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NEWS AND VIEWS

Foreign Newsletter—Puerto Rico

TO THE EDITOR:

Only ten or fifteen years ago, in travelling across the Island, one could easily pick up by the road-side almost any number of cases of severe, so-called hookworm anemia. They were pale, edematous, weak, usually barefooted subjects. Today it is hard to find such cases, although the incidence of necator americanus infestation has not materially diminished. It may very well be that the severity of the infestation is not as high but most probably better nutrition through education and improvement of the economic status is the real answer.

The same statement holds true for sprue. Only a relatively few years ago Ashford would report on series of hundreds and even thousands of cases. Today in order to get 2 or 3 suitable cases for study and investigation one has to travel the Island from north to south and from east to west, to correspond with physicians practicing in the smaller towns and rural areas or to publish advertisements in the daily papers.

There is no doubt that educational, economic and nutritional factors have played a role on the practical disappearance of severe anemias on the Island.

On the other hand it is our impression that we have been seeing more cases of aplastic anemia during the last few years. As far as leukemia in its acute and chronic forms is concerned—thrombocytopenic purpura, primary and secondary, and hemolytic anemias—the incidence is probably similar to that observed elsewhere. The high incidence of schistosomiasis mansoni in certain regions of the Island could explain many of our cases of splenomegaly and of hypersplenism. Malarial fever as a cause of anemia and splenomegaly has practically vanished since World War II.

Sprue

Over one hundred cases of sprue have been kept in hematologic and clinical remissions for over five years with the daily oral administration of 2.5 mg. of folic acid (Lederle). No neurologic manifestations have developed during the administration of folic acid, but a sprue patient who had mild signs and symptoms of combined system disease developed a most fulminating degeneration of the postero-lateral cords while receiving diopterin (pteroyldiglutamic acid).

It has been suggested that Addisonian pernicious anemia is the clinical result of a deficiency of vitamin B_{12} and that in nutritional macrocytic anemia the predominant deficiency is of pteroylglutamic acid.[1]

It might be interesting to state that sprue patients respond to the parenteral administration of vitamin B_{12} in the same or similar fashion that they do to oral or parenteral folic acid. We have at present 20 sprue patients who have been maintained in excellent clinical and hematologic remission for nearly two years with a weekly injection of 15 μg. of vitamin B_{12} (Chas. Pfizer & Co.).

The oral and simultaneous administration of vitamin B_{12} and folic acid in subminimal doses (25 μg. of the former and 1.67 mg. of the latter) was found effective in the treatment of 4 sprue patients by Meyer and collaborators.[2] The administration of vitamin B_{12} in 100 and 500 mg. oral single doses had previously been found ineffective in the treatment of sprue by Suárez, who also had reported that although 2.5 mg. daily of folic acid given orally is probably adequate as a maintenance therapy, 10 or 15 mg. should be given daily in the treatment of acute cases to induce maximal clinical and hematologic responses.

The combination of 10 μg. vitamin B_{12}, and 0.67 mg. folic acid given orally was found inadequate in the treatment of 3 cases. The additional intravenous administration of ascorbic acid did not seem to enhance the effect of the combination of vitamin B_{12} and folic acid.

A mixture of ferrous sulfate, vitamin B_{12}, folic acid and ascorbic acid (Rubraferrate,

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E. R. Squibb) was found useful in the treatment of sprue patients who had suffered blood loss or who harbored heavy intestinal parasitism.

Folinic acid and citrovorum factor have been tried on sprue patients by Rodriguez, Molina and Romero and by Suárez and collaborators respectively. A paper by the latter authors has appeared in the June number of the Boletin de la Asociación Médica de Puerto Rico. Citrovorum factor in doses of 20 million units daily given parenterally was found effective both clinically and hematologically.

Paniagua, Casas and Hernández-Morales[3] reported on the adrenocortical function in 10 untreated sprue patients using the subcutaneous administration of 0.3 cc. adrenalin 1/1000 solution. In all cases but one who had complicating schistosomal and syphilitic infections, there was a definite decrease, which varied from 40 to 92 per cent in the circulating eosinophils. We have repeated the Thorn test on another 10 cases of acute sprue using 25 mg. of ACTH instead of adrenalin and our unpublished results showed also a satisfactory adrenocortical response in all cases.

In February 1950 we tried ACTH in doses of 20 mg. every six hours in 2 severe sprue patients. Both had initial red blood cell counts of less than one million, the reticulocytic increase was only 14 per cent, subjective improvement and a sense of well being and euphoria was observed, but there was no real clinical nor hematologic improvement after fourteen days of treatment.

Megaloblastic Anemia of Pregnancy and the Puerperium

During the annual meeting of the Puerto Rico Medical Society held in December last year, Leonard J. Piccoli of E. R. Squibb & Son showed an interesting moving picture on anemia made in Havana, Cuba and in Puerto Rico, and edited both in the Spanish and English language. He also read a paper on "Recent developments in vitamin B_{12} therapy."

In the discussion of Dr. Piccoli's paper, Ramón Suárez, Sr. reported a series of 12 cases of megaloblastic anemia of pregnancy and the puerperium all of which responded to liver extract injection. This was long before the discovery and synthesis of folic acid. A recent case diagnosed and treated at the Bayamón Charity District Hospital responded nicely to vitamin B_{12} injections. This last case showed purpura and a palpable spleen and was admitted with tentative diagnoses of either aplastic anemia or aleukemic leukemia. Only after the bone marrow was obtained and studied could the diagnosis of megaloblastic anemia be established. It is Suárez' opinion that probably some of the cases of megaloblastic anemia of pregnancy observed in Puerto Rico are in reality cases of tropical sprue and that all of them respond to liver extract or to vitamin B_{12} as well as the cases observed in northern climates respond to folic acid.

Thorn Test in Patients with Eosinophilia Related to Parasitic Infection

Hernández Morales and Carmen Casas reported[4] on the effect of epinephrin on the circulating eosinophils of 12 patients suffering from filariasis or schistosomiasis. In 10 of the 12 patients the number of eosinophils decreased over 40 per cent after a four hour rest period following the injection of 0.3 mg. of epinephrin. This result seems to indicate that parasitic infections may not interfere with such a test for adrenocortical function. A future communication will deal with a similar study in which pituitary adrenocorticotropic hormone (ACTH) will be used instead of the adrenergic drug.

Rh Antibody Tests and Circulating Anticoagulant

There are two papers in press; the first one is by Mercedes V. de Torregrosa, "Prognostic value of prenatal Rh antibody tests." She studied a series of 163 Rh-negative women through one or more pregnancies. Of the 86 women in their first pregnancy, none of the babies had complications that could be attributed to the Rh factor, and there was no in vitro evidence of isosensitization except in one, who had received a blood transfusion. There were 3 erythroblastotic babies due to Rh isosensitization among the 53 women in their second pregnancy, and 1 case due to sensitization of a group O mother to the blood factor B present in the baby. In this group she also encountered a stillborn hydropic baby

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the cause of which has not been determined. Of the 24 women studied during the third, fourth and fifth pregnancies, 18 had negative Rh antibody tests and they delivered normal babies. Five had Rh antibodies that increased in titer during the pregnancy, and all five delivered erythroblastotic babies. One of these five patients had positive Rh antibody tests at the beginning of her fifth pregnancy; the Rh antibodies did not increase in titer and she delivered a healthy Rh-negative baby. The Rh antibodies were a residue of her fourth pregnancy which had terminated in the birth of a hydropic baby. The titers of Rh antibodies varied from 8 to 8,192 by the conglutination method, only 2 of the patients exhibited anti-Rh agglutinins of low titer. Trypsinized cells were used in a small group of cases only. This is in accordance with the finding of Wiener and others, that incomplete or blocking antibodies are more important in causing erythroblastosis than agglutinins. Prenatal Rh antibody tests have proved to be of great prognostic value.

The other paper, presented by Eduardo R. Pons and Mercedes V. de Torregrosa, which will appear in a future number of BLOOD, is the report of a case showing hemorrhagic diathesis in whom the presence of an anticoagulant in the patient's blood and plasma could be demonstrated. The anticoagulant was shown to be active in dilutions up to 1/350. It retained its potency after heating to 61 C. for 10 minutes and after storage, either in a refrigerator or at room temperature, for twenty-four hours. The anticoagulant was not neutralized by protamine sulfate or by toluidine blue. Placental plasma corrected the clotting defect in vitro but was ineffective when administered intravenously to the patient. Evidence is presented suggesting that the second and third stages of coagulation in this case were normal, that the patient's plasma had antithromboplastic activity, and that the anticoagulant may be antithromboplastin.

Hypersplenism

Noya Benítez read a paper entitled "Splenectomy in the treatment of hypersplenism and esophageal varices," which has not as yet been published. There were 49 cases of schistosomiasis mansoni, all showing splenomegaly, anemia, leukopenia, thrombocytopenia and cirrhosis of the liver. Splenectomies were performed at the University Hospital of the School of Tropical Medicine in San Juan, P.R. in the five years period from 1945 to 1950. The six additional successful cases performed at the City Hospital of San Juan, P.R. were not included. They were all typical cases of portal hypertension and beautiful examples of the hypersplenic syndrome. Hypersplenism became, therefore, the main reason for splenectomy. All the cases had a complete work-up, which included urinalysis, stool examination, determination of blood proteins, platelet counts, Hanger cephalin flocculation and Bromsulfalein tests and x-ray of the esophagus. In the follow-up the patients were checked every three months during the first year postoperatively, and every six months thereafter. All the cases, except the first two and the fourth, had biopsies of the liver performed at operation, but studies on the portal venous pressure were not made. (These studies are being performed at present in Noya Benítez' series of porto-caval anastomosis.) Forty of the 49 cases gave a history of hematemesis, melena, or both. In 9 cases there was no such history. One patient died following operation. The operative mortality was 2.04 per cent. One case, who was subjected to splenectomy and cholecystectomy (for a fatty infiltrated gall-bladder), suffered a dehisced wound on the second day after operation, which was repaired under pentothal and curare. Subsequently he developed pulmonary atelectasis, pneumonia, liver failure and died on the fifth postoperative day. One case died from intercurrent disease (postpartum eclampsia) twenty-six months after splenectomy. In 5 cases splenectomy seemed to be absolute failures in preventing hematemesis and melena. Three of these died. Another 3 cases were considered partial failures, although they have not bled during the last three years; but as cases have been seen to bleed eight years after splenectomy, these figures could not be considered final. Thirty-nine patients have gained weight and strength, have improved their blood picture, and are today practically normal subjects and useful citizens.

The spleen removed from these patients ranged in weight from 500 to 2,250 Gm. the average weight being 1,000 Gm.

Based on the fact that the operative mortality of porto-caval anastomosis (including

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spleno-renal) for cases of intrahepatic portal bed block ranges from 18 to 35 per cent, and that a certain percentage (4 to 10 per cent) of the successful cases bled after operation, Noya Benítez concluded tentatively as follows:

"Splenectomy and splenectomy alone is indicated in cases of splenomegaly due to schistosomiasis mansoni with anemia, leukopenia, thrombocytopenia and cirrhosis of the liver. Porto-caval shunts should be reserved for the cases that continue to bleed after splenectomy."

RAMÓN SUÁREZ

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Foreign Newsletter—Japan

TO THE EDITOR:

I have been intending to write you and report to you the recent activities of the Japan Hematological Society. The big event was of course the annual session of the Society which this year was held in Tokyo as Section VIII of the Thirteenth Japan Medical Congress which meets once every four years, comprising 41 specialty societies. The total attendance at this Congress is reported to be over 15,000 assembled from all over Japan. The Emperor of Japan attended the opening meeting of the Congress. This was the first time that the Emperor has ever been present at a scientific meeting. The hematologic sessions were held over a period of three days in which three special lectures and 265 different papers and reports were heard by over 300 members. The subjects dealt with on the first day were chiefly those of the hemopoietic organs, particularly the bone marrow, spleen and reticuloendothelial system. The noteworthy papers concerned with the structure of the bone marrow vascular system, the method of measuring the oxidation and reduction of the marrow, the problem of leukotaxin, and the special lecture by Prof. Komiya dealt with the question of specific "poietin" for each strain of blood cells on the basis of his observations on the nervous regulation of blood cells. Another series of papers was concerned with the problem of blood platelets and blood coagulation.

The papers presented on the second day were chiefly on various aspects of leukemias and the special lecture by Prof. Takeda brought out a new idea regarding the immunizing or antigenic effect of leukemic or malignant cells. Using Yoshida sarcoma cells as the research material he demonstrated that the clinical manifestations of leukemia, which was a transplantation leukemia, varied according to immunity reaction and state of allergy. During the last stage of transplantation when the animal was in a state of anergy, the malignant cells appeared in the blood stream, while during the stage of allergy no free cells appeared in the peripheral blood. This suggested a method of treating leukemia with immune serum, which seemed fully confirmed by his data.

The program of the third day comprised such subjects as metabolism, anemias, the defense mechanism and a few others. One of the interesting papers took up the question of acatalasemia, a disease of certain enzymic deficiency, presumably catalase, in the blood,

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which produced peculiar discoloration of the red cells. Metabolic studies using radioactive iron have also begun to appear on the program and recent news that cyclotrons are again to be permitted to be built in Japan will undoubtedly lead to a larger number of metabolic studies using radioactivity as a method in the hematologic laboratories of Japan in the future. A few papers on the relation of lymphocytes to plasma cells were very stimulating although none too conclusive.

The Society has been holding semi-annual meetings in the past four years and the coming autumn meetings will be held in Matsumoto near Asma Hot Spring on October 13–14. The principal theme of this meeting will be the bone marrow.

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