THE ÆTIOLOGY OF CÆLIAC DISEASE: PRELIMINARY COMMUNICATION ON THE BLOOD FAT.

BY

ALAN MONCRIEFF, M.D., M.R.C.P.

and

W. W. PAYNE, M.B., B.S.

(From the Hospital for Sick Children, Great Ormond Street, London.)

For the purpose of this paper we will take as a definition of cœliac disease that put forward by R. Miller¹ in one of his recent communications on the subject: 'Cœliac disease is a digestive disorder arising in infants and young children who show no evidence of chronic intestinal or other organic abdominal disease: it is characterised by a persistent mal-absorption of dietetic fat which causes large stools containing an excess of split fat, enlargement of the abdomen, lack of growth and other symptoms.' As we hope to show later in this paper the term 'mal-absorption' is, we believe, incorrect, but for the moment the definition will serve. It excludes all forms of chronic enteritis and abdominal tuberculosis. For further details as to differential diagnosis on clinical evidence, Miller's paper should be consulted. The peculiar stools which are such a feature of cœliac disease are, however, also found in other diseases. In their recent paper on fæcal fat analysis in children Harrison and Sheldon² mention this point: 'the figures in tuberculous peritonitis show the same deviation from the normal as in cœliac disease.' Indeed the similarity between the stools of cœliac disease and those of abdominal tuberculosis in which there is obstruction of the lacteals has led Ryle³ to put forward the suggestion that cœliac disease is due to lacteal obstruction. Two cases recently in the Hospital for Sick Children under the care of Dr. Thursfield illustrate this point.

Case 1. B. B., girl, aged $1\frac{9}{10}$ years. Admitted for loss of weight for three months following measles. The child had obviously wasted and the abdomen was enlarged with a large mass in the right lower part. The stools were pale, bulky and offensive. Analysis of the stool showed 67·8 per cent. of dried fæces was fat and of this 84 per cent. was split and 16 per cent. was unsplit. The blood fat was 0·145 per cent. (as fatty acid) 2 hours after a feed consisting of skimmed milk and Casec. The child went rapidly down and died.

At necropsy the abdomen was found to be filled with large masses of tuberculous glands, matting the intestines and obviously causing gross obstruction to the lacteals. No ulceration of intestine was found and there was no definite enteritis.

Case 2. F. A., boy aged $1\frac{3}{4}$ years. Admitted for wasting since the age of 11 months with bulky, offensive motions. The child was very wasted; abdomen distended, but without any signs of free fluid; no lumps could be felt. Analysis of the stools showed 38·97 per cent. of the dried fæces was fat, of which 74·05 per cent. was split fat. Blood fat 2 hours after a fat-free meal was 0·422 per cent. (as fatty acid). The child had curious attacks with sudden loss of consciousness. The temperature rose a few days after admission and he died.

At necropsy broncho-pneumonia was found. There were no changes whatever in the intestine, no enlargement of the mesenteric glands and microscopically the intestine and pancreas were normal.

These two cases, one of abdominal tuberculosis and the other regarded as coeliac disease, both showed many points of similarity in the wasting, the character of the stools and the passage of excess of fat in the fæces, mostly split in a normal manner. The striking difference lies in the blood fat estimated under almost identical conditions as to diet, time of taking blood, etc. It is so frequent in coeliac disease to talk of the mal-absorption of fat and to look upon the disease as essentially characterised by a failure of the intestine to absorb fat that it might be expected that the fat in the blood would be considerably reduced below normal. One year ago one of us (A. M.) had the fat in the blood of a coeliac child* estimated at the Middlesex Hospital and it was found to be higher than in a normal child of the same age. This surprising result, which was repeated on several occasions, led to the consideration that the fault in coeliac disease could scarcely be due to a faulty absorption. The work embodied in this paper was undertaken to investigate this subject still further.

METHOD OF BLOOD-FAT ESTIMATION.

The estimation of the blood fats in the small quantities of blood necessarily used in repeated observations in children is technically a difficult process and is liable to both individual and systematic errors. It is therefore desirable at present for each individual worker to establish his own normal values with the method he chooses to adopt.

With regard to the method to be used, the nature of the fat to be estimated must be considered. The ether-soluble fraction of the blood contains fats proper, lecithins and cholesterol and cholesterol esters. As the significance of these fractions differs it is necessary to make some attempt to distinguish them. It is now considered that cholesterol and its esters have but little to do with fat metabolism and that the lecithins and fats are probably of equal importance.

The more recent methods aim at estimating only the saponifiable matter, that is, the fats proper and the fatty acid fraction of the lecithins. The estimation of the ether soluble phosphorus will give an indication of the proportion of the fatty acids to allot to the lecithins. The method at present used differs somewhat from other methods in that only fatty acids yielding insoluble calcium soaps are estimated. The values obtained do not differ greatly from those given by other workers.

As with blood sugar, so with blood fat, the time and nature of the preceeding meal must be considered. The amount of information at present available with regard to the effect of fat meals on the blood fat is not by any means as complete as could be desired. That there is a rise, with a maximum between two and five hours after a fat meal is generally agreed. The degree of this rise varies considerably according to various factors, e.g., a smaller rise occurs when animal fat is given than when vegetable fat is given. In dogs frequent repetition of the fat meal (which presumably was greater than that normally taken) resulted in a progressively smaller increase in the blood fat.

* Dr. C. E. Lakin has kindly allowed us to mention this patient who was under his care.

Again, the nature of the food taken with the meal causes a difference, there being a larger rise with meat and fat than with bread and fat (Bang⁴). These results have mainly been obtained in dogs and adult men. Pending the investigation of these various points in children, it has been considered sufficiently accurate for purposes of comparison to take the blood at the same time of day in each child without disturbing their usual diet.

ETIOLOGY OF CÆLIAC DISEASE.

The problem of the cause of cœliac disease has attracted the attention of many workers. Herter⁵ in his original publication on intestinal infantilism in 1908, believed that the disorder began as a chronic inflammatory process in the intestines, and he was inclined to favour a bacterial cause. This view is still prevalent in American literature, and Sauer⁶ in a recent paper has called attention to certain evidence which he believes shows that cœliac disease may be transmitted from one child to another. It is probable that confusion has arisen with regard to a possible bacterial origin because "chronic intestinal indigestion" and "chronic enteritis" have not been sufficiently separated from cœliac disease by many writers. Miller and others have particularly gone into this point, and Miller's paper already mentioned should be consulted as to details. The pancreas has been blamed, but tests for pancreatic efficiency are normal in cœliac disease. In any case the fat in the fæces is normally split and Bauer⁷ has investigated the intestinal ferments by means of a duodenal tube in a case of cœliac disease and has shown that they are present in the same amounts in the presumably normal child with similar variations as regards feeding and fasting. Their digestive powers are also similar. (The actual substances investigated were bile, lipase, trypsin and amylase). The view that the lacteals are obstructed has already been mentioned and may be dismissed by saying that there is not sufficient evidence in its favour and the facts that cœliac cases do not develop tuberculosis, nor can mesenteric glands be felt, seems to dispose of it as the cause of cœliac disease. Miller's own view on deficiency of the bile-salts is admittedly arrived at by a process of exclusion and has not much evidence in its favour, and at the moment it may be said that the ætiology of cœliac disease is unknown. This is, we believe, largely because of a fundamental misconception of the meaning of excess of fat in the stools.

The common view is that absorption is at fault and that by cutting down fat in the diet this can be prevented to a large extent by presenting the intestines with a limited amount of fat to deal with. Bauer⁷ has indicated that absorption of fat seems to be as readily attained experimentally in the child with cœliac disease as in the normal child, and the work of Hill and Bloor⁸ and of Speery and Bloor⁹ seems to indicate that the fat in the fæces appears to have no direct relationship to the fat in the food in many cases 'but represents rather some form of excretion from the intestinal tract' (Hill and Bloor, 1922). In the early experiments these workers reached the conclusion that fatty substances were to be found in the fæces whether present in the food or not and that fat in the food increases the fæcal fat, but only to a comparatively small extent.

Of the experiments Hill and Bloor said "taken altogether they indicate a continuous output of 'fat' in the fæces of a constant composition independent of the diet." In a later paper Speery and Bloor⁹ described further experiments on the 'fæcal lipoids' and they concluded that 'the most probable source of the fæcal fat seems to be excretion from the blood, either directly or indirectly, as is evidenced by similarity of the fæcal lipoids to those of the plasma.' They believed that there were two possible ways in which fat could be excreted from the blood: either as a true excretion of unusable material, waste fat from lipid metabolism, or as a leakage of usable fat due to a fat plethora and analagous to alimentary glycosuria on a high sugar intake.

The conclusions only are quoted here, but the original papers contain records of many experiments in support of the views put forward, and if the work is accepted as correct, then a possible explanation for coeliac disease lies in the high blood fat associated with excretion in the fæces of fat which has "leaked" from the blood. In other words the primary fault in coeliac disease is not a mal-absorption of fat, but a mal-utilisation of fat, a defect of fat metabolism possibly analagous to the defective utilisation of sugar in diabetes. It is suggestive in this connection that in many cases of coeliac disease carbohydrates are not normally dealt with, and indeed the association of coeliac disease and diabetes mellitus has been described in a child of seven years old by Poynton and Cole¹⁰. It is also interesting to note that a high blood fat is found in many cases of diabetes where it is fairly definite that there is a failure of fat metabolism as well as carbohydrate metabolism.

CONCLUSION.

We have not investigated sufficient cases to establish the theory here put forward, but as a working hypothesis for further investigation we would suggest that coeliac disease is a primary disorder of fat metabolism associated with an increase in the fat in the blood and in the fæces, where possibly it is being excreted.

We are indebted to the Physicians of the Hospital for Sick Children, Great Ormond Street, for permission to make use of their cases.

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BLOOD FAT IN CÆLIAC DISEASE

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TABLE 1.

BLOOD-FAT ESTIMATIONS IN NORMAL CONTROLS.

Case.	Age in years.	Disease.	Fatty acid in blood, %
E. K.	1 $\frac{2}{3}$	Otitis Media	·163
B. W.	4	Rheumatic Carditis	·142
E. P.	2 $\frac{3}{4}$	Cerebral Tumour	·208
P. D.	2 $\frac{2}{3}$	Unresolved Pneumonia ..	·173
M. R.	2 $\frac{1}{2}$	Diarrhoea (stools normal) ..	·142

Blood taken in each case about 11 a.m., that is, 2 $\frac{1}{2}$ hours after a light meal.

TABLE 2.

BLOOD-FAT ESTIMATIONS IN PROBABLE CASES OF CÆLIAC DISEASE.

Case.	Age in years.	Comments.	Fatty acid in blood, %
D. B.	3	Improving	·275
E. B.	2 $\frac{7}{8}$	Improving	·280
D. S.	3 $\frac{1}{2}$	Not doing well	·530
J. A.	3 $\frac{9}{10}$	Improving	·280
B. R.	2 $\frac{1}{2}$	(See note below)	1·17
"	"	" " "	1·15
"	"	" " "	·51
J. S.	4 $\frac{1}{2}$	" " "	·62

The blood in each case taken about 11 a.m. after a small meal at 8.30 a.m. containing no fat. The last two cases were private patients. Blood was taken three hours after a meal very low in fat. These two cases were investigated before treatment was begun.