The Mechanisms of Cataract Formation

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Summary: This review summarizes current knowledge concerning cataract formation. Metabolically induced forms of cataract are discussed, but mainly aspects of cataract formation in older patients are described, especially with respect to lens protein modifications and epidemiological results. In most cases, cataract in older people is a multifactorial process and therefore cataracts appear in a multitude of different morphological types. Only accurate documentation of lens disturbances and the use of reproducible methods can provide more detailed information about the complexity of the disease cataract.

Attempts to explain the disease 'cataract' are as old as the disease itself. One of the first ideas concerning the pathological mechanisms led to the term cataract because of the assumption that humour flowing down from the brain (καταφείν) would close the pupillary region. In the meantime, considerable progress has been made in the field of cataract research. This is especially the case where the cataract is associated with diseases in which the pathogenic mechanisms could be found. Moreover, there exist countless biochemical, histological and epidemiological results which have made contributions to a better understanding of this extraordinarily complex disease. Nevertheless, the mechanisms leading to the most frequent lens opacifications, namely opacifications with increasing age, are nearly unknown. Hypotheses and model systems have been developed which in combination with experimental results and epidemiological surveys have become the essential basis for further research in cataract development.

METABOLIC CATARACTS

Metabolically induced cataracts mostly appear in early childhood since the underlying inborn disorders of metabolism often cause damage to the very susceptible developing pre- or postnatal lens. One of these cataracts is the diabetic cataract, which thanks to optimized insulin substitution hardly develops to its full extent. The following mechanism is believed to cause the development of cataracts in untreated diabetes. Lack of insulin causes glucose accumulation not only in blood but also in the aqueous humour and in the lens. Within the lens reduction of glucose to sorbitol takes place via the aldose reductase pathway. Further sorbitol metabolism proceeds very slowly; the resulting accumulation of sorbitol is followed by an osmotic swelling of the lens.
fibres. Typical findings of a fully developed diabetic cataract are snowflake-like opacifications of the anterior and posterior lens cortex. This kind of lens disturbance is fairly seldom seen in older diabetic patients, whose lens changes do not really vary from those of other ‘normal’ people. However, diabetic patients have an earlier onset of cataracts (Anthonisen, 1936; Kinoshita, 1964).

Also osmotically induced are the cataracts of galactosaemia which is caused by a lack of galactose-1-P-uridylytransferase in its classical form, or a lack of galactokinase. By reducing the C-1-aldehyde group the osmotically effective sugar polyol galactitol is formed from the excess galactose. Its accumulation within the lens leads to opacifications of the embryonic nucleus (Kinoshita, 1965). In the case of α-mannosidosis the accumulation of mannose-enriched oligosaccharides gives rise to opacifications of the posterior lens capsule.

Besides these inborn errors of sugar metabolism disorders of amino acid metabolism can play an important role in cataract development. In Lowe’s syndrome, for example, we find different kinds of opacifications probably as the result of synthesis of abnormal lens proteins. As a consequence of disturbed lens growth, the lenses moreover remain smaller and thinner than usual. Of interest in disorders of amino acid metabolism is the observation of cataract development in phenylketonuric animals after feeding with 4-chlorophenylalanine. In man, however, there is no evident relationship between phenylketonuria and cataract development (Wegener et al., 1984). Also well known is cataract formation in rats after feeding with a tryptophan-free diet (Ohrloff et al., 1978).

In addition to the diseases already mentioned, there are many cataract associated syndromes. Last but not least are the cataracts which develop following intrauterine viral infections such as rubella, toxoplasmosis and cytomegalic virus as well as cataracts secondary to other eye diseases or cataracts resulting from traumatic injuries to the eye.

CATARACTS OF OLD AGE

All types of metabolic cataract together only constitute a very small number compared to the most common cataract, the cataract of old age, unfortunately often called ‘senile cataract’. Biochemical investigations of age-related changes in lens metabolism as well as studies of experimentally induced cataracts have made essential contributions to the elucidation of the mechanisms involved in cataract formation with increasing age. Different cataract models give proof of the fact that quite different pathological actions produce morphologically widely varying kinds of cataracts. This, together with the findings following combined treatment of animals with different cataractogenic factors, emphasizes the complexity of cataract formation (Hockwin et al., 1969). Cataract formation in old age depends on many damaging influences and must be considered as a multifactorial process in most cases. One major factor which has hindered the research on cataract formation in older people and sometimes still hinders further progress today is the uncritical and undifferentiated grouping of a great variety of morphologically different cataract types under the term ‘senile cataract’.

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