plasma-volume depletion, such as are induced by fluid restriction and cleansing enemas before intravenous pyelography. Elevated plasma-renin levels have been measured after relatively mild salt deprivation.[8] We have repeatedly observed resistance to angiotensin-infusion under such circumstances, and have advised that the test should be repeated, in all patients who are resistant, immediately after infusion of 250–500 ml. of physiological saline solution.[7] Patients with renovascular hypertension remain resistant, whereas those with resistance secondary to shrinkage of plasma-volume become sensitive. Perhaps this source of error could be obviated by giving this amount of saline to all patients before performing the test, particularly since it is necessary to start an intravenous infusion and to give the blood-pressure adequate time to reach basal levels before starting the infusion of angiotensin.

We agree with Dr. Breckenridge that the test is reproducible, uninfluenced by antihypertensive treatment, and unrelated to responsiveness to other pressor agents.

Department of Internal Medicine,
Southwestern Medical School,
University of Texas,
Dallas, Texas 75235. NORMAN M. KAPLAN.

ERYTHROCYTE LIPIDS IN AMAUROTIC IDIOCY

SIR,—As part of a programme for the investigation of lipidoses, erythrocyte-lipids were studied in affected and non-affected members of families in which an anatomically verified case of late infantile amaurotic idiocy (L.I.A.I.) or juvenile amaurotic idiocy (J.A.I.) had occurred. Blood-samples were taken in the non-fasting state from one case of L.I.A.I., four cases of J.A.I., eight parents from necropsy-proven cases of L.I.A.I., and five parents from necropsy proven cases of J.A.I. Extraction of lipids from erythrocytes was performed within five hours after the sample had been taken. Thoroughly washed erythrocytes were extracted in sequence with methanol, twice with a mixture of methanol and chloroform in equal volume proportions, and with chloroform. Phospholipids, cholesterol, and triglycerides were analysed by methods described in detail elsewhere,[9] but the results were unremarkable. N-acetyl neuraminic acid (N.A.N.A.) was determined in the lipid extracts by a method described by Warren.[10] The experimental error involved in this determination was assayed by sending six portions of a 300-ml. sample taken from a normal subject to the laboratory, without laboratory personnel being aware of this blind test. The variation in the values obtained for these portions proved to be equivalent to the variation observed in five samples from five normals in the non-fasting state. As an interesting, unexplained side observation, a group of ten normals in the fasting state proved to have lower values for lipid-N.A.N.A. than the group of six normals examined in the non-fasting state.

The accompanying table shows that the N.A.N.A. values in the groups of parents and in the patients are significantly higher than the levels in the six normal, non-fasting individuals. This increase of lipid-N.A.N.A. in clinically normal parents may be tentatively regarded as a biochemical expression of the heterozygous state. A recessive autosomal transmission is now generally accepted as the mode of inheritance in J.A.I. As is shown elsewhere,[11] the mode of inheritance in L.I.A.I. is not yet clarified. None of the seven families with L.I.A.I. accessible in the Netherlands showed consanguinity, nor could they be traced to the same geographical area.

In the reported cases consanguinity of the parents is also an exception rather than a rule.[11] The present study shows that an increased lipid-N.A.N.A. content of the erythrocytes may be an additional diagnostic characteristic in amaurotic idiocy, and may also serve as one of the factors on which genetic counselling could be based. The study of the chemical composition of red blood-cells for genetic purposes has also been proposed for other forms of lipidoses.[12] The pathochemical significance of the increase in lipid-N.A.N.A. values in amaurotic idiocy is still unexplained. Accumulation of gangliosides (i.e., N.A.N.A.-containing glycolipids) is one of the main pathochemical characteristics of nervous tissue in infantile amaurotic idiocy or Tay Sachs' disease, and a concomitant characteristic of nerve-tissue in Niemann Pick's disease and in gargoylism.[13] In L.I.A.I. and in J.A.I. a possible accumulation of gangliosides in the neurons is indicated histochemically but not proven biochemically. For the time being it is tempting to relate the observations on erythrocyte-lipid-N.A.N.A. to possible abnormalities in the N.A.N.A.-containing glycolipid fraction of the red blood-cells. Whether this abnormality is due to an increase, to an abnormal molecular constitution, or to abnormal physicochemical properties leading to abnormalities in solubility is uncertain. Studies are in progress to isolate and further characterise the N.A.N.A.-containing glycolipid fractions from larger blood-samples by means of thin-layer chromatographical and analytical methods.

N.A.N.A. IN LIPID EXTRACTS OF ERYTHROCYTES (mg. per 100 ml. packed cells)

Subjects	Mean	Range	Individual observations
10 Normals (fasting) ..	1·00	0·77–1·09	0·77* .. .. 0·85* 1·09*
5 Normals (non-fasting)	1·08	0·91–1·26	0·91* 0·98 1·04 1·19* 1·26*
1 Normal	1·11†	1·00–1·24	1·00 1·05 1·10 1·12 1·14 1·24
8 Parents (L.I.A.I.)‡: ..	1·36	1·00–1·63	
Mothers			1·63 1·39 1·49 1·00 1·34
Fathers§			1·45 1·20 1·30
5 Parents (J.A.I.)¶: ..	1·79	1·00–3·06	
Mothers			1·98 3·06 1·54
Fathers§			1·00 1·41
1 Patient L.I.A.I. ..			1·58
4 Patients J.A.I. ..		1·76–5·70	3·20 5·70 3·35 1·76

* N.A.N.A. values measured in the same individual.
† 6 independent determinations on a 300-ml. sample.
‡ L.I.A.I.
§ Values for mothers and fathers presented in vertical rows relate to parents of one patient.
¶ J.A.I.

Institute for Epilepsy Research,
Meer en Bosch, Heemstede, and
Institute for Human Biology,
State University of
Utrecht, Holland. G. W. F. EDGAR.

Department of
Medical Chemistry,
State University of
Leiden, Holland. G. J. M. HOOGHWINKEL
P. BORRI.

PULMONARY EMBOLISM IN HEALTHY PEOPLE

SIR,—The report of an inquest[14] on a young woman who died of massive pulmonary embolism while taking oral contraceptives has been given considerable publicity in the lay press.

The evaluation of any possible relation between thrombosis and oral contraceptives will be very difficult, for there are few reports of the incidence of massive pulmonary emboli in healthy people. I am jointly preparing a detailed study[15] of this condition as it presents in Cambridge, and my co-worker and I have confirmed a suspicion[16] that sudden death due to massive pulmonary embolism is not rare in healthy people. From 9280 consecutive autopsy reports in the Cambridge University department of pathology covering 1946–63, we have collected 27 cases under the age of 70. Of these 27, 21 were female and 6 male. Only 3 women were under the age of 45, and they were either pregnant at the time or had recently been pregnant. Thus we found no examples of young non-pregnant women in this series. Our study of an even larger series of non-fatal cases gives a similar result. Breckenridge and Ratnoff,[17] however, found cases in normal non-pregnant young women. They surveyed coroners' necropsy records for 1951–62 of persons between the ages of 15 and 45. Of their 26 cases, 11 occurred in non-pregnant women, 5 in pregnant women, and 10 in men. There is obviously a need for further study of this type.

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