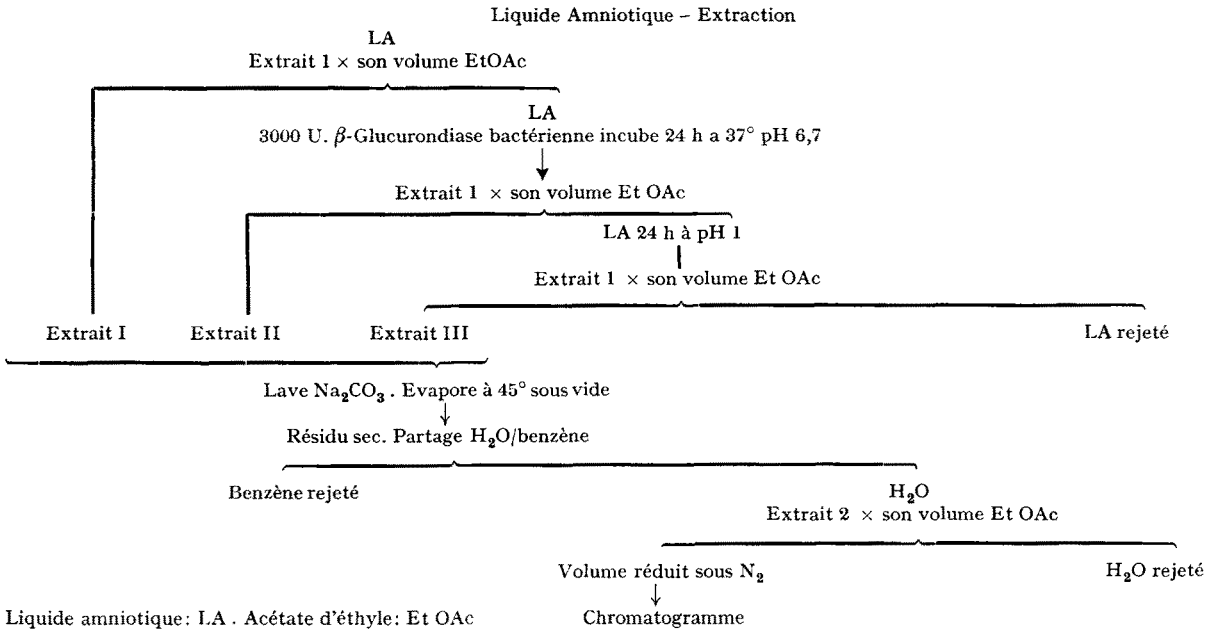

Fig. 2.

Ces substances ont été mis en évidence dans le liquide amniotique d'une femme diabétique dont le nouveau-né présente l'aspect particulier dit «Cushing» et une anomalie congénitale. Leur quantité a été appréciée entre 25 et 50 μg dans le volume de 650 ml de liquide amniotique. Ce liquide contenait un taux anormalement élevé de protéines de 0,7 g%.

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Summary

Paper chromatography was applied to corticoids extracted from amniotic fluid of a diabetic mother.

Normal amniotic fluid contains no 17-hydroxycorticosterone and cortisone, as defined by paper chromatography.

The extract of amniotic fluid of a diabetic mother, insulin treated from the 4th month and giving birth to a child with a congenital anomaly of cervical vertebras (KLIPPEL-FEIL syndrome) and with typical "Cushing" aspect, has been chromatographed. It contains 25–50 μg of 17-hydroxycorticosterone and cortisone. The protein content of this fluid was 0·7 g %.

The Diphenylamine Test on Leukemic Sera

According to AYALA and his coworkers[1], and NIAZI and STATE[2] the intensity of the purple color from the DISCHE diphenylamine test[1] is greatest with sera from patients with carcinoma, pulmonary tuberculosis, and rheumatic fever.

We found that the diphenylamine (DPA) reagent is extremely useful as an aid in diagnosing leukoproliferative disorders.

Our normal controls were 500 healthy, hospital staff adults, 18 to 50 years of age. Another group of 1,852 patients, 3 to 88 years of age, were selected at random from routine hospital admissions to represent various pathological states. We divided these cases into three groups; 1,670 non-malignant pathological conditions, 104 malignant neoplasms non-leukoproliferative, and 78 leukoproliferative disorders. All diagnoses were made by complete medical and clinical observations. The leukoproliferative group had complete blood counts, including supra-vital stain of peripheral blood and bone-marrow, and autopsy findings, when feasible. Cases with doubtful diagnoses were omitted.

The DPA reagent was made according to DISCHE[2]. Among the slight modifications we made in the analytical procedure of AYALA[3] was the use of only 0·2 ml of serum to permit analysis of samples from infants and small children. The optical density of the clear purple reaction mixture was read from a BECKMAN Model B Spectrophotometer at 530 mμ with distilled water as the reference solution. The optical density of the solution multiplied by 1,000 gives the DPA index.

The DPA index for 500 normal controls ranged from 180 to 350 units, with a mean value of 248 units, and a probable error of 5·35 units.

The 1,670 non-malignant pathological cases, 15 to 65 years of age, consisted of pregnancies, cardiacs, infectious mononucleosis, hepatobiliary diseases, benign tumors, poliomyelitis, nephrosis and uremia, gastric ulcers, burns, anemias, non-specific infections, collagen diseases, diabetes mellitus, tuberculosis, lupus erythema-

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[1] Z. DISCHE, Mikrochemie *8*, 4 (1930); *7*, 33 (1929); J. Biol. Chem. *167*, 189 (1947).

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[3] W. AYALA, L. V. MOORE, and E. L. HESS, J. Clin. Invest. *30*, 781 (1951).

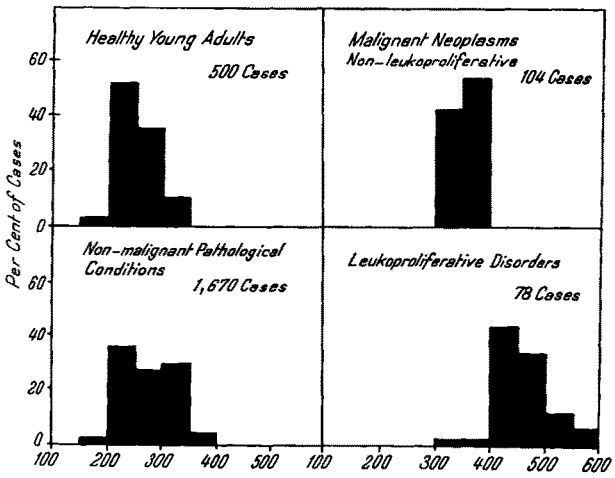

Fig. 1.–Distribution of the DPA indices in four groups of human sera.

tosus, polycythemia vera, and ADDISON's disease. The DPA index ranged from 160 to 376 units, with a mean value of 274 units, and a probable error of 4·78 units.

The third group was 104 persons, 5 to 88 years of age, with maignant neoplasms, not leukoproliferative, consisting of breast tumor, cancer of the prostate, cancer of the liver, ovarian tumor, skin cancer, brain tumor, osteogenic sarcoidosis, cancer of the esophagus, lung cancer, intestinal cancer, cancer of the tongue, and kidney tumor. The DPA index ranged from 303 to 406 units, with a mean value of 370 units, and a probable error of 5·02 units.

The fourth group, consisting of 78 leukoproliferative conditions or those involving the blood forming organs, 3 to 75 years of age, included acute and chronic leukemia, acute monocytic leukemia, and chronic granulocytic leukemia, reticulum cell sarcoma, lymphosarcoma, lymphoblastoma, multiple myeloma, and HODGKIN's disease. The DPA index ranged from 298 to 600 units, with a mean value of 448 units. The probable error was 5,38 units.

We were fortunate to be able to test several extremely early cases of lymphatic leukemia. These cases gave DPA indices of 298 to 304 units. All other cases of leukoproliferative disorders had a DPA index of 400 units or higher when we first tested them.

The mean values for the normal controls and the non-malignant pathological states differed by 26 units, but the mean value for the malignant neoplasms was 122 units higher than the normal. The mean value of the leukoproliferative disorders was 78 units higher than the malignant neoplasms and 200 units higher than the normals. This difference from malignant neoplasms is sufficiently high to be useful in the diagnoses of leukemia.

The figure shows the distribution of the DPA indices in the four groups of subjects. The highest DPA index values correspond to the leukoproliferative conditions. Multiple myeloma gave especially high values, 520 to 606 units. The index always becomes higher as the leukemia progresses. When drugs such as ACTH, Cortisone, Aminopterin (Lederle), triethylene melamine (Lederle), nitrogen mustards, or X-radiation were given to control the leukoproliferative disorders of patients, the steady increase in the DPA index nevertheless persisted. Even through the disease was in a state of remission or relapse, as revealed by the blood and bone-marrow studies, the DPA index continued to increase and always remained elevated. All other diseases showed a decrease to the normal index range when the patient was in the recovery stage.

The range, 303 to 406 DPA index units, for malignant neoplasms indicates that the test might also be useful as a screening test for malignancy. Leukemia may be easily distinguished from these processes during the advanced stages when the index is high. Border-line cases will require additional laboratory investigation.

Infectious mononucleosis gave no abnormal rise in the index reading, and therefore, it may be distinguished from leukemia even if the cytologic picture sometimes may be confusing.

Knowledge that the basic abnormality of a leukoproliferative disorder was present would lead to an earlier diagnosis and provide a basis upon which to begin the available therapeutic measures and to study new ones.

Further details of this work will be published elsewhere.

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Zusammenfassung

Alle leukämischen Kranken hatten einen hohen Diphenylamin(DPA)-Index. Falls das mikroskopische Blutbild keine sichere Aufklärung gibt, kann der DPA-Index zur diagnostischen Unterscheidung zwischen Pseudoleukämie und echter Leukämie angewendet werden.

Alkali-Resistant Cooley's Anemia Hemoglobin is Different from Alkali-Resistant Fetal Hemoglobin

An alkali-resistant hemoglobin that has all the properties of normal fetal hemoglobin has been described in COOLEY's anemia[1] and related Mediterranean hemopathic syndromes[2].

This Hb and the fetal Hb react identically to the denaturation in aqueous alkaline solutions, move the same distance on paper electrophoresis, show the same properties in crystallization, solubility and ultraviolet absorption spectra.

Most authors are therefore inclined to believe that such hemopatic conditions are associated with a congenital inability to pass from fetal to adult mechanism of hemoglobin synthesis.

We all know the importance of the application of several independent methods to check the homogeneity of the protein specimens.

The following differences between fetal and COOLEY's anemia Hb already have been demonstrated in our Institute:

(1) While their correspondent oxyhemoglobins are known to be denaturated by alkali at the same rate, they are denaturated by acids at different rates[3];

(2) their carbon monoxide derivatives are denaturated both by alkali and by acids at different rates[1].

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