THE ROLE OF RETINOL IN, AND THE ACTION OF ANTI-INFLAMMATORY DRUGS ON, HEREDITARY RETINAL DEGENERATION

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Inherited retinal dystrophy in the rat is transmitted by an autosomal recessive gene and blindness occurs after birth as a result of degeneration of the photoreceptor cells (1,2). This resembles the situation in certain forms of inherited retinitis pigmentosa in man. Degeneration of the retina in the strain of albino dystrophic rats known as "Campbells" (1) is associated with an increase in the level of "free" lytic enzymes which appear to originate from lysosomes in the adjacent pigment epithelium (3). It has been suggested (4) that the degeneration of the visual cells is produced by breakdown of lysosomal membranes in pigment epithelium and retina. This breakdown is thought to be due to an abnormal build up of vitamin A alcohol (retinol) in the pigment epithelium which arises from the action of light on an unusually labile type of visual pigment (5).

We have attempted to provide further biochemical evidence for the above hypothesis and, to devise methods of retarding the degeneration by:

1. Studying the effect of light deprivation on the progress of retinal degeneration.
2. Studying the effect of retinol on retinal lysosomal stability in vitro.

There is evidence that retinol damages liver lysosomes (6) and bovine retinal and pigment epithelial lysosomes (7).

The Effect of Light Deprivation on the Progress of Retinal Degeneration

The effect of eye pigmentation. In the albino dystrophic rats visual cell degeneration can be retarded by raising the animals in the dark (2). This may have been due to a reduction in the amount of retinol released by the action of light on the visual pigment and on this basis it seemed likely that a similar delay in the onset of blindness could be obtained by the presence of melanin in the dystrophic eye.

A strain of pigmented dystrophic rats was bred in our laboratory by crossing the white-coated, tan hooded, pink eyed Campbell rats, homozygous for retinal degeneration, with sighted pigmented Piebald Virol Glaxo (PVG) rats. This new true breeding strain (known as "Hunter") has been established for over two years and the viability of the rats does not differ significantly from the PVG, albino Wistar or Campbell strains. The full details of the breeding programme have been published elsewhere (8). The four different rat strains are illustrated in Figure 1.

A full scale comparative study of the histology and biochemistry of the two dystrophic strains and the sighted PVG and albino Wistar rats, all male and aged 12 weeks.