ABSTRACTS

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Coagulation


In 31 cases of leukemia (11 chronic myeloid, 11 chronic lymphatic, 8 acute, 1 erythroleukemia) the following tests were performed: prothrombin time; labile factor; factor VII, prothrombin concentration (according to Owen); prothrombin time in serum. In over one third of the cases, a prolonged prothrombin time was observed. A moderate but definite reduction of prothrombin concentration was often observed in chronic leukemia. A decrease of the labile factor was frequently noticed in acute leukemias. Proconvertin (factor VII) was decreased in almost all forms. No definite connections were observed with the hemorrhagic symptoms.-P. d. N.


Infants have been studied during the first 12 weeks of life with prothrombin, proconvertin, and proaccelerin assayed by the author's microtechnic. In the current study cord blood and maternal blood samples were evaluated with and without vitamin K to the mother and infant and both. The data show deficiencies of prothrombin and proconvertin to be present at birth, becoming more severe during the first two days of life. Proaccelerin activity is found to be equivalent to 300 per cent of the normal adult levels. Vitamin K did not appear to alter the mean values obtained in any of the various groups. In a carefully controlled in vitro system, the effect of varying concentrations of proaccelerin in the presence of low levels of proconvertin and prothrombin was studied. With the latter two factors at low levels comparable to those encountered in the neonatal period, increasing concentrations of proaccelerin from 15 to 300 per cent produced progressively shorter clotting times. The authors pose a challenging question as to whether or not the hypoprophosphorbinemic, hypoproconvertinemic infant is protected from bleeding by the presence of high levels of proaccelerin. This interesting concept needs further study and these findings need confirmation. The role of potentially dangerous vitamin K in newborn care is minimized by these studies.-N. J. S.

The paper deals with thrombin time in liver patients. Theories explaining the prolongation of the thrombin time are discussed, e.g. qualitative deficiency of fibrinogen, deficiency of a coagulopathic factor of the plasma or a nonspecific physico-chemical disorder of the platelets. None of these is entirely satisfactory and it seems plausible that in the liver patient, several of these factors cooperate in prolonging the thrombin time.—J.D.

Tissue Cells


Mast cells are credited with many functions, one of which is the secretion of mucopolysaccharides. They have also been variously described cytologically, but their finer structure has been heretofore obscured by the metachromatic granules in relatively thick sections as seen with the light microscope. However, ultrathin sections of the skin of newly born mice are suitable for electron microscopy of the mast cells adjacent to the primordium of hair follicles in the presumptive dermis. The mast granules are markedly electron dense and irregular in shape. They vary from 0.3μ to 1μ in diameter but are usually about 0.5μ wide. The periphery of a granule is denser than the interior. The latter has the appearance of a network of filamentous elements. There is usually a cytoplasmic space surrounding each granule, but no limiting membrane lining the space has been observed. Mast granules have not been found extracellularly. Spaces with no granules appear in the cytoplasm, and since granules are found predominantly at the cell periphery, it is possible that they are extruded from the cell. Mitochondria, both rounded and rod-shaped, were observed and the Golgi apparatus appeared as a well organized system of closely packed membranes in an oval configuration. Very little endoplasmic reticulum with attached cytoplasmic particles was found. All of these features are consistent with the appearances to be expected in a cell actively engaged in secretion.—O. P. J.


The number of mast cells in peritoneal fluid of rats is quite high, and since they are a source of heparin perhaps this eventually makes its way into the circulatory system. In order to test this theory, loops of intestine in 85 normal rats were exposed and the location of mast cells in their areas of mesentery was plotted. The mesentery was returned to the peritoneal cavity and the abdominal wall sutured. One, two, and three days later these areas were relocated and the "marked" areas studied for lost and new mast cells. The average value for three days showed that 66 per cent of its original cells were lost. The reappearance of normal peritoneal mast cells following their destruction or degranulation after treatment with compound 48-80 was complete after injection. The concentration of heparin or heparin-like compounds in whole peritoneal fluid and in blood serum was determined by a method depending upon the sulfur content of a benzidine-sulfate-heparin-complex. In all experiments, the peritoneal fluid showed, per unit weight of fluid, a markedly higher concentration of heparin or heparin-like substance than did the blood serum in a ratio of 9:1. These results justify the conclusion that mast cells leave the mesentery at a fairly rapid rate and that their presence in the peritoneal fluid offers a possible source of heparin available by absorption to the circulatory system.—O. P. J.

The occurrence of mast cells in the mouse vagina was studied after hysterectomy and bilateral oophorectomy. Growth induced by prolonged oestrogenic treatment was accompanied by a significant increase in the number of mast cells compared to untreated controls.—O. P. J.


Mast cells are found in varying numbers in the connective tissue of most regions of the body; the umbilical cord is no exception. The solubility of the granules of mast cells in fixatives containing water has long been argued, and in order to test this requirement, 120 umbilical cords from full-term infants were fixed in various solutions. The results of these studies indicate that nonaqueous fixative, basic lead acetate, nonaqueous solutions of metachromatic dye, and the use of hyaluronidase are unnecessary. Instead, the critical factors were found to be a dilute solution of dye and relatively short staining period.—O. P. J.


The importance of taking exact measurements of the cell sizes in the blood and the bone marrow is pointed out as a diagnostic procedure in disorders accompanied by an increase in plasma cells. In bone marrow films the mean diameter of the plasma cells and their nuclei was determined. The mean nucleus-cell-ratio was calculated. The intensity of the coloration of the cytoplasm after equal staining of the films was used as an additional diagnostic mean.—H. H.


In order to understand the pathogenesis of the virus-induced leukemias and to ascertain which part of the cell is most directly engaged, it is essential to find out the localization of the virus in the cell. Both the nucleus and the cytoplasm of the leukemia cell show characteristic cytological and cytochemical changes as compared with normal blood cells. In the process of separating the cytoplasm and the nucleus it is impossible to exclude contamination of one fraction with the other. The present paper describes a separation procedure yielding a relatively pure cytoplasmic fraction of the leukemia cell. Since the virus can be identified and assayed only by its capacity to induce leukemia, animal inoculation must be used for this purpose. The present experiments seem to indicate that the virus of a fully developed leukemia cell is mainly located in the cytoplasm. The erythroleukotic cytoplasm is especially rich in ribonucleotides, and if the cytoplasm is further divided on a silica column no greater loss of virus takes place. The activity seems to follow the ribonucleotide fraction very closely, which further suggests an intracytoplasmic localization.—O. P. J.


In previous studies on the hemolymph of higher Diptera, most of the work has been on the function of hemocytes rather than the morphology. Most investigators found two main kinds of hemocytes and some described four kinds. In the present study the hemocytes are described and classified as they appear under the phase microscope in unfixed wet mounts and in sectioned or smeared stained material from representative stages of the life cycle. The hemocytes were roughly classified into four categories: prohemocytes, plasmatocytes, granular hemocytes and spherule cells. There are two well known functions of insect hemocytes — phagocytosis and synthesis of tyrosinase.—O. P. J.
COMPLICATIONS OF THERAPY


Carbutamide (BZ55) has recently undergone extensive trial as a drug that might be given by mouth for the treatment of diabetes mellitus. It has been shown in a few instances to cause leukopenia, and now it is reported to be liable to cause thrombocytopenic purpura and possibly increased capillary fragility. Our knowledge of the platelet count in diabetes is inadequate, so this was investigated. Of 72 diabetic patients not receiving carbutamide, 12 had low platelet counts (130,000 to 200,000 per cu. mm.). Published reports suggest that increased capillary fragility (positive pressure method) might occur in half the cases here investigated.

The majority of the 40 patients treated with carbutamide were middle-aged or elderly women with mild diabetes of some years' standing. The dosage was 1.5 Gm. per day for seven days and 0.5 to 1.5 Gm. daily thereafter. No important changes occurred in the hemoglobin or red cell levels in any patients. In many instances there was a substantial fall in the white cell count soon after carbutamide therapy was instituted, but in all cases except one the count rose again as treatment was continued. Otherwise the main general feature was that several patients developed depression of the platelet count, but this was not marked and took time to appear. Individuals showing more serious effects were as follows:

A 51-year old woman developed persistent vaginal bleeding after 15 weeks of treatment. Her platelets fell from 320,000 to 180,000 and Tourniquet test was positive.

A 71-year old woman, whose platelet count was 190,00 before treatment, developed neutropenia and petechiae. The marrow was fatty but myelocytes were plentiful. Tolbutamide was given in place of carbutamide, and extensive purpura developed without leukopenia.

A 64-year old woman with an initial low platelet count developed thrombocytopenia and was found to have marrow aplasia.

A 68-year old woman developed thrombocytopenic purpura which cleared rapidly when carbutamide treatment was stopped and recurred when it was started again. Tolbutamide also depressed the platelet count.

In all cases, cessation of carbutamide treatment cured the abnormality. Carbutamide patch tests were negative in the eight instances in which they were tried, including the above patients. Platelet agglutinins were not found.

Possibly a weakly antigenic carbutamide platelet complex occurs and most patients can maintain the level of circulating platelets by an increase in production, but in others this is not possible. The destruction of platelets is probably peripheral. Carbutamide also probably accentuates the increased capillary fragility of diabetes itself. There is an antigenic similarity of capillary endothelium and platelets. Carbutamide is not a safe substitute for insulin in the routine control of diabetes.—R. H. G.


There have been reported seven cases of marrow depression with this antithyroid drug; two were fatal. Of 21 cases treated by the author with carbimazole, two had depression of polymorphs and one, a man aged 86, developed agranulocytosis and died. Nitrofurantoin was also being administered just before the leukopenia developed. The dosage of carbimazole was 30 mg. daily for 50 days.—R. H. G.

Case report in a 41-year old man. The toxic agent was contained in a fluid for work on wood, called progyl. It was identified as sodium pentachlorophenate. The contact with the toxic agent took place five months prior to admission. The first symptoms began three months later and were characterized by tiredness, dyspnea, vertigo and tinnitus. Marked anemia, prolonged bleeding time, positive tourniquet test, and subnormal platelet count were found in the laboratory examinations. The bone marrow was aplastic. A marked hemorrhagic syndrome appeared and the patient died four months later. No other cases due to the same toxic agent were found in the literature.—P. d. N.


An unusual situation is reported involving profound thrombocytopenia in a mother and newly born infant following the ingestion of 720 mg. of quinine within two hours prior to delivery. Bleeding began in the mother two hours after delivery and in the infant 22 hours after birth. Spontaneous and complete recovery occurred in both mother and infant. It is of interest that the mother had taken quinine 13 to 14 years previously without incident. In vitro studies suggested the presence of platelet agglutinins of maternal origin, active in systems involving quinine. The agglutination reactions in the mother’s serum were positive five months postpartum.—N. J. S.


A case of a 32-year old female patient is reported who was treated for agranulocytosis with ACTH and cortisone. The administration of the hormones induced a fast remission in the bone marrow and the peripheral blood. After four days of treatment a severe relapse was observed followed by the sudden death of the patient. On autopsy, multiple ulcerations of the gastrointestinal tract with perforations of the ileum were demonstrated. The effect and the complications of ACTH and cortisone therapy are discussed.—M. H. H.


Seven cases of aplastic anemia following the administration of chloramphenicol are described. Five had received more than one course, but two had only a single course. The first symptoms of a blood disease occurred within five to eight weeks of the termination of a course of chloramphenicol, a bleeding tendency usually being the first manifestation. Six cases were fatal and the seventh recovered after a prolonged illness and more than 90 blood transfusions.—G. C. de G.


A report is given of 44,770 transfusions to surgical patients of mixed dried (lyophilized) human blood plasma produced in Czechoslovakia. Altogether, 1.81 per cent of the patients presented any kind of reaction; the results obtained were satisfactory and were substantially better than those observed in nonsurgical patients.—M. N.