I. Definitions:
Several terms should be clearly defined to differentiate between the various types of nutritional deficiencies.

1. Nutrient:
Nutrient is any substance provided from food that performs one of three functions: (a) provides energy; (b) promotes growth and maintenance of tissue or (c) regulates body processes (Dietz and Trowbridge, 1990). Examples may include constituents in food such as energy, protein, minerals, vitamins, water and some constituents of dietary fiber.

2. Undernutrition:
Undernutrition is a term used synonymously to hunger. Both are interpreted to signify the effect of intake of an insufficient quantity of food. The energy value of the diet is the limiting factor in hunger and undernutrition. People who are undernourished are simply getting too few calories to maintain normal body weight and normal activity (Allen, 1990; Mayer, 1990; Dietz, 1990; Peterson and Chen, 1990; Trowbridge and Wang, 1990).

3. Malnutrition:
When there is an inadequacy in nutritional quality of the diet, deficiency of certain nutrients such as
protein, minerals, or vitamins, the term malnutrition is used (Dietz and Trowbridge, 1990). Undernutrition and malnutrition are not mutually exclusive, people who are undernourished may also be malnourished. The malnourished individual may get enough calories but insufficient amounts of needed food nutrients such as minerals, vitamins, and proteins. The individual does not develop normally during growth period and is unable at any time of life to maintain himself in good health and to resist disease.

4. Protein-Calorie Malnutrition:

The term "protein-calorie malnutrition" (PCM) was first introduced by Jelliffe in 1959. It can be defined as a range of pathological conditions arising from simultaneous deficiency of protein and calories and commonly associated with infections. It occurs most frequently in infants and young children.

The use of the term "protein-calorie deficiency" rather than Protein-calorie malnutrition, was proposed by the Joint FAO/WHO Expert Committee on Nutrition in its sixth report (1962). The former term underlines the fact that diets of those suffering from the condition are almost invariably deficient in both protein and calories. Protein-calorie malnutrition, on the other hand, is a broader term, indicating states of malnutrition occurring in individuals whose
diets are deficient in protein and calories, but in practice often precipitated by other factors, particularly bacterial and viral infections.

5. Protein-Energy Malnutrition:

Protein energy malnutrition (PEM) has been defined (WHO and FAO, 1973) as a range of pathological conditions arising from coincident lack in varying proportions, of protein and calories and is commonly associated with infections. The term has great advantage of bringing forward the main cause while avoiding an emphasis on clinical signs (Jelliffe, 1959, 1969). It occurs more frequently in infants and young children but is also observed in adolescents and adults. It is recognized that the etiology of the entire spectrum of infants and child malnutrition is not fully reflected in the PEM and that not only protein and energy deficiencies but other nutrient deficiencies and infections are involved (Joint FAO/WHO Expert Committee on Nutrition, 1971). The time is apposite for changing from the anteceder term, protein-calorie malnutrition (PCM), as the joule is replacing the calories as the measure of energy in nutrition, energy is the property whereas calories or joules are merely units to measure it.
Protein-energy malnutrition is an old disease under new designation. Severe protein-energy malnutrition is made up of a spectrum of conditions. The two extremes, starvation marasmus and the sugar-baby variant of Kwashiorkor comprise separate clinical syndromes (Waterlow, 1968). It is recognized that, for clinical purposes, it is possible to distinguish Kwashiorkor from marasmus (Lancet, 1970). The presence of edema in kwashiorkor is considered the crucial difference, but is also possible to make distinction at a biochemical level. These metabolic dietary diseases in infants and young children were known and intensively studied in Europe particularly in Germany in the first decade of the twentieth century. What we call "marasmus" today was known as "starchy food dystrophy" (Czerny and Keller, 1906) and the present kwashiorkor was known as the wet (edematous) from of marasmus, caused mainly by an excessively high ratio of carbohydrate to protein with an absolute protein intake usually far below the requirement. The Jamaican edematous "sugar-babies" observed by Platt (1945), offer a typical picture of the more "modern" kwashiorkor. The nutritional marasmus and kwashiorkor can be defined as follows:
a) **Nutritional Marasmus**

A condition characterized by very low body weight for age, loss of subcutaneous fat, gross muscle wasting and absence of edema. It is observed more frequently in infants and very young children. There is general agreement that marasmus is the end result of chronic semistarvation often due to failure of lactation or the use of dilute breast milk substitutes (Barltrop and Sandhu, 1985). Food intake is inadequate to support growth initially and leads to the characteristic wasting of fat and muscle tissue eventually. Factors other than lack of enough food e.g., infection, often play a part in causation.

b) **Kwashiorkor**

The link between malnutrition and the syndrome now called kwashiorkor was long unrecognized. It was Dr. Cicely Williams who in 1933 showed its relationship to diet (Williams, 1933) and introduced to the world its name in the Ga language from Gold Coast (now Ghana) which means "the disease of the deposed baby" (Williams, 1963; Williams and Jelliffe, 1972). Kwashiorkor is characterized by muscle wasting with preservation of fat stores and in particular by hypoalbuminemia and edema. It was originally thought to be due to protein deficiency in the presence of an adequate energy intake (FAO/WHO Expert Committee on Nutrition, 1953). However,
others have been unable to demonstrate convincingly that nutritional background of those with kwashiorkor differs from that of those with marasmus (Gopalan, 1968; Whitehead et al., 1977). Also, what determines whether a particular infant will manifest with marasmus or with kwashiorkor remains a subject of debate (Truswell, 1981; Waterlow, 1984a). This has led to a proliferation of alternative theories to explain the failed adaptation by which some children adapt appropriately (marasmus) to protein-energy deficiency whereas others do not and develop kwashiorkor (Jaya Rao, 1978).

Intermediate between nutritional marasmus and kwashiorkor, i.e. between a clinical picture associated primarily with deficiency of calories and one resulting primarily from deficiency of protein, is a series of conditions combining some of the features of both. Retardation in growth is common to all forms of protein energy malnutrition and the degree of retardation can be roughly assessed by classifications based on the difference between observed weight and a chosen standard. A widely used classification is that of Gómez et al. (1955).

II. Historical Background:

In every age and in every land, people have been subjected to famine conditions and ancient history
has several accounts of human experience with starvation. Some of these ancient and historic accounts have been referred to in the excellent monographs of Keys et al. (1950) and McCance (1951). An indication of the severity of some famine situations is obtained from reports of the nature of foods to which men had resorted. Dogs, Cats, rats and even the bodies of children and adults were reported to have been consumed (Fisher, 1927).

Pringle (1764) perhaps has given the first account of hunger edema in the medical literature (Hottinger et al., 1948). Hecker (1844) referred to what was probably famine edema in the sixteenth century. There are several references to famine edema in the nineteenth century literature. Gaspard (1821) gave a good description of the physiological effects of famine in France in 1816. Other famines occurred in Ireland in 1845-47 (Mareska, 1846, 1849-50) and in southern India in 1876-78 (Porter, 1889).

More recently, scientific interest in the subject of famine edema was aroused by reports, which began to appear in 1915 in the wake of World War I. Budzynski and Chelchowski (1916) described "dropsical condition" in undernourished subjects in Poland. The prevalence of edema among prisoners of war was common occurrence.
and German authors in 1916 described this condition as "edema disease of the prison camps". These early reports were followed by many other reports (Knack and Neumann, 1917; Schiff, 1917; Masse and Zondek, 1920). In 1918 famine edema was common in all parts of central Europe. The aetiology of this syndrome was debated and only in 1918 was it connected with dietary deficiency of calories and proteins.

Starvation and its effects received particular attention during and after the Second World War when innumerable victims in prisons or concentration camps were barely surviving on minimal rations. In Netherlands, Holland, Greece, France, Belgium and Italy famine conditions prevailed for several months. As a result of the Japanese occupation of Burma, China and East Indies, famine conditions were widely prevalent in India and the Far East.

During the German occupation of Belgium, Brull, et al. (1945) reported some studies on undernourished population. Simonart (1948) as a prison physician made extensive observations and wrote about edema, its genesis, treatment and also about the effects of starvation on circulation, digestion, excretion and basal metabolism. The acute starvation picture in the Warsaw Ghetto in 1941 and 1942 has been referred to in Maladie de famine edited by Apfelbaum (1946). The German blockade of Leningrad in
1941 produced severe food shortage and starvation. The subject of starvation has been reviewed in vol. 3 & 5 of the periodical studies of Leningrad physicians during the years of "Patriotic War" published by the Leningrad branch of the State Medical Publishing House (Medgiz). The effects of war on nutrition in Holland during the 1944-45 famine have been discussed in a monograph Ed. by Boerema (1947). Details regarding the victims of concentration camps have been published by Debray et al. (1946) and Lamy et al. (1948).

Two outstanding reports on starvation and its effects by Keys et al. (1950) and by McCance (1951). Keys et al. (1950) had induced starvation in human volunteers and studied several aspects of the pathology of famine, a study which as indeed considered a classic.

Famine in India

Famine in India has been a recurring phenomenon. Several famines have been reported in 1148-59 and in the years 1344-45. During the latter, even the Moghul Emperor is reported to have bound himself unable to obtain the necessities for his household. In the year 1769-70 there was a great famine in Bengal when a third of the population is said to have perished. In the year 1866-69 famine prevailed in Bengal, Orissa, Rajputana and Bihar. Between the years 1876-78
population in Madras, Bombay and Mysore were again affected by severe famine and food shortage. In 1943 Bengal was the scene of one of the worst famines in human history.

III. Studies on Malnutrition

The strategies investigators have used to study the long-term effects of malnutrition have derived mainly from their view of human malnutrition. One group considers malnutrition as an acute disorder, more or less sharply delimited in time. This attitude has led to field studies such as that of Hiermaux (1964) in Rwanda and to human experiments utilizing volunteers, such as the series carried out by keys et al. (1950). Another view is that of malnutrition as a chronic state, which may or may not have acute exacerbations related both to social conditions and to the age and physiologic status of the individuals at risk (Gopalan and Ramalingaswami, 1955; Rnoetal1959; Doen 1960). Increasingly it is recognized that except under highly special conditions like war or natural catastrophe, the major problem of human malnutrition is its chronicity with only occasional exacerbations of acute diseases. Complimentary approaches have been developed to clarify the causal factors and consequences associated with the most prevalent variety of human undernutrition, protein-calorie malnutrition. In all these
approaches the young child is the primary focus of study, in as much as, the consequences of even severe malnutrition in adults have been remarkably transient (Cravioto, 1963), whereas the young child has been shown to be highly vulnerable to permanent damage (Cravioto and Robles, 1962, 1965; Cravioto et al., 1966).

**Animal Studies**

Many studies have been made on the effect of undernutrition on various species of growing animals. These include the rat (Jackson and Stewart, 1920; McCay et al., 1939; Ross, 1961; Widdowson and McCance, 1963; Miller, et al., 1985; Lewis et al., 1986; Oldfors and Sourander, 1986; Ahmed et al., 1987; Eberhardt and Halls, 1987; Testar et al., 1988; Tonkiss et al., 1988; Badi et al., 1989; Kawai et al., 1989; Sieck et al., 1989; Warren et al., 1989; Goncalves et al., 1990; Keller et al., 1990; Koski et al., 1990; Martin et al., 1990; Rao et al., 1990); mice (Berk et al., 1975; Castellano and Oliverio, 1976; Zane, 1976; Heard and Blevins, 1989; Gross and Frohaska, 1990; Koizumi et al., 1990; Meydani et al., 1990; Spindler et al., 1990; Umezawa et al., 1990; Watanabe and Ando, 1991); pigs (McMeekan, 1940a, b; McCance and Widdowson, 1962; Pond et al., 1987); Guinea pigs (Fabianek, 1967; Biesalski et al., 1990); rabbit (Simard and Srivastava, 1974; Turner et al., 1976; Baker and Campbell, 1989); Cat (Lehmann et al., 1990);
dog (Aron, 1911); sheep (Palsson and Verges, 1952); goat (Wilson, 1960); chick (Tolosa de Talamoni et al., 1990) and hamster (Shanker et al., 1990).

Animal investigations have mainly utilized the deprivation model. Undernutrition before weaning in laboratory animals has been imposed by different techniques: changes in maternal diet (Chow and Lee, 1964), ingastric feeding (Dymsza et al., 1964), limitation of the quantity of milk available to nursing pups by dilution of milk (Miller, 1970), removal of pups from the mother for different lengths of time (Howard and Granoff, 1968) or by partial mammectomy (Galler and Turkewitz, 1977) or by increasing the litter size (Schultz, 1954).

After the Second World War people became concerned about the malnutrition of children throughout the more backward countries of the world and some experiments made in the late 1950s (Kennedy, 1957a,b; Widdowson & McCance, 1960, 1963; McCance, 1962; McCance and Widdowson, 1962) opened up a way of varying the plane of nutrition of rats experimentally immediately after they were born. This technique which made it possible both to accelerate and delay the normal rate of growth, has frequently been exploited since that time. Animals have been used not so much to replicate the human conditions of chronic and
moderate deprivation, but to examine the effects of severe malnutrition. Animals have been nutritionally deprived qualitatively and quantitatively to determine the effects of specific nutritional deficits on growth and development. The work of Lat et al. (1961), Widdowson et al. (1960), McCance (1964), Platt et al. (1964), Winnick and Noble (1966), Barnes et al. (1968), Winick et al. (1968), Howarth and Baldwin (1971), Dickerson and McAnulty (1975), Dobbing (1964), Srivastava (1985), Glore and Layman (1987), Smart et al. (1987, 1989), Dureuil et al. (1989) and Firmanzalah et al. (1989a,b) among others have provided clear evidence for at least three developmental consequences of severe malnutrition. First, animals exposed to nutritional deprivations early in life exhibited growth failures not fully repaired by subsequent rehabilitation. Second, such early severe malnutrition resulted in lags in maturation accompanied by the development of abnormal metabolic and enzymatic patterns. Third, in almost all instances in which behaviour, as well as, central nervous system structure and composition has been carefully studied, the exposure of the animal to malnutrition has resulted in central nervous system abnormality and some degree of behavioural incompetence.

The dramatic effects of severe nutritional deprivation have led several groups to examine conditions in animals
that more fully mimic the human condition. These investigators have provided animals with moderate, but persistent, degree of nutritional deprivation and have studied the effects on subsequent generations. Chow (1964), and Chow and Lee (1964) have shown that offspring of rat mothers fed sufficient calories, but protein of poor quality, were stunted at birth and remained stunted even when a full ad libitum diet was available after weaning. Cowley and Griesel (1963) and Platt et al. (1965) have focussed less on physical characteristics and more on the functional and behavioural consequences of chronic malnutrition. Cowley and Griesel (1963) produced evidence suggesting that such deprivation has cumulative effects on learning capacity. They have demonstrated that rats nutritionally deprived over successive generations manifest increasing degrees of learning deficit. Platt et.al. (1965) have studied pigs rather than rats to demonstrate behavioural, anatomic and neurophysiologic consequences associated with chronic malnutrition.

Animal studies based on the deprivation model have been extremely valuable, since they permit an examination of the effects of malnutrition on biologic structures utilizing controlled condition which would be impossible and immoral to achieve in the human organism. They have provided data on specific organs, systems and mechanisms
of biological organization most likely to be affected when exposed to malnutrition. Moreover, they have inspired such specific studies as those of Flexner et. al. (1963, 1965), who have used metabolic blocking agents to study the effects of the deprivation of nutritional elements on memory.

b. **Human Studies**

Animal studies cannot provide a complete analogy to the human conditions. Experimental animals lack the social substrate against which human nutritional deprivation takes place and with which it interacts. Furthermore, the effects on behaviour have necessarily been limited to the simple types of behavioural adaptation possible for the lower animal. Therefore, the effects of malnutrition on complex behavioural and social functions could not be studied and the analogy though useful is incomplete and complements rather than substitutes for the study of the effects of malnutrition in man. Interestingly, Winick (1969) has found that brain from children who died from protein calorie malnutrition showed a reduction in cell number roughly equivalent to that obtained in severely malnourished rats.
One of the first studies on human starvation was conducted by Benedict (1915) on a single subject for a period of 31 days. In the study of Keys et al. (1950) semistarvation was imposed in study for 24 weeks. Except for studies of subacute malnutrition in adult human volunteers carried out by Keys et al. (1950), almost all studies have capitalized on malnutrition spontaneously occurring under conditions of social dislocation. These conditions may have been acute as in the case of Antonov's study of pregnancy during the siege of Leningrad (Antonov, 1947) and Smith's study of acute food deprivation in Holland (Smith, 1947) or chronic as in the case of Dean's studies in Kampala (Dean, 1960). The population studies have ranged from a series of individuals hospitalized for malnutrition to whole communities studied by epidemiologic methods (Perez-Navarrete et al., 1960). Moreover, Dr. C. Gopalan had carried out an elaborate study on protein-calorie malnutrition in children with special emphasis on the protein deficiency syndrome (kwashiorkor) in India and abroad (Gopalan, 1950, 1956, 1968a,b; 1969; 1973; Gopalan and Venkatachalam, 1952; Gopalan and Srikantia, 1957; 1959; Gopalan and Ramalingaswami, 1955; Gopalan and Mehta, 1956; Gopalan and Narasinga Rao, 1957; Gopalan and
Padmavathi, 1957; Gopalan and Ramanathan, 1957; Gopalan et al., 1952; 1953a,b; 1954a,b; 1955a,b,c; 1956a,b,c; 1957, 1963, 1964a,b; 1968a,b; 1970, 1973). Another study on children with kwashiorkor include the works of Rama-
ingaswami et. al., (1948) and Champakam et. al. (1968) in India, Berrera-Monica (1963) in Venezuela, Cravioto and Robels (1965) in Mexico and Hansen et. al (1971) in South Africa. Also, the early sign of PCM was reviewed by Jelliffe and Welbourn (1963), and Arroyave (1963).

Waterlow and Alleyne (1971) have discussed the assessment of marginal protein malnutrition in an excellent review. Behar (1972) has discussed the various methods of nutritional assessments as they are related to natural history of disease (Laevell and Clark, 1965). More recently, many investigators have studied in detail the effect of undernutrition on human subjects (Forbes, 1986; Linhares, et. al., 1986; Bagenholm et al., 1988; Gershoff et. al. 1988; Hallak and Nomani, 1988; Hendler and Bonde 1988; Lewis and Belman 1988; Poole and Henson 1988; Bruce et al. 1989; De Luise and Harker, 1989; Koski and Hill, 1990).

IV. Effect of Malnutrition on Body and Organ Weight

One of the earliest reviews of literature about the effect of malnutrition on body and organ weight in very young malnourished animals is found in the publications
of Aron (1911) and Jackson (1925, 1929). Recently it has been confirmed that body and organ weight fail to increase normally in dietary insulted animals (Srivastava, 1985; Smart et al., 1987, 1989; Dureuil et al., 1989; Firmansyah et. al., 1989b).

Body weight of female rats subjected to different models of dietary restriction and of their neonatal and 21 day-old progeny failed to increase normally in comparison to their corresponding controls (Srivastava and Malchelosse, 1976; Srivastava et. al., 1974a,b; 1978a,b; 1979; Goswami and Srivastava,1978; Goswami et. al., 1971; 1974; Smart et al., 1987, 1989; Dureuil et. al.,1989; Firmansyah et. al.,1989b). According to some researchers (Venkatachal and Ramanthan,1964; Altman et. al., 1970; Howarth and Ford, 1972), dietary restriction during gestation generally has little influence on the weight of the young at birth, but growth may be stunted during the weanling period. Chow and Stephan (1971) noted a slight difference at birth between the weight of the young born to well-fed groups as compared to those whose mothers were undernourished during gestation. Zeman and Stanbrough (1969) also reported similar changes in the body weight of newborns of females maintained on a protein deficit diet. In the study by Chow and Stephan (1971), dietary restriction imposed during gestation and lactation caused severe, irreversible growth retardation in weanlings, confirming their earlier investigation (Chow and
Lee, 1964). If the dietary insult was inflicted during gestation only, then the resulting changes were the same but of a lesser degree than those noted above (Simonson et al., 1969). In experiments by Venkatachalam and Ramanthan (1964), the progeny of food-deprived dams having a similar weight at birth as the progeny of control dams were less strong and suckled less milk so that they experienced severe growth retardation in the weanling period, even though they were suckled by well-fed dams (Zeman, 1970). This was further confirmed by Knittle (1972), who found nearly one-half the quantity of milk in the stomachs of the young of undernourished female rats. According to Zeman (1970), this growth retardation was due to a decreased absorption capacity and heightened protein catabolism in the pups of dietary insulted rats.

V. Effect of Malnutrition in Cell Growth

Classically, growth has been measured in increments of weight, height or length, or by using other anthropomorphic criteria. Only recently, however, has it become possible to measure growth by determining the number of cells within an organ or the size or density of individual cells. In 1962 Enesco and Leblond determined total DNA content of various rat organs and knowing that DNA per diploid nucleus of any species is a constant, actually
calculated the number of cells in the organs of the rat. Once the number of cells had been calculated, the average weight per cell was determined simply by dividing the total organ weight by the number of cells. Regardless of whether actual cell number is calculated, the hypothesis that DNA content reflects cell number is valid except in tissues containing a significant number of non-diploid nucleus e.g. liver or testis, or in tissues containing many multinucleated cells, e.g. pancreas in the older animal. With these exceptions, then, serial analysis of total organ DNA during development will determine the rate of increase in the number of cells. Weight/DNA or protein/DNA ratios reflects the average weight or protein per cell in tissues where extracellular material is minimal. These ratio provide an estimation of cell size and/or cell density. RNA/DNA ratios reflect the average RNA per cell.

In the experiments of Enesco and Leblond (1962) and Winick and Noble (1965, 1966) normal and retarded growth studied by serially measuring the nucleic acid and protein content of various tissues. With this chemical approach, the pattern of normal growth in the various organs of the rat was observed from ten days after conception until adulthood. Three phases of growth could be defined in all organs, hyperplasia, hyperplasia and hypertrophy, and hypertrophy alone. The transition from
one phase into another was entirely dependant on slowing down and finally a cessation of DNA synthesis. The time that this occurred varied from organ to organ, (Winick and Noble, 1965), but in all cases DNA synthesis as measured both by total organ analysis and by incorporation of $^{14}$C thymidine ceased before weight gain and net protein synthesis stopped. From these data, it was concluded that the same stimulus might interfere with growth differently, depending on the cellular events occurring at the time the stimulus was active (Jasper and Brasel, 1974). Because of experiments suggesting that the recovery pattern of early and late malnutrition differed (McCance and Widdowson, 1962) the effects of malnutrition on these cellular growth pattern were investigated (Winick & Noble, 1966).

Winick (1968) reported that the amount and availability of anterior pituitary hormones are also very important in controlling the rate of cell division as well as in determining the time at which cell division stops. Moreover, in the presence of anterior pituitary hormone the rate of cell division will not increase with increased caloric intake. It may even be possible that one of the ways in which undernutrition retards cell division is by reducing secretion of or receptivity to growth hormone.
VI. Effect of Malnutrition on Protein Content of Muscle

At the turn of this century Folin (1905a) studied the effect of both adequate and low nitrogen intakes on the chemical composition of urine. Folin developed his theory of protein metabolism (Folin, 1905b) which he separated into endogenous and exogenous components postulate that was later invalidated by the isotopic tracer studies of Schoenheimer (1942). Since those early developments reviewed in their historical context by Munro (1964), a considerable literature has been captured in a series of excellent volumes (Munro and Allison, 1964; Munro, 1969, 1970). Recently, it was also reviewed by Waterlow et al., (1978); Waterlow and Stephen (1981); Blaxter and Waterlow, (1985) and Young and Marchini (1990).

First report on the effect of malnutrition on protein content of different organs in the rat was clearly illustrated by Addis et al. (1936a,b,c), who showed rapid and extensive changes in the total amount of protein in the liver of the rat under conditions of starvation or protein deficiency but much slower changes in the case of carcass, a large part in which is muscle. The liver and the skeletal musculature each made a quantitatively important contribution to the rates of whole body protein synthesis and breakdown (Garlick, 1980; Waterlow, 1984b).
Effects of diet on muscle and liver protein synthesis were reviewed extensively (Millward et al., 1976; Waterlow et al., 1978; Garlick, 1980; Millward, 1980). Munro (1956) concluded from a survey of the literature that the liver of the rat has completed its adaptation of protein deficiency with 3 days of consuming a protein free diet, whereas muscle does not begin to lose protein significantly until after this time. Waterlow and Stephen (1966) demonstrated no loss of muscle protein during the first 3 days on low-protein diet but a loss of 56% of original muscle protein content after 6 weeks of this regimen. Thus during prolonged protein-calorie malnutrition muscle eventually loses a greater percentage of its initial protein content than does liver and in terms of total protein lost from the body, skeletal muscle contributes much more protein than does liver (Waterlow, 1956; Hagan and Scow, 1957; Mendes and Waterlow, 1958; Widdowson et al., 1960; Allison et al., 1962).

In man, Kerpel-Fronius and Frank (1949), and Winick and Brasel (1973) showed in malnourished infants that the loss of muscle mass was considerably greater than the reduction in body weight. Muscle protein is catabolized during protein calorie malnutrition in order to provide amino acids for the liver and other vital organs (Widdowson et al., 1960; Young and Marchini, 1990).
Somewhat recently, studies showed that malnutrition has a differential effect on the constituent cells of skeletal muscle. The proteins of the contractile fibers (fibrillar and sarcoplasmic) diminish whereas the extracellular proteins (chiefly collagen) are not reduced during a period of malnutrition. There is evidence from studies on animals (Hagan and Scow, 1957; Mendes and Waterlow, 1958; Widdowson et al., 1960; Caback et al., 1963) and on man (Picou et al., 1966) that muscle collagen can continue to accumulate during severe malnutrition a phenomenon that also occurs with body collagen generally (Harkness et al., 1958). Part of the collagen increment is contributed by a reduction in collagen catabolism during malnutrition (Picou et al., 1965). Within the contractile cells, it has been concluded from studies on pigs (Widdowson et al., 1960) and rats (Waterlow and Stephen, 1966) that prolonged malnutrition has little effect on the ratio of fibrillar to sarcoplasmic proteins. However, other studies on rats (Yamatami and Kandatsu, 1967; Hagan and Scow, 1957) and on cocks (Dickerson and McCance, 1960; Montgomery et al., 1964) have shown a greater proportional loss of sarcoplasmic protein.

VII. Effect of Malnutrition on Chromosome Aberrations;

There are few reports on the chromosomal aberrations due to malnutrition in rats (Sadasivan and Raghuram, 1973;
Vijayalaxmi, 1975; Murthy, 1984) and human lymphocytes (Armendares et al., 1971; Khouri and McLaren, 1973; Betancourt et al., 1974; Upadhyaya et al., 1975) and bone marrow (Tolani et al., 1978). In rats, the incidence of chromosomal abnormalities was higher in the embryos whose mothers had low-protein diet compared to controls (Murthy, 1984) and also in the progeny of dams fed protein-deficient diet during gestation and lactation (Sadasivan and Raghuram, 1973). Similar, results have been observed in weaned rats fed a low-protein diet for 8 or 12 weeks (Vijayalaxmi, 1975). In humans, the lymphocytes of severely malnourished children showed an increased number of chromosome abnormalities as compared to control (Armendares et al., 1971; Khouri and McLaren, 1973; Betancourt et al., 1974 and Upadhyaya et al., 1975). Similar results have been observed in the study of bone-marrow chromosome preparation from children suffering from protein calorie malnutrition (Tolani et al., 1978).

There is a lot of controversy in the studies of the effect of malnutrition on chromosomal damage (Sadasivan and Raghuram, 1973). While Armendares et al., (1971) found that chromosomal aberrations were six times commoner in malnourished children than in normal ones, Thorburn et al. (1972) and Khouri and McLaren (1973) reported that malnutrition per se may not influence chromosomal
abnormalities. Even in the data of Armendares et al. (1971) it was difficult to assess the extent to which malnutrition per se had contributed to the increased incidence of chromosomal anomalies, since environmental factors such as radiation, chemical agents and viral infections are also known to produce chromosomal aberrations. However, recent studies suggest that malnutrition may also produce chromosomal damages. In advanced protein calorie malnutrition cell division would fail and chromosomes would become structurally abnormal either spontaneously or as an exaggerated response to environmental factors such as radiation, chemical agents or viral infection (Evans, 1970; Krause, 1988). Murthy et al. (1982) showed that cell cycle duration of lymphocytes was prolonged in cultures from children suffering from Kwashiorkor. Also, Ortiz and Betancourt (1984) reported that malnutrition during the lactation period produced a prolongation in the time of proliferation of bone-marrow cells in the rat.

VIII. Effect of Malnutrition on Muscle Histology

At the cellular level numerous reports confirmed that protein-calorie malnutrition causes a decrease in mean fiber diameter in the muscle of man (Vincent and Radermecker, 1959; Montgomery, 1962) and the mouse (Goldspink,
1964, 1965; Rowe, 1968). In the mouse, there is a bimodal distribution of fibers into large phase and small phase and inadequate food decreased the relative proportion of large phase fibers (Goldspink, 1964; Rowe, 1968). Starvation decreases the number and diameter of myofibrils in the fibers (Goldspink, 1965) and in the rat undernutrition reduces the number of myofilaments at the outer periphery of the myofibril (Nechsler, 1964). Whether there is an actual diminution in the number of muscle fibers during undernutrition is not certain.

Many investigators have concluded that only the mean diameter of the fibers changes, without an alteration in fiber number. In contrast, Elliott and Cheek (1968) observed a loss of muscle DNA from food restricted weanling rats and concluded that there must have been a decrease in fiber number. However, Mendes and Waterlow (1958) fed a low-protein diet to rats at a level that caused even greater restriction on growth than that imposed in Elliott and Cheek's study but failed to obtain a loss of muscle DNA. It may be that calorie restriction is more severe than protein restriction alone. In human infant there is histological evidence that protein-calorie malnutrition leads to loss of muscle fibers (Frank and Freund, 1986; Montgomery, 1962).
The effect of a period of undernutrition, on subsequent muscle development has been investigated by Winick and Noble (1966) as part of their survey of tissue responses to malnutrition. If the period of malnutrition is applied for a short period while the muscle cell population is still increasing, the amount of DNA in the muscle reaches a final plateau at a lower level than it would in normally nourished animals, even if some time elapses between the time of terminating the malnutrition and the end of the growing period.