

Sprue in Puerto Rico¹

A CLINICAL STUDY OF 100 CASES

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THE HEMATOLOGY of sprue² is the subject of a previous communication, and comprises a study of the initial peripheral blood picture before treatment in one hundred individuals of both sexes suffering from uncomplicated sprue. The present report analyses the clinical picture and includes other laboratory data obtained in the same group of patients. A brief discussion on the etiology of sprue is also included.

Sprue is found in certain regions of the tropics and the subtropics. It was first described by Katelaer in 1669, but William Hillary's description³ of the disease as he observed it in the Barbadoes in 1759 is better known. More than a century later Van der Berg⁴ and Patrick Manson⁵ described the condition in the East Indies and China, but it was not until 1908 that Ashford⁶ called attention to its existence in Puerto Rico and in the American tropics. Since then, the sprue syndrome has occupied a position of prominence in the medical history of Puerto Rico. Along with the pioneer work of Ashford,⁷ Serra,⁸ Jenaro Suárez,⁹ Ramon Suárez,¹⁰ Pons,¹¹ Koppisch,¹² Castle and Rhoads,¹³ have all made important contributions.

Sprue is a chronic, wasting disease, which in the light of modern medical science may be classified among the deficiency states. In

the earlier writings, great importance was ascribed to the differential diagnosis between sprue and Addisonian or pernicious anemia of temperate climates. Mainly through the work of Castle and associates we now consider these conditions closely related in etiology, symptomatology and treatment.

MATERIAL FOR STUDY

There were 57 males and 43 females ranging from 12 to 78 years of age, the mean age for the entire group being 40.14 years. Fifty-three individuals were under 40 years of age and 47, over 40. There were 87 white and 13 colored individuals, among which two full-blooded negroes were included, the others in the colored group being mulattoes. The oldest was a white man of 78, and the youngest, a white girl of 12. The cases were observed either at the clinic or in the wards of the University Hospital of the School of Tropical Medicine, San Juan. As far as we know, 98 persons were natives of Puerto Rico, of either Spanish or colored extraction and, of the remaining two, one was a male Venezuelan mulatto and the other a continental American who had resided in the Island for several years before the onset of sprue. With very few exceptions the individuals studied were of the indigent or underprivileged class, and when seen by us they usually presented a fully developed picture of the sprue syndrome. A few cases of this series were first observed by the late Bailey K. Ashford in 1930, under whom it was the author's privilege to work until his untimely death in 1934. The group of cases comprises 73 individuals seen at the out-patient department and 27 in the wards of the University Hospital. The latter group represents 15 percent of all sprue cases admitted to this Hospital during the period of 1929 to 1936. Six percent of all admissions during this period were sprue cases.

In selecting the group of 100 individuals with uncomplicated sprue, over 50 percent of the records of other sprue patients observed by us were discarded as presenting various intercurrent and complicating conditions in addition to sprue. Notably among these were syphilis, chronic coledocystitis, and tuberculosis.

Sixteen percent of the group under study harbored intestinal parasites such as hookworm, strongyloides, ascaris, whipworms and amebae (cysts). Intestinal parasitism was not considered significant in altering the clinical pattern of sprue.

1. Received for publication April 3, 1941.

2. R. Rodríguez Molina, *The Puerto Rico J. of Pub. Health & Trop. Med.*, XV: 89. 1939.

3. W. Hillary, "Observations on the Changes of the Air and the Concomitant Epidemical Diseases, in the Island of Barbadoes," 1st. ed., C. Hitch and L. Hawes, London. 1759.

4. C. L. van der Berg, "Indische Spruw (Aphthae Tropicae)," Ernst and Co., Batavia. 1880.

5. P. Manson, "Notes on Sprue," Medical Reports, China Imperial Maritime Customs, Shanghai, 1879-1880.

6. B. K. Ashford, *Bol. Asoc. Méd. de Puerto Rico*, CXLI:1-26, March, 1923.

7. B. K. Ashford, "Sprue," Chapter XXVII in Tice's *Practice of Medicine*, Vol. IV, W. F. Prior Co., Inc., Hagerstown, Md. 1929.

8. A. Serra, *Am. J. Trop. Med.*, IX:49, 1929.

9. J. Suárez, *Puerto Rico J. Pub. Health & Trop. Med.*, VII:145. 1931.

10. R. M. Suárez, *Ann. Int. Med.*, XII:529. 1938.

11. J. Pons and R. Rodríguez Molina, *Bol. Asoc. Méd. de Puerto Rico*, XXVI:60. 1934.

12. B. K. Ashford (quoted), *Tice's Practice of Medicine*, loc. cit.

13. W. B. Castle, C. P. Rhoads, H. A. Lawson, and G. C. Payne, *Arch. Int. Med.*, LVI:627-699. October, 1935.

SYMPTOMS AND SIGNS

In figures nos. 1 and 2 are shown by means of a bar diagram the relative frequency of recorded symptoms and physical signs in this series of sprue cases. Ninety-seven percent complained of gastro-intestinal disturbances which have been grouped under the term "Dyspepsia." This term comprises (in order of their frequency) abdominal distention, epigastric distress—not necessarily related to taking of food—, heartburn and abdominal discomfort and pain following ingestion of food. In over 90 percent asthenia, weakness or prostration, diarrhea, loss of weight, carbohydrate and fat intolerance, soreness or pain of tongue and mouth, and anorexia occurred. By intolerance to certain foods we mean the aggravation of gastro-intestinal symptomatology, particularly diarrhea following ingestion of rice, beans and fried foods. These articles of diet are consumed in large quantities in the daily menu of Puerto Ricans. Gastro-intestinal disturbances constituted the earliest subjective manifestations of sprue in this group of patients. As a rule they did not appear following a dietary indiscretion or alcoholic abuse. Flatulence, eructations, heartburn, meteorism and diarrhea as mentioned above were made worse by the ingestion of rice and beans, cereals, bread or potatoes and fried foods in general. Curiously enough, these food stuffs are not excluded from the daily fare until later, when the tongue and mouth are too sore or painful to tolerate even water. Indigestion may persist for months before the more disabling and aggravating symptoms ensue, but soreness of the tongue or mouth accompanied by looseness of the bowels appears after two or more months of dyspepsia. Watery, frothy, yellowish, fermentative, acid stools, occasionally grayish or light colored, which may or may not be ushered by tenesmus or cramp-like pains, soon dominate the picture. Movements are almost constantly preceded by an imperative desire to go to stool and not infrequently stools are passed involuntarily before the patient is able to reach the toilet. Their frequency is quite variable, from two, or three, to twenty motions or more during the day. The number of stools occurring during the day is by far higher than those taking place by night. One to three movements before breakfast in the early hours of the morning is characteristic. As diarrhetic stools are precipitated by ingestion of food, particularly in the solid state, the patient, though hungry, is afraid to eat and soon loses appetite and is repelled by the sight and odor of food. Soreness and pain of the tongue and mouth progress, complicating the clinical picture, and from then on loss of

BAR DIAGRAM SHOWING THE RELATIVE FREQUENCY OF RECORDED SYMPTOMS IN SPRUE

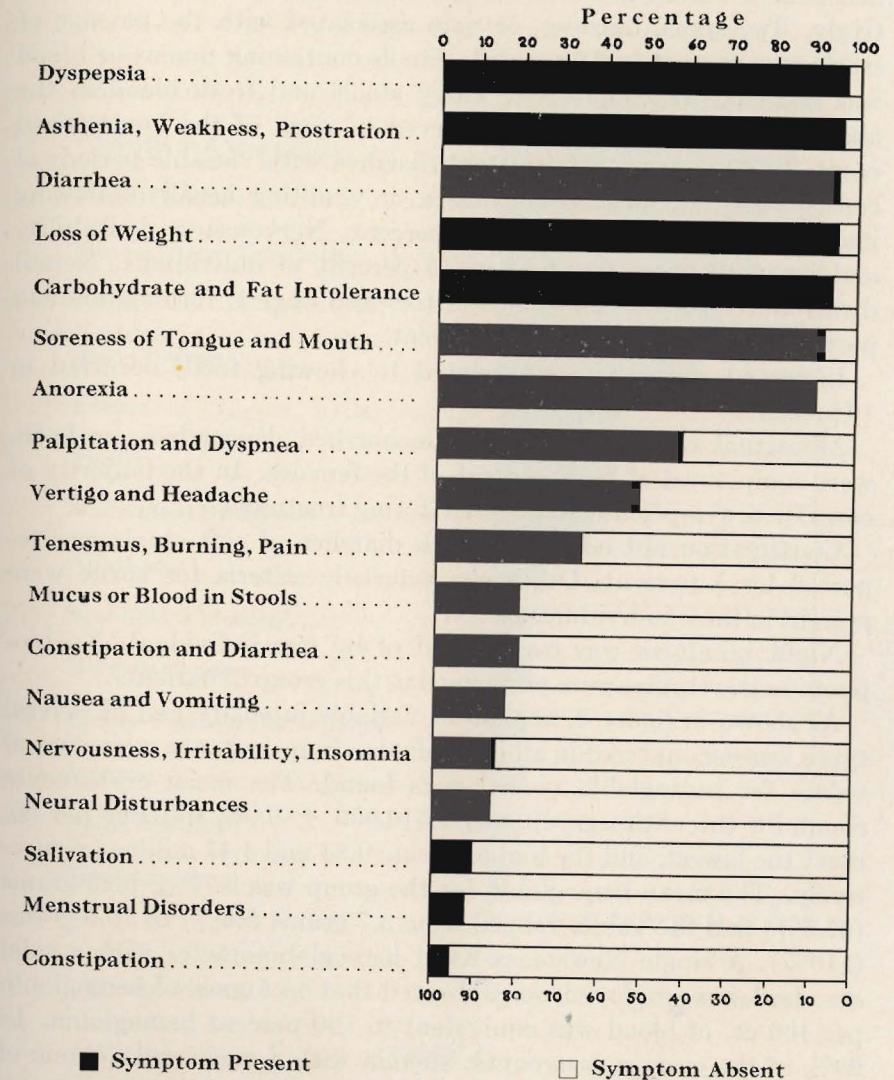


Figure 1

weight and strength is rapid. A loss of 50 lbs. in four to six months in a person normally weighing 120 to 130 lbs. is not infrequently seen.

Palpitation of the heart and dyspnea on exertion, vertigo and headache occurred in 58 and 48 percent of the individuals, respectively. Tenesmus, burning, or pain associated with the passage of stools was present in 35 percent. Stools containing mucus or blood was reported by 20 percent. Tarry stools and fresh blood in the absence of hemorrhoids was observed in some of the hospitalized cases. In 20 percent, intermittent diarrhea with variable periods of constipation was observed. Nausea or vomiting usually following ingestion of food occurred in 17 percent. Nervousness, irritability and insomnia were reported in 15 percent of individuals. Neural disturbances such as numbness of toes and fingers, formication and paresthesias were noticed in 14 percent.

Increased salivation, not related to chewing food, occurred in 10 percent.

Menstrual disorders, usually amenorrhea, leucorrhea, or both, were complained of by 8 percent of the females. In the majority of cases these symptoms disappeared during treatment.

Constipation not connected with diarrhea or soft stools was reported by 5 percent. Other characteristic criteria for sprue were present in these individuals.

Night blindness was complained of by one individual. No biophotometric studies were performed in this group of patients.

As shown in figure 2, anemia of variable intensity and of several types was encountered in all individuals. In no instance were normal values for hemoglobin or red cells found. The mean erythrocyte count for the entire group was $2,510,000 \pm 0.064$ millions per cu. mm., the lowest, and the highest being 0.84 and 4.47 millions respectively. The mean hemoglobin for the group was 9.77 ± 0.23 grams (67.5%) and the values ranged from 3.7 grams (26%) to 16.0 grams (110%). A single Newcomer-Klett hemoglobinometer with a solid standard was employed, so calibrated that 14.5 gms. of hemoglobin per 100 cc. of blood was equivalent to 100 percent hemoglobin. In 90% of the cases a macrocytic anemia with a mean cell volume of 119.14 ± 1.45 cu. mm. was observed; the normocytic type was reported in 7 percent, simple microcytic in 1 percent and hypochromic in 2 percent of the cases. In this connection we disagree with a statement recently made by Vedder¹⁴ that the anemia of sprue is

BAR DIAGRAM SHOWING THE RELATIVE FREQUENCY OF DIFFERENT SIGNS IN SPRUE

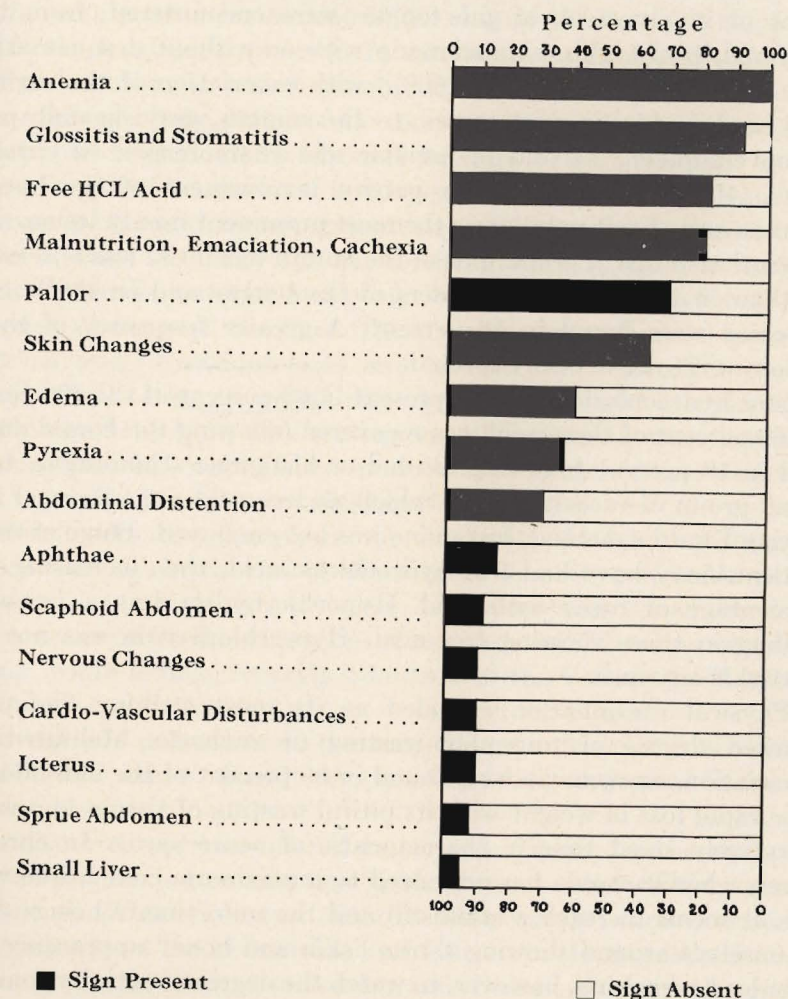


Figure 2

14. E. B. Vedder, *Am. J. of Trop. Med.*, XX:345, No. 3. 1940.

normocytic in the beginning. In our experience, as well as in that of R. M. Suárez,¹⁵ when macrocytosis occurs it is an early manifestation of the syndrome.

Glossitis and stomatitis was present in 92 percent. Various degrees of involvement of the tongue were encountered, from the fiery red, beefy, glossy appearance with or without desquamation and atrophy of the papillae (60%) with excoriation of the surface and borders seen in acute cases, to the smooth, grayish, dull, pale organ completely devoid of papillae and characteristic of chronic cases (40%). Stomatitis with patchy involvement of the buccal mucosa and of soft palate was the most prominent mouth lesion. No ulceration of lips or of margins of the mouth (cheilitis) was observed. Aphthae on the surface or borders of the tongue and on the buccal mucosae were found in 16 percent. A greater frequency of these lesions was to have been expected.

Free hydrochloric acid was present in 82 percent of the 100 cases. In 60 percent of these acid was recovered following the Ewald meal, and in 40 percent following alcohol or histamine stimulation. In a small group of earlier cases in which no free acid was observed following Ewald's method, histamine was not employed. Some of these patients may have had free hydrochloric acid, thus increasing the percentage of cases with acid. Hypochlorhydria was a frequent finding in those showing free acid. Hyperchlorhydria was not reported in any case.

Physical examination revealed as its most striking finding a marked degree of muscular wasting or cachexia. Malnutrition, emaciation, or cachexia were found in 80 percent of the individuals. The rapid loss of weight with its pitiful wasting of tissues in a comparatively short time is characteristic of acute sprue. In chronic cases, when cachexia has advanced to a maximum compatible with life, it seems to reach a standstill and the unfortunate beings drag themselves around showing a true "skin and bone" appearance. It is indeed surprising, however, to watch the degree of activity some of them display, going on their way with a million red cells per cmm. and looking like ghosts. This apparently effortless activity is a contrast to that of patients with hookworm disease and anemia, in which cases the individuals may have anywhere from three to four millions of red cells per cu.mm., yet exhibit great effort in moving about; their actions are sluggish and dyspnea on the slightest exer-

15. R. M. Suárez, personal communication.

tion is obvious. However, their hemoglobin is much lower (20 to 30 per cent, 2.9-4.4 grms.) in proportion to the number of red cells—the reverse of that which usually occurs in sprue.

Pallor of the skin, usually generalized, occurred in 69 percent. In white individuals a lemon tint of the skin of the face and the forehead was frequently present. In others, the skin had assumed a dull gray or dirtyish yellow, parchment-like appearance, reminiscent of a mummy. True pallor of the skin in white individuals living in the tropics is difficult to discover because of sun tanning. Other skin changes were observed in 63 percent. These consisted mainly of areas of brownish hyperpigmentation with roughening, located (in order of their frequency) on the forehead, cheeks, extensor surface of the forearms, anterior and posterior aspects of the neck and the anterior surfaces of the legs. These lesions were invariably symmetrical and of various sizes and intensity of color. They were usually dry, often presented discrete borders, slight atrophy and wrinkling of the skin, with scaling resembling *echthymosis*. The hair of many patients, particularly those below 30 years of age, was fine, dry, scant, in the axillae or pubis, and lacked luster.

Occasionally the changes in the skin were similar to pellagroid lesions, but no erythemas or ulcerations were observed. No petechiae or purpuric spots were seen. As already mentioned, cheilitis was not encountered in this series of cases, though it was present in a young, white female, recently admitted to the University Hospital with acute sprue.

Edema was present in 40 percent, the most frequent sites being the feet and ankles. Rarely was edema of face or general anasarca observed.

Hospitalized patients offered ample opportunity for the study of pyrexia not related to infection in the present series. Thirty-seven percent of all cases showed elevated temperature when first seen. The majority of the 27 individuals admitted to the wards had some degree of temperature on admission and during sojourn in hospital. As a rule the fever was remittent in type with rises to 101° F. or 102° F. in the evening, with remissions to normal or subnormal values in the morning. Fever receded by lysis as the clinical condition improved. Subnormal temperatures as low as 95° F. are reported in some individuals before improvement began.

Along with symptoms so common as epigastric distress, flatulence and abdominal discomfort found in over 90 percent of cases, abdominal distension would be expected to occur in a larger number of cases.

It was observed in only 30 percent. Tenderness either over the epigastrium, descending colon, or generalized, was present in 70 percent. This is not shown in figure 2. Thinning out of the abdominal wall to the extent that peristalsis was seen, was quite frequent. A scaphoid type of abdomen was found in only 12 percent. This was surprising in the presence of the high incidence of emaciation and cachexia. However, the higher incidence of abdominal distension may account for it.

Nervous changes occurred in 10 percent. These consisted mainly in diminution or absence of tendon reflexes and of absence or diminished vibratory sensations at malleoli, dorsum of feet, or along legs to iliac crests. No ataxia was encountered.

Icterus of sclerae or of skin was observed in 10 percent. Usually it was correlated with increased bilirubin in the blood.

Cardiovascular disturbances such as heart murmurs, apparently haemic in character, coldness of extremities, arteriosclerosis of peripheral arteries in some of the elderly individuals were observed in 10 percent of the cases. Blood pressure readings were usually low, the systolic values ranging from 80 and 120 mm. and diastolic between 30 and 60 mm. The Danzer ratio indicating size of heart to the X-ray was computed in a few cases, with results of less than one, indicating a normal sized organ. The shape of the heart to the X-ray was sometimes described as of "hanging drop" appearance by the roentgenologist, Dr. G. Ruiz Cestero. Determination of hemodynamic tests such as blood volume, circulation time or venous pressure readings were not carried out in this series.

Sprue, abdomen and small liver, which are believed to be characteristic of sprue by Manson Bahr¹⁶ and Ashford, was noticed in less than 10 percent of the cases. This term refers to abdominal distension, particularly below the umbilicus and along the flanks, the lower abdomen presenting a dome-shaped appearance. A small liver to percussion or palpation (above costal margin) was also not considered typical (5%) in this group of individuals.

CLINICAL PATHOLOGY OF SPRUE

Reference has already been made to the number, corpuscular volume, and hemoglobin content of the peripheral red cells. Studies of the leucocytes and platelets were also included in a previous communication (*loc. cit.*). Determination of bleeding and coagula-

tion time, fragility of red cells and clot retraction were performed in some cases. All of these tests gave results within normal limits. Recently, Dr. R. M. Suárez¹⁷ has confirmed the latter findings in other sprue cases.

Results obtained of the frequency of hydrochloric acid following gastric expression have already been discussed.

Stools: The amount, consistency, color, odor and chemical composition are affected. We believe the normal stool of the rice-eating people of this Island to be unduly large and bulky. In sprue, however, a small sized stool passed with plenty of gas is typical. This is likely to be due to the fact that the usually liberal amounts of rice, beans, pork fat, and undigestible material in the diet has been avoided, and to the frequency of bowel movements. Watery, foamy, fermentative dejections with an acid or sour odor are characteristic of acute sprue. An offensive, putrid, foul odor was frequently encountered, particularly in chronic cases. The reaction is strongly acid. Under suitable diet and liver extract they soon became semi-solid, the odor changing to that of normal movements. Semi-solid stools may persist for months or years before formed, normal movements are passed. As to color, we must admit that the copious pale, grayish, fatty, foul stool, described in the literature as typical of sprue, has been rare in our experience. A light yellow, golden or brown stool, mixed with variable amounts of foam, is the rule. We have seen tarry stools in some cases of sprue, as well as fresh blood, and 20 percent of the cases stated they had passed blood or mucus.

As to the chemical composition of the stools, no studies have been performed in connection with the present work. Increased abnormal amounts of split fats, as well as normal quantities of bile pigments have been reported by Ashford.

Urine: No pathologic changes in the urine were found in this series of cases. In some patients a low grade genito-urinary infection, such as cystitis or pyelonephritis may be encountered, but this is to be considered a complication. A few patients complained of marked nocturnal polyuria, that is, during the period when bowel movements are less numerous. The significance of this observation is not known.

Blood Chemistry: Studies in blood chemistry were performed, in hospitalized cases and in several dispensary patients. The blood glucose was found to lie within normal figures, but the results usually

16. P. Manson-Bahr, "The Dysenteric Disorders," Williams & Wilkins Company, 1939.

17. R. M. Suárez, personal communication.

fell below 100 milligrams per hundred cc. of blood, often around 80, occasionally around 70; the lowest was 68 milligrams. As expected, glucose tolerance tests showed flat curves that are considered characteristic of the sprue syndrome. We have not performed this test when glucose is given by vein.

Urea nitrogen and non protein nitrogen figures were normal as well as the uric acid and creatinine. Total plasma proteins fell within normal variations except in cases with edema, in which the results were invariably below 5 percent. Values between 5 and 5½ percent were frequent. Low plasma protein levels indicate, of course, an abnormal state of nutrition, which may be correlated with the rapid wasting of tissues seen in sprue. The albumin and globulin fractions were reduced without disturbance of the proportion between the two. One middle-aged female showed 2.2 percent of total protein. She had general anasarca with marked edema of the lower extremities and ascites, which at first were thought to be due to a blockage of the pelvic venous circulation. Under liver therapy and high protein diet, the plasma proteins rose to 6.5 percent in two months and the edema disappeared completely.

Cholesterol determinations showed low values, the highest being 133 mgs. and 90 mgs., the lowest. It is our impression that normal cholesterol values are lower in Puerto Rico than in the North, but data on what constitutes "normal," is lacking.

The chlorides (whole blood) fell within normal variation, and below normal in some individuals. The results obtained were similar to values accepted as normal.

Icteric indices were usually observed below 6 units, but in three instances it was increased, the highest result being 14 units. The serum bilirubin in this case as determined by the Van der Berg test was 0.95 units.

Calcium and phosphorus determinations showed normal figures. However, values between 8.5 and 9 mgs. for the calcium and 2.5-3.0 mgs. for phosphorus were common. Again, the question of what constitutes normal calcium and phosphorus values in a country where the daily per capita intake of calcium is low, requires further investigation. It is opportune to mention that in no case there occurred clinical manifestations of calcium or phosphorus deficiency. However, a search into the occurrence of osteoporosis or osteomalacia was not made.

The determination of basal metabolic rates showed normal values.

Recently, however, we have observed several cases with low rates—over—10, and two young females in whom sprue was associated with hyperthyroidism.

GASTROSCOPIC AND RECTOSIGMOIDOSCOPIC FINDINGS IN SPRUE

Through the courtesy and assistance of Drs. A. Rodríguez Olleros and F. Hernández Morales it was possible to perform gastroscopic and rectosigmoidoscopic observations in twenty individuals of this series before and during treatment. We believe that such studies¹⁸ and those which are being carried out at present by Hernández Morales have thrown much light on the understanding of the pathological physiology of sprue. These investigators have repeatedly observed a patchy and generalized atrophic gastritis and rectosigmoiditis in our group and in other cases of sprue. The gastritis was not necessarily associated with a histamine achlorhydria in all individuals. More recently Hernández Morales¹⁹ was able to visualize the gastric mucosa of early, acute and full-blown cases of sprue. Changes in the gastric, rectal and sigmoid wall, similar and corresponding to those of the acute glossitis and stomatitis were observed, that is, a beefy red, glossed, hyperemic mucosa. A reversion to normal appearance was further observed at different intervals during liver therapy coincident with improvement of the glossitis, stomatitis and general condition of patients. In chronic cases, or in elderly individuals, however, the atrophic changes in the stomach and large bowel persisted during and following treatment.

The findings discussed above would appear to fit into the accepted views on the postmortem gastro-intestinal pathology of sprue. These consist of degeneration and atrophy of the absorptive and secretory epithelium of the entire tract with thinning out of the gut. The physiological implications derived from the appearance of the stomach and large bowel *in vivo* point clearly, in our opinion, to faulty absorption of food products by the gut. As to the etiology of such condition, it is as yet impossible to define, but a deficiency state, the nature and *modus operandi* of which is still obscure, seems to be responsible in bringing about the sprue syndrome.

18. A. Rodríguez Olleros, *The Puerto Rico J. of Pub. Health & Trop. Med.*, XIII:503-521. 1938.

19. F. Hernández Morales, personal communication.

DIAGNOSIS

The diagnosis of sprue was comparatively simple in the group under study. In the majority of cases a correct diagnosis was arrived at from the chief complaints alone. On the other hand, this series comprises a particular type of individual in whom the classical features of the disease in full bloom were observed when the patient received medical attention. We realize, however, that in private practice diagnosis might be difficult, as anemia may be present without marked lingual or intestinal symptoms, or vice versa.

We believe the diagnosis of the sprue syndrome is based upon the following criteria: (1) Insidious onset, chronicity of symptoms and rarity of spontaneous remissions; (2) Mouth lesions (stomatoglossitis); (3) Gastro-intestinal disturbances (dyspepsia, diarrhea); (4) History of recent weight loss accompanied by increasing weakness or prostration; (5) The presence of a macrocytic, hyperchromic anemia and (6) a flat glucose tolerance curve. Secondary in importance but also characteristic, are (7) the presence of free hydrochloric acid in the stomach in a high percentage of cases; (8) Hyperpigmentation of the skin; (9) Absence of neural manifestations in the majority of cases; (10) "Inflammation" and atrophy of the gastric and rectosigmoid mucosa. Difference in degree or intensity and in frequency of these symptoms and signs may be quite variable in different individuals, but in our experience during the past fifteen years a general uniformity about the clinical picture has been the rule, particularly so in the present group of patients.

Differential Diagnosis. The clinical picture of sprue resembles in a qualitative way that of Addisonian or pernicious anemia, in that gastro-intestinal abnormalities, anemia and neural manifestations are encountered. The emphasis on these symptoms is, however, very differently placed. The observations in individuals studied by us confirm the statements of others^{20,21} that the outstanding manifestations of the disease other than that of anemia are referable to the tongue and the gastro-intestinal tract. Symptoms and signs pertaining to the spinal cord and peripheral nerves are found in only a small percentage of cases. With relation to pellagra, there is a definite similarity to sprue in that stomatoglossitis, anemia, and skin manifestations are present as in sprue; however, true pellagroid lesions are very rare in sprue (we have never seen them). Although

20. W. B. Castle and G. K. Minot, "Pathological Physiology and Clinical Description of the Anemias," Oxford University Press. 1936.

21. P. Manson-Bahr, *loc.cit.*

there is often some degree of mental depression in some advanced cases of sprue, psychosis as seen in pellagra is not found in sprue.

Other conditions that were considered in the differential diagnosis in selecting the present group of cases were chronic cholecystitis, intestinal tuberculosis, carcinoma of the stomach, and syphilis. These entities were the most frequent responsible for a clinical picture very suggestive of sprue. In fact, chronic gall bladder disease and carcinoma of the stomach may simulate the sprue syndrome. Several times we have arrived at the diagnosis of sprue in a middle aged or elderly individual with glossitis, history of weight loss, diarrhea and dyspepsia, the presence of a macrocytic anemia, and when an X-ray study of the stomach and duodenum was made, carcinoma of the stomach was the answer. We recall two other cases (not included in this group) with typical gastro-intestinal symptoms in which a chronic gall bladder infection was present. Cholecystectomy having been performed, a relapse of sprue occurred in both cases within a year following operation.

With regards to non-tropical sprue (chronic idiopathic steatorrhea) and Gee-Herter's disease, our experience with these conditions is very meager, but judging from the literature our personal opinion is that these entities offer a clinical picture somewhat different from what we have come to call "Sprue" in Puerto Rico.

Although no individual of this series harbored ova of *Schistosoma mansoni*, it is important to bear in mind the gastro-intestinal disturbances such as dyspepsia and diarrhea which occur in individuals infected with this trematode, and which resemble those of sprue. However, the bloody and mucous diarrhea accompanied by tenesmus and cramps is characteristic of schistosomiasis, and not the usual findings in sprue. Tenesmus and pain is more marked and the character of the stools is different in the former condition. The gastro-intestinal disturbances with the chronic dysentery of schistosomiasis give rise to a symptomatology not unlike that of mucous colitis and chronic amoebic dysentery.

PROGNOSIS

In a future communication dealing with treatment in the present series of cases, more details will be given in connection with the prognosis of this condition. However, we will make a few appropriate remarks on our observations. In the average patient the prognosis was good; only one death occurred, a white male aged 56,

hospitalized in a state of sprue cachexia, dehydration and marked prostration. Such practically hopeless cases, with the capacity for absorption totally destroyed, were fortunately few.

In general, the prognosis depended on the age of the patients and on whether they were able to receive adequate treatment. The outlook for those below forty is directly good, but by no means favorable in persons of either sex over fifty years of age. However bad the symptoms may be, the patient, if under middle age, can be assured of a permanent restoration to health if proper treatment is instituted and continued.

DISCUSSION

Now that analysis of the clinical picture has been made, we shall discuss and attempt to explain the changes in the blood and gastro-intestinal tract occurring in sprue in the light of what is now known of the abnormal physiology of this condition.

Our good friends, the pathologists, have found few changes other than those of marked wasting of tissues and organs, a hyperplastic bone marrow, a fatty liver, and atrophy with degeneration of the absorptive and secretory epithelium, with thinning out of the intestinal wall. These changes do not, in the opinion of some investigators²² and in our own, give a picture of the actual primary lesions of sprue. For this reason, pathological studies have so far failed to elucidate further the etiology of this condition. That degenerative and atrophic changes other than on the tongue also occur in the living subject has been demonstrated by Rodríguez Olleros and Hernández Morales at this institution, where they have encountered a generalized or patchy atrophic gastritis and rectosigmoiditis. Noya and Hernández Morales²³ observed at operation the intestinal wall of the ilium of a patient with acute sprue. The wall presented an edematous, grayish appearance, and the gut seemed unduly distended.

The work of Castle, Rhoads and associates in 1935 established on a scientific basis the intimate etiological relationship of sprue and pernicious anemia. The former, like the latter, is a deficiency disease, the extrinsic factor in the diet being absent as is the intrinsic in pernicious anemia. This opinion correlates well with the existing evidence of dietary deficiency in many patients preceding

the development of sprue, and with the much lower incidence of achlorhydria in the patients with sprue than in pernicious anemia. However, we believe this view does not appear tenable in individuals who develop sprue in spite of a well balanced diet of foods and vitamins. It does seem to us that a defect of intestinal absorption occurring in the intestinal tract of individuals with sprue is more fitting with the course of events as has been brought out in the analysis of the present group of patients. And in this connection we must not forget the hereditary factor in sprue as one requiring further investigation, for we have seen the syndrome to occur in several members of a family living far apart and in different climates.

Castle's explanation for the development of the macrocytic hyperchromic anemia in sprue is convincing, but how about the derangement of the gastro-intestinal system, which is much more marked in sprue than in pernicious anemia? Which are the conditions or factors that initiate the gastro-intestinal disturbances, the sore and inflamed tongue²⁴ and mouth, the atrophic gastritis and rectosigmoiditis, the hypermotility of the intestinal tract and the looseness of the bowels? These are questions which future research will have to answer. When 90 percent of the individuals studied by us present as chief complaint symptoms referable to the intestinal system, one must admit that derangement with dysfunction of such system is just as important and as distinct as is the presence of anemia.

The late Dr. Ashford from his wide clinical experience was led to believe that the character of the food in Puerto Rico was one important predisposing factor in the bringing about of sprue. The widespread and daily consumption of greasy foods such as fritters, fried meats, syrupy sweets and of cereals, particularly rice and beans, leads to an irritability of the entire alimentary tract which in due time and in susceptible individuals is followed by dyspepsia and diarrhea. From our observations we concur with this opinion. This course of events appears to be the usual sequence in the life history of sprue. At what stage does anemia develop, we cannot at present definitely say, but it is our impression that gastro-intestinal disturbances precede the appearance of the anemia in the majority of cases. It is to be expected that the severe diarrhea interferes with the proper absorption of fats, carbohydrates, proteins and vitamins.

22. P. Manson-Bahr, *loc. cit.*

23. F. Noya and F. Hernández Morales, personal communication.

24. For lack of a better term "inflammatory" has been employed to describe the appearance of tongue and mouth lesions. We do not believe these changes are to be regarded as inflammatory in nature, that is, as produced by an infectious agent.