complete upper and lower dentures. In this same enlightened era I see children in their first year of school life losing the use of most of their primary teeth before their permanent teeth have begun to erupt. Am I right in observing that the minimum age for the occurrence of coronary thrombosis is getting progressively lower? Am I justified in suggesting that if all the instances of acute otitis media now occurring in young children were not countered by the fortunate availability of chemotherapy and antibiotics the incidence of chronic otorrhoea and mastoiditis and deafness would be vastly on the increase? In other words, may there not be a state of reduced resistance to infection disguised by prompt and efficient therapy? And could not these dental disasters, these early coronaries, this reduced resistance, be laid at the door of fundamental habitual nutritional errors in the early years of life?

The family doctor can make little claim to either skill or consistency in the role of instructor in nutrition, and, in any case, has been jostled out of his rightful position as chief adviser by the midwife, the health visitor, the press, and the commercial advertiser. Yet he is in the ideal position to observe what is going on in the home, to observe and to instruct. If I am right in saying that this is the first ever postgraduate symposium for general practitioners which has chosen to deal with the subject of human nutrition, then perhaps today marks the beginning of the end in this regard of just sitting back and whistling Lillabullero.

FOOD, GROWTH, AND DEVELOPMENT

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I do not know that I can answer many of the questions or conundrums put to you by Dr McCulloch. I hope that you won't go away afterwards feeling like the sheep in " Lycidas " that you have looked up without being intellectually fed. I can only do my best to give you a short paper on a subject which certainly does concern food, growth, and development and I would like to begin with nutrition *in utero*.

The food of the foetus is looked after in the early stages by the trophoblast. We do not know exactly what food the trophoblast provides for the foetus, but we suspect that it is very largely protein in nature and we know that it always provides enough. There is no evidence whatever that the foetus in the early stages of its existence is ever short of food. When we come to consider the development of the foetus while it is linked up with the placenta, we have to take into account several characteristics of placental nutrition. In the first place, the supply of food is continuous, not discontinuous as it is after birth, and of course the materials do not just float across the placental barrier—most of them are delivered by active transport. The amino-acids in the blood of the foetus are mostly at a higher concentration than they are in the maternal plasma, and the same applies to the vitamins. The supplies of fat to the foetus are in a very special position, because the foetus makes all its own fatty acids, except possibly the so-called "essential" ones. The placenta may absorb fat from the maternal blood, but it is broken down there and passed on to the foetus in the form of two-carbon atom residues. From these the foetus builds up its own fatty acids and sterols.

It will not be possible to study the nutrition of the foetus directly until there is some method of feeding it outside the uterus and making a proper metabolic balance. One has to rely upon the development of the foetus *in utero* and its size at birth to obtain an idea of what its nutrition has been—in other words one has to work backwards through the mother. Fortunately, nutrition during foetal life can be followed in this way, because most of the things which might be expected to interfere appear not to do so. Temperature can be ruled out and genetics hardly come in, because the great experiment of Hammond and Walton, in which they crossed Shire horses with Shetland ponies, led to the discovery that the size of the foals at birth depended almost entirely on the size of the mother. This is because her size determines the amount of food she can supply and the extent of the accommodation she can provide. It is similar in man; big babies on the whole are the product of big mothers, and if you want your offspring to win a prize at the local baby show, you ought to marry a big woman!

There is never any trouble over nutrition in the early stages of pregnancy when the foetus always gets plenty of food; it is the last part of pregnancy which is the real test. It is at this time that the weight of the foetus is going up very rapidly, more and more rapidly every day, whilst at the same time the placenta has practically stopped growing, and is becoming a little old and arteriosclerotic and not so good at its job as it was when it was young and vigorous about the third month of foetal life. In all species the rate of transmission of sodium across the placenta rises throughout pregnancy until a short time before term, at which point it begins to fall. The placenta indeed is often ageing so rapidly at this time that it is unable to transmit the food required by the foetus; this leads to a fall in the rate of growth, even of single foetuses in the last week or two of pregnancy.

It might be supposed that the maternal plane of nutrition would make an enormous difference to the growth of the foetus, and in some species this is so. The weight of twin lambs can be halved quite easily by reducing the food supply to the mother in the last half of pregnancy, but it is very difficult to make any difference to the weight of newborn pigs by reducing the food supply of the sow. It makes a difference to the weight of the human baby at birth if the mother is very undernourished, but the difference is small and the matter can only be demonstrated statistically. We demonstrated it in Germany after the war and it has been shown by other people, but one has to look carefully to find it. If the mother is a heavy smoker it makes almost as much difference to the size of her offspring as it would if she were in a state of severe undernutrition and the reason is probably the same, namely that nicotine leads to constriction of the uterine arteries and so limits the supply of food to the foetus.

Many other things affect size at birth. In animals, the numbers in a litter are well known to affect the size of the individual foetus, and this of course applies to the human too, for twins as you know are generally smaller than singletons. The position in the uterus makes a considerable difference in some animals, and this has been beautifully worked out in the mouse and shown to depend on the nutritional supply of the individual foetuses. The blood supply to the placenta must make a difference to the amount of all the nutrients supplied to a foetus and consequently its growth. The size of the placenta is also to some extent important, but very large foetuses may be associated with quite small placentas, because the efficiency of the placenta seems to be just as important as its size.

The length of gestation matters and the size of twins, triplets, and quadruplets depends upon this as much as it does upon the quantity of nutrients supplied to them. This is where the size of the mother comes in again, for the greater the amount of accommodation she can provide the longer she can retain the foetuses *in utero*, and therefore the larger they can become. When the growth rates of human singletons, twins, triplets, and quadruplets are compared, it is found that from the 26th week the growth rate of quadruplets beings to fall off while their placentas are still in their prime, because the mother cannot supply more blood to the uterus. The uterus is already getting all the blood supply it can, and therefore all of the nutrients which the mother can provide for the foetuses is being provided, and if this has to be shared between four foetuses then each one will get less than if there were only three. The growth rate of triplets starts to fall about the 27th—28th week, and that of twins from the 30th, whilst the growth rate of singletons is still maintained. The reason, however, why twins, triplets, and quadruplets are generally born so small is not so much because they are undernourished from the 26th or 27th week, but because the mother is unable to continue to provide accommodation for them after the uterus has reached a certain degree of distension. The time of delivery depends mainly upon this, as the progeny are born when the uterus has become distended to the extent which the mother can tolerate neurologically and hormonally. Consequently, quadruplets come out before triplets and the triplets before twins, prematurity, as well as undernutrition, controlling their size at birth.

The food supply of the newborn is rather different from the food supply of the foetus, because it is intermittent and contains large amounts of fats which the newborn animal is now able to metabolize. The supply of phosphate to the foetus through the placenta may be one of the things which limits the growth rate and ossification of the bones *in utero*, and there is evidence that after birth phosphates may again limit the calcification of the bones of breast-fed children. There must be a limiting factor, and this appears not to be proteins, fats, or calories; we think it is quite likely to be phosphates.

Some newborn animals absorb large quantities of gamma globulins or lactoglobulins unchanged through the intestinal wall, and this is how many animals get the passive immunity which enables them to survive the hazards and infections of the farmyards and their natural surroundings. In rabbits this is not the case, nor is it the case in man. In rabbits, the antibodies reach the foetus through the everted yolk-sac, which is also a sort of embryonic intestine, but in man the gamma globulins seem to enter the foetus through the placenta.

If ever there was a race against time so far as nutrition and development are concerned, development *in utero* is one. One might suppose that, after birth, time would be more on the side of the developing organism, and to a point this is true. The development of the large member of a litter presents few problems once it is safely born, but the small one is always a risk, particularly in nature. The runt is handicapped by weakness and poor temperature regulation; he cannot compete for food supplies and consequently tends to go on growing more slowly. He does not catch up at all readily, even if given unlimited food, and this is also true of man. The small baby tends to remain the small child, and to continue as such until puberty and even afterwards.

There is no evidence that the children of today are born larger than they were fifty years ago, but there is no doubt whatever that children are larger than they used to be, and this increase in the size of children is well documented, and generally referred to as the " secular trend " in development. With this increase in height and weight goes earlier maturity and puberty, and all that this involves in social relationships. Some people have said that the increase in height and weight is all nutritional. Tanner attributes it to the introduction of the " bicycle ", using the bicycle as a symbol of the increased transportation which has led to very much more out-breeding than was the case a hundred years ago. I think myself that the reduction in infections in the early years of life is probably a more important reason. There is no kwashiorkor in the Gambia, for example, and no reason why children there should not wean off quite successfully. They start growing at exactly the same rate as English children, but between six months and two years of age they are bombarded with all kinds of infections and parasites. All receive a severe check in their growth rates and about half of them die, but the survivors go on growing thereafter at about the same rate as English and American children. They are, however, always that much behind. The increased growth rates in England are well established before the children ever get to school, because at five years of age children today are taller than they were at the same age ten to 50 years ago, but whether this is due to better nutrition, fewer infections, or more outbreeding no one can say.

In the race against time which characterizes growth *in utero* and development after birth, undernutrition is always a disadvantage. The well-nourished animal is much less liable to infections, grows faster, and in some species, such as the rat, becomes a larger adult. The prolongation of life after the attainment of maturity is a trial of endurance rather than a race against time, and there is considerable evidence that in this test of endurance over-nutrition is a disadvantage rather than an advantage, and that, once you have attained adult size, you are better to be a little undernourished than over-nourished. It is difficult to prove this from work done on animals, because few people have had the patience to keep animals for long enough, but it has been shown quite clearly that in mice, for instance, which become obese for genetic reasons, limiting the amount of food they are able to get does prolong their life extensively. Prolonged under-nutrition of rats from an early age may lead to a great many deaths from infection while the animals are growing, but it does enable the male, once he has become an adult, to live longer, perhaps three times as long as his well-nourished fellows. There is no doubt from the evidence of insurance companies that over-nutrition later in life tends to shorten the length of time that a man is likely to live to enjoy it. This is a subject in itself, one largely concerned with food and time but rather outside my terms or reference, as growth is no longer on the " agenda ".

REFERENCE

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NUTRITIONAL INDIVIDUALITY*

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A hundred years ago Claude Bernard wrote in his *Introduction to Experimental Medicine:* " Physiologists and physicians must never forget that the living being is an organism with its own individuality ". A lot of us have forgotten this, especially the administrators, because they always think in terms of population and averages—the average body-weight for a given age or height, the average requirement for this or that. If they think of the individual at all, it is the average man weighing 70 kg., and probably this hypothetical average man never existed. The doctor, on the other hand, deals with the individual, and to him the range of variation that can exist from one perfectly normal person to another is much more important than a single mean, which is often wrongly interpreted as being synonymous with the normal. We are now beginning to realize how very widely normal healthy people differ from each other in all sorts of ways, and I would like to discuss a few of the physiological characteristics over which we have little or no control, and which influence our nutritional requirements.

My attention was first drawn to this in 1936, when I studied the individual food intakes of 63 men and 63 women of the English middle classes. Up to that time dietary surveys had generally been made on families, and no information was obtained about the individuals within those families. I was at once struck by the enormous variation in calorie intake from one person to another. Both groups contained men or women who were taking half as many calories as others. This is not peculiar to adults, for when I later made a similar study on over 1,000 children I found that in every age group from 1 to 18 years one boy or girl out of the 20 or

*Based on a paper given at a Symposium held by the Nutrition Society on Individual Variation. *Proc. Nutr. Soc.* (1962) **21,** 121.