Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Porphyria

SIR,—Numerous attempts have been made during recent years to provide a satisfactory classification of the porphyrias. All workers are agreed that congenital porphyria (Günther) is a distinct clinical and pathological entity in which abnormality resides in the haemopoietic system. The acute porphyria and porphyria cutanea tarda of Waldenström¹ appear to involve the liver rather than the haemopoietic system and were therefore grouped under the heading "hepatic porphyria" by Watson *et al.*,² to distinguish them from the "haemopoietic" congenital porphyria. Schmid, Schwartz, and Watson³ later recognized a mixed porphyria of hepatic type to accommodate cases in which symptoms were present resembling those of both acute intermittent porphyria and porphyria cutanea tarda.

My own investigations led me⁴ from 1952 to emphasize the biochemical differences between those patients exhibiting abdominal colic, large output of urinary porphobilinogen, not infrequently nervous symptoms but without photosensitivity or other lesions of the skin (acute intermittent porphyria) from patients on whom lesions of the skin were present. These latter excreted little if any urinary porphobilinogen but large quantities of faecal porphyrins; they seemed to be best accommodated under porphyria cutanea tarda, and familial incidence could frequently be demonstrated (see Holti, Rimington, Tate, and Thomas⁵). At the same time, evidence was steadily accumulating that a condition very similar to porphyria cutanea tarda could arise as a result of chronic alcoholism⁶ or malnutrition associated possibly with other hepatotoxic factors.⁷ Convincing proof of the possibility of symptomatic cutaneous porphyria was afforded by the case of a woman with a porphyrin-producing liver-cell adenoma.^{10,11} The classification of the hepatic porphyrias required revision, and this has been admirably accomplished, to my mind, by Waldenström,¹² who proposes the following:

- (1) Porphyria cutanea tarda symptomatica:
 - (i) Alcoholic cirrhosis
 - (ii) Bantu cirrhosis
 - (iii) Exceptional cases
- (2) Porphyria cutanea tarda hereditaria:
 - Protocoproporphyrin
- (3) Acute intermittent porphyria.

In their recent publication Drs. Geoffrey Dean and H. D. Barnes (*Journal*, February 8, p. 298), however, discard acute intermittent porphyria and propose to recognize the "Swedish type of porphyria hepatica" and the "South African type." The latter differs essentially from the former in just those features which I have already insisted serve to distinguish porphyria cutanea tarda from acute intermittent porphyria—namely, in the presence of skin lesions, a continued large production of porphyrins which are eliminated mainly in the stool (even during clinical remission), and absence of porphobilinogen from the urine or its excretion in only relatively small amount during acute exacerbations of the disease. Until the precise biochemical error has been revealed which is in each case responsible for the manifestations of disease in porphyria patients, a truly satisfactory classification cannot be drawn up. I submit, however, that in our present state of knowledge the classification of choice is that due to Waldenström.¹²—I am, etc.,

London, W.C.1.

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Indicators of Irradiation Damage

SIR,—I was interested to read Surgeon Commander P. W. Edmondson's paper (*Journal*, February 15, p. 363) on the effects of chronic gamma irradiation in female guinea-pigs and also the annotation (p. 391) on indicators of chronic irradiation. A preliminary report has been published¹ on quantitative examinations of bone marrow in young male guinea-pigs after acute whole-body gamma irradiation using a cobalt-60 unit as source. Subsequent experiments have confirmed the findings in this report. In the same experiments estimations of blood leucocyte levels were also made at various periods after irradiation.

Quantitative analysis of the immature neutrophils in the marrow shows a steady decline from the fourth hour after irradiation until the fourth day. After an initial and transient polymorphonuclear leucocytosis occurring at the fourth hour, the blood neutrophil level remains within normal limits until about the fourth day, when a decline commences. A partial recovery of the immature neutrophils in the marrow occurs from the fourth to the eighth day and this is followed, after an interval of four days, by the well-known "abortive rise"² in blood neutrophils which occurs from the eighth until the twelfth day. A second decline, which is both marked and progressive, occurs in the marrow levels of immature neutrophils after the eighth day, and this is reflected four days later—i.e., from the twelfth day—by a precipitous fall in blood neutrophils. There is the same lag period of four days in the recovery phase. The immature cells show a marked increase after the sixteenth day, but blood neutrophil levels do not show a definite increase until after the twentieth day. Thus at all times there is a lag period of four days between changes in the marrow population of immature neutrophils and the blood population of mature neutrophils.

Recovery of erythropoiesis in the marrow, as shown by increasing numbers of erythroblasts, occurs from the tenth day after irradiation and is followed, after four days, by a rise in blood reticulocytes and the presence of substantial numbers of polychromatic and orthochromatic erythroblasts in the peripheral blood. The increase in marrow erythroblasts, which is particularly rapid and marked between the fourteenth and sixteenth days, is quickly reflected in the peripheral blood (within two days) by the presence of large numbers of polychromatic and orthochromatic erythroblasts and also reticulocytes.

A correlation can be made between blood and bone marrow cellular levels, especially if the marrow cells are estimated by a quantitative technique rather than by a percentage count. The fallacy of estimating blood leucocyte levels solely by percentage count is widely recognized by clinicians, and the same reasoning should be applied to estimations of bone-marrow populations. Unfortunately, in the human, quantitative estimations of marrow cells tend to be rather variable owing to the varying dilution of marrow aspirate by blood.

One realizes, of course, that the effects of chronic irradiation on the haemopoietic organs differ from those after acute irradiation. However, the effects of the latter are of significance in the event of atomic warfare or after accidents involving peaceful uses of radioactive materials. Thus a knowledge of the time lapse, in man, between changes in marrow and blood granulocyte levels might be of some application, firstly, in assessing cases where exposure to severe acute irradiation had occurred but dosage was indefinite, and, secondly, in assessing the response to myelo-therapeutic measures such as bone-marrow transfusion.—I am, etc.,

Bristol, 8.

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