INCIDENCE OF CORNEAL CHANGES IN CONGENITAL SYPHILIS*†

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The purpose of this investigation was to find the incidence of interstitial keratitis among patients known to have congenital syphilis whether treated or untreated.

Previous estimates have varied widely. Green (1920) reviewed the literature and found that the incidence reported by different authors varied from 6.5 to 96 per cent., the average in the 2,000 reported cases that he studied being 50 per cent. It is clear that the widely differing results of most of the published series (Table I) do not indicate the total incidence of interstitial keratitis among congenital syphilitics. In only one series, that reported by Green (1920), were all the patients examined by means of the slit-lamp microscope. Green examined one hundred children and found evidence of interstitial keratitis in nineteen; this series showed clearly that age is an important factor, for 24 of the children were under 2 years old and the remainder from 2 to 14 years of age, so that the apparently low incidence of corneal change is explained by the youth of the patients.

Cannon (1927) found interstitial keratitis in seventy of 202 cases of congenital syphilis (35 per cent.). It is perhaps significant that this figure corresponds exactly with the number of patients who attended because of the development of symptoms of keratitis. In this group 143 of the patients were under 15 years of age, 36 were aged 15 to 20, and twenty were over 20 years of age.

Cole and others (1937) found that of 1,010 congenital syphilitics aged 2 years and over, 428 (42.3 per cent.) had evidence of interstitial keratitis or developed it during observation periods of 2 years or more. When first seen, 788 of these patients were aged between 2 and 15 years.

Fournier (1886) reported the presence of clinically detectable interstitial keratitis in 88 of 212 patients with congenital syphilis (42 per cent.). This great observer noted that in rare cases complete resolution of the cornea seemed to have occurred, and that in others interstitial keratitis remained unnoticed for a time because only the peripheral cornea had been

involved. He did not report the ages of all his patients but noted that the time of onset of keratitis varied up to 20 years of age, the maximal incidence occurring between the ages of 10 and 12.

Howles (1939) studied 147 patients with congenital syphilis who were 3 years of age or older, the great majority being under 10 and none over 23 years of age. He found evidence of interstitial keratitis in 48 patients (32.7 per cent.).

Jeans and Cooke (1930) studied 707 syphilitic children over 2 years of age, and found interstitial

TABLE I
REPORTED INCIDENCE OF INTERSTITIAL KERATITIS IN CONGENITAL SYPHILIS

Author	Date	Number of Cases	Age (yrs)	Examination By Slit Lamp in all Cases	Evidence of Interstitial Keratitis	
					Cases	Percentage
Cannon	1927	202	143 < 15 36 = 15 to 20 20 > 20	No	70	35
Cole and others	1937	1,010	—	No	428	42.3
Fournier	1886	212	—	No	88	42
Green	1920	100	24 < 2 76 = 2 to 14	Yes	19	19
Howles	1939	147	3 to 23 Most < 10	No	48	32.7
Jeans and Cooke	1930	707	—	No	193	27.1
Laird	1950	115	—	No	45	39.1
Lemoine	1934	1,017	—	No	118	11.6
Lemoine	1934	262	—	No	28	10.7
Lennarson and Jeans	1937	174	2 to 16	No	75	43
McLeod and Lemoine	1940	1,520	—	No	—	5.3
Smith	1927	1,000	708 < 15 100 > 20	No	641	64.1
Stokes	1926	—	—	No	—	52
Wile and Mundt	1942	402	—	No	177	44
Present Study	1954	117	5 to 70 (Average 34)	Yes	74	63

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keratitis, active or residual, in 193 (27.1 per cent.). These authors are paediatricians and it seems likely that the majority of these patients were young children.

Laird (1950) found evidence of interstitial keratitis in 45 out of 115 patients with congenital syphilis. He recorded that 39 of the patients with such evidence were aged from 1 to 29 years and the remaining six between 30 and 49 years of age.

Lemoine (1934) studied the records of 1,017 cases of congenital syphilis diagnosed at a children's hospital. There was evidence of interstitial keratitis in 118 cases (11.6 per cent.). A personal study of 262 patients by Lemoine resulted in the finding of interstitial keratitis in 28 (10.7 per cent.). Examination of the cornea in this second group was carried out with the aid of a loupe and focal illumination. In a later review from the same hospital, McLeod and Lemoine (1940) stated that 5.3 per cent. of 1,520 patients suffering from congenital syphilis had evidence of interstitial keratitis. Of the patients with congenital syphilis who had undergone ophthalmic examination, 22.9 per cent. had been found to have interstitial keratitis. It is not clear whether this ophthalmic examination included the use of the slit-lamp microscope. This hospital does not normally admit children over 16 years of age and it appears likely that the majority of these patients also were young children.

Lennarson and Jeans (1937) found evidence of interstitial keratitis in 75 (43 per cent.) of 174 children with congenital syphilis who were aged between 2 and 16 years. These authors commented that a detailed ocular study by an ophthalmologist was planned for all syphilitic patients coming to their children's hospital because of the valuable information afforded by such investigation; 124 of the 174 children had been so studied.

Smith (1927) analysed the findings in 1,000 cases of congenital syphilis. He found that 641 patients had evidence of interstitial keratitis and accounted for this abnormally high incidence by the close affiliation of his clinic with the Massachusetts Eye and Ear Infirmary; 708 of his patients were aged 14 years or less, and 100 were aged 21 years or more.

Stokes, Beerman, and Ingraham (1944) estimated that 52 per cent. of all patients brought to medical attention because of congenital syphilis had signs of past or present interstitial keratitis.

Wile and Mundt (1942) found evidence of interstitial keratitis in 177 (44 per cent.) of 402 patients with congenital syphilis. None of the patients was under 2 years of age; the oldest patient with active interstitial keratitis was 42 years of age and active disease was commonest between the ages of 6 and 15 years.

These reports vary widely in their estimates. The disparity is due to differences in the ages of the

patients at the time of review and in the completeness of the ophthalmic examination; also, in some series, such as that of Smith (1927), it is due to the special selection of cases. It is clear that the older the age group and the more complete the ophthalmic examination, the higher is the observed incidence of interstitial keratitis.

Selection of Cases

For the purpose of the investigation we reviewed the cases of all patients attending the Whitechapel Clinic, The London Hospital, in which the diagnosis of congenital syphilis had been made. In addition, we examined a number of similar patients from St. Bartholomew's Hospital and from hospitals in the county of Essex. In each case the diagnosis was reconsidered carefully in the light of history and clinical findings, as well as the results of investigation of contacts and of families, and each patient was examined or re-examined with the slit-lamp microscope by the method outlined below.

Conclusions as to the type of infection, whether congenital or acquired, must sometimes be made on the balance of probabilities and, for this reason, the selection of cases presented difficulties. The first essential in attempting to make an estimate of the incidence of interstitial keratitis is to include only those cases in which the diagnosis of congenital syphilis appears certain. In this series there were 117 such cases, and there were fourteen in which the evidence was strong but not conclusive. These groups are considered separately.

The difficulties of selection are well illustrated by the case of a patient reviewed when she was 32 years of age. At the age of 24 she had been found to be suffering from *tabes dorsalis*, when, according to her case record, the clinical findings were Argyll Robertson pupils and absent ankle jerks, but tests of the cerebrospinal fluid gave normal results. At that time she stated that she had been married for 6 years and that her husband's blood had been tested at another hospital with negative result. All these facts supported the diagnosis of congenital syphilis, but it was also recorded that the patient's six sisters were said to have negative blood tests for syphilis. When her case was reviewed, the patient gave information which she had previously withheld, namely, that she had attended the Whitechapel Clinic at the age of 18 years. Her original record was then traced and it was found that she had been a contact of a patient suffering from secondary syphilis. Four weeks after her first attendance she had developed a syphilitic chancre in serum from which *Treponema pallidum* was found, and serological tests had become positive although negative at first. After two injections of arsenic and bismuth she did not attend until 6 years later, when she returned showing the signs of *tabes dorsalis*, as already described. This experience impressed upon our minds the necessity for extreme care in the selection of cases and the importance of the individual assessment of every patient.

Apparatus

In order to examine the cornea thoroughly it is necessary to use the slit-lamp microscope. This examination

FIG. 1.—Basic components of optical system (after Vogt).

1. Lamp, 6 v. 5 amp. spiral filament bulb
2. Collecting system, two plano-convex lenses each of 22 D. with convex surfaces in apposition
3. Vertical slit 10 mm. in height and adjustable in width
4. Illuminating lens, adjustable and capable of focusing image of slit on eye.

is essential to the investigation and the appearances seen will be described below. The slit-lamp microscope, first demonstrated by Gullstrand (1911), had its optical system changed by Vogt (1920, 1931), and, in its modern form, consists of two parts :

(1) *Slit Lamp*.—This consists of a source of light and a collecting system which directs the light through a slit and focuses it on to the posterior surface of an illuminating lens. The slit is used as a diaphragm to control the size of the beam, and the image of this homogeneously lighted slit is focused upon the cornea by the illuminating lens (Fig. 1).

(2) *Corneal Microscope*.—This preceded the slit lamp in its development and was originally introduced by Abbe (1881). The forerunner of the modern instrument was developed by Zeiss from a

microscope devised by Czapski (1899). The microscope is binocular, producing an erect stereoscopic image, and various objectives enable magnifications of from $\times 8$ to $\times 103$ to be obtained, though for practical purposes $\times 20$ and $\times 40$ are most commonly used.

The instrument used in this investigation was the Haag-Streit slit-lamp microscope (Fig. 2). It is coupled so that the microscope is always directed to the focus of the illuminating beam. By suitable adjustment the intensity of the illumination, the size and shape of the slit, and its focus may be varied.

FIG. 2.—General view of Haag-Streit slit-lamp microscope. (Photograph by The London Hospital Photographic Department.)

1. Housing for electric lamp, condensing lens, and disk with slit
2. Illuminating lens
3. Screw for focusing illuminating lens
4. Screw for regulating width of slit
5. Catch for locking illuminating arm
6. Head-rest
7. Chin-rest
8. Lever for control of combined movement of illuminating and microscope arm in all directions in horizontal plane
9. Height regulating screw
10. Binocular microscope
11. Lever for interchanging microscope objectives

Clinical Procedure

Examination by means of the slit lamp is carried out in a darkened room. The patient is seated on an adjustable stool, and the head is steadied by placing the chin on the chin-rest and forehead against the bar of the head-rest. The beam of light and the microscope are then focused on the tissue to be examined.

When the broad beam of the slit lamp is focused on the cornea, the illuminated area appears as a truncated prism or parallelopiped (Fig. 3). An optical section of the cornea can be obtained by narrowing the beam of light. In this way the anatomy of the cornea may be studied with ease and any morbid changes observed in detail. By retro-illumination, whereby light is reflected from the iris or anterior surface of the lens on to the posterior surface of the cornea, the presence of blood vessels or their remnants, and even the circulation of individual red blood corpuscles, can be distinguished clearly.

FIG. 3.—1. Corneal parallelopiped as seen with broad beam of light
2. Optical section of cornea as seen with narrow beam of light
Ep. epithelium D. Descemet's membrane
B. Bowman's membrane En. endothelium
S.P. substantia propria
3. Optical section to show scarring left by interstitial keratitis in posterior layers of cornea.

Pathology

The main feature of interstitial keratitis is a necrosis of the corneal lamellae, associated with massive cellular infiltration in which lymphocytes predominate. The posterior layers of the cornea are most severely attacked, and the affected area soon becomes heavily vascularized. Vascular invasion of the deeper layers of the substantia propria is then the most conspicuous feature, the vessels running in at various levels corresponding to the sites of active inflammation. The most densely infiltrated part of the cornea is usually at the periphery. In severe cases the anterior epithelium may be considerably affected, with some loss of the basal and deeper layers, and oedema and partial

necrosis of the superficial layers. Bowman's membrane usually remains intact. The posterior endothelium tends to disappear and clumps of lymphocytes are commonly seen adhering to the back of Descemet's membrane, giving rise to the appearance known as keratitis punctata. This membrane may be very wrinkled and irregular or even ruptured. Together with the pathological processes taking place in the cornea there is always a uveitis, the degree of involvement of the uveal tract varying in severity. Many authorities believe that the uveitis is the primary condition, but that it tends to be masked by the more obvious interstitial keratitis. The significance of this uveal involvement will be mentioned later.

The vascular invasion which forms so prominent a feature of this process appears to be a defensive reaction. Repair is effected at a later stage, partly by the proliferation of fixed corneal cells and partly by the fibrous tissue derived from the invading elements. As the condition resolves, the majority of the vessels cease to contain blood, although the outline of their walls may remain permanently as the so-called "ghost vessels". Nevertheless, we have observed in most cases a few vessels which continue to carry blood corpuscles for an indefinite period and it is possible that this may continue throughout life. These vascular remnants afford lasting evidence of the previous disease. Appreciable thinning of the cornea usually accompanies resolution.

Although considerable clearing of the cornea does take place, some permanent opacity usually remains, situated in the deeper layers. This is commonly seen as a diffuse steaming of the most posterior layers of the cornea, or as islets of opacity denser than the diffuse steaming and separated from one another by clear channels, the whole rather resembling a delta in appearance. As already described, some vessels persist throughout life as fine lines, although most of them ultimately cease to contain blood. Their characteristic course and distribution, together with the presence of opacities, offer lasting proof of a previous attack of interstitial keratitis and evidence of congenital syphilis, which may well be diagnostic (Fig. 4a, b, opposite).

Clinical Course.—The clinical course of interstitial keratitis due to congenital syphilis is, in a typical case, characterized by a rapidly developing corneal haze, followed by the appearance of blood vessels, and associated with signs of irido-cyclitis. This initial stage, sometimes called the progressive stage, is usually of short duration measured in weeks. It is followed by the florid stage, when the disease is at its height, which may last for several months. This, in turn, is succeeded by the stage of retrogression, in which gradual

FIG. 4(a).—Section of cornea showing deep vessels. Haematoxylin and eosin. $\times 93$.

1. Epithelium	4. Descemet's membrane
2. Bowman's membrane	5. Endothelium
3. Substantia propria	6. Vessels in posterior fifth of cornea.

FIG. 4(b).—Section of posterior third of cornea, showing deep vessels. Haematoxylin and eosin. $\times 340$. (Microphotographs by courtesy of The London Hospital Medical College, Department of Photography, Institute of Pathology.)

recovery occurs over a period which may last for anything up to 2 years. Recovery is then complete, except for the residual corneal appearances described above and evidence of old irido-cyclitis. Both eyes are usually involved sooner or later, the intervals between the involvement of the first and second eye varying from a few days to many years.

Other Clinical Types of Interstitial Keratitis.—A less common form, though by no means so rare as the literature would lead us to suppose, is the avascular type: in this a collection of small infiltrates, which frequently coalesce, appears near the centre or sometimes the upper part of the cornea. This type, as its name suggests, is associated with little or no vascularization and appears to have a quite different prognosis from the classical form.

A further variant is the annular type described by Vossius (1885), which is characterized by an endo-

thelial catarrh with the deposition thereupon of plastic exudates in annular distribution with a clear centre. We saw no cases of this kind.

Effect of Treatment on the Corneal Appearances.

The course of the corneal changes was not significantly affected by treatment before the use of cortisone. In the present study acute interstitial keratitis was seen in fourteen eyes. Six of these received local cortisone treatment; in three of the six the disease was avascular and cleared to such an extent that no residual signs of any kind are present; in the three remaining eyes the keratitis was of the classical type and the effect of local cortisone was to produce marked regression of existing vascularization, together with lessening of the corneal oedema and infiltration, thereby changing the clinical picture to one more nearly resembling that of avascular interstitial keratitis.

Corneal Stigmata following Interstitial Keratitis.—A diffuse steaming of the most posterior layers of the cornea, associated with some opacification in all layers, together with the presence of deep vessels or their remnants, forms the usual picture which follows a classical attack of interstitial keratitis.

Quite a different picture seems to follow an attack of the avascular variety, which was present in five out of the fourteen eyes observed with acute interstitial keratitis. All five, of whom two were not treated with cortisone, have cleared without residual signs of any kind. From this it would appear that the avascular form can heal without permanent damage.

Results of Assessment

A series of 117 congenital syphilitics aged from 5 to 70 years (average 34 years), was examined with the slit-lamp microscope and 74 (63 per cent.) showed undoubted evidence of interstitial keratitis past or present. None of the fourteen patients who were only *probably* suffering from congenital syphilis had evidence of interstitial keratitis, and if they are considered together with the previous group the incidence of interstitial keratitis is reduced to 56 per cent. of the 131 patients examined (Table II).

TABLE II
ANALYSIS OF RESULTS

Congenital Syphilis		Male	Female	Total	Per-centage with Inter-stitial Keratitis
Certain	Interstitial keratitis	21	53	74	63
	No interstitial keratitis	5	35	40	34
	Doubtful corneal change	1	2	3	—
	Total			117	48
Prob-able	No interstitial keratitis	4	8	12	—
	Doubtful corneal change	1	1	2	—
	Total			14	—
Total of Both Groups				131	56

Interpretation of Results.—The point to be considered is whether the incidence of interstitial keratitis in this group of patients represents the true incidence in congenital syphilitics in general. Was there, in fact, any bias in the method of selection of cases? In this connexion it is of interest to review the reasons for which these patients presented at the clinic, and to determine, if possible, whether the sources from which the patients were drawn were responsible for some inherent bias. Table II shows that the proportion of female patients was high, namely 53 females to 21 males with interstitial keratitis, and 35 females to 5

males with normal corneae. Interstitial keratitis is known to be commoner in women than in men; this preponderance was described by Hutchinson (1863) when he found that, of 102 cases of interstitial keratitis, 64 occurred in women. Fournier (1886) drew attention to the fact that 46 of his 83 patients with interstitial keratitis and 22 of Parinaud's 32 patients were women. Many authors have confirmed these earlier findings, amongst them Spicer (1924), who found that of 596 cases of interstitial keratitis due to congenital syphilis 61 per cent. occurred in women. In the present study, however, it seems reasonable to suppose that there has been an element of special selection, for in this country more women than men have routine serological tests and no less than 13 per cent. of the patients with undoubted congenital syphilis were sent for investigation because routine serological tests during pregnancy were found to be positive (Table III).

TABLE III
ANALYSIS OF MODE OF PRESENTATION OF 117 CONGENITAL SYPHILITICS

Reason for Reference to Clinic							Total
Serological Tests for Syphilis Positive	Routine	12	61	}	Antenatal	15	
	Investigation of syphilitic lesion	32					
	Persistent	2					
Interstitial Keratitis	Initial	23	40	}	Subsequent	6	
	Scarring	11					
Contact tracing	.. .. .	7					
Gonorrhoea, non-specific urethritis	.. .. .	2					
Patient	.. .. .	6					
Continue Treatment	.. .. .	1					
Total	.. .. .	117					

It seems certain, too, that any estimate of the incidence of interstitial keratitis among known congenital syphilitics must be higher than the true incidence, because it is most likely that some patients, particularly those who do not develop keratitis, go through life with undiagnosed congenital syphilis. Thus the development of interstitial keratitis is an important means by which the patient with congenital syphilis is brought to notice. In the case of the patient who does not develop corneal changes the disease may remain undiagnosed unless routine serological tests are done for some other reason. Of the 74 patients with interstitial keratitis, 28 had no history or other sign diagnostic of congenital syphilis; but for the keratitis it is most likely that the diagnosis would not have been made (Table IV, opposite).

This is particularly true of three female patients with old interstitial keratitis whose serological tests for syphilis were negative at the time of examination and who had no record of previous serological tests.

TABLE IV
PATIENTS WITH INTERSTITIAL KERATITIS

Interstitial keratitis with other diagnostic signs	46
Acute interstitial keratitis S.T.S. positive	24
Old interstitial keratitis S.T.S. positive	1
Old interstitial keratitis S.T.S. negative	3
Total	74

The first of these was 62 years old when typical corneal changes were found, the second 42, and the third 56 years of age. In each case the family history suggested the diagnosis of congenital syphilis and there was a history of an attack of mistiness of vision in childhood which had been treated with eye drops only. The second of these three patients has been under observation for 8 years and serological tests for syphilis have remained negative throughout, except for weakly positive precipitation tests on two occasions.

Nevertheless it should be noted that the fact that a patient develops interstitial keratitis does not always lead to the correct diagnosis. Of 74 patients with evidence of interstitial keratitis, only forty came to a clinic for that reason (Table III). Of 64 patients whose first symptoms were due to interstitial keratitis only 35 (55 per cent.) began adequate anti-syphilitic treatment within 6 months of the onset.

The age of the patient when the case is reviewed is an important factor to be considered in estimating the total incidence of interstitial keratitis occurring in congenital syphilitics. In this series the age of review was late, the average being 34 years. Thus it is probable that most of the patients who were likely to develop interstitial keratitis would have done so by the time of review. This is one reason for the apparently

high incidence of interstitial keratitis which was found. Fig. 5(b) shows the ages of the patients at the time of review, varying from 5 to 70 years (average 34). Fig. 5(a) shows the age of onset of interstitial keratitis in 67 cases varying from 2 to 38 years.

No mention has been made of the effect of anti-syphilitic treatment, for it is a factor which cannot be assessed in this study.

For these reasons, therefore, the results described indicate only that evidence of interstitial keratitis was found in 63 per cent. of cases of congenital syphilis in clinic practice at the present time. Because forty patients first attended the clinic on account of interstitial keratitis (Table III) they have, for that reason, caused bias in the selection of cases. If this group is omitted, 77 patients remain, of whom 34 (44·2 per cent.) had keratitis. It is likely that the true incidence of interstitial keratitis occurring among congenital syphilitics, as distinct from that found in clinic practice, may lie between these figures of 44 and 63 per cent.

Corneal Changes of Doubtful Significance

Three patients with undoubted evidence of congenital syphilis were found to have corneal changes which might have been due to old interstitial keratitis but were not diagnostic of this condition. These changes were sufficiently interesting to merit description in some detail:

(1) **Case 58.**—Opacity in the right cornea, deeply situated for the most part, but with some superficial nebulæ in addition. Few vessels were present and these were superficially placed except for one in the posterior layers of the cornea. There was no evidence of activity, although some of the vessels contained red blood corpuscles. The patient did not give a history suggestive of old interstitial keratitis. He was 69 years of age at the time of review and said that his eyes had been "red" at the age of 57. He showed stigmata of infection in early life including a sabre-shaped tibia and perforation of the palate. Serological tests for syphilis performed on his blood serum gave strongly positive results.

(2) **Case 163.**—Corneal microscopy showed ghost vessels running in a sheaf from the periphery of the cornea in the 12 o'clock meridian, starting at the level of the junction of the middle and posterior thirds of the

FIG. 5(a).—Age at onset of interstitial keratitis in 67 patients (2–38 years).
(b).—Age at review of 112 patients with congenital syphilis (5–70 years).

cornea and becoming deeper centrally but not completely posterior. There was "pocking" of the endothelium in relation to these vessels. This patient was 59 at the time of review. She gave no clear history to suggest old interstitial keratitis but remembered an episode of watery discharge from the right eye at the age of 20, without mistiness of vision. The condition had been treated with hot fomentations. At the age of 36 the patient had been found to have evidence of old healed choroido-retinitis and Hutchinsonian teeth while her blood serum gave a positive Wassermann reaction.

(3) **Case 165.**—A girl aged 15 was found to have small discrete white maculae on Descemet's membrane at the periphery of one cornea; there was no vascularization. She gave a history of transient loss of vision at the age of 14 years but this had affected the other eye only. She had been found to have positive blood serological tests for syphilis at 11 years of age during an attack of what was described as "toxic nephritis". Her mother was found to be suffering from syphilis of old standing.

Iritis without Corneal Change.—Apart from the 74 patients with definite evidence of interstitial keratitis and the three with corneal changes of doubtful significance, four were suffering from congenital syphilis, with signs of old iritis without evidence of involvement of the cornea. It is possible that some or all of these patients had suffered from kerato-iritis and that the corneal inflammation had resolved completely, for we observed the phenomenon of complete resolution of corneal changes in five eyes with active interstitial keratitis, but it should be added that three of these were treated with cortisone.

Other Findings.—From the study of this group of patients there emerged certain further points of interest from which conclusions may be drawn:

(1) **History of Misty Vision.**—The history of an episode of misty vision, extending over a period of weeks or months, was obtained originally or on further questioning in the case of 77 patients, no less than 66 per cent. of all patients with congenital syphilis. Of these 77 patients, 73 had evidence of interstitial keratitis and four of iritis.

It appears that such a history of misty vision is probably the most important single symptom in the diagnosis of congenital syphilis. The direct question "Have you ever had an attack of mistiness of vision?" should always be put to any patient in whose case the diagnosis of congenital syphilis is a possibility. Evidence of old interstitial keratitis in the absence of such a history of misty vision is rare and is most easily explained by an attack that occurred in infancy. Only one patient (Case 93) in this group had evidence of old interstitial keratitis without such a history. He was found to have characteristic, although scanty,

corneal vascularization and scarring. Another patient (Case 191), who was probably suffering from congenital syphilis and gave no history of misty vision, was found to have opacities of the posterior layers of the cornea at the periphery; these might have been the result of "clinically silent" interstitial keratitis, but were not diagnostic. Yet another patient (Case 36) had similar peripheral opacities in one eye with the classical signs of old interstitial keratitis in the other eye. This patient had undoubted congenital syphilis and gave the history of an attack of mistiness of vision in the eye which showed the classical signs, but not in that which showed the peripheral opacities. It is possible that both these patients had had attacks of acute avascular keratitis without symptoms because only the peripheral parts of the cornea were involved.

(2) **Macroscopic Examination.**—The routine inspection of the eye by the physician is of less value than the careful history in suggesting the diagnosis of old interstitial keratitis. In 21 of the 74 patients who showed typical changes on slit-lamp examination, the cornea had been described as clear on routine inspection. In five other cases, opacity of one cornea was found on routine inspection but examination with the slit-lamp microscope showed characteristic changes in the other eye also.

(3) **Unilateral Involvement.**—As might be expected in a group of patients whose cases were assessed relatively late, the large majority (84 per cent.) of those affected had evidence of involvement of both corneae. In each of thirteen cases, however, only one cornea was involved; of these, one patient had been under observation for only 4 months since the first attack, and another had developed changes in the second eye during the period of observation. The second patient had been seen for slit-lamp microscopy 16 years after an original attack of interstitial keratitis which had affected the left eye. Examination of the left cornea showed old scarring and no present activity, but the anterior chamber of the right eye contained an excess of cells and 2 months later the changes of interstitial keratitis developed in that eye. In the remaining eleven patients, the interval from the first attack of interstitial keratitis to the time of reassessment was from 2 to 40 years (average 12.3).

(4) **Excess of Cells in Anterior Chamber.**—The finding of an excess of cells in the anterior chamber of an eye followed by the development of interstitial keratitis in that eye was noted in three cases. It seems probable that interstitial keratitis, or kerato-iritis as it is also called, may be heralded by an increase in cells in the anterior chamber. Vogt (1931) has stated that the first sign of the disease is seen by slit-lamp examination as an endothelial catarrh in an apparently

sound eye, before symptoms are obvious. Our observations lead us to suppose that this endothelial change may be preceded by the presence of cells in the anterior chamber. The duration of this "warning sign" is at present uncertain, and whether it always precedes the development of corneal opacity remains to be determined. In the event of finding evidence of endothelial catarrh or an excess of cells in the anterior chamber of one eye when the other is affected by interstitial keratitis, it would be advisable to treat both eyes with cortisone.

(5) *Non-Specific Corneal Scars*.—Corneal microscopy with the slit lamp played an important part in amending the diagnosis of one in ten of all the cases reviewed. It not only established the diagnosis of interstitial keratitis but it also excluded from the group under assessment a number of patients whose corneal scarring was of non-syphilitic origin.

Summary and Conclusions

(1) Previous estimates of the incidence of interstitial keratitis among patients with congenital syphilis are reviewed.

(2) The use of the slit-lamp microscope in the investigation of ocular disease in congenital syphilis is described and the findings in 131 cases examined by this method are outlined.

(3) The incidence of interstitial keratitis in cases of congenital syphilis in clinic practice was 63 per cent. This incidence is reduced to 44 per cent. by excluding all those who *presented* at the clinic because of interstitial keratitis. Thus the true incidence, as distinct from that seen in clinic practice, may lie between 44 and 63 per cent.

(4) In 63 (84 per cent.) of the 74 patients with evidence of interstitial keratitis, both corneae were involved; the change was unilateral in eleven patients observed for an average of 12.3 years since the first attack.

(5) A history of misty vision lasting more than a few days is the most important single symptom in the diagnosis of former interstitial keratitis and of congenital syphilis. Macroscopic examination of the eye is of less value and frequently misleading. The direct question "Have you ever had an attack of mistiness of vision?" should always be put to any patient in whose case the diagnosis of congenital syphilis is a possibility.

(6) Complete clearing of the cornea was observed in five eyes affected by avascular interstitial keratitis.

Three of these had been treated with cortisone. It is also possible that corneal clearing, although short of complete resolution, may leave only traces from which no diagnosis can be made. Three patients were seen who had corneal changes which may have been due to old interstitial keratitis but were not diagnostic of this condition.

(7) An increase of cells in the anterior chamber of the eye, as seen with the aid of the slit-lamp microscope, is a valuable sign and may precede the development of interstitial keratitis.

(8) It is desirable that all patients in whom the diagnosis of congenital syphilis is a probability should be examined with the aid of the slit-lamp microscope; any such patient giving a history of mistiness of vision should certainly be so examined.

(9) Corneal microscopy with the slit lamp played an important part in amending the diagnosis of one in ten of all the cases reviewed.

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