amounts of labelled adenosine diphosphate (ADP) and guanosine diphosphate (GDP) were also observed. Further on, a large labelled peak was eluted after GTP. It contained adenosine, and could possibly be identical with the ATP–2,3-diphosphoglycerate complex described by Hashimoto and Yoshikawa[16]. Quite unexpectedly, a large quantity of ^{32}P was eluted from the 'Dowex-1' column, despite preliminary separation by filtration on the 'Sephadex *G*-25' column. The reason for the appearance of this ^{32}P peak is not clear. When the labelled lipoprotein complex was precipitated directly by TCA, without previous incubation with TCA-soluble nucleotides from the red-cell haemolysate, the same labelling pattern of slightly ultra-violet-absorbing peaks appeared on the 'Dowex-1' column chromatogram[17]. The small amounts of material available did not permit any closer identification. Another interesting observation was made when the lipoprotein complex had been rapidly frozen to −186° C in liquid nitrogen[2] before incubation with ^{32}P. When the material was rapidly thawed and incubated with ^{32}P, and mixed with nucleotides as described here, it was not possible to observe any labelled nucleotide peaks in the eluate from the 'Dowex-1' column chromatography.

One of the reasons why the mechanism of ATP formation in red-cell ghosts has been difficult to investigate is the strong ATPase activity, strongly fixed to the insoluble membrane residues left after exhaustive extraction with *tris*-glycylglycine buffer in the Spinco ultracentrifuge, whereas the lipoprotein complex is devoid of such enzymatic activity.

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IMMUNOLOGY

Vitamin A-induced Rejection of Autografts and Homografts

Hypervitaminosis A has been shown to suppress delayed hypersensitivity reactions in the guinea-pig[1]. Large doses of vitamin A were also shown to cause the release of lysosomal proteolytic enzymes, both *in vitro* and *in vivo*[2]. In an earlier publication we suggested that proteolytic processes may be of importance in graft rejection[3]. In the present investigation the effects of hypervitaminosis A on transplantation of auto- and homografts in rabbits are described.

Local wild rabbits of 2·5–3 kg were used. Autografts were made on 10 rabbits by grafting pieces of full-thickness abdominal skin, 2 cm × 2 cm in area, to the rabbit's own back. Homografts of identical size were exchanged between 14 rabbits grouped in pairs. Vitamin A palmitate, 1,700,000 units/kg, was injected intraperitoneally every second day, starting on the day of the skin grafting. As controls, autografts were performed on 10 rabbits and homografts were exchanged between five pairs of rabbits not receiving vitamin A.

Autografts in untreated rabbits were consistently successful and after 12–14 days showed evidence of permanent take. Homografts in the control animals were constantly rejected, the longest survival being 13 days.

Autografts in vitamin A-treated rabbits already appeared pale on the 6th day, at the time of removal of the compressive bandages. Between the 10th and 15th post-operative day the grafted skin was detached from the graft bed. The detachment occurred either spontaneously or at the slightest touch. The graft bed was slightly bleeding at the time of detachment and the grafted skin was whitish-grey in colour and appeared non-viable.

The fate of the homografts in the vitamin A-treated rabbits was similar to that of the autografts. On the 7th post-operative day the homografts appeared non-viable. They lost their attachment to the bed between the 7th and 9th day. In spite of the spontaneous separation from the graft bed, no haematomata, serous accumulations or pus were found beneath the graft.

Serial biopsies taken from the grafts of the vitamin A-treated rabbits showed early epidermal and dermal degenerative changes and/or necrosis despite an almost normal graft bed in which the only unusual finding was a peculiar paucity of blood vessels. The homografts of vitamin A-treated animals showed a mild round cell infiltration only. The similar fate of both auto- and homografts in the vitamin A-treated rabbits excludes the possibility that an immune mechanism is involved in this 'graft rejection'.

Unsuccessful autografts have been reported in sublethally irradiated rats, possibly due to interference with the vascularization of the graft[4]. Assuming that the rejection of both auto- and homo-grafts in the vitamin A-treated rabbits was also due to interference with the vascularization of the graft, the effects of vitamin A on neovascularization were studied. In these experiments, an account of which is being prepared, the effect of hypervitaminosis A on vascular neoformation in the rabbit cornea was examined. It was found that, in rabbits which received injections of 0·1 N HCl intracorneally, vitamin A palmitate administration completely prevented neovascularization of the cornea[5]. The mode of action of vitamin A in preventing vascular neoformation and consequent 'graft rejection' is not yet clear.

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