ERYTHROCYTIC DISEASE


By means of the *Euglena* assay, serum vitamin B12 estimations were done on thirty-three patients with pernicious anemia in relapse and thirteen with other forms of megaloblastic anemia. Injections of 20 to 1000 μg. of vitamin B12 were given to untreated pernicious anemia patients. In all the latter patients, when the marrows were normoblastic the serum vitamin B12 levels ranged from 80 to 860 μg. per ml., with a mean concentration of 250 μg. per ml. When it was megaloblastic the concentrations ranged from 50 to 120 μg. per ml. (mean 83 μg. per ml.) with one exception.

Concentrations remained within the normal range for from six to more than eighteen days after injections of 20 μg.; from two to twenty-two days after 40 μg.; from eleven to at least thirty-five days after 80 μg.; from eleven to at least forty-eight days after 160 μg.; from thirty-nine to ninety-eight days after 320 μg.; and from thirty-four to at least fifty-eight days after 1000 μg. However, in all treatment groups the mean concentration of vitamin B12 in the serum fell within a few days of the injection below the mean concentration found in normal persons.

In patients with megaloblastic anemia due to sprue or pregnancy the serum vitamin B12 levels were normal before treatment. There was no response to vitamin B12 therapy, and no change occurred in the serum level with folic or folinic acid treatment.

The authors consider that the serum vitamin B12 level can be maintained within the normal range with very little vitamin B12 in store, and that a much larger amount in store is needed to keep the serum level at the mean normal concentration.

On theoretic grounds, it is suggested that the initial therapeutic dose should be of the order of 5000 μg. by injection.—R.H.G.


Twenty two Indian patients with uncomplicated nutritional macrocytic anemia were chosen for study. All had a megaloblastic bone marrow. They were given a diet relatively poor in animal protein. Vitamin B12 was given intramuscularly to twenty-one patients, the total dosage varying from 30 to 600 μg. The improvement was very good in ten cases, good in four, and fair in four, but was sustained in only four. Six of these patients were given vitamin B12 by mouth, in five instances before parenteral therapy, in a total dosage of 30 to 500 μg. There was usually a better response to parenteral than to oral therapy.

Folic acid by mouth produced greater improvement in six cases than did parenterally administered vitamin B12, equal response in four and less response in four. The folic acid
was given when there was no improvement with vitamin B₁₂ or when the improvement was not sustained.

Injections of a crude liver extract in a dosage of 3 to 4 ml. daily produced better response than vitamin B₁₂ or folic acid in one case, equal response in three cases, and less response in three.

The degree of improvement was calculated according to the formula of Della Vida and Dyke.

The authors conclude that nutritional macrocytic anemia represents deficiency of both folic acid and vitamin B₁₂, deficiency of folic acid being the major and primary factor.—R.H.G.


Five cases are described. A man aged 60 had an ileotransverse colostomy for what was later shown to be a chromaffinoma of the terminal ileum. The operation produced a blind loop, and the patient developed megaloblastic anemia which responded in successive relapses to parenteral but not oral vitamin B₁₂, to aureomycin, and to folic acid. The relapses were due to cessation of treatment. A man aged 62 had a gastroenterostomy with enteroanastomosis and developed macrocytic anemia, peripheral neuritis together with extensor plantar responses, and steatorrhea. The anemia and neuritis improved with injections of vitamin B₁₂. The third was a man aged 48 who developed steatorrhea after a gastrectomy of the Polya type. This was cured by restoring the normal intestinal pathway and eliminating a stagnant loop. The fourth man, aged 55, developed steatorrhea and normochromic anemia after gastroenterostomy and was found to have an enormously dilated duodenum, while the fifth, aged 55, had a gastroenterostomy, followed by an antecolic Polya gastrectomy for a jejunal ulcer. He had a dilated afferent loop with antiperistalsis therein, and developed megaloblastic anemia.—R. H. G.


Using technics involving preparative paper strip electrophoresis, active material which seems to be mucoprotein in nature has been isolated from pig gastric mucosa and human gastric juice. Intrinsic factor activity was demonstrated by studying the fecal excretion of radioactive vitamin B₁₂ after oral administration to patients with pernicious anemia.—R. H. G.


Hemoglobin estimations were carried out on one hundred and ninety-six consecutive cases of H. influenzae meningitis in infants and children. In 45 per cent of them the hemoglobin level was less than 55 per cent (100 per cent = 14.5 Gm. per 100 ml.), and in 70 per cent of these it was less than 75 per cent. Anemia was more prevalent where the infection was severe, as measured by the concentration of glucose in the cerebrospinal fluid. Anemia often developed during the course of the illness, the hemoglobin level sometimes falling rapidly in twenty-four to forty-eight hours; this made it likely that intravascular hemolysis was occurring.

The incidence of anemia in one hundred and forty-one cases of meningococcal meningitis was only 8 per cent.—R. H. G.


The condition is frequent in the North of Ireland. In sixteen cases investigated where possible by endoscopy and x-ray, organic obstruction was demonstrated. There was stenosis
in the upper esophagus at or just distal to the introitus of the esophagus. Sometimes the lumen appeared in the middle of a diaphragm-like obstruction; sometimes just beyond the sphincter there was a web of mucosa with a free crescentic edge. There was no muscular spasm or achalasia. A negative barium swallow does not exclude the condition. The condition is precancerous and dilatation of the stricture is the essential treatment. Iron therapy will not correct the dysphagia.—R. H. G.


A woman aged 48 had irregular menstruation without menorrhagia. The face was congested and the eyes blood shot. Large abdominal masses were present. The hemoglobin level was 148 per cent, red cells, 7,280,000 per cu. mm. The blood volume was 7286 ml. The abdominal masses were multiple fibroids, and total hysterectomy, bilateral salpingo-oophorectomy and appendectomy were done without excessive hemorrhage.

A week after operation, the hemoglobin value had fallen to 114 per cent and normal blood counts have now been present for two years.—R. H. G.


The standard method of examining for sickle cells after overnight incubation in a moist chamber was used successfully in one one hundred and fifty cases of sickle cell anemia. It was of limited value in transfused patients or in those with preclinical disease. A thin, wet marrow preparation, sealed with melted paraffin, was inspected immediately under the high power objective. Bizarre formations made up of numerous hemoglobin filaments were found in fifteen cases of sickle cell anemia, five cases of preclinical sickle cell anemia (siblings of sickle cell anemia patients with various signs in the blood suggesting S. C. A.), and ten cases of sickle cell anemia that had been treated with transfusion together with other therapy. The marrow smears were negative in two further patients of this last group and in twelve patients with sickle cell trait superimposed upon another form of anemia.—R. H. G.


The Veddooids of Southern India have many physical features in common with the Australian aboriginals. The rhesus chromosome CDE (R) which is rare or absent in most parts of the world is relatively frequently seen in Australian aboriginals and in South Indian Veddooids. In the latter, the sickle cell trait is common and the present investigation was an examination of the bloods of seventy-two Australian aboriginals for the sickle cell trait. The samples were examined both by incubation with sodium-metabisulphite and with sodium hydrosulphite. No sample showed the sickle cell trait.—R. H. G.


The technic of examining for sickle cells by sealing up the blood for long periods without added reagent, frequently shows "false sickling." Samples of blood were sent by air to London from one hundred and ten unselected Greeks, fifty born in Athens and sixty in other parts of Greece but not in Petromagoula where the sickle cell trait is known to exist. The samples were incubated with sodium metabisulphite and with sodium hydrosulphite. No sickling was found in any of these bloods. The bloods were also tested for the A, A₂ BO Rh
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and MNS blood group systems. In the Rh system a frequency of 9.6 per cent was found for the cDe chromosome, which appears to have its highest incidence in the East Mediterranean region.—R. H. G.


In two thousand two hundred fifty-five Africans, sickling of the erythrocytes was found in four hundred and seven instances, but in only one was sickle cell anemia present. However, thirty-two cases of sickle cell anemia were seen on other occasions and in twenty of these patients, clinical and laboratory investigations were performed. All the parents who could be examined showed the sickle cell trait. In sickle cell anemia, the common symptoms were joint pains, and the most frequent type of anemia was the normochromic, orthochytic variety. Target cells were frequent in thin blood smears. Megaloblasts were not found in the marrow.

No satisfactory method of treatment was found.—R. H. G.


Of one hundred sixty-five “healthy” boys aged 8 to 18 years, sixty-one showed target cells in percentages varying from 0.2 to 81. Of these, twenty-six showed more than 4 per cent of target cells in the peripheral blood. In addition the blood was examined for target cells in three hundred and sixty-five normal Africans, one hundred and sixty with the sickle cell trait and thirty-three with sickle cell anemia; moreover fifty hospital patients with blood slides showing many target cells were investigated for sickle cell anemia or sickle cell trait.

The incidence of target cells was not greater in those with sickle cell trait than in those with normal erythrocytes, but target cells were present in 100 per cent of those with sickle cell anemia. The presence of target cells is not diagnostic of sickle cell anemia, but its absence renders the possibility of a diagnosis of sickle cell anemia unlikely. No case of Cooley’s anemia was found. The target cell is probably formed in the peripheral circulation and is probably due to an alteration in the constituents of the plasma proteins.—R. H. G.

LEUKOCYTES


A man aged 23 was admitted with upper abdominal pain and was found to have a ruptured spleen. After operation the white cell count was 22,000 and there were 13 per cent monocytes and 39.5 per cent lymphocytes, many of which were atypical. The Paul Bunell test became positive at 1 in 96 and the spleen showed an unusually cellular pulp with atypical mononuclears and distension of some of the sinuses with these.—R. H. G.


It has been shown that when adrenalectomized animals are subjected to stressors, a lymphocytosis occurs which is greater than that which follows adrenalectomy alone. The response is the inverse image of the lymphopenic response of intact animals known to be mediated by adrenocortical hormones and has been termed the lymphocytotic response.

In addition, blood films taken from adrenalectomized and stressed adrenalectomized mice revealed morphologic alterations of the lymphocytes as compared to intact non-stressed mice.
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It was found that two morphologic types of lymphocytes exist in the normal intact mouse: (1) normal lymphocytes, and (2) stress lymphocytes which are large cells with increased amounts of poorly basophilic cytoplasm.

The lymphopenia induced by adrenocortical mediation of stress in intact mice was due to a decrease in numbers of normal lymphocytes, whereas the stress lymphocytes did not decrease, or actually increased. It is suggested that stress lymphocytes are more resistant to the lytic effects of adrenocortical hormones than normal lymphocytes.

The lymphopenia induced by stress in adrenalectomized mice was due primarily to an increase in numbers of stress lymphocytes.

It is concluded that the production of stress lymphocytes is due to nonadrenocortically mediated effects of stressors which bring factors into play which increase the number of lymphocytes and induce specific cytologic changes.—T. R. T.

BLOOD COAGULATION and HEMORRHAGIC DISEASE

THE DETERMINATION OF PLASMA FIBRINOGEN BY TURBIDITY WITH AMMONIUM Sulfate.

I. A. Parfentjev, M. L. Johnson, and E. E. Clifton. From the Department of Microbiology, Yale University School of Medicine, New Haven, Conn. Arch. Biochem. 46: 470–479, 1953.

A simple method for routine analysis of fibrinogen by turbidity with (NH₄)₂ SO₄ is described and compared with other procedures. The (NH₄)₂ SO₄ solution is prepared so that one part of the diluted plasma plus nine parts of the salt solution give a final (NH₄)₂ SO₄ concentration of 12 per cent. This concentration assures complete precipitation of plasma protein. This plasma protein mixture is redissolved and the fibrinogen is completely coagulated by thrombin or by heating to 55 C. —C. E. R.

HEREDITARY HEMORRHAGIC TELANGIECTASIA WITH GASTRO-INTESTINAL HEMORRHAGE AND HEPATO-SPLENOMEGALY.


In a family of thirty-two individuals, twelve have evidence of hereditary hemorrhagic telangiectasia, and five of the affected persons have had gastrointestinal hemorrhage. Of these five cases, two have hepatosplenomegaly and in one the presence of this is doubtful. The hepatosplenomegaly is believed to be associated with cirrhosis of the liver but the author considers that the gastrointestinal bleeding is due to telangiectases in the gut. —R. H. G.

ENDOCRINE INFLUENCE ON THE PLASMIN-PLASMIN INHIBITOR SYSTEM IN THE BLOOD OF RATS.


This work was done in an attempt to determine the role played by endocrine glands on the amount of plasmin inhibitor found in the blood. The work was done on male Sprague-Dawley rats weighing 220–250 Gm. The subcutaneous administration of adrenocorticotropic hormone, thyrotropic hormone, and thyroxine caused elevation of the plasmin inhibitor in blood. Cortisone, in contrast, produced no change. The plasmin inhibitor titer of rat plasma ten days after the removal of the hypophysis or the adrenals was found to be greatly reduced. Splenectomy did not alter the plasmin inhibitor level of plasma. In splenectomized rats adrenocorticotropic hormone did not produce any change in the plasmin inhibitor of the blood. On the other hand, administration of thyroxine to these splenectomized rats was found to produce an elevation of the titer. —R. C.

EFFECT OF INTRAVENOUSLY INJECTED BONE MARROW CELL SUSPENSIONS ON THYMIC REGENERATION IN IRRADIATED C 57 BLACK MICE.

Previous work has shown that the development of thymic lymphomas in systemically irradiated C57 black mice is effectively inhibited by placing a lead shield over one thigh during exposure, despite the fact that the thymus receives the same x-ray dose. In addition, it has recently been shown that although the initial radiation injury of the thymus is not prevented, thymic regeneration is significantly accelerated by thigh shielding. The present work is concerned with a series of four experiments indicating that this effect of thigh shielding may be largely reproduced by intravenous injections of homologous bone marrow cell suspensions into systemically irradiated mice. Regeneration of the thymus begins less promptly, however, and requires the injection of relatively large amounts of bone marrow. The intraperitoneal implantation of skeletal muscle and the intravenous injection of exogenous thymic cell suspensions were not effective in promoting thymic recovery.—R.C.


The portion of febrile reactions due to blood transfusion that are caused by viable bacteria is not known. Eighteen severe or fatal reactions have come to the attention of the author at the Laboratory of Biologic Control, and there are undoubtedly many more that are not reported. The present study of the implicated blood, plasma, or albumin. In addition ninety-eight cultures from blood or blood products and eleven from vaccines and antigens were studied.

Of the eighteen severe or fatal reactions due to blood, thirteen were studied by culture. Eight were Pseudomonas (none of which were P. aeroginosa); two Paracolobactrum aerogenoides; and three escherichia freundii.

Eighty-five other cultures from blood products, not associated with reactions, were also studied. From both plasma and albumin, micrococci predominated. Streptococci came only from plasma.

The growth temperature range of all strains associated with reactions and of representative ones from plasma and albumin was determined. All strains associated with reactions and all other gram negative rods grew at blood storage temperatures, some did not grow at 37 C. The range at which all cultures grew readily was limited to above 25 C. and below 30 C.

This report is extremely well documented and re-emphasizes the importance of nonpathogenic bacteria as a source of contamination of blood and blood products and defines the proper temperature for the sterility tests.—T.R.T.


The intravenous administration of hemoglobin, adrenaline, and noradrenaline resulted in an immediate rise in the urinary pH of rabbits. To learn whether the urinary pH change was of adrenergic origin, experiments were carried out measuring the effects on blood pressure of intravenously injected hemoglobin. A rise in blood pressure was seen, which could be blocked by Regitine, and the rise in urine pH was also prevented. If the animal was rendered deficient in sodium, the rise in pH did not occur.

In the Regitine and hemoglobin group of animals, casts were seen in the urine and the BUN was elevated for one or more days.

No direct application of these data to humans is attempted.—T.R.T.


A technic is described for visualization of the splenic-portal system by percutaneous injection of radio opaque material into the spleen.
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Under local or general anesthesia, an 18 gage needle is introduced percutaneously into the spleen and 12 to 40 cc. of 70 per cent Diodrast is injected in two to three seconds with a 20 or 50 cc. syringe. Serial films or a single film at the completion of the injection are taken.

By this technic the portal system was well visualized which aided in planning the surgical procedure. No bleeding or thrombotic complications were noted.—C.E.R.


Forty-six cases of portal hypertension were treated by splenectomy with or without splenorenal anastomosis. Splenectomy relieved the leukopenia and thrombocytopenia, and the authors consider that this favors the concept of hypersplenism in portal hypertension. Ligation of the splenic artery in five cases did not lead to generalized atrophy of splenic tissue or to relief of the leukopenia and thrombocytopenia. In seven cases, portocaval anastomosis was done, but there was no improvement in the white cells or platelets.

None of the operations appeared to benefit the red cell and hemoglobin levels by mechanisms other than control and prevention of esophageal bleeding.—R.H.G.


Observations have indicated that hypoproteinemia occurs in eclamptic toxemia and that the extracellular fluid volume shows an increase greater than that occurring in normal gestation. The authors present data on six patients with eclamptic toxemia who were treated with salt-poor human serum albumin. This was administered in 50 Gm. doses intravenously in total amounts varying from 75 to 250 Gm. Transient hemodilution and diuresis were produced. No pulmonary edema or urinary suppression occurred. Hypertension and edema were unchanged and the patients' courses were not appreciably affected.—R.B.C.