration of hemoglobin that started during the second stage can either be curtailed or reversed. Thus this helps to a larger extent in augmenting the concentration of hemoglobin even at the cost of body stores of iron (Marsh et al, 1959; Gorten and Cross, 1964; Andelman and Sered, 1966; Lundstrom et al, 1977).

According to Worwood (1977) the premature or low birth weight infant has poorer body stores because of a smaller body since iron content is proportional to body weight. According to Widdowson (1950) even if the concentration of iron varies with gestational age, the values (mg/kg) for whole body iron are 71, 80 and 91 for very premature, premature and full term infants respectively. In any case, infants of low birth weight have a more rapid rate of postnatal growth and are liable to exhaust their iron stores at an earlier age. The requirements for exogenous iron are greater for low birth weight and

preterm infants than in the term infant (Schulman and Smith, 1954; Gorten and Cross, 1964; Committee on Nutrition, 1976; Lundstrom et al, 1977), in whom the third stage of iron nutrition begins earlier (Layrisse et al, 1974; Bezwoda et al, 1979). In normal infants the postnatal fall in hemoglobin concentration to a low value between 6 weeks and 2 months of age occurs before iron stores have become depleted and is not influenced by iron supplementation. However, in infants of low birth weight, the 'nadir' in the concentration of hemoglobin is much lower than in the term infant and is followed by a rise in reticulocyte count, which is higher than in term infants. If the supply of dietary iron is adequate, the concentration of hemoglobin in preterm infants gradually catches up with that of term infants until mean values are equal by nine months of age (Lundstrom et al, 1980). In the absence of such supplies the preterm infant is at risk of iron deficiency. Iron stores at birth vary depending on the nutritional status of the mother which, consequently, may influence the infant's hematological values at birth (Bhatt et al, 1969; Cavill et al, 1977; Bogden et al, 1978). Even in the west, where iron deficiency is relatively less of a problem than in this country the iron content of the liver is found to be five times greater in infants born of mothers with a better nutritional

status than those born of mothers consuming the usual western diets. Significantly greater cord levels of blood hemoglobin and serum iron have been found in infants of mothers supplemented with iron during pregnancy as compared to controls. A number of investigators have shown that infants born of anemic mothers are likely to develop hypochromic microcytic anemia during the first year (Strauss, 1933; Woodruff and Bridgeforth, 1953; Lanzkowsky, 1961), thus emphasizing the importance of iron nutrition during pregnancy and immediately after delivery.

Magnesium nutrition during pregnancy

A number of studies emphasize the need for adequate magnesium nutrition during pregnancy and lactation. Balance studies by Macy and Hunscher (1934) suggest an increase in magnesium requirement during human gestation. This is because of increased protein synthesis and other biochemical changes probably related to the growth of the fetus and maternal accessory tissues. Further, the acquisition of cumulative reserves of magnesium along with other minerals during the early stages of pregnancy and their later transfer to the fetus have been suggested (Macy and Hunscher, 1934) and clearly demonstrated in the case of calcium during the last trimester

(Mitchell, 1962). The extent of transfer depends on maternal stores, fetal requirements and placental function.

A number of investigators showed that maternal serum magnesium decreases significantly during pregnancy especially in last trimester (Watchorn and McCance, 1932; Hall, 1957; Carvalho and Daptary, 1959; Lim et al, 1969; Hurley, 1971; Caddell et al, 1973; NIN Report, 1978). Studies in Kerala conducted by this laboratory have, on the other hand, shown a progressive decline in serum magnesium levels with gestation, presumably because of the magnesium content of diets in this region (Peramma, 1985).

As in the case of other nutrients, the proportion of magnesium in fat free body rises during gestation in the fetus. The full term neonate contains 780 mg of magnesium (Widdowson, 1960) as against the value of 25 g in the adult. Magnesium is distributed between hard and soft tissues in roughly equal proportions. Bone contains about half of the total body magnesium in adult. The concentration in the nonosseous tissues, liver and striated muscle, for example, being 240 mg/kg as against 1080 mg/kg in the skeleton (Eichelberger and McLean, 1942; Conway and Hingerty, 1946; Cotlove et al, 1951; Widdowson et al, 1951;

Baldwin et al, 1952) whereas brain and kidney contain 156 and 204 mg/kg respectively (Shohl, 1939).

It is known that development is associated with a fall in the proportion of water and an increase in the proportion of nitrogen in all tissues. Fetal heart, liver and kidney reach their adult composition before skin and skeletal muscle and this is related to their early functional development. It is also known that skeletal muscle alone accounts for 25% of the total body weight at term whereas it accounts for 43% of the total in the adult. Further, the increments of minerals at each stage are partly due to the increasing size of the body and partly as a result of changing chemical composition. Widdowson and Dickerson (1960) showed an increase in magnesium stores with development. Studies by Apte and Iyengar (1972) also showed an increase in the magnesium content of the fetus with the progress of gestation and found a greater correlation of magnesium content with fetal size rather than with gestational age. An increase in the body stores of magnesium was found upto 1.7 kg of body weight and no further. No data are available on the relationship between maternal magnesium status and fetal stores.
A number of animal studies suggest the relationship between magnesium deficiency and pregnancy outcome. Pregnant rats fed diets severely deficient in this mineral

showed fetal malformation, and resorption, embryonic death, teratogenic effects in full term off-spring and fetal anemia. A reduction in body weights and carcass nitrogen and magnesium content was found in the newborn off-spring of depleted dams (Cohlan et al, 1970; Dancis et al, 1971; Feng Lai Wang et al, 1971; Hurley, 1971; Hurley and Cosens, 1971).

Like iron, magnesium is transferred from the mother to the fetus, this transfer being a unidirectional active process involving energy. The concentration of magnesium is higher in the newborn infant than in the mother (Salmi, 1954, 1955; Mavron and McCance, 1958; Hillman et al, 1977; Bogden et al, 1978; Vobecky et al, 1982). Some investigators have found a positive correlation between maternal and cord serum magnesium levels (Bogden et al,1978; Cockburla et al, 1980; Vobecky et al, 1982). Preterm infants have been found to have lower serum magnesium levels than full term infants and a significant incidence of hypomagnesemia was observed through out the first five days of life in infants with gestational age less than 35 weeks (Jukarainen, 1971). But the incidence of hypomagnesemia was higher in low birth weight infants born to mothers having toxemia of pregnancy, diabetes and sprue (Tsang and Oh, 1970; Jukarainen, 1971). This may have been due to associated hypocalcemia. On the other hand,

Hillman et al. (1977) failed to show any difference in serum magnesium levels between premature and full term infants. In addition, Bogden et al. (1978) reported no correlation between either maternal or cord serum magnesium and birth weight. Studies conducted by this laboratory in Kerala, where diets are marginally deficient in magnesium, the serum magnesium levels were lower in premature and small-for-date infants and their mothers as compared to full term infants.

Lactation also involves considerable depletion of magnesium, the concentration of this mineral in breast milk being 3.3 mg/dl so that a daily loss of 24.5 - 35.0 mg can be expected with milk production at 0.7 - 1.0 litre. In spite of the increased demands for magnesium during lactation, hypomagnesemia has not been reported during lactation. However, parenteral magnesium load tests in post-partum American women showed a high retention of magnesium in biologically immature multiparous women suggestive of deficiency (Caddell et al, 1975). A better magnesium balance was found in the older subjects who had the longest interpregnancy interval presumably because of adequate repletion in the inter-pregnancy interval. Some of the investigators have

failed to find any correlation between the dietary intakes of magnesium and their levels in milk (Vaughan et al, 1979). Animal studies on magnesium deficiency during lactation resulted in 55% maternal mortality by the 21st day of lactation, and reduction of blood and bone magnesium content. Postnatal growth of the pups was also retarded (Feng Lai Wang et al, 1971; Buck and Bales, 1983).

These observations raise the question whether marginal deficiency of magnesium could be one of the critical factors involved in the etiology of prematurity and fetal growth retardation.

In view of the above observations, studies were undertaken on the following aspects :-

1. Fetal tissue stores of iron in relation to maternal iron status, gestational age and fetal growth status.

2. Neonatal iron status in relation to maternal iron status, gestational age and birth weight.

3. Fetal and neonatal magnesium status in relation to maternal magnesium status, gestational age and growth status.

4. Effects of food supplementation on pregnancy weight gain and outcome.

5. Pattern of organ growth during human fetal development in relation to maternal nutritional status, gestational age and fetal growth status.

6. Somatic measurements of the human fetus and neonate in relation to plane of maternal nutrition, gestational age and growth status.