

(4) Obese subjects make greater use of the hexose monophosphate pathway so providing NADPH₂ which is needed for synthesis of fatty acids. The evidence for this is that if obese and lean subjects are given glucose labelled in the C₁ and C₆ positions, a larger proportion of the labelled C₁ appears in the expired air of the obese than in the normal subject. The C₁ carbon atom is primarily involved in the oxidation of glucose via the hexose monophosphate pathway.

(5) Obese patients have a diminished urinary excretion of the adrenal androgen, dehydroepiandrosterone. This hormone inhibits the activity of glucose-6-phosphate dehydrogenase which is involved in the first stage of the hexose monophosphate pathway.

However, it is not clear whether any of these changes are the cause or the consequence of the obese state. None of them allows a sharp demarcation of the obese from the non-obese. There is no evidence that the specific dynamic action is less well-marked in the obese than in normal subjects.

Homo sapiens evolved in an environment in which the food supply was often scarce. He learnt to adapt to this and is able to survive when his food intake is reduced to about half the normal amount. It is only recently that a significant proportion of the species has lived in an environment with an abundant supply of food, which can be obtained without physical effort. There is no evidence of any regulatory mechanism which can protect him against overeating and the consequent storing of excess energy as fat. Although, as indicated above, there are possible mechanisms whereby a higher proportion of dietary energy could be dissipated as heat without being associated with the corresponding amount of work, it seems very unlikely that obesity arises as a result of any such changes. In the vast majority of cases of human obesity, the condition appears to arise from changes in behavioural activity which are not compensated by any physiological control system.

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Food intake and growth in the newly-born

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So long as it is in the uterus the foetus receives its supplies of nutrients and energy from the blood reaching it from its mother through the placenta. The

calories are provided mainly as glucose and amino acids. Appetite control as we understand it does not come in at this stage of development, though the mechanisms that will be responsible for it later are developing and will be ready to come into play at the right time. Much of our knowledge of the hypothalamic aspects of appetite control has been obtained on the rat, but the newborn rat is very immature compared with the newborn of many other species and it is thought to have no means of restraining its food intake until it is about 14 d old (Kennedy, 1957). The more milk it can get the more it will take and the faster it will grow. Myelination of the brain begins about this time (Davison & Dobbing, 1966), but the brain is developing rapidly in other ways too, and there is no proof that myelination is necessary for hypothalamic control of appetite.

Newborn babies are much more highly developed than newborn rats, and the evidence goes to show that they do have the ability to match their intake of food to their requirements for it from very soon after birth. It is thought that they do this entirely by hypothalamic control, and that only later do they acquire the more complicated feeding patterns and habits initiated by the cerebral cortex (Anand, 1961).

A supply of food is needed first and foremost to provide nutrients and energy for all the vital processes of the body, both at organ and cellular level, and in homeothermic animals after birth to maintain the body temperature high enough to enable these processes to continue at an optimal rate. The metabolic requirements of an animal are approximately proportional to its surface area and, therefore, the smaller the body the greater will be the requirements for energy per unit of body-weight.

In the growing animal 'energy' in the form of protein, carbohydrate and fat is also needed to lay down and maintain the new tissues, and this is true too during recovery from a wasting disease or lack of food. Generally speaking, however, far more of the food intake is used to provide for the tissues already there than for laying down new ones and it is, therefore, the metabolic rate of the animal that sets the pace for its demands for calories. Only soon after birth in animals that grow very rapidly do the requirements for growth ever exceed those for general metabolism. Table 1 illustrates this. It compares the gain in the calorie value of the body of the rat, calculated from the amounts of protein and fat in it, with the estimated calorie intake during the first 5 weeks after birth. The values for the composition of the rats' bodies are from our own analyses, and those for the calorie intakes are based on the observations of Kennedy (1957); these may be too high in the early stages since they are calculated from the increase in the mother's intake of food. Growth does not take place with 100% efficiency, so that a higher proportion of the calories ingested would probably be required for growth of the body tissues than the values set out here, but it is impossible to know what allowance to make for this. The rat can deposit 80% of its food intake, reckoned in terms of calories, as new body tissue during the first week because it is almost poikilothermic at this stage of its existence. The warmth of its mother's body and the proximity of the rest of the litter provide it with the heat it requires to maintain its temperature sufficiently high

Table 1. *Comparison of the gain in calories in the body of the rat with its calorie intake during the first 5 weeks after birth*

Week after birth	Body-wt (g)	Fat in body (g)	Protein in body (g)	Calorific value of body (kcal)	Gain in body calories during week (kcal)	Calorie intake during week (kcal)	Gain in body calories (% calorie intake)
0	5	0.03	0.49	2.3			
1	12	0.96	1.29	14.2	11.9	14.8	80
2	22	2.02	2.88	29.6	15.4	55	28
3	35	3.2	4.6	49.3	19.7	87	23
4	51	3.2	7.2	59.6	10.3	134	8
5	71	3.6	10.5	76.0	16.4	179	9

for the body's metabolic processes to proceed satisfactorily. It does not have to expend many of the calories derived from its food on maintaining its body temperature. By the 2nd week it is becoming homoeothermic. It is a very small animal and its metabolic requirements per unit of body-weight are therefore high. Three-quarters of its intake of food are now used to support its rapid rate of metabolism and about one-quarter for purposes of growth. By the 3rd week it is fully homoeothermic. It is also becoming quite active and it is beginning to take food other than milk. It is still growing very rapidly, however, and nearly a quarter of the calorific value of its food is deposited as protein and fat in the body. At the end of the 3rd week these rats were weaned, and this reduced the deposition of fat during the 4th week and the percentage of the calorie intake used for growth fell to 8.

Table 2. *Comparison of the gain in calories in the body of the pig with its calorie intake during the first 4 weeks after birth*

Week after birth	Body-wt (kg)	Fat in body (g)	Protein in body (g)	Calorific value of body (kcal)	Gain in body calories during week (kcal)	Calorie intake during week (kcal)	Gain in body calories (% calorie intake)
0	1.5	18	174	882			
1	3.2	306	437	4 640	3758	6 830	55
2	5.5	796	770	10 500	5860	11 450	51
3	8.0	1280	1098	16 380	5880	11 600	50
4	10.0	1763	1427	22 250	5870	12 200	48

Table 2 shows figures for newborn pigs set out in a similar way. The pig, like the rat, is born with hardly any fat in its body. It grows exceedingly fast, and at the same time the fat in the body increases from 1% at birth to 18% of the weight at 4 weeks. These calculations are based on experimental evidence for the growth and composition of young piglets (Manners & McCrea, 1963), the volume of milk drunk by young piglets while growing at this rate and the composition of sow's milk (Blair, Diack & MacPherson, 1963). The pig is homoeothermic from the time of birth and therefore it has to utilize some of the energy value of its food to maintain its body temperature in an environment which may be quite cold, yet about half the calories it derived from its mother's milk were deposited as protein and fat in its body over the first 4 weeks of its postnatal life while it was being fully

suckled. The percentage must fall later but there are no figures available from which to make the calculations.

The human baby grows much more slowly than the rat or pig. Similar calculations, based on intake of food while the birth weight is being doubled (McCance & Widdowson, 1964; Chilver & McCance, 1967), the composition of a full-term baby at birth (Widdowson & Spray, 1951) and an estimate of its composition at 4-6 months, lead to the conclusion that 7-9% of the baby's intake of calories are used to form new body tissue during this time.

It is energy expenditure that regulates calorie intake in every species, and the young babies and animals have to adjust their intake of food continually to meet their changing metabolic requirements. Because they are becoming heavier they need more and more food, but less and less of it per unit of body-weight. The percentage of the total calorie value of the food used for growth may be high initially, but the percentage falls as the animal becomes larger and the rate of incremental growth slows down. This is a far more complicated situation than the one facing an adult and yet the young of many species seem to be able to take the right amount of food for their requirements from the time they are born, even though these requirements are changing all the time.

In a litter of pigs there is sometimes one weighing only a half or even a third as much as the largest at birth. Even when only these two pigs are left with the mother, so that there is no question of a shortage of food, the small pig grows at a slower absolute rate than the big one so that it does not catch up the big one in weight, and the weights fall farther and farther apart (Fig. 1). Its rate of incremental growth,

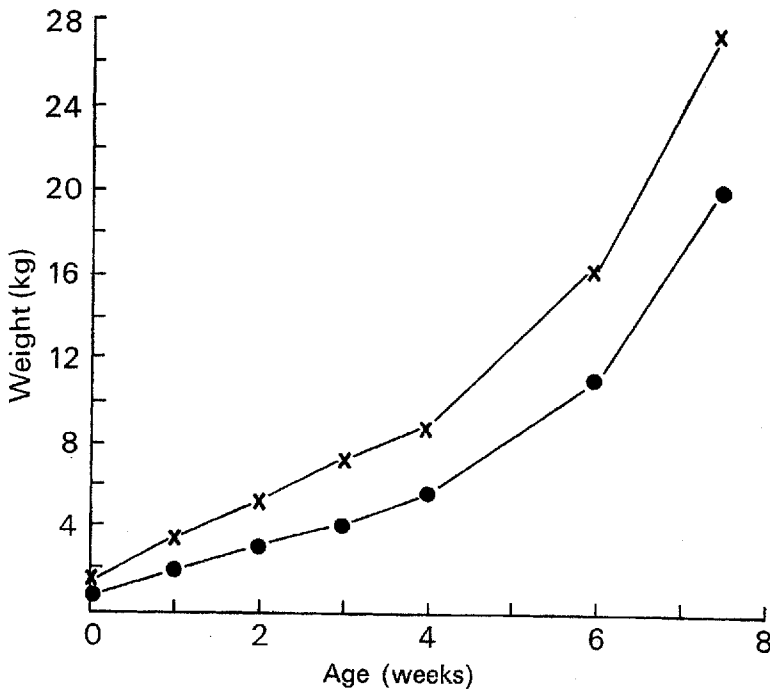


Fig. 1. Gain in weight of litter-mate pigs of different weights at birth.

however, may be greater than that of its larger litter-mate and, in fact, the small pig generally doubles its birth weight before the large one. The question at once arises as to which hypothalamic regulatory mechanism is most likely to be operative in the early days of postnatal life, whether a thermostatic (Brobeck, 1948), gluco-static (Mayer, 1953) or lipostatic (Kennedy, 1953) one. It is characteristic of the suckling period that fat is laid down in the body, whether the newly born has subcutaneous fat like the human baby, or has practically no fat inside it like the rat and pig (Widdowson, 1950). A regulation of appetite by a feedback mechanism associated with the amount of fat in the body does not fit the facts, and Kennedy (1967) himself considers that a lipostatic mechanism would not be likely to interfere with the high food intake associated with rapid growth. The level of circulating blood glucose and the body temperature are both more labile in the very young than in the adult, and it seems probable that a fall in one or both of them may be important in calling forth a desire for food, and a rise in producing a feeling of satiety. Most sucking animals feed at more frequent intervals than the adult of the same species and it is possible that there is no long-term regulation of appetite in early life. The rabbit is an exception to this. It is suckled only once a day and it then takes in the space of 2-3 min enough milk to suffice it for the next 24 h (Davies, Widdowson & McCance, 1964). The milk is 'squirted' into the young rabbit's mouth by contraction of the muscles of the mammary gland in much the same way that young marine mammals are fed under water. In this situation it is difficult to see how the young rabbit can take advantage of any mechanism of appetite control that it may have. It has a large stomach which empties slowly and even after 24 h there is usually some milk left in it. There must be some control, for the small rabbit in the litter, like the small pig, remains smaller than its larger litter-mates at birth. The fact that rabbits feed their young in this strange way makes it easy to find out how much milk the young animals take at each daily meal. Fig. 2 shows the results for two rabbits in one litter during the first 2 weeks from their 1st day after birth. One weighed 70 g, the other 53 g at the beginning. The larger one gained 218 g and the smaller one 145 g during the 2 weeks of study. Table 3 shows the total amount of milk they took during each of the 2 weeks, and it is obvious that the

Table 3. *Milk intake of largest and smallest rabbits within a litter*

	Total milk intake (g)	
	Week 1	Week 2
Large	133	260
Small	83	187
Milk intake (g/100 g mean body-weight)		
	Week 1	Week 2
Large	124	127
Small	117	126
Milk intake (g/g gain in body-weight)		
	Week 1	Week 2
Large	2.10	1.67
Small	2.07	1.77

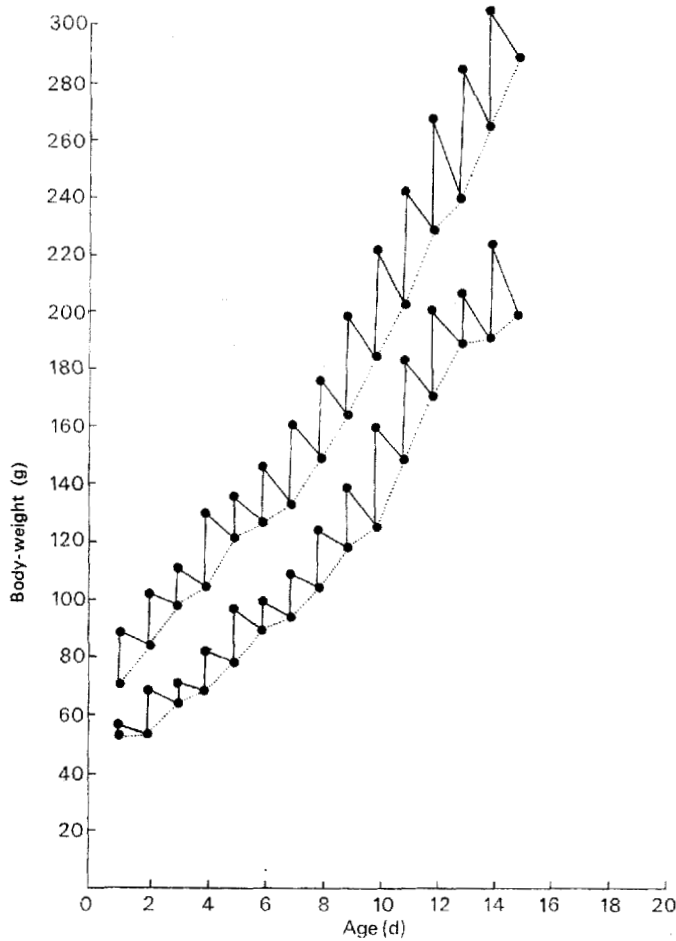


Fig. 2. Weight of two rabbits in a litter before and after their daily feed.

smaller one took less than the larger. When the intakes are expressed per 100 g mean body-weight during the week, the values for the two animals are very much the same. Both appeared to use their milk for growth with remarkable efficiency, for they needed only 1.7 g of milk to build 1 g of body tissue during the 2nd week. In fact, rabbit's milk contains about 10% less water than the newborn young it is produced to feed and it is considerably more calorific. The adult rabbit is a nibbler and like all herbivores it needs to feed continuously to get enough calories from its bulky diet, so appetite control must undergo a dramatic change in this species at the time of weaning.

The pig or rabbit that is smaller than its litter-mates at birth has been undernourished *in utero*. Rats are much more uniform in weight at birth than the young of many species, possibly because they are born at such an early stage of development. They take more or less food than the average depending on whether the mother has few or many to suckle, and they grow at rates correspondingly fast or slow (Kennedy, 1953; Widdowson & McCance, 1960). Once set on a course of rapid or

slow growth, and large and small size for age, they continue to feed and grow in the same way when hypothalamic control takes over at 14 d or so, and the rat that has grown slowly to this age will not now take sufficient food to enable it to increase its rate of growth, and it does not catch up its larger fellows. The rat now adjusts its food intake to its body size, which is the situation from birth in other species that are more mature when they are born.

I am going to finish by saying something about food intake and growth in the human baby. Many years ago I was impressed by the way in which calorie intakes of individual children of the same age and sex varied from each other. Of the twenty or more boys and girls in every yearly age group from 1 to 18 there was without exception one who ate enough food to provide twice as many calories as the food of another (Widdowson, 1947). The differences were already evident by the 1st year and more recent studies in the United States show that there is a variation from the time of birth (Fomon, Owen & Thomas, 1964; Beal, 1969). As we have seen, human growth is so slow compared with that of the rat or pig that even during the first few months of a baby's life growth accounts for only a small proportion of the total calorie intake. Calorie requirements throughout human life, therefore, largely depend upon the demands for maintenance. Unlike the rapidly growing rat, rabbit and pig, where food intake is closely related to body size, big babies do not necessarily need more calories than small ones, and the calorie intake per kg body-weight varies almost as much as the total calories a baby takes. Fomon *et al.* (1964) measured the voluntary food intake of eighty-two infants fed *ad lib.* Milk was the sole source of calories and it provided 67 kcal per 100 ml. Besides showing the variation in volume of milk taken by the children per kg body-weight, the results of this investigation demonstrated how the food and, therefore, calorie intake per kg body-weight, decreased with age. Most children took more than 180 ml of milk per kg, providing 120 kcal during the first 2 months, but few of them accepted this amount after 3 months.

During the last weeks of gestation, the male foetus grows faster than the female, and it is well known that, when large numbers are considered, boys weigh more than girls at birth. They continue to gain weight faster after birth (Fig. 3), and Fomon, Filer, Thomas, Rogers & Proksch (1969) have shown that they have bigger appetites and take more milk in order to do so.

The quantity of food a baby will consume voluntarily is determined by bulk as well as by energy needs, and calorie intakes therefore depend to some extent on the composition of the food and its calorific value per 100 ml. This was demonstrated by Doxiadis & Paschos (1962) and by Fomon *et al.* (1969). Both groups of investigators gave one group of full-term infants a relatively dilute formula and another a more concentrated one. Those given the dilute formula took larger volumes, but not enough to compensate for the difference in calorific value, so that their total calorie intake was significantly less than that of the infants receiving the more concentrated feeding. The babies having the dilute formula gained weight more slowly than those having the one that was more concentrated. Premature babies have been shown to gain more weight when fed a milk with a higher calorific

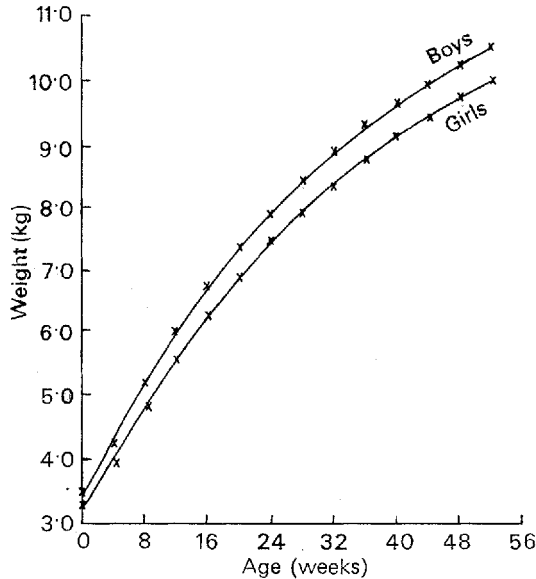


Fig. 3. Growth of first-born boys and girls fully breast-fed for 3 months.

value than breast-milk, but – and this is very important – their long bones did not grow any faster (Snyderman & Holt, 1961; Combes & Pratt, 1961). We may think the baby has rather poor appetite control if it can be fooled like this, but what we must remember is that a milk diet is always one of low calorie density because it contains so much water. At 67 kcal per 100 ml, which is the value for both cow's milk and human breast-milk, an adult would have to drink 4–4.5 l per d to get his quota of calories. I wonder how good we should be at regulating our calorie intake to our needs if we were forced to take all that water in order to get them!

There is one question we must ask ourselves in this connection – though I am afraid I have not got the experience or knowledge to answer it. Are those in charge of young babies sowing the seeds of obesity in later years by giving them concentrated feeds to make them gain more weight than they would have done had they been fed on breast-milk?

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Physiological changes affecting voluntary food intake in ruminants

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Although the basic control of voluntary food intake in ruminants is imperfectly understood, it has been possible to study and describe the response in food intake to various changes in the environment (especially the diet) and within the animal. This paper deals with the effects within animals of physiological changes on voluntary intake. There have been many observations made on the effects of growth, development, reproduction and pregnancy on intake and, recently, some experimental work has begun to explain these observations.

The literature on the effects of pregnancy and lactation on voluntary intake has been reviewed (Forbes, 1970a) and this paper will attempt to correlate the results of some recent experiments with the more general framework of ideas which has been put forward elsewhere.

The early post-weaning period

Even when unlimited amounts of milk are offered to young calves and lambs, they begin to chew solid food at about 2 weeks of age and crave for it if it is not available. Under natural conditions, weaning is slow and the transition to solid food intake is prolonged and may not be complete until 6 months of age. Under modern husbandry conditions, calves are weaned at about 4 weeks old, at a time when their solid food intake is still very low. The withdrawal of milk does, however, rapidly stimulate the intake of solids (e.g. Hodgson, 1971a).

Diets with a high concentration of metabolizable energy are usually offered during and after weaning. It is unlikely that rumen capacity limits voluntary intake of such diets immediately after weaning because feeding fibrous materials at this time results in a greater volume of rumen contents (Hodgson, 1971b).

To study the importance of rumen fill in limiting the voluntary food intake of growing calves, Hodgson (1971c) added food to, or removed digesta from, the rumens of fistulated calves. Fig. 1 shows the change in intake of the two diets