

## **Nutritional science in medicine / Sir Edward Mellanby.**

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### **Publication/Creation**

[Place of publication not identified] : [publisher not identified], 1944?  
[(Colchester) : [Spottiswoode, Ballantyne.]]

### **Persistent URL**

<https://wellcomecollection.org/works/k9dbpgcy>



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## NUTRITIONAL SCIENCE IN MEDICINE

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Nutritional research has now come to occupy a dominant position in the study of problems both of health and of biological science. In regard to disease, it began as a small flame in 1897, when Eijkman correlated his observations on beri among Javanese prisoners with his experimental results on polyneuritis gallinarum, finding that these conditions in man and bird were both due to the consumption of polished rice, and preventable by addition of the pericarp of the grain. The flame was fanned by Holst and Frölich in 1907, when they studied scurvy in guinea-pigs and found it could be prevented and cured by something in fresh vegetables and fruits. As both beriberi and scurvy were then seen in western countries, the average medical man was not particularly interested in these clinical discoveries. It was only in 1918, when it was shown by experiments on dogs that rickets, one of the most common diseases of childhood, was due to the absence from the diet of a fat-soluble substance associated with fish and animal fats, that the importance of diet in relation to human health and disease was appreciated.

### **Cognition of Dietary Deficiency as a Cause of Disease**

From 1920 onwards, the flame of dietetic and nutritional research became a fire extending over all countries of the world. In particular, the idea of "deficiency diseases"—diseases due to the absence from the body of specific chemical substances—was generally accepted. It was realized that, for the maintenance of health, certain vitamins and other accessory factors must be present in the food in



sufficient quantities, as the animal body was either incapable of synthesizing them, or its power in this respect was limited.

It is now known that this idea of "deficiency diseases" is not always so simple as when Grijns first formulated it in 1901, and that there are other dietetic and nutritional factors which often determine the development of such illnesses. Thus, the amount of aneurin necessary to prevent beriberi and allied conditions is governed by the amount of carbohydrate or alcohol also consumed; similarly the amount of vitamin D necessary to produce perfect calcification of bone and teeth is conditioned by the amount of calcium and phosphorus in the food and their relationship to one another. In other words, there are sometimes positive as well as negative factors to be taken into account in such diseases.

It would be unfair, in recording the successes that have followed the establishment of "deficiency disease" as a factor in animal and human life, to forget that the idea of such an ætiology had been advanced so long ago as 1817 by Chatin, following extensive estimations of iodine in foodstuffs, when he related the development of simple goitre to a deficient intake of iodine. This hypothesis was, however, formally suppressed by the French *Académie des Sciences* in 1860. The recognition, as a result of the discoveries of Pasteur, Lister and Koch, that a major cause of disease was the invasion of the body by micro-organisms, was responsible for an outlook which made it difficult, and at times apparently impossible, to imagine a deficiency or an excess of something from the body as being a cause of disease. It was only the discovery by Baumann in 1895 of iodine in the thyroid gland that allowed the resuscitation of Chatin's original hypothesis of the cause of thyroid enlargement. Research from that time has more and more confirmed his views.

If this disregard of dietary deficiency as a factor in disease were the only suppressive effect that could be ascribed to Pasteur's remarkable work, it would probably not be sufficiently important to stress here, but it must also be remembered that it had a similar influence on the attitude towards Bernard's hypothesis that many diseases are due to



abnormal working of bodily processes which, when physiological or optimal, result in good health. It will be remembered that Claude Bernard claimed, on this basis, that medical science was essentially experimental physiology. This again was an overstatement of the case, but the success of the *matrices morbi* hypothesis, as achieved by Pasteur, Lister and Koch, again delayed, but did not prevent, the ultimate acceptance of Bernard's hypothesis. Indeed the development of research on "deficiency diseases" has tended only to emphasize the truth of the Bernard teaching.

### Dangers of a Specialized Outlook

There is surely a lesson to be learnt from these historical facts—namely, that we must avoid allowing the very success of research on the relation of nutrition and disease to cloak and possibly even to suppress, temporarily at least, other pathological hypotheses and theories. The specialist is the backbone of medical, as of all research, but the concentration that leads to discovery is apt to be associated with blindness to other views, and this must be guarded against. Probably the danger is not so great nowadays, when many more men and women are engaged in medical research and when publication of results is so easy and widespread, but it would be well if the danger were more widely recognized. What is more likely to happen now is, not the suppression of new points of view and new lines of scientific investigation, but too rapid development, and adoption as a fetish by an advertisement-goaded public, of new discoveries in medicine. This undesirable reaction as regards vitamins has not been absent from some countries, and scientific men ought to combat it. Except in infancy and childhood, there are but few instances where good health cannot be maintained by eating properly chosen food without the constant administration of vitamin preparations.

### Biological Problems

Surveying now the general field of nutritional science, what do we find? We see that physiologists and biochemists, mainly by means of experiments on the growth of



young rats, have detected a large and increasing number of chemical substances which must be present in the diet, often in minute quantities, either for the maintenance of life itself or for proper growth. The chemical constitution of most of these vitamins is known. The chemists' success has indeed been great. But what about the biological side: can it be said why these substances are essential and/or in what way they work? From this angle the success has not been so outstanding: a biological problem is usually much more difficult than a chemical problem, for the living cell and animal body are not limited in their actions by the known rules and regulations of the chemist's laboratory. Besides, the physiological technique which led to the discovery of many of these substances, namely growth in young animals, is so crude, and the factors involved are so many and complicated, that little knowledge of biological function can be deduced from them.

Thus, there is hardly any knowledge of how the vitamins work in performing their functions. Even when the ultimate action of a vitamin is known, as in the case of vitamin D, whose main function is certainly so to control calcium and phosphorus metabolism as to bring about the calcification of bones and teeth, there is still no knowledge of how it works. Does it simply bring about the absorption from the intestine of sufficient calcium and phosphorus to maintain these elements at an optimum level in the blood, leave the calcifiable tissues to select their needs from the blood stream, or does it actually assist the calcification process of the bones and teeth? Even when there is sure evidence that vitamin D acts in either or both these ways, there still remain the problem of how it performs these functions. Does it, for instance, form part of an enzymic complex analogous to the co-carboxylase in which vitamin B<sub>12</sub> is known to participate? In the case of vitamin D we have at least reached the stage of formulating the problem, and the same applies to vitamin K, but with most other vitamins we have not even reached this stage. Clearly this is a challenge to all interested in experimental biology—physiologists, biochemists, pathologists, pharmacologists



clinicians. To pathologists the appeal is specially strong, even to those concerned with morbid anatomy, for one outstanding result of modern work on nutrition is that it is gradually making that subject into an experimental science. Few things are more interesting than to see how, one by one, it is becoming possible to reproduce under experimental dietary conditions the long-known classical changes seen in morbid tissues, one of the most interesting in recent times being the fatty infiltration, necrosis and cirrhosis of the liver induced by dietary defects of choline and the amino-acid methionine.

### Nutrition and Infection

Nothing seems to be more certain than that nutritional defect is at least part of the ætiological basis of many of the more common illnesses, and yet, in most of these cases, this is only conviction without satisfactory proof. For instance, it will probably be found that a dietetic or nutritional factor is involved in the ætiology of enlarged tonsils and adenoids, peptic ulcer, diabetes mellitus, pernicious anæmia, arteriosclerosis and rheumatic disease. The relation of nutrition and infection remains an unsolved problem, but that there is a relationship is not to be doubted. Tuberculosis and other infective diseases increase when the nutritional condition of a population is greatly lowered. What is even more certain is that in badly-fed populations infective invasions by micro-organisms are much more deadly than in the well-fed. In the great field of investigations which lies before us, we must keep a balanced view of the relative importance of the factors—infection and resistance to infection—as influenced by nutrition. The bacteriologist and epidemiologist at times, be inclined to lay all stress on the infective agents and the pathogenicity of the micro-organisms; the nutritionist, on the resistance of the body. The relative importance of these factors will no doubt vary greatly in particular infective process studied, but that both must be regarded as of major importance in many cases is undoubted. We have recently seen how fruitful has been the use of some chemotherapeutic agents, especially the



sulphonamides, when considered from the point of view the chemistry of the bacteria upon which they act, and it not to be doubted that knowledge of the chemical processes which underlie the toxic action of pathogenic micro-organisms and the resistance of the tissues to them, and of how they are affected by nutrition, will shed great light on infectious disease. In some cases it may even be found that passage of an infective agent through a series of people in good nutritional state will lower the pathogenicity of the invading micro-organisms.

In some types of infection it will probably be found that diet, acting during the period of development of the affected tissues and after their formation, is the main controlling factor as, for instance, in dental caries, gingivitis and periodontal disease. In other cases good nutritional conditions may only modify the severity of the disease by increasing the resistance of the body to the infective agent, as for instance in tuberculosis, while in some types of infection the diet and nutritional state may have little or no effect on the incidence and severity of the condition.

To what extent, if any, dietary factors will be found to have a specific anti-infective action remains for future investigation. Some investigators on nutrition have already had experience in the search for this El Dorado, and in the sequence regard the problem with more respect. None could have been more promising than the indications of a specific anti-infective action of vitamin A in young rats which die almost without exception with multiple intestinal foci when deprived of vitamin A, and recover rapidly when vitamin or carotene is added to the diet within reasonable time. In endeavouring to extend these facts to bacterial infection in human beings two points were not realized: first, that rats hold a special place among animals in their susceptibility to infection when deprived of vitamin A because of their great liability to develop hyperplasia and metaplasia of epithelial surfaces under this condition; second, that it seldom happens that human beings are deprived of vitamin A to the extent produced experimentally in the rat experiments. Although it is undoubtedly



that a great deficiency of vitamin A in the body lowers man's resistance to bacterial infection, it is improbable that a degree of deficiency of this vitamin, such as is met with in Britain and comparable countries, is an ætiological factor in infective disease of great significance, except possibly in infants. Nor is there any substantial evidence in the case of vitamin A that added resistance to infection results from giving more of it than is physiologically needed. Indeed there is but little evidence that giving amounts of any vitamin larger than those physiologically necessary makes the body functionally more effective. An exception to this is nicotinamide which, in larger doses than are necessary for health, appears to produce an effect on the neuro-muscular mechanism in man which lowers the time needed to carry out strenuous exercises associated with good co-ordination.

### Nutritional Science and Food Policy

War conditions in Britain have made it essential for the maintenance of health that modern knowledge of nutrition revealed by research should play an important part in framing food policy. War-time food policy in this country, carried out by the Ministry of Food, is described in a separate article below.\* It might be of interest to say something from the point of view of the scientist on this question. It can be said at once that during war-time nutritional experts in Britain have had an opportunity to express their views and to give their advice either through the *Medical Research Council* or through the Food Policy Committee of the War Cabinet. Generally speaking, actions by the Ministry of Food have followed the lines of this advice, sometimes on the basis of its nutritional advantages to the nation, and occasionally because the shipping and economic conditions enforced its adoption. As the scientists' advice on food policy in war-time was based on both of these factors, it came to the same thing in the end, but this will not necessarily continue to be so when the time comes to adopt long-term policy for the days of peace. When that time

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\* [see BMB 492]



arrives, policies dependent on scientific and economic factors respectively will often be divergent and, unless the nutritional needs of the people are given precedence over economic claims, much of the progress in health standards of the population may be lost.

The war has emphasized the lesson that in industrialized countries two foodstuffs have pre-eminent claims to national control. The first is milk and the second cereals, especially bread. So far as milk is concerned, the policy of Britain is satisfactory and will probably remain so in peace-time. In this case the Government policy to ensure that all pregnant and nursing mothers and all infants and children receive, if they so wish, a reasonable quantity of milk can only be commended. It is true that in war-time many adolescents and adults have had to go short of milk, especially in the winter months, and it is also true that too high a proportion of the milk is neither clean nor bacteriologically safe. Determined action is required both to increase the supplies and improve the quality, and the Government seems inclined to press on with both of these policies.

### The Bread Question

In the case of cereals and cereal products, the situation is not so satisfactory. Bread made from wheat has in the past formed, and undoubtedly will in the future, a substantial part of the British diet. The bread eaten before the war was made of a low-extraction flour (70 to 73% of the berry) and consisted entirely of the endosperm, while the bran, aleurone layer, scutellum and embryo were extracted by millers and sold for cattle, pig, and poultry food. Thus most of the vitamin and mineral contents of the wheat berry which are known to be essential for health went to animals while the residue formed a substantial part of human diet. Nutritional scientists are agreed that this policy is wrong but unfortunately there are two schools of thought as to the best method of dealing with this important national problem. One school, represented by British scientists, thinks that bread for human consumption should be made of flour containing as much of the wheat berry as is physiologically



insoluble, i.e. the whole grain except for the outer coarse  
bran. The second school, represented by some North-  
American scientists, thinks that flour should be of the old  
low-extraction, white type, with the addition of those vitamins  
prepared by synthetic or other methods which are known to  
be present in the original berry. This second method is  
based on the assumption that the main vitamin contents of  
cereals are known, and that their physiological importance  
to the body is understood. These assumptions many physi-  
cologists will find difficult to accept. It is probable that the  
policy of the British Ministry of Food in war-time as regards  
bread production, namely of producing 85%-extraction  
flour with a minimum of fibre and with high vitamin-B<sub>1</sub> and  
iron content, has depended more upon shipping difficulties  
than upon nutritional grounds. Consequently, when the  
wartime situation is eased, there will be a powerful move to  
return to the meretricious attractions of the old white bread for  
mass consumption, thus releasing to the farmer, poultry-  
breeder and manufacturer of proprietary food-products more  
of the valuable offal for their own purposes. Possibly as a  
countermeasure to those with knowledge of nutrition there will be  
added to the bread aneurin, nicotinamide, riboflavin and  
iron, as is now being done in North America.

This solution of the bread problem, which consists  
essentially of depriving flour of most of the chemical entities  
which are necessary to life and then restoring a few  
of these substances, seems wrong in principle. In fact,  
the method is also wrong, because the low-extraction white  
bread will undoubtedly be more and more eaten in tropical  
and other countries in which the addition of the vitamins  
will not take place. There will be a repetition of the polished  
bread story, only in this case it will be soulless bread.

### **Need for International Agreement**

It is obvious that scientists of different countries cannot  
easily differ on this important question of the best utiliza-  
tion of available foodstuffs. In the case of cereals, and par-  
ticularly bread, it is very desirable that after the war they  
should come together and see whether they cannot reach



agreement on the optimum composition, both from a nutritional and from an æsthetic point of view, of those cereal preparations which form such a large proportion of the normal diet. The path to such an agreement in policy has already been blazed by the Health Section of the League of Nations. This body achieved the outstanding feat, both in setting up international standardization of vitamins, and also of determining standards of nutrition in terms of common foodstuffs. Probably after the war either this body or its successor will be able to bring about further international co-operation in matters of diet and nutrition and, among other things, agree on a common policy as regards the optimal composition of bread and other cereal products. It may be that new milling techniques will have to be introduced to secure the production in peace-time of bread which fully accords with the principles advocated by British scientists: namely, bread made from a flour which contains all the nutritionally important contents of the wheat berry and is at the same time æsthetically excellent.

All that is demanded is that the factor controlling the constitution of bread should be primarily the health of the consumer, and that milling and other interests should be secondary to this condition. Indeed, no nutritional policy adopted by governments can be wrong if it places the health and needs of the community as its first and guiding principle.