We hope that the publication of these exceptional findings will be followed by the study of the ascendants in other cases of 'primary macroglobulinæmia'.

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Hæmogram of Normal and Starved Rats

THE bioassay of plasma erythropoietin by the starved rat method was introduced by Fried *et al.* in 1957¹ and has since been utilized by other investigators for evaluating erythropoietic stimuli. Gross changes in peripheral blood are apparent in all rats prepared for assay by withdrawal of food for varying periods of time.

The hæmograms of Sprague-Dawley rats before and after starvation for 80-96 h are shown in Table 1. The rats were kept singly in cages and had previously been fed on standard 'Purina' laboratory chow. Water *ad lib.* was provided during the starvation period. Pre-starvation body-weights were 155-170 g; after starvation, weights ranged from 100 to 121 g.

Mean levels of hæmoglobin, hæmatocrit and red blood cell count before starvation are comparable with other published values on 'normal' laboratory rats^{2,3}. The hypochromia and microcytosis of the erythrocytes may be indicative of relative iron-deficiency, though iron (3 mg/10 g food) was included in the rat diet. High red blood cell, platelet and reticulocyte counts are a striking feature of the normal rat hæmogram. The intense reticulocytosis in the Sprague-Dawley rats before starvation is higher than that noted in an early investigation of normal albino rats by Orten and Smith². Their figures reveal a mean of about 8 per cent reticulocytes in rats of comparable size.

The polycythæmia and hæmoconcentration seen after starvation (Table 1) are probably a reflexion of the degree of dehydration in the starved animals. Similar changes occur in rats given food but no water.

Inanition was accompanied by leukopænia which varied in individual rats from 1,600 to 4,300 white blood cells per cubic millimetre of blood. Differential leukocyte counts were not averaged because of marked variation from one animal to another. Granulocytes were generally less than 20 per cent of peripheral white cells in normal rats and no real differences were found in the starved animals.

Specific nutritional deficiencies known to influence hæmatopoiesis were not delineated in the starved rats. It seems possible, however, that part of the response of the starved rats to anæmic plasma, and indeed the slight erythropoietic effect of normal plasma or saline, may be the result of factors other than a specific hormonal erythropoietic factor. The suggestion has been made that polycythæmia plasma contains an inhibitor to erythropoiesis⁴. Any such inhibition is apparently easily overcome by anæmic plasma and even to some extent by normal plasma or

saline. Reticulocytes in the starved rats increased from a mean of 0.8 per cent on the fourth day of starvation to 3.0 per cent 24 h after normal saline (3.0 ml.) alone was given intravenously.

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¹ Fried, W., Plzak, L. F., Jacobson, L. O., and Goldwasser, E., *Proc. Soc. Exp. Biol. Med.*, **94**, 237 (1957).

² Orten, J. M., and Smith, A. H., *Amer. J. Physiol.*, **108**, 66 (1934).

³ Wintrobe, M. M., *Clinical Hematology* (Lea and Febiger, 1961).

⁴ Krzymowski, T., and Krzymowska, H., *Blood*, **19**, 38 (1962).

PATHOLOGY

Pathological Proliferation of the Trophoblast Homograft in Women

ABOUT 1 g of trophoblast tissue, obtained in the course of legal interruptions in the second and third month of pregnancy, was grafted into the abdominal wall (mm. recti abd.) of: (a) 5 elderly women suffering from incurable cervical cancer; (b) 25 elderly women suffering from incurable cervical cancer and treated daily with 5 mg of oestrone acetate 3 weeks prior to grafting and consecutively until the removal of the graft; (c) 3 patients suffering from endogenous hyperoestrogenism.

5-7 weeks later the grafts were removed and examined histologically, about one half of the tissue being reserved for the estimation of chorionic gonadotropin (HCG).

The grafts from the cancer patients not treated with oestrogens were found, according to expectation, to have degenerated (Fig. 1), and no HCG could be detected by the Galli Mainini test. The grafts from oestrogen-treated patients showed no homograft reaction, were viable, and in addition marked proliferation with polymorphism of the nuclei and metachromasia were also present (Fig. 2). In some instances syncytial cells were found dispersed in the connective tissue (Fig. 3). Similar findings were obtained in cases suffering from endogenous hyperoestrogenism (Fig. 4).

The results demonstrate clearly that a high oestrogen-level suppresses the reaction of the host to homologous trophoblast tissue, and permits this not only to proliferate but also to synthesize HCG. It remains to be seen whether this action of oestrogen

Fig. 1. Trophoblast implanted without oestrogen treatment. Degenerated villi, inflammatory infiltration. (Hæmatoxylin-eosin stain. $\times$ c. 150)

Table 1. MEAN HÆMATOLOGICAL VALUES IN 88 SPRAGUE-DAWLEY RATS BEFORE AND AFTER STARVATION

	Before starvation	After starvation
Body-weight (g)	155-170	100-121
Hæmoglobin (g/100 ml.)	12.8	17.9
Hæmatocrit (%)	46	58
R.B.C. (million/mm ³)	6.86	9.18
Reticulocytes (% of R.B.C.)	19	0.8
W.B.C. (per mm ³)	19,400	3,680
Platelets (direct count/mm ³)	954,000	669,000