

time-consuming, and precise quantitation of lymphocyte transformation by morphological criteria is not easy.

Mixed-lymphocyte culture, on the other hand, is an accepted in-vitro immunological reaction which depends upon immunogenetic differences at or related to the HL-A locus. Thus it seems a more relevant and, probably, a more sensitive assay of immunological competence than is P.H.A. stimulation. Measurement of the incorporation of radioisotopically labelled precursors in D.N.A. seems to be so far the most reliable and easiest way of evaluating the degree of transformation.

Our results suggest that the ability of lymphocytes to react to antigenic stimulation is not impaired in most patients with Hodgkin's disease, and that there is no frequent inherent defect of these cells. The same impression was reported by others<sup>26</sup> using purified tuberculin derivative and streptolysin-O stimulation of peripheral-blood lymphocytes from twenty patients. Recent extensive studies<sup>27,28</sup> have shown that the incidence of anergy in vivo in Hodgkin's disease is much lower than previously reported. The immunological competence of patients with Hodgkin's disease needs re-evaluation by both in-vivo and in-vitro methods.

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## FAILURE OF PROGESTERONE TO PRODUCE HIGH BLOOD-PRESSURE IN RABBITS AND RATS

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**Summary** Contrary to earlier claims, daily administration of 50 mg. progesterone over ten days did not increase the blood-pressure of 6 rabbits. Daily injection of 10 mg. progesterone had no influence on the blood-pressure of rats. The weight-gain of female rats was significantly increased by this treatment.

#### Introduction

DAILY administration of large doses of progesterone was found by Horrobin<sup>1</sup> to increase the blood-pressure of rabbits and produce glomerular tuft enlargement and endothelial swelling. Horrobin claimed,<sup>2,3</sup> on the basis of his experimental findings, that over-production of progesterone might be responsible for the clinical and pathological manifestations of pre-eclamptic toxæmia in man.

Horrobin's blood-pressure findings disagree with other experiments performed on rats and dogs,<sup>4,5</sup> and we thought it worth while to investigate this effect in rabbits and rats.

#### Methods

Rabbits of both sexes with a body-weight of approximately 2500 g. were used. Blood-pressure was measured by the ear-capsule method of Grant and Rothschild<sup>6</sup> in a quiet dark-room. The animals were placed on a board without restraint, and the experiments were started after the rabbits became accustomed to the procedure. A small mark was made over the ear artery and on the rubber capsule, which ensured that the blood-pressure was always measured on the same arterial segment. Determination of the diastolic pressure did not seem to be feasible by this method.

Rats of both sexes, weighing 170–200 g., were trained to remain quietly in a small cage and their blood-pressure was measured daily using the photoelectric method of Kersten et al., as modified by Leenen and de Jong.<sup>7</sup> Systolic blood-pressure values obtained by this method corresponded quite well with the intra-arterial pressure.

Progesterone was administered in the form of an oily solution containing 10 or 25 mg. per ml. ('Progestin', Organon).

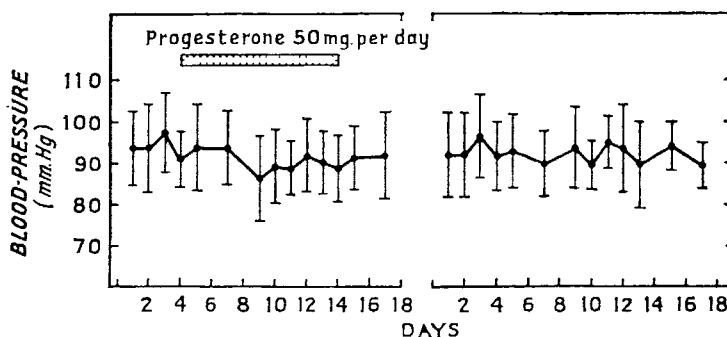


Fig. 1—Average daily systolic blood-pressure  $\pm$  S.D. of 6 treated (left) and 4 control rabbits (right).

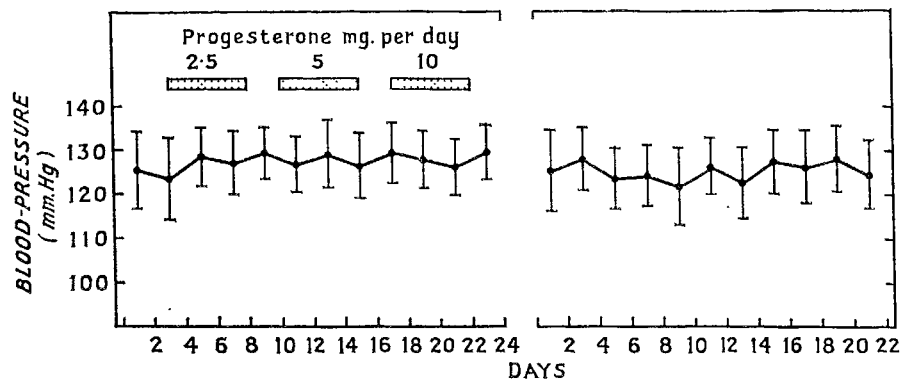


Fig. 2—Average daily systolic blood-pressure  $\pm$  S.D. of 28 treated (left) and 12 control rats (right).

Results

Rabbits

In a preliminary trial 4 rabbits were injected with 25 mg. progesterone daily for ten days. Because their blood-pressure was completely unchanged, 6 other rabbits were treated twice daily with this dosage. 4 rabbits served as controls. The average daily blood-pressure of the two groups is shown in fig. 1. The daily administration of 50 mg. progesterone over ten days did not produce any change in the blood-pressure. The animals remained in good health, and did not show an excessive weight-gain over the controls; and their blood-urea-nitrogen and serum creatinine, electrolyte, and total protein values were normal at the end of the experiment. The animals were killed and their kidneys examined histologically by C. J. Kooiker. Glomerular enlargement, endothelial swelling, capillary narrowing or obliteration as described by Horrobin<sup>1</sup> were not found.

Rats

The average systolic blood-pressure of 40 rats was 125 mm. Hg (S.D.  $\pm$  9.28). 28 rats were treated with progesterone and 12 were untreated. The starting dose of progesterone was 2.5 mg. per day, which was increased to 5 and then 10 mg. per day. Each dose was injected five times. The results are shown in fig. 2. There was no significant change in blood-pressure.

The average daily weight-gain of progesterone-treated female rats was 1.7 g., compared with the corresponding value of 0.7 g. in the untreated animals. The weight-gain of male rats was much higher (2.0 g. per day) and was not influenced by the progesterone treatment. These findings agree with other observations.<sup>8,9</sup> Large doses of oestradiol benzoate caused a significant loss of weight in female rats, without influencing the blood-pressure (unpublished observations).

Discussion

Horrobin<sup>1</sup> reported a slight increase of 15–20 mm. Hg in the blood-pressure of 4 progesterone-treated rabbits. Weir<sup>10</sup> reported similar observations in 3 rabbits. Our findings do not agree with these reports, although the method and dosage were the same. We cannot explain the discrepancy. Although the rabbit is not an ideal animal for short-term blood-pressure studies, we feel that our negative results indicate the ineffectiveness of the hormone treatment.

Progesterone had a slight blood-pressure-lowering effect in hypertensive rats, dogs, and man.<sup>5,11</sup> If progesterone is involved in the pathogenesis of eclampsia one would expect that, as in man, animals that are already hypertensive would be more sensitive to progesterone. In 6 rats with deoxycortone-acetate hypertension, blood-pressure tended to decrease when progesterone was given. These experiments were not pursued. In our studies relatively large doses of progesterone did not increase the blood-pressure of normotensive rats. Even if the possibility of a species difference is accepted, it is questionable whether far-reaching pathophysiological conclusions can be drawn from the observations of Horrobin.<sup>1</sup> The typical pattern of weight-gain in the female rat<sup>8,9</sup> is proof of the effectiveness of the treatment in our experiments, but there was no change in the blood-pressure.

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INADVERTENT INTRAVENOUS INFUSION OF MILK

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**Summary** A patient with an exacerbation of a duodenal ulcer received 100 ml. of pasteurised cow's milk by intravenous infusion. An immediate hypersensitivity reaction, disseminated intravascular coagulation, and evidence of fat embolism developed. No acquired sensitivity to milk has been demonstrated.

"Then, gentlemen," I said, "I am about to try the experiment of transfusing milk into his veins."—"If you do, you will kill him," was the reply.—E. HODDER.<sup>1</sup>

Introduction

WE would like to draw attention to the danger of describing the intragastric administration of plain or alkalised milk as a "milk drip", and to record the successful treatment of a patient accidentally given 100 ml. pasteurised milk intravenously. No similar case has been reported, and the Scottish Poisons Information Bureau has no record of such an incident.

Case-report

The patient was a 34-year-old male hotel porter who had