

The Lumleian Lectures

ON

COELIAC DISEASE.

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LECTURE III.*

MR. PRESIDENT AND FELLOWS.—In this, my third lecture, I propose to consider the treatment of coeliac disease.

This section of my subject I approach with considerable diffidence, for in face of the modern therapeutics which the brilliant investigations of laboratory workers in chemistry and bacteriology have made applicable to many diseases, one feels almost out-of-date in offering suggestions and observations based chiefly on clinical experience.

As, however, I have shown in the previous lecture, it has not been possible to trace coeliac disease to one specific cause. Until this has been done, or until the clinical grouping which has been called by this name is shown to be divisible into several different specific entities, the treatment must necessarily be more or less symptomatic and empirical. In the meantime experience has shown that certain lines of treatment are definitely valuable in many cases included under this heading, and these I shall try to indicate; moreover, as negative observations are sometimes hardly less important than positive, I shall refer also to the failure of various methods which on theoretical grounds have been thought worthy of trial.

DIETETIC TREATMENT.

One of the outstanding features of coeliac disease is failure of fat assimilation.

This failure has not only a negative result in depriving the child of important material for nutrition, but also a positive result in leaving in the food-residue in the bowel an excess of fatty substances which favours putrefactive change, and in this way may lead to local irritation and secondary infections, and more remotely may cause symptoms of toxic absorption. Possibly also the excess of fat remaining unabsorbed may interfere with the digestion of other food by covering it with an oily coating which digestive secretions have difficulty in penetrating. Failure of assimilation of any element of food is liable, in various ways, to have a more profound effect upon nutrition than the mere loss of that particular element would entail, for by its secondary effects in the bowel it may, and evidently does, interfere with the absorption of other food elements.

Reduction of Fresh Cow's Milk.

I suppose this to be the reason of the value of a diet from which fresh cow's milk is altogether excluded. I place this point foremost in the treatment of "coeliac disease," for I know of no other item of equal importance. Experience shows also that it requires emphasis, for the tendency is to put such a case upon milk and more milk, as the one thing needful, whereas nothing is more likely to retard recovery.

Dr. Gee's experience led him to the same conclusion. "Cow's milk," he says, "is the least suited kind of food for them"; but he attributes this intolerance of milk to the curd, not to the fat. "Nothing is more certain," he adds, "than that coeliac children cannot digest the hard curd of ruminants' milk."

I think the balance of evidence is against this explanation of the harmfulness of cow's milk in this disorder. As he himself points out, peptonising milk does not make it any more suitable for these cases, as it should do if the difficulty were chiefly or entirely curd indigestion. I would add that the use of dried milk, the curd from which is much less tough and consequently much more easily digested than that of cow's milk, produces little or no improvement in the stool unless the proportion of fat in the dried milk is much less than that in the fresh milk. The stools show no evidence of curd indigestion, whereas they do show very marked deficiency of fat absorption. Cream, even much diluted, is not tolerated, as it should be if the milk difficulty was due only to the curd.

My own observations, in agreement with those of other clinicians, show that the best results are to be obtained in the dieting of these children by reducing the fats to a minimum, and as the food in which fat is chiefly given at the age when these children come under treatment is cow's milk these observations have applied chiefly to this particular form of fat.

Dried Milk with Reduced Fat.

I have found most successful the replacement of fresh milk altogether by a dried milk containing only a small proportion of milk fat.

The particular brand—"Cow and Gate Half Cream"—which I have used is stated to contain half the proportion of fat present in milk.

Analyses showed that dried milk requires using with special precautions, otherwise the proportion of fat in the food may be very different from that intended. The very light, almost flaky, powder is very easily compressed, so that if on opening a full tin of this half-cream dried milk a fully-heaped, large-sized teaspoonful is taken and added to 1 oz. of water the resulting proportion of fat is no less than 3.1 per cent. (the amount of the powder taken thus was found to be about 75 gr.), whereas if the powder be turned out of the tin or shaken up, as it would be in a partially emptied tin, the same teaspoon heaped fully with the loose powder contains barely 50 gr. and gives with 1 oz. of water only 1.8 per cent. of fat.

Why the small amount of cow's milk fat contained in the dried milk should be better tolerated than the same proportion of fat in fresh cow's milk is not apparent.

Indeed, one would rather have expected the reverse, for the emulsion of the fat in a solution of dried milk is so imperfect that it tends to form into visible droplets on the surface and forms a greasy coating on the vessel in which it is given. Sometimes, indeed, I have wondered whether the loss of a certain amount of fat to the child in this way may not have facilitated the digestion of these preparations.

Human and Other Milk.

It might very reasonably be argued that if the fat is the difficulty then any milk which contains as high a proportion of fat as cow's milk should be equally unsuitable.

This, however, is not so. The difficulty of assimilating the fat of fresh cow's milk seems to be a specialised intolerance, for the fat of human milk, though present in larger proportion than is often found in cow's milk, is seemingly tolerated excellently by these children.

Usually their age makes it difficult to utilise this form of feeding, but in two cases where life seemed to be seriously threatened by coeliac disease, I was able to obtain human milk, which was used in one of them from the age of 2½ years for nearly a year, and in the other from the age of 20½ months until the child was 2 years and 11 months old.

In both cases the human milk seemed to be the turning point in the illness, and its use was followed by great improvement in the stools and in the child's general condition, so that one case made a complete recovery, though with some stunting of growth, and the other, last seen at 3 years and 10 months, showed no arrest whatever of growth and was able by this time to take both cow's milk and goat's milk.

In connexion with this special value of human milk I would recall a fact which I have already mentioned, that none of my cases of coeliac disease began in an infant who was still at the breast.

One of the most successful substitutes for cow's milk is asses' milk.

This might be expected from the very low proportion of fat which it contains, commonly not more than 1 per cent. Whether this is the whole explanation may, however, be doubted, for cow's milk, even when diluted so as to reduce the proportion of fat to this extent, or when used in the form of whey, which contains usually not more than 1 per cent. of fat, is still much more liable to render the stools loose and offensive.

Apart from the proportion of fat present it is recognised that there are differences in the characters of the fat in the milk of different animals, notably in their melting point, also in the proportion of butyric acid present as well as in other respects, and it may be that these differences determine the digestibility of different kinds of milk fat, and therefore their relative suitability in such a condition as coeliac disease.

Fat Derived from Other Sources.

Fats other than those present in milks have also proved unsuitable.

I have tried the oil obtained from soya bean in the form of an artificial milk, Solac, containing 3.3 per cent. of fat according to one analysis, and 3.75 per cent. according to another, but in spite of good emulsion this was not successful; it aggravated the looseness of the bowels.

Cod-liver oil also is not available to replace the milk fats, for it is usually tolerated badly in this disorder.

Another form of fat which, though tolerated by some of these children in small quantities, increases the symptoms in others, is that present in the yolk of egg.

The evidence of intolerance of these various fats is the increased looseness of the stools and still more their offensive character. The reduction of the proportion of fat in the diet produces not only diminution of looseness but a better colour and less offensive odour of the stools, and therewith a definite improvement in the child's general condition, and particularly in the weight.

Carbohydrates.

The diet, however, must needs consist of something more than a milk very poor in fat if any continuous improvement of nutrition is to be obtained.

There is apparently some difficulty in dealing with starches, though much less than with fats.

Unfortunately, one form of starch which seems particularly liable to aggravate the symptoms is bread. I know of no adequate substitute. Rusks have seemed less harmful than bread, probably owing to the fact that the starch in them is partially dextrinised; they help to satisfy the child's craving for something solid. For this reason, though they contain very little carbohydrate, I have used biscuits made with dried

* Lectures I. and II. were published in THE LANCET of August 10th (p. 163) and 17th (p. 193), 1918.
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milk, with just enough wheaten flour to give a crisp consistency; there have been at least two such in the market, "Nurso" and "Malac" biscuits. Sugar is allowable only in small quantity.

A form of carbohydrate which generally suits these cases is "Revalenta," prepared from lentils; this made thin with a solution of the dried milk and sweetened with sugar, though not very palatable, is generally taken well. Rice boiled in water for three or four hours so that it is almost a jelly is another form of carbohydrate which has usually succeeded.

These foods, with the addition of chicken broth or veal broth and sweet jellies, have made up the total dietary, in some cases, for a year or more, and if anyone tries to draw up a menu from this list he will find that it is meagre indeed. If eggs are tolerated it eases the difficulty considerably. Pounded chicken, or fish, or meat, or brains, generally make the looseness of the bowel worse, and are only suitable when the child is already improving.

Apart from the fact that such a diet is unsatisfying to the child, it is definitely scorbutic.

Five of my cases developed scurvy at ages varying from $4\frac{1}{2}$ years to $10\frac{1}{2}$ years. All of these were on dried milk and the diet I have mentioned, a proof incidentally that these dried milks, if they contain vitamins at all, do not contain sufficient to prevent scurvy. Obviously, it is important to give some antiscorbutic, and sometimes there is no difficulty, for grape-juice can be given to some without increasing the looseness of the bowels, but usually fruit juices and green vegetables have to be avoided on this account.

Other Diets.

Various have been the efforts to find a diet upon which these children will do well.

One of the most remarkable is that mentioned by Dr. Gee: "A child who was fed upon a quart of the best Dutch mussels daily thrived wonderfully well, but relapsed when the season for mussels was over; next season he could not be prevailed upon to take them. This is an experiment," he says, "which I have not yet been able to repeat."

There may have been more reason in this method of feeding than at first appears, for, like most of the diets which have succeeded, it is one containing a low proportion of fat. Moreover, while containing a high proportion of proteid, it contains, of course, no carbohydrate. The mussel contains 12.5 per cent. of proteid and only 1.6 per cent. of fat.

I have tried in some cases a so-called "fat-free" diet with marked success.

From this even the dried milk and egg are excluded, and the diet consists of rusks, Robb's biscuits, jellies, chicken and veal broth, rice boiled in water, revalenta, mashed potato, pounded chicken or fish, barley water or weak tea with sugar. On this diet there has usually been great improvement and in six cases slow but steady recovery.

In this diet the potato fulfils a double purpose by not only providing a considerable number of calories, but also a most effective antiscorbutic. It has seemed to me to be better tolerated in this fat-free diet than when given in a diet including milk, dried or otherwise. This impression is confirmed by one's experience in some of the commoner digestive disturbances of childhood, where one has often noticed that the combination of oily substances—for instance, butter—with potato seems to render the potato particularly indigestible, possibly for the reason already suggested, that the fatty material forms an envelope around the starch granules preventing the diastasic action of the amylase of the salivary and pancreatic secretions.

Diet with Little or No Fat: Freedom from Rickets.

It might be thought that a diet practically devoid of fat, or even such a régime as that previously mentioned in which the fat is reduced to an extremely small amount without being excluded altogether, would, when continued for months, or, as has been necessary in some cases, for two or three years, produce serious harm; especially when it is used, as it is almost always in this disease, at an age which should be that of rapid development. I have already pointed out that in spite of the deficient fat assimilation caused by the disease rickets is strikingly absent in the large majority of children with coeliac disease; and now I will add that even when fat is eliminated entirely or almost entirely from the diet these children still show a remarkable freedom from rickets.

Other Routes of Introducing Fat: Inunction.

Admitting, however, that in this direction the low proportion of fat in the diet does no harm, it must still be desirable from the point of view of general nutrition to secure the absorption of fat if possible, and the question arises whether for purposes of tissue building fat can be introduced by any other route than the alimentary canal.

There is some evidence not only that it can be absorbed but that it can be used for tissue building when injected into the subcutaneous tissues. Such a mode of administration is obviously undesirable for children, especially as it would have to be repeated many times and for a long period.

Can fat be introduced by inunction?

If so, it would be simple enough to compensate for the deficiency of fat digestion. There is plenty of evidence that various substances applied in oils or ointments are absorbed—e.g., mercury in mercurial ointment or iodoforn in oil or in vaseline; but this is no proof that the fat of the oily vehicle is absorbed also.

I have sought in vain for confirmation of statements that cod-liver oil and other fats can be introduced through the skin. The only experimental evidence which I have been able to find was that obtained by Lassar, who smeared the shaven skin of rabbits with rapeseed oil three times a day for two or three days, and found that the liver and kidneys after this short time were full of fat globules. He stated also that olive oil and cod-liver oil passed through the skin into the deep organs.

As far as I know, these experiments have not been confirmed, and it has been pointed out (Reid¹⁵) that the skin of mammals usually employed for such experiments is thinner than that of man and more vascular, and in the case of the rabbit in particular contains hair follicles with wide mouth, so that the conditions are not strictly comparable.

If fat can be absorbed through the skin it must presumably be without the fat-splitting and subsequent synthesising which are supposed to be necessary to its absorption through the bowel. It is difficult to believe that if with such special adaptation to absorption as is shown in the structure of the intestinal mucosa such an elaborate process is necessary to the absorption of fat it can be absorbed without any preparation at all through such a structure as the skin.

It is much to be desired that careful clinical observations under strict conditions could be made on this particular point.

Most of us have ordered inunctions of oil many times for wasting children, who sometimes have thereupon gained weight and sometimes not, but there are so many possible fallacies, and so few cases offer the exact conditions favourable to any decisive conclusion, that such inunctions are usually rather the therapeutics of hopefulness than the therapeutics of conviction. Personally, I have been under the impression that any good accruing was due rather to the friction and perhaps the warm covering of oil than to any real absorption.

It is important for investigation that the cause of the wasting should be mainly, if not entirely, failure of fat absorption by the bowel. The presence of some other cause of wasting, such as tuberculosis or any general failure of digestion, will make the results of inunction even more doubtful, as any gain from skin absorption may be counterbalanced by loss of nutrition from other causes. In "coeliac disease" we have a condition in which presumably the predominating factor in the failure of nutrition is failure of fat absorption from the bowel, and therefore a state of things particularly suited to this investigation.

Results in Cases Treated by Inunction.

With this point in mind, I tried the effect of inunction with peanut oil (*oleum arachis*), two drachms being rubbed in twice daily for about 15 minutes.

The patient was a boy aged $7\frac{1}{2}$ years who had been under my care in hospital for five weeks with coeliac disease without gaining weight. On admission he weighed 28 lb.; at the end of five weeks only 25½ lb. At this stage the daily inunction was begun, and the boy's weight steadily rose so that in the next eight weeks he gained 8½ lb., and this in spite of the stool being often very pale and slimy and purpura appearing most of the time.

This observation is certainly suggestive of the possibility of fat absorption through the skin, but I am bound to admit that even with such a favourable opportunity for investigation as coeliac disease my results in other cases have been equivocal.

In one case the inunction, done with cotton-seed oil, and subsequently with peanut oil, produced no definite gain in weight, whereas in another case of coeliac disease in the same ward, where the weight had been stationary for many weeks, the weight began to rise almost steadily, and the child's condition improved enormously without any change in the treatment, and in particular without any inunction.

An unexplained improvement like this has happened in several cases where the disease had already lasted two or three years without any permanent progress. It behoves us, therefore, to be careful in attributing results to our treatment, whether it be fat inunction or any other.

TREATMENT BY DRUGS, ORGANIC EXTRACTS, AND VACCINES.

Another method of overcoming the fat difficulty which has been tried in these cases is the administration of digestive extracts.

In view of the striking results obtained by Dr. Byrom Bramwell in cases of pancreatic infantilism, a condition associated, like that we are considering, with failure of fat assimilation, it seemed possible that pancreatic extracts would be of value in coeliac disease.

I have repeatedly used them, trying in various cases the glycerine extract specially recommended by Dr. Bramwell, also the preparation sold under the name of "holadin," and that sold as "trypsinogen," but none of them have appeared to me to have any obvious beneficial effect, a confirmation, incidentally, of the conclusions reached in my previous lecture that the failure of fat assimilation is not due to the failure of the pancreatic secretion.

I have also tried ox-gall on the theory that the biliary secretion was deficient, but without any improvement in the stools or in the child's condition.

Calomel.—Digestive Extracts.

Dr. Cheadle recommended calomel as stimulating hepatic secretion, as well as having some antiseptic value.

So far as my own experience goes, the facts certainly do not fit the theory, for calomel, and even grey powder, seem to aggravate the bowel disturbance and to be particularly unsuitable for these cases.

Dr. Cammidge quotes one observer as having found that calomel, so far from diminishing the number of bacteria in the faeces, may actually cause an increase, presumably by increasing the mucus which serves as a favourable nidus for bacteria. Whatever may be the explanation it certainly does not improve either the stools or the patient in coeliac disease.

The difficulty in digestion of carbohydrates, particularly of starch, which is only less than the fat difficulty, naturally suggests the administration of malt for its diastasic effect. This, however, is also found to be inadmissible in most cases, for it seems rather to promote flatulence and looseness.

It would seem, indeed, so far as any direct influence can be exerted upon the absorption of fats and carbohydrates in coeliac disease, it is rather to be accomplished by rigorous dieting than by any drugs or digestive extracts.

Astringents.

Drugs, however, even if they are of but little assistance in this affection to the digestive processes which prepare the food for absorption, may still be of real value if they can render the intestinal mucosa more healthy, and therefore more capable of absorbing.

Post-mortem examination has shown that, at any rate in a fatal case there may be definite inflammatory change in the intestine, and the

presence of much mucus in the stools during life, especially when the disease has already been present for a long time, shows that there is at least much intestinal catarrh, and these changes are apparently due, in part at least, to bacterial irritation and partly to the irritating effect of putrefaction.

It might be supposed that this could be diminished in two ways, either by drugs which exert an astringent effect upon the mucosa, or by those which have some antiseptic value and in this way prevent bacterial growth and putrefactive changes.

Most of the astringents, whether vegetable or mineral, have proved useless in my hands; the only one which has an undoubtedly good effect is castor oil.

Given in small doses, three times daily, it usually causes more or less improvement.

A mixture of 5-minim doses of castor oil with salol 2 or 3 gr. in mucilage and water has such a pronounced effect in improving the stools and checking looseness that in several cases the child took it almost continuously for some years, and the parents stated that any attempt to discontinue it was usually followed before long by deterioration in the character of the stools, so that the medicine had to be resumed.

It has always seemed to me difficult to understand how five drops of castor-oil can have any astringent effect on 20 feet of intestine, but however it is to be explained there is no doubt that it has a very definite action in this respect.

Another astringent which, though much less reliable than castor oil, is certainly sometimes useful in coeliac disease is silver nitrate, which in doses of $\frac{1}{4}$ or $\frac{1}{2}$ gr. ter die seems to reduce the looseness of the stools in some cases.

Bismuth has seemed to me to be usually of little, if any, value in these cases, perhaps because it was used in the traditional doses of 10 gr. or even 5 gr. three or four times a day, whereas the radiographers have taught us that bismuth can be taken by the ounce without ill effect, so that recently infants in my ward sometimes have 30 gr. of bismuth carbonate every three hours, and a child of three as much as 60 or 70 gr. several times a day.

Chromo-santonin.

Having in mind the resemblance in many points between coeliac disease and sprue, I have tried in three cases the chromo-santonin, which Dr. Charles Begg has found to have remarkably beneficial effects in sprue.

It was given, as he directs, in a gelatine capsule. There were no records from which the dosage proper to children of this age and suffering from coeliac disease could be gauged, so I was obliged to feel my way cautiously, beginning with amounts which, no doubt, were too small, and perhaps even finally not reaching a sufficient dose. A child 6½ years old, weighing 21 lb., took 2 grains twice daily without any definite effect.

In one case, the girl aged 17½ years whom I have mentioned before, the administration of the chromo-santonin was followed by immediate improvement of the stools, which became less offensive and less loose, and there was rapid gain in weight.

In another, a girl aged 3½ years, and weighing 15½ lb., there was no marked alteration of the stools whilst the chromo-santonin was given—increasing doses up to 1 grain twice daily were used—but just after the course of this drug was stopped there was great improvement in their character; they became firmer and a better colour than they had been for months.

Clearly, further observations are needed on the value of this drug in coeliac disease. In the doses used it produced no ill-effects of any kind; the greenish-yellow discolouration of the urine due to santonin was observed in 15 hours after it was taken, but this is of no importance.

Dr. Begg considers that the chromo-santonin has a bactericidal action.

Intestinal Antisepsis.

Other drugs have been tried in this affection with the idea of intestinal antisepsis.

In one, at the age of about six years, iodoform gr. $\frac{1}{2}$ was given for six months, apparently with markedly beneficial effect.

Salol has also seemed to do good.

Perhaps in the same category should be mentioned ionisation with sodium salicylate at one electrode; this was done in one case under my observation. A 2 per cent. solution of sodium salicylate was used on one pole on the abdomen. During this treatment, which was carried out for many weeks, the child very definitely improved, though she subsequently relapsed and died.

In one case I tried radium water; half a pint was given daily by mouth, without the slightest benefit.

In one of the recorded cases appendicostomy was done with a view to overcoming intestinal infection by irrigation through the appendix. Some improvement of the child's general condition started after this was done. Autopsy, however, showed that there was inflammation involving the whole of the small intestine as well as the large, so that it could hardly be expected that this treatment could do more than palliate symptoms.

Vaccine Therapy.

The discovery that a considerable proportion of the cases examined gave evidence of intestinal infection with a dysentery bacillus, as shown either by the finding of the organism in the stools or in the mucus from the bowel, or by the positive result with the agglutination test, naturally suggested that a vaccine might be of value.

I have used an autogenous vaccine of the dysentery bacillus in two cases where the bacillus had been obtained from the stools and a stock vaccine of dysentery bacillus where, although the organism could not be found in the stools, the agglutination test gave a positive result.

In both the cases where the autogenous vaccine was used there was very definite temporary improvement both of the stools and of the child's nutrition for about a fortnight, after which the condition again deteriorated in spite of continued use of the vaccine. The vaccine was

administered in the one case in doses of 5 millions, increased gradually up to 200 millions; in the other the initial dose was 60 millions, increased later up to 150 millions.

In the third case, where only a stock vaccine was available, and was used in doses increasing from 25 millions gradually to 150 millions, no effect whatever was observed.

In one case where the dysentery bacillus was absent, but the stools showed many streptococci and pneumo-bacilli, a vaccine was used of pneumo-bacilli and streptococci in increasing doses up to 100 millions of each; no effect whatever, either for good or ill, was observed.

Internal Secretions.

The striking arrest of growth in these cases has raised a suspicion that one or other of the internal secretions might be deficient.

In three cases under my observation thyroid was given, but without the slightest advantage. It did not seem to promote growth nor to improve the general condition; indeed, one of them seemed rather the worse while taking it. This symptom is one for which treatment is specially sought in the cases which reach convalescence. The child herself is distressed by the difference between herself and those of her own age.

In one such case the administration of polyglandin, a preparation of mixed organic extracts, was followed by an increase of height of $\frac{3}{4}$ inch in 14 days and another $\frac{1}{2}$ inch in the next 12 weeks, but the child at the same time had improved so much in her power of assimilation that she was able to take an ordinary diet in place of the restricted special diet, so that growth might have been due to this rather than to the drug.

If we have no certain means of promoting growth in these cases where it has been arrested by the disease I suspect that we can do something to prevent the stunting by the diet adopted during the earlier and more acute stage of the disease, for I have noticed that cases fed on human milk or on asses' milk have shown much less interference with growth than those in which such feeding was not obtainable.

Anyone who has seen the remarkable stunting of growth which can be produced in rats by regulating the diet so as to exclude some elements will realise that there is no necessity, in children with this disease, to seek for the primary cause of the arrest of growth in any failure of internal secretions. Nevertheless, it is quite conceivable that the general interference with nutrition, caused by the failure of fat absorption, may affect also the internal secretions which are known to play a part in the regulation of growth.

The point is one of practical importance. For if the arrest of growth is due simply to deficiency of calcium absorption, through the loss of calcium in the soaped fat passed in the faeces, one might suppose an increase of the intake of calcium by administration of calcium salts—for instance, the lactate or the chloride—would compensate to some degree for the loss in the faeces, assuming that the wastage in the form of soap remains unaltered.

But I know of no evidence that growth is promoted by the giving of calcium in this way; I am not even satisfied that calcium salts given thus have any effect upon bone formation; certainly one's experience is that, judging from clinical evidence, calcium in the form of lime-water has little, if any, effect in the prevention or in the cure of rickets. Moreover, in some experiments upon the feeding of rats with a diet deficient in fat, the arrest of growth occurred in spite of the administration of calcium in the form of calcium lactate.

IMPORTANCE OF DIET.

To sum up, it would seem that drugs, while not entirely impotent in the treatment of this condition, have a very limited scope, and that chief reliance is to be placed upon scrupulous care in dieting. The element in the food which requires most consideration is the fat, and the form of fat which seems most obnoxious to children affected with coeliac disease is the fat of cow's milk. If this be borne in mind it is nearly always possible to obtain marked improvement in these cases, and a large proportion of them can be coaxed back after many months or years of patient perseverance with a very restricted diet, to health and even to an average power of assimilation.

CONCLUSION.

In conclusion, Gentlemen, I can only regret that I have not been able to throw more light upon the obscure problems raised by this group of cases, and that the working hypothesis with which I started, that it can be pigeon-holed as one specific morbid entity, coeliac disease or intestinal infantilism, name it what you will, remains still nothing more than a working hypothesis.

I have raised many questions, I have answered few, and if any apology is needed, I would say, in the words of Heraclitus, χρυσόν οἱ διζήμενοι γῆν πολλήν ὀρύσσουσι καὶ εὐρίσκουσιν ὄλιγον.

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