THE BRITISH JOURNAL OF OPHTHALMOLOGY

OCTOBER, 1922

COMMUNICATIONS

THE DOYNE MEMORIAL LECTURE, 1922*

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(Concluded)

We come now to consider cataract associated with well-marked constitutional conditions, diabetes being one of the most important of these. There is no doubt that genuine diabetic cataract exists. It is a disease of early life, and is seen typically in the rapidly-developing cataract of the serious and generally fatal glycosuria of young subjects. In a child it has been known to occur in a few hours and in other cases in a few days. It is subject to regressive metamorphosis and the whole lens may liquify and become absorbed. Spontaneous cure is commoner than in the ordinary senile type. The disease mainly involves the outermost layers of the cortex, and in its appearance resembles rapidly swelling traumatic cataract, presenting bluish-white asbestos striped opacity. Since it may appear at various ages, it occurs in many different forms. It cannot be differentiated with certainty in older people, as in them the prominent features may be those of senile cataract, and the diagnosis can only be certain when the disease is associated with cataract in early life. Its proportion to other forms, owing to this fact, varies considerably. Becker gave 1 per cent., Williams 8 per

* Read at the Oxford Ophthalmological Congress, August 7, 1922.

cent., Koineg 11 per cent. The true value probably lies between 2 and 5 per cent. It is quite usual to find types of cataract associated with diabetes which have nothing to do with the disease at all. In the case of punctate and subcapsular varieties it is most difficult to determine whether they are senile manifestations or are due to the disease. A rapid increase of myopia would be the clinical sign indicating diabetic cataract in an elderly person though hypermetropia has been known to occur. Myopia is probably the result of imbibition of water by the cortex lessening its refractive index and so reducing the strength of the concave meniscus relative to the nucleus. In certain cases of senile diabetes alterations in the epithelium of the ciliary body are present, and these in turn interfere with the proper nutrition of the lens. Diabetes as a cause of cataract was first reported by Berndt as early as 1834, and since his day observers have been divided as to the actual cause of the crystalline changes. Some attribute them to the presence of sugar in the blood and intra-ocular fluids. Koch in 1881 and Vansonneau in 1904 showed that the cause was not so much the presence of glucose on the intra-ocular fluids as the vicious influence of the diabetic state on the whole uveal tract. Hess thinks diabetic cataract is due to changes in the posterior surface of the iris similar to those observed in the ciliary body by Peters; others that the lens changes are coincidental, and are only indirectly due to the diabetic condition. We ask ourselves, naturally, what causes the ciliary alterations that produce the cataract? What is it that interferes with secretory activity of the ciliary epithelium, the analogue of the renal cells? Is it glucose or is it a factor of which the latter is only an indication? Magnus' experiments on the injections of glucose do not help much. It cannot be due to sugar concentration in the aqueous, as in grave cases with 6 per cent. to 10 per cent. of sugar in the urine the amount in the aqueous is 0.5 per cent. In the case I personally determined many years ago it was 0.4 per cent. with 7 per cent. of sugar in the urine. This amount is utterly unable to effect an opacity in the clear lens removed from the eye, and, in addition, sugar has been found in good healthy lenses in experimental pancreatic diabetes. A sharp distinction ought to be drawn between diabetic opacity and cataract. A lens rendered opaque by sugar can be cleared by placing it in water, provided no decomposition has taken place. Deutschmann's idea probably is the correct one, that there is local death of the cells through which abnormal diffusion takes place. What the factor is in determining this is at present unknown. Botlazzie and Scalinci think it is the organic acids which precipitate the alkaline proteid of the lens, but I have found the aqueous alkaline. The idea, I think, at present is that it is due to glucose. Diabetic cataracts are invariably white and unpigmented. This would imply an absence of

oxygen. The increased amount of cholesterin found in diabetic cataract seems to confirm this, as the latter, I believe, is a reduction product of a previously formed acid.

Viterbi and Foa say it does not depend on molecular concentration of the aqueous, and may possibly be due to slow chemical action of the glucose. Roemer suggests specific cyto-toxins formed in connection with products of intermediary metabolism; in short, a similar explanation to that which he gives for senile cataract, with which it is one and the same disease, and according to this view the diabetes would not be a direct but an indirect cause. In spite of all that has been done, our ideas as to aetiology are still inaccurate.

Of cataract occurring in diphtheria, typhus, meningitis, scarlet fever, variola, and loss of blood, we know nothing. That occurring in cholera has been attributed to the abstraction of water but is probably of cyto-toxic origin. The part played by syphilis, congenital or acquired, is not yet settled. There is a leaning to Von Michel's theory that specific lesions of the ramifications of the internal carotid, principally those supplying the retina and choroid, cause disturbances of nutrition and opacity.

It is freely admitted that recurring uveitis, usually syphilitic, gives rise to cataract. Regarding auto-toxaemia and intestinal toxaemia in particular, Professor Lewis, speaking some time ago on the aetiology of lenticular changes, stated that every patient presenting such a condition of the lens was suffering from intestinal toxaemia. In a series of 100 cases of incipient cataract taken at random to test the accuracy of this statement I found 80 per cent. showed a well-marked indicanuria.

Cataract is frequently met with in localities after epidemic poisoning by ergot. The general symptoms associated with it are muscle cramps and disturbances of sensation, and the cataract is usually bilateral, and in young people. Meyer attributed it to spasm of the internal ocular muscles. Kortnoff found that ergot cataract usually took three to twelve months to ripen, and then had all the appearances of senile cataract. The spasms produced by ergot affect unstriated muscle tissue. Many attribute it to spasm of the blood vessels and consequent interference with nutrition. So far, it has not been produced experimentally by ergotin.

The occurrence of cataract in tetany and convulsions has long been known, the exact aetiology being still a matter of investigation. Dor believes that the occurrence of convulsions, malformations of the thyroid cells, and defects of the enamel of the teeth form a symptomatic triad not to be ignored. He is of the opinion that we are no more justified in charging tetany or strumous teeth with the cataract than we are in blaming the cataract for the convulsions. Can tetanic convulsions produce cataract? This has been answered

in the affirmative by Peters, Schoen, Dor and others, who have reported cases of tetany followed by cataract. Possibly an accompanying cramp of accommodation, ciliary spasm and rupture of the zonular fibres may bring it about. Peters thinks that the lenticular changes are the result of a cyclitis. Dor, after sifting up the evidence, thinks that both the cataract and the convulsions are the result of some thyroid ferment circulating in the blood. Hesse and Phelps do not think that zonular cataract is the only affection of the lens in tetany since they observed within three years 34 juvenile cases in which tetany existed or had done so. These had total cataract or some other form of opacity in the lens. They concluded that it may be assumed with great probability that tetany is the aetiological element in zonular and many other forms of cataract at a pre-senile age. They do not identify tetany with tetanic convulsions and do not attribute the cause of the lens affection to these. The convulsions are only a partial phenomenon. Motor, sensory and vaso-motor disturbances and changes of metabolism are present in well-marked tetany, and it is from these that the characteristic trophic abnormalities, especially ectodermal ones effecting skin, hair, nails and teeth, and the lens, develop.

From experiments on rats it would appear that complicated nutritive disturbances due to a morbid condition of the blood are the aetiological factors.

The observations of Noël Paton and Findlay suggest that tetany is due to a defective action of the parathyroids. These ordinarily detoxicate a guanidin compound derived from muscular metamorphosis. Tetany occurs if this process is interfered with. Fuchs and Tribenstein claim to have found tetany and latent tetany in 88.2 per cent. of cases in pre-senile cataract, whereas such evidences were only found in 8.3 per cent. of control cases free from the disease. Cataract may follow removal of the thyroid and parathyroid either for experimental purposes or for surgical reasons. The aetiology of this cataract is uncertain, but the balance of evidence points to the cause being toxæmic and uncontrolled by sufficient thyroid and parathyroid secretion. Thyroidectomy is not always followed by cataract, and assuming the operation to be complete, some additional factor must be present to cause the disease in such cases. Major Kirkpatrick, from whose paper on the aetiology of cataract, kindly lent me for this lecture, I now quote, has seen cataract associated with hypothyroidism, and he suggests that the ocular condition might be dependent upon a deficient endocrine function to which tetany in all probability is to be attributed. The number of cataracts which may be ascribed to convulsions represent only a small proportion of primary cataracts met with, but it is quite possible that minor degrees of parathyroid deficiency which in itself

may be insufficient to cause convulsions, may be comparatively common and exert an important influence.

An interesting and important cataract from an aetiological point of view is that produced by naphthalene, first investigated in 1886 by Bouchard; it is finally accepted now that this cataract is due to a poisoning of the lens. Panas thought that it was due to retinitis produced by naphthalene, but Hess showed that the opacity preceded the retinitis which may be absent. Magnus and Peters thought it due to a shrinkage of the nucleus due to increased osmosis by the presence of salt in the aqueous, the outcome of alterations in the epithelium of the ciliary body, a conclusion arrived at through a study of the electrical conductivity of the aqueous. Hess showed that there was an increase in volume of the lens at the commencement with shallowing of the anterior chamber, and Salfner that the lens had increased both in weight and volume before any changes took place, the first visible indication of opacity being an augmentation in weight and volume amounting to 16 per cent. The first change results from the inability of the capsular epithelium to prevent the entrance of water. That the epithelium is involved is shown in its looser connection with the lens, and the occurrence of proliferation and mitotic division of its cells. An interesting feature is that naphthalene must be given by the mouth before cataract can occur. Animal lenses remain clear in a concentrated solution of the drug, and administration by any other method has failed to produce opacity. How the naphthalene acts, whether by producing some poison in its passage through the intestinal tract and final absorption by the blood, or that other substances are formed by the poisoning of the body we do not know, but it has been discovered that lenses absorb water quicker in the serum of animals poisoned with naphthalene than in the normal.

Naphthalene cataract is one of *the* most important experimental cataracts, as of all the types it most resembles the subcapsular senile variety, and it gives us some indication where to look for the cause of the human disease.

Cataract due to heat and light, owing to its industrial importance, has received considerable attention during the last 15 years. We are largely indebted to the work of the Royal Society Committee, appointed in 1908 to investigate the aetiology of glassblowers' cataract, and numerous individual workers, among whom we may mention the late Dr. Burch, Gunn, Parsons, Anderson, Legge, Abney, Crookes, Hartridge, Hill, Robinson and Cridland in this country, and Meyhoefer, Hirschberg, Hess, Arlt, Peters, Burge, Birch-Hirschfeld and others abroad.

In order to appreciate how heat and light affect the eye it is necessary to refer to the spectrum, which to suit our purpose may be divided into three divisions. The invisible infra-red or heat

rays of wave lengths varying between 60000 and 7300 A-units, all of which, according to Hartridge and Hill, are absorbed by the iris. The visible spectrum comprised between 7200 and 3970, rays of which, when extremely intense, damage the retina, as in eclipse blindness, and the invisible ultra-violet or actinic rays which are most active chemically. Of the latter, those in close proximity to the violet of about 3550 may, if intense, reach the retina and cause damage. Those of shorter wave length still, and comprised between 3500-2950, are absorbed by the lens and converted by it into heat. It is these rays which are the active factor in the ultra-violet portion of the light given off from molten glass or metal. They are not the chief set but are only supplementary to the invisible heat rays beyond the red, which are by far the most potent. The lens absorbs probably all rays between 4000 and 2950. In the infra-red, rays longer than 23000 do not penetrate the eye at all. The larger amount comprised between 11000 and 13000, are absorbed by the lens, and are the active factor. Crookes and Dr. Burch have shown that it cannot be X-rays which produce post-cortical cataract, as none are emitted from molten metal or glass, and it is extremely improbable that it is purely ultra-violet light, as Crookes found that few ultra-violet rays emanated from the bottle makers' tank and that the infra-red rays were far more abundant. Schanz and Stockhausen found, on the contrary, a fairly rich emanation. As it is only those comprised between 3000 and 3500 (a comparatively small number) which could damage the lens and only a small fraction of these are absorbed by it and converted into heat, their effect must be small, but as they exist they cannot be ignored. The truth probably lies with both schools, and we may summarise it by saying that the cause is really absorption of the rays of light from both ends of the spectrum, namely, those between 11000 and 13000 in the infra-red and those lying between 3000-3500 in the ultra-violet and their conversion into heat in the lens. It is, in reality, the heat rays which determine the cataract and Cridland's designation "ray cataract" is as good a term as we could have. It is a matter of clinical experience that cataract is common in those exposed to great heat. Cridland has described at least two cases of post-cortical cataract in a puddler and it occurs in other occupations where extreme heat is used. Burge found that cataract could not be produced by radiation from the region of the visible spectrum or infra-red provided the temperature effect be excluded, and the work of Martin, Hess, Birch-Hirschfeld and others goes to show that ultra-violet light is without influence on the lens, and probably its capsule, in the absence of heat. As a great amount of heat is absorbed by the iris, Parsons thinks that the cataract is caused by changes in the ciliary body, with corresponding nutritive changes in the lens. So far, there is no evidence in favour of this theory.

The cataract of bottle makers is primary and posterior cortical, and is not due to gross mischief in the choroid or retina. Meyhoefer and Birch-Hirschfeld attribute it to extreme heat; Arlt to light; Leber to concentration of the aqueous by sudden evaporation from the surface of the cornea and intense sweating; Peters to the changes in the aqueous consequent on congestion of the vortex veins; and Scalinci to accumulation of carbonic acid by venous stasis through the act of blowing. There is no doubt whatever that extreme heat predisposes to premature cataract. Cataract occurring in blacksmiths and foundries between 40 and 50 years of age shows a course more like ordinary senile cataract and the aetiology cannot be regarded as similar. Vogt has shown that it takes a white heat to produce infra-red radiation sufficient to penetrate the lens and produce its effect. Bottlemakers' cataract begins on the left side with discolouration of the face of the same side. It has been suggested that it cannot, owing to the protection of the aqueous, be produced by heat (Druké and Helmholtz), but Vogt has shown that it takes a much deeper layer of water to absorb the red rays than is afforded by the aqueous. According to Finson, blood and colouring matter afford the greatest obstacle to the entrance of chemical rays and these are abundantly furnished by the iris, so that if due to actinic light its occurrence in the pupillary area first is easily explained. The skin trouble is stated by the supporters of the actinic theory to be due to pigment formation in the upper strata of the skin, which according to Unna and Widmark is the result of ultra-violet rays and not heat. The mixture of sand, lime, soda and clay, according to Cramer, may be the source of this light. The truth probably lies with both, and if we look upon all cases of true cataract as a chemical change we are not justified in excluding either, as it has been shown that infra-red rays hasten hydrolysis, and actinic light is capable of modifying the lento-proteid and aiding ferment action. Its position at the posterior pole is largely a question of physics concerning the transformation of one form of energy into another—and I see no physical reason why the effect of this should not be greater the deeper we go into the lens—it is ridiculous to imagine, as has been done, that the rays are concentrated at the nodal point. The nodal point is not this by definition, but that point to which, if a ray of light be directed, it continues its course unchanged. My own feeling is that light is necessary as well as heat, but is of far less importance in these posterior-cortical cataracts, and it is not surprising that the changes both are capable of working occur at a position in the lens, not only in keeping with our ideas of physics but of physiology too, seeing that it is here the lens is unprotected from the intra-ocular fluid.

Cataract due to traumatism may be divided into two groups: those in which the coats of the eye are involved and those, much

rarer, in which they are not. The latter can be further sub-divided according as to whether the capsule is intact or not.

The group includes Vossius' cataract, cataract following blows and contusion, and fulguration cataract. The former group has been well studied and good accounts of the histo-pathology are to be found in the textbooks. Transient contusion opacity is rare and the cases clear up in a week or so. The aetiological factor in these cases is a limited damage to the capsular epithelium, permitting imbibition of aqueous by the lens. These lesions ought to be called opacities and not cataract, and the prognosis should be guarded as many spontaneous recoveries have occurred. Concussion changes have been well studied during the late war, both anterior and posterior cortical, the former presenting many different varieties. An excellent study of posterior cortical cataract was made by Hudson some years ago. Hudson considered the changes due to distension of the lymph spaces in the lens, or to definite but usually transient changes in the lens fibres themselves.

Ormond suggests that the change giving rise to concussion posterior cortical cataract is not in the lens at all, but at the posterior surface, and is the result of fluid finding its way beneath the posterior lens capsule owing to a slight movement of the lens in the patellar fossa. Against Hudson's theory is the fact that lymph spaces in the lens have been disproved by Leber and it is a little difficult to reconcile definite alterations in the lens fibres with the transient character of the cataract. My own idea of these cases is that they owe their cause to the same set of changes that occur in the development of posterior cortical cataract, the result of disease of the *uvea* or deeper parts of the eye, and that they are the evidence of a reaction on the part of the lens to faulty nutritive supply. It is not difficult to imagine either a severe contusion or perforating wound producing effusion from either blood or lymph channels which would profoundly alter the composition and vital properties of the aqueous. We know that any slight alteration of the aqueous will affect the lens; the temporary character is explained by the fact that in repair the exciting cause comes to an end.

Of the anterior cortical, concussion or contusion cataract, there are several different varieties. The classical one is that first described by Vossius in 1903. Whiting has added another five varieties to the original annular variety. The interest in these types of cataract centres around the discussion which has been forthcoming regarding their cause. Vossius assumed that the ring opacities were due to the pupillary margin of the iris being pressed upon the anterior surface of the lens by the cornea, and that pigment cells were fixed thereto by fibrin, or in the case of the unpigmented grey ringed type to degeneration of the capsular epithelium at the point of contact with the pupillary border of the

iris. His theory is based on Schirmer's researches. The latter produced contusion cataract by traumatism of the capsular epithelium, which later regenerated without leaving a sign of injury. The case reported by Krusius seems to confirm this theory as he found a greyish opacity on Descemet's membrane exactly opposite the corresponding opacity in the lens. There are many difficult points to solve. Indentation of the cornea is not requisite; a small perforating injury anterior or posterior to the lens may produce it and the site of the traumatism may not be anterior to the lens. Hoeg says that a displacement of the aqueous necessary to produce a trauma which would bring the cornea and lens in contact over an area of 3 mm. diameter could not occur without rupture of the iris or cornea. He believes it is due to a sudden rise in hydraulic pressure forcing the iris against the lens. Others believe that where the pressure is applied posterior to the lens the vitreous drives the lens against the iris. Coats, on the other hand, says it is quite impossible unless the iris becomes imprisoned between the lens and the cornea as the iris will give way before the advancing lens. The occurrence of pigment granules within the Vossius ring is difficult to explain. Beresford has recently established a theory based on Bach's work on the changes following traumatism of the eye ball. According to him it is the result of a contusion with mild iridocyclitis set up with exudation from the vessels of the iris and ciliary body. The fibrin agglutinates the pupillary border to the lens capsule, which in a short space of time frees itself, leaving the fibrous ring. The pigment, both within and without the area of the opacity, he attributes to leucocytic migration from the ring itself or pigment containing leucocytes or red blood corpuscles, as blood is not infrequently present in this type of lesion.

I cannot conclude this account of the aetiology of cataract without some reference to heredity, though so little is known about it. No part of the eye exhibits in a more striking way the influence and character of heredity than the lens. Many have been content with an attempt to explain the aetiological changes which may be responsible for the formation of congenital cataract, and have done but little to explain heredity and I need not inflict you with detailed accounts. Suffice it to say that opinions are divided into two groups regarding the explanation by which congenital deformities of the lens are produced: first, those who believe the basic cause is toxic, and secondly those who believe there is an alteration in the development of the lens due to some inherent abnormality in the germ cell.

The evidence is strongly in favour of both, and it is probable that neither singly explains the cause, and that in some cases both may be active. Treacher Collins truly remarks that to attribute a condition to arrest of development offers only a partial explanation of its

aetiology, leaving the cause of the arrest to be accounted for. Variations in development can be traced with a fair degree of accuracy to a group of cells in the embryo, but an inquiry into the cause of this variation leads to a very complex situation, about which surmises only exist.

Nash thinks that as regards certain developmental defects there seems to be no reasonable doubt that, on the whole, their descent follows the system of the Mendelian dominant and that they are due to the presence of special factors, individuals not possessing these factors being unable to transmit them. The whole body may be influenced by abnormalities in the functions of glandular organs and through what Garrod has termed "inborn errors of metabolism," which latter, at any rate, appear to run in families. Cataract running in families behaves as a dominant, that is, there is something in the organism which produces cataract; there is a determiner in the germ cells for that something which causes cataract. The person who has received the determiner for cataract from one parent will have it in half of his germ cells, so that half of his children will show congenital cataract. If it could be possible by chemical or other means to rid the germ cells of the determiner for early cataract then those germ cells should produce individuals without cataract for an indefinite time. So long as people with determiner for early cataract marry they are bound to perpetuate the trait in half of their descendants. So far there is no authoritative statement on heredity, and the study of the causes underlying the facts has just begun. As Conklin says, in the absence of such knowledge it has been necessary to form theories of heredity to account for the facts, but these are only a temporary scaffold to bridge the gaps in our knowledge, and if we knew all that could be known about the germ cells and their development we should have little need for theories.

I thank you, Gentlemen, for the kind attention you have given to this lecture which, I beg you, Sir, to accept as a tribute, all too feeble on my part I know, to the memory of Robert Doyne, to whom we are one and all so deeply indebted.

FIG. 13.

Tyrosin : from hydrolysis of the human nail.

FIG. 14.

First specimen obtained from aqueous after needling for high myopia.

FIG. 15.

Cholesterin and tyrosin in lens in diabetic cataract.

FIG. 16.

Tyrosin in lens in senile cataract.

FIG. 17.
Another specimen.

FIG. 18.
Aqueous in diabetes showing tyrosin.

FIG. 19.
Tyrosin in lens in diabetic cataract.

FIG. 20.
Tyrosin in lens in albuminuria (Bright's Disease.)

FIG. 21.

Tyrosin in lens in albuminuria (Bright's disease.)

FIG. 22.

Another specimen.

FIG. 23.

Tyrosin in aqueous in albuminuria.

FIG. 24.

Tyrosin in lens of an ox (cataractous).

FIG. 25.

Aqueous from same eye.

FIG. 26.

Tyrosin from lens which had lain 18 years in anterior chamber. Lens one mass of tyrosin.

FIGS. 27 and 28.

Showing method of demonstrating tyrosin amid a mass of debris and sodium chloride: by breathing on the specimen the common salt, being hygroscopic, dissolves, leaving the insoluble tyrosin quite clearly defined.

(27 before, and 28 after, breathing on slide.)