

## A village epidemic of brucellosis

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### INTRODUCTION

The problem of brucellosis in Israel has assumed greater importance since there have been increasing numbers of flocks of sheep in the country districts. Widespread outbreaks of the disease have occurred, especially in settlements established by immigrants lacking adequate experience in agriculture and animal husbandry (Rozansky, Weber, Lehman & Bali, 1956; Cohen, 1958; Olitzki, Sulitzean, Arnan & Rasooly, 1960). One such outbreak is the subject of the present communication.

Melilot, a village in the Beer-Sheva district, was founded in 1953 by immigrants from Kurdistan and in 1957 its total population was 309. At the beginning of that year there was an outbreak of brucellosis in the village involving more than a quarter of the population. Because of its high morbidity and the fact that the investigation covered almost all the inhabitants who were seriously exposed to risk of infection it was considered that it might be of interest to place on record the more important observations made during a study of the outbreak.

### THE OUTBREAK

#### *Infection in the village livestock*

The village livestock in January 1957 included 390 sheep and 57 goats. Although the individual animals were privately owned, the sheep were kept together as a common herd. As soon as it was known that cases of human brucellosis were occurring in the village, veterinary inspection of the animals was undertaken and the veterinary surgeon took samples of blood from sixty-one sheep and fifteen goats for examination for brucella agglutinins; fifteen of the sheep sera and eight of the goat sera were found to be positive. In addition, *Brucella melitensis* was isolated from uterine cultures of one sheep and one goat.

Every family owned either sheep or goats or both and it was known that in every family where there were cases of human brucellosis there was infection among the animals owned by that family. The detail of this relationship was not worked out since the original veterinary survey was not repeated and the extent of the spread of infection among the animals was not determined. Nevertheless, from the information obtained about the occurrence of human cases it seems probable that the spread of infection in the herd was considerable.

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There were no bacteriological examinations of the milk of either the sheep or goats, but epidemiological evidence indicates that the soft country cheese made from sheep's milk was sometimes infective. This cheese appears to have been consumed widely and even included in the diet of very young children who would be susceptible to infection by this means. It was known that some of the villagers drank goat's milk which had previously been boiled but detailed information on the extent of this practice was not available.

### *Infection among the villagers*

The population of Melilot at the time of the outbreak was 309 and this was made up of 46 families, the size of which varied from three to eleven persons (average 6.7 persons). All the families were of similar social and cultural levels and the distribution of the sexes throughout the age groups of those involved in the outbreak was approximately equal (see Table 1). But there were nine of the families, comprising sixty-two persons, in which all members remained free from infection throughout the epidemic. It was not possible to obtain information which would offer a satisfactory explanation for this freedom from infection in these particular families.

Table 1. *Incidence of brucellosis in village outbreak in Melilot 1957 according to age and sex*

Age group	Population			No. examined	Brucella infections			
	Males	Females	Total		Sero-logical evidence only	Clinical brucellosis with serological and/or bacteriological evidence		
						Males	Females	Total
0-2	24	27	51	10	—	1	2	3
3-5	18	19	37	15	—	0	2	2
6-10	22	14	36	28	1	2	1	3
11-15	25	17	42	41	1	7	4	11
16-20	21	18	39	36	3	6	4	10
21-50	45	43	88	86	—	21	19	40
51-82	7	9	16	16	—	3	7	10
Totals	162	147	309	232	5	40	39	79

## INVESTIGATION OF THE OUTBREAK

### *Epidemiology*

Although the outbreak was considered to have started in February, when the notification was received, it is possible that it commenced a little before this because several of the cases were clinically very mild. In planning the investigation of the outbreak it was necessary to have the co-operation of the whole of the village, and it was therefore decided that the examination of the inhabitants should be as complete as possible except where the very young children were concerned. Experience of previous outbreaks had clearly indicated that exposure to risk of infection was almost entirely confined to those having direct contact

with animals and that, normally, children under the age of 5 years would not be exposed to this type of risk. Except, therefore, where there was a special reason for including them in the routine medical examination the very young children were not examined, but, with few other exceptions, all persons, male and female, over the age of 5 years were fully investigated by interrogation (where feasible), clinical examination and also by the various laboratory procedures. Out of the total population of 309 there were seventy-seven persons not examined; this number includes sixty-three apparently healthy children under the age of 5 years. There were adequate reasons for not examining the remaining fourteen. It is possible that if all the sixty-three children under 5 years had been fully investigated one or two might have shown evidence of infection but it seems unlikely that any significant number of additional infections would have been revealed. There were twenty-five children in the 0-5 years age-group who were fully investigated because of some clinical illness or other reason and in only five was there any evidence of brucellosis.

The original examination of the villagers in February showed that thirty-seven were suffering from brucellosis; the clinical diagnosis was confirmed by serological tests or by the isolation of *Brucella melitensis* from blood cultures. Subsequently forty-two other persons developed the disease (four in March, thirty-six between April and July, and in September there were two) making seventy-nine who were clinically ill with brucellosis. In addition there were five with serological evidence of infection without being clinically ill.

The age of the population at risk influenced the incidence. Thus under the age of 5 years the incidence was about 6%, from 6-10 years 8%, from 11-20 years 25%, from 21-50 years 50% and in those over 50 years the incidence was 66%. The age of the patient could be related to the degree of exposure to risk of infection; in this village it was the older age group which was most in contact with the sick animals.

The arrangements for the care of the livestock varied according to the particular village settlement. In the one under consideration it could be said that children under the age of 5 years had no direct contact with the village livestock but after that age they often began to help with the animals although the major part of this work, especially the care of sick animals, was undertaken by the older members of the settlement. Indeed, as indicated, above, the elderly folk were most frequently given this task, the reason being that their advancing years made them ill fitted for the hard manual labour in the fields. It was no surprise therefore to find such a high incidence in those over 50 years, but the very steep rise in incidence after the age of 10 years reflects the increasing degree of contact with animals through adolescence to adulthood.

The age incidence noted in this epidemic is not always observed in outbreaks of brucellosis in Israel. In another village in the Beer-Sheva district there was an outbreak of brucellosis in 1953-54 and there the highest incidence of the disease occurred in children under the age of 10 years. The epidemiological study of this outbreak revealed the fact that most of the adolescents and adults in the settlement were fully employed in the field or in a nearby factory and that the care of

the animals was left almost entirely to quite young children and thus this young age-group was most heavily exposed to the risk of infection (Rozansky *et al.* 1956).

The lack of sex differentiation in village outbreaks of brucellosis is a reflexion of the equal employment in Israel of men and women in the care of livestock. In other places, however, such as Iowa and Minnesota in the U.S.A., it is mainly the men who are employed in animal husbandry and there brucellosis is predominantly a disease of males (Feig, 1952; Jordan, 1949).

As indicated above, the part played by milk from diseased animals in the outbreak was not directly investigated. One 5-months-old baby who had no direct contact with any of the sheep or goats developed a severe attack of brucellosis. It was found, however, that she received soft cheese made from sheep's milk as part of her diet and it is presumed that the infection came from this source. This soft country cheese was widely consumed by all age groups in the village and although it is possible that one or two of the other very young children who contracted the disease were also infected from this source, since this age group is highly susceptible to infection, the epidemiological evidence does not support the view that contaminated milk products were a serious hazard in this outbreak.

The serious danger was in the infected herd and the whole of the remaining stock was slaughtered in May. This did not immediately cut short the epidemic for a few cases appeared in June and the beginning of July, but by then the epidemic may be said to have come to an end. The two clinical cases that appeared in September were, without doubt, contracted from the infected ground where the herd was slaughtered some 3 months previously. Two men were employed in digging over the ground by hand because mechanical equipment was not available at the time; within 2 weeks of accomplishing this task the men became ill with clinical brucellosis which was later confirmed in both cases as *Br. melitensis* infection.

#### *Clinical picture of the disease and response of patients to antibiotics*

There was considerable variation from patient to patient in the severity of the symptoms and the course of the disease but the qualitative picture was fairly constant. Most of the patients complained of arthralgia and myalgia but heavy sweating was less frequently noted. In nearly three-quarters of the patients the spleen and liver were enlarged and the lymph nodes palpable. The degree of pyrexia was very variable and only half of the patients had temperatures of 38° C. (100.4° F.) or more. One-third of those affected were severely ill, several being unable to move even in bed. The severity of the illness was unrelated to age or sex. Haematological and urinary investigations were undertaken on all the patients admitted to hospital (twenty-six in all) but they did not reveal information of great value.

There were no fatalities and all the patients responded well to antibiotic therapy. The standard treatment for adults was dihydro-streptomycin intramuscularly in daily doses of 1 g. and oxytetracycline orally in daily doses of 2 g. for 3 weeks, with suitably adjusted doses for those in the younger age-groups. In most cases the temperature dropped within 4-5 days and there was significant clinical

improvement, but in a few cases the immediate response was a Herxheimer-like reaction (Bertrand, 1955) in which the pyrexia first increased. In eleven patients the picture resembled an undulant type of fever; the interval between the two waves varying from 2 to 9 months and in two the illness during the second wave was more severe than during the first. It is suggested that these examples might support the view that sensitization of the body to the brucella endotoxin is of importance in the pathogenesis of brucellosis (Spink & Anderson, 1954; Abernethy & Spink, 1958).

#### *Bacteriology and serology*

*Brucella melitensis* was cultured from twenty-four of the twenty-six patients admitted to hospital. Blood culture was also attempted on ten of the patients, less severely ill, who were treated in their homes; *Br. melitensis* was isolated from four of these. Castaneda bottles containing trypticase soya broth and trypticase soya agar were used for all the blood culture work.

The cultures isolated were H<sub>2</sub>S negative, decomposed urea, grew in the presence of thionine and basic fuchsin and did not require CO<sub>2</sub>. The identity of the organisms was confirmed as *Br. melitensis* by Dr O. Neeman of the Brucella Reference Laboratory, Government Veterinary Institute by their biochemical and serological reactions. All the strains were found to be sensitive to streptomycin and the tetracyclines. Growth was inhibited by 1 µg./ml. dihydro-streptomycin and by 3 µg./ml. of oxytetracycline, the two antibiotics used in therapy.

The serum agglutination tests were performed by the technique recommended by the World Health Organization (Stableforth, 1954). The International Standard Brucella Agglutinating Serum was used to standardize the antigen used in these tests, which was prepared by the Brucella Reference Laboratory. The end-point was taken at the 50 % agglutination level. The results were expressed as reciprocals of the serum titre giving that degree of agglutination or translated into Standard Agglutinin Units in accordance with the sensitivity of the antigen as determined by the Standard Serum (80 units or more per ml. serum was regarded as diagnostic of recent infection).

Out of a total of 232 persons examined there were seventy-nine clinically ill with brucellosis. *Br. melitensis* was isolated from the blood of twenty-eight of these patients and brucella agglutinins in a concentration of eighty Standard Units or more per ml. of serum were demonstrated in seventy-six. There were two patients with agglutinins below the accepted level and a 5-month-old baby from whose blood *Br. melitensis* had been isolated without demonstrable agglutinins in her serum. Among the 153 persons who showed no sign of illness throughout the period of the outbreak there were only five whose sera contained brucella agglutinins; one had 40 units and four had 80 units or more per ml.

The persistence of brucella agglutinins after recovery from the clinical disease was investigated in a limited number of cases. In one series of twelve there were six patients with agglutinins at diagnostic levels more than a year after recovery and in another eleven cases agglutinins persisted in five of the patients for a period of 2 years.



There were four patients who contracted the disease at the time they were lactating and three showed agglutinins in their milk at approximately the same level as in their blood serum.

#### DISCUSSION

The village outbreak of brucellosis described in this paper has several points of epidemiological interest. The population was composed entirely of immigrants of Kurdistan origin who had been 'settled' in the Beer-Sheva district of Israel some 4 years previously. Although there was no evidence of any earlier experience of brucellosis, the fact that sheep's milk cheese was freely consumed by the population of the village without causing illness, except in very young susceptible children, suggests either a low degree of infectivity or some immunity against the disease. While it is possible that several of the children, other than the young baby, contracted their infections through the consumption of the soft cheese or even the raw goat's milk, there can be no doubt that the great majority of the illnesses arose out of direct contact with brucella-infected animals. This would be in keeping with the general experience of rural outbreaks in Israel and most other countries; in the United States, Spink (1956) concluded that not more than 10% of cases came from the consumption of raw milk. In Great Britain, however, great emphasis is placed on the dangers of drinking milk which has not been heat-treated; in a recent survey in Oxfordshire, Bothwell (1960) found that only 22% of the cases of brucellosis in adults could be traced to direct contact with infected animals, but the observations were made on a small number of cases only. The disease in Great Britain is not notifiable and there is no reliable information about the incidence in that country, but it would appear (Dalrymple-Champneys, 1960) that the chronic and latent forms, both due to infection with *Br. abortus*, are more common than is frequently supposed. In our outbreak in Melilot more than one-quarter of the population of the village fell ill with acute brucellosis due to infection with *Br. melitensis*, but there were only five who showed evidence of infection without clinical manifestation of the disease. In endemic areas of brucellosis it is often assumed that an outbreak of the disease results in many more persons being infected than could be judged by the number who develop the full clinical manifestations, but in the outbreak described here where almost all those exposed to the risk of infection were fully investigated, there were only five cases out of the eighty-four, where there was evidence of infection, which could be regarded as examples of sub-clinical infections.

Reliable information about the severity, and the spread, of infection in the village livestock is not available but there can be little doubt that the villagers, for the most part, contracted brucellosis by direct contact with heavily infected animals. Although the slaughter of the infected herd may be said to have terminated the epidemic, a few cases occurred after this had taken place. Some of these were probably incubating the disease at the time of the slaughter, but, in addition to the two men who fell ill in September and whose source of infection is known, there were one or two who developed clinical brucellosis outside the usual incubation period. There is no satisfactory explanation for these illnesses except the

possibility that some material, contaminated at the slaughter, was taken back to the village where it could have been the source of these later infections.

It is well known that the soil on which the slaughter of brucella-infected animals is carried out may remain infective, in favourable circumstances, for several weeks. The slaughter of the infected herd in Melilot must have caused heavy contamination of the ground with *Br. melitensis* and although it was 3 months later when the two men dug over the soil the heavy task took them a number of days to complete so that their exposure to infection was of a high order. They both developed clinical brucellosis about 2 weeks after completing the work.

#### SUMMARY

A village epidemic of brucellosis, due to *Brucella melitensis*, contracted from infected sheep and goats owned by the villagers is described. Of the 309 inhabitants eighty-four became infected and seventy-nine were clinically ill with brucellosis. The investigation covered 232 of the total population and nearly all those not examined belonged to the age group, 0-5 years, not directly exposed to infection by contact with diseased animals.

The population of the village was made up of forty-six families, only nine of which escaped infection. In the affected families, the incidence varied from one to seven in each case. The size of the family varied from three to eleven but there was no correlation between the size of the family and the number contracting brucellosis, neither did sex play any part in the incidence. All age groups were susceptible but the morbidity increased with age and this was correlated with increased risk of exposure to infection of the older age groups.

There was considerable variation in the severity of the clinical illness but there were no fatalities and all patients responded to antibiotic therapy.

*Brucella melitensis* was isolated from twenty-eight of the thirty-six patients subjected to blood culture and specific agglutinins at an acceptable level were demonstrated in all but three of those with a clinical illness.

The number of persons without evidence of clinical brucellosis who possessed significant brucella agglutinins was very small and the assumption that in an endemic area the number of infected persons is much greater than the number clinically ill was not borne out in the outbreak described here.

Persistence of specific agglutinins up to 2 years after recovery from the clinical illness is recorded.

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## REFERENCES

- ABERNETHY, R. S. & SPINK, W. W. (1958). Studies with *Brucella* Endotoxin in Humans. The significance of susceptibility to endotoxin in the pathogenesis of brucellosis. *J. clin. Invest.* **37**, 219.
- BERTRAND, L. (1955). Le traitement actuel de la brucellose humaine. *Rev. Prat.* **5**, 253.
- BOTHWELL, P. W. (1960). III. Brucellosis: an anachronism in Public Health. *Vet. Rec.* **72**, 425.
- COHEN, J. (1958). Epidemiology of brucellosis in Israel. *Harefuah*, **54**, 258.
- DALRYMPLE-CHAMPNEYS, W. (1960). *Brucella Infection and Undulant Fever in Man*. Oxford University Press.
- FEIG, M. (1952). Some epidemiological aspects of brucellosis in Midwest. *Amer. J. Publ. Hlth*, **42**, 1253.
- JORDAN, C. F. (1949). *The Epidemiology of Brucellosis*, a symposium, p. 102. Maryland: Bethesda.
- OLITZKI, A. L., SULITZEAN, D., ARNAN, A. & RASOOLY, G. (1960). Observations on men vaccinated with a streptomycin dependent *Brucella* strain. *J. infect. Dis.* **106**, 77.
- ROZANSKY, R., WEBER, D., LEHMAN, E. & BALI, S. (1956). Brucellosis in Northern Negev. *Harefuah*, **51**, 1.
- SPINK, W. W. (1956). *The Nature of Brucellosis*. Minneapolis: University of Minnesota Press.
- SPINK, W. W. & ANDERSON, D. (1954). Experimental studies on the significance of endotoxin in the pathogenesis of brucellosis. *J. clin. Invest.* **33**, 540.
- STABLEFORTH, A. W. (1954). The international standard for anti-*Brucella abortus* serum. *Bull. Wld Hlth Org.* **10**, 927.