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The Primary Lung Focus of Tuberculosis in Children.[1]

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ABSTRACT.—Of 1,800 consecutive autopsies on children whose ages ranged from a few hours to between 12 and 13 years, and who lived in Glasgow and the West of Scotland, 283 (15·7%) were found to have tuberculous lesions.—Of the total tuberculous cases, the lungs or tracheo-bronchial lymph nodes were the seat of tuberculous lesions in 173 (61·1%), and of these 168 (97·1%) died as a result of the tuberculous disease.—A primary lung lesion was found in 148 of the cases classified as having the primary site of infection in the thorax. The primary lung lesion consisted of a localized patch of caseous broncho-pneumonia and in the great majority of cases was single. Calcification of these lesions was unusual and only about one-third showed evidence of surrounding fibrosis, the incidence of which increased with the age of the children.—Most of the primary lung lesions were subpleural in position and the right lung was more often the seat of such lesions than the left; the right upper lobe being most frequently involved and then, in order, the right lower, left upper, left lower, and right middle.—The tuberculous adenitis in the tracheo-bronchial glands was related both anatomically and pathologically to the primary lesion in the lungs, the involvement of the glands being secondary to the lung lesion.—In 25 of the cases considered as primary thoracic infections, no primary lung lesions were found.—In a series of cases in which the type of infection was investigated, 173 human and 3 (2·7%) bovine strains were found in cases with the primary site of the infection in the thorax.—Only human strains were obtained from cases with primary lung lesions.—These findings were in marked contrast to those found in children in the same series with the primary site of infection in the abdomen where 81·8% of the infecting bacilli were of the bovine type, and also in cases of bone and joint tuberculosis—a blood-borne infection, in which 34·6% of the causal organisms were bovine strains.—From the pathological and bacteriological evidence, it is concluded that the focus described as the primary lung lesion is indeed such, and that it is due to direct infection of the lungs through the air passages.

DURING the last seven years we have found 283 cases (15·7%) with tuberculous lesions in a consecutive series of 1,800 autopsies performed at the Royal Hospital for Sick Children, Glasgow. The ages of the children coming to *post mortem* in this series ranged from a few hours to between 12 and 13 years, and they were mostly children of poor or working-class people. The 283 tuberculous cases were classified according to what was considered the primary site of the infection as follows:—

Thoracic	...	173 (61·1%)	Cervical glands	...	6 (2·1%)
Abdominal	...	101 (35·7%)	Not found	... ...	7 (2·5%)

1 The expenses of this work were partly paid by a grant from the Medical Research Council to whom I wish to acknowledge my indebtedness.

Four cases had double primary sites of infection, one in the thorax and the other in the abdomen. It is the primary thoracic lesions which we wish to discuss more particularly in this communication, as the results of the whole investigation are being published shortly by the Medical Research Council as a special report. The greatest number of children with primary intrathoracic tuberculous disease was found in the first year of life, though in the first three months they were rare. After the first year, the greatest number was found in the second year, and then in the third (Table I). After the third year, the number of cases in any one year was always less than half of that in the third, and for convenience the cases have been arranged in groups of three years in the Table. Nearly all the lesions had been responsible for death, only in five (2·9 %) of the 173 cases could they be regarded as accidental post-mortem findings. In only two of these five, however, which were not responsible for death, was there naked-eye and microscopic evidence that the disease was in the process of being arrested. In one of these children, aged 4 years and 1 month, the lesion in the lung was partly calcified and surrounded by fibrous tissue (fig. 6), and the glands at the root showed slight calcification with marked chronic periadenitis; in the other child, aged 5 years, a few chronic partly calcified caseous glands were found at the root of the left lung in which no primary lesion was discovered. Thus nearly all these children with tuberculous lesions in the lungs and tracheo-bronchial lymph nodes died as a result of the tuberculous disease.

TABLE I.

Age incidence, etc., of 173 cases with primary intrathoracic tuberculosis in 1,800 consecutive autopsies.

Type of case	Result of lesion	0 to 1 year	1+ to 2 yrs.	2+ to 3 yrs.	3+ to 6 yrs.	6+ to 9 yrs.	9+ to 13 yrs.	Totals	
148 cases with primary lung lesions	Caused death ...	52	37	18	15	17	6	145	148
	Not cause of death	...	...	...	2	1	...	3	
25 cases with no primary lung lesions	Caused death ...	5	3	4	7	3	1	23	25
	Not cause of death	...	...	1	1	...	...	2	
Total primary thoracic cases = 173 ...		57	40	23	25	21	7	173	
Total autopsies		1,204	235	87	135	97	42	1,800	

We have divided the 173 cases with primary intrathoracic infections into two groups:—

(1) Those in which primary lung lesions were found; (2) those in which *no* primary lung lesions were discovered.

(1) CASES IN WHICH PRIMARY LUNG FOCI WERE FOUND.

In this group there were 148 cases. The primary lung lesion was originally described by Parrot (1876) and later by Kuss (1898), E. Albrecht (1907), H. Albrecht (1909), Ghon and Roman (1913), Ghon (1916), Opie (1917), Canti (1919), Schürmann (1926), and Ranke (1928). Zarfl (1913), Ghon and Pototschnig (1918) have described very early stages of the lesion, while Gardner (1922) and Pagel (1926) have experimentally produced in animals lesions similar to those in the child.

Characters of the primary lung lesion.—In our cases the primary lesion was found to be a small localized caseous area in the lung substance (fig. 1). Microscopically it consisted of a patch of caseating tuberculous broncho-pneumonia which was fairly sharply marked off from the surrounding lung tissue, and which nearly always showed on microscopic examination some evidence of an attempt at arrest (figs. 2 to 6). Histologically a small bronchiole plugged with caseous material could often

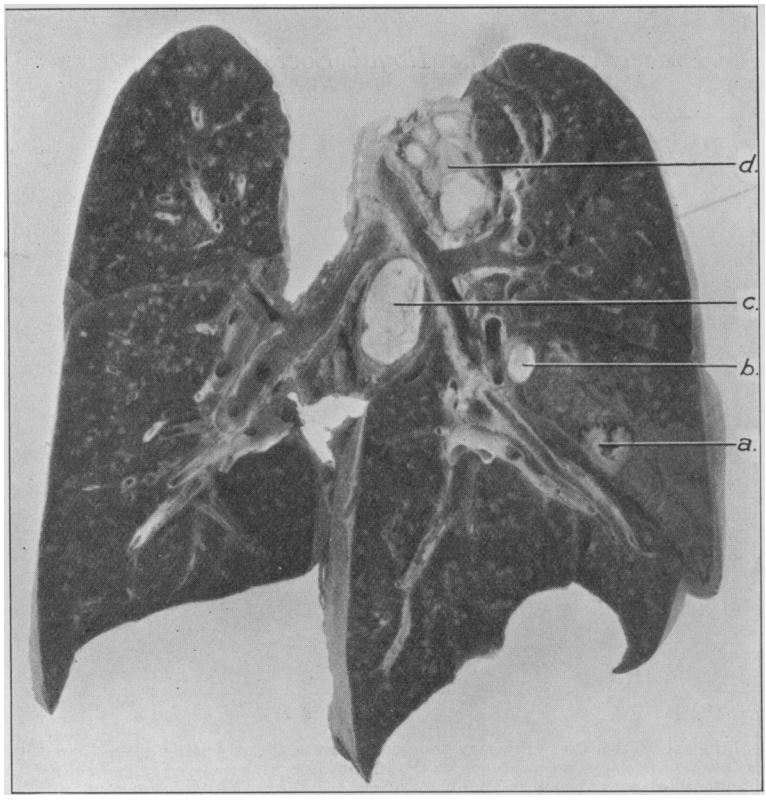

FIG. 1.—Lungs of child aged 1 year and 7 months, with primary lesion in lower part of right middle lobe. The specimen is viewed from the posterior aspect. The primary lesion (*a*) is caseous with central cavity formation. In the outer part of the lobe there is some early broncho-pneumonic tuberculosis, while scattered throughout the rest of the lungs numerous subacute miliary tubercles are present. A small caseous broncho-pulmonary gland (*b*) is present at the root of the middle lobe and the right inferior (*c*) and the right superior (*d*) glands related to the primary lesion are enlarged and caseous. No diseased glands are present at the root of the left lung.

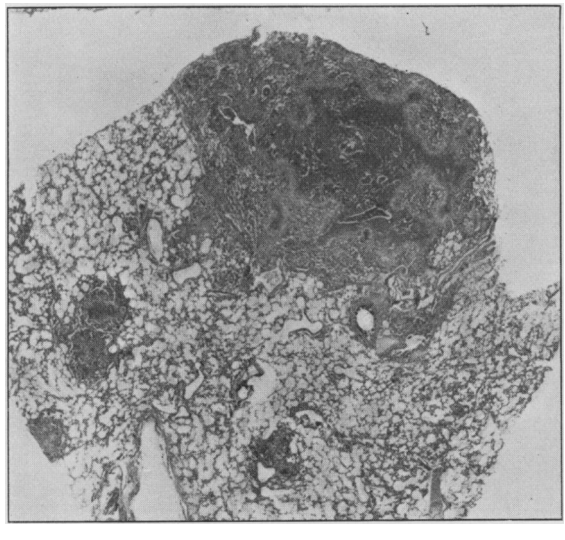

FIG. 2.—Child aged 7 months; a primary lung lesion at an early stage. The lesion is situated immediately under the pleural surface and is fairly sharply demarcated from the surrounding lung tissue. Numerous small vessels and bronchioles are involved in the lesion, the central part of which is caseous and shows early softening, while in the outer part there is a zone of cellular reaction. The small foci in the lower part of the figure are secondary subacute miliary lesions. Hæmatoxylin and eosin × 6½.

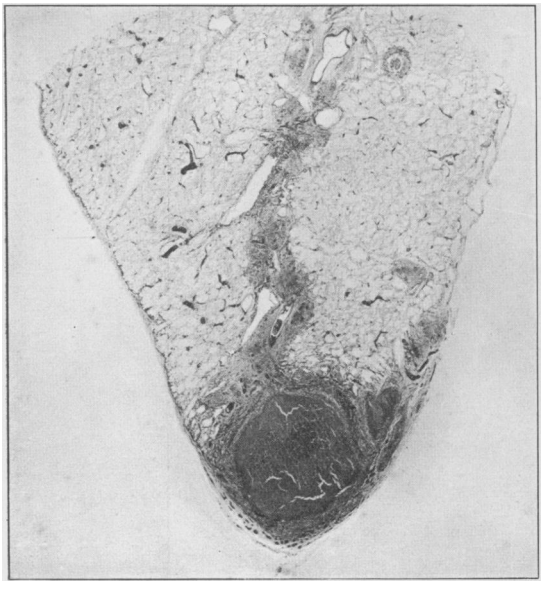

FIG. 3.

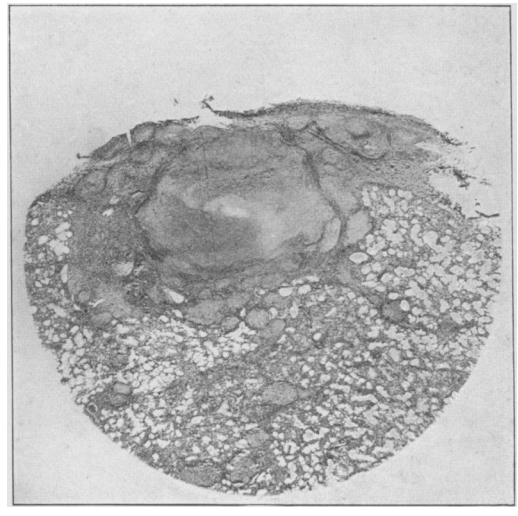

FIG. 4.

FIG. 3.—Child aged 6 months. Primary lung lesion at a slightly later stage than that in Fig. 2. The subpleural lesion is completely caseous, with, at the margin, scanty cellular infiltration and early fibrosis. The pleura over the lesion is slightly thickened and many small tubercles are found in the line of a small bronchiole, part of which is seen in the upper part of the figure. Such involvement of the peribronchial lymphatics was not often observed. Hæmatoxylin and eosin × 10.

FIG. 4.—Child aged 7 years. Caseous subpleural primary lesion at a later stage than that in fig. 3. There is well-marked surrounding fibrosis both at the edge of the main lesion and also around the numerous secondary tubercles. The caseous material in the centre is beginning to break down. Gallego's modification of Mallory's stain × 5.

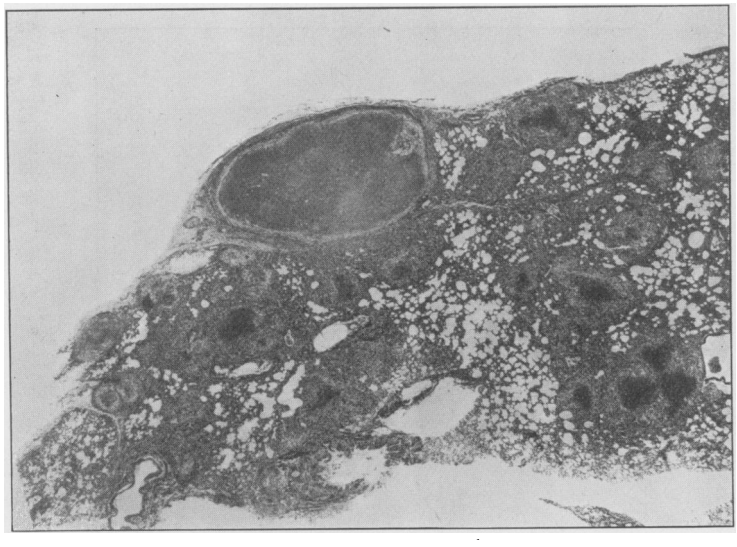

FIG. 5.—Child aged 7 months. Caseous subpleural primary lesion at a later stage than that in fig. 4. The lesion is completely surrounded by fibrous tissue. Numerous subacute miliary tubercles and areas of early broncho-pneumonic tubercle are present in the lower part of the figure.
Gallego's modification of Mallory's stain × 10.

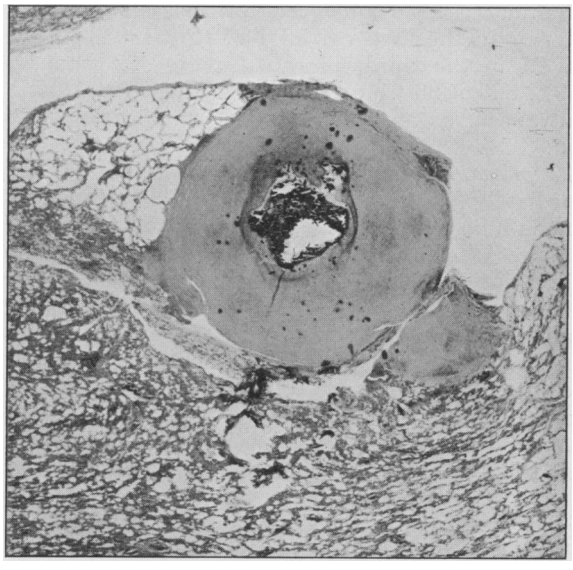

FIG. 6.—Child aged 4 years and 1 month. Died from chronic meningococcal meningitis. Section from the primary lesion which showed the most advanced evidence of arrest of any found in the whole investigation. The lesion (subpleural in position) is well encapsulated and there is only one secondary tubercle at the right edge. The central darkly-staining area is calcified and part of this has fallen out in the preparation of the section. The pleura over the lesion is slightly thickened and there is a little emphysema in the surrounding lung tissue.
Von Kossa's silver method and carmalum × 6½.

be found leading into the primary lung lesion which, when stained for elastic tissue, showed the normal pattern and architectural arrangement of the lung tissue persisting in the consolidated area. Though a large number of primary lesions were cut in serial sections, we could never demonstrate any of them to have a vascular origin. In the majority of cases only a single lesion was present, but in a few cases where they were multiple one lesion was often found, on naked-eye and histological examination, to be older than the others. In this series of 148 cases the actual distribution of the primary lesions was found to be as follows:—

133 cases had	1 primary lesion each.
10 cases had	2 primary lesions each.
3 cases had	3 primary lesions each.
2 cases had	4 primary lesions each.
148 cases had	170 primary lesions.

The fact that the greatest proportion (89·9%) of the cases had only one primary lung lesion is difficult to explain, as a child in contact with a patient suffering from "open" pulmonary tuberculosis would inhale large numbers of bacilli and multiple lesions would be expected. Accordingly, unknown factors must be at work in determining the localization of the lesion in the lung substance. Most of the above 170 primary lung lesions were small, 140 (82·4%) being the size of a hazel-nut or smaller. In all of them caseous change had taken place, and in 52, cavities had formed. Only 11 (6·5%) showed definite macroscopic evidence of calcium deposit, while in 55 (32·4%), included in which are those showing calcification, surrounding fibrosis was noted at the site of the lesion. No completely fibrosed or calcified primary lesion was found in the whole investigation, and in this finding we are at variance with many of the Continental and American workers already quoted. The

age incidence of this macroscopic evidence of healing is of interest. One case (1·7%) out of 58 showed this in the first year of life, 15 (34·9%) out of 43 in the second, 8 (38·1%) out of 21 in the third, 11 (50%) out of 22 from the fourth to sixth year, and 20 (76·9%) out of 26 from the seventh to twelfth year. Thus, as the age of the children advanced, so a greater proportion of cases showed an attempt at arrest of the lesion.

Situation of the primary lesions.—The majority (70%) of the primary lesions were found immediately under the pleural surface while the remainder were situated deeper in the lung substance, but generally nearer one surface than another. Of the 170 lesions regarded as primary 112 (65·9%) were found in the right lung. When the lobar distribution of the lesions was investigated, the greatest number was found in the right upper lobe, and then, in order, the right lower, left upper, left lower, and right middle. In the upper lobes these lesions were most often found in the upper two-thirds of the anterior surface; the apex, however, was very seldom involved. In the lower lobes, the lower third of the posterior aspect was the commonest site, and in the middle lobe the middle third of the anterior surface.

Relation of primary foci to the tracheo-bronchial lymphatic glands.—The lymphatic glands into which the lymph from the lungs and pleuræ drain are the tracheo-bronchial. The right and left superior groups of glands situated above the main bronchi on either side drain the corresponding upper lobes. The right inferior group situated below the right main bronchus receives lymph from the right lower and middle lobes, and the left inferior group from the left lower lobe. Although this is mainly so, yet there is a certain amount of overlapping of the lymphatic territories draining into these groups due, as Most (1908) pointed out, to the lymphatics from the contiguous pleural surfaces of neighbouring lobes draining into a common deep lymphatic channel in the depths of each interlobar fissure.

For the study of the anatomical relationship of the primary lesions to the glands, we considered chiefly those cases with only one lesion. Where there were multiple lesions, either of a primary or secondary nature, scattered throughout different lobes, the anatomical relationships to the lymph nodes were not so clearly demonstrable. This was also true, to a certain extent, of multiple lesions in one lobe, as the lymph glands in these cases often showed extensive lesions on account of the greater size of the diseased area. We found in cases with only one primary lung lesion that the situation and extent of the tuberculous adenitis in the tracheo-bronchial glands was a very good indication as to the site of the primary lesion in the lung substance. Space does not permit of a complete analysis of the situation and extent of the glandular lesions in those cases with single primary foci, but in general we found that the glands on the right side showed the most advanced tuberculous disease, when the primary lung lesion was on that side, the superior group, when the primary lesion was in the upper lobe, and the inferior group, when the lesion was in the middle or lower lobes. The same was true of the glands on the left side related to primary lesions in the left lung. The tuberculous disease did not, however, long remain localized to the glands in direct anatomical relation to the various lobes, and in the great majority of cases there was spread, upwards or downwards, to the lymph nodes on the same side, and then across to the glands on the other side. In these cases with extensive glandular involvement, however, the glands in direct anatomical relation to the primary lesion in the lung always showed the most advanced pathological change. As most of the lesions were in the right lung, the glands on the right side were more often diseased than those on the left. In the few exceptional cases where the glands were not involved in accordance with their anatomical relations to the lobes of the lungs, the lesions were situated in the upper parts or interlobar surfaces of the middle or lower lobes, and probably the infection had passed through the pleural lymphatics to the lymphatic channel in the deep part of the interlobar fissure already mentioned. In our series of cases all the primary

lung lesions studied were associated with tuberculous adenitis in the tracheo-bronchial glands. It was also noted that the extent and degree of involvement of these glands were less in older children than in infants.

The pathological changes in the glands were found, on both naked-eye and histological examination, to be at the same or an earlier stage than those present in the associated primary lung lesion. By using the delicate silver nitrate test of von Kossa for the demonstration of calcium salts, we were able to show in a large number of cases that early deposit of calcium salts was present in the primary lung lesion, but not in the related glands. These observations on the age of the lung lesions and glands were of importance as they showed that the disease in the latter was secondary to the lesion in the lungs.

The important facts obtained from this study of the tuberculous adenitis associated with the primary lung lesions were that the glandular disease was most marked on the side of the lesion and very often in relation to the actual lobe in which the lesion was present. Further, the broncho-pulmonary glands situated between the branches of the bronchi to the various lobes, and also, occasionally, those within the lung substance, were always diseased on the side of the primary lesion in the lung, while those in relation to the lung on the other side showed no morbid change. In addition to these observations, we noted that the further the diseased glands were traced away from the lesion in the lung, the less intense did the tuberculous adenitis become. Thus a retrogressive spread from diseased glands, a process which we never observed, having been the cause of the primary lung lesion seemed most unlikely.

(2) Cases in which No Primary Lung Foci were discovered.

In twenty-five of the 173 cases considered as primary intrathoracic infections, no primary lung lesions were found. In all of these cases except two in which double portals of infection were present, the tuberculous adenitis in the thoracic glands was advanced and tuberculous lesions elsewhere were of a secondary nature. In twelve of the subjects, a primary lesion in the lung might have been present, as the distribution of the tuberculous adenitis in the tracheo-bronchial lymph nodes in these children corresponded to cases in which primary lung lesions were found. On the other hand, in these cases it is possible that the infecting bacilli passed through the bronchial mucosa without leaving any trace of their passage, as in the case of the intestinal or pharyngeal mucosa in subjects with tuberculous adenitis in the mesenteric or cervical glands. Most of the other workers on this subject, quoted above, state that this does not occur, and that in such cases the primary lung lesion has been missed. Until we have had further experience, however, of cases without primary lung lesions, we feel that such a view is rather extreme. In other nine children, the tuberculous lesions in the lungs were so extensive that the finding of a primary lesion was impossible. In the remaining four cases, the most advanced tuberculous disease was in the thoracic paratracheal glands, and the site of the primary infection in these cases was uncertain, though it may have been in the trachea or one of the main bronchi.

Bacteriological Findings.

From the pathological part of the investigation we have shown that the primary lung lesion was most probably the first site of the tuberculous infection, and was due to infection through the air passages. One thing remained to make the proof of this more or less complete, namely, what was the type of infecting bacillus in those lesions or associated glands? Conditions in Scotland favoured this part of the investigation, for, as Fraser (1912), Mitchell (1914), Griffith (1915 and 1930), Tulloch and his co-workers (1924), Munro and Cumming (1926) and Munro (1930) have shown, a very large proportion of tuberculous lesions

in that country were due to infection with bovine strains. As infection with that type of tubercle bacillus nearly always takes place through the alimentary system, we tried to isolate the infecting organisms from the first 216 cases with tuberculous lesions occurring in this series of autopsies, and were successful in obtaining strains from 183 cases. These organisms were typed according to their cultural characters, and also by the results they produced on inoculation into rabbits. From lesions considered as primary abdominal, 54 bovine (81·8%) and 12 (18·2%) human strains were obtained (Table II). Now, according to von Behring (1903) and Calmette (1922), practically all tuberculous infection enters the body by way of the alimentary tract. If their views are correct, and as the children

TABLE II.

Types of tubercle bacilli found in (1) *primary thoracic tuberculosis*, (2) *primary abdominal tuberculosis*, (3) *tuberculosis of bones and joints.*

Source of strain		Human		Bovine		Bovine percentage
Cases with primary lung lesions	Primary lesion	32	94	—		—
	Related glands	62				
Cases with no primary lung lesions	Tracheo-bronchial glands	11	13	2	3	18·8
	Paratracheal glands ...	2		1		
All primary thoracic lesions		107		3		2·7
Primary abdominal lesions		12		54		81·8
Tuberculosis of bones and joints		17		9		34·6

with primary abdominal infections from which we isolated the above high percentage of bovine strains were from the same series of autopsies as those with the primary thoracic lesions, then we ought to have found a high percentage of cases in this latter group infected with bovine strains. This was not the case, however, for from subjects in whom the primary site of the infection was in the thorax, 107 (97·3%) human and three (2·7%) bovine strains were isolated from the primary lung lesions or tuberculous tracheo-bronchial glands. Only human strains were isolated from cases with primary lung lesions, while the three bovine strains were obtained from subjects in whom no such lesions were discovered (in two of these there was tuberculosis of the tracheo-bronchial lymph nodes, the right superior group being involved in the one, and the right inferior in the other, while in the remaining case one of the left thoracic paratracheal glands was the seat of the most advanced disease). Thus there was a very marked difference in the type of infection in the cases classified as primary abdominal and in those with the primary seat of the disease in the thorax. So marked was the difference that the conclusion was justified that the subjects with the primary seat of the tuberculous disease in the thorax were not infected by way of the alimentary system. Further, in view of the fact that 97·3% of the thoracic cases were infected with human strains, we concluded that the path of infection was directly through the air passages. The three thoracic cases in which no primary lung lesions were found, but which were infected with bovine strains, may appear to be against this conclusion. This, however, is not necessarily so, for, as Griffith (1930) has pointed out, "open" respiratory carriers of the bovine type of bacillus are relatively common in Scotland where they constitute 3·8% of patients expectorating viable tubercle bacilli, as against 1% in England, and 0·3% on the Continent. Thus it is possible that these three children were infected directly through the air passages from subjects with "open" tuberculous lesions in the lungs due to bovine strains. Further proof that the primary lung lesions did not have a hæmatogenous origin was obtained from a small series of cases of

tuberculosis of bones and joints occurring in children in the surgical wards of the hospital, from whom 20 strains were isolated from material obtained from the diseased bones or joints. In six other cases which came to post-mortem, bone lesions were found, but were secondary to abdominal or thoracic disease, and in these cases the infecting bacilli were only isolated from the primary lesions. Of the total 26 strains thus obtained, nine (34·6%) were found to be bovine strains. Tuberculous disease of bones and joints is nearly always due to a blood-borne infection, and the percentage of bovine strains which we found in such cases was more than ten times higher than in cases with primary thoracic tuberculosis.

Most of the photographs in this article are the work of Mr. John Kirkpatrick of the Pathology Department at the University of Glasgow. I would like to express my appreciation for the care which he has taken with the work.

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