I am not going to give an extensive classification of cataracts, and I refer for that to the excellent work by Nicholas Brown (1976). I would like to discuss some specific genetic problems based on observations of lens pathology.

Most of us senesce while keeping our sight, with sometimes the exception of interference from some haze due to nuclear sclerosis. However, we all see families in which cataracts occur in consecutive generations as presenile or senile cataracts. Their mode of inheritance seems at times compatible with autosomal dominant inheritance with delayed onset. However, other modes of inheritance cannot be excluded with certainty.

Why do we know so little about a possible genetic basis of this most common of all eye diseases? There are some obvious reasons. Patients who are now in their 50's or 60's usually know vaguely whether their parents had ocular problems, and of what type; but they usually do not know why their grandparents went blind, the exact reason why they were operated upon, and certainly not what type of cataract they had. Another problem lies in the phenotypic overlap between various types of cataracts as they mature and come to the attention of the ophthalmologist. Also, the segregation frequencies — as aspected under autosomal dominant, autosomal recessive with high gene frequency, and polygenic inheritance — are not all that different (Barrai & Cann, 1965; Neel, 1967). Nor is it known what influence environment has, and so it is again difficult to differentiate between familial disease due to a common genetic background and that due to a shared environment. Thus, any disease with delayed age of onset and with probable heterogeneity but phenotypic overlap is not very amenable to genetic studies; and all these results will be open to much criticism such as the studies of open-angle glaucoma or diabetes have encountered. Thus, large numbers of families are needed for us to come possibly to a conclusion about the inheritance pattern or patterns of presenile and/or senile nuclear lenticular sclerosis, and posterior subcapsular or other types of cataracts.

The situation is much clearer for congenital cataracts not associated with other ocular or systemic pathology. Several clinical types — which breed

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true, although they may show a variable amount of severity – are recognized: anterior and posterior polar, nuclear, zonular pulverulent, nuclear pulverulent, etc. The vast majority of them are inherited as autosomal dominant diseases. Autosomal recessive and X-linked inheritance are also recognized, although both are considerably rarer.

Why should most cataracts, congenital or senile, be inherited as autosomal dominant diseases? Nicholas Brown (1978) recognizes three basic mechanisms for the formation of lens fiber opacities: 1) previously clear lens fibers become opaque; 2) newly-formed fibers may be opaque at the time of their formation; 3) granular material may be laid down in the subcapsular region in a lens which has lost the ability to produce properly formed fibers. What happens in autosomal dominant diseases? The old statement that one gene produces one polypeptide (or protein) still holds. In the lens and the cornea the autosomal dominant dystrophies are the more common types, and both tissues are made up of highly organized structural proteins. In case of a mixture of products of a normal and an abnormal gene, slight abnormalities can lead to interference with the physical properties of the lens and hence to a cataract. Neither the actual sequence nor the number of amino acids in the lens fibers or in the proteins of the lens capsule are known, but most polypeptide chains are composed of some 100 to 200 amino acids, each coded for by three bases, for each of which three different base substitutions can occur. Thus, the number of different possible mutation is very large, and these are likely to become clinically manifest, although phenotypic differences are not to be expected for all the different mutational events. It seems clear that much more research on cataracts is needed before the mutational event and the phenotypic appearance can be correlated, as has been done for mutations of the human hemoglobin chains. By 1976, 102 mutations were recognized for the α-chain and 166 for the β-chain (McKusick, 1976).

How can the blinding disorder of cataract reach as high an incidence as 5 million new cases in India a year? Are such figures evidence against a genetic basis for this disease? Any gene frequency in a given population depends upon mutation rate and selection with selection being the reciprocal of fitness. There is no reason to assume that presenile and senile cataracts give rise to a measurable reduction in fitness in Western countries, since their onset occurs after the end of a patient's reproductive age and leads to little interference with a patient's earning capacity. However, in countries such as India where the mean age of blindness from cataracts is 45 years (Vyas, personal communication) and surgery is not readily available, there may be an effect on the survivorship of the later-born children. However, cataracts have a high incidence in India and therefore a large non-genetic component for presenile and senile cataract formation cannot be excluded. It would be very interesting to examine a group of Indians living in a different country under improved socio-economic conditions, to evaluate the respective effects of environment and genes on this condition.

The majority of cases of congenital cataracts arise as new dominant mutations in view of the strong selective disadvantage of those affected. If there were only one recessive and one dominant type of cataract, and each type