Early Nutrition and Later Development

Edited by

A W Wilkinson

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Foreword

The provision of enough food for the increasing population of the world is the greatest material problem which faces mankind today. Improvements in the control of what were formerly endemic diseases like smallpox, plague and malaria without control of the birth rate means the nutritional problem can only increase. The future well being and mental and physical development of a child may be greatly influenced by the way in which it is fed and the quality of the food it receives in the days soon after birth and in this way paediatricians have a lasting responsibility far beyond their immediate interest in the baby. In this book eighteen authors of widely different backgrounds review various aspects of the effects of nutrition in early life in a number of species other than man on later development. Although the emphasis in it is on human nutrition there is much interesting information about early nutrition in other mammals which contributes to our knowledge and understanding of early nutrition during pregnancy and soon after birth.

All mammals suckle their young, whether they are harvest mice or 90 ton blue whales, but there are enormous differences in the number of young born of one pregnancy, their individual and collective weights at birth and the rate at which they grow soon after birth. It is not surprising, therefore, that there are very big differences in the composition of the milk produced by the mammary glands of different species.

There are considerable morphological species differences in the structure and function of the placenta but there is still too little information about the relationship between placental function and fetal growth and well being in man.

The factors which affect fetal growth and determine size at birth are discussed as well as the nutritional endowments at birth and the development and use of glycogen stores and glucose homeostasis soon after birth and the storage, supply and utilisation of fatty acids. Even the baby born at full term is in some respects biochemically immature and drug kinetics in the neonate are much different to those in the older child or adult, but there are at any age important relationships between nutrition and some drugs.

Recently there has been renewed interest in breast feeding and the physiological, immunological and psychological aspects are discussed together with the choice of an artificial milk and its possible effects on the composition of the body of the baby. There are often difficult clinical problems in the nutrition of the very small premature infant and these are accentuated when the baby is born also with an anomaly of the intestinal tract which requires emergency surgical treatment just after birth. The effects of such operations in human neonates and in piglets may be very severe.

Too much food may be almost as bad for the baby and young child as too little and may have adverse effects in early life or in old age but these are difficult to study in man except for short periods. Food intake may also be markedly affected by variations in appetite and family habits. Much important information has been derived from the study of the effects of the treatment of infants with severe malnutrition associated with marasmus and Kwashiorkor. There appears to be an important connection between breast feeding and resistance to infection, and 'weaning diarrhoea' in some countries may be largely due to the substitution of an artificial milk for breast feeding with the consequent greater risk of contamination of poorer quality milk. This book describes many nutritional problems and shows where even more may lie and for some it proposes possible answers.

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Pregnancy and Lactation: The Comparative Point of View

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PREGNANCY

In 1940 a collection of essays by JBS Haldane was published and among them was one entitled 'On being the right size'. This essay begins "The most obvious differences between animals are differences of size, but for some reason the zoologists have paid singularly little attention to them. In a large textbook of zoology before me I find no indication that the eagle is larger than the sparrow, or the hippopotamus bigger than the hare, though some grudging admissions are made in the case of the mouse and the whale. But yet it is easy to show that a hare could not be as large as a hippopotamus, or a whale as small as a herring. For every type of animal there is a most convenient size, and a large change in size inevitably carries with it a change of form". Haldane was writing about adult animals, but what he says in this essay applies with just as much force to the newborn. It is obvious that the mother has to deliver her young while they are still smaller than herself, but the amount by which they are smaller is not the same in all species. Leitch et al (1959), who also complained that zoologists rarely record weights of mothers and newborn young, did manage to find information about the weights of mothers and newborn of over 100 species of mammals. Weights for some small and large mammals are shown in Table I. The smallest mother was the lesser horseshoe bat which weighs 6 gram and the largest was the blue whale which weighs 79,000 kilograms, a difference in weight of over 10 million times. Both produce one young and both, incidentally, deliver their young in a remarkable way – the bat produces her offspring hanging upside down, and the whale delivers her young into the sea. The bat's young weighs 2 gram, over 30% of her own weight, the whale's 2000 kg, which is 2.5% of the weight of

TABLE I. Relation Between the Weights of the Mother and that of her Offspring at Term

Species	Mother's weight	Weight as per cent mother's weight Whole litter	One Young
Lesser horseshoe bat	6.1 g	34	34
Mouse	25 g	40	5
Rat	200 g	25	2.5
Guinea pig	560 g	68	17
Rabbit	1,175 g	19	3.8
Dog	9 kg	12	2.4
Sheep	50 kg	10	10
Woman	56 kg	6	6
Pig	200 kg	6	0.6
Cow	600 kg	7	7
Horse	800 kg	9	9
Elephant	2,590 kg	3.6	3.6
Blue whale	79,000 kg	2.5	2.5

the mother. This illustrates the general principle set out by Leitch et al, that, although the weight of offspring increases as the size of the mother increases, it does not increase in proportion and, generally speaking, the total weight of offspring at birth forms a much larger percentage of the mother's weight in small species than in large ones. The lesser horseshoe bat is rather exceptional among small mammals in only having one young and she must have something rather special in the way of a birth canal. Most small mammals have large litters, so that the total weight is divided among a number of young. The mouse's litter for example, which is 40% of the mother's weight, is divided among 8 individuals; the guinea pig, which produces a greater weight of young in relation to her own weight than any other species, over 60%, has an average litter of 4.

So far we have taken no account of length of gestation, which must clearly be included in any consideration of the demands of pregnancy on mothers of different species. Payne and Wheeler (1968) related maternal weight to gain in weight of total litter in unit time, averaged over the whole of gestation. Table II shows that the total offspring of small mammals are not only heavy in proportion to the weight of the mother at birth but, because their periods of gestation are short, their growth rate before birth related to the mother's weight is even more different from that of large species. For example the litter of the mouse gains nearly 2% of the mother's weight each day of gestation, whereas the fetus of the whale gains only 0.077% of her weight daily, in spite of its great weight of two thousand kilograms at term.

Growth in the early stages of gestation is brought about entirely by cell division

TABLE II. Relation Between the Daily Gain in Fetal Weight, Averaged over the Whole of Gestation, and the Weight of the Mother

Species	Mother's weight	Length of gestation (days)	Weight litter at birth (g)	Gain in weight of litter per day as per cent of mother's weight
Mouse	25 g	21	10	1.90
Rat	200 g	21	50	1.19
Guinea pig	560 g	67	380	1.01
Rabbit	1,175 g	28	225	0.68
Dog	9,000 g	63	1100	0.19
Sheep	50 kg	150	5	0.07
Woman	56 kg	280	3.5	0.02
Pig	200 kg	115	12	0.05
Cow	600 kg	280	42	0.03
Horse	800 kg	340	71	0.03
Elephant	2,590 kg	600	93	0.006
Blue whale	79,000	330	2000	0.0077

without any increase in cell size, so the fetus can only grow as fast as its cells divide. Cell division goes on much more rapidly in the fetuses of small animals than in those of large ones. The rat, for example, increases from a single cell to two to three thousand million during the three weeks of gestation, whereas the human fetus only achieves about a third of this number of cells in its first eight weeks. I know nothing about cell division in the fetal whale. It is true the human fetus and the fetal whale ultimately grow much larger than the rat, but this is because they stay in the uterus so much longer, so the cells have much more time

TABLE III. Relation Between Basal Metabolism and Body Weight of Adult Mammals

Species	Body weight (kg)	Basal metabolism (kCal/kg/day)
Mouse	0.025	182
Rat	0.200	88
Guinea pig	0.560	63
Rabbit	1.175	46
Dog	9.0	36
Sheep	50	23
Woman	56	26
Pig	200	14
Cow	600	15

to double and redouble their number. To bring the rat fetus to 5 gram the complete cell population has got to divide and redivide 30 times. If growth of the human fetus through the whole of gestation were entirely by cell division, then division of all the cells of the body 10 times over would take it from 5 gram, the weight of the newborn rat to 3.5 kg, the weight of the full term baby. Growth of the human fetus is not entirely by cell division, however, but also by growth in size of cells (Widdowson et al, 1972), so the cell population does not have to divide even 10 times over, but something considerably less than this during the last 7 months of gestation.

The problem is, how does all this come about? We can put it all down to genetics, but this rather begs the question as to how the young of small mammals are able to grow so much faster than those of large mammals before they are born.

Another characteristic of small and large species of mammals concerns their basal metabolism. The amount of heat they produce and oxygen they consume each day increase with increasing body weight, though they do not increase in proportion to it but at a much slower rate. In other words small animals have a higher rate of metabolism per kilogram than large ones. Table III shows some of the values given by Voit (1901) and others for the heat production of various species of mammals. A mouse, for example, produces heat at the rate of 212 kCal per kg body weight per day, and a horse 11 kCal per kg per day. Man comes in between with a basal heat production of 32 kCal per kg per day. If these are expressed per square metre of surface area they all come to about 1000 kCal per day.

We do not know for certain how closely the metabolic rate of the fetus in the uterus corresponds to that of its mother. Clearly surface area does not have much meaning for this comparison, and indeed it seems that the placental circulation has the capacity for dissipating all or nearly all the heat produced by the human fetus in its metabolism (Adamsons & Towell, 1965), though there is evidence in man and other species that at term the body temperature is higher in the fetus than in the mother (Wood & Beard, 1964; Adamsons & Towell, 1965; Mann, 1968; Abrams et al, 1969a,b). Earlier investigators (Bohr, 1900; Murlin, 1910), working with animals, concluded that the metabolic rate of the fetus was the same as that of its mother per kilogram of weight, so that it behaved in this respect as if it were part of the mother's body. However, more recent studies have suggested that in the sheep at any rate fetal metabolic rate may be a little higher than maternal per kilogram of weight (Meschia et al, 1967), and indeed one would expect it to be so in view of the cellular activity that is going on. The figure obtained by Romney et al (1955) for the oxygen consumption of the human fetus of 5 ml per min suggests that in our species too fetal metabolism may be a little higher than maternal. Even if this is so I think we can safely assume that there is a close relationship between maternal and fetal rates of metabolism per unit weight. It follows from this that the metabolic rates per unit weight of the fetus of small mammals like the mouse and rat are much higher than those of fetuses of larger species, for example man or the pig, horse or elephant. Even between man and the pig there is a difference and the fetal pig at term probably has a lower heat production than the human fetus. Yet it only weighs one-third as much, so that when it is born the pig needs to increase heat production far more than the human baby to maintain its body temperature. The high rate of metabolism in small adult mammals is made possible by their rapid heart rate and circulation and hence a greater blood supply to the tissues, in fact blood supply is proportional to metabolic intensity as this varies with body size. Small mammals have wide tracheas and aortas for their size, and the number of capillaries per square millimetre cross section of muscle is much greater for small mammals than for large ones. Oxygenation of the fetus and circulation of blood within it are outside my province, but I think we can assume that the placental and fetal circulations of the small mammal shares in the general rapid turnover, so that the fetus of the small mammal is supplied with the oxygen and nutrients required for the high rate of metabolism and high rate of growth.

Pregnancy, therefore, makes far greater demands on the mothers of small mammalian species than on those of large ones and they have to eat correspondingly more food to provide for the requirements of their unborn young. Not only so, but all species so far studied deposit considerable amounts of fat in their own bodies during pregnancy. The amount of fat laid down may be considerable. Hytten and Leitch (1971) suggest that the average amount is about 4 kg during a full human pregnancy, which is quite a lot of fat. It weighs more than the average baby and may well add a third to the amount of fat the mother had in her body before she became pregnant. The fat seems to be deposited at specific sites, over the abdomen, the back and the upper thighs, but not over the arms (Taggart, 1961). Pregnant rats and mice deposit fat too. Spray (1950) found the fat in the bodies of rats to increase from 51 to 72 gram during pregnancy and in mice from 1.2 to 2.8 gram.

LACTATION

In many species lactation makes a far more exacting test than pregnancy. Table IV shows for eleven species the weight, expressed as a percentage of the mother's weight, of the young at birth and at the end of the time when they depend entirely on milk for their sustenance, and the difference between the two, which gives the gain during suckling. First on the list I have placed the small rodents, the mouse and rat, and then rather surprisingly, a carnivore, the cat. Their young are born in an immature state, but grow extremely rapidly after birth and soon become quite fat. The rabbit, sheep and pig follow the cat, and in all these species the demands on the mother for nutrition of the young after birth are far greater than those for nutrition of the fetus before birth. On the other hand the guinea pig, which has a long gestation period and is born large and mature, makes considerably more demands on the mother before birth than after. It depends on mother's milk for a very short time, and in fact begins to nibble other food very

TABLE IV. Weight of Young as per cent of Mother's Weight

Species	At birth	At end of full suckling	Gain during suckling
Mouse	40	170	130
Rat	25	120	95
Cat	12	100	88
Rabbit	19	50	31
Sheep	10	40	30
Man	6	12	6
Pig	6	40	34
Calf	7	14	7
Elephant	3.6	23	19.4
Blue whale	2.5	20	17.5
Guinea pig	68	–	–

soon after it is born.

For the human species pregnancy and lactation appear from this table to make equal demands, but this is not true for several reasons. In the first place time must be taken into account, and this applies also to the other mammals. The human baby takes twice as long to grow to 3.5 kg before birth as it does nowadays to double this weight after birth. Moreover, to provide milk for the growth of the young after birth is a less efficient process than to supply the fetus in the uterus with what it needs. Neither the production of milk by the mammary gland nor the digestion and absorption of the nutrients in the milk by the young animal or baby are carried out with 100% efficiency. The cost of lactation to the mother includes not only the nutrients in the milk and their energy value, but also the energy required to synthesise the lactose, protein and fat. It used to be thought that the energy efficiency of milk production was no more than 60%, but Thomson et al (1971) have been steadily raising their estimate and their latest figure is about 90% efficiency. So far as the utilisation of nutrients by the infant for growth are concerned, this is more efficient than at any other time of life but, even so, the infant retains only about half the nitrogen in breast milk for the synthesis of protein for growth (Fomon, 1974). The rabbit, that grows much more rapidly than the human baby retains about 70% of the nitrogen in its milk for growth (Davies et al, 1964).

A far more important reason why nutrition after birth is a less efficient process than nutrition before birth is because a great deal of the energy taken in in the milk, at any rate in some species, must be used for maintenance in an environment that is almost certainly cooler than the uterus. The more slowly the young animal grows the greater is the proportion of its energy intake which is used for maintenance, and the smaller is the proportion which is used for the deposition of new body tissue. The human baby is a particularly slow grower and Table V

TABLE V. Percentage of Energy Intake Used by Infants for Maintenance and for Growth (kCal/kg/day)

Age months	Intake	Expenditure	
		Maintenance	Increment in body i.e. growth
0–2	126	93	33
2–4	111	93	18
4–6	100	93	7

shows the average energy intake of the infant at three ages, and the amount of this that is expended on maintenance, and on increments of protein and fat in the body, that is, on growth. Even during the first two months after birth only 26% of the total is used for growth and by 4–6 months the percentage has fallen to 7.

Women who breast-feed their babies probably lose most of the fat they acquired during pregnancy, and the 36000 kCal of energy stored in this way should provide a third to a half of the energy required for the production of breast milk. Rats too lose the fat deposited in their bodies during pregnancy and far more as well. The rats that had increased their fat from 51 to 72 gram during pregnancy lost all but 9 gram of it during lactation.

Other mammals do this too, and an extreme example is the grey seal. The female lays down a great deal of fat during the latter part of pregnancy in July and August. She has her young on shore in September, and the weight of the newborn is about 15 kg. The mother suckles her pup for about two weeks, during which time it puts on 20 kg in weight or 1.5 kg a day (Amoroso & Matthews, 1951; Amoroso et al, 1951). It becomes very fat indeed – seal milk contains 53% of fat. Meantime the mother takes no food at all and she loses twice the weight gained by her pup. All that the pup needs for maintenance and rapid growth comes from within the mother's body.

Most mammals, however, increase their food intakes during lactation, and a small mammal like the mouse or rat with a weight of young at the end of lactation greater than her own weight, must eat a great deal more food during lactation to provide for the rapidly growing young. In fact more food is eaten by rats in full lactation than after lesions have been made in the hypothalamus (Kennedy, 1952–53). Kennedy (1952–53) and Anderson and Turner (1963) found that the food consumption of rats in full lactation was more than double that of non-pregnant non-lactating females. The digestive tract enlarges in response to all this extra food, the stomach by some 60%, the small intestine by over 100% and the caecum by 65% (Fell et al, 1963). The increase in weight of the intestine was found to be brought about by dilation of the wall (Boyne et al, 1966) so that the surface area of the mucosa almost doubled. The liver, too, increases greatly in size in response to all this extra food, and Kennedy et al (1958) found that the enlargement was greater the more young were being suckled. When there were 8–11 young in the litter the liver doubled in size. Growth of the liver was brought about by an increase both in number and size of its cells. After lactation was over and the rats were eating less food the size of the liver returned to what it was before. There was loss of protein from it, but no loss of DNA, so the livers of parous rats have more cells in their livers than rats that have not lactated. Similar changes have been shown to occur in the livers of lactating sheep (Campbell & Fell, 1970).

Enlargement of the gastrointestinal tracts and livers of women during lactation has not been reported. There seems no reason why it should not occur, but if it does its magnitude is likely to be considerably less than that observed in the animals that have been studied.

TABLE VI. Composition of Milks of Various Species (per 100 ml)

Species	Protein (g)	Fat (g)	Carbohydrate (g)	Energy (kCal)
Rat	9	9	3	129
Guinea pig	8	6	3	98
Rabbit	13	15	2	195
Cat	11	11	3	155
Dog	8	9	4	129
Sheep	6	8	4	128
Cow	3	4	5	68
Horse	2	2	6	50
Ass	2	2	6	50
Rhinoceros	2	0.5	6	37
Elephant	8	9	4	129
Pig	6	9	5	125
Hippopotamus	7	18	2	198
Man	1	4	7	68
Monkey	2	4	6	68
Seal	11	53	3	533
Whale	12	40	1	412

The milk of rodents and carnivores that have young that are immature and helpless at birth but that grow very rapidly after birth are characterised by a low percentage of carbohydrate, a high percentage of protein and fat and a high energy value (Table VI). The milk of ruminants, cow's milk for example, has less protein than the milk of rodents and carnivores, a little less fat and more carbohydrate. The milk of ruminants differs from all other milks in containing appreciable amounts of short chain saturated fatty acids, notably butyric acid.