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II. Coproporphyrin I Metabolism and Hematopoietic Activity.

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In a previous communication concerning the porphyrin excretion in normal individuals[1] we have briefly outlined a concept of the dualism of the porphyrins, stating that in certain pathological conditions increased or decreased Type III porphyrin construction associated with hematopoietic activity may lead to a proportionally increased or decreased Type I porphyrin construction and excretion. This communication presents data which bear out this concept.

A classical case of hemolytic jaundice with 1,600,000 R.B.C., 4.5 gm. of hemoglobin per 100 cc., 21,000 nucleated R.B.C., 5,800 W.B.C., 10% reticulocytes, icterus index 30, Van den Berg (indirect) 3.1 mg.%, and markedly increased R.B.C. fragility was studied. The patient was maintained throughout the period of observation on a bland diet containing small amounts of meat. After 3 blood transfusions splenectomy was performed, following which R.B.C. increased to 2,500,000, hemoglobin to 9.0 gm. per 100 cc., the reticulocytes decreased to 2%, and the icterus index decreased to 10. Porphyrin and stercobilin excretion were followed quantitatively before and after operation.

In the 7 days previous to operation the average daily value for urinary and fecal coproporphyrin was 718 micrograms. The stercobilin averaged 407 mg. during the same period. During the first 6 post-operative days the total coproporphyrin I excretion averaged 648 micrograms per diem. In the same period the stercobilin values fell rapidly to 157 mg. per day. The average coproporphyrin excretion for the next 6 days was 371 micrograms and the stercobilin 73 mg., both within normal range.

These data strongly indicate that physiologically increased hematopoietic activity is accompanied by increased coproporphyrin I excretion. The excretion reverts to normal coincident with decreased hematopoietic activity.

A second patient with hemolytic jaundice, followed for 20 days

[1] Dobriner, K., Strain, W. H., and Localio, S. A., Proc. Soc. Exp. Biol. and Med., 1937, **36**, 752.

and not operated upon, showed a daily average total coproporphyrin I excretion of 652 micrograms.

To prove these data further we investigated quantitatively the coproporphyrin I output in therapeutic hemolysis in a case of polycythemia vera. The patient, a known polycythemia vera with characteristic bluish-red discoloration of the skin and mucous membranes, enlarged spleen, and R.B.C., hemoglobin, hematocrit, blood volume, and viscosity increased to polycythemia levels, received a total of 1.4 gm. of phenylhydrazine-HCl over a 7-day period. This resulted in a decrease of the R.B.C. from 7,700,000 to 4,070,000, hemoglobin from 18.0 to 10.5 gm. per 100 cc., hematocrit from 59 to 36, and viscosity from 7 to 3.8. The icterus index increased from 7 to 30 and the reticulocytes from 1.0 to 5.0%. Throughout the study the patient was maintained on a constant diet.

During the 6 days prior to therapy the average daily total coproporphyrin I excretion was 371 micrograms and the stercobilin 143 mg. No significant changes in porphyrin or stercobilin values were observed during the first 3 days of therapy. In the next 3 days there was however a definite rise of the stercobilin from 148 to 254 mg. a day, the porphyrin values remaining unchanged. On the seventh day of treatment destruction of hemoglobin was manifested by falling blood hemoglobin. During this period the coproporphyrin I excretion rose to 739 micrograms and there was a simultaneous rise in the reticulocytes. The previous elevated stercobilin values reached a peak of 836 mg. These values decreased slightly during the remaining 18 days of observation.

The final evidence was derived from study of a patient manifesting decreased hematopoietic activity. Severe anemia was associated with a neurocytoma of the adrenal with massive metastasis to the bones and destruction of bone marrow. The coproporphyrin excretion averaged only 131 micrograms per day during a 7-day observation period.

Three patients exhibited increased coproporphyrin I excretion during periods of increased hematopoietic activity. One patient showed a return to normal excretion following splenectomy and coincidental with return to normal hematopoiesis. A fourth patient showed a decreased coproporphyrin I excretion associated with decreased hematopoiesis. It is concluded that the production and excretion of coproporphyrin I is parallel to the physiological hematopoietic activity.