Hereditary Crystalline Degeneration of the Cornea

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(Summary. A paper will be published in extenso)

Clinical and genetic particulars

Description of 2 families in which this condition occurs. The first family is the same as the one described by Van Went and Wibaut in 1924. The condition occurred 20 times in 5 generations. The clinical picture shows considerable variations. The association of genu valgum in 15 of the 20 affected members of the family is noteworthy. In one case genu valgum was found without cornea dystrophy. Autosomal dominant heredity was clearly indicated in this family. The genu valgum and the cornea dystrophy were presumably determined by separate genes which showed quite a high degree of coupling. The cases in which only one of the 2 conditions occurred could be explained by crossing over.

The second family included two generations, in which cornea dystrophy occurred in 4 out of 5 children in the second generation.

Therapy and histology

Although this condition is generally considered to be clinically of no great importance, in 5 patients from these two families corneal grafts were performed on the grounds of insufficient vision. Four of these patients are described. In three the graft was penetrating and in one lamellar. The condition reappeared eventually in all the grafts, but most rapidly in the lamellar graft. The visual improvement was also greater after the penetrating than after the lamellar grafts. By means of microscopy with polarized light, fat staining and Schulz's histochemical reaction for cholesterol, it could be proved that the crystals are composed of cholesterol. An autosomal domi-

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nant hereditary disturbance of the cholesterol metabolism, probably enzymatic, seems to be the cause of the condition, and the question as to whether this is restricted to the cornea or is more generalized remains as yet unanswered.

Discussion

Vclzebo€Γ points out that the cornea is a favourite site for metabolic disturbances. In patients with angiokeratoma, in whom the lipoid metabolism is disturbed, the typical vertebra-shaped opacity in the cornea was always found, even when no clinical symptoms were present. In these patients only the skin biopsy and the corneal examination were positive.

Waardenburg: My congratulations on these beautiful pedigrees. Van Went and Wibaut, with their less specialized instruments, also saw that the opacities were not restricted to the anterior layers of the cornea. In your second pedigree one must assume that the albinism of one child out of the consanguineous marriage is due to recessive heredity, but that the affected father of the

affected children is not married to a heterozygotic woman, but that here also, although this is not known in the case of the grandparents, dominant heredity has taken place.

In connection with the frequent association of the corneal condition with a severe form of genu valgum, in addition to the coupling of genes on one chromosome, there is the possibility of one polyphenic gene, i.e. of a syndrome. To decide which postulate is the true one, the pedigree will have to be carried further by a new generation of ophthalmologists.

If two genes are concerned, which may become separated by the crossing over of homologous chromosomes, the descendants of persons with genu valgum only will not be affected further with the corneal condition; if, however, a polyphenic (pleiotropic) gene is concerned, and the separate symptoms have not sufficient penetrance, the genu valgum may, for example, after being absent for a time, later reappear in sufferers of the corneal condition.