CHAPTER - I

I N T R O D U C T I O N

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INTRODUCTION

In many poor countries food supply fails to meet the calorie needs of the people even if we go by per capita intakes. In some parts of the world where starchy tubers, sugarcane or sago form the major providers of calories, the supply of protein is also precarious (FAO, 1971, 1973, 1975). Limited food resources combined with inequitable distribution lead to a wide prevalence of undernutrition. That this is not just a theoretical shortage is suggested by several indices such as the high prevalence of low birth weights, growth retardation, stunted physical stature as adults and the generally poor productivity of undernourished individuals.

On the other hand, the performance of the individual undernourished with regard to food energy and other nutrients, is not as bad as might be expected. Children continue to grow on intakes that are barely above levels expected to be required for basal metabolism. The fertility of undernourished individuals continues to be distressingly satisfactory and the gestation and lactation performance of the poor woman on a low plane of nutrition compares favourably in many respects with that of the upper class woman. Most of the production of material goods in poor countries is accomplished by apparently undernourished individuals.

As emphasized by Hegsted (1974), the adaptability of the organism under stress is great, at least within a certain range of what we now consider as'suboptimal' nutrition. Studies in this direction are important as they may help provide a more realistic appraisal of the consequences of undernutrition.

Some of the reports dealing with the adverse consequences of nutritional stress in man and in experimental animals, their reversibility on rehabilitation, the evidence for the operation of adaptive mechanisms in undernutrition and the baneful effects of excessive nutrition are briefly reviewed below :

Consequences of undernutrition on man

Undernutrition during the fetal and neonatal period

Undernutrition may begin even before birth as evidenced by the high proportion of full term singletons born with low birth weights. Since the fetus gets all its nutrition from the mother, it stands to reason that the wellbeing of the fetus is directly dependent on the nutrition of the mother during pregnancy. The Indian Council of Medical Research (Gopalan and Narsingarao, 1971) recommends a daily allowance of 1900-2500 Kcals, 40-50g protein, 400-500 mg calcium and 750 µg vitamin A for non-pregnant, non-lactating women with an increased allowance of 150-300 Kcal., 10g protein, 300-500 mg calcium and 600-1000 µg vitamin A during pregnancy. The corresponding figures for lactation are 500 Kcals., 20g.,

500-600 mg and 600-1000 µg. As against this, the diet of the majority of poor women in India provides only about 1600 Kcals, 40g protein, 400 mg calcium and 800 µg vitamin A. This does not increase appreciably during either pregnancy or lactation (Sengupta and Bagchi, 1961; Shankar, 1962; Rajalakshmi and Ramakrishnan, 1969(b); Rajalakshmi, 1971; Srikantia and Iyengar, 1972). Even if we go by the amounts of nutrients transferred to the fetus and the growing infant (Table 1) the supply of many nutrients must be considered rather precarious.

Better obstetric performance has been associated with better nutrition in several studies in this country (Gopalan, 1949; Varkki et al, 1955; Arora et al, 1963; Nirmala et al, 1966(a); Ankegawada and Sumitra Devi, 1976) and elsewhere (Toverud et al, 1950; Dean, 1951; Hamlin, 1952; Berry, 1955; Woodhill et al, 1955; Monckeberg, 1968; Stein et al, 1976; Pitkin, 1977). A number of studies have reported a striking increase in mean birth weights when the mothers were given a food supplement (Iyengar, 1967; Higgins et al, 1972; Srikantia and Iyengar, 1972; Habitch et al, 1973(a), (b), 1974; Higgins,1973; Quereshi et al, 1973; Chavez et al, 1974; Iyengar, 1975; Read, 1975; Adams et al, 1978; Mora et al, 1979) or even supplements of individual nutrients such as folic acid and iron (Iyengar, 1971; NIN, 1974; Gandy and Jacobson, 1977).

On the other hand, the lack of a relation between the adequacy of the maternal diet and obstetric performance has

Table 1 : Nutritional demands of the growing fetus and the nursing infant in relation to maternal diet (Rajalakshmi, 1979).

	Amount in diet*	Transferred to	
		The growing** fetus	The nursing*** infant
Kilo calories	1500-1600	160-170	400-500
Protein (g)	35 - 40	1.4	10
Fat (g)	30	1.6	30 - 35
Calcium (mg)	400	100	140
Vitamin C (mg)	10 - 15	3 - 5	20 - 30
Vitamin A (ug)	125	10 - 15	210
Iron (mg)	20 - 25	0.75	1.4
Folate (mg)	0.5 - 0.7	0.0013	0.0018
B_{12} (ug)	0.5	0.045	0.0672
B_1 (mg)	1.0 - 1.5	-	0.06-0.08
B_2 (mg)	0.5	-	0.15-0.18
Niacin (mg)	5-6	-	0.8-0.9

* Based on intakes of poor women in urban Baroda (Rajalakshmi and Ramakrishnan, 1969(b).

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

*** On the basis of secretion of milk as 700 ml/day and the analytical values obtained in our studies (Karmarkar and Ramakrishnan, 1959; Deodhar and Ramakrishnan, 1960).

also been reported (Williams and Fralin, 1942; Mc Ganity et al, 1954, 1955). This is supported by the fact that in spite of inadequate dietary intakes, the poor woman, on an average, achieves a satisfactory weight gain of about 7 kg during pregnancy (Venkatachalam et al, 1960; Bagchi and Bose, 1962; Rajalakshmi and Ramakrishnan, 1969(b); Bhatt et al, 1972) and produces a reasonably healthy infant weighing on an average 2.6-3.0 kg which is only about 200-300 g less than that of the upper class infant (Sen,1956; Singh and Ahluwalia, 1957; Kulkarni,et al,1959; Achar and Yankauer, 1962; Bagchi and Bose, 1962; Currimbhoy, 1963; Banik et al, 1967; Iyengar, 1967; Rajalakshmi and Ramakrishnan,1969(b)). However, this small difference in average birth weights masks a serious phenomenon, namely the high prevalance of low birth weights of full term singletons among the poor. Infants weighing less than 2 kg at birth account for 8-14% of the total among the urban poor as against a negligible proportion in the upper class (Rajalakshmi and Ramakrishnan, 1969(b); Achar and Yankauer, 1962; Udani, 1963). This proportion could be higher among the poor in rural areas.

Also, the prevalence of still births and perinatal mortality has also been found to be some what greater in the poor group (Gopalan and Raghavan, 1969; Rajalakshmi and Ramakrishnan, 1969(b); Aiyer, 1972; Bhatt et al, 1972; Parekh et al, 1972; Banik, 1978; Purohit, 1979).

On the other hand, compared to the upper class woman,the poor woman appears less prone to prolonged labor and toxemia of pregnancy and less in need of surgical intervention for or during delivery (Bagchi and Bose, 1962; Rajalakshmi and Ramakrishnan, 1969(b)).

The smaller stature of the poor woman has been implicated in the prevalence of low birth weights among the poor but the major factors responsible for fetal growth retardation appears to be poor weight gains during pregnancy and low placental weights associated with poor food intakes (Rajalakshmi and Ramakrishnan, 1969(b); Munro, 1973; Desai et al, 1974; Sen and Agrawal,1975; 1976; Rajalakshmi et al, 1978;Rosso and Cramoy, 1979; Woods et al, 1980).

The reasonably good gestation performance of poor women would suggest the operation of adaptive mechanisms during pregnancy. This is suggested by the more efficient conservation of nitrogen associated with satisfactory retention of nitrogen even with no increase over customary intakes (Beaton et al,1954; Rao and Rao, 1974).

The more efficient conservation of N seems to be associated with decreased urea formation during pregnancy (Mc Ganity et al, 1949; Rao and Rao, 1974) and lower levels of blood amino nitrogen (Beaton et al, 1951). Similar observations have been made regarding an increased efficiency in the utilization of

iron (Balfour et al, 1942; Thomson and Hytten, 1964; NIN, Annual Report, 1968) and calcium (Thomson and Hytten, 1966; NIN Annual Report, 1968).

Although lactation involves the transfer of nutrients to the nursing infant in significant amounts, and the nutritional stress of lactation is greater than that of pregnancy (Table 1), the lactation performance of the poor woman is found to be generally satisfactory in several studies (Walker, 1958; Pearson, 1968; Rajalakshmi and Ramakrishnan, 1969(b))and surpasses that of the relatively better nourished upper class women in this country. The average milk production of the poor woman is of the order of 700-800 ml (Gopalan, 1958; Belavady et al, 1959; Rajalakshmi, 1971; Lonnerdal et al, 1976, 1977; Jenson et al, 1978; Whitehead et al, 1978; Khin et al, 1980; Van Steenberger, 1980) and the maintenance of this for a prolonged period, despite low intakes of foodenergy poses a theoretical problem. However, some infants fail to reach a weight of 6 kg at six months, presumably because of inadequate lactation, and this proportion is found to be of the order of 10% in previous studies in this laboratory (Rajalakshmi and Ramakrishnan,1969(b)) and may be higher in poor rural areas on the basis of studies directed otherwise in this laboratory (Ramakrishnan, 1980).

In conclusion, the reasonably satisfactory gestation performance on a low plane of nutrition is clouded by the

higher proportion of still births, low birth weights and undernourished infants at weaning age.

The prognosis for growth in full term singletons with low birth weights is not clear on the basis of existing information. Beargie and associates (1970) found that at about $4\frac{1}{2}$ years of age, one third of the small-for-date babies studied looked undergrown and one fifth showed a moderate developmental lag. Lubchenko (1970) observed growth retardation in small-for-dates even at 10 years of age. Fitzhardinge and Stevens (1972) studied such children whose birth weights were 70% of average values and found that even at 4 yrs of age they were growth retarded as judged by mean height and weight which were between the 10th and 25th percentile. Cruire (1973) reported that catchup growth at 2-3 yrs. of age was less satisfactory in full term small-for-dates than in prematures. Continued growth retardation as judged by height and weight of small-for-dates has been reported by several investigators (Rajalakshmi and Ramakrishnan, 1969(b); 1972 Aiyer, 1972; Srivastava et al, 1978; Desai, 1980; Savkur, 1980; Ramakrishnan, 1982). These children also showed deficits with regard to other somatic measurements such as head circumference (Fitzhardinge and Stevens, 1972; Srivastava et al, 1978).

On the other hand, reports to the contrary are also available. In the well known Dutch famine study (Stein et al, 1975), individuals with low birth weights were not found to differ from

controls with regard to physical stature, body weight or psychological development. Complete catch-up was observed even in the first year of life in singletons born with body weights of about 1500 g. (Davies and Stewart, 1975).

The pattern of brain growth relative to birth differs appreciably in different mammalian species (Dobbing, 1974). In man, the late fetal period and early neonatal period are believed critical for the development of the nervous system. According to the vulnerable period hypothesis propounded by Dobbing (1974) and Winick and Noble (1965), the effects of nutritional deprivation on any tissue are influenced by the normal rate of growth of that tissue at the age when nutritional stress is in operation. We should therefore expect nutritional stress during the late fetal and early neonatal periods to have a greater effect on brain development than that at subsequent stages.

Empirical evidence for this view was provided by several studies reporting the higher prevalence of mental retardation in low birth weight babies (Wiener,1962; Knobloch and Pasamanic, 1963; Harper and Wiener, 1965; Bacola et al,1966; Jackson,1968; Winick, 1968; Kaelber and Pogh, 1969; Birch et al,1970; Butler, 1972; Drillien, 1972; Fitzhardinge and Steven, 1972; Parekh et al, 1972; Davies and Stewart,1975). However, such small-for-dates are not found to differ from controls in other studies (De Silva,1962; Rossen, 1962;

Rajalakshmi and Ramakrishnan, 1969(a); 1972; Chase and Martin, 1970; Ghosh et al,1972; Fitzhardinge and Ramsay, 1973; Francis-Williams and Davies, 1974; Davies and Tizard, 1975; Stein et al, 1975; Douglas and Gear, 1976).

The complicated findings with regard to the above aspects are perhaps explicable. At least some of the effects observed may have been due to the hospitalization of the babies and the artificial hazards imposed on them such as hypoxia and kernictus in the 1950's and early 1960's (Davies and Stewart, 1975; Douglas and Gear, 1976). Also, as pointed out by Dobbing (1974), the effects of fetal growth retardation may well depend on the circumstances after birth. In studies carried out in this laboratory at Trivandrum and Madurai on cases of severe protein-calorie malnutrition, children who were small at birth and continued to grow poorly during the neonatal and post-weaning periods were among the most affected cases (~~Rajalakshmi, 1979~~) and the least responsive to treatment (Ramakrishnan,1980). The poor performance of such children could be due in major measure to the constraints on development during the postnatal and postweaning periods (Pratapkumar, 1982) rather than to their low birth weights.

The picture has been clouded by the fact that in many studies the small-for-date babies have not been compared with controls matched for socio-economic status, family size etc. Often comparisons have been made between the prematures and

full term babies in the group and the latter found to be worse (Davies and Stewart, 1975). This could well be due to the fact that the former are to be found in all segments of the population whereas the latter are found mainly among the poor. In this connection, according to Davies and Stewart (1975), the prognosis for normal development of the low birth weight infant is improving due to centres specializing in the development of modern methods of perinatal care.

Undernutrition in early infancy

Most poor women nurse their infant with success for at least the first 4-5 months of life, producing on an average, 700-750 ml of milk per day (Rao et al, 1959; Venkatachalam, et al, 1967; Rajalakshmi and Ramakrishnan, 1969(b); Rajalakshmi, 1971; Lönnerdal et al, 1976, 1977; Jensen et al, 1978; Whitehead et al, 1978; Khin et al, 1980; Van Steenberger,1980). The composition of this milk compares favourably with values for upper class and western women with regard to proximate principles (Karmarker et al, 1959) and minerals (Karmarkar and Ramakrishnan, 1960). The concentration of vitamins is comparatively less (Belavady and Gopalan, 1959; Deodhar and Ramakrishnan, 1960; Deodhar et al, 1963) but seem adequate on the basis of theoretical and practical criteria (Rajalakshmi and Ramakrishnan, 1969(b) (Table 2). The poor often manage this performance through successive parities without losing weight in the bargain (Rajalakshmi and Ramakrishnan,1969(b);

Rajalakshmi et al, 1978) and without deterioration in the health of the new born. In fact, the birth weight of the infant is found to increase slightly till the fifth or sixth parity in a number of studies (Achar and Yankauer, 1962; Banik et al, 1967; Rajalakshmi and Ramakrishnan,1969(b); Basu and Puri, 1963; Billewicz and Thomson, 1973; Rajalakshmi et al, 1978). The problem posed by this has been the subject of investigation and discussion in several studies in this laboratory (Rajalakshmi and Ramakrishnan,1969(b); Subbulakshmi, 1970; Rajalakshmi et al, 1978; Rajalakshmi, 1979; Rajalakshmi, 1980(a)).

A conservative estimate of the requirement of the poor woman would be about 1600 Kcals on the basis of intakes of non-pregnant, non-lactating women. The milk output of the nursing mother is found to be of the order of 700 ml estimated in the Baroda studies by weighing the infant, duly diapered, before and after each feed, an estimate consistent with several other reports as mentioned earlier. The calorie value of the milk is 65 Kcal per 100 ml (Rajalakshmi, 1974). This would impose an additional burden of about 450 Kcals, even assuming a 100% efficiency of conversion of food energy to milk. A deficit between expected requirement and observed intakes still remains even when allowance is made for some decrease in activity and some increase in intake (Table 2).

Table 2 : Intakes of critical nutrients as compared to the nutritional requirements of pregnancy and lactation[a].

	Amount in diet[1] (rounded figures)	Demands of		Amount left for maternal metabolism during	
		Pregnancy — last trimester[2]	Lactation[3]	Pregnancy	Lactation
Calories	1500-1600	300	500	1200	1100
Protein (g)	40	10	10	30	30
Calcium (mg)	400	230	230	170	170
Vitamin A } i.u. Carotene }	50 1250	40 -	500-700 -	?	?
Vitamin C (mg)	15 - 20	?	21	?	Nil
Riboflavin (mg)	0.5	?	0.2	?	0.3

1. Based on collection and analysis of matched amounts of all the foods consumed (Rajalakshmi and Ramakrishnan, 1969(a)).
2. On the basis of maternal or fetal stores according to Mitchell (1962) or other sources.
3. Amounts provided by 700 ml of milk on the basis of analysed values obtained in previous studies (Deodhaf and Ramakrishnan, 1960; Deodhar et al, 1963).

a. Rajalakshmi (1980(a)).

The hypothesis of tissue depletion during lactation and repletion before the next pregnancy is difficult to sustain in cases where pregnancy occurs before the termination of the previous lactation.

In spite of the overall satisfactory performance, as mentioned earlier, an appreciable proportion of children, about 10% in studies carried out in Baroda, fail to double their birth weights by 6 months of age, suggesting that milk production in such cases falls short of requirements (Rajalakshmi and Ramakrishnan, 1969(b)). In such cases, and in cases of total lactation failure, early introduction of weaning foods and milk substitutes may be called for, the absence of which may result in growth retardation (Trowell and Davies, 1952; Monckeberg,1968; McCance,1971; Chavez et al, 1972; Rajalakshmi and Ramakrishnan,1972; Gopalan and Srikantia, 1973; McLaren,1973; Jelliffe,1977).

It is found that where breast milk is not available, the child is often given dilute cow or buffalo milk. In the commonly prevailing unsanitary conditions, bottle feeding during this age often results in diarrhoea, resulting from both, undernutrition and bacterial infections in response to which the mother substitutes even more unsatisfactory foods. Studies the world over have shown the increased susceptibility of the bottle-fed infant to infections, both because of increased exposure and decreased resistence (Goldman and Smith, 1973;Larsen and Homer,1978; Totterdell et al,1980; Cravano, 1982).

The prevalence of neonatal mortality is increased in full term infants with low birth weights (Yerushalmy et al, 1965; Lubchenko, 1970) even though this rate is less than that found for prematures (Yerushalmy et al, 1965). However, the former may manifest a higher prevalence of congenital abnormalities (Yerushalmy et al, 1965; Lubchenko, 1970), hypoglycemia (Usher, 1970; Lubchenko and Bard, 1971), chronic intrauterine infections (Lubchenko, 1970), a limited ability to conserve body heat, inspite of a normal response to cold and a narrower range of thermoregulation (Sinclair, 1970), asphyxia (Usher, 1970), disturbed acid base balance at birth (Shah and Acharya, 1970(a)) and hypocalcemia and hyponatremia (Shah and Acharya, 1976(b)) impaired cell mediated immunity (Chandra, 1982) and low stores of adipose tissue (Hull, 1976) and iron (Bhatt et al, 1969) at birth. Such infants have been found to be more susceptible to chest infections, septicemia, respiratory distress syndrome, cold injury during winter months, intracranial complications and still births (Verma and Dhar,1976). The postnatal nutrition of these children may suffer if an infant shows decreased vigour of the suckling reflex and fails to elicit normal lactation and maternal response (Graham, 1972; Cortial and Lazino,1974).

Even where breast milk supply is insufficient and infants fail to double their body weight by the weaning age of 6 months, most of them are found to reach, at or ahead of the expected

ages, landmarks of development such as lifting the head, turning over, crawling, sitting, standing and walking. These children do well on standard scales of development (Rajalakshmi, 1976). However, in children subjected to severe malnutrition, the proportion of children who fail to reach land-marks of development at appropriate ages may be considerable (Ramakrishnan, 1980; Pratapkumar et al, 1982).

Questions also arise regarding the prospective reproductive performance of females who were undernourished in early life. Thomson and Billewicz (1963) and Stewart (1972) have indicated the possibility that the mother who has been undernourished in early life may produce more small-for-dates babies than her well-nourished counterparts.

In this connection, an appreciable proportion of poor mothers are of slender build with weights less than 35 kg and heights less than 150 cm. This group must be deemed to include at least some who were undernourished in early infancy. The performance of this group as a whole seems reasonably satisfactory on the basis of previous studies in Baroda (Rajalakshmi and Ramakrishnan, 1969(b)) and elsewhere (Rao et al, 1959; Gopalan, 1958; Venkatachalam et al, 1967).

As mentioned earlier, undernutrition which may begin even before weaning age, becomes a high probability after this age among the poor. In cases of lactation failure leading to early

introduction of substitute foods, the child is given diluted milk, often contaminated, resulting in chronic and/or severe episodes of diarrhoea resulting from both undernutrition and infections (Achar, 1950; Trovell and Davies, 1952; De Silva et al, 1953; Jelliffe et al, 1954; Venkatachalam et al, 1954; Gopalan and Ramalingaswamy, 1955; Pretorius et al, 1956). Other diseases common in children include respiratory illness (Pereira and Begum, 1974) and intestinal intestation. These recurrent episodes of diarrhoea and infections are treated by diluting the milk further or starving the child fully or partially, a procedure which eventually results in decreasing food supplies at a time of increased needs and thus in severe undernutrition. Even where lactation is satisfactory, breast milk supply dwindles and more so in relation to increased needs (Gopalan, 1958; Whitehead et al, 1978).

Several investigators have reported that a decline in or inadequacy of breast feeding and early weaning on to the adult diet which is unsatisfactory for the child are the major causes leading to protein calorie malnutrition (Trowell and Davies, 1952; Waterlow and Vergara, 1956; Monckeberg, 1968; McCance, 1971; Chavez, Martines and Bourge, 1972; Rajalakshmi and Ramakrishnan, 1972; Gopalan and Srikantia, 1973; McLaren, 1973; Jelliffe, 1977). In some areas such as Gujarat (Rajalakshmi, 1975) the child is given the family foods but the unsatisfactory texture of the foods offered such as thick hard 'roti's and highly spiced side dishes make it difficult

for the child to eat adequate quantities of the foods which, moreover, are offered in two major meals without adequate spacing of the meals during the day. In other regions, including rice-eating areas ~~including~~ (ONR Report, 1972-75; Ramakrishnan,1980; Pratapkumar et al, 1982) the child is not offered all the foods consumed by the family. Protein-rich foods such as fish and dals are omitted and starchy foods such as the surplus starchy fluid from cooked rice or gruels made of sago, or arrowroot are either added or substituted. In regions such as Kerala, the problem is aggravated by the high proportion of tapioca consumed by the family and offered to the child. Fish, which is part of the family diet is often withheld from the child. Weaning foods such as ragi, coconut water and coconut milk which were commonly in use in the last generation are now used by very few families. Also, the trend is towards substitution of home made pazhinjee (fermented rice) for black coffee and appam which are more expensive so that the amount of food available is reduced. These patterns of child feeding become even worse if the child is prone to respiratory illness or fever in which case black coffee is considered a suitable drink, or diarrhoea, in which case starchy gruels are considered appropriate. The result is a malnourished child, who is also more prone to infections (Scrimshaw, Taylor and Gordon,1968; Chandra, 1976; Brown,1977) and diarrhoea, as discussed earlier.

This sequence of events results in severe clinically recognisable malnutrition in the form of marasmus or kwashiorkor.

Marasmus is generally considered to be the result of prolonged semistarvation where intake of both calories and protein is insufficient whereas kwashiorkor is attributed to a lack of protein relative to the intake of calories (Dengoa,1974; Gopalan, 1975; Gravesx, 1976; Sharda and Bhandari,1977; Pollitt and Thomson,1977). These two conditions, however,are thought to form the extremes of a continuum describing severe protein calorie malnutrition. More commonly, severely malnourished children exhibit signs of both conditions and lie at some point between these two extremes or alternate between the two (Scrimshaw and Behar, 1961). Marasmic kwashiorkor is sometimes used to describe a condition where signs of the two syndromes are seen in combination. Classification of these conditions follows the following definitions : marasmus:no edema, weight/age < 60%; kwashiorkor; edema, weight/age < 80% (but ⩾ 60%), marasmic kwashiorkor:edema, weight/age < 60%. (Food and nutrition Technology, 1973; Editorial, Lancet,1970).

Waterloo and Rutishauser (1974)believe that marasmus and kwashiorkor have different natural histories and they described two distinct growth patterns for the two. Nelson and associates (1969) have shown that in kwashiorkor there is a nearly normal growth pattern until around 6-8 months after which weight for age begins to decrease sharply. They are approximately 60-80% of the Boston growth norms by 14-18 months. In marasmus on the other hand, poor growth is reported from birth and large

deficits in weight for age are apparent during the first few months of life. Similar differences between the two syndromes have also been suggested by McLaren (1966). In studies carried out in this laboratory, the marasmic child is more likely than the kwashiorkor child to have been small-at-birth, to have been weaned from the breasts either too early or too late, and to have manifested growth retardation in infancy (Ramakrishnan, 1980).

Thus, the categorisation of kwashiorkor and marasmus as distinct conditions arising from the difference in the relative proportions of protein and calories in the diet may be an over simplification of the etiological situation (Whitehead,1969).

Marasmus is associated with dehydration, wasting of muscle and wrinkled skin. These children are irritable and tend to be cry babies. Kwashiorkor, on the other hand,is associated with edema, moon face, dermatitis, discolorâtion of hair and often eye symptoms. Extreme apathy is a common characteristic in kwashiorkor. Serum protein levels may be nearly normal in maramus but are reduced mainly due to reduced plasma albumin in kwashiorkor (Pollitt and Thomson, 1977). Plasma globulin levels may sometimes be higher than normal in PCM in response to infedtions (Gurson, 1972). Serum transferrin levels may be reduced in kwashiorkor (Pollitt and Thomson, 1977). In fact, transferrin levels have been found to cofrelate with albumin levels (Morgan and Peters, 1972).

However, with regard to many features, including biochemical status, clear cut differences between kwashiorkor and marasmus are not always found (Whitehead, 1969; Ramakrishnan, 1980; Pratapkumar et al, 1982).

In studies in this laboratory carried out in Trivandrum (ONR Report, 1972-75; Ramakrishnan, 1980), the biochemical status of kwashiorkor children was as expected and was characterized by low levels of blood hemoglobin, serum protein and albumin, a low A/G ratio and decreased activity of alkaline phosphatase. However, contrary to expectation, marasmic children showed a similar pattern except for the fact that they showed a greater range with some showing normal or near normal values with regard to serum total protein and albumins. Serum levels of calcium and phosphorus tended to be variable with quite a few children showing very low values.

Parallel studies, carried out by this laboratory at Madurai suggested differences with regard to biochemical status of malnourished children in Madurai and Trivandrum (Ramakrishnan, 1980; Pratapkumar et al, 1982). In Trivandrum, vitamin A deficiency was seldom found in association with protein energy malnutrition, whereas in Madurai, 55% of the severely malnourished children had mild to severe symptoms of vitamin A deficiency. In Madurai children with eye lesions had serum albumin levels similar to those without lesions but had lower

A/G ratios and a higher prevalence of intestinal infestation. In contrast to Trivandrum, in Madurai children suffering from marasmus has higher levels of serum protein and albumin than those suffering from marasmic kwashiorkor and kwashiorkor. The Madurai children also showed an increase in edema following rehabilitation in some cases. Serum levels of magnesium as well as phosphorus were higher in the children studied in Madurai.

The biochemical response to the conditions may be affected by several other factors, as pointed out by Whitehead (1969) and may include the restriction of calories on a low protein diet due to anorexia, diarrhoea, vomiting, etc. the proportion of calories provided by fat and carbohydrate and those provided by starch or sucrose, the presence of subsidiary dietary deficiencies of vitamins and minerals, the period of chronic malnutrition before the acute episode of clinical malnutrition, genetic factors e.g. the amount of jejunal lactase and other more subtle variations of more general importance, and age. As mentioned earlier, kwashiorkor usually occurs around 2 years of age and marasmus, before one year of age. However, this is not always the case. For instance, in Jamaica and Sudan the peak incidence of kwahiorkor is reported to be at 9-10 months of age, while in Guatemala, several cases are 4-5 years of age. (Whitehead, 1969). In one study in this country (Gupta and Mehta,1971), the peak incidence of marasmus is reported to be around 3 years of age

and of kwashiorkor, around 16 months. Studies in this laboratory (Pratapkumar, 1982) have found the peak incidence of marasmus and kwashiorkor to be respectively 27 and 33 months in Trivandrum and 20 and 29 months in Madurai in cases without eye lesions, and 31 and 32 months in cases with eye lesions. It is important in this context that the metabolic response to stress can be expected to differ at different ages, thus accounting for the differences in findings in different regions, and perhaps even for the differences reported for kwashiorkor and marasmus.

Although growth retardation is a concomitant of severe protein calorie malnutrition, about a quarter of the children affected may exhibit very severe growth retardation with body weights less than 30-40% of Boston norms as against the cut off point of 60%. In the studies carried out in Trivandrum and Madurai, more than half have body weights less than 50% (Rajalakshmi and Ramakrishnan, 1969(a); Ramakrishnan, 1980; Pratapkumar et al, 1982). Growth is resumed on refeeding and voluntary intakes may be as much as 200 Kcal or more per kg of body weight but the extent of catch up depends on several factors.

Studies on children who were treated for severe protein calorie malnutrition in early childhood and who were monitored upto 4-6 years thereafter indicate a steady but incomplete catchup as measured by physical stature (Stock and Smythe, 1963;

Chase and Martin,1970; Satyanarayan et al, 1981). A similar view has been expressed by Srikantia (1968) and Thomson (1968). Evans and associates (1971) report a complete catch-up after a rehabilitation period of 8-9 years.

Differences in the severity and age at onset, the nature of the diet used for immediate rehabilitation, the adequacy of the home diet after partial recovery are all likely to influence the outcome.

The early studies on the pathology of severe malnutrition were concerned with the effects of protein deficiency on the structure and function of organs and systems such as the liver. The nervous system was considered as one not affected by malnutrition because of the metabolic priority enjoyed by this system(e.g. NAS-NRC, 1959).

For many years, little attention was paid to the mental condition of malnourished children, although apathy, listlessnes, irritability and general misery were constant findings (Trowell et al,1954). Platt (1961) was the first to suggest that the malnourished child dies a central nervous death, emphasizing that even the central nervous system is not spared in severe protein-calorie malnutrition. These early observations were supported by a number of studies suggesting not only the adverse effects of malnutrition on behavioral development (Stock and Smythe, 1963; Monckeberg, 1968), but also their

irreversibility, as judged by such measures as deficits in intelligence, memory, perception, abstraction, verbal development, intersensory development, language and cognitive development (Cabak and Najdanvic, 1965; Cravioto and Robles, 1965; Pollitt and Granoff,1967; Champakam et al, 1968; Monckeberg, 1968; Birch et al, 1970; Chase and Martin, 1970; Yatkin and McLaren, 1970; Brockman and Ricciuti, 1971; Evans et al, 1971; Fisher et al,1972; Herzig et al, 1972; McLaren et al, 1973; DeLicardie and Cravioto, 1974; Cravioto et al, 1974; Cravioto and DeLicardie, 1975; Lloyd-still, 1976; Greene,1977; Brozek, 1979; Griesel,1980).

However, complete reversibility of the effects of early malnutrition on rehabilitation have also been reported (Richardson et al, 1973,1975; Rajalakshmi and Ramakrishnan, 1972; Winick et al, 1975; Clarke and Clarke, 1974; Tizard, 1974; Rajalakshmi, 1981).

Age at the onset of malnutrition was considered as a crucial factor for reversibility in the light of the hypothesis of vulnerable periods advanced by Dobbing (Dobbing and Sands, 1970; 1973; Dobbing,1974) and Winick and Noble (1965) and discussed earlier. However, the prevalence and severity of psychological deficits associated with severe malnutrition in young children do not seem to depend on the age at onset and admission, as had been found in studies in this laboratory (Ramakrishnan, 1980) and can be seen from those reviewed by

Pollitt and Thomson (1977). Further, children of the same age with comparable degrees of malnutrition are found to show a very wide variation in the extent, if any, of psychological retardation suggesting a complex interplay of nutritional and non-nutritional factors (Rajalakshmi and Ramakrishnan,1969(a), 1972; Winick et al, 1975; Ramakrishnan, 1980; Rajalakshmi,1981; Mundy-Castle, 1982; Ricciuti , 1982).

Another aspect now receiving attention is the importance of mother-child interactions and interpersonal relations in precipitating and reversing the effects of severe malnutrition (Pollitt and Wirtz, 1981; Ricciuti, 1982). These are found to influence and to be influenced by the nutritional state and its impact on the responsiveness to each other of the mother and the child (Denenberg et al, 1976; Chavez and Martinez, 1979; Denenberg, 1979; Levine, 1979; Strobel,1979). Appreciable differences may be found in this regard between different cultures. For instance, in the study of Stock and Smythe (1963), the undernourished group consisted of 62% illegitimate children and in 14% the fathers had absconded. The mothers appeared lazy and too apathetic to care for the well-being of the children. This situation contrasts remarkably with that prevailing in India where the children do not apparently lack affective care (Rajalakshmi and Ramakrishnan, 1972).

Further, as has been pointed out by several investigators, the relative importance of different factors may vary with the

age and developmental stage of the child (Cravioto and Robles, 1965; Cabak and Najdanvic, 1965; Monckeberg, 1968; Rajalakshmi, 1968; Rajalakshmi and Ramakrishnan, 1972; McLaren et al, 1973; DeLicardie and Cravioto, 1975; Rajalakshmi, 1981). In fact, the factors involved has been codified by Hebb (1960) and recently by Rajalakshmi (1981) (Table 3).

Adult physical stature and productivity

Chronic undernutrition during the growth period with varying degrees of impact on growth rate at different ages culminates in smaller physical stature as an adult. This results in a smaller lung capacity and vO_2 max which can be expected to influence work capacity (Astrand and Rodahl, 1970). This expectation is reinforced by the generally low productivity of the undernourished individual.

However, a geniune physiological adaptation to a smaller body size in relation to productivity is suggested (Guharay, 1972; Davies et al, 1976; Spurr et al, 1977; Barac Nieto et al, 1978). Guharay (1972) found Indian miners to use less energy for the same work than Polish miners, in both absolute terms and relative to BMR. Highly motivated sugar cane cutters are found to maintain reasonable rates of productivity (as judged by weight of the cane cut which determined the wages to be paid) by working at rates theoretically above expected capacity for sustained work. Their oxygen consumption is estimated to have been somewhat more than 40% of vO_2 max (Spurr et al,1977).

Table 3 : Classes of factors in behavioral development.*

Genetic	Physiological properties of the fertilized ovum.
Chemical, prenatal	Nutritive or toxic influence in the uterine environment.
Chemical, postnatal	Nutritive or toxic influence - food, water, oxygen, drugs etc.
Sensory, constant	Pre- and postnatal experience normally inevitable for all members of the species.
Sensory, variable	Experience that varies from one member of the species to another.
Traumatic	Physical-events tending to destroy cells; an "abnormal" class of events to which an animal might conceivably never be exposed, unlike above factors.

* From Hebb (1960).

In fact, despite the environmental heat stress of the tropics, Sudanese cane cutters maintained work rates well in excess of those recommended for most European factory workers (Davies et al, 1976). Thus, the small statured individual seems to display a remarkable capacity for work.

In fact, most of the hard work in adverse environments such as in sugar cane, cotton, tea, coffee and rubber plantations is done by workers who are of a smaller physical stature and poorer nutritional status than their employers. Hundred to two hundred years ago they were imported as bonded labourers or slaves.

The low productivity of an apparently undernourished individual may be not only and not mainly due to his current body size but due to continued inadequate intakes of food energy and other nutrients. It stands to reason that only the calories available over and above basal metabolic requirements can be expended for physical activity and their availability depends on the supply of other nutrients. In fact, productivity has been found to increase with the availability of better food supplies (Correan, 1975). For instance, the productivity of factory workers in Germany fell during and after World War II and rose to normal levels when food supplies became adequate (Keller and Kraut, 1962).

On the other hand, it has been reported onthebasis of a study conducted in East Java (Edmundson,1977, 1979) that the output of work is not affected by calorie intake. The authors suggest the operation of compensatory mechanisms such as higher levels of metabolic efficiency, lower basal metabolic rate, greater physical fitness and stronger incentives to work enabling those on a low energy diet to produce more work per unit energy intake than individuals with relatively high energy intakes (Nutr. Rev., 1980).

Incidentally, alterations in the rate of growth mightbe one of the mechanisms by which the organism adapts to dietary stress. Survival and maximum physical development probably have different nutritional requirements (Allen,1968). Pearson (1968) speculates that in countries where nutritional levels have been depressed for a long time, slower growth and smaller body size with a lower plane of nutritional requirements may have greater survival potential in a Darwinian sense, than rapid growth and a larger body size.

In view of the growing concefn about the effects of nutritional stress on growth and development, reproductive efficiency and productivity as adults, a number of studies have been carried out on experimental animals on these aspects mostly using the rat as the model in spite of differences in ontogenetic development (Table 4) and stress of reproductive performance (Table 5).

Table 4 : Critical phases in the developing brain.

Developmental features	Age at manifestation or completion	
	Man	Rat
Multiplication of neurons and astroglial cells	26th fetal week	Until birth
Multiplication of glial cells and microneurons, outgrowth of dendrites and axons and synaptic formation	26th fetal week to birth	birth to 10th day of age.
Continued synaptogenesis oligodendroglial proliferation; onset of myelination	Birth to 6th months	11-21 days
More myelination and further development.	After 6 months	After 21 days
Adult EEG pattons	10 years	14-16 days
Psychological development	Early twenties	-

* From Lindley,1974; Caley and Maxwell, 1968 and Svennerholm, 1974.

Table 5 : The nutritional stress of reproduction in rat and man[a].

	Rat	Man
Body weight (g) of mother	250	50000
period (in days) of		
Gestation	21	270
Lactation	21	180
Weight (g) of progeny		
at birth	4	3500
at weaning	400	7500
Weight of progeny as % of mother		
at birth	16	7
at weaning	160	15
Weight (g) gained by progeny per day		
Prenatal	1.9	13
Neonatal	17	22
Weight gained by progeny as % maternal weight		
Prenatal	0.76	0.026
Neonatal	6.8	0.044

a. Rajalakshmi and Ramakrishnan, 1969(b).

Undernutrition during the fetal period :

Undernutrition during the fetal and neonatal periods has been induced by feeding the mothers either a low protein diet (Cowley and Griesel, 1963; Barnes et al, 1966) or a normal diet in restricted amounts (Simonson et al, 1969). During the neonatal period increasing litter size has been used (Widdowson and McCance,1960). The net effect in all these cases appears to be a restricted supply of milk and therefore of nutrients to the progeny. The composition of the milk itself is not believed to be significantly altered. The effects of such restriction have been widely discussed and include low birth weight of progeny (Stewart, 1973; Hsueh et al, 1974; Rider and Simonson, 1974).,increased perinatal mortality (Roeder, 1973; Stewart, 1973), subsequent growth retardation (Widdowson and McCance, 1960; Chow,1964; Chow and Lee,1964; Hsueh et al, 1967, 1973, 1974; Lee and Chow, 1965; Blackwell et al, 1969; Rider and Simonson, 1973,1974), abnormalities of behavior (Lat et al, 1961; Guthrie and Brown, 1968; Barnes et al, 1970; Levitsky and Barnes,1970; Hsueh et al, 1973; Rider and Simonson,1973; Simonson et al, 1973) and an increased food intake per unit body weight (McCance and Widdowson, 1962; Blackwell et al, 1969; Barnes et al, 1973; Hsueh et al, 1974; Rider and Simonson, 1973).

The findings in animals contrast with the situation found in humans as discussed earlier, where the gestation performance of poor mothers on the whole is quite satisfactory. In this

connection, it is well to remember as pointed out earlier (Rajalakshmi, 1968; Rajalakshmi and Ramakrishnan, 1969(b)) that the stress of reproduction in the rat is of a much greater order than in man (Table 5) so that comparisons of studies on humans and animals should be made with caution.

The normal gestation performance of a larger proportion of poor women inspite of an apparently low plane of nutrition suggests the operation of adaptive mechanisms during pregnancy, This suggestion is supported by several animal studies. In one study (Spray, 1950) post-parturient rats weighed 75g more than virgin rats matched for age and initial weight with whom they were pairfed. To this must be added fetal weight gain. This gain, on the basis of carcass analysis, represented a gain in the maternal tissues of about 9g of protein, 21g of fat, 30 mg of calcium and 140 mg of phosphorus. Again, additional amounts must have accrued in the fetal tissues. Pregnant rats when pair fed with non-pregnant ones are found to retain more nitrogen (Rombaults et al, 1950; Naismith and Fears, 1971). In another study, pregnant rats fed a protein free diet from the 11th day of gestation produced viable progeny (Seegers, 1938). These observations are all the more remarkable because of the severe nutritional stress imposed by reproduction on rats and suggest the remarkable efficiency with which nutrients are utilized in the undernourished pregnant female.

According to many investigators, the growth of the animal subjected to fetal malnutrition is permanently impaired even when it is fed adequately after birth (Lee and Chow, 1965; Hsueh et al, 1974; Massaro et al, 1977; Rider and Simonson, 1973). This is reported to be accompanied by impairment of the efficiency of food utilization, which cannot be reversed by refeeding (Blackwell et al, 1969; Hsueh et al, 1974; Rider and Simonson, 1973). However, complete catch-up growth following fetal undernutrition has been observed in other studies (Stein et al, 1975).

Maternal protein deficiency induced during gestation has been found to delay the development of certain reflexes such as righting, negative geotaxis and cliff avoidance which appear soon after birth but other indices such as free fall righting, palmer grasp, vibrissae placing and responsiveness to auditory stimuli, which appear somewhat later remain unaffected (Rajalakshmi and Ramakrishnan, 1969(a); Rajalakshmi, 1975(b)).

Rats subjected to fetal growth retardation and subsequent rehabilitation are found to show an increased latency and decreased activity in the open field (Hsueh et al, 1974), a less developed locomotion pattern and self feeding behavior, increased conditioned emotional response (Rider and Simonson, 1974,1974) and increased shock avoidance (Smart et al, 1973).

Undernutrition during the suckling period

A 50% restriction of calories to mothers during lactation has been reported to result in permanent stunting of progeny which fail to achieve catch-up growth even after rehabilitation during the postweaning period (Chow, 1964; Chow and Lee, 1964; Hsueh et al, 1967, 1973, 1974; Lee and Chow, 1965; Blackwell et al, 1969; Rider and Simonson,1973, 1974). Similar findings have been made when undernutrition is induced by increasing litter size (Widdowson and McCance, 1960).

However, catch-up growth has been found in other studies. Knittle (1972) fed dams either a qualitatively adequate diet restricted to 50% of the amount consumed by controls fed ad lib or a 3% protein diet during lactation. No effects were apparent at weaning. However, when these pups were fed ad lib. after weaning, the deprived groups had smaller body weights than controls (83 and 74% respectively) after 2 weeks. Five weeks later, at the age of 10 weeks, the body weights of animals reared by calorie deprived mothers did not differ significantly from those of controls but those reared by protein deficient mothers continued to have smaller body weights.

Efficiency in the utilization of food for tissue production as measured by weight gain per g food intake, was lower in the progeny of undernourished mothers (McCance and Widdowson, 1962; Blackwell et al, 1969; Barnes et al, 1973; Rider and Simonson, 1973; Hsueh et al, 1974).

Animals subjected to neonatal undernutrition by manipulation of the maternal diet show behavioral aberrations such as heightened emotionality and excitability (Lat et al, 1961; Barnes et al, 1970; Levitsky and Barnes, 1970; Hsueh et al, 1973; Simonson et al, 1973). However, the learning ability of the progeny does not seem to be affected by neonatal undernutrition when this is followed by adequate nutrition during lactation (D'Amato, 1960; Barnes et al, 1966, 1968; Frankova and Barnes, 1968; Myslivecek, et al, 1968; Rajalakshmi, 1967; Rajalakshmi and Ramakrishnan 1969(a); Guthrie, 1968; Howard and Granoff,1968; Knittle, 1972; Frankova, 1981; Myslivecek, 1982).

Acceleration or retardation of growth of female rats in the neonatal period by manipulation of litter size has no effect on their reproductive performance as judged by number of pups born, survival at meaning and growth rate till weaning once sexual maturity is reached (Widdowson and McCance, 1960). However, attainment of sexual maturity is delayed (Widdowson et al, 1964). Lactation is found to be particularly good in the group fed restricted calories in early life and rehabilitated thereafter (Widdowson and Cowen, 1972). In dairy cattle, a mild degree of undernutrition beginning neonatally is found to improve reproductive performance in later life (Crichton et al, 1959; Reid et al, 1964; Allden, 1970; Ura, 1972).

Undernutrition during the postweaning period

Protein deficiency in the rat during the postweaning period has been found to be associated with deficits in performance on the Hebb Williams maze and the water maze as well as deficits in visual discrimination, reversal learning, activity in the open field and tasks involving neuromotor co-ordination such as crossing a gulf on two parallel bars or negotiating a small hole (Rajalakshmi et al, 1965; Rajalakshmi and Ramakrishnan, 1969(a), Polidora et al 1, 1966; Whimbley and Denenberg, 1967; Cowley and Griesel, 1966). Some of these effects do not seem to be reversible on rehabilitation on the basis of studies on rats and pigs (Levitsky and Barnes, 1972; Barnes et al, 1970). However, it has been shown that behavioral features in monkeys such as aversion to novel stimuli and preference for high protein diets, which developed following protein deprivation (Zimmerman et al, 1972) were eliminated after 180 days of nutritional rehabilitation (Pettus et al, 1974).

Rats fed low protein (6-8%) diets from weaning throughout life were found to show impaired reproductive performance as judged by a reduced litter size, smaller size of pups, increased neonatal mortality and behavioral disturbances of the progeny. (Stewart, 1973). In another study, the subsequent number of pups born was unaltered but their size was smaller (Turner, 1973). Delayed puberty, decreased fertility and ovulation rates have been reported (Widdowson and Cowen, 1972). However,

when the animals were rehabilitated before mating no impairment in reproductive performance was seen (Widdowson, 1967; Widdowson and Cowen, 1972). Radhakrishnan (1966) fed groups of rats protein free diets for 4 week intervals at different ages and found no impairment in reproductive performance unless depletion was effected just prior to mating, resulting in significantly lower body weights at the time of mating. On the other hand, female rats subjected to neonatal undernutrition by feeding the mothers a low protein diet for 42 days after weaning and rehabilitated showed impaired maternal behavior even after rehabilitation (Frankova, 1974) as judged by impaired efficiency and/or intensity with which the mother seeks her pups when separated. This, however, may not effect development of the pups if the pups are healthy and have access to the mother. More recently, Galler and Propert (1981(a)) have reported the persistence of an increase in active nursing-related behaviors in rats that were rehabilitated following prolonged intergenerational malnutrition.

Further, when control pups were nursed by rehabilitated mothers and rehabilitated pups by control mothers (Galler and Propert, 1981(b)) it was found that maternal factors were dominant in determining the amount of active nursing and that pups factors modified the maternal influence on other lactation oriented behaviors.

Effects of Undernutrition on Metabolism

It is well known that ATP forms the major source of energy in the body although it forms quantitatively a minor component because of the fact that it is constantly synthesized and degraded. The energy needed for ATP synthesis is derived from the oxidation of selected nutrients such as fatty acids, carbohydrates, glycerol and appropriate carbon derivatives of aminoacids, namely, acetate or intermediates of the TCA cycle. The total energy requirement of the body is made up of two major components, namely, basal metabolism and the activity increment.

The former represents the energy consumption of the body when free from overt physical and mental work although the vital organs continue to be active even in the so called resting state. The ability of the animal to survive shortages infood supply implies a reduction in the requirements of one or more of these components during undernutrition.

Data reported by Benedict (1915) on a fasting subject suggest a reduction by 28% in BMR with 31 days of fasting. In subsequent studies (Benedict, 1935) on 25 young men, subjected to semi-starvation whose calorie intake was reduced from a range of 3200-3600 to 1400 Kcals/day, the subjects lost 12% of their initial body weight in 3-10 weeks. Thereafter, they could maintain this weight on a diet providing 1950 Kcals/day. Their BMR was found to be reduced by 18%, but

no appreciable decrease in activity increment as measured by pedometer records was found. In another study, Taylor and Keys (1950) found that with 55% calorie restriction (i.e. from 3500 to about 1500 Kcalories) calorie equilibrium was established at 75% of original body weight namely, 50-55 kg. At this point, reached in 24 weeks, BMR was reduced by 39% on an average and expenditure in muscular activity diminished by 71 %. Shrinkage in metabolizing mass of tissue was believed to account for 65% of the reduction in BMR and a decrease in intensity of metabolism, for 35%.

A reduction in the BMR of growing and adult animals, subjected to varying degrees of undernutrition has been reported in a number of studies (Stewart,1916; Horst et al, 1934; Jackson, 1937; McCance and Mount, 1950). On rehabilitation and resumption of normal growth, BMR has been found to rise to normal values (Horst et al, 1934),food intake being more than that of non-deprived controls (Carobi et al, 1972). A stimulatory effect on growth has also been observed so that the undernourished young animals were found to weigh even more than the controls when restriction was moderate but not when it was severe (Quimby, 1948).

Effects on life expectancy

A few studies on animals have also been concerned with the effects of early or continued undernutrition on long term effects such as longevity. Different techniques have been used to induce undernutrition experimentally, such as feeding restricted amounts of stock diet (McKay et al, 1935; Berg and Simms, 1961; Ross, 1961; Nolen, 1970, 1972; Kahn, 1972), meal feeding (one meal per day) of a qualitatively adequate diet (Levielle, 1972), low protein diets in restricted or ad lib feeding schedules (McKay et al, 1941; Miller and Payne, 1958; Ross et al, 1976) and intermittent starvation (Carlson and Hoelzel, 1946).

McKay and Coworkers (1935) found young animals subjected to almost complete growth arrest by a period of severe food restriction to live longer than controls fed ad libitum. Similar observations have been made on adult animals fed 54% of ad lib intakes on an 8% protein diet (935 days of life as compared to 730 days in controls) (Ross, 1961) and animals fed 54% of ad lib intakes on a stock diet (1000 days of life as compared to 800 days in controls Berg and Simms, 1961). The growth rates in the

restricted and control groups in the two studies were0.9g and 5.0 g per day and 2.9 g and 5.0g per day. In another study (Levielle, 1972), young growing animals had access to food only for a 2h period daily, restricting their food intake by 26%. These animals lived on an average 15% longer. Similarly, Nolen (1972) found an increased life span of animals fed 60% of ad lib intakes from 12 weeks of life (927 days of life compared to 706 days in controls).

Thus, it is apparent that the life expectancy of adult animals can be increased by dietary manipulations. However, experimental data are not in agreement regarding the effectiveness of various methods of imposing dietary restriction. In addition, Kepec (1928) and David et al (1971) have shown that dietary restriction in adult Drosophila was ineffective. Similarly, Barrows and Roeder (1965) did not demonstrate an increase in life span in 13 or 19 month old female adult rats whose dietary intake was reduced by 50%. Thus, as pointed out by Barrows and Kakkonen (1981) further studies must be carried out to define effective ways of consistently increasing the life span of adult organisms.

The observation of the beneficial effects of dietary restriction on longevity in the adult rats, may be of considerable importance for man. According to the Society of Actuaries in America, individuals whose weights are lower than average have a greater life expectancy (Payne, 1972). In this connection, as Comfort (1969) has pointed out, a critical need exists for controlled trials with human volunteers. According to Prof. Oomen (personal discussion with Dr. Rajalakshmi) young inmates of concentration camps during World War II, now in their seventies are on the whole healthier, more active and have maintained their adult weights more successfully than their age peers who were fortunate or unfortunate enough to miss this experiance.

Consequences of Overnutrition

Except in man and some hybernating and domesticated animals, the appetite mechanism regulates food intake with such precision that obesity as a consequence of overnutrition is rare. The hypothalamus regulates the appetite for food intake through the mechanism of interaction between a 'feeding centre' and a 'satiety centre'. It is believed that the feeding centre is chronically active and its activity is governed by the activity in the satiety centre. Activity in the satiety centre is in turn governed in part by the level of glucose utilization with in certain cells in the satiety

centre, called glucostats, and in part by the size of body fat depots sensed either by neural or hormonal signals (Lipostatic control). The net effect is adjustment of food intake to the point where calorie intake balances energy expenditures with the result that body weight is maintained (Ganong,1977).

However, evenwhen body weights are maintained, a one-to-one correlation between the day-to-day energy expenditure and intake is not generally found although over a reasonable interval of a week or a fortnight such a correlation is found, suggesting the operation of a simple banking and credit system the mechanism for which is yet to be elucidated. The existence of such a mechanism is supported by several studies (Widdowson, 1951; Fox, 1953; Edholm et al, 1955; Aneegers, 1973). For example, African farmers are found to recover their nutritional debts when the new harvest comes in (Fox, 1953; Aneeger, 1973). Germans who were obliged to restrict their food intakes in 1945-46 ate enough food to provide themselves with 6000 Kcals/day for weeks on end when they were given the chance till they reached their weights prior to food deprivation (Widdowson, 1951). Even in obese people, such a mechanism adjusted to a new homeostatic point for body weight seems to operate as obese people put on strict dieting tend to regain their original weight but no more as soon as they give up dieting. The mechanism of this

belated adjustment of the intake of food to correct for an expenditure of energy incurred days, weeks or months earlier seems difficult to explain by any theory which relates the sensations of appetite and hunger solely to the level of some metabolite such as glucose in the plasma or even in some specialized cellular sense organ (Mayer, Vitale and Bates, 1951) and suggests the operation of both, long term and short term regulation. The importance of such a regulation from the biological point of view is obvious as in nature animals have to adjust to intermittent food deprivation by feasting when food is available and fasting when it is not.

When the regulation of appetite is efficient, indulgence in one meal is followed by reduced intake at a subsequent meal but this often fails to happen in many individuals because of culturally established patterns of food consumption and food preferences, resulting in accumulation of excess calories in the form of adipose tissue, and, consequently obesity. A small disturbance in the overall equilibrium between energy intake and expenditure by as little as 5% could theoretically result ina gradual accumulation of adipose tissue at the rate of 6 kg per year.

Although obesity is more prevalent in maturity, it may begin even in infancy and appears to be associated with the early introduction of energy rich solid foods and conventional

commercial formulas (Nut, Rev., 1977(c), Fomon et al, 1977) and is relatively rare in breast-fed infants (Fomon et al, 1977). Obesity is found frequently in young children who are coaxed to eat generously of protein rich and energy rich foods and discouraged from vigorous physical activity by the parents.

In adolescents obesity is more characteristically associated with inactivity than with intakes much in excess of normal (Johnson et al, 1956; Stefanik et al, 1959).

In adults, the decrease in activity levels and in basal metabolism with age is not always accompanied by a concomitant decrease in food intake although such a reduction may follow in due course. With a small positive balance for a prolonged period of time the damage is done before equilibrium is eventually reached (Mayer et al, 1956).

Though it would seem logical to attribute obesity to food intakes in excess of requirement, this does not seem to be the only factor involved. Evidence suggests that to some degree obesity may be genetically related (Schlenker et al, 1973). This view is consistent with the higher prevalence of obesity in children born of obese parents (Davenport, 1922; Gurney, 1936; Angel, 1949), although this could be due to the fact that such children are raised on diets conducive to obesity. It has been observed that during the first year of life the number of adipose cells in individual children varies by as

much as 100% and those with a greater number of adipocytes are more prone to developing obesity (Hirsch and Knittle, 1970). In a cross-sectional study of children ranging from pre-school age to adolescence, Knittle (1969) observed that obese children have a greater number of fat cells compared to age matched non-obese. It is to be noted that birth weights were found to be normal for people with childhood onset obesity (Gscheiden and Roderuck, 1960). A genetic factor has been implicated in the eventual number of adipocytes formed in an individual (Schlenker et al, 1973). On the other hand, contrary to general belief, evidence is also available that the increase in adipocyte number due to overfeeding in early life does not predispose to obesity in later life (Hausberger, 1981). This view is borne out by other reports which suggest no relation between early obesity and later proneness to the same (Nutr. Rev., 1977(b); 1978; Poskilt and Cole, 1977). Some of the other factors leading to obesity are body types (Seltzer and Mayer, 1964, 1965, 1969), physical inactivity (Bullen et al, 1964; Dorris and Stunkand, 1957) and psychological factors (Bruch, 1956; 1957; Rome, 1960). Preferred foods are used not only as rewards but also to relieve stress such as physical injury in children. Many individuals seem to persist in seeking satisfaction in eating whenever they are bored or stressed (Bruch, 1957).

In the case of nutrients such as minerals and vitamins, intakes in excess of requirements are taken care of by decreased absorption and increased excretion although there are physiological limits to this capacity. This is also true of nitrogenous components of protein. But in the case of carbon compounds which enter the oxidative pathway and provide energy, no such mechanism exists for the disposal of unwanted nutrients and homeostasis is mainly achieved by regulation of intakes. When this regulation fails even slightly, the result is an imbalance between metabolic supply and demand of food energy, resulting in obesity. No increase in BMR is evident following luxus consumption (Means, 1916; Gulick, 1922; Mitchell et al, 1932) in contrast to the increased turnover found in the case of nutrients such as protein (McFarlane, 1963; Garlick et al, 1975; Golden et al, 1977). Some reports have been made regarding increases in post prandial thermogenesis with surfeit feeding (Stock, 1966; Swindells,1972) but these have been questioned (Davidson et al, 1975). The fact remains that the failure of the body to respond in other ways to excess energy is highly visible in the form of unwanted adipose tissue. In fact, obesity may aggravate the energy imbalance if it results in reduced physical activity as it normally does.

Apart from posing a psychological problem in Societies where fat people are regarded as unattractive (although in certain cultures, obesity indicating affluence is prestigious

(De Garine, 1982), obesity is reported to be associated with several serious disorders including increased mortality, hypertension, carbohydrate intolerance leading to diabetes, and increased levels of blood lipids and uric acid associated with increased incidence of gout, cardiovascular disease, arthritis, and gall bladder disease (Nutr.Rev., 1976).

However, complex the etiological factors leading to obesity may be, it is generally agreed that obesity is associated with life styles characterised by luxus consumption, overall reduction in physical activity and absence of periodic fasting practiced in nature and by many ancient cultures. It is also found that it can be prevented and controlled by dietary means and altered life styles including changes in diet patterns. In the same ethnic group, obesity is more prevalent in the affluent with more access to food, as in poor countries; or in the poor, with greater access to cheaper high calorie foods and less opportunity for vigorous physical activity such as swimming or playing tennis, in affluent countries (Davidson et al, 1975).

The serious consequences of overnutrition in affluent populations have led to the formulation of dietary goals for the United States (Select Committee on Nutrition and Human Needs, 1977 [illegible]) which recommended that Americans should eat less fat, particularly saturated fat, less cholesterol, less

sugar and less salt and more fruits, vegetables, gain products and unsaturated oils thereby reducing fat consumption with a simultaneous increase in carbohydrates and the proportion of complex carbohydrates at the cost of sugar.

The successful lactation performance of poor women as compared to frequent lactation failure in the upper class and the practice in dairy farming of underfeeding dairy calves so as to promote their subsequent lactation efficiency (Allden, 1970) raises questions regarding relation between growth in early life, adult weight and obesity and lactation performance. This aspect has received little attention in studies using animal models except for the studies on dairy animals expected to perform artificial feats of lactation.

Specific Nutritional Deficiencies

Diets consumed by the poor are inadequate not only in calories but also in other nutrients, particularly protein, calcium, vitamin A and vitamin C.

Protein

Common diets in India contain 8 - 10% protein calories. However, the protein is of poor quality and in about 25-30% of the individuals serum levels of protein and albumin are deficient according to ICNND norms (Rajalakshmi, 1975) Symptoms of protein deficiency are often evident in children but seldom in adults.

As mentioned earlier, in young children, severe protein deficiency manifests itself as kwashiorkor associated with biochemical, biophysical, anatomical and psychological changes. Biochemical changes include low values for plasma proteins, specially albumin, (Autret and Behar, 1954), an imbalance between essential and non-essential aminoacids, reduced secretions of enzymes and edema appearing in various areas of the body (Autret and Behar, 1954; Waterloo and Alleyne, 1971; Pereira and Begum, 1974). Biophysical changes include EEG abnormalities, hypothermia (Botha-Antoun et al, 1968; Jelliffe, 1965), alterations in the mucous ~~x~~ membranes and depigmentation of the skin (Autret and Behar, 1954). Anatomical changes which include skeletal, muscular, glandular and neurological change (Marcondes et al, 1973), hypotonia and poorly developed motor skills (Pollitt and Thomson, 1977) are almost always present.

As discussed earlier, the apathy, mental arrest and poor psychological status of the malnourished child observed by pioneers such as Platt (1961), Carothers and Dean have led to the widespread recognition that severe malnutrition carries with it the risk of irreversible mental retardation although the role of non-nutritional factors is receiving increasing recognition.

Magendie's pioneering observations on the need of protein for survival were followed by the studies of Voit and Atwater

who concluded on the basis of customary intakes of well-nourished individuals that adult man should consume approximately 120g. of protein daily. This amount was demonstrated to be an exaggeration by Chittenden and his colleagues (Chittenden, 1907) who found themselves able to thrive and increase their functional efficiency, physical condition and feeling of well-being by cutting down their protein intakes to 40 g.

The amounts consumed by individuals in balance studies have varied widely, raising questions about the validity of balance studies. Even within a group relatively homogeneous with regard to body build, food intake and life style the amount needed for balance may vary appreciably, raising a question regarding the effects of prior dietary history and errors in the balance technique itself (Hegsted, 1978).

Part of the confusion could well be due to the fact that when individuals living habitually on high protein diets are switched to low protein diets, they may manifest negative nitrogen balance in the beginning but reach equilibrium later (Yoshimura, 1961).

Adaptation to low intakes of protein has been suggested by studies on rats (Jackson, 1937; Khan and Bender, 1974) and is suggested by the fact that in human population groups protein intakes may vary from 20-30g in New Guinea to more

than 100g in Eskimoes. In many groups the intakes are even less than conservative estimates.

It would be logical to expect that adaptation to low protein diets is mediated at least partially, through altered rates of tissue protein anabolism and/or catabolism. As the liver is the site of urea formation from amino acids, it has a key role in the adaptive processes. An immediate consequence of decreased protein intake is a decrease in the synthesis of body proteins followed by a more gradual decrease in catabolic rate. As a consequence, serum protein levels are reduced initially but maintained thereafter (Mcfarlane, 1963; Garlick et al, 1975; Golden et al, 1977; Waterlow et al, 1977).

The reduced rates of synthesis and catabolism are borne out by the observation that when a labelled amino acid is injected intraperitoneally in protein and/or calorie deficient animals, not only the rate of incorporation of label in liver protein (Simon et al, 1975) but also the rate of loss of label are decreased (Narasinga Rao and Radhakrishnan, 1966; Goto and Kametaka, 1974; Milenkovic et al, 1974; Nettleton and Hegsted, 1974a,b; Peng et al, 1974; NIN Annual Report, 1976).

The protein value of a diet depends not only on the amount of protein but also on its availability which in turn is determined by digestibility and amino acid composition, as deficits in essential amino acids can limit the value of a

protein for synthesis of body compounds derived from amino acids. The amount of protein required is often stated in terms of a standard protein such as egg albumin, which is efficiently utilized. The amount of test protein required is sought to be determined in terms of its biological availability, the assessment of which is made by several criteria including the comparison of its amino acid composition with that of either a standard protein or a standard pattern formulated on the basis of studies on essential amino acid requirements in different groups. The criteria used in these studies vary with regard to the amount and type of nitrogen source, composition of the essential amino acid mixture used, the proportions of essential and non-essential nitrogen, the period of observation, the graded amounts of the test amino acid used to decide the point of equilibrium and the criteria used for nitrogen balance (Rose, 1949, 1957; Holt et al, 1960; Leverton, 1959; Swendseid et al, 1956, 1959) and are discussed by Irvin and Hegsted (1971).

However, a consensus emerges that lysine is the first limiting amino acid in most cereals and is likely to be deficient in poor diets based on cereals providing little or no meat. Fortification of rice or wheat (the most common staple cereals of India) with lysine has been found to increase net protein utilization (NPU) in young rats and has been advocated as a solution for bridging the protein gap in cereal based diets (Rosenberg et al, 1954; Westerman et al, 1957(a),(b);

Scrimshaw et al, 1958; Bressani et al, 1958; FAO, 1965; United Nations, 1967).

It is well known that lysine requirement is greater for the young animal than the adult animal (McLaughlan, 1972). For instance, differences in biological value between lysine rich and lysine poor foods such as egg albumin and wheat gluten are much greater (97 and 40 respectively) in young animals than in adult animals(94 and 65 respectively)(Munro, 1964). One would therefore, expect lysine requirement to vary with growth rate. This aspect was ignored by the previous recommendations of the FAO (FAO, 1965) but the recent recommendations of the FAO committee (1973) take into account the probability of age differences with regard to amino acid requirements. However, their recommendations of 0.32, 0.47 and 0.14 g. lysine/g N intake for infants, children and adults in this regard presents a major anomally in that the amino acid requirement for school children is suggested to be higher than that for infants although the latter have a higher growth rate. The higher recommendation for school boys is apparently based solely on the study of Nakagawa et al (1961) which suffers from a number of limitations, a major one being that the step wise increments in the amounts of lysine used for determining the point of nitrogen equilibrium are too far apart (namely 2.4, 1.6, 1.2 and 0g. in a diet providing 12g. of nitrogen). In this study more graded doses may have given a different picture.

Adaptive mechanisms which conserve amino acids when they are in short supply have been reported (Yamashita and Ashida, 1969; Said et al, 1970,1974). Absence of specific amino acid deficiencies on diets deficient in methionine, cystine, tryptophan and histidine have been reported in adult Indian groups habitually consuming these diets (Chitre et al, 1976). The degree of adaptation varies for different essential amino acids and appears to be maximal in animals fed a lysine free diet (Said and Hegsted, 1970; Said et al, 1974). The adaptive response represents modifications in the catabolic rate of lysine (Chu and Hegsted, 1976), its conservation in the liver as a result of high reutilization (Garlick et al, 1974), modifications of the urea cycle enzymes in the liver (Das and Waterlow, 1974), or reduction in the synthesis of all liver proteins (Ganfield and Chytil, 1978).

High protein diets may not only be unnecessary but also harmful as the waste products of protein metabolism impose a stress in metabolism as pointed out by Chittenden (1907). Such diets place an obvious load on the kidney and increase water requirements (Hoag et al, 1927; Hodes, 1936; Gamble, 1946,1947; Calloway, 1960). In fact, growth ceases in rats when protein content exceeds critical amounts (Allison, 1964).

High protein diets also make for increased requirements of calcium (Johnson et al, 1970; Anand and Linkswiler, 1974; Linkswiler et al, 1974). While dietary protein enhances

calcium absorption upto a certain point (McCance et al, 1942; Hegsted et al, 1952; Wasserman et al, 1956; Walker and Linkswiler, 1972), it also results in its increased urinary excretion (Pitmann and Kunerth, 1939; Margen and Calloway, 1968; Margen et al, 1970; Chu et al, 1971; Walker and Linkswiler, 1972; Margen et al, 1974). Linkswiler and associates attribute the increase in urinary calcium to both, increased absorption and increased bone resorption. This is probably because high meat diets which are usually high protein diets are also high in phosphorous. This may cause an imbalance in the calcium: phosphorous ratio if the diet is also not high in calcium. This results in greater resorption of calcium from the bone (Draper et al, 1972; Anderson and Draper, 1972; Krishnahara and Draper, 1972; Laflamme and Jowsey, 1972; Bell et al, 1975). The adverse effects of high phosphorous on calcium utilization is suggested by the observation of Whiting and Draper (1981) who found that when the Ca:P equilibrium was maintained on high protein and high phosphorous diets by appropriate additions of calcium, bone loss was prevented.

A clear cut effect of high protein diets in increasing nutritional requirements is demonstrated inthe case of vitamin A. Inspite of the fact that the absorption, storage and retrieval of vitamin A are all reported to be adversely affected in protein deficiency (Rechcigl et al, 1962) animals fed a vitamin A free, high protein diet develop deficiency

symptoms much faster than those fed low protein diets and their liver stores are also more rapidly depleted (McLaren, 1970; Rajalakshmi and Ramakrishnan, 1978).

Not long ago, nutritionists were advocating not only high protein diets but also those rich in animal protein because of the consideration that their biological utilization is higher. But it is now realized that foods such as mutton and beef are rich not only in saturated fats but also methionine and other lipogenic amino acids both of which are conducive to the elevation of cholesterol levels in serum, which, in turn, have been linked with arteriosclerosis and atherosclerosis. Epidemiological data show that the association between animal protein in the diet and mortality from coronary heart disease is as strong as that between dietary fat and heart disease (Yudkin, 1957; Yerushalmy and Hilleboe, 1957; Connor and Connor, 1972). American vegetarians are known to have lower plasma lipid levels than other segments of the American population (Hardinge and Stare, 1954; Sacks et al, 1975).

The level of plasma cholesterol is found to be reduced in man by substituting plant protein for animal protein in the diet (Carroll and Hamilton, 1975; Sirtori et al, 1977) a finding consistent with differences between the two particularly with regard to amino acids such as methionine (Huff et al, 1977).

Calcium

Calcium is another nutrient which has come in for a fair amount of discussion and re-evaluation. Earlier thinking about this was governed by the high prevalence of rickets, osteomalacia and growth retardation in certain areas of the world. The studies carried out by Mellanby (1926,1949) pointed to the adverse effects of phytate on bone calcification. Phytate has been found to interfere in the absorption of calcium in animals (Harrison and Mellanby, 1937; McCance and Widdowson, 1942(a),(b) and man (Hoff-Jorgensen et al, 1946).

However, many studies negate the effects of phytate on mineral absorption. Such studies include those on Indian boys and adults (Basu et al, 1939; Wilson and Widdowson, 1942), Ceylonese children (Nicolls and Nimalasuriya, 1939), Bantu boys and adults (Henderson and Kelley, 1929-1930;Walker et al, 1948) and the French obliged to consume a high phytate diet during World War II (Paris letter, 1942,1946).

As phytate is present in appreciable amounts in cereal based diets, concern continues about the calcium status of population groups subsisting largely on cereals and millets without adequate intakes of calcium (Ford et al, 1972; Berlyne et al, 1973; Reinhold et al, 1973).

This concern is partly because of the very marked effects of phytate on zinc status inthe middle East resulting in

hypogonadal & dwarfism in the rural areas of Iran (Prasad et al, 1961).

Young children require more calcium in proportion to body weight than adults in order to meet the requirement of the growing skeleton. According to Mitchell (1964) daily calcium accretions inthe skeleton are of the order of 163 mg for infants, 70-110 mg for young children upto 5 years of age, 140-160 mg for older children upto 10 years of age and 65-190 mg for adolescents. The FAO recommended allowance (FAO, 1962) for the 1-9 years old is 400-500 mg and for the 10-15 year old is 600-700 mg. Intakes of poor children in this country are of the order of 250-300 mg and 300-350 mg respectively (Rajalakshmi, 1974) suggesting deficits of 150-200 mg and 300-350 mg according to these recommendations and of a smaller order of 50-100 mg in other age groups.

The role of vitamin D, phosphorous and the Ca:P ratio in the utilization of dietary calcium is well known. Studies in this laboratory (Rajalakshmi et al, 1977; Rajalakshmi, 1980(b)) have shown retardation of skeletal growth to some extent in school boys is attributable mainly to a deficient supply of calcium and to a greater extent in young children attributable to lack of vitamin D. Some degree of deficient mineralization has been found in the middle aged.

If food or protein restriction in early life promotes longevity, presumably by affecting cellular turnover and cell loss (Barrows and Kakkonen, 1981), questions arise regarding the impact of similar variations with regard to other nutrients in early life on subsequent metabolic performance. The question is of particular importance for nutrients such as bone minerals in view of the major problems posed by osteoporosis in later life.

In this connection Sherman and Booher (1931) and Henry and Kon (1953) have reported that animals on low calcium diets have less calcium per unit body weight than well nourished controls, for a considerable part of their lives, but ultimately their bodies acquire the usual adult proportion of calcium, indicating slower skeletal growth but no permanent drawbacks. However, in the opinion of Widdowson and Dickerson (1960), further experimental evidence is required to make any categorical statement in this regard.

The problem is complicated by the fact that the etiological factors resulting in malnutrition and growth retardation in early life may differ in their consequences after middle age. For instance, while high phosphorous diets are implicated in the etiology of senile osteoporosis inadequate supply of phosphorus either because of a poor dietary supply or lack of vitamins may result in skeletal retardation and rickets (Leitch, 1964).

In studies reviewed by Hess (1929), as early as 1921, McCollum and associates (Shipley et al, 1921) suggested that under certain conditions phosphate may also be a limiting factor in the calcification process. Several recent observations in both children and experimental animals tend to support this view (Bronner, 1976). The beneficial effects of phosphate supplementation have been reported in patients suffering from fractures and in infantile rickets arising from phosphate depletion (Lapatsanis et al, 1976). The phosphorus requirements of young children in relation to protein and calcium requirements are estimated to be greater than those of adults (Mitchell, 1962, 1964), a fact consistent with the higher levels of serum phosphorus in younger children (Hegsted, 1973) and animals (Dutcher et al, 1925) as compared to adults.

The etiology of osteoporosis appears to be complex, involving dietary, hormonal and genetic factors. Rather interestingly, it has been found that osteoporosis is about ten times more prevalent among the Whites in S. Africa than among the native Bantus even though the diet of the former contains more calcium than that of the latter (Walker et al, 1971). However, in studies on the same ethnic groups with differing calcium intakes, osteoporosis is often found to be more prevalent in groups subsisting on low intakes (Gershon-Cohen, 1964; Jowsey et al, 1964; Heaney et al, 1978; Matkovic et al, 1979; Nordin et al, 1979). Similar observations have been

made in this laboratory (Shah, unpublished). Beneficial effects of calcium supplementation on bone density have also been reported in osteoporotic females with an average age of 70 years (Lee et al, 1981).

The observations on Bantu women (Walker et al, 1971) and the studies of Henry and Kon (1953) underline the need for more detailed investigations on the impact of variations in calcium intakes onbone status at different ages.

Iron

Iron is yet another nutrient the supply and/or utilization of which poses problems. Iron deficiency anemia is widespread in all age groups and not all that uncommon in the affluent west (Finch and Monsen, 1972; Rajalakshmi, 1975). The prevalence rates are higher in women and children than in men (Widdowson and McCance, 1942; Hoglund, 1969; Finch and Monsen,1972; Rajalakshmi, 1975) and higher in rural areas with poor facilities than in urban areas because of the greater incidence of inteatinal parasite infdstation (Rajalakshmi, 1975; Wadsworth, 1975). Poor stores at birth combined with a poor supply and utilization may be the major factors involved in the case of young children (Bhatt et al,1969).

Vitamin A

The supply of vitamin A may be precarious in most Indian diets, specially in interior regions where rice is the staple

and fish are not consumed. In these regions, symptoms such as conjunctival and corneal xerosis are found in all age groups although an increased prevalence with age is found (Srikantia, 1975, 1978; Prahlad Rao, 1982). However, although young children are less prone to cornealxerosis, they show a greater prevalence of severe keratomalacia following periods of severe food deprivation and infections (McLaren,1956; Gopalan et al, 1960) and the consequences of this could be most tragic as severe keratomalacia often culminates in partial or total blindness. Preformed vitamin A is found only in animal foods so that most poor people are obliged to depend largely on its major precursor, β-carotene, present in many vegetables and fruits and some food grains although the content and utilization vary widely.

Much uncertainty prevails about the efficiency with which carotene is utilized. The FAO committee (1967) assumes that 6 ug of carotene are needed to derive 1 µg of vitamin A. This is supported by some of the findings reviewed by Moore (1957), ARC (1967) and NRC (1971). These figures are presumably arrived at from the results of studies conducted on Western subjects who usually get a fair amount of the preformed vitamin in their diets. Moreover, in many of these studies (e.g. Kemmerrer and Fraps, 1938) sources such as alfaalfa which may not be the best sources of utilizable carotene are used. Further, several studies suggest a much higher utilization

in widely different species such as pigs and chicks. Table 6 shows the conversion ratio arrived at by different investigators.

In studies in this laboratory (Rajalakshmi et al,1974(b), 1975; Rajalakshmi and Ramakrishnan, 1978) a normal vitamin A status could be maintained on 30g leafy vegetable in young children and 50g in older children. Assuming 33% cooking losses (Chari, 1967; Sail, 1970; Rajalakshmi et al, 1975), these would provide about 800 ug and 1400 µg of carotene respectively as against the recommended amounts of 200 µg and 600 ug of vitamin A. In adult men, the response of serum vitamin A to 50g leafy vegetable providing about 650 ug of carotene was found to compare well with that to 600 µg vitamin A as palmitate. In contrast to the FAO ratio of six to one these studies suggest that less than 4 mg carotene may yield 1 mg vitamin A. Similar observations in young children have been made by other investigators at Vellore (Pereira and Begum, 1968) and supported by Pirie (1975).

The differences in conversion ratio in the different studies may be due to differences in test conditions. Dietary fat aids carotene utilization according to some reports (Kemmerer and Fraps, 1938; De, 1937) but not others (Wilson et al, 1936; Kemmerer and Fraps, 1945; Pirie, 1975; Rajalakshmi et al, 1975). The latter observation may be due to the small

Table 6 : Variability in conversion ratios of Carotene to Vitamin A.

Reference	Approximate conversion	Species	Carotene source	Vitamin A source	Level	Criteria used
ARC (1963, 1965, 1967)	5 : 1	Poultry, Ruminants, Pigs				
Blaxter et al (1946)	8 : 1	Cattle	Pure β-Carotene	Retinol	50-500 µg/kg live weight	Liver vitamin A
Branion and Emslie (1966)	2-6 : 1	Poultry				
"	12 : 1	Fox				
"	4-10: 1	Domestic animals, Man				
Brandd et al (1941)	6 : 1	Pigs	Pure β-Carotene	Retinol and Retinyl ester		Growth
Faruque and Walker (1970(b))	5-25 : 1	Milk fed lamb	Pure β-carotene	Retinyl palmitate as retinol		Serum protein
Jones et al (1962)	6 : 1	Cattle	Pure β-Carotene	Retinol	50-500 µg/kg live weight	Liver vitamin A
Marusich and Bauernfield (1963)	2 : 1	Poultry	Dry stabilized gelatin beadlet preparations		660 µg/kg dry weight	Livestock

contd...

Table 6 : contd.

Reference	Approximate conversion	Species	Carotene source	Vitamin A source	Level	Criteria used
Marusich and Bauernfield (1963)	6 : 1	Poultry	Dry stabilized gelatin beadlet preparations		5x660 µg/kg dry weight	Livestock
"	10 : 1	"	"		10x660 µg/kg dry weight	"
NRC	8 : 1	Sheep, Cattle Swine Poultry				
Parisch et al (1963)	2 : 1	Poultry			660 µg	
Rajalakshmi (1974)	3 : 1	Adult Men (accustomed to diets based mainly on plant foods)	Leafy vegetables	Palmitate in oil	1800 µg	Serum Carotene and Vitamin A
Rajalakshmi et al (1975)	3 : 1	Weanling albino rats	Pure-β-Carotene or leafy vegetables	Vitamin A acetate	300 µg	Serum and liver vitamin A
Ullrey (1972)	12.5 : 1	Pigs	Maize			

amount of fat associated by food grains when consumed as whole grains.

A positive correlation between dietary protein and β-carotene utilization has been suggested by several investigators (Arnrich and Peterson, 1959; Berger et al, 1962; Mathew and Beaton, 1963; Deshmukh and Ganguly, 1964; Hillers and Arnrich, 1964; Nirmala et al, 1966(b); Kamath and Arnrich, 1973). However, no such correlation is indicated in other studies (Murray, 1961; Anderson et al, 1962; Rajalakshmi et al, 1975). The differences in results could be due to differences in the levels of protein and carotene used. In this connection, Gronovska, Senger and Coworkers (1970) found maximum activity of the enzyme carotene deoxygenase in animals on 10% protein as compared to 5, 20 and 40% protein indicating adverse effects of both very low and high protein diets.

Vitamin C

Vitamin C is another nutrient which is consumed in much smaller amounts (10-15 mg or less after allowing for cooking losses (Mitra, 1958; Rajalakshmi and Kothari, 1964) than the amounts of 30-70 mg recommended by various sources (RDA of NRC, 1968; Gopalan et al, 1963). However, 5-10 mg havebeen found sufficient to ward off scurvy (British Medical Council, 1946; Abt et al, 1963; Baker et al, 1969) and frank scurvy is seldom seen in the tropics including in nursing mothers who

lose more than they consume in milk (Ingalls et al, 1938; Bagchi, 1952; Pathak, 1958; Rajalakshmi and Ramakrishnan, 1969(b). Serum and blood levels of vitamin C are satisfactory (Rajalakshmi and Kothari, 1964; Rajalakshmi and Ramakrishnan 1969(b); Rajalakshmi et al, 1974). But higher intakes of the vitamin are probably desirable as anemia is widely prevalent and blood hemoglobin shows a better response to iron when supplemented with vitamin C than to iron alone presumably because of the favourable effect of vitamin C on iron utilization (Bagchi and Chaudhary, 1954; Hussain et al, 1965; Kuhn et al, 1968).

In conclusion, the major deficiencies in poor diets in this and other similar regions are of food energy, protein, calcium, iron and vitamin A. While evidence for these deficiencies is manifest in the form of impaired growth, poor productivity, skeletal retardation, anemia, night blindness, xerophthalmia etc. an appreciable proportion of the people in such regions, specially, adults do much better than one might expect on the basis of intakes, raising questions about the short term response and long term adaptation to diets lacking in one or other of the nutrients or globally poor diets in relation to age.

The present studies conducted on rats were designed in this context and were concerned with the following aspects :

(1) Growth, food utilization, activity levels as judged by activity in an open field and in an activity wheel, reproductive performance and maternal behavior of rats subjected to food restriction in the neonatal and/or postweaning periods.

(2) Comparative studies on two generations of rats fed diets simulating those consumed by different population groups with regard to reproductive performance, and nutritional status and nitrogen balance during gestation and lactation.

(3) Response of rats to variations in dietary protein content and to changes in the same as judged by growth, nutritional status, nitrogen balance and incorporation of a labelled amino acid in serum protein.

(4) Response of rats fed on a wheat diet with and without addition of lysine at different ages as judged by growth, nutritional status and incorporation of a labelled amino acid in serum protein.

(5) Response of bone composition to different amounts of dietary calcium in relation to age at ~~a~~ treatment.

(6) The utilization of carotene in rats depleted of vitamin A in relation to dietary vitamin A source (vitamin A or carotene) prior to depletion.