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COMMUNICATIONS

ECZEMATOUS KERATO-CONJUNCTIVITIS *

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BY

ARTHUR BERNARD CRIDLAND, F.R.C.S.ED., D.O.Oxon.,
WOLVERHAMPTON.

It is first my pleasant duty to thank the Committee of Selection of the Richard Middlemore Post-Graduate Lectureship for inviting me to deliver the Lecture for 1917 and to express to them my deep appreciation of the honour so conferred, the more so as I do not practise in Birmingham.

In selecting a subject my thoughts were directed towards those in which general practitioner and specialist might find much in common, for in doing so I felt that I should be making my best endeavour to fulfil the trust bequeathed by the great oculist who founded this Lecture.

One of the commonest diseases of the eye and one with which all should be familiar is that which is now usually termed "Eczematous Kerato-conjunctivitis."

It is a common disease in more senses than one, for it is common amongst the common people.

The sight of the dirty and slatternly mother dragging two or three children equally dirty and slatternly, with eyes tightly closed

* Delivered on December 4, 1917, at the Birmingham and Midland Eye Hospital.

is, unfortunately, too familiar in our out-patient clinics, and forms a sad picture, not wholly relieved by the fact that we can do a great deal for them.

This disease, occurring as it does between the ages of two and twelve, the happy years of childhood, throws much sadness upon these young lives, to say nothing of the interference with their education and quite apart from the low standard of general health of which its presence is an indication.

Although it seldom is seen after puberty, and the majority of the eyes fortunately recover completely, yet for many the matter does not end there. The resultant scars of the cornea cause more or less permanent diminution of vision, and so prove a lasting handicap to good citizenship, whilst the worst cases may even be forced into our blind institutions.

The figures given by the late Simeon Snell show that 5 per cent. of the inmates of the Blind School at Sheffield are there on account of ulcers and other lesions of the cornea.

Those of the Blind Institute of Birmingham show that 12.5 per cent. of the inmates are blind from the same cause.

I do not wish it to be thought that I regard all these cases as examples of advanced eczematous kerato-conjunctivitis, but as the result of a recent examination of the inmates of the Wolverhampton Society for the Blind I found three cases out of 22 (i.e., 13.6 per cent.) to have suffered from corneal troubles; in two of them the evidence of scrofulosis together with the appearance of the eyes was so undoubted as to make it certain that eczematous kerato-conjunctivitis played a great part in the tragedy.

It is because this disease is so common and because its effects may be so far-reaching that I have ventured to make it the subject of this lecture.

Nomenclature

Before attempting to recall to your minds an outline of the disease some criticism may be directed towards its title, "Eczematous kerato-conjunctivitis," more particularly, of course, to "eczematous," a word for which, I believe, we are indebted to Horner, though I cannot give the reference. Other names by which it has been designated are "strumous," "scrofulous," "phlyctenular," and where the cornea alone is involved "fascicular"; of these, if we are not to accept the word eczematous, scrofulous would appear to be as good as any.

When, however, years ago Robert Koch found the tubercle bacillus in scrofulous glands, belief in the existence of scrofulosis as an entity was so shaken that medical men hardly dared to breathe the word; but of late, opinions have been modified, and in an interesting communication made to the Oxford Ophthalmological

Congress in 1912, the late Professor Straub²⁰, of Amsterdam, expressed himself as a believer in the existence of scrofulosis as something apart from tuberculosis, or, if a tuberculosis, certainly a distinct form; and he further showed himself a strong supporter of the reintroduction of the term, and of its applicability to this disease.

Our predecessors knew scrofulosis by its signs, although they did not possess a satisfactory theory to explain it, and the results of many generations of medical experience cannot be cast aside even by the most excellent histological and bacteriological work.

On the other hand, "eczematous" is the word found in textbooks, and most commonly used to distinguish this form of kerato-conjunctivitis, and a plea for its continuance is found in the work of Sydney Stephenson¹⁷, for in 765 cases of phlyctenular disease seen by him in three clinics for children in London, more than 63 per cent. showed eczema of the skin. He also found analogous changes in mucous membranes other than the conjunctiva, as, for example, those which line the nose, mouth, and palate, and he argued that the existence of such changes strengthened the view according to which phlyctenular disease was believed to be eczema of the conjunctiva. He concluded that phlyctenular disease was due remotely to the tuberculous diathesis and immediately to an eruption of eczema or impetigo upon the surface of the eyeball.

Against this it has been established by Weekers²², of Liège, that the ocular phlyctenule is something quite different from the vesicle of eczema, so that, histologically, eczematous is not a true descriptive title to apply.

For the same reason phlyctenular is incorrect, for does not *φλύκταινα* the Greek derivative signify a vesicle, whilst the sub-epithelial nodule which it is intended to describe is an efflorescence which is never a vesicle?

There appears to be no good reason why we should not revert to the old term "scrofulous." The word "scrofula" itself, meaning as it does "a little pig," is one which must appeal to all, for how many do we not see suffering from this form of kerato-conjunctivitis who resemble that plain though useful animal. There appears to be only one objection to the term, and that from the patient's point of view, for is it not almost a term of opprobrium to call a patient "scrofulous," or to tell parents their children are so?

Clinical Picture

Although the clinical picture of scrofulous kerato-conjunctivitis is one which is very familiar to us all, it is necessary to take a brief glance at it.

The essential feature is the presence of the efflorescence, or so-

called phlycten, on the conjunctiva or cornea, and very frequently at the junction of these two structures.

Discrete in character, it never involves more than a portion of the surface of the conjunctiva, and so, unlike a diffuse inflammation of that membrane, it is not in its pure form accompanied by an abnormal secretion.

Just as the follicle and the process of contraction are clinically diagnostic in trachoma, so the nodules form clinically the fundamental characteristic in scrofulous kerato-conjunctivitis, but the nodules differ in appearance as these are situated on the conjunctiva or the cornea.

Considering the conjunctiva first, the simplest type of the disease is represented by the solitary efflorescence at the limbus, which appears as a round or oval whitish-grey sub-epithelial nodule as large as a pin's head with some hyperaemic vessels arranged in triangular form, the nodule being at the apex, and the rest of the conjunctiva being perfectly well.

There may, however, be two or three, each with its corresponding patch of injection, and when they are more numerous the whole globe may appear reddened.

The more numerous they are the smaller they are, so much so that the entire limbus may present a raised granular appearance with much conjunctival injection—a condition sometimes described as "sand-grain efflorescences."

The single efflorescence may appear at some distance from the limbus and is then distinctly large, more obstinate in its course, and takes longer to clear up.

Occasionally the efflorescences appear near the margins of the lid, as has been especially noted by Stephenson.

When the cornea is involved, i.e., when the condition may be described as *keratitis eczematosa* or *scrofulosa*, four distinct clinical pictures are produced which may be present either singly or in various combinations. These fundamental types are :

1. Eczematous infiltration.
2. Round eczematous ulcer of the cornea.
3. Eczematous ulcer migrans or fascicular keratitis.
4. Eczematous pannus.

1. In the first type, *eczematous infiltration*, the condition may be otherwise described as a marginal keratitis, for the nodules occur at the margin of the cornea and may be single or in great numbers.

They are very common, and, as in the conjunctival condition, they may vary in size and number.

Sometimes the whole surface of the cornea is studded with very small ones, causing minute losses of substance after the epithelial covering has broken down.

They are the same as the sand-grain efflorescences of the limbus

and in the initial stage the cornea looks as if it were sprinkled with sand.

On account of the irritation of the terminal filaments of the nerves of the cornea, much photophobia and blepharospasm are set up, making examination exceedingly difficult.

2. *Ulcus eczematosum*.—This is a round or oval ulcer which may appear in any part of the cornea and represents an advanced stage of the eczematous nodular infiltrate in which the process is more malignant.

The infiltration rapidly becomes purulent, assumes a yellowish, almost pustular, appearance, and produces ulceration. Iritis usually co-exists.

This ulcer has a characteristic tendency to perforate the cornea, and in its most acute stages is not infrequently accompanied by hypopyon or pus in the anterior chamber; this is, I think, due in many cases to a secondary infection with micro-organisms, although presumably the intensity of the toxin, whatever it may be which gives rise to the ulcer, is sufficient cause in itself.

After perforation, the iris is often seen to be adherent to the back of the cornea and the condition known as leucoma adherens follows, usually with a deplorable interference with vision as a sequel.

As a rule one eye alone is so affected.

3. *Eczematous ulcer migrans* or *fascicular keratitis*.

The appearance which this type presents is that of a crescentic efflorescence on the cornea with small blood-vessels running to it.

The infiltration is formed primarily at the margin and breaks down into an ulcer in which vessels extend from the margin.

The peripheral portion heals, but on the opposite side the ulcer spreads towards the centre of the cornea pushing before it its infiltrated edge, the grey crescent.

As the infiltration and subsequent breaking down extend, the vessels follow, and a narrow groove is formed which is filled by them.

The course is slow, often lasting for weeks, while the ulcer may extend to, and even beyond, the centre of the cornea.

It remains superficial and never perforates, but it leaves a permanent narrow cicatricial band of opacity, which may sometimes be forked, showing that the ulceration has advanced in two divergent directions.

The interference with vision which inevitably follows corresponds with the density and site of the opacity.

The appearance and behaviour of this form may be likened to that of a comet rushing across the sky.

4. *Eczematous pannus*.

In this last form the whole or greater part of the cornea is reddened by a superficial vascularisation with its typical ramification.

Numerous superficial infiltrations appear in the cornea, soon become confluent, and give rise to the great vascularization, the cornea being cloudy between the vascular twigs.

So it is seen that there are about nine different types of scrofulous kerato-conjunctivitis; they are not met with, however, in such distinctive forms, but usually combined in various ways.

Thus marginal efflorescences with leucomata, infiltrates, and ulcers are seen in one cornea, pannus and conjunctival efflorescences in another, and so on.

The histological changes are as follows :

On the conjunctiva there are three stages through which the efflorescence passes; the stages of infiltration, ulceration, and cicatrization.

1. *Stage of infiltration.*—The conjunctiva presents dilatations chiefly of the lymphatic vessels, diapedesis of leucocytes, and serous transudations into the interstices of the conjunctival tissues. The epithelium shows leucocytes on the surface, a thickening and degeneration of certain cells, together with the formation of vacuoles filled with serum. Towards the centre of the nodule the leucocytes are principally polymorphonuclear, whilst those around are chiefly mononuclear. The blood-vessels in the neighbourhood are dilated and their endothelium shows proliferation.

2. *Stage of ulceration.*—Prior to ulceration, the epithelium becomes raised and attenuated. As a rule, the ulcerations appear at several points. Sometimes the epithelium may disappear completely, or, on the other hand, it may disappear only from the summit of the phlyctenule. Beyond the ulcerated part, the epithelium is infiltrated and shows here and there vacuolation of its cells. At other places it may be thickened and proliferating. The base of the ulcer is occupied by masses of polymorphonuclear leucocytes covered with fibrin. The conjunctival cells are frequently degenerated. The vessels have become greatly dilated, their endothelium has proliferated, and a large number of plasma and basophile mast cells have made their appearance.

3. *Stage of cicatrization.*—The epithelium proliferates abundantly, and shows prolongations. Karyomitosis can be recognized in the superficial strata. Fissures form between the superficial necrotic layers and the deeper sound layers. Numbers of fine new vessels with proliferating endothelium appear in the sub-epithelial tissue, and scattered among these are large numbers of mast cells with remains of the mononuclear and polymorphonuclear exudation. Finally, infiltration is replaced by connective tissue fibres.

Occasionally, instead of an ulcer forming, the cavity becomes lined by epithelium growing down over its surface, and a cyst results.

Phlyctenulae occurring in adults, those supervening during the

course of a microbic conjunctivitis, and those complicating an ophthalmo-reaction due to tuberculin, possess the same histological structure.

In the cornea the same three stages can be recognized, modified only by the structure of the tissue itself, and the histological changes seen in each stage are similar to those of the ordinary corneal ulcer arising from other causes.

As is well known, the disease is one of childhood, appearing at latest at puberty, although it may be seen later in those who have previously suffered from it; I can recall quite a number of cases of phlyctenular conjunctivitis somewhere about the age of 40, but I do not remember seeing one later than at 47. Most commonly it is the single phlycten which occurs in adults.

The great tendency to relapse, the presence during the attack of photophobia, blepharospasm, and an increased lacrymal secretion, especially when the cornea is involved, inflammation of the lid margins with the excoriations at the outer canthi, all these are features so well known as to require no further comment.

Occasionally, a considerable amount of general conjunctival congestion, with discharge of muco-pus, is seen associated with the phlyctenular condition, and this must, in my opinion, be regarded as an added infection from micro-organisms, and the treatment be modified accordingly.

The appearance so presented must not be confounded with that seen during the course of an attack of acute conjunctivitis due to the pneumococcus or Weeks's bacillus or the Morax diplobacillus, when typical phlyctenulae may be seen at the limbus; these clear up with no other treatment than that directed against the infection, and the explanation of their presence by most authors is that the micro-organisms have fallen upon scrofulous soil.

Diathesis

Eczema is found in a great number of cases, as mentioned before, and this, together with, in so many cases, the "little pig aspect" of the patient, brings us to the diathesis which is so frequently present as a background to the ocular signs.

Broadly speaking, two types may be seen, the torpid and the erethistic.

In the torpid type the children appear coarse and bloated, with pale skins, thick noses, puffy lips, short thick necks, and are slow mentally and physically.

In the erethistic or nervous type, the children are of slight build, lacking in subcutaneous fat, but with good mental capacity; their skins are pale, but flush easily.

A characteristic feature of both is the enlargement of the lymphatic glands, especially in the torpid type.

A tendency to catarrh of mucous membranes in general is found, rhinitis especially is common, whilst the frequent accompaniment of adenoids and enlarged tonsils is well known. In addition, catarrh of the Eustachian tube and middle ear may be present.

Digestive troubles are extremely frequent on account of irritability of the mucous membrane of the intestinal tract.

Lastly, secondary anaemia is not uncommon.

This, then, is the clinical picture of the disease which, in a greater or lesser degree, we usually find set in a scrofulous frame.

Before bringing before you a review of the various theories on the aetiology of the condition, I wish to say something as to its frequency.

Incidence

At the outset the statement was made that the disease was a common one, and when I chose it as my subject I believed that it was very common. This statement needs qualifying, however, for with an open mind I have endeavoured to obtain some idea as to its incidence in various parts of the country, and the statistics show that it is much more common in some than in others.

This may be already an established fact, and on the grounds of the loose expression "bad housing," might well be thought to be so, but I have not seen any comparison of figures which proves it.

I will avoid figures as much as possible and will simply give the percentages of cases of the disease which have occurred amongst the out-patient clinics of various hospitals, excluding the "accident" cases.

No case diagnosed simply as corneal ulcer was taken, although, doubtless, a number must have been of the eczematous type.

Working upward from the South they are as follows:

Plymouth.—1·42 per cent. for one year, 1916.

Exeter.—1·54 per cent. for one year, 1916.

Southampton.—1·98 per cent. for one year, 1916.

Bristol.—3·23 per cent. for one year, 1914.

Oxford.—1·2 per cent. (average for past 12 years).

Birmingham.—3·01 per cent. for one year, 1916.

Wolverhampton.—7·84 per cent. (average for past 35 years).

Shrewsbury.—2·53 per cent. for 1 year, 1916.

Manchester.—3·13 per cent. (average for past 25 years).

Sheffield.—4·76 per cent. (average for 1912).

Sunderland.—8·82 per cent. for three years, 1912, 1913, and 1916.

Glasgow.—7·54 per cent. for one year, 1916.

In a few towns and cities where I have been unable to get any statistics, I have obtained an expression of opinion from the following ophthalmic surgeons:

Margate. I chose Margate especially for, as is well known, it is

a place which attracts, by reason of its climate, numbers of young sufferers from surgical tuberculosis, and I thought it would be very interesting to know something of the frequency of the disease amongst them.

Dr. G. F. C. Wallis, to whom I wrote, is the ophthalmic surgeon attached to the Royal Sea Bathing Hospital for surgical tuberculosis and he kindly replied as follows: "I am afraid I cannot give you any hospital statistics, because those of the Royal Sea Bathing Hospital (for surgical T.B.), to which I am attached, only refer to the general condition. I think I can safely say, however, that I have seldom seen so little phlyctenular keratitis or conjunctivitis either in hospital or private life as in practice here: whilst in normal times I should think there is more tuberculous trouble of all sorts—glands and joints in particular, but also phthisis—treated in the district than in any other in the kingdom. I have always looked upon the whole régime of the general treatment adopted as an efficient preventive of this ocular affection."

I may say that I had quite an open mind as to what might be the frequency of the disease in Margate, and I think that Dr. Wallis's remarks are of much interest.

Newport. Captain R. J. Coulter kindly informed me that he thought the condition fairly common.

Leamington, Coventry, and Birmingham. Of these towns and cities Mr. T. Harrison Butler says "It is common in Birmingham, less so at Leamington and much less so at Coventry."

Norwich. Mr. Johnson Taylor writes that he would not say eczematous kerato-conjunctivitis is very common in the City and he attributes it to the fact that Norwich, called "The City of Churches and Gardens," is open, and that Norfolk is a dry county.

My own statistics in *Wolverhampton* extend over a period of 35 years and actually give the highest percentage of any except one, so that you will see I had reason for believing that, according to my own experience, the disease was a distinctly common one.

During these 35 years there has been a variation of the yearly percentage from 3.32 per cent., which occurred in 1909, to as much as 15.41 per cent. in 1897, the latter occurring in a series of high percentages extending over the seven years from 1892-1898 inclusive, when all were well over 10 per cent. Curiously enough, the two highest annual percentages, amounting to just over 4 per cent. each, which occurred in the Manchester series of 25 years, took place during the same years.

This series stands out from amongst the other years so prominently that one is tempted to look for a special cause to account for it, and a feasible one being the weather I looked up the weather records for those years.

Beyond, however, the fact that 1893 was a year of maximum

sunspots, whilst 1896 showed a predominance of N.N.W. wind, nothing out of the average was found either in rainfall, temperature, wind, earthquake or other phenomena. The weather records consulted were those made of the district from 1874-1900; incidentally the author of the work had once been a patient of the late Richard Middlemore.

The *Sunderland* figures are those for in-patients only, and it might be thought that they ought not to be compared with those of out-patients; since, however, they closely correspond with my own in-patient figures, and the two hospitals are nearly the same size, I felt justified in including them.

Opinions are of course of less value than actual figures, but I am most grateful to the above gentlemen who have been good enough to express them, and I cannot let this opportunity pass without tendering my cordial thanks to those who have so kindly assisted with figures; I allude specially to: Mr. J. Gray Clegg, of Manchester; Captain P. H. Adams, of Oxford; Mr. A. C. Roper, of Exeter; and Major G. H. Pooley, of Sheffield. The help of all has been most valuable.

The other results were obtained by an examination of the Reports of the various hospitals.

What conclusions may be drawn from such statistics as these?

The figures are not so divergent that a definite deduction can be made at once, and yet there is sufficient variation to merit more than a passing consideration.

At first glance it seems that the south country towns are more free than those more northern, as probably most people would think, and to some extent this is so, for the first towns mentioned, namely, Plymouth, Exeter, Southampton, etc., showed very low percentages.

Against temperature as a factor, however, we have the evidence of Colin, of Nice, who in 1910 stated that he found the disease very common in that health resort, putting it down to "bad housing" amongst the Italians. I am not able to give you any percentage of the incidence. And again, Bristol, Birmingham, and Manchester are within 0.1 of each other in the percentages found, and the difference in temperature in the three cities is well enough known to all.

If, however, we take them in three groups, according to nearness of percentages, we find we have:

Group 1. Plymouth, Exeter, Southampton, and Oxford all under 2 per cent. and averaging 1.5 per cent., and to these we can add Norwich and Margate, where the disease is said to be not common.

Group 2. Bristol, Birmingham, Manchester, and Shrewsbury all between 2.5 per cent. and 3.23 per cent. and averaging 2.9 per cent.

Group 3. Wolverhampton, Sheffield, Sunderland, and Glasgow all between 4·7 per cent. and 8·84 per cent., Sheffield only being the former, the average being 7·24 per cent.

Now, if on a map of England a line be drawn from Plymouth to the Wash a Southern area is cut off which includes Group 1, and is a part of the country where, with the insignificant exception of the Kent field, no coal is found.

In Group 2 the towns and cities are all close to, but not actually on, coal-beds, or if they are the bed lies extremely deep.

In Group 3 all are situated on coal-beds, practically the centre in each case, and as stated the percentage in each is strikingly high.

I suggest, therefore, that broadly the disease is distinctly more common in towns and cities where coal is found immediately beneath the surface than in those otherwise situated.

Where there is coal there are also iron-works, and it may be that the nature of this industry is a factor—in fact, a number of ideas spring to one's mind in seeking an explanation of the difference in the above figures. To mention a few: dust and smoke in the air and the prevalence of spitting, the health of the miner, the health of the iron worker, the clay soil, the rawness of the climate where coal is found, the effect of high wages and alcoholism, etc.

“Bad housing” alone, however, cannot explain the differences, for no one who knows them will contest the fact that the slums of Plymouth can hold their own in undesirableness with those of Bristol, Birmingham, Wolverhampton, Glasgow, etc.

In attempting this investigation it had been in my mind to compare the frequency of eczematous kerato-conjunctivitis with that of surgical tuberculosis or of tuberculosis in general, for the close relationship between the two is well established in the majority of cases, but strange as it may sound I am given to understand on good authority that there is no information as to the relative incidence of any form of tuberculosis in different parts of this country other than might be obtained by enumerating the deaths from phthisis.

Surgical tuberculosis is common in Wolverhampton and I am informed that it is so in Glasgow.

Probably it will be found that its frequency corresponds to a large extent with that of eczematous kerato-conjunctivitis in the towns and cities to which I have previously referred.

I cannot help feeling that such statistics would be of value and are needed, for if a disease is found to be more common in some districts than in others, there must be one or more conditions to account for it, and it naturally follows that those are the districts in which investigation is best made and the disease itself most successfully attacked.

I therefore very respectfully hold out these small beginnings to

investigators of tuberculosis and say: "Here and there, as the case may be, you will find eczematous kerato-conjunctivitis in plenty, an acknowledged finger-post to the presence of the tubercle bacillus; search the conditions under which life is carried on in those districts and so you may perhaps add another proof to the old adage 'prevention is better than cure.'"

Incidence among Healthy Children

Owing to the kindness of Dr. J. Priestley, Senior School Medical Officer of Staffordshire, to whom I am greatly indebted, I am able to present to you statistics from another point of view, namely, that of the occurrence of the disease amongst apparently healthy children or rather children who are well enough to attend school.

Dr. Priestley has given me the figures obtained by an examination of 8,575 children made up of, roughly, an equal number of boys and girls and all between the ages of 5 and 6, the first period in school life when these children are examined.

Excluding refraction cases, there were 126 cases of external eye disease amongst the boys, and 155 amongst the girls, 281 all told.

Dr. Priestley says that this is in accordance with his usual findings, namely, that eye diseases, including visual defects, are more common amongst girls than boys.

Amongst these 281 cases of miscellaneous external eye diseases there were 8 cases of phlyctenular disease in boys, and 14, including one case of staphyloma, in girls, the percentage being 6.45 per cent. and 9.09 per cent. respectively, or a total of 7.77 per cent., a high figure considering that coarse refraction errors were excluded. The remainder included many cases of blepharitis and catarrhal conjunctivitis, and also 14 cases of corneal opacities, and it is probable that a percentage of these, especially the opacities, were of the eczematous type.

Amongst these eye cases, as a whole, "bad housing," as evidenced by overcrowding, neglected and dirty clothing, and personal uncleanness, seems to have had little influence, as the proportion of these amongst the entire group of children was but little different from that amongst the eye diseases, and amongst the phlyctenular cases the proportion was as follows:—

Overcrowding—i.e., a family living in a three-roomed dwelling.—Not a single case of phlyctenular kerato-conjunctivitis came from such a dwelling. The usual proportion amongst the entire groups examined was 7.7 per cent.

Neglected and dirty clothing.—One case, or 7 per cent., amongst the girls and none amongst the boys. In the total groups there are 5 per cent. girls and 8 per cent. boys.

Personal uncleanness.—No case amongst the boys, but five of the girls were unclean, or 35 per cent. The usual findings in entire

groups were boys 12 per cent., girls 40 per cent. The difference is accounted for by the state of the head, the long hair of the girl being doubtless the reason.

As regards the general health of the 281 eye cases as indicated by the state of nutrition, it was found that there was nearly twice the amount of malnutrition amongst them as in the entire group of children, and that in the phlyctenular cases there occurred three amongst the girls, or 21.4 per cent., and four amongst the boys, or 50 per cent. The averages of malnutrition in the entire group were girls 14.5 per cent., boys 15.2 per cent.

It is clear, then, that these phlyctenular cases showed an excessive proportion of malnutrition.

Dr. Priestley comments as follows :

"Allowing for the very small number of cases, 14 girls and 8 boys, it would seem that narrow houses and incidences of personal neglect, uncleanliness, etc., which we associate with poverty, had unexpectedly small influence in inducing kerato-conjunctivitis ; but that malnutrition (which I am convinced generally means *disease* and not lack of nourishment, bad food, stuffy bedrooms, etc., as is so often assumed) had a great deal to do with it."

(The incidence, according to geographical distribution into North, Mid, and South Staffordshire, showed such little variation as to call for no comment.)

An interesting finding was that among the total 8,575 children there were 59 with definite tuberculous disease, and yet not one of these tuberculous children was found in the group of eye disease cases.

The investigation of these figures, small though they are, goes to show: (1) the high frequency of mild cases of the disease in Staffordshire ; (2) "bad housing," as expressed by overcrowding, personal uncleanliness, and dirty clothing, has but little effect as a causal factor, a finding which agrees with my investigations as to the comparative incidence in various large towns ; (3) malnutrition is a frequent association, but whether it is cause or effect in the evolution of the disease must be an open question at present.

I may say that I had an entirely open mind as to what might be found when I enlisted Dr. Priestley's kind help. I think that the results are distinctly interesting and open up paths along which it would be well worth while to proceed further and so enable us to throw more light on the still somewhat obscure aetiology of this disease.

Aetiology

The aetiology of eczematous kerato-conjunctivitis has received in the past twenty years more consideration than formerly.

Most of the work done has been in the direction of trying to

show the close relationship between it and tuberculosis, and the generally accepted opinion is that the phlycten is the ocular manifestation of a toxæmia arising from a tuberculous focus situated somewhere in the body.

The proof is almost complete but some of the links in the chain are wanting.

It is well established that the phlycten itself is not a true tuberculosis, for no tubercle bacilli alive or dead have ever been found in one; in fact, no micro-organisms have ever yet been found to exist in them, though they have been specially looked for by many investigators.

There is, however, a good deal of evidence to show that a tuberculous focus exists somewhere in the body in many cases.

Nias and Paton¹⁴ stated in 1906 that as a result of the examination of 50 patients suffering from phlyctenular disease the opsonic index was lowered for tubercle, and rose as the lesion improved, and they concluded that the phlyctenules were caused by attenuated or dead tubercle bacilli.

In 1910 Stephenson and Jamieson¹⁹ found that in 20 children suffering from phlyctenules, 50 per cent. showed clinical signs of medical or surgical tuberculosis, whilst 75 per cent. gave a family history of tubercle, and all the 20 cases reacted positively to von Pirquet's test; and, again, Stephenson¹⁷ found that in 669 cases with phlyctenular affections tubercle was present in 31·98 per cent.

Bywater,³ of Preston, in the same year found that Moro's test was positive in every one of 12 cases, and later in the same year repeated the test in all, and in three others besides, but with bovine tuberculin instead of human; in 13 out of the 15 the test was positive.

Harrison Butler² in 1913, stated that he regarded phlyctenular ophthalmia as being the result of a tuberculo-toxæmia, and that a tuberculous aetiology was exceedingly probable in 70 per cent. of his cases.

In 1912, Belenky-Raskin¹, of Berne, working in Siegrist's clinic, submitted one hundred consecutive cases of phlyctenular disease to von Pirquet's and Moro's tests, with the results that the von Pirquet reaction was positive in 90 per cent., and the Moro reaction in 85 per cent. I have not had the opportunity of consulting the original article, but the reviewer goes on to say that of the remainder 8 were carefully examined, and in all there was a strong family history of tuberculosis, or the patient showed obvious signs of tuberculosis. This leaves two cases, the subjects of phlyctenular disease, in which von Pirquet's test and also Moro's were negative, and in which there was no history or evidence of tuberculosis. I call attention to this as a weak point in what would otherwise have been a very strong link in the chain of evidence.

Davis and Vaughan⁹, two American authors, found in 1912, that

as the result of the examination of 40 cases of phlyctenular conjunctivitis, 70 per cent. gave a positive von Pirquet reaction and 30 per cent. a negative. I again call attention to this 30 per cent. of negative results, especially as this test is of far greater value negatively than positively. The authors believe that tuberculosis is the underlying cause in all cases, and that the phlycten occurs only in those who are the subjects of tuberculosis, latent or otherwise, or are "candidates for tuberculosis."

These references are a few amongst the many which have been brought forward in the past few years, but are sufficient to show that in the large majority of cases the tubercle bacillus is present in some form in the individual who suffers from the disease; or, to put it in another way, "the phlycten is an almost sure finger-post to the presence of that micro-organism."

I say "almost sure" because there does exist good evidence that in a small minority of the cases the proof of the presence of the tubercle bacillus is wanting. The failure to react to tuberculin tests in a certain percentage is a fact which cannot lightly be disregarded.

How, then, are we to explain the aetiology of the phlycten?

All are agreed as to the importance which a careful and suitable diet plays in the treatment of the condition, pointing to the association of gastro-intestinal disturbance as being a more or less constant factor present, and it is interesting to remember that in a great number of cases indican is found in excess in the urine. (Colobomo⁵, of Parma, found that 82 per cent. of cases of phlyctenular disease showed an increase in indican.)

Czerny⁸ in 1909 published a thoughtful article, in which he spoke of the "exudative diathesis," a condition found in infants in the first twelve months of life, and caused, he thinks, by an abnormality in the power of the fat metabolism. In the first six months the condition expresses itself in the presence of milk-scab, thrush, scurf, geographical tongue, and sometimes catarrh of the nose, pharynx, and bronchi. Later, eczema appears, and the child is an easy prey to infections, amongst which, of course, tuberculosis holds its place, though it must be remembered that tuberculosis is rare in the first year of life.

This diathesis is not more common or more strikingly apparent in tuberculous families than in others, but is frequently found in nervous families. He considers that overfeeding with milk and eggs, and also carbohydrates, brings out the symptoms, but that flesh food has no bad effect on these children. He finds that phlyctenulae are common, and a sign of this diathesis, and that with suitable feeding the symptoms disappear. He regards the status lymphaticus as representing the condition in its most severe form.

Again,¹³ Lafon, of Périgueux, in 1910, gives an even more interesting contribution on the subject, which, did time permit, I should like to quote in full. Briefly, he recognizes a complex and a simple group of cases of phlyctenular mischief, and the latter he arranges in three categories:

1. Patients who are already tuberculous when the eye trouble begins. The cause of the ocular disturbance in this class must be the toxin of the tubercle bacillus.

2. Patients free from a family or personal history of tubercle, in whom the eye mischief comes on after an infective malady, such as measles, scarlatina, whooping-cough, varicella, blennorrhagia, etc.

3. Patients free from tubercle and who appear to enjoy robust health when the ophthalmia makes its appearance.

It is this third class that Lafon has studied with particular attention and in support of the existence of such a class Victor Morax, of Paris, may be quoted, for he says: "Phlyctenular disease may be observed equally in children whose health is in the rudest possible condition, among whom all local tuberculous infection may be surely eliminated, and to whom we are not at liberty to apply the word scrofulous."

Lafon finds that these children, although said to be well by their parents, suffer from gastro-intestinal disturbances as the result of injudicious feeding; that they are the subjects of a chronic auto-intoxication of gastro-intestinal origin; and that the organism, in trying to rid itself of the toxins in various ways, provokes the formation of ocular phlyctenules.

The position as conceived by Lafon may be summed up as follows: If phlyctenular ophthalmia may in certain cases be attributed to toxins derived from a virulent bacillary focus, in other cases the lesions may depend upon digestive disturbances. At the same time that it provokes the formation of phlyctenulae, gastro-intestinal auto-intoxication diminishes the resistance of the organism against other infections. It creates a soil favourable to the evolution of all micro-organisms, notably of the tubercle bacillus. The conclusion is that phlyctenular ophthalmia may be due to different causes, amongst which gastro-intestinal auto-intoxication occupies the preponderating place.

Such is a brief consideration of the endogenous causes of the disease, but the possibility of an exogenous factor as an exciting cause is not beyond reason.

It has been well established that staphylococci are found in abundance in many cases of phlyctenular conjunctivitis, but their presence has not been detected in the efflorescences themselves. As to what part, if any, they play is a matter open to much question and remains undecided.

Straub²⁰ considered that an exogenous cause was more than likely

for several reasons, namely, the superficiality of the eruptions, their situation at the limbus, which shows alterations in almost every case of conjunctivitis, and from which he concluded that it is an excellent point of attack for exogenous infection, and, lastly, the often rapid success of external treatment. From the fact that staphylococci are so often found, he thought that they play an important rôle.

One might add that it is curious that the single phlycten so frequently appears on the conjunctiva in the palpebral fissure, thus suggesting an external irritation.

Axenfeld considers that the phlycten is the specific reaction of the scrofulous individual to all kinds of infection and that there is no need to accept only one cause for it.

One author, Gradle,¹⁰ of Chicago, has treated the condition with staphylococcus vaccine. Nine cases in which recurrences had taken place, and which had failed to improve under ordinary treatment, were submitted to the measure, but the results were not too conclusive.

In 1912, Rubert,¹⁵ of Kieft, recorded the results of a series of experiments in tuberculous animals. Instillations of staphylococcus vaccine, staphylococcus toxins, and tuberculin were made in the conjunctival sacs, and it was then found possible to produce experimentally lesions which clinically and histologically resembled the phlycten of the human conjunctiva.

Pooley, of Sheffield, has tried instillations of tuberculin in the conjunctival sac as a form of treatment. In one case, he informs me, tuberculous iritis occurred, whilst another case was very suspicious. His results have not been published, but he has kindly permitted me to mention them.

It is well to remember the fact that phlyctenulae may appear in the course of a conjunctivitis due to the pneumococcus, Weeks's bacillus or the diplobacillus of Morax, and that the efflorescences themselves are the same histologically as those found in eczematous conjunctivitis.

Although in the last four or five years no further research appears to have been made in this direction, there is some evidence pointing to the existence of an exciting cause (which may provoke an attack in a suitable *terrain*) as being highly probable.

My own views, if I may be permitted to express them, are much in accordance with those of Lafon, that, with the evidence we have at present, the phlycten is the ocular manifestation of a toxaemia, which in many cases is undoubtedly tuberculous, but in a number, probably mild ones only, is of gastro-intestinal origin, the exact nature of which is unknown.

The phlycten in the majority of cases is undoubtedly a finger-post to the presence of the tubercle bacillus, but the fact that a number

of mild cases of the disease occur which clear up by treatment with local antiseptics, such as a little yellow oxide of mercury ointment, and a few doses of grey powder, combined with advice as to diet, especially this last-named, is one which is hard to reconcile with any set statement that a tuberculous toxæmia is the cause in all cases.

I think that we should recognize the existence of an hereditary diathesis, call it the exudative or what you will, but a condition which forms a bed-rock upon which infection readily takes place. Faulty hygiene, bad and improper food chiefly, opens the road still further to infection by micro-organisms. The tubercle bacillus, which is so wide-spread, is the one most successful, and perhaps the one most suitable, to such a soil, which then becomes scrofulous, but other infections may occur, any of which by their toxins may give rise to the phlycten.

As to an exciting cause, I think it is more than probable that such exists in every case, but whether it is mechanical, chemical, bacterial or not, it is impossible to say. Perhaps an unknown organism may be found.

The differential diagnosis of the disease should present but little difficulty.

Differential Diagnosis

An important point to bear in mind is the superficial nature of the lesion.

The age of the patient and the association in the majority of cases with the various signs of scrofulosis form valuable clues. When the conjunctiva alone is attacked, the condition may be confounded with other forms of conjunctivitis, but the localization of the red patch with the greyish-white phlycten, together with the absence of secretion, differentiates it at once.

Sometimes, as stated previously, phlyctenulæ appear in the course of an acute conjunctivitis due to the pneumococcus, the Weeks's bacillus, or the diplobacillus of Morax, and I recall some five or six years ago an epidemic of such cases at the Wolverhampton Eye Infirmary; but smears of the secretion were taken, and showed either the pneumococcus or the Weeks's bacillus, and these findings, together with the subsequent progress of the cases, made it quite clear as to what was the condition.

Occasionally, an episcleritis may be confounded with a single phlyctenule in its later stages, but a few drops of adrenalin solution, as a rule, place the matter beyond doubt.

That interesting disease, spring catarrh, in its milder forms, presents an appearance not unlike that of an eczematous conjunctivitis in its later stages, but the smoky-yellowish, or sometimes brown, appearance of the conjunctiva in spring catarrh, together with the history, as a rule, form a sufficient differentiation.

In the bulbar form the nodules at the limbus simulate phlyctenulae, but the latter ulcerate rapidly and become resorbed, whilst the former never break down, and, finally, in both forms a smear to reveal the presence or absence of eosinophils is all but infallible in the diagnosis.

In the cornea, if we again remember the superficial nature of the lesion in eczematous keratitis, there will be little difficulty in coming to a conclusion, but there are a few conditions which may be mistaken for each other.

Trachomatous pannus is generally limited by a more or less horizontal line to the upper part of the cornea, and associated with it is cicatrization of the palpebral conjunctiva, especially in the superior fornix.

Ecematous pannus occurs on the cornea in any position and is often associated with an ulcer.

It is well to remember, however, that a scrofulous patient may be infected with trachoma, and the condition consequently then presents great difficulties in diagnosis.

A somewhat rare and interesting condition, namely, rosacea of the cornea, requires mention, for it may be confused with a troublesome case of eczematous keratitis, and not without reason, for in many ways the two diseases resemble one another in a striking manner. It occurs usually in women in middle life and is associated with rosacea of the face. The appearance on the cornea is that of a superficial keratitis with nodules of opacity which break down and ulcerate. Recurrence is frequent and the patient suffers from chronic indigestion. The age of the patient, the association of rosacea on the face and the chronicity of the complaint are guides to the differentiation from eczematous keratitis. Attention has been drawn to this disease by Cross,⁶ Stephenson,¹⁸ and Cruise,⁷ the two first-named of whom specially note the resemblance to the phlyctenule of the cornea, and there is no doubt that the two diseases have much in common.

Treatment

In the treatment of this disease, with which I shall not detain you long, we must remember that practically all our patients are of the poor class. I can only recall about five or six private patients in 14 years. Captain P. H. Adams tells me he only remembers one in 12 years, and something like this is the experience of all ophthalmic surgeons. That being so, such measures as a trip to the Riviera or a sea-voyage are quite out of the question; and we have to consider treatment which it is within the capability of the patient to carry out.

Considering the local treatment first, we find that calomel

powdered on the eye in the case of limbal or conjunctival efflorescences is most useful, and that in all other forms Pagenstecher's ointment, i.e., the yellow oxide of mercury ointment, is the best, and should be combined with light massage.

It is noteworthy that a mercurial compound is the most successful.

If secretion is present suggesting an infection by micro-organisms, an antiseptic lotion is necessary, together with drops of silver nitrate, argyrol, protargol, or one of the many well known silver compounds.

Atropin is seldom necessary, except in the case of deep ulcers, and when hypopyon has occurred.

Some advise eserin in the severe cases, notably Kaz, of Petrograd, who states that it acts in a miraculous manner and he gives the usual explanation.

A number of drugs have been brought forward by various authors from time to time, but none seems to take the place of the two mercurial compounds which are so much in use, and there is no good purpose in enumerating them.

A word in praise of subconjunctival injections is necessary, however, and there is no doubt that in many cases they are beneficial. Ordinary saline solution or cyanide of mercury solution (1 in 5,000), combined with acoin solution to relieve the pain, would seem to be as effective as anything, although a number of other solutions has been extolled. My own experience is that some cases respond to this measure as though it were a charm, but that in others no effect is produced. I have never been able to decide as to what class of case is likely to be benefited, but they are well worth trying in all obstinate cases.

Side by side with subconjunctival injections must be mentioned dionin in drops of 2 or 3 per cent. solution, which acts in the same way, though much less actively. Especially are these remedies stated to be useful in helping to clear up opacities.

The general treatment is as important as, perhaps more important than, the local. Mostly it is directed against the scrofulous diathesis, and it is unnecessary to go further than to say that "light, air, movement and nutrition are the fundamental supports of both the prophylaxis and treatment."

The value of treating these sufferers as in-patients of a hospital is recognized by all surgeons who have to deal with them in anything like a large number, but too often after discharge do they relapse, are taken in again and again relapse. It would seem to be well worth while to have separate wards set apart in the hospitals where phlyctenular disease is very frequent, and this has been in my mind for some time with regard to Wolverhampton.

Regarding medicinal treatment, it is again striking that grey

powder, or small doses of calomel, should prove so beneficial, and its success in improving the general condition of these children bears out the opinion that gastro-intestinal auto-intoxication holds an important place in the aetiology. The exhibition of these drugs seems to be especially satisfactory in the fat, apparently over-nourished, cases that we meet with. The ill-nourished demand the usual building up with cod-liver oil, combined with the phosphate or iodide of iron; but even in these the mercurial drugs are very valuable.

The diet is summed up in little starchy food, and more meat, vegetables, and fruit.

These old-fashioned measures, about which, did time permit, more might be said, are not to be lightly put aside in favour of the more modern inoculation forms of treatment.

Reference has already been made to the injection of staphylococcus vaccine and its somewhat dubious success.

As to injections of tuberculin, it is now well established that they are of great value, but it may be presumed that no surgeon undertakes them before the simpler old-fashioned remedies have been tried. They should be, I think, and probably are by most, reserved for the more advanced and troublesome cases, which will not yield to simpler measures, and it would be wise to bear in mind the fact that in a number of cases evidence of the tuberculous focus is wanting though it probably exists, and that being so, the amount of vaccine administered should be a small one. Even in those cases where there is trustworthy evidence that the tubercle bacillus is present, the site and the extent of the trouble it has caused may be unknown, and the injection of tuberculin becomes a "shot in the dark." It is wise to begin with the smallest doses and to work up gradually.

As to surgical treatment, the procedure adopted by Hicks,¹¹ of New Brighton, N.Y., who excises a large phlycten, would seem to most of us, I think, to be unnecessary.

One small point as an adjunct in the management of these cases which I would like to mention, is the value of the correction of errors of refraction when present, and, in my experience, they are not uncommon. It has been my impression for some time that they existed to an unusual extent, and to satisfy myself on this point I took a few cases in succession and examined the refraction, with the result that about one-half showed an error, nearly always hypermetropia and hypermetropic astigmatism, and that in the majority of those the eye which showed the greater refraction error was the one which had been most affected. Needless to say, the error was obviously a previously existing one, and was not of the nature which might be put down to scarring of the cornea as the results of ulceration, *i.e.*, an irregular astigmatism.

In conclusion, I think that a great deal remains to be done in the direction of the preventive treatment of this disease.

Quite apart from the close association of tuberculosis, the chief aetiological factor which is usually assigned to it is summed up in the words "bad housing," and there the matter seems to end without any, or at least without sufficient, consideration as to what the phrase means.

Do not Dr. Priestley's figures, as well as my own, tend to show that "bad housing," as evidenced by overcrowding, personal uncleanness, and ragged clothing, has but little effect, whilst malnutrition is undoubtedly a factor?

Speaking in a general way with regard to children, Dr. Priestley regards malnutrition as evidence of disease and not necessarily as evidence of insufficient or bad food.

Applying this to the evolution of eczematous kerato-conjunctivitis, we have to decide whether malnutrition is cause or effect; but whichever it is there is one constant factor present in the disease for which there are many proofs, namely, gastro-intestinal disturbance, and does not this point to food, contaminated and improper, as being in some way the beginning of the whole trouble?

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PHLYCTENULAR DISEASE AND ITS RELATION TO TUBERCULOSIS

BY

R. BEATSON HIRD, M.D., F.R.C.S.Ed., CAPT. R.A.M.C. (T.)

HON. OPHTHALMIC SURGEON TO THE GENERAL HOSPITAL, BIRMINGHAM; HON.
ASSISTANT SURGEON TO THE BIRMINGHAM EYE HOSPITAL.

THE substance of my present remarks on the relationship of tuberculosis to phlyctenular disease formed the subject of a short paper read before the Midland Medical Society in April, 1914. I have purposely delayed its publication in order that the cases might be kept under observation for some time to see if the results were satisfactory. The number of cases dealt with is not large, but I have had scores since then and have had no reason to change my opinion of four years ago. Much has been written on this subject during the last few years, and I offer this contribution to confirm and strengthen the growing opinion that there is a relationship between phlyctenular disease and tuberculosis. If this is correct, then phlyctenular disease assumes an importance beyond that of a superficial local inflammation. It is undoubtedly the commonest cause of corneal opacities in children. During the last four years as ophthalmic surgeon to the City of Birmingham Education Committee, I have had 4,702 new cases of children suffering from ocular defects referred to me, and amongst these, 308, or over six per cent., had corneal scars in one or both eyes. Many in consequence have had to be educated at one of the special schools for the partially-blind and blind. The children in these schools are frequently leaving or being transferred to other schools, but the following was the result of an examination of all the scholars attending one of the schools for the partially-blind inspected by me a little while ago. I found no less than 64 per cent. suffering from corneal opacities which had rendered their education there a necessity. The commonest cause was phlyctenular keratitis which accounted for 50 per cent. for certain. There were some doubtful cases which might well have come into this group, but I excluded