ABSTRACTS

ERNST R. JAFFÉ, M.D., Editor

LEUKOCYTES


A patient was presented in whom splenectomy, performed for mild thrombocytopenia, was followed by an immediate rise in peripheral leukocyte count from 27,000 to 210,000 per mm.³ on the afternoon of surgery. The extreme leukocytosis persisted until the patient's death more than 5 ½ years after splenectomy and it reached levels as high as 302,000. The heukocytes were strongly alkaline phosphatase positive and apparently consisted almost entirely of segmented and band neutrophils, most of which contained Döhle bodies. The removed spleen weighed 2000 Gm. and contained a large number of foam cells which stained positively with fat stains. At autopsy the patient was found to have generalized amyloidosis.—T. E. B.


Rhesus monkeys, immunized repeatedly with homologous skin grafts or with blood given intravenously, produced potent leukoagglutinating iso-

antibodies. The antisera were directed against more than one antigenic determinant, though immunization was done with skin or blood from one donor only. It seemed likely that monkeys can be used in studying the relevance of leukocyte compatibility to transplantation of homologous tissues other than bone marrow.—T. E. B.


Although the main morphologic characteristics of polymorphonuclear leukocytes and their structures have been carefully investigated, correlation between morphologic and functional changes has not been studied sufficiently. The very early metabolic changes caused by phagocytosis in guinea pig polymorphonuclear leukocytes could not be related to lytic release of oxidase systems during degranulation. This change occurred later and reflected the morphologic aspect of the decline in oxidative activities.—O. P. J.

The effect of clumping and scattering of the cells upon the paths taken by rabbit polymorphonuclear leukocytes was studied in slide-cover-slip preparations. Scattered leukocytes, in the absence of introduced chemotactic substances, moved at random and avoided aggregation. Clumped leukocytes moved away from the clump until they were widely scattered and thereafter remained dispersed. It was suggested that the clumped leukocytes were displaying negative chemotaxis to some substance, presumably a metabolite, diffusing from the clump.—T. E. B.


Methods were described for the isolation of eosinophils and basophils from human blood. After 72 hours of suspension in physiologic saline, almost all eosinophils contained a Charcot-Leyden crystal in their cytoplasm. Charcot-Leyden crystals formed within two minutes when basophils were suspended in hypotonic saline and when saline extracts of eosinophils or of basophils were concentrated by ultrafiltration through dialysis tubing. Fractions obtained from nuclei, cytoplasm and granules of eosinophils were studied. Crystals seemed to come from the cytoplasmic fraction, but not from the nuclear or granular fractions. The crystals were protein in nature. It was hypothesized that the cytoplasmic proteins of eosinophils possess special ability to form stable complexes with RNA and that depolymerization of RNA may permit crystalization of the cytoplasmic proteins. Charcot-Leyden crystals were not observed in human neutrophils, lymphocytes or monocytes.—T. E. B.


Increasing cell concentration results in inhibition of division of cultured cells. Data are presented to show that granulocytes exert an inhibitory effect on the division of cultured lymphocytes. This inhibitory effect surpasses that associated with cell number per se. The data obtained are thought to provide some support for the notion that lymphocytes represent multipotential stem cells.—T. E. B.


Chloroquine is shown to be capable of inhibiting the response (the development of large cells and of mitoses) of cultured human lymphocytes to phytohemagglutinin and to antigens. In the low chloroquine doses used (10⁻² mg. per ml.), inhibition is seen only if the drug is added at the beginning of the culture period. Larger doses are suppressive, no matter when they are added. Although chloroquine is known to be able to bind DNA, it seems probable that it inhibits the lymphocyte response by another means, possibly the stabilization of lysosomal membranes in the lymphocytes so that lysosomal enzymes are not released. It seems reasonable to assume that the controlled release of lysosomal enzymes is required during the initiation of derepression of lymphocytes. Chloroquine may be able to suppress lymphocytes capable of responding to foreign histocompatibility antigens without producing permanent damage to the immunologic system.—T. E. B.


The cytocidal effect of specifically sensitized lymphoid cells on homologous target cells in culture can be inhibited by small quantities of Imuran, an imidazole derivative of 6-mercaptopurine. This inhibition takes place at Imuran concentrations which do not seem to affect the viability of the attacking lymphoid cells. The continuous presence of Imuran is apparently required for this inhibition to be demonstrable. Imuran is thought to act by interfering with RNA metabolism in the lymphoid cells. These results are consistent with the contention that RNA-dependent protein synthesis on the part...
of the lymphoid cells is necessary for a destructive interaction between sensitized node cells and homologous target cells in vitro.—T. E. B.


The mesenchymal origin of the lymphocyte, generally accepted for many years, has been challenged recently by the authors as a result of extensive morphologic, histochemical, and electron microscopic studies of the bursa of Fabricius. Sequential cytologic changes in the development of the hamster thymus into an active lymphoepithelial organ were interpreted as indicating that lymphoblasts develop by gradual proliferation and transformation of "undifferentiated" epithelial cells comprising the primordial thymus. "Undifferentiated" epithelial cells undergo 2 distinct lines of differentiation: into lymphoblasts and into stellate reticular-epithelial cells which form the organ parenchyma. This observation suggested diversity, rather than uniformity, in the origin of lymphocytes.—O. P. J.


Pycnotic nuclei are conventionally used as indicators of cell death in histologic preparations. The author studied rat thymocytes irradiated in vitro. Low pH values, addition of respiratory inhibitors (dinitrophenol, cyanide, arsenite, iodoacetamide) after irradiation, high doses of x-radiation, and "cationic condensing agents" (e.g., agmatine, excess sodium ion) were able to prevent pycnosis in irradiated thymocytes, though other signs of cell degeneration remained. It was suggested that pycnosis represents a physical dispersion of nuclear components which can be prevented by irreversibly denaturing the nuclear proteins or by causing a reversible gelation of the nucleoplasm. The absence of nuclear pycnosis does not necessarily indicate absence of cell damage.—T. E. B.


Hematopoietic tissues are difficult to grow in vitro because they usually dedifferentiate quickly with fibroblasts being the only surviving cells. Better results have been obtained with cultures of lymphoid tissues obtained from preimmunized donors, but what is usually obtained is survival, rather than real growth and differentiation. The author reports the results of tissue cultures of spleen cells from normal humans and from animals of different species, strains and ages. The splenic tissues have been successfully cultured for long periods of time (even greater than a year) during which they underwent a continuous process of differentiation, forming mature types of plasma cells. Subculturing is easily accomplished. The explanation for these successful results is not yet clear.—T. E. B.


Histamine release reactions and energy metabolism should be studied in the same sample of isolated mast cells. With the Cartesian ampulla diver technic used in this study, sampling difficulties were circumvented because the diver was the pipette and the cells which entered the diver were counted directly. The respiration rates at 37 C., in μl O2 per cell per hour, were 0.29 × 10−6 without substrate and 0.47 × 10−6 with glucose. The rates of anaerobic glycolysis, expressed as CO2 released from bicarbonate, were 1.70 × 10−6 μl and 1.43 × 10−6 μl per cell per hour with and without glucose, respectively. The aerobic glycolysis rate in the presence of glucose was 0.93 × 10−6 μl CO2 per cell per hour. CO2 production by mast cells in both anaerobic and aerobic media was much higher than respiratory oxygen uptake. This metabolic property of mast cells resembled that of leukocytes.—O. P. J.

ERYTHROCYTES


A 74-year-old male with disseminated lymphosarcoma and moderate hemolytic anemia associated with warm and cold autoagglutinins was

Krebs-Ringer phosphate buffer, pH 7.4 (10 parts). .01 M aqueous methylene blue (2) and 5 per cent glucose in isotonic saline (1) were mixed daily. Blood, collected in heparinized capillary tubes, was spun 5 minutes and the red cells were transferred to a second capillary tube which contained an equal volume of the mixed solution. After 4 hours of incubation at 37 C., tubes open and horizontal, smears were examined under low power; 8 to 17 per cent of erythrocytes from normal males showed varying intensities of blue coloration. Among G-6-PD deficient males, less than 1 per cent of the cells showed any blueness. The test was not evaluated in homozygous or heterozygous females or during a hemolytic episode.—H. S. J.

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The use of “Sorbo”-rubber insoles in shoes decreased the rate of hemolysis in a case of exertional hemoglobinuria. In this syndrome, hemolysis may result from damage to erythrocytes in the soles of the feet.—F. B.


Polyninosic acid and other activators of the first component of complement (C'), such as dextran sulfate, markedly enhance PNH red cell lysis in vitro and induce normal red cell lysis. Evidence is presented that lysis results from evolution in the suspending medium of later components of complement which are hematologically active, despite the lack of an antibody coat on the red cell. This “indifferent” C' activation may explain the exacerbation of hemolysis in various acquired hemolytic anemias, including PNH, during infections, wherein interactions between antibody and the invading agent may indirectly activate the C' system in plasma. Hemolysis in PNH may be due entirely to such a mechanism, since the sera of many PNH patients have been shown to contain antiglobulins whose reactions with native globulins might continuously activate the C' system in vivo. (See M. E. Kaplan, et al., Clin. Res. 12:236, 1964.)—H. S. J.

Indophenol oxidase activity was found in mammalian erythrocytes under conditions indicating its identity with cytochrome oxidase. Peroxidase activity was found in the nonhemoglobin constituents of red cells.—O. P. J.


There was more plasma trapped among centrifuged red cells of thalassemic than of normal children. Trapping varied inversely with the density of the red cells, as estimated by mean hemoglobin concentration.—H. H. F.


Differential titration of oxyhemoglobin at different temperatures and oxygen equilibrium measurements in buffered solutions of various pH values indicated that the Bohr effect decreases with increasing temperature. The heat of ionization of
the group responsible for the normal Bohr effect was 7 to 9 kilo-calories per mole, consistent with its being an imidazole.—H. S. J.


Intravenous injection of radioactive iron-tagged hemoglobin solution in 10 patients with anemia of infection was followed by poor reutilization of iron. Methods utilizing in vitro or in vivo iron-tagging gave similar results. Retention of iron by the reticuloendothelial system may result from the increased oxidative metabolism associated with inflammation.—R. O. W.


Iron absorption studies were performed by the double tracer technic (Fe59 by mouth, Fe55 intravenously). Normal women averaged 22.9 per cent absorption and normal men 16.7 per cent. Patients with chronic blood loss absorbed at approximately 3 times the normal rate. Nine of 11 patients who had had Billroth II gastrectomies absorbed slightly increased amounts of iron. Five patients with sprue or regional ileitis absorbed at only one-third the normal rate. Most interestingly, a group of 10 patients with anemia of infection or malignancy and low serum iron absorbed extremely small amounts of iron.—R. O. W.


Studies in man showed that folate was removed from the blood by the liver and secreted in the bile at a higher concentration than was present in serum, even in the absence of the gallbladder. There was no correlation with the serum folate level. It was suggested that folate, like vitamin-B12, has an enterohepatic circulation.—P. B.


Experimental evidence obtained in mice supports the suggestion that the erythropoietic effect of testosterone is mediated through erythropoietin production.—P. B.


Testosterone caused an increase in the uptake of Fe59 in polycythemic and in starved mice. Since this effect, in contrast to that of erythropoietin, was inversely related to the degree of polycythemia, the authors concluded that testosterone probably has no direct effect on the primitive red cell precursors. They favored the hypothesis that testosterone influences the rate of production of erythropoietin. They also showed that triiodothyronine had no effect on the Fe59 utilization of severely polycythemic mice. This finding was consistent with the hypothesis that triiodothyronine has an erythropoietic effect because it causes an increase in oxygen demand, a demand which is met when many red cells are available for oxygen transport. The opposite conclusion, however, was reported in a recent paper by Meineke and Crafts (Proc. Soc. Exp. Biol. Med. 117:520, 1964); these authors found that polycythemia did not abolish the erythropoietic effect of triiodothyronine.—A. J. E.


A technically sophisticated procedure was used to perfuse one kidney with venous atrial blood, thereby inducing localized renal hypoxia in an almost intact dog. Erythropoietin titers, measured in polycythemic mice, did not increase in 3 hours, but after 5 hours of perfusion the authors concluded that 50 per cent or more had a significant increase in erythropoietin level. The titer of blood obtained from the right atrium generally was consistently higher than that of blood from the right atrium. In control animals with the kidney perfused by blood obtained from the femoral artery, erythropoietin titers did not
change significantly. The procedure was far more physiologic than those reported previously in which the isolated kidney was found to produce erythropoietin. The significance of the increase in erythropoietin titer, however, is somewhat questionable; in half of the significant cases, the results were statistically significant only at the 0.1 level and some cases had titers which vacillated between significant and nonsignificant.—A. J. E.

Erythropoietin studies were not performed. A transient increase in red cell production was unexplained. 2 months and the cause for the temporary in-

crease disappeared spontaneously after traumatic occlusion of the middle cerebral artery.

The granularity of the juxtaglomerular cells increased during chronic intermittent exposure to low oxygen tension. The authors related the con-

comitant increase in erythropoietin titer to this increase in secretory activity of the J.G. cells. Extraction of normal renal cortex under nitrogen resulted in a preparation which had erythropoietic activity when injected into starved rats. Cortical erythropoietic activity was absent, if the rats had been salt loaded first, a procedure which de-

creases the secretory activity of the J.G. cells. —A. J. E.

Neurogenic Polycythemia. Report of a Pa-

tient with Transient Erythrocytosis As-

sociated with Occlusion of a Middle Cere-

bral Artery, and Review of the Literature. H. B. 

Demopoulos, B. Highman, P. D. Altland, M. A. 

Garvng and G. Kaley. From the National 

Institute of Arthritis and Metabolic Diseases, 


A useful review of the literature on neurogenic polycythemia with a case report of a 27-year-old man who had a transient true erythremia after traumatic occlusion of the middle cerebral artery. The erythrocytemia disappeared spontaneously after 2 months and the cause for the temporary in-

crease in red cell production was unexplained. Erythropoietin studies were not performed. —A. J. E.

Erythropoiesis in Subjects with Chronic 

Bronchitis. D. Massaro, A. M. Cusick and S. 

Katz. From the Veterans Administration Hos- 


This paper adds a number of thoroughly studied cases to the many previous reports of patients with chronic bronchitis, arterial oxygen unsaturation and a suboptimal erythropoietic response. The conclusions are that, in many cases, the erythrocyte mass and the erythropoietin titer are appropriate to the degree of arterial oxygen unsaturation. In other cases, however, there is a definitely inadequate erythropoietic response, the reason for which is completely unknown.—A. J. E.

Erythropoietic Stimulating Activity during 

the First Ninety Days of Life. D. L. Mann, 


From St. Louis University School of Medicine, 


212, 1965.

Erythropoietin titers of cord blood and blood obtained on days 4, 30, 60 and 90 following birth were measured and correlated with the hemoglo-

bin level. Assays, done with polycythemic mice, indicated that the titer was elevated in cord blood, reduced to normal during the early polycythemic postpartum period and then increased gradually as the hemoglobin concentration returned toward normal. The results were certainly compatible with a physiologic control of erythropoiesis by erythropoietin during the newborn period.—A. J. E.

Intestinal Absorption of Bile Pigments. III. 

The Enterohepatic Circulation of Uro-

bilinogen in the Rat. R. Lester and R. 

Schmid. From University of Chicago, Chicago, 


bilinogen Absorption in Man. R. Lester, W. 


The behavior of mesobilirubinogen-C14, a mem-

ber of the class of bile pigment chromogens com-

monly termed "ubobilinogens," was investigated in rats and humans with biliary fistulae. When labeled pigment was infused into the small in-

testine, the rate and magnitude of its biliary excretion (enterohepatic circulation) was much greater than when injected into the colon. Urinary, in contrast to biliary, excretion of absorbed pigment was minimal, except under conditions of biliary obstruction or hepatic parenchymal dis-

case. Since bilirubin is reduced by intestinal bact-

eria to ubobilinogens and since the latter are more readily absorbed in the small intestine, it
was suggested that the urobilinogenuria in hepatic disease reflects both invasion of the small intestine by bacteria and impaired hepatic excretion.—H. S. J.


Tubular fibers, 270 A in diameter, were isolated from erythrocytes of the western salamander, Taricha granulosa, by the spreading forces of the Langmuir trough. The substructure of these fibers and their occurrence adjacent to the cell membrane suggested that they were isolated microtubules. They may help maintain the rigidity of cell shape.—O. F. J.

HEMOSTASIS


Two individuals believed to be homozygous for von Willebrand’s disease (v.W.d.) had markedly prolonged bleeding times. AHF levels too low to be titrated and a severe bleeding disorder. The parents of one appeared to be normal by laboratory tests. The parents of the other had slightly prolonged bleeding times, low normal AHF levels and showed extensive new synthesis of AHF when transfused with hemophilia A plasma, as did a group of 4 patients considered to be heterozygous for v.W.d. The two individuals considered to be homozygous showed only ¼ as much new synthesis as the latter set of parents and as the unrelated group of v.W.d. heterozygotes. The authors previously had suggested that the autosomal von Willebrand’s locus might be regulatory, influencing the quantity of AHF without affecting the structure of the molecule. If the only defect were diminished production of AHF because of reduced effector substance, then both homozygotes and heterozygotes should respond essentially equally when given large transfusions of hemophilia A plasma deficient in AHF, but rich in the hypothetical effector. The results, however, showed much less synthesis by homozygotes. This finding was interpreted as indicating that the v.W.d. locus is not occupied by a regulatory gene. The finding was consistent with the hypothesis that both the autosomal and the x-locus which affect AHF biosynthesis are occupied by structural genes coding subunits of the molecule.—R. G.


The levels of Factor XI in pregnant women fell throughout the last trimester to below those of the normal adult and were intermediate between normal adult and cord blood levels. Neonatal levels were significantly lower than maternal levels at term and rose gradually within 60 days to near normal adult values. Serial measurements in 4 infants in the first 5 days of life did not demonstrate a fall, as was seen in prothrombin and Factors VII, IX and X which are vitamin K-dependent. Vitamin K did not alter the levels within the first 5 days and had no effect on the rate of rise to adult levels. Three newborn infants with symptoms of hemorrhagic disease were found to be deficient in Factor XI. Bleeding symptoms were not controlled by vitamin K. Factor XI, probably formed in the liver, did not cross the placenta from mother to infant and was not dependent on vitamin K for formation. It was probably produced in amounts proportional to the maturity of the liver. It was pointed out that decreased activity of Factor XI in the neonatal period may be responsible for bleeding which will not respond to vitamin K.—R. G.


Two brothers had histories of severe epistaxes, either spontaneously or after slight trauma, and excessive bleeding after tooth extractions. One had had two severe episodes of gastrointestinal bleeding. Coagulation studies were normal in both, except for low normal levels of fibrinogen and increased solubility of their fibrin clots in urea solutions. Although the whole blood clots were firm, there was increased red-cell fallout. There was no evidence of increased fibrinolytic activity. Both had increased capillary fragility.
with the suction-cup technic but normal fragility when the venous stasis technic was used. Fibrinase (FSF or Factor XIII) activity was decreased in the plasma and serum of both patients, although immunoelectrophoresis appeared to indicate that fibrinase protein was present. —R. G.


In a 12-year-old boy, the first hemorrhagic manifestation occurred a few days after birth after separation of the umbilical cord. Bleeding began and continued for 3 weeks. From that time on, he suffered multiple ecchymoses and hematomas. Hemorrhagic manifestations always occurred at least 24 hours after trauma. On at least 3 occasions, trauma caused serious hemorrhage: huge hematoma of the thigh, subdural hematoma, and hemarthrosis. Improvement followed blood or plasma transfusions. The mother, father and 3 siblings had no history of a bleeding tendency. One brother had died at age 19 days from cerebral hemorrhage and one sister, 6 months of age, appeared to bruise easily. Studies which included bleeding time, tourniquet test, clotting time, clot retraction, prothrombin time, prothrombin consumption cephalin time, levels of Factors II, V, VII, VIII, IX, X and fibrinogen, thromboplastin generation and euglobulin fibrinolysis were all normal. The only abnormality was the lack of fibrin-stabilizing factor, revealed by the solubility of the fibrin clot in urea and monochloroacetic acid. By a semiquantitative assay method, it was found that both the mother and father had less of this factor than normal, indicating that perhaps they were heterozygous. These findings would support an autosomal recessive mode of transmission. Following administration of 500 ml. of plasma, clot solubility was corrected until 14 days after transfusion. —R. G.


Rats fed atherogenic diets developed high levels of many blood coagulation factors, including Factors VII and X. The production of Factor VII-X by liver slices incubated in vitro was assessed. The assay was sensitive for both factors, but it was felt that the increases reflected mainly increases in Factor VII. Expressed as a ratio (test: control), the median value of Factor VII-X production per mg. protein was 1.9. It appeared, therefore, that there was an increasing Factor VII-X in flasks containing liver slices from test rats, though the possibility of delayed degradation could not be excluded. —R. G.


Factor X was purified by combined BaSO₄ treatment and DEAE chromatography. Activation of purified Factor X by trypsin or Russell's viper venom resulted in an apparent reduction in molecular size or shape, as revealed by chromatography on Sephadex G-100. In the presence of Ca²⁺, a further pronounced decrease in molecular weight was evident. Examination of the various species of Factor X on electrophoresis showed that activation resulted in a sharp decrease in net negative charge on the molecule. Activated Factor X was capable of activating plasma Factor X, whereas 25 per cent citrate, reportedly an activator, did not have an effect. The affinity of plasma Factor X and activated Factor X for purified phospholipids was followed by gel filtration on Sephadex C-200. Formation of a stable complex between Factor X activity and phospholipids (phosphatidyl serine/phosphatidyl choline, equimolar mixture) was effected only when Factor X was activated and then only in the presence of Ca²⁺. The net charge on protein and phospholipid molecules appeared to be of considerable import in these interactions. —R. G.


Ca7, a highly purified proteolytic enzyme from Aspergillus oryze, acts on a number of coagulation factors. In low concentration, its immediate action is to shorten the recalcification time of
plasma. It does this by converting prothrombin to thrombin and its action is similar to that of tissue thromboplastin. During incubation, particularly with increasing concentrations, it destroys prothrombin, thrombin, and fibrinogen. It destroys normal plasma antithrombin, but also generates a thrombin inhibiting activity, probably by its proteolytic action on fibrinogen.—R. G.


Dextran coating of platelets inhibited the release of PF 3 activity. Clot retraction, platelet adhesiveness and the platelet thromboplastin test were normal. Serum prothrombin time was abnormal in some subjects. Clinical dextran had a more deleterious effect on PF 3 activity than did low molecular weight dextran, but the majority of subjects had normal bleeding times associated with their reduced levels of PF 3 activity.—H. H. F.


Thrombin, trypsin and papain inactivated the clottable protein of human platelets and released serotonin and ATP. Platelets freed of clottable protein by treatment with these enzymes did not aggregate when subsequently incubated with thrombin and calcium, but retained their ability to support clot retraction when suspended in a medium containing fibrinogen. Plasmin and α-chymotrypsin in concentrations equivalent to trypsin in proteolytic activity did not inactivate clottable protein or release significant amounts of serotonin or ATP from intact platelets, although they rendered the clottable protein incoagulable in platelet lysates. Platelets treated with plasmin and α-chymotrypsin did not aggregate, but released serotonin and ATP when subsequently incubated with thrombin and calcium. Fragments of plasmin-digested fibrinogen that were unable to polymerize were, however, capable of being split by thrombin. Thrombin may produce release of serotonin from plasmin-treated platelets by further splitting of plasmin-digested platelet fibrinogen. The release of serotonin under these circumstances may not be due to an effect on platelet fibrinogen, but may involve another mechanism. It was pointed out that platelets from certain patients with thrombocytopenic purpura have been found to be deficient in platelet fibrinogen and were not aggregated by thrombin, but did release serotonin and ATP following exposure to thrombin. The authors concluded that their data were compatible with the hypothesis that platelet fibrinogen is a functional part of the structure of normal platelets and that aggregation of platelets by thrombin depends on a multiphase reaction involving platelet fibrinogen, possibly with polymerization of fibrinogen. Release of serotonin and adenosine nucleotides by thrombin may depend only on proteolysis of platelet fibrinogen, but other mechanisms are possible.—R. G.

AN INVESTIGATION OF THE HEMORRHAGIC DIATHESIS IN PATIENTS RECEIVING COUMARIN AND INDANEDIONE ANTICOAGULANTS. C. W. Baugh.


Coagulation studies were carried out on 10 patients who bled during anticoagulation therapy without other underlying causes and on 10 patients with a similar degree of prolongation of the prothrombin time who did not bleed. The average age and sex distribution of the groups was similar. No association was noted between occurrence of hemorrhage and type of anticoagulant, duration of treatment, or nature of underlying disease. There were no differences in the levels of Factors II, VII, IX and X, or in the glass and silicone clotting time, the thromboplastin generation test or the thrombo test. All patients on anticoagulant drugs with prothrombin times in the therapeutic range or longer may be potential bleeders. One cannot predict who will bleed on the basis of coagulation studies.—R. G.


It has been postulated by others that defects of intrinsic thromboplastin production are responsible for bleeding when Quick prothrombin times are in the accepted therapeutic range. In this study, purpura, occult blood in stool (guaiac 2+ or greater) or hematuria, either gross or
microscopic (greater than 5 red cells per HPF), was considered evidence of bleeding. There was poor correlation between bleeding and defects of intrinsic thromboplastin production, as measured by the activated PTT. There was good correlation between bleeding and reduction of prothrombic activity below 10 per cent, as determined by the Ware and Stragnell test. There were no instances of hemorrhage when the activity was above 15 per cent. There was good correlation between bleeding and elevation of the prothrombin time above 20 seconds when control values were 11 to 12. When the prothrombin time was over 20 seconds, Ware-Stragnell prothrombic activity was less than 10 per cent in the majority of instances. The author suggested that, for Simplastin giving control values of 11 to 12, either duration or therapeutic range probably would be different, but this could be established by correlating prothrombin times with prothrombic activity.—R. G.

MISCELLANEOUS


Antinuclear antibodies were studied by immunofluorescence in 3000 sera. A positive test was found in almost 100 per cent of L.E. cases with a positive correlation between titer and phase of the disease; in acute phases, the titer was very high. Anti-DNA antibodies were almost specific for L.E., but were inconstantly found in treated patients. Antinucleoprotein antibodies evolved parallel to the L.E. phenomenon. Antinuclear antibodies were detected in rheumatoid arthritis, scleroderma, myasthenia gravis, erythroleukemic anemia with thymic tumor and in 20 per cent of cases of chronic lymphatic leukemia or lymphosarcoma. They were also found in some normal patients, especially older women, and in patients with tuberculosis after long-term treatment with isoniazide.—J. C.

STEROID THERAPY OF SYSTEMIC LUPUS ERYTHEMATOSUS BASED ON IMMUNOLOGIC CONSIDERA-


Nineteen patients were treated continuously with large doses of glucocorticoids until the immunologic abnormalities had returned to normal, regardless of prior relief from subjective complaints. Thereafter, prolonged intermittent steroid therapy with large doses was used, guided by immunologic data, for at least 2 years. Immunosuppression was maintained. The disease was controlled, side-effects were minimal and lost renal function improved markedly, even in advanced cases. Serum complement levels were the most sensitive immune indicators, becoming normal last on therapy and subnormal first on relapse.—H. H. F.

SURFACE SPECIALIZATIONS OF ABSORBING CELLS.


Since hematologists would not necessarily be inclined to read this article, at least one portion of it should be brought to their attention. Thin sections of a suspension of normal guinea pig bone marrow were studied by electron microscopy after glutaraldehyde and osmium tetroxide fixation. The cell membrane (plasmalemma) of erythroblasts was, for the most part, a typical smooth-surfaced unit membrane, but in certain small plaques destined to form micropinocytosis vesicles the membrane exhibited faint vertical striations. Dense particles of ferritin adhered to the outer surface of the filamentous coating on these thickened patches, but were not found on unspecialized areas of the cell surface. In dividing cells, an unusual number of specialized sites with adherent ferritin was found, but there was no invagination to form vesicles. The latter activity was apparently suspended temporarily during mitosis.—O. P. J.


Cameron and Staveley showed in 1957 that the fluid in hydatid (echinococcus) cysts contained a strong P blood group substance. P; negative patients with hydatid cysts developed anti-P; antibodies. It was found that anti-P; may be produced in P; negative individuals without
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Hydatid cysts when they were given hydatid antigen in the course of Casoni Tests. Such individuals also developed positive hydatid complement fixation tests. Since positive reactions were found only in patients with various cancers, it may be that neoplastic conditions are associated with an increased susceptibility to sensitization by the P substance in hydatid-cyst fluid.—F. W. G.


A simple crossmatch method is described which will assist in preventing the inadvertent administration of D and D" blood to Rh negative persons. It involves the addition of a drop of anti-D serum to the mixture of recipient serum and donor cells, followed by 30 minutes' incubation and an antiglobulin test. (Abstracter's comment: The simple and economical test seems eminently reasonable and should probably be routine in all Rh-negative recipients.)—H. H. F.


Alpha lipoprotein was shown to exist in two forms: LP_a and LP_b. Antisera, prepared in 3 different animal species, revealed that LP_a and LP_b were only partially cross-reactive. Alpha LP_a may be the native form in which these lipoproteins circulate. Alpha LP_b was shown to be formed from alpha LP_a by partial delipidation.—H. H. F.