dextran were resistant to doses of 0·05, 0·2 and 0·8 ml. per 100 gm. when tested at weekly intervals. Similar results were obtained when fresh egg white (10 ml./kgm.) or a second brand of dextran was used. The rats which did not respond to dextran also failed to respond when subjected to stress (withdrawal of food for 24 hr.). They were not diabetic, and the weights of their adrenal glands were similar to those of control rats. There was no deficiency in the 5-hydroxytryptamine content of the skin of rats not responding to dextran, and dextran was ineffective in these rats even when pre-treated with 5-hydroxytryptophan. The intravenous toxicity of histamine was also unchanged.

Procedures which potentiate the anaphylactoid reaction in control rats were then tried in animals not responding to dextran. Pre-treatment of the rats with insulin (4 I.U./kgm.) or chlorpropamide (100 mgm./kgm.) failed to facilitate the response, and so did adrenalectomy when the animals were tested at 6, 13 and 20 days after the operation. In these experiments, up to 50 per cent of the control animals died after showing the anaphylactoid reaction. When insulin and the stress of food withdrawal were used in adrenalectomized rats, the resistant animals again failed to show the anaphylactoid reaction.

In this work, 832 rats have been used, and no fewer than 162 (about 19·5 per cent) have failed to respond to dextran or egg white. When, however, some of the experiments were repeated using Sprague Dawley and hooded Lister rats, the anaphylactoid reaction developed at a fast rate, and no failures were obtained. Further work is now in progress to determine the characteristics of the strain specificity with regard to dextran. The immunological aspects of the problem may be of paramount importance in the study of human allergies.

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[1] Selye, *Endocrinology*, **21**, 169 (1937).

Treatment of Thrombocytopænic Hæmorrhage with Œstriol Succinate

The therapeutic indications for œstriol have, until now, been limited to the treatment of superficial conditions of the cervix, vagina and vulva, and to the relief of menopausal symptoms. At the dosage-level effective in these cases, œstriol has no effect on the endometrium and does not, therefore, lead to irregularities in the menstrual cycle or to uterine hæmorrhage.

I have recently carried out an investigation into the hæmostatic properties of a pure intravenous preparation of œstriol succinate (kindly supplied by N.V. Organon, Oss, Holland) in hæmorrhages of varying pathogenesis. It became clear very early in our investigations that this substance has a rapid effect on all types of thrombocytopænic bleeding, its action being particularly marked in the acute toxic and allergic thrombocytopænias.

The substance was administered to patients of normal weight in intravenous doses of 10 mgm. and provided adequate protection from hæmorrhages for about 48 hr. None of the 100 patients so far treated in this way has shown side-effects.

My investigations into the mechanism of the normal clotting process have demonstrated that œstriol succinate acts on this mechanism in two distinct ways: (1), a direct action on the blood vessels, reducing their permeability; and (2), an effect closely similar to that of thrombocyte factor 3. The latter action can be irrefutably demonstrated using the thrombokinase-formation test. Details of my work on the clotting mechanism will be published elsewhere.

No significant increase in thrombocyte count was observed during the above treatment. The dangerous incidents which occur all too frequently in the course of thrombocytopænia can, nevertheless, be rapidly and economically controlled in this way until such time as a more normal thrombocyte count can be restored by other means. I have had frequent recourse to œstriol succinate in cases with symptomatic thrombocytopænia consequent on leukosis, panmyelopathy and overdosage of cytotoxic agents. In addition, hæmorrhages following overdosage with anticoagulants, as well as post-traumatic bleeding in patients on anticoagulant therapy, can be better controlled when œstriol succinate is administered than on vitamin K therapy alone. This effect must be attributed to the direct vascular action of the preparation. Œstriol succinate, in view of its high therapeutic efficiency and its very good tolerance, has proved to have a wide field of application in this hospital, and one must hope that it will become generally available in the near future.

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Effect of Enzyme Injections on Mitosis in Regenerating Liver

The addition of deoxyribonuclease to tissue-culture media affected mitosis in tissue cultures[1,2]. In mice bearing Ehrlich ascites tumours, injections of the enzyme decreased the incidence of mitoses in the tumour cells and increased the survival-time of the animals[3]. Similarly, injections of xanthine oxidase and ribonuclease affected the rate of tumour growth and the survival time[4–6].

In view of these facts, it has been thought of interest to study the effect of deoxyribonuclease (DNase), ribonuclease (RNase) and xanthine oxidase on a rapidly dividing normal tissue such as regenerating liver following partial hepatectomy. (Deoxyribonuclease and ribonuclease were purchased from Worthington Biochemical Corporation, Freehold, New Jersey. The xanthine oxidase was a gift from Prof. F. Bergel, Chester Beatty Research Institute, London.)

Wistar rats of average weight 218 gm. (194–242 gm.) were partially hepatectomized (66 per cent) according to the method of Higgins and Anderson[7] between 9.30 and 11.30 a.m. to eliminate the variations due to the periodicity of mitotic activity[8]. The hepatectomized rats were injected intraperitoneally with sodium chloride 0·85 per cent or solutions of albumin, DNase, RNase (5 mgm./ml.), or xanthine oxidase in sodium chloride 0·85 per cent. The original solution of xanthine oxidase prepared in phosphate buffer containing sodium salicylate and ethylenediamine tetraacetic acid as preservatives