A SURVEY OF RECENT METHODS OF DIAGNOSIS AND TREATMENT OF INTERSTITIAL KERATITIS, AND AN ANALYSIS OF THE RESULTS OF TREATMENT IN A SERIES OF 105 CASES.

A Thesis presented to the University of Edinburgh, for the Degree of Doctor of Medicine, By Dorothy M. Taylor.

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INTRODUCTION.
A SURVEY OF RECENT METHODS OF DIAGNOSIS AND TREATMENT OF INTERSTITIAL KERATITIS, AND AN ANALYSIS OF THE RESULTS OF TREATMENT IN A SERIES OF 105 CASES.

INTRODUCTION.

Interstitial keratitis was for a long time regarded as a definite disease affecting the eye, and it was not until 1863 that Jonathan Hutchinson\(^1\), in his "Clinical Memoirs", established it as being directly due to Inherited Syphilis. In this work Hutchinson mentions that Dr Mackenzie\(^2\) had already devoted a section of his treatise to a description of what he termed, "Scrofulous Corneitis", 
and stated, "that it is specifically different from every other ophthalmia".

We are indebted to Jonathan Hutchinson for the first classical description of the condition, and also for his pioneer work in establishing it as a definite manifestation of Inherited Syphilis.

Briefly, Interstitial Keratitis may be described as a cellular infiltration of the middle and posterior layers of the cornea, which is thereby given a ground-glass appearance. The disease is commonest in childhood, notably occurring between the ages of five and eighteen years in patients who are the subjects of Congenital Syphilis. It is somewhat chronic in its course, and is characterised by the absence of any tendency to ulceration.
AETIOLOGY.
Many, and widely varying, explanations have been vouchsafed as to the reason for the occurrence of interstitial keratitis during the growing years of life, one of these being the suspicion that the influence of the hormones of growth are concerned. Its greatest incidence in girls, during the age periods of eleven to fifteen, has led to the sex hormones being implicated, particularly those of the ovaries.

Igersheimer\(^3\) quotes Hippel, Rheis, Scafelder and Cathanes as having shown anatomically
that keratitis parenchymatous may occur in foetal life, but it is a great rarity. However it is generally admitted that the corneal lesion is due either directly or indirectly to the spirochaeta pallida. Whether this lesion is a result of the actual presence in the cornea of the spirochaete, or of its endotoxins, is still a subject for discussion. Igersheimer made an exhaustive study of rabbits in which both direct and metastatic interstitial keratitis was produced, he was then able to demonstrate the presence of spirochaeta pallida throughout the layers of the cornea, as far down as Decemet's membrane. Lowenstein, however, did not show spirochaetes but observed a cellular infiltration around the ciliary vessels, and concluded that it caused nutritional changes, and so produced the keratitis. This was a later publication than that of Igersheimer.

Another investigator, Brown, believed
that certain strains of spirochaetes have a greater affinity for the corneal tissue than others. An interesting case was reported by McDiarmid\textsuperscript{7} illustrating that the soil, i.e. the cornea, and not the spirochaete, may be the determining factor. He quoted a case of twins, where one twin showed a positive Wassermann reaction, and had repeated attacks of interstitial keratitis. The mother's Wassermann reaction was positive, while the father's, and the other twin's, was negative, and keratitis never developed in this child.

The question of trauma might be mentioned here as being an aetiological factor, or rather an exciting cause. It has aroused widespread attention on account of its industrial insurance aspect. Butler\textsuperscript{8} said that in 20 per cent of his cases there was a history of trauma, while Spicer\textsuperscript{9} gave 3 per cent and Cunningham\textsuperscript{10} 1.5 per cent. In this series of 105 cases there
was a history of trauma in 2.8 per cent of the number.

Another point in the aetiology that is stressed by certain European authorities, namely Euroth, Hagop, and Kraupe, is that some constitutional condition is usually present, and is the exciting cause. Still others believe that an unbalanced endocrine system is an important factor. Among those who hold this view is Alexander who studied interstitial keratitis in a hypothyroid case which cleared up quickly with thyroid extract.

Mention must also be made of focal infection as being concerned in the aetiology, and this view may be illustrated by the following case reported by Jones. He studied this aspect in a boy, aged 16 years, who had a typical interstitial keratitis. The Wassermann reactions in both parents and child were negative, and antisyphilitic
measures failed to affect the condition. The tonsils were seen to have pus in the crypts, and X-rays of the teeth showed nine apical abscesses. The affected teeth and tonsils were removed, and an uninterrupted recovery took place. The boy had full vision 20/20 at the end of seven months. A bacteriological report of pus from the teeth and tonsils showed the presence of the streptococcus haemolyticus, micrococcus catarrhalis, and pneumococci.

Still another authority, Spicer, believes that the interstitial keratitis depends on the presence in the eye of the spirochaeta pallida - if it is present an attack of keratitis is bound to develop at some time. However, if the organism present has not attained the required state of evolu:c:tion, then there will be no attack. If this state of evolution has been reached then an attack of interstitial keratitis will develop in the absence
of any further stimulus, or, in spite of anything, that can be done.

Another point which is raised by studying the preponderance of interstitial keratitis incidence in congenital, as compared with acquired syphilis, is, whether the cornea during its developmental stage is more susceptible to the invasion by the spirochaete, than is the avascular adult cornea. This latter view, as a possible explanation, is held by Mr C. Mills.16

On reviewing the mass of material collected by various authors, the following conclusions may be drawn.
Conclusions.

1. That the spirochaetes and their endotoxins present in the cornea are responsible for the keratitis.

2. Trauma is undoubtedly a contributing factor and must be considered.

3. The presence of focal infection and disturbance of the endocrine balance may have an influence, but it should be realised that these factors themselves are often influenced by the specific infection.

4. Finally, we are brought to the conclusion, that the true cause of interstitial keratitis is the spirochaeta pallida.
PATHOLOGY.
PATHOLOGY.

Macroscopic Appearances.

Interstitial keratitis, as the name implies, is a cellular infiltration of the middle and posterior layers of the cornea, which results in a generalised corneal haziness or cloudiness.

This infiltration may begin at the margin or periphery of the cornea, and spread until the whole cornea is affected. Once the
infiltration has become general the cornea softens and assumes a dense grayish colour, so that the iris is no longer visible, and vision is reduced to little more than perception of light. The corneal surface, at this stage, is steamy and of a ground-glass appearance.

At this point, deep-seated blood-vessels, derived from the anterior ciliary begin to appear, and pervade the substance of the cornea. This vascularization gives rise to a reddish dis-coloration which is known as the salmon patch. The inflammation then commences to subside, and in favourable cases, after a couple of months, nothing remains but a faint central opacity, or perhaps evidence of a few, minute, peripheral vessels.

Microscopic Findings.

Two well-known ophthalmologists,
Spicer$^{17}$ and Jaeger$^{25}$ affirm that before the succession of changes occurring in the cornea during an attack of acute interstitial keratitis can be accurately ascertained, a series of histological examinations should be made at various stages of the different kinds of onset in an attack.

As a result of animal inoculations certain changes have been observed, and confirmed by various authorities.

Gilbert$^{18}$ studied the eye of a boy of 19 years with a typical attack of interstitial keratitis, and found marked variability in the thickness of the corneal epithelium, as a result of the corneal infiltration, but he did not demonstrate spirochaetes in the tissue. Suganuma$^{19}$ found general atrophy of the epithelial layers. Others, namely Weill,$^{20}$ Kesterbaum$^{21}$ and Nakaisumi$^{22}$ believe that the lines sometimes seen in the affected cornea are the results of a proliferative inflammation.
As before stated, Igersheimer\textsuperscript{23} found endothelial thickenings containing spirochaetes in experimental keratitis produced in rabbits, while Lowenstein\textsuperscript{24} failed to demonstrate them, but showed there was a round-cell infiltration around the ciliary vessels. Still another observer, Jaeger\textsuperscript{25} stated that a histological study of a case of interstitial keratitis showed no changes to support a nutritional disturbance theory.

Ebsching\textsuperscript{26} attributes the process of interstitial keratitis to toxins reaching the cornea from the limbus, while Rheis\textsuperscript{27} claims that the toxins attain the cornea from the amniotic fluid and produce cell infiltration by chemotaxis.

One may thus conclude from the results of animal inoculations, that the general clouding of the cornea is more frequently due to a round-celled infiltration, than it is to the presence of the spirochaeta pallida itself.
Although it is as far back as 1863 that Hutchinson first recognised the condition to be part of an inherited syphilis and not a purely local eye disease, yet it is only within recent years that this view has been accepted universally as regards treatment. After much controversy the ophthalmologists have now realised this aspect of the disease, and are referring cases to a syphilologist for treatment. Prior to this, the
prognosis of the disease was bad as regards vision because it was only being attacked locally. This subject will be dealt with in greater detail later on.
OTHER CONDITIONS GIVING RISE TO INTERSTITIAL KERATITIS SIMULATING THE SYPHILITIC FORM.

Keratitis is commonly divided into two forms - namely, suppurative and non-suppurative, and, as previously stated, interstitial keratitis belongs to the non-suppurative class. Although, in the vast majority of cases, interstitial keratitis is syphilitic in origin, there are other conditions which give rise to a similar appearance of the cornea, and these must be considered before a definite diagnosis can be made. There is a form of keratitis occurring in patients who are the subjects of tuberculosis. It closely resembles the
appearance of the syphilitic variety, and can only be distinguished by the presence of other signs of active tuberculosis on the one hand, and the absence of any evidence of inherited syphilis on the other. The Wassermann reaction is, of course, negative in these cases, and there is no response to antisyphilitic remedies.

Keratitis profundo, as the name implies, is a deep-seated inflammation of the cornea, and is recognised by the development of a gray central opacity of the cornea, accompanied by irritative symptoms. It becomes absorbed entirely, or almost perfectly, in a few weeks and is treated along similar lines to those adopted for interstitial keratitis. This variety of keratitis occurs chiefly in adults.

Another form of keratitis, with which interstitial keratitis may be confused, is keratitis
punctata. This is the name given to dot-like deposits on the posterior surface of the cornea, due to an exudation occurring in inflammation of the uveal tract, e.g. iritis, cyclitis and irido-cyclitis. The condition is never limited to the cornea as in interstitial keratitis proper, and the deposits are usually absorbed.

There are other rare forms of keratitis namely, leprous interstitial keratitis, and malarial keratitis, - in the latter disease the condition is usually uniocular and avascular, and runs a rapid course to recovery.

Still rarer forms have been reported, e.g. influenzal, rheumatic, reflex, dysmenorrheic, but in all such conditions there are signs of the primary disease, and the absence of any manifestations of syphilis to aid in the diagnosis.
A further list of various forms of keratitis from which the interstitial variety must be distinguished is given by Dr Alfredo Roma\textsuperscript{28} and these need only be enumerated.

1. Disciform.  
2. Lattice.  
3. Sclerosing.  
5. Marginal  
6. Traumatic.  
7. Seriated, etc. etc.
DIAGNOSIS OF INTERSTITIAL KERATITIS.
THE DIAGNOSIS OF INTERSTITIAL KERATITIS.

The diagnosis of interstitial keratitis is based upon at least three factors:

1. Local appearances in the eye.
2. Other signs of congenital syphilis.
3. Serological confirmation of the Wassermann reaction.

I. Local Appearances.
Local Appearances.

The condition of interstitial keratitis commences as a diffuse haziness near the centre of the cornea of one eye, with very little evidence of congestion. The patient usually complains of some irritability of the eye - there is photophobia, lacrimation and some dimness of vision. Pain is usually absent at this stage. The central opacity spreads until the whole cornea is involved, except perhaps a band near the periphery. The surface is steamy and is said to have a ground-glass appearance. At this period deep-seated blood-vessels appear, and give rise to the vascularization known as the salmon patch, which is so distinctive of the disease. About this time pain around the orbit may be marked, and all the other irritative symptoms are intensified. This
process may continue for one to two months, and at the end of this time, the inflammation may begin to subside, depending on the severity of the attack and the institution of treatment. About this time the second eye may become involved and go through a similar process. Spicer\textsuperscript{29} reports a case where one eye had a mild attack, and seven years later the second eye was more severely involved than the first. In 75 per cent of his 700 cases, both eyes were involved together or overlapped, with no greater interval than twelve months – many cases had longer intervals and two cases had intervals of 18 years.

Igersheimer\textsuperscript{30} states that, intensive treatment by arsenobenzol or mercury at the beginning of the inflammation in the first eye, does not always prevent involvement of the second eye, and that the inflammation of the second eye may reach the same degree as in the first. Fucks\textsuperscript{31} believes that
interstitial keratitis attacks both eyes and more frequently two in succession than two at once. There may be an interval of several years between this involvement of the two eyes. Cunningham found 19 years to be the longest interval before the second eye was attacked.

In the present series of 105 cases there were 50 cases in which both eyes were involved at intervals varying from one month to three years.

Recurrences in one eye after the institution of treatment was noticed in 10 cases or 0.9 per cent.

The process of clearing of the cornea may take several months or even a year - the centre usually being the last portion to clear.
At any stage this resolution of the exudates may come to a standstill leaving a dense opacity resulting in varying degrees of loss of vision.

II. Other Signs of Syphilis.

There are a large percentage of cases of interstitial keratitis which have the typical congenital facies - the broad square forehead, sunken or broadened bridge of nose, flattened malar bones, and perhaps most constant of all - Hutchinsonian teeth. These teeth have characteristic notching of the central
incisors, the teeth themselves being peg-shaped and deficient in enamel. In other cases, there is a doming of the cusps of the first molar teeth as described by Moon.

Rhagades, or the cicatrices of old fissures at the angles of the mouth, may be seen frequently.

Additional, and confirmatory signs, are thickenings of the sterno-clavicular joints, periosteal nodes, and sabre-blade tibiae.

Cervical adenitis is generally present, and enlargement of the epitrochlear, axillary and inguinal glands may be noticed as well.

An analysis of the present series of cases reveals the frequency with which these various
stigmata have occurred. In many of the cases, several signs were present, while in the most typical and grosser cases of inherited syphilis, in addition to the interstitial keratitis, it was common to find the unmistakeable facies, with the harsh, inelastic skin, broad nose, perhaps with a sunken bridge, flattened malar bones, and Hutchinsonian teeth associated with a narrow high-arched palate, or Moon's molar teeth. In such a case it was usual to find enlarged tonsils and cervical adenitis.

On the other hand, 19 of the cases showed no physical defect which could be attributed to inherited syphilis, apart from the interstitial keratitis - this and the existence of the positive Wassermann reaction in the blood, were the only evidences that the patient suffered from inherited syphilis.

Various combinations were found
intermediate between these two extreme types. These findings were borne out by C. H. Mills\textsuperscript{16} who recorded many cases of interstitial keratitis occurring in congenital syphilis during the War. Many of these patients were perfect in physique with no congenital stigmata. Usually interstitial keratitis developed 3 to 5 weeks after some local trauma and the Wassermann test was found to be positive. He is of the opinion that many congenital cases go through life without showing any definite lesion of the disease.

Analysis of 105 cases to show signs of congenital syphilis other than interstitial keratitis.
Analysis of 105 cases to show signs of congenital syphilis other than interstitial keratitis.

Suggestive facies 30 cases
Hutchinsonian teeth 61 "
High-arched palate 45 "
Bone lesions 15 "
Deafness 9 "
Rhagades 5 "
No stigmata noticed apart from interstitial keratitis 19 "

III Serological./
III  Serological.

The Wassermann reaction should be performed in every case of interstitial keratitis, as has been previously stated, because there may be no congenital stigmata to point to the diagnosis. It is exceptional in a case of acute keratitis to get a negative reaction.

Guy states, that, in interstitial keratitis in association with congenital syphilis, it is diagnostic but not pathognomonic. He found the Wassermann test positive in 144 cases out of a series of 150, leaving 6 cases or 4 per cent with a negative reaction.

In these series of 105 cases the serological results were as follows:

Wassermann reaction positive in 99 cases - 94%
Wassermann reaction negative in 6 cases - 5.7%
THE VALUE OF THE PROVOCATIVE TEST.

In the rare cases where a negative result in the Wassermann reaction is obtained repeatedly, and in the absence of other evidence of syphilis, it is often a valuable procedure to administer an injection of .15 gm. or .3 gm. of an arsenobenzol preparation, according to the age of the patient. If the Wassermann is repeated three days to a week later, after such a provocative injection, it is found frequently to be positive.

Age periods./
Age periods.

The incidence of interstitial keratitis is greatest during the age periods of 5 to 15 years. This was noted first by Hutchinson, who added also, that he had never seen a case beyond the age of 26 years. In his series of cases the average age of incidence was 10 years. The figures given by Guy in his cases, numbering 150, are as follows:

<table>
<thead>
<tr>
<th>Age</th>
<th>Cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 - 2 years</td>
<td>5</td>
<td>3%</td>
</tr>
<tr>
<td>5 - 10 years</td>
<td>80</td>
<td>50%</td>
</tr>
<tr>
<td>10 - 15 years</td>
<td>41</td>
<td>25%</td>
</tr>
<tr>
<td>15 - 20 years</td>
<td>22</td>
<td>13%</td>
</tr>
<tr>
<td>20 - 30 years</td>
<td>10</td>
<td>6%</td>
</tr>
<tr>
<td>Over 30 years</td>
<td>2</td>
<td>1%</td>
</tr>
</tbody>
</table>

The earliest age in his series was 1 week.
The latest age in his series was 39 years.
In the present series of 105 cases the following figures were obtained:

<table>
<thead>
<tr>
<th>Age Period</th>
<th>Number of Cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 - 2 years</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>3 - 4 years</td>
<td>4 cases</td>
<td>3.8%</td>
</tr>
<tr>
<td>5 - 10</td>
<td>24 cases</td>
<td>22.2%</td>
</tr>
<tr>
<td>10 - 15</td>
<td>31 cases</td>
<td>29.5%</td>
</tr>
<tr>
<td>15 - 20</td>
<td>25 cases</td>
<td>23.8%</td>
</tr>
<tr>
<td>20 - 30</td>
<td>9 cases</td>
<td>8.5%</td>
</tr>
<tr>
<td>Over 30</td>
<td>7 cases</td>
<td>6.6%</td>
</tr>
</tbody>
</table>

Earliest age - 4 years.
Latest age - 48 years.

In this series the age period of the greatest incidence was 4 to 18 years - 90 cases - 85%

The peak of the incidence was between the years of 10 and 18, while the year of greatest incidence was 10, at which age there were 11 cases. Other authorities have given varying figures but the
majority attain their greatest number of cases at 10 years. Their figures are as follows:

<table>
<thead>
<tr>
<th>Name</th>
<th>Cases</th>
<th>Peak of curve</th>
</tr>
</thead>
<tbody>
<tr>
<td>Greef</td>
<td>279</td>
<td>10 - 20 years</td>
</tr>
<tr>
<td>Hoor</td>
<td>109</td>
<td>10 - 20</td>
</tr>
<tr>
<td>Cunningham</td>
<td>336</td>
<td>10 - 15</td>
</tr>
<tr>
<td>Spicer</td>
<td>556</td>
<td>5 - 10</td>
</tr>
<tr>
<td>Igersheimer</td>
<td>256</td>
<td>5 - 10</td>
</tr>
<tr>
<td>Carvill and</td>
<td>322</td>
<td>5 - 10</td>
</tr>
<tr>
<td>Derby</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Sex Incidence.**

All observers agree that the female sex is more liable to interstitial keratitis than the male, but their actual figures vary considerably. The incidence in the present
105 cases is:-

Total number of cases  -  105
Females      -    79  -  70.4%
Males        -    26  -  43.8%

Guy \(^{33}\) found the following incidence in his 150 cases:-

93 females  -  59%
67 males    -  41%

Carvill and Derby \(^{34}\) report 61% female, 39% male.

Spicer's analysis is almost identical.

Cunningham \(^{32}\) recorded 54% female, 46% male.

Hutchinson \(^{1}\) 63% female, 37% male.

Igersheimer \(^{34}\) 50.6% female, 49.4% male.
FREQUENCY OF INHERITED SYPHILIS AS OPPOSED TO ACQUIRED SYPHILIS AS THE CAUSE OF INTERSTITIAL KERATITIS.

Since the time of Hutchinson it has been recognised that interstitial keratitis occurs much more frequently in inherited than in acquired syphilis. Various, and diverse reason, for this have been brought forward.

In the case of inherited syphilis the disease is, from the very beginning, widely disseminated, so that in certain tissues the infection is lying latent from birth.

When keratitis occurs as a result of acquired syphilis it is usually, according to
De Schwenitz\textsuperscript{38} a late secondary or tertiary manifestation; it is apt to be unilateral, the onset is more rapid and the disease is more amenable to treatment than in the case of interstitial keratitis occurring in a subject of congenital syphilis. Schwenitz cites Stephenson as finding 2 – 10 per cent of interstitial keratitis in syphilis of acquired type. Igersheimer,\textsuperscript{36} in investigating 247 cases, found only one case in which there was a chancre, and Beensheimer found no such case in 280 patients. Cases have been reported where it was claimed that both congenital and acquired syphilis were present. Critchley\textsuperscript{37} reports a case of interstitial keratitis occurring with an acquired syphilitic infection. This patient developed the interstitial keratitis five days after receiving an injection of "914" for mucous patches. There was a history of a penile sore four months previously.

All the cases in this series occurred as a result of inherited syphilis.
CLINICAL CLASSIFICATION IN THIS SERIES.

This series of 105 cases of interstitial keratitis may be divided into three groups:

1. Acute interstitial keratitis 76
2. Subacute interstitial keratitis 12
3. Chronic interstitial keratitis 17

The term "chronic" requires explanation. Examples of this form were seen, for the most part, in cases examined in the Royal Blind School in Edinburgh. The majority of these were old-standing cases of interstitial keratitis, which had either passed unrecognised, or had not been submitted to treatment until the damage to the eye was so gross as to cause blindness. These cases will be discussed later under a separate heading.
The patients demonstrated certain groups of well-recognised symptoms, and it is of interest to give an analysis of those most frequently met with. In the more acute cases, the most prominent symptoms were pain, photophobia and lacrimation. The actual number of cases in which this triad occurred is as follows:

- Pain: 31
- Photophobia: 82
- Lacrimation: 78
- Ulceration and Suppuration: 2

As will be seen from the figures photophobia and lacrimation were much the most
frequent symptoms. Pain is more prevalent when the complication of iritis is present, but may manifest itself in the absence of this condition. It has been mentioned elsewhere that ulceration and suppuration are very rarely seen in interstitial keratitis, and hence it is of interest to note that there were two patients in the series who showed definite evidence of both these complications.

One patient, a woman of 29 years, who was pregnant, developed interstitial keratitis of the right eye in July 1931. She had definite stigmata of congenital syphilis. The Wassermann reaction was triple positive. She was an inmate of the Eye Wards for nine weeks during which the condition improved under atropin, etc. Six months later the patient was confined in the Maternity Hospital. She returned home ten days after delivery and soon after the left eye became affected. She was re-admitted to hospital with the following clinical picture:-
Right Eye - showed dense corneal opacities, the pupil was not well seen.
Vision - fingers at 3 metres.

Left Eye - showed acute interstitial keratitis with haziness of the cornea and pus in the anterior chamber; there was a typical hypopyon ulcer present.

The eye condition rapidly cleared up under antisyphilitic treatment, in addition to the local application of atropin.

The second case, illustrating ulceration of the cornea, was also a case of recurring interstitial keratitis occurring in a child of six and a half years. She was a delicate, under-sized child who developed interstitial keratitis of the right eye in November 1928. Her blood gave a triple positive Wassermann reaction. The keratitis was very resistant to treatment, and from November 1928 to September 1931 she received, in all, 5.25 gm.
"914", and 6.9 gm. metallic bismuth. In September she developed albuminuria and casts were found in the urine; antisyphilitic treatment had to be restricted. In December 1931 the corneal condition flared up in the right eye, and she was admitted to hospital with an acute interstitial keratitis of that eye which also showed ulceration of the cornea. Antisyphilitic treatment was started again and the condition gradually improved.
We are indebted to Hutchinson\(^1\) for first recording the fact that interstitial keratitis is often either accompanied, or preceded, by iritis, and that it is followed, not infrequently, by certain changes in the choroid which are seen frequently in herido-syphilitic patients.

These observations are borne out to a certain extent in this series of cases - but perhaps the fact that the patients have come under more intensive treatment, and at an earlier period of the disease may account for the diminished incidence in the number of complications noted in our cases.
Complications and their Sequelae.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Number of Eyes Invol.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iritis</td>
<td>7</td>
</tr>
<tr>
<td>Irido-cyclitis</td>
<td>6</td>
</tr>
<tr>
<td>Choroiditis</td>
<td>3</td>
</tr>
<tr>
<td>Blepharitis</td>
<td>4</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>3</td>
</tr>
<tr>
<td>Nystagmus</td>
<td>3</td>
</tr>
<tr>
<td>Retinitis</td>
<td>2</td>
</tr>
<tr>
<td>Episcleritis</td>
<td>2</td>
</tr>
<tr>
<td>Strumous keratitis</td>
<td>2</td>
</tr>
<tr>
<td>Increased ocular tension</td>
<td>2</td>
</tr>
<tr>
<td>Optic atrophy</td>
<td>1</td>
</tr>
<tr>
<td>Dacryocystitis</td>
<td>1</td>
</tr>
<tr>
<td>Ulceration of cornea</td>
<td>1</td>
</tr>
<tr>
<td>Suppuration of cornea</td>
<td>1</td>
</tr>
</tbody>
</table>

Number of Eyes Involved.

It has been recognised from early days that interstitial keratitis attacks first one eye, and then the second
eye after a period of several months has elapsed. Sometimes the second eye becomes involved even while the patient is undergoing intensive antisyphilitic treatment for the keratitis in the first one - this occurrence is, however, rare. It is generally admitted, that the institution of early and active treatment for the interstitial keratitis of the one eye, is a means of preventing its onset in the other eye.

In this series the cases have been divided up as follows:

Number in which interstitial keratitis was present in both eyes when patient first came for observation

- 55

One eye affected only

- 50

Recurrences after institution of treatment

- 10
Duration of Symptoms.

It is difficult to estimate the rapidity of clearing of symptoms, but an attempt has been made to do so in terms of cessation of all signs of inflammation of the cornea. The usual time taken, before the acute symptoms subside, is recorded as two to three months by most authorities - notably Guy. He gives the following figures in his series of 150 cases of interstitial keratitis.

<table>
<thead>
<tr>
<th>Time</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 months</td>
<td>61</td>
</tr>
<tr>
<td>Less than 2 months</td>
<td>10</td>
</tr>
<tr>
<td>3 months to 1 year</td>
<td>27</td>
</tr>
</tbody>
</table>

In this particular series only 90 cases could be estimated, as the 15 chronic cases from the Royal Blind School could not be included. It was found that the larger number of cases took rather more than eight weeks for the cornea to
clear - the average time being twelve weeks. Many of the cases were more intractable and over a year elapsed before symptoms and signs completely subsided, while one particularly stubborn case, which at first resisted all forms of treatment, took three years before the acute symptoms were relieved. The visual results at the end of this period were:

Right eye $V = 6/12$
Left eye $V = 6/24$

The patient could read Print $4 = .75$

The discs were normal, and the Wassermann reaction was a weak positive. This patient is still under treatment; her general health is excellent and she is able to earn her living as a domestic servant.

The actual figures of the results obtained are given below:

Table of Duration of Symptoms.
Table of Duration of Symptoms.

<table>
<thead>
<tr>
<th>Duration</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 months</td>
<td>15</td>
</tr>
<tr>
<td>3 months</td>
<td>30</td>
</tr>
<tr>
<td>4 months</td>
<td>13</td>
</tr>
<tr>
<td>5 months</td>
<td>4</td>
</tr>
<tr>
<td>6 months</td>
<td>14</td>
</tr>
<tr>
<td>6 months to 1 year</td>
<td>5</td>
</tr>
<tr>
<td>1 - 2 years</td>
<td>-</td>
</tr>
<tr>
<td>2 - 3 years</td>
<td>1</td>
</tr>
<tr>
<td>Uncertain duration</td>
<td>2</td>
</tr>
<tr>
<td><strong>Total cases</strong></td>
<td><strong>90</strong></td>
</tr>
</tbody>
</table>

At the end of these intervals the cornea was clear in 47 cases, giving the patient full vision, while the remaining 34 had corneal opacities of varying degrees. The final results as regards vision are considered at a later period. One authority, Igersheimer, states that as regards vision the results are misleading - a clear central
cornea with an opaque periphery gives better vision than a clear periphery and an opaque central cornea.

OBSERVATIONS ON THE FIFTEEN CHRONIC CASES OF INTERSTITIAL KERATITIS.

A special study has been made of cases of congenital syphilis who were inmates of the Royal Blind School, Edinburgh. During a period of six months, sixty-seven children were examined, and the Wassermann reaction tested and twenty-one of
these were found to be suffering from inherited syphilis both clinically and serologically. Of these twenty-one cases fifteen were found to have had interstitial keratitis, and these fifteen children have been included in this series.

These children, all residents in the Blind School, came from all parts of Scotland, and great difficulty was experienced in obtaining clinical histories and notes regarding the onset of the disease and the duration of symptoms, etc. In several cases the children had attended V. D. clinics elsewhere, and received varying amounts of treatment. Where possible, details of this treatment was obtained. An analysis of the cases was attempted and the following figures obtained.

Total number of cases 15
Number of patients who had had no previous treatment 1
Number of patients who had received treatment after onset of blindness 8
Number of patients who became blind during treatment 4
Number of patients with uncertain history 2

15
All these children showed evidence of having suffered from the very severest forms of interstitial keratitis, and in several cases the eyeball had been destroyed, and in others, removed. They illustrated the various facial and other stigmata associated with congenital syphilis - one being a deaf mute, while many were deaf as well as blind. The majority were of poor physique and were undersized. It was of definite clinical interest and importance to note that their physical health and well-being improved markedly while they were undergoing courses of treatment with arsenobenzol and bismuth, even when the sight had been lost. Treatment was continued usually until the Wassermann and cerebro-spinal fluid became negative.

**Degrees of Blindness.**

<table>
<thead>
<tr>
<th>Degree</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total blindness</td>
<td>1</td>
</tr>
<tr>
<td>Perception of light</td>
<td>4</td>
</tr>
<tr>
<td>V. = fingers at 3 metres</td>
<td>8</td>
</tr>
<tr>
<td>V. = 5/60</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>15</td>
</tr>
</tbody>
</table>
TREATMENT OF INTERSTITIAL KERATITIS.
TREATMENT.

Methods adopted in this series. These may be classified under three headings.

1. General
2. Local.
3. Specific.

The treatment was varied to suit the requirements of each individual case, and was dependent on the tolerance of the patient, and the therapeutic effects obtained with the various drugs.
I. General Treatment.

This was based on the results of a thorough systematic examination of the patient. Special attention was paid to the presence of such defects as carious teeth, or septic tonsils, which would be a source of toxic absorption, and would on this account interfere with the carrying out of intensive antisyphilitic therapy. Where practicable such defects were dealt with before starting full treatment. The importance of maintaining the general health of the patient at the highest possible level was recognised in every case. Adequate nourishment, fresh air, regular exercise and a sufficiency of sleep were recommended, and carried out when ever possible. In many instances it was necessary to admit the patient to hospital to insure this part of the treatment. Regular daily action of the bowels was another important factor which had to be emphasized.
Any cases showing evidence of anaemia or loss of weight during treatment were given general tonics containing iron or strychnine as indicated. During the intervals of rest between course of injections the majority of the children were kept on syrup ferri iodidi, especially when debilitated or anaemic, while adults received Hyd. c.cret. qt I, t.i.d. or Pot. Iod. qt xv, t.i.d.p.c.

II. Local Treatment.

This naturally varies in detail with the demands and indications of each individual case. Speaking generally, in the more acute cases with intense photophobia, an eye-shade was necessary to relieve the distressing symptoms: unless contraindicated by increased intra-orbital tension, 1% atropin was instilled once or
twice daily either as drops or in the form of an ointment.

Where there was much pain, a common symptom occurring in those cases with accompanying iritis, hot compresses or even blisters in the temple region were employed.

Guy advocates the use of atropin until all ciliary irritation is relieved.

Once the acute symptoms had subsided, mild stimulating ointments were tried in the more obstinate cases — to hasten the clearing of the cornea. The ointment usually employed was the yellow oxide of mercury or 1% dionin. The application of the ointment was often combined with gentle massage. This inunction was found necessary in a few cases only — the majority of the corneas clearing with the specific therapy in a remarkably short time. Fisher avers that mercurial inunction always clears the eye in the
acquired form of interstitial keratitis, whereas in
the congenital variety no amount of local treatment
arrests or modifies the disorder.

Subconjunctival injections are
employed in some clinics and satisfactory results are
reported. Harrison has used subconjunctival
injections of salvarsanised serum with good effect;
this measure was not employed in any of these cases
under discussion.

III. Specific Therapy.

With certain exceptions, which will be referred to later, all
the cases in this series received arsenobenzol
therapy during some part of their treatment. The
amount of arsenic administered to children varies
with the age of the child, its weight, and the type of lesion present. In the majority of these cases dual therapy with arsenobenzol and bismuth was given concurrently, and it is now recognised as the most potent combination of drugs available for administration in this condition. Where possible, in the more urgent cases, the first few injections of "914" were given intravenously. Subsequently the intramuscular route was adopted, as being simpler of administration as well as insuring a more prolonged action of the drug in the tissues by virtue of its slower rate of excretion.

The usual method of treatment adopted in a typical case of interstitial keratitis was as follows:

1. General and local treatment was instituted as already indicated, and the patient was started with a double course of Neokharsivan and bismuth,
(subject, of course, to a satisfactory examination of the urine). The arsenical preparation most frequently selected, was one of the "914" group, namely Neokharsivan for intravenous injection, and Kharsulphan or Sulfarsenol for intramuscular use. An average dose for a child of 8-10 years was 0.1 gm. dissolved in 10 c.c. doubly distilled sterile water; 0.15 gm. for one 12-14 years and 0.3 gm. as an initial dose for an adult. This injection was followed two to three days later by an intramuscular injection of bismuth - generally given in its metallic form as Bicreol or Hypoloid Bismuth, in similar doses.

These alternate bi-weekly injections of arsenic and bismuth were continued according to the patient's tolerance, until a course of 3 gm. of a "914" preparation had been given. At this point, usually after three months had elapsed, injections of arsenobenzol were temporarily discontinued, but weekly injections of bismuth were continued until about
4 gms. had been injected. In addition to the injections, iodides were prescribed by mouth, usually in the form of syrup ferri iodidi in the case of children, and of pot. iod. for the adults. At the end of such a course of treatment occupying about four months, the eye symptoms had entirely subsided in most cases making it possible to give the patient an interval of rest from treatment for one month. The routine was to ask the patient to continue taking the iodide mixture by mouth for three weeks, then to discontinue all treatment for one week, at the expiry of which, the patient returned to the clinic when the Wassermann reaction was taken and a full clinical examination made. It was thus possible to assess the effects of the past course of therapy and to determine the most suitable combination of drugs for the next or second course.

When it had been possible to give the arsenobenzol preparation intravenously in the first course, and when the clinical condition of the
patient permitted it — the second course of treatment was frequently one of bismuth alone, given in weekly injections. When the response to treatment was less satisfactory the double course of arsenobenzol and bismuth was repeated, the former drug being given by the intramuscular route, either as Sulfarsan or Kharsulphan.

When dealing with children it was found that if the selected "914" preparation was dissolved in a solvent containing —

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Guaicol</td>
<td>1 part</td>
<td></td>
</tr>
<tr>
<td>Glucose</td>
<td>50 parts</td>
<td></td>
</tr>
<tr>
<td>Aq. Dest.</td>
<td>100 parts</td>
<td></td>
</tr>
</tbody>
</table>

and injected deeply into the buttock, the whole operation could be carried out quite painlessly and without any unpleasant after-effects.

The second course was followed by a similar period of rest, after which another Wassermann test was taken and a further clinical review of the case was made. It was usual at this stage,
namely, eight months after the commencement of treatment, to find the cornea completely cleared, and the sight restored to full vision. Subsequent courses of treatment were then dependent on the results of therapy and on the tolerance of the patient.

It might be emphasized at this point, that once the clinical signs in the eye have subsided, it is most important to prolong treatment until both the blood and the cerebro-spinal fluid give negative reactions. It is advisable to extend treatment over a prolonged period rather than to try by more intensive measures to reduce the Wassermann to negative in a shorter period of time. In any case the patient must be kept under observation for a minimum period of two years.

So far, we have been dealing with an uncomplicated, straight-forward case of interstitial keratitis which has responded well to treatment.
There are many cases, however, which are most intractable and resistant even to the most intensive treatment administered over long periods. In some of these resistant cases, where "914" preparations given both intravenously and intramuscularly have failed, the use of Tryparsamide (T.P.A.) injected intravenously, has given favourable results. For intravenous purposes it is dissolved in 20 c.c. sterile, doubly-distilled water, the average dose for an adult being 2 - 3 gms. given weekly until the patient has received 20 - 24 gms. The Tryparsamide may be given alone or in combination with alternate injections of bismuth. Children seem to tolerate this drug well, and it may be repeated in successive courses. The dose for a child of 10 years is about 1 gm. weekly. In addition to its spirillicidal effect, it stimulates the natural resistance of the body tissues and is tonic in its effect.

*Acetylarasan* is a very mild
pentavalent preparation of arsenic and may be employed with advantage when the patient has proved intolerant to more potent varieties of "914".

**Bismuth.**

In 1921 Levaditi and Sazerae were able to prove that experimental syphilis in rabbits could be treated successfully with bismuth; since then it has been recognised as a valuable drug in the treatment of syphilis and as a valuable adjunct to "914" preparations.

Lees was perhaps the first syphilologist in this country to use and advocate bismuth, and he published his earliest results in 1923. He observed the results of treatment with bismuth alone, and in combination with arsenic, in 150 cases of all stages of syphilitic infection, and came to the conclusion that intramuscular injections of bismuth salts were more effective than
mercury, but less so than the Salvarsan derivatives. He used, and recommended a suspension of precipitated bismuth in a creocamph base containing 100 per cent bismuth. One cubic centimetre of this preparation contained 0.15 gm. metallic bismuth.

In 1927 Lees, in opening a discussion on the "Place of Bismuth in the Treatment of Syphilis," at the annual meeting of the British Medical Association in Edinburgh, said he was able to amplify his original observations. His final conclusions were based on the clinical experience of the use of bismuth in over six thousand cases of syphilis. The number of injections in the series being over one hundred thousand. In some of his cases, bismuth was the only drug used, in others it was combined with N.A.R., T.P.A., mercury and iodides.

Mercury.

Mercury is the drug which has
been associated with the treatment of syphilis right down the ages. It still has its uses, although it is inferior to the arsenical remedies in its spirochaeticidal properties; it is now being largely superceded by bismuth.

In this series of cases mercury was only used as an adjuvant, and mainly during the intervals of rest between courses. It was administered in the form of Hyd. c. cret. gv.i. One tablet being taken thrice daily for a period of three weeks at a time. It is important for the patient to maintain a high standard of oral cleanliness while taking mercury, otherwise unpleasant symptoms of stomatitis may arise. This state of affairs is usually preceded by a warning blue line of the gums which should always be looked for. When this is observed the intake of mercury should be suspended for the time being.
Iodides.

The action of iodides, as is well known, is that of opening up the tissues, and dissolving newly formed fibrous tissue. Hence their great value is to enhance the action of the antisyphilitic drugs.

The children in this series of cases were given syrup ferri iodide in doses 3 i t.i.d. either, as an adjunct to the purely specific remedies, or during the intervals of rest between courses. The adults generally received pot. iodid. gr. 15 - 20 t.i.d.p.c. well diluted in water. It was found advisable to prescribe the iodide in combination with sod. bicarb. and spirit ammon. aromat. to counteract the depression so often induced by the prolonged administration of iodides.

A few of the more resistant cases in the series were given weekly injections of 10 per cent Sod. Iod. 10 - 20 c.c. given intravenously, with, it
it was thought, good results. This method of administering iodide was also advocated by Dr Puris. 44

SUPPLEMENTARY FORMS OF TREATMENT.

In addition to the lines of treatment which have been outlined, there are many other methods, which have been tried and advocated by different workers. Certain of these supplementary methods may be briefly mentioned.
I. Malarial Therapy in the Treatment of Interstitial Keratitis.

Mrazmova tried therapeutic inoculations with benign tertian malaria in twelve cases of interstitial keratitis, combining them with preliminary and subsequent antisyphilitic treatment. She found that the subjective and objective symptoms were relieved during an attack of malaria, but that they recurred, and were, in some cases even intensified. Appreciable improvement was only noted in two cases. It was discovered by this observer that malaria did not prevent recurrences, or have any prophylactic effect, and that the Wassermann reaction remained positive throughout, and after, the treatment by therapeutic malaria.
II. X-ray Therapy.

Two workers on this line of treatment, Japiot and Busey \(^6\) maintain, "that there is no disease of the eye in which the method is more indicated". Interstitial keratitis is a disease characterised by an infiltration into the corneal layers of young connective tissue cells which are susceptible to the action of X-rays, without causing severe lesions in the cornea or changes in its structure. They aver, that to be successful, the treatment should be employed in the period of infiltration before deep lesions of the cornea cause indelible scars. They also affirm that, "the younger the patient, the greater the infiltration, the more favourable the results; the greatest benefits occurring in cases of congenital syphilis". They advocate irradiation of the closed eyes with very small doses, without special protection or localisation, and recommend five applications of five
minutes with a week's interval as being sufficient. This treatment is intended as an adjunct to, and not instead of, antisyphilitic treatment. It results, they claim, in very rapid relief of pain, photophobia, and blepharospasm, and shortens the course of the disease.

This X-ray treatment was first advocated by De Courcy and Mather in Liverpool in 1924. Among other authorities who uphold this local therapy with Röntgen rays may be mentioned:— Bywater and Plummer, Nicolee and Ravendino. Hensen believed that the quartz light treatment gave good results.

III. Atoxyl. This drug was found to be very successful when administered with mercury,
by Stephenson. He advised intramuscular injections of 0.25 to 0.5 gm. repeated once weekly in mild cases, and oftener in more severe ones. He advocated not more than 6 gm. being given in all. He found that twelve injections were usually sufficient to cure almost all cases.

IV. Thymol Iodide.

One of the most recent suggestions in the treatment of the disease is that of thymol iodide, or Aristol. It was used by Pranash Chandra who obtained rapid results in a chronic case of interstitial keratitis which had been refused antisyphilitic treatment. He applied the drug locally by dusting it on to the cornea.
V. Fever Therapy in Parenchymatous Keratitis.

This method was used by Huber\textsuperscript{54} who tried injections of milk, typhoid vaccine, arsephenamine, and bismuth. While his results are good one can hardly evaluate the different preparations used.

VI. Corneo-sclerotomy.

This operative procedure was carried out by Basil Lang\textsuperscript{55} with marked improvement of vision in three cases which he reported.
Old Methods of Treatment.

Before leaving this subject of treatment, it is interesting to compare the modern, and more elaborate methods, with the old ideas of mercury and the iodides. Inunction of the patient with mercurial ointment was the most popular form of treatment and was strongly recommended by Jonathan Hutchinson in his "Memoirs". He was also a believer in the value of pot. iod., the iodide of iron and tinc. nux. vomica. Many of the cases yielded to this form of treatment, but recurrences and relapses were so common that the treatment of interstitial keratitis fell into disrepute.

It is only in recent years since intensive antisyphilitic treatment has been insisted upon by syphilologists, and proved to be effective, that the pessimistic prognosis of the disease has been revised.
Duration of Treatment.

However rapidly a case reacts to treatment it is advisable to keep the patient under observation at least for two years, and, in addition to recovery of the eye, all other symptoms and both the Wassermann and cerebro-spinal fluid should be negative.

An analysis has been made in this series to show the length of time the cases have been observed, and it will be seen how frequently the two year's limit has been extended.
Time under observation:

<table>
<thead>
<tr>
<th>Time Range</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Under 6/12</td>
<td>3</td>
</tr>
<tr>
<td>1 year</td>
<td>4</td>
</tr>
<tr>
<td>Over 1 year</td>
<td>9</td>
</tr>
<tr>
<td>2 years</td>
<td>33</td>
</tr>
<tr>
<td>3</td>
<td>12</td>
</tr>
<tr>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>6</td>
<td>13</td>
</tr>
<tr>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>9</td>
<td>3</td>
</tr>
<tr>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td>11</td>
<td>3</td>
</tr>
</tbody>
</table>

105 cases.

Total Amount of Treatment Given in this Series.

Naturally the amount of treatment varies with the individual case, depending on how the patient reacts to, and tolerates, the drugs given.
The following analysis shows the treatment given, under two headings:

1. Total treatment given.

2. Amount of treatment given before symptoms were relieved and the Wassermann became negative.

<table>
<thead>
<tr>
<th>Total Treatment</th>
<th>Amount given before W.R. became negative.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grams &quot;914&quot; Bis.</td>
<td>&quot;914&quot; Bis.</td>
</tr>
<tr>
<td>1  2 cases 2 cases</td>
<td>- 3 cases</td>
</tr>
<tr>
<td>2  - 4 cases</td>
<td>3 cases 2 &quot;</td>
</tr>
<tr>
<td>3  8 &quot; 9 &quot;</td>
<td>5 &quot; 7 &quot;</td>
</tr>
<tr>
<td>4  2 &quot; 12 &quot;</td>
<td>2 &quot; 5 &quot;</td>
</tr>
<tr>
<td>5  13 &quot; 1 &quot;</td>
<td>8 &quot; 2 &quot;</td>
</tr>
<tr>
<td>6  7 &quot; 3 &quot;</td>
<td>- 3 &quot;</td>
</tr>
<tr>
<td>7  4 &quot; 5 &quot;</td>
<td>3 &quot; 4 &quot;</td>
</tr>
<tr>
<td>8  4 &quot; 4 &quot;</td>
<td>8 &quot; 2 &quot;</td>
</tr>
<tr>
<td>9  8 &quot; 6 &quot;</td>
<td>1 &quot; 1 &quot;</td>
</tr>
<tr>
<td>10  9 &quot; 5 &quot;</td>
<td>9 &quot; 2 &quot;</td>
</tr>
<tr>
<td>11  - 7 &quot;</td>
<td>1 &quot; 2 &quot;</td>
</tr>
<tr>
<td>12  1 &quot; 5 &quot;</td>
<td>2 &quot; -</td>
</tr>
<tr>
<td>13  2 &quot; 1 &quot;</td>
<td>2 &quot; -</td>
</tr>
<tr>
<td>14  -  -</td>
<td>1 &quot; 2 &quot;</td>
</tr>
<tr>
<td>15/</td>
<td></td>
</tr>
<tr>
<td>Grams</td>
<td>&quot;914&quot;</td>
</tr>
<tr>
<td>-------</td>
<td>-------</td>
</tr>
<tr>
<td>15</td>
<td>5 cases</td>
</tr>
<tr>
<td>16</td>
<td>3 &quot;</td>
</tr>
<tr>
<td>17</td>
<td>4 &quot;</td>
</tr>
<tr>
<td>18</td>
<td>3 &quot;</td>
</tr>
<tr>
<td>19</td>
<td>-</td>
</tr>
<tr>
<td>20</td>
<td>5 &quot;</td>
</tr>
<tr>
<td>21</td>
<td>1 &quot;</td>
</tr>
<tr>
<td>22</td>
<td>-</td>
</tr>
<tr>
<td>23</td>
<td>4 &quot;</td>
</tr>
<tr>
<td>24</td>
<td>1 &quot;</td>
</tr>
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<td>25</td>
<td>1 &quot;</td>
</tr>
<tr>
<td>26</td>
<td>-</td>
</tr>
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<td>27</td>
<td>-</td>
</tr>
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<td>28</td>
<td>-</td>
</tr>
<tr>
<td>29</td>
<td>-</td>
</tr>
<tr>
<td>30</td>
<td>-</td>
</tr>
</tbody>
</table>
THE EFFECTS OF TREATMENT.
THE EFFECTS OF TREATMENT.

These may be considered as threefold:

1. On the eye.
2. On the Wassermann reaction.
3. On the generalised syphilis.

I. Effect on the Eye.

The object in view in treating interstitial keratitis is to restore full vision to the patient, failing that, the best that is possible. In the majority of cases of acute keratitis which come under treatment at a sufficiently early date, full vision is attained, although several months may elapse before this stage is reached. The more chronic the course, the
more difficult it is to clear the cornea, but it is often remarkable how well some of the most obstinate opacities yield eventually to intensive treatment. In all these cases under consideration, (with the exception of the fifteen chronic cases), the optic discs were examined and found to be normal.

I. Effect of Treatment on the Eye in 105 Cases.

<table>
<thead>
<tr>
<th>Vision</th>
<th>Total no of eyes</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full vision</td>
<td>50</td>
<td>30.8</td>
</tr>
<tr>
<td>6/6</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>6/9</td>
<td>12</td>
<td>14.2</td>
</tr>
<tr>
<td>6/12</td>
<td>5</td>
<td>7.4</td>
</tr>
<tr>
<td>6/18</td>
<td>9</td>
<td>6.7</td>
</tr>
<tr>
<td>6/24</td>
<td>7</td>
<td>8.6</td>
</tr>
<tr>
<td>6/36</td>
<td>6</td>
<td>5.5</td>
</tr>
<tr>
<td>6/60</td>
<td>5</td>
<td>6.2</td>
</tr>
</tbody>
</table>

Vision - fingers - 5 cases, - 3.1
" - blind - 3 " - 1.8
" - perception of light only - 1 case - 0.6
No note of vision obtainable in 8 cases - 4.9

It is interesting to consider the figures obtained by Igersheimer in his series of
118 cases, in which the media and central fundi were normal. Years after the active process had ceased, examination gave the following results.

Normal sharpness of vision 5/4 5/5 8 eyes - 6.8%  
Good " " " 5/7 5/10 25 eyes - 21.8%  
Workable eye 5/15 5/20 50 eyes - 42.4%  
Recognition of fingers 5/35 5/50 8 eyes - 6.8%

II. Effect on the Wassermann Reaction.

As interstitial keratitis is part of a generalised syphilis, it is essential to continue treatment even after all local symptoms have subsided, until the Wassermann reaction is negative, and for some time afterwards. In those cases which are more resistant, and the Wassermann reaction
remains positive in spite of intensive treatment, this should be continued until the patient has received sufficient to safeguard him against the development of further manifestations of the disease. Generally speaking this point has been reached after the adult patient has received 10 – 20 grams arsenic and an equivalent, or even more, bismuth. In this series the effect of treatment on the Wassermann reaction is seen by the figures:

Wassermann reaction negative in 54 cases - 51%

" " weak positive in 12 cases - 11%

" " moderately strong positive in 9 cases - 8.5%

" " strong positive in 15 cases 14.5%

Cases still under treatment - 15 - 14.5%
III. Effect of Treatment on the Generalised Syphilis.

The effect was estimated after a thorough systematic examination of the patient, including that of the central nervous system and heart. In 41 out of the 105 cases the cerebro-spinal fluid was examined and found to be negative: and these cases have been discharged as cured. Forty-three of the other cases were still under treatment and in the remaining twenty-one it had not been possible to do a cerebro-spinal examination, but clinically, the condition of the central nervous system was satisfactory.

<table>
<thead>
<tr>
<th>Cases with negative C.S.F.</th>
<th>41</th>
<th>39%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases still under treatment</td>
<td>43</td>
<td>41%</td>
</tr>
<tr>
<td>C.S.F. not done but cases clinically satisfactory</td>
<td>21</td>
<td>20%</td>
</tr>
</tbody>
</table>

Total 105
The Advantage of Cases being Treated as Cases of Syphilis.

On reviewing these results of treatment, bearing not only on the local conditions of the eye, but on the generalised syphilis, it is bound to emphasize the paramount importance of recognising these cases of interstitial keratitis as subjects of inherited syphilis and treating them as such. Once this attitude is accepted it naturally leads to more intensive and more general treatment. It also illustrates the urgent need for the closest co-operation and correlation between the ophthalmologist and the syphilologist. Naturally, the disease is most frequently discovered and diagnosed in the Eye Departments of general hospitals or in school clinics, and here, very often, the Wassermann reaction is first taken. Once the
diagnosis is confirmed it should follow naturally that the case be referred to the venereal diseases department to carry on the prolonged and specialised treatment which is indicated. It is an ideal system when it is possible to refer the case back to the ophthalmologist at frequent intervals for a report on the progress of the eye condition.

This method has been tried and proved successful in many instances in this series.

In an interesting discussion on congenital or inherited syphilis opened by Mr Lees in 1924, Dr Paterson said he had observed the results of Mr Lees' intensive treatment very critically, and in his opinion, and that of his ophthalmic colleagues, the treatment had been of real service in shortening the disease and rendering its results less fatal to the eye.

When this method is more universally adopted the former depressing prognosis of
interstitial keratitis should be materially improved. This view was supported by Mr T. H. Browning who stated that he had treated many hundreds of cases of keratitis with the new methods - salvarsan, neosalvarsan, and bismuth, though nearly always combined with mercury. He was convinced that his cases did better with intensive antisyphilitic treatment, and some of his results had been almost dramatic.

This opinion was also most emphatically upheld by Dr David Nabarro of Great Ormond Street Children's V. D. Department. His results had been extremely good - nearly all children who had received efficient treatment, had what appeared to be normal eyes - very few having nebulae at all. The few cases of blindness were due to choroiditis, and they were blind when they came under his observation. He was non-plussed when he read papers by ophthalmic surgeons who said they did not believe in the value of arsenobenzol.
preparations in interstitial keratitis. At the same meeting Dr Fowler Ward\textsuperscript{61} said that five years ago he was struck by the mournful view of ophthalmic surgeons in keratitis, and he kept careful notes of forty cases, thirty of whom were still under observation. Practically all rapidly improved, the earlier they came the less scarring they had. When there was scarring, it was in children who had not had treatment until after three months had elapsed. He kept every case of interstitial keratitis for as many years as possible for observation.

American opinion is very strong in favour of the syphilologists carrying out the treatment of interstitial keratitis. Dr Stokes\textsuperscript{62} says that the disease constitutes a special problem in syphilo-therapy, and believes the ophthalmologists must bear the brunt of a charge of backwardness in failure to avail themselves more generally of the intensive modern methods. Few eye-men, he continues, have ever seen what really intensive
treatment can do for interstitial keratitis. He predicts the passing of the old slogan, "that interstitial keratitis always involves the other eye", and hopes to witness the percentage of relapses reduced from 23 to 2 or 3, and the course of the vast majority of cases reduced from months to weeks, with a permanently damaged residuum of almost zero instead of 40–60 per cent.

Such results are not too much to expect when ophthalmologists are finally willing to discard their prejudice. These are the views of one of the most eminent of the American authorities, and we can but hope for their widespread recognition throughout the world, to reduce the disastrous results of neglected interstitial keratitis.
Permanence of Results.

Since the adoption of more intensive therapy, recurrences of interstitial keratitis have steadily diminished, although unfortunately they still occur, often in spite of most efficient treatment.

In these 105 cases, recurrences occurred in only 10 patients or 0.9 per cent, and of these two occurred in patients who had failed to continue to come for treatment, and only returned when the second eye became involved. However, there is reason to believe that the number of recurrences will decrease as treatment increases, and once a case has received adequate treatment, resulting in the absence of any signs of generalised syphilis with negative blood and cerebro-spinal fluid, then the permanence of such results should be assured. This view was justified and illustrated in at least
41 of the 105 cases in this series, where the patients were examined in many cases years after they had been discharged, and the permanence of the results of treatment ratified.
PREVENTIVE MEDICINE ASPECT.
PREVENTIVE MEDICINE ASPECT.

I should like to diverge for a little from the consideration of the individual case, and regard the subject from a wider aspect, namely that of Preventive Medicine.

When a case of interstitial keratitis is discovered in a child it has been our practice, once the diagnosis has been confirmed, to examine all the other members of the family, both the parents and the other children. In this way many unsuspected cases of congenital syphilis have been discovered before any symptoms have arisen. Where the Wassermann reaction was found to be positive,
similar courses of treatment have been instituted in these patients. In this way latent syphilis can be discovered and treated before the important structures have been damaged. It has been interesting and instructive to investigate the family history of many of these cases. In some instances they have proved most illustrative of the ravages of syphilis, both as regards mortality and morbidity of child life. In 42 out of the 105 cases a definite history of syphilis was obtained and confirmed in the parents, and other children in the family suffered from syphilis. The value of this following-up of families is inestimable, and should do much in lessening the morbidity caused by congenital syphilis, and what is even more vital, the lessening of the incidence of blindness. This brings up the important question of the incidence of blindness due to congenital syphilis.
INHERITED SYPHILIS AS A CAUSE OF BLINDNESS.
INHERITED SYPHILIS AS A CAUSE OF BLINDNESS.

To illustrate the great havoc caused by untreated interstitial keratitis in children, and the resultant blindness, I should like to quote figures obtained from the final report of the Royal Commission on Venereal Diseases 1926. In this report Mr Bishop Harman states that of the 1,100 children in the London Blind Schools, 31.2 per cent of the cases were certainly, and an additional 2.8 per cent probably, due to syphilis. He found that more than half of all cases of blindness among children are the result of venereal disease in the parents and gives the following striking figures.
268 cases or 24.4% due to gonorrhoea.
343 cases or 31.2% due to syphilis,
and probably 2.8% in addition are due to the latter cause. These figures give a total of 55.6%
certainly of V. D. origin and 58.4% probably venereal in origin.

The conclusions adopted by the Report are of interest in their bearing on this subject.

1. That venereal disease affecting the parents is responsible for more than half of all cases of blindness occurring amongst children.

2. That the total blindness due to venereal disease does not appear great in relation to the total population, as the effects of the disease are largely masked by the heavy incidence of miscarriages, still-births and infant deaths, among the affected population.

3. The effective treatment of affected parents
would result in an appreciable reduction in cases of blindness amongst children and also the disabilities arising therefrom.

My final reference to this Report is to show the relative incidence of interstitial keratitis as a cause of blindness.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ophthalmic neonatorum</td>
<td>24%</td>
</tr>
<tr>
<td>Purulent conjunctivitis</td>
<td>4.2%</td>
</tr>
<tr>
<td>Phlyctenular keratitis</td>
<td>3.8%</td>
</tr>
<tr>
<td>Sympathetic ophthalmia</td>
<td>1.5%</td>
</tr>
<tr>
<td>Interstitial keratitis and iritis</td>
<td>17.8%</td>
</tr>
<tr>
<td>Choroiditis and optic atrophy</td>
<td>11.8%</td>
</tr>
<tr>
<td>Congenital defects</td>
<td>1.5%</td>
</tr>
</tbody>
</table>

A more recent investigation on these lines only serves to further emphasize the part played by interstitial keratitis as an important factor in the cause of blindness in young children.

In a report on the Control of Ocular Diseases of Venereal Origin, Mackay states that in the years 1924 to 1928 there were 6,596 cases of
syphilis treated in Edinburgh. Two-thirds (4,400) of these came from Edinburgh and the rest from surrounding districts. Of these cases, 136 suffered from interstitial keratitis and about 40 more had some eye trouble, for example, iritis, choroiditis or optic atrophy. At the Royal Blind School in Edinburgh where the Wassermann test is now systematically applied to every applicant for admission, out of 67 children examined in a period of six months, 21 were found to be suffering from inherited syphilis, both clinically and serologically. I might add that 15 of the 21 cases mentioned in the above report have been included in this series of cases, under the classification of chronic interstitial keratitis.

In a discussion on inherited syphilis in 1924, Dr Sinclair gave some interesting figures on the incidence of interstitial keratitis in the Eye Department of the Royal Infirmary, Edinburgh.
Number of cases of congenital syphilis.

1921 . . . . . 35) equal to 116 cases
1922 . . . . . 32) in 3 years.
1923 . . . . . 49) in 3 years.

Of these 116 cases:-

100 had interstitial keratitis.
7 " choroido-cyclitis.
1 " double optic atrophy.
1 " syphilitic iritis.
1 " congenital cataract.
1 " superficial keratitis, Wassermann reaction positive.
1 " nubuleum, Wassermann reaction positive.
1 " convergent concomitant squint, Wassermann reaction positive.

In the 100 cases of interstitial keratitis choroidal lesions were observed in 16 cases.

The cases of inherited syphilis were 6.98 per cent of the total new cases entering the Department during the three years under consideration.
The American figures on this question are of interest for purposes of comparison. In a report made by Derby and Walker\textsuperscript{65} on congenital syphilis the figures for interstitial keratitis were 0.4 per cent to 0.6 per cent of all eye disturbances in a total of 77,000 eye cases. Hoor\textsuperscript{66} gives the same percentage for a total of 375,000 cases.

The figures given by Stokes\textsuperscript{67} are rather more instructive. He found 52 per cent of all persons brought to medical attention because of congenital syphilis have, or have had, interstitial keratitis, and only 22 per cent have entirely normal eues.

In a more recent investigation undertaken in this country by the Council of British Ophthalmologists on the Causes of Blindness in 1922, Mr Bishop Harman\textsuperscript{68} gives the following analysis:

In 1855 blind children – 399 (21.5\%) had interstitial keratitis. 359 showed signs of syphilis.
The same authority in his analysis of the causes of blindness in 601 persons of all ages found 28 cases of interstitial keratitis - 24 of which were due to syphilis.

These figures, culled from so many different sources, all indicate the appalling ravages of interstitial keratitis in the absence of early recognition and treatment. Once it is admitted and universally realised that so many of these sequelae can be avoided, surely, it is to be hoped, that the figures of the future will show a substantial decline.
CONCLUSIONS AND SUMMARY.
CONCLUSIONS AND SUMMARY.

In this survey of interstitial keratitis I have tried to epitomize modern methods of diagnosis and treatment of the condition and to analyse the results so obtained.

Compared with the unfavourable prognosis formerly accorded to the disease, the results in this series fully justify the greater consideration and expenditure which such methods demand.

I should like to express my gratitude to Mr Lees, Venereal Diseases Department, Royal Infirmary, Edinburgh, for
his inspiration and for his kindness in extending me facilities, without which, this Thesis could not have been compiled.

M.B., Ch.B., D.P.H.
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50./


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61. Ward, Fowler. Discussion at above meeting.
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