ABSTRACTS

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LEUKOCYTES


The thoracic duct lymph of rats contains an almost pure population of lymphocytes which can be sampled by an experimental fistula. Hence, this material is most suitable for the study of the survival of lymphocytes labeled with P³² in the desoxyribonucleic acid. The results indicate that the rat lymphocyte has a long life span—6 or more weeks. Additional experiments are now being undertaken to determine whether the β radiation from the P³² may have caused a significant effect upon the lymphocyte life span.—O. P. J.


Hydrocortisone increases both in vitro and in vivo the desoxyribonuclease activity of lymphoid tissues in rats. In contrast, desoxycorticosterone decreases the enzyme activity, but only in vivo. Changes in enzyme activity were associated with changes in the DNA content and the weight of the organs. Desoxycorticosterone at certain concentrations lessens the desoxyribonuclease-activating effect of hydrocortisone.—S. R. H.


Using the slide method, the influence of surgical trauma and muscular exercise on active motility of human leukocytes and on the absolute number of neutrophils was studied. A rise in leukocyte motility occurs immediately after operation or after strenuous muscular work. One week after operation the motility of leukocytes returned to original values. A positive linear correlation between the motility of leukocytes and the absolute number of neutrophils was found. The increase in leukocyte motility in man is a part of the alarm reaction.—L. D.

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Using the slide method, the authors observed leukocyte motility at a temperature of 37 C. and compared it with motility at 30 C. and 40 C. They found that at 30 C. the ameboid activity of the leukocytes was significantly decreased. At higher temperatures (40 C.) the motility of the leukocytes in the first hours of incubations was significantly increased.—L. D.

ENDOCRINE INFLUENCES ON THE OSMOTIC FRAGILITY OF LEUKOCYTES. V. Schreiber, L. Kučera, J. Kučerová and V. Kmentová. From the Third Medical Clinic, Charles University, Prague, Czechoslovakia. Cas.lék.čes. 96:1299–1302, 1957.

The authors described a simple and reliable modification of the method of Storti and Pederzini for the determination of the osmotic fragility of leukocytes in peripheral blood. The method can be used in a simply equipped laboratory. Cortisone increases osmotic fragility in human mononuclear cells; methylthiouracil decreases the fragility of granulocytes and mononuclear cells, and thyroid hormone increases the fragility of granulocytes in the rat.—L. D.


A method is described for detection of antibodies by a complement consumption test. To make the reaction more sensitive, tanned leukocytes are employed. It will probably be possible to use this method for detection of antibodies against thrombocytes and erythrocytes, and to estimate tissue antibodies.—L. D.


Colloidal solutions and suspensions, given intravenously, induce leukopenia in rabbits, followed by leukocytosis. These reactions are mainly due to the changes in the number of the pseudo-eosinophils, but lymphocytes are also involved. Red cell counts and the blood volume remain unchanged. The leukopenia and leukocytosis observed are not due to changes in the distribution of the blood cells, cannot be abolished by antihistamine drugs and can be transmitted through the serum of the rabbits.—S. B. H.


Sixteen patients, all from one hospital, developed agranulocytosis following administration of chlorpromazine. Granulocytopenia seemed to be of gradual onset and usually followed prolonged treatment with a large cumulative dose of chlorpromazine. Routine blood counts were useful in detecting serious granulocytopenia before overwhelming infection had occurred.

At the height of leukopenia the patients’ bone marrows showed a highly selective aplasia of the cells of the granulocytic series. Extensive immunologic studies on all patients failed to show evidence of antileukocyte antibodies. It is likely that individual biochemical idiosyncrasies play a role in the development of chlorpromazine agranulocytosis. There was no evidence to support an immunological mechanism as the pathogenetic factor.

Adrenal corticosteroids had no demonstrable value in treatment.
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Most cases of chlorpromazine agranulocytosis have occurred in women and in the mentally ill.—T. E. B.

RETICULOSSES AND EXPERIMENTALLY INDUCED RETICULOSSES DUE TO STORAGE OF METHYLCELLULOSE. S. Benkő. From the Department of Medicine, Medical University, Szeged, Hungary. Acta Med.Hung. 12:115–137, 1958.

Reticulosis associated with dysproteinemia and hemolysis was induced in rats by means of methylcellulose injected intraperitoneally twice a week for 4 to 5 weeks. The author claims this to be a good reproduction of the reticuloses in human pathology.—S. R. H.


A case of splenomegaly in a man aged 61 is described. There was storage within the spleen of both phospholipids and glycolipids, and there were multiple angiomata and thrombocytopenic purpura. It is possible that the association between the angiomata and the accumulation of lipid were aspects of a common failure of splenic development. The lipidosis failed to conform chemically with any of the usually recognized types.—O. P. J.


Patients exposed to strong light (100 Watts from a distance of 1.5 feet) developed marked eosinopenia. Red, green and blue lights were found to produce the same effect.—S. R. H.


Recent interest in the experimental production of atherosclerosis and the possible relation of tissue mast cells to the pathogenesis of this disease has made it necessary to quantify the distribution of mast cells. Before doing this, it is necessary to know what influence time after death, temperature prior to fixation and length of fixation of the tissues have upon the mast cell population. The authors did not find significant changes in the number of these cells due to these things under the conditions of their experiments. Mast cell counts, representing the number of cells present during life, may be done on refrigerated human tissues which have been fixed in formalin within 24 hours of death.—O. P. J.


The authors injected into AkR and C3H mice, within 24 hours after birth, a nucleic acid extract of AkR leukemic cells. Seven animals, of 51 which received the extract, developed malignant tumors, often multiple (epithelial tumors of the parotids, mammary carcinomas, subcutaneous sarcomas, leukemias).

The authors did not observe such tumors among the other animals. Controls given nucleic acids from veal thymus or pneumococci did not develop any similar tumor. It would be tempting to conclude that the nucleic acid extracted from AkR leukemic tissues has a carcinogenic power for isologous or homologous mice, provided these have a certain degree of tissue compatibility with the donors.—G. M.

When an acellular extract of leukemic tissues from Ak mice is injected into newborn C3H animals, there are produced C3H type leukemias and, less commonly, tumors of the parotid glands (L. Gross. Proc.Soc.Exper.Biol.& Med. 76:27, 1951). The injection of this same extract into Ak newborn mice increases the occurrence of leukemia, shortens the latent period and induces salivary tumors in some animals. When administered to Ak mice, extracts of grafted Ak lymphosarcoma prepared with a solution of sucrose in water provoke the formation of sarcomas and various epithelial tumors (R. Rogel and G. Rudali: Bull. Cancer. 44:483, 1958.

This paper refers to an extract of Ak leukemic tissues obtained from several cases of spontaneous leukemia and kept for a month at -20 C. Injected into AkR newborn animals of the same brood, this extract has induced the development of multiple cancers of several types and in various sites.—G. M.


It is well known that extracts of Ak leukemic tissues made with water or saline contain a leukemogenic factor. But if the extracts are made with a very concentrated solution of sucrose, one obtains in Ak mice injected at the moment of birth with these extracts, besides the expected leukemias, multiple epithelial tumors occurring at the same time in a given animal. These include salivary tumors, mammary carcinomas and lung adenocarcinomas. However most of the animals treated with the saccharose extracts remain normal.—G. M.


Preliminary results of an electron microscope study of a leukemia of the mouse transmissible by cell-free filtrates are reported. In 12 of 47 specimens examined, virus-like particles were observed. So far, these particles have not been observed in control, non-leukemic animals. They are located inside the cytoplasm of leukemic cells which infiltrate the spleen or the liver. Their diameter is approximately 78 mµ. Their resemblance to other particles recently described in different mouse tumors is stressed. Three possibilities must be considered in seeking the general physiopathologic meaning of the virus-like particles in leukemic material: (1) the particle is a contaminant, (2) the particle is a normal cell component, and (3) the particle is the etiologic infective factor. If the latter is true, then the similarity of the particles observed in the leukemia to those previously described in other mouse tumors must be stressed. A great deal of work is still necessary to clarify the relationship of these particles to one another.—O. P. J.


This study deals with the electron microscopic examination of 47 cases of fowl erythroblasticosis and of numerous normal controls. In the leukemic chickens, virus particles, approximately 80 mµ in diameter, were demonstrated in the bone marrow in 37 cases and in the spleen in 21 cases. In cases of advanced leukemia, in which a high percentage of paraerythroblastic cells were found in the hematopoietic tissue, 90 per cent of the animals were positive. The virus particles were found either in the intercellular spaces or in intracytoplasmic vacuoles of reticulum cells, macrophages or paraerythroblasts. A peculiar process of budding from the cell membrane, possibly related to virus formation, was demonstrated. Virus particles, intact or partly disintegrated, were found in the plasma of the leukemic chickens. The particles were morphologically identical to those demonstrated...
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in other neoplastic diseases of the chicken. They were also demonstrated in the tissues of 12.5 per cent of the control cases considered to be normal. Avian tumors in general and erythroblastosis in particular show the existence of only a morphologic family of virus particles in the neoplastic tissues of the chicken. The electron microscope is not able, at this time, to distinguish one from the other, and the proof of their specific action in a given neoplasm is brought out only by biologic experimentation. Moreover, the existence in normal tissues of particles morphologically identical to those which in certain circumstances release a cancerous process is of the highest theoretical interest.—O. P. J.


Experiments on transmission of C57 Black mouse irradiation leukemia in the 51st passage to young Wistar A rats on standard diet are reported. The mortality rate of the process as well as the pathologic changes, including hematologic, cytologic, histopathologic and roentgenologic observations, are given. The recorded changes are in accordance with criteria established for the hematoblastic process in a laboratory animal. The inoculated rats were observed for 10 to 11 months, with the exception of the third passage, for which the period of observation lasted 4 months.—L. D.

II. REACTIVE AND PATHOLOGICAL CHANGES IN RATS AFTER INOCULATION WITH HUMAN LEUKEMIA. Ibid. 4:100–112, 1957.

Hematologic, cytologic and histologic observations of pathologic changes, occurring as a result of experimental transmission of leukemia from man to rats, are described. In one group of experiments human leukemia was transmitted by means of instillation of whole cells or isolated cell particles into the embryos of pregnant rats. Descendants of the rats of both sexes which had previously been inoculated with human leukemia (the “pathologic” litters) developed reticulosis, possibly by “verticle” transmission via the reproductive cells.—L. D.


In 1953, Kidd discovered that normal guinea pig serum, when administered intraperitoneally, brought about regression of the Gardner lymphosarcoma carried by C3H mice. Consequently, it would be of interest to determine whether the tumor inhibitory principle is peculiar to guinea pig serum or whether serum from other animals may also contain the substance. Results of the present study indicate that complete inhibition of tumor growth was obtained with guinea pig serum; slight or inconstant inhibition was demonstrated with sheep and human sera; and no inhibition was noted with rat, chicken, dog, bovine, horse, calf and rabbit sera, or with sheep or human plasma.—O. P. J.


The authors have treated the mouse leukemia 1210 with a combination (by diazotization) of Amethopterin and gamma globulins from hamsters to which that leukemia had been given by heterologous graft.

The activity of this combination is markedly higher than that of Amethopterin alone, or the gamma globulins alone, or the addition of the two without diazotization, or a combination of Amethopterin and gamma globulins from nonimmunized hamsters.
The combination destroys practically all leumkemmlic cells and has rendered possible one complete cure. Therefore, it seems likely that, according to the working hypothesis of the authors, the gamma globulins of hamsters immunized by the heterologous graft transport Amethopterin selectively into leukemic cells.—G. M.


One hundred patients with malignant disease have been treated with E39 (Dipropyloxy-2, 5 diethylene-imino-3,6 benzoquinone 1,4). Sixty-two had chronic malignant blood disease, and 38 had other kinds of neoplasm. A daily intravenous dose of 10 mg. was used and was generally well tolerated. After a total dose of about 200 mg. a fall in the leukocyte count often occurred; this was reversible, either by spacing the dosage, or by the addition of prednisone without altering the dose.

E39 offers an advance in the chemotherapeutic treatment of lympho- and reticulosarcoma and sarcomatosis (17 of 20 cases were sensitive), and in cases resistant to radiotherapy or previous chemotherapeutic agents. E39 was less frequently of benefit than previous agents in Hodgkin's disease. If it is of use in chronic lymphoid or myeloid leukemia, it probably should not replace either chloramllino-phenyl-butyrie acid or 1-4 dimethane-sulfonyl-oxy-butane.—G. M.

"SPONTANEOUS" REMISSION IN LEUKEMIA WITH PARTICULAR REFERENCE TO THE QUESTION OF ASSOCIATED INFECTION. J.T. Libáňsky. From the Institute for Hematology and Blood Transfusion, Prague, Czechoslovakia. Cas.lék.čes. 96:1092–1097, 1957.

The causes of so-called spontaneous remission in leukemia are discussed. It does not appear probable that these can be explained only by the effect of blood transfusion. Three cases are presented in which remission occurred simultaneously with an infectious process and similar cases from the literature are presented. The question is raised as to why only rare cases of associated infection lead to a marked improvement in the course of the leukemia, whereas the same stimulus in most patients leads to aggravation. The concept is advanced that the infectious agent probably modifies leukemia in a nonspecific manner so that the multiplying micro-organisms act as powerful antigenic stimulus, mobilizing mesenchymal tissue. This may influence the course of tissue maturation and, thus, the course of leukemic leukopoiesis. Much would depend on the host, its defense mechanisms, and on the stage of the leukemic process.—L. D.

BONE CHANGES IN CHRONIC LEUKEMIA IN ADULTS. V. Šolb. From the Radiological Clinic, Charles University, Prague, Czechoslovakia. Čsl.rentgenologie 11:100, 1957.

In contrast with the frequently found opinions in the literature concerning the incidence of bony changes in adult chronic leukemia, the author argues that small, detailed changes in the form of small translucencies may be recognized in this form of the disease in the region of the epiphysis or diaphysis of marrow bones, most easily seen in the metacarpals. The marrow cavity is enlarged and not evenly lined. The appearance of these changes may be due to lacunar resorption of bone from the pressure of leukemic marrow. These changes may be regularly found in chronic leukemia. They are not, however, pathognomonic. There are often, moreover, longitudinal translucencies in the tibial diaphysis.—L. D.


The serum level of vitamin B₁₂ was studied in 32 leukemic subjects (10 acute leukemias, 13 chronic leukemia myelosis and 9 chronic leukemic lymphoadenosis). The microbiologic test was used (Lactobacillus leichmanii 7830 ATCC). An increase of the vitamin B₁₂ serum level was observed in all types of leukemia, but it was statistically significant only
in chronic myeloid leukemia. The changes resulted both from the disease itself and from the possible presence of liver damage.—P. d. N.


Whole blood of patients suffering from acute leukemias was injected into the chorioallantoic membrane of chick embryos. This was followed by up to 18 passages onto other chick embryos. The allantoic fluid was then injected into mice, of which 20 per cent (28 of 136) developed leukemia within three to four months. Blood from normal people, treated in the same way, produced leukemia in only 3 per cent of mice (two of 72). The presence of a human leukemic factor is postulated.—J. J. B.


Dopan, 4-methyl-5-di(2 chlorethyl) aminouracyl, was given to 15 patients suffering from chronic myelogenous leukemia, in most of whom other forms of therapy were no longer effective. A remission of 7 to 10 months was obtained in seven. Others improved a little. Toxic symptoms, such as nausea and vomiting, were rare. Repeated courses were much less effective.—J. J. B.


The presence of the antibiotic in the diet in 1 to 3 per cent concentration did not produce any specific effect. With a concentration of 5 per cent in the diet, the animals developed profound leukopenia, while it took twice as long for similar change to appear in pair-fed controls. The incidence of death in animals fed chloramphenicol was found to be significantly higher than those fed the 'diamine' derivative or pair-fed.—J. B. C.


Myeloid leukemia, agranulocytosis and persistent leukopenia in a member of a family with hereditary neutropenia is described. A possible relationship between the development of leukemia and the familial benign leukocyte abnormality is discussed. The literature related to this subject is extensively reviewed.—B. R.


The authors describe two cases of congenital, transient neutropenia in newborn infants of neutropenic mothers. In one case neutropenia appeared to be due to the transplacental transmission of a neutropenic factor (demonstrated by both leukoagglutination in vitro and by a plasma transfusion experiment). The mechanism operating in the other case could not be identified despite very extensive and careful studies. The authors have observed two additional patients with immune neutropenia probably due to a demonstrable circulating leukoagglutinin, who have delivered normal children.—T. E. B.

Four patients suffering from severe agranulocytosis were treated with leukocyte suspensions. Within 24 hours young granulocytes appeared in the peripheral blood. Patients showed dramatic improvement during the next two or three days and all recovered. Antibiotics were also given, but alone they had no effect. In two cases previous ingestion of pyramidon was established. The recommended dose is 100 ml. of the suspension in one intravenous dose which may be repeated after a few days.—J. J. B.


Respiration of purified human leukocytes was investigated with the aid of Cartesian divers in presence of varying concentrations of erythrocytes. The leukocyte oxygen uptake was found to rise when red cells were added to the suspension. The positive effect of erythrocytes on leukocyte respiration was shown to be characterized by an insignificant initial rise in oxygen uptake intensity and subsequent pronounced extension of its duration. An optimum concentration of erythrocytes at which leukocyte respiration is most intensive is likely to exist.—E. K.


Total and differential white blood cell counts were determined repeatedly in 50 patients undergoing thoracotomy. The average of all peripheral white counts showed a rise from 9389/cu.mm. preoperatively to a maximum of 32,060/cu.mm. two hours after intubation had been performed. The leukocytosis is attributed to the combined effect of corticotrophin released by stress plus probable loss of the ability of the lung to act as a reservoir for the granulocytic series of cells.—T. E. B.


An increase in the adhesiveness of leukocytes is an established component of a variety of seemingly unrelated biologic phenomena. A detailed study was therefore made of nonantibody causes of leukocyte agglutination and of the inhibition of such nonspecific agglutination in vitro by heparin and by hydrocortisone.—T. E. B.


The complement fixation reaction with human sera and with a leukocyte antigen in chronic myeloid leukemia is described. The antigen was obtained by breaking leukocytes in an electrical hand-mill or with ultrasound waves. The antigen could be kept for several weeks frozen or in a lyophilized state. The accuracy of the reaction has been investigated in 44 sera derived from patients with various leukocytic diseases. Six sera gave a strongly positive result in the complement fixation reaction; all the sera also gave a strongly positive leukoagglutination reaction. Four sera yielded a weakly positive complement fixation reaction; one of them was strongly positive, one weakly positive, and two negative in the leukoagglutination reaction.

The remaining 34 sera were negative in both reactions. The specificity of reactions was checked on 472 sera from the syphilis laboratory. Five of them gave a weakly positive result, and the remaining ones a negative result. The authors are of the opinion that the reaction described by them may find practical application in the immunohematologic laboratories.—E. K.
HEMOSTASIS


When resin plasma is incubated at 28 C. with magnesium or manganese (final concentration about 0.02 M) for 30 to 40 minutes, and a suspension of fresh, carefully prepared, washed platelets is added, the platelets agglutinate within 15 seconds. Washing the platelets 10 times did not decrease activity. Frozen and thawed platelets or platelets heated to 60 C. did not agglutinate. Calcium could not be substituted for magnesium or manganese. Frozen plasma, plasma collected with citrate, oxalate or EDTA, BaSO₄ plasma and plasma from hemophilic dogs were active. Thrombin preparations had variable activity. Purified prothrombin preparations were inactive. Although fibrinogen preparations were active, so were serum and citrated plasma from which fibrinogen had been adsorbed. The plasma factor, called TAg (thrombocyte agglutinating factor), was inactivated by heating at 53 C., was nondialysable and was found in the globulin fraction. It appears to act independently of the coagulation process.—M. B. Z.


The patient under study had an unexplained thrombocytosis with platelet counts between 1.2 and 2 million per cu.mm. His serum potassium varied between 7 and 8 mEq. per liter. However, when serum obtained from platelet-poor plasma was allowed to clot, the serum potassium level was normal. Among a group of additional thrombocytemics, a few others also showed this phenomenon. Platelets of the propositus released some of their potassium when incubated in thrombin clotted plasma, but additional potassium was released when these platelets were subjected to repeated freezing and thawing. No demonstrable contribution of potassium could be attributed to erythrocytes, or to leukocytes. The possibility of formed elements contributing to serum potassium levels was also excluded. It is concluded that the blood platelet count must be considered in interpreting serum potassium levels.—T. H. S.

EVALUATION OF PULMONARY MEGAKARYOCYTES. J. G. Sharnoff and E. S. Kim. From Department of Pathology, Mount Vernon Hospital, Mount Vernon, N. Y. A.M.A. Arch. Path. 66:176-182, 1958.

The finding of megakaryocytes in the lung in no way negates the original observation by Wright that the bone marrow is a site for platelet formation. Lungs from humans of all ages and a wide variety of animals show that pulmonary megakaryocytes may be observed routinely. Histochemical procedures indicate that their cytoplasm is positive for polysaccharides. When epinephrine is administered to rabbits there is a striking disappearance of megakaryocytes from the lungs and a concomitant elevation of blood platelets. Megakaryocytes are apparently transported by means of the venous circulation from the bone marrow to the pulmonary capillary bed where, by filtering through the vessels and their anastomoses, they are broken up to form platelets.—O. P. J.

MISCELLANEOUS

The effect of intracardial heparin on the activity of esterase in rabbit serum was studied. There was no statistically significant change of activity after injection. This supports the idea that post-heparin esterase in humans is different from clearing factor, which develops in the rabbit after injection of heparin.—L. D.


Experiments carried out in rabbits showed that one to three hours after the intravenous injection of 10,000 to 15,000 U. of heparin (Heparin Novo), an increase occurred in the volume of the red cells (evaluated by the hematocrit method). In the control rabbits, on the other hand, from which blood was collected for examination at the same intervals, a decrease in volume took place. These changes are interpreted as an expression of non-specific stress and confirm the antagonism between the action of heparin and activation of the suprarenal glands in the course of general adaptation. Together with volume changes, there were also differences between the two groups as regards changes in the total number of red blood cells: a decrease in the heparin group and an increase in the control group.—L. D.


The authors have studied changes in the levels of Fe and Cu in serum, and the excretion of these metals after the administration of Na-Ca EDTA in a group of healthy individuals and a group of subjects with chronic lead poisoning. After injection, serum Fe and Cu increased to a maximum level in both groups from 4 to 5 hours later. The urinary excretion of both metals was the same in control and experimental groups. On the day of injection about 12-fold more Fe and four-fold more Cu appeared in the urine. With repeated administration Fe excretion decreased, suggesting exhaustion of body stores.—L. D.


This study is concerned with 26 macroglobulinemic sera and 7 isolated macroglobulins. The main protein abnormality is a considerable increase, without any immuno-chemical alteration, of a $\beta_2$-globulin, which is present only in very small quantities in normal serum; its molecular weight is probably very high, and this protein has been termed $\beta_2$-M-globulin by the authors.

The only immunochemical abnormalities which have been observed were those concerning $\alpha$-globulins that have been noticed in 10 out of 14 sera investigated. Those could account for the individual immunologic specificity of macroglobulins. The global pathologic specificity reported by some workers was not confirmed.

Isolated macroglobulins contained this $\beta_2$-M-globulin and most often normal $\gamma$-globulins.—G. M.