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Coeliac Disease

II. *The Presence in Wheat of a Factor Having a Deleterious Effect in Cases of Coeliac Disease*

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A basic principle of current opinion on the dietary treatment of coeliac disease is that all starch-containing foodstuffs (with the exception of bananas) are injurious for the patient and must be avoided (HAAS, ANDERSEN, SHELDON, LOWE and others).

In contra-distinction to this view, we have learnt in the course of many years' experience in the treatment of cases of coeliac disease that it makes a great difference to the patient what kinds of starch-containing foodstuffs (cereals and starches) are included in the diet; in particular, whether or not wheat is used. If wheat is banished from the diet and rice flour, maize starch, peeled, boiled potatoes are given instead, the anorexia, vomiting and abdominal pain disappear, the acute attacks of diarrhoea cease, the faeces become darker in colour, the patient gains in weight and finally the growth in height becomes normal, or even more than normal. If wheat is given again, the anorexia returns, the attacks of diarrhoea reappear, the stools become more liquid and lighter in colour, the weight decreases and growth slows down or is arrested.

This clinical observation was confirmed by experimental investigation (DICKE and WEIJERS), by a method which has been described elsewhere (VAN DE KAMER, TEN BOKKEL HUININK and WEIJERS; WEIJERS and VAN DE KAMER).

For this purpose patients with coeliac disease were placed on a diet consisting of milk (standardized at 2 $\frac{1}{2}$ % of fat) or protein milk, eggs, lean meat, butter, margarine, vegetables, fruit juices, sugar, glucose and cereals and/or starches in measured amounts for each patient. Only the kinds of starch-containing foodstuffs were varied, but always in equivalent amounts with respect to starch content, while the other components of the diet remained unchanged. Sometimes a correction was made for the different protein contents of the various cereals and starches, by varying the amount of lean meat.

Mean Coefficient of Fat Absorption per Test Period, as Percentage: (All Periods were Consecutive, without Interruption) ¹						
Case and Test	Sex	Age (yrs)	Rice flour or maize starch + potato	Wheat flour	Rice flour or maize starch + potato	
A	M	15	87.6	71.4	85.5	
C ¹	M	4		86.7	92.5	
C ²	M	4	94.9	81.3	94.3	
D ²	M	8		86.7	93.9	
E ¹	M	5	95.1	84.8	93.9	
			Rice flour or maize starch + potato	Wheat flour	Wheat starch	
B	F	3	83.9	63.9	86.7	
D ¹	M	8	95.4	74.9	94.1	
			Maize starch + potato	Rye flour	Maize starch + potato	
D ³	M	8	93.9	85.6	89	
			Maize starch + potato	Oats	Maize starch + potato	Oats
G	M	9	91.3 ²	85.3	95.5	89.6
			Maize starch + potato	Only 6 g maize starch no potato	Maize starch + potato	
E ²	M	5	91.8 ²	93.1	95.1	

¹ The percentages were calculated after having attained the new level.
² First period after admission to the hospital.

Every day or every second day the amount of faeces per 24 or 48 hrs was measured and the fat content of the wet stools was determined by the method of VAN DE KAMER, the fat excretion being calculated in grams per day. As the amount of fat ingested was known, the fat absorption coefficient could be calculated (WEIJERS and VAN DE KAMER).

Each diet period lasted 3—4 weeks; this is long enough to give the patient a chance to become adapted to the new diet, i.e. to reach a new level if necessary. This is usually attained after 10—14 days, but may take longer. Further, it is necessary to get sufficient data at the new level to permit a statistical analysis. The results are shown graphically (figs. 1, 2, 3 and 4) and in the table above. It should be noted that a descent of the absorption coeffi-

cient from 90 % to 80 % means a doubling of the number of grams of fat eliminated in 24 hrs.

Example of one of the tests: (D¹, D², D³). An 8 year-old boy with coeliac disease: The test extended from 22nd Jan. 1949 to 10th Jan. 1950. The diet contained 68 g protein; approx. 50 g fat; approx. 245 g carbohydrate and approx. 1750 calories.

Period I. 22 Jan.—12 Feb.: Diet: 950 g milk (2 1/2 % fat), 76 g glucose, 15 g sugar, 125 g carrots, 125 g apple purée, 150 g raw apple, 10 g butter, 10 g margarine, 1 egg, 100 g meat, 57 g maize starch and 250 g potato.

Period II. 12 Feb.—4 March. Diet: The 57 g maize starch were replaced by 57 g of rice flour; the meat was cut down to 80 g. The fat absorption coefficient over periods I and II was 95.4 % (faeces 56 g/24 hrs, fat content 4.6 %).

Period III. 4 March—23 March. Diet: The 57 g of rice flour were replaced by 65 g of wheat flour; the meat was reduced to 65 g.

Period IV. 23 March—13 April. The 250 g of potatoes were replaced by 55 g of wheat flour; the meat ration was increased to 85 g. Coefficient of fat absorption over periods III and IV was 74.9 % (faeces 121 g/24 hrs, fat content 10.3 %).

Period V. 13 April—30 May. The whole 120 g of wheat flour were replaced by 110 g of wheat *starch* (*amylum tritici*), the meat ration was raised to 120 g. The coefficient of fat absorption was 94.1 % (faeces 49 g/24 hrs, fat content 5.5 %).

Period VI. 30 May—22 June. The 110 g of wheat starch were replaced by 130 g of corn flour and the meat was cut down to 60 g. The fat absorption coefficient over periods V and VI was 94.2 % (faeces 57 g/24 hrs, fat content 4.6 %).

In order to ascertain that the patient had not undergone a spontaneous improvement but was still sensitive to wheat flour, a new wheat flour period was instituted.

Period VII. 22 June—28 Aug.: The 130 g corn flour were replaced by 130 g of wheat flour. The coefficient of fat absorption was 86.7 % (faeces 75.2 g/24 hrs, fat content 8.4 %).

Period VIII. 28 Aug.—11 Nov. Diet as in period I. Coefficient of fat absorption 93.9 % (faeces 57 g/24 hrs, fat content 5.3 %).

Period IX. 11 Nov.—9 Dec. The 57 g maize starch and 250 g potato were replaced by 130 g of rye flour. Coefficient of absorption 85.6 % (faeces 98 g/24 hrs, fat content 14.4 %).

Period X. 9 Dec.—10 Jan. Diet again as in periods I and VIII. Coefficient of absorption 89 % (faeces 88 g/24 hrs, fat content 5.9 %).

Upon statistical analysis of the coefficient of absorption it was found that the two wheat flour periods III + IV and VII showed significant differences from the preceding and succeeding periods without wheat flour. $P = < 0.001$.

The periods without wheat flour which were close together in time (I plus II and V plus VI, V being a period with wheat *starch*) showed no significant difference from each other. $P = 0.22$.

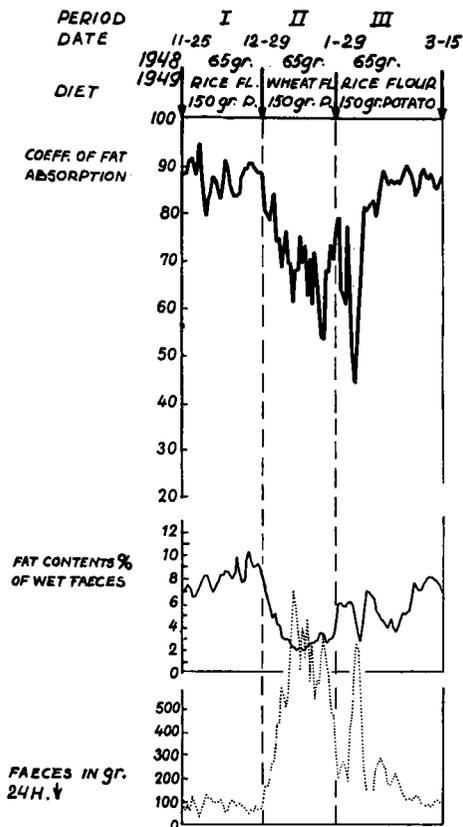


Fig. 1. Case A.

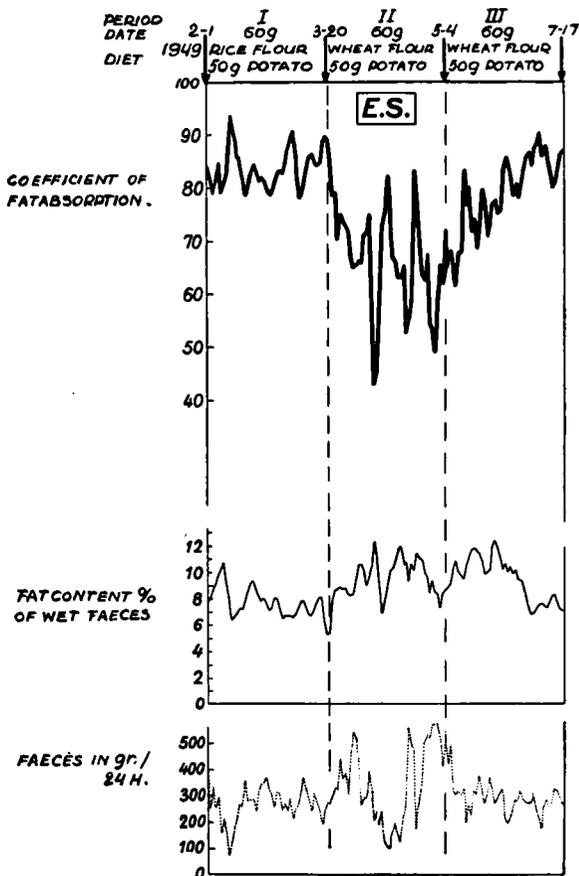


Fig. 2. Case B.

The two periods VIII and X without wheat flour are less satisfactorily comparable, because the recovery in X proceeded slowly, the period was short and the calculation was started immediately after the change of diet. In spite of this, period IX shows a significant difference from period VIII and period X. $P = < 0.001$ and $P = 0.032$. If we look at the periods IX and X on the graph we see a descending line in IX and an ascending line in X. Upon calculating the regression coefficients we find these to be of opposite sign and greater than $2 \times S_b$.

The wheat used was grown in the Netherlands; the flour was of 75 % extraction as provided at the experimental mill of the Cereals Department of the Institute for Research on Nutrition T. N. O. Analysis: protein 8.6 %; fat 1.3 %, carbohydrate 76 %; crude fibre 0.15 %. Free from baking additives and bleaching agents.

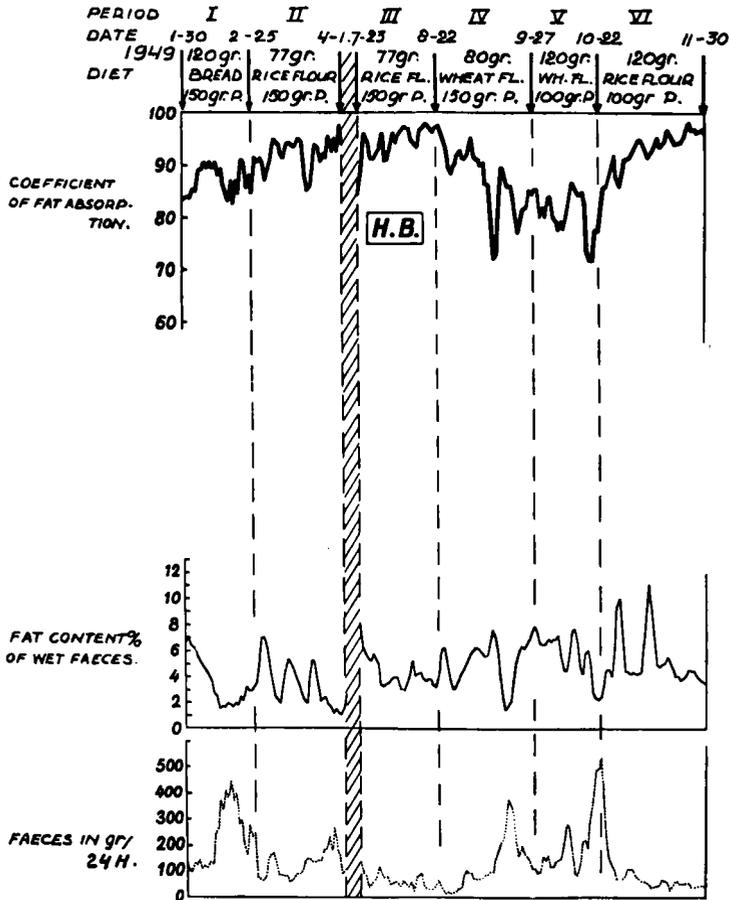


Fig. 3. Case C.

In addition to the data reported above, we are also in possession of the results of experiments with wheat flour on a fat free diet; these point in the same direction but will be published in another article.

Of the starch containing foodstuffs as far as investigated, the following are harmless; wheat starch, cornflour, maize starch, rice flour, and peeled, boiled potatoes.

Of the cereals and starches, wheat flour and rye flour and oats have a very unfavourable effect on the patient.

The other starch containing foods, such as barley, peas and beans, have not yet been tried and it is not known to which group they belong.

It was found, however, that no conclusions can be drawn as to the quantitative interrelations of the above-mentioned phenomena, since in one

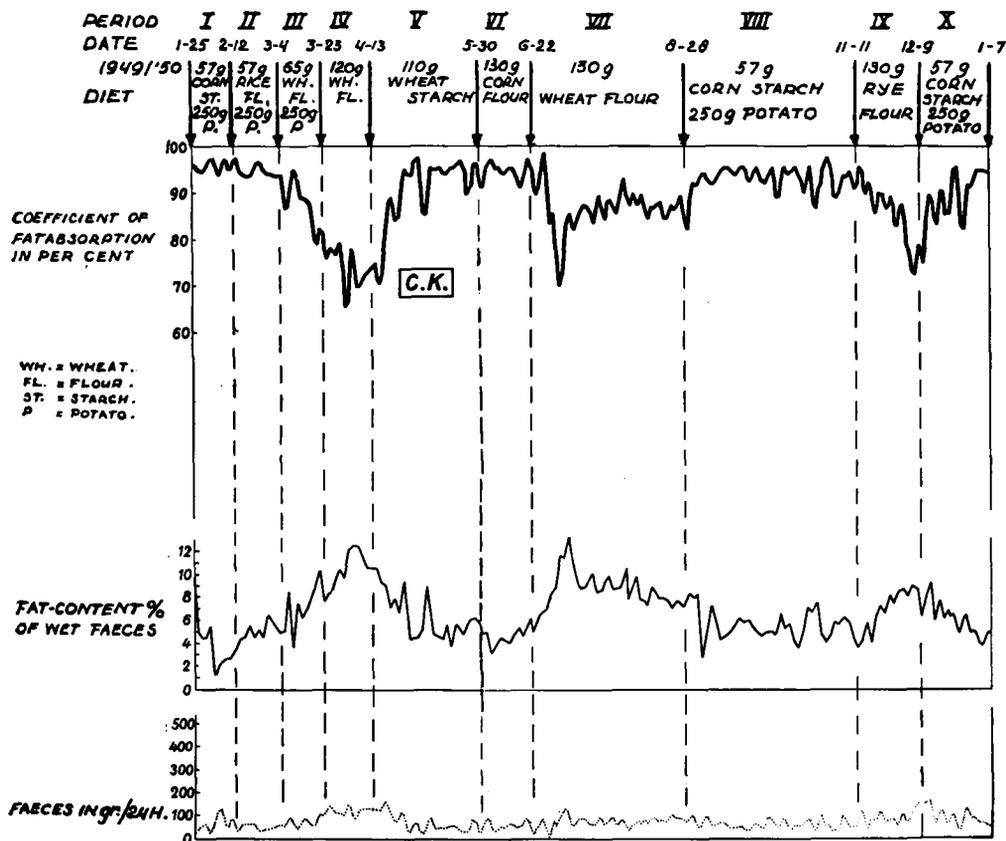


Fig. 4. Case D.

test period the increase in the volume of faeces may be the chief sign, while in another the fat content-percentage or perhaps the clinical signs may come more to the foreground. This is unpredictable. (See graphs 1-4.)

Discussion

A very remarkable and important fact is that while wheat flour shows the deleterious effect, wheat starch does not. Wheat starch is obtained by washing out kneaded wheat flour and allowing the starch to settle out of the washings, after which it is dried. Since the starch does not produce the harmful effect, one of the other components of the wheat flour must be responsible for this. Which component this is we do not yet know. For the time being we call it the "wheat factor."

The effect of rye and oats is supposed to be due to the same factor. We do not know whether the factor in question is also present in other starch containing foods.

As criteria for the diagnosis of coeliac disease we employed those which are in general use, as described, for instance, in the textbook of MITCHELL and NELSON. But even, should the reader make use of other criteria, this still does not in any way alter the wheat phenomenon as such.

It is also probable that this "wheat factor" is active over a wider field than in coeliac disease only. It is our clinical experience that some cases of dyspepsia and subacute enteritis in infants and young children respond very favourably to the wheatless diet. Exact laboratory proof is, however, not yet forthcoming.

However not all forms of steatorrhoea (e.g. fibrosis of the pancreas) are influenced by the "wheat factor." It still remains to be seen whether the difference in behaviour with respect to wheat will form a useful basis for a classification in which coeliac disease and related diseases can be brought together and also a clearer insight can be gained in the abortive forms.

It has by now become obvious that behind the alleged deleterious influence of carbohydrates on absorption there looms another still unknown harmful food constituent which exerts its damaging activities in the patient with coeliac disease either in the intestinal wall or deeper in the organism.

Conclusions

(1) A factor exists in wheat, which is the cause of anorexia, vomiting, diarrhoea and a large proportion of the fat elimination in patients with coeliac disease. However, this factor is not the wheat starch.

(2) Although anorexia, vomiting, diarrhoea and steatorrhoea are produced or exacerbated by the "wheat factor", there is no quantitative interrelation between these symptoms.

(3) The "wheat factor" has so far been encountered only in wheat, rye and oats.

(4) It is possible and perhaps even probable that this factor will also be found in certain other foodstuffs which have not yet been tested.

(5) It is probable that the "wheat factor" is active in other disturbances as well as coeliac disease (indigenous sprue, some forms of subacute dyspepsia and enteritis in infants and small children).

(6) The effect of the "wheat factor" may be of importance for the recognition and understanding of nutritional and intestinal disturbances.

(7) In investigations of improvements produced by medication or vitamins in cases of coeliac disease, the experimental set-up must take the "wheat factor" into account, in order to avoid wrong conclusions.

Summary

Attention is drawn to the different effects of different kinds of cereals and starches on patients with coeliac disease. The effect of wheat flour is unfavourable while that of wheat starch is harmless. The harmful effect is produced by a still unknown substance and not by starch. The substance in question is provisionally called the "wheat factor." The effect of this factor is judged according to its ability to produce or aggravate anorexia, vomiting, diarrhoea and steatorrhoea. Several conclusions as to the significance of this factor are presented.

Présence dans le blé d'un facteur ayant un effet nuisible dans les cas de maladie coeliaque.

On attire ici l'attention sur les différents effets des diverses sortes de céréales et d'amidon chez les malades atteints de maladie coeliaque. L'effet de la farine de blé est nuisible tandis que l'amidon de blé est inoffensif. Cet effet défavorable est produit par une substance encore inconnue et non par l'amidon. La substance en question est provisoirement appelée « facteur du blé ». L'effet de ce facteur est jugé selon qu'il est capable de produire ou d'aggraver l'anorexie, les vomissements, la diarrhée et la stéatorrhée. Plusieurs conclusions sont présentées au sujet de la signification de ce facteur.

Ein im Weizen vorhandener, bei Coeliakie schädlicher Faktor.

Die Aufmerksamkeit wurde auf die verschiedenen Effekte verschiedener Arten von Getreide und Stärke auf Coeliakie-Patienten gelenkt. Der Einfluss von Weizenmehl ist ungünstig, während Weizenstärke harmlos ist. Dieser ungünstige Effekt wird durch eine bis jetzt nicht bekannte Substanz ausgelöst, und nicht durch Stärke. Diese Substanz wird vorläufig als „Weizenfaktor“ bezeichnet. Die Wirkung dieses Faktors besteht in der Fähigkeit Anorexie, Erbrechen, Diarrhoe und Steatorrhoe zu verschlimmern. Einige Schlüsse über die Bedeutung des Faktors werden vorgetragen.

Presencia en el trigo de un factor mostrando efectos nocivos en casos de enfermedad celiaca.

Se llama la atención sobre los diversos efectos de diferentes clases de cereales y almidones en pacientes con enfermedad celiaca. El efecto de la harina de trigo es desfavorable, mientras que el almidón de trigo no es nocivo. Este efecto desfavorable es producido por una substancia todavía desconocida y no por el almidón. La substancia en cuestión es provisionalmente llamada « factor trigo ». La acción de dicho factor se juzga de acuerdo con su capacidad para producir o agravar la anorexia, vómitos, diarrea y esteatorrea existentes. Se presentan varias conclusiones sobre la significación de dicho factor.

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Note during the correction: Our results have been confirmed by ANDERSON *et al*, SHELDON and LAWSON, and SÖDERHJELM:

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Received 1.4. 1952.

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