CHRONIC MILIARY TUBERCULOSIS IN CHILDREN*

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Survey of literature

The existence of a chronic form of miliary tuberculosis which is not invariably fatal has recently begun to attract the attention of British clinicians. The subject formed the basis of a leading article in the 'British Medical Journal' in November, 1934¹, and a paper on it was read by Sayé of Barcelona at the last provincial meeting of the Tuberculosis Association at Cambridge². Nevertheless the condition is still looked upon by many as a medical curiosity and only five cases reported by writers from this country have been found. The earliest of these was described by Preston and Jeaffreson³ in 1925; later three were mentioned by Burton Wood^{4, 5}, and in 1935 one was reported by Deaner⁶ entitled 'Chronic Disseminated Tuberculosis with Erythema Nodosum.' A case showing multiple calcified nodules in both lungs was reported by O'Reilly⁷ who regarded it as intermediate in form between the primary focus and miliary tuberculosis.

A study of the foreign literature gives a different impression of the matter. As early as 1845 Waller⁸ in Germany made the statement that miliary tuberculosis was not always fatal, and in 1861 in the same country Wunderlich⁹ maintained that he often saw evidences of healed miliary tuberculosis while making autopsies. The first detailed report of cases of chronic miliary tuberculosis was by Burkart¹⁰ in 1873: he described four in which the character of miliary tubercles observed in the lungs post-mortem suggested that they had existed for a considerable period before death. In America an early writer on the subject is Longcope¹¹ who in 1906 described eight cases in which he considered life was prolonged sufficiently for them to be classed as chronic. In 1914 Northrup¹², in the same country, described seven cases. In 1924 Blaine¹³ reported three that he had discovered in the stage of calcification. In the French literature the classical work on the subject is that of Burnand and Sayé¹⁴ in 1924, entitled 'Granulies Froides et Granulies Chroniques.' These writers described nine cases. All their patients were in fair general health and afebrile when first examined: two of them died from meningitis, and the diagnosis based on the radiological findings was confirmed at autopsy; of the remainder, all except one had improved, and one had cleared up completely.

With the wider use of radiology that has developed during the last decade, many more publications on the subject under discussion have

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appeared in France, Germany, America, and a few other countries. From America an excellent account is given by Fishberg¹⁵, who states that 'such cases are seen by everyone who meets with many chest cases.' From Germany a good review is provided by Hein¹⁶; he describes twenty cases, and gives a long list of references. From France, in June, 1934, twenty-four cases were reported in a critical discussion on the subject that took place in Paris¹⁷. Among these was a patient described by Ferru and Perochon who recovered and remained well for seven years although tubercle bacilli were demonstrated in the sputum. Finally, there is the paper by Sayé², referred to previously, in which the writer described a large number of cases classified into different types and even went so far as to say that he had detected miliary tuberculosis by routine x-ray examination in a number of healthy students.

A good account of the condition as it occurs in children is given by Armand-Delille and Lestocquoy¹⁸ in their recently published manual on juvenile pulmonary tuberculosis: the former writer, from his wide experience of tuberculosis in children, has reported many cases of chronic miliary tuberculosis in a number of different publications. Another interesting paper is by Rist et al¹⁹, who describe seven cases of miliary tuberculosis of the lungs of which three were relatively acute while the remaining four recovered; they demonstrate the gradual transition between the acute and chronic forms of the disease. Jochims²⁰ describes four cases occurring in children: he considers the occurrence of extra-pulmonary manifestations, such as tuberculous arthritis and terminal meningitis, as evidence of the haematogenous origin of the pulmonary nodules. Duken²¹ describes eight cases, also in children, in which haematogenous tuberculous lesions of the skin were a prominent feature. Miller²² describes several others in a long thesis in which he expounds on the subject of haematogenous pulmonary tuberculosis in general. Sachs²³ describes two cases supported by the presence of tubercle bacilli in the sputum that cleared up completely. Valette and Rosenkranz²⁴ have reported three cases, Edel²⁵ three, and Marlow²⁶ two, also associated with cutaneous lesions.

In the majority of cases mentioned so far it was only possible to demonstrate a pulmonary form of chronic miliary tuberculosis. There is evidence, however, that even generalized miliary tuberculosis may pursue a prolonged course and sometimes end in recovery. Among the cases described by Duken²¹ is one showing multiple calcified deposits on radiographical examination in both liver and spleen. Similar cases are described by Miller²² and Hellgren²⁷. Opie and Anderson²⁸ took x-ray photographs of the organs removed from a large number of post-mortem subjects: they report a case in which not only were the lungs, liver, and spleen thickly studded with calcified nodules, but a number of these were also observed on the pia mater over the frontal lobes of the brain. It might be contended that the findings of multiple calcified deposits is insufficient evidence on which to make a diagnosis of healed miliary tuberculosis. Assmann²⁹, however, describes a patient in whom, in addition to the miliary picture in the chest skiagram, miliary tubercles were observed on the retina; yet the patient became apparently quite well, and remained so for six months before developing urogenital tuberculosis, of which she finally died. The most striking case of all is the following, reported by Cohn³⁰ as far back as 1921. In a girl, aged fourteen, the spleen was removed on grounds of a diagnosis of Banti's disease. The organ was found to be studded with typical macroscopic and microscopic miliary tubercles, and similar tubercles were observed on the peritoneal surface of the liver. Following the operation an x-ray photograph was taken of the chest, and this revealed the typical picture of miliary tuberculosis. The girl lived and was observed

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over several years. At the end of this period she was quite well; and, except for a slight increase in the physiological pulmonary striation, the radiological appearance of her chest was normal.

Other writers who have reported cases of either chronic or calcified miliary tuberculosis are Baer³¹, Kahn³², Kern³³, Lorey³⁴, Middleton³⁵, Pierson³⁶, Stivelman³⁷, and Wallgren³⁸.

Differential diagnosis

In face of the formidable amount of literature on the subject referred to in the foregoing survey, there can be little doubt not only that miliary tuberculosis sometimes runs a chronic course, but also that complete recovery from the disease occasionally takes place. Nevertheless, in view of the scarcity of reports of cases of this type emanating from British writers, a record of further examples occurring in this country should be of interest. Before describing a new series of cases, however, it is necessary to point out that the diagnosis of miliary tuberculosis is not infrequently made on insufficient evidence. A discussion of the possible sources of error in this connexion will therefore not be out of place.

With a skiagram of the chest suggestive of miliary tuberculosis, i.e., showing reasonably small opacities densely distributed over both lung fields, before this diagnosis can be accepted, it must be shown, first, that the opacities seen in the picture represent tuberculous nodules, and second, that these nodules resulted from a dissemination of organisms by the blood stream. In regard to the first of these points a considerable number of non-tuberculous conditions may be mentioned which are liable to simulate the x-ray picture of miliary tuberculosis: among these are pneumoconiosis, carcinomatosis, broncho-pneumonia or bronchiolitis, chronic vascular congestion due to cardiac insufficiency, and disseminated blood following haemoptysis. In regard to the second point, that is the mode of implantation of the nodules, there are two other possibilities besides that of a haematogenous spread. The lesions may be the result of a dissemination of disease via the air passages; the radiographical appearance of a tuberculous broncho-pneumonia is often similar to that of miliary tuberculosis. The other possibility is a disseminated lymphatic pulmonary tuberculosis. The pathology of this is a little difficult to understand as it would appear to entail a spread of disease in a direction contrary to that of the normal lymph flow; nevertheless Pleininger³⁹ has described a case under the title of 'lymphangitis reticularis tuberculosa,' and Duken²¹ also refers to this condition when discussing chronic miliary tuberculosis.

Finally, in relation to the question of the mode of origin of the nodules in chronic miliary tuberculosis, reference must be made to certain hypotheses which, although they do not necessarily indicate a revision of the diagnosis, might nevertheless provide an explanation for the benign course of the illness in these cases and serve to distinguish them pathologically from the

more common acute type of the disease. Burton Wood⁴ has drawn attention to the frequent occurrence in these cases of exudative or allergic manifestations such as epituberculosis and the benign juvenile type of pleural effusion; he suggests that chronic miliary tuberculosis may itself be a similar exudative type of phenomenon. He points out that the skin reaction to tuberculin is usually strongly positive in chronic miliary tuberculosis, whereas in acute miliary tuberculosis it is not infrequently negative. He also remarks that the opacities seen in the skiagrams in chronic miliary tuberculosis tend to be of a coarse type with a somewhat blurred outline, and that their resolution often occurs with surprising rapidity. In relation to Burton Wood's observations, experiments that were carried out by Nicaud¹⁷ are of considerable interest. By the intravenous injection of dead tubercle bacilli he was able to produce, in the lungs of rabbits, lesions similar to those he had found at autopsy in a case of chronic miliary tuberculosis in which the patient had died following an operation for pyloric stenosis. Nicaud interpreted this experiment as an indication that tuberculous toxins alone could give rise to x-ray appearances simulating miliary tuberculosis. Taking cognisance of Burton Wood's observations, it might be suggested as an alternative possibility that the stippling of the skiagrams in the recoverable variety of the illness is a manifestation of an exudative or allergic reaction produced by dead tubercle bacilli disseminated throughout the lungs. All these theories require further investigation.

Report of cases at High Wood Hospital

After this discussion of the possibilities that may lead to an erroneous diagnosis of chronic miliary tuberculosis, it is proposed to report a number of cases which are considered to be genuine examples of this condition observed among children admitted to High Wood Hospital during the last four years. Like the acute variety of the disease, chronic miliary tuberculosis appears to occur particularly frequently in young subjects. High Wood Hospital is a favourable institution for cases of this type because it receives all children affected with pulmonary tuberculosis requiring institutional treatment under the London County Council tuberculosis scheme. First will be described six fatal cases, and then four in which recovery has taken place.

Case 1. SUBACUTE MILIARY TUBERCULOSIS OF LUNGS.

A boy, aged ten years, was admitted with a history of influenzal pneumonia nine months previously, with cough and gradual emaciation since. A right pleural effusion had occurred three months previously and a skiagram one month previously showed 'mottling of both lungs.' On admission he showed a fair general condition, was rather pale and thin, with slight cough, and a subnormal temperature. There were harsh breath sounds all over the chest with a few fine crepitations at both apices. There were some enlarged cervical glands. His other systems were normal. Sputum was unobtainable and gastric lavage was not carried out. The

Mantoux reaction was negative to 1 in 10,000, but positive to 1 in 1,000. A skiagram of the chest showed dense stippling of both lung fields, and slight pleural thickening on right side (fig. 1).

The boy was kept lying flat in bed on an open air balcony. His condition gradually deteriorated. Pyrexia developed three months after admission, and he died in a cachetic condition, five-and-a-half months after the pulmonary stippling was first detected radiographically.

Autopsy (at another hospital) revealed both lungs densely studded with miliary tubercles; further details were not obtainable.

FIG. 1.

Case 2. CHRONIC MILIARY TUBERCULOSIS OF LUNGS WITH DEATH FROM TUBERCULOUS ENTERITIS.

A boy, aged thirteen years, had never recovered since an illness diagnosed as left basal pneumonia three months before admission. On admission his general condition was very poor; there was emaciation, a malar flush and cyanosis, but no cough. His temperature was subnormal. Examination of the chest showed a slightly impaired percussion note and diminished air entry at left base. The breath sounds were a little harsh, with crepitations at both apices. There were some enlarged glands on both sides of neck. The other systems were normal. Sputum was unobtainable but gastric lavage revealed tubercle bacilli on direct examination of centrifugalized material, a finding which was confirmed by inoculation of a guinea pig. The Mantoux reaction (1 in 10,000) was positive. A skiagram of the

Case 2.

Case 4.

Case 5.

Case 6.

FIG. 2.—Shows detail of pulmonary stippling in cases 2, 4, 5 and 6. In case 6 note also bulging upper mediastinum and shadow extending downwards from right hilum.

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FIG. 3.—Healing miliary tubercles.

FIG. 4.—As fig. 3 under $\frac{1}{8}$ objective.

chest showed a fine fluffy stippling of both lung fields with some larger shadows at the apices (fig. 2), and some haziness in the left costo-phrenic angle suggesting a resolving pleural effusion.

The boy was kept lying flat in bed and given a course of intramuscular injections of solganal B. oleosum. His condition remained about stationary at first, but later began to deteriorate. A sudden turn for the worse with pyrexia of 99–100° F. set in about six months after admission. Diarrhoea appeared with tumidity of the abdomen. Death however did not take place till seven months after admission.

Autopsy revealed both lungs studded with miliary tubercles and a few larger caseous nodules, mainly in upper lobes. There were also numerous caseous cervical and mediastinal glands, and tuberculous ulceration of small intestine. Other organs were unaffected.

Microscopical sections of lung tissue showed numerous miliary tubercles containing tubercle bacilli and giant cells. Many of these tubercles showed evidence of healing; they were ringed round by and infiltrated with fibrous tissue staining pink in van Giesen preparations (fig. 3 and 4).

Case 3. CHRONIC MILIARY TUBERCULOSIS OF LUNGS WITH DEATH FROM MENINGITIS.

A girl, aged one-and-a-half years, was admitted to a general hospital for double otorrhoea and debility. A skiagram of chest showed mottling of both lung fields, a wide upper mediastinum, and an epituberculous type of shadow extending out from the right hilum (fig. 5). She was transferred to

FIG. 5.

High Wood two months later and on admission there she was an emaciated, ill-looking child with slight cyanosis and a troublesome cough. The temperature range was 97°–99° F. Examination of the chest showed normal percussion and prolonged expiration all over with scattered crepitations on

both sides, especially at right base. The abdomen was distended and resistant to palpation. The urine was normal. There was profuse bilateral aural discharge which was not examined for tubercle bacilli. Numerous large matted glands bulged out on both sides of the neck. No other clinical abnormalities were found. The sputum was unobtainable and gastric lavage was not carried out. The Mantoux reaction (1 in 10,000) was positive. A skiagram of chest showed little change from previous one, except that the shadow extending out from right hilum was smaller.

The child was kept in bed as still as possible with aid of restrainers. Cardboard splints were applied to her neck. Her condition improved considerably at first, although intermittent pyrexia persisted. Her weight increased until, six months after admission, she had gained five-and-a-half pounds. At this stage the pyrexia began to increase again and the child became drowsy. She finally died in state of coma ten months after the first skiagram was taken.

Autopsy revealed tuberculous meningitis, numerous large caseous cervical and mediastinal glands, and in the left kidney a large tuberculous pyonephrosis. Small punctate miliary tubercles were scattered through both lungs.

Microscopical sections of lung tissue showed two distinct types of miliary tubercles. The first, containing tubercle bacilli and giant cells, were presumably of recent origin; the second, showing as nodules of pink-staining, fibrous tissue in van Gieson preparations, were presumably of long standing. It seems probable that these latter had been responsible for the original pulmonary stippling, and that a fresh haematogenous dissemination of organisms had occurred recently giving rise to fresh miliary deposits in the lungs and also to meningitis.

Case 4. CHRONIC MILIARY TUBERCULOSIS OF LUNGS WITH TEMPORARY IMPROVEMENT FOLLOWED BY FATAL MENINGITIS.

A girl, aged nine years, with history of recent pain in right chest, of uncertain duration, with slight cough, anorexia, and loss of weight was admitted in a poor general condition, pale and emaciated. She had a slight cough and complained of pain in the right side of chest. The temperature range was 97.5–99.5° F. The percussion note over the chest was impaired and the breath sounds were faint at right base; there were harsh breath sounds and a few crepitations at right apex. No other clinical abnormalities were found. A specimen of sputum was obtained and found to contain tubercle bacilli. The Mantoux reaction (1 in 10,000) was strongly positive. A skiagram of the chest showed a moderate-sized pleural effusion on the right side, slight upper mediastinal widening, and a fine generalized stippling of both lung fields.

The child was kept at rest in bed for five months, during which time her condition improved steadily. At the end of this period she had gained 7 lb. in weight and had been completely free from pyrexia for a month. A fresh skiagram showed the pulmonary stippling still present (fig. 2), although the effusion had absorbed. The child was allowed to get up for periods increasing up to four hours a day. At this point pyrexia reappeared and she was returned to bed. Signs of meningitis soon appeared, and death followed, nine months after pulmonary stippling was first demonstrated in a skiagram.

Autopsy revealed tuberculous meningitis, caseous hilar and mediastinal glands, and numerous small miliary tubercles throughout both lungs.

Case 5. CHRONIC MILIARY TUBERCULOSIS OF LUNGS SHOWING TEMPORARY IMPROVEMENT.

A girl, aged twelve years, with a history of left pleural effusion ten weeks previously was admitted in a fair general condition, pale but moderately well nourished. There was no cough or sputum. The temperature range was 97-98.6°. There was an impaired percussion note and weak air entry at both bases, particularly at the left and a few fine crepitations at both apices. No other clinical abnormalities were present. The Mantoux reaction (1 in 10,000) was positive. A chest skiagram showed a wide upper mediastinum, pleural thickening on both sides, and a fine stippling all over both lung fields (fig. 2).

The child was kept in bed for four months, during most of which time she was afebrile, and then allowed to get up for gradually increasing periods. By six months after admission she had gained 10 lb. in weight, but a fresh skiagram taken at this time still showed the pulmonary stippling little changed. She had reached the stage of six hours up in the day, when the pyrexia reappeared; from this time on, despite return to bed, her condition steadily deteriorated. A cough developed, and tubercle bacilli were demonstrated in the sputum. The pyrexia increased and the child died in a cachectic state eleven months after the disease had been first detected by x-ray. Autopsy was not carried out, as the child was transferred to another hospital a few days before death.

Case 6. CHRONIC MILIARY TUBERCULOSIS OF LUNGS WITH TEMPORARY IMPROVEMENT FOLLOWED BY FATAL MENINGITIS.

A girl, aged one year, with a history of cough following measles two months previously, had spent two months in a general hospital where skiagrams showed 'mottling throughout both lungs.' On admission she was in poor general condition, underweight for her age, but not markedly emaciated. Cough was present, and wheezy respiration. The temperature range was 97.5-101.1° F. There was slight impairment of percussion note and some coarse crepitations at the right base, the breath sounds being a little harsh all over. There were some large glands on both sides of neck. No other clinical abnormalities were noted. Sputum was unobtainable. Tubercle bacilli were demonstrated by inoculation of gastric lavage material into a guinea pig. The organisms were shown to be of human type by culture on Jensen's modification of Loewenstein's medium. The Mantoux reaction (1 in 10,000) was positive. A skiagram of the chest showed a fine, fluffy stippling of both lung fields, upper mediastinal widening, and a shadow of irregular outline extending downwards from the right hilum (fig. 2).

The child was kept in bed as still as possible with the aid of restrainers. Her condition gradually improved for seven months, at the end of which time her temperature had been normal for six weeks and she had gained 8 lb. in weight. At this point she developed an attack of tonsillitis, and from this time on her condition began to deteriorate. Pyrexia recurred a month later, and increased gradually until meningitis set in leading to the death of the child twelve months after pulmonary stippling was first demonstrated by x-ray.

Autopsy revealed tuberculous meningitis, caseous cervical glands, and large caseous glands in upper mediastinum. Both lungs were densely studded with miliary tubercles.

Microscopical sections of lung tissue showed both recent and healed miliary tubercles as in case 3, but intermediate stages in the healing process

were also demonstrable. Fig. 6 shows on the right a healed nodule of fibrous tissue, and on the left a recent miliary tubercle containing a giant cell. Fig. 7 shows the healed nodule under the $\frac{1}{6}$ objective.

FIG. 6.

FIG. 7.

Case 7. MILIARY TUBERCULOSIS OF LUNGS WITH OSSEOUS LESIONS. MARKED IMPROVEMENT AFTER SIXTEEN MONTHS' ILLNESS.

A boy, aged three years, with a history of contact with a phthisical mother, had had before admission six months' intermittent pyrexia following

whooping cough. On admission he was in a poor general condition, pale and emaciated. There was no cough. The temperature range was 97–100° F. There were harsh breath sounds all over the chest, and a few post-tussive crepitations at both bases. There were numerous enlarged cervical glands. No other clinical abnormalities were noted. The sputum was unobtainable. Tubercle bacilli were demonstrated by inoculation of gastric lavage material into a guinea pig. The Mantoux reaction was negative to 1 in 10,000 but positive to 1 in 1,000. A skiagram of the chest showed a wide upper mediastinum and a somewhat coarse type of mottling over both lung fields (fig. 8).

The boy was kept in bed, as still as possible with restrainers, and given a course of injections of solganal B. oleosum. His condition gradually deteriorated during the next nine months, during which time the pyrexia persisted and he lost 4 lb. in weight. Three months after admission he developed tuberculous disease in the right elbow. Nine months after admission tuberculosis of the cervical spine manifested itself by a retropharyngeal abscess. The boy was then transferred to Queen Mary's Hospital, Carshalton, where he was treated on a spinal frame. In a skiagram taken at this time the pulmonary stippling remained little changed. Rupture of the retropharyngeal abscess occurred with discharge of tuberculous pus. Later, tubercle bacilli were also demonstrated in pus from an abscess over the right elbow. Since being placed on the frame the boy's condition improved steadily, and seven months after this (sixteen months after pulmonary mottling was first detected by x-rays) he was stated to be in fair general condition and to have had a subnormal temperature for five months.

Case 8. MILIARY TUBERCULOSIS OF LUNGS WITH RECOVERY.

A boy, aged ten years, with a history of increasing lethargy following pneumonia nine months previously, and the report that a skiagram had shown miliary tuberculosis two-and-a-half months before was admitted acutely ill. He showed a marked malar flush, emaciation, dyspnoea, and a slight cough. The temperature range was 99–101·2° F. The only abnormal physical signs in the chest were a few fine crepitations in left anterior axillary line. Other systems were normal. Sputum was unobtainable. Gastric lavage revealed tubercle bacilli after inoculation of a guinea pig. The Mantoux reaction (1 in 10,000) was positive. A skiagram of the chest showed typical dense miliary stippling of whole of both lungs, a fluffy wedge-shaped shadow extending outwards from the right hilum, and a wide upper mediastinum (fig. 8 and 9).

The boy was put on absolute rest in bed, and the temperature subsided in a week's time. He was kept in bed and given a course of injections of solganal B. oleosum. Six weeks after admission there was a sudden recurrence of pyrexia (101° F.) which coincided with the appearance of three typical papulo-vesicular tuberculides on the dorsum of the left hand. After this his condition improved steadily. Pulmonary stippling was still present in a skiagram taken five months after admission, but six months after this both lung fields appeared clear (fig. 10). Only then was the boy allowed to get up. He gained weight steadily, and at the present time, eighteen months after pulmonary stippling was first demonstrated, he is up all day and appears extremely fit.

Case 7.

Case 8.

Case 9.

Case 10.

FIG. 8.—Shows detail of pulmonary stippling in cases 7 to 10,

FIG. 9.—Case 8 on admission.

FIG. 10.—Case 8 eleven months later,

Case 9. MILIARY TUBERCULOSIS WITH RECOVERY. LUNGS AND POSSIBLY LIVER AND SPLEEN AFFECTED.

A boy, aged three years, was admitted to a general hospital with ascites five months before transfer to High Wood. Tubercle bacilli were found in the sputum at this time, and miliary tuberculosis was diagnosed from x-ray pictures. On admission to High Wood he was in fair general condition, rather fat, but flabby and a little flushed. There was no cough or sputum. The temperature range was 97–99° F. There was an impaired percussion note at the base of the right lung with harsh breath sounds all over the chest and crepitations at right base. Examination of the abdomen showed no free

FIG. 11.

fluid. The liver edge was palpable one inch below the costal margin and the tip of the spleen was palpable. A fluctuant swelling over the left mastoid process was incised, and yielded pus containing tubercle bacilli. The Mantoux reaction (1 in 10,000) was positive. A skiagram of chest showed marked widening of upper mediastinum, a shadow in the right mid zone of the epituberculosis type (possibly due to collapse of the middle lobe), and a faint but definite stippling of both lung fields (fig. 8 and 11).

The boy was kept in bed as still as possible, and a course of injections of solganal *B. oleosum* was given. Pyrexia persisted for six months, but ultimately subsided. By ten months after admission the liver and spleen were no longer palpable, and the sinus over the mastoid process had healed. Since this time his condition has continued to improve, and at the present time, twenty-one months since the disease was first demonstrated by x-rays, he is getting up all day and very fit. A recent skiagram shows no evidence of pulmonary stippling.

Case 10. CHRONIC MILIARY TUBERCULOSIS OF LUNGS, WITH ABDOMINAL, CUTANEOUS, OSSEOUS, AND CEREBRAL TUBERCULOUS LESIONS, TERMINATING IN RECOVERY.

A boy, aged six years, with a history of persistent pyrexia following measles five months before was admitted with fair general condition and nutrition. He had a slight cough. The temperature range was 97–99.5° F. There was an impaired percussion note at the left base with crepitations at both bases, more on the left. The abdomen was prominent and 'doughy.' There was discharge from the right ear. No other clinical abnormalities were noted. The Mantoux reaction (1 in 10,000) was positive. A skiagram of the chest showed a wide upper mediastinum, a shadow of epituberculous type in the left lower zone, and a rather coarse fluffy type of mottling of both lung fields (fig. 8 and 12).

The boy was kept in bed as still as possible. Pyrexia persisted continuously for one year and intermittently for most of a second year. Tubercle bacilli were demonstrated in the sputum on two occasions. In serial skiagrams the pulmonary stippling gradually became less definite, but it was still detectable two years after admission. At this time the boy had gained 7 lb. in weight since admission and had reached the stage of being up all day and afebrile. After a few weeks, however, the pyrexia recurred, and a number of small crusty papules appeared on both buttocks. A large abscess full of tuberculous pus next appeared on the left buttock, and a skiagram showed rarification of the greater trochanter of the left femur. The papules healed leaving pitted scars, and the disease of the femur was successfully treated by open operation at Queen Mary's Hospital, Carshalton.

The boy was allowed up again, and was then found to be blind in the right eye; examination of the fundus showed complete optic atrophy. Further examination revealed exaggerated deep reflexes and an extensor plantar response on the right side. Lumbar puncture and x-ray examination of the skull revealed no abnormalities; nevertheless a diagnosis of healed cerebral tuberculomata seems the most likely one. The other possibility is a healed meningitis. At the present time, three-and-a-half years after admission, the boy has been up all day for nine months and is very fit. A skiagram taken three years after admission showed both lung fields quite clear except for a calcified patch at the left base and a few tiny calcified spots in the right lung (fig. 13).

Discussion

There can be little doubt that all the fatal cases described above, i.e., cases 1 to 6, represent genuine examples of miliary tuberculosis of a chronic type. The post-mortem findings were conclusive in five out of the six, and in the remaining one, case 5, the characteristic x-ray picture combined with the presence of tubercle bacilli in the sputum and the fatal termination of the illness should satisfy most critics. Nevertheless the duration of the illness in these cases varied from five-and-a-half to eleven months taken from the time the disease was first demonstrated by x-rays, and in all but the first two members of the group indubitable clinical improvement took place although this was only of a temporary nature. The most important feature of these cases is the demonstration of both healed and healing miliary tubercles in microscopic section of the lungs. All intermediate stages could be observed between typical acute miliary tubercles and nodules of pure fibrous tissue. These nodules were situated in the interstitial tissue disconnected from the bronchial tree; they were also isolated from each other

FIG. 12.—Case 10 on admission.

FIG. 13.—Case 10 three years later.

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which would not have been the case if they had represented an infiltration of the pulmonary lymphatic network. Further it was possible to demonstrate multiple tubercle bacilli in many of them: this finding excludes the possibility that the pathological changes were produced by toxins from dead organisms as was suggested by Nicaud.

Cases 7, 8, 9 and 10 are of particular interest because of the favourable course taken by the illness. Post-mortem findings are necessarily lacking here, but nevertheless the similarity between these cases and the other six fatal ones is extremely suggestive. The finding of tubercle bacilli in the sputum or gastric contents in these cases is evidence against a diagnosis of any non-tuberculous condition. Among other possibilities, carcinomatosis may be excluded as being practically unheard of in childhood; the same applies to pneumoconiosis particularly as there was in no instance a history of exposure to any special dust that might have given rise to this condition. The persistence of the stippling over periods of many months excludes a non-specific broncho-pneumonia or bronchiolitis and also disseminated blood. The absence of cardiac lesions excludes vascular congestion.

A feature of particular significance in regard to the pathology of cases 7 to 10 is the occurrence in all four of them, at some period during the course of the illness, of definitely established extra-pulmonary tuberculous lesions which could only have arisen following a discharge of tubercle bacilli into the blood stream. The presence of these lesions constitutes a strong piece of evidence in favour of the haematogenous origin of the original deposits. In case 7 the right elbow and cervical spine were affected; in case 8 cutaneous tuberculides occurred; in case 9 there was a tuberculous abscess over the left mastoid process, and the hepatic and splenic enlargement pointed towards a haematogenous abdominal tuberculosis. The most striking example, however, is case 10: here, in the first instance, the skiagram of the lungs indicating miliary lesions was associated with tuberculous peritonitis and with a chronic otitis media which may well also have been of tuberculous origin. Two years later a fresh generalization of infection occurred, resulting in tuberculous disease of the femur, cutaneous tubercles, and probably tuberculomata of the brain. It is of interest to note that extrapulmonary tuberculous lesions were also a feature of three of the similar but fatal cases described previously. In case 3 there was a tuberculous kidney, and also, as in case 10, otitis media of undetermined etiology; tuberculous meningitis occurred in three instances, cases 3, 4 and 6. It is noteworthy that in both groups of cases, in every instance in which the development of an extra-pulmonary lesion was observed, the appearance of the latter was heralded by an increase or recrudescence of pyrexia such as might be expected to accompany a discharge of organisms into the blood,

It is evident that all these cases, whether fatal or otherwise, were of a type showing a tendency to recurrent episodes of tuberculous bacillaemia. It is surely more than probable on this ground alone that the initial deposition of organisms in the lungs in all of them followed a similar episode of this nature.

In both fatal and non-fatal cases an interesting feature of the skiagrams was the marked widening of the upper mediastinal shadow. In cases 3, 4 and 6, at autopsy, this x-ray appearance was shown to be due to the presence of numerous large caseous paratracheal glands. It is now generally accepted that the spread of tuberculous disease in a child, following primary infection of the lung, takes place first along the pulmonary lymphatics to the hilar glands. From the hilar glands the disease may spread further to the tracheo-bronchial glands, and thence to the paratracheal glands in the upper mediastinum. This group forms the subject's last line of defence in the struggle to obstruct the organisms in their passage towards the blood-stream: the final stage of the journey, in cases where this last barrier has been passed, may reasonably be supposed to occur with little difficulty through either the thoracic duct or the main right lymph duct. A tendency to tuberculous bacillaemia is thus to be expected in association with caseation of the upper mediastinal glands; the presence of the latter feature in a large proportion of the cases in the series is a further point in favour of a haematogenous origin for the pulmonary lesions. It is noteworthy that cases 1 and 2, in which upper mediastinal widening was not evident in the skiagrams, are the only ones in which there was no evidence whatever of a recurrence of bacillaemia after the initial pulmonary dissemination of the virus.

It still remains to consider Nicaud's suggestion that a dissemination of dead tubercle bacilli might be responsible for the lesions in certain non-fatal instances of miliary tuberculosis; there are, however, strong arguments against the applicability of this hypothesis to any of the cases in the present series. The finding of numerous tubercle bacilli in a single nodule in the microscopic sections from three fatal cases has already been referred to. In the other cases, if the causative organisms had been dead at the time of their implantation in the lungs, it would seem impossible that they should have been found apparently intact in the sputum or gastric contents many months later. What is more, in four instances the organisms obtained by gastric lavage proved virulent to guinea pigs. With regard to Burton Wood's conception of a benign exudative variety of miliary tuberculosis, there are certain features of the cases which would at first sight appear to favour this. Epituberculous manifestations occurred in five

members of the series and pleural effusion in four, also the Mantoux test was positive in all cases; further a coarse variety of pulmonary stippling with a blurred outline to the individual opacity was observable in many of the skiagrams. But these last features were by no means constant findings throughout the series: in cases 3 and 4 for example, the skiagrams showed an abnormally fine variety of stippling, and in case 8 the opacities appeared small and well defined although they ultimately cleared up completely. A significant point against Burton Wood's view as applied to these cases is the long period over which the stippling persisted in the skiagrams in most instances. In case 10 the opacities could still be detected in the films two years after they were first demonstrated; it is unlikely that this would have been the case if the lesions had been of a purely exudative nature. Thus, taking everything into consideration, the hypotheses of Nicaud and Burton Wood both appear insufficient to explain the pathology of the examples of chronic miliary tuberculosis reported in this series. There seems no reason to suppose that in the initial stage of the illness the nodules present in the lungs of these cases differed in any essential feature from the tubercles of the acute miliary disease.

A final point worth mentioning is the gradual transition in type that appears from case to case throughout the series. The absence of any sharp line of demarcation between the acute and chronic forms of miliary tuberculosis has already been demonstrated by Rist et al¹⁷, whose work was referred to in the survey of the literature given above. The present set of cases, arranged for this purpose in order of severity, help to bear out this point. In case 1 the illness pursued an inexorable course towards a fatal termination without any signs of a remission occurring. Since the lesions were confined to the lungs and the picture was not complicated by meningitis, the six months duration of the illness here is not much longer than might be expected in accordance with the prevalent conception of miliary tuberculosis as an inevitably fatal disease. The cases in the series gradually become more chronic until case 10 in which the child has been under observation for over three years. It would appear that all intermediate degrees of severity of the condition may be met with between classical acute miliary tuberculosis and a chronic form which may last several years and ultimately clear up altogether. This observation is a strong argument in support of the pathological unity between all these cases.

An abortive form of miliary tuberculosis

Cases 1 to 10 were selected for publication as being particularly striking examples of chronic miliary tuberculosis. Actually among children at High Wood Hospital the writer has observed a considerable number of other

similar cases which, although not quite so convincing, nevertheless showed clinical and radiological features strongly suggestive of the same condition in a milder form. In some of these the disease was of a localized type limited for example to one lung or only part of one lung; in others the stippling seen in the skiagrams covered both lung fields, but was of a fine punctate variety that tended to clear up relatively rapidly. The latter x-ray appearance was frequently seen in conjunction with a shadow of the epituberculosis type extending out from the hilar region; it was also almost invariably associated with x-ray evidence of tuberculous glands in the upper mediastinum. The course of the illness was usually favourable in this type of case; nevertheless in two instances recorded meningitis developed shortly after the child was allowed exercise. It seems probable that these cases were examples of an abortive form of miliary tuberculosis in which the growth of the nodules was checked at an early stage: possibly the organisms deposited in the lungs were of an abnormally low virulence. Although it must be admitted that gross examples of chronic tuberculosis are of comparatively rare occurrence, these abortive forms appear to be considerably more common. With the spread of the practice of examining juvenile contacts by x-ray, they are likely to be detected increasingly frequently. Their early recognition and treatment should assist materially in reducing the incidence of tuberculous meningitis which is still an important cause of death in childhood.

Treatment

A study of cases 1 to 10 makes it clear, not only that no sharp line of demarcation exists between the acute and chronic forms of miliary tuberculosis, but also that it is frequently impossible to determine the prognosis of any given case at the outset. Patients appearing desperately ill may sometimes recover, while others in relatively good general condition are liable to go steadily downhill. It follows therefore that treatment should be considered in every case. One point stands out above all others; that is the paramount importance of rest. Any child whose chest skiagram suggests miliary tuberculosis should be kept in bed until the stippling has completely disappeared from the picture. Any earlier termination than this involves risk of disaster. Certainly it is not enough to wait only until the pulse and temperature become normal; tragic evidence of the truth of this is provided by cases 4 and 5, and the two other instances mentioned in the last section, in which a fatal relapse followed shortly after exercise was allowed. Absolute rest, as opposed to simple confinement to bed, is a matter very difficult of attainment in a young patient; nevertheless an attempt should be made to keep the child lying flat at least until the acute

stage of the illness has passed. The remarkable improvement that took place in case 7 after the boy was placed in a spinal frame suggests that in certain instances this method of treatment might just turn the balance, even in the absence of spinal disease.

All the children in this series were treated on open air balconies. In view of the good results obtained, it seems likely that this factor was beneficial. The only other form of treatment used in these cases was gold therapy. Good results have been claimed from this method by Sayé¹⁰; and three out of the four cases on which it was used at High Wood Hospital did well. Solganal, which can be given intramuscularly, is probably the best form to give the metal in these toxic cases owing to the slow absorption by this route. In a child aged three the initial dose given was 0.005 gm.; this was increased up to a final dose of 0.2 gm. after fifteen weekly injections.

Summary and conclusions

After a survey of the literature and a discussion of the differential diagnosis, a series of ten cases of chronic miliary tuberculosis occurring in childhood is described. Recovery took place in four of these cases; microscopic sections of the lungs in three of the fatal examples demonstrated the healing process in individual miliary nodules. The cases are discussed and the following conclusions are reached.

(1) Miliary tuberculosis runs a chronic course more frequently than is generally recognized; recovery occurs in a fair proportion of these chronic cases.

(2) Recovery is commonest when the nodules are confined to the lungs, but it may also take place in generalized cases and even when the onset of the illness is moderately acute.

(3) The pathology of the lesions in chronic and acute cases is essentially the same.

(4) Healing of individual miliary tubercles takes place by a process of fibrosis which usually leads to their complete disappearance from the pulmonary skiagrams.

(5) Massive caseous glands in the upper mediastinum are a frequent finding in the juvenile type of chronic miliary tuberculosis; the presence of these glands may be responsible for the tendency to recurrent episodes of tuberculous bacillaemia which is a feature of these cases.

(6) Any one of these episodes may give rise to fatal meningitis; the risk of this complication occurring is, however, considerably diminished if strict rest in bed is maintained until the x-ray picture is clear.

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