Sprue in Puerto Rico—Ten Years Later[1]

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INTRODUCTION

PREVIOUS communications[2] embody a study of the peripheral blood before treatment and analysis of the clinical picture in one hundred individuals of both sexes, suffering from uncomplicated sprue. The present report includes a follow up of these cases during a period of ten years, together with a record of the treatment instituted. Its original purpose was to evaluate the condition of a group of consecutive cases at the end of a given period of time and, as the therapy administered was similar for all individuals, an opportunity was thus offered to study the life history of the sprue syndrome as it occurs in Puerto Rico. Originality for any of the therapeutic measures carried out on this group of patients is not claimed; due credit is given herein to the late Dr. B. K. Ashford for establishing the routine of treatment administered, and to Dr. W. B. Castle for instructions in the preparation of parenteral liver extract, employed in all the cases.

When fully developed, the sprue syndrome is a chronic deficiency state characterized by its insidious onset, chronicity of symptoms, progressive development of gastrointestinal disturbances—mainly, dyspepsia,[3] soreness of tongue and mouth, meteorism, and diarrhea. The stools are usually liquid, foamy, grayish, foul smelling, frequently voluminous and fatty. Stomato-glossitis, atrophic gastritis, and rectosigmoiditis are important findings. A macrocytic hyperchromic type of anemia with a megaloblastic marrow accompanies over 90 percent of the cases. Loss of weight occurs in the same percentage of cases; fever in about 40 percent.

The symptomatology of sprue may appear and become fully developed in the course of weeks, usually months. However, as the chronicity of symptoms is typical, this symptom complex may continue, if untreated, for several years before death ensues. Relapses

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2. R. Rodríguez Molina, *P.R.J.Pub.Health & Trop.Med.*, XV (1939), 89; XVII (1941), 134.

3. Under the term "dyspepsia," the following symptomatology is included: abdominal distention, epigastric distress and fullness, heartburn, abdominal discomfort, and pain following ingestion of food.

are common, but spontaneous remissions of gastrointestinal symptomatology or of the anemia have been rare in the experience of the writer.

The rapid loss of weight and strength is associated with intestinal hypermotility, with resulting malabsorption, and chronic and progressive starvation. Derangement of the metabolism of fats, carbohydrates, and proteins is closely related to the failure of the absorptive intestinal function, and is believed to be intimately linked with the clinical picture of the syndrome.

Nevertheless, this deficiency state in sprue is amenable to replacement therapy and symptoms can be cured by liver extract.

MATERIAL AND METHODS

The group of individuals studied comprised fifty-one males and forty-nine females, ranging from twelve to seventy-eight years of age, the mean age for the group being 40.14 years. The oldest patient was a white man of seventy-eight and the youngest, a white girl of twelve. There were eighty-seven white and thirteen colored individuals; among the latter group were two full-blooded Negroes, the others being mulattoes. Seventy-two of the cases were observed at the Outpatient Department, twenty-seven in the wards of the University Hospital; hospital cases were later followed up in the clinic. As far as was known, ninety-eight persons were natives of the Island, of either Spanish or colored extraction; of the remaining two, one was a male Venezuelan mulatto and the other a continental American who had lived in Puerto Rico for several years prior to the onset of sprue. With very few exceptions the individuals were indigent or underprivileged and, when first examined, presented a fully developed picture of the sprue syndrome.

The liver extract employed for intramuscular use was prepared according to instructions given the University Hospital by Dr. W. B. Castle in 1931. This consisted of a crude, unconcentrated product prepared from 343 Liver Powder Lilly, but its efficacy for sprue and other macrocytic anemias had been repeatedly tested and demonstrated in our own, and other local, hospitals. The following was its method of preparation:

Four boxes of powdered liver extract Lilly 343, each containing 24 vials, are required to prepare two liters of the finished product. The powdered extract is emptied in a two-liter Erlemmeyer flask and 600 cc. of freshly redistilled water are added. No rubber tubing should be used in the distillation

of this water. The contents are heated and stirred until all the liver is dissolved, when it turns dark in color. The flask is left in the icebox overnight. Next morning the contents are filtered and, as the Ph is low, it requires neutralization with concentrated sodium hydroxide until the reaction is neutral to litmus. Three cc. of tricresol per liter are added. Seventy-five grams of permutit are also added with the object of absorbing the free amino acids. The solution of liver extract is now filtered to separate the permutit and, in the process of filtration, acetic acid and water are used to wash the permutit. Once this is done, filtration through filter paper is repeated. Redistilled water is then added to make 2,000 cc. and the liver extract is bottled in 250 cc. vials with rubber cap. The vials are then sterilized in a water bath for one hour. A hypodermic needle should be inserted through the rubber cap of each vial during the process of sterilization.

One cc. of this extract was equivalent to about 5 gm. of fresh liver and contained one unit per cc. In the Outpatient Department it was given intramuscularly in doses of 5 to 10 cc., usually 5 cc. three times a week. Injections of 5, 8, and 10 cc. were often given daily in the wards. One individual received as much as 20 cc. intravenously every day.

A standard technique was used in performing the peripheral red, white, and platelet counts at definite intervals. Whenever possible, reticulocytes were counted daily during the first two weeks of liver therapy and Wintrobe's hematocrit employed to determine the volume of packed red cells, with a Newcomer-Klett hemoglobinometer to estimate the hemoglobin in grams and percentages.

The diet prescribed for hospitalized cases and used, as far as possible, by ambulatory patients was originally described by the late Dr. Ashford.[4] In principle it was a low residue, high protein, low fat, and low carbohydrate diet that procured assimilation of absorbable foods in the presence of marked diarrhea. In practice, however, it included certain carbohydrate foods produced on the Island, such as plantains, bananas, *yautías* (a tuber somewhat similar to the potato) which, for some unknown reason, had been found to be tolerated and absorbed by the sprue patient. The purpose of this diet was to eliminate the excess carbohydrates (particularly rice and beans) and fats present in the daily fare of Puerto Ricans, replacing them by meat, eggs, milk, green vegetables, and fruits. It is not within the scope of the present report to include detailed menus of the above diet, yet they are available and can supply from 1,500

4. B. K. Ashford, *Am.J.Trop.Dis.*, III (1915–1916), 377.

to 2,000 calories per day. The majority of these foodstuffs was prepared by boiling and broiling; practically no fats were used with the exception of small quantities of butter in the final serving of meats, eggs, and vegetables. Condiments and alcoholic beverages were completely excluded from this diet.

Some of the cases received diet alone as the sole therapeutic agent during variable periods before liver extract was administered; others received liver extract without a special diet. The various drugs mentioned below were used in all cases, along with the liver extract or diet.

As to the drugs to be taken orally, a few were suggested by the late Dr. Ashford and employed in this group of cases. They were a digestant and stimulant containing dilute hydrochloric acid, pepsin, and a very small amount of strychnine, referred to herein as S. H. P.; another preparation contained tincture of opium, calcium, and bismuth subcarbonate, used for stubborn cases of diarrhea and known as O. B. C. Equal parts of dilute hydrochloric acid and elixir lactopepsin were also utilized.

The following were the prescriptions given to the patients:

S. H. P.

R/	Strychnine sulphate	0.079	gm.
	Hydrochloric acid, dilute	16.0	cc.
	Pepsin	12.0	cc.
	Comp. Tr. of Card	30.0	cc.
	Water q. s	240.0	cc.
Sig.	½ teaspoonful in water before meals.		

O. B. C.

R/	Tr. of deodorized opium	0.10	gm.
	Bismuth subcarbonate	6.5	cc.
	Prepared chalk	6.5	cc.
	Syrup of acacia	50.0	gm.
	Cinnamon water	100.0	gm.
Sig.	A teaspoonful in water q. 3 hours.		

DEATHS AND DEATH RATES FROM SPRUE IN PUERTO RICO FOR THE YEARS 1928–38

Table 1 shows the number of deaths and the death rates from sprue per 100,000 of population in Puerto Rico during the years 1928 to 1938. For purposes of comparison similar data for deaths due to

other anemias are also shown. Thus, while deaths and the death rates from other anemias increased during this period, those due to sprue remained more or less stationary. In 1928 there were reported 88 deaths from this condition with a rate of 5.9 percent; in 1938 the total number of deaths reached 103 and the rate, 5.8 percent.

TABLE 1

Deaths and Death Rates per 100,000 Population from Sprue and Anemias in Puerto Rico for the Years 1928–1938

Year	Sprue		Anemias	
	Deaths	Rate per 100,000 Population	Deaths	Rate per 100,000 Population
1928	88	5.9	185	12.3
1929	196	12.8	272	17.8
1930	105	6.8	145	9.4
1931	92	5.8	191	12.1
1932	109	6.8	211	13.2
1933	161	9.9	266	16.4
1934	139	8.4	269	16.3
1935	109	6.5	284	17.0
1936	104	6.1	414	24.4
1937	115	6.5	421	23.7
1938	104	5.8	382	21.3

It is assumed that in 1938 physicians all over the Island were more familiar with, and were better prepared to recognize, this condition than in 1928; it is believed, however, that more accurate diagnoses and a more widespread use of liver extract by the laity and the medical profession accounted for the decrease in deaths, reported above.

OBSERVATIONS ON THE FOLLOW UP OF CASES FROM 1931–41

Table 2 presents a distribution of cases according to age at first observation and to sex and race. In the white individuals, the age groups showing the greatest number of persons affected were the 20–29 for females, and the 20–29 and 40–49 for males. Twenty-six white males, or about one-half of the total male group, were affected between the ages of 20 and 50. The remaining male groups affected according to age were those from 50–59, 60–69, 70 and over, and from 10–19.

TABLE 2

Distribution by Age at First Observation and by Sex and Race of 100 Individuals with Sprue, Observed from 1931–1940

Age	White		Colored	
	Males	Females	Males	Females
10–19 yrs.	1	2	0	2
20–29 yrs.	9	11	2	3
30–39 yrs.	8	7	2	1
40–49 yrs.	9	10	2	0
50–59 yrs.	7	8	0	0
60–69 yrs.	7	4	0	1
70 and over	4	0	0	0
Totals	45	42	6	7

There were eleven white women in the 20–29 group, a higher number than in any other. This increase was considered a significant indication that sprue attacked women more often during the period when pregnancy was most likely to occur and that its onset occurred, not during pregnancy, but following delivery. However, while there seemed to be a high correlation between child-bearing and the incidence of this disease, nine of the eleven white women in the 20–29 age group were discharged improved and have had no relapses to date (Table 3). Groups 40–49, 50–59, 30–39, and 60–69 followed the first in order of sprue incidence.

Not much can be said as to the colored population of only thirteen individuals. The largest number of males and females affected, however, fell in the group 20–29 of both sexes.

By means of a master table (3), various combinations are presented on the data gathered in the follow up of these one hundred cases. This table classifies individuals according to race, sex, and age at first observation; also as to whether they were discharged improved, were still under treatment or had abandoned treatment, and as to those whose whereabouts were unknown.

In addition, and for arbitrary reasons, the cases were further divided into two groups; one comprised eighty-three persons first seen from 1931 to 1936, and the other made up of the seventeen cases admitted between 1936 and 1941. The reason is obvious for the great decrease in the size of the second group. The University Hospital closed for repairs from November, 1936 to April, 1940, and, though the Outpatient Department functioned during this interim, the

TABLE 3

Follow-up of 100 Individuals with Sprue, Observed from February 1, 1931 to February 28, 1941, Distributed According to Age at Entry and to Sex and Race

			83 Cases Admitted 1931–1936							17 Cases Admitted 1936–1941							
			10 to 19 Yrs.	20 to 29 Yrs.	30 to 39 Yrs.	40 to 49 Yrs.	50 to 59 Yrs.	60 to 69 Yrs.	70 and Over	10 to 19 Yrs.	20 to 29 Yrs.	30 to 39 Yrs.	40 to 49 Yrs.	50 to 59 Yrs.	60 to 69 Yrs.	70 and Over	Totals
White	Discharged Improved	♂	1	6	5	6	3	4	4	—	—	1	1	3	—	—	34
		♀	2	9	4	6	3	3	—	—	—	—	1	4	—	—	32
	Still under Treatment	♂	—	—	—	1	—	1	—	—	1	—	—	—	1	—	4
		♀	—	2	1	3	—	—	—	—	—	—	—	1	—	—	7
	Course Unknown	♂	—	1	2	1	1[a]	1	—	—	1	—	—	—	—	—	7
		♀	—	—	2	—	—	—	—	—	—	—	—	—	1	—	3
Colored	Discharged Improved	♂	—	2	1	1	—	—	—	—	—	—	—	—	—	—	4
		♀	1	2	1	—	—	—	—	1	—	—	1	—	—	—	5
	Still under Treatment	♂	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1
		♀	—	1	—	—	—	—	—	—	—	—	—	—	—	—	1
	Course Unknown	♂	—	—	1	—	—	—	—	—	—	—	—	—	—	—	1
		♀	—	—	—	—	—	1	—	—	—	—	—	—	—	—	1
	Totals		4	23	17	18	7	10	4	1	2	1	3	8	2	—	100

[a]Died in hospital 4 days after entry under observation.

number of new cases decreased surprisingly. One individual belonging to this group of one hundred cases died during hospitalization.

In February, 1941, sixty-six whites were discharged improved and up to the present time had not returned; eleven were still under treatment; ten had stopped treatment, their present condition unknown. Of the thirteen colored individuals, nine were discharged improved, two were still receiving treatment, and there were two whose course was not known. There is no record of those discharged improved who may have since had a relapse or may have died from sprue or from other causes. However, it can be said in general, judging from the interest shown by the patients under treatment, that the majority of cases would have returned had they suffered a relapse.

A total, then, of seventy-five white and colored individuals were discharged as improved and did not return during the ten-year period of 1931–1941. The average duration of treatment for all individuals was three years, with a range of from one month to ten years; the average hospital sojourn for twenty-seven cases was forty days. Twenty-five of these were later followed up in the Outpatient Department.

It is interesting to note that fifty-five patients were first observed in 1933, a number several times greater than in any other year; twenty-five of these, however, were discharged improved during that period. It is believed that the devastating hurricane which in 1932 struck the northeastern coastal plain of Puerto Rico, bringing destruction to sugar-cane plantations and factories and a subsequent lowering of economic and health conditions among agricultural workers, was responsible for the large number of sprue cases recorded in 1933. Of these about half responded rapidly to treatment and were discharged within the same year—fifteen within six months. On the other hand, fewer cases were treated at the University Hospital after 1939, a year when economic conditions throughout the Island improved greatly as the result of an expanding National Defense Program. During the first three months of 1942 one case only was admitted to the Outpatient Department.

The number of relapses and visits to the dispensary was generally less in patients below forty years than in the older age groups, though it was about the same for both men and women. Women came more often than men, though they did not get well any sooner. Upper respiratory infections were responsible for the greatest number of relapses in all age groups of both sexes. Dietary indiscretions, such

as ingestion of fried foods, rice, and beans, or barbecued pork, were next in order; cessation of liver therapy by those discharged improved was also a cause, irrespective of whether or not the diet had been followed during this time. However, relapses were more frequent in those who had abandoned their diet after discharge. In a country where many of the staple foods are imported and expensive, strict adherence to any form of diet is practically impossible for many of the underprivileged. Once improvement set in, younger people remained well longer and suffered fewer relapses than those over forty.

OBSERVATIONS ON THE EFFECT OF THERAPY IN THE GASTROINTESTINAL TRACT, GENERAL CONDITION, AND BLOOD OF PATIENTS WITH SPRUE

The earliest indication of improvement under liver therapy was a rapid and progressive disappearance of the lingual and buccal symptoms, accompanied by an equally rapid change in the appearance of tongue and mouth lesions. The beefy, red, angry, glazed appearance of the tongue dramatically vanished in the course of five to twelve days and, along with it, the bothersome soreness, rawness, and pain. Often within a week the tongue acquired a normal healthy color and new papillae could be seen on its previously red, smooth, atrophic borders and tip. Moreover, under diet alone, this process of improvement and repair was, as a rule, not only more delayed since it required several weeks, but also a complete return of all papillae, with complete disappearance of the affected areas, was rare.

The return of the long-lost appetite was also an early indication yet, if this were not properly controlled, it proved detrimental, as the ingestion of large amounts of food tended to produce diarrhea. On the other hand, relief of gastrointestinal symptoms including diarrhea and the frequency and character of the stools was not apparent until a later date, usually the second or third week. Such improvement was gradual and total disappearance of the symptoms might not follow for months. Epigastric distress or pain, heart-burn, abdominal distention, and borborygmi were diminished and might disappear completely.

However, it was believed that improvement was more rapid under liver and diet than under liver alone; a return of gastrointestinal symptoms under liver therapy, without a proper diet, was frequently observed and demonstrated in several hospital cases, even when blood values and the character of the tongue improved. These

first reappeared in a mild form and were not difficult to control. Occasionally hospitalized patients who were purposely given a general diet would not touch starchy or fried foods, which they knew from experience to be harmful.

As to the frequency and character of the stools under liver extract and diet, or under liver or diet alone, the change for the better was more delayed by the use of either regime than by the combined action of both. Under liver therapy and diet, the number of movements might diminish as early as the second or third week, even though the character was not altered until after several weeks of treatment. The watery, foamy, fermentative, foul dejections, accompanied by a great deal of gas and tenesmus, were then replaced by a soft, mushy, or semisolid stool without the characteristic foul odor or appearance, but the return to a hard-formed stool of normal appearance was infrequent. The change, with therapy well under way, was generally to a semisolid yellow stool, passed in the morning and evening and not accompanied by tenesmus or gas.

It was observed that any slight indiscretion in the diet of the majority of patients—even those who were relatively symptom-free, with blood values kept at normal or subnormal levels under adequate maintenance doses of liver extract—always resulted in a change in the appearance and frequency of the stools, with the accompanying complications. This observation occurred so often that it is worth mentioning now. It was also our belief that some individuals required larger amounts of liver extract to maintain a sustained improvement of gastrointestinal symptoms than to maintain normal hematologic values.

During the first few days after beginning treatment and usually preceding improvement of tongue and mouth, little evidence of betterment appeared in the general condition of patients; occasionally their condition seemed less satisfactory than before. Sometimes, however, coincident with improvement of mouth lesions, or following it, a striking change for the better took place. A feeling of intense well-being ensued. The long-lost appetite returned; quite suddenly strength also came back and the depressed or irritable state rapidly changed to one that was agreeable and cheerful. During the following few days, when the tongue and mouth were no longer sore or raw, hunger increased and a ravenous appetite appeared. (The speed with which this most striking change in the patients' condition took place is seldom paralleled by the treatment in other diseased states.) Such a rapid effect of liver therapy on sprue should not convey the impression that the successful and

final cure of the condition was necessarily of short duration. As has been stated before, the mean duration of treatment for this group of patients, taken as a unit, was three years.

What was the effect of liver therapy on the peripheral blood of sprue patients? A rise in reticulocytes might be said to mark the earliest indication of blood regeneration following the administration of liver. The peak of this increase usually occurred from the fifth to the twelfth day, often on the ninth, and was proportional to the degree of anemia present (number of red cells). With an initial count of one to two million erythrocytes per cmm., a peak ranging between 20 and 40 percent was observed, while with a count fluctuating between two and three million the maximum rise was seldom over 15 percent. When the red cells were more than three million, the reticulocyte count was rarely higher than 10 percent. As a rule, the increase in reticulocytes normalized (1 to 2 percent) by the end of the second week. An earlier communication[5] states that the initial reticulocyte count in untreated sprue ranged between 1 and 12 percent, but that it fell between 1 and 2 percent in the majority of cases. In general, it is believed that reticulocyte peaks were lower in sprue than in pernicious anemia, that is, given corresponding conditions of anemia and adequate amounts of liver therapy.

The changes in the morphology of the red cells, such as anisocytosis and poikilocytosis, were greatly diminished during the first few weeks of treatment but might persist for months, particularly when macrocytosis is present. A reversion to these changes occurred in relapses. Pronormoblasts, erythroblasts, normoblasts, and macrocytes disappeared rather early. Maturation of megaloblasts to normoblasts, and the restoration of normal morphology in the marrow and in the peripheral blood, followed the administration of liver, as in Addisonian pernicious anemia. As to the macrocytosis of the erythrocytes, the mean cell volume diminished as the number of cells and the volume of packed cells increased. Within a month of liver therapy, a mean corpuscular volume of 200 cubic microns might steadily return to within normal values (80–94 cu. u.). In about 50 percent of the cases the mean corpuscular volume rose shortly after administration of liver extract, as the amount of cells and their packed volume increased. This might be explained by the rise in reticulocytes which had a greater volume than the adult erythrocytes. However, this was not always the case and, in some

5. R. Rodríguez Molina, *P.R.J.Pub.Health & Trop.Med.*, XVII (1941), 134.

instances, the volume of packed cells rose faster in proportion to the number of cells per cmm., thus resulting in a higher mean cell volume. In still other individuals, such as Cases 2, 3, and 4 reported here, the packed red cells remained higher than the number of cells, after months and even years of therapy. Sometimes the red count might drop somewhat before rising steadily, while the packed cells remained stationary or were increased. Again, when a clinical relapse occurred, the number of red cells dropped sooner and faster than their volume, thus producing marked increase in the mean corpuscular volume. Though it was fully realized that the extremely small values in question were subject to fluctuations within the elements of chance and errors of technique, the above observations were so consistently repeated in different cases that they are worth reporting. Macrocytosis of the red cells had been observed in some cases to increase during the first, second, or third weeks of adequate treatment.

As a rule, when adequate amounts of liver extract had been given, as demonstrated in hospitalized cases, macrocytosis of the red cells disappeared and the mean corpuscular volume returned and remained within normal values. There was a like reaction in the mean corpuscular hemoglobin. As to the mean corpuscular hemoglobin concentration, this remained above 30 percent, providing it was not below 29 percent before treatment. Macrocytosis with hypochromia, that is, a mean corpuscular hemoglobin concentration below 29 percent, occurred in 15 percent of the cases before treatment. As red cells increased under liver therapy, the hemoglobin concentration tended to decrease further; the use of iron salts was quite helpful in building up the hemoglobin. However, as the only treatment in these cases, iron ammonium citrate and iron sulphate were tried with poor results, either clinically or in the blood. Liver extract was later required by all to bring about improvement.

The leukocyte count, if low, usually returned to normal between the fourth and fifth weeks of treatment, and the differential count returned to normal also. Macrocytosis of the leukocytes, described in a previous communication,[6] promptly disappeared in the majority of cases.

When subnormal values were present, the number of platelets per cmm. rapidly returned to normal variations (200,000 to 300,000 per cmm.), but not before the third or fourth weeks of treatment.

6. R. Rodríguez Molina, *ibid.*

The amount of liver extract required to maintain a person with a high threshold requirement in good health, once a full remission of symptoms had occurred, varied widely with different individuals. In the cases under study and, particularly in those of the Outpatient Department, the blood picture returned to five million red cells per cmm. during the course of treatment in only 25 percent of the cases. This might simply have indicated an insufficient amount of liver, because the majority of patients could not report for daily injections. However, clinical improvement with cessation of gastrointestinal symptoms and even a gain in weight was often attained with a subnormal erythrocyte count of three to four million per cmm. It appeared, then, that the liver extract administered was just enough to compensate for the lack of an adequate supportive diet and to maintain the patient up and about at a fair threshold of health and activity, but was insufficient to build up his blood to normal levels. It did not seem too much to expect from this or any other form of therapy. If relief of gastrointestinal manifestations, particularly the diarrhea and soreness of tongue, was obtained, the patients felt satisfied and resumed their work.

The amount of activity some of them could display with subnormal blood values was surprising. The erythrocyte and hemoglobin responded much more rapidly, but normal or subnormal levels were maintained for longer periods in individuals below forty years of age of both sexes and race than in those over this age. In the older age groups, clinical improvement with disappearance of gastrointestinal symptomatology was frequently observed in association with subnormal blood levels. In some cases the blood cell count did not rise above three and a half million, in spite of continued and apparently sufficient administration of liver extract. The patients were quite coöperative and persistent in their treatment.

Ideally, the criteria for a complete cure in sprue should include a sustained normal red cell count and hemoglobin, plus complete absence of all gastrointestinal symptoms under a general unrestricted dietary. However, experience proved that these requirements could not be met by the majority of the underprivileged patients. The disappearance of gastrointestinal disturbances together with an increase in strength and in weight were therefore the most important and common subjective and objective factors in determining such criteria. In many patients these states were frequently observed before normal blood values were produced.

The opportunity for observing permanent cures in sprue is lacking in the present work, which comprises the study of the life-history of the disease during ten years only. It is known, however, that of the seventy-five individuals discharged as improved, sixty-five have apparently remained well after five years without treatment. Knowledge is lacking, of course, as to how many of these have since received maintenance doses of liver extract in order to remain well, but it is believed that such a course is unlikely, given the type of patient observed in this series of sprue cases.

Liver extract was given one individual daily by the intravenous route in 10 and 20 cc. doses. No reaction resulted except pyrexia of 103° F., but clinical and hematological improvement was no more effective nor did it appear any sooner than when liver was administered intramuscularly.

REPORT OF CASES

Though several case histories are discussed herein, a more detailed summary of each case is presented in chart form. It is believed that they are representative of each group studied, that is, of those discharged as improved, those whose course is unknown, and those still under treatment. The report of one case that died is also included.

CASE 1. *J. O.:* O. P. D. No. 8040 (Chart I). Female mulatto age seventeen, suffering from acute sprue of three months' duration. Moderate macrocytic anemia with hypochromia found on examination (mean corpuscular hemoglobin concentration, 23 percent). Liver extract, iron sulfate, S. H. P., and sprue diet prescribed. (A note of interest is that an attack of upper respiratory infection, lasting two months during course of treatment, did not produce significant changes in blood picture, though it did aggravate intestinal symptoms.) Patient discharged sixteen months after first visit with slight macrocytosis of red cells still present; known to be in good health having suffered no relapses.

CASE 2. *C. B.:* O. P. D. No. 2935 (Chart II). White male age thirty-one, first treated by the late Dr. Bailey K. Ashford in 1932; seen again during first relapse of condition in 1936 after losing ten pounds in two months. Diarrhea, glossitis, epigastric distress, and moderate macrocytic anemia present; gastroscopic examination revealed chronic gastritis. As patient could not give up work during treatment and was thereby unable to receive regular liver injections, condition worsened after nearly two years' observation; four relapses were suffered during interim. Marked anemia and macrocytosis with hypochromia (mean corpuscular hemoglobin concentration, 27 percent) present when last seen; has not been heard of since final visit.

CASE 3. *J. R. E.:* O. P. D. No. 8544 (Chart III). First seen May 12, 1938; patient hardly able to walk, having lost fifty-eight pounds in six months. Acute sprue of six months' duration with extreme weakness and diarrhea found; also marked anemia with 1.11 million red cells, macrocytic in type with many normoblasts and thrombocytopenia. Reticulocyte peak of 24 percent observed on eighth day of liver therapy. Patient showed remarkable subjective and objective improvement, having gained fifty-four pounds in seven months and sixty-four by the end of the first year's treatment; hematologic response, however, not parallel to clinical improvement, but showing slight anemia with macrocytosis and hypochromia. Discharged April, 1940, with normal blood picture and symptom-free. Following attack of influenza, patient had anorexia and several aphthae seen on tongue. In February, 1941, no gastrointestinal symptoms, except flatulence and anorexia, present; blood picture subnormal; diet followed strictly. Patient last seen in July, 1941, doing fairly well; weekly liver therapy since February, 1941; weight, 143 pounds.

CASE 4. *R. L.:* U. H. No. 1725 (Chart IV). White male age forty; first seen March, 1934, with sprue of five months' duration, glossitis, and foamy diarrhea. Response to treatment, fair, with four relapses up to present; still under treatment. Discharged January, 1941, with fairly good (same as in 1934) blood values and symptom-free; weight sixteen pounds more. Last seen in August, 1941, blood count of four million red cells per cc. Case represents general type of patient, unable to come regularly for liver injections or to follow sprue diet because of economic condition. In 1937 given several samples of Jeculin, liver preparation taken orally.

CASE 5. *E. R.:* O. P. D. No. 8353 (Chart V). White female age fifty-seven, suffering chronic sprue of two years' duration; first seen December 1937. Atrophic gastritis and chronic proctitis found. No relapses from 1937 to 1940. General condition fair in May, 1940, with generally good blood values, though unable to follow diet or receive regular liver injections; seen in December, 1941, after relapse of condition, having moderate macrocytic anemia; still receiving liver therapy.

CASE 6. *R. R. M.:* O. P. D. No. 9765 (Chart VI). White male age fifty, with chronic sprue; originally diagnosed in 1916 but first seen in relapse in August, 1931, this last occurring while patient followed sprue diet but had not received liver therapy for several months previously. Patient was white-collar worker, more intelligent and better educated than average patient; realized his condition well. Marked pallor with lemon-yellow tint to skin noted; diarrhea, glossitis, and edema of ankles found. Marked macrocytic anemia (1.43 million red cells, 6.2 gm. hemoglobin, and mean corpuscular volume of 121 cubic microns); numerous nucleated red forms, giant staff neutrophils, and macropolycytes found. Extraordinary improvement, both clinically and hematologically, followed within six months of regular liver therapy (8 cc. biweekly), plus diet; red cells reached 4.91 million and hemoglobin 14 gm., or 96 percent, after 285 cc. of liver extract. Attack of recurrent tropical lymphangitis of left leg brought about loss of approximately one million red cells and 2½ gm. hemoglobin. Last seen in July, 1941, in excellent condition with normal blood values; no liver therapy since January, 1941. Patient had for years followed a practically fat-free dietary, the only carbohydrates allowed him being bananas, plantain, *yautía*, and citrus fruits. He realized, and had repeatedly proved to himself, that the slightest dietary indiscretion would produce flatulence and anorexia, followed by diarrhea. His rapid recovery and continued improvement, in spite of advanced age, was believed due to his ability and willingness to maintain a strict diet, one that could be tolerated by his incompetent intestinal tract.

CASE 7. *J. D. N.:* U. H. No. 1463. White male age fifty-five, first observed September, 1933, complaining of marked diarrhea and weakness of ten months' duration; loss of eighty pounds in weight claimed. Patient found to be well-developed cachetic individual with marked anemia, chronically and critically ill. Generalized lemon-yellow color of skin; prostration so marked patient could hardly talk or move, answering questions with great difficulty; mind clear. Sclerae subicteric; tongue pale and atrophic; heart sounds distant and muffled; systolic apical blowing murmur, not transmitted but audible; extrasystoles frequent. Abdomen scaphoid; lower border of liver palpable, small round tender movable mass felt at midclavicular line; spleen not palpable; marked evidences of peripheral arteriosclerosis. Blood pressure, 70 systolic and 0 diastolic. Patient collapsed in Outpatient Department and immediately hospitalized.

Macrocytic hyperchronic anemia, with red cell count of 990,000 per cmm., and hemoglobin of 27 percent (3.95 gm.) found; volume of packed red cells, 10.9 per cc.; mean corpuscular volume, 111 cubic microns; mean corpuscular hemoglobin, 39 micromicrograms; mean corpuscular hemoglobin concentration, 36 percent. Numerous normoblasts and megaloblasts observed in stained smears. White blood cell count, 4,000 with 45.5 percent polymorphonuclear neutrophils, 52.5 percent lymphocytes, and 1.5 percent monocytes. Urine contained heavy traces of albumin and bile; sediment negative. Blood Kahn also negative; blood cholesterol, 90.0 mg. and icteric index, 10 units. Feces positive for hookworm ova.

Course of illness in hospital: Patient became increasingly weak; intramuscular daily doses of 20 cc. of liver; temperature subnormal. Opiates would not control diarrhea. No donors for blood transfusion. Patient dyspneic and comatose, dying on fifth hospital day apparently from asthenia and circulatory failure.

Clinical diagnosis: Sprue, chronic cholecystitis and cholelithiasis, and uncinariasis.

Anatomical diagnosis: (Dr. A. Rivero). Sprue with severe primary anemia; hyperplasia of bone marrow; hemosiderosis of spleen and kidneys; chronic glossitis with atrophy of mucosa; cholelithiasis with numerous calculi in gall bladder, cystic, and common bile ducts; chronic cholecystitis; portal cirrhosis of liver; slight arteriosclerosis of aorta and coronary arteries; arteriosclerotic scarred kidneys; Monckeberg sclerosis of peripheral arteries. A final note from the pathologist's report (Dr. E. Koppisch) is included: "A case of sprue of approximately one year duration presenting profound emaciation, advanced anemia, intense hyperplasia of the bone marrow, hemosiderosis of the spleen and glossitis with atrophy of the lingual mucosa, as the main autopsy findings. There are no distinct anatomical changes in the stomach and the intestines. The bone marrow of the femur was not characteristic in that it abounded in normoblasts, but this is probably the result of administration of liver extract. Atrophic changes were not in evidence in any of the organs. The amount of hemosiderin in the spleen is greater than usual. An incidental finding is that of calculi in the cystic and common bile ducts, as well as in the gall-bladder with gross evidence of chronic inflammation of the latter organs. The liver is the seat of cirrhotic changes. Although one or two nodules suggestive of completely healed schistosome pseudotubercles were found microscopically, there is not enough evidence to ascribe the process to infection with *S. mansoni*."

An interesting note in this case was that the suprarenal glands were negative; cirrhosis of liver also mentioned in view of recent work establishing relationship of liver cirrhosis with nutritional deficiency.[7]

DISCUSSION

The foregoing study has shown that seventy-five individuals of the group under observation were discharged improved and have not returned during the ten-year period of the study. Thirteen cases are still under treatment and twelve have abandoned it, their course being at present unknown. Of those discharged as improved, sixty individuals have apparently remained well for over five years, that is, they were discharged over five years ago and have not, as far as is known, suffered a relapse of their condition.

With seventy-five patients discharged improved and sixty of them to all appearances cured for over five years, one must consider the prognosis in sprue as very good, depending on the patient's age. The outlook for those below forty is distinctly good but not very favorable for persons of either sex or race who are nearing fifty years of age. However marked the symptoms, the less than middled-aged patient can be assured prompt and sustained restoration if proper treatment is instituted and continued.

7. A. J. Patek, Jr. and J. Post, *J.Clin.Invest.*, XX (1941), 481.

The above results constitute a high tribute to the efficacy of liver therapy, though it must be borne in mind that the group studied comprised individuals of low economic status, many of whom were unable to receive regular liver injections or to follow the recommended diet for sprue. These factors doubtlessly influenced the duration of treatment, which had a mean length of three years, fluctuating from one month to ten years. Nevertheless, liver treatment did more than merely prolong the lives of these patients; it restored their health and their capacity for work. Before the introduction of liver therapy, the average life duration of the sprue patient was estimated at two years in Puerto Rico; the life span has therefore been increased by several years, as shown in the present work. Furthermore, inasmuch as the weakness produced by the accompanying anemia and diarrhea of sprue are likely to limit the patient's working efficiency, it is obvious that the lengthened life span is now accompanied by an increased activity for a similar period of years. It is believed that the life expectancy of a sprue patient, who is receiving adequate treatment, is that of the average person for the same age group.

More than half of the patients were first observed in the year 1933. The number of cases seen during that time was significant, since this was several times greater than the entries for any other year during the period of this study. The increase was believed due to, and intimately associated with, the disturbed economic and health conditions following the hurricane of 1932. The dietary deficiency resulting from that state of affairs was instrumental in producing a greater incidence of sprue several months later.

With regard to the thirteen patients still under treatment, nine are females, four males, eleven whites and two colored individuals. Their ages fluctuate between twenty-one and sixty-five, with only five patients below forty years of age. All but two patients have been treated over five years and one of these had received treatment for ten, eight for eight, one for seven, and another for six years.

Of the twelve patients who abandoned treatment or were discharged as unimproved, there were eight males and four females, ten whites and two colored, with ages ranging from twenty-one to fifty years. The length of treatment received was from one to three months in seven cases, and from six to seven years in five.

Regarding the use of a diet in the treatment of sprue in Puerto Rico, the author is convinced of its value as a supportive measure, second only in importance to liver therapy, and is entirely in dis-

agreement with the statement, made several years ago by Rhoads and Miller,[8] to the effect that the "idea of treatment by diet in sprue is so thoroughly ingrained in the medical consciousness that it is difficult for it to abandon the conception of some beneficial quality of the diet, simply as a regimen." They do admit, notwithstanding, that diet offers an "uncertain method" of obtaining liver extract for the pitiful victims of sprue. Long before the discovery of liver therapy for sprue, many cases here in Puerto Rico and other tropical regions had been improved and even cured by diet alone. The effectiveness of the Ashford diet in the successful treatment of sprue is clear and conclusive.

It is believed that every symptom of this illness can be cured by liver therapy, though some cases will require maintenance doses for months or years. However, if relapses are to be avoided, diet must be adhered to in the majority of cases, though patients can, in the absence of gastrointestinal symptoms, become more liberal in the use of carbohydrates; fatty foods and sweets must be avoided at all costs.

SUMMARY

1. The treatment and follow up of one hundred uncomplicated cases of sprue observed during a ten-year period is presented.

2. The material studied included fifty-one males and forty-nine females, ranging from twelve to seventy-eight years in age, with a mean age of 40.14 years; eighty-seven were whites and thirteen colored.

3. The method followed in preparing liver extract is outlined and other drugs employed mentioned; a consideration of the diet used is also included.

4. The effect of liver extract and diet on the gastrointestinal symptomatology, on the blood, and on the general condition of the patient is discussed in detail.

5. Several case histories, representing various groups of patients, are included, with postmortem findings in the one fatal case.

6. Tables and charts attached show: deaths and death rates from sprue for the years 1928–38; distribution of sprue cases according to age at first observation, sex, and race; classification of individuals according to race, sex, and age at first observation, as to whether they were discharged as improved, were still under treatment, or had abandoned treatment.

8. C. P. Rhoads and D. K. Miller, *J.A.M.A.*, CIII (Aug. 11, 1934), 387.

TABLE 1

J.O.—COLORED FEMALE, AGE 17—O.P.D. 8040

Date		*R.B.C.*	*Hgb. Gms.–%*	*Vol. P.R.B.C. cc.*	*M.C.V. Cu^3*	*M.C.H. γγ*	*M.C.H.C. %*	*Leucocytes*
1937 May 11	Acute sprue; epigastric distress; soreness of tongue; diarrhea; amenorrhea, 3 months duration; wt. 107; glossitis; free HCl. ℞: S.H.P.; sprue diet; liver extract, 5 cc. bi-weekly. Macrocytosis and hypochromia	3.47	11.4–78.3	48.0	135	32	23	11,000
July 22	Improved; wt. 115; no diarrhea or soreness of tongue; epigastric fullness after meals. ℞: ferrous sulphate 0.25 gm. q.i.d.	4.00	10.4–71.5	45.0	112	26	23	8,300
Sept. 30	Feels stronger; wt. 118; good appetite; epigastric distress unchanged; one daily stool; tongue, normal appearance. ℞: Iron sulphate 0.25 gm. t.i.d. Has received 50 cc. liver extract to date.	4.37	12.6–87.	45.0	102	28	28	7,000
Oct. 14	Upper respiratory infection, 1 week; wt. 115; slight soreness of tongue; no diarrhea. ℞: In bed; cough mixture; 5 cc. liver extract weekly.							
Oct. 21	Bothersome cough and pain in chest; bronchitis; X-ray of chest, neg.; sputum neg. for acid fast bacilli.							
Nov. 11	Temp. 99° F.; history of fever and chills; blood for malaria, neg.; bronchitis still present.							
Nov. 18	Respiratory condition unchanged; wt. 113; tongue sore; glossitis; no diarrhea; epigastric distress worse. ℞: Liver extract, 5 cc. bi-weekly; ferrous sulphate 0.25 gm. b.i.d.	4.50	12.8–88.	46.0	102	28	27	6,200
Dec. 16	Much improved; wt. 117; glossitis and epigastric distress still present; menses regular. Patient has not received liver extract injections as prescribed. Total amount: 75 cc. To return Jan. 20, 1939.	4.16	13.8–95.	42.0	100	33	32	7,400
1938 Jan. 20	Pt. did not return for appointment.							
Sept. 15	Mild upper respiratory infection; wt. 118; was 139 four months ago; no G.I. symptoms. ℞: Cod-liver oil.							

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Sept. 30	Feels stronger; wt. 118; good appetite; epigastric distress unchanged; one daily stool; tongue, normal appearance. ℞: Iron sulphate 0.25 gm. t.i.d. Has received 50 cc. liver extract to date.	4.37	12.6–87.	45.0	102	28	28	7,000
Oct. 14	Upper respiratory infection, 1 week; wt. 115; slight soreness of tongue; no diarrhea. ℞: In bed; cough mixture; 5 cc. liver extract weekly.							
Oct. 21	Bothersome cough and pain in chest; bronchitis; X-ray of chest, neg.; sputum neg. for acid fast bacilli.							
Nov. 11	Temp. 99° F.; history of fever and chills; blood for malaria, neg.; bronchitis still present.							
Nov. 18	Respiratory condition unchanged; wt. 113; tongue sore; glossitis; no diarrhea; epigastric distress worse. ℞: Liver extract, 5 cc. bi-weekly; ferrous sulphate 0.25 gm. b.i.d.	4.50	12.8–88.	46.0	102	28	27	6,200
Dec. 16	Much improved; wt. 117; glossitis and epigastric distress still present; menses regular. Patient has not received liver extract injections as prescribed. Total amount: 75 cc. To return Jan. 20, 1939.	4.16	13.8–95.	42.0	100	33	32	7,400
1938 Jan. 20	Pt. did not return for appointment.							
Sept. 15	Mild upper respiratory infection; wt. 118; was 139 four months ago; no G.I. symptoms. ℞: Cod-liver oil.							

Date		R.B.C.	Hgb. Gms.–%	Vol. P.R.B.C. cc.	M.C.V. Cu^3	M.C.H. γγ	M.C.H.C. %	Leucocytes
1936								
May 28	First seen by Dr. Ashford, 6–11–32; well, up to 1936. Relapse No. 1. Diarrhea; sore tongue; glossitis; has lost 10 lbs. in 2 mos.; epigastric distress; wt. 138; free HCl. Liver extract therapy begun 6–1–36.	3.49	11.8–80.7	36.0	103	33	32	9,800
July 10	Stronger; wt. 143; G.I. symptoms improved.	3.42	12.0–82.					
Aug. 6	Improved; unable to receive liver injections regularly; mild glossitis; no diarrhea; 60 cc. liver extract received from 6–1–36 to 7–29–36; none since.							
1937								
Mar. 11	Relapse No. 2. Wt. 135; glossitis and diarrhea; liver therapy resumed; 5 cc. three times a week.	2.44	11.1–76.	28.0	116	42	39	8,350
Apr. 14		3.76	10.6–72.9					9,200
Apr. 22	Wt. 146; much stronger; at work; no diarrhea as long as sprue diet is followed; tongue, normal appearance.							
May 27	Symptom free, except for occasional epigastric distress; working; wt. 142. Advised to avoid manual labor. ℞: Iron sulphate 0.25 gm. b.i.d. Has received 45 cc. of liver extract since March 11.	4.96	12.8–88.	44.0	88	25	28	8,400
July 15	Diarrhea; glossitis; heartburn. Relapse No. 3. Wt. 136 after 6 weeks of work and while under liver therapy.	3.60	8.0–55.5					
Aug. 12	Wt. 140; slight subjective improvement; last liver injection 8–16–37.	2.40	8.6–59.					
Sept. 16	Stronger; no diarrhea; tongue covered; wt. 148. Mucosa of rectosigmoid colon is atrophic.	3.47	11.4–78.					
Dec. 16	No liver extract from Aug. 16 to Dec. 20. Relapse No. 4. Wt. 134; loss of 14 lbs. since Sept.; felt strong and symptom free up to one month ago; diarrhea; sore tongue; epigastric distress. Has not stopped working; follows diet.	3.33	11.5–78.8					
Dec. 20	Gastroscopic exam.: chronic gastritis.							
1938								
Jan. 20	No change in symptomatology; wt. 139.							
Mar. 31	Unable to work because of weakness; gastro-intestinal symptoms worse; wt. 134. Patient has not returned to clinic. Course unknown.	2.23	7.2–49.5	26.0	118	32	27	6,000

J.R.E., WAITER—WHITE MALE, AGE 25—O.P.D. 8544

Date		R.B.C.	Hgb. Gms.–%	Vol. P.R.B.C. cc.	M.C.V. Cu^3	M.C.H. γγ	M.C.H.C. %	Leucocytes
1938								
May 12	Acute sprue of 6 months duration. Extreme weakness; hardly able to walk; claims to have lost 58 lbs. in 6 mos.; epigastric distress; soreness of tongue; edema of ankles; diarrhea; wt. 98. ℞: Liver extract 5 cc. biweekly starting 5–13–38. Sprue diet. Anisocytosis; poikilocytosis; normoblasts; platelets: 134,000.	1.11	5.4–36	16.0	145	49	33	3,400
May 21	Reticulocytes peak: 24%.							
June 2	Marked subjective improvement; wt. 110; no diarrhea; epigastric distress; vertigo; tongue still sore and atrophic.							
July 28	Wt. 111.	1.84	7.6–52	28.0	155	42	27	5,600
Dec. 15	Marked objective improvement; wt. 142; no G.I. symptoms; no edema. Total amount of liver extract received: 200 cc. ℞: Iron sulphate 0.25 gm. b.i.d. Pt. discharged; return in 6 months. Platelets: 200,000.	3.42	11.6–80					10,200
1939								
June 29	Wt. 162, a gain of 64 lbs. since admission; no G.I. complaints. Hematologic response not parallel to clinical improvement.	3.57	13.8–95	50.0	140	38	27	
1940								
Jan. 23	After working as laborer in city sewerage construction, has lost 11 lbs. in one month; wt. 152; no G.I. symptoms. Pt. states to have followed diet during illness, and still does. Macrocytosis and hypochromia.	4.04	13.0–90	55.0	137	32	23	
Feb. 8	Iron sulphate 0.25 gm. g.i.d. To return in 2 months.							
Apr. 18	No symptoms; wt. 150; follows diet. Discharged.	5.41	14.5–100	44.0	81	26	32	
Aug. 16	Influenza one month ago. Since then does not feel well: no G.I. symptoms but frequently there is anorexia. Tongue presents aphthae on borders. Wt. 147 lbs. Blood values not as good as formerly. No macrocytosis.	4.90	13.1–91	43.0	87	26	30	
Nov. 15	Condition satisfactory: weight 146 lbs.							
1941								
Feb. 14	Feels tired; No. G.I symptoms except flatulence and anorexia. Tongue of normal appearance. Wt. 143 lbs. ℞: Liver extract 5 cc. thrice weekly. Iron Sulphate							

Date		R.B.C.	Hgb. Gms.-%	Vol. P.R.B.C. cc.	M.C.V. Cu³	M.C.H. γγ	M.C.H.C. %	Leucocytes
1934								
Mar. 8	Acute sprue of 5 months duration; wt. 102; soreness of tongue and mouth; diarrhea; stools: liquid, foamy, fetid, grayish, 1–5 daily, 1–3 nightly; intolerance to sweets and fatty foods. Free HCl.	3.18	14.5–100	37.0	116	45	36	6,300
Mar. 15	Hospitalization; liver extract 5 cc. daily; Retcs. 2.8% 7th day.	3.15	13.4–92	34.8	110	42	38	4,100
Apr. 2	Discharged improved; wt. 107; no diarrhea; no soreness of tongue. Liver therapy to be continued at O.P.D.							
Oct. 9	Improvement continues; wt. 128; no diarrhea; normal tongue, but feels weak. Received 64 cc. liver extract since discharge; last injection 4–30; liver therapy again resumed.	3.20	10.3–70					
1935								
Apr. 4	No complaints; wt. 135; 60 cc. liver extract since 10–9–34; to return in 3 months.	4.00	10.5–72					
1936								
June 4	Relapse No. 1; wt. 115; anorexia; weakness; diarrhea; flatulence; glossitis; unable to follow diet. Patient did not return to our clinic until 1937, but continued to receive liver extract to 7–24–36: 72 cc.	2.35	11.0–76					
1937								
July 22	Relapse No. 2. Felt fairly well up to 3 mos. ago; glossitis; weakness; diarrhea; wt. 114 lbs. Jeculin per os–16 cc. daily as he is unable to come for liver injections.	2.90	7.5–51.5					
Sept. 2	Improved; wt. 117; follows sprue diet.							
Oct. 7	Stronger; no diarrhea; wt. 119; mild glossitis.	2.04	9.6–66					
Dec. 12	Has taken 720 cc. of Jeculin since 7–22. Subjective improvement continues, however. Parenteral liver extract therapy resumed.	1.88	10.3–70	32.0	170	54	32	6,700

TABLE 4—Continued

R.L., CIGAR MAKER—WHITE MALE, AGE 40—U.H. 1725—*Continued*

Date		R.B.C.	Hgb. Gms.-%	Vol. P.R.B.C. cc.	M.C.V. Cu³	M.C.H. γγ	M.C.H.C. %	Leucocytes
1938								
Jan. 20	Stronger; no G.I. symptoms; wt. 120. Has received only 30 cc. of liver extract since 12–12–37.	3.57	13.0–89	37.5	105	36	34	10,400
Mar. 17	Wt. 115; symptom free; suffered fall; in bed several weeks; liver extract discontinued.	4.05	12.0–82					
Mar. 30	Wt. 126 lbs.							
July 7	Continues symptom free; working; wt. 119; discharged improved.							
1939								
Oct. 5	Relapse No. 3. Well up to one month ago; anorexia; weakness; diarrhea; wt. 112 lbs. Liver extract, 5 and 8 cc. weekly.	2.99	8.8–60	27.0	90	29	32	8,000
Dec. 7	Improved; unable to follow diet; wt. 115 lbs.	3.16	11.4–78					
1940								
Jan. 11	No G.I. symptoms; stronger and active at work; wt. 115; 70 cc. of liver extract since 10–5–37. Discharged improved.	4.06	14.5–100	45.0	111	35	32	6,400
Feb. 15	Improvement continues; cannot follow diet; wt. 113.	4.38	14.2–97	44.0	100	32	31	7,600
Apr. 18	Relapse No. 4. Flatulence; glossitis; no diarrhea; wt. 114. Under treatment with liver extract.	3.73	11.2–75	38.0	102	30	29	
June 21	Stronger: diarrhea occasionally; tongue, normal appearance; wt. 108 lbs. Under treatment with liver extract. Unable to follow diet.	2.37	9.3–64	33.0	139	40	29	
Sept. 16	Feels stronger; two solid stools daily: No G.I. symptoms. Since January 11, 1940 has received 90 cc. liver extract; wt. 112 lbs. Stools culture for B. Typhosus. For a typhosus and shigella, neg.							
1941								
Jan. 20	No symptoms, except slight flatulence; stronger; wt. 118 lbs. Since Sept. 16, 1940 has received 30 cc.							

Table 5

E.R.—WHITE FEMALE, AGE 57—O.P.D. 8353

Date		R.B.C.	Hgb. Gms.-%	Vol. P.R.B.C. cc.	M.C.V. Cu^3	M.C.H. $\gamma\gamma$	M.C.H.C.	Leucocytes
1937								
Dec. 23	Sprue of 2 yrs. duration; weakness; soreness of tongue; numbness of feet; diarrhea; marked glossitis and stomatitis; wt. 79; free HCl. Platelets: 196,000.	3.11	11.4–78	39.5	127	36	28	3,900
Dec. 27	Atrophic gastritis. Patient looks 10 yrs. older than given age. ℞: Sprue diet; S.H.P., Liver extract 5 cc. bi-weekly begun 1–17–38.							
1938								
Jan. 13	Chronic proctitis.							
Feb. 24	Good appetite; stronger; no diarrhea; follows diet.							
Mar. 17	Improvement continues; tongue covered; one formed stool daily; wt. 74. Total liver extract received to date: 45 cc.	4.15	13.0–89.6	54.0	130	31	24	6,800
Apr. 14	Wt. 87; symptom free; ℞: ferrous sulphate 0.25 gm. q.i.d.							
May 10	Relapse No. 1, following respiratory infection; anorexia; weakness; no diarrhea; relapse occurred while under liver therapy, which has been irregularly administered; wt. 75.	3.69	12.2–84	54.0	146	33	22	7,000
Aug. 4	Improved; anorexia and epigastric distress; wt. 77.	3.88	12.8–88					
Sept. 22	Wt. 86; objective improvement, in spite of complaints of weakness, aches and lamentations.							

Table 5—Continued

E.R.—WHITE FEMALE, AGE 57—O.P.D. 8353—*Continued*

Date		R.B.C.	Hgb. Gms.-%	Vol. P.R.B.C. cc.	M.C.V. Cu^3	M.C.H. $\gamma\gamma$	M.C.H.C.	Leucocytes
1939								
Jan. 19	Relapse No. 2; wt. 76; diarrhea; soreness of tongue; unable to receive liver extract regularly. Ferrous sulphate 0.25 gm. t.i.d.	3.23	11.2–77	44.0	137	35	25	
Mar. 16	Slight subjective improvement; tongue covered; wt. 76.	3.00	11.8–80.5					
May 18	Wt. 78; improvement continues; no diarrhea.	3.44	10.6–73					
Aug. 3	Relapse No. 3, following respiratory infection; wt. 75; weakness, glossitis; diarrhea. ℞: 8 cc. weekly of liver extract (one injection).	3.57	10.3–70					
Oct. 10	Stronger, more active; no G.I. symptoms; wt. 76.	3.55	11.0–76	43.0	121	30	25	4,800
Dec. 14	Good appetite; has to eat what she is able to get; wt. 76. No G.I. symptoms; one hard movement daily. Pt. has received liver therapy during all of 1939, a total of 393 cc.							
1940								
Feb. 20	Pt. did not report for appointment Feb. 8, 1940. Active at work; no diarrhea; no soreness of tongue; aphthae in mouth; wt. 76: liver extract irregularly administered.	3.37	12.9–89	42.0	124	36	30	10,000
May 31	Condition is fair: 1–2 soft stools daily: normal tongue. Cannot follow diet or receive liver injections regularly; wt. 77 lbs. Blood values pretty good: no macrocytosis or hyperchromia.	4.68	13.0–90	40.0	87	28	32	7,300

TABLE 6

R.R.M., CLERK—WHITE MALE AGE 50—O.P.D. 9765

Date		*R.B.C.*	*Hgb. Gms.-%*	*Vol. P.R.B.C. cc.*	*M.C.V. Cu³*	*M.C.H. γγ*	*M.C.H.C.*	*Leucocytes*
1939								
Aug. 22	Sprue in relapse; first diagnosed in 1916 at Institute of Tropical Medicine; wt. 120 lbs., marked pallor with lemon yellow tinge of skin; diarrhea; glossitis; edema of ankles and feet. Free HCl present. Anisocytosis; numerous nucleated red cells; macrocytes; giant staff neutrophiles; macropolycytes.	1.43	43–6.2	17.0	121	44	36	5,400
Sept. 21	Reticulocyte peak—19%. 8 cc. liver extract bi-weekly begun 9–14–39.							
Oct. 19	Wt. 118 lbs. Much stronger; no diarrhea; tongue covered; slight redness of tip and borders.	2.65	36.5–9.7	38.0	143	36	25	6,400
1940								
Jan. 16	Extraordinary improvement; Ruddy complexion; very active and cheerful; wt. 130 lbs. No. G.I. symptoms. Tongue of normal appearance. Total amount of liver extract received 285 cc. Clinical improvement as marked as hematologic response.	4.91	96–14.0	96.0	93	28	30	5,000
Jan. 30	Wt. 131 lbs. Slightest dietary indiscretion produces flatulence and heartburn; no diarrhea; one formed stool daily of normal appearance; no therapy, except diet.							
Mar. 28	Symptom free; working; one daily formed stool. Follows diet; wt. 132½ lbs. Macrocytosis, hypochromia. A loss of one million cells and 2.5 gms. hemoglobin probably result of attack of so called "recurrent tropical lymphangitis," left leg.	3.99	11.5–80	41.0	103	29	28	5,200
May 10	No sprue symptoms; active at work. ℞: liver extract 5 cc. bi-weekly; wt. 138 lbs.							
1941								
Jan. 10	No symptoms; feels strong; has not received liver regularly. 140 cc. since May 10, 1940; wt. 146 lbs.; follows diet.	4.20	12.4–85	43.0	102	29	28	