

he cannot compete, occupational therapy lays the groundwork for more satisfactory vocational adjustment at a later date.

Occupational therapy of this type must be carefully planned and coordinated with physical therapy and speech therapy. Treatment, either by the occupational therapist or at home with frequent check-ups by the physician and therapist, must be continued for a number of years. Providing there is normal or nearly normal intelligence and there is cooperation from the home, the child with minimal to moderately severe handicaps may be expected to show progressive objective improvement during the period of growth. By progressing from simple tasks, such as feeding, drinking, and dressing, to self expression and vocational training the otherwise useless individual may be able to make his contribution to society.

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## PULMONARY MANIFESTATIONS OF BRUCELLOSIS

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Pulmonary brucellosis has received scant attention, although it has long been known that all three types of brucellosis may attack any body tissue. As early as 1861, in discussing Malta fever, Marston<sup>1</sup> wrote: "There is no fever so irregular in its course and symptoms." Craig<sup>2</sup> in 1906 said: "It is extremely difficult to describe accurately all the forms which this truly protean disease may assume." The largest number of autopsies in brucellosis have been reported by Hughes.<sup>3</sup> He frequently noted pleural adhesions, pleural effusion, and patchy or lobular consolidation. Others have more recently reported pulmonary involvement. Bogart<sup>4</sup> described massive bronchopneumonic infiltration due to both acute and chronic inflammation. Beatty<sup>5</sup> thinks the most common pulmonary manifestation is hilar and bronchovascular infiltration and reported 12 patients showing this finding. Hemoptysis with tracheal ulceration,<sup>5,6</sup> infiltration and consolidation,<sup>6,7,8,9,10,11,12</sup> unresolved pneumonia,<sup>6</sup> lung abscess,<sup>9</sup> and pleural effusion<sup>9</sup> have been recorded by others. Hardy<sup>9</sup> once recovered the *Brucella* from pleural fluid by guinea

pig inoculation. Debono<sup>9</sup> found positive blood cultures in patients with lung involvement.

The following group of patients is reported to illustrate various types of pulmonary diseases observed in the study of several hundred patients with brucellosis at Cleveland Clinic. Most patients had a chronic type of infection.

**Case 1.** A white man, aged 48, entered Cleveland Clinic May 10, 1938, with a dry, hacking cough and substernal discomfort of five weeks' duration. There was also a history of headaches, chills, fever, drenching sweats, and loss of 23 pounds of weight. His temperature was recorded as high as 102° and the pulse rate 110. The chest was clear to physical examination and to x-ray. Agglutination for brucellosis was positive, 1:2560. This patient responded remarkably to sulphanilamide and has been previously reported by one of us.<sup>14</sup>

**Case 2.** A white woman, aged 25, entered Cleveland Clinic May 22, 1946, with persistent hoarseness, cough, and fever of several months' duration.

During the preceding year she had suffered in succession with a chondritis of the nose, acute hepatitis with jaundice, arthritic involvement of the spine and ankles,

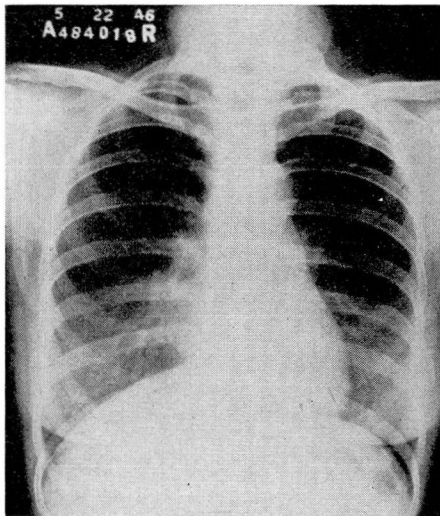


FIG. 1. Case 2. Hilar and bronchovascular infiltration in right lung.

and recurrent pharyngitis. She had had fever as high as 104° and lost 25 pounds of weight. There was a further history of chondritis of the left ear in 1943 and of the right ear in 1942.

The only positive physical findings were a pulse rate of 120, temperature 99.0°, harshness of breath sounds at the hilar areas, husky voice, and diffuse edema of the entire larynx with fullness or piling up of tissue in both ventricles.

The reddish elevation on the superior surface of each vocal cord was stripped off laterally to the ventricles. Sections of this material showed edema and hyperemia of subendothelial stroma with moderate lymphocytic infiltration beneath a normal

epithelium. A chest film at this time revealed prominent hilar and bronchovascular markings in the right lung (fig. 1). A bronchogram was negative. Brucella agglutination was negative, but an intradermal test proved strongly positive. The patient returned to the Clinic on July 18 with a right orbital cellulitis and a chondritis of the left ear, which followed her first two injections of Brucella vaccine. The hoarseness had cleared, and the blood agglutination was still negative.

**Case 3.** A white boy, aged 14, came to Cleveland Clinic Hospital May 13, 1931, because of persistent fever and stiffness in the muscles. His illness had begun in February, 1930, with fever, malaise, and stiffness in the joints. He had developed a patchy skin eruption resembling urticaria. There had been pain and swelling in the testes for a time. Fever had been as high as 104°. He had had severe sweats. Six weeks after the onset of illness he had developed a pleural effusion. Ten cc. of fluid had been aspirated from the left side and reinjected into the subcutaneous tissues. After two to three weeks the effusion disappeared, and he was improved until March, 1931, at which time fever returned with muscular stiffness but no joint pains.

When he was examined two months later there were no significant physical findings in the heart or lungs. There was slight nystagmus, slight digital tremor, and slight ankle clonus with normal reflexes. A chest film revealed very shallow costophrenic angles. The temperature was as high as 104° and the pulse rate 150. Agglutination for brucellosis was positive, 1:80, and an intradermal test gave a markedly positive reaction. The patient had improved under a course of specific vaccine but relapsed in March, 1932, with high fever, swollen and painful breasts, and an audible friction rub over the lower right side of the chest. He was given brucellin and apparently had a good result. However, the breasts remained prominent.

He was seen again in 1940 complaining of fatigability, grating in the neck with aching pain in the left shoulder, back of head, and neck. In 1944 he had another febrile relapse accompanied by an erythema multiforme-like eruption similar to that of his original illness. He likewise had episodes of fever in December, 1945, and in May, 1946. Each of these relapses was accompanied by pain and swelling in the breasts and appeared to respond to sulphonamides. He was last seen July 30, 1946, and still had some grating and soreness of the neck. The breasts were hypertrophied and the testes small but firm.

A chest film showed the same obliteration of costophrenic angles as in 1931. The blood agglutination was negative, and other tests were reported negative during the intervening years. The remains of another strongly positive intradermal test, done several months previously, were clearly visible on his arm.

**Case 4.** A white girl, aged 15, was first seen at Cleveland Clinic on January 12, 1932, with acute mastoiditis without a bulging drum or middle ear discharge. The leukocyte count was only 2000 with 35 per cent granulocytes. There was, in addition, a history of three and a half years of ill health characterized by weakness, nervousness, tachycardia, and headaches with cough, postnasal discharge, and occasional fever during the past year. A tonsillectomy had been performed in July, 1931. For a month before her initial visit she had had a hard cough with foul greenish sputum and temperature of 100° to 103° each afternoon, accompanied by chilliness and sweats. The ear symptoms were of only two days' duration.

At examination coarse rales and a few wheezes were audible in both lungs, most marked over the right base. There was definite mastoid tenderness on the left. X-ray examination revealed some nontuberculous infiltration in the base of the right lung. Blood culture and agglutination for brucellosis were both negative.

At mastoidectomy, bone cells were found to be filled with a thick purulent material having the appearance of an acute process superimposed on an old chronic infection. Convalescence was uneventful, but the temperature again became elevated after the

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patient returned home, and her cough and headache continued. She began to have fever associated with each menstrual period, and on May 24, 1932, agglutination for brucellosis was positive, 1:80. By August, 1932, an abscess had developed in the mid right lung. No definite pathogen could be cultured. She was treated with repeated artificial pneumothoraces, and by January, 1934, the abscess had entirely healed. Meanwhile other agglutinations were positive in a titer as high as 1:360. Fever and headache continued with no evidence of increased intracranial pressure. She had several abscessed teeth and at one time complained of blurred vision with the finding of definite neuroretinitis. She was treated with Brucella vaccine and was apparently greatly improved but later had a recurrence of fever that was not helped by vaccine. She continued to have fever and headaches and on November 30, 1934, her leukocyte count was only 1400.

It is of interest to note that in 1932 and 1933, seven cows belonging to the family were condemned because of Bang's disease.

The patient died elsewhere December 10, 1934, with a clinical diagnosis of peritonitis. Necropsy findings were reported as generalized peritonitis, chronic pleurisy, and terminal pneumonia. There was no examination of the skull, and no cultures were reported.

**Case 5.** A white woman, aged 24, came to Cleveland Clinic February 28, 1946, because of recurring hemoptysis during the preceding ten days. In the fall of 1944 she had had a respiratory infection that was diagnosed pneumonia. X-ray examination at that time showed a lesion suggestive of tuberculosis, but a patch test and the sputum were negative. Dyspnea and a productive cough persisted, and she complained of bouts of pleuritic pain over the diaphragm and costovertebral angle. She had gained from 25 to 30 pounds since the onset of illness.

Examination of the chest was negative, and during a week's observation her highest temperature was 99.6°. The chest film was entirely comparable to one made elsewhere a year earlier and revealed a somewhat rounded, not definitely margined area of in-

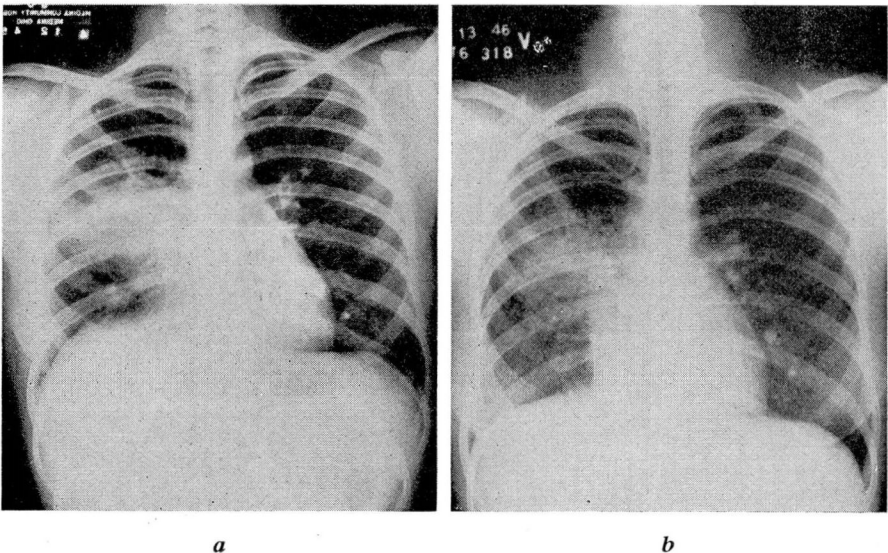


FIG. 2. Case 5. (a) Pneumonic infiltration of six months' duration (4-12-45) in right lung (b) clearing gradually after twenty-two months (8-13-46).

creased density extending outward several inches from the right upper hilus. It was impossible to identify a neoplasm bronchoscopically. A small amount of purulent mucus came from the orifice of the right upper lobe bronchus. Culture of this material showed streptococci, and the sputum was again negative for acid-fast bacilli. A small amount of bloody fluid was aspirated by needle puncture from the area of the lesion, and its culture was sterile. This patient had a negative agglutination for brucellosis but a strongly positive intradermal test. A course of penicillin was given. When last seen August 13, she appeared entirely well; the agglutination test was positive, 1:16, and follow-up x-ray examination showed some clearing of the chest lesion (fig. 2).

In this case there was also a history of contact with cattle infected with Bang's disease eight years previously.

**Case 6.** A white man, aged 42, came to Cleveland Clinic April 26, 1932, with a draining sinus of the right anterior chest wall of seven months' duration. He had acquired Malta fever as a foreign missionary in May, 1931, and at the same time developed a painful area in the right side of the chest. Some peculiar changes in the lungs from the time of the original infection were reported. A large abscess had developed in the right buttock in August, 1931, had been drained, and had healed.

He now had no cough, a good appetite, and was gaining in weight. Temperature was normal, pulse 100. There was a sinus opening with excess granulation tissue between the right fifth and sixth ribs medial to the midclavicular line, and a few scattered rales

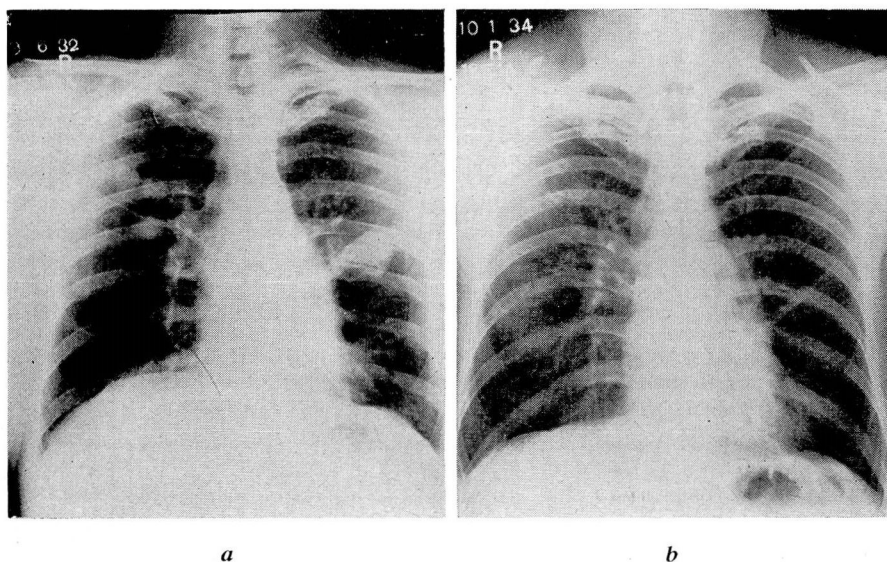


FIG. 3. Case 6. (a) Nodular granulomas in both lungs (9-6-32) with (b) residual scarring (10-1-34).

were present in both lungs, though most numerous at the right apex. The thyroid was diffusely enlarged, and a nodule 1 cm. in diameter was present in the epididymis above the left testicle. The brucellosis agglutination test was positive, 1:640. A chest film showed a linear density between the right mid and upper lobes and several discrete, round nodules of homogenous density, approximately 2 cm. in diameter, lying between the second and third interspaces. The left lung contained a similar nodule 4 cm. in

diameter (fig. 3). All of these had the appearance of metastatic malignant disease. Cultures from the sinus yielded *Staphylococcus aureus*. The patient was treated with iodides, bacteriophage, and nearsphenamine. On June 5, 1933, the nodules were smaller and less dense, and by October 1, 1934, nothing remained but residual scarring. Meanwhile the sinus in the chest wall had healed, but another abscess developed in the right gluteal region and was incised. Culture revealed a gram-positive bacillus. Healing took place after several months. Other superficial infections appeared in the left parieto-occipital region and upper portion of the left thigh in 1933 and 1934 and healed after several months' drainage. Chest films were again negative in 1936, and the blood agglutination varied from negative to 1:40. A communication received in 1938 reported that the patient had remained in good health.

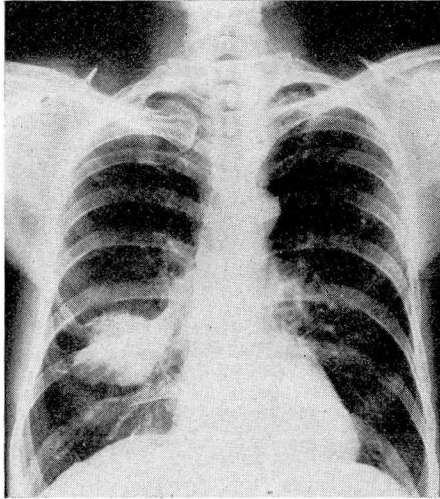


FIG. 4. Case 7. Large granulomatous infiltration in right lung.

**Case 7.** A white man, aged 48, came to Cleveland Clinic Hospital July 17, 1946, because of pain in the left flank and fever of one month's duration. He also had a slight, hacking, nonproductive cough. There had been some increased frequency of urination and pyuria at the onset. He had received courses of sulphonamides and penicillin without benefit. His previous examination had revealed an afternoon temperature of 100° to 101°, a positive brucellosis agglutination, 1:360, and a strongly positive intradermal test. Urologic studies were negative. There was a history of recent use of raw milk. A chest film had revealed a large, solitary, nodular infiltration extending 6 cm. from the lower portion of the right hilus into the lower anterior aspect of the right lung (fig. 4). Little additional information of a positive nature was gained during a two-week period of observation. There was no evidence of neoplasm by bronchoscopic examination, and cultures were negative. This patient was known to have had a negative chest x-ray examination three years prior to his present illness.

### Discussion

Chronic brucellosis may be difficult to diagnose. Often the diagnosis has to be made on the clinical characteristics, the exclusion of other

disease, and a positive skin test. We have not made a diagnosis on a positive skin test alone. We feel reasonably certain that the diagnosis is correct in the cases cited, although the causative organism has not been recovered in any patient.

Case 1 is presented as an example of a common type of pulmonary localization that is more apt to occur in the acute variety of brucellosis and does not exhibit any changes on x-ray examination. The laryngitis in case 2 was pronounced. Hilar and bronchovascular infiltration is characteristic of the most common type of pulmonary pathology reported in this disease. Pleurisy and pleural effusion, as illustrated by case 3, are apparently uncommon manifestations, but brucellosis undoubtedly should be considered more often in cases of pleural effusion when acid-fast infection cannot be demonstrated. In case 4 the lung abscess was merely another step in the adverse progress of the disease.

Case 5 probably represents an unresolved pneumonic process. Cases 6 and 7 are believed to represent pulmonary granulomas and are like nothing else reported in the literature of brucellosis. They could easily be confused with neoplasms, and only the course of the disease can rule this out. In case 7 a benign course remains to be demonstrated.

Among 227 case records of brucellosis which we have recently reviewed, x-ray evidence of hilar and peribronchial infiltration was present in 10 additional cases, cough was recorded as a prominent symptom in 28, a respiratory infection marked the onset in 7, recurrent respiratory infection was present in 19, and hemoptysis was recorded in 4 cases.

### Conclusion

Brucellosis may be easily overlooked as the cause of pulmonary disease.

The pulmonary tract is frequently affected in brucellosis, hence this disease should always be considered when otherwise unexplained disease of the bronchi, lungs, or pleura is present.

Seven patients who illustrate different phases of pulmonary disease due to brucellosis are reported.

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## CLINICAL OBSERVATIONS ON THE MECHANISM OF HYPERTENSIVE HEADACHE AND THE RESULTS OF ITS TREATMENT WITH DIHYDROERGOTAMINE TARTRATE

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Suggestive evidence indicates that hypertensive headaches are in some respects similar to migraine (Janeway<sup>1</sup>) and may be due to dilatation and distention of branches of the external carotid rather than intracranial arteries (Schumacher and Wolff<sup>2</sup>). As reported by Steiner,<sup>3</sup> migraine can often be relieved by vasoconstriction and the resultant decreased amplitude of arterial pulsation induced by ergotamine tartrate. However, this drug is not without unpleasant side effects such as nausea and vomiting. Although it has also been shown to elevate the blood pressure of human beings, the elevation is not of great magnitude, since Pool, von Storch, and Lennox<sup>4</sup> showed that subjects who were given injections of 0.5 mg. intravenously had an average rise of only 13 mm. Hg in both systolic and diastolic pressure.

Recently, dihydroergotamine tartrate has been made available for clinical trial and is believed to be less toxic than the parent drug. The