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ON THE RELATIONSHIP BETWEEN CHRONIC IRIDOCYCLITIS AND TUBERCULOSIS, AND THE APPROPRIATE THERAPY

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Introduction

FOR more than a decade continental ophthalmologists have repeatedly emphasized the importance of tuberculosis in the aetiology of a wide variety of ocular diseases. It is generally agreed that certain diseases affecting the eye are caused by tuberculosis, for a characteristic histology and the demonstration of the bacillus in the lesion have provided conclusive proof of their nature. In this group may be mentioned tuberculosis of the conjunctiva, caseating iridocyclitis with perforation of the sclera, and miliary tubercle in the choroid. Other disorders of the eye, however, have on less certain evidence been attributed to tuberculosis, particularly by the above-mentioned continental authorities, and in this country clinical opinion, especially where allergic phenomena are invoked, has in the past and still to-day regards their case as non-proven. Pathological lesions in this category include phlyctenular conjunctivitis, recurring haemorrhage into

the vitreous or retina in young adults (Eales' disease), chronic iridocyclitis, uveo-parotitis, and solitary exudative choroiditis.

It is with the relationship between tuberculosis and chronic iridocyclitis, and the closely associated disorder uveo-parotitis that this paper deals.

The evidence in regard to the Aetiology of Chronic Iridocyclitis.—It has been held that tuberculosis is seldom a cause of iridocyclitis because the bulk of the available evidence as regards the aetiology of the latter is conflicting. Thus, associated tuberculous manifestations have generally been found to be rare, furthermore, chronic iridocyclitis is said to be encountered infrequently in sanatoria, and in hospitals for diseases of the lungs. Of more importance is the fact that tubercle bacilli have never satisfactorily been demonstrated in the local lesion, nor is the histology of chronic iridocyclitis characterised by tuberculous caseation. Moreover, the aetiological importance of foci of sepsis has in this country particularly been stressed in this disease. Here, also, clear-cut evidence of a relationship is lacking, and, while appropriate treatment of associated infection of the teeth, sinuses, or intestinal or uro-genital tracts has in a minority of cases been attended by brilliant results, all too frequently relentless relapses occur and in the course of months or years blindness ensues.

The hypothesis that chronic iridocyclitis is a tuberculous manifestation rested originally on histological findings in excised eyes. The literature of this aspect of the subject has recently been classified and exhaustively discussed by Igersheimer.¹⁹ He stresses the rarity of caseation, and the persistent failure of all efforts to detect the bacillus in the lesion. He notes also that while a characteristic histology is not uncommon, tuberculous giant-cell systems are by no means always found, and even when present are very frequently atypical in appearance. Morbid anatomical evidence therefore is suggestive but not fully convincing.

Löwenstein²² has claimed by the use of special culture media to have recovered tubercle bacilli from the blood in cases of the type under consideration. He had previously reported the presence of a tuberculous bacillaemia in 100 per cent. of cases of advanced, and in 15 per cent. of moderately severe cases of phthisis. Similar positive results were obtained in approximately 15 per cent. in the series of cases of chronic iridocyclitis above mentioned. In spite of the repeated efforts of many investigators including Calmette and Saenz,⁴ and Butler,³ Löwenstein's work has not been confirmed. Subsequent investigation indeed has shown that while a tuberculous bacillaemia does occur, it is probably quite rare even in advanced cases of phthisis, and its detection is in any

case a tedious, uncertain and difficult matter. Furthermore, the danger of contamination of the culture by other acid-fast bacilli is not inconsiderable, and finally, a positive result is not of course diagnostic of the nature of a local ocular lesion. The report, therefore, of Meller²⁴ (who used Löwenstein's technique) that tubercle bacilli could be recovered from the blood in 14 per cent. of cases of chronic iridocyclitis is open to some criticism, and cannot be accepted as proof that the disease is due to tuberculosis, although such a finding if it were undoubtedly true would add to the probability of such an aetiology in this disease.

In recent years improvement in radiological technique has been considerable, and has made possible earlier and more accurate diagnosis of many intrathoracic lesions. This technical advance has led to the demonstrations that in chronic iridocyclitis lesions in the lungs and in the lymphatic glands of the mediastinum are frequently present, and that these lesions show the radiological characteristics of tuberculosis in many instances. (Werdenberg⁴¹ Meisner,²³ Brown² and others.) The importance of this finding remains unrecognised by the majority of British ophthalmologists, indeed the literature of the subject in this country is barren in this respect with the exception of a few papers for the most part by clinicians in regard to the relatively rare uveo-parotitis. (Garland & Thompson,¹² Tanner & McCurry,⁴⁰ Lewis, Raines and Stewart,²¹ Stallard and Tait.³⁹)

The significance of the association of tuberculous intrathoracic lesions in a disease such as chronic iridocyclitis can best be appreciated from a brief consideration of the accepted pathogenesis of tuberculosis in man.

The generally accepted view of the development of tuberculosis in human subjects implies the occurrence of an initial lesion, usually in the lungs or intestinal tract, with consecutive involvement of the lymphatic system immediately draining the area concerned. Thereafter, the patient is allergic, and subsequent reinfection produces a generalised reaction, as well as an intense local allergic response in the lungs to the inhaled tubercle bacilli. The glands at the hilum of the lung may be reinfected, but as a rule the inflammatory reaction satisfactorily encloses and walls off the infection. In a majority of individuals the new secondary pulmonary lesion heals, while organisms in the mediastinal glands may remain dormant for years, often for the remainder of the subject's life. He is now not only allergic to tuberculin but has, as a rule, a considerable immunity to tubercle bacilli. These hilar glands, however, constitute the last wall of defence to the blood stream, for their normal channel of excretion consists of a few inches only of thoracic duct or right lymph duct before the opening into the venous system occurs. Tubercle bacilli may

therefore on occasion pass from infected glands by this route into the blood stream, and, returning to the lungs, give rise to further secondary lesions or to miliary tuberculosis there; or they may pass that filter and reach the systemic circulation to give disseminated lesions throughout the body. In this way the escape of relatively small numbers of tubercle bacilli into the systemic circulation may well be attended by isolated disseminated lesions, such as are found, for example, in the epididymis, the eye, or in joints, while when the bacilli are actively virulent and widely disseminated miliary tuberculosis results, and the patient as a rule rapidly dies of meningitis.

Chronic Miliary Tuberculosis.—Recent work suggests that even in miliary tuberculosis the course may be chronic and occasionally recovery is possible. Hoyle and Vaizey¹⁸ in a comprehensive survey have amassed 120 cases from the world's literature, and added ten of their own, which were diagnosed on adequate evidence as having chronic miliary tuberculosis. Some of these patients died after little more than six months of the probable onset, others survived several years only to die of the disease later, while a few recovered and remained alive and well. Fish¹¹ has also reported ten cases of chronic miliary tuberculosis in children, four of whom survived, the others eventually dying of meningitis. Blood borne complications in his series comprised a unilateral optic atrophy, probably from an intracranial tuberculoma, tuberculides in the skin, and lesions in the abdomen, liver and spleen. All his cases showed enlargement of mediastinal or hilar glands. He also recognises that such cases vary very much in severity. We can, therefore, no longer regard miliary tuberculosis as necessarily a rapidly fatal disease.

In this connection the experimental work of Innes²⁰ is of interest. By means of intravenous injections of B.C.G. (avirulent tubercle bacilli) he was able in animals regularly to produce miliary tuberculous foci in the lungs, and considerable enlargement of the hilar lymph glands. Microscopically these glands did not show evidence of caseation, rather there was present sinus catarrh—the sinusoids being full of solid masses of macrophages and endothelioid cells. The lesions usually cleared completely in eight or ten months. Reinjection after an interval produced an intense allergic response which with the relatively enormous doses used, often killed the animal, but in those which survived, identical pulmonary and lymphatic changes were observed to occur. Variations in the generalised reaction as well as the lung lesions of animals injected with small doses were purely quantitative in extent and cleared correspondingly more rapidly.

It is also noteworthy that among the cases of miliary tuberculosis which pursue a chronic course, a group exists in which

retrograde lymphatic extension of the disease occurs throughout the lungs from the hilar glands. The process tends, as Schurmann³⁴ has shown, to be relatively slow and the cases present the clinical and radiological appearances of increasing pulmonary lymphatic stasis and permeation. In some of the cases of this group the disorder is confined to the lungs, while in others disseminated presumably haematogenous lesions are also found.

Chronic haematogenous tuberculosis has also recently been discussed by Simmonds and Pagel³⁵ who hold that there is good reason for thinking that by this method of re-infection the common chronic pulmonary form of the disease may be produced. Thus, Pagel³⁷ has produced haematogenous typical lung lesions in rabbits by intravenous injection of virulent bacilli after previous immunization of the animals by infection with living avirulent or killed bacilli. Nicaud²⁶ in 1934 had obtained similar results in animals using dead tubercle bacilli.

Generalised, as well as isolated forms of haematogenous disseminated tuberculosis are thus well-recognised both clinically and in the laboratory, and it is now realised that in both the lesions may be acute, sub-acute, or chronic.

The hypothesis that chronic iridocyclitis is a variety of disseminated haematogenous tuberculosis therefore postulates the presence of a focus of tuberculosis elsewhere in the body from which the organisms gain entry into the blood stream. Proof of the hypothesis requires the demonstration first of tubercle bacilli and of classical tuberculous changes within the eye, secondly of occasional tuberculous bacillaemia, and finally the presence of a tuberculous focus elsewhere. We have seen that in chronic iridocyclitis the histology of the ocular lesion is suggestive but not always typical of tuberculosis, and that tuberculous bacillaemia though rare, does occur. What of the third requisite? At the beginning of the century Naegeli²⁵ showed that at post-mortem traces of tuberculosis were evident in 98 per cent. of adults, whatever the cause of death, and subsequent work by many other pathologists has confirmed his findings. In the vast majority of patients these lesions are healed or quiescent, and can only rarely be demonstrated during life by clinical examination. Radiological investigation discloses a greater proportion of these healed foci, though even in this way only a minority can be demonstrated in life. The response of the individual to tuberculin, however, usually provides a means of determining, as will be shown, whether or not a previous tuberculous infection has occurred. On the other hand, if an active tuberculous focus is present in the body, its demonstration is as a rule possible by clinical and radiological tests.

While, *a priori*, an active tuberculous focus is more likely to give rise to disseminate lesions via the blood stream than are healed or quiescent foci, the latter are by no means innocent in this respect. Cobbett⁵ was able to show, for example, that quiescent foci, particularly glandular foci, as had been suggested by Cornet, frequently contained avirulent or dead bacilli, and this finding, together with the animal experiments quoted above, led to the suggestion (as yet unproved), that chronic ocular disease of the type under consideration might well follow the liberation of dead or avirulent organisms into the blood stream, and their subsequent deposition in the uveal tracts.

It may be assumed therefore, that in the vast majority of adults living in civilised communities, a focus of tuberculosis exists from which systemic haematogenous infection may occur. The probability of such dissemination increases with the activity of the disease in the focus, and with its size.

In any given case, therefore, when a possibly tuberculous peripheral lesion is discovered, the likelihood of the diagnosis proving in fact to be tuberculosis is increased if a manifestly tuberculous focus is discovered elsewhere in the body, and considerably increased if that focus is extensive and active.

Allergy in Tuberculosis.—The occasional atypical nature of the local pathology in chronic iridocyclitis also induced proponents of the tuberculous theory of its aetiology to suggest that, following the original local bacterial infection which as a rule subsides, subsequent exacerbations of inflammation are allergic, and in response to the liberation of tuberculin from the active focus elsewhere in the body. Final proof of this theory is lacking, although it is of course well-known that allergic inflammatory reactions around foci of tuberculosis do follow the injection of varying amounts of tuberculin. It has been, indeed, the clinical experience of many that in cases of chronic iridocyclitis, injudicious use of large doses of tuberculin is not seldom followed by severe exacerbations in the ocular condition. Until recently such accidents in therapy have been regarded as strong evidence of the tuberculous nature of the disease. However, Almroth Wright's work, as quoted by Williamson-Noble,⁴² has shown that a variety of antigens, of which tuberculin is one example, are capable of eliciting non-specific as well as specific responses in distant organs on intra-muscular injection. It would seem, therefore, that the above response is not certainly specific in character, and therefore its value as evidence of tuberculosis in the aetiology of the disease is slight.

The Mantoux Reaction.—Apart from ocular reactions to relatively large doses of tuberculin given intramuscularly or hypodermically, the local response to small intradermal injections

has been used extensively in diagnosis. Indeed, in the continental literature on chronic iridocyclitis, "proof" of the tuberculous nature of this disease seems usually to be dependent on the results of such tests, of which the "Mantoux" reaction is perhaps most widely employed. It cannot be too strongly asserted that this reaction measures only the allergic state of the individual. Hart,¹⁶ in an extensive report on tuberculin skin reactions, found that amongst the London population as high a proportion as 25 per cent. of those aged 5 years, 45 per cent. of those aged 10 years, and 70 per cent. of those aged 16 years were positive. Such findings are in agreement with the pathological evidence previously quoted.

A positive reaction, therefore, is no proof of the aetiology of any lesion the adult individual may present. It signifies only that he has become sensitised by infection with tuberculosis on some previous occasion. A positive response, indeed, is usually consistent with good health in town dwellers. Furthermore, such a reaction is no certain sign of immunity, for immunity and allergy are not only not identical or necessarily co-existent (Lyle Cummins),⁸ but have been successfully separated experimentally (Rice Rich).³⁰

On the other hand, a negative reaction particularly in an adult, may be of value as evidence against tuberculosis as the cause of a given lesion. However, occasionally in advanced cases of undoubted chronic pulmonary tuberculosis, and quite frequently in miliary tuberculosis, a negative Mantoux reaction may be obtained, presumably because the patients have become desensitised by the relatively enormous doses of tuberculin their own lesions are producing throughout the body. The finding, therefore, of a negative Mantoux reaction is not necessarily proof that a given lesion is not tuberculous. A negative reaction is also not unusual in certain rare disorders (possibly of tuberculous aetiology, and of importance in regard to chronic iridocyclitis because they present certain similar clinical features) such as Schaumann's disease, lupus pernio, lupus miliaris, and Boeck's sarcoid. The skin reactions to tuberculin are therefore of limited value in the diagnosis of a local ocular lesion.

We may conclude from the literature, then, that many children and nearly all adults carry within them a focus of (usually healed) tuberculosis: that dissemination of bacilli by the blood stream may on occasion take place from such foci and give rise to distant lesions in, for example, the eyes. In the particular case of chronic iridocyclitis the above potentialities of course exist, but the local pathology though highly suggestive of tuberculosis has never been proved to be due to this cause.

Clinical Records

Forty cases of chronic iridocyclitis were investigated. These patients were chosen from among those attending the Royal London Ophthalmic Hospital, St. Mary's Hospital, Paddington, and the Hospital for Consumption and Diseases of the Chest, Brompton. The sole criterion governing the selection of these cases was the presence of undoubted chronic iridocyclitis.

In every case the clinical history, physical examination, radiological examination of the chest, and the Wassermann and Mantoux reactions were obtained. A variety of laboratory determinations, which seemed relevant to each case and are considered in detail below, were also made; while, in addition, in a majority of the cases careful search for focal sepsis, including extensive bacteriological investigation, was instituted.

In most of the cases the period of observation extended over several years; in every case that period exceeded six months, so that frequently in individual patients several phases of in-patient investigation and treatment were carried out. In the intervals the patients were seen from time to time as out-patients. Close study of alterations in their clinical condition, and in the changing results of investigations, was thereby permitted, and we were thus enabled to form some estimate of the value of the various methods of treatment employed.

Details of each of the cases included in the series are presented in the appendix.

General Condition

Of the forty cases investigated fifteen were male and twenty-five female. Their ages at the onset of the ocular lesion varied from four to fifty-two years, while in twenty-three cases the onset occurred during the third decade. The mean age at the onset of the iridocyclitis was 28.21 years.

The chronicity of the disease can be judged from the fact that in this series, to the end of the period of observation, the duration of the disease varied from a few months to thirty years, with a mean duration of 7.5 years.

In seven cases of the forty, there was a family history of pulmonary tuberculosis in a near relative with prolonged contact, while in one other case contact with known cases of phthisis had occurred for three years prior to the onset of the disease.

Significant uniformity of occupation or social position was not found, nor was any seasonal incidence in the disease noted.

In twenty-seven cases iridocyclitis was the presenting disorder. Outstanding modes of onset of the disease other than the above were parotitis, an acute febrile illness resembling influenza,

pleurisy, pharyngitis, laryngitis and herpes zoster. Once the disease was established the following extra-ocular clinical features were frequently encountered; cough productive of sputum, parotitis, lymphadenitis, dyspepsia sometimes associated with vomiting, irregular recurrent pyrexia, amenorrhoea, tuberculides of the skin, dyspnoea, cyanosis and loss of weight. Often, however, there were no symptoms other than those immediately referable to the ocular lesion.

One of the cases investigated died during the period of observation, and it is regrettable that permission to perform a post-mortem examination could not be obtained.

The ocular lesions, the radiological appearances of the chest, and the results of the pathological investigations in these cases are separately discussed in detail below.

Considerable variety existed in the clinical manifestations presented by the patients comprising this series. For the purposes, however, of an investigation of the significance of tuberculosis in the aetiology of chronic iridocyclitis it is convenient to divide the cases into five groups.

Group 1. Uveo-parotitis, 6 cases. (Nos. 1-6)

These patients all showed bilateral severe iridocyclitis, bilateral but not necessarily symmetrical parotitis, and generalised lymphadenitis at some stage of their illness. Usually these features were most marked at the onset, but there was in every case a tendency for phases of renewed activity, persisting sometimes for months, to recur during the period of some years over which they were observed. In such relapses, as at the onset, irregular pyrexia, malaise, dyspnoea, cyanosis, hyperidrosis, anorexia, amenorrhoea, and loss of weight were prominent features of a typically systemic disease in which ocular symptoms and signs were dramatic but incidental characteristics.

Five of the six cases had persistent splenomegaly, in two cases very considerable in degree; three cases showed a cutaneous tuberculide, maculo-erythematous in type, and for the most part affecting the legs and arms, while in two cases a VIIth nerve palsy lasting for some weeks complicated the clinical picture during the early stages of the disease in which parotitis was a feature.

Radiological examination of the chest disclosed in each of these patients the appearances of chronic miliary tuberculosis (lymphogenous type) associated with gross hilar lymphadenitis. (See Figs. 1 to 12.) In striking contrast, abnormal physical signs obtained on examination of the chest were either minimal or absent.

Four cases of this group (Nos. 2, 4, 5, 6) were observed from the onset of the disease. Of these, two cases (Nos. 4 and 5) became blind in both eyes within a few months of the onset. Case 6 ran a slightly less severe course, one eye becoming useless after eighteen months, while the second eye still retains 6/60 vision some three and a half years after the onset. In Case 2 the ocular lesion initially was much less severe, and fair vision is retained in both eyes some fifteen months after the onset.

Cases 1 and 3 were seen for the first time respectively five and two years after the onset. Case 1 was blind in both eyes, and Case 3 had good vision in both.

Group 2. Chronic Miliary Tuberculosis without Parotitis, 6 cases (Nos. 7-12)

These cases differed from the first group in that parotitis with or without VIIth nerve palsy did not occur, and that clinically-recognisable lymphadenitis and splenomegaly were not constant. The clinical course of the disease, with its irregular exacerbations and remissions, and the symptomatology were, however, essentially similar. It was also characteristic that while physical examination of the chest failed as a rule to show any abnormality, radiological investigation revealed changes consistent with the diagnosis of chronic miliary tuberculosis (usually of the haematogenous type). (See Figs. 13 to 18 inclusive.)

It is of particular interest that two of the cases (Nos. 11 and 12), after periods respectively of ten and three years, are now clinically and radiologically cured; Case 11 having only a few scattered peripheral calcified foci to mark the site of some of the original miliary tubercles in the lung (Figs. 13 and 14); Case 12 now showing an entirely normal chest. The ocular condition in both these cases is also arrested, the iridocyclitis having been quiescent and productive of no symptoms for seven and two years respectively. In Case 8, in which marked recurrent generalised symptoms were a feature, very considerable hilar lymphadenopathy was present, and fine miliary deposits of the lymphogenous type developed in the lungs. (Figs. 17 and 18.)

The damage caused by the iridocyclitis to the sight of these five patients, however, tended usually to be as severe as that found in the previous group.

Group 3. Tuberculous Lymphadenitis, 3 cases (Nos. 13-15)

In these patients, though the ocular lesion tended to be as severe as in the preceding groups, as a rule there were less well-marked general symptoms.

In Case 13, apart from the iridocyclitis, widespread tuberculous

lymphadenitis and Bazin's disease of nineteen years' duration provided evidence of generalised dissemination from an early stage of the illness.

In Cases 14 and 15, tuberculous cervical lymphadenitis was present. Clinically and radiologically the lungs of these patients were within normal limits during the period of observation.

Group 4. Chronic Pulmonary Tuberculosis, 10 cases (Nos. 16-25)

Four of these patients (Nos. 19, 20, 24, and 25) were to every test examples of arrested pulmonary tuberculosis. Examination of the chest either revealed the signs of pulmonary fibrosis or was entirely negative, while radiologically typical hard fibroid scars and calcification marked the site of previous infiltration. There were in these four patients no symptoms suggestive of an active generalised disease. None the less, the ocular lesion, although quiescent in one, was irregularly recurrent and active in the remaining three.

In the remaining six cases the symptomatology was typical of active chronic pulmonary tuberculosis, and included lassitude, loss of weight, dyspnoea, night sweats, cough, sputum, anorexia, and amenorrhoea. During the period of observation in these patients the pulmonary and ocular disease ran its slow, irregularly progressive course, having long intervals in which healing of the lesions took place interrupted by relapses in which fresh spread of the disease occurred.

The extent of the pulmonary disorder was in the majority considerable but varied in different cases, and in those most severely affected, signs of infiltration and fibrosis were obtained on clinical examination. As a rule, however, radiological examination disclosed far more extensive lesions than physical examination would have suggested were present.

In these respects these six cases were fairly typical examples of chronic pulmonary tuberculosis. As a group they were, however, remarkable, first in that in nearly every case the distribution of the lesions in the lungs was widespread and suggestive of haematogenous rather than bronchogenic dissemination, and secondly that in spite of the considerable extent of the lesions the general condition of these patients was as a whole extraordinarily good. It was noteworthy, furthermore, that no direct relationship between the lesions existed; thus, for example, on more than one occasion in these patients gross increase in the pulmonary disorder occurred synchronously with improvement in the iridocyclitis. In three cases only, after many such examinations, was the sputum found to contain tubercle bacilli. In three

other of these patients systemic haematogenous dissemination other than in the eye, was shown to have occurred by the discovery respectively of tuberculous enteritis, tuberculous epididymitis and tuberculous ischio-rectal abscess, from which lesions tubercle bacilli were recovered.

**Group 5. Fifteen Cases—No direct evidence of Tuberculosis.
(Nos. 26-40)**

In this group there were no generalised symptoms, while investigations such as those undertaken in the previous groups (other than the Mantoux reaction) failed to disclose any evidence of pulmonary or other tuberculosis. However, the ocular condition was in general similar both as regards severity and course. In two cases (Nos. 27 and 33) X-ray of the chest revealed thickening of the pleura which corresponded with a history of pleurisy in each case. There was no evidence, however, of any kind that the pleurisy was caused by tuberculosis.

Radiological Observations

Radiological examination of the chest was made in each of the forty cases of chronic iridocyclitis.

No less than twenty-four cases could be termed "chest-positive," indicating that abnormal changes were present either in the lung parenchyma or in the mediastinal and hilar lymph nodes. Stress must be laid immediately on the fact that we rejected borderline cases of possible hilar adenopathy and considered these "negative." The differentiation between pathological and non-pathological opacities in the hilar complexes is so dependent on technical variations, and is so much a matter of personal opinion, that we felt it would be wiser to class borderline cases as "negative." It may therefore be assumed that a definite pathological lesion is present in the "chest-positive" cases.

The "chest-positive" cases may be analysed briefly thus:—

(a) Old healed fibrotic or calcified pulmonary tuberculous foci—with no change noted in the lesions over long control periods, 4 cases.

(b) Active chronic pulmonary tuberculosis—the activity being assessed by frequent clinical, bacteriological and radiological controls, 6 cases.

(c) Massive mediastinal and hilar lymph node enlargement without pulmonary changes, 2 cases.

(d) Diffuse miliary and reticular pulmonary changes, with or without hilar adenitis, 12 cases.

During the period of observation, two cases initially showing only gross hilar adenitis developed diffuse pulmonary changes and these are grouped with the last class in the table above.

The radiological appearances seen in classes (a) and (b) present no peculiar features, save those characteristic of pulmonary tuberculosis, and our main interest lies in classes (c) and (d): these fourteen cases are included in Groups 1, 2, and 3 of the clinical classification given earlier in the paper.

Radiological interpretation of the abnormal appearances observed has had to be made on theoretical grounds alone because, as stated earlier in the paper, no post-mortem study has been available. For guidance, we have turned to the relatively few published illustrations of chest radiographs in chronic pulmonary miliary tuberculosis. The fine diffuse pulmonary lesions that have been observed are very difficult to reproduce in illustrations, especially when only reductions are presented. We have therefore, felt it necessary to illustrate some of our cases by contact (actual size) reproductions as well as by reductions of the whole chest films.

In the fourteen cases under particular discussion the outstanding radiological features were, variously:—

1. Massive hilar and mediastinal lymph node enlargement.
2. Diffuse pulmonary miliary and reticular opacities.
3. Total lack of cavitation or lung contracture.

Massive Hilar and Mediastinal Adenopathy.—This is seldom observed in the common forms of chronic pulmonary tuberculosis in adults. There is little doubt that mediastinal node enlargement has to be considerable before it can be definitely appreciated radiologically. Hence, in those of our fourteen cases which showed massive adenopathy it must be assumed that the enlargement was really gross.

The type of lymphadenitis we have observed bears a very close resemblance to that seen in intrathoracic Hodgkin's disease or lymphosarcoma (see Fig. 17).

Diffuse Pulmonary Changes.—All the cases with uveo-parotitis and six other cases (Groups 1 and 2) showed diffuse pulmonary changes consisting of:—

(a) Small soft round opacities with a distribution similar to that seen in acute haematogenous pulmonary miliary tuberculosis, and (b) a reticular striation of peculiar but striking appearance, in some cases very fine and web-like, in others coarse and irregular.

With an advancing lesion, the superimposition of the different types of opacity, together with an accentuation of linear and "end-on" vascular markings from the vascular stasis, makes the radiological dissection of individual lesions impossible.

The net-like opacities appear to be most pronounced in the

juxta-hilar zones of the lungs, especially in those cases showing gross hilar adenitis. It is our impression that the lymph node enlargement precedes the parenchymal changes but this sequence was not always demonstrated. The process then tends to spread peripherally until the whole lung field is affected. Generally speaking, the grosser the nodal enlargement, the coarser the pulmonary striation and miliary foci.

These appearances bear a close resemblance to those discussed and shown by Cohn,⁷ and Hantschmann,¹⁵ Schurmann³⁴ and Hoyle and Vaizey.¹⁸ Especial attention is called to Case 1 in Hoyle and Vaizey's personal series.

It therefore seems reasonable to suggest that the predominant lesion responsible for the radiological changes observed is *lymphogenous miliary pulmonary tuberculosis*. The reticular shadowing is very probably due to the "Lymphangitis reticularis chronica" described by Schurmann.³⁴ It is impossible to prove the suggestions because of the lack of post-mortem evidence: that certain of the changes may be of haematogenous origin is likely in some cases.

Radiological Differential diagnosis.—Many conditions, some rarely seen, have to be considered in differential diagnosis when such changes as we have described are observed. For example, the radiological appearances in congestive heart failure, lymphangitis carcinomatosa, early pneumokoniosis, chronic broncho-pneumonia, Hodgkin's disease with pulmonary invasion, diffuse pulmonary syphilis, Boeck's sarcoid with pulmonary changes, and in xanthomatosis with lung involvement may closely resemble those of chronic miliary pulmonary tuberculosis. For a full discussion of the differential diagnosis, reference should be made to Hoyle and Vaizey's monograph.¹⁸

From radiological observation alone, the association between chronic iridocyclitis and chronic miliary tuberculosis in both typical and atypical forms is very striking. It must be emphasised that chronic miliary tuberculosis is a relatively rare condition and yet twelve apparent cases (six with uveo-parotid fever) are found in the investigation of forty unselected cases of chronic iridocyclitis.

The Ocular Condition

As already stated, the forty cases in this report have been collected from patients attending (1) The Hospital for Consumption and Diseases of the Chest, Brompton, (2) the Ophthalmic Department of St. Mary's Hospital, Paddington, and Moorfields Eye Hospital. From the first source came ten cases, and criticism may be made that as a consequence the proportion of cases showing intra-thoracic abnormality might be unduly increased. Whilst

this is true, it is important that they should not be omitted, for apart from their intrinsic interest, they controvert the statement that ocular disease is a great rarity in hospitals for tuberculosis.

The incidence of extra-ocular lesions in cases of chronic iridocyclitis encountered in ordinary ophthalmic practice is better illustrated in the second division. Moreover, most of these cases have been personally observed from the early phases of the ocular disease.

Of the thirty cases in this division, we have been able to watch twenty-eight for considerable periods, and these twenty-eight may be classified according to the ocular conditions as follows:—

(A) Three cases (Nos. 4-6) clinically uveo-parotitis. In two of these, the ocular disease was very severe from the commencement, blindness of both eyes ensued after a few months and there has been no recovery. The third (No. 6) ran a more chronic and relapsing course, with mutton-fat corneal deposits and opacities in the vitreous of both eyes. Improvement occurred later (after strict confinement to bed and deep X-ray treatment), and one eye has retained 6/36 vision.

(B) Thirteen cases (Nos. 8, 9, 15, 18, 21, 22, 23, 25, 33, 34, 35, 37, 38) clinically chronic cyclitis. This type of disease tends to affect young adult females. It starts insidiously and usually affects both eyes, the one often some months after the other. Gradually posterior corneal deposits appear, at first fine but soon becoming of the "mutton-fat" type: vitreous opacities are usual and may be dust-like or dense: posterior synechiae are not the rule in the early stages. Later the whole anterior uveal tract is involved: the tendency is for relapse to occur, with deterioration of vision after each attack. Some cases respond to general measures, and there is considerable variation in the clinical course, but most traverse a downhill path. In the last two decades these cases seem to have occurred more frequently.

Three of these patients are now blind, in two others the sight is very impaired: in two the issue is still doubtful, but in the remaining six vision is still excellent whilst the ocular condition has been quiescent for some time. We have reason to hope that the form of therapy which was carried out played a considerable part in the improved result in these half-dozen cases. (See section on treatment.)

Of these thirteen cases, ten were women and three were men. The lesion was bilateral in all. The age of onset was between 20 and 30 in eight, between 32 and 40 in three, whilst in the two oldest it was 46 and 50 years respectively. In six of these, X-ray findings in the chest were negative. Of the other seven, four cases showed adult pulmonary tuberculosis, one with hilar adenopathy

as well. Two showed hilar lymphadenopathy alone, and in one calcified foci were present.

(C) Five cases (Nos. 10, 13, 24, 30, 36) presented tuberculous-like masses on the iris. Two of these (Nos. 10 and 24) had solitary hemispherical protrusions affecting the peripheral part of the iris, associated with "mutton-fat" precipitates, posterior synechiae and vitreous haze (Fig. C). In both of these cases the condition has remained unilateral, the tuberculomata subsided, but the affected eyes have become blind. In one of these (No. 10) the incidence of secondary glaucoma led to excision of the eye two years and four months after the first symptoms of the disease. Microscopical examination produced evidence suggestive of tuberculosis. In one adult pulmonary tuberculosis was present, which was quiescent, in the other active lymphogenous miliary tuberculosis was found.

In three cases (Nos. 13, 30, 36) small nodules on the iris were present, these were near the pupillary margin or near the base of the iris: in two cases they had visible vessels on the surface and localised exudate in the anterior chamber. The cornea was affected by superficial vesiculation, deep haze or striation, which in one case became vascularised. After resolution good vision was regained in two cases—moderate vision in one. The chest was normal to investigation in two, but hilar lymphadenitis was present in the other case.

(D) Seven cases (Nos. 19, 20, 28, 29, 31, 33, 40) of old-standing severe recurring iridocyclitis in women. Of these six were bilateral. In all of them vision was seriously affected. Three could only count fingers at close range with their better eye; the unilateral case had only 6/60 vision on the affected side, whilst the better eye of the other three had only 6/60, 6/36, and 6/18 respectively. Their chest X-rays were negative in five cases, the other two showed calcified foci, and one of these had a definite thickening of the pleura.

(E) One case (No. 27) was a chronic unilateral heterochromic cyclitis. The chest was normal to clinical and X-ray examination.

Laboratory Investigations

A Wassermann reaction in the blood was obtained and was negative in every case.

The Mantoux reaction in each patient was in the first place tested with a dilution of 1/10,000 of tuberculin. If the reaction at that dilution proved negative, the test was repeated successively in dilutions of 1/1,000 and 1/100 until either a positive reaction or the latter dilution was attained. Control injections of the diluent were made in every case.

In Group 1 (uveo-parotitis) two cases (Nos. 1 and 5) were negative to 1/100, while the remainder gave positive reactions. It is significant, however, that the remaining four cases were all negative to 1/1,000 and only weakly positive to 1/100.

In Group 2 (chronic miliary tuberculosis without parotitis), of the six patients two were negative to 1/100, while three of the remaining four were positive to that dilution but negative to 1/1,000. In the fifth case (No. 11), in which healing had occurred and persisted for seven years, the Mantoux reaction was positive to 1/1,000 but negative to 1/10,000.

In Group 3 (tuberculous lymphadenitis) the Mantoux reaction was positive at a dilution of 1/10,000 in all.

In Group 4 (pulmonary tuberculosis) the Mantoux reaction was obtained in eight of the ten patients and was negative in two only (Nos. 18 and 23). In the remaining six positive results were obtained, usually with a dilution of 1/10,000.

In Group 5 (no other evidence of tuberculosis) the Mantoux reaction was determined in thirteen of the fifteen cases, and was positive, usually to a dilution of 1/10,000 in all.

Consideration of these results shows that in the thirty-six cases of chronic iridocyclitis in which a Mantoux reaction was performed a positive result was obtained in thirty, using dilutions up to a strength of 1/100. Since these patients were all above the age of sixteen this result is approximately what would be expected in any un-selected group of the English urban population above that age. It was of interest, and might also have been anticipated, that those cases in which clinical and radiological evidence of wide-spread disseminated tuberculosis was present tended to show relatively little or no allergic response to tuberculin when tested in this way.

Biological Tests

In two cases the anterior chamber was aspirated (Nos. 8 and 10). The aqueous was in each case then injected into a guinea-pig and the animal observed for a period of more than eight weeks, after which it was killed and examined. In neither case could tubercle bacilli be demonstrated in this way.

Biopsy

In six cases (Nos. 1, 4, 6, 9, 13, 14) enlarged subcutaneous lymphatic glands were removed. In each case the gland was divided into two halves, one half being submitted to the pathologist for section and report, while the other was ground up, a smear stained for tubercle bacilli, and an extract injected into a guinea-pig which was subsequently killed and examined. In this

way histological proof of tuberculosis was obtained in five of the above cases, while biological proof of tuberculous lymphadenitis was also obtained in two cases (Nos. 13 and 14). Detailed histological reports of two of the glands are appended below, while the appearances are also illustrated in figures A and B.

Case 4. Fig. A.—"The lymph gland contains numerous small rounded inflammatory foci. Some are almost entirely fibrous, most contain a fibrous capsule, endothelioid cells and a few lymphocytes. A few contain giant cells, and small calcified nodules, but no large areas of necrosis are present. It appears to be a very chronic healing miliary tuberculosis of a lymph gland. No tubercle bacilli have been demonstrated."

In this case, where the history and clinical course are similar to those of, for example, Nos. 1 and 9, we feel confident that tuberculosis is the underlying cause. In the following example, however, the aetiology is less certain for while tuberculosis may have caused the changes mentioned, the possibility of the diagnosis of, for example, Boeck's Sarcoid arises.

Case 6. Fig. B.—"The gland is enlarged, owing to the formation of numerous rounded nodules consisting of concentrically arranged endothelial cells. In a few instances cells with two or three nuclei are present, but most of them are rather large mononuclear cells. A few lymphocytes and eosinophiles are seen in the nodules.

No caseation or necrosis can be seen.

No tubercle bacilli have been demonstrated: a form of reticulosis is the most likely diagnosis."

The histology of glands removed in cases 13 and 14 was that of typical tuberculous lymphadenitis with caseation, and living tubercle bacilli were shown to be present by guinea-pig inoculation.

In two of the cases (Nos. 1 and 3) in which a tuberculide was present, a section of skin revealed changes typical of tuberculosis, the bacilli being seen in Case 1, while chronic inflammatory changes only were found in the skin in Case 13, which was an example of Bazin's disease. In Case 18 examination of the wall of an ischio-rectal abscess, which was treated surgically, revealed the presence of tubercle bacilli and tuberculous granulation tissue. Similarly, in Case 17, the pus from an abscess in the epididymis was shown to contain tubercle bacilli. In Case 24 a tuberculous appendix was removed.

In three patients (Nos. 16, 17 and 24) tubercle bacilli were found in the sputum after several examinations. In the remaining thirty-seven cases, however, when sputum was present, in spite of repeated and extensive searches, tubercle bacilli could not be found. This was the more remarkable since many of these patients

FIG. A.

Section of lymph node from Case 4. Low power view showing rounded inflammatory foci, some of which are almost entirely fibrous: most have a fibrous capsule and contain endothelioid cells and a few lymphocytes; some contain giant cells, and calcified debris.

FIG. B (1).

Section of lymph node from Case 6. There are numerous rounded nodules consisting of concentrically arranged epithelioid cells. Some have several nuclei, but most are rather large mononuclear cells. A few lymphocytes and eosinophiles are seen in the nodules.

FIG. B (2).

High power view of Fig. B (1) showing the numerous epithelioid cells.

FIG. C.

Case 24. Sketch showing the large inflammatory tumour of the iris. It was yellowish in colour, and had numerous vessels on the surface. Large deposits were present on the back of the cornea.

showed wide-spread pulmonary lesions which approximated to the ordinary adult type. Gastric lavage was not undertaken.

In the twelve cases of Groups 1 and 2 having chronic miliary tuberculosis, examination of the urine and faeces failed to demonstrate the presence of tubercle bacilli.

In all, therefore, tubercle bacilli were isolated by various means in seven cases (Nos. 1, 13, 14, 16, 17, 18, 24). Histological evidence in addition, added three other cases (Nos. 3, 4, 9) to the number in which co-existent active tuberculosis was proved. In two patients (Nos. 10 and 12) in which the radiological appearances of the lungs were those of chronic miliary tuberculosis, an eye was removed. Histological section of these eyes showed giant cells and chronic inflammatory changes which, since neither tubercles nor tubercle bacilli could be demonstrated, were not certainly due to tuberculosis but might well have been caused by that disease, or indeed by any other chronic inflammatory process.

Focal Sepsis

Search for focal sepsis was undertaken in every case by clinical methods, and by radiological and bacteriological means when these were suggested by the symptomatology and clinical findings. Dental sepsis, chronic tonsillitis, antritis, pharyngitis and cholecystitis were found in various patients. Wherever necessary surgical treatment was undertaken and vaccine therapy given for a prolonged period after the operation. In other patients a chronic infection of the throat, usually streptococcal in type, or the persistence of preponderating numbers of streptococci in cultures of the faeces also led to the preparation of a vaccine and its subsequent use. The response to this form of treatment will be discussed in the section dealing with therapy.

Blood counts unfortunately were obtained in only seven cases (Nos. 1, 2, 5, 8, 9, 10). They were remarkable for the fact that an increase in the mononuclear leucocytes up to a maximum of 25 per cent. in the presence usually of an otherwise normal white count was constantly found.

Treatment

Apart altogether from local symptomatic measures, the variety of treatment which has in the past been used and is still recommended for chronic iridocyclitis of the type under consideration, is evidence of the relative failure of any particular type of therapy in this disease: ultra-violet light, tuberculin, protein shock, novarsenobillon, the eradication of focal sepsis, vaccine therapy, therapeutic rest over long periods and sanatorium treatment, all have had their advocates.

In this series of cases a variety of treatments and at least one new method of therapy were employed. In some instances, moreover, patients came to us who had had the disease for several years, and had already received one or more of the above types of treatment.

Our experience, and that of many others, in dealing with tuberculosis had made us extremely cautious in advising the use of either ultra-violet light or tuberculin in the treatment of any condition in which involvement of the lungs by tuberculosis might concurrently be present. In one patient of the series (No. 18) who had until then only presented local ocular symptoms and signs, it was perhaps significant that a vigorous course of generalised ultra-violet light baths had been given before she came under our care, and the exposures had been quickly followed by symptoms and signs suggestive of the presence of pulmonary tuberculosis. Radiological investigation disclosed the presence of relatively acute pulmonary tuberculosis. The development of such a lesion is in accordance with the findings of Gosse and Erwin¹³, and others.

In five of our cases (Nos. 8, 13, 19, 28, 38) reactivation of the ocular disease seemed to have been precipitated by the use of ultra-violet light. It is also of interest that eight patients (Nos. 4, 6, 7, 13, 16, 28, 34, 38) experienced immediate and disastrous reactivity in previously quiescent ocular lesions following therapeutic injections of tuberculin before they came under our care.

The recent experience of a medical student (not included in this series) in this connection is relevant and of interest. For experimental purposes he injected himself subcutaneously with 5 minims of the purified protein derivative of tuberculin (second strength 0.05 mgm. in 1 c.c.) in a mistaken attempt to determine whether or not his Mantoux reaction was positive. He thus received a hypodermic dose of 0.015 mgm. of P.P.D. Within twenty-four hours there occurred a severe focal reaction at the site of the injection, and a generalised reaction with pyrexia. His eyes became irritable one week later, and after a few days "floaters" were observed in the visual field. A fortnight after the injection fine corneal precipitates and vitreous opacities were seen on examination. Clinically and radiologically there was no evidence of tuberculosis elsewhere in the body, and the general and local reaction subsided without event. His progress during the subsequent nine months was unremarkable, and there has been no evidence at all that permanent ocular damage has been sustained.

In spite, therefore, of favourable reports of the value of ultra-violet light and tuberculin in this disease, there is little doubt that both measures carry with them the danger of reactivation of tuberculosis within the lungs, and also in the eyes themselves.

Furthermore, within our own series, no case occurred in which there was undoubted improvement attributable to either or both these therapeutic measures. We felt, therefore, that the continued use of these two methods was unjustified.

One of us (W.D.W.B.) suggested that in view of the remarkable success which has sometimes attended the use of deep X-ray therapy in cases of tuberculous cervical adenitis, an adaptation of this method might well be of value in this disease. Since the probable focus from which, *ex hypothesi*, the tubercle bacilli most frequently gain entry into the blood stream is the lymphatic glands at the hila of the lungs, it seemed worth while to give these patients a course of deep X-ray therapy to this region.

The mediastinal and hilar areas were irradiated through two anterior and two posterior ports: fractional dosage was used, no field receiving more than 200 r units (measured at the skin) at one application. Treatment was given at 2-3 day intervals over a period of three weeks. The delivery was at the rate of 200 r per minute at 180 kilovolts.

There was no immediate reduction in the size of the nodal masses but in certain cases these masses became smaller after a latent period of 3-6 months. No febrile disturbances or unpleasant reactions attributable to the irradiation were observed. Patients receiving X-ray therapy were under in-patient observation.

In this way it was hoped that fibrosis in the infected glands might be promoted, and the chance of haematogenous dissemination in the future thereby considerably reduced. The method was used in six cases (Nos. 4, 6, 8, 9, 10, 13), and although the interval of time is as yet too short to permit accurate assessment of the value of the method, we report that the results are sufficiently encouraging to justify further extensive trial. In no case has the procedure caused any objectionable reaction, while in five cases the ocular lesion subsided and fresh activity has not occurred.

Apart from this measure, we have become convinced that by far the most important therapeutic procedure in chronic iridocyclitis is prolonged rest in bed, irrespective of whether or no consecutive pulmonary disease is present. The duration of the period of rest in bed should always exceed six weeks, and should subsequently be determined by the progress of the ocular and other lesions presented by the individual case. The activity of the lesion, as well as the general toxaemia, can well be followed by repeated determinations of the sedimentation rate when such other factors as temperature and pulse have fallen to within normal limits. Subsequently, graduated exercise and the return to normal life is best undertaken at a sanatorium and we are strongly of the opinion that any substitute for this is likely to be considerably inferior.

Ancillary methods of treatment are those devised to improve the general health, and include a generous diet, fresh air, cod-liver oil or related products of high vitamin content.

We are aware that bilateral artificial pneumothorax has been advocated in the treatment of chronic miliary tuberculosis in those cases in which the lesions predominantly affect the lungs. Preparations containing gold in various forms have also been used. Both methods may have value in selected cases, but they have not been used in the cases comprising this series.

In patients in whom the syndrome of uveo-parotitis is present, treatment of the parotid glands includes counter-irritation and deep X-ray therapy. Paresis of the facial nerve, if it occurs, may be treated with facial hook and electro-therapy to the paralysed muscles. In our experience, however, such palsies do not tend to persist.

When focal sepsis, especially in the upper respiratory tract was shown to be present, and particularly when bacteriological investigation showed that the infecting organism was a streptococcus, measures designed to eradicate the focus were instituted, a vaccine was prepared, and in some cases a prolonged course of injections given. In nine cases (Nos. 15, 20, 25, 26, 30, 31, 33, 35, 40) this method was given an extended trial. Occasionally (Cases 20 and 33) improvement seemed to result, and has persisted. In the remaining seven cases, however, relapses varying in severity sooner or later followed. In one patient (No. 31) the use of the vaccine produced a focal reaction within the eye, and it is perhaps significant that this patient had also long been a subject of chronic arthritis. In her case evidence of co-existent tuberculosis was dependent upon the radiological recognition of healed calcified foci within the lungs and hilar glands. Study of the case reports, however, shows that both the eradication of focal sepsis and the raising of immunity to the organism isolated by means of vaccine treatment failed to give results which could with any certainty be attributed to the procedure. Our experience has led us to believe that, while focal sepsis may be a factor in some of these cases, its importance in the aetiology of this disease has probably been overrated.

The local treatment of the iridocyclitis has followed the ordinary lines, namely, atropine, mydrine, heat, leeches and diathermy. Glaucomatous attacks in the more severe types and in the later stages are best relieved by paracentesis, repeated if necessary, whilst occasionally iridectomy has to be undertaken. In the experience of one of us it is well to avoid the latter if possible, as in severe cases the later tendency is for a reduction of tension to occur, and a severe reaction from an iridectomy is likely to hasten such a complication. Occasionally, however, iridectomy is unavoidable, and helps to a satisfactory result.

Schieck's treatment by the introduction of whole blood into the anterior chamber was carried out several times in case No. 6, and the result was not beneficial. It is not a method which we commend either in theory or in practice.

Results of Treatment

Since the significance of tuberculosis in these cases was realised and the patients have been treated in the manner described above, there has been an improvement in the ocular lesions. The time which has elapsed is too short for us to be dogmatic, but we feel that the change for the better is a real one.

Many of the forty cases in this series had been under treatment before rest and sanatorium therapy was instituted, and most of these had suffered very gross damage to sight. More recently several have come whilst still in the early stage of disease, and the results have been on the whole gratifying. Another group of cases comprises those which were treated on the usual lines up to the early part of 1937, when the rest, sanatorium or convalescent home and cod-liver oil regime was insisted upon. The results in these cases point to a slowing down of the active cyclitis, so that further damage has not occurred, and the vision has remained stationary or has improved.

The preceding statements may be amplified as follows:

(a) Six Cases. (Nos. 8, 9, 10, 21, 22, 27) have been treated in which the onset occurred not earlier than 1936. Of these, one (No. 22) went to a sanatorium and has not been traced since: four others, all bilateral cases, have retained so far 6/6 or 6/9 in each eye: the sixth, with a large unilateral iris tuberculoma, developed secondary cataract and glaucoma. In four of these cases, there has been some advance in the pulmonary condition.

(b) Sixteen cases (Nos. 3, 4, 5, 15, 20, 23, 24, 25, 27, 28, 29, 30, 31, 33, 35, 36, 38) treated chiefly before 1937. Of these only four have retained vision of 6/9 or 6/6; three retain 6/18, 6/24 and 6/36 in the better eye; two have 6/60 in the better eye, finger-counting in the other, whilst the remaining seven have bare perception of light, or at most finger-counting ability.

(c) Six cases (Nos. 6, 13, 18, 19, 32, 34) seemed to show improvement after the sanatorium régime had been started.

In No. 6, the cyclitis ran a severe course for two years, but since 1937, with prolonged rest in bed, etc., the eyes have been quiescent. No. 13 had recurring cyclitis for 12 years, but since May, 1938 the relapses have been mild. She has not, however, been in a sanatorium. Reference to the details in the appendix of the other cases will confirm the statement at the commencement of this paragraph.

Discussion

The outstanding finding which emerges from the study of these forty cases is that in a high proportion clinical and radiological evidence was found suggestive of the presence of tuberculosis elsewhere in the body. This result is in accordance with that of Derby and Carvill,⁹ who, in sixty-three cases of ocular disease of possibly tuberculous aetiology (phlyctenular keratitis, sclero-keratitis, uveitis and tuberculous keratitis), found pulmonary involvement in nineteen, tuberculous adenitis in twenty-one, pleurisy in three, and tuberculous mediastinal adenitis in three, while in eleven others there was evidence of tuberculosis in other sites of the body.

If forty individuals of similar age distribution to the patients of our series were chosen at random from the urban population of England, it would be expected that clinical and radiological investigation would provide evidence of tuberculosis in perhaps one or at the most two instances. Wingfield and McPherson's⁴³ findings indeed, would suggest that in such a group evidence of active tuberculosis would probably not be forthcoming.

The forty cases in this series had in common a chronic ocular lesion, but were otherwise unselected. The fact that twenty-five of these cases showed evidence suggestive of tuberculosis on clinical and radiological examination is therefore beyond the limits of coincidence, and strongly supports the view that chronic iridocyclitis is caused by tuberculosis.

It has been shown that of the twenty-five cases presenting evidence of tuberculosis elsewhere in the body, ten had the radiological and clinical features of chronic pulmonary tuberculosis. Of these ten cases, although the organism was isolated from the sputum in three only, there can be little or no question of the accuracy of the diagnosis. We are of opinion, furthermore, that the very considerable difficulty in isolating the organism, not only in cases showing typical chronic pulmonary tuberculosis but also in those others in which wide-spread dissemination had occurred, is itself of the utmost significance in regard to the pathology of chronic iridocyclitis, as will be shown.

There is evidence that many of the patients in this series exhibited responses to a Mantoux reaction suggestive of a relatively low tissue sensitivity to tuberculin. The clinical course in almost every case suggested that at the same time their immunity was, except during the phases of re-activity, as a rule high.

These findings are in agreement with those of Woods, Friedenwald and their co-workers,⁴⁴ who have shown that the extension of local tuberculous ocular lesions is associated with

hyper-sensitivity in the presence of a low immunity, while limitation and healing are associated with low tissue sensitivity and high immunity.

Garland and Thompson,¹² it will be remembered, published a review of forty-seven cases of uveo-parotitis from the literature, and concluded that this disease, originally described by Heerfordt, was caused by tuberculosis of a particularly fibrosing and non-caseating type: that it ran a chronic course, with marked tendency to spontaneous recovery, and that when death occurred, which was rare, it was due to miliary tuberculosis. In our series, of those twelve cases in which the clinical and radiological appearances suggested chronic miliary tuberculosis, tubercle bacilli or indisputable histological tuberculosis were demonstrated in four cases.

We are of the opinion that all these patients are particular examples of what may be called chronic disseminated tuberculosis, and that the occurrence of either parotitis or iridocyclitis, or both, is nothing more than an incidental feature of a generalised disease. The extent and severity of the disease would seem logically to depend on the number and virulence of the organisms discharged into the blood stream, and also upon the allergic condition and immunity of the patient at and after the time when dissemination occurs. In this group particularly, allergy was shown to be, as a rule, relatively low, while the clinical course indicated a very high degree of immunity. We suggest the hypothesis that this finding, and also the difficulty in demonstrating the organism in spite of every endeavour, may be due in these cases to the fact that when dissemination occurs these organisms are already dead, or of such low virulence that local necrosis and caseation is absent or relatively slight in the metastatic lesions.

If such a theory were true the particular glandular pathology shown in some of these cases would be explained, since it is apparently identical with that found by Innes (*loc. cit.*) in animals following the injection of avirulent or dead tubercle bacilli.

In these patients particularly the differential diagnosis includes Schurmann's³⁴ disease and Boeck's¹ sarcoid. In regard to the former (chronic miliary tuberculosis with lymphangitis reticularis), sufficient pathological evidence exists, and was indeed presented by Schurmann himself, to prove the tuberculous aetiology conclusively. The radiological appearances in eleven of our cases are similar to those presented in this type of chronic miliary tuberculosis.

The latter syndrome, first recognised by Jonathan Hutchinson and described in 1899 by Boeck,¹ was thought by the latter probably to be a localised form of tuberculosis. More or less widespread visceral lesions were shown to accompany the disease

by Schurmann and gradually an ill-defined group of disorders, including lupus pernio, lupus miliaris, angio-lupoid, erythrodermia sarcoidique, cystoid formation in small bones, and uveo-parotid fever, have been tentatively incorporated in the syndrome which is now known as sarcoidosis. It has become realised that sarcoidosis is a generalised disease of the reticulo-endothelial system, and that it affects particularly lymph structures, spleen, liver, skin, eyes, bones, lungs, salivary glands and the central nervous system. Its outstanding features are those of a chronic recurrent toxæmia, a low or complete insensitivity to tuberculin, an absence or paucity of caseation in the lesions which have otherwise a histological structure closely similar to that caused by tuberculosis, and finally, within the lesions tubercle bacilli cannot usually be demonstrated. It is known, however, that when such patients die they are very often found at post-mortem to have generalised tuberculosis. Recently, Snapper³⁷ and Scott³⁵ have reviewed the literature, have added cases of their own, and have concluded that insufficient evidence exists to prove that the disorder is a manifestation of tuberculosis, preferring to regard it as a reticulosis of unknown aetiology somewhat akin to Hodgkin's disease. A similar conclusion is tentatively announced by Pautrier,²⁸ and by Stallard and Tait.³⁹

On the other hand and equally recently, the studies of Schaumann (*loc. cit.*), Cohen⁶ and Rubin,³¹ have directed particular attention to the probably tuberculous aetiology of the disease. In many of the cases reported by these authors, Hoyle and Vaizey (*loc. cit.*), Souter³⁸ and others, tubercle bacilli have in fact been demonstrated to be present.

Of our cases, Nos. 1 to 12 inclusive could possibly be regarded as examples of (Boeck's) sarcoidosis. In five of these (Nos. 1, 3, 4, 6, 9), histological examination of either enlarged glands or skin nodules was obtained, and in four (Nos. 1, 3, 4, 9) the appearances were such that a confident diagnosis of tuberculosis was made and was confirmed by expert pathological opinion in each case. The appearance of the gland in Case 4 (Fig. A) is typical of the group. In Case 6, the histology of the excised gland was sufficiently atypical of tuberculosis to make the diagnosis a matter of opinion. The appearances are shown in Fig. B. In only one of these twelve cases could tubercle bacilli be isolated. The major clinical, radiological and laboratory findings in these twelve cases were, however, essentially the same in all, while the ocular disease differed in no important characteristic from that presented by the remainder of our patients.

While the aetiology of sarcoidosis cannot be said to be a matter of certainty, in our opinion the available evidence suggests that the disorder is a manifestation of disseminated tuberculosis. The

hypothesis that in these cases moribund or dead tubercle bacilli pass into the circulation and give rise to the generalised lesions, would well explain the particular features of this disorder.

Consideration of the Mantoux reaction in the patients of our series, is of especial interest when regard is paid to the dilution at which a positive result was obtained. It was noteworthy that when evidence of gross disseminated tuberculosis was present the Mantoux reaction tended to be either negative or positive only in the more concentrated solutions. This was also true in regard to the cases showing chronic pulmonary tuberculosis, for in these, widespread lesions were frequently associated with evidence of relatively low allergy, while sparse lesions often gave strong positive Mantoux reactions to the most dilute solution of tuberculin used.

In the group in which no clinical or radiological evidence of tuberculosis outside the eye existed, the Mantoux reaction was, as a rule, strongly positive in the lower dilutions, suggesting that in these patients tuberculo-allergy was frequently high. Woods, Burke and Friedenwald⁴⁴ have recently shown that cutaneous sensitivity to tuberculin gives a fairly reliable index of the degree of ocular sensitivity, and on this basis, together with the reports of Rich and his associates at Johns Hopkins University that allergy and immunity are two distinct processes, have recommended that if tuberculin be used in the treatment of ocular tuberculosis it should be used with a view to desensitisation rather than with a view to producing perifocal lesions which might conceivably themselves produce immune bodies. Our findings are in entire agreement with such a concept.

Summary

1. Forty cases of chronic iridocyclitis were studied with a view to investigating the importance of tuberculosis in the aetiology of the condition.
2. The clinical features, the ophthalmological features, the radiological findings and laboratory data are presented and discussed.
3. Treatment, both as regards the local lesion and the patient as a whole, is discussed in the light of the responses shown by these patients to the various methods which were employed, and these favour a prolonged rest and sanatorium régime.
4. Post-mortem examination was not possible in any of our cases and in only two was an eye excised. Blood cultures were not attempted. Clinical and radiological evidence of tuberculosis elsewhere in the body was present in twenty-five of the forty patients: tubercle bacilli were demonstrated in seven (Nos. 1, 13,

14, 16, 17, 18, 24), while histological evidence of undoubted tuberculosis following biopsy was forthcoming in nine cases (Nos. 1, 3, 4, 9, 13, 14, 17, 18 and 24).

5. The Mantoux reaction and its value are discussed at length. In thirty-six of the forty cases this reaction was performed and was positive in thirty. Analysis of these results in regard to the dilutions employed showed that when evidence of extensive dissemination was present the reaction was either negative, or else the more concentrated solutions were, as a rule, necessary to give a positive result.

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Finally, we are indebted to Sir Frederick Menzies and the authorities of the London County Council for their permission to incorporate the histological report on the eye excised in Case 12.

APPENDIX OF CASE REPORTS

No. 1. D.E., female, aged 29 years. (B.H., Dr. C. Hoyle)

Uveo-Parotitis resulting in blindness

Family and past history were without significant events. Onset with misty vision, pain in both eyes and pyrexia in December, 1932. She was admitted to St. Thomas's Hospital in January, 1933, where bilateral parotitis, splenomegaly, L. 7th nerve palsy, transient deafness, and absent knee and ankle jerks developed. A diagnosis of uveo-parotitis was made. Irregular pyrexia, progressive bilateral iridocyclitis with deterioration of vision, and amenorrhoea persisted, but the parotid swelling and the facial palsy subsided within a few weeks. The cerebro-spinal fluid was found to be normal, and the W.R. negative in this fluid and in the blood. She was transferred to a convalescent home in May, 1933, and there a course of injections of bacillary emulsion (O.T.) was given. A macular rash appeared on the legs late in May of that year. By October, 1933, she was completely blind. The course of injections was completed in April, 1934, iridectomy was performed for iris bombé. In 1936 she had an illness diagnosed as whooping cough.

She was admitted to the Brompton Hospital for investigation in December, 1937. Continued irregular pyrexia was present, as were amenorrhoea, blindness and dyspnoea on exertion. Positive signs included those of infiltration in the upper zones of both lungs, a greatly enlarged spleen, and a maculo-erythematous tuberculide on the arms and legs. She was not unduly thin. The eyes were quiescent showing a few k.p., bilateral iritic adhesions and lenticular opacities.

Mantoux reaction negative to 1/100 tuberculin. W.R. negative. Blood count normal save leucopenia (W.B.C. = 4,000 per c.mm. of which 24 per cent. were monocytes). Sedimentation rate (Westergren) = 70 mm. in 1 hr. Vital capacity 1,200 c.c. (about $\frac{1}{2}$ normal for her size). X-ray of the chest showed chronic miliary (lymphogenous) tuberculosis with enlarged hilar glands. A few minute areas of calcification were visible in the mass of glands at the left hilum. X-ray of the spleen and liver showed no calcification. X-ray of the dorsal and lumbar spine, hands and feet revealed normal bones. Sputum contained no tubercle bacilli. Urine was normal to routine tests and contained no tubercle bacilli.

Histological section of an area of affected skin showed tuberculosis of the dermis, tubercle bacilli being seen in the section. She was treated by rest in bed for some eight weeks, and subsequently returned to her home clinically unchanged.

No. 2. J.G., male, aged 20 years. (B.H., Dr. G. E. Beaumont)

Uveo-Parotitis with recovery of vision

This patient had scarlet fever in childhood. Tuberculosis was not known to have affected his family. Onset with a pyrexial illness resembling influenza in January, 1937. Cough, productive of scanty sputum persisted, and he lost weight (1 stone in 3 months). Bilateral iridocyclitis, R. > L., began in March, 1937, for which he received treatment at the Central London Eye Hospital whence in April he was transferred to a convalescent home. The ocular and general condition progressed irregularly until June, 1937, when bilateral parotitis and R. 7th nerve palsy developed. He was then transferred to University College Hospital where investigation disclosed the pulmonary abnormality which led to his admission to the Brompton Hospital in August of that year.

Examination revealed a somewhat emaciated young man. Râles were heard in the upper zone of the right lung, the chest being otherwise normal. Generalised enlargement of the subcutaneous lymphatic glands was found, but the parotid and submaxillary glands were not then enlarged, nor was the spleen palpable. Slight right facial weakness was present. There was slight impairment of vision in both eyes, more marked in the right, and here the iridocyclitis was the more severe. Circumcorneal injection, and mutton-fat k.p. and a slight vitreous haze were present in both eyes throughout his stay in hospital.

Pyrexial incidents did not occur. Sputum (six samples) contained no Tb. W.R. —ve. Sedimentation rate was normal. Blood count normal (W.B.C. = 7,000 per c.mm., of which 17 per cent. were monocytes). Mantoux +ve 1/100 O.T. X-ray of the chest showed bilateral hilar lymphadenopathy with early generalised (lymphogenous) miliary tuberculosis. X-ray of the liver and spleen did not show calcification. Biopsy was not obtained.

Therapy consisted of rest in bed for six weeks at hospital followed by seven months sanatorium treatment. He responded very well so that the ocular and generalised lesions became quiescent and have remained so ever since. Vision improved steadily and sight is not now noticeably affected. The radiological appearances in the lungs remain unchanged.

No. 3. A.H., female, aged 30 years. (S.M.H.)

Uveo-parotitis with recovery of vision

Father alive and known to have had pulmonary tuberculosis for many years. Two brothers died in childhood of tuberculous meningitis. The patient had mumps in childhood.

Onset in March, 1936, with pain and misty vision in the left eye, followed in May of that year by similar symptoms in the right eye. Vision in the left eye was said to have been temporarily lost. She was admitted to R.L.O.H. where after some weeks the ocular condition improved. Thereafter she was transferred to the London Hospital for a further six months in-patient therapy. In December, 1936, she became severely dyspnoeic and pyrexial, developed a cough and began rapidly to lose weight. The left parotid gland and the lymph glands of the neck enlarged, and she "lost the use of her left arm," tingling was felt in the forearm and hand to the little, ring and middle fingers. Thereafter the

clinical course of the illness progressed with irregular remissions and relapses in both the generalised and ocular lesions.

In August, 1937, bilateral iridocyclitis was present without severe impairment of vision. Both irides were adherent, k.p. present in both eyes, and a lenticular opacity (slight) was found in the left eye. The parotid glands were normal to palpation, but generalised enlargement of the lymph glands and spleen was found. Râles were audible all over both lungs. The heart and central nervous system were normal. Sputum —ve Tb. Mantoux reaction +ve 1/100. X-ray of the chest showed enlarged hilar glands and generalised mottling and reticulation throughout the lungs, suggestive of chronic (lymphogenous) miliary tuberculosis. (Figs. 11 and 12.)

Therapy consisted of local applications to the eyes, prolonged rest in bed followed by an equally prolonged convalescence in the country while taking cod-liver oil. Under these conditions she slowly improved and when last seen in August, 1938, little impairment of vision had resulted, the ocular lesion was quiescent, and her general condition was excellent.

No. 4. A.W., male, aged 29 years. (S.M.H.)

Uveo-parotitis ending in blindness

Past history not relevant. He had been an agricultural labourer. The patient's sister died of pulmonary tuberculosis at the age of 21 years.

Onset with pyrexia, anorexia and pleurisy in March, 1934. Three weeks later both eyes became painful and vision misty, and in June, 1934, both parotid glands became enlarged. Irregular pyrexia, anorexia, loss of weight, cough and night sweats recurred occasionally for the next four years, and during these exacerbations, further enlargement of the parotid glands occurred. In the intervals of quiescence these glands decreased in size. During this time vision deteriorated rapidly so that he had become nearly blind by May, 1935, and throughout the next four years exacerbations in the local ocular inflammation occurred.

In May and June in 1935, he was an in-patient of St. Mary's Hospital. Clinically then no abnormal physical signs were found in the chest. The spleen was enlarged, as were lymph glands in the neck, axillae and groins. Vision was reduced to the perception of hand movements. In both eyes there was typical advanced iridocyclitis, the ocular tension was normal, and at this time the left eye was red and inflamed and precipitates were present. Temperature varied between 97° and 100°, and he complained only of ocular pain and a feeling of weakness. X-ray of the teeth and sinuses was normal. Six specimens of sputum contained no tubercle bacilli. X-ray of the chest showed extensive bilateral enlargement of the hilar lymph glands, with a scattered nodulation throughout the lung fields, most marked in the right mid zone, apparently spreading out from the hila. (Figs. 1 and 2.) Blood count was normal. Urine was normal chemically and sterile on culture. Search for foci of infection revealed the presence of streptococci (viridans) in the nasopharynx, and from these a vaccine was prepared. He received a course of injections from this vaccine while at home during the next year, and after that a course of injections of tuberculin. His condition was, however, unaffected. He was readmitted in May, 1937, and was then quite blind. D'Espine's sign was then positive, but the chest was otherwise normal to clinical examination. Splenomegaly and generalised lymph gland enlargement were found. The parotids and submaxillary glands were also enlarged. The eyes were both inflamed, k.p. present bilaterally, and lenticular opacities and iritic adhesions were noted. He was occasionally pyrexial and complained of ocular pain and weakness again. Mantoux reaction +ve 1/1000. Sputum —ve Tb. A cervical gland was excised and section showed numerous small rounded inflammatory foci, some of which were almost entirely fibrous, most containing a fibrous capsule, endothelioid cells and a few lymphocytes, and some few giant cells also. (Fig. A.) Some of these foci were calcified. "The appearances suggested a very chronic healing miliary tuberculosis of the gland." (Prof. Newcombe.) No tubercle bacilli could be seen. A portion of the gland was emulsified and injected into a guinea pig. The animal was killed five months later but showed no tuberculosis. X-ray of the chest revealed similar but more advanced changes as compared with those found two

years previously. (Figs. 3 and 4.) X-ray of the spleen demonstrated enlargement, but showed no calcification. He received a course of deep X-ray therapy to the hilar glands, and rested in hospital for one month, after which he returned home to continue rest. During the next six months he took cod-liver oil regularly. He attended the out-patient department in November, 1937. The clinical signs were essentially similar. There was no active ocular inflammation. He had gained in weight and strength and reported that he had had no further pyrexia and no ocular pain.

X-ray of the chest then showed considerable diminution in the size of all the peripheral deposits and a shrinkage of the hilar glands. (Figs. 5 and 6.)

No. 5. K.B., male, aged 29 years. (S.M.H.)

Uveo-parotitis ending in blindness

Onset with fever and painless bilateral parotitis in January, 1936, followed a fortnight later by pain in both eyes, photophobia and dimness of vision. Family and past history were irrelevant.

He rapidly lost weight and strength and was admitted to St. Mary's Hospital in March, 1936. There the ocular condition was found to be typical subacute iridocyclitis, both eyes being involved. Apart from the ocular lesions, his parotid glands were both slightly enlarged as were the cervical lymphatic glands and the spleen. A vague persistent mass was palpable between the umbilicus and the right anterior iliac crest which was thought to be a mass of enlarged mesenteric glands. Persistent nausea and vomiting was a troublesome symptom which lasted irregularly throughout March. D'Espine's sign was positive, but the chest was otherwise normal to clinical examination. X-ray of the chest revealed very marked hilar lymphadenopathy without parenchymal lung disease. W.R. —ve. Mantoux reaction negative in all dilutions. Blood count normal save that mononuclears were 11 per cent. in a total white cell count of 8,000 per c.mm. During the next two months he was occasionally pyrexial. An infected right maxillary antrum was found and an antrostomy was performed. Three teeth shown clinically and radiologically to be infected were removed, and well marked marginal gingivitis received local gingivectomy. Throat swab and culture of the faeces revealed the presence of a haemolytic and viridans streptococcal infection from which a vaccine was prepared. During the next three months he received a course of injections of increasing doses of this vaccine without appreciable effect. At the same time a course of carefully graduated general ultra-violet light baths was given, while both eyes were treated with local diathermy. His general condition slowly improved. The ocular lesions, however, grew progressively more serious. He was discharged at the end of April, 1936, at which time the spleen, peripheral lymphatic and hilar glands were somewhat smaller in size. The parotid glands, however, were no longer appreciably enlarged.

Deterioration in the state of the eyes led to his re-admission in May, 1936. Cervical and axillary lymphadenopathy of the same firm painless type and equal in degree, was present. The spleen could just be felt. X-ray of the chest showed no change. Sputum —ve Tb. Blood count showed an 18 per cent. mononuclear leucocytosis but was otherwise unchanged. Mantoux reaction again —ve in all dilutions. Ocular condition worse and necessitating bilateral paracentesis. Therapy consisted of further rest, radiostoleum, and a course of injections of tuberculin. His general condition improved. He was discharged at the end of June and continued therapy as an out-patient. Weekly injections of Tuberculin (O.T. 1/10,000) were given until a maximum dose of 1 c.c. was attained, and this dosage was repeated until February, 1937.

During this time serial radiological examination of the chest showed progressive marked diminution of the hilar shadows, but in October, 1936, a diffuse irregular fine fibrosis became noticeable in the right mid and left upper zones, which increased in extent and degree slightly till January, 1937, but has since remained stationary. His general condition has remained good, though occasional slight enlargement of the lymphatic glands has occurred only later to regress. Vision is, however, now reduced to perception of light in both eyes. He has learnt Braille and has obtained regular employment. His only extra-ocular symptoms during the last two years have been occasional attacks of nausea and vomiting, and X-ray of the chest in January, 1939, is essentially similar to that of January, 1937.

No. 6. Marjorie C., female, aged 27 years. (R.L.O.H. and S.M.H.)

Uveo-parotitis resulting in severe damage to sight

Brother known to have had tuberculous cervical adenitis in childhood. Her brother-in-law died of pulmonary tuberculosis in 1937. Past history irrelevant.

Onset with bilateral parotitis in June, 1935. Generalised lymphadenitis was noticeable within a few days, and was particularly marked in the neck. Both the parotid and lymphatic glands have varied in size, but have remained enlarged ever since. Iridocyclitis started in the left eye in July, 1935, and became evident in the right eye in September. She was admitted to St. Mary's Hospital in October, when apart from the above, no abnormal physical signs were found. X-ray of the teeth and antra was unexceptionable. Faeces contained no abnormal organisms. Urine was sterile. W.R. —ve. Culture from the throat grew streptococci, and during the next two months she was given a course of injections from the vaccine thus prepared. She did not improve, and a course of generalised ultra-violet therapy was undertaken with no beneficial effect, and during the ensuing months at home, sight deteriorated further.

She was re-admitted in March, 1936, and a course of injections of tuberculin was given (doses T.R. 0.00001 to 0.0001 mgr.). She lost weight and was occasionally pyrexial and her sight continued to deteriorate. Lassitude became a pronounced symptom.

She was transferred to R.L.O.H. where on four occasions injections of her own blood were made into the anterior chambers of her eyes. No noticeable improvement resulted. Iridectomy was performed on the right eye in February, 1937, for iris bombé.

She was re-admitted to St. Mary's Hospital in March, 1937. Clinically then she was underweight and complained of cough and lassitude. The cheeks and lips were cyanosed and she was dyspnoeic on slight exertion. Generalised enlargement of the lymphatic glands was present and the spleen could just be felt. Both parotid glands were enlarged. No abnormal signs were present in the chest save that D'Espine's sign was positive. The central nervous system and heart were normal. Periods were regular but scanty. Occasional pyrexia was noticeable but no significant foci of infection were found. X-ray of the chest showed well marked hilar lymphadenopathy with chronic miliary tuberculosis of the lymphogenous type. She had no sputum. W.R. —ve. Blood culture —ve for Tb. Mantoux reaction +ve 1/1000. A cervical gland was removed and section of half showed an enlarged soft and rather tough lymph gland. "The enlargement is due to the formation of numerous rounded nodules consisting of concentrically arranged endothelioid cells. (Fig. B.) In a few instances cells with two or three nuclei are present but most of them are rather large mononuclear cells with oxyphile protoplasm and rather large and vesicular nuclei. Many of the nodules have a definite thin fibrous capsule. A few lymphocytes and eosinophiles are seen in the nodules. Although the nodules are often confluent the normal architecture of the gland is still obvious. No caseation or necrosis can be seen. No tubercle bacilli have been demonstrated and a form of reticulosis is the most likely diagnosis." (Prof. Newcombe.) The remaining half of the gland was minced and an extract injected into a guinea pig. The pig was killed six months later and showed at autopsy no evidence of tuberculosis.

The patient was kept at absolute rest while in hospital and improved symptomatically. Furthermore, a course of deep X-ray therapy to the hilar glands was given. The ocular condition slowly improved and she was discharged in May. She has attended the O.P.D. at St. Mary's at intervals since. There has been no evidence of fresh activity in the eyes and sight has improved as is shown. She has gained more than a stone in weight, and her general condition is good. Radiological control of the pulmonary condition showed that a definite increase of parenchymal lesions occurred in December, 1937, and this lasted till May, but that since that time progressive improvement has occurred, so that by December, 1938, the hilar and paratracheal glands were smaller and the peripheral shadows much smaller and harder in type.

OCULAR COURSE

When first seen in July, 1935, the left showed k.p. and by October the R.V. was 6/12, the L.V. 6/24, with mutton-fat deposits on the L. cornea, and vitreous opacities. After courses of vaccine and ultra-violet therapy during three months, there was little change until a further relapse occurred in February, 1936, with gross k.p. in each eye. The vision in March was 6/18 and 6/60, and in May 3/60 in the R., finger counting in the L. at $\frac{1}{2}$ metre. After tuberculin and Schieck's treatment (own blood into anterior chamber) there was further deterioration so that in December, 1936, R.V. was hand movements, and L.V. was fingers at 1 metre. In February, 1937, R. iris bombé necessitated iridectomy but this eye degenerated. In March, 1937, the tension was low in both eyes and the left vision was fingers at 1 metre. In April and May (during a period of strict confinement to bed) the deep X-ray treatment was carried out. In January, 1938, the eyes were quiescent and L.V. was 6/36. In June, 1938, the R.V. was p.l., tension plus: the L.V. was 6/36, tension normal, no k.p. In December, 1938, the eyes were quiescent.

No. 7. G.H., male, aged 24 years. (B.H., Dr. L. S. T. Burrell)

Chronic miliary tuberculosis with recurring iridocyclitis ending in blindness

Onset with pain, redness and dim vision in the left eye in October, 1933, followed a week later by similar symptoms in the right eye.

Since the onset, the ocular lesion has been progressively but irregularly active and has produced blindness.

He complained of no other symptoms and had had no other serious illness. Family history was not significant. He was treated at home with local applications to the eyes for eight months but the deterioration in vision led in June, 1934, to an X-ray examination of the chest being made. It showed considerable enlargement of the hilar glands and generally increased fine markings apparently spreading out into the lungs from the hila.

He was admitted to Brompton Hospital in June, 1935, when apart from the ocular symptoms he had no complaints, and there were no abnormal signs in the lungs or elsewhere other than in the eyes. Sputum —ve Tb. (10 tests.) He was apyrexial throughout stay in hospital. Mantoux reaction —ve in all dilutions. W.R. —ve. Enlargement of the parotid and lymphatic glands, and of the spleen was not found. E.S.R. = 9/200 in 1 hr. X-ray showed enlarged hilar glands and a rather coarse mottling throughout both lungs, suggestive of chronic miliary tuberculosis. He was transferred to Frimley where he received sanatorium therapy for two months, but continued indiscipline led to his discharge.

Subsequently, while his general condition continued to be good, the eyes deteriorated and he became blind. X-ray of the chest in July, 1936, was similar to that in 1935 save that all shadows were harder in character and the hilar glands smaller, while in January, 1937, the clinical and radiological appearances were reported as being essentially unaltered.

OCULAR DETAILS

October, 1933. Attacks of mistiness of vision commenced.

June 6, 1934. R.V. 6/18. L.V. 6/9: cyclitis: post. syn.

July 3, 1935. R. and L. mutton-fat k.p. post. syn.: gelatinous nodules on irides. (Mr. Stallard.)

January 5, 1937. Report from Ipswich: Eyes, marked injection. R. pupil occluded: L. pupil partially occluded. Blind.

No. 8. D.C., female, aged 30 years. (R.L.O.H. and S.M.H.)

Bilateral cyclitis. Worse after dental extractions and U.V.L. therapy;

improved remarkably after deep X-ray therapy to hilar glands

? *Chronic miliary tuberculosis*

?? *Boeck's Sarcoid*

Personal and family history without significant events. Onset September, 1936, with "pertussis" during which blurred vision and pain began in the left eye. Three weeks later similar symptoms started in the right eye. The cough and

malaise associated with the fever decreased after about one month, but both eyes steadily became worse. Complete dental extraction was undertaken in December, 1936, and this was followed by an exacerbation in the ocular lesions which led to her admission to St. Mary's Hospital in January, 1937. She then had a slight unproductive cough, and had lost nearly a stone in weight. Clinically, apart from the ocular lesions, and a positive D'Espine's sign, no abnormality was found. Mantoux reaction 1/10,000 +ve. W.R. -ve. Sedimentation rate 10/200 in 1 hr. X-ray of the chest showed very marked enlargement of the hilar and paratracheal lymph glands without definite pulmonary disease. (Fig. 17.) Radiograms of the long bones, hands and feet were normal. Blood count was within normal limits. One specimen of sputum was obtained, but no tubercle bacilli could be found. A specimen of the aqueous (obtained by paracentesis), and a specimen from a gastric lavage were injected into guinea pigs. Post-mortem on these animals eight months later showed no evidence of tuberculosis.

Therapy consisted of two month's rest in bed, general ultra-violet light baths and local measures to the eyes. The ultra-violet light treatment was continued for three months as an out-patient. During this time her general condition was excellent and she gained a stone in weight. The ocular lesion however, grew steadily worse. She was re-admitted in June, 1937. D'Espine's sign was still positive, and the clinical and radiological condition of the chest was the same as that shown six months before.

She received a course of deep X-ray therapy to the mediastinal glands together with a month's rest in bed. She returned home to continue rest there and has reported at intervals as an out-patient since. The ocular condition has steadily and considerably improved. Her health has remained excellent. Serial X-ray control shows marked reduction in the size of the mediastinal glands so that they are now only slightly larger than is normal. There appeared, however, a fine miliary spread throughout both lungs, most marked in the left lower zone. (Fig. 18.) She was last seen in April, 1939, when clinically no abnormality could be found, in the lungs or elsewhere, and the ocular lesion was apparently healed. The radiological appearances were, however, unaltered.

OCULAR COURSE

November 16, 1936. R.V. 5/12, L.V. 5/12 partly. B.E. slight injection; fine k.p., fine vitreous haze. Atropine. Heat.
 December 31, 1936. K.p. worse: pupils dilated.
 January 24, 1937. R. 6/36, L. 6/24, k.p. worse.
 March 19, 1937. R. 6/60, L. 6/60, k.p., vitreous haze.
 June 18, 1937. R. 3/60, L. 3/60. T. Full, corneal oedema, gross k.p., gross vitreous opacity.
 July 16, 1937. R. 3/60, L. 3/60.
 October 15, 1937. R. <6/60, L. 6/36, k.p., eyes white.
 February 18, 1938. R. 6/18, L. 6/9, remains of k.p., vitreous opacities.
 May 20, 1938. R. 6/12 pt., L. 6/9, eyes quiet.
 April 28, 1939. R. 6/9, L. 6/6 pt., health excellent.

No. 9. C.S., female, aged 34 years. (S.M.H.)

Iridocyclitis, severe in R., slight in L., responding well to rest and sanatorium treatment; later advance of miliary tuberculosis within the lungs

Family history irrelevant. The patient had worked at a sanatorium as a maid for eighteen months at the age of 21 (1924).

Onset with misty vision and pain in both eyes, more marked in right in February, 1937, led to her admission to hospital. Loss of weight (1 stone in three months), an unproductive cough, scanty periods and general malaise were associated symptoms. At this time there were no abnormal physical signs save those in the eyes. W.R. -ve. Sputum -ve for Tb. X-ray showed bilateral hilar lymph gland enlargement, and vascular congestion in otherwise normal lung fields. Mantoux reaction +ve 1/10,000. Blood count was not remarkable save that it showed 18 per cent. mononuclears out of a total white cell count of 5,600 per cu. mm. While in hospital, thrombosis of a retinal vein in the right eye occurred. Local therapy to the eyes was supplemented by rest in bed,

cod-liver oil and malt, and a course of deep X-ray therapy to the hilar glands. Controlled radiological examination showed that the hilar glands decreased in size over a period of two months, and they have remained unaltered since. She had a month's convalescence at a convalescent home and returned to work as a domestic servant in June, 1937.

She attended O.P.D. regularly and the ocular condition which had greatly improved continued slowly to heal. She continued well till January, 1938, when lassitude, amenorrhoea, and an unproductive cough developed. The cervical and inguinal glands enlarged, and she lost a stone in weight. X-ray of the chest in February of that year was unchanged but her condition failed to improve. In April, 1938, X-ray showed widespread diffuse reticular shadowing throughout both lungs, although the hilar glands remained within normal limits. (Figs. 15 and 16.) She was re-admitted. E.S.R. 45/200 in 1 hr. Sputum —ve Tb. on two occasions. Blood count as before was unremarkable save that a 16 per cent. mononuclear leucocytosis was present. Mantoux reaction 1/10,000 +ve. Occasional slight pyrexia was present at first, but rest in bed rapidly restored normality in that respect. She gained in weight and scanty menstruation began once more in June. The ocular condition continued completely unaffected by the generalised illness through which she was passing. An enlarged subcutaneous lymph gland was removed and on section was reported to show "typical chronic granulomatous tuberculosis of a lymph gland." Special staining failed to show tubercle bacilli.

Her general condition continued to improve and she left hospital for sanatorium in July. There her progress was uninterrupted and she began work again in November, 1938. She was last seen in January, 1939, when she looked and felt well. The ocular lesion was then quiescent, and X-ray of the chest showed essentially the same condition as that which obtained in April, 1938.

OCULAR COURSE

March, 1937. Vision misty.

March 30, 1937. R. c̄ gl. 6/9, L. c̄ gl. 6/6. R.E. gross mutton-fat k.p., with two or three small gelatinous swellings on pupillary margin of iris below. L.E. some k.p.

In-patient. April 12, 1937, until June 1, 1937. *Bed. Ol. Morrh. deep X-ray therapy* from April 16 until May 4.

May 9, 1937. R.T. +, phlebitis of superior nasal retinal vein (followed varicose vein injection).

Sanatorium. June and part of July.

July 16, 1937. R.V. c̄ gl. 6/12, L.V. c̄ gl. 6/9. Residue of k.p. in R., none in L.

November 12, 1937. R.V. c̄ gl. 6/9, L.V. c̄ gl. 6/6 partly. Vitreous clear. No k.p.

January, 1939. Eyes quiet. R. +3 Sph. = 6/9. L. +2.5 Sph. = 6/9.

No. 10. D.P., female, aged 21 years. (S.M.H. and R.L.O.H.)

Severe unilateral iridocyclitis with a large iris tuberculoma and degenerative changes in the eye
Chronic miliary tuberculosis

The patient had erythema nodosum at the age of nineteen. Family history was not significant.

Onset with misty vision and pain in the right eye in June, 1937. There were no generalised symptoms and the left eye was and has remained unaffected. She was treated as an out-patient at R.L.O.H. Tonsillectomy was performed in August, 1939, and subsequently she had two months' convalescence at Broadstairs. The condition of the right eye did not improve, however, and she was admitted to St. Mary's in December, 1937. Apart from the ocular lesion she then presented no abnormal physical signs, the lymph glands and spleen were not enlarged, and her general condition was excellent. W.R. —ve. Mantoux reaction 1/1,000 +ve. She had no sputum, and a twenty-four hour specimen of urine contained no tubercle bacilli. Sedimentation rate was 15 mm. in 1 hr. X-ray of the chest revealed generalised vascular congestion throughout the lungs.

The heart and mediastinum were normal. In the middle zone of the right lung, multiple fine scattered non-vascular opacities were apparent. During the next two months, while resting in bed, she was occasionally slightly pyrexial (99.8°). Blood count was not remarkable save that a leucocytosis of 1,400 cells per c.mm. was present, and of this 9 per cent. were mononuclears, 75 per cent. were polymorphs, 3 per cent. eosinophils, and 13 per cent. lymphocytes. Her general condition, however, continued to be good, and the sedimentation rate fell to 3 mm. in 200 in 1 hr. X-ray of the chest showed no definite change to have occurred. A specimen of the aqueous taken from the right eye was injected into a guinea pig. The pig was killed six months later and was found to be normal. The patient returned home and reported to the out-patient department at intervals. Her general condition continued to be excellent. X-ray, however, in May, 1938, showed that a spread of the fine opacities had occurred, the appearance now being that of lymphogenous miliary tuberculosis. The hilar glands were not visibly enlarged.

In May, 1938, she became pregnant, and this was confirmed with certainty in July. She was re-admitted, and the pregnancy was terminated by hysterotomy. No evidence of intra-abdominal tuberculosis could be seen at the operation. After a few days pyrexia she made an uninterrupted recovery, leaving hospital at the end of August. X-ray then showed slight but definite retrogression in the pulmonary lesions. She continued in good health, her weight remained constant, and the affected eye quiescent while resting quietly at home until October, 1939, when glaucoma developed and necessitated enucleation.

Ocular details.—Gross precipitates were present in the R.E. from the start in June, 1937; a large tuberculoma on the lower part of the iris was noticed in December, 1937, when vision was reduced to fingers at 1 metre. After a paracentesis, iris bombé developed, and iridotomy and iridectomy were necessary in January, 1938. The tuberculoma shrank after the paracentesis. Congestion gradually diminished but the tension, low in April, increased at the end of the year, by which time the lens was opaque. The eye was removed on account of pain and raised tension in October, 1939. Section of the eye revealed the usual peripheral anterior synechiae, and the cupping of the optic disc associated with glaucoma. The choroid was free from inflammatory changes, but the iris and ciliary body showed atrophy and fibrosis. Near the base of the iris were several giant cells suggestive of tuberculosis but there was practically no active cellular infiltration in the surrounding area. No caseation was detected nor could tubercle bacilli be demonstrated.

No. 11. M.P., female, aged 47 years. (B.H., Dr. T. Nelson)

Severe bilateral iridocyclitis with chronic miliary tuberculosis resulting in healing of all the lesions

No relevant past or family history. Onset in April, 1928 (aged 37 years) with redness, dim vision, and pain in the right eye, followed a week later by similar symptoms and signs in the left eye. During the remainder of this year, and the next, the ocular condition was intermittently active and there occurred also phases in which pyrexia was accompanied by headaches, loss of weight, night sweats, and pain in the limbs. She was admitted to Brompton Hospital in December, 1929, and there was occasional pyrexia during the next eleven weeks while resting in bed. Râles were audible posteriorly over the upper zones of both lungs. Enlargement of lymphatic or parotid glands was not present, and the spleen was not palpable. Both eyes were red and painful during her stay in hospital, though slowly improving. K.p., present. At her discharge right vision was reduced to perception of light, and left vision was noted as "very poor." Sputum —ve for Tb. on three occasions. W.R. —ve. Mantoux reaction was not obtained.

X-ray of the lungs showed chronic miliary tuberculosis (Fig. 13). She was treated by rest in bed, by a course of injections of very small doses of B.E. (0.1 c.c. of 1 in 10,000,000 increasing gradually to 0.5 c.c. of the same strength solution) over a period of four months, and by sanatorium treatment at Frimley for some five months. During this time she slowly improved, the ocular lesion finally becoming quiescent by June, 1930, by which time vision had greatly

improved. She returned to her home in the Autumn of 1930, resumed work as a schoolmistress, and has continued to lead a normal life since. In December, 1937, she had no symptoms, and examination disclosed the following: Eyes no evidence of active disease and vision was good in both. Old iritic adhesions present in both, lenticular opacity (small) in left. K.p., not present. No abnormal signs in chest or elsewhere. Sputum —ve. E.S.R. = 6/200 in 1 hour. X-ray of the chest showed slightly emphysematous lungs with a few peripheral calcified foci only remaining to mark the site of the previous miliary tubercles (Fig. 14).

No. 12. D.E., male, aged 16 years. (B.H., Dr. A. Hope Gosse)

*Unilateral iridocyclitis, resulting in enucleation
Miliary tuberculosis with recovery*

Family and past history irrelevant. Onset with pyrexia, loss of weight, redness of left eye and dimness of vision. Treated at Royal Eye Hospital, Swanley, and St. Olave's (L.C.C.) Hospital. The left eye was enucleated on March 5, 1936, section showing chronic inflammation of the iris and ciliary body.

X-ray of the chest in March, 1936, showed multiple fine opacities in all areas of both lungs, and a diagnosis of miliary tuberculosis was made. He was transferred to the Brompton Hospital in August, 1936, and there the remaining (Rt.) eye was found to be normal, while clinically the lungs presented no abnormal physical signs. There was no enlargement of the lymphatic, or parotid glands, nor was the spleen palpable. A maculo-erythematous tuberculide was present on both forearms and wrists. Four specimens of sputum contained no tubercle bacilli, and a further specimen was injected into a guinea pig with negative results. During his stay in hospital, severe bouts of pyrexia occurred, accompanied by nausea and vomiting, sweating and loss of weight. X-ray October, 1936, showed persistent fine mottling throughout the lungs, without demonstrable enlargement of the hilar glands. He was transferred to sanatorium and remained there until October, 1937, having made slow but steady progress. During this year, X-ray showed progressive clearing of all the pulmonary lesions, and by October the radiogram of the chest could be classed as within normal limits. He was seen at another hospital in July, 1938, when his general condition was good and clinically and radiologically the lungs were normal. The right eye also had remained unaffected.

No. 13. M.S., female, aged 35 years. (S.M.H.)

*Bilateral iridocyclitis, severe in one eye
Nodules in iris. Bazin's disease
Tubercle bacilli in glands*

The patient showed Bazin's disease with recurring ulceration of legs, which started in 1920 at the age of 18 years, and had recurred irregularly, usually in the summer, since.

Glands were removed from the neck at the age of 4 years, and again at 11 years. A further gland was removed at the age of 34.

She had *ultra-violet light* baths and *tuberculin* injections at the age of 23 years: 4 months after the injections, L. iritis commenced. R.E. affected one year later.

September 8, 1933. R.V. 6/5, small post. synechiae.

L.V. <6/60; many post. synechiae, no k.p., eye quiet.

February 9, 1934. L.V. 6/36 (1).

October 21, 1937. R. 6/5, L. 6/60. L. vitreous haze: slight injection.

January 20, 1938. L. recurring inflammation.

In-patient S.M.H., March 14, 1938, to April 2, 1938. Family history not significant. No abnormal signs were present in the chest. Chronic cervical adenitis, and bilateral typical Bazin's ulceration of the legs were present.

X-ray of the chest showed slight calcification in right hilar lymph nodes and no pulmonary infiltration.

March 21, 1938. Pyrexia slight: occasional. W.R. negative. Sedimentation rate—14 mm. 1 hour, 32 mm. 2 hours. Mantoux positive at 1/10,000. W.R. —ve.

In-patient S.M.H., May 5, 1938, to June 3, 1938.

May 6, 1938. R.V. gl. 6/6 (2); slight injection; post. synechiae; fine k.p., iris vascular, small nodule on periphery at "8 o'clock," with large vessels on surface. L.V. bare p.l.

May 18, 1938. Rest: Ol. Morrh. X-ray therapy to hilar and cervical glands. This was carried out between May 19 and June 1.

Biopsy of a cervical gland was performed on March 31, 1938, and showed chronic typical granulomatous tuberculosis of lymph gland. An emulsified fragment of the gland was injected into a guinea pig which was killed on June 6, 1938, and was found to be riddled with tuberculosis, the regional glands being caseous and broken down, and the spleen, lungs and liver were full of tubercles.

In October, 1938, she was reported to be living quietly by the South Coast, the eyes being quiescent. In April, 1939, however, activity had recurred both in the left eye, and in the ulceration in the left leg. X-ray examination of the chest at this time, however, revealed no change. The cervical glands also were clinically unaltered. The vision was 6/5 in the R., fingers at 1 metre in the L.

**No. 14. A.W., female, aged 34 years. (R.L.O.H. and B.H.,
Dr. J. L. Livingstone)**

Bilateral recurring iridocyclitis, severe, with tuberculous lymphadenitis

Admitted to R.L.O.H. (Mr. Foster Moore) in 1932, with scleritis and iridocyclitis R. and L. Right eye had nebula, dating from infancy. L.V. 6/24.

1933, January to August, attended twice monthly with peri-corneal injection, k.p., and fluctuating vision, L.E. Treatment, Potass. Iodide, Sod. Salicyl. and Hyoscine.

1934, February, L.V. 6/12; 1936, September, R.E. injected. Attended monthly to February, 1937. R.E. k.p. +++ Post. syn. T.n., V. Hd. mts. L.E. injected: post. syn. K.p., V = 6/9.

1937, April, admitted R.L.O.H. for L.E. treatment.

1937, May 17, discharged. R.E. white. C.F., old k.p. L.V. 6/12 partly, slight flush: confluent k.p., organised exudate at bottom of a.c. T.n.

May 30. R. iridectomy below.

June 21. R.V. = C.F., L.V. = 6/18 pt., white: mutton-fat k.p.

July 14. L. fresh k.p., injected.

The patient was admitted to the Brompton Hospital in July, 1937, giving a history of chronic iridocyclitis in both eyes since 1927, and stating that she had been conscious of a swelling on the left side of the neck for some months. Family and personal history was otherwise irrelevant. A chain of soft adherent glands was found extending downwards from the angle of the left jaw, but apart from this and the ocular condition, there were no abnormal physical signs. There was no evidence of focal sepsis in the mouth or throat. X-ray of the chest revealed normal lungs. Sputum —ve Tb. (twice). W.R. —ve. Mantoux reaction +ve 1/10,000. Sedimentation rate (Westergren) 5/200 in 1 hour. The lowest of the abnormal chain of cervical glands was removed and section showed typical tuberculous lymphadenitis with caseation toward the centre of the gland. Apart from local measures to the eyes, therapy consisted of rest for a prolonged period at home, together with the administration of cod-liver oil.

No. 15. S.M., male, aged 38 years. (R.L.O.H. and S.M.H.)

Mild bilateral cyclitis, recurring

Family history not relevant. He had suffered from chronic cervical and axillary lymphadenitis for years. Seen February 10, 1937, when clinically there were no abnormal physical signs to be found in the chest. Hard enlarged matted glands were palpable in the neck and left axilla. Mantoux reaction +ve 1/10,000. X-ray of the chest revealed no abnormality in the lungs or mediastinum. W.R. —ve.

His eyes were under observation from 1926 until the end of 1938. In 1936 at the age of 25 years the vision was first affected with active iridocyclitis in the R.E., two spots of k.p. in the L.E. This subsided in three months, but relapses occurred in the R.E. in 1928 and 1930 with well marked k.p. After tonsillectomy in April, 1931, further relapses took place in May, 1931, and in February, 1932. In the latter, the corneal deposit was of the mutton-fat variety, but improvement followed in two months' time. In 1934 both eyes were affected with impairment of vision. After a stay in a convalescent home resolution occurred and in six months vision was R. 6/6 partly, L. 6/6. In 1937, after dental extractions, three relapses of the same kind attacked the left eye and one attacked the right eye. The left vision, however, recovered to 6/9, following a course of novarsenobillon. In December, 1938, however, a further relapse in the left occurred after influenza, and a vaccine prepared from a nasopharyngeal swab did not sensibly improve his condition.

No. 16. O.D., female, aged 33 years. (B.H., Dr. F. H. Young)

Unilateral chronic iridocyclitis and chronic pulmonary tuberculosis

No significant family history. Onset probably with iridocyclitis in the left eye at the age of four years. Recurrent pains and redness of left eye ever since with loss of vision. From the age of fifteen she had attacks of asthma associated with chronic bronchitis. In January, 1937, however, lassitude, persistent cough and sputum, loss of weight and dyspnoea led to her attending Brompton Hospital. There clinical signs suggestive of chronic bronchitis and emphysema were found, but X-ray of the chest revealed extensive infiltration of both lungs without excavation, the appearances suggesting haematogenous dissemination. A calcified focus was present in the left upper lobe. Eight consecutive specimens of sputum contained no demonstrable tubercle bacilli. W.R. —ve. Sedimentation rate (Westergren) was 54 mm. in 1 hour. Mantoux reaction was not obtained. The parotid and lymphatic glands were not enlarged, nor was the spleen palpable.

She was for five months treated at sanatorium with improvement both in the ocular and the general condition. Since June, 1937, she has attended the out-patient department at intervals while working as a secretary. The pulmonary lesions have remained essentially static, but in October, 1938, sputum for the first time contained tubercle bacilli. The ocular lesion has only occasionally been slightly active during the last two years. The right eye is normal; the left has k.p., and an opaque lens, while vision is reduced to perception to light.

No. 17. R.B., male, aged 24 years. (B.H., Dr. M. Davidson)

*Unilateral uveitis, occurring one month before death from pulmonary tuberculosis
Other haematogenous tuberculous metastases present*

No significant family history. Onset of cough and hoarseness, 1927, aged 15 years. No other symptoms. Admitted to B.H. for 2/12. Bilateral signs of infiltration present. Sputum —ve Tb. Tuberculous laryngitis present. X-ray; infiltration upper and middle zones of both lungs. Thence to sanatorium for 3/12, then returned to work. Cough continued. Pleurisy 1932 (aged 20 years).

1933. Developed an ulcer on the hard palate. W.R. —ve. Sputum —ve. X-ray: rarefaction of bone between incisors due to bone destruction. Biopsy of edge of ulcer showed tuberculous granulation tissue. Larynx better. Chest: Signs *in statu quo*. X-ray, R. lung: shadows harder, L. lung, further infiltration.

1934. Swelling developed in L. scrotum following trauma, and the left testis was removed. Biopsy: Tuberculous epididymitis. Tb. in pus from wound. Sputum —ve. Chest: clinically unaltered. X-ray: further fibrosis and no further infiltration. Ulcer of palate nearly healed. Tuberculous laryngitis still active.

1935. Sputum —ve. General condition good. Prostate and L. seminal vesicle enlarged and tender. X-ray therapy to these.

1936. Cough +. Sputum +. Loss of weight and appetite. Sweats +. Fresh ulcers of palate and lips following dental extraction.

1937. Pharynx, larynx, and mouth all became much worse. Lungs — advancing terminal disease clinically. X-ray: Fibrosis and further infiltration both lungs with cavitation in right mid zone.

March, 1937. Swallowing was by now intolerable. Both superior laryngeal nerves injected with alcohol, with some relief of pain.

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April, 1937. Rt. eye. Ciliary injection and iritic adhesions. Vitreous opacities present. Vision = hand movements. Left eye normal. (Seen by Mr. C. Dee Shapland.)
Died May, 1937.

No. 18. F.H., aged 31 years. (R.L.O.H., L.H., S.M.H., and B.H.)

Mild bilateral recurring cyclitis, with pulmonary tuberculosis

No relevant family history. The patient had pneumonia at the age of eight years, and mumps at 10 years. At the age of 24 she was investigated at a voluntary hospital for loss of weight and no definite cause was found. X-ray of the chest at this time was normal.

Onset with "influenza" aged 25 years, followed by iridocyclitis in the right eye. Fluctuating course for four years, with k.p. in both eyes, but with no general symptoms. When 29 years of age, she developed a fistula in ano and felt "run down." Synchronously the ocular condition became worse. She received ultra-violet light general baths at another hospital, but her general condition deteriorated. Examination then (1937) revealed pyrexia with flushing. Râles could be heard over the upper part of the right chest, but physical examination was otherwise negative apart from the ocular condition which was now bilateral. W.R. —ve. Mantoux reaction —ve 1/10,000. X-ray of the chest showed infiltration in the upper lobe of the right lung with some fibrosis. Sputum contained no tubercle bacilli.

She was transferred to the Brompton Hospital where she reacted well to some ten weeks' rest in bed. The ocular lesion became quiescent, while the pulmonary condition became clinically and radiologically arrested. Eight consecutive specimens of sputum contained no tubercle bacilli. Sedimentation rate varied from normal limits to 20 mm. in 200 in 1 hour. Mantoux reaction —ve 1/100. She was transferred to sanatorium in October, 1937, and during the next eleven months there progressed irregularly. She received a full course of sanocrysin during this period without noticeable benefit. During this interval the ocular lesions became quiescent and have in fact remained healed ever since. The pulmonary disease has, however, slowly and irregularly spread throughout both lungs and she now (1939) has bilateral infiltration and fibrosis in both lungs without excavation. During the last eighteen months she has worked part-time, and has been free of symptoms and gained weight in spite of the advancing pulmonary disease. Sputum has been consistently free of tubercle bacilli and the signs in the chest have always been minimal. Glandular enlargement has never been a feature of the case. Vision is 6/9 in each eye.

No. 19. E.P., female, aged 50 years. (S.M.H.)

Unilateral kerato-iridocyclitis, improving after residence in Convalescent Home

Family history irrelevant. Onset with anterior choroiditis in left eye at the age of 18 years, followed by kerato-iritis in the right eye at the age of 47 years. She had been a subject of flatulent dyspepsia for more than 20 years.

Clinical examination revealed no abnormal signs over the lungs. Sputum on three occasions over two years contained no tubercle bacilli. Mantoux reaction 1/1,000 +ve. X-ray of the chest revealed two calcified foci of healed tuberculosis in the upper part of the right lower lobe, but was otherwise normal. Extensive search for foci of infection showed the presence of excess streptococci in the faeces, and clinical and radiological evidence of chronic cholecystitis. X-rays of bones of hands and feet were normal. She received a prolonged course of vaccine therapy, and biliary drainage (medical) during 1937, and 1938. During the former year she also had some four months at a convalescent home. Symptomatically and clinically as regards the ocular lesion, definite improvement occurred. The left eye had always been defective, but with the right, in spite of a nebula, she was able to read J.4 type, and the eyes have remained free from inflammation, although at one time (July, 1936) gross k.p. was present in the right eye.

FIG. 1.

CASE 4. March, 1936. Gross hilar and mediastinal adenitis with generalised chronic pulmonary miliary tuberculosis: ? mainly lymphogenous.

FIG. 2.

CASE 4. Contact study of right upper zone of Fig. 1.

FIG. 3.

CASE 4. February, 1937. Fewer miliary foci but reticular lymphangitis remains.

FIG. 4.

CASE 4. Contact study of right upper zone of Fig. 3.

FIG. 5.

CASE 4. October, 1937. Considerable clearance of diffuse pulmonary changes. Well marked residual hilar and central node enlargement.

FIG. 6.

CASE 4. Contact study of right upper zone of Fig. 5.

FIG. 7.

CASE 6. May, 1937. Hilar and paratracheal node enlargement with early lymphogenous spread into lung.

FIG. 8.

CASE 6. Contact study of left upper zone of Fig. 7.

FIG. 9.

CASE 6. May, 1938. Generalised pulmonary miliary tuberculosis, probably lymphogenous.

Fig. 10.

CASE 6. Contact study of left upper zone of Fig. 9.

FIG. 11.

CASE 3. Chronic pulmonary miliary tuberculosis with unequal pulmonary involvement.

FIG. 12.

CASE 3. Contact study of right upper zone of Fig. 11.

FIG. 13.

CASE 11. December, 1929. Chronic pulmonary miliary tuberculosis, probably haematogenous.

FIG. 14.

CASE 11. April, 1937. Complete clearance of miliary lesions except for a few minute calcified foci.

FIG. 15.

CASE 9. Generalised chronic pulmonary miliary tuberculosis. Six months previously this patient showed only borderline hilar node enlargement, without pulmonary changes. Probably haematogenous spread.

FIG 16.

CASE 9. Contact study of right upper zone of Fig. 15.

FIG. 17.

CASE 8. February, 1937. Massive hilar and mediastinal node enlargement.

FIG. 18.

CASE 8. August, 1938. Recession of lymph nodes. Spreading pulmonary lymphangitis.

No. 20. K.J., female, aged 55 years. (R.L.O.H. and S.M.H.)

Mild bilateral uveitis, apparently responding to vaccine therapy

Onset with uveitis at first in the right eye and soon after and more severely in the left eye at the age of thirty years. At irregular intervals the ocular lesion was active in both eyes during the next twenty years. Neither at the onset nor subsequently, were there generalised symptoms associated with the ocular lesion. She had had a "nervous breakdown" with considerable loss of weight at the age of twenty-six years, but no more accurate diagnosis was made at the time. At the age of forty-eight years she had pleurisy without effusion on the right side. Phthisis or other tuberculosis was not known to have occurred in her family.

She was transferred from R.L.O.H. to St. Mary's Hospital in December, 1933. Clinically then apart from the ocular condition, no abnormality was found on examination. Bacteriological investigation disclosed a streptococcal infection in the stools, and *B. coli* bacilluria. A vaccine was prepared from these sources, no other foci of infection having been found. W.R. —ve.

She responded well to a prolonged course of injections during 1934, and in fact the inflammation previously present has remained entirely quiescent in both eyes ever since. Re-examination of the stools in 1935 showed a heavy infection with *B. epidemic* jaundice and streptococci, a fresh and stronger vaccine was made, and the injections were continued. In 1936, further examination of the stools revealed no significant infection, and this type of therapy was discontinued.

In 1937 clinically, apart from the evidence of the healed ocular disease, she presented no abnormal physical signs. Mantoux reaction 1/10,000 +ve.

X-ray of the chest in 1937 revealed two peripheral calcified foci of healed pulmonary tuberculosis in the mid zone of the right lung, while peripherally in the right upper zone was an ill-defined oval opacity which with serial X-ray control remained unaltered. It could not be ascertained with certainty whether this opacity was situated in the lung or was in fact a local pleural thickening.

She has attended the out-patient department regularly since, has had no further ocular trouble, and has remained quite well. The vision is poor, owing to degenerative changes in the lens, vitreous, and fundi: R. 6/60, L. 6/36.

No. 21. Mary C., female, aged 54 years. (R.L.O.H. and S.M.H.)

A cyclo-choroiditis in which the eyes have cleared well after sanatorium treatment, but the lung and general condition have deteriorated

A sister died of renal tuberculosis. The patient had for years been particularly subject to colds accompanied by an unproductive cough, hoarseness and occasional aphonia. After the onset of cyclitis in 1936, these symptoms persisted but did not become noticeably worse.

Examination in June, 1937, revealed a well-built, slightly cyanosed woman of 52 years of age. Glands were not enlarged and the spleen was not palpable. Over the chest râles were present in the upper zone on the right side. Sputum contained no tubercle bacilli (2 examinations). Mantoux reaction +ve 1/1,000. W.R. —ve. X-ray of the chest showed calcified tuberculous cervical adenitis, while in the lungs in both upper lobes, typical infiltration with calcification was present. She was occasionally pyrexial while at rest in bed. The ocular lesion and her general condition improved with rest and she was transferred to sanatorium in October, 1937. She made fair progress during the next three months and in particular had by February, 1938, improved clinically and symptomatically as regards the ocular lesion. Râles, however, could be heard over both lungs and she had not gained in weight. X-ray of the chest showed considerable increase in the infiltration in both upper lobes, many of the foci having now become confluent. She continued to rest at home and further improvement in the ocular condition occurred. During the next three months she lost weight and strength, the cough became much more troublesome and productive of more sputum, and the appetite diminished.

X-ray in July, 1938, showed still further spread of infiltration which now involved all zones of both lungs. It was noteworthy that while deterioration of

the pulmonary condition was occurring (June, 1937, to July, 1938) the ocular lesions improved and became quiescent.

OCULAR DETAILS AND COURSE

July, 1936. R.E. inflamed and painful.
 September, 1936. Cobwebs in vision, especially L.
 May, 1937. R.V. 6/18, L.V. 6/12: mutton fat k.p. eyes white.
 October, 1937. R.V. 6/9, few k.p., pupil free; fine vitreous opacity; old anterior choroidal patch.
 L.V. 6/9, greasy k.p., dense vitreous opacity, a few old foci in choroid.
 February, 1938. R. 6/36, L. 6/12, greasy k.p. in both. Vitreous opacity slight.
 May, 1938. R. 6/6, L. 6/6, no injection, k.p., still present, vitreous opacity slight.

No. 22. A.B., female, aged 48 years. (R.L.O.H. and S.M.H.)

A recurring bilateral cyclitis with chronic pulmonary tuberculosis

The patient's father died of pulmonary tuberculosis at the age of 50 years. At the age of 26 years the patient had a pyrexial illness called "influenza," with which she was ill for several months, and since that time has suffered from recurrent colds and a cough occasionally productive of purulent sputum. A pregnancy was terminated at 5 months, aged 39 years—reason unknown. She lost weight and strength, and complained of a persistent productive cough. Periods became scanty and irregular and by 1937 recurred at approximately three-monthly intervals. Night sweats had occurred during the last 6 months. Examination showed a cyanosed, slightly dyspnoeic, rather thin female, in whom physical signs suggested bilateral infiltration and fibrosis. Lymphatic glands were not enlarged and the spleen was not palpable. She was occasionally pyrexial while at rest in bed. Sputum contained no tubercle bacilli (one examination). Mantoux reaction +ve 1/1,000. W.R. —ve.

X-ray of the chest, September, 1937, showed widespread typical infiltration and fibrosis in the upper and mid zones of both lungs due to pulmonary tuberculosis. In the right upper lobe, excavation had occurred. Though some of the foci were confluent, the distribution of the majority suggested haematogenous spread. Hilar lymph nodes were not apparently enlarged. With rest in bed, while taking cod-liver oil and malt, the pyrexia settled and the ocular lesions remained *in statu quo ante*. She was transferred for a prolonged period of sanatorium therapy in October, 1937, and has not since then been seen.

Ocular signs.—Her history suggested an attack of cyclitis in 1930 and again in 1935. When seen in 1937 she had k.p. in both eyes chiefly in the L.E., which was injected and contained vitreous opacities. V.R. 6/9, V.L. 6/24.

No. 23. J.P., male, aged 68 years. (R.L.O.H. and S.M.H.)

A recurring bilateral cyclitis, with increasing severity of attacks, culminating in secondary glaucoma and blindness

Onset with cyclitis at the age of 45 years. Family and personal history irrelevant. Examined in June, 1937, when signs over the chest suggested chronic bronchitis and emphysema. Lymphatic glands were not enlarged and the spleen was not palpable. A considerable degree of peripheral arterio-sclerosis was present and was associated with an increased blood pressure. W.R. —ve. Sputum contained no tubercle bacilli. Mantoux reaction —ve 1/100.

X-ray of the chest showed emphysematous lungs with a calcified left paratracheal gland. The heart was enlarged and the aorta somewhat uncoiled, a calcified plaque being visible on the arch.

OCULAR CONDITION

March 19, 1936. Aged 65 years. Had recurring ocular inflammation for 20 years. Vision failed after influenza, December, 1935.
 R.V. Hand movements. Tension full, large k.p., post. syn.
 L.V. 6/12, tension full, fine k.p., dental sepsis.

March 21, 1936. R. paracentesis.
 April 2, 1936. All teeth removed.
 May, 1936. R. iridectomy.
 June 22, 1936. R.V. hand movements, k.p., vitreous opacity. Disc white and cupped.
 L.V. 6/12, k.p., tension normal.
 September 28, 1936. Rt. tension ++. L.V. c.f. 3 metres. Tension ++.
 October 5, 1936. L. iridectomy.
 December 31, 1936. L.E. fresh large k.p.
 May 20, 1937. R.E. tension full, large mutton fat k.p.
 June 17, 1937. R.E. no p.l., tension ++.
 L.V. hand movements, Tension ++.
 June 18, 1937. R. paracentesis.
 June 19, 1937. L. paracentesis.
 July 6, 1937. L. tension normal for 10 days. No improvement in vision.

No. 24. R.L., male, aged 24 years. (S.M.H.)

A severe unilateral cyclitis with a large iris tuberculoma, resulting in blindness. (v. Fig. C.)

No known tuberculosis in his family. In 1929 abdominal pain and vomiting led to the diagnosis of appendicitis. At operation tabes mesenterica was suspected and subsequent section of the appendix showed the presence of tuberculous inflammation. Examination of the chest then resulted in the diagnosis of pulmonary tuberculosis which was confirmed by the discovery of tubercle bacilli in his sputum. He was treated in sanatorium for six months and greatly improved. He remained at work until 1935. In May, 1935, he developed misty vision and pain in the left eye following slight local trauma while at work. Examination revealed the presence of a tuberculoma on the iris of the left eye, and greasy k.p. (Fig. C.) Right eye was normal. W.R. —ve.

There were signs over the upper lobes of both lungs, suggestive of fibrosis, and X-ray showed bilateral infiltration with fibrosis in these areas. Sputum was not available. He was treated by rest in bed and subsequently by a further course of sanatorium therapy. Later he returned to work and has remained well ever since.

In the eye the tuberculoma of the iris subsided in two months, but k.p. persisted and gross vitreous opacity developed. With the onset of secondary cataract, the tension of the eye diminished and vision was reduced to finger counting in under 12 months.

In 1938, the general and ocular conditions were unaltered. The chest showed some slight signs of bilateral apical fibrosis. Mantoux reaction +ve 1/10,000. X-ray of the chest showed fibroid changes in both apices, the appearances suggesting (as compared with those of 1935), healed pulmonary tuberculosis. The right eye remained unaffected.

No. 25. A.T., male, aged 46 years. (S.M.H.)

A recurring severe bilateral cyclitis, ending in blindness in spite of eradication of sepsis and a variety of treatment

Onset with iridocyclitis in the right eye in 1928. Family and past history unknown. No abnormal physical signs were found in the chest, and the lymphatic system was clinically normal. Mantoux reaction +ve 1/10,000. W.R. —ve. X-ray of the chest — calcified foci in right upper and lower lobes, and, probably also calcified cervical adenitis due to healed tuberculosis. During the period of observation 1933—1936, as indeed was the case from the onset in 1928, the course was one of temporary arrest of the ocular inflammation, followed by relapse recurring at irregular intervals in spite of intensive treatment of focal sepsis, vaccines, ultra-violet light, rest, protein shock, iridectomy and a variety of other therapeutic measures.

No. 26. R.K.A., male, aged 33 years. (S.M.H.)

Severe bilateral chronic iridocyclitis treated with tuberculin

Onset in May, 1936, with pain and dimness of vision in both eyes while in U.S.A. Examination then revealed bilateral chronic iridocyclitis and chronic tonsillitis. There were no abnormal physical signs elsewhere in the body. Family history included diabetes mellitus in the father, but was otherwise insignificant. He had had no other serious illness.

Treatment while in U.S.A. included vaccine therapy, prolonged rest in bed, and a course of tuberculin injections. A severe ocular reaction followed an early injection in this course, after which the dose was reduced and subsequently again cautiously increased. In October, 1936, he developed an acute streptococcal pharyngitis with otitis media, but the ocular lesion did not become concurrently worse. In March, 1937, the tonsils were removed. However, the iridocyclitis which, ever since the onset had been irregularly active, was not sensibly improved, and vision continued to deteriorate.

He was seen by one of us in May, 1937, when circumcorneal redness was present in the left eye, and there were bilateral iritic adhesions and bilateral lenticular opacities. Vision was poor but he could just read newspaper headlines. There was no evidence of abnormality elsewhere in the body. Sputum —ve Tb. Mantoux reaction +ve 1/1,000. Glucose tolerance curve normal. W.R. —ve. X-ray of the chest showed normal lungs. Activity in the ocular lesion soon subsided. Further therapy included a modified rest régime, cod-liver oil and malt, and continuation of the tuberculin injections. Including the course given in U.S.A., the dosage employed varied from 0.0001 to 0.25 mgms. P.P.D. When last seen in September, 1937, on his return to U.S.A., the ocular lesion was quiescent.

No. 27. J.L., male, aged 45 years. (S.M.H.)

A unilateral heterochromic cyclitis with secondary glaucoma

When first seen in 1929, he had the atrophic iris with fine k.p. and vitreous opacities of a chronic heterochromic cyclitis. The condition appeared to have commenced in 1922, when teeth were removed and he was given tuberculin with resulting benefit. In 1936, chronic glaucoma necessitated a trephining operation, which was well tolerated, for in 1938, the eye was quiescent, the vision was 6/12, and the field of vision showed no further contraction.

The patient's mother and sister died of pulmonary tuberculosis after many years' illness—the former at the age of 56 years, so that prolonged contact was virtually certain. His past history was uneventful. At no time during the course of the disease were there any generalised symptoms. Examination revealed no abnormal signs in any system save the eyes. Sputum —ve Tb. Mantoux reaction 1/1,000 +ve. W.R. —ve. X-ray of the chest revealed a dense fibrotic band crossing the right upper lung field obliquely. It seemed probable that this abnormality was pleural in site. No change had occurred eighteen months later in the radiological appearances. Accordingly he was regarded as a case in which while there was strong presumptive evidence of tuberculosis, such an aetiology for the abnormalities he presented could not be considered proven.

No. 28. R.M., female, aged 30 years. (S.M.H.)

Bilateral chronic cyclitis ending in blindness, after a course of ten years, in spite of varied treatments

Onset with bilateral iridocyclitis in 1928 (aged 19 years). No significant family or past history. At no time were there any symptoms suggestive of generalised disease. Prolonged therapy, including removal of foci of infection, protein shock, vaccines and tuberculin, failed to prevent repeated relapses leading to blindness. In 1937, there were, apart from the ocular disease, no abnormal physical signs in any system. X-ray of the chest was normal. W.R. —ve. Sputum —ve for Tb. Mantoux reaction +ve 1/1,000.

No. 29. E.S., female, aged 51 years. (S.M.H.)

Relapsing bilateral iridocyclitis of many years' duration, with secondary glaucoma, resulting in blindness

Onset with bilateral iridocyclitis previous to 1931. No significant family or past history. At no time during the course of the disease were there any symptoms suggestive of a systemic illness. Examination in 1937 revealed no evidence of glandular abnormality. The lungs were emphysematous but otherwise normal. Other systems were unremarkable. Sputum —ve for Tb. Mantoux reaction 1/10,000 +ve. X-ray of the chest was normal, save for emphysema of the lungs.

In 1932, iris bombé necessitated bilateral iridectomy. In 1933 and 1934, relapsing uveitis reduced the visual acuity to perception of light in one eye and finger counting in the other. A variety of treatments included antrostomy, ultra-violet light, tuberculin and novarsenobillon were without effect.

No. 30. E.B., female, aged 32 years. (S.M.H. and R.L.O.H.)

*Unilateral iridocyclitis of two years' duration with small tuberculoma of iris.
Issue still doubtful*

Onset with kerato-iritis in the right eye in December, 1936. Family and past history insignificant. At no time were there symptoms or signs suggestive of generalised disease. Physical examination revealed no abnormality save the ocular lesion. W.R. —ve. Sputum not available. Mantoux reaction 1/10,000 +ve. X-ray of the chest was normal. Vaccine therapy was unavailing.

Ocular condition.—The eye developed a deep keratitis with vascularisation and a small nodule or exudate from the iris in the lower part of the anterior chamber, together with another small nodule close to the iris margin. With local treatment the inflammation subsided after six months. A recurrence, however, took place in June, 1938, with "mutton fat" k.p. in the same eye. This resolved in three months time with resulting vision of 6/24.

No. 31. M.S., female, aged 64 years. (S.M.H.)

Recurring iridocyclitis of many years' duration: bilateral: with gross deterioration of vision

Onset with iridocyclitis and rheumatism many years previously. No other significant past or family history. Since the onset she had a series of relapses in the ocular lesion, sometimes accompanied by fresh rheumatic pains, which seem probably to have been mainly attacks of fibrositis, and osteoarthritis.

In January, 1937, a severe relapse occurred, following influenza, and persisted until the summer of that year. Clinical examination revealed marked pulmonary emphysema, generalised arteriosclerosis with hypertension, and well marked osteoarthritis in the hands, shoulders and spine. She was mentally unstable. There was no evidence of tuberculosis or lymphadenopathy. Sputum —ve for Tb. Mantoux reaction +ve 1/10,000. W.R. —ve. X-ray of the chest revealed pulmonary emphysema and a somewhat dilated and elongated aorta but no other pathology. Haemolytic and viridans streptococci were found abundantly in the throat and faeces, and a combined vaccine was made. No other foci of infection were found. A course of injections was given from October, 1936, until April, 1937. A severe relapse in the ocular lesion coincided with this course and it was therefore abandoned. Subsequently, she once more improved, and remained fairly stable until May, 1936, when she was last seen. During the last year of observation she slowly developed mental symptoms suggestive of involutional psychosis.

During the period in which she was under observation, the vision in the right eye was approximately finger counting, that of the left was similar but at times improved to 6/60. Iridectomy in both eyes was necessary for occlusion of the pupil.

No. 32. D.W., female, aged 38 years. (C.L.O.H. and S.M.H.,
Mr. F. Ridley's case)

Recurring bilateral kerato-iridocyclitis, active for over four years: apparently rendered quiescent by three months Sanatorium treatment

Onset in 1930, aged 29 years, with "blood poisoning" which left behind it several hard enlarged cervical glands. Iridocyclitis followed three months later in the right eye, and a year later a similar lesion developed in the left eye. Subsequently symptoms entirely ocular. Family history and past history were not significant. Physical examination in 1937 apart from the ocular lesions, was wholly negative. No enlarged glands were then found. Sputum not available. Mantoux reaction +ve 1/1,000. W.R. —ve. X-ray of the chest normal.

OCULAR COURSE

1930, aged 29 years.

February. R. inflamed some months. V 6/6 partly post. syn. L. 6/6.

October. L. inflamed two weeks; injected. Keratitis: post. syn. W.R. negative.

Relapses occurred in December and March, 1931, when tonsillectomy was performed. In May, 1931, interstitial vessels in L. cornea. W.R. again negative. From May till October she had U.V.L. therapy, thyroid and radiostoleum. Throughout 1932 the eyes remained quiet and vision R. 6/36, L. 6/60. In April, 1933, gross k.p. occurred in R. E. and she was an in-patient for some months. Relapses occurred occasionally and in April, 1934, R.V. 6/60, L.V. <6/60 with injection of both eyes. In May, 1934, L. iridectomy was performed and later she was in a sanatorium for three months. She says this brought about considerable improvement and the eyes have since remained quiescent. On December 13, 1935, R.V. 6/24, L.V. 6/36, with glasses. In 1937, the eyes were quiet.

No. 33. D.B., female, aged 53 years. (R.L.O.H. and S.M.H.)

Relapsing uveitis, of doubtful aetiology: quiescent for two years, benefited by vaccine

Onset in 1932 with influenza and bronchitis followed by bilateral iridocyclitis which caused rapid loss of vision during the next eight months. Family history not significant. Past history included many attacks of bronchitis which had become chronic while since the menopause she had suffered from rheumatic pains in the hands and legs.

Clinical examination revealed obesity, generalised arteriosclerosis with hypertension, chronic bronchitis and emphysema. There was no clinical evidence of tuberculosis and no enlargement of the spleen or glands was found. Osteoarthritis was present in the knees and shoulders. Sputum —ve for Tb. W.R. —ve. Mantoux reaction —ve 1/1,000. X-ray of the chest showed emphysema of the lungs and cardiac enlargement, but no evidence of tuberculosis. Antral sepsis suspected on clinical grounds led to a bilateral antrostomy being performed in 1935, whilst her teeth and tonsils had been removed soon after the onset of the disease. Haemolytic and viridans streptococci were present in the throat, sputum and faeces, and a combined vaccine was made. A prolonged course of injections was given during 1936 and 1937. The ocular lesion became quiescent and the rheumatic pains were relieved, and she has been relatively well ever since.

Her vision, which in 1934 was 6/24 in each eye, was in 1937 6/18 in the right, 6/60 in the left. In addition to the ciliary body, the anterior part of the choroid was definitely involved.

No. 34. I.C., female, aged 32 years. (R.L.O.H. and S.M.H.)

Recurring iridocyclitis of eight years' duration, made worse by tuberculin given in increasing small doses

Family history not significant. Past history included pleurisy in 1930. In November, 1935, when aged 28 years, her R.E., which had been inflamed at

intervals after haemorrhage in pregnancy in 1933, had become useless and soft. The L.E. had become inflamed recently: k.p. ++, post. syn. T.n. V=4/60.

L. iridectomy was performed in January, 1936, and vision a week later was 6/36. In September a relapse occurred with vitreous haze, and vision 3/60. Tuberculin B.E. was given in small doses whilst in hospital and later at the Tuberculosis Dispensary at weekly intervals, starting in October, 1936, with 0.1 c.c. of 1/10⁶ mgm. per c.c., increasing the dose by 0.1 c.c. weekly until she was having 1 c.c. of 1/10,000 mgm. per c.c. in March, 1937. It was then reported (Dr. Richardson), that she had lost one stone in weight in three months, and that X-ray suggested a "hilar adenopathy" where none had been present before. In April, 1937, the L.E. was quiet and V=6/60, but there was a relapse in June. V=4/60. General U.V.L. therapy was used extensively until December, 1937, 16 minutes exposure twice weekly. Since April, 1937, she has lived quietly and put on weight again and is taking cod-liver oil and malt. In February, 1939, there had been no further attacks since June, 1937, and V.L. = 6/60.

No. 35. C.F., male, aged 39 years. (S.M.H.)

Bilateral recurring iridocyclitis of mild type

The family and past history are unknown. No severe generalised illness would seem to have occurred during the course of the disease. The patient's eyes have been watched since 1932. There have been numerous mild relapses with fine k.p. in each eye, but recovery has occurred. The last attack in October, 1937, cleared and vision was 6/6 with glasses, in each eye in January, 1938. W.R. —ve. He had various treatments, including prolonged courses of vaccines (strept. viridans from the post nasal space, the bac. of epidemic jaundice from the faeces) tuberculin, U.V.L. therapy and N.A.B.

General examination revealed no abnormality in the chest or sinuses, and there was never any glandular or splenic enlargement. X-ray of the chest in 1932 revealed rather exaggerated hilar shadows of uncertain nature and probably not glandular. In 1936 X-ray of the chest was entirely normal. The Mantoux reaction was not obtained.

No. 36. F.B., male, aged 26 years. (R.L.O.H. and S.M.H.)

Unilateral iridocyclitis with small iris nodule

Onset occurred with iridocyclitis in the right eye in January, 1936. He was admitted in March, when a small tuberculoma was present on the iris. In April there was a relapse of the iridocyclitis with corneal vesiculation and deep haze, together with fine k.p., but by June the eye had cleared, leaving vision of 6/9 and some vitreous opacity.

Family and past history insignificant. Examination revealed a normal chest. No enlargement of glands or spleen was found. Other systems were also normal. Sputum —ve for Tb. Mantoux reaction +ve 1/10,000. X-ray of the chest showed normal lungs and heart. Early response to conservative therapy was satisfactory but his subsequent progress is unknown.

No. 37. E.B., female, aged 23 years. (S.M.H.)

Mild bilateral iridocyclitis

The family history indicated the death of a sister from acute pulmonary tuberculosis shortly before the onset of the disease in the patient. The general health of the latter had been good, except for a certain lassitude and some loss of weight about the time when the eyes were first affected in 1936. In February, 1937, the R.E. developed "greasy k.p.," and the L.E. became congested in March. There were no abnormal signs in the chest. W.R. —ve. Mantoux reaction was not done. X-ray of the chest* showed "definite glandular enlargement at both hila." She was sent to a seaside home for a few weeks, and the cyclitis, still active in May, resolved during June with vision of 6/9 in each eye. The X-ray of the chest taken 9 weeks after the first, showed normal lungs and normal hilar shadows. In April, 1938, her ocular and general condition was still satisfactory, and she had been living quietly at home, where her *only* other treatment had been cod-liver oil.

*Not seen by the authors.

No. 38. A.R., female, aged 41 years. (S.M.H.)

Recurring bilateral iridocyclitis, resulting in blindness, in spite of various treatments

The onset with herpes zoster (L. vth nerve) was followed by left iridocyclitis in 1930. Family history insignificant. The patient had pleurisy at the age of 21 years. Past history otherwise uneventful. No generalised symptoms but iridocyclitis followed in the right eye in 1932. Clinically, in 1936 and 1937, physical examination revealed no abnormal signs in the chest or in any other system save the eyes. Sputum —ve for Tb. Mantoux reaction 1/10,000 +ve. W.R. —ve. X-ray of the chest was normal. In spite of ultra-violet light, tuberculin, vaccine therapy from focus of infection in the throat, her progress was steadily downhill and blindness followed.

In-patient S.M.H., February, 1932, aged 36 years, for iridocyclitis both eyes following herpes ophthalmicus. On discharge, she attended elsewhere for U.V.L. therapy.

April 6, 1932. R. fine k.p. L. gross k.p.

June 7, 1932. R. 6/9 partly. L.V. 6/9. In February, 1933, the L. had mutton-fat k.p., and the R. was affected in March.

January 10, 1936. R. 6/18, L. c.f. at 1 m. K.p. in both.

January 17, 1936. Small doses of tuberculin started.

January 31, 1936. Iritis. R.V. = c.f. at $\frac{1}{2}$ metre. L.V. = c.f. at $1\frac{1}{2}$ m.

Readmitted. February, 1936. Pupils occluded.

March 12, 1936. Protein shock therapy with T.A.B.

May 7, 1936. K.p. gone.

May 8, 1936. R. iridectomy followed by vomiting, hyphaema, corneal blood staining and shrinkage of the globe.

September 8, 1936. L.V. 6/18.

November 12, 1936. L.V. 4/60. T. low.

October 12, 1937. L.V. = c.f. T. low. Eye quiet.

No. 39. W.S., male, aged 49 years. (S.M.H.)

Unilateral iritis without loss of vision

Onset with iritis in right eye in April, 1936, at the age of 48 years. Second attack March, 1937. Family and past history not significant save that he had had a winter cough since aged 29 years.

Clinically he presented the signs of chronic bronchitis and emphysema of the lungs, without other abnormal physical signs. There was no enlargement of glands or spleen.

Sputum —ve for Tb. W.R. —ve. X-ray showed emphysematous lungs but no other abnormality. Mantoux reaction not obtained. Therapy included rest and cod-liver oil and malt under the care of his local doctor at his own home, where he made good progress.

No. 40. D.R., female, aged 44 years. (S.M.H.)

Chronic iridocyclitis not improved by vaccine therapy: secondary glaucoma: blindness

Onset with pain and misty vision in the right eye in 1925, followed a year later by similar symptoms in the left eye. During the intervening fourteen years, periods of quiescence and activity occurred regularly in the eyes, and vision deteriorated in both to perception of hand movements only. Throughout this period there have been no significant generalised symptoms.

Her past history included an attack of jaundice during adolescence, and she had also been subject to occasional attacks of bronchitis and vague rheumatic pains. Her family history contained no significant feature.

In 1932, corneo-scleral trephining became necessary on account of glaucoma in the right eye, and this was followed in 1933 by paracentesis oculi. An iridectomy was performed on the left eye in 1934. During the second of these periods of treatment in hospital, extensive search for focal infection revealed

the presence of haemolytic and viridans streptococci in the throat. Clinical and radiological investigation also showed the presence of dental caries and alveolar erosion. Appropriate dental extraction was done and the remaining teeth have remained clinically and radiologically normal. A vaccine prepared from the culture of the throat was given at regular intervals in increasing doses during 1933 and 1934, and had no discernible effect on the ocular condition. During 1936, a course of four injections of Tuberculin (0.0001 to 0.0002 mgm.) was given, and the second injection was followed by a slight general reaction with pyrexia. She was readmitted in December, 1937, and paracentesis was performed on both eyes. At that time no abnormal signs were found in the chest, lymph glands and spleen were not enlarged, and no significant focal sepsis could be found. X-ray of the chest showed slightly emphysematous lungs but no other abnormality. Mantoux reaction +ve 1/10,000. Sedimentation rate (Westergren) 11 mm. in 1 hour. She was given a period of rest in hospital together with cod-liver oil and malt, and thereafter had six weeks' further rest in a convalescent home. She has subsequently attended the out-patient department and her ocular condition has ever since remained essentially static, but vision is reduced to perception of light in one eye, and hand movements in the other. (January, 1939.)

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ANNOTATION

"My eyes are dim"

The fact that one of the marching songs of the British army in the current war begins "My eyes are dim, I cannot see," is of interest as we believe it to be the first instance of an ophthalmic sentiment being made use of in this connexion. In the Great War "Tipperary" held the field; in the present "Roll out the barrel" bids fair to be as popular. The Marseillaise must, we think, be the most famous marching song in history, though "John Brown's body" runs it close. The fact that Uncle Toby was addicted to whistling half-a-dozen bars of "Lillibullero" leads one to the conclusion that those British soldiers, who swore so terribly in Flanders, got rid of some of their superfluous energy with this tune. The French are said to have used "Malbrouk s'en va-t-en guerre" during the Revolution. Brewer, in his Dictionary of Phrase and Fable, says that this song dates from the Crusades and has nothing to do with the Duke of Marlborough; and it is now chiefly memorable for Thackeray's ridiculous drawing of Duchess Sarah taking leave of her husband. Was Kipling's "Absent minded beggar" much used in the South African war of 1899-1902? Our Scottish readers, if any chance upon this note, will doubtless hum "Hey Johnny Cope"; and it is common knowledge that Cromwell's Ironsides went into action singing psalms. Napoleon gave orders that French troops in the Peninsula should be supplied with at least three different songs, and for all we know to the contrary William the Conqueror may have countenanced a marching song at Hastings. Marching songs are probably as old as armies themselves.

We have even heard of an example of ophthalmic humour in the eye ward of one of the London Hospitals where the children greeted the dawn with the roundelay "Dancing with tears in my eyes."