ERYTHROCYTES AND ERYTHROCYTIC DISEASE


The human red blood corpuscle was studied with bright- and darkfield microscopy in the untreated and treated condition. There is considerable evidence to indicate that there is a plasma membrane, which remains intact even after hemolysis occurs. This membrane contains certain acetone and alcohol extractable lipids which, according to the author, are demonstrable with Sudan black after saturation of the unsaturated bonds. Ralph has confirmed a previous observation (Cowdry, N. H.: Biol. Bull. 32: 196, 1917) that mitochondria may be present in immature erythrocytes which he has unfortunately referred to as primitive erythrocytes.

After cells had been exposed to neutral red for 15-30 minutes, some of them developed refractive globules which were designated as the 'A' granule. The ability of the red blood corpuscle to segregate basic dyes in newly formed vacuoles was first studied by Israel and Pappenheim (Virchows Arch. 143: 419, 1896) and has been investigated recently by Dustin (Bull. Acad. Belg. Cl. Sci. 28: 230, 1942). These, along with reticulation, mitochondria and the vacuole, are signs of immaturity.

O. P. J.


Before red blood corpuscles are hemolyzed there is a loss of potassium with a replacement by sodium derived from the media in which the cells are suspended. When red blood corpuscles were suspended in certain alcoholic solutions it was possible to study large losses of potassium, since the amount of lysis was unusually small. As much as 50 per cent of the potassium may be lost from a cell without greatly affecting the disk-sphere transformation and resistance to osmotic hemolysis.

O. P. J.


The problem analyzed and discussed in this paper concerns what happens to the internal composition, the pH, the ionization of hemoglobin, and water content of erythrocytes, if they are placed in a medium containing known quantities of penetrating and nonpenetrating anions, cations, neutral molecules and ionized and nonionized proteins.

O. P. J.


The authors study the action of several substances: aesculoside, rutinoside, d-epicatechine (which are supposed to possess vitamin P activity) on guinea pigs red cells twice washed with saline. They use a
colorimetric method of measuring the hemolysis and express the results in percentage of the total hemolysis. Rutoside has a very poor solubility in water and it is impossible to obtain a concentration higher than 1.3 per cent. Aesculoside and d-epicatechine are very soluble and higher concentrations were studied. These three substances appear to increase the globular resistance to hypotonic solutions. This action is not stronger with large concentrations than with the very dilute solutions first tested (less than 1.3 per cent for the rutoside). Among the three, the d-epicatechine seems to be the more active: as small doses as 2.5 per cent definitely increase the globular resistance. Although the authors do not discuss the specificity of this in vivo antihemolytic activity (physical interferences, or pH), these experiments seem worthwhile reporting; any new method of testing the activity of the so-called vitamin P (here, by modifications of the cellular permeability of the red cell) is welcome, since the usual tests for capillary permeability (or resistance) are far from being satisfactory.

J. P. S.


The three major factors which may contribute to modifying hematologic values on the Witwatersrand are the 6,000 foot elevation, the unclouded skies and the general occupation of deep level mining. The results were obtained by examining blood from 100 males and 50 females who were robust and healthy adults, usually between the ages of 20 and 40 years. Medical students were considered unsatisfactory for such studies. There was an erythrocytosis, increased amount of hemoglobin and a slightly elevated color index. Erythrocytes were slightly smaller in diameter and surface area than those from Europeans living at sea level. Leukocyte level was unaltered. Three hundred cases of macrocytic anemia were analyzed statistically. In view of the high normal counts, a large number of patients would be relieved of their symptoms if they were not treated before they had fewer than 4.0 million erythrocytes.

O. P. J.


This study deals with the non-mining population, mostly members of Reef Benefit Society Panels, residing on the Witwatersrand in the vicinity of Johannesburg at an elevation of approximately 6,000 feet. From a potential reservoir of 50,000 individuals, 300 persons (0.6 per cent) were found to have abnormalities of the erythrocyte in the direction of macrocytosis and hyperchromatosis. In this area, 6.0 million cells per cu. mm. and 20.0 grams of hemoglobin per 100 cc. of blood are considered average normal values. The mean values for the cases included in the author’s series were as follows: erythrocyte count 4.04 million, hemoglobin 18.3 grams, color index 1.37, erythrocyte diameter 7.8 microns, and erythrocyte surface area 102 square microns. The range of the red cell counts in this group was from 1.0 to 7.0 millions. Considerable emphasis is placed upon the hemoglobin surface concentration index which is a measure of the breathing surface of the blood and is calculated by the formula:

\[ \text{H.S.C.I.} = \frac{\text{color index}}{\text{mean erythrocyte surface area}} \times 100. \]

In the group of cases under consideration, the mean H.S.C.I. was 0.86 compared with the normal mean of 1.57, and this is taken as a measure of the lack of physiologic efficiency of the macrocytes. Anisocytosis was regularly present and often marked, while poikilocytosis was less commonly noted (in contrast to pernicious anemia).

Although response to parenteral liver therapy was very good, no conclusions could be drawn as to pathogenesis or epidemiologic factors. The possible roles of constitutional defects, endocrinopathies and urinary infections are discussed. It is suggested that if certain constitutional types fail to achieve adequate adaptation to high altitudes, hypofunction of hemopoietic tissues may be one result.

L. E. Y.

FAMILIAL HYPOPLASTIC ANAEMIA OF CHILDHOOD. REPORT OF EIGHT CASES IN TWO FAMILIES WITH BENEFICIAL EFFECT OF SPLENECTOMY IN ONE CASE. S. Estren and W. Dameshek. From the Blood Labora-
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This report is concerned with the first recorded instances in which hypoplasia of the marrow has been noted as the sole familial trait. It is pointed out that the closest similar cases in the literature are those of Fanconi, in which hypoplasia of the marrow was one of a number of congenital and familial abnormalities.

Three of 7 siblings in one family and 3 of 14 in another family had apparently identical disorders characterized by peripheral pancytopenia, pallor, weakness, and bleeding tendency. In the 2 cases in which the marrow was examined, there was quantitative hypoplasia of all elements, but the proportions of erythroid cells were somewhat higher than normal. In one of the cases splenectomy resulted in cessation of the hemorrhagic tendency together with some increase in red cells and leukocytes and a more marked increase in platelets. The spleen was not enlarged and showed no abnormalities.

It is the opinion of the authors that in cases of complete or almost complete aplasia of the marrow, and in cases in which a reduction of platelets is accompanied by a reduction of megakaryocytes in the marrow, splenectomy will probably be of little value. When megakaryocytes are present to some degree in the marrow, however, and particularly when lack of platelet production in the megakaryocytes can be demonstrated, and when, in addition, erythroid elements show some evidence of regenerative activity, splenectomy is deemed worthy of consideration. It is suggested that extirpation of a normal spleen under such circumstances removes the regulatory (inhibitory, ?humoral) effect on red cells, granulocytes and platelets in the marrow.


Idiopathic methemoglobinemia was studied in a girl aged 2.5 years who had had a dusky cyanotic hue of the face, hands, lips, ears and fingernails for as long as she could remember. Total hemoglobin was 17.0 Gm. per 100 ml. Oxygen carrying hemoglobin was 10.8 Gm. per 100 ml. The 36 per cent difference consisted of 6.2 Gm. of methemoglobin. Plasma ascorbic acid concentration was low. The optimum amount of ascorbic acid was between 2.00 and 300 mg. per day. Under such therapy the oxygen capacity of the blood rose and cyanosis lessened in three days and the latter disappeared within a week. Similar results were obtained with methylene blue. When treatment was discontinued there was a gradual return to the previous status. In vitro studies indicate a probable defect in the erythrocyte enzyme system.


Properly controlled blood studies were made on men and women from 60 to 100 years old. Red cell, hematocrit, mean corpuscular volume, color index and white counts showed completely normal values, with the usual sex difference. These data, in agreement with other reports, indicate the pathologic importance of any degree of anemia in old age.

BLOOD GROUPS, THE Rh FACTOR AND BLOOD TRANSFUSIONS


The author points out that with the advent of more detailed knowledge of the pathogenesis and treatment of erythroblastosis fetalis, interest is being focused on possible untoward effects of therapy that may result in a live but helpless infant with kernicterus. Wiener's hypothesis regarding the pathogenesis of kernicterus is cited. According to this concept, agglutinated red cells plug the capillaries of the brain,
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cauing anoxemia. Ganglion cells, being most easily injured by lack of oxygen, die and are then stained by bilirubin.

Follow-up records of 35 cases of erythroblastosis were reviewed. All patients included in the series had neonatal jaundice or anemia and were Rh positive children born of Rh negative mothers. In the 6 fatal cases no correlation could be shown between severity and extent of clinical manifestations of neurologic involvement and the findings on pathologic examination; only 2 of the 6 showed kernicterus. Of the 29 living children, 4 showed neurologic signs attributed to kernicterus, but in only 1 of these patients was involvement of the central nervous system noted during the neonatal period. These figures are compared with those reported by other observers.

L. E. Y.


There is in the Poitou district of France, a disease, well studied by Sausseau, which affects 8 per cent of new-born mules. It is an acute hemolytic jaundice with hemoglobinuria appearing within a few hours after birth and usually terminating in death. Following the time a mare gave birth to a jaundiced mule, all its offspring will die of icterus gravis. But if this mare is covered by a stallion, the colt will always be healthy. These features, so similar to the hemolytic disease of the human new-born, caught the attention of Caroli and Bessis, and these authors sought for a heteroimmunisation of the mare covered by an ass.

The hematologic examination of the new-born mule with hemolytic jaundice, shows a striking auto-agglutination of the red cells, spindle-shaped red cells, microspherocytosis. The anatomic findings are the same as those found in rats treated by hemolytic serum: Dilation of the hepatic sinus, generalized pigmentar infiltration, but no hydrops foetalis and no kernicterus, as often seen in the human new-born disease. The serologic study shows a very high titer of antibodies against the ass and mule red cells in the sera of the diseased mare, while the other mares have only a few or no antibodies. The antibodies often are incomplete (blocking antibodies). Intravenous injections of an ass blood to the mare increases the titer of the antibodies much more in the immunized mares than in the others.

The authors compare this mule disease to experimental hemolytic jaundice, and to the human hemolytic disease: the mule disease is very close to the experimental disease of the rat and differs from the human disease only by the lack of cytotoxic lesions (cirrhosis, nervous lesions). The parasitic etiology, first considered, is eliminated by these immunologic findings concerning the prophylaxis and therapeutics of the Poitou mule disease, which findings may prove of considerable importance to cattle breeders. The study of this animal disease can also lead to a better understanding of the human hemolytic disease of the new-born.

J. P. S.


The author presents a well-organized summary of the present status of the Rh-Hr system with particular reference to inheritance and isoimmunization. Readers who are relatively unacquainted with the voluminous and confusing literature in this field will find this review helpful. Some authorities would disagree with the rather firm recommendation that early induction of labor be considered when the mother's serum contains a high titer of blocking antibodies.

L. E. Y.


The author reviews the literature favoring direct blood transfusion against the citrated method. Reactions and “shock” are rare with the former method. He used the metallic apparatus devised by Luis de Marval and the cannula of E. F. Fischietto.

In 20 cases studied, using both the direct and the citrate methods, there were no reactions with the former, and four post-transfusion reactions with the latter. Blood clotting time was definitely
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diminished in all cases where the direct method was used, and in only 4 of 10 cases where the citrate method was used.

The direct method is, according to the author, the method of choice, whenever blood coagulation time should be shortened preoperatively. It is indicated especially in neurosurgery, in hemophilia, anemias, and hepatic insufficiency.

The transfusion should be made twenty-four hours before operation.

R. M. S.

LOSS OF VIRULENCE OF TREPONEMA PALLIDUM DURING PROCESSING OF DRIED BLOOD SERUM. T. F. Probey.


A saline suspension of treponemes of the Nichols strain was prepared from rabbit testicles and mixed with normal horse serum. A portion of the mixture was then used for immediate inoculation into control rabbits and the remainder frozen under vacuum in a bath of carbon dioxide and cellusolve for thirty minutes. Drying of the frozen material was then continued under vacuum for twenty hours with the ampules exposed to room temperature, a procedure which had previously been shown to reduce moisture content to less than 1 per cent. One group of rabbits was inoculated with restored dried material soon after completion of the drying cycle, and a second group was inoculated two days later. Dark-field examination of the resuspended material showed some atypical forms of what appeared to be nonmotile treponemes.

All 5 of the control rabbits developed syphilitic lesions within forty-two days, while none of the 6 rabbits inoculated with processed material developed evidence of syphilis during the observation period of one hundred and forty days. Three successive subtransfers observed for thirteen, seven, and 9 months respectively also remained negative.

These observations confirm the results of Turner, Bauer, and Kluth, and offer somewhat more conclusive evidence that the danger of transmitting syphilis is eliminated by proper freezing and drying of plasma or serum. The author points out that Turner has demonstrated that motility and virulence of T. pallidum are not altered appreciably by freezing at -78°C. and maintenance of this temperature for at least one year. Turner has also showed that freezing at -10°C. or -20°C. does not adversely affect treponemes, but that maintenance at these temperatures for two months causes their death. The practical importance of these studies is obvious.

L. E. Y.

HEMOGLOBINURIA


Hemoglobin solutions containing stroma were injected intraperitoneally in single doses into 37 rats (5 to 7 Gm./Kg.) and 16 guinea pigs (1 to 3.5 Gm./Kg.) which had been fed and offered water up to the time of injection. Microscopic examination of the kidneys following this procedure revealed an occasional cast in only 2 rats. Sections from the remaining 35 rats and from the 16 guinea pigs showed no casts or tubular changes.

Water was withheld from 16 rabbits for periods of one to five days after which stroma-free hemoglobin solutions were injected intravenously at one time or in divided doses on successive days toward the end of the dehydration period. Water was then withheld for a period of eighteen to 14 hours after the last injection. Thereafter varying amounts of water were given daily for one week. The quantity of hemoglobin injected varied from a single dose of 1.3 Gm./Kg. to 2.8 Gm./Kg. in eight divided doses on two consecutive days. In the 3 rabbits dying prior to the fourth day following hemoglobin injection, the kidneys were congested and a reddish yellow substance of homogeneous glasslike consistency was observed in the tubular lumina. These collections were not considered to represent formed casts. In 12 of 13 rabbits examined from four to forty days after hemoglobin injection, characteristic pigmented casts and associated tubular dilatation were demonstrated. Minimal necrosis of tubular epithelium in 5 of 13 rabbits was thought to have followed, rather than preceded, the plugging of tubules by casts. Lesions in other organs were of no particular significance.
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It is emphasized that consistent reproduction of hemoglobinuric nephrosis has not been previously accomplished without preliminary direct trauma to the kidneys, and that there is need for studying the role of dehydration in other species, particularly man. It should be pointed out that urinary pH was not controlled in this study, and that the hydrated control animals were rats and guinea pigs rather than rabbits.

L. E. Y.

FOLIC ACID


This monograph, comprising a series of thirteen articles by various authors on pteroylglutamic (folic) acid, covers in detail its chemistry, synthesis, pharmacology, physiology, and clinical applications. Published in 1946, it brings together theoretic and clinical investigations available up to the middle of that year. Much of the material has since been recorded in reviews and individual articles elsewhere, especially the description of the synthesis of pteroylglutamic acid and the observations on the patients in the clinic.

It is of interest that the mode of action of folic acid and the absence of marked activity of conjugated forms, are yet controversial. Heinle and Welch (pp. 343-346) note the failure of other components of the vitamin B complex, and of biotin, paraaminobenzoic acid, choline, and inositol, to augment the effect of pteroylglutamic acid. The yeast conjugate, they found, was not utilized by human beings; although more recent findings suggest that, in sufficiently large doses, yeast-conjugate is effective (Spies, Experiments with Folic Acid, New York, Interscience Publishers 1947, p. 101). Nor is conjugated folic acid the “extrinsic factor” of hematopoiesis. The exact role of folic acid is today, as a year ago, still obscure.

This is a valuable and complete collection of observations on pteroylglutamic acid as of May 1946.

S. E.


In a lecture given at Clínica Pila in Ponce, Puerto Rico, the author gave the results obtained in 4 cases of sprue treated with conjugated forms of folic acid. Fermentation folic acid in daily doses, equivalent to 3.1 mg. of folic acid administered intramuscularly, was used in 2 cases; Bc conjugate in daily oral doses of 7 cc., equivalent to 8.4 mg. of folic acid, in one case; and another case of sprue was treated with 2. G in daily oral doses of 20 mg.

Both cases treated with fermentation folic acid showed, not only clinical and hematologic improvement, but also an increased urinary output of free folic acid.

The case treated with Bc conjugate showed a striking clinical and hematologic response, but only a slight urinary elimination of free folic acid, and the case treated with 2. G failed to show definite improvement.

As already reported by Suárez, Welch et al., the urinary output of free folic acid increased when concentrated liver extract was added.

It is stated that the mechanism of action of free folic acid, and of its conjugated forms, is unknown, but that it is definitely established that folic acid is not the intrinsic factor of Castle. It may be that folic acid is somehow related to the extrinsic factor, but until more is known about the biochemistry of the antianemic compounds, premature speculations should be avoided.

R. M. S.


The administration of methyl-folic acid to one patient with sprue and one with pernicious anemia was followed by no changes in the peripheral blood, the bone marrow, or the clinical course of the patient. Administration of ordinary folic acid, on the other hand, was followed by a prompt improvement.

The authors argue from this that the particular chemical configuration known as folic acid is highly specific in its effect on erythropoiesis. It would have been of interest to have included sufficient details.
concerning the patients to note whether they became worse, since methylfolic acid has actions antagonistic to folic acid, i.e., it is an "anti-folic acid material." (Arch. Biochem. 12: 318, 1947.) Alterations in the glutamic acid portion of the folic acid molecule do not qualitatively affect its activity, since the triglutamyl and heptaglutamyl compounds corresponding to pteroylglutamic acid are both antianemic. Methylfolic acid consists of an alteration in the pteridine portion of the molecule, and antagonizes the action of folic acid. The significance of this chemical alteration, and the uses of antifolic acid compounds, are yet to be determined.

S. E.


During the course of studies on the antianemic activities of pteroylglutamic (folic) acid, a number of related compounds were tested for their possible similar action. Pteroylglutamic acid itself, and pteroyltriglutamic acid (the fermentation factor, also written pteroyl-diglutamyl glutamic acid) were found to have similar actions in pernicious and related anemias. Pteroyl-heptaglutamic acid (also called pteroyl-hexaglutamyl-glutamic acid; the B0 conjugate material) was also found to give a good response, contradicting in this regard previous findings by Bethell (Univ. Mich. Hosp. Bull. 12: 42, 1940) and Heinle (Proc. Centr. Soc. Clin. Res. 19: 27, 1946), who had found the heptaglutamic compound to have no effect. According to Spies, this difference is probably a matter of dosage: the body is able to release folic acid from the heptaglutamic compound only in small amounts, but if sufficiently large doses of the compound are given, a good antianemic effect is obtained.

In contrast, there was no antianemic effect from pteroic acid, glutamic acid, or xanthopterin, all chemically related to folic acid.

S. E.


Materials which are chemically related but physiologically antagonistic to certain substances have recently become important as "displacing agents" or "anti-" substances (paraaminobenzoic acid for sulfanilamide; methylfolic acid for folic acid; antivitamins). The present report deals with the changes produced in lymphoid and hematopoietic tissues by two antipyridoxine substances, desoxypyridoxine and methoxypyridoxine.

Interesting findings, produced alike by pyridoxine deficiency and by administration of antipyridoxine compounds, included a reduction in the bulk of the spleen due to hypoplasia of the lymphoid elements. In some species of experimental animals, atrophy of the thymus and the lymph nodes was also present. Concomitant with these abnormalities occurred the development of a microcytic hypochromic anemia, leukopenia, and lymphocytopenia: and reduction in the erythroid and myeloid elements of the bone marrow.

An important finding in the adrenal glands consisted of a depletion in the lipid content, with an enlargement of the adrenals. The authors, therefore, speculate—since a relationship between adrenal cortex and lymphopoiesis has been suggested—whether the lymphoid atrophy might be the result of adrenal stimulation rather than the result of a direct action of the antipyridoxines. This question has not yet been answered.

Not all findings were present in all species of animals studied. Variations in species response and doubt as to manner of action make it difficult to attempt to translate these results to human experience.

S. E.

Leucocytic Disease

Twelve cases of leukopenia following arsenical therapy are reported. In 7 there was complete absence of polymorphonuclear leucocytes in the peripheral blood and the remainder varied between 5 and 15 per cent. All patients were febrile and 10 showed agranulocytic angina. Treatment consisted of injections of BAL in peanut oil 2.5 mg/kilo every four hours for the first two days, then 1-2 times a day for six days. Penicillin and sulfonamide drugs were not employed. Recovery occurred in all cases and provides further convincing evidence of the effectiveness of BAL in countering toxic manifestations of arsenic and other heavy metals.

C. A. F.


This is the third case published in France of infectious mononucleosis with a genital ulceration and inguinal adenopathy (the others published by P. Chevallier and by Chassagne & Forgeois). The patient, 23 years old, noticed on the first of May a slight genital erosion on the penis; the tenth of May an inguinal adenopathy appeared. The patient was seen for the first time on the sixteenth of May. He was tired, with 38.8°C. fever. The genital ulceration had disappeared, but several lymph nodes formed in the left groin. The twenty-eighth of May, the adenopathies were generalized, especially in the cervical area. The volume of the spleen was increased. On the second of June the fever receded. The hematologic examination (twenty-fourth of May) gave the following results: leucocytes, 7400; polynuclears, 35; lymphocytes, 43; monocytes, 3.3. On the thirtieth of May a Paul and Bunnell reaction was strongly positive: serum alone, 1:12.2.12.12; serum + guinea pig kidney, 1:12.2.12.12; serum + beef red cells 0.000-000.000. On the twenty-second of June, the mononucleosis predominated in the blood, the Paul and Bunnell also was still slightly positive. How should one interpret this genital ulceration? Since it was the first symptom and a transitory one it cannot be a trophic ulceration due to the hypogranulocytosis. Was it the point of entrance of the unknown virus of the disease? Another venereal contamination is possible, but there was no reason to suspect it and the wife of the patient remained healthy.

J. P. S.


The reported higher incidence of tumors in female mice led the present authors to investigate the association of oestrogenic stimulation and neoplasms in male castrate mice. Two strains of male mice were used in 3 groups from each. Group I was castrated and then painted with oestrone. Group 2 was painted but not castrated. Group 3 was the control group. The incidence of lymphoid tissue changes in both test groups was much higher than in the control and higher in the castrate than non-castrate. It has not been determined whether or not these lymphoid changes were of a truly malignant nature.

O. P. J.

LYMPHOMA AND BONE TUMORS


Jean Bernard, author with P. Chevallier of an excellent monograph on Hodgkin's disease, reports the results of surgical attempts to treat Hodgkin's disease.

In 6 children, a cervical lymph node which was hypertrophic was removed. In these cases, there were no other adenopathies, and the mediastinum and the spleen were not involved. There was no fever. The diagnosis of Hodgkin's disease was made on histologic examination: Tuberculin reactions were negative, and then were only slight modifications of the white cell counts (neutrophilia and slight eosinophilia).

Two of the 6 children, are still alive and in perfect health, 6 and 8 years after the operation. In the other 4 cases the disease progressed as if no surgical attempt had been made. After 3 to 12 months new adenopathies appeared. The surgical procedure was excision of the hypertrophic lymph node; without
"évidemment ganglionnaire." At this initial period, the clinical diagnosis of Hodgkin's disease is only presumptive before histologic examination. The unnecessary removal of an inflammatory lymph node is preferable to losing precious time awaiting a more characteristic picture.

These observations have a theoretic interest: Hodgkin's disease seems to have a short, localized, initial stage, even if it is a system disease (as the fowl-leucosis has a first, medullary, localized stage). The practical interest is considerable. Since the surgical removal has no detrimental effects on the course of the disease, two successful results in six attempts bring hope in the treatment of this fatal disease.

J. P. S.


The clinical hematologist who is often called upon to assist in the differential diagnosis of bone tumors will find much of interest in this straightforward presentation. The significance of abnormal blood levels of calcium, inorganic phosphate, alkaline phosphatase, acid phosphatase and serum proteins is given in tabular form and briefly explained. Recent advances in medical treatment of bone tumors are cited as examples of current trends but are not discussed.

L. E. Y.


This concise presentation, like the above, merits attention from those interested in the blood and blood-forming organs. The pathologic and some of the clinical features of the most important bone tumors are clearly described. The author recognizes two general cytologic groups of multiple myeloma, namely, the 'plasma cell myeloma' or 'plasmacytoma,' and a group of more varied cytology dominated by cells larger than plasma cells. The pathognomonic findings in the kidneys in this disease and the presence of amyloid in some cases are stressed. With regard to roentgenographic evidence of multiple myeloma, it is emphasized that when films of the other bones do not show the conventional picture, the calvarium as a rule also fails to show it.

L. E. Y.

LYMPHOMATOUS DISEASE


An analysis of the clinical and pathological features of 130 cases of malignant lymphoma is presented. A close correlation existed between the histology of the tumor and the life expectancy of the patient. Sixty-seven cases were subjected to radical surgery and 63 of these survived the operation. Twenty-one of these patients received no other form of therapy and 12 of these survived 5 years or longer, and showed no evidence of disease at the time of the report.

Forty cases received adequate radiation therapy following radical removal of the tumor. Eighteen of these patients survived and 9 were without evidence of disease at the time of the report.

From reports such as this it is apparent that radical excision of localized accessible lymphomatous tumors should be attempted. Hellwig stresses the fact that radiation therapy alone does not produce cure of malignant lymphomatous disease and actually prolongs the life of its victims very little. In contrast, radical excision of the tumor may occasionally result in complete cure, and frequently prolongs life.

J. F. R.


Details of the technic of aspiration biopsy are given and the simplicity of the procedure is emphasized.
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In no instance in the 300 aspirations did serious complications result and there were no cases in which fungation from the needle puncture occurred. One hundred and ninety-seven of the 300 aspirations were successful in that either tumor or lymphoid tissue was secured. Of these, 160 showed the presence of metastatic cancer. One hundred and three cases represented technical failure to obtain sufficient tissue but subsequent clinical course proved only 34 of these to be in error in that the patients subsequently developed cancer.

The greatest value of this technic is in the diagnosis of metastatic cancer. It is of much less value in the diagnosis of malignant lymphomatous disease since it usually is necessary to have an entire lymph node for examination in order adequately to establish this diagnosis.

I. F. R.


The authors of this article review in some detail the entire subject of Hodgkin’s disease from the points of view of history, etiology, clinical diagnosis and differential diagnosis, and pathological distribution, and then summarize the modes of x-ray therapy with regard to technic and results. Their own experiences have led them to formulate a procedure of irradiation which is somewhat different from that of others.

There are 3 principles in this technic. Recurrences of Hodgkin’s tissue are more radioresistant than the original areas; hence it is considered advisable to give a relatively heavier dose at the start of therapy. By the same token, the total amount of irradiation is given in as short a time as possible, not exceeding 2 weeks. Furthermore, since the site of recurrence is unpredictable, prophylactic irradiation is not utilized. The authors’ technic, correspondingly, consists of intensive irradiation as soon as the diagnosis is made, a full course of treatment being given to each area involved, starting with the adenopathy which is giving the worst symptoms. Each course consists of between 1000 and 2000 tissue roentgens given in not over 14 days. By this method, the authors have, in a series of 185 cases, a 5-year survival rate of 12 per cent; and a 10-year survival of 8 per cent.

This report discusses, in passing, local resection of Hodgkin’s tissue with subsequent irradiation, and discards it in favor of heavy irradiation. It also mentions ordinary spray therapy, as well as prolonged spray therapy in small doses, only to prefer heavier intensive irradiation. There is no discussion of therapy with the nitrogen mustards.

S. E.

BLOOD COAGULATION, ANTICOAGULANTS AND HEMORRHAGIC DISEASES


When fibrin is formed during coagulation there is a progressive increase in turbidity. Photometric methods were devised to measure the light scatter and optical density during this process. Nonclottable proteins influenced the optical properties of this system and were believed to enter into the fibrin structure by being trapped in the process of fibrin formation. Evidence was presented to indicate that the clotting of fibrinogen by thrombin occurs in two stages. First the thrombin activates some of the fibrinogen, then these activated molecules react with nonactivated fibrinogen in a progressive polymerization reaction.

O. P. J.


Experience over a six year period with dicumarol is reported. Complications due to the use of the drug were limited to a 3.4 per cent incidence of hemorrhage which was considered serious in 1.8 per cent and included 2 cases of fatal bleeding. In a group of 819 patients with either pulmonary embolism or peripheral venous thrombosis there was a 2 per cent incidence of a further vascular complication while under
therapy. The one fatal pulmonary embolus occurred after the patient's prothrombin had returned to normal. These data show a marked reduction in expected mortality when compared with its incidence without anticoagulant therapy. This report further justifies the spirit of general enthusiasm over the use of anticoagulants in thrombo-embolic disease.

C. A. F.


This article comprises a concise authoritative review of the origin, chemistry, action and therapeutic applications of heparin. The material is dealt with more fully in the author's monograph on Heparin in Thrombosis, 1946 edition.

C. A. F.


Concentrated aqueous heparin was used containing 100 mg./cc. and injected intramuscularly at 8 to 12 hour intervals in doses of 50 to 180 mg. Maximum effect was attained 4 to 6 hours after injection. In 2 per cent of injections local reactions were observed consisting of a small nodule or local discomfort. This was felt by the authors to be a simple, safe and therapeutically satisfactory method of administration of heparin.

Single injections, however, showed considerable variation in duration of action and insufficient data is reported for the reader to judge the predictability of anticoagulant effect on repeated injections.

C. A. F.


In this very interesting preliminary report the authors question whether the amount of circulating heparin may be increased in thrombocytopenic purpura. By titration of heparinized blood against varying concentrations of protamine sulfate, they find that a greater amount of protamine is required to return the clotting time to normal in thrombocytopenic patients than in controls.

Toluidine blue (2.5 mg./kilo body weight) was injected intravenously into 6 patients with thrombocytopenia in view of its known antagonism to heparin. Four of these patients had leukemia and 2 had idiopathic thrombocytopenic purpura. To judge from the illustration presented, the patients experienced dramatic remission in spontaneous purpura. Platelet counts and bleeding times did not appear to be affected, and the authors emphasize that bleeding from ulcerated areas may be little improved. Certain inconsistencies in the behavior of the patients to treatment along with the as yet limited data make it necessary to withhold any definite opinion as to the therapeutic value of antiheparin drugs in thrombocytopenic purpura.

C. A. F.


In these two communications, P. Fredericq reports the method of cultivating the prodigiosus or the actinomyces on a sheet of cellophane. The cellophane is washed in distilled water, then the solution is filtered through a Jena filter G 5/3. Then the filtrate is precipitated by five volumes of alcohol (94°C.). The precipitate is used to make different dilutions. Thus an enzyme is isolated: the "prodigiosicoagulase" and the "actinomyceticocoagulase" which are able to clot an oxalated plasma. This coagulase is not a thrombin, since a pure solution of fibrinogen is not clotted. The presence of prothrombin is necessary (absorption of prothrombin suppresses in the absence of calcium—trypsin-like activity). Both enzymes are as proteolytic as the trypsin itself and the plasma-protease (called by Fredericq, "tryptase").

J. P. S.
RADIOACTIVITY AND RADIOACTIVE ISOTOPES


The deleterious effects upon the blood of atomic energy and high voltage x-ray brings up the necessity for a thorough study of the problem, and of the more practical methods of immunization.

The penetrating and pernicious effects of the radiations are similar to those produced by the gamma rays of radium. There are three such effects: (1) those produced by a sudden and intense irradiation, as observed among the victims of atomic bomb explosion; (2) those produced by repeated small, well-tolerated doses, as observed in workers with radioactive substances and in investigators of nuclear physics; and (3) the effects secondary to continuous internal irradiation given off by radioactive substances accumulated in the marrow.

The inhabitants of Hiroshima and Nagasaki subjected to intense and penetrating acute irradiation, showed, first, a latent period; then granulocytopenia, which occurred during the first three weeks; three to five weeks later, thrombocytopenia, with hemorrhagic diathesis, made its appearance; and from five to seven weeks after the explosion, cases of aplastic anemia developed. The sternal marrow in these cases, was found aplastic, physiologically if not always anatomically.

Bones absorb radium, thorium, and radioactive calcium and strontium. The bone marrow is subjected to a continuous bombardment of destructive alpha rays, as observed in workers in the manufacture of luminous watches. Aplastic anemia with an aplastic marrow, or with a hyperplastic impotent marrow, develops as a result of this internal irradiation, and the hematologic picture is similar to that observed in the victims of atomic bomb explosion.

R. M. S.


Since radiophosphorus is chiefly deposited in the bone and bone marrow, it is understandable why its therapeutic value should be tested for modifying disturbances in the hematopoietic organs. Hall and Watkins review the cases reported in the literature and add some of their own. Radiophosphorus therapy is an effective method of controlling polycythemia vera. Besides the high cost of material another disadvantage is that the occurrence of leukemia may be accelerated.

O. P. J.