PROCEEDINGS OF THE NUTRITION SOCIETY
The Boyd Orr Memorial Lecture was held at the Royal Society of Medicine, London, on 6 December 1988

BOYD ORR MEMORIAL LECTURE

Early nutrition and later achievement

BY JOHN DOBBING
Department of Child Health, University of Manchester, The Medical School, Oxford Road, Manchester M13 9PT

'Après le pain l'éducation est le premier besoin du peuple', Danton*

At least two things separate me from previous Boyd Orr lecturers: firstly I am not a nutritionist, and I therefore appear before this Society with unusual humility; and secondly I neither knew, nor even saw Lord Boyd Orr.

Reading accounts of his life leaves me with an impression of a large person, both physically and intellectually, and a nutritionist whose prime concern was that his science should contribute to the betterment of mankind, and this at three levels: the international, the national and the personal.

The subject of my lecture might well therefore have interested him for a time, since it promises to contain elements bearing on all three of these concerns. Alas, as we shall see, the topic is a great deal more elusive than might appear, and it is likely that it would not have taken Lord Boyd Orr decades of his life, as it has taken me and many others, to discover the hopelessness of resolving the matter in purely nutritional or even scientific terms. I will try to explain this in my present valedictory lecture.

We will first try to define, in the sense that Humpty Dumpty used the word, the five terms in our title: Early Nutrition and Later Achievement. "When I use a word", Humpty Dumpty said, in a rather scornful tone, "it means just what I choose it to mean, neither more nor less" (Carroll, 1871).

By 'Early', I mean from conception into human toddlerhood. This includes the various stages of fetal life which, in physical growth and development, are nearly all imperceptibly continuous with the first two or three postnatal years, the main exceptions being in the respiratory and cardiovascular systems. It is sometimes forgotten that, for most developmental processes, birth is not the revolution that it is for the heart and lungs.

By 'nutrition' I think I mean food. I shall not be very much concerned primarily with any particular class of dietary constituents, nor with any single one, except to express scepticism, and this is likely to lose me the sympathy of some nutritionists. In this context I shall mainly mean 'undernutrition', scarcely a more precise term. The experimental approach to the problem has almost always used undernutrition, meaning a reduced amount of the whole diet, although at a time when it was widely believed that the

---

* Education is the greatest need of the people, but first they must be fed'. I am grateful to the late Herbert Birch for pointing this out to me on Danton's memorial in the Place de l'Odéon in Paris.

important shortage was of protein (McLaren, 1974), a specific protein malnutrition was imposed.

The word 'and' in our title implies, of course, a causal relationship between food and later achievement.

'Later', in this context, is deliberately vague. It carries a connotation of 'ultimate', and it is there mainly to absolve me from considering contemporaneous effects. Thus the very different behaviour, for example, of children with kwashiorkor and those with marasmus, does not concern us, since it is their outcome in the later life of the successfully treated child which we shall be discussing, and this has not been shown to differ between them. Nor will we discuss transient effects on mood, nor the somnolence which in me and many others accompanies satiety.

The final word in the title, 'achievement', is one which would have been abundantly clear to my grandmother, but for the scientist it sounds like a fudge. It is sometimes used to describe physical, or growth attainment; but here it is also a device for avoiding the terms 'intelligence' or 'intellect', which no one can meaningfully define either; and for avoiding the seductively simple expression 'I.Q.'. I.Q. is the product of two quite separate attributes: the capacity to perform an arbitrary task and, very importantly, the current motivation to do so. A widespread reluctance to remember the motivational component has led to its erroneous use outside behavioural science as a simple, numerical measure of intelligence itself, which can be conveniently fed into a computer analysis. In any case, there are many different tests of I.Q., all of them arbitrary, although most of them are reproducible. Differences between them, together with a wide range of degrees of motivation amongst the subjects at the time of testing, mean that I.Q. is *not* simply a measure of intelligence, whatever that may be.

It can therefore be said that our subject includes childhood malnutrition, the most widespread scourge inflicted by mankind on his own children and on their mothers, together with higher mental function, which in many ways is quite the most important of human attributes; and it is therefore small wonder that it has engaged the attention and the imagination of investigators, in several bursts of enthusiasm, since the turn of the century. We are now towards the end of the latest of these bursts, which began in the late 1950s and is only now being laid to rest: a period which coincides with my own life as an investigator. This paper is therefore valedictory. The earlier burst of research activity, in the first part of the century, was largely a response of scientists who themselves witnessed childhood poverty in their own communities, both here and in the United States; just as Boyd Orr himself did in Glasgow at the turn of the century, and later in what were our colonies (Boyd Orr, 1966).

Until fairly recently it was often assumed, and still is for many nutritionists, that malnutrition reduced the potential for later intellectual attainment by affecting the physical development of the brain. This may seem to be a reasonable hypothesis, but implicit in it is the dangerous assumption that higher mental function was exclusively mediated by the brain; as well as the even more doubtful corollary that any anatomical, compositional or biochemical changes shown to be imposed on the brain will inevitably be significant for intelligence.

Thus for many it seems that a statistically significant change in brain composition or metabolism which has been induced by dietary means, is inevitably significant in the more interesting sense: i.e. that it matters. Laboratory scientists understandably have a vested interest in the wider significance of their findings, but, especially since techniques

of measurement have become increasingly sensitive, it has become easier to demonstrate changes with statistical significance which nevertheless may still lack meaningfulness. It must not be automatically assumed that such findings 'matter', especially in the brain, where we still have almost no understanding of the physical basis of higher mental function. These two meanings of the word 'significant', the statistically so as opposed to the meaningful, have parallels in the two meanings of the word 'important' in France. '*Important*' in French still means 'to be of consequence' ('*qui est de conséquence*') (Robert, 1987) as it does in English; but it is more frequently used by the French to mean 'big': '*dont la mesure est grande*'. In calculating our P values we should, perhaps, reflect on this. At the same time we must agree that this very ignorance of the relation of brain composition to higher mental function should make us take such changes in composition seriously until they can be shown *not* to matter.

It seems to me that one example (and I could cite several) may be found in current thinking about dietary lipids and their effects on brain lipids, and hence, it is said, on intelligence. It is true that certain essential fatty acids are important components of brain membranes, structures which in turn are 'important' in the brain in the French, quantitative sense, and for all we know they may be the seat of the soul; but the latter remains to be shown, and seems to me doubtful. It is also true that some modifications in composition can be induced by extreme dietary manipulation, probably well outside ordinary human experience, though these are nothing like the rapid and dramatic changes that can be induced in the liver and in the more labile bodily fat outside the nervous system (Bourre *et al.* 1988). However, it cannot be assumed that such changes in the brain are significant to higher mental function until directly shown to be so, and this is where this corner of the subject becomes difficult.

The experiment is out of the question in humans, especially when we are interested in long-term effects. This is not only for ethical reasons, but also because of the long time scale of our lives, making it necessary to follow the results of early manipulation for at least a decade, and perhaps even longer, before a direct intellectual assessment can be usefully made. The same long duration of the experiment would also be required for the detection of long-term physical changes in human brain, but this can never be tested in our species. No human brains ever become available whose earlier histories are either known or appropriate to the enquiry, so there is no useful information anywhere, in either the anatomical or biochemical literature.

We must therefore consider using experimental animals of short lifespan for what may be a uniquely human question (Smart, 1987), and it is here particularly that non-behavioural scientists, including anatomists, biochemists and nutritionists, often rush in where the more instructed fear to tread. They rarely understand, and nearly always underestimate the complexity of the experimental behavioural science involved in the testing of behaviour in the long term. No biochemist would pay any attention to metabolic results obtained by untrained and inexperienced behavioural scientists: and yet they often seem quite happy to tackle experimental behaviour themselves, in the belief that running a maze for punishment or reward, chasing a rat from one side of a shuttle box to another with electric shocks, or setting an animal 'learning' tasks or even testing its intelligence, are easy and within their own capability. Experimental behaviour, including, and perhaps especially, in non-human species, is probably a much more complex discipline in the design, execution and interpretation of experiments than anything in biochemistry or nutrition; caveat amateur! Much of the extensive literature

in which those not properly familiar with behavioural technology purport to show that dietary manipulation directly affects performance, is glib and worthless: an observation which does not prevent a widespread, ready and eager acceptance of it. Such work is endlessly quoted to impress an equally uninstructed audience.

Claims that human intellect is affected by changing the dietary fatty acid spectrum has even descended on occasions to such ludicrous propositions such that, for example, Japanese children are more intelligent than British or American children because of the greater preponderance of fish in their diets. No parallel mention is made of Eskimo children, nor, more seriously, of the extreme difficulties of making cross-cultural assessments of intellect. P. G. Wodehouse is clearly still alive. I must confess, however, that I cannot explain the apparent coincidence that Jeeves was indeed given a diet rich in substances now known to be important brain membrane fatty acid constituents, a fact which cannot have been biochemically known to his master, his creator nor to the grandmothers of nations across the world, from China to England, whose identical folklore long antedated this.

Similar mythology has grown up around those amino acids which are the precursors of neurotransmitters. It simply will not do to say, as some have said, that because inborn errors of amino acid metabolism are known to be associated with severe mental retardation, that any amino acid in the diet of normal people may therefore have intellectual significance; nor that simply because neurotransmitters have important functions in the brain, that modification of their levels or metabolism may be expected also to have this sort of effect. To say that something 'may' be so is incontrovertible; anything 'may' be so. What is desperately required, and in my view is still lacking, is satisfactory direct evidence from competent and suitably humble behavioural scientists that it *is* so. Potentially interesting observations are there for the testing, not for concluding, but they must be tested properly to be credible.

Even at the simple, biochemical level, investigators have often ignored the extra-ordinary autonomy of the brain, especially of its developmental processes, in the face of widely fluctuating systemic levels of nutrients and precursors. The developing brain seems remarkably able to abstract materials necessary for its growth reasonably satisfactorily, and as a priority, even in the face of considerable systemic shortage. The blood–brain barrier is as facilitatory as it is sometimes restrictive, and is ill-named. We are touching here on what is presumably the basis for the phenomenon known as 'brain sparing', a term invented to express the very much smaller effect undernutrition has on the brain than on the body as a whole. At the same time, the term 'brain sparing' is itself an exaggeration, since brain size and composition during development can indeed be shown to be affected by undernutrition.

In the adult, starvation unto death has long been known to have astonishingly little effect on the physical brain (Dobbing, 1968) at a time when other tissues are profoundly affected, both in their composition, size and metabolism. However, it is equally well known that the developing brain does not have the same protection. There are periods of development when the brain is much more vulnerable to fluctuations in supply, including those produced by undernutrition, even though it is quantitatively less affected than other organs and tissues.

The discovery of these periods of vulnerability of the developing brain, approximating in timing to the duration of what came to be known as the brain growth spurt, was very exciting for those, like myself, who entered this field with an unashamed mixture of

emotional and scientific zeal. It had been missed during the first phase of research activity in the first quarter of the century. At that time experiments were usually not begun until the time of weaning in rats, since it was much easier to manipulate their diets after separating them from their mothers: and, after all, they had still to pass through the most rapid period of their bodily growth. The brain growth spurt in this species is over and the brain is already reaching its stage of adult invulnerability. Small wonder, then, that it seemed invulnerable. It was not realized that although the whole body growth spurt and that of other tissues is at its height in the few weeks after weaning, the weanling brain is almost adult. The negligible changes measured in these early experiments are probably responsible for the subject being abandoned for a time, until vulnerability of the developing brain of suckling rats was demonstrated later.

Reports from Kennedy (1957) and Widdowson & McCance (1960, 1963) in the late 1950s and early 1960s of the results of dietary manipulation in the suckling period were a great stimulus in the field of developmental undernutrition. They showed that early, postnatal growth retardation encompassing the suckling period in rats, led to permanent restrictions on the growth attainment of the whole body, and the same was later shown to be true for the brain itself. Plots of growth in brain weight as well as in its other compositional and structural components, identified the suckling period with the brain growth spurt, and it became clear that bodily, as well as brain vulnerability in this sense, coincided with the brain growth spurt period and not with the whole body growth spurt (Dobbing, 1968). That the same resetting downwards of the bodily growth trajectory almost certainly occurs in man has sometimes been denied, but mainly by those who have ignored the rules of proper cross-species extrapolation in their reasoning. The equivalent early experience in man to that of the early growth-restricted Widdowson and McCance rats from artificially large litters can only be estimated properly by obeying these rules (Dobbing, 1981a). Humans would have to be growth-restricted for most of the period from 30 weeks of gestation until about the second birthday to be analogous to these rats. By the same analogy restriction for short times within this period would be recoverable, as would restriction over the age of two, provided it was not too severe. As in other matters in developmental undernutrition, all three factors: the duration, severity and, above all, the timing, need to be taken into account in any extrapolation. The subject is important to our present discussion, since we are speaking of the effects on the brain of bodily growth restriction during the period of the brain growth spurt, which in humans covers the last trimester of gestation and at least the first two postnatal years (Dobbing & Sands, 1973).

Proper cross-species extrapolation during brain development (Dobbing, 1973; Dobbing & Sands, 1979) begins with a recognition that it is the *stage* of brain growth when undernutrition occurs which decides what is affected in the brain, and we will return to this; and that birth occurs at very different stages of brain growth from one species to another. The latter is another way of saying that the young of different species are born at very different stages of maturity. One has only to compare the immediate postnatal behaviour of the guinea-pig with that of the rat or mouse, all of them rodents: newborn rats and mice are naked, with their eyes closed, and very dependent, even for urination and defecation as well as for suckling, on maternal help; whereas the fully furred newborn guinea-pig with open eyes scarcely needs to suckle and can be hard to catch. The reindeer is born while the herd is on the march in the extreme weather conditions of the tundra in winter, and is able, of necessity, to keep up with the migrating herd from the start.

As might be expected the stage of brain development reached by birth in different species matches their apparent degree of maturity. To illustrate this it is necessary to outline very simply the stages through which the developing brain passes, since it is the components of each of these developmental stages which are affected by restrictions imposed at the time they normally occur.

Towards the end of the period of embryogenesis, which occupies the first trimester of human gestation, it is possible to detect the beginning of a new phase of brain cell multiplication which is thought to be that of the neuroblasts, the precursors of the nerve cells of the central nervous system (Dobbing & Sands, 1973). Almost all cell multiplication from about 10 to 12 weeks until about the 18th week of gestation concerns neuroblasts, so that when they eventually differentiate into neurons in mid-human gestation, the fetus already possesses the adult number of neurons. Subsequently, at about mid-gestation, the phase of glial cell multiplication begins, and continues well into the second human postnatal year (Dobbing & Sands, 1973). There are about eight times as many glial cells in the finished brain as there are neurons, so the glial multiplication phase is much larger. The majority of the glia, the oligodendroglia, are responsible for making the myelin sheaths, so myelination follows glial multiplication and mostly occurs postnatally in the human brain. At about the same time, and again mostly postnatally, the dendritic trees of the rather primitive neurons begin to grow, and over the first 2 years or so accomplish their extraordinary complex branching (Conel, 1939, 1955, 1959; Dobbing, 1981b). Concurrent with this is the establishment of synaptic connectivity. Quantitatively, the rat brain is said to have about 150 million neurons, and we know that many of them in the cerebral cortex have up to about 25 000 synpatic connections each (Bedi et al. 1980b). The human brain is about 700 times as large as that of the rat. This scheme of brain growth, and the astronomical figures just quoted, conceals an even greater complexity of the histological architecture and its heterogeneity from one small region of the brain to another, some of it accomplished by cell migration, as well as two other well-known facts: one, that each region or tract system passes through these stages of development at somewhat different times; and, two, that there is initially a substantial overproduction of cells, followed by the disappearance of a great many of them. Indeed the development of the brain seems to depend as much on the pattern of cell death as on that of their arrival and subsequent migration. At the same time, crude accretion rates in large brain regions, measured by means of chemical markers, allow us to discern the general scheme of development just outlined, in spite of the brain's developmental heterogeneity both in space and time (Dickerson & Dobbing, 1966a; Dobbing, 1968; Dobbing & Sands, 1970, 1973).

Thus we can speak, in crude, whole brain terms, of an early, relatively small phase of neuroblast multiplication, followed by a larger phase of glial proliferation, followed in turn by the period of myelination, with growth in dendritic complexity and the establishment of synpatic connectivity coinciding with and following these later phases (Dobbing, 1981c). An exception outside this general scheme is the phase of multiplication of the so-called microneurons of the cerebellum and hippocampus which is much later than that for most neurons.

Now, the same general rough sequence of development is found in all the species studied, and the individual histological units are similar, if not identical, from species to species. Mouse is distinguished for these purposes from man in its obviously very different degree of complexity in the final, mature product. For those obsessed with

brain size, or relative brain size, as a determinant of function, however, it may be devastating to learn that the brain of the mouse is relatively larger than that of man.

In rats and mice, with a 3 week gestation, neuronal multiplication mainly occurs before birth, and occupies the last week of gestation, except for those cerebellar and other microneurons which arrive postnatally. In man the same major phase occurs before mid-gestation, from about 12 to 18 weeks of gestation (Dobbing & Sands, 1973). Glial multiplication begins in the rat after birth and, together with the related phase of myelination, continues until about the time of traditional weaning at 21–25 d (Dobbing, 1968). In man the same phase begins at about 30 weeks of gestation and continues into the second postnatal year. In rats mature dendritic complexity is achieved by about 25 d; in man by about the second to third birthday (Conel, 1939, 1955, 1959). Expressed another way, the traditional weaning of the laboratory rat, at 21–25 postnatal days, corresponds to the stage of brain development reached by human children by approximately the second birthday. Rat birth corresponds to human mid-gestation, and birth in the human corresponds to about 5 or 6 postnatal days in the much faster-growing rat. In the guinea-pig, and presumably in the other praecocial species such as the reindeer, horse, sheep and cow, all these processes are virtually completed before birth.

The single, extremely important lesson for our present discussion from this digression on brain growth in different species is that, since the components of the developing brain are affected by nutritional growth restriction according to the stages of brain growth at the time of the undernutrition, one can only properly compare the stage in one species with the stage in another: and not age with age. The vulnerable brain growth spurt is entirely postnatal in the rat and prenatal in the guinea-pig: and in man it is perinatal, but much closer to the rat than to the guinea-pig. Even the sub-human primate is not much like man in the timing of its brain growth spurt, being much more mature at birth (Dobbing & Sands, 1979). All this has a crucial bearing on the design of experiments in different non-human species if the object is to extrapolate to the human.

This is not the place to catalogue the many aspects of brain growth which seem to be affected, permanently or not, only by growth retardation during the brain growth spurt period. It needs to be emphasized, however, as has been already mentioned, that for a structure or a process in the developing brain to be affected, the growth restriction must cover the period when that structure is arriving and accumulating or the process developing. The brain does not grow like a crystal grows, as R. A. McCance would say, an adage which is even more true of the brain than of the body as a whole. It follows a complex but orderly sequence in the building up and interlinking of its myriad components, and only the parts of the sequence which coincide with the restriction are affected by it.

In this there are close parallels with teratology. In both cases the most important feature is the timing of the insult in relation to the normal timing of developmental events, rather than the nature of the insult, which can be a whole range of apparently unconnected things. There are several interesting differences, however, which may be more apparent than real: in the brain the insult may occur at any time throughout its development, during fetal life and as late as about the second birthday in humans; it is a late, and prolonged teratology. Classical teratology is a matter for the first trimester. Also the nutritional insult to the brain throughout this period must be applied for a duration corresponding closely to the duration of the process being affected, compared with the very short exposure to insults required during embryogenesis. At all events the

concept we derived from our teachers that teratology was a matter of gross malformation resulting from an insult in the first trimester of our existence is now a limited one. In the brain a later teratology results, not in gross malformations, but in a more subtle distortion of the architecture, combined with deficits in quantity.

This led me to describe the neuropathology of nutritional growth restriction as one of deficits and distortions. A good example to explain this is the effect of properly timed undernutrition on the cerebellum, a part of the brain which grows much faster than the rest, and therefore over a shorter period (Dickerson & Dobbing, 1966b). Nutritional growth restriction of the whole brain during the brain growth spurt leads to a permanently smaller brain, but the cerebellum is considerably more reduced in size than is the brain as a whole (Dobbing et al. 1970). There are therefore deficits in both brain and cerebellum, but it may be more important functionally that there is a gross distortion of their quantitative relationships. A similar distortion follows X-irradiation (Dobbing et al. 1970) as well as corticosteroid treatment during the brain growth spurt (Howard, 1968). The cerebellum provides one other good illustration of the deficit and distortion pathology, this time in its histology. It has two phases of neuronal multiplication: one concerns its macroneurons, the Purkinje cells amongst them, and these arrive at the same time as most of the other brain neurons, before mid-gestation in humans. The other period of neuroblast multiplication concerns the microneurons, and is much later. Unlike the main phase it is a component of the brain growth spurt. It might be expected, there-fore, that the effects of undernutrition during the brain growth spurt would selectively reduce the number of microneurons in the cerebellum, and would spare the number of Purkinje cells, so that in the mature brain there would be a distortion of the quantitative relationship between the two types: and this in fact does happen (Bedi et al. 1980a).

Before leaving our discussion of the nature of the neuropathology of nutritional growth restriction, it is worth emphasizing that these examples in the cerebellum are gross, and have only been possible to detect because of the ease with which the region can be anatomically defined and dissected out. Its architecture also has a very much simpler geometry than most others in the brain. Other systems, such as the hippocam-pus, for example, which is also a site of late proliferation of microneurons, is much less easy to treat in this way, since it is anatomically less well defined, and has scarcely been investigated, although effects on it may be functionally much more important.

Notice also in passing that the deficit and distortion pathology is very much more difficult to detect, since it requires very laborious quantitative neurohistology of a kind which is quite beyond the scope of general pathology. Notice further that the easy-to-detect lesion pathologies, consisting of foci of damage or their scars, are never caused by undernutrition. This is why, in the underprivileged world, one does not find a profusion of physical neurological focal signs, since these are the consequence of focal damage.

Not all the effects produced by early restrictions are irrecoverable. Some appear to be so, but others recover slowly, and some even seem to recover completely. If we knew which of them were significant for higher mental function we would be in a better position to interpret these findings in behavioural terms. As it is we do not know whether it matters to have a few lamellae permanently missing from the myelin sheath, a less-than-usual number of glial cells, a slightly different fatty acid composition of myelin or neuronal membranes, a reduction of the complexity of dendritic branching (McConnel & Berry, 1977, 1978) or a profound but temporary shortage of synapses per neuron (Thomas et al. 1980). We may suspect that this short list has been cited in

ascending order of importance, such that slightly slimmed down myelin may be less functionally important, if at all, than a shortage of glia; in turn than a very slightly changed membrane structure: the myelin deficits could presumably occur without any change in its insulatory properties, nor in the more important spacing of the nodes of Ranvier which is responsible for nerve impulse conduction. Dendritic complexity and synaptic connectivity sound much more likely requirements for good function, but we have little but our suspicions to work with.

We have mentioned the astronomical number of structures in the brain, as well as the incredible complexity of their histological arrangement. Many bodily organs and tissues are known to have immense functional reserve, and the same may well be true of the brain, although such comparisons with liver or kidney, for example, may be dangerous in the face of the striking relative heterogeneity of structure in the brain. Removing half the liver, or replacing much of it with metastases, may have very little effect on liver function, but removing special, tiny parts of the brain can certainly be devastating in a way that the removal of a similar proportion of liver would not be noticed. Nutritional experiments have only been able to consider gross quantities in major regions, or in the brain as a whole, and it may well be that the deficits we have been able to demonstrate are quite unimportant to function. We simply do not know.

More important, as we have said, we know nothing of what to look for in the histology, any more than in the biochemistry, if we are interested in intellect. Certainly brain size, which is the most permanently affected by suitable early nutrition, may be of no significance whatever, provided it is appropriate in size for the body in which it is found. No one would seriously suggest that a ranking of brain size amongst members of this audience would tell us anything about your relative intellectual capacity; or that the intellectual function of women is in any way related to the smaller average size of their brains, appropriate as it is to the smaller lean body mass. Microcephaly is known to be associated with a severe degree of mental retardation, but for this to be true, microcephaly must itself be severe, and properly defined as a brain considerably smaller than it should be for the body size: not merely a small brain on the centile charts for age. Paediatricians particularly are prone to misinterpret the significance of 'small' brains, since severe microcephaly is of more significance to them. They also often misinterpret the meaning of small full-term newborns and small people. Five per cent of all babies are below the fifth centile, and are by definition normal. It is only those who are abnormally so who should detain us, and in the case of the brain, and excluding obvious lesions in it, this mainly means those whose small brains are abnormally so for the body size.

Even the number of nerve cells in a brain, within quite wide limits, may not be significant for mental function, compared, for example, with their disposition, their degree of dendritic branching or their synaptic connectivity. We simply do not know. However, we do know that almost all the adult nerve cell number is produced before mid-pregnancy in the human (Dobbing & Sands, 1973), at a period of fetal growth which is not affected by maternal undernutrition. Nerve cell number should therefore be out of the reach of undernutrition. It is not until later, in the early third trimester of gestation, that the fetus begins to be affected in its bodily growth, and this happens also to be the beginning of the human brain growth spurt. Therefore, by analogy with animals, general maternal undernutrition will affect fetal nerve cell numbers in rats, which arrive in the last one-third of gestation, but not in humans. This is as well for us, since nerve cell multiplication is one of the developmental processes for which there is a once-only opportunity as mentioned above. A threat to it, by such environmental factors as viruses,

toxins, anti-mitotic drugs and irradiation are likely to reduce nerve cell number irrevocably and may even be a root cause of true microcephaly (Dobbing, 1984a,b). No nutritional factor or shortage has ever been shown to affect nerve cell numbers, but only glial cells and microneurons; any more than undernutrition has ever been shown to produce brain damage, by which we mean lesions, in otherwise normal individuals. An exception may turn out to be the possible effect of certain vitamin deficiencies at a specific time during embryogenesis on neural tube closure (Dobbing, 1983), although this will have to be shown to be a direct effect of vitamins on nerve cells to deny the above generalization, and that is almost certainly not the case. Wernicke's encephalopathy, in which lesions are specially related to deficiencies in B group vitamins, may be another rare exception, but it does not reach detectable proportions amongst the masses of malnourished people in the underprivileged world. Growth in dendritic complexity and synaptic connectivity is known to be reduced substantially by properly timed undernutrition in experimental animals (McConnel & Berry, 1977, 1978; Bedi et al. 1980a,b), and the same is likely in humans. These are predominantly postnatal processes in our species (Dobbing, 1981b), coinciding with the greater part of the brain growth spurt when human malnutrition is common. The large deficit in numbers of synapses per neuron in undernourished animals is thought, however, to be recoverable (Thomas et al. 1980): which is not to say that even a temporary deficit will not be without later significance to educational attainment.

For an enormous literature on the detailed effects on the physical brain of early undernutrition I refer you to the library (Dobbing, 1981b,c,1984b). There is little question about the effects: only about their functional significance.

As I have repeatedly said, effects on achievement can only be investigated directly, by competent behavioural scientists who, however, may often be as poorly versed in nutrition as are nutritionists in experimental behaviour. A little respectful collaboration is all that is required.

The difficulties in investigating the long-term behavioural outcome of early undernutrition in experimental animals are in many ways the same as those encountered in human field studies. The single greatest obstacle is the problem of distinguishing a specific nutritional cause for the undoubted behavioural differences encountered in both previously undernourished animals (Katz, 1982; Rogers et al. 1985; Smart, 1986, 1987) and people (Galler, 1987). Such is the complexity of the array of other, interdependent, non-nutritional confounding factors in the environment of early-undernourished subjects, all of which are perfectly capable of producing similar behavioural changes, that an analysis of them is probably impossible, even when the most sophisticated techniques are used. At least that is my view. I cannot see how any multivariate analysis can produce convincing answers when the different factors themselves can be neither separately identified, nor quantified. Even if an analytical method allows an unidentified residue, the identified components can only be scored arbitrarily by making unwarranted assumptions which may invalidate the answer. For example, how does one quantify social class, itself an enormous, heterogeneous galaxy of different aspects of underprivilege? How is another collection of powerful influences, the real quality of the home, to be expressed? There have been valiant attempts to produce scores, or indices, but these have often only lulled us into a glib acceptance of them without contributing much to the subject. To what extent does acute and chronic disease in third world children, never far from their ordinary existence, compromise their eventual achievement,

recognizing that it is not just the fact of it which is likely to be important, but also its nature, its duration, severity and timing, and that this will vary from one child to another? When parents are themselves quite ignorant of even the simplest principles of hygiene, nutrition and education and their importance, how can one quantify the influence of this on their children's future achievement, bearing in mind that only quantification can contribute to a multifactorial analysis?

In underprivileged societies, parents, often especially mothers, have insufficient time to stimulate, care for and educate their children, even if they realize its importance. Mothers are often the main work force, both in the home and outside, and there is often little incentive to have fewer children, since the more children the greater the family work force, a situation continuously conspiring to prevent improvement.

Many investigators have thought a great deal about the influence of the degree of impoverishment or enrichment of the emotional and psychological environment, in early childhood, which is likely to be a large influence on later achievement. Animal experiments which have shown that enrichment or impoverishment interacts with poor or satisfactory nutrition, either synergistically or by compensation to produce morphological changes in the brain (Katz *et al.* 1980, 1982; Davies & Katz, 1983; Katz & Davies, 1983, 1984), have sometimes been criticized (Bedi & Bhide, 1988). Functionally, however, the idea has a ring of truth, judged by several observations in humans. Severe malnutrition at all the 'right' times, as a consequence of paediatric disease (Lloyd-Still, 1976), can leave the otherwise privileged child apparently untouched. The same is true even when the underprivileged previously malnourished third world child is subsequently adopted into rich, middle class America (Winick *et al.* 1975): while non-physical, non-nutritional emotional deprivation can apparently act synergistically with undernutrition to reduce achievement. It is therefore very difficult to identify a specific role for nutrition behind the very common deficits in the later achievement of malnourished children in globally impoverished communities (Grantham-McGregor, 1987).

I learnt a great deal about many of these things at the feet of the best respected field investigators of the 1960s and 1970s, as well as from my colleagues who are experimental behavioural scientists. In North, Central and South America, the likes of Birch, Cravioto, Richardson, Tizard and Monckeberg (Cravioto *et al.* 1966; Hertzig *et al.* 1972) spent many years reliably showing us that previously malnourished children performed demonstrably and importantly less well than their relatively non-malnourished friends. But why was this? As we have seen, children in a community who came to suffer from malnutritional disease were mostly those who also suffered from its non-nutritional, social and family concomitants. The really malnourished children have the least competent parents, the dirtiest and poorest homes, both materially and intellectually, and therefore the greatest exposure to disease and environmental impoverishment: indeed a shortage of food may well have been amongst the least of their problems. Evidence for this comes from the realization that nutritional rehabilitation by no means always produces a happy behavioural outcome, unless it is accompanied by appropriate environmental 'stimulation', which in many cases can simply mean playing with children and being nice to them. Anyone who doubts the effects that kindness may have on physical growth, almost regardless of dietary intake, and almost certainly without any changes in the brain, should read the extraordinary story by Widdowson about the two post-war German orphanages (Widdowson, 1951).

I have not mentioned the possibility of inherited behaviour, since I do not like to

accept that it is important in either the French or the English sense. We know something, at least from animals, of the so-called 'maternal' (Smart, 1983) and even 'grand-maternal effect', by which behavioural traits which are environmentally induced in a female rat can be transmitted at least in part across one or more generations, and will be mistaken by the ignorant or even the ill-intentioned as inherited. Certainly the effects of a culture, whether local or regional, are powerful influences on people's later attitudes and reasoning. They are probably frequently confused with inherited traits, and are also likely to confuse any investigation based on our own, somewhat more predictable cultures. If I resemble my father in my ways of thinking and my mannerisms, could it not be that I copied him for nearly 50 years?

Most of what we have discussed stems from a concern for the problems of mal-nourished children in impoverished communities throughout the world; but can it have any implications for our own more privileged society?

I will first mention two issues of current, and perhaps evanescent interest. We have recently seen an eager acceptance in some quarters of two claims: one that vitamin and mineral supplements in British children's diets (Benton & Roberts, 1988; Naismith *et al.* 1988), and the other that very small doses of lead from petrol exhaust fumes, are important to 'intelligence'. A not unrelated issue, though a rather more nebulous one than these two, is does the processed food we all eat contain additives which affect children's behaviour and even their intelligence? From what I have said about the extreme difficulties in measuring such an ill-defined commodity, especially epidemi-ologically in large samples untrammelled by the multitude of confounders in everyone's environment, I believe that none of these propositions has yet been satisfactorily established, and some border on the cranky. Perhaps my beliefs are not relevant, but similar considerations have not deterred others from exercising their own. The greater the public, political, commercial and scientific thirst for such information, the lower it seems is the level of criticism which is applied to the evidence. For the beneficial effects of vitamin and mineral supplementation on intelligence the evidence is so scanty and preliminary that it would probably not have been accepted for publication in any more rigorous scientific field (Bates *et al.* 1988; Benton & Roberts, 1988; Emery *et al.* 1988; Naismith *et al.* 1988); whereas in the case of Pb there is only one recent study (Fulton *et al.* 1987) amongst many other very careful ones (Medical Research Council, 1988*a,b*) which shows any significant correlation at all between exposure to Pb and scores in various estimations of I.Q. The excessive Pb found in these particular children came largely from the water supply, with only a very tiny fraction coming from petrol, and there are several other factors which make the data difficult to interpret. In the first case parents have promptly rushed to buy the vitamin pills, since who could resist a promise that their children's intelligence can be boosted by them? The second example is being used to support a case for a nationwide change to unleaded petrol, a move of great benefit to the platinum industry, although the case may be strong on other grounds. In both cases, however, there is a background of truly deleterious effects of severe vitamin deficiency disease and of massive Pb poisoning, and this has no doubt influenced people's attitudes to relatively tiny versions of the same phenomena.

Leaving popular belief, and turning to more analogous examples of nutritional growth retardation in children in our own community, we are immediately up against all the same difficulties, with the same confounding factors we have seen when considering the much more severe examples in the children in the underprivileged third world.

As far as I know, there is no evidence for fetal growth restriction being caused by maternal undernutrition during the first two-thirds of gestation in any mammalian species. In the last trimester, however, there are abundant indications that it is, certainly in non-human species, but also in some circumstances in humans (Lechtig & Klein, 1981). In general 'small-for-dates' babies due to maternal undernutrition may be born to mothers with an energy intake habitually below a certain threshold, this being influenced by an habitual high energy output and close birth spacing. It is therefore plausible that the lower birth weights in large, seriously impoverished populations of mothers engaged in hard manual labour, should be largely due to poor nutrition. There is, however, a multitude of other environmental and obstetric factors in these surroundings, as well as in our richer countries, which contribute to third trimester growth retardation, chief amongst them in our own country being maternal smoking. It is highly unlikely that maternal undernutrition accounts for many British small-for-dates babies, and much of the reason is the priority which has been arranged for fetal growth in the pregnant mother's metabolic economy, together with our cultural practice of reasonable birth spacing and smaller numbers of children.

However, the other environmental contributors to intra-uterine growth retardation may also act by effectively depriving the fetus of an adequate nutritional supply, so that the question is still theoretically open. Two things lead me largely to discount smallness-for-dates as a serious restriction on later achievement (Dobbing, 1985), other than what we might call 'fetal sparing'. Within the fetus there is the second, similar protection for fetal brain growth which we have called 'brain sparing', so that brain size and functional maturity are comparatively little affected. Indeed the head at birth is disproportionately large in these babies, due to the much greater effect of the restriction on the rest of the body. Secondly, with the important proviso that the conditions into which the child is born are reasonably favourable, there is an in-built tendency for the small-for-dates newborn to embark on a prompt postnatal catch-up trajectory, and for a normal size to be achieved well within the period of the brain growth spurt. At the same time there does seem to be a tendency for children who were born small-for-dates to be minimally clumsy in later life, and for their growth attainment to be sometimes reduced, and it has been claimed (Fogelman & Manor, 1988) that a small intellectual deficit may also be detected in later life; but these are observations on large populations, and we cannot know individual circumstances. I have often wondered if a selective effect on the cerebellum, comparable with that mentioned above in undernourished experimental animals, might sometimes be responsible.

Prematurely born babies have their own reasons, connected with their physiological immaturity, for sustaining brain damage, but if this is avoided, and provided their management promotes adequate proper growth, there is no obvious reason why they should be affected by the neuropathology of nutritional growth restriction we have described. 'Proper growth' implies reasonable conformity to normal bodily composition, as well as increase in size.

Intra-uterine growth retardation before the third trimester, which is a common accompaniment, for example, of congenital malformations and chromosome disorders, may well affect the early second trimester phase of neuronal multiplication, which undernutrition cannot do, and this may be responsible for the much more serious neurological and intellectual deficits often found in such cases.

Except for the last case, it seems to be an advantage for the human species that most of

its brain growth spurt is postnatal, giving us an opportunity, as well as a duty, to promote good brain growth in the first two postnatal years, by promoting good bodily growth; and much of this promotion is therefore indirectly nutritional.

What, then, of the future?

I am one of those who think that yet more studies in human third world communities are unlikely to be illuminating of our question, even though our subject, or our main interest in it, is a particularly human one. Its enormous complexity defies analysis. I think such matters as the interplay between the non-nutritional environment, such as its enrichment and impoverishment, and nutrition can still be profitably further explored in experimental animals. Another non-nutritional set of confounding influences on later achievement comes from the impoverished mother, and even the grandmother: and the new techniques of artificial rearing of both experimental animals and their controls can theoretically help to control these. This matter is quite impossible to investigate in humans.

I think there are likely to be great dividends from more investigation by neuro-anatomists using quantitative neurohistology, but their techniques are enormously laborious, even when automated, and it is most unlikely that they can ever be applied to humans. It is possible that a greater use of modern, non-invasive imaging and other investigative techniques would get useful results in future human field studies, but I do not see precisely how. And after all this we will still not have bridged that chasm of ignorance between effects of undernutrition on the brain and their possible relation to behaviour. I think Danton understood very well. Of course early undernutrition is important, for all sorts of reasons, but not so specifically for the brain or behaviour. It is what he called 'education', which, in his language is defined as the proper means of assuring the good development of a human being (Robert, 1987), that is quite the most powerful influence. The Shorter Oxford Dictionary, however, defines education even more interestingly as 'the process of nourishing and rearing'.

How much further are we than merely being able to pronounce, rather obviously, that we should feed children? Not much, I fear. I think there are some beginnings of scientific dividends, but there are two generalities of practical importance which might not have been so obvious if we had not done all this work: the fact that there are periods of especial vulnerability, which in the present state of knowledge, and in the present chronic shortage of food, should lead us to pay particular nutritional and other attention as a priority to fetuses and children of those special ages; but perhaps most important of all, the paramount need to accompany our nutritional and other physical relief efforts with encouragement for everybody to stimulate the children: in other words to be ordinarily nice to them as a means of promoting both their physical and their future higher mental well-being.

REFERENCES

Bates, C. J., Thurnam, D. I. & Powers, H. J. (1988). Letter. *Lancet* **i,** 407.

Bedi, K. S. & Bhide, P. G. (1988). Effects of environmental diversity on brain morphology. *Early Human Development* **17,** 107–144.

Bedi, K. S., Hall, R., Davies, C. A. & Dobbing, J. A. (1980a). Stereological analysis of the cerebellar granule and Purkinje cells of 30-day-old and adult rats undernourished during early postnatal life. *Journal of Comparative Neurology* **193,** 863–870.

Bedi, K. S., Thomas, Y. M., Davies, C. A. & Dobbing, J. (1980b). Synapse-to-neuron ratios of the frontal and cerebellar cortex of 30-day-old and adult rats undernourished during early postnatal life. *Journal of Comparative Neurology* **193,** 49–56.

Benton, D. & Roberts, G. (1988). Effect of vitamin and mineral supplementation on intelligence of a sample of school children. *Lancet* i, 140–143.

Bourre, J.-M., Bonneil, M., Dumont, O., Piciotti, M., Nalbone, G. & Lafont, H. (1988). High dietary fish oil alters the brain polyunsaturated fatty acid composition. *Biochimica et Biophysica Acta* **960**, 458–461.

Boyd Orr, J. (1966). *As I Recall*. London: MacGibbon & Kee.

Carroll, L. (1871). Chapter VI, Humpty Dumpty. In *Through the Looking Glass*.

Conel, J. L. (1939, 1955, 1959). *The Postnatal Development of the Human Cerebral Cortex*, volumes I, V and VI, Figs 36, 28 and 24 respectively. Cambridge, Mass: Harvard University Press.

Cravioto, J., de Licardie, E. R. & Birch, H. G. (1966). Nutrition, growth and neurointegrative development: an experimental and ecologic study. *Pediatrics* **38**, 319–372.

Davies, C. A. & Katz, H. B. (1983). The comparative effects of early life undernutrition and subsequent differential environments on the dendritic branching of pyramidal cells in rat visual cortex. *Journal of Comparative Neurology* **218**, 345–350.

Dickerson, J. W. T. & Dobbing, J. (1966a). Prenatal and postnatal growth and development of the central nervous system of the pig. *Proceedings of the Royal Society, B* **166**, 384–395.

Dickerson, J. W. T. & Dobbing, J. (1966b). Some peculiarities of cerebellar growth. *Proceedings of the Royal Society of Medicine* **59**, 1088.

Dobbing, J. (1968). Effects of experimental undernutrition on development of the nervous system. In *Malnutrition, Learning and Behaviour*, pp. 181–202 [N. S. Scrimshaw and J. E. Gordon, editors]. Boston: M.I.T. Press.

Dobbing, J. (1973). The developing brain: a plea for more critical interspecies extrapolation. *Nutrition Reports International* **7**, 401–406.

Dobbing, J. (1981a). Vulnerable periods in somatic growth. In *Infant and Child Feeding*, pp. 399–411 [J. T. Bond, L. T. Filer, G. A. Leveille, A. Thomson and W. B. Weill Jr, editors]. New York: Academic Press.

Dobbing, J. (1981b). Nutritional growth restriction and the nervous system. In *The Molecular Basis of Neuropathology*, pp. 221–233 [R. H. S. Thomson and A. N. Davison, editors]. London: Edward Arnold.

Dobbing, J. (1981c). The later development of the brain and its vulnerability. In *Scientific Foundations of Paediatrics*, 2nd ed., pp. 744–759 [J. A. Davis and J. Dobbing, editors]. London: Heinemann.

Dobbing, J. [editor] (1983). *Prevention of Spina Bifida and Other Neural Tube Defects*. London: Academic Press.

Dobbing, J. (1984a). The pathogenesis of microcephaly with mental retardation. In *Effects of Prenatal Irradiation with Special Emphasis on Late Effects*, pp. 199–212 [C. Streffner and G. Patrick, editors]. Commission of the European Communities, Radiation Protection, Report no. EUR 8067EN.

Dobbing, J. [editor] (1984b). Pathology and vulnerability of the developing brain. In *Scientific Studies in Mental Retardation*, pp. 89–106. London: Royal Society of Medicine. and Macmillan Press.

Dobbing, J. (1985). Maternal nutrition in pregnancy and later achievement of offspring: a personal interpretation. *Early Human Development* **12**, 1–8.

Dobbing, J., Hopewell, J. W., Lynch, A. & Sands, J. (1970). Vulnerability of developing brain: 1. Some lasting effects of X-irradiation. *Experimental Neurology* **28**, 442–449.

Dobbing, J. & Sands, J. (1970). Growth and development of the brain and spinal cord of the guinea pig. *Brain Research* **17**, 115–123.

Dobbing, J. & Sands, J. (1973). The quantitative growth and development of the human brain. *Archives of Disease in Childhood* **48**, 757–767.

Dobbing, J. & Sands, J. (1979). Comparative aspects of the brain growth spurt. *Early Human Development* **3**, 79–83.

Emery, P. W., Nelson, M., Geissler, C. G., Sanders, T. A. B., Judd, P. A., Thomas, J. E. & Naismith, D. J. (1988). Letter. *Lancet* i, 407.

Fogelman, K. R. & Manor, O. (1988). Smoking in pregnancy and development into early childhood. *British Medical Journal* **297**, 1233–1236.

Fulton, M., Raab, G., Thomson, G., Laxen, D., Hunter, R. & Hepburn, W. (1987). Influence of blood lead on the ability and attainment of children in Edinburgh. *Lancet* i, 1221–1226.

Galler, J. R. (1987). The interaction of nutrition and environment in behavioural development. In *Early Nutrition and Later Achievement*, pp. 175–207 [J. Dobbing, editor]. London: Academic Press.

Grantham-McGregor, S. (1987). Field studies in early nutrition and later achievement. In *Early Nutrition and Later Achievement*, pp. 128–174 [J. Dobbing, editor]. London: Academic Press.

Hertzig, M. E., Birch, H. G., Richardson, S. A. & Tizard, J. (1972). Intellectual levels of school children severely malnourished during the first two years of life. *Pediatrics* **49**, 814–824.

Howard, E. (1968). Reductions in size and total DNA of cerebrum and cerebellum in adult mice after corticosterone treatment in infancy. *Experimental Neurology* **22**, 191–208.

Katz, H. B. (1982). Superior learning performances by malnourished animals? In *Psychophysiology*, pp. 140–145 [R. Sinz and M. R. Rozenzweig, editors]. Amsterdam: Elsevier.

Katz, H. B. & Davies, C. A. (1983). The separate and combined effects of early undernutrition and environmental complexity at different ages on cerebral measures in rats. *Developmental Psychobiology* **16**, 47–58.

Katz, H. B. & Davies, C. A. (1984). Effects of differential environments on the cerebral anatomy of rats as a function of previous and subsequent housing conditions. *Experimental Neurology* **83**, 274–287.

Katz, H. B., Davies, C. A. & Dobbing, J. (1980). The effect of environmental stimulation on brain weight in previously undernourished rats. *Behavioural Brain Research* **1**, 445–449.

Katz, H. B., Davies, C. A. & Dobbing, J. (1982). Effects of undernutrition at different ages early in life and later environmental complexity on parameters of the cerebrum and hippocampus in rats. *Journal of Nutrition* **112**, 1362–1368.

Kennedy, G. C. (1957). The development with age of hypothalamic restraint upon the appetite of the rat. *Journal of Endocrinology* **16**, 9–17.

Lechtig, A. & Klein, R. E. (1981). Pre-natal nutrition and birth weight: is there a causal association? In *Maternal Nutrition in Pregnancy: Eating for Two?*, pp. 131–174 [J. Dobbing, editor]. London: Academic Press.

Lloyd-Still, J. D. (1976). Clinical studies on the effects of malnutrition during infancy and subsequent physical and intellectual development. In *Malnutrition and Intellectual Development*, pp. 48–61 [J. D. Lloyd-Still, editor]. Lancaster: MTP Press.

McConnel, P. & Berry, M. (1977). The effects of undernutrition on Purkinje cell dendritic growth in the rat. *Journal of Comparative Neurology* **177**, 159–172.

McConnel, P. & Berry, M. (1978). The effect of refeeding after neonatal starvation on Purkinje cell dendritic growth in the rat. *Journal of Comparative Neurology* **178**, 759–772.

McLaren, D. S. (1974). The great protein fiasco. *Lancet* ii, 93–96.

Medical Research Council (1988a). *The Neuropsychological Effects of Lead in Children: A Review of Recent Research, 1979–1983*. London: Medical Research Council.

Medical Research Council (1988b). *The Neuropsychological Effects of Lead in Children: A Review of Recent Research, 1984–1988*. London: Medical Research Council.

Naismith, D. J., Nelson, M., Burley, V. J. & Gatenby, S. J. (1988). Can children's intelligence be increased by vitamin and mineral supplements? *Lancet* ii, 335.

Robert, P. (1987). *Le Petit Robert*. Paris: Dictionnaires Le Robert.

Rogers, P. J., Tonkiss, J. & Smart, J. L. (1985). Incidental learning is impaired during early-life undernutrition. *Developmental Psychobiology* **19**, 113–124.

Smart, J. L. (1983). Undernutrition, maternal behaviour and pup development. In *Parental Behaviour of Rodents*, pp. 82–96 [R. W. Elwood, editor]. Bristol: John Wiley.

Smart, J. L. (1986). Undernutrition, learning and memory: review of experimental studies. In *Proceedings of the XIII International Congress of Nutrition 1985*, pp. 74–78 [T. G. Taylor and N. K. Jenkins, editors]. London: John Libbey.

Smart, J. L. (1987). The need for and the relevance of animal studies of early undernutrition. In *Early Nutrition and Later Achievement*, pp. 50–85 [J. Dobbing, editor]. London: Academic Press.

Thomas, Y. M., Peeling, A., Bedi, K. S., Davis, C. A. & Dobbing, J. (1980). Deficits in synapse-to-neuron ratio due to early undernutrition show evidence of catch-up in later life. *Experientia* **36**, 556–557.

Widdowson, E. M. (1951). Mental contentment and physical growth. *Lancet* i, 1316–1318.

Widdowson, E. M. & McCance, R. A. (1960). Some effects of accelerating growth. 1. General somatic development. *Proceedings of the Royal Society, B* **152**, 188–206.

Widdowson, E. M. & McCance, R. A. (1963). The effect of finite periods of undernutrition at different stages on the composition and subsequent development of the rat. *Proceedings of the Royal Society, B* **158**, 329–342.

Winick, M., Meger, K. K. & Harris, R. C. (1975). Malnutrition and environmental enrichment by early adoption. *Science* **190**, 1173–1175.

Printed in Great Britain