ABNORMAL HEMOGLOBINS

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TERMINOLOGY OF HEREDITARY HAEMOGLOBINOPATHIES INVOLVING HAEMOGLOBIN VARIANTS.


Some idea of the various recommendations given by this Working Party may be obtained from the table which they give to exemplify known Hemoglobin Combinations.

<table>
<thead>
<tr>
<th>A</th>
<th>Normal adult</th>
</tr>
</thead>
<tbody>
<tr>
<td>A + F</td>
<td>Infants</td>
</tr>
<tr>
<td>A + S</td>
<td>Sickle-cell trait</td>
</tr>
<tr>
<td>A + S + F</td>
<td>Sickle-cell/thalassemia</td>
</tr>
<tr>
<td>C (+ F)</td>
<td>Hb--C disease</td>
</tr>
<tr>
<td>A + C</td>
<td>Hb--C trait</td>
</tr>
<tr>
<td>A + C + F</td>
<td>Hb--C/thalassemia</td>
</tr>
<tr>
<td>S + C (+ F)</td>
<td>Sickle-cell/Hb--C disease</td>
</tr>
<tr>
<td>D</td>
<td>Hb--D disease</td>
</tr>
</tbody>
</table>

A + D Hb--D trait
S + D ( + F) Sickle-cell/Hb--D disease
A + E Hb--E trait
E + F ( + A) Hb--E/thalassemia
G Hb--G disease
A + G Hb--G trait
A + I Hb--I trait
A + H Hb--H trait
A + J Hb--J trait

—R. H. G.


The blood of a patient born in the Mianwali District of Pakistan was investigated when he was admitted to hospital in London for erythema nodosum. His hemoglobin consisted of two fractions one of which was hemoglobin A and the other a minor component moving at pH 8.6 more slowly. It was not one of the known hemoglobins and moved between hemoglobins S and G. The abnormal component formed 28% of the total hemoglobin. The patient’s mother’s hemoglobin consisted of hemoglobin A and a component moving more slowly than A but faster than S or D. The name hemoglobin L is given to the abnormal component in the patient’s hemoglobin.—R. H. G.


The subjects surveyed were 326 Indians living in and near Kampala, Uganda, and nearly all were first, second or third generation immigrants from the Bombay region of
India. The survey was for hemoglobin D, and two unrelated subjects were found to exhibit both hemoglobins A and D. One woman who came from Gujarat had an abnormal hemoglobin with greater mobility than hemoglobin A at pH 8.6. It was unassociated with any abnormality in the blood. The properties were those of hemoglobin J.-R. H. G.

**Haemoglobin K in an East Indian and His Family. J. A. M. Ager and H. Lehmann.**


The abnormal hemoglobins so far described in East Indians are S, D and E. This South African of Indian (Madras) extraction, living in London, had hemoglobin with the electrophoretic properties of hemoglobin K. One son showed the same abnormality. Hemoglobin K has previously been seen in Kabyles, Liberians and Dagombas, all from Africa.—R. H. G.

**Sickle-Cell-Thalassaemia Disease in South Turkey. M. Aksoy and H. Lehmann.**


When both the genes controlling the formation of normal adult hemoglobin are replaced by alleles responsible for the sickle cell hemoglobin variant, sickle cell anemia (S.C.A.) results. If only one A gene is thus replaced, the subject is usually a symptomless carrier of the sickle cell trait (S.C.T.). However, if an AS heterozygote inherits a single thalassaemia gene, suppression of hemoglobin A formation with a subsequent preponderance of hemoglobin S may produce a state which resembles S.C.A. This is called sickle cell–thalassaemia disease (S.C.Th.D.) or microdyserythrocytic disease.

In the Eti-Turks, a small Arabic-speaking population enclave near Mersin, in Southern Turkey, five cases of S.C.Th.D. were seen in four families. In addition two people were discovered who were heterozygous for the thalassaemia and sickling genes but were not anemic. The incidence of the hemoglobinopathy among the Eti-Turks is equalled only in Sicily.—R. H. G.

**Sickle Cell Anaemia in Assam. J. N. Batabyal and J. M. G. Wilson.**


Sickle cell anemia is described in a boy aged 4½ years (Hb. 4.5 Gm.) and his infant sister aged 1 year (Hb. 6.0 Gm.). Parents of these patients were immigrants from Orrissa and were settled in Assam.—J. B. C.

**Occurrence of Sickle Cell Anaemia and Cases of Sickle Cell Trait in Nagpur, R. N. Shukla and A. S. Parande.**

From the Department of Pathology and Bacteriology, Nagpur, India. Ind. J. M. Sc. 10:892–895, 1956.

Details of Sickle cell anaemia in a 13-year-old male, Mahar by caste, is described.—J. B. C.


Incidence of Hb. E trait and of thalassemia trait in a series of 700 Bengalees was found to be 3.9% and 3.7% respectively.—J. B. C.


From the Haematological Unit, I.C.M.R., School of Tropical Medicine, Calcutta. Indian J. M. Sc. 11:554–564, 1957.
Abstracts

Details of 20 patients with Hb. E-thalassemia disease are presented. Clinical and hematologic features were similar to those of homozygous thalassemia from which the condition could be differentiated by electrophoretic analysis of hemoglobin. Splenectomy done in 7 patients produced only partial improvement.—J. B. C.


In a series of 700 unrelated Bengalees, the incidence of Hb. E was 3.9% and that of thalassemia trait about 3.7%.—J. B. C.


Sickle cell thalassemia is described in a 2½-year-old female child and her 11-year-old sister belonging to a Maratha Kunbi family.—J. B. C.


An instance of Hb. S-thalassemia is described in a 10-year-old Indian girl. The patient presented hemolytic anemia of moderate degree. This was the only case of Hb. S-thalassemia in a series of 200 cases of thalassemia syndrome investigated in Calcutta.—J. B. C.

Radiation Disease


When bone marrow suspensions from within an inbred strain of mice (isologous) and between strains (homologous) are injected intravenously into lethally irradiated mice, delayed deaths occur in the latter group 2 to 3 months after irradiation. The delayed death is caused by a homologous bone marrow reaction involving a proliferation of foreign bone marrow cells in the irradiated host. These reactions can be interpreted as evidence of a hypersensitive state resulting from a chronic in vivo tissue antigen–antibody reaction.—O.P.J.


Mice of the CBA/H strain, aged 3 to 4 months, were given a generalized lymphoid leukemia (151/1) by intravenous or subcutaneous passage of cells. When mice are given an otherwise lethal dose of x-rays to the whole body they can recover if injected intravenously with homologous myeloid cells. It is now established that their depleted hemopoietic and lymphopoietic tissues are colonized by cells derived from those that have been injected. Therefore, a method of treatment of leukemia might be to give a dose of x-rays that would be sufficiently lethal to normal cells of the bone marrow and lymphatic tissue to cause death of the animal, and completely lethal to leukemia cells, then to treat the irradiated animal with normal isologous bone marrow from the same strain of mouse, thereby perhaps preventing its death.

Accordingly, one week after receiving the 151/1 leukemia the mice were given x-
irradiation to the whole body in doses approximating to the LD$_{100}$. They were then treated with intravenous injections of isologous (CBA) myeloid tissue (a few with homologous bone marrow from other strains of mice) in order to recolonize hemopoietic and lymphopoietic tissue. Given 950 rads at high intensity (14 minutes) the mice were not cured of leukemia, but when the dose was 1,500 rads in 25 hours there were 25 survivors out of 35 animals after 3 months.—R.H.G.


When lethally irradiated mice were injected with whole blood showing a marked granulocytosis, 10–70% survived, and this seemed to be due to the formed elements and not the plasma. In order to determine how leukemoid blood causes this recovery, leukocytes from several sources were tested for recovery activity. Leukocytes from BALB/c JAX mice bearing a transplantable squamous-cell carcinoma (A280) cause a recovery of lethally irradiated BALB/c mice. One hundred per cent survival is usually obtained with 100.0 x 10$^6$ or more leukocytes. Heterologous leukocytes from normal rats and rabbits, and from man with leukemia proved ineffective in these experiments.—O.P.J.


Studying the synthesis of hemoglobin in vitro, Nizet has established that incubation at 37° for 24 hours confers to plasma some stimulating properties. Progressive fractionation resulted in a concentrated fraction (C fraction) which at a very low concentration stimulates the hemoglobin synthesis in vitro (5 γ cu. mm.). This factor was present in normal as well as in anemic dogs’ plasma.

On the other hand, Nizet and Herve have established that plasma of irradiated dogs contained also a factor stimulating hemoglobin synthesis in vitro. Chemical characterization of this factor has not yet been achieved. It has not been evidenced that the two factors are identical.

In order to see whether survival was affected the authors injected the C fraction (from incubated plasma) in mice after a lethal dose of x-rays. Three mice survived definitely. The mean survival time of injected mice was greater than that of the controls. The difference was statistically significant.

Although the differences obtained are small, it is considered that further studies should be made on its efficiency. The identification of the C fraction and of the factor stimulating hematopoiesis in the irradiated dog may prove of value in the study of irradiation sickness.—O.P.J.

**The Effect of Narcotics and Anesthetics on the Mortality of Animals After Lethal Irradiation with X-rays.** Z. Dienstbier, J. Símský and V. Kofránek. From the 1st Medical Clinic and the Institute for Aviation Physiology, Charles University, Prague, Czechoslovakia. Cas. lék. čes. 95:889–894, 1956.

The possibility of decreasing the mortality of young laboratory rats irradiated with lethal doses of x-rays by the administration of several narcotics or substances possessing an anesthetic action (dial, dorminal, pentothal, ether, urethane, procaine, ethanol) was investigated; no protective action of any of these substances against the effects of x-ray irradiation was noted.

The conclusions drawn by other authors claiming that some of these substances may have a blocking action on the irradiated animals are described and the reasons for these conflicting results are discussed. The authors emphasize the necessity of considering the
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organism as a whole; the contemporary knowledge of this subject being still inadequate, further studies of the nervous system in irradiation sickness are necessary.—M.N.


In 18 cases of lymphogranuloma, lymphosarcoma, leukemia, lung carcinoma, the leukocytic resistance was studied during roentgen irradiations. A significant decrease of the resistance was detected even before the onset of leukopenia.—P.d.N.


Previous studies indicate that x-rays may produce different primary or immediate effects in different cells, namely, rabbit lymphocytes and amphibian ova. Hence, they may have more than one effect in the same cell. In order to test this, suspensions of rabbit thymus in 50% rabbit serum were exposed to different amounts of irradiation. The preparations were incubated at 37 C. and photographed by time-lapse cinemicrography. After 10,000 r some of the cells developed early degenerative changes, including irregularities in the shape of the nuclei. In one of three hours all of the cells were seen to undergo death, as indicated by loss of oscillatory and rotational movements, rounding up of the nucleus, and increased transparency of the nucleoplasm. After irradiation with 1000 r, the lymphocytes died by intranuclear vacuolation, lobulation, and pycnosis.—O.P.J.

LEUKEMIA


This is a thoughtful assessment, particularly with relation to recent work on etiology, course and treatment, inspired by the rise in incidence of leukemia and by the discovery of new therapeutic drugs. The disease is still relatively uncommon, and is commoner in rich than in poor. Acute leukemia is becoming commoner than chronic, and chronic lymphatic more frequently seen than chronic myeloid. To a certain extent the increase is due to improved medical care and ageing of the population, but this is not the whole story. A familial incidence is unusual. Leukemia is unduly frequent in doctors and nurses who work with x-rays, after x-ray treatment of ankylosing spondylitis and other non-malignant conditions, and in survivors of atomic bomb explosions. In all these the dosage was probably more than 100 r over a short period or 200 r over a longer period. The normal background radiation in man in a generation is about 3 r. A gastrointestinal examination may expose the patient to 15 r per minute.

It has been reported (Stewart et al., Lancet 2:447, 1956) that about twice as many of the mothers of children who died of leukemia or malignant disease before the age of 10 in the years 1953–5 had an x-ray examination of the abdomen in pregnancy compared with a control group. A Medical Research Commission committee considered that there would be little increased risk of leukemia if an individual received a total dose of 200 r in his lifetime in addition to background radiation, provided the dose was distributed over tens of years and that the maximum weekly exposure, averaged over any period of 13 weeks, did not exceed 0.3 r. However there is probably no threshold below which x-rays are harmless. The greatest care must be taken in exposing ourselves, our patients and above all pregnant women to x-rays and radioactive agents.

However, most of the leukemias occurring after radiotherapy for spondylitis and most cases after atomic bombs have been myeloid, while the increase in spontaneous cases has been largely in chronic lymphatic.
One of the most interesting occurrences in leukemia, and one which makes therapeutic trials difficult, is the spontaneous remission of acute leukemia. It is essential to have organized therapeutic trials of new forms of treatment.—R.H.G.


These articles are the text of three Lettsonian lectures given to the Medical Society of London in February, 1957. They deal first with the incidence and etiology of leukemia and then in turn with acute leukemia, chronic myeloid, and chronic lymphatic. Clinical features, the blood pictures, pitfalls of diagnosis and methods of treatment are considered. The full text should be read.

The incidence of the disease is rising, its cause is unknown, and treatment seldom prolongs life, let alone preserves it. Reports of the cure of experimental leukemia in mice may give a gleam of light for the future.—R.H.G.


A survey of the incidence of the various types of leukemia, lymphosarcoma and Hodgkin’s disease is made in two large hospitals of Sao Paulo: Santa Casa de Misericordia, for the period of 1934 up to 1944, and Hospital das Clinicas of the Sao Paulo University Medical School, for the period of 1945 up to 1954. An actual increase was observed in the incidence of the various forms of leukemia, greater in the acute form, predominantly in March–April (autumn in the area studied) and September–October (spring in this area). Lymphatic leukemia and lymphosarcoma do not exhibit any significant variation.—M.A.J.


The records were examined of 624 cases of leukemia occurring in members of the Armed Forces in 1940–54. There was a significant increase during that period in the mean age at onset of the acute type whether the term “acute” included cases with a duration of up to 6 months or up to 12 months. No significant change was found in the mean age at onset of chronic leukemia in that period. Statistical comparison with tables of death rates from leukemia in England and Wales for 1911–1953 showed differences which were interpreted as showing nonsignificant increases in deaths from leukemia for the age groups 20–24, 25–29 and 30–34, but rapidly growing significant increases for the older age groups. The authors conclude that it is probable that environmental factors are responsible for the changes and that one such factor may be man-made additions to background radiation.—R.H.G.

IRON METABOLISM


The present work is divided into two parts: (1) case history of a very peculiar affection, combining hemochromatosis and hypochromic anemia without abnormal hemoglobin; (2) study of the liver, medulla and blood of the patient with the electronic microscope, which investigations afforded a substantial aid to the physiopathologic interpretation of
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the clinical case. Electronic microscopy has exhibited an iron overload (ferritin and derivatives, in the mitochondrias) of the reticulocytes and hypochromic erythrocytes.

The hypochromia therefore seemed to be related to the nonutilization of the iron at the level of erythroblasts. Stress is placed on the exceptional character of that combination of hemochromatosis with hypochromic anemia without fetal hemoglobin.

The authors discuss the diagnosis of Cooley’s disease and Heilmeyer siderochrestic anemia, and finally they consider the syndrome to be different from these two diseases.—J.D.


If the interpretation of the observations reported in this brief note are correct, then it will be necessary to revise the concept of iron metabolism. Bessis and Breton-Gorius examined ultrathin sections of human bone marrow by electron microscopy. They believe that particulate iron is passed from marrow macrophages to erythroblasts by a process similar to pinocytosis.—O.P.J.


THREE ASPECTS OF IRON IN ORGAN SECTIONS EXAMINED WITH THE ELECTRON MICROSCOPE. M. Bessis et J. Breton-Gorius.

The authors have observed in histocytes, and described previously, iron granules proceeding from the digestion of phagocyted erythrocytes. Those particles penetrate the young erythroblasts. A larger magnification reveals that the granules observed are ferritin granules, whose molecules penetrate in the erythroblast mitochondria where they undergo a transformation, after which the mitochondria break up and iron is released into the cytoplasm and takes part in the synthesis of hemoglobin. Ferritin molecules were also formed in the jejunal epithelial cells of the small intestine.—J.D.


In a series of 12 patients with nutritional macrocytic anemia, significant and sharp drop in serum iron level was consistently observed between 2 to 4 days in all the 10 patients showing satisfactory erythropoietic response. This fall in serum iron usually appeared before the reticulocytic peak.—J.B.C.


Using the radioactive isotope Fe² in polycythemia vera, a clearance curve of the plasma iron of the sideropenic type was noticed. Also the index “erythropoetic iron utilization,” defined as the ratio between the radioactivity, measured in the erythrocytes at fifth and at first day, pointed to a sideropenic state. After the therapeutic use of P² there was a renormalization of the iron plasma content and of the intestinal absorption.—M.A.J.

A case of idiopathic hemosiderosis of the lungs diagnosed on a 5-year-old girl and confirmed by autopsy is reported. Repeated treatment with ACTH and cortisone had only temporary success. Splenectomy had no effect. At autopsy, the finding of an atelectatic segment of the lung which was not affected by hemosiderosis, was interesting from the pathogenetic point of view. The content of iron in the pulmonary tissue was ten times higher than in normal tissue of an adult person. The origin of the disease on the immunotoxic basis seems to be the most probable with respect to the case described.—M.N.

The Other Journals of Hematology


