

appearances, the foetal ovary of the giraffe may be capable of adult secretory functions in addition to gametogenic functions. In view of the similar character of the ovarian changes in the human and giraffe ovary at birth, the occurrence of gonadotrophins in the urine of pregnant giraffe<sup>13</sup> becomes a matter of special interest. On the other hand, it is possible to envisage an endocrine picture in which maternal (or placental) oestrogen acting directly, or indirectly through the foetal pituitary, plays a dominant part.

L. M. KELLAS

Department of Histology and Embryology,  
University of Glasgow Veterinary School.

E. W. VAN LENNEP

Faculty of Veterinary Science,  
University of Khartoum.

E. C. AMOROSO

Department of Physiology,  
Royal Veterinary College, London.  
Nov. 19.

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### Avoidance of 'Secondary Disease' in Radiation Chimæras

IN the experience of this laboratory the radiation chimæras<sup>1</sup>, produced by irradiating CBA mice with 950 rads of X-rays and then injecting them intravenously with bone marrow from C<sub>57</sub>BL mice, invariably die within 4 months from 'secondary disease'. Congdon *et al.*<sup>2</sup> have worked on the lines that this condition might be due to recovery of the host animals' capacity to eliminate the foreign graft. We<sup>3</sup> and Uphoff<sup>4</sup> have favoured the idea that it was due to reaction by the graft against the host.

To test the latter hypothesis with its corollary that material from immature donors may be less reactive, similar irradiated CBA mice (950 rads of X-rays; 250 kV. constant potential, 15 m.amp., half-value layer 1.2 mm. copper, 43 rads/min. at 70 cm.) have been given myeloid tissue from foetal and newborn C<sub>57</sub>BL mice with the following results (Table 1).

Two of the survivors in group (b) and seven of those in group (c), when they had survived more

Table 1. SURVIVORS OF IRRADIATED CBA MICE (950 RAD X-RAYS) GIVEN MYELOID TISSUE FROM C<sub>57</sub>BL MICE

Myeloid tissue given	Survivors at 120 days
(a) Adult bone marrow	0/30
(b) Newborn spleen	11/20
(c) Embryo spleen	9/15
(d) Embryo liver	4/10

than three months and were in good condition, were grafted with skin from C<sub>57</sub>BL mice of the same stock. One animal died (? pylephlebitis) during the procedure of deplastering, one skin graft was shed after ten days; the other seven grafts were intact after 2 months.

These results are in accord with our original hypothesis.

D. W. H. BARNES  
P. L. T. ILBERY  
J. F. LOUIT

M.R.C. Radiobiological Research Unit,  
Atomic Energy Research Establishment,  
Harwell, Didcot, Berks.  
Nov. 21.

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### Transformation of Megaloblasts to Normoblasts by cultivating Human Bone Marrow in Presence of Vitamin B<sub>12</sub> and Vitamin B<sub>12</sub>-binding Protein

Callender and Lajtha<sup>1</sup> observed that little or no conversion of megaloblasts to normoblasts occurred when pernicious anaemia marrow was cultivated in pernicious anaemia serum by itself or together with vitamin B<sub>12</sub>. However, if bone marrow is cultivated in pernicious anaemia serum containing vitamin B<sub>12</sub> and normal gastric juice or in normal serum with vitamin B<sub>12</sub> megaloblasts are partly converted into normoblasts within twenty-four hours. Swan *et al.*<sup>2</sup> did not find this influence of vitamin B<sub>12</sub> and gastric juice, but Astaldi and Cardinali<sup>3</sup> have recently confirmed the findings of Callender and Lajtha<sup>1</sup>.

We cultivated human megaloblastic marrow in suspension in pernicious anaemia serum or in normal human serum as described by Osgood<sup>4</sup> and Lajtha<sup>5</sup>, and were able to confirm the findings of Callender and Lajtha<sup>1</sup> and Astaldi and Cardinali<sup>3</sup>.

It seems that the effective principle in gastric juice and normal human serum necessary for the activity of vitamin B<sub>12</sub> in the conversion of megaloblastic marrow to normoblastic marrow is the vitamin B<sub>12</sub>-binding protein. By zone electrophoresis or fractionation with ammonium sulphate we prepared vitamin B<sub>12</sub>-binding protein from normal gastric juice. When this was added to the bone-marrow cultures together with vitamin B<sub>12</sub>, the conversion of megaloblastic marrow to normoblastic marrow showed decisive improvement. In some of these cultures we found 50 per cent of the nucleated red cells as normoblasts after twenty-four hours. In the same cultures containing only vitamin B<sub>12</sub> there were no normoblasts at all. Bone marrow cultivated in normal human serum with vitamin B<sub>12</sub> contained about 10 per cent of the nucleated red cells as normoblasts after twenty-four hours. The effect was not achieved when some other protein of gastric juice, having no binding capacity for vitamin B<sub>12</sub>, was added to the cultures. Due to its binding capacity for vitamin B<sub>12</sub> the  $\alpha$ -globulin fraction of normal human serum also showed a marked effect on the conversion.

These investigations were performed on bone-marrow cultures of nine patients with pernicious anaemia in relapse and all yielded the same results.