CHRONIC BRUCELLOSIS IN GENERAL PRACTICE*

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Acute brucellosis is a disease entity the clinical picture of which is fully described in all standard textbooks of medicine. Only in recent years, however, has it become recognized that brucellosis may present and persist for many years in a more chronic form. Evans *et al.* (1938) and Evans (1939) emphasized that many cases of brucellosis were overlooked because of the chronic and insidious nature of the disease. Spink (1951), recognizing the controversy that existed with regard to the reliability of the criteria for diagnosis, followed up 65 cases of proved acute brucellosis that had not been treated by any antibiotic known to be effective in brucellosis and found that 46% were still complaining after 12 months. In a second series that had had antibiotic treatment, 39% were still unwell after a year. He concluded that, in spite of effective antibiotic treatment, a small but significant number of patients continued to show manifestations of active disease.

In this country, Dalrymple-Champneys (1952) and Barrett and Rickards (1953) have described the condition in detail, and the latter workers, in an excellent survey of 35 cases occurring in Lancaster, have shown how chronic brucellosis can occur without a preceding recognizable acute attack. They have drawn attention to the value of aspiration liver biopsy in assisting in the diagnosis.

The present investigation was carried out in general practice and was originally prompted by the fact that I contracted brucellosis four years ago and became aware that several patients who were repeatedly attending my surgery on account of chronic and recurrent ill-health had themselves the same symptoms and signs. It is the purpose of this paper to discuss 11 cases all occurring in one rural practice. Two of the 11 had acute brucellosis in the beginning and, after being followed up for nearly a year, failed to show a return to normal health, and had manifestations of active disease, although during this time the agglutination titre had become negative. The other nine cases were diagnosed in their chronic state.

Great attention was paid to the history, and wherever possible a verbatim description of symptoms was used in the history-taking. The results of clinical and haematological investigations have been recorded, together with temperature charts. Use has been made of the intradermal brucellin test and the subsequent rise in antibody titre that followed. Wherever appropriate, full investigation has been carried out to exclude alternative conditions.

The one constant symptom has been periodic muscle weakness with easy fatigability. In view of the similarity of this to periodic familial paralysis, and remembering that chronic brucellosis is presumed to be due to an intracellular parasitism by the brucella organisms, and also that nine-tenths of the potassium in the body is intracellular, it was decided to investigate the serum potassium levels in these patients. These have been recorded at different phases of the disease.

Table I provides a summary of the principal features of the cases under review. The agglutination titres recorded are the highest titres reached. The serum potassium figures are the readings obtained before and after antibiotic treatment. Details of treatment are given at a later stage of this paper.

Symptomatology

The cardinal symptoms of chronic brucellosis noted in this series of cases were: (1) muscle weakness with easy fatigability and generalized lassitude; (2) muscle pains and joint pains; (3) sweats and chills; (4) abdominal symptoms, chiefly of pain and flatulence; and (5) neurological symptoms.

1.—*Muscle Weakness*.—This is the only symptom common to all cases. It is periodic, in that it is present at certain times and not at others, it comes on suddenly, and it usually gets worse at the end of the day. It bears no relation to the amount of work done. Apart from a generalized lassitude, weakness is maximal in the upper arms and legs, particularly in the extensor muscles of the arm and the quadriceps group of muscles in the legs. There is a rapid fatigue of these muscles, especially when used to maintain a posture, and patients often state that they cannot stand for any length of time, and that their arms soon tire when they are holding up a book to read or are shaving. General lassitude produces a disinclination for exercise, and weight increase is often the result. It is easy to understand why many of these patients, often looking fairly well and yet complaining of a degree of lassitude that is out of all proportion to their appearance, are labelled neurotic, neurasthenic individuals. Spink (1954) has shown how these symptoms can be reproduced in a clinically cured case by the injection of a brucella endotoxin, and they could be partially allayed by the intravenous injection of 20 mg. of corticotrophin. The former is a lipoprotein carbohydrate which resides on or near the surface of the bacterial cell from smooth cultures.

2. *Muscle and Joint Pains*.—These are transitory and are felt chiefly in the limbs, the back of the calf muscles, and the back of the neck. Three patients complained of pain in the pectoral and subscapular group of muscles. Transient enlargement of the posterior triangle cervical glands may occur. Other groups of glands may also enlarge and become tender. Joint involvement is usually transitory and any joint may become painful and swollen for a few days. Case 10 showed a bilateral hydrarthrosis of knee-joints, destructive changes were not noted in the inflamed joints, and the sedimentation rate, radiological appearances, and blood uric acid were within normal limits. Apart from local symptoms, several patients complained of a generalized stiffness, most commonly felt in the early mornings. One patient remarked that it was just as if he had done a hard day's haymaking the day before. Another likened it to the morning after the first game of football of the season. Stiffness would seem to be out of all proportion to the previous day's exercise. Harris (1950) quotes the remarks of a physician suffering from chronic brucellosis—he states: "If fatigue is due to neurosis, continuation of graded exercise should result in improvement and greater tolerance; in chronic brucellosis, if one continues to exercise in spite of fatigue, then exhaustion, tremor, lack of muscular control and co-ordination develops." He points out that the muscular sensation of the patient who has brucellosis is exactly similar to that of the well person who has exercised too vigorously.

3. *Sweats*.—Excessive sweating was noticed in five cases. It was most pronounced in the two acute cases, but became less noticeable in the chronic state. Recurrence of sweating seemed to herald the return of a bout of brucellosis and was particularly marked at night.

4. *Abdominal Symptoms*.—Eight patients complained of abdominal pain. This was described as an ache in the right iliac fossa or in the right hypochondrium. The former

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suggested an appendicular origin, and two cases had had an appendicectomy without relief of symptoms. Four complained of excessive intestinal flatulence associated with the passage per rectum of an irritating mucous discharge which excoriated the perianal skin. The latter symptom was noted before antibiotic treatment, was not associated with any radiological or bacteriological abnormality in the bowel, and was cured by antibiotic therapy. Case 5, besides complaining of lassitude and sweats for several years, had a history of chronic pain in the right loin with frequency of micturition. The day after an intradermal brucella skin test he developed a frank haematuria and a fever. Laboratory examination of the urine showed no organisms or casts, and culture for tubercle bacilli was negative. The intravenous pyelogram was normal. This case and all the others were relieved of their abdominal symptoms by antibiotic therapy. Abernathy *et al.* (1955) reported a remarkable case of proved brucella pyelonephritis. Their patient, who underwent nephrectomy, exhibited caseation and calcification, and microscopical examination showed multinucleated giant cells in numerous granulomatous lesions: in fact, macroscopically and microscopically, lesions typical of tuberculosis, and yet the Mantoux test was negative and no tubercle bacilli were isolated from the kidney. They concluded that in all chronic granu-

lomatous lesions the specific aetiological agent should be found, and suggested that in the search for the aetiological agent the index of suspicion for brucellosis should be high.

5. Neurological Symptoms.—Two of the cases showed signs of a peripheral neuritis and also had blurring of vision. Another patient, not included in the series, though suffering from multiple sclerosis, showed a strongly positive brucella test and developed a sustained antibody rise. She was so improved after combined antibiotic and steroid therapy that one could not but wonder whether her neurological condition might have been related to a brucella hypersensitivity.

Physical Signs

Physical examination of these cases revealed the following features.

1. Hepatic Enlargement in All Cases.—The liver edge was found to be firm, tender, and smooth. The degree of enlargement was between 1 and 2 in. (2.5 and 5 cm.) below the right costal margin. Barrett and Rickards (1953) have shown by aspiration liver biopsy that there is a return to normal hepatic cytology in brucellosis after antibiotic therapy.

2. Splenic Enlargement.—This was detected in two cases. It was not tender. Neither hepatic nor splenic enlargement could be detected after adequate antibiotic therapy.

TABLE I.—Summary of Cases

Case No.	Age and Sex	Duration of Disease	Milk Supply	Symptoms	Physical Signs		Agglutination Titre		Treatment	Serum Potassium (mg./100 ml.)		Results
					Hepato-megaly	Spleno-megaly	Before Skin Test	After Skin Test		Before Treatment	After Treatment	
1	40 M	9 mths	Pos. Brucella isolated from own milk	Fever, sweats, muscle pains, lassitude	Yes	No	1: 640	Not done	Combined antibiotics (4 courses)	16.5	21.0	Afebrile. Symptom-free, back at work as nurse
2	36 M	3 years	" "	Lassitude, muscle pains, abdominal pains	"	"	1: 1,000	1: 30	Combined antibiotics (3 courses)	17.2	21.5	Afebrile. Only minimal symptoms after second course of antibiotics
3	40 F	4 "	Abortion in own herd 4 years ago	Lassitude, fever, sweats, joint pains, abdominal pains	"	"	Negative	1: 160	Combined antibiotics (2 courses) antibiotic + prednisone	16.8	18.5	Afebrile. No symptoms, working well as farmer
4	50 M	12 mths	Raw milk drinker	3 febrile bouts, prodromal lassitude, aching in arms	"	"	"	1: 80	Combined antibiotics (2 courses)	Not examined	17.8	No further bouts of fever, feels well. Working as shop assistant
5	31 M	4 years	Abortion in own herd 4 years ago	Chronic lassitude, sweats, muscle pains, dysuria, abdominal pains	"	Yes	"	1: 640	Combined antibiotics (2 courses) antibiotic + prednisone (1)	16.4	17.5	Afebrile. Working as farmer, greatly improved. Minimal symptoms
6	33 F	10 "	Raw milk drinker	Lassitude, persistent fever, muscle and joint pains, abdominal pains	"	No	"	1: 160	Combined antibiotics (2 courses)	16	17	Was greatly improved after 2nd course but had recurrence now of polyarthritic symptoms. Working. Afebrile. Only partial improvement
7	67 M	6 mths	" "	Lassitude, muscle and abdominal pains, colitis	"	Yes	"	1: 160	" "	17	20	No symptoms. Has plenty of energy
8	47 M	2 years	" "	Lassitude, easily fatigued, pains in arm and neck	"	No	"	1: 40	" "	15.5	21	Afebrile and back at work but still has minimal symptoms
9	58 M	2 "	" "	Lassitude, sweats abdominal pains	"	"	"	1: 2,560	" "	16	23	Back at work as farmer. No sweats or fatigue. Abdominal symptoms cured
10	38 M	4 mths	" "	Lassitude, muscle pains, bilateral effusion in both knees	"	"	"	1: 80	Combined antibiotics (1 course)	16.5	17.5	No symptoms, except both knees are stiff and swollen
11	63 M	2 years	" "	Weakness, sweats, pain in calves, abdominal symptoms + colitis	"	"	1: 160	1: 1,280	" "	17	21.5	Has only recently completed treatment. Afebrile. No abdominal symptoms, but not yet regained full strength

3. Evening Pyrexia.—In this series of cases, six were found to have an evening pyrexia which disappeared after treatment. Griggs (1942), in a survey of 100 cases of chronic brucellosis, recommended that the temperature should be recorded for five minutes night and morning. He detected a pyrexia of 1° F. or more in 20% of cases. The same procedure was adopted.

Haematological Investigation

In all cases a full blood count was made and the sedimentation rate estimated. Two cases showed a mild degree of iron-deficiency anaemia. The sedimentation rate was normal in all cases. Scarlett (1948) regarded this as an important aid in differential diagnosis. Lymphocytosis was noticed in five cases. Where appropriate, blood sugar and uric acid were estimated. Blood culture, using Castañeda's (1946) technique, was carried out in five cases. All were negative. This has been the experience in larger series of cases.

Intradermal Skin Test

All the cases had a positive skin reaction. Brucellin, a killed whole organism suspension prepared and supplied by the Central Public Health Laboratory, Colindale, has been used as the intradermal antigen.

Technique.—0.1 ml. was injected intradermally in the right forearm. In most cases a short-bevel needle was used and care was taken to see that a visible and definite vesicle was produced. In a few cases the Heaf multiple-puncture technique was used; this had no special advantages. The test was read at 48 hours, and after one week; a positive reaction was interpreted if there was (1) induration of the site, (2) erythema of 1 cm. or more, (3) or both erythema and induration. Harris (1950) classifies the positive results of the skin test as (1) weakly positive (+), this being a reddened indurated area of about 5 mm. in diameter appearing from the fourth to eighth day; (2) positive (++), an area of induration of more than 5 mm.; (3) strongly positive (+++), an area of redness and marked induration greater than 10 mm.; (4) a violent positive reaction (++++), which is a

markedly swollen indurated area with erythema, often with lymphangitis, axillary adenitis, systemic reaction, and occasionally with central necrosis. This classification was used to read the results of the skin test. Equivocal results encountered in a series of controls were clarified by the inspection one week after the skin test. In most of the positive cases the intradermal mark could still be detected several weeks afterwards.

The significance of the skin test is analogous to the tuberculin test. A positive skin reaction indicates past or present infection, but does not in itself indicate current infection.

Thanks to the co-operation of the medical staff of the hospitals in this area, it was possible to estimate the incidence of the positive skin reaction to brucellin in a group of patients. In this survey I was greatly assisted by the consultant bacteriologist, and we conducted skin tests on a group of patients in the mental hospital, the sanatorium, and the medical ward in the general hospital. The results are shown in Table II.

TABLE II.—Results of Skin Tests

Hospital	No. of Cases Tested	Positive Tests	
		No.	%
Male wards of mental hospital ..	40	11	27
Female admission block of mental hospital ..	33	7	21
Medical ward of general hospital ..	24	3	12
Sanatorium ..	29	6	20
Total ..	126	27	21

The incidence of dermal sensitivity to brucellin in a group of controls was found to be 21%. This would suggest that in a rural area risk of exposure to brucella has not been insignificant.

Agglutination Reaction

The agglutination response to *Brucella abortus* in the patients of this series are recorded in Table III. Three cases had an agglutination titre prior to skin testing. Cases 1 and

TABLE III.—Agglutination Response to *Br. abortus*

Case No.	Date and Result of Brucellin Test	Agglutination Titres (with Dates)						
		10/4/56	13/4/56	28/4/56	28/6/56	7/9/56	15/9/56	
1	Not done	1: 640	1: 640	1: 250	1: 640	Trace 1: 50	Neg. (less than 1: 20)	
2	23/1-29/5/56 ++ 1/1,000-1/100 dilution ++	29/9/53	26/2/54	16/3/54	8/4/54	4/3/55	15/6/56	21/10/56
		1: 1,000	1: 80	1: 125	Neg.	Neg.	Neg.	1: 20 1: 3; 1: 120 (incomplete antibodies)
3	9/5/56 +++	9/5/56	24/5/56	30/5/56	2/6/56	19/6/56	2/8/56	22/9/56
		Neg.	1: 40	1: 40	1: 160	1: 80	1: 160	1: 40
4	9/5/56 +++	22/5/56	22/6/56	10/8/56				
		Neg.	1: 80	1: 80				
5	18/5/56 ++++	24/5/56	18/6/56	2/7/56	12/8/56			
		1: 80	1: 320	1: 640	1: 320			
6	1/6/56 ++	3/1/55	12/6/56	24/7/56	6/8/56	4/10/56		
		Neg.	1: 160	1: 80	1: 40	1: 40		
7	12/5/56 ++	13/6/56	2/7/56	3/8/56				
		1: 160	1: 160	Neg.				
8	12/7/56 ++	5/7/56	30/7/56	22/8/56	7/9/56			
		Neg.	1: 40	1: 40	Neg.			
9	18.4.46 +++	24/4/56	5/5/56	2/6/56	29/6/56	11/7/56	11/8/56	
		Neg.	Neg.	1: 80	1: 2,560	1: 160	Neg.	
10	30/6/56 ++	27/6/56	3/7/56	18/7/56	2/8/56			
		Neg.	Neg.	1: 80	Neg.			
11	27.6/56 ++	1/10/54	27/6/56	17/7/56	25/10/56			
		Neg.	1: 160	1: 2,560	1: 320			

2, in that they had a titre which was diagnostic of acute brucellosis at the onset of their disease, were not subjected to a diagnostic intradermal test, although Case 2 received several intradermal doses of 1/1,000+1/100 brucellin in January, 1956, as vaccine therapy. It will be noted that after two years, during which time the agglutination titre had fallen to less than 1:20, antibodies were found to reappear in the case as a result of the antigenic stimuli. Case 11 had a titre of 1:160 prior to the skin test.

The appearance of antibodies in the blood following skin testing was first noted by Giordano (1929). He showed that a response could occur in skin-positive or skin-negative cases. Since then much controversy has occurred, and a wide variation in the response has been reported by different workers (Goldstein, 1934; Elton, 1948; Carpenter *et al.*, 1950). This controversy has arisen chiefly on account of the variation in dosage and the type of antigen used. Krakauer *et al.* (1951) studied the effect of brucellergen on the agglutination titre of 34 cases suffering from probable brucellosis whose serum, prior to skin testing, failed to agglutinate brucella in a significant titre. A titre of 1:80 or above developed in 32 out of the 34. In contrast, 85 patients suffering from diseases other than brucellosis failed to show any antibody rise. Elton (1948), in a survey of the literature on this point, concluded that the antibody response following skin testing is chiefly dependent upon the amount and type of antigen used.

It was therefore decided to estimate the antigenic power of the solution of brucellin which had been used in the present series of cases. Patients in the mental hospital, in a near-by sanatorium, and in general practice were examined and tested as controls. A sample of blood was taken before the skin test in order to ascertain that there were no antibodies to *Br. abortus* in the circulating blood. The intradermal test was then carried out, recorded, and after 14 days the blood was re-examined for antibodies. In a number of cases the blood was re-examined 28 days and 56 days after the intradermal test. The results are given in Table IV.

TABLE IV

	No. of Cases	Agglutinations Present Before Skin Test	Negative Agglutination 14 Days After Skin Test	Positive Agglutination 14 Days After Skin Test
Mental hospital	40	0	32	8
Sanatorium	21	0	15	6
General practice	11	0	10	1
Total	72	0	57	15

Of the 72 controls examined, 57 demonstrated no rise in antibodies 14 days after a brucellin skin test. In the remaining 15 the agglutination was positive at 1:25 in 6, 1:50 in 6, and 1:125 in 3.

Those cases in the general practice and sanatorium groups which had shown this antibody rise were examined again 28 days after the skin test. They were then all found to be negative.

In the mental hospital group of controls, serial blood examination was carried out on all 40 cases. The results are shown in Table V.

TABLE V

	Total No.	No. of Cases with Negative Agglutination	No. of Cases Showing Positive Agglutination
14 days after test	40	32	8 (6, 1:25; 2, 1:50)
28 " " "	40	37	3 (1:25)
56 " " "	40	40	0

It was also found that of the 15 controls showing an antibody rise five were skin positive and ten skin negative.

The results of this experiment showed, therefore, that (1) the intradermal injection of brucellin resulted in the appearance of antibodies in a group of controls in a small number of cases; (2) this non-specific rise in antibody titre, when it appeared, was neither of high titre nor sustained;

and (3) the appearance of antibodies was not related to the original dermal sensitivity of the case.

These results are similar to those of Huddelson *et al.* (1939) with brucellergen. They stated that "one injection of brucellergen may give rise to brucella agglutinins in a small proportion of cases."

Diagnostic Criteria

The above findings suggested that emphasis could be laid on the following diagnostic features. (1) A typical history, especially of muscular weakness, together with positive physical signs. (2) In the presence of the history, either (a) the isolation of the organism from the blood or tissues or the detection of antibodies to *Br. abortus* in the blood, or (b) the appearance of antibodies in high or sustained titre following a positive intradermal brucellin test. If these conditions appertained, antibiotic therapy was begun and the response provided the third criterion. (3) Therapeutic result: three patients, not included in this series, with suggestive symptoms and a positive skin test failed to show any antibody response or any improvement following antibiotic therapy.

Serum Potassium

For reasons already mentioned it was decided to determine the level of serum potassium in all 11 cases. Estimations were made in the chronic phase of the disease. The potassium was calculated by the use of a flame photometer employing coal-gas and compressed air, a light-filter system, and an external standard.

The results, which are expressed in mg. per 100 ml., are shown in Table VI.

TABLE VI.—Serum Potassium Values Before and After Treatment

Case:	1	2	3	4	5	6	7	8	9	10	11	Mean
Before	16.5	17.2	16.8	Not done	16.4	17	17	15.5	16	16.5	17	16.59
After	21	21.5	18.5	17.8	17.5	17	20	21	23	17.5	21	19.6

In a group of controls from patients in the mental hospital and the sanatorium the figures shown in Table VII were obtained.

TABLE VII.—Mean Serum Potassium Values in Controls

	Female	Male	Total
No. of cases	30	36	66
Mean serum K (mg./100 ml.)	18.7	19.2	19.0

The level of the serum potassium in the cases of chronic brucellosis before they had effective treatment were all below the mean figure obtained from the controls. Josephson and Dahlberg (1952), in a survey of a number of healthy men and women, calculated the mean values for potassium, and these are shown in Table VIII.

TABLE VIII.—Mean Serum Potassium Values (mg./100 ml.) in Healthy Men and Women

	Men	Women
20–30 years	18.67 ± 0.43 σ2.05	18.49 ± 0.35 σ1.55
16–50 " "	19.34 ± 0.16 σ1.9	—
<50 " "	—	18.5 ± 0.14 σ1.7
60–65 " "	20.5 ± 0.25 σ1.92	—
>70 " "	—	20.03 ± 0.25 σ1.81

Wootton and King (1953), in an analysis of the inter-hospital differences for the normal constituents of blood, have shown that it is necessary to return to the use of ranges of normality. Whilst the figures obtained for the serum potassium in this series of cases all fall within this range, it may be of some significance that they are all at the lower level.

Serial examination of the serum potassium at times seemed to show some correlation to the clinical state of the patient. Potassium chloride tablets, 15 gr. (1 g.) three times a day

given by mouth, however, had no effect on the symptomatology or fever of the patient, although a rise in serum potassium level was observed after their administration. An improvement in the general health of patients was noticed when the serum potassium level rose as a result of antibiotic therapy; no such amelioration of symptoms was noticed when potassium chloride was given by mouth to four cases for a short period, even though the serum potassium might have increased. It seems possible that the intracellular potassium metabolism is disturbed by the activity of the *Br. abortus*, and the serum potassium figure is an index of the activity of this organism.

Electrocardiographic tracings of Cases 1, 3, 5, and 6 showed no evidence of potassium deficiency.

It is quite obvious that no conclusion can be drawn from such a small number of cases of brucellosis, especially as basal conditions were not assured. Nevertheless, so far as this series was concerned, a low "normal" value for the serum potassium was observed in all the cases. Furthermore, there was a general correlation between the clinical improvement of the patient and the level of the serum potassium after treatment. It may well be that these fluctuations are coincidental, but they are described in the hope that workers with large series of cases at their disposal might feel that in view of the above findings the fluctuation of the serum potassium in chronic brucellosis is worth looking into.

Treatment

Combined antibiotic therapy was used in all cases. Tetracycline and streptomycin sulphate were given for 14 days in most instances. Tetracycline, 2 g., was given daily and streptomycin, 5 g., by injection night and morning. In several instances it was necessary to repeat this course two or three times on account of a relapse. An improvement was noticed about one week after the completion of a course, and even if there was a return of symptoms there seemed to be an overall improvement after each course of antibiotics. Cases 3 and 5 were the exception in that they showed only a transient improvement with the above routine. It was necessary in these cases to combine the antibiotics with prednisone. Prednisone was used because of its property in reducing hypersensitivity and its ability to liberate organisms from a fibrotic lesion. The dosage was 15 mg. twice daily for the first two days, 10 mg. twice daily for the next two days, and 5 mg. twice daily for the rest of the 14 days. The usual precautions for steroid therapy were taken (preliminary radiograph of chest and inquiry about any history of peptic ulceration) and supplementary vitamin-B therapy was given with the antibiotic.

The results of treatment are given in Table I. It is not possible to speak in terms of a cure in a disease that is notorious for its tendency to relapse, but the results of treatment have been assessed with regard to improvement of symptoms and ability to carry on a normal day's work.

Discussion

The study of these cases of chronic brucellosis would seem to suggest that the disease is a relatively common one. On the basis of these observations it must surely be of significance that 11 cases have occurred in one rural practice in less than a year. Survey of the herds in this area in recent years has not suggested that infection with *Br. abortus* is any more prevalent here than in other rural areas. There has, however, been a considerable decline in the drinking of pasteurized milk, largely as a result of the publicity given to the Tuberculosis Milk Scheme. The tuberculin-tested milk has come to be regarded as a synonym for the "safe milk," and little attention has been paid to the brucella risk.

That this risk is not insignificant is suggested by Dalrymple-Champneys (1950) in a survey of the incidence in cattle in this country. He has reliably estimated that 15 to 20% of our adult bovine cattle are infected. It is further suggested by the results of the examination of a group of

controls in this series: these have shown that at some time or another approximately 20% of the adult population have had their tissues infected with the *Br. abortus*, with the results and production of skin allergy to brucellin.

Analysis of the mode of onset of the 11 cases has shown that in one only was the onset of the disease heralded by a high fever; all the other cases demonstrated a period of ill-health with no recognized acute onset—in fact, one case was found to have a positive titre as high as 1 in 1,000, although on no occasion did the fever exceed 99° F. (37.2° C.). It was further noted that in three cases a bout of brucellosis was either precipitated or aggravated by a surgical operation. As these operations were performed in different hospitals and the milk supply in one of them was known to be pasteurized, it was unlikely that the hospital milk supply was at fault. The impression was gained that trauma excited a latent brucella focus.

When it is recognized that infection with *Br. abortus* can present and persist in this insidious way, it is obvious that many cases are either missed altogether or not diagnosed in the acute stage. It is only in the acute stage of the disease that laboratory diagnosis, by blood culture or high agglutination titre, is positive. It is necessary to utilize ancillary laboratory procedures in the diagnosis of the chronic state. The follow-up of the agglutination titre in these cases has shown that there is often a high and sustained agglutination response following a single intradermal injection of brucellin. There was also a strongly positive skin reaction and a low normal serum potassium. In view of the fact that these criteria were not found in the controls, it is not justifiable to dismiss the *Br. abortus* in any investigation on the strength of a single negative agglutination in the blood.

The importance of recognizing the chronic brucella state serves a twofold purpose. Firstly, in order to raise the index of suspicion of brucella in several chronic debilitating diseases. It has already been mentioned that transient polyarthritic symptoms were found to develop and reoccur in two of the cases, and a third case showed features suggestive of chronic brucella pyelitis. In view of Spink's remarkable case of chronic brucella pyelonephritis which showed caseation, calcification, and giant cell formation, it is surely justifiable to apply full brucella diagnostic procedures to most chronic granulomatous conditions where no pathological organism has been isolated. Secondly, to offer hope to a not insignificant group of patients who have often wandered from physician to physician (or surgeon) ever hopeful of seeking help and relief from their symptoms, and who, if left undiagnosed, may remain in chronic ill-health for many years.

It has been the purpose of this paper to attempt to show that these cases may be diagnosed if care is taken in interpreting the patients' histories, if the physical examination is thorough, if the temperature is recorded for five minutes, and if the laboratory and dermal sensitivity findings are all correlated together.

Summary

The essential clinical and laboratory features of cases of chronic brucellosis which have occurred in a rural practice are described.

In a survey of a group of people in a rural area the incidence of sensitivity to brucellin was found to be 21%.

The single intradermal injection of brucellin in a group of controls was followed by the appearance of antibodies in only a small number of cases. Such a rise, when it appeared, was not of high titre nor was it sustained.

The possible disturbance of potassium metabolism resulting from the intracellular habitat of *Brucella abortus* is discussed.

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The patient seemed an admirable one as a test case; at term she would have survived more than a two-year period after pneumonectomy, she was multiparous, had excellent respiratory reserve, and was quite without apprehension regarding the outcome. The result of the trial was most encouraging.

Present Series

The following small series of cases illustrates this and some further experiences.

Eighteen cases are reported. Two patients who were advised against carrying on with pregnancy had the pregnancy terminated, and were sterilized. Sixteen have been delivered (see Table): twelve at the Queen Victoria Memorial Hospital, where I was personally able to supervise the chest condition; three at the Royal Women's Hospital; and one at the Base Hospital, Geelong. It is notable that one patient had pneumonectomy performed during pregnancy.

Details of Cases (16 Patients)

State of Chest	Primigravidae	Multigravidae
Left pneumonectomy; clear right lung ..	3	2
Right pneumonectomy; clear left lung ..	3	2
Left pneumonectomy; some disease right lung ..	4	1
Right pneumonectomy; some disease in left lung ..	0	1

PREGNANCY AFTER PNEUMONECTOMY FOR PULMONARY TUBERCULOSIS

BY

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During the past decade a number of patients have undergone pneumonectomy as part of their treatment for pulmonary tuberculosis, and some of them have subsequently returned to a life of reasonable activity. They have almost invariably had a prolonged and severe illness. Work with patients needing such an extensive operation as pneumonectomy is usually regarded as largely salvage work.

It was inevitable that some of this salvage work would be done on women in the child-bearing period of life, and that sooner or later we would be asked to advise for or against pregnancy, and, if advising in favour of it, to care for the patient during and after pregnancy. The problem is twofold. Firstly, can a woman with only one lung undergo pregnancy and normal delivery safely? Secondly, can such a woman subsequently recover and maintain herself in sufficiently good health to undertake and continue with family responsibilities?

It is well known from past experience that a woman with extensive bilateral pulmonary tuberculosis and little respiratory reserve can deliver herself normally of a healthy infant. It would seem, then, on theoretical grounds, that the absence of one lung should be no bar to pregnancy and normal delivery. But the answer to the second part of the problem is not so easy to deduce, for no one can yet be sure of the ultimate prognosis of the patient with one lung and a past history of pulmonary tuberculosis.

When the first such pneumonectomy patient presented me with this problem late in 1950, I advised her, with a certain amount of trepidation, to carry on with the pregnancy. The problem had to be solved by clinical trial.

The average time interval between pneumonectomy and delivery was 26 months (variation between four months and four years). The average length of labour for primigravidae was approximately 26 hours (variation between 3½ and 50 hours) and for multigravidae 4½ hours (variation between 1½ and 7½ hours).

With one exception (Case 9) labour proceeded without undue respiratory distress; with one exception (Case 12) a living healthy child was born. All patients have been followed up for a minimum of one year.

A certain number of complications were associated with these pregnancies and deliveries, both respiratory and obstetrical.

Respiratory Complications.—Immediate: Two patients suffered respiratory distress during labour, one very mild, one severe. Both recovered completely after delivery and have shown no evidence since of respiratory damage due to stress in labour. The patient with severe distress was sterilized after delivery; the other was later delivered of a second child without any distress whatever. Late: One patient reactivated disease in her remaining lung six months after delivery, and required further antituberculous treatment.

Obstetrical Complications.—One patient developed mild hypertension at 36 weeks. Two patients developed toxæmia, one mild, one moderately severe. One patient developed severe hydramnios at 38 weeks. One had a post-partum hæmorrhage requiring blood transfusion. One had a premature but healthy infant. One had a stillborn child due to blood incompatibility between mother and foetus. One later aborted a second pregnancy.

The following cases are selected from the series:

Case 1

The patient was found to have pulmonary tuberculosis in 1947, some time after the birth of her second child. She was then aged 26. After a period of sanatorium treatment, left artificial pneumothorax was tried, but it failed to control the disease. Bronchoscopy showed that there was acute disease of the left main bronchus. A small area of infiltration in the right lung had cleared without leaving radiological signs. After 22 months' sanatorium treatment left pneumonectomy was done for uncontrolled cavitation in