A Lecture

ON

THE PRACTICAL IMPORTANCE OF VITAMINES.*

BY

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In many departments of human knowledge the teaching and guidance of science are accepted as final because in these departments the knowledge arose in the first instance from scientific studies and from these alone. Progress in such categories depends entirely upon controlled and recorded observation or upon experiment, and these are the methods of science.

It is otherwise, one might be tempted to say, in regions where mankind can claim abundant and accumulated empirical experience. In connexion with his own nutrition man's experience has, needless to say, been co-terminous with his whole existence. Science may explain that experience, but is unlikely, it might seem, to improve upon experience as a guide. It may supply theory, but where experience has been so great and so continuous it seems unlikely that it could do much to guide practice. This consideration, consciously or subconsciously, accounts, I think, for a widespread feeling that the teachings of science about our food supply are of academic interest only.

I am to deal, however, with some facts which indicate that, in one direction at least, practice, for lack of knowledge, has for a long time been in danger of going wrong. Experience might doubtless have eventually corrected the error; but it may be hoped that in this case scientific study will forestall experience, which is a much slower and more expensive teacher.

So long as a community can command not only a sufficiency of food, but also a variety of foods, and uses these foods in fresh condition, as nature made them, appetite and instincts (if unperverted) are usually sufficient to secure efficient nutrition for the individual. But when natural foodstuffs are treated artificially—when, for instance, one kind of food material is fractionated, and the consumer presented with a part of it only; or when another material is dried or heated for preservative or other purposes; or, again, when natural foods are sealed up and kept for long periods, it by no means follows that the food materials any longer subserve proper nutrition, even though they are eaten in sufficient quantity and satisfy the appetite.

Now questions of diet are proverbially liable to stimulate quackery, and if I were here to discuss the merits of "natural" foods without giving objective facts I might be suspected of merely supporting certain doctrinaires—self-styled "food reformers"—whose zeal outruns their knowledge. There are facts, however, which support the view that where commercial or other enterprise supplies the public with articles of diet which have been treated or "refined" so as to please the eye or to accord with a fashion or convenience, it may be encouraging very wrong practice. Related facts show that the public, when employing tinned or dried or preserved foods, should use them with discretion, and supplement them properly.

To the naive view that the one important factor in nutrition is the quantity eaten, the science of the last century added one discriminative fact—namely, that quality must be considered as well as quantity, in so far that the food eaten must in any case contain a certain minimum of protein. It taught that the essential constituents of a diet which promotes proper nutrition are protein, carbohydrate, fat, and mineral salts, the organic materials being always provided in sufficient amount to supply the demands of the body for energy.

What we have lately learnt—though it is remarkable how slowly came a recognition of the facts—is that, in addition to the above constituents, which our diets always contain in tangible and easily ascertainable amounts, an efficient diet must also comprise other substances, of which the characteristic is that their nutritive importance is out

of all proportion to the minute quantity in which they are normally consumed. This, I would repeat, is one essential fact in connexion with what we have agreed to call accessory food substances or "vitamines." Their influence on the body is great; their amount as they exist in natural foods is apparently exceedingly small. This is one reason why they have for so long eluded recognition.

An Illustration: Milled Rice and Beri-beri.

Before giving further details I will illustrate how great may be the importance to the body of very small amounts of a nutritional factor by reminding you of what still remains the most vivid instance of the phenomena with which we are concerned.

In certain rice-eating communities of the East, in Japan, the Malay Peninsula, the Dutch Indies, the Philippines, etc.—where, owing to various circumstances, the diet is more exclusively confined to the single cereal than is the case in the wheat-eating West—the very serious disease beri-beri is endemic. It is natural for pathologists to look for a positive rather than what may be called negative causation in disease, and after the development of modern bacteriology many unsuccessful efforts were made to find a microbic origin for beri-beri. Long before this, it is true, the view had been held that diet played a part in its production, and the use of rice was blamed. But the view taken was that the cause was *bad rice*—rice infected with moulds or other organisms. Only slowly did the understanding arise, and not till quite lately was proof driven home, that the disease only follows when the rice eaten has been so treated as to lose some essential constituent. The natural grain contains a special constituent necessary to the body. Overmilling removes this. Polished rice, unlike whole rice, is a deficient food. Beri-beri is a deficiency disease, due to reliance upon this food.

Though not duly appreciated at first, evidence for this really came with the arrival in the East of modern milling machinery from the West. This brought a very great increase in the number of cases of beri-beri. Now the native methods of treating rice before eating had been such as to leave essentially untouched certain parts of the grain which the steam mill on the other hand completely removes.

The advent of steam milling and the increase of disease were not at once recognized as being correlated; but, so far back as 1897, there was brought forward what was irrefutable proof that beri-beri depends not upon infection or staleness in the rice taken as food, but upon the treatment the grain had received in the mill. This proof was due to the Dutch physician Eijkman. His statistics dealt with no fewer than 279,621 individuals, all of them at different times prisoners in the jails of the Dutch East Indies. The different prisons, owing to their different situations, with different and settled local customs, were supplied with different kinds of rice, so the conditions for controlled observations were ready to hand.

In thirty-seven prisons unpolished rice was employed; only one of these prisons developed cases of beri-beri. In thirteen prisons the rice used was polished rice mixed with unpolished; in six of them beri-beri developed. Out of fifty-one prisons, where the rice eaten was entirely of the polished variety, so many as 36, or over 70 per cent., developed cases of the disease. If instead of considering the prisons we count individuals, we find from Eijkman's data that for each 10,000 of the prison population there was only one case among those eating unpolished rice, 416 on the mixed rice dietary, and no less than 3,900 on polished rice. Confirmatory observations have in later years been made elsewhere, but Eijkman's figures are so conclusive that I need bring forward no others. What, then, is removed by the steam mill, of which the importance becomes so evident in its absence? Not the main husk of the grain, for that had nearly always been removed in oriental practice, but just a very thin layer—the "silver skin"—which lies on the outer part of the husk-free seed, together with what we now know to be also important—the germ or embryo. But these structures represent but a very small proportion, indeed, of the total weight of the grain, and we know, as a matter of fact, that the essential thing or things contained in them can amount to but a minute fraction of the material removed. Polished and unpolished rice, as one looks at them side by side, seem to differ so little, that it is almost

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unbelievable that while the latter is an efficient food the exclusive use of the former may lead to fatal results.

But even Eijkman's striking statistics and the facts they brought out did not at once lead to the conception of vitamins. The thought of the pathologist is so accustomed to deal with the positive causes of disease—with bacteria, with some intruder, some *materies morbi*—that he develops a certain habit of mind, and with difficulty believes in causation which has, so to speak, a *minus* sign.

Necessity of Accessory Substances.

I will return later to this particular instance of the evil effects of fractionating a natural food material; for the moment, lest you should associate the subject too closely with the idea of actual disease, I will turn your attention into another channel.

As I have already reminded you, the scientific assumption until a few years ago was that the only essential organic constituents of foods are proteins, fats, and carbohydrates. But the scientific data were mostly obtained during the use of natural foodstuffs, meats, cereals, vegetables, etc. These were of course known to contain many other substances besides those held to be essential, but because, for the most part, they are present in small amounts, the possibility of their importance was always ignored. Clearly the ability of proteins, fats, carbohydrates, and inorganic salts by themselves to support life could only be proved by giving them *pure*.

Suppose now we feed animals with a mixture containing really pure protein, such as purified casein from milk, purified starch, and pure sugar, together with a vegetable fat (I say vegetable fat for a reason which will shortly be made clear), and the requisite mineral salts—what is the result? Not normal nutrition by any means. On such a food young animals fail to grow, and all animals, even adults, sooner or later go to ground.

The full significance of these facts will not be appreciated unless it be recognized that these purified diets are perfectly wholesome; they are fully digested, and may be eaten, so far as quantity is concerned, in ample amount for normal growth and maintenance. Something, however—something clearly of the greatest importance—is lacking. Experiments which prove these statements, and the further discriminative experiments to which I shall refer, have hitherto been made almost exclusively upon animals; for the most part, indeed, upon rats, because of the extreme convenience of these subjects. But for those who feel prejudice against applying results so obtained to the nutrition of man (an unjustifiable prejudice, let me say), I shall later offer facts which make a bridge to the case of human nutrition.

The striking thing, the point that we are now concerned with, is the extremely small amount of material which as an addition will, if rightly chosen, convert these wholly inefficient artificial diets into efficient ones. In some early experiments of my own, for example, the addition was a minute amount of milk. The amount of solid matter contained in this added milk represented at most 3 or 4 per cent. of the whole food eaten by the animals, and as most of the constituents supplied in it were already in the diet, any special substance must have formed a very small proportion indeed of the whole supply of food. Yet without this small addition young animals did not grow; with it they grew satisfactorily. With it they lived; without it they ultimately died. Similar results are got by the addition of equally small amounts of other materials, but they must be preparations made from plant or animal tissues. They must contain something made originally by living cells. All our natural foods are parts of tissues which have lived. We ultimately owe our supply of them to the plant, and the plant evidently makes and stores in very small quantity certain substances which are, as experiment proves, as important to the animal and to the human body as the proteins and the starch which it makes in so much larger quantity. Except for those who view nutrition too exclusively from the standpoint of energy supply, there is no reason for surprise in this circumstance.

What should be clearly grasped is the fact that, without the minute quantities of accessory substances, perfectly wholesome and, indeed, from the standpoint of their own functions, absolutely necessary foodstuffs, are not, in any complete and proper sense, utilized at all. They are absorbed, and the energy contained in them is liberated in

the body, but the co-ordination of metabolism is absent, and neither material nor energy is employed aright. When the minute addition is supplied these very same foodstuffs become perfectly available as a whole. We may think of such facts in terms of a very rough analogy. If a house is to be built it is bricks and wood which bulk largely in the necessary supply. The bulk of necessary nails is out of all proportion small, and even that of the mortar is relatively small; but it would be impossible to erect a normal house without at least a minimal supply of nails and mortar. Without them the rest of the building materials would, from the standpoint of a future tenant, be useless. From the facts just dealt with, and from those brought to light from the study of beri-beri, the conception of vitamins emerges. The analogy just used may indeed be wrong. Vitamins may not be concerned with the structure of the tissues, but rather as stimulants or catalysts, with dynamic processes in the tissues. In any case they are nutritive essentials not directly concerned with the supply of potential energy.

Varieties of Accessory Substances.

The question will be immediately asked: What, then, is the actual nature of such substances? It must be confessed that we do not yet know. Patient efforts have already been made to effect their isolation, but success has not yet come. But their nature is perfectly objective. We can extract them, precipitate them, redissolve them, but we cannot yet get them completely separated from other substances, and until we can do so we cannot determine their chemical nature. But many facts have been garnered concerning their general character and behaviour, and what in particular we have learned in the last four or five years is to be sure that there is more than one of these substances. There are indeed at least three, each one of them having its own function in nutrition.

Consider first, very briefly, the evidence for the existence of two of them. Suppose an animal to be upon artificial diet such as I have already described; normal growth will fail as we have seen. But suppose the fat supplied in the artificial mixture to have been butter or almost any other animal fat. Then growth will occur if we merely add to the mixture small quantities of watery extracts made from various plant or animal tissues. A watery extract of the wheat grain, for instance, and especially of the cortex or embryo of the wheat; or, as it is interesting to know, of the "polishings" which are removed when rice is milled. A substance soluble in water, and that in small quantity, is all that is necessary to convert the, by itself, useless diet into a useful one. Suppose, however, that instead of an animal fat we have supplied in the original mixture a pure vegetable fat. Then the addition of the just mentioned watery extracts alone may be quite ineffective; they fail to make the dietary one which will sustain the animal. Replace, however, the vegetable fat with butter once more, and, given the watery extract, the animal will thrive. Now the vegetable fat is a perfectly good food. As fat, as serving the special purpose of fat itself in the body, there is no reason to doubt that it is as good as animal fat. But it lacks some constituent which the latter contains, though that something is once more present in very small amounts. It will be seen at once to what this evidence tends. There are at least two vitamins of importance to nutrition: one associated with certain fats, and one soluble in water. Both must be present in sufficient amount in any dietary providing proper nutrition. Following American suggestion, we now speak of them respectively as the "Fat-soluble A" and the "Water-soluble B."

The absence of the fat-soluble vitamin from vegetable fats is not due to its absence from the vegetable structures—seeds, etc.—from which the fats are derived, but to the fact that it is left behind when the fats and oils are expressed or extracted. It is abundant in butter, and is present, as I have said, in most animal fats, but it is, strange to say, absent—or said to be absent—from lard. Now of the water-soluble substance there is one statement which I think can to-day be safely made. It is of special interest because it links these animal experiments with human experience. The water-soluble vitamin, proved requisite for growth, is the very substance which is necessary for the prevention of beri-beri. It is the substance which rice loses when it is "polished."

TABLE I.—Showing the Relative Distribution of "Fat-soluble A" and "Water-soluble B" Substances in Certain Natural Products. The relative quantity of either, when present, is indicated by the number of plus signs.

	Fat-soluble A.	Water-soluble B.
Wheat embryo	++	+++
Wheat bran	+?	++
Wheat endosperm	—	—
Lean meat	+	+
Egg yolk	+++	++
Milk	+	+
Butter	+++	—
Vegetable fats	—	—
Cabbage	++	+
Potatoes	+	+
Yeast	+	+++

I return to beri-beri for a moment. One of the special characteristics of that disease is a disturbance in the nutrition of the nerves. A degeneration of the nerves occurs, with accompanying paralysis. Now birds, when fed exclusively upon polished rice, display this particular symptom in a very typical manner, and the fact enables us to perform careful controlled experiments, such as are necessary for determining the distribution of the water-soluble vitamin or, as it may also now be termed, the "antineuritic" substance. After, say, three weeks upon a diet of polished rice a pigeon or a fowl will suddenly develop acute symptoms of paralysis. It is quite easy to cure or prevent these symptoms by adding other foodstuffs to the rice, and if known amounts of them are added it is possible to estimate approximately the relative richness of various foods in this water-soluble or antineuritic factor.

So much for the water-soluble vitamin. Is, now, the deprivation of the factor associated with fats also followed by symptoms of actual disease? The experimental study of its effects is more difficult than in the case of the other factor. Deprivation of the latter is almost immediately felt; but in their own fat stores animals possess a supply of the fat-soluble vitamin, and when it is absent from their diet they seem able to mobilize this supply for the purposes of their active tissues. Not till this internal store is exhausted, or reduced to some minimal value, is its absence from the diet fully felt. Clearly, different individuals will, either from differences in their previous nutrition, or from idiosyncrasy, vary in respect of their store of fat and its associated vitamin. It is more difficult, therefore, in the case of the fat-soluble factor to obtain completely consistent results during experimental feeding. Nevertheless, all animals ultimately fail when this factor is missing from their food.

Rickets.

The probability is growing that there is one disease—and it is a disease of serious import to the community—in which a dietetic error related to a deficiency in the fat-soluble vitamin plays a causative part. I allude to rickets. We have in this connexion, it is true, not yet the concordant evidence from various sources which exists in proof of the origin of beri-beri or of the general importance of vitamins. The case depends at the moment mainly upon the remarkable experimental results obtained by my friend and former pupil Dr. Edward Mellanby; but his work is by no means without the support of other evidence. It is easy, he has found, to construct a diet upon which dogs, though kept in healthy surroundings and given exercise, speedily develop the characteristic symptoms of rickets. It is easy to prevent this by suitable additions to the dietary, in particular by giving certain fats. The fats which are specially efficacious are those which, from other evidence, we know to be rich in the fat-soluble vitamin. Vegetable fats, free from the vitamin, are without effect. The conclusion seems to be inevitable that in some way—on lines, perhaps, not yet fully cleared up—rickets arises when fat-soluble vitamin is deficient in the food. Other factors, such as a generally deficient hygiene, may be contributory, but I for one am quite convinced that the

dietetic error is the primary cause. No whit less important is the fact demonstrated by Mrs. Edward Mellanby that deficient diets, such as those which induce rickets, also involve grave errors in the growth of teeth in young animals. We have had little suspicion until lately that the quality of the fat supply in the diet could have an effect such as this.

As a fat rich in the vitamin and capable of preventing rickets in dogs cod-liver oil stands pre-eminent. It has been long known that the oil favourably influences the course of rickets in infants, a fact discovered empirically and without knowledge of vitamins, but a successful therapeutic measure is much more likely to gain general credence and to establish itself in practice if a rational basis for it is made clear. Moreover, the recent attention given to the importance of qualitative factors in food has led to the use of cod-liver oil in the prevention of rickets, with successful results. These bring observations upon human infants directly into line with Dr. Mellanby's experiments. The following are striking figures relating to infants in a negro community of the United States. In this community the dietetic standards are low and unsatisfactory, and its children are greatly prone to rickets.

TABLE II.—Showing the Results of Administering Cod-liver Oil to Children for the Prophylaxis of Rickets.

Total Oil Administered.	Duration of Treatment.	No. of Infants.	Infants Developing Rickets.	Percentage of Non-rachitic.
54 oz.	6 months	32	2	93
23 oz.	6 "	5	1	80
21 oz.	4 "	12	5	58
None	—	16	15	6

Scurvy.

In the case of the disease scurvy, which arises when no fresh foods are available, the cause is again deficiency in a subtle but indispensable element for nutrition. We learn from this disease that at least one other vitamin exists quite distinct from the two hitherto considered. The antiscorbutic factor, unlike the antineuritic or the fat-soluble substance, is very unstable. These last show considerable resistance to heat and do not necessarily disappear when foodstuffs are kept, even for long periods, whereas the antiscorbutic substance is rapidly destroyed when fresh foodstuffs are heated, dried even at low temperatures, or kept too long.

Pellagra.

Another disease which may be mentioned is one to which maize-eating communities are prone. I allude to pellagra. I do not propose to discuss it; but, to show how wide a ground the subject of this lecture may ultimately be found to cover, I would point out that the many theories as to the origin of pellagra which have previously held the ground seem at the moment to be giving way under the pressure of facts, and to be yielding to the view that pellagra, too, is due to the absence of some specific necessary nutritional factor from the diet.

Effects of Partial Deficiency of Accessory Substances.

It would be grave error to deny that such facts and considerations as have been now discussed are of practical and even of national importance. Our troops abroad during this war have suffered from scurvy, as they have in previous wars. Wherever bodies of men—soldiers, sailors, or explorers—are long removed from the sources of fresh foods, scurvy is wellnigh inevitable. But the severe sufferings which were undergone during the siege of Kut, for instance, might never have occurred if the authorities responsible for the equipment of the expedition had had real belief, such as grows from scientific study, in the importance of antiscorbutics rather than the half-faith which is common, especially had they possessed the quantitative information available as to the distribution of the antiscorbutic factor in different materials.

At home the variety in our foods may be sufficient to secure that actual deficiency disease shall, so far as adults are concerned, remain absent. If the necessary accessory

factors are missing from one article of diet they will probably be supplied in others. It is by no means so sure that this remains true in the case of the child population. I would ask you here to give your attention to certain matters of fact, hoping that you will not think them trivial because they concern foodstuffs that are so familiar.

First consider our bread supply. The ancient controversy concerning the relative merits of brown and white bread has been tainted by prejudice. We have had enthusiasm without knowledge on the one side, and, to some extent at least, we have had the influence of trade interests on the other side. I hold no brief for whole-meal bread. I think the well-fed and well-to-do public may be justified, now the war is over, in insisting upon returning to its very white loaf, if this loaf suits its tastes and appetite better than any other. Other articles eaten will surely supply any deficiency. It is well to face the facts, however. The elaborate milling, the "refining" which the wheat grain suffers before it appears in the form of our white flours, deprives it entirely of its water-soluble vitamine. If our pure white wheaten flour were in this country to form so large a proportion of the whole diet as rice does in the East, beri-beri would with certainty appear among us. Indeed, in certain limited communities it is said to have followed the use of white bread. The wheat grain, no less than the rice grain, shows that an essential nutritive factor may have an unequal and limited distribution in a natural product, and illustrates the danger of "fractionating" natural foods to which I referred in my opening remarks.

It is clear that the danger of any deficiency in bread becomes the greater the more it bulks as a constituent of the whole diet. In the case of the poor—and especially the children of the poor—it undoubtedly bulks largely. Consider again the question of margarine as a substitute for butter. If the margarine is made wholly of vegetable fats, it lacks the fat-soluble vitamine. It is not by any means a trivial point to remember that brown bread and butter is, from the standpoint of vitamine supply, an excellent combination, while white bread and margarine may be a desperately bad one. Speaking in parenthesis, I may say that I happen to be aware from personal knowledge that the margarine industry in this country is quite alive to the significance of the facts. Given full liberty of action, the trade is, I believe, both willing and able to turn out products free from the reproach of this deficiency.

We must remember, again, that polished rice contributes not a little to the table of the poor, especially in some districts, and is often eaten plain boiled. Many of the advertised proprietary breakfast foods and invalid foods are practically devoid of vitamine.

In connexion with the antiscorbutic vitamine in particular, let it be called to mind that tinned foods are largely used in poor households—for one thing, because they often need no cooking. In these very households salads are rare, and during those periods of the year when fruit is dear extraordinarily small amounts of fresh foodstuffs are consumed.

Yet, it may be said, in spite of all this, beri-beri or pellagra or any disease like them is unknown in this country; and scurvy is, to say the least of it, very rare. But disturbances in health may exist without arriving at the extreme stage when the appearance of a severe set of symptoms leads to the recognition of actual disease. In particular is this true of conditions of malnutrition, and, unless the considerations I have put before you are wholly baseless, malnutrition may arise irrespective of the quantity of food eaten. It may depend not upon insufficient food but upon badly treated foods or upon an ill-chosen combination of foods. There is no point in all that I have said that I would like to emphasize more than this: Absence of an essential vitamine from the food means disease; but no more than a relative deficiency of a vitamine may mean bad nutrition. In my own opinion at least the diets of the poor—and once again it is the children who are chiefly concerned—often display such deficiency. In connexion with a point such as this a study of national supply, or even of family budgets, gives only partial information. Even when the total family food-budget is satisfactory, ignorant and ill-judged feeding of the child members is both possible and common.

The worst of it is that at present the facts are not generally recognized, even by the medical profession, and the ill health with which such deficiencies as we have been considering are associated is, in my belief, misunderstood and wrongly treated.

The case of rickets, however, stands out. Rickets is very common in this country. True rickets is a disease which, though crippling, is not fatal in itself. It is, nevertheless, a factor of supreme importance to the country because of its indirect effect upon the infantile death-rate. The child who is rickety is much more prone to other ailments—much more vulnerable in all respects—than a normal child. I will not dogmatize with regard to its origin. The mere suspicion that it may be due to a specific dietetic error, such as a deficiency in the supply of the fat-soluble vitamine, should awaken instant interest. Once we are convinced of the primary importance of this factor it will become of national importance to look to the question not alone of the quantity, but of the quality, of the fat in the diets of infants and of nursing mothers.

Mention of the nursing mother brings me to my last point. Evidence has accumulated to suggest that vitamins are not made in the animal body. The animal depends ultimately upon the plant for a supply. They accumulate in the tissues of herbivorous animals, and there, as well as in the plant, they are available for human consumption. But if vitamins are not made in the body at all, this means, in the case of the nursing mother, that if she consume a diet deficient in vitamins her milk may ultimately become deficient—to the complete detriment of the nutrition of her child. Animal experiments have already revealed such deficiencies in milk. It will be seen that the whole question of infant feeding is one in which a knowledge of these special accessory food factors is particularly important. The deficiencies which we have been considering are indeed of more urgent importance in connexion with the nutrition of the young than when adults are concerned. Hence what I believe to be the national importance of the subject. Whether this importance prove ultimately to be less than some of us believe, or whether—for this is quite possible—it may prove to be of as yet unsuspected importance, it should in any case awaken public interest. We are yet at the bare beginning of its study.

A Collective Investigation OF TEN THOUSAND RECRUITS WITH DOUBTFUL HEART CONDITIONS.

Conducted at the National Hospital for Diseases of the Heart by C. CHAPMAN GIBBES, R. O. MOON, S. RUSSELL WELLS, P. HAMILL, FREDERICK W. PRICE, and J. STRICKLAND GOODALL.

REPORT III,*

COMPILED BY

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THE ETIOLOGY OF AORTIC REGURGITATION.

It has been found extremely difficult, on account of the large amount of material with which we have to deal, and the number and variety of the problems that present themselves, to treat the different questions in logical order. In many cases the questions at issue are so intermixed that when the solution of any particular problem is attempted it is found necessary to solve another first. In our last report we dealt with the incidence of certain general diseases in our whole 10,000 cases, and arrived at the conclusion that there was a slight but definite correlation between a history of rheumatic fever and chorea, but no correlation between a history of rheumatic fever and either a history of "rheumatism," growing pains, or tonsillitis. We stated that the importance of these disorders as

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