ABSTRACTS OF SPECIAL INTEREST


In vitro studies showed that the iron-binding capacity of desferrioxamine, a new chelating agent, exceeds that of transferrin. Intravenous infusion of desferrioxamine to patients with hemochromatosis caused a significant rise in urinary iron output which, within limits, was dose dependent. The maximal iron excretion rate was 2.5 mg. per hour. This maximum is not imposed by renal function but may be a function of the maximal rate of iron mobilization from iron deposits. Observations on calcium excretion after desferrioxamine are inconclusive.—S. A. K.


Desferrioxamine-B (DFOM, Desferal) is a watersoluble substance of 3 molecules trihydroxamic acid, 1 molecule of which binds 1 mole of Fe++ ions. It has considerably higher affinity for iron than for other metals. It can remove iron from ferritin and transferrin. When the material was given in doses of 400-1200 mg. daily intramuscularly to four patients with transfusion hemosiderosis, iron in amounts of 15-39.9 mg./day with a total maximum of 7348 mg. in 16 months was excreted in the urine. No toxic effects were noted.—R. O. W.


Intramuscular injection of desferrioxamine increased the urinary output of iron in two patients. Maximum daily excretion was 3.5 mg. and 10.1 mg. respectively. There was no untoward effect.—J. B. C.


Sera from 294 persons above the age of 70, admitted for social rather than medical reasons to homes for old people, or to a mental institution, were studied by paper electrophoresis. Nine
sera contained proteins of M-component type. A complete work-up including x-ray studies and bone marrow aspiration was done in these individuals. One patient had metastasizing prostatic carcinoma. Two other patients had previously been treated for basa cell carcinoma and adenocarcinoma of the stomach, respectively. The remaining patients were (relatively) healthy. In none of these nine individuals could a diagnosis of myeloma or Waldenstrom's macroglobulinemia be made. Considering that the population sample studied approaches a random selection of aged persons, the incidence of M-components is strikingly high.—S. A. K.


Yttrium-90, chelated to diethylene triamine when infused into animals, provides relatively selective irradiation to lymph nodes. Six of eight dogs given 150–210 rads to lymph nodes had no ill effects. Of the formed elements in the blood, only the lymphocytes were depressed. Lymph node doses over 373 rads resulted in six out of eight dogs dying by 14 days. Experiments in which dogs given this amount of irradiation could be protected with autologous bone marrow showed that the mortality in this group was due to hematopoietic failure. Experiments to test the ability of homologous bone marrow to protect lethally irradiated dogs is still in progress. These preliminary data suggest that homologous bone marrow is protective, the irradiation to the lymph nodes being therefore sufficient to depress the homograft reaction of the host animals. The authors conclude by suggesting that selective irradiation to the lymph nodes with Y90 may be clinically applicable to human homograft therapy.—I. G.

ERYTHROCYTES


Suggestive evidence that porphyrin and heme synthesis are regulated, in part, by the rate of turnover of the tricarboxylic acid cycle was obtained in studies of rat liver hemogotenes.—E. R. J.


The hazards inherent in applying data obtained with Cr51-tagging in one species to another species are exemplified in these studies in which it was shown that hemolysates of rat erythrocytes labeled with sodium chromate contained two fractions of almost equal concentration that were removed from the circulation of rats differently: hemoglobin-bound Cr51 was removed slowly and radioactivity accumulated in tissues, whereas metabolically inert fraction II (reduced, unbound Cr51) appeared rapidly in the urine and failed to label tissues. Human and canine erythrocytes apparently contained little fraction II-type Cr51. Homogobin-bound Cr51 was cleared from blood at the same rate as was 131I-hemoglobin.—E. R. J.


By employing rebreathing in a closed system for 2 to 5 hours and a sensitive technic for the determination of carbon monoxide in 2 ml. blood samples with an infrared CO meter, endogenous CO production in 10 hematologically normal adult males was found to average 0.42 ± S.D. 0.07 ml. per hour. It appeared unlikely that the increase in blood CO resulted from exogenous CO or from displacement of tissue-bound CO. Other possible sources of error were evaluated. Previous investigators had suggested endogenous CO production in man, but with less critical data. A major source of endogenous CO may be the catabolism of heme with release of the α-methene bridge carbon atom of the porphyrin ring. These findings are of significance in determining the risks of prolonged space travel and in the study of pathologic states associated with erythrocyte destruction or altered hemoglobin catabolism.—E. R. J.

FURTHER STUDES ON THE NATURE AND SOURCE OF THE CONJUGATED BILE PIGMENTS. L. J. Schoenfield and J. L. Bollman. From the Mayo
ABSTRACTS


Studies of rat-fistula bile, bile from isolated rat liver, the product of liver slices incubated with bilirubin, and plasma of hepatectomized dogs, employing reverse-phase column, chemical-partition and paper chromatography, suggested that pigment I is formed in extrahepatic sites and that it may be a monoglucuronide. These conclusions are in conflict with other recently reported studies, and further evaluations, especially of species variations, will be required.—E. R. J.


Tritiated bilirubin was injected into the jugular vein of surgically exposed 19- to 21-day old fetal rats and the maternal bile was collected for 2 hours. Despite low fetal serum bilirubin concentrations (less than 1.4 mg. per cent), 93 to 98 per cent of the dose remained in the fetus 2 hours later and maternal serum and liver could not have contained more than 2.5 per cent. Less than 1 per cent of injected bilirubin appeared in maternal bile. Most of the radioactivity was concentrated in the carcass, serum, liver and intestine with significant amounts in lungs, brain, kidney and stomach and only traces in heart, placenta, umbilical veins and spleen. Although bilirubin did cross the placenta from fetus to mother, the rate appeared to be too slow to account for normally low fetal serum bilirubin concentrations. Thus, it was suggested that slower production or greater tissue storage was important in explaining normally low fetal serum bilirubin concentrations. At pH 8.6, 1 mole of human serum albumin bound 2 moles of bilirubin so tightly that it was virtually nondialyzable. At higher concentrations, some bilirubin was rapidly oxidized to products that remained attached to albumin and a-globulins or were lost into dialyses. It appears unlikely, therefore, that a specific globulin with high affinity but limited binding capacity for bilirubin exists in human or rat serum.—E. R. J.


Beef erythrocyte protein, freed of hemoglobin, incubated with xanthine and phosphoribosylpyrophosphate produced a compound that differed from xanthyl acid upon spectroscopic, chromatographic and hydrolytic examination. By analogy with (3-ribosyluric)5'-phosphate, the new compound was tentatively identified as (3-ribosylxanthine)5'-phosphate.—E. R. J.


In contrast to high-K+ human erythrocytes, low-K+ beef cells had lower ATPase activity, and K+ activation of this enzyme decreased rapidly at K+ concentrations greater than 5 mM.—E. R. J.


A detailed study in which, with the aid of isotopically labeled bilirubin and continuous-flow and starch-block electrophoresis, it was possible to demonstrate that bilirubin is bound solely to albumin at or near physiologic concentrations in human and rat serum. A small, but variable amount of radioactivity was noted in the a-globulin fraction, but could be accounted for by the formation of diazo-negative derivatives of C14-bilirubin during the experiment. Only in hypoalbuminemic serum was any diazo-positive material found in the a-globulin fraction. At pH 8.6, 1 mole of human serum albumin bound 2 moles of bilirubin so tightly that it was virtually nondialyzable. At higher concentrations, some bilirubin was rapidly oxidized to products that remained attached to albumin and a-globulins or were lost into dialyses. It appears unlikely, therefore, that a specific globulin with high affinity but limited binding capacity for bilirubin exists in human or rat serum.—E. R. J.


Preliminary data obtained with ultrasonicated fragments indicated that either Na+ or K+ activated the ATPase and did not require both ions. It was suggested that the linkage of ATPase activity and cation pumping may not be a property of the enzyme per se.—E. R. J.
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Malic dehydrogenase, purified 3000-fold from mature human erythrocytes, had a broad pH optimum, could be inhibited by mercury, cadmium and ammonium ions only, had no diaphorase activity, resembled the enzyme isolated from various other mammalian tissues and had the characteristics of the cytoplasmic, rather than the mitochondrial form of the enzyme. What function the relatively high activity of this enzyme in mature erythrocytes serves in the absence of significant activity of most other enzymes of the citric acid cycle remains unknown.—E. R. J.


Production of a severe hemolytic anemia in rabbits by administration of phenylhydrazine HCl did not result in an increase in lactic, malic or glucose-6-phosphate dehydrogenase or glutamic oxaloacetic transaminase activities in plasma. Simple destruction of erythrocytes apparently does not contribute to plasma enzyme activities. —E. R. J.


Thin-layer starch gel electrophoresis at pH 8.6 of hemolysates suggested the occurrence of an atypical catalase in six members in three genera of a family of Scandinavian-British extraction. All six were presumed to be heterozygous for the autosomal character, had normal total erythrocyte catalase activity, and were free of clinical or subclinical disease. Heterogeneity of catalase was suggested, but could not be proved.—E. R. J.


Washed erythrocytes from normal rabbits or reticulocytes from rabbits made severely anemic by administration of acetylphenylhydrazine were incubated at 37 C. for 4 hours with glucose, glutamine, inorganic phosphate and nicotinic acid-7-C14 or nicotinamide-7-C14. DPN and TPN were isolated from acid extracts of these cells by chromatographic methods. Significant incorporation of nicotinic acid into DPN had occurred after incubation with mature erythrocytes, but there was no radioactivity in the TPN; limited labeling of TPN was noted only after 8 hours. Thirty-fold greater incorporation of nicotinamide into DPN than of nicotinic acid occurred and TPN was labeled after 4 hours. The incorporation of both nicotinic acid and nicotinamide into DPN of reticulocytes was 4 to 5 times greater than incorporation into DPN of mature erythrocytes. The labeling of TPN of reticulocytes was also much greater than that of TPN of mature erythrocytes. Net synthesis of total oxidized pyridine nucleotides was not observed with either precursor. The greater incorporation of nicotinamide than of nicotinic acid into pyridine nucleotides of rabbit erythrocytes was in marked contrast to the findings with human erythrocytes. The precise mechanism that determines the striking reduction in capacity to incorporate nicotinic acid and nicotinamide into pyridine nucleotides when rabbit reticulocytes mature to become nonreticulated erythrocytes remains to be defined.—E. R. J.


Extensive studies of five children with severe hemolytic anemia beginning in infancy demonstrated a Dacie type II abnormality that was associated with a severe deficiency in erythrocyte pyruvic kinase activity in three of five patients. Intermediate enzyme activities were found in erythrocytes of both parents of all affected individuals. The families were Amish and distantly related, and pedigrees were compatible with an autosomal recessive mode of inheritance. Splenomegaly was present in all affected subjects and splenectomy halted transfusion requirements. Some differences between the clinical and laboratory findings in these patients and those previously described were noted.—E. R. J.

Red-Cell and Plasma Lipids in Acanthocytosis. P. Ways, C. F. Reed and D. J. Hanahan. From

Careful analyses with sensitive chromatographic methods of the lipids of erythrocytes and their "membranes" obtained from three patients with acanthocytosis revealed a consistent and significant decrease in the relative and absolute amount of lecithin and a corresponding increase in sphingomyelin. Similar alterations in distribution of plasma phospholipids were noted. Absent low-density lipoprotein levels, confirmed by immunoelectrophoresis, and decreased high-density lipoprotein concentrations were found. Erythrocyte plasmalogens were decreased. A striking absolute and relative deficiency in linoleic acid (not over 3 per cent; normal 10 to 14 per cent) was noted in acanthocytes and their "membranes." Erythrocytes from patients with other types of steatorrhea or malnutrition had less striking decreases in linoleic acid content and no reversal of the lecithin:sphingomyelin ratio. Increased reticulocyte content appeared to contribute to lower linoleic acid percentage, but not to significant alterations in distribution of major phosphatides. Studies of plasma and erythrocytes obtained from close relatives of one patient failed to reveal significant abnormalities. The most striking finding appeared to be the altered phosphatide distribution in acanthocytes and suggested that an abnormality in absorption of linoleic acid was not the primary defect. The influence of the composition of the plasma lipids on erythrocyte membrane lipids could not be evaluated from the present data. —E. R. J.


G-6-PD activities of the erythrocytes of 131 normal white women were significantly higher than those of 126 normal white males, a difference not correlated with the pre- or post-menopausal state of the women and not in agreement with previous reports. Studies of erythrocytes of patients with X chromosome anomalies failed to demonstrate altered G-6-PD activity, confirming other investigations. Thus, dosage compensation appears to operate in respect to erythrocyte G-6-PD activity, but not completely. Further evaluations are essential to resolve the contradictions. —E. R. J.


Washed erythrocytes, obtained from normal adults and from adult Negro male subjects whose erythrocytes were found to be deficient in G-6-PD activity, were incubated at 37 C. in sodium phosphate buffer at a packed cell volume of 35 per cent with glucose, 2 mg./ml., and with or without acetylphenylhydrazine (APH), 2.5 mg./ml., for up to 7½ hours. Incubation of normal cells with APH resulted in decreased formation of lactic acid and an equivalent rise in accumulation of pyruvic acid. More marked alterations in glycolysis occurred in G-6-PD-deficient erythrocytes, but the increased pyruvate accumulation did not fully compensate for the marked diminution in lactate formation. These observations were made under conditions in which about 50 per cent of the initial GSH remained in normal erythrocytes, but no appreciable GSH remained in G-6-PD-deficient cells. A greater decrease in utilization of glucose, after preincubation with APH, occurred in G-6-PD-deficient than in normal erythrocytes. Activities of glyceraldehyde-3-phosphate dehydrogenase and lactic acid dehydrogenase were not affected significantly in either type of erythrocyte by incubation with APH. A diminished availability of DPNH in the presence of APH was implied, and it was found that oxidation of DPNH by APH was accelerated in the presence of hemolysate and that GSH afforded protection. The diminution in glycolysis in G-6-PD-deficient erythrocytes depleted of their GSH suggested a possible role of GSH in preventing the oxidation of DPNH by agents such as APH. The possibility that these findings are a function of altered hexokinase activity is postulated.—E. R. J.


In Hb E-thalassemia disease, a high percentage of subjects had instability of erythrocytic GSH
with normal G-6-PD. The instability was not due to any defect in glutathione reductase.—J. B. C.


The staining reagent consisted of 50 mg. benzidine hydrochloride dissolved in 100 ml. of distilled water to which was added 2 ml. glacial acid, 1 ml. of 2 per cent sodium nitroprusside and 1 ml. of 30 per cent H2O2. The hemoglobin and the haptoglobin bands on paper took a deep blue color.—J. B. C.


During extracorporeal circulation, introduction of large volumes of homologous blood results in a fall in plasma and red-cell volumes that may continue into the first postoperative day. Subsequently, with an unchanged blood balance, there is a substantial increase in both compartments. When large amounts of blood are given for postperfusion hypotension, with associated blood-volume deficit, hypervolemia eventually ensues. It is concluded that the deficit represents sequestration of blood and that the subsequent blood-volume rise reflects dessequestration. The association between the severity of the blood-volume deficit and serious pulmonary complications appears to implicate the lungs as a sequestration site. Appreciation of the sequestration-dessequestration phenomenon has been of help in the management of postperfusion patients for the following reasons: the volume of homologous blood is reduced by hemodilution, and flow rate is not reduced; measured blood loss during the perfusion is replaced by the blood-diluent mixture; blood collecting in the pleural and pericardial cavities is preferentially returned to the heart-lung machine; and additional blood is administered as necessary for postperfusion hypotension. If there is no immediate response, cardiotonic agents and vasopressors are used. No attempt is made to maintain isotopic normovolemia after operation. Late blood loss is incompletely replaced in anticipation of dessequestration.—H. H. F.


Erythrocytes coated with bacterial capsular polysaccharides, notably the Vi antigen, were no longer agglutinated by antibodies directed against the various antigens native to the red cell surface. These effects could not be attributed to prevention of antibody uptake, even though in some systems the uptake of antibody was diminished. In fact, agglutination by Rh-incomplete antibody was brought back to the original titer only after the sensitized Vi-coated cells had been subjected to ten alternating exposures to globulin and antoglobulin. Hemaggulination by Newcastle, mumps, and influenza viruses were also suppressed. Erythrocytes coated with Vi polysaccharide assumed the distinctive physicochemical attributes of this acidic polymer which results in a stabilization of the erythrocyte suspension as manifested by increased electrophoretic mobility and a striking decrease in the rate of sedimentation. Among the possible models for explaining the nature of the Vi effect on immune agglutination, the data favor interference with lattice formation.—H. H. F.


Vitamin B12 content of 15 varieties of Indian fish was estimated both in the natural raw state and after boiling the materials with distilled water for 15 minutes. Vitamin B12 was assayed with Euglena gracilis. In the raw state, the activity varied between 0.7 and 8.0 μg. per 100 Gm., and in the boiled state the value varied from 1.0 to 4.85 μg. per 100 Gm. Vitamin B12 activity in the boiled state was lower than that in the raw state in nine varieties of fish.—J. B. C.


Serum incubated with vitamin B12-Co57 was separated by high voltage electrophoresis in Peri-con. Radioactivity was found in the α1-, β1- and
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In the natural state in vivo, in normals and in chronic myeloid leukemia, vitamin B₁₂ was bound primarily to α-1 globulin. After intramuscular injection, the chief binding protein was α-2. With in vitro addition, the chief binding protein was α-1 in chronic myeloid and α-2 in normals. —J. B. C.


Under conditions of the experiment, the microbiologic activities of normal and chronic myeloid leukemia sera to alkali treatment were essentially similar. —J. B. C.


Some clinicians still prefer liver extract to vitamin B₁₂, believing in some additional hematopoietic factor in liver. The report deals with 43 patients with pernicious anemia treated with aqueous vitamin B₁₂ for from 2 to 10 years, on an average 4½ years. Twenty-one patients had previously had other types of therapy. Doses of vitamin B₁₂ varied, from a minimum of 60 μg. every 4 weeks to a maximum of 500 μg. every week. Most patients had 60 μg. every 2 weeks. Optimal hematologic status was maintained in all patients. No neurologic manifestations developed. It is concluded that liver extract has no advantage over aqueous vitamin B₁₂. —S. A. K.


A detailed report of a 20 year old man presenting with refractory anemia and a brief report of a similar case from an unrelated family. —J. B. C.


The metabolism of transferrin was studied in normal and anemic subjects, using ¹³¹I as a label. Half-time plasma disappearance in normal subjects ranged from 8 to 10.4 days. Total plasma values ranged from 3.79 to 7.10 Gm. and were related to body weight. There was equal distribution between intra- and extravascular compartments. Plasma disappearance rates did not correlate with degree of erythropoiesis or radioiron clearance. Transferrin levels were considerably elevated in iron deficiency anemia. —R. O. W.


Apoferitin and ferritin solutions were prepared from horse spleen, and crystallized hemoglobin was prepared from normal adult human blood. The fate of the ferritin molecules in vitro after degradation with oxidizing agents and trypsin digestion was determined by using chemical, serologic and electron optical techniques. The denaturation products of oxidized ferritin were compared with hemosiderin. The results indicated that hemosiderin in vivo is a denaturation product of ferritin. They also demonstrated that iron release in the presence of ascorbate was more rapid from hemosiderin than from undenatured ferritin. Perhaps such a pathway may operate in vivo as a source of mobile iron. —O. P. I.


Total marrow storage iron was determined by an isotope diluting technic in adults undergoing
thoracotomy. Radioiron was given intravenously 18–24 hours prior to surgery, to give maximal marrow radioactivity. The rib removed at surgery was squeezed dry, the marrow weighed, its radioactivity counted and its iron measured chemically.

Radioiron was given intravenously to 24 white males, and 1629 mg. (304-4820 mg.) in 17 white females, 288 mg. (10-833 mg.) in 24 white males, and 1629 mg. in 15 Bantu males. Chemical estimations of iron concentration agreed fairly well with histologic assessment.—R. O. W.

**LEUKOCYTES**


Although blood films have often been the material of choice when developing cytochemical methods, the position of the metallic constituents of leukocytes has remained obscure. Hence it was thought desirable to subject relatively pure fractions of equine leukocytes, isolated from peripheral blood, to spectrochemical analysis. Sodium, potassium, magnesium and calcium were observed to be present in all samples. Of these metals of biological interest, manganese, molybdenum, vanadium, strontium, and zinc were, if present at all, below the limits of detection. Nickel and chromium were occasionally found in trace but significant amounts. In contrast, there was, in the case of both copper and iron, a pronounced and consistent increase from platelet to neutrophil, eosinophil, and lymphocyte.—O. P. J.


Leukocyte extracts showed in vitro hemolytic activity in 9 out of 29 patients investigated. —J. B. C.


Inbred mice were thymectomized within 12 hours after birth and implanted at 3–4 weeks of age with Millipore (45 μ) diffusion chambers (MDC) containing isologous newborn thymus. A control group was only thymectomized. The latter group of animals died within 7–8 weeks with a syndrome of weight loss, diarrhea and hunching. The lymphoid organs of these mice were small and showed marked lymphocyte depletion. The peripheral blood also showed decreased numbers of lymphocytes. In the mice implanted with the MDC containing isologous thymus, these gross and microscopic changes did not occur. The authors conclude that the thymus is a source of a humoral substance affecting lymphocytes production and/or maturation. [Abstractor's note: Since M. Fishman has shown that MDC have an adjuvant effect on antibody production, a necessary control for the above experiment would be implantation of empty MDC and MDC containing other living non-thymic tissue.]—I. G.


This paper reports experiments to quantitate by the granule count technique several histochemically demonstrable enzymes in rabbit mononuclear and polymorphonuclear exudate cells (MN and PMN) and pulmonary alveolar macrophages (AM). The authors were successful with acid phosphatase in MN and partially successful with succinic dehydrogenase in all three types of phagocyte. With the others (cytochrome oxidase, aminopeptidase, and esterase) the method became semiquantitative in nature, because part of the color produced was diffuse and not amenable to granule counting. Apparently alkaline phosphatase was not present in rabbit MN and AM, but only in PMN.—O. P. J.


The object of the experiments reported in this paper was to examine the metabolic basis of the phagocytic event in mononuclear cells (MN)
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and in alveolar macrophages (AM) and to compare these cells with polymorphonuclear leukocytes (PMN). The reasons for the very large increase in oxygen uptake PMN during phagocytosis and the associated stimulation of conversion of glucose carbon-1 to CO₂ have been shown to be due to the presence of a cyanide-insensitive oxidase for reduced pyridine nucleotides. The AM differed from both PMN and MN in that the resting respiration of the AM was high and phagocytosis caused only a small increase in oxygen uptake and in glucose oxidation. It has been noted that the stimulation of labeling of lipids, particularly phosphatides, in phagocytizing PMN was most notable in the case of phosphatidic acid, phosphatidyl serine and inositol phosphatide. The failure to detect an increased labeling of lipids in the case of AM when they were engulfing particles was possible due to the greater rate of conversion of inorganic phosphate to ATP in these cells and the rapid equilibration of inorganic ester and anhydride phosphates.—O. P. J.


A historical and clinicopathologic review of Schüller-Christian disease has been presented and its clinical manifestations, course, and response to therapy summarized. A review of 10 years experience with adrenocorticoid therapy (1951–1961) in 40 patients revealed differences in steroid medication, dosage, therapeutic intervals and, in many instances, the coincident use of other forms of therapy. The over-all effectiveness of corticoid therapy in these patients was equivocal and difficult to assess. Finally, clinical and laboratory evaluations of 10 children with active Schüller-Christian disease have been made and their response to large doses of prednisone evaluated. The results indicate that adrenocorticoid therapy is capable of reversing all the skeletal and visceral manifestations of the disease. When large doses of prednisone were administered for relatively short intervals, remissions were obtained and sustained for periods of 12 to 30 months.—H. H. F.


This paper describes a histochemical technic for the study of the kinetics of an enzyme-catalyzed reaction, the derivation of kinetic constants from the data obtained, and the significance of these data in the characterization in human mast cells of an amidase and esterase activity having similarities to trypsin. Apparently a single enzyme or closely related enzymes in this site were responsible for the hydrolysis of both the amide and ester substrates and that typical trypsin substrates acted as competitive inhibitors of their hydrolysis.—O. P. J.

HEMOSTASIS


Three systemic factors, arterial wall damage (DHT), dietary fats (butter) and acute hemodynamic change (adrenaline) were investigated for producing blood hypercoagulability and arterial thrombosis in experimental rats. Butter and DHT feeding caused significant shortening of plasma fibrinolytic activity. Adrenaline did not alter the prothrombin time but tended to increase plasma fibrinolysis. Coronary thrombosis was produced as a result of the combined effects of all the three systemic factors. DHT administration produced a rise of serum cholesterol and lipid phosphate, but the other factors did not affect these parameters.—J. B. C.


EEN FAMILIALE VORM VAN IDIOPATHISCHE HYPOPROTHROMBINEMIE. C. R. Post, G. J. H. Den Ottolander and P. G. Hooiveld. From the Central Laboratory of the Blood Transfusion Service

Van Creveld (1954) published on the clinical features and the coagulation defect in a family with true congenital hypoprothrombinemia. Four boys and two girls, out of 13 siblings, had recurrent hemarthroses and other severe hemorrhages occurring after the slightest trauma. The prothrombin (factor II) concentration in the plasma of these children was found to be 5–10 per cent of normal, as measured by the two-stage technic. Consanguinity between the parents could not be demonstrated. Interestingly enough, the proconvertin (factor VII) activity also appeared to be lowered, to about 30 per cent of normal. In 1961 the family was restudied by Hart et al. (1963)

By means of the one-stage technic, values of about 1 per cent prothrombin were found in the five "bleeders." The concomitant slight hypoproconvertinemia was confirmed. The parents and six of the seven apparently non-affected children displayed prothrombin values between 47–75 per cent, 58 per cent on the average (normal value: 97 ± 7 per cent). Post et al. (1956) described another Dutch family suffering from true congenital hypoprothrombinemia. In the parents and in two of the five children, about 50 per cent; in one child 100 per cent, and in the two other children 5 per cent prothrombin was found. The two severely affected members had repeated hemorrhagic manifestations, although much less pronounced than Van Creveld's cases. There group of monkeys was used as controls for the was no concomitant hypoproconvertinemia. Coagulation studies in these two Dutch families support the view that congenital hypoprothrombinemia is due to an autosomal gene defect with intermediate expression and complete penetrance.

—E. A. L.

MISCELLANEOUS


Intravenous inoculation with KFD virus was given to two groups of M. radiata monkeys, one nonimmune and one partially immune, for a clinicopathologic study of the disease with particular reference to the hemopoietic system. A third effect of repeated bleedings. Liver and bone marrow specimens were taken for examination from each group of monkeys during the test for comparative studies. A marked leukopenia and erythropenia developed in relation to the viremia in the nonimmune monkeys. Some degree of thrombocytopenia was also seen. These findings were not observed in either the partially immune monkeys or in the controls. Circulation of virus was not demonstrated in the partially immune monkeys. Leuko-, erythro- and platelet phagocytosis were observed in the peripheral blood from the 8th to the 11th day in the nonimmune virus-circulating monkeys. It is suggested that phagocytosis, mediated in all probability through an immunologic (agglutinating) mechanism, plays a part in causing the leukopenia, erythropenia and thrombocytopenia seen in the monkeys that circulated virus. It is further suggested that consideration be given to the possibility that this phagocytosis by the reticuloendothelial system contributes to the leukopenia seen in other virus diseases.—J. B. C.


In Kyasanur forest disease, an arthropod-borne virus disease of South India, the significant findings were: leukopenia, thrombocytopenia, presence of leuko- and thrombo-agglutinins, low serum albumin, slightly increased γ-globulin and raised serum alkaline phosphatase activity.—J. B. C.


(Balb/c x DBA/2) F1 female mice were irradiated with an LD50 30 days with a cobalt source or Van de Graaff generator. Colchicine (40 μg.) was given 2 days prior to irradiation. Trimethylcolchicinic acid (0.5 mg.) was given 1 day before irradiation. A third group of mice was not treated. Peripheral blood counts and longitudinal sections of femur were made. Serial examination of bone marrow showed in the treated groups an increase in bone marrow cellularity 3
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days after LD₅₀ irradiation, a significant increase in the lymphocyte count and advance in the time of recovery of the granulocyte count. These findings explain the increased survival that is seen in irradiated mice pretreated with colchicine.

—J. G.


The bifunctional reagent p,p’ difluoro—m,m’ dinitrodiphenyl sulfone has been used for conjugation of antibodies to ferritin in a one-step procedure. In this brief report are discussed some details of the characterization of the antibody-ferritin conjugates and the advantage of this procedure over the previous methods.—O. P. J.

RHEUMATOID FACTOR IN HEPATIC AND NON-RHEUMATIC HYPERGAMMAGLOBULINEMIA. P. Sfikakis, X. Kourkourneli and D. Loukopoulos. From the Faculty of Medicine, Athens, Greece. Rev. franç. Etudes clin. biol. 8:51–58, 1963.

Sera from 57 patients with hepatic disease were studied serologically. Patients were selected on the basis of having raised γ-globulin concentrations. The Heller-Swartz hemagglutination test was positive in 70 per cent, and the Singer-Plotz latex F-II test was positive in 44 per cent. The rapid slide R.A. test was positive in 89.5 per cent. The tests were more commonly positive if the increase in serum γ-globulin was well marked. A significant correlation was found between the hemagglutination test and the γ-globulin concentration estimated by paper electrophoresis. Correlation was also present between the latex-F-II test and the thymol and zinc flocculation tests as well as the electrophoretic γ-globulin concentration.—H. H. F.


A report of a man, 33, with primary congenital agammaglobulinemia. Malabsorption of fat, glucose, xylose, and vitamins A and B₁₂ were demonstrated. Suction biopsies of gastric, duodenal and sigmoid mucosa revealed profound changes. Family studies disclosed hypogammaglobulinemia in the patient’s son, brother, and identical twin brother. The latter died from malignant reticulosis, probably Hodgkin’s disease. The relationship between the malabsorption and the agammaglobulinemia is not clear.—S. A. K.


Relevant data on blood from 100, and bone marrow from 12 adult guinea-pigs are recorded. —J. B. C.