LYMPHOMA


To the hematologist interested in the pathogenesis of leukemia and lymphomas, the possibility of psychogenic factors of etiologic importance comes as a startling suggestion. However, this is one of a series of reports in which the antecedent roles of psychosomatic factors are investigated in various patients with lymphoma and leukemia. The authors studied 32 women over 20 years of age who had leukemia, Hodgkin's disease, lymphosarcoma, and reticulum-cell sarcoma, and delineated 4 psychologic categories: "mothering," "manly," "clinging," and "pseudoindependent or isolated." Further similar psychologic analyses are extensively detailed: family characterization, senses of guilt and shame, etc. From all their data, the authors make one major suggestion: that separation from a key object or goal, with ensuing depression, may be one of the multiple conditions which determine the development of leukemia or lymphoma, and may contribute to development of relapse in a patient with one of these disorders. Such a psychologic loss includes death of a significant person, loss of home, and onset of menopause. It is interesting, in this regard, that the authors themselves found that similar losses, however, were found in other patients not afflicted with these disorders; but they consider that the losses in the lymphoma-leukemia group occurred within only a few years prior to onset of their illness. The significance of these data, and the validity of the authors' interpretations, must remain subject to long-time evaluation.—S. E.


Of 76 patients with various lymphomata who were examined by autopsy, it was found that 25 (33%) had had clinical signs and symptoms of neurological involvement, but only 18 (25%) showed neurological involvement at autopsy. The cases included Hodgkin's disease, lymphosarcoma, reticulum-cell sarcoma, and giant follicular lymphoma. Neurologic symptoms included low back pain, leg pain, weakness, hoarseness and convulsions. Signs included involvement of cranial nerves, diminished reflexes, spinal cord involvement. Cranial involvement was rare, and was due to local extension to the basal structures or to diffuse meningeal involvement. Intracerebral lymphomas were exceedingly rare.—S. E.
ABSTRACTS

AN UNUSUAL NEUROLOGIC SYNDROME IN HODGKIN’S DISEASE. J. E. Sokal and G. H. Glaser.
From the Dept. of Internal Medicine, Yale University School of Medicine, New Haven, Conn. Ann. Int. Med. 44: 1250-1259, 1956.

Two patients with Hodgkin’s disease complicated by central nervous system manifestations developed weakness, tremor, difficulties in speech, and generalized convulsions. Nitrogen mustard therapy produced dramatic and prolonged remissions in both patients. Neurologic signs did not recur, although other manifestations of Hodgkin’s disease subsequently developed and required treatment.—S. E.

GASTRIC LESIONS IN HODGKIN’S DISEASE AND LEUKEMIA. H. R. Wahl and J. H. Hill. From Department of Pathology and Oncology, University of Kansas School of Medicine, Kansas City, Kansas. Am. J. Path. 32: 235-251, 1956.

Of 45 cases of Hodgkin’s disease, 9 showed characteristic lesions in the stomach at autopsy. Of 64 cases of leukemia, 7 showed gastric involvement. The lesions in Hodgkin’s disease included ulcerations of the mucosa, ulcerating infiltrations, infiltration of the stomach wall with enlargement of the rugae, and nodular infiltration. In this series, the lesions of Hodgkin’s disease were never restricted to the stomach alone; and, in the literature, solitary Hodgkin’s disease of the stomach is rare. The 7 patients with leukemia involving the stomach showed nodular infiltration of mucosa and submucosa, with or without ulceration, or diffuse cellular infiltration with formation of giant rugae. Myelocytic leukemia did not involve the stomach: 6 of the cases were chronic lymphocytic, and one was monocytic.—S. E.

LYMPHOMAS OF THE SMALL INTESTINE AND CECUM. S. O. Burman and F. A. K. van Wyk.

According to the authors, lymphomas of the small intestine comprise one third to one half of all small bowel tumors. This study of 25 cases revealed that lymphoma shows more extensive involvement than carcinoma of the small bowel, and that lymphoma may exhibit diffuse infiltration or may be polypoid, but rarely spreads concentrically. Pain is almost always present, an abdominal mass is almost always palpable, and anemia is rare. Only once in the authors’ series did the peripheral blood show lymphocytosis. Treatment recommended is extirpation if possible, with irradiation following. The prognosis is poor, and in this group 13 of the cases were dead in less than 1 year after onset. Review of the literature suggested that lymphoma of the cecum had a better average survival (8 years) than lymphoma of the small bowel (9 months).—S. E.


The primary localization of lymphosarcoma in the digestive tract is reviewed, focusing on the Argentinian published cases more attentively. Very rare was the gastric or colonic localization, almost all cases being of the small intestine.—M. A. J.


A critical review of several cases personally studied and published by the author since 1928 is made. In addition a table of the cases registered in Argentina is also presented. The varieties of small-round-cell, large-round-cell and reticulum-cell sarcomas are distinguished. The gastric localization occurred about 1 in 10,000 necropsies. A localized and a generalized form are considered.—M. A. J.


This is a detailed study of giant follicle lymphoma or macrofollicular lymphoma (MFL) as demonstrated in 136 cases of definite MFL and 14 cases in which the diagnosis lay between
ABSTRACTS

MFL and follicular hyperplasia. MFL is considered to be a diffuse disease, as the interstitial tissue separating the follicles is also part of the neoplastic process. Transition of MFL into lymphosarcoma and leukemia is discussed. Different nodes in the same patient showed MFL in one place, diffuse lymphosarcoma in others. The same node in different regions might also show MFL and diffuse lymphosarcoma. No cases in the author's experience, and very few in the literature, showed transformation to Hodgkin's disease. Differentiation from hyperplastic lymphoid tissue is discussed, and the occurrence of the latter (benign) condition in rheumatoid arthritis and in monarticular arthritis is mentioned. In the author's experience with this series, 3-year survival occurred in 49% of the patients, and 5-year survival in 36%. Complete cures were noted in 8% of the cases of MFL: in all such cases, the disease was localized when the patient came to the attention of the physician. MFL must be considered always a malignant disease, with a prognosis, according to the author, poorer than that noted in other series.—S. E.

EVALUATION OF CB 1348 IN HODGKIN'S DISEASE AND ALLIED DISORDERS. B. A. Bouroncle, C. A. Doan, B. K. Wiseman, and W. J. Frajola. From the Herman A. Hoster Research Laboratory, Department of Medicine, Ohio State University College of Medicine, Columbus, Ohio. Arch. Int. Med. 97: 703-714, 1956.

The nitrogen mustard derivative known as CB 1348 was given to 42 patients with various proliferative disorders of the hematopoietic system. The regime consisted of a 3 to 4 week course of 0.2 to 0.4 mg/Kg/day, followed by a maintenance dose of 0.05 mg/Kg/day. Side reactions were few and uncommon, and consisted of nausea and nervousness. In most cases, moderate pancytopenia occurred some 6 weeks after beginning of therapy, and was reversible in all cases. Of 24 patients with Hodgkin's disease, 6 showed excellent remissions, and 9 others showed improvement. Excellent remissions were also obtained in 1 case of reticulum-cell sarcoma and in 1 of 10 cases of acute monocytic leukemia. No effect occurred in cases of chronic lymphocytic leukemia (in this report), lymphosarcoma, acute lymphocytic leukemia, mycosis fungoides, or multiple myeloma. When remissions occurred, there was relief of fever, lymphadenopathy, and hepatosplenomegaly, but remissions were notably short (2 to 9 months). The drug was used without difficulty in the presence of thrombocytopenia.—S. E.

BLOOD GROUPS


In representative groups of the population of Venezuela the incidence of a new “private” blood group, the “Diego factor,” was determined. It behaves like a mendelian dominant character. In Caribbean Indians the incidence was very high: 35.54 per cent. It is suggested that the name of “Indian factor” be given to this blood factor.—M.A.J.


The Diego blood factor occurs relatively commonly in Caribe and Arawaco Indians and in anthropologically independent Indians in Brazil and Venezuela. It has not been found in United States Caucasoids or in Dutch, Spaniards or Italians. The present investigation was undertaken because Indians of the American continent are considered to be anthropologically related to the Mongoloid people of the Old World. One hundred unrelated male Chinese from Canton living in Venezuela were studied. Of these 5 were Diego positive. Of 68 unrelated Japanese, 8 were Diego positive.—R.H.G.
**THE BLOOD GROUP ANTIGEN DIEGO IN NORTH AMERICAN INDIANS AND IN JAPANESE.**


The antigen Diego was present in 16 of 148 unrelated Chippewa Indians in North Minnesota and 6 of 77 unrelated Japanese in Winnipeg.—R.H.G.

**ANTI-H IN TWO SIBLINGS IN AN INDIAN FAMILY.**


Two cases of blood group O (H-) with anti-H in their sera are reported in the sibship of one family. Four similar cases had previously been reported from India.—J.L.C.

**BLOOD GROUP FREQUENCIES IN NATIVES OF THE CENTRAL HIGHLANDS OF NEW GUINEA, AND IN THE BAININGS OF NEW BRITAIN.**


The A-B-O, M-N-S, Rh, Le, P, Fy and K blood groups, together with the secretion of A, B or H substances in the saliva and taste-blindness to phenyl thiocarbamide, have been determined in New Guinea natives from four localities in the Central Highlands, and in the Bainings from the Gazelle Peninsula of New Britain. The gene frequencies calculated for 485 natives of the Central Highlands are as follows: A = 0.195, B = 0.159, O = 0.646, ns = 0.042, nS = 0.005, ns = 0.588, nS = 0.115, R1 = 0.829, R2 = 0.081, R3 = 0.028. The gene frequencies calculated for 77 Bainings are: A = 0.297, B = 0.252, O = 0.451, n = 0, n = 1, S = 0, R1 = 0.818, R2 = 0.182, R3 = 0.014. All of 316 New Guinea subjects tested were Le (a-), and 239 out of 242 (98.7%) were secretors of A, B or H substances in saliva. In Bainings, 15 out of 75 (20.0%) were Le (a+), but no secretion tests were performed. In New Guinea natives, 182 of 318 (57.2%), and in Bainings 34 of 38 (89.5%) were considered P positive. All of 79 New Guinea natives, and all of 22 Bainings were Fy (a+). In New Guinea samples one out of 52 (1.9%) was K positive. The results obtained have been compared with other data from New Guinea and neighboring regions, and the significance of the findings has been discussed.—G.C.de G.

**IMMUNIZATION BY THE BLOOD ANTIGEN KELL IN HAEMOLYTIC DISEASE OF THE NEWBORN AND IN BLOOD TRANSFUSION.**


This paper reviews the work on the Kell antigen with special reference to eleven anti-Kell sera encountered in Australia. The antigenicity of the K antigen is compared with that of the C, D, and E antigens, and it is stressed that the K antigen must be considered seriously in problems of immunization due either to pregnancy or transfusion. Of random blood samples from the white Australians 9.375% were Kell positive.—G.C.de G.

**BLOOD GROUPS AND AGGLUTINATION OF LEUCOCYTES.**


This paper reports the results of agglutination tests carried out by directly cross-matching leukocyte suspensions and serum.

Positive results were obtained in 40 to 60 per cent of mixtures in which there was an ABO incompatibility and in 10 to 15 per cent of "compatible" mixtures. Absorption studies supported the belief that leukocytes carry A and B antigens in accordance with the corresponding red cell group.

Agglutination in mixtures expected to be compatible was caused by 13 of the 71 sera used, particularly by sera from donors of blood group AB. The serum of one patient who had been pregnant caused agglutination in 18 out of 20 samples of cells. Another, from a
male, gave positive results against seven of 11 test samples. Both patients had normal leukocyte counts, and neither had ever received a transfusion. Strong leuko-agglutinins were found in the serum of a patient with aleukemic leukemia, and in that of another with hemolytic anemia associated with a cryoglobulin.

The possible significance of leuko-agglutinins in relation to blood groups of leukocytes, blood transfusion, leukopenia and tissue transplantation has been discussed.—G.C.de.G.


If skin epidermal cells of a person of blood group A possess the A antigen, then, accepting that ordinary agglutinating antibodies are at least bivalent, it would be expected that such epidermal cells would be able to be linked by anti-A to group A cells. To test this a suspension of epidermal cells from a group A person could be exposed to anti-A, and the cells subsequently washed free from uncombined antibody. Group A red cells should then combine with extending anti-A receptors on the treated epidermal cells. In the nine group A persons, five group O persons and three group B persons so examined it has been shown in all instances that the expected antigens were contained on the membrane of the epidermal cells. The occurrence of the A and B antigens on epidermal cells is not limited to persons possessing the secretor gene.—H.H.G.


The Coombs and Bedford test for the demonstration of A and B antigens in platelets was performed and superimposable results were obtained. The thrombocytic-erythrocytic agglutination was observed only when platelet suspensions from A and B group subjects, sensitized with the corresponding antisera, were incubated with homologous red cells.—P.d.N.


In a report on the medicolegal applications of blood grouping, the American Medical Association’s Committee on Medicolegal Problems recommend that the C-D-E notations should be discarded and the Rh-Hr nomenclature retained. This suggestion will cause surprise in Britain, where the C-D-E nomenclature has been in constant use for over a decade, and where no other is used by the more recently qualified pathologist. Wiener does not accept the Fisher-Race theory of 3 allelomorphic pairs of linked genes, and prefers an explanation based on the existence of multiple allelomorphs of a single complex gene. This is highly academic. Only the C-D-E notation indicates which antigens and genes are present, and for practical use the C-D-E system is the more satisfactory. It seems unlikely that, outside the United States, pathologists and others will wish to change from the Fisher-Race to the Wiener nomenclature. The author of the article in Lancet concludes, however, that it is unlikely that American workers will retire into serological isolation and points out that certain American experts disagree with the report!—R.H.G.


Data are presented on the testing of 62,869 sera for Rh antibodies. Two hundred fifty (3.2%) of the Rh-negative women had or developed antibodies as demonstrated by the saline, trypsin and antiglobulin techniques. Apparently normal infants were delivered in 123 instances (49.2%), 5 (2.0%) had miscarriages, 31 (12.4%) had stillborn infants, and 91 (36.4%) had infants with hemolytic disease of the newborn. Evaluation of 230 cases where clinical data were available suggests that the occurrence of hemolytic disease is more
closely related to the level of antibody in the mother than to the number of pregnancies. However, the data are incomplete in that such factors as the genotype of the father, history of previous hemolytic disease of the newborn, and type of Rh-antibody are not included. Therefore, the study has only limited value.—J.H.A.


This paper is concerned with the study of a number of anti-A and anti-B sera produced by immunization to a variety of blood group substances to see whether all such immune sera behaved in a uniform manner in tests for immune antibodies (Coombs test, Coombs test following neutralization of the agglutinin titer by A or B substance). The antisera for the study were obtained from persons who had been immunized by blood group substances from the following sources: heterospecific pregnancy, human A substance (saliva), group A blood, hog A substance plus horse A and B substance, hog A substance, horse A substance, horse substance without blood-group activity, horse B substance with a trace of A activity, horse A and B substance, horse B substance, hog O substance, human B substance, and serum from a group-O donor whose blood produced a severe hemolytic transfusion reaction in a group-A recipient. Pooled anti-human-gamma-globulin-rabbit serum having about 200 mg. antibody nitrogen per ml. was used. By agar diffusion technic, using normal human serum as antigen this anti-gamma-globulin serum showed only one band.

From the results of the Coombs tests in block titration and after neutralization by blood group substances, the authors conclude that no distinction can be made, as to whether antibodies are “natural” or immune, between those antibodies showing enhancement in Coombs titer over the saline agglutinin titer and those failing to show enhancement.—J.H.A.


When a comparison was made of agglutinating power between β(AO) isohemagglutinin of normal serum and β(AO) isohemagglutinin of the same serum to which glucose had been previously added, a larger amount of antibody nitrogen specifically fixed on B stroma was found in the latter case.—J.D.


Three cases of accidental interchange of babies in Maternity Hospitals are presented. It was possible to reach definite results employing adequate methods of blood antigen typing. The several agglutinogens studied is given in detail. In one of the cases the interchange is proved, in the other one there was some results pointing to illegitimacy or interchange, while in the last case studied the possibility of interchange was excluded.—M.A.J.

BLOOD GROUPS—RELATION TO DISEASE


It is fashionable to investigate the statistical relationship between various diseases and blood groups. This investigation in 516 women showed no substantial differences between the various blood groups and the average age of the menarche or in its dispersion about the average.—R. H. G.

Unlike what was found in a previous series, no excess of group O was found in 262 women suffering from toxemia of pregnancy as compared with 1,523 nontoxemic pregnant women. When the 3,651 patients formerly reported were re-examined, with stricter criteria for the diagnosis of toxemia, and the two series combined, no significant excess of group O was found.—R. H. G.


There was no significant difference in the ABO blood group distribution between 675 women with toxemia of pregnancy and 10,411 not so afflicted.—R. H. G.


Of 32 patients believed to have sarcoidosis, 21 had Rh-negative blood and radiographic evidence of hilar or lung involvement. Of 11 whose blood was Rh positive, 4 had normal chest radiographs. Of 1000 patients of all departments who had their Rh (D) factor determined about the same time, 17.3% were Rh negative.—R. H. G.


Investigations were on 1,333 diabetic patients and 14,249 controls. These were divided into three geographical areas. In each there was a fairly highly significant increase in diabetic men of group A. The women diabetics did not differ significantly from the controls. In men there was some evidence that the excess of group A was greater in those with a close relative suffering from diabetes. There was no evidence of this in women. In neither sex was there any association between the age of onset of diabetes and ABO blood group frequencies or of association with insulin requirements.

In 500 patients in the Oxford area Rhesus and MN groupings did not differ from the findings in controls.—R. H. G.


The study is of 119 patients in the surgical unit most of whom were operated on by the same surgeon for gastric carcinoma. As others have found, there was an excess of group A over group O, and this was due to an association between group A and carcinoma of the pyloric end of the stomach. There was no such excess in carcinoma arising in the body of the stomach. This does not support the suggestion that group A is associated with atrophy of the acid-producing mucosa and achlorhydria. It is possible that the antral mucosa is more frequently inflamed in group A, and that this predisposes both to simple ulcers and to carcinoma.—R. H. G.


This reports the results of a survey into the ABO Rh(D) blood group distribution in 2,039 patients suffering from peptic ulcer. A total of 5,808 consecutive donor registrations
at the Blood Transfusion Centre supplied a control series. There was an increased frequency of group 0 in patients with duodenal ulcer, but no significant difference with gastric ulcer, the numbers here, however, being small. The frequency of group 0 was greatly increased in patients with stomal ulcers. There was no difference from controls as regards Rh-negative grouping.

In 276 patients with duodenal or gastric ulcer there was no correlation between acid output and ABO group.—R. H. G.


Recent studies in the United States and Europe have strongly suggested that there is an association between blood group 0 and duodenal ulcer. These findings are criticized on the grounds that the controls used, unaffected people living in the same area, are a population of mixed origin and this way contain elements with a high frequency both of group 0 and of duodenal ulcer without the two being causally connected. Data on 293 duodenal ulcer sibships are presented in which the unaffected siblings were used as controls. No evidence was found that a group 0 person is more likely to have a duodenal ulcer than his A, B or AB siblings. These findings are discussed as being due to a material effect.

The ability to secrete ABO blood group substances was investigated in 514 unrelated duodenal ulcer patients and 491 controls. There was a significantly higher proportion of nonsecretors in the patient group (35.0%) than in the controls (24.2%). This suggests that nonsecretors have a 45% greater chance of developing duodenal ulcers than secretors. A study of 262 families suggest that the relationship between nonsecretion and duodenal ulcer may hold within families. That the A, B and Lewis blood group substances may have some protective action against duodenal ulceration by virtue of their mucoid character is discussed.—J. H. A.


An analysis of the distribution of the ABO blood group in 1114 cases of pernicious anaemia collected from six English cities plus 111 cases from Copenhagen shows, with a fairly high degree of significance, that this disease is commoner in persons of blood group A than in persons of group 0 and, for the small number reported, of group B. An analysis of the English series shows that the greater incidence in group A is equal in both sexes.—J. H. A.


The authors report the comparative results of the blood groups A, A2, B, O, D, M, N, the secretor state and sex in 1000 consecutive cases of proved malignant disease collected over a three-year period. Generally no statistically significant differences were found although there were suggestive trends associated with certain malignancies. For instance, carcinoma of the breast showed low O and Rh-negative and high N frequency; carcinoma of the prostate showed a tendency to high Rh-negative frequency; carcinoma of the bladder is mainly in patients of group O and mostly in males; sarcomas show an excess of A2; all patients with esophageal cancer were secretors; most of the patients with biliary cancer were women and were group O; and all laryngeal cancer patients were men. Since progress in this field is beyond the scope of any single hospital, the data are presented mainly so they can be available for inclusion in other series.—J. H. A.
SUSPECTED CORRELATION BETWEEN BLOOD GROUP FREQUENCY AND PITUITARY ADENOMAS.

The ABO blood group frequencies in patients in Boston hospitals were found to be 42.08 percent for group A in carcinoma of the stomach (N = 663) and 61.11 percent for group O in duodenal ulcer (N = 144). The frequency for the A group in the Massachusetts population (N = 120,281) is 39.7 per cent and for the O group 45.8 per cent. This indicates that deviations from neutrality can be demonstrated in the racially heterogeneous North American population. An analysis of the ABO blood group frequencies of 637 cases of brain tumors showed that there was little if any deviation from those of the Massachusetts population. The distribution of the ABO blood groups in chromophobe adenoma of the pituitary (N = 123) in three Boston and two New York hospitals showed a considerable excess of blood group O (60.16%) associated with a deficiency of group A (19.51%). There was no duration for group B or AB. It is interesting to note that in other established cases of an association between the ABO blood groups and pathological conditions the correlation has been with the intestinal tract directly or indirectly. These findings are in keeping with the broad concept that genes have pleiotropic effects. The rarity of blood group B in the European and North American population is mentioned and it is suggested that some childhood or infectious disease may account for its low frequency since this blood group has not been found to be discriminated against in any pathological condition. The abstractor suggests that future studies include other blood group systems, thus adding more points for analysis.—J. H. A.

RETICULOENDOTHELIAL SYSTEM

STUDIES ON THE DEVELOPMENT OF CONNECTIVE TISSUE FIBERS AND MAST CELLS IN HUMAN EMBRYOS, WITH SPECIAL REFERENCE TO THEIR HISTOCHEMICAL RELATIONSHIP. Thoshiko Kitanishi. From the Department of Pathology, Medical Faculty, University of Kyoto, Kyoto. Acta Haematologica Japonica. 19: 53-63, 1956.

Various mesenchymal tissues of the arm from 74 human embryos of various stages were studied histochemically, being interested in the course of development of reticulin, collagen and elastic fibers on the one hand and the appearance of the tissue mast cells on the other. In this study reticulain fibers which originate from fibroblasts and tendon cells and which are to develop into collagen fibers were mainly examined. The earliest sign of collagen fiber formation in the primordial corium was found in 102 days of fetus, closely paralleled with the first appearance of tissue mast cells in the neighborhood. This indicates that the heparin from the mast cells plays some role in the formation of the collagen fibers.—K.M.


In order to determine the existence of hormonal control over the mast-cell population, various endocrine procedures such as adrenalectomy, hypophysectomy and sham-adrenalectomy were performed on adult male rats of a modified Long-Evans strain. Peritoneal fluid was examined for qualitative and quantitative changes in mast cells. Mesenteric spread preparations were studied for comparison but were found unreliable because of inherent artifacts of technic. Hypophysectomy resulted in aberrations in mast-cell shape and in an increase in the average size of the population. The abnormality in the shape of mast cells was corrected by replacement treatment with growth hormone. Both adrenalectomized and sham-operated animals had smaller mast cells and they remained unchanged following replacement technics. The hormonal control is probably indirect because experiments in vitro were negative after two hours’ contact.—O.P.J.
ABSTRACTS


Numerous large lymphoid cells appear in the first regional lymph node of rabbits following skin homografts, but they do not appear after autografts of skin. Since it is known that systemic administration of cortisone acetate prolongs the survival of skin homografts, it was thought that perhaps cortisone might affect the large lymphoid cell response and the source of systemic immunity. When administered systemically in a dosage of 10 mg. per day, or applied locally to the surface of the graft in a dosage of 2 mg. every third day, cortisone prolonged the survival of skin homografts and reduced the large lymphoid cell response. Cortisone injected subcutaneously between the graft and the regional node did not do this. These findings are consistent with the hypothesis that the large lymphoid cell is actively involved in the production of antibodies against skin homografts. The mode of action in prolonging homograft survival is probably due to cortisone's reducing the power of the graft to elicit the immune response.—O.P.J.

ON THE LYMPHATIC TISSUE OF GERM-FREE ANIMALS. Masasumi Miyakawa. From the Department of Pathology, School of Medicine, University of Nagoya, Nagoya. Acta Haematologica Japonica 18: 406-424, 1955.

In germ-free guinea pigs reared by the author's own apparatus of M-51 type, the state of lymphatic tissue was studied. In these animals, the lymph nodes at any site of the body and the subepithelial lymphatic tissue of the respiratory and gastrointestinal tract developed very poorly and new ones did not grow in the postnatal life. It is also revealed that the so called Flemming's secondary nodules were absent in the lymphatic tissue of such animals. When germ-free animals were infected with a single bacteria, a number of Flemming's secondary nodules were recognized on the cortex and some pyronine-stained cells on the medullary cords. However, by the injection of ovo-albumin, DNA or RNA into the foot pad of the animals, no lymphatic secondary nodules with clear center were seen in the popliteal lymph nodes. The injection of cortisone or ACTH in the same way resulted in a reduction of the small sized lymphocytes of the popliteal lymph nodes as in normal animals. From these observations, it is considered that the appearance of the typical Flemming's secondary nodules with clear center and dark ring depends upon contamination by the natural bacterial environment and has some connection with antibody formation.—K.M.

PERIODIC ACID-SCHIFF-POSITIVE RETICULO-ENDOTHELIAL CELLS PRODUCING GLYCOPROTEIN. FUNCTIONAL SIGNIFICANCE DURING FORMATION OF AMYLOID. G. Teilum. From the Laboratory of Rheumatic Research, University Institute of Pathological Anatomy, Copenhagen, Denmark. Am. J. Path. 32: 945-959, 1956.

The author has a theory which accounts for the association of amyloidosis, not only with rheumatoid arthritis, but with other conditions. It is based upon histologic and experimental studies of reaction of mesenchymal and reticuloendothelial cells in various conditions, and the control of the protein-synthesizing function of the reticuloendothelial system and its pyroninophilic derivations, the plasma cells and their immediate precursors, by the actions of adrenal corticoids and ascorbic acid. The breakdown of this control in persistent antigenic stimulation or other form of stress results in the local formation of amyloid. In order to test this, 80 female mice of C3H strain were divided into 5 groups as follows: control; those injected subcutaneously with sodium caseinate; the latter plus cortisone or ACTH, and a group which received nitrogen mustard. In addition, a group of 48 rabbits were hyperimmunized with a formaldehyde-killed Pfeiffer bacillus culture. There resulted a widespread proliferation of reticuloendothelial and other cells derived from mesenchyme, characterized cytochemically by the presence of periodic acid-Schiff-positive material in the cytoplasm. This suggests a most important function of reticuloendothelial cells in producing polysaccharide-containing globulins (mucoproteins or glyco-proteins) in response to diverse stimuli or injuries. Following over-stimulation, a varying proportion of these cells will show a decreasing amount of pyronine-positive material (ribo-
nucleic acid) and an increasing content of PAS-positive substance (mucoprotein). Obviously, the proliferation of PAS cells can be considered a general adaptation reaction, closely related to pyroninophilic cellular reaction.—O.P.J.


By the use of an electrochemical circuit previously described, measurements were made on the respiration of rat connective tissue cells multiplying in vitro. These experiments show that rat connective-tissue cells are able to multiply at the normal rate under anaerobic conditions. When cysteine was added to the medium routinely, disintegration of the cells never occurred, and it shows that multiplication took place at the normal rate in medium containing no detectable amount of oxygen.—O.P.J.

Hemolysis and Hemolytic Disease


The amount of hemoglobin in single red blood cells can be studied by micro-absorptionmetry, phase contrast microscopy or micro-interferometry. The first method is based on the specific absorption of the red blood cell pigment; while in the interference method the total cell mass can be estimated. Large differences in the optical retardation have been demonstrated between intact red cells and ghosts. Such a difference seemed to offer considerable advantages in the determination of the rate of hemoglobin liberation in a fluid containing Michaelis-Veronal-Acetate Buffer after introducing small quantities of digitonin or teepol. Great variation in the sensitivity of individual erythrocytes to the lysing agents was recorded by a cine camera attached to a Dyson interferometer microscope. The duration of hemolysis varied considerably and seemed related in part to the concentration of lysin.—O. P. J.


In a series of 35 patients with Cooley’s anemia, the mean value of plasma hemoglobin as measured with a modified method of Bing and Baker was 16.98 mg.% and the range varied from 4.30 to 56.50 mg.%. High level of plasma hemoglobin indicates that intravascular hemolysis of significant degree is a feature in Cooley’s anemia.—J. B. C.


Case report in a 38 year old man. The most important patterns were as follows: after a not extremely extended burn, a marked hemolytic anemia suddenly developed. Autoantibodies against erythrocytes were detected. Marked thrombocytopenia, hemorrhagic diathesis (retinal hemorrhages, hematuria, subcutaneous homorrhages), vascular thrombosis, especially in retinal vessels, severe cerebral manifestations, particularly irritative in nature. Death occurred owing to cerebral coma.—P. d. N.


Marrow was obtained by sternal puncture from patients with highly active erythropoiesis (e.g. hemolytic anemia or hemorrhage). Parallel cultures were set up in normal
serum and in uremic serum. Nine such experiments were done. In each instance, culture of marrow in normal serum resulted in a significant increase in the proportion of orthochromatic normoblasts present in 24-hour cultures, and a corresponding decrease in earlier forms. With uremic serum a similar trend occurred, but the proportion of orthochromatic normoblasts was lower, and of immature forms higher, at 24 hours. Uremic serum appears to inhibit the maturation of marrow normoblasts, and the defect may be one of hemoglobin synthesis.—R. H. G.


A negro infant had a gradual onset of anemia during the first 6 weeks of life. Appropriate data are presented to establish the diagnosis of hereditary spherocytosis. A discussion of differential diagnosis deals principally with unusual infections in the newborn and ABO isoimmunization. The controversial problem of elective splenectomy in early life is discussed in relation to increased susceptibility to severe sepsis of splenectomized children. The problem of severe hemolytic crisis in the first few days of life is not mentioned.

This paper draws attention to the occurrence of severe anemia in newborn infants with hereditary spherocytosis, a problem unduly neglected in the past.—N. J. S.


The authors can trace no other instance of megaloblastic erythropoiesis occurring in idiopathic acquired hemolytic anemia although it has been reported in the congenital form. The patient, a married woman aged 29, had a frankly megaloblastic marrow, spherocytosis and Pappenheimer bodies. Red cell fragility in hypotonic saline was increased and reticulocytes were 20%; the direct Coombs test was negative and no autoagglutinins were demonstrated at 4°C or 37°C in either saline or albumin. Trypsinized normal cells were agglutinated by the patient's serum. There was considerable hematological and clinical improvement with blood transfusion, and then cyanocobalamin injections were given. Five days after the first injection the reticulocytes rose to a peak of 25%. (They had first fallen from their previous high level.) After the hemoglobin levels had risen to a relatively satisfactory height, a second hemolytic crisis occurred during the period of administration of cyanocobalamin. The marrow remained normoblastic. Two years later all evidence of hemolysis had disappeared. A test meal showed free hydrochloric acid to be present, and glucose absorption was normal. The serum vitamin B₁₂ level was not measured, nor was absorption of labelled cyanocobalamin or of folic acid. The gastric juice was not tested for intrinsic factor activity. Because of the improvement after cyanocobalamin therapy the case is considered to be one of vitamin B₁₂ deficiency, and this is attributed not to increased demand alone but also to depression of intrinsic factor or alteration in intestinal flora or both.—R. H. G.


In twelve patients with ictero-hemoglobinuric favism, the hemolytic threshold of erythrocytes was studied. Three phases were described: 1) during the hemoglobinuric phase, the hemolytic threshold was decreased; 2) in the second phase, when hemoglobinuria is minimal, the threshold is increased; 3) in the third phase, when normal conditions are present, intermediate values are obtained. Hyporesistant erythrocytes are assumed to be
present during the first phase. Young erythrocytes should characterize the increase of the second phase.—P. d. N.

HEMOGLOBINOPATHIES


A brief review of the subject, in English, by a well-known European worker in this field. An account is given of the amino acid composition of hemoglobins A, S, C and E as measured in the author's laboratory.—R. H. G.


Since the discovery of the abnormal hemoglobin H three other abnormal hemoglobin types, I, J and K have been found to migrate faster in paper electrophoresis than normal adult hemoglobin at a pH of 8.6. This is the first report of the occurrence of hemoglobin J in an Indonesian family. It occurred in a young female of Javanese extraction and her four year old daughter.—R. H. G.


A Jamaican negro immigrant, found at routine antenatal investigation to be severely anemic, was shown by electrophoresis to have hemoglobin C only. The bone marrow was partially megaloblastic, but the patient was pregnant at the time. There was no previous history of ill-health attributable to anemia. The patient's husband had only adult hemoglobin (A) and her two children had a mixture of A and C. Two of her half-brothers (copaternal) were investigated: one had homozygous C (AC) and one A only.—R. H. G.

HOMOZYGOTIC HAEMOGLOBIN E DISEASE IN INDONESIA. L. Luan Eng and O. H. Giok. From the Department of Parasitology and General Pathology, University of Indonesia, Djakarta. Lancet 1: 20-23. 1957.

In Eastern countries there have been recognized the hemoglobin E trait, which is the homozygous form of the gene for this abnormal hemoglobin, pure hemoglobin E disease (homozygous) and hemoglobin E/thalassemia disease (heterozygous for hemoglobin E and thalassemia genes). The present report is of three cases of pure hemoglobin E disease in Indonesians. In two of the three cases both parents were carriers of hemoglobin E; the parents of the third case, father of one of the other two, could not be examined.—R. H. G.


Eighteen patients from 4 to 28 months of age suffering from hypochromic microcytic anemia were studied. The values for fetal hemoglobin in the anemic infants did not differ from those in 102 normal controls.—N. J. S.

SICKLE CELL GENE IN INDONESIA. Lie-Ingo Luan Eng. From the Department of Parasitology and General Pathology, University of Indonesia, Djakarta. Nature 179: 381, 1957.

More than 4,000 samples of blood from different islands in Indonesia have been examined during a mass survey on pathological hemoglobins. This communication describes the discovery of the sickling gene, hitherto not found in Indonesia. Two sickle cell trait
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carriers were found during the survey. The ethnological implications are discussed.—R. H. G.


Four children with well established diagnoses of sickle cell anemia were seen with clinically typical sickle cell anemia crises. The remarkable feature of each crisis was the reticulocytopenia and erythroid hypoplasia found in the bone marrow. It is also of interest that the crises occurred almost simultaneously in the siblings of the same family, suggesting to the author that some infectious process initiated the crises. Rather extensive studies failed to reveal any evidence of bacterial or viral infection.

In none of the patients was there evidence of impaired production of blood platelets or leukocytes. The peripheral counts and bone marrow findings were not remarkable in regard to these elements. Thus one might question the use of the term "Aplastic" in referring to these crises.—N. J. S.

STORAGE OF BLOOD


We studied the free amino acids in whole human blood, and also in the separated plasma and erythrocytes at various periods of its storage at 4 C. The amino acid content was analyzed by the method of evenly ascending chromatography on paper. For separation of the majority of amino acids we employed a solvent of butanol, acetic acid and water. We succeeded in discovering up to 12 amino acids. It was shown that the content of the individual amino acids in the plasma and the erythrocytes is different. In the process of conserving banked blood we discovered regular cyclical changes in the content of the free amino acids: in the plasma, in the first days of storage, the content of the majority of the amino acids increased, after which there was a perceptible reduction in their concentration; after this there was a secondary increase and in the later periods of storage the concentration of amino acids again decreased. In the erythrocytes the regularity of the changes of some free amino acids (cysteine, asparaginic acid plus histidine, glycine, methionine, plus tryptophane, leucine) are the same as in plasma; the content of the other amino acids (serine, glutamic acid, alanine, tyrosine plus valine, norleucine) undergoes a change opposite to that taking place in plasma in the course of 20 to 25 days of storage of the blood.

The increase in the content of the amino acids in plasma in the first days of storage is explained by the exit of the amino acids from the erythrocytes. The decrease in the content of the amino acids in the plasma in the later period of the storage of the blood (35th day) is evidently the result of the disintegration of the amino acid during storage. It is noted that the free amino acids undergo changes and conversions during the time of storage, indicating the possibility of the employment of certain amino acids for lengthening the periods which stored blood will keep.—A. A. B.


One studied the influence of the addition of adenilic acid prepared with various media, on the lengthening of the period of keeping stored blood. For the preservation of blood we employed solutions of sodium citrate with the addition both of glucose and a mixture of glucose and saccharose. The intensity of the retardation of the latent hemolysis of the blood was an index of its preservation. On the basis of the increase in the blood of "ammonia nitrogen" one determined the degree of splitting of the added adenilic acid. The change in the content of sugar indicated participation of the added adenilic acid in the carbohydrate
exchange of the blood. As a result of the rapid fermentative splitting of the added adenilic acid, a single addition of it to the preservative solution, in the preparation of blood, did not insure lengthening of the period of conservation. The repeated aseptic addition of adenilic acid, during storage of the blood, or a single addition, only during storage lengthens by 10 to 14 days the period of time before the onset of hemolysis.

It was shown that adenilic acid, added to the blood during storage is not split very much in long periods of storage of the blood and does not participate in the process of glycolysis. Addition at one time and repeatedly of adenilic acid keeps at a definite level, for a long time, the processes of glycolysis and lengthens the time that passes before the appearance and development of hemolysis.—A. A. B.


A new method is proposed for increasing the time that banked blood will keep. It involves the study of the participation of ferments of the hydrolase group in the destruction of erythrocytes and the seeking of a method for suppressing their activity. It is shown that the derivatives of the phenothiazine series of diprosin and etisin reduce considerably the activity of the esterases of blood plasma and do not effect the activity of fibrinolysin. The introduction of the aforementioned preparations into the blood lengthens by 20 to 30 days the period before which there takes place hemolysis, it considerably increases the osmotic resistance of the erythrocytes and it makes possible prolonged preservation in the blood of the morphological value of the erythrocytes. Due to the specific action of the preparations tested on the structural integrity of the red blood cells they are called anticytolyzing substances.

The method proposed for storage of blood making it possible to keep blood for 60-80 or more days in a condition suitable for transfusion, consists of the addition to the preservative solutions of certain anticytolyzing preparations of diprosin and etisin.
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