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GEE-THAYSEN DISEASE

(IDIOPATHIC STEATORRHOEA OF ADULTS AND ADOLESCENTS IN NON-TROPICAL COUNTRIES)

BY

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WITH A NOTE AND A POSTSCRIPTUM

BY

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This disease, of which two cases are recorded here, has received considerable attention during the past decade. Coeliac disease was first described by Samuel Gee (1888) of London, and the condition as it occurs in adults and adolescents of non-tropical countries was first extensively studied by Thaysen (1929, 1932); hence the reason for the nomenclature, Gee-Thaysen disease, a name first suggested by Moore, O'Farrell, Geraghty, Hayden, and Moriarty (1936) and later supported by Mogensén (1937).

These two cases came under the care of Prof. Henry Moore in the Mater Misericordiae Hospital, Dublin, since the publication of the ten cases described by him and his co-workers in the paper mentioned above. Each has been fully investigated on the basis of the criteria then advanced. The recent work of Kantor (1939) has added what may prove another important diagnostic feature—i.e., roentgenological changes in the small intestine. These are (a) obliteration of the usual markings of the valvulae conniventes—the “moulage” sign; and (b) dilatation of the small intestine and segmentation of the contained barium into “clumps.” In neither of our cases can it be said that Kantor's findings were discovered. In the previous series of cases from this hospital (Moore and others, 1936) three had duodenal abnormalities, and one of these (Case 4) showed “duodenal and jejunal delay with marked diminution of the typical markings of these bowel segments.”

Treatment in both of our cases proved very gratifying. In this connexion the experiments of Barker and Rhoads (1937) are of interest. These authors concluded that in tropical sprue the parenteral administration of liver extract exerts some specific effect upon the absorptive power of the small intestine. Blood-fat determinations in sprue patients before and after liver therapy, with normal subjects as controls, support their conclusions. Snell (1939) reports that the appearance of the small intestine, as shown by roentgenological observation, was restored to practically normal by the parenteral administration of liver extract. In our second case satisfactory clinical response may have been to some extent influenced by the liver extract therapy, but this is doubtful.

Case I

An unmarried man aged 28 was admitted to hospital on November 7, 1938. The family history was negative. His own history was uneventful up to the age of 18, when he was treated for “glands in the neck,” which disappeared. His present trouble began some months before admission with loss of appetite, lack of energy, and loss of weight, which he estimated at a stone and a half; at that time also he began to suffer from diarrhoea.

Physical Examination.—His weight was 93½ lb. and height 63½ in. He was thin and pale, the tongue was too red and too clean, and papillae were scanty. Beard and moustache were absent. Examination of the lungs revealed some scattered rhonchi in both. The abdomen was slightly distended, while the descending colon was palpable and tender. The testicles were small; the pubic and axillary hair was scanty, and the former was feminine in distribution. Chvostek's and Trousseau's signs were negative and the clinical physical examination was otherwise normal.

Laboratory Investigations.—Blood chemistry (in mg. per 100 c.cm.): Serum calcium, 8.9; inorganic phosphorus, 3.1; urea, 42; cholesterol, 115. A blood examination showed 3,860,000 erythrocytes and 4,100 leucocytes per c.mm., with a normal differential leucocyte count; haemoglobin, 60%; and colour index 0.77. A blood smear revealed slight anisocytosis and poikilocytosis. A fractional test meal disclosed a very low curve of free HCl, the maximum being 16 units. The basal metabolic rate was -24%. The peroral glucose-tolerance test (ingestion of 50 grammes of glucose) gave the following results:

Time	Blood Sugar
Fasting	76 mg. per 100 c.cm.
In 30 minutes	85
In 1 hour	83
In 2 hours	63
In 3 hours	61

The curve was “depressed,” the greatest increase of blood-sugar value being 9 mg. per 100 c.cm. (normal increase, 40 mg.). The faeces were light, clay-coloured, foul-smelling, and porridge-like. Microscopical examination did not reveal starch, undigested muscle fibres, or neutral fat; there was an excess of soaps, fatty acids, and other fat combinations, but no pus, blood, or mucus. On ordinary ward diet the weight of the stools averaged 40 oz. a day over a period of one week after admission. Chemical analysis of the twenty-four-hour stool (under ward dietary conditions) gave 46.23% total

lipids, with normal fat splitting and a nitrogen output in the faeces of 8.34 grammes; the nitrogen figure, however, fell to a more normal one while the patient was under treatment. The results of the twenty-four-hour chemical stool analysis are summarized in the accompanying table, along with those of Case II.)

Table showing Chemical Analyses of 24 Hours' Faeces

Case	Date	Total Weight of Moist Stool	Dry Matter	Total Lipoids	Neutral Fat	Free Fatty Acid	Soap Fat	Total Lipoids	Neutral Fat	Nitrogen	Approx. Fat in Diet
I	18/11/38 17/1/39	gm. 1,140 653	% 14.33 9.02	% 46.23 58.53	% 10.85 9.72	% 29.54 21.35	% 5.84 27.47	gm. 75.47 34.48	gm. 17.64 5.70	gm. 8.34 3.02	gm. Full diet, 77
II	29/9/39 3/11/39	436 203	19.15 16.47	54.01 20.18	21.68 6.26	13.23 12.02	19.10 1.90	45.12 7.06	18.00 2.05	4.30 1.96	Full diet, 69

Röntgenological Examination.—No evidence of pulmonary disease was observed. There was a rapid passage of barium meal through the small intestine, and very marked redundancy of the large bowel with associated stasis and dilatation of the lumen due to intestinal gas. The epiphyses of the lower ends of the ulnae were not united to the shafts, while those of the lower ends of the radii, tibiae, and femora, and the upper ends of the tibiae were but partially united. A moderate degree of bony subcalcification was shown by controlled radiography of the hand. Barium enema examination emphasized the marked redundancy and dilatation of the colon; owing to the large amount of enema required to fill the entire colon it was considered inadvisable to fill the large bowel completely.

Examination of the eyes revealed normal refraction, and slit-lamp examination showed no abnormality of the lenses.

Treatment.—The patient was put on a low-fat diet consisting approximately of carbohydrate 218 grammes, protein 88 grammes, and fat 77 grammes per twenty-four hours. He was given 25 minims of dilute HCl with a little pepsin thrice daily by mouth after meals, and daily in addition, orally, 9 grains of ferrous sulphate, 40 grammes of calcium gluconate, 25 mg. of calciferol, and a vitamin preparation which furnished a daily intake of 18,600 international units of vitamin A, 150 international units of vitamin B₁, 30 Sherman units of vitamin B₂, 600 international units of vitamin C, and 2,700 international units of vitamin D. Under this treatment the bulk of the faeces was reduced considerably: over a period of two weeks before discharge they averaged about 22 oz. a day. Diarrhoea was completely relieved and steatorrhoea was reduced from 75.47 to 34.48 grammes of total lipid per twenty-four hours (see table). Nine weeks after admission the blood count showed: erythrocytes, 3,800,000 per c.mm., haemoglobin 70%, and colour index 0.92. The patient left hospital on the above treatment on January 25, 1939.

Re-examination on July 20, 1939, after approximately six months of this treatment at home, showed a gain in weight of 30½ lb. and an increase in height of almost one inch (2½ cm.); the axillary and pubic hair was more plentiful, but the latter was still feminine in distribution. The patient had had no diarrhoea since his stay in hospital and he stated that he felt, and he certainly looked, extremely well. There was apparently no anaemia (no blood count was done). He was seen again in May, 1940. For the previous twelve months or so his only treatment was a low-fat diet. His weight was approximately 10 stone, and he reported that he felt well, was able to do a full day's manual labour on a farm, and had no diarrhoea, the stools being well formed and normally coloured. The pubic and axillary hair had increased, and he stated that libido was present. A test meal was normal and the blood count showed 4,210,000 erythrocytes and 101% of haemoglobin. He certainly looked in very good health.

Summary.—A man aged 28 suffering from diarrhoea, lack of energy, loss of appetite, loss of weight. Examination showed a mild hypochromic anaemia, moderate bony subcalcification, ununited epiphyses, infantilism, and steatorrhoea. Treatment with a low-fat diet, iron, and

vitamins produced striking improvement clinically, a gain in weight of more than 3 stone, and an increase in height of 2½ cm.

Comments on Case I

1. The diagnosis of Gee-Thaysen disease might seem to be in doubt because of the high faecal nitrogen (8.34 grammes). This would suggest pancreatogenous steatorrhoea: Thaysen (1932) considered that a faecal nitrogen which much exceeds 3 grammes daily indicates this latter condition. The faecal nitrogen estimation in the present case was reported on four occasions during the next fortnight, with the following results: 3.58, 4.19, 4.68, and 3.65 grammes. These figures are considerably lower than the first analysis, although still somewhat above Thaysen's figure; but when considered with the "flat" type of blood-sugar curve, the absence of muscle fibres in the stools, and the clinical course of the case, the diagnosis of pancreatogenous steatorrhoea may be discarded.

2. After reduction of the fat intake the percentage of lipid in the faeces did not become reduced; indeed, it increased from 46.23% of the total dry matter to 58.53%. Nevertheless, although the percentage of total lipid did not fall on treatment, the amount of lipoids in the stools by weight fell from 75.47 to 34.48 grammes, and of neutral fat from 17.64 to 5.7 grammes—a drop of 55% and 70% respectively. The effect of curtailment of fat on the faecal lipid output was considered by Moore and his co-workers (1936) in the previous series of cases studied in this hospital; it was concluded that usually the percentage of lipid in the faeces varied directly with the fat intake. Nevertheless inconsistent results were obtained (Cases 6 and 10) in which the percentage output was greater after the restrictions in the diet. Bennett, Hunter, and Vaughan (1932) made a special investigation of this point on one patient (Case 1); they found that the percentage faecal output was reduced with a low-fat diet although even then on the average the fat comprised more than 25% of the dried faeces. Clinically in the present case the fat-poor diet controlled the diarrhoea, although it cannot be exactly stated to what extent fat absorption was influenced by the treatment.

3. At 28 years the patient increased in height by almost one inch (2½ cm.). Epiphyses were ununited before treatment began. Two cases in the series reported by Moore *et al.* (1936) (Cases 4 and 7, aged 22½ and 19 years) also increased in height while under treatment. Thaysen suggested that hypovitaminosis of the fat-soluble vitamin A is an important factor in causing the infantilism of this disease. Mogensen (1937) investigated one patient for vitamin A deficiency according to the method of Edmund and Clemmesen (1936), and he concluded that there was probably a deficiency even though there were no clinical signs. He suggested, therefore, that therapy should include regular administration of vitamin A. In patients with ununited epiphyses this ought to be particularly valuable. In the present case 18,600 international units of vitamin A were given daily.

Case II

A male aged 19 was admitted to hospital on September 21, 1939, with the complaint that he had not increased in weight during the previous two years despite an inordinate appetite. For four years he had been treated for anaemia with liver orally and later on with liver extract. He was listless, easily fatigued, and disinclined for any considerable exertion. He stated that for as long as he could remember he had had diarrhoea (three to four motions a day), with the exception of an interval of three years at a boarding-school when apparently he was unwittingly being treated by a low-fat diet. With the exception of bronchopneumonia at the age of 2 years there had been no other serious illness, and the family history was not significant.

declared that a relatively high nitrogen intake was essential for the maintenance of a positive nitrogen balance in idiopathic steatorrhoea; in a series of experiments on patients he maintained a positive balance on diets with a daily protein equivalent of 80 to 90 grammes. In both of our cases an allowance of about 2 grammes of protein per kilogramme of body weight was made, which meant that each patient received approximately 90 grammes of protein daily. A liberal protein intake is therefore apparently advisable in treatment.

I wish to express my thanks to Prof. Henry Moore for his suggestion to publish these two cases and also for his invaluable advice and criticism in the preparation of this paper.

PROFESSOR MOORE'S OBSERVATIONS

Little is known of the pathogeny of this interesting but complex disease. My own view is that in the great majority of cases the fundamental fault lies in imperfect absorption from the small intestine; in a small minority, however, lacteal obstruction may possibly play a part. The most important factor in the causation of the symptoms would seem to be imperfect lipid absorption: the presence of the abnormal amount of lipoids in the bowel would appear to be to a large extent responsible not only for the diarrhoea but also for the imperfect absorption of calcium, phosphorus, haematopoietic bodies, and vitamins, in varying degrees in different cases. This view is supported by the following observation. We have been able to follow eleven of our twelve cases for from fourteen months to fifteen years—seven of them for over five years and two for over three years. After the initial period of some months on low-fat diet and "replacement" therapy seven of them remained in quite good health for prolonged periods on the low-fat diet alone. In addition to the low-fat diet, one took calcium gluconate, one took a few daily drops of haliverol, one had occasional doses of marmite, and one had occasional doses of dry vitamins; all four continued well for years. It is probable, therefore, that the chief factor in the production of disability in the Gee-Thaysen disease is the abnormally increased lipid content of the bowel due to malabsorption of lipoids by the small intestine.

In the paper by Bennett, Hunter, and Vaughan (1932) it is stated that in adult and adolescent cases of idiopathic steatorrhoea the results of treatment in general are more disappointing than in children suffering from coeliac disease, and that, although some cases respond more satisfactorily than others, in the majority all that is accomplished is the alleviation of one or more symptoms and the temporary arrest of downward progress. Our experience, on the contrary, is that the results of treatment are most satisfactory, and this notwithstanding the fact that six of our twelve cases could be classified as very severe and four as severe; three of them had multiple pathological fractures, all of which healed under treatment. Of our twelve patients one died of the disease itself—this was a case seen in 1926 (Case 2 in our original paper), when we were not in a position to carry out the successful treatment elaborated later; one died of acute lobar pneumonia in 1936, but for three years from discharge enjoyed excellent health; and one died of pulmonary tuberculosis, symptoms of which appeared three and a half years after discharge from hospital. Of the nine cases surviving to date the results can be stated to be excellent in six (of which one was observed for fourteen months, one for two years, and the remaining four for from five to fifteen years) and good in three (all of these three cases were observed for over five years).

Accordingly, our belief is that treatment—which in the initial stages should be carried out in hospital, which must

be individualized, and which may have to be continued for considerable periods—gives on the whole very satisfactory results.

POSTSCRIPTUM

Since the above note was written a paper by Bennett and Hardwick (1940) has appeared in which these authors, in relation to cases of "non-tropical sprue" in adults, state: "We find no justification for classing such cases with coeliac disease or for describing them, as has been done by H. Moore *et al.* (1936) and E. Mogensen (1937), as Gee-Thaysen disease." "This situation is not improved by the endeavour of Moore and others to identify the infantile cases with those appearing in later life to the exclusion of the tropical cases, for the cases arising in adult life resemble the tropical cases closely, but have only superficial resemblance to the infantile and adolescent ones."

It was precisely to bring out the difference between the infantile and the adult cases that we proposed the name Gee-Herter disease for the former and Gee-Thaysen disease for the latter. There are certain resemblances between the infantile and the adult cases, but there are also differences even whether the adult cases persist from infancy into adult life or arise in adult life: these symptomatological differences are probably due largely to the different age incidence and to the different mode of life led by the adult as compared with the child. Many adult cases in some respects resemble tropical sprue, but many do not—e.g., some cases of "non-tropical sprue" apparently beginning in adult life show marked osteomalacia and even fractures, whereas such conditions are not, so far as I am aware, found in tropical sprue. So far as I can understand their paper Bennett and Hardwick seem to wish to establish the close resemblance between cases of idiopathic steatorrhoea beginning in adult life and cases of tropical sprue. Resemblances there certainly are, but there are also notable differences. For example, as reported in our paper (Moore *et al.*, 1936), Cases 1, 5, and 10 (aged respectively 28, 29, and 63) had marked osteomalacia, with fractures in Cases 1 and 5; yet the onset, so far as could be judged from the history, did not begin in childhood and the symptoms did not closely resemble sprue. On the other hand, in Case 2 (aged 43), which did resemble sprue, the onset was probably in adult life, whereas in Case 6 (aged 40), which also resembled sprue, loose motions had been present since childhood. Again, Case 1 of the present paper did not resemble sprue, and the onset, judged by the roentgenological appearances of the bones, may have begun at about early adolescence, but could not be traced back to childhood.

The point raised by Bennett and Hardwick seems to be the nomenclature of those cases of "idiopathic steatorrhoea" which appear first in infancy and persist until adult life, and of those which first appear in adult life: are the latter more allied to tropical sprue than to coeliac disease? I confess that I do not believe we have enough exact information to give a definite answer to this question. There seems to be little doubt that the one aetiological factor running through (a) coeliac disease, either in infancy or persisting to adult life, (b) "idiopathic steatorrhoea" beginning in adult life, and (c) tropical sprue is, as Bennett and Hardwick put it, chronic jejuno-ileal insufficiency; but the manifestations of this deficiency might be different according to the age of the patient, the time of onset, the duration of the deficiency, the environment of the sufferer, and other factors. With a common fundamental defect it might not always be easy to say whether an adult case was more closely allied to tropical sprue than to infantile coeliac disease.

Gee (1888), describing the coeliac affection, wrote (*italics mine*): "There is a kind of chronic indigestion which is met with in persons of *all ages*, yet is especially apt to affect children between 1 and 5 years old"; and again: "The coeliac disease is commonest in patients between 1 and 5 years old; it often begins during the second year of life. Sometimes from India Englishmen return sick with the coeliac affection; seldom is it met with in *adults* who have never left our island." Gee therefore was almost certainly aware of the existence of adult cases of "non-tropical sprue" as well as of the infantile cases of coeliac disease and of tropical sprue. Tropical sprue was described before Gee's time. Gee's original paper was apparently forgotten until in 1906 Herter, in the U.S.A., gave a good account of the disease in children. Thaysen gave excellent descriptions of adult cases of idiopathic steatorrhoea in 1929 and 1932. With these facts in mind my co-workers and I (Moore *et al.*, 1936) wrote as follows:

"In the interest of clarity, and in order to give credit to those observers who have been chiefly instrumental in the recognition, description, or separation of these three interesting disease entities, we suggest that coeliac disease of children be called the Gee-Herter disease, that idiopathic steatorrhoea as it occurs in adults and adolescents of non-tropical countries be called the Gee-Thaysen disease, and that the name sprue be retained for the disease as it occurs in adult residents of tropical countries. It may be that a better nomenclature will become apparent as the obscurity at present surrounding the pathogeny and aetiology of the idiopathic steatorrhoeas becomes more clear. The name idiopathic steatorrhoea is not a suitable one, for steatorrhoea is common to all three and the term idiopathic is simply a teleological confession of ignorance: steatorrhoea, also, occurs under other conditions."

Bennett and Hardwick would probably argue that it is wrong to use the name Gee-Thaysen disease with reference to an adult case in which the disease began many years back in childhood and persisted into adult life, as well as for the case in which the malady first appeared in adult life or middle age; on the other hand, the symptomatology may not be quite the same in infancy as in adult life, even in those cases in which the disease originated in infancy and with persistence of symptoms into adult life, although not infrequently the resemblance may be close. In the latter case it is admittedly not wholly desirable to call a disease of infancy by one name and to use another when it persists to a later age. While we await the further information necessary for a final nomenclature Gee's name can be attached to both; in the infantile cases the name of Herter and in the adult cases that of Thaysen could be added to denote the changing symptomatology coincident with increasing age.

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I. S. Cormanschi (*Thèse de Paris*, 1940, No. 252), who records three cases in patients aged from 19 to 29, one of which is original, describes a disease characterized by the triad of iritis, genital ulceration, and buccal aphthae. The aetiology is still obscure. Recurrent iritis with hypopyon is found in both sexes. The genital ulcers and buccal lesions are slight. The ocular lesions as a rule consist not only of iritis or iridocyclitis but also of uveitis.

BLOOD AND PLASMA TRANSFUSION IN ALIMENTARY HAEMORRHAGE

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The infusion of serum or plasma has been shown to exert a favourable effect not only in experimental shock in animals (Bond and Wright, 1938; Mahoney, 1938; Best and Solandt, 1940) but also in shock from burns (Trusler *et al.*, 1939) and wound shock (Edwards *et al.*, 1940) in the human subject. It has been argued that even in acute haemorrhage the absolute deficiency of red cells is of less importance than the vascular and circulatory derangement which prevents the effective access of blood to the tissues, and that the improvement of circulation following plasma infusion would outweigh the reduction in the number of red cells per unit volume of blood. If this were the whole story the ready availability of stored plasma and the absence of delay required to group the recipient would render it a valuable preliminary treatment of haemorrhage, even if it were necessary to give whole blood at some later time.

The object of this paper is to compare the effects of citrated whole blood with those of plasma in treating patients with massive bleeding from the stomach or duodenum. For a study of this type patients with haematemesis and melaena offer the advantages that the lesion causing haemorrhage is uniform in type, enabling a fair comparison to be made; reasonably good quantitative indications of the severity and progress of the case are given by measurements of the blood volume (Bennett *et al.*, 1938) and blood urea; and the indications for transfusion are comparatively definite. These last have been summarized by Witts (1937) as a pulse rate above 140, systolic blood pressure below 90 mm., blood urea above 100 mg. per 100 c.cm., or haemoglobin lower than 40%.

Clinical Material and Methods

The nine patients studied were all suffering from severe bleeding from the stomach or duodenum, and were kept at rest in bed on an adequate intake of food and fluid in the form of two-hourly feeds of milk and cream, with added vitamins. The first three were treated with massive transfusion of citrated blood by slow drip, and in one of them three transfusions of a litre or more were given. The fourth patient was treated with reconstituted dried serum in fourfold strength, but showed so severe an immediate reaction that this experiment was not repeated. In Cases 5 and 6 plasma infusion was started, but had to be supplemented straight away by blood transfusion; in Cases 7, 8, and 9 it was possible initially to give plasma alone, by slow drip, although Case 8 required whole-blood transfusion five days later. The plasma used was obtained by allowing blood of Group AB to stand in M.R.C. citrate bottles for forty-eight to seventy-two hours at 4° C., and aspirating the plasma into clean bottles with sterile precautions; it may be of importance that plasma so obtained is diluted bulk for bulk with citrate solution, and it may perhaps be best described as half-strength plasma.

In addition to observations on the general state of the patients, estimations of the blood urea were carried out