PLATE XX

A VITAMIN B DEFICIENCY SYNDROME ALLIED TO SPRUE : A. B. COOK. PAGE 429.

Fig. 1.—An advanced case which failed to respond to treatment.

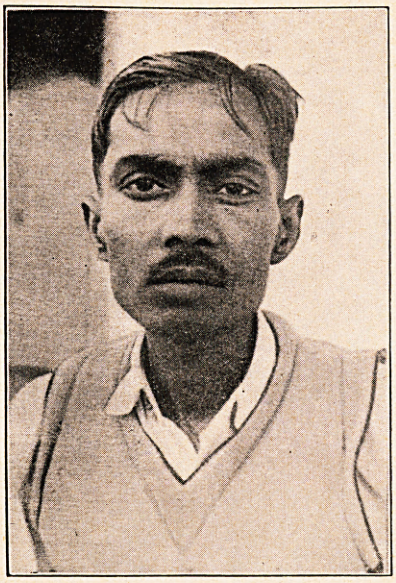

Fig. 2.—Before treatment.

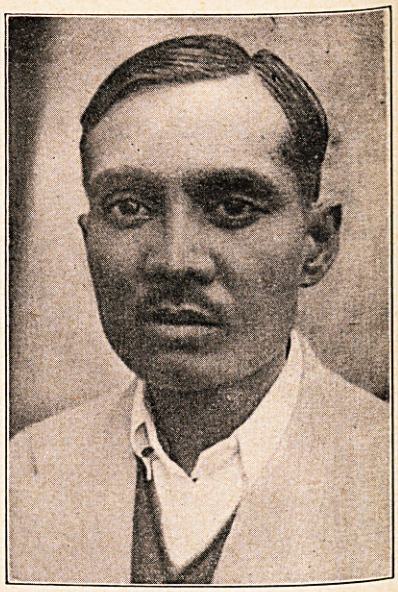

Fig. 3.—After treatment.

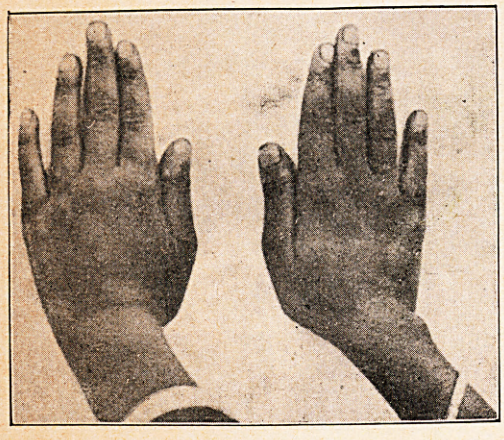

Fig. 4.—The characteristic blackness of the knuckles. It is not a rash as in pellagra.

A NEW METHOD OF ARTIFICIAL RESPIRATION : R. VISWANATHAN. PAGE 400.

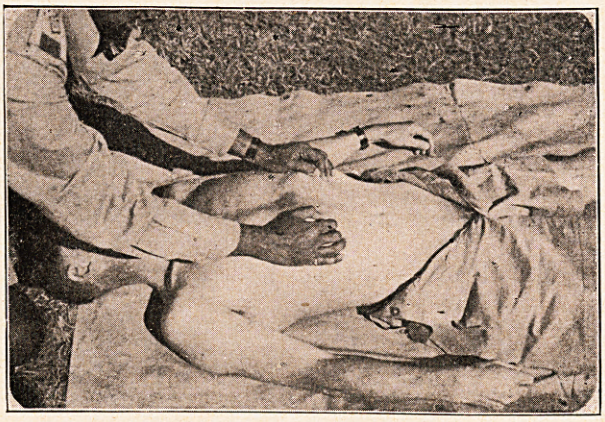

Fig. 1.—Process of inspiration.

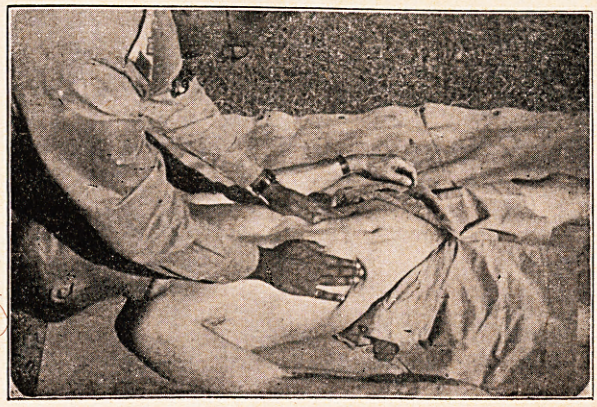

Fig. 2.—Process of expiration.

Special Article

A VITAMIN B DEFICIENCY SYNDROME ALLIED TO SPRUE*

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EVERY practitioner in Gujerat frequently meets patients suffering from a triad of symptoms, diarrhœa, glossitis, and anæmia. In one year I have seen over 200 cases, clinical details of 50 which I have kept for analysis. Hardly a day passes without seeing a typical case. The indigenous practitioner recognizes such cases as 'sprue'. The relative frequency of this disease, if it is really sprue, conflicts with the idea commonly quoted in standard textbooks, *e.g.* Manson-Bahr in 'Manson's Tropical Diseases', 11th edition. 'Sprue is a disease which pre-eminently affects Europeans. Doubt was formerly expressed as to the existence of sprue in native races'. Hamilton Fairley in 'The British Encyclopædia of Medical Practice' writes that 'the disease is very rare amongst Indians'. These statements are true or not according to whether the syndrome I am elaborating is really sprue or not. There is no doubt as to the frequency of this syndrome, but there is doubt in my mind as to whether it is classical sprue or a vitamin B deficiency syndrome allied to sprue.

The salient features are :—

(*a*) Diarrhœa, the motions being watery and copious and in colour white or yellow. They may be passed at any time of the day, especially after meals and be accompanied by exhaustion.

(*b*) Glossitis, the tongue is inflamed. It is usually clean and may be red in spots or be glazed in appearance. The patient complains of soreness of the mouth and of inability to eat spices. The glossitis may precede the diarrhœa or occur simultaneously with it or follow it.

(*c*) Anæmia is usually marked and is frequently macrocytic. In many cases however the anæmia is microcytic.

(*d*) Pigmentation of the skin. The knuckles of the fingers are black and the face is sallow.

The critical difference from sprue as classically described in textbooks is in the nature of the motions.

Hamilton Fairley in 'The British Encyclopædia of Medical Practice' describes the stools of sprue as being 'bulky and loose in consistence, pale, or occasionally even white in colour and gaseous. Exceptionally during acute exacerbations, an enteritic type of diarrhœa may develop with frequent, brownish, fluid stools'. Manson-Bahr in 'Manson's Tropical Diseases' describes the diarrhœa as of two kinds, 'One chronic and habitual, the other more acute and in the early stages, evanescent. The former is characterized by one or more daily discharges of a copious, pale, greyish, pasty fermenting, acid, mawkish, evil smelling material; the latter is of a watery character, also pale and fermenting, the dejecta containing undigested food, and as a rule, an abnormally large amount of oil and fatty acids'.

The loose type of diarrhœa in sprue is thus described by two authorities as being 'exceptional' and 'evanescent'. In the syndrome I am reviewing, however, the loose, watery diarrhœa is the characteristic, habitual feature. The porridge-like, bulky, frothy stool of classical sprue is seldom met with.

This difference in the nature of the diarrhœa constitutes an essential variant from classical sprue, and justifies the isolation of the disease as a syndrome allied to sprue.

Tropical sprue, non-tropical sprue, idiopathic steatorrhœa and cœliac disease are classified together as the 'sprue syndrome'. In the same way this variant of sprue may be accepted as a member of the group of conditions known as 'the sprue syndrome'. Apart from the nature of the diarrhœa, the syndrome is similar to sprue as classically described.

The recent researches into the part played by the vitamin B complex in the physiology of the small bowel, the well-known deficiency of vitamin B in the diet of Indians, and the successful treatment of the syndrome by the administration of vitamin B complex, lead one to the conclusion that the syndrome is due to vitamin B deficiency.

For more than 20 years, it has been known that deficiency of vitamin B is associated with abnormal gastro-intestinal function. Radiological researches in more recent years seem to give the clue to the mechanism of this association. The work began with observation on the small intestine in cases of sprue (Pillai and Murthi, 1931; Mackie, 1933). In these and later studies, mainly by American workers, it was found that characteristic changes occurred in the small intestine in several diseases such as sprue, cœliac disease and idiopathic steatorrhœa. The *valvulæ conniventes* of the duodenum and jejunum normally present a feathery or herring-bone appearance. This appearance is absent in these diseases, and the opaque material separates into smooth, outlined masses of various lengths. These radiological changes are now referred to as the 'deficiency pattern' of the small intestine.

There is growing evidence that one or more components of the vitamin B complex is associated with the development of this 'deficiency pattern'. The deficiency has been produced in dogs on a diet lacking vitamin B, and was only completely cured by the administration of the whole complex (Crandall *et al.*, 1939). Martin and his colleagues (1941) experimenting on dogs found that inositol increased peristalsis in both stomach and small intestine, whereas nicotinic acid decreased peristalsis and induced a state of repose. The authors suggest that the balance of these two factors might determine the motility of the gastro-intestinal tract.

Therapeutic tests also support the theory that the vitamin B complex is probably responsible for the deficiency pattern. Lepore and Golden (1941) describe a series of patients in whom the deficiency pattern was demonstrated and who complained of a series of symptoms which they claim form a clean-out syndrome due to deficiency of the vitamin B complex. The oral administration of yeast or the parenteral injection of liver extract relieved the symptoms, and the deficiency pattern disappeared.

* Being a paper read at the All-India Medical Conference held at Ahmedabad, December 1943.

The deficiency pattern is due to the flattening out or disappearance of the *valvulæ conniventes* as a result of paralysis of the main layer of the *muscularis mucosæ.*

This paralysis of the *muscularis mucosæ* leads to loss of pumping action of the villi into the larger lacteals (Hurst). Fat would thus cease to be absorbed, and the stools would thus contain a great excess of split fat, as in sprue. Such a paralysis would not alter the microscopical appearance of the mucous membrane. If the activity of the *muscularis mucosæ* is regained, the mucous membrane being unimpaired, the villi would start to function again and so normal fat absorption would be resumed.

The cause of this paralysis of the *muscularis mucosa,* if this is the correct explanation of the sprue syndrome, may be vitamin deficiency.

This disturbance of the normal physiological activity of the small intestine, presumably due to vitamin B deficiency, results in a corresponding functional disturbance.

Bennett and Hardwick (1940) have coined the term 'chronic jejuno-ileal insufficiency' to denote the resulting syndrome. The symptoms are gaseous, generalized abdominal distension after meals, borborygmi and gas pains in the area of the small intestine, constipation or diarrhœa with loose stools. The biochemical features are achlorhydria or hypochlorhydria, a flattened glucose tolerance curve due to failure of carbohydrate absorption, faulty absorption of fat with increased fatty acids and calcium soaps in the stools, calcium deficiency due to mal-absorption or retention of calcium in the intestinal tract as calcium salts, failure of absorption of iron and of the anti-anæmic principle, resulting in anæmia. Thus is compounded a syndrome of clinical and biochemical features which gives a complete picture of sprue. Stannus (1942) advances a new hypothesis to explain the defect in intestinal absorption. He believes that the physiological lesion in sprue is failure of phosphorylation, an essential process for the absorption of fatty acid glycerol, cholesterol and glucose by the intestinal mucosa. He suggests that this failure of phosphorylation is due to a defect in the enzyme system which is made up of members of the vitamin B_2 complex, including riboflavin, nicotinic acid, pyroxidine and choline.

The name 'jejuno-ileal insufficiency' places the emphasis on the small bowel and not on the colon. Sprue may be preceded by an attack of amœbiasis which attacks the large bowel essentially—but the symptoms of sprue do not supervene until, due to vitamin B deficiency, as a result of dietetic restriction or failure of absorption, the syndrome of 'jejuno-ileal insufficiency' is produced. Colitis itself does not lead to the clinical and biochemical picture of sprue. In amœbiasis, there may be some secondary anæmia, but never a megalocytic anæmia. The glossitis, achlorhydria, flat glucose tolerance curve, and low serum calcium seen in sprue are not to be found in colitis; they arise when the pathology shifts to the jejuno-ileum.

The evidence that vitamin B deficiency lies at the root of this jejuno-ileal insufficiency is at present practically wholly therapeutic. Lepore and Golden (1941), Mackie (1933), May *et al.* (1942), Manson-Bahr (1941), etc., have shown the remarkable response clinically to an intensive course of vitamin B complex given orally and parenterally. The symptoms disappear, the deficiency pattern radiologically returns to normal, weight is gained. Some experimental work on dogs (Martin and his colleagues) also lends proof to the theory that vitamin B deficiency is responsible for the deficiency pattern. Circumstantial evidence for the theory that vitamin B deficiency is the cause of the sprue syndrome is gained by studying Indian diets. 'The richest sources of vitamin B_1 are unmilled cereals, pulses and nuts. A diet largely composed of raw milled rice contains insufficient vitamin B_1. The greatest danger of vitamin B_1 deficiency arises when a highly milled raw rice is consumed as the main ingredient in a diet containing other foods, such as pulses, in very small quantities. There is good evidence that poor Indian diets, which contain little milk or meat, are often very deficient in vitamin B_2 group' (Aykroyd). The deficiency in the vitamin B complex may be relative and not absolute. Sydenstricker (1941) has shown that on a diet consisting largely of carbohydrate, acute riboflavin and nicotinic acid deficiency is apt to occur. Thiamin, nicotinic acid and riboflavin are concerned with the continuous processes of cellular nutrition and respiration. They are essential for the metabolism of carbohydrates. On a diet with a preponderance of carbohydrate, a correspondingly large 'cover' of vitamin B complex is essential. If this is lacking, then symptoms of deficiency may arise. Moore (1939) commented on the 'sore tongue syndrome' on a staple diet of rice.

Experience confirms the above observations. In any particular case, it is difficult to elicit evidence of any gross deficiency in the diet apart from the general deficiency common to all Indian diets. On being questioned, a patient usually replies, 'I eat rice, dhal, wheat and vegetables'. It is not uncommon however to meet with patients who eat only rice and do not eat bajri or vegetables—or others who have dieted themselves for a long period on buttermilk and pulse water only. In such cases there is a manifest deficiency of the vitamin B complex.

Another observation that lends force to the argument that a dietetic deficiency is the cause of the syndrome is that several cases may be met within one family. A husband and wife may be similarly affected. I have met a family in whom the mother and the three children all had glossitis. In another family, the son at first presented himself with the syndrome in all its features. After some time, when he was showing steady improvement, the father asked that he might take his son's bed as he was not well. He had glossitis, anæmia and weakness, but constipation instead of diarrhœa as in the son's case. Turning to the mother, I found she had also glossitis and anæmia. Probably in the father's case, nicotinic acid deficiency was less marked than deficiency of the other elements of the vitamin B complex, and so he did not have diarrhœa.

I consider this disease is the most serious nutritional defect in Gujerat. I speak as a clinician and not as a nutritional research worker. But I recognize this deficiency disease so frequently and see its debilitating effects in so many of my patients that I know of no other avitaminosis which is responsible for as much ill health in the community.

CLINICAL FEATURES

Diarrhœa

(*a*) *Nature of stools.*—The stools are watery and are often described by the patient as looking like curds and consisting of undigested food. The colour may be yellow or white or greenish. The thick, frothy, bulky, pasty, pale stool of sprue is only occasionally seen.

(*b*) *Time of day.*—The motion may be passed at any time of the day but not particularly in

the early morning as in sprue. A few patients however specify the night and early morning as the time when the diarrhœa occurs, but most patients, on being questioned, say the stools are passed at any time.

(*c*) *Lienteric diarrhœa.*—A very characteristic feature is that there is an urgent desire to defæcate after taking food. There may be a motion every time the patient takes food.

(*d*) *Exhaustion* is felt after passage of the stool.

(*e*) *Quantity.*—The stool may be profuse and exceed in quantity any food intake of the patient.

(*f*) *Number.*—The number of motions may vary from 2 or 3 to 10 or 15 in the day.

(*g*) *Mucus or even blood* may appear in the motion at times. This is not due to chronic dysentery, but due to an acute exacerbation of the disease in which the rectal mucous membrane is injected and inflamed due to the frequent passage of motions.

(*h*) *Gurgling* and sometimes colic accompany the passage of motions.

Constipation may alternate with diarrhœa. One may see a patient who complains of constipation and all the other symptoms suggestive of this syndrome, but in whom diarrhœa had occurred at the onset and only at irregular intervals since.

Pigmentation.—A characteristic feature is a dark or even black pigmentation of the knuckles of the fingers. It seems to be an increase of the natural pigment of the skin overlying the joints, and not a rash on the skin as in pellagra. This blackness of the knuckles is very commonly seen, but it is not invariable. Typical cases may be seen with a normal appearance of the skin.

The common sites of pigmentation are : on the knuckles, the tongue (black spots may appear on the dorsum of the tongue), around the lips and in the nasolabial folds, on the forehead, under the eyes, on the dorsum of the ankles, back of the wrist, extensor surface of the arms, front of the neck, front of the legs below the knees.

The effect is a characteristic sallowness or murkiness of the complexion. The sallow face with the muddy skin and the sunken cheeks at once suggests the probable diagnosis.

Glossitis.—In marked cases, the tongue is clean, smooth, glazed and red. The whole dorsum of the tongue may be red, or the tip only or spots at the sides of the tongue may be red. The redness may extend to the palate and pharynx, and in extreme cases, the whole oropharynx may be inflamed so that the patient has marked dysphagia. Aphthæ of the lower lip frequently occur. When the disease is not so pronounced, the tongue however may not be red and may not even be clean. The tongue may be red and clean during relapses only, regaining its normal colour and even a fur in a remission.

In a series of 50 cases, the tongue was described as :—

Clean and glazed	6
Clean and fiery red all over ..	4
Clean and red at tips or sides ..	20
Slightly furred	3
Clean but normal	17

Angular stomatitis due to riboflavin deficiency was noticed in 3 cases.

The time relationship between the glossitis and the onset of diarrhœa was noted in each case.

Diarrhœa occurred first in 20 cases; glossitis occurred first in 25 cases; the glossitis and diarrhœa commenced simultaneously in 5 cases.

A frequent observation was that the patient had suffered from glossitis on and off for many years, in one case 15 years, before the onset of diarrhœa. One patient said she had suffered from sore tongue since childhood.

Even in cases where there is no gross change in the appearance of the tongue, the patient complains that he cannot eat chillies or hot food.

Dyspepsia.—The patient complains that he is unable to take any food. The prominent features are :—

Gurgling in the abdomen. An urgent desire to defæcate after food, loss of appetite (at times there is excessive appetite but the patient is unable to eat because of the stomatitis), vomiting, a feeling of weight and distension after food, heartburn, pain in the epigastrium and occasional colic is complained of.

Constitutional effects.—Loss of weight is marked in all cases; exhaustion and weakness are prominent; lack of mental power, inability to concentrate, incapacity to work, and mental depression are seen, and irritability of mind is often noted.

Paræsthesia, probably due to thiamin deficiency, is frequently complained of, especially tingling and burning in the legs, soles of the feet, and the palms of the hands. There may be loss of knee jerks. I have observed ataxia in one case.

Fever of a low degree 99 to 100 may often be observed. The temperature may persist for some time, as long as the patient is weak, and automatically disappear as he regains strength. Fever may occur at the onset of a relapse and then gradually disappear.

PHYSICAL EXAMINATION

The general appearance, the sallow muddy face and pigmented knuckles frequently give a clue. The appearance of the tongue and mouth is described above, and the anæmia is described later.

The skin may be dry and scaly over the forearms and legs. There may be evident signs of loss of weight. In advanced cases, there is œdema of the feet due to hypoproteinæmia. The

œdema I have observed to disappear with the use of nicotinic acid alone (oral and parenteral).

The abdomen may be normal in contour and consistency in early cases, but in more advanced cases there is wasting of the subcutaneous fat, and the intestines are outlined against the parietes. Gurgling of the intestines may be audible and palpable. The abdomen may be distended and tympanitic on percussion.

In 44 cases out of 50, it was noted that the descending colon and cæcum were not palpable. In 6 patients giving a clinical history of dysentery, the colon was felt thickened and tender. A low blood pressure was frequently observed during relapses (*e.g.* readings of 90 mm. Hg. systolic and 60 mm. Hg. diastolic—or 110 mm. Hg. systolic and 65 mm. Hg. diastolic).

Varieties of syndrome.—It is important to realize that for every fully-fledged case as described above that is seen, there may be several cases met with which exhibit only part of the syndrome. These may be called 'larval forms' or 'formes frustes'.

There may be glossitis, anæmia and constipation. The patient may complain of indigestion and gurgling and loss of weight, but gives no history of diarrhœa. There may be only anæmia, blackness of the skin and debility; or glossitis and loss of weight only. Any such combination of symptoms may be met with. Such cases are only too commonly labelled as anæmia, debility, neurasthenia or indigestion, and the true significance of the vitamin B deficiency is missed.

Biochemical and pathological features

Hæmatological findings.—The anæmia is typically of the megalocytic type.

In 5 cases, the size of the red cells was measured by Eve's halometer.

In 3 cases, the size was 8 microns and in 2 cases 8.2 microns.

The colour index was in most cases 0.9 or higher.

2	cases	showed	a	colour	index	of	0.7
6	„	„	„	„	„	„	0.8
9	„	„	„	„	„	„	0.9
4	„	„	„	„	„	„	1.0
11	„	„	„	„	„	„	1.1
1	case	„	„	„	„	„	1.3
3	cases	„	„	„	„	„	1.4
1	case	„	„	„	„	„	1.5

A typical blood picture is as follows :—

Patient, male—		
Hæmoglobin	.. ..	58 per cent
Red corpuscles	.. ..	3,100,000
Colour index	.. ..	1.0
White corpuscles	.. ..	5,950
Polymorphs	.. ..	65 per cent
Lymphocytes	.. ..	34 „
Mononuclears	.. ..	1 „

Marked anisocytosis and poikilocytosis. Many megalocytes showed hyperchromia. Basophilic degeneration. A few microcytic cells. No normoblasts nor megaloblasts.

A patient was admitted in a very advanced state of anæmia. He had lost 50 lb. in weight and was very emaciated. Blood transfusion was done but he only temporarily revived and succumbed soon afterwards. His blood picture was as follows :—

Hæmoglobin	.. ..	25 per cent
Red corpuscles	.. ..	910,000
Colour index	.. ..	1.5
White corpuscles	.. ..	3,800
Polymorphs	.. ..	34 per cent
Lymphocytes	.. ..	50 „
Mononuclears	.. ..	16 „

Severe anisocytosis and poikilocytosis, slight hypochromia with a tendency to enlargement of cells. No normoblasts nor megaloblasts.

In such advanced cases of anæmia, the absence of regenerative cells is explained by the aplastic degeneration of the bone marrow. The fatal conclusion even after a blood transfusion is due to the same aplasia.

The gastric secretion

There may be absolute achlorhydria or hypochlorhydria. In 7 cases, absolute achlorhydria was found, and in 5 cases a marked hypochlorhydria. Two cases showed a practically normal curve.

Glucose tolerance.—The glucose tolerance test after ingestion of 50 grammes of glucose shows a flattened or delayed curve due to deficient absorption of glucose from the small bowel. A typical curve is as follows :—

Resting blood sugar	..	90 mg.	per 100 c.c.
One hour after glucose	..	130 „	„ 100 „
Two hours after glucose	..	85 „	„ 100 „

Sigmoidoscopy.—The typical appearance in an uncomplicated case of the syndrome is a pale, thin-walled mucous membrane of the rectum.

In several cases, scrapings of the mucosa were taken directly via the sigmoidoscope and examined for ova and cysts, always with negative results.

In an acute relapse, the rectal mucosa may be reddened and œdematous and covered with mucus. In such cases, a difficulty in diagnosis may arise, and the appearance suggests at first ulcerative colitis. A scraping will be negative for cysts and amœbæ. The diagnosis is determined by the therapeutic test. As the glossitis subsides and the general condition of the patient improves, the rectal congestion settles down.

Fæces.—In sprue, the stools have a high total fat content varying from 25 to 60 per cent of the dried fæces. The fats are split normally as there is no deficiency of enzymes but the fats are not absorbed. The neutral fats to the fatty acids and soaps are as 1:3.

The estimation of neutral fat, fatty acids and soaps by laborious laboratory methods is not necessary. The presence of excessive fat in the stools can be satisfactorily recognized by microscopical examination alone.

In the syndrome I am describing, there may be no increased content of fat. Under the

microscope, occasional fat cells and fatty acid crystals may be seen, but they are not present in any marked degree. There is evidence of undigested food with no increased fat.

I have however seen stools exactly like those of classical sprue, pale, frothy, bulky stools, full of fat and fatty acids, in patients who exhibited no other recognizable feature distinguishing them from the syndrome under discussion.

I can only come to the conclusion that the two conditions are closely related. The difference may be in the preponderance of carbohydrate in the Gujrati diet compared with the mixed diet of Europeans in whom sprue is classically described—or in some particular deficiency of the vitamin B complex resulting in a variation of the syndrome.

The onset of the condition

The onset may be insidious, the initial symptoms being progressive weakness, anæmia and loss of weight. The patient complains that he is getting weaker day by day, and often notices that his skin is getting black. The skin overlying the knuckles of the fingers looks darker than normal, and his complexion is sallow and muddy. There may be darkness of the skin around the neck and the lips. The patient is conscious and concerned about his blackness, and realizes he is suffering from some obscure disease. He feels weak and disinclined to work, his appetite fails, and he loses weight from no apparent cause. The tongue may be sore at this stage, or glossitis may precede other symptoms by a long period. Then, after some time, he begins to get diarrhœa. There is gurgling in the abdomen, and irregular loose motions are passed. As the disease progresses, digestion becomes more and more disturbed. At this stage the diet is usually limited to buttermilk, as is always prescribed by indigenous practitioners. Often the patient will exist for months on buttermilk only.

As soon as heavier food is taken, the patient complains that he gets borborygmi and diarrhœa, and so he hesitates to add anything more to his diet. This extremely limited diet eventually leads to other dietetic deficiencies, and to a state of nutritional œdema due to hypoproteinæmia.

The onset may be precipitate with vomiting and diarrhœa. Often the patient will attribute the attack to the water of some place he may be residing in, *e.g.* Bombay, or it may have commenced while on pilgrimage, the strain and fatigue associated with which probably being the determining factor.

The diarrhœa weakens the patient. He rapidly loses weight. Glossitis may set in at the same time, or shortly afterwards, or may precede the attack.

The diarrhœa subsides for a time with treatment, only to relapse every two or three months.

Varieties of onset

Onset with—	
Diarrhœa	7 cases
Diarrhœa and glossitis	3 „
Glossitis	6 „
Anæmia	4 „
Pregnancy	13 „
Malaria	10 „
Dysentery	7 „
	50 cases

Precipitating factors

Pregnancy is cited as a precipitating factor in 13 cases.

A common history is that the patient develops diarrhœa, or what she calls dysentery, in the last month or so of pregnancy. There may be some blood and mucus in the stools, or there may be only watery motions. The diarrhœa may persist for some time after delivery, and all the symptoms associated with the syndrome we are discussing develop, *viz,* glossitis, anæmia, loss of weight, etc. The diarrhœa may relapse with each pregnancy, the patient having more or less normal health in between pregnancies.

(1) *Case* 13.—Female, age 35 years, Patel caste.

Diarrhœa commenced one month before delivery. Also with 2 previous pregnancies—normal health in between. Diarrhœa 10 to 20 motions a day—watery with mucus. Lienteric in type.

Glossitis, pain in throat on swallowing. Burning palms and soles and substernal. Dryness and blackness around mouth and feet and knuckles. Angular stomatitis present.

Tongue clean, red spots at tip. Dyspepsia—gurgling. Distension, achlorhydria. Loss of weight. Abdomen distended and thin walled. Hæmoglobin 32 per cent. Total red cells 1,400,000. Colour index 1.1.

(2) *Case* 7.—Muslim female, age 28 years.

Glossitis since childhood.

Diarrhœa, watery motions, yellow, copious, lienteric.

Always worse with pregnancy—4 children. Glossitis, fiery red tongue, stomatitis and pharyngitis, pain in throat on swallowing.

Tongue glazed, clean, pale. Burning palms and soles and substernal. Pigmentation of lips and angles of mouth. Abdomen—tympanitic, visible peristalsis, gurgling. Loss of weight. Hypochlorhydria. Hæmoglobin 62 per cent. Red cells 3,216,000. Colour index 0.9.

(3) *Case* 32.—Female, Bania, age 35 years, 3 pregnancies.

Diarrhœa with first pregnancy diagnosed as sprue—no glossitis then—sick for 6 to 7 months.

Constipation with second pregnancy.

Third pregnancy during last month, diarrhœa with blood and pus for 7 days and then after delivery diarrhœa continued as watery, yellow motion without blood and pus. Gurgling and glossitis now appeared.

Glossitis—clean tongue, pale.

Skin—very black back hands and all way up arms to axillæ—very dry black skin and face and lips in front of knuckles. B.P. 110/70.

Marked loss of weight. Abdomen—distended, thin walled. Gurgling, flatulence, heartburn, vomiting. Hæmoglobin 28 per cent. Total red cells 1,232,000. Colour index 1.1. Glucose tolerance 110—180—100. Hypochlorhydria.

Discussion.—These cases differ in no way from the other cases not associated with pregnancy. They are not examples of tropical megalocytic anæmia of pregnancy.

In tropical megalocytic anæmia, the gastric secretion is normal in most patients and

diarrhœa is quite rare (*British Encycl. Med. Practice*, Vol. I, p. 439). In the 3 cases detailed above, the outstanding clinical feature is the diarrhœa. Achlorhydria was found in one case and marked hypochlorhydria in 3 cases. They therefore resemble clinically the syndrome under discussion, and not tropical megalocytic anæmia. It is recognized that in pregnancy, there is an increased demand for vitamin B. These patients are probably living on the threshold of vitamin B deficiency. The added strain of pregnancy just tips the scale in the adverse direction, so that now there is a definite deficiency of vitamin B.

Fever is mentioned in 10 cases as one of the initial symptoms. Malaria may precipitate the syndrome in one who is on the border-line of vitamin B deficiency. The extra metabolic strain imposed by the attack of malaria results in a breakdown of the defences.

(1) *Case* 48.—Female, Bania, age 25 years.
First had malaria fever for one week—and then diarrhœa commenced—watery white motions—with glossitis. Admitted as a typical case with glossitis, angular stomatitis, rough dry scaly skin of legs, anæmia. Hæmoglobin 50 per cent. Red cells 2,814,000.

Dysentery is frequently mentioned by the patients, but the term is a clinical one only, not verified in the majority of cases by laboratory methods.

In only 2 out of 50 cases were *Entamœba histolytica* cysts isolated. No bacteriological examinations were made to isolate the organism of bacillary dysentery. Blood and pus are at times reported by the patients, but their mere presence in the motion is not necessarily indicative of dysentery. Blood and pus may be due to piles or to straining due to the excessive diarrhœa or to pelvic congestion due to pregnancy. Blood and mucus may also be passed in an acute relapse of the syndrome, when the whole alimentary mucous membrane from the mouth to the anus is in a state of congestion. The tongue is red and raw, the pharynx is inflamed, there is dysphagia and heartburn probably due to a similar rawness of the œsophagus. Sigmoidoscopy in such a condition will reveal an œdematous, red, rectal mucous membrane covered with mucus.

In 7 of the 50 cases, there seems to have occurred a definite attack of amœbic dysentery. I do not think there is any argument in support of the theory that dysentery is the cause of the syndrome. The relationship can be explained in terms of a conditioned deficiency. Dysentery is essentially a large bowel disease, whereas this syndrome is a small bowel dysfunction. Patients who have suffered from dysentery, and notoriously Gujrati patients, diet themselves most rigorously over very prolonged periods. They exclude all vegetables and the richer cereal foods from their diet, and live only on curds and conjee and dhal water. The dietetic restriction may be voluntary and therapeutic, or it may be enforced by the patient's inability to take heavier food, or by his lack of appetite. The primary dysentery symptoms, due to a large bowel lesion, are loose motions containing blood and pus, abdominal colic, weakness and loss of weight. With the switchover to a small bowel dysfunction, due to a conditioned vitamin B deficiency, symptoms due to jejuno-ileal insufficiency become paramount. The nature of the stools alters, the blood and pus disappear and the motions become watery and copious. The patient complains of gurgling and an urgent desire to defæcate after food. Soon anæmia and glossitis and a feeling of exhaustion set in. Several patients have clearly described this transition from large bowel to small bowel pathology in recounting their history. As one patient remarked 'Dysentery stopped and sprue began'.

(1) *Case* 29.—Male, age 33 years, Patel caste.
Dysentery (clinical diagnosis only) 5 years ago blood and pus—dysentery lasted 2 months—20 to 25 motions a day.
Then the bowel motions less, with no blood and pus. Gurgling and swelling of the abdomen commenced, and glossitis started one month ago.
Motions 7 to 8 a day—watery and yellow—any time of day—exhaustion after motion. General sallowness of skin of face, back of hands and shins.
B.P. 80/40. Tongue clean, glazed. Abdomen—distension, thin-walled, gurgling. Loss of weight. Wasted skin. Hypochlorhydria. Colon thick and tender. Hæmoglobin 44 per cent. Total red cells 1,944,000. Colour index 1.1. Sigmoidoscopy—normal mucous membrane except for pallor.
Treatment—Patient improved greatly on nicotinic acid, liver extract, hydrochloric acid and fersolate. Increase of weight 11 lb.

Sex.—In a series of 50 cases, 30 were in males. The condition shows no preference for either sex.

Age.—The age of the patients varied from 20 to 40 years. In a few cases, patients of 50 years and over presented themselves with the syndrome, but in such cases a careful history elicited the fact that they had suffered from the same condition many years previously, and this attack was but a recrudescence.

Caste.—In the series of 50 cases, 11 were Muslim and 39 were Hindu. This is of no significance, as the population varies in the same degree. Of the Hindu patients, 11 were Brahmin, 12 were Bania, 3 were Patel, 2 were Jains, 1 Soni ; there were no cases from the depressed classes. This observation may be of some significance. The higher caste eat more wheat and polished rice, the lower caste subsist more on bajri and coarser grains and often eat home-pounded rice which has a considerable content of vitamin B.

Acute relapse

This is exemplified by the following two cases :—

Case A.—Muslim male, aged 24 years.
History of diarrhœa for 10 months. Acute glossitis for the last 10 to 15 days—tongue fiery red glazed patches on the dorsum. Whole pharynx inflamed, so that he is unable to eat food.
Diarrhœa, 4 to 5 profuse watery yellow motions, marked exhaustion after motions—motions passed at all times of the day.

No history of dysentery. B.P. 100/50. Marked loss of weight, and strength. Achlorhydria—absolute. Dyspepsia—gurgling and distension and heartburn. Blood. Hæmoglobin 62 per cent. Red cells 2,616,000. Leucocytes 64,000. Colour index 1.1. Size of red cells 8 microns.

Sigmoidoscopy—very œdematous, reddened, gelatinous, mucous membrane. Liquid white fæces with much mucus.

Treatment—immediate relief in 24 hours with nicotinic acid. The redness of the tongue disappeared and patient was able to swallow the Ryle's tube for gastric analysis.

Case B.—A Hindu patient presented himself for examination with what I considered the typical syndrome of this variant of sprue. To my surprise he came again in a few days with what he described as dysentery. He was pouring bloody stools and was too weak to stand. His tongue and mouth were fiery red and he was unable even to drink fluids. In spite of the bloody stools, I adhered to my original diagnosis. I prescribed only nicotinic acid by mouth and injection. In 24 hours there was marked improvement and by 48 hours all blood had stopped. Sigmoidoscopy revealed a red, swollen, gelatinous mucous membrane, covered with mucus. I came to the conclusion that his whole intestinal tract was injected and inflamed right from his lips to his anus.

The patient made steady progress with treatment only for the sprue syndrome and without any amœbicidal measures.

Treatment

The main object in treatment is to supply the vitamin B complex orally and parenterally.

Baker's yeast is obtained fresh every day from a local baker and given to the patients in quantities of half an ounce three times a day.

Peanut butter is advised. The patients are instructed to grind up fresh peanuts finely and add a little peanut oil till it is of the consistency of butter. Spies *et al.* recommend a mixture containing 25 per cent dried brewer's yeast, 64 per cent peanut butter and 8 per cent peanut oil. The peanut contains about 25 to 30 per cent protein, 40 to 50 per cent fat and 10 to 20 per cent carbohydrate. It is a rich source of vitamin B complex.

Wheat bran is made into a porridge with milk. Proprietary products such as marmite and bemax are almost unobtainable nowadays due to the war.

Nicotinic acid at once relieves the glossitis and stomatitis, and also controls the diarrhœa. Given in maximum doses by mouth and by injection, a patient miserable with glossitis and dehydrated with diarrhœa can be transformed in 24 to 48 hours. The dramatic relief confirms one in the belief that nicotinic acid deficiency is responsible for at least part of the syndrome.

Riboflavin.—Certain cases of glossitis do not respond to nicotinic acid. If the sore tongue does not improve with the latter therapy, then a few injections of riboflavin (lactoflavin) may produce a beneficial change.

The whole vitamin B complex may be prescribed in convenient form as manibee, multivitamindon, or B-G-phos elixir, to name a few proprietary products which have been tried with success.

Hydrochloric acid is given if there is hypochlorhydria. It may be combined with judicious doses of tincture of opium if there is diarrhœa.

A useful formula is :—

Acid hydrochloric dil.	.. ..	30 minims
Tincture opii	.. ..	10 „

Water to half an ounce.

Half an ounce three times a day.

Pulv os sepiæ (*Batavia powder*) is very helpful in controlling diarrhœa if persistent.

Liver extract is indicated for three reasons: it supplies the hæmopoietic factor which is deficient in megalocytic anæmia; it is a rich source of vitamin B complex; it improves the absorption of amino-acids from the small intestine.

Crude liver extract gives the best results. Preparations such as campolon, hepatex T, hepolon, plexen are used in large doses daily or on alternate days.

Iron is necessary to overcome the anæmia. It is particularly difficult to administer iron, as it tends to aggravate the diarrhœa. Ferri et ammon citrate especially will frequently cause an attack of diarrhœa in a patient otherwise doing well. If a covering dose of tincture of opium is given with the ferri et ammon citrate, the latter may be tolerated. Another method is to give pil ferri redactum 5 grains three times a day, or fersolate or ribothiron tablets.

Ultra-violet light has been found helpful in toning up the system generally, and has been frequently prescribed.

Tongue.—Two per cent chromic acid applied to the tongue relieves the glossitis.

Diet.—The classical indigenous treatment is buttermilk and curds.

I have seen a patient live solely on buttermilk of which he drank 12 seers a day. He increased in weight by 30 to 40 lb.

In early cases, this treatment is advised : buttermilk, fruit juice, mashed up bananas and tea constitute the sole diet. Later, rice and milk, curds and kigdi and pulse water and bajri are added. Ghee and all fried foods are rigidly forbidden. In Muslim patients, liver soup and minced meat are advised from the beginning.

Sprulac (Cow and Gate), a specially prepared dried milk powder with diminished fat content, is a very valuable foodstuff, but it has not been used in this series.

A note on nicotinic acid therapy.—Nicotinic acid alone frequently dramatically relieves not only the glossitis, but also the vomiting and diarrhœa. Three cases quoted below were treated on admission with nicotinic acid only. In 2 or 3 days, the loose diarrhœa was controlled, the tongue was relieved, and the œdema lessened. Then other treatment was added to improve the blood. The improvement with nicotinic acid alone lends considerable weight to the hypothesis that deficiency of the vitamin B complex is one of the causal factors in producing the syndrome.

Case 1.—Male, Brahmin, age 40 years.
Previous history.

(*i*) Onset 1937—gradually progressive mental and physical depression accompanied by anæmia. Treated in hospital for 1½ months.

(*ii*) Relapse 1939—weakness, vomiting and diarrhœa, loss of weight, anæmia.
Cysts *Entamœba histolytica* present in fæces—treated with enterovioform, hepatex T, campolon, plastules—recovered.

(*iii*) Relapse every following monsoon with weakness, anæmia, depression, loss of weight and diarrhœa. Glossitis recurred each time now with the attack of diarrhœa.

(*iv*) 1942. Admitted to hospital again with weakness, tingling soles of feet and palms of hands, diarrhœa and anæmia. Tingling became a prominent symptom; treated with hydrochloric acid, hepolon, nicotinic acid, iron, hepatex T and berin. All the symptoms subsided except the complaint of tingling. His legs felt stiff and he experienced difficulties in walking. The knee reflexes were absent.

(*v*) Monsoon 1943. Admitted again in a very debilitated state. He complained of :—

(*a*) Prostration.
(*b*) Vomiting.
(*c*) Diarrhœa. Watery, yellow motions—7 or 8 a day—passed at any time of day or night.
(*d*) Sore tongue and throat.
(*e*) Tingling of hands and legs.
(*f*) Loss of weight.
(*g*) Slight fever.
(*h*) On physical examination the following clinical features were noted :—

(*a*) Tongue—dry, clean, raw red with glazed patches on dorsum. No angular stomatitis.
(*b*) Sallow complexion. Muddy appearance. Skin of knuckles of fingers blackish.
(*c*) Marked anæmia.
(*d*) Abdomen—normal contour. Liver not enlarged, colon not palpable nor tender.

Laboratory findings :—

(*a*) Absolute achlorhydria.
(*b*) Fæces—no cysts present and no ova.
(*c*) Blood—red corpuscles 1,326,000.
(*d*) Hæmoglobin 30 per cent, colour index 1.1. Size of red cells 8.2 microns.

On admission the patient was given only nicotinic acid tablets and injections of nicotinic acid twice a day intravenously. The effect was most striking. With two injections of nicotinic acid, the vomiting was controlled and the tongue felt and looked better and the motions were reduced from 8 to 4. The next day, on the same treatment the motions were reduced to three and on the third day, he passed one hard motion only. The motion was formed and digested. The tongue looked much better, the patient's general expression was much improved, and he felt distinctly better.

After 3 days on nicotinic acid only, the patient passing one motion a day only, the treatment was amplified. Baker's yeast, fersolate tablets and hepolon injections were given. Hydrochloric acid was administered because of the achlorhydria.

Discussion.—The whole syndrome from the beginning is attributable to vitamin B complex deficiency.

There is a superficial resemblance to sprue, and locally the indigenous practitioner calls such cases sprue. But the stools in this case never approximated to those characteristic of sprue. The motions were always watery yellow or like curds with no increased fat content. It is true that *Entamœba histolytica* cysts were detected in fæces on one occasion, but this finding was never confirmed later. The glossitis and macrocytic anæmia and the achlorhydria are not typical of chronic dysentery.

The response to nicotinic acid therapy was most dramatic, and confirms one in the belief that nicotinic acid deficiency lies at the root of the trouble. The complaint of tingling and stiffness in walking points to a thiamine deficiency, although vigorous treatment with thiamine preparation did not alleviate the symptoms.

PROGRESS UNDER TREATMENT

As the patient improves, the gurgling in the abdomen disappears, the motion becomes better formed and the patient looks healthier and brighter. There is visible a distinct change in his facial expression. Not every case, however, steadily improves. The stools may become constipated but the blood does not seem to improve. In spite of intensive liver extract therapy, there is no progress in the blood condition. This is always disappointing to both doctor and patient. It is probably due to hypoplasia of the bone marrow.

There may be actual aplasia of the marrow and such cases steadily deteriorate to a fatal conclusion.

At times one meets with an intractable diarrhœa. No amount of sedatives, opiates or vitamins will check the diarrhœa. The motion becomes profuse, incontinent and the patient becomes collapsed and œdematous, and dies. This is probably explainable as a state of jejuno-ileal insufficiency which has become so advanced as to be irreversible and unresponsive to all remedial measures.

Relapses frequently occur, even after many years. I have met a patient who had his first attack in 1917, with a relapse in 1924 and again in 1943. In the intervening years, he was quite well.

Relapses occur frequently in the monsoon and winter. Some patients say they relapse every year in these seasons.

DIFFERENTIAL DIAGNOSIS

Amœbiasis.—I have repeatedly seen patients referred with the diagnosis of amœbic dysentery. As one swallow does not make a summer, so the occasional discovery of a cyst of *Entamœba histolytica* does not constitute amœbiasis. The syndrome as a whole must be studied.

In amœbiasis, the anæmia is seldom severe and is always secondary and microcytic. Glossitis does not occur in amœbiasis. The liver tenderness and thickened colon point to amœbiasis, rather than sprue. The mental sluggishness and debility and constitutional upset are more suggestive of the sprue syndrome.

Achlorhydria and a flat glucose curve denote the small intestine disturbance typical of the sprue syndrome. Above all, the sigmoidoscopic appearance should clinch the differential diagnosis.

Tuberculosis of the abdomen.—Glands in the neck, a family history, fever, an old history of pleurisy may serve to give the clue to the diagnosis of tuberculosis.

Pellagra.—Pellagra is not uncommonly met with in Gujerat. Full-fledged cases may be seen with the classical pigmentation of the back of the hands and the front of the ankles. In my experience, diarrhœa is uncommon, the patients usually complaining of constipation.

The glossitis is much the same as in the sprue syndrome. The pigmentation of pellagra is a rash on the skin which can be removed by keratolytic ointments. In sprue the pigmentation is in the skin and is only a deepening of the normal pigment and is not a rash.

Summary

A syndrome commonly occurring in Gujerat is described which differs from sprue as described in textbooks of tropical medicine only in the nature of the stools. The stools are nearly always watery and passed at any time of the day.

The syndrome is believed to be a variant of the sprue syndrome, the nature of the stool being conditioned either by (*a*) the predominantly carbohydrate nature of the diet or by (*b*) some particular deficiency of the vitamin B complex.

The syndrome is believed to be due to a primary dietetic deficiency of the vitamin B complex leading to jejuno-ileal insufficiency.

The syndrome is relieved by therapy supplying the vitamin B complex orally, and parenterally.

Thirteen cases are quoted in which the syndrome was precipitated by pregnancy.

An explanation is offered as to the mechanism of the syndrome being implanted on dysentery. A conditioned deficiency of vitamin B due to dietetic restriction or defective absorption leads to jejuno-ileal insufficiency. It is possible to trace the change-over from a colitis to a small bowel disorder.

Acute relapse of the syndrome mimics dysentery. Sigmoidoscopic appearance typical of a relapse is described.

Acknowledgment.—Grateful recognition is given of the valuable assistance and stimulating criticism of my colleague, Dr. Stanley E. Beer, in the preparation of this paper.

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Medical News

FEEDING OF CHILDREN IN WAR-TIME

SUBSTITUTES FOR IMPORTED FOODS

A COMMITTEE of experts appointed by the Indian Research Fund Association to suggest satisfactory substitutes for imported infant foods and breakfast cereals has issued a pamphlet on the feeding of children from six months to six years in war-time.

The committee has dealt with the problem of feeding in general apart from the present war emergency. Alternative methods of feeding which would ensure good health and development have been discussed without reference to their cost.

The pamphlet deals with nutritional requirements of young children, planning the child's diet, weaning and diets suitable at different ages. In planning the diet of the growing child, it says, the first essential is to ensure that sufficient quantities of body-building and protective foods are included. Once requirements in this respect are fulfilled, a healthy child's appetite will determine its intake of energy-producing foods.

All the three categories of foods have been tabulated and the requirements of children from six months to six years are given with the planned diet for all meals.

Apart from the general principles of feeding, the pamphlet also deals with the palatability and attractiveness of meals and gives hints for their preparation and cooking. A few recipes for soups and other preparations are included in the pamphlet which is being distributed by the Indian Research Fund Association Office, New Delhi, and the Maternity and Child Welfare Bureau of the Indian Red Cross Society.

THE SIR NILRATAN SIRCAR FUND

THE Calcutta Medical Club has decided to perpetuate the memory of the late Sir Nilratan Sircar, *Kt.*, M.A., M.D., D.C.L., LL.D., the founder and as first president, by instituting a Fund of Rs. 25,000 from the interest of which, as a first step, will be created an Annual Oration called Sir Nilratan Sircar Memorial Oration which will be delivered annually, at the Calcutta Medical Club, by a medical man of outstanding abilities from all over India. The Committee appeal to the public to donate to the above Fund, which should be sent to the Honorary Secretaries, Calcutta Medical Club, C.M.C. House, 91B, Chittaranjan Avenue, Calcutta.