CHAPTER I

GENERAL: AETIOLOGY

DEFINITION

The condition to be described is that of an eye which has become enlarged under the influence of increased intra-ocular pressure. As the ability of the ocular tissues to stretch is practically limited to the period of childhood, and as glaucoma in the first few years of life is almost always associated with ocular distension, the term "Congenital Glaucoma" appears suitable for this condition. By congenital glaucoma we mean a state of raised tension due to an intra-uterine defect and manifest during the first few years of life.

The definition excludes from the scope of this work true cases of infantile staphyloma, which show evidence of perforation, in which the iris is incorporated with the cornea. Of course, the hypertension that is the cause of enlargement in congenital glaucoma may not be in evidence at the time of examination. The state of raised tension may have passed, but before doing so it sets up a series of degenerative changes and interferes with the nutrition of the various tissues to such an extent that ultimate blindness is almost inevitable.

Glaucoma in children, as in adults, may be primary or secondary. The term primary is reserved for cases of obscure origin, and simply implies ignorance as to the cause. It is hoped that in time the term may become obsolete. This study is mainly concerned with primary infantile glaucoma.

Some cases of glaucoma in children are obviously due to certain malformations, of which the most common are aniridia and microphthalmia. In aniridia, glaucoma is undoubtedly often caused by the union of the iris root and the posterior surface of the cornea. In microphthalmia the narrowness of the circumlental space plays a part. As the finer changes which may hinder the function of the drainage channels are beyond our knowledge at present, our conceptions are largely hypothetical.

TITLE

Of the many different names given in the past to the condition under discussion, "Hydrophthalmia" and "Buphthalmia" have been most widely used. A. Fuchs (1924) reserved the term "buphthalmos" for

the condition in which an anterior staphyloma arises in infancy and "hydrophthalmos" for "primary infantile (congenital) glaucoma".

The term buphthalmia, though picturesque and of ancient origin, should be excluded, for in these days of scientific exactitude long-continued usage does not warrant the perpetuation of a term that is clinically inaccurate. Ambroise Paré (1517–90) wrote "Œil de bœuf (*βοῦς ὀφθαλμός*) est une maladie d'œil quand il est gros et éminent, sortant hors la teste, comme on voit les bœufs les avoir". The eye of the bull does not suggest the failing vision or the raised tension, which are essential features. This term has been applied more suitably to the condition of megalocornea or megalophthalmia. The dual application of this term, and the following multiplicity of synonyms, make it desirable for us to adhere to the one or two most suitable titles. Amongst the terms used for congenital glaucoma and for megalocornea are the following: keratoglobus, keratomegalia, cornea globus, cornea bulbosa, hydrophthalmos congenitus anterior, hydrops camera anterior, and others. The terms keratoglobus turbidus and keratoglobus pellucidus have been used to distinguish congenital glaucoma from megalocornea.

In this work we shall use only the terms congenital glaucoma and hydrophthalmia, which will be considered as synonymous. It is suggested that all others be discarded.[1]

RETROSPECT

In the opinion of Julia Bell (1932) the early writers, Hippocrates, Galen, Celsus, and others, did not clearly describe as an entity the condition now known as hydrophthalmia.

Saint-'Yves, in 1722, described the various forms of ocular enlargement in a chapter entitled "De la grosseur démesurée du Globe de l'Œil". They were grouped as

(*a*) the naturally large eye;
(*b*) exophthalmos due to causes other than increase in the size of the globe;
(*c*) an increase in the size of the globe with too great an abundance of the aqueous humour constituting a hydropsy of the globe (Bell).

[1] After consultation with two classical scholars, it appears that the widely used endings -ophthalmos and -ophthalmus are incorrect, the word for the morbid state being hydrophthalmia. In medical terminology, hydro- is prefixed to names of parts of the body to denote that such part is dropsical. According to the Sydenham Society *Lexicon*, the meaning of this term is "expansion of the whole eye with increase of its fluid contents". Quoted by *Shorter Oxford Dictionary*.

Terson (1925) considered that the first reference to hypertension in hydrophthalmia was made by Beger in his thesis presented at Tübingen in 1744.

Von Muralt (1869) emphasised the fact that this condition was a form of glaucoma. He and von Graefe considered that the enlargement of the cornea was primary and that hypertension followed the atrophy of the corneal nerves. Raab (1876), Gallenga (1885) and Mauthner (1882) were the earliest observers to state that the glaucoma was secondary to a uveal inflammation. Manz (1883) and Grahamer (1884) found no signs of inflammation.

The earliest series of cases with detailed histological reports appears to have been that of Schiess-Gemuseus (1884). Then followed Gallenga (1885), Dürr and Schlegtendal (1889), Cross (1896), von Hippel (1897), Collins (1900), Reis (1905) and Seefelder (1906).

Even after hypertension was recognised as a factor producing enlargement, there was much confusion between pathological "hydrophthalmia" and the physiologically large eye or cornea now known as "megalophthalmia" or "megalocornea". This considerably delayed a true understanding of the disease. The definitions given by Kestenbaum (1919) are now generally recognised.

SUMMARY OF QUESTIONNAIRE

As a result of sending out forms to oculists in most countries, information was collected concerning 205 eyes of 116 patients. 874 forms were sent to 346 oculists living in thirty-two different countries. Of these 111 completed forms were returned from thirty-one oculists in fifteen countries. Six doctors wrote to say that they had not treated a single patient with congenital glaucoma. One—Colonel R. E. Wright of Madras—sent notes of twenty-nine patients, and Zeeman of Holland reported twenty-four patients. The staff of the Royal London Ophthalmic Hospital sent reports of ten cases, and Lindner of Vienna described seven. One oculist reported five cases, one four cases, four reported two cases each, seven reported one case each.

Reports of	9	cases	came from Australia
,,	7	,,	,, Austria
,,	2	,,	,, Belgium
,,	1	case	,, Canada
,,	5	cases	,, Czecho-Slovakia
,,	2	,,	,, Finland
,,	1	case	,, France

Reports of	6	cases came from	Germany
,,	15	,, ,,	Great Britain
,,	24	,, ,,	Holland
,,	7	,, ,,	Hungary
,,	29	,, ,,	India
,,	1	case ,,	Italy
,,	1	,, ,,	New Zealand
,,	6	cases ,,	U.S.A.

Of these cases 147 eyes of ninety patients were operated on. Several have been omitted as they were possibly examples of juvenile glaucoma or interstitial keratitis. The total number of the remainder was 139 eyes of eighty-four patients. They received approximately 243 operations.

24	eyes	received only	1 operation
24	,,	,,	2 operations
16	,,	,,	3 ,,
9	,,	,,	4 ,,
4	,,	,,	more than 4 operations

An analysis of the type of operation used shows a great preference for the operation of sclerectomy, and particularly by means of a trephine, viz. ninety-five eyes of fifty-six patients.

Trephine	was performed	126	times on	95	eyes
Anterior sclerotomy	,,	27	,,	17	,,
Cyclodialysis	,,	31	,,	24	,,
Paracentesis (one or a series)	,,	9	,,	9	,,
Iridencleisis	,,	8	,,	8	,,
Herbert's sclerotomy	,,	5	,,	2	,,
Iridectomy	,,	11	,,	8	,,

Thirty-one eyes were enucleated. As a rule this followed an injury such as a bump against a chair or other obstacle.

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Incidence. The rareness of the disease is seen from the following reports. In Seefelder's clinic (1906) only forty-six examples were found amongst 129,520 patients from 1891 to 1905, percentage 0·035. In the Tübingen clinic from 1875 to 1903, 0·079 % of the patients had the disease. Gallenga considered that the majority of

these patients came from hilly or marshy country. Seefelder's patients came chiefly from plain country. Kaminsky (1913) found this disease in 0·041 % of Breslau patients, and Jaensch (1927) in the same centre found twenty-three cases (0·032 %) amongst 72,681 admittances from 1916 to 1925. Carvill (1932) found the incidence to be 0·01 % amongst 31,648 patients with ophthalmic disorders. In another American series, amongst almost a quarter of a million patients, the incidence was 0·011 % compared with that of 0·78 % for patients with glaucoma of all types (Lehrfeld and Reber, 1937).

The relative frequency of this disease may become greater now that blindness due to ophthalmia neonatorum has almost ceased and the treatment of other acquired conditions in early life has become more effective. Hydrophthalmia is one of the chief causes of blindness amongst children, and is the most common of the developmental causes. Dürr and Schlegtendal (1889) stated that in 1885 the Clinic for the Blind contained ninety-nine pupils, of whom nine were blind from congenital glaucoma. Priestley Smith (1896) found 5 % of the inmates of a blind school with congenital glaucoma. During the first twenty-five years of this century it caused 13·5 % of the admissions to the Institute for Blind Children in Lausanne (Gonin, 1925). Lamb (1925) reported that 5·3 % of the pupils in the Missouri School for the Blind had become blind from this disease.

During the years 1919–24, 4·75 % of the admissions to the German Institutes for the blind were the result of glaucoma. Of this percentage half, or sixty persons, suffered from the congenital form. Hübner (1926) and Hirsch (1902) found that 2·4 % of the inmates of blind institutes were affected by this disease.

Bilateral incidence. In approximately two out of every three patients with hydrophthalmia both eyes are affected. This is similar to the finding for retinal detachment. In

de Grosz's series,	64 %	were	bilateral
Zahn's	,, 70 %		,,
Seefelder's	,, 67 %		,,
Jaensch's	,, 60 %		,,

Of the ninety-four cases of hydrophthalmia reported in answer to the questionnaire recently issued by us, 86 % were bilateral. The right eye was affected in four of the eight unilateral cases.

There may be a difference in the time of onset and in the degree of the disorder in the two eyes.

Bell found that relatively few unilateral cases were hereditary. In the hereditary group of fifty-eight cases, approximately 10 % were unilateral, and in the non-hereditary group of 268 cases, 35 % were unilateral.

Information is too meagre to enable us to decide whether or not the former are mainly primarily inherent affections and the latter secondary to infection or local injury.

Kiehle and Pugmire (1934) found unilateral hydrophthalmia in different degrees in opposite eyes in identical twins. The affected eye of one was trephined successfully and that of the other, being blind, was excised. Bilateral hydrophthalmia was found by Gault (1937) in identical twins aged $6\frac{1}{2}$ years. They were practically blind. An iridectomy had been performed on one eye. All these had been treated with eserine. Duncan (1937) examined female twins, aged seven months, who had bilateral hydrophthalmia and almost complete retinal detachments. Several months later one died and an intraocular neuro-epithelioma with widespread dissemination was found.

Influence of sex. The predominance of males amongst hydrophthalmic patients is as unexplained as it is marked. While adult glaucoma affects three females to two males, the following figures have been given for congenital glaucoma:

de Grosz (1932)	116 patients,	62 % males
Zahn (1904)	73 ,,	58·9 % ,,
Kunzmann (1899)	37 ,,	70 % ,,
Seefelder (1906)	47 ,,	67 % ,,
Lamb (1925)	28 ,,	71 % ,,
Lehrfeld & Reber (1937)	28 ,,	71 % ,,

Haag (1915) and Lawford (1907) found the sexes affected equally by juvenile glaucoma. Löhlein (1913), in his study of 1640 cases of glaucoma under thirty years of age, found a slight predominance of males.

Bell wrote: "Sex incidence for purely hereditary cases does not differ significantly from that calculated from 304 due to all causes, which is of interest in view of the fact that hereditary disease does on the whole tend to become manifest in men more frequently than in women."

In the predominance of the male sex, hydrophthalmia resembles juvenile glaucoma and differs from the senile form which is more common amongst females (Lehrfeld and Reber, 1937).

Time of origin. It is difficult to determine the time of origin of the glaucomatous process. When we consider the degree of distension that is sometimes present at birth, we realise that hypertension must have developed soon after the anterior chamber first appeared and the activity of the filtration process began. The time of this is probably about the middle of the sixth month. Seefelder (1920) considered that the fourth month was the probable time of origin of hydrophthalmia in his specimen associated with an iris coloboma, a retinal detachment and an orbital cyst. Lagrange (1925) described the angle in his eighth specimen as being foetal in type, resembling that found in the sixth month of intra-uterine life.

In Christel's specimen (1912) the posterior part of the lens was covered with epithelial cells and the lens fibres were incompletely developed. Schlemm's canal was absent. The lens was absent in Schlaefke's specimen (1913) and in Seefelder's specimen II and III (1906). Spielberg's specimen (1911) was enlarged at birth even though the child was premature. These findings suggest an early origin.

Age of onset. While the defect producing hydrophthalmia is usually congenital, the disease may not become evident for some time after birth. Different criteria have been adopted by different people in determining the age of onset. Seefelder relies on the first appearance of acute signs. The common statement that the eyes were large at birth he did disregard as certain evidence that the disease was congenital, especially if the acute symptoms appeared later. He did not contradict the view that intra-uterine glaucoma might occur with the later development of acute symptoms, but he considered such findings to be rare in his series. Few would agree with his belief that hydrophthalmia may arise at any stage of juvenile life and lead to excessive ocular distension.

Here, as in many other sections of this work, the need for careful study of eyes in early life is felt. Until this is done we will remain unable to decide whether the so-called onset is truly such or an exacerbation. Many of the late onsets are probably recrudescences of intra-uterine developments. In these the same changes in Schlemm's canal are reported by Reis (1920), Seefelder, and others, as are found in those cases where the parents recognised the disease early.

Cross (1891) considered that in one of his series the onset was very late. The patient was a machinist, who had always been shortsighted (R. −19·0 D., L. −23·5 D.) and who had observed failing sight only during her twenty-fourth year. The corneae were enlarged (R.

14·0 mm., L. 13·5 mm.), the tension raised and no cupping was detected. It is difficult to know whether this patient had congenital glaucoma in her myopic and somewhat enlarged eyes. There is, however, little support for the theory that she developed hydrophthalmia when twenty-four years old.

Of Seefelder's forty-seven cases the onset was given as at birth in nine cases and during the first year in twenty-four; in Zahn's fifty-seven cases the figures were twenty-four and twenty-eight, in Grosz's forty-five cases twenty-seven and six, and in Golomb's twenty-seven cases fourteen and eleven. So in 81·3 % the onset was probably before the end of the first year.

If we summarise the information contained in Seefelder's, Dettmering's, Stölting's, Fleischer's and the questionnaire series, we obtain the following:

At or before birth in 102 cases, that is 40 % of those with reliable information.
At 6/12 months or under in 86, that is 34 % of those with reliable information.
At 1 year or under in 30, that is 12 % of those with reliable information.
At 6 years or under in 28, that is 11 % of those with reliable information.
At over 6 years in 5, that is 2 % of those with reliable information.
No, or unreliable, information in 80.

Thus in 87 % of these cases the condition was recognised under the age of one year. On the other hand, five patients were more than six years old before their eyes became affected. This brings us to the relationship of hydrophthalmia to juvenile glaucoma.

Relationship to juvenile glaucoma. No absolute distinctions can be made to separate juvenile glaucoma from hydrophthalmia on the one hand and senile glaucoma on the other. It is probable that at one end of the scale, that is, in early life, an innate defect in structure is the cause of hypertension and that degeneration is merely a secondary phenomenon. At the other end of the scale raised tension is due almost entirely to various degenerative changes associated with old age, and inherited defects play a minor part. There is an intermediate group in which both factors appear to be pathogenic in varying degrees.

Probably thirty or thirty-five years might be taken as an upper age limit for juvenile cases. In deciding the lower limit, between

juvenile glaucoma and hydrophthalmia, we have taken as a criterion the absence or presence of the most characteristic sign of congenital glaucoma, viz. distension of the eyeball. Thus glaucoma due to a congenital defect may be classed as juvenile if it fails to develop until the eye is no longer distensible.

The ocular disorder then, that we are to consider, is that which is due to a rise in tension occurring at so early an age that the coats of the globe distend. It is necessary now to ask two questions. First, is raised tension always found in the condition we are calling congenital glaucoma? Just as the answer to a similar question relating to glaucoma of later life is in the negative, so it is here. The association with normal tension is certainly much rarer in the adult group. Such a finding does not disprove the pathogenic influence of hypertension, but simply suggests that it is transient, though with permanent and characteristic results. It is easier to understand the occurrence of normal tension or even hypotension in a distended eye than in one that cannot distend because of the inelasticity that comes with age. One can imagine the results of distension counteracting its causes. Yet, though the tension may return to normal, degenerative changes are set in motion which may persist and produce results that make the actual causes of raised tension difficult to recognise. This has led to considerable confusion in interpreting the late lesions found in an affected globe.

The second question is, can distension develop as the result of raised tension in later life? It is known that areas of local distension, staphylomata, can arise as a result of inflammation where a weakened area bulges in response to even normal tension. But can uniform distension occur as a result of hypertension in the mature eye in the absence of the weakening effect on the sclera of inflammation? This question is very difficult to answer. Certain cases observed by Colonel Wright suggest that, at any rate in Indian races, such distension is possible up to the age of twenty-five. Thiele (1930) referred to other instances of a late onset. On the other hand, the majority of observations made in Europe indicate that the cornea and sclera are not distensible after about seven years of age. Probably a considerable proportion of such late cases have suffered from interstitial keratitis.

Thus among the forty-five cases of hydrophthalmia (reported by de Grosz) the disease was evident in twenty-seven at birth or during the first week of life, in six during the first year, in eight during the third year and in two at eight years. A study of most of the reputed instances of a late onset has unconvincing results. As examples let

us consider the two with the latest onsets in the forty-five cases. It is said of these that hydrophthalmia was not present till the age of fourteen. One case, Derby's (1882), was a man aged twenty, whose sight and that of three other children of a blind father failed at about fourteen years of age. The condition was undoubtedly hydrophthalmia in this patient, but the age of onset is not definitely stated. The second case is one reported by Grahamer (1884), and is an example of an inaccurate reference. The author's account is of a girl who was examined at the age of fourteen years. The left eye at birth, however, had been larger than normal, and of bluish appearance. The right eye was emmetropic and of normal tension.

Thirdly, it might be asked what degree of tension can exist in childhood without scleral stretching? This again we cannot answer. It is possible that in some cases congenital defects produce a low degree of hypertension without distension, so that the process is not evident until aggravated by disease or at puberty. This might explain the occasional finding of congenital and juvenile glaucoma respectively in the two eyes of one individual, or in two members of one family.

There are certain similarities between congenital glaucoma and juvenile glaucoma that help to confirm the affinity between the two conditions. In both forms, congenital anomalies are common. These include persistent hyaloid arteries, persistent pupillary membrane, anomalies of the retinal vessels, lamellar cataracts, aniridia, colobomata, and other deformities of the globe and very high myopia.

As we shall see later, there is ample evidence in the majority of cases to prove the dependence of congenital glaucoma upon anomalies. Schmidt-Rimpler (1877) considered that 50 % of cases with juvenile glaucoma have a defective canal of Schlemm. Löhlein postulated a milder degree of defect than that required to produce the congenital form of glaucoma. Verhoeff examined histologically the eyes of two patients with juvenile glaucoma and found a defective form of filtration angle as in hydrophthalmia. He considered these two forms of glaucoma to represent differences in degree of the same condition.

Löhlein (1913) found that

38·8 % of cases of juvenile glaucoma were recognised between 15 and 20 years.

21·3 % of cases of juvenile glaucoma were recognised between 20 and 25 years.

1·3 % of cases of juvenile glaucoma were recognised under the age of 5 years.