ABSTRACTS

Theodore H. Spaet, M.D., Editor

ABSTRACTS OF SPECIAL INTEREST


The frequency of chromosomal abnormalities in peripheral leukocytes of eight men accidentally exposed to irradiation in 1958 were re-investigated. The present study was done 42 months after exposure; an earlier study on the same men had been done 29 months after exposure. These men continue to show both major and minor type of chromosomal aberrations. However, the frequency of these abnormalities decreased in the interval from the first to second examination.—I. G.


Enhancement of the leukemogenicity of AKR leukemia virus has been achieved by serial cell-free passages through newborn AKR and Zb mice, and it was possible to induce lymphocytic leukemia in 62 per cent of AKR and 60 per cent of Zb mice inoculated. In addition, the leukemia virus also induced leukemia in RF mice and AKRxC3H/He hybrids. The amount of the leukemic virus contained in leukemic brains is smaller than that of leukemic liver, spleen, lymph nodes and thymus. A dominant hereditary trait is suggested as regards the transmission of susceptibility to the AKR leukemia virus. The AKR leukemia virus can be inactivated by heating at 56 C. for 30 minutes, or by exposing it to ethyl ether, has an isoelectric point at about pH 4.5, and is antigenic. The virus cannot be sedimented by centrifugation at 10,000 rpm for 20 minutes, and passes through Glass filter G4, Selas filter, Berkefeld N, or Chamberland L3. Fluorocarbon extraction of the virus from leukemic tissues does not result in the loss of its leukemogenicity. The fluorocarbon extracts exhibit an ultraviolet absorption curve characteristic of nucleic acids, and contain only RNA but no DNA. These findings indicate that the AKR leukemia virus is a lipid-containing, medium-sized virus of the RNA type. The authors have succeeded in cell-free transmission of lymphocytic leukemia induced by 20-methylcholanthrene in RF mice. Although the mechanism by which leukemia is elicited is normally carried in RF mice in a latent form, the carcinogen acts as to increase the number of infective viral particles to the dose level where a leukemia transformation ensues.—K. F.
ABSTRACTS


This is the first report of a working party set up to evaluate therapy in leukemia. The purpose of this trial was to compare the results of therapy in acute leukemia with prednisone and 6-MP, and 6-MP alone. All the patients received 6-MP at a daily dose of 2.5 mg./Kg. of body weight. One group received in addition prednisone at a daily dose level of 40 mg., and another prednisone at a daily dose level of 250 mg. In all, 108 patients were admitted to the trial (“myeloid” 86; lymphoblastic 19; undifferentiated 2; plasma cell leukemia 1). The remission rate was 47 per cent in the lymphoblastic cases but only 7 per cent in the myeloid cases. Treatment with high steroid dosage and 6-MP proved definitely harmful. There was no significant difference in survival between patients treated with 6-MP alone and those treated with 6-MP and prednisone (40 mg./day). There was not a close correlation between completeness of remission and duration of survival. In fact some of the longest-surviving patients never remitted at all.—I. C.

HEMOSTASIS


Activities of various clotting factors in thoracic-duct lymph of rabbit were determined. From the results obtained, all plasma clotting factors were present. The lipoid materials being transported seem to behave as platelets in thromboplastin generation, since no platelets were detected in lymph. Although lanolin-feeding increased turbidity of lymph, no significant difference was found in the coagulation properties, except for a more incomplete consumption of prothrombin. Treatment with warfarin lowered the activities of the following factors: serum thromboplastic factors, prothrombin and factor VII complex.—K. F.


Prothrombin preparation satisfying the usual criteria of purity as determined by ultracentrifugal and electrophoretic studies was subjected to partial degradation by chemical, enzymatic and ultrasonic methods. The different fractions thus obtained (particularly the lipid component) were further purified and tested biologically and chemically for vitamin K activity. The composite data indicate that vitamin K is not an integral part of prothrombin.—J. B. C.

THE TISSUE ACTIVATOR OF FIBRINOLYSIS. M. Bielaciot. From the Medical School, Bialystok, Poland. Postepy Hig. Med. Dośw. 16:531, 1962.

Plasminogen activator was obtained by a 5-minute extraction of non-homogenized tissues with saline. Homogenization and prolonged extraction did not increase the extraction yield because of inhibitor release.—E. K.


Addition of phenol to a purified system accelerated clot formation, but phenol had no influence on esterase activity of thrombin and did not influence the stabilization of “desmo fibrin” (urea-insoluble clot, according to the nomenclature of the author). The authors are of the opinion that phenol precipitates intermediary products of fibrinogenesis, and they compare the observed phenomena with “paracoagulation.” Clots formed in the presence of phenol are “incomplete” and are copolymers, containing less fibrin than clots produced in the absence of phenol.—E. K.


By fractionation of plasmin-digested fibrinogen on DEAE-cellulose columns, at least 12 nondialyzable products could be obtained. Thus, during prolonged proteolysis, fibrinogen splits into many breakdown products; most seem to be of high or intermediate-molecular weight. At the time of fibrin clot solubilization, relatively small amounts of low molecular breakdown products appear.—E. K.

As shown by the euglobulin lysis time, there was inhibition of fibrinolysis by alimentary lipemia. Elimination of chylomicrons from the system by filtration resulted in activated fibrinolysis. Activation was more pronounced in lipemic plasma, it was inhibited with re-addition of chylomicrons. Addition of chylomicron-poor plasma to the sample of filtrated plasma did not inhibit fibrinolysis. Cod liver oil or cream added to plasma did not influence fibrinolysis. The authors feel that fibrinolysis inhibition by chylomicrons is a specific process and may be due to the lipoprotein part of chylomicrons.—E. K.


It is known that platelets take up 5-hydroxytryptamine (5-HT) rapidly by an active mechanism. The possible effect of platelet antibodies on this uptake was explored. Platelets incubated with normal serum or saline took up about 41 to 52 per cent of C14-labeled 5-HT after 1½-2 hours. By contrast the uptake of 5-HT by platelets which had been incubated with a serum containing platelet antibodies was less than 1 per cent. A similar effect was observed with serum from patients who had received multiple transfusions. However these sera behaved as isoantibodies since they were effective on donor platelets and ineffective on the patients' own platelets. Sera from six patients with idiopathic thrombocytopenic purpura were ineffective in blocking the uptake of 5-HT by donor platelets.—I. C.


Hemostatic and thromboplastic activity of blood platelet preparations was studied under different storage conditions. Isolated platelets suspended in citrate, and stored at +4 C. were found to be best preserved. Clot retraction was supported until the 7th day of storage; thromboplastic activity was more stable, and was found during the 28 days of experiment. Gelatin suspension, lyophilization or freezing were not suitable for storing the platelets, but thromboplastic effect and complete activity of frozen platelets factors was noted on the 1st, 3rd and 4th day of observation. Frozen or lyophilized platelets gave no retraction of a thrombogenic plasma clot. Gelatin failed to protect the platelets against lysis, and their hemostatic effect lasted only a few hours. The authors conclude that in selected cases of thrombogenic hemorrhage, only transfusion of undamaged, fresh platelets is effective.—E. K.


Thrombocytopenic purpura was produced by injecting large doses of stilbesterol into rabbits. These animals were divided into four groups: (1) injected with swine bone marrow extract; (2) injected with an extract of calf bone marrow; (3) injected with the bone marrow of human blood donors; and (4) non-treated control. Bone marrow transplantation as well as extracts of bone marrow corrected the disorder. There was normalization of the megakaryocyteopoiesis, megakaryocyte development and platelet formation. A thrombocyto poetic factor present in the bone marrow and in aqueous extracts of the bone marrow is postulated.—E. K.


Platelets from patients with Von Willebrand's disease did not adhere when fresh citrated blood was passed through a column of glass beads. Fresh normal plasma restored platelet adhesiveness to normal, whereas the patients' plasma was ineffective. Results obtained, however, were dependent on suitable batches of glass beads.—I. C.


The ratio ATP/ADP was found to be abnormal in disease states in which it has been suggested there is an anomaly in the adhesion of platelets.
ABSTRACTS

to the vessel wall. Thus ATP was elevated and the ratio elevated in Von Willebrand’s disease. The opposite was the case in Glanzmann disease.—I. C.

ANTITHROMBIN IN CHRONIC RECURRENT PANCREATITIS. S. Laskowski, J. Borowska-Kuzniacka and A. Stach. From the Medical School, Lodz, Poland. Polski tygodnik lek. 17:1622, 1962.

Antithrombin activity (Quick et al.) was studied in 50 patients with chronic recurrent pancreatitis. The control group consisted of 20 patients with exacerbated cholecystitis, 20 with peptic ulcer and 10 diabetics. Of 50 patients with chronic recurrent pancreatitis and tenderness of the pancreatic trunk (Grott method), increased antithrombin activity was noted in 66, a moderate rise of the serum diastase activity in 24, of the urine diastase in 28, and serum lipase in 8 per cent of the cases. Abnormal hyperglycemic curves after oral administration of glucose were noted in 88 per cent of the patients. In the control group, normal antithrombin activity was noted in 92, was slightly increased in 4 and markedly elevated in 4 per cent of the patients. Accordingly, the antithrombin test may be considered as a valuable adjunct in the diagnosis of chronic recurrent pancreatitis.—E. K.


The patients were divided into three groups according to the severity and extent of the operation. The studies were performed before the operation and on the 1st, 8th and 18th day postoperatively. The first group consisted of patients with simple operations (e.g., appendectomy). No changes were noted in this group. The second group consisted of patients after operations of moderate severity (e.g., cholecystectomy). The thromboelastographic clotting time \((r + k)\) was delayed in the first few postoperative days, but then it became normal. Increased clot retraction and firmness were noted in most of the patients, and were associated with an increase of plasma fibrinogen. The third group consisted of patients with major operations (e.g., gastrectomy). Shortened clotting time \((r + k)\), increased clot retraction and firmness \((mE)\), and increased fibrinolysis \((f_4)\), with increased plasma fibrinogen were found among those patients.—E. K.


Three cases are presented with severe bleeding associated with a “hypercoagulable” state. The evidence for this was a shortened coagulation time using a 9.5 x 100 mm. plastic tube (normal range 17.5 to 32.9 minutes) and a shortened plasma-recalcification time. There was increased antihemophilic activity (factor VIII) and fibrinolysis. Heparin was found to have a normalizing effect and was used successfully in therapy.—I. C.

Patients receiving these drugs and also receiving anticoagulant therapy required a reduction in the maintenance dose of anticoagulant. The extent of the change varied widely. The mechanism of the change is not understood.—I. C.


Details of a 8-year-old girl are recorded. The blood was incoagulable with virtual absence of fibrinogen. The fibrinogen content was 33 mg. in the father’s blood and 35 mg. in the mother’s.

—J. B. C.


Five cases aged 7 to 10 presented with rubella and severe purpuric manifestations. The platelet count was low. All the cases recovered, normal platelet counts being noted from 16 to 100 days after the onset.—I. C.


A male infant with this sex-linked syndrome is described in whom eczema, repeated furunculosis, hepatosplenomegaly and generalized lymphadenopathy were associated with thrombocytopenia, repeated nasal and gastric hemorrhage, recurrent pneumonia and otitis media. Bilateral vitreous hemorrhages developed, and splenectomy was performed when the patient was 3 years old, following which the platelet count stabilized at about 150,000/mm.³ At 3½ years, precipitins to several components of whole cow’s milk were noted in the patient’s serum. Elimination of milk seemed to cause a decrease in diarrhea and fever. Shortly thereafter he developed measles, complicated by severe pneumonia, from which he succumbed. Autopsy revealed the presence of widespread giant cell pneumonia. Cells typical of cytomegalic inclusion disease were present in several viscera. In addition the liver, spleen, lymph nodes and bone marrow were diffusely infiltrated with large mononuclear cells.—J. B. S.
ABSTRACTS

Percentage of labeled cells increased for a further 2-3 hours followed by a plateau and a further rise in the percentage of labeled metamyelocytes after 14 hours. Thirty-seven per cent of myelocytes were labeled 1/2 hour after injection of tritiated thymidine (turnover of 7.5 per cent per hour). The turnover rate for metamyelocytes was 5 per cent per hour. Since the marrow smears showed 1 myelocyte to 0.75 metamyelocytes, the data suggested that only 1 myelocyte out of 2 was being transformed to a metamyelocyte and hence to a neutrophil. Thus there was evidence of "ineffective" granulocytopoiesis, a considerable number of myelocytes not undergoing mitosis and being lost in some way.—I. C.


The intravascular life of granulocytes was measured in four dogs before and after irradiation. Before irradiation the disappearance curve of labeled granulocytes is similar to that found in man, with a half disappearance time of about 6 to 8 hours. After a total irradiation of 250 to 350 r the curves are similar and there is no evidence of an accelerated disappearance.—G. M.


Crystalline aggregates, apparently representing the infecting virus, were found in more than 40 polymorphonuclear leukocytes in areas of poliomyelitis in three experimentally infected animals. It is suggested that PMN leukocytes may phagocytose virus as they do bacteria and thus be important in body defense against viral infections, or that the leukocyte may be utilized by the virus as a host cell for virus replication.—T. E. B.


Total thymectomy was carried out in nursing hamsters 1-4 weeks of age. The majority of the males developed a rapid wasting disease with anemia but slight reticulocytosis and reduction in circulating lymphocytes. The females were unaffected. The resemblance of these animals to those affected by 'runt disease' is noted.—I. C.


Lymph from the thoracic duct of unanesthetized rats was allowed to drain away from a fistula for 5 days, after which the fistulae were closed. The output from the thoracic duct fell progressively during the 5-day period, and severe peripheral blood lymphopenia occurred. The lymph nodes at the end of this time were found to show gross depletion of the cortical small lymphocytes. The lymphocyte-depleted animals showed a severely depressed primary immune response to tetanus toxoid and sheep erythrocytes but interestingly a normal secondary immune response when they had been given a first dose of tetanus toxoid 3 weeks before lymph drainage was begun. The poor primary immune response was corrected by intravenous administration of thoracic duct cells from normal non-immunized rats of the same strain. Spontaneous complete recovery of ability to respond to primary stimuli apparently occurred over a period of 4 weeks after the fistula had been closed.—T. E. B.


To evaluate damage to the leukocytic system after exposure of rabbits to high x-ray doses, the leukocytic response was used. The conclusions were as follows: (1) 100 r or 900 r skin dose at 100 r weekly gave no difference in reaction to intravenous injection of 10^6 killed Bacterium coli per Kg. of weight; (2) 2000 r at 500 r per week markedly inhibited the reactivity of the granulocytic system; return of the reaction to normal appeared about 3-4 weeks after irradiation; (3) The leukocytic reaction to Bact. coli was checked cytochemically (glycogen) and by means of the leukocytic test ("stickiness" of granulocytes). The impaired function of bone-marrow (inhibition of leukocyte production) speaks for partially preserved regenerative power of leukocytic system.—E. K.

Lethally irradiated mice were injected with bone-marrow, together with lymph-node or thymus cells. The progeny of the bone-marrow and lymphoid inocula could be distinguished from each other and from the cells of the host by means of chromosome markers. Restoration of lymphoid elements in the irradiated mice occurred sooner in the thymus than in the lymph nodes. The cells re-colonizing the thymus came from injected bone marrow only, whereas lymph-nodes were re-colonized by both bone marrow and lymphoid elements. It is possible that in the normal animal the thymus is continuously being re-seeded from bone marrow and the authors suggest that the thymus may possess a selective attraction for circulating lymphoid precursors.—I. C.

The Histophysiology of the Antibody Response

The author has attempted to clarify one aspect of the lymphocyte-plasma cell relationship by studying the changes in the lymphocytes of the periarteriolar sheaths of the splenic white pulp, following a single, primary, antigenic stimulus. This excellent paper should be read in the original, but the author makes a plausible case for direct lymphocyte-plasmablast transformation. His view is that the "transitional cell" of Fagraeus is not the first step in the lymphocyte-plasma cell change, but comes after the lymphocyte-plasmablast metamorphosis.—C. R. M.


A 5-year-old girl with acute leukemia was given 200 μc. of tritiated thymidine/Kg. intravenously. Serial autoradiographs of blood and marrow were prepared after the injection. Seven and a half per cent of the leukemic cells contained the label at 1 hour, although only 20 per cent were heavily labeled. The proportion of heavily labeled cells reached a maximum at 3 hours and thereafter declined. It would appear that a considerable part of the leukemic population did not divide at all or only very slowly. The generation time of the labeled cells appeared to be about 20–22 hours.—I. C.


Chromosomal preparations using peripheral blood were studied during treatment with 6-azauridine of three patients with acute leukemia. Globule-like bodies, which appeared to have a chromosomal origin, were seen in these cultures and persisted until cessation of therapy. It was suggested that these abnormal structures resulted from faulty synthesis of nucleic acid due to 6-azauridine.—I. C.


The Sr90 content was lower in the bones of seven patients who died of leukemia than in the non-leukemic group. The authors suggest that this might be due to disturbed calcium metabolism in leukemia.—E. K.


A method has been used for concentrating nucleated cells in the blood to find circulating neoplastic cells in patients with non-leukemic hematosarcoma. Positive results were obtained in the following: in 5 of 23 patients with Hodgkin’s disease; 4 of 9 patients with lymphoblastosarcoma; 2 of 6 patients with reticulosarcoma; and in 1 of 2 with histiocytosarcoma. With treatment (chemotherapy or radiotherapy) the circulating neoplastic cells disappeared, except in terminal or very advanced cases.—G. M.

ABSTRACTS

Plasma was collected from patients with chronic granulocytic leukemia and chronic lymphocytic leukemia before and after local splenic irradiation. A total of 11 experiments was performed in 7 patients. In 10 of 11 studies the plasma taken shortly after irradiation to the spleen had a leukopenic effect upon subsequent administration (after the WBC had risen). Plasma taken before Splenic irradiation had such an effect in only one instance. The effect of the post-radiation plasma had an onset within 12 hours; duration of decrease was 4 days. The author suggests that a humoral factor is liberated from the x-irradiated spleen, causing this decrease.—I. G.


The author infected (intraperitoneally) normal chicks, and chicks infected with mycoblastosis virus, with cultures of Aspergillus fumigatus. The leukemic birds showed a more fulminating type of infection with more extraperitoneal spread. The hope is that this will shed some light on the increased incidence of fungus infection in the human leukemic patients. Unfortunately, no counts were made of normal leukocytes, and the lifespan after the appearance of leukemia is very short (2–4 days). With another animal leukemia system, allowing for a longer period of study, the method might provide useful results.—C. R. M.


The authors describe in detail and with very good photomicrographs a case in a 3-year-old Mongol who died finally of pulmonary aspergillosis. They define the criteria for making the diagnosis, review the literature, making a good case for the existence of this entity.—C. R. M.


An analysis of 544 cases. During the first 5-year period (1949–1953) there were only 67 cases; during the second 5-year period (1954–1958) there were as many as 240 cases. During the next 3-year period the number mounted to 237. The incidence of different types is discussed in the light of the causative role of alleged environmental factors.—J. B. C.


A great number of sophisticated but remarkably unrewarding erythropoietic studies were carried out on 12 patients with multiple myeloma. The hemoglobin concentration ranged from 7.4 Gm. per cent to 15.4 Gm. per cent and the severity and manifestation of the disease varied greatly. The not too surprising conclusion was that anemia, when present, was caused by some hemolysis, some erythropoietic suppression, some iron deficiency and some blood loss.—A. J. E.

ERYTHROCYTES


Estimation of molecular size and shape of biologically active compounds can be made by measuring the inactivating effects of irradiation upon biological activity. An attempt was made here to determine size and shape of erythropoietin molecules in urine obtained from a patient with aplastic anemia, and in cyst-fluids (renal and cerebellar) from two patients with “secondary” erythremia. These biologically active fluids were subjected to inactivation by high-energy electrons and low energy x-rays. The molecular weight of erythropoietin was estimated to be about 27,000 and it was suggested that it is asymmetric, and 10 times as long as it is wide.—A. J. E.


The renal juxtaglomerular cells, located near the afferent arterioles, are believed to be sensitive to stretch and work as volume receptors. When the blood volume is decreased the cells show an increased granularity, and it is believed that this increase in granularity denotes an increased production of renin. It has been suggested that erythropoietin is produced by these cells, and it
It has been reported that there is an increased granularity of the cells in anemias associated with high plasma erythropoietin titers. In the first paper, the authors show that hypoxia without hypovolemia (exposure to low oxygen) will not change the granularity of the juxtaglomerular cells in the rat. They consequently suggest that there may be two separate renal erythropoietic substances, one of which is secreted by the juxtaglomerular cells in response to underdistension of the arterial bed, and the other by some unknown renal cells in response to hypoxia alone. In the second paper, the authors show that increased granularity of the juxtaglomerular cells produced by a low sodium diet is associated with a high content of erythropoietic material in the kidney. The content of erythropoietic material in the kidneys of a number of different control groups was significantly lower. The authors quite prudently conclude that this does not conclusively prove or disprove the juxtaglomerular origin of erythropoietin. One can only regret that the authors attempt to prove the existence of an accelerated production of erythropoietin by assaying kidney extract (which so far has been shown to be only borderline active despite high serum titers of erythropoietin), and fail to do the obvious: observe whether or not the rats which were kept on a sodium-free diet for 10 weeks had accelerated rates of red cell production. —A. J. E.


The rat spleen will respond to erythropoietin, bleeding, or phenylhydrazine with an increase in DNA synthesis, reflecting the emergence of erythroid elements (the rate of DNA synthesis in the thymus gland is unaltered). The author found that the splenic uptake of tritiated thymidine did not begin until more than 8 hours after the injection of erythropoietin. This observation was interpreted to indicate that erythropoietin has no direct effect on DNA synthesis but acts on differentiating cells (presumably reticuloendothelial cells). The increased rate of DNA synthesis observed after the first 8 hours is believed to reflect subsequent mitotic activity of the differentiated cells. Data on radiated rats are also given but are difficult to interpret. —A. J. E.


Sheep erythropoietin was administered to polycythemic rats, and the 18-hour Fe59 utilization and the reticulocyte response were determined at various times afterwards. A definite response was first observed 48 hours after the injection of erythropoietin. However, if a second dose of erythropoietin was administered, its effect could be observed 24 hours after injection. The prompt response to the second dose suggests that erythropoietin, in addition to its action on stem cell, may influence red cell production at a later stage of development. —A. J. E.


Inbred C-57 black mice were divided into three groups, each containing about 100 animals as follows: (1) splenectomized mice (2) mice in which splenectomy was followed by a subcutaneous implantation of an isologous spleen, (3) controls. The studies were performed during the 4th and 8th week after operation in order to eliminate the side-effect of surgical hemorrhage and shock. Morphologic studies were done on peripheral blood and bone marrow; additional experiments were performed with Fe59 and Ca51. Plasma iron and iron stores (ferritin and hemosiderin) in the heme-marrow, liver and spleen were measured. The existence of hemopoietic hormones originating in the spleen was suggested. These may normally be transferred into the liver via the portal circulation and be transformed by the liver cell. The author has analyzed their complex mode of action on the proliferative activity of medullary erythroblasts and on maturation and release in the medullary red cell system. Co-ordination between spleen and liver seems to be instrumental in maintaining constant levels of circulating iron, of the iron-stores and in preserving a constant circulating erythrocyte mass. —E. K.


Moderate anemia associated with a slight reticulocytosis was induced in rats by means of tur-
ABSTRACTS

1) pentane abscesses. Daily administration of erythropoietin in relatively large doses resulted in an increase in Hb, Hct and red cell mass, but not to the same extent as in normal controls. Exposure to a simulated altitude of 20,000 feet also resulted in a suboptimal response. These results are interpreted to indicate that rats having a tumor abscess are capable of producing and utilizing erythropoietin in a normal manner. It appears, at least to this reviewer, that the data are even more consistent with the thesis that the bone marrow (stem cell) response to erythropoietin is suboptimal.—A. J. E.


The authors have compared the reticulocyte count (method of Brecker and Schneiderman) with red cell iron turnover as an indication of the rate of erythropoiesis in 68 cases of hematologic disease. The paper should be read in the original, but they conclude that if the level of 40,000 reticulocytes per cu. mm. is taken as significant, only 75 per cent of patients with counts above this will have “at least a normal rate of red cell synthesis” whereas of those falling below, 90 per cent will have a “decreased rate of red cell synthesis.” There were occasional striking discrepancies between the reticulocyte count and hemoglobin renewal rate, and in two cases of Hodgkin’s disease there was a two-fold difference between the red cell iron turnover and the red cell survival time. The conclusion is that the reticulocyte count is a useful guide to the rate of erythrocyte renewal in most cases, but that caution in interpretation is very necessary.—C. R. M.


A 20-page review of the erythropoietic effect of large doses of androgens. The author describes the accelerated rate of red cell production observed in women with carcinoma of the breast treated with large amounts of various androgenic preparations and the possible therapeutic use of this “pharmacologic side-effect.” Occasional, but unquestionably beneficial responses were observed by the author in aplastic anemia, anemias of myelosclerosis and anemia of chronic renal disease. These responses were observed especially when treatment was maintained for more than 2 months.—A. J. E.


Erythropoietin assays were carried out on serum and cyst fluid from nine patients with renal cysts (three without polycythemia, one with polycythemia vera and five with secondary polycythemia). The bioassay was made on polychromic mice using untreated serum and cyst fluid. The results were disturbing in that cyst fluid from six patients, three without polycythemia, one with polycythemia vera and two with secondary polycythemia, showed erythropoietic activity. The authors attempt bravely to fit these results with the hypothesis that erythropoietin may be secreted by the cyst wall in cases of erythrocytosis complicating renal cysts. However, they have to conclude that the only certain evidence of a causal relationship between renal cyst and polycythemia is remission of the polycythemia on removal of the cyst.—A. J. E.


A good review of the many case reports in which erythremia and various tumors have occurred simultaneously (79 references). Four new cases are added, one with bronchogenic carcinoma, two with renal tumors and one with hepatic cell carcinoma. Erythropoietin studies were done in the three cases with renal and hepatic tumors and erythropoietin was found to be high in two (renal tumors and hepatomas) and moderately high in the third.—A. J. E.


During investigation of a Puerto-Rican family with sickle-cell anemia, a hitherto undetected variant of hemoglobin A_2 (hemoglobin Flatbush) was detected. This hemoglobin could be separated with difficulty by elution following a 40-hour electrophoresis on starch granules at pH 8.6. In
each of the nine carriers of Hb Flat., hemoglobin A₂ was decreased. Hb A₂ values were 1.8 to 3.2 per cent and Hb Flat. 1 to 2 per cent, the rest being Hb A. In three individuals with sickle cell trait, Hb Flat. could not be demonstrated directly, but its presence was inferred from decreased amounts of Hb A₂. Evidence is presented that Hb Flat. contained an altered γ-chain.—I. C.


This paper is based on measurements in 10 patients where A-A blood was transfused into SS and CC recipients. The survival was followed by demonstrating survival of A-A hemoglobin on starch block electrophoresis, which is a less sensitive technic than radioisotope or Ashby methods. It can be applied where these other technics are for one reason or another not applicable—surely a small segment of the population, but it could be of value.—C. R. M.


(1) The reduced glutathione content of erythrocytes from two patients with paroxysmal nocturnal hemoglobinuria (PNH) was 16 per cent higher than in the erythrocytes of healthy people, but glutathione restoration rate was lower in PNH. (2) The erythrocytes in PNH were normally resistant to the factors increasing glutathione oxidation and had a normal content of oxidized glutathione; therefore, they did not resemble erythrocytes with glucose-6-phosphate dehydrogenase deficiency. (3) The N-acetylneuraminic acid content of the erythrocytes of healthy people was about 242 µg. in 1 ml. of packed red cells. In PNH the level was about 7 per cent lower. The erythrocytes which remained intact after the Ham or Kirchmayer test showed slightly elevated N-acetylneuraminic acid as compared to the control erythrocytes incubated in unacidified serum. (4) The erythrocyte content of the N-acetylneuraminic acid inaccessible to papain action seemed to be slightly higher in PNH than in healthy subjects. Incubation of the erythrocytes with papain led not only to a fall of N-acetylneuraminic acid content but also to a decrease of acetylcholinesterase activity. It indicates an extensive erythrocyte membrane impairment by papain.—E. K.


Using a diet consisting primarily of foods whose folate had been extracted by thrice-boiling in large quantities of water, the sequence of events in developing folate deficiency in a normal adult male was shown to be: low serum folate after 3 weeks, neutrophilic hypersegmentation after 7 weeks, high urine FIGLU after 13 weeks, low erythrocyte folate after 17 weeks, macrocytosis after 18 weeks, megaloblastic bone marrow after almost 19 weeks, and anemia after a little more than 19 weeks. No gastroenterological abnormalities developed except for a gradual change in the buccal mucosal cells.—V. H.


Cobalt was determined by an original chromatographic-spectrometric method. The findings showed parallel cobalt and B₁₂ levels.—E. K.


Leukocyte cultures were set up using cells from patients with untreated pernicious anemia and sera of very low B₁₂ content. Chromosome numbers and morphology were normal in all four patients studied.—I. C.


In attempting to confirm a possible relationship between diabetes and pernicious anemia, serum
vitamin B₁₂, serum pepsinogen, and hemoglobin concentrations were estimated on single blood samples obtained from 100 randomly selected diabetics. Three cases of pernicious anaemia were found in this limited survey.—I. C.


Twelve patients with Addisonian pernicious anemia were treated with a preparation containing 1000 µg B₁₂ as a tannin-complex in aluminum-nanostearate/oil suspension. This was given every 2 months. No side effects were observed. Hemoglobin and serum B₁₂ levels were maintained in the normal range for over one year.—I. C.

CHLORAMPHENICOL AND ITS SULFAMOYL ANALOGUE. E. J. Ganganosa and F. de la Macorra. From the University of Maryland, School of Medicine, Baltimore, Md. Arch. Int. Med. 111: 70, 1963.

An important and carefully executed study of the hematologic effect of tetracycline (two normals receiving 50 mg./Kg./day), chloramphenicol (seven normals receiving 50–60 mg./Kg./day) and a sulfamoyl analogue of chloramphenicol (three normals receiving 55–70 mg./Kg./day). The sulfamoyl-analogue is a compound in which the NO₂ group of chloramphenicol is replaced by a NH₂-SO₂ group. (This compound has been shown to have insignificant toxic effects on human bone marrow in vitro: Erslev and Lossifides. Acta Haemat. July 1962). The two patients treated with tetracycline showed no hematologic side effects, but five of the seven cases receiving chloramphenicol and all three receiving the sulfamoyl analogue had clear-cut evidence of bone marrow suppression. There was vacuolization of normoblasts, reticulocytopenia, thrombocytopenia, a definite rise in serum iron, impaired iron turnover, and moderate leukopenia. When the drugs were discontinued after 20–40 days there was subsequent reticulocytosis and thrombocytosis and a complete restoration of normal bone marrow function in all. The sulfamoyl analogue appeared to be more toxic than chloramphenicol in that anemia came earlier and reticulocytopenia was more pronounced. It was concluded that chloramphenicol in normals induced a consistent and reproducible bone marrow suppression and that the nitro radical of chloramphenicol cannot be responsible for this toxic effect.—A. J. E.


A remarkable paper showing that chloramphenicol, when given in large doses to desperately ill patients, has little or no suppressive effect on the bone marrow. Chloramphenicol was administered i.v. in a single dose of 8–12 Gm. a day in 95 patients. The mean total dose administered was 64 Gm. All patients were described as having "severe, life-threatening infections." In no instance did aplastic anemia or overt bone marrow suppression develop. Hematologically, however, the paper is not very sophisticated, and the data are difficult to evaluate. In only one case were serial blood counts obtained, but this case is impressive, since it shows that a normal reticulocyte response to a bleeding could be observed despite administration of 6 Gm. of chloramphenicol a day. The "pooled data" given are of little scientific value although they do show that definite bone marrow suppression must have been very rare. This paper supports previous impressions that the severe bone marrow suppression noted after chloramphenicol occurs most often in people receiving the drug for trivial diseases (doctors’ children treated with samples) and much more rarely in severely ill patients. However, the lack of erythropoietic impairment in this series is still most unusual in view of many others showing a consistent and reproducible effect of chloramphenicol on the bone marrow. Is it possible that a single i.v. injection with its brief elevation of chloramphenicol levels is less toxic than oral doses causing a sustained elevation?—A. J. E.


In a 24-year-old male, an acute episode of hemoglobinuria was possibly due to deficiency of G-6-PD in red cells.—J. B. C.


Macrocytic anemia was found to be about 5 times as frequent among patients with rheumatoid arthritis as compared to a control group.
The majority had Addisonian pernicious anemia; one patient had $B_{12}$ deficiency due to jejunal diverticulosis. Finally, eight patients with megaloblastic anemia formed a rather confused group. Thus, although in some of these patients Addisonian pernicious anemia appeared to be the probable diagnosis, this was excluded because Co$^{57}$-B$12$ absorption (using the fecal excretion method) was apparently normal. Although these patients were not receiving steroids at the time of carrying out the $B_{12}$ absorption test, it appears likely that at least in some cases an apparently normal absorption may have been due to incomplete fecal collection. Three of these patients were subsequently shown to have impaired $B_{12}$ absorption. Three patients in this group had free acid in the gastric juice following an augmented dose of histamine. One of these had been taking barbiturates for 10 years.—I. C.


Hereditary spherocytosis was diagnosed in a Bantu male by the usual clinical and hematologic criteria. Twelve other members of the family were examined and two sons were found to be affected. This is only the second instance in which hereditary spherocytosis has been recognized in a South African Bantu family.—T. H. B.


The authors have investigated the reactions of the blood group antibody, anti-C, using $I^{131}$ as the antibody label. Purification of the $I^{131}$-labeled antibody was achieved by allowing $I^{131}$-labeled antibody attached to red cells to dissociate into saline. It was shown that the reaction between antibody and red cells is reversible and obeys the law of mass action. Using a derivation of the law of mass action, it was calculated that there are approximately 60,000 c antigen sites on each red cell (genotype cde/cde). The following average values of the kinetic constants were obtained: rate constant for association, $3.2 \times 10^4$ 1.mole$^{-1}$ sec.$^{-1}$; rate constant for dissociation, $4 \times 10^{-4}$ sec.$^{-1}$; minimum range of equilibrium constant, $0.19 \times 10^8$ to $1.8 \times 10^8$ 1.mole$^{-1}$. Heterogeneity of the antibody was found with respect to all the constants.—I. C.


The author points out that the methods described for calculating corpuscular volume by means of the Coulter Counter do not allow for osmotic error. This is quite significant with minor variations in salinity in the region of physiologic normality. A method of correcting for this error is described in detail.—C. R. M.


This describes in detail the preparation of the recommended bilirubin standard. It emphasizes the fallacy of relying on minor changes in serum bilirubin, as estimated in virtually any laboratory.—C. R. M.

MISCELLANEOUS


In addition to urine, a major excretory pathway for ascorbic acid was shown to be the degradation to carbon dioxide excreted via the alveoli. Based on measured values of radioactivity in urine and expired air, the authors calculate the minimum human daily ascorbic acid requirement for the adult to be 1 to 3 mg. On the other hand, there may be an increased requirement for ascorbic acid in wound healing, infections and other abnormal conditions. The authors feel a reasonable adequate dietary allowance of ascorbic acid for the normal adult is in the range of 30 mg.—V. H.