PATHOGENESIS OF NON-PULMONARY TUBERCULOSIS

BY

M. C. WILKINSON, M.B., B.S.

Medical Superintendent, Essex County Council Sanatorium,
Black Notley

Calmette (1923) has argued on experimental and pathological evidence that the tubercle bacillus enters the body and may first be held up in the lymphatic glands, and that it may pass through the lymphatic chain into the blood stream, where it causes tuberculous bacillaemia. The clinical manifestations of this process are tuberculosis of the lymphatic glands and tuberculous lesions of haematogenous origin. The haematogenous tuberculous lesions are most often found in the skeleton, genito-urinary organs, peritoneum, or lungs. Some clinical observations on these forms of tuberculosis will be submitted in this paper, and the relation between tuberculosis of the lymphatic glands and haematogenous forms of tuberculosis will be discussed. The observations are based on the examination of 593 patients suffering from non-pulmonary tuberculosis admitted consecutively to the Essex County Council Sanatorium, Black Notley, during the years 1930-7. This number does not indicate all those persons who developed non-pulmonary tuberculous lesions in the County of Essex during those years, since many children with tuberculosis of the cervical and abdominal glands were treated at other sanatoria, and only an unknown proportion of patients suffering from genito-urinary and abdominal tuberculosis were passed to sanatoria for treatment. The patients who were admitted to the Black Notley Sanatorium are enumerated in Table I

TABLE I.—Sex-Age Incidence of Patients Admitted for Treatment of Non-pulmonary Tuberculous Lesions during 1930-7

Age	Male							Female						
	Cervical Glands	Abdominal Glands	Tuberculous Peritonitis	Skeletal Tuberculosis	Renal Tuberculosis	Genital Tuberculosis	Total	Cervical Glands	Abdominal Glands	Tuberculous Peritonitis	Tuberculous Salpingitis	Tuberculous Caecum	Skeletal Tuberculosis	Renal Tuberculosis
1-10	32	9	2	67	2	0	112	24	9	3	0	0	59	1
11-15	12	6	1				17	17	3	3	0	1		
16-20	4	0	3	35	3	2	66	11	5	8	5	1	47	1
21-30	3	2	1	32	8	0	46	9	3	4	4	1	38	2
31-40	1	1	1	14	9	3	29	3	2	3	4	2	17	5
41-50	0	0	0	10	4	1	15	1	0	0	0	0	9	3
51-60	0	0	0	9	2	1	11	2	0	0	0	0	3	1
Total	52	18	8	167	28	6	279	67	22	21	13	5	173	13

in sex and age groups. It will be seen that skeletal tuberculosis was the most common form of non-pulmonary tuberculosis occurring at all ages, that renal tuberculosis developed most often in young adult males, that tuberculous peritonitis was commoner in females than in males and was most frequent in adolescence, and that the majority of patients admitted on account of tuberculosis of the lymphatic glands were children. Patients admitted for the treatment of tuberculosis of the thoracic glands have not been included in this series.

Haematogenous Nature of Non-pulmonary Tuberculosis

The result of tuberculous bacillaemia must be the insemination in various parts of the body of foci most of which remain latent. Sometimes the haematogenous nature of a non-pulmonary tuberculous lesion may be demonstrated by its association with miliary tuberculosis

of the lungs, the presence of which may be revealed by radiographic examination. The factors governing the development of a lesion are doubtful, but sites with an abundant blood supply appear to be favoured. For example, the blood-borne lesion in the child usually develops in bone near an epiphysis. Trauma appears to play a part in the production of a tuberculous lesion if it occurs in an area which is inseminated with tubercle bacilli.

If skeletal, genito-urinary, and peritoneal tuberculosis were all caused by blood-stream infection it would be expected that in many patients more than one tuberculous lesion would be present at a distance from each other or in organs not connected by their lymphatic systems. On the other hand, if tuberculosis of the lymphatic glands is not the result of blood-stream infection there would be no associated lesions in the majority of patients. These suppositions were confirmed by the findings in this series of patients. Table II shows the proportion of patients

TABLE II.—Incidence of Additional Tuberculous Lesions associated with Non-pulmonary Tuberculous Lesions

Site of Tuberculosis for which Patient was Admitted	No. of Patients	No. of Patients with One or More Additional Tuberculous Lesions
Tuberculous cervical adenitis ..	119	0
Tuberculous abdominal adenitis ..	40	0
Tuberculous peritonitis, salpingitis, or tuberculosis of caecum ..	47	13 (27.7%)
Genito-urinary tuberculosis ..	47	30 (64%)
Skeletal tuberculosis ..	340	86 (25.3%)

who had additional tuberculous lesions in other parts of the body. These associated tuberculous lesions were commonest in the skeleton, lungs, and kidneys.

Not only would lesions in more than one organ be expected as the result of haematogenous tuberculous infection but the foci of insemination in each organ would be multiple. There is abundant evidence that this is the case. At operations upon tuberculous bone it is usual to find multiple areas of tuberculous infection; and so, for example, the removal of an extra-articular focus near a joint may not prevent the development of tuberculosis in the joint (Cholmeley, 1939). Multiple calcified foci which are the result of tuberculous bacillaemia may be observed radiographically in the spleen in association with extra-pulmonary tuberculous lesions. Tuberculous lesions found in the kidney are multiple. A particular type of pulmonary tuberculosis which occurs in association with haematogenous tuberculous lesions has been described by Reisner (1934). This type consists of parenchymatous tuberculous lesions which tend to spread from apex to base in the form of miliary nodules. These nodules are comparable to the multiple haematogenous foci of infection in other parts of the body.

It is reasonable to suppose that tuberculous infection by the blood stream would be evenly distributed and therefore bilateral. This was found to be the case. The haematogenous form of pulmonary tuberculosis described by Reisner is bilateral. Twenty-two of the patients in this series who suffered from renal tuberculosis had a complete examination of both kidneys. Twenty showed evidence of bilateral infection. Similarly, tuberculous epididymitis was found to be bilateral in the majority of patients, although disease in both epididymides was not always manifest simultaneously. Tuberculous salpingitis is also found to be bilateral in the majority of patients. Nine of the 13 patients suffering from tuberculous salpingitis were known to have bilateral disease. Jameson (1935) states that 90% of patients with tuberculous salpingitis in a series investigated by him had bilateral

disease and 50% also had tuberculous infection of the uterus.

Tuberculous peritonitis may occur as a direct extension from tuberculous abdominal glands, but in my opinion it occurs more commonly as a haematogenous tuberculous infection or as an ascending peritonitis from tuberculous Fallopian tubes. When the infection is haematogenous miliary tubercle along the course of the blood vessels may be seen at operation. Tuberculous pleurisy is common as an associated tuberculous lesion, and occurred in six of our patients.

Tuberculosis of the Lymphatic Glands

Patients in this series suffering from tuberculosis of the lymphatic glands may be divided into two groups: those who were admitted for the treatment of tuberculous glands, and those admitted for the treatment of tuberculous lesions elsewhere and in whom tuberculous glands were also found. In the first group 119 patients were admitted for tuberculous cervical adenitis and 40 for tuberculous abdominal glands. Symptoms and signs had attracted attention to the disease, and these patients may be regarded as individuals in the community whose glands became affected with gross tuberculous disease as the result of primary infection. On examination no associated tuberculous lesions were found (Table II). Follow-up reports were received of 81 at periods varying from a few months to seven years after discharge, and in no case had a fresh tuberculous lesion developed in another part of the body. It was therefore concluded that patients treated for tuberculous cervical or abdominal adenitis did not develop tuberculosis elsewhere.

Glandular tuberculosis in patients of our second group was in the majority of cases diagnosed by the presence of calcifications in radiographs of the chest or abdomen. Active glandular tuberculosis was found in only a few children. None of the patients in this group showed evidence of tuberculosis of the cervical glands. The results of examination are shown in Table III. Only

TABLE III.—Results of Examination for Evidence of Past or Present Glandular Tuberculosis in Patients Suffering from Skeletal, Peritoneal, and Genito-urinary Tuberculosis

	Tuberculosis of Thoracic Glands	Tuberculosis of Abdominal Glands	No Evidence of Glandular Tuberculosis	Percentage Positive
Adults :				
Renal ..	9	5	26	
Peritoneal ..	0	0	4	
Skeletal ..	1	4	57	
Total ..	10	9	87	17.9
Children :				
Renal ..	1	0	0	
Peritoneal ..	0	0	2	
Skeletal ..	23	8	45	
Total ..	24	8	47	40.5

patients with definite calcifications or hilum gland enlargement have been included.

Table III shows that in the majority of the patients suffering from renal, peritoneal, or skeletal tuberculosis there was no gross evidence of past or present glandular tuberculosis. This, however, does not indicate that these patients did not suffer from some degree of tuberculosis of the lymphatic glands at the time of their primary infection, because in some cases the glandular tuberculosis may have subsided before the radiograph was taken or, in others, enough time may not have elapsed for calcifications in the glands to have developed. But the table tends to confirm the finding in the first group of patients, who had gross glandular tuberculosis but no haematogenous lesions; for it shows that, conversely,

patients with haematogenous tuberculous lesions do not necessarily reveal evidence of previous gross glandular tuberculosis. It may be inferred, then, that gross glandular tuberculosis is not necessarily associated with severe tuberculous bacillaemia, and may, on the contrary, be a means by which severe haematogenous infection is prevented.

Discussion

It appears that the severity of haematogenous tuberculous infection is not proportional to the severity of glandular tuberculosis, and that haematogenous tuberculous lesions are not likely to appear if the glandular tuberculous lesion following primary infection is treated by constitutional measures. This suggests that under favourable conditions the lymphatic system may afford some protection against the entrance of tubercle bacilli into the blood stream. It may be supposed that not only do the cervical, thoracic, and abdominal glands present a barrier to the entrance of tubercle bacilli into the blood stream from the site of primary infection but that the regional glands exert the same function in preventing haematogenous spread from a tuberculous focus in bones or other organs. The disastrous effects of tuberculous infection in infants are well known. It appears, however, that the child is to some extent protected if the lymphoid tissue is well developed and if the child's environment and nutrition are good.

Conclusions

From an examination of these findings it may be concluded, first, that patients suffering from gross tuberculous adenitis do not under favourable conditions develop tuberculosis in other parts of the body, and, secondly, that those suffering from tuberculosis of the bones, joints, kidney, peritoneum, and genital organs do not usually show evidence of active glandular tuberculosis. It may therefore be inferred that if the degree of tuberculous infection in a series of patients were constant the intensity of tuberculous bacillaemia resulting would be in inverse proportion to the glandular reaction at the site of infection. As the lymphatic tissues are most active in childhood, an explanation is offered for the small proportion of infected children who develop haematogenous tuberculous lesions. The absence of heavy calcifications in the cervical, thoracic, or abdominal fluids and an absence of a history of glandular infection in the majority of adults suffering from haematogenous tuberculous infections suggest that patients who have had a heavy glandular infection are protected from haematogenous forms of tuberculosis in adult life.

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J. Gough (*J. Path. Bact.*, 1940, **51**, 277) records the post-mortem findings in twelve Cardiff steam-coal trimmers, together with their clinical histories. All showed evidence of pneumoconiosis and five had died of the disease. The pulmonary fibrosis was of two types, massive and nodular. The nodules differed from those of classical silicosis in being less densely fibrosed and in showing radiating rather than concentric fibrosis. Gough concludes that inhalation of Welsh steam coal dust for many years leads to serious and sometimes fatal lung fibrosis.