THE INFLUENCE OF TUBERCULOSIS UPON THE DEVELOPMENT OF *BRUCELLA ABORTUS* INFECTION

By E. J. PULLINGER

From the Research Institute in Animal Pathology, Royal Veterinary College, London

In a survey of some of the milk supplies of London for contamination with tubercle bacilli and *Br. abortus* by Pullinger (1934), difficulty was experienced in isolating the latter organism from bulk milk samples collected from ordinary herds, though no such difficulty was experienced when examining "clean milk" from graded herds. While 70 out of 101 herd samples* of certified or grade A T.T. milk collected in England contained *Br. abortus*, only 20 out of 104 herd samples from ordinary or non-graded herds in Somerset, and 39 out of 105 samples from similar herds in Cheshire were proved to contain this contaminant. Although extensive figures for the incidence of *Br. abortus* in "herd milks" of graded herds are not available for comparison, it would be most unlikely that any difference such as that just mentioned could be real, and indeed it would be logical to expect the incidence to be higher in ordinary than in graded herds. There can be little doubt that the figures obtained in the aforementioned survey are misleading, in that the incidence for ordinary herds is too low, and in the same connexion it is significant that it was often impossible to cultivate *Br. abortus* from guinea-pigs inoculated with ordinary milk, though the development of specific agglutinins in a low titre indicated that some degree of infection must have occurred.

Various explanations of these findings were considered. There was firstly the possibility that *Br. abortus* was destroyed owing to the relatively high acidity of the ordinary milk. It was thought more probable, however, that the tissue reaction set up in guinea-pigs by the inoculation of large numbers of saprophytic organisms might stimulate phagocytosis, and so destroy the *Br. abortus* when small numbers of this organism were present. At the same time, it was remembered that ordinary milk samples are sometimes contaminated with tubercle bacilli, whereas this is not the case with graded milk. It is conceivable that, following the combined inoculation of tubercle bacilli and *Br. abortus*, the less resistant organism might succumb as a result of the phagocytic reaction stimulated by the tubercle bacilli.

The object of the present investigation was to test these hypotheses, and to provide an explanation for the seemingly low incidence of *Br. abortus* in ordinary milk.

* Mixed product of all milking cows in a herd, except in the case of certified milk, which is always bottled on the farm.

A. EFFECT OF SAPROPHYTIC BACTERIA IN MILK UPON THE DEVELOPMENT OF *BRUCELLA* INFECTION

The influence of the bacterial flora of milk upon the development of *Brucella* was studied by adding known numbers of these organisms to samples of "clean" and of "dirty" *Brucella*-free milk. Milk so treated was inoculated into guinea-pigs after samples had been standing for various periods. In Exp. 1 they were allowed to stand for 1 hour at 18° C., in Exp. 2 the milk was stored at 18° C. and guinea-pigs were inoculated after intervals of 1, 5 and 18 hours. In both experiments an old laboratory culture of *Br. abortus* (B 22) of bovine origin, which was no longer CO_2-sensitive, was used, as it was thought that this would be of low virulence and so likely to give clear-cut results. Throughout the investigation suspensions of *Br. abortus* were prepared by growing the organism for 3 days on potato-extract agar, when the growth was washed off with saline and diluted to an opacity corresponding to Brown's dilution tube No. 3. Serial tenfold dilutions of this suspension were set up in saline, using a fresh sterile pipette for each dilution. A dilution of 10^{-7} generally contained between 100 and 500 organisms per c.c. Counts for viable *Br. abortus* were made at the time the suspensions were inoculated into guinea-pigs, by sowing 1 c.c. amounts of dilutions 10^{-7} to 10^{-9} in deep potato-extract agar plates, three plates being seeded from each dilution. Colonies were counted after incubation for 4 days.

The "clean milk" was taken, under good hygienic conditions, and about 3 hours before it was used, from a cow which was free from tubercle and *Br. abortus* infections. "Dirty milk" was similar milk which had been allowed to stand at room temperature overnight, after a small quantity of cowshed dust and sour milk had been added to it. When samples were to be used for inoculation, they were first thoroughly shaken and then 1·5 c.c. quantities were injected intramuscularly into the thighs of guinea-pigs. The total bacterial count of the milk sample at the time of each inoculation was estimated by standard methods. Guinea-pigs were examined 4–6 weeks later by methods previously described (Pullinger, 1934). Their serum was tested for specific antibodies, and tissue emulsion, prepared from the spleen, was seeded on to potato-extract agar slopes for the isolation of *Br. abortus*.

Results

The full data are recorded in Table I and the results summarized in Table II.

Exp. 1. With the small groups of animals examined, there was no significant difference whether the milk used was "clean" or "dirty".

In each group 15 animals survived, of which 11 developed infection with *Br. abortus* and 4 resisted.

Exp. 2. From the summary it will be seen that of 22 guinea-pigs receiving "clean" milk, 21 became infected and 1 resisted, whereas 18 of the 23 which received "dirty" milk became infected, and 5 resisted.

These differences are of little significance, for one reason because all 7

Table I. *Survival of* Br. abortus *in milk with low and high bacterial count*

	"Clean" milk								"Dirty" milk							
Exp. No.	Age hours	Total bacterial count per c.c.	*Bact. coli* in c.c.	Dose of *Br. abortus*	No. of guinea-pigs	*Br. abortus* (6 weeks) Agglut. titre	Cult.	Diag.	Age hours	Total bacterial count per c.c.	*Bact. coli* in c.c.	Dose of *Br. abortus*	No. of guinea-pigs	*Br. abortus* (6 weeks) Agglut. titre	Cult.	Diag.
1	1	500	—	80,000	4	160- -	+	+	1	150,000,000	0·001	80,000	3	160- -	+	+
	1	500	—	8,000	3	160- -	+	+	1	150,000,000	0·001	8,000	3	160- -	+	+
										150,000,000	0·001	8,000	1	80	+	+
	1	500	—	675	2	160- -	+	+	1	150,000,000	0·001	675	1	160- -	+	+
	1	500	—	675	2	—	—	—	1	150,000,000	0·001	675	1	80	+	+
									1	150,000,000	0·001	675	2	—	—	—
	1	500	—	80	2	160- -	+	+	1	150,000,000	0·001	80	2	160- -	+	+
	1	500	—	80	2	—	—	—	1	150,000,000	0·001	80	2	—	—	—
2	1	79,300	1·0	5,000	2	160- -	+	+	1	12,540,000	0·01	5,000	4	160- -	+	+
	1	79,300	1·0	5,000	1	20	−	+								
	5	97,370	1·0	5,000	3	160- -	+	+	5	178,400,000	0·001	5,000	2	160- -	+	+
	5	97,370	1·0	5,000	1	80	+	+	5	178,400,000	0·001	5,000	2	—	—	—
	18	557,000	0·1	5,000	3	160- -	+	+	18	5,000,000,000	0·001	5,000	2	160- -	+	+
	18	557,000	0·1	5,000	1	40	+	+	18	5,000,000,000	0·001	5,000	1	80	+	+
	1	79,300	1·0	500	3	160- -	+	+	1	12,540,000	0·01	500	1	160	+	+
	1	79,300	1·0	500	1	40	+	+	1	12,540,000	0·01	500	3	—	—	—
	5	97,370	1·0	500	2	160- -	+	+	5	178,400,000	0·001	500	3	160- -	+	+
	5	97,370	1·0	500	1	10	+	+	5	178,400,000	0·001	500	1	80	+	+
	18	557,000	0·1	500	2	160- -	+	+	18	5,000,000,000	0·001	500	3	160- -	+	+
	18	557,000	0·1	500	1	80	+	+	18	5,000,000,000	0·001	500	1	80	+	+
	18	557,000	0·1	500	1	—	—	—								

In this and subsequent tables 160- - indicates that the agglutinin titre was at least the reciprocal of this figure; when no - - sign is shown the figure indicates the end-titre.

Table II. *Summary of results of Exps.* 1 *and* 2

Exp. No.	"Clean" milk: Total bacterial count per c.c.	Dose of *Br. abortus*	No. of guinea-pigs	*Br. abortus* +	*Br. abortus* −	"Dirty" milk: Total bacterial count per c.c.	Dose of *Br. abortus*	No. of guinea-pigs	*Br. abortus* +	*Br. abortus* −
1	500	80,000	4	4	0	150,000,000	80,000	3	3	0
	500	8,000	3	3	0	150,000,000	8,000	4	4	0
	500	675	4	2	2	150,000,000	675	4	2	2
	500	80	4	2	2	150,000,000	80	4	2	2
2	79,300	5,000	3	3	0	12,540,000	5,000	4	4	0
	97,370	5,000	4	4	0	178,400,000	5,000	4	2	2
	557,000	5,000	4	4	0	75,000,000,000	5,000	3	3	0
	79,300	500	4	4	0	12,540,000	500	4	1	3
	97,370	500	3	3	0	178,400,000	500	4	4	0
	557,000	500	4	3	1	75,000,000,000	500	4	4	0

guinea-pigs which received the 18-hour-old sample of "dirty" milk developed infection, whilst 3 out of 8 animals receiving the 1-hour-old sample escaped infection. From these results it was concluded that the failure to isolate *Br. abortus* from "dirty" milk could not be explained by the concomitant presence in milk of large numbers of saprophytic organisms. No estimations of titratable acidity or hydrogen-ion concentration were carried out, but it was very unlikely that either of these factors played an important part, because "dirty" samples used in both experiments were already tainted when seeded with *Brucella*; whilst in Exp. 2, after 18 hours' storage, the sample was definitely sour and unfit for consumption. Such milk would have a *p*H of at least 4·8, but in spite of this *Br. abortus* was not destroyed.

B. The effect of tuberculosis upon the development of *Br. Abortus* infection

A certain proportion of samples of milk from ordinary herds are contaminated with tubercle bacilli, and it was thought that the presence of these organisms in the inoculum might have some bearing upon the problem. Although there has been but little work done in this connexion, two views are held. According to Schroeder & Cotton (1911) and Schoenfeld & Cotton (1925), the two infections are mutually helpful, whilst according to Wilson & Nutt (1926) they exert no influence upon one another.

Schoenfeld & Cotton carried out an investigation especially designed to clarify the problem. A total of 22 guinea-pigs was inoculated with *Br. abortus* at the same time as or subsequent to an inoculation of tubercle bacilli. Of these, 4 were completely resistant to the dose of *Brucella*, whilst 3 others developed agglutinins, but the organism could not be isolated by culture, which suggests that the infection had died out. The remaining 15 were infected. Unfortunately, only 4 non-tuberculous control animals were injected with *Br. abortus*, though all four developed infection. When it is realized that the inoculum consisted of tissue suspension taken from guinea-pigs, which had been infected with a reputedly virulent strain of *Br. abortus*, or of a culture

suspension of the same organism containing at least 5 million organisms per dose, the conclusion that the presence of tubercle infection assisted the development of *Br. abortus*, a conclusion based upon the rate of development of the dual infection, seems hardly justified.

Wilson & Nutt tested, by guinea-pig inoculation, bulk samples of tuberculous milk and similar non-tuberculous samples. From statistical analysis of their results, they considered that *Br. abortus* and tubercle bacilli were without influence upon one another. They found 17·5 per cent. of 40 tubercular samples and 6·2 per cent. of 130 non-tubercular samples to be contaminated with *Br. abortus*, that is, altogether 8·8 per cent. of 170 samples. The incidence of *Brucella* contamination, particularly in the non-tuberculous group, is extremely low. In my own investigation 70 per cent. of herd samples from graded herds, 20–40 per cent. from non-graded herds and 80 per cent. of "rail tank"* samples were contaminated with this organism. J. Smith (1932) found this contaminant in 28 per cent. and Beattie (1932) in 35 per cent. of market milk samples in Scotland, whilst Rowlands (1933) in Wales found 16 per cent. and Gaiger & Davies (1933) in England 43 per cent. of herd samples to be thus contaminated. The low figures recorded by Wilson & Nutt suggest that, apart from any question of tuberculosis, these results were being influenced by some other factor. Thus, it may be noted that, for diagnosis, reliance was placed on the cultivation of the organism from the guinea-pigs and that the serum was not tested for antibodies. An analysis of the examination of *Brucella*-infected guinea-pigs (Pullinger, 1934) indicated the danger of depending entirely upon culture, particularly when guinea-pigs had been inoculated with "ordinary" milk. The figures were as follows:

Class of milk	No. of guinea-pigs	Agg. + Cult. +	Agg. + Cult. −	Agg. − Cult. +
Graded	128	112	12	4
Ordinary	40	11	26	3

It was decided to reinvestigate the problem from the point of view that tubercle infection might hinder the development of *Br. abortus* in the guinea-pig. It is well known, from the work of a number of investigators, some of which has been recently reviewed by Dienes (1936), that the injection of certain substances into guinea-pigs is followed, within a few hours, by the accumulation of mononuclear cells at the site of inoculation. Thus, Gay *et al.* (1926) injected aleuronat or gum arabic intrapleurally into guinea-pigs, and this was followed by an accumulation of tissue macrophages in the pleura as well as an increase in the number of these phagocytes in the cavity itself. Resistance of the cavity to injection of streptococci was proportional to numbers of macrophages present in the pleural exudate. Even the adjacent unprepared peritoneal cavity sometimes benefited from this protective action, though the peritoneal lining showed no increase of macrophages. Dienes & Mallory (1932) found that the local cellular reaction following the injection of protein into a previously sensitized animal was of a mononuclear type. There

* 3000-gallon tanks containing the mixed milk of many herds.

is, therefore, much reason for believing that, following the simultaneous inoculation of tubercle bacilli and *Br. abortus*, a mononuclear reaction is stimulated which, whilst unable to offer effective resistance to the progress of tubercle infection, may prevent the establishment of *Br. abortus*. The fact that both organisms generally spread via the lymph stream increases the likelihood of *Brucella* being destroyed by any cellular reaction stimulated by the tubercle bacilli.

In the experiments mentioned below, strains of tubercle bacilli and of *Br. abortus* judged to be of high or of low virulence were used. The virulence of the tubercle bacilli was gauged by the speed and extent of spread of infection. Data regarding these points will be found in the tables. The strain of *Br. abortus* of low virulence was B 22, the one used in Exps. 1 and 2; that of high virulence was specially chosen on account of its reputed high pathogenicity for guinea-pigs. With the culture of tubercle bacilli, no attempt was made to standardize dosage, an amount sufficient to cause progressive infection being administered. The dose of *Br. abortus* was estimated as already described. In Exp. 3 varying amounts of *Br. abortus* were administered, but in subsequent experiments one large dose was always used. The suspension to be inoculated into each guinea-pig was placed in a separate tube and the required dose of tubercle bacilli was added. The bulk was then made up with saline to 1·0 c.c. which was inoculated intramuscularly into the animal's thigh.

Results

Results are recorded in Table III and summarized in Table IV.

Exp. 3 was of a preliminary nature, small groups of animals being used. The group of guinea-pigs receiving the smallest dose of *Br. abortus* (20 organisms) may be neglected, since none developed infection. Of the remaining 15 tuberculous guinea-pigs, 2 developed *Brucella* infection and 13 resisted. Of the 7 non-tuberculous control animals, 5 became infected and 2 resisted.

Exp. 4. The simultaneous inoculation of tubercle bacilli and *Br. abortus*, both of low virulence.

Out of 22 tuberculous guinea-pigs, 20 developed *Brucella* infection and 2 resisted. From 3 of the 20 infected animals it proved impossible to isolate the organism by culture. All 20 non-tuberculous control animals were found to be infected with *Brucella*.

Exp. 5. The simultaneous inoculation of highly virulent tubercle bacilli and of *Br. abortus* of low virulence.

Out of 26 tuberculous guinea-pigs, 1 developed *Brucella* infection, whilst 25 resisted this disease. All 30 non-tuberculous control guinea-pigs were found to be infected with *Brucella*.

Exp. 6. The simultaneous inoculation of virulent tubercle bacilli and virulent *Br. abortus*.

Out of 26 tuberculous guinea-pigs, 5 developed *Brucella* infection, whilst 21 resisted. It should be noted, however, that *Br. abortus* could not be cultivated

Table III. *Simultaneous inoculation of* Br. abortus *and tubercle bacilli into guinea-pigs*

				Tubercle bacilli injected [Strain 18]									No tubercle bacilli injected				
	Virulence		Incubation	Dose of	No. of	Lesions of tuberculosis in glands				*Br. abortus*			Dose of	No. of	*Br. abortus*		
Exp. No.	Tubercle bacilli	*Br. abortus*	period (weeks)	*Br. abortus*	guinea-pigs	Femoral	Sub-lumbar	Portal	Spleen	Agglut. titre	Cult.	Diag.	*Br. abortus*	guinea-pigs	Agglut. titre	Cult.	Diag.
3	High	Low	6	1,880	1	+	+	+	+	160--	+	+	1,880	2	160--	+	+
	,,	,,	6	1,880	1	+	+	+	+	80	+	+					
	,,	,,	6	1,880	1	+	+	+	+	—	–	–					
	,,	,,	6	1,880	2	+	+	–	–	—	–	–					
	,,	,,	6	1,880	1	+	–	–	–	—	–	–					
	,,	,,	6	188	5	+	+	+	+	—	–	–	188	2	160--	+	+
	,,	,,	6	188	2	+	+	+	–	—	–	–	188	1	160	+	+
	,,	,,	6	188	2	+	+	–	–	—	–	–	188	2	—	–	–
	,,	,,	6	20	7	+	+	+	+	—	–	–	20	3	—	–	–
	,,	,,	6	20	1	+	+	+	–	—	–	–					
	,,	,,	6	20	2	+	+	–	–	—	–	–					
4	Low	,,	6	1,000	16	+	+	–	–	160--	+	+	1,000	6	160--	+	+
	,,	,,	6	1,000	1	+	+	–	–	80	+	+	1,000	4	160	+	+
	,,	,,	6	1,000	1	+	+	–	–	80	–	+	1,000	3	80	+	+
	,,	,,	6	1,000	1	+	+	–	–	20	–	+	1,000	5	40	+	+
	,,	,,	6	1,000	1	+	+	–	–	10	–	+	1,000	2	20	+	+
	,,	,,	6	1,000	2	+	+	+	+	—	–	–					
5	High	,,	4	500,000	3	+	+	+	+	—	–	–	500,000	26	160--	+	+
	,,	,,	4	500,000	22	+	+	–	–	—	–	–	500,000	3	80	+	+
	,,	,,	4	500,000	1	+	+	–	–	160--	+	+	500,000	1	20	+	+
6	,,	High	5	225	21	+	+	+	+	—	–	–	500,000	23	160--	+	+
	,,	,,	5	225	2	+	+	+	+	40	–	+	500,000	2	80	+	+
	,,	,,	5	225	3	+	+	+	+	10	–	+	500,000	2	—	–	–
7	,,	Low	4	25,000	18	+	+	+	+	—	–	–	25,000	21	160--	+	+
	,,	,,	4	25,000	3	+	+	+	–	—	–	–	25,000	2	80	+	+
	,,	,,	4	25,000	5	+	+	–	–	—	–	–	25.000	4	40	+	+

Table IV. *Summary of results of Exps.* 3–7

Exp. No.	Tubercle bacilli injected: Extent of tuberculous lesions	Dose of *Br. abortus*	No. of guinea-pigs	*Br. abortus* +	*Br. abortus* −	No tubercle bacilli injected: Dose of *Br. abortus*	No. of guinea-pigs	*Br. abortus* +	*Br. abortus* −
3	Medium	1,880	6	2	4	1,880	2	2	0
		188	9	0	9	188	5	3	2
4	Slight	1,000	22	20	2	1,000	20	20	0
5	Medium	500,000	26	1	25	500,000	30	30	0
6	Advanced	225	26	5	21	225	27	25	2
7	Advanced	25,000	26	0	26	25,000	27	27	0

from the spleens of these five animals, and diagnosis was based on the presence of specific antibodies in low titre. Out of 27 non-tuberculous control animals, 25 developed *Brucella* infection, whilst 2 resisted.

Exp. 7. This was a repetition of Exp. 5, but "clean" milk instead of saline for suspending the organism was used. None of the 26 tuberculous guinea-pigs developed *Brucella* infection, whilst all 27 non-tuberculous control animals became infected.

The influence of the presence of tubercle bacilli upon the development of *Br. abortus* appeared to be so striking that a further experiment was carried out to study the phenomenon more closely. The possibility that *Br. abortus* was being destroyed by the tubercle bacilli *in vitro*, though unlikely, could not be ignored. Also, if the destruction was taking place within the guinea-pig, it was desirable to ascertain whether the reaction was confined to the site of inoculation. Opportunity was also taken to see if the presence of *Brucella* infection had any obvious influence on the development of tuberculosis.

Exp. 8. Guinea-pigs were inoculated in groups of ten with highly virulent tubercle bacilli and *Br. abortus* of low virulence.

Group 1. A mixture of the two suspensions inoculated with a single syringe.

Group 2. Suspensions inoculated into the same site with separate syringes.

Group 3. Suspensions inoculated into opposite thighs with separate syringes.

Group 4. *Br. abortus* inoculated alone.

Group 5. Tubercle bacilli inoculated alone.

The results are recorded in Table V and summarized in Table VI. Out of a total of 30 guinea-pigs, which received both tubercle bacilli and *Br. abortus*, 5 developed *Brucella* infection and 25 resisted. The 10 control animals, which received *Br. abortus* alone, were found to be infected. The possibility that *Brucella* is destroyed *in vitro* by tubercle bacilli is excluded, since the 10 animals inoculated with both suspensions by means of separate syringes escaped *Brucella* infection. The fact that 5 out of the 10 animals which received the two doses on opposite sides escaped *Brucella* infection suggests that the destruction of organism is not purely a local phenomenon. Judging from the extent of the tuberculous lesions in any fixed tissue in the different groups, the

Table V. *The inoculation of* Br. abortus *of low virulence and tubercle bacilli of high virulence at the same or at different sites*

Tubercle bacilli injected									No tubercle bacilli injected				
Group No. [See text Exp. 8]	No. of guinea-pigs	Lesions of tuberculosis in glands				*Br. abortus*			Group No. [See text Exp. 8]	No. of guinea-pigs	*Br. abortus*		
		Femoral	Sub-lumbar	Portal	Spleen	Agglut. titre	Cult.	Diag.			Agglut. titre	Cult.	Diag.
1	10	+	+	+	+	—	−	−	4	10	160--	+	+
2	10	+	+	+	+	—	−	−					
3	5	+	+	+	+	—	−	−					
	4	+	+	+	+	160--	+	+					
	1	+	+	+	+	40	−	+					
5	10	+	+	+	+	—	−	−					

Table VI. *Summary of results of Exp.* 8

Tubercle bacilli injected							No tubercle bacilli injected						
Site of inoculation		Method of injection	Dose of *Br. abortus*	No. of guinea-pigs	*Br. abortus*		Site of inoculation		Method of injection	Dose of *Br. abortus*	No. of guinea-pigs	*Br. abortus*	
Tubercle bacilli	*Br. abortus*				+	−	Tubercle bacilli	*Br. abortus*				+	−
Left thigh	Left thigh	Same syringe	800	10	0	10	None	Left thigh	Single syringe	800	10	10	0
,,	,,	Different syringe	800	10	0	10							
,,	Right thigh	,,	800	10	5	5							
,,	None	Single syringe	800	10	0	10							

development of tuberculosis appeared to be unaffected by the presence of *Br. abortus*.

General discussion

In the course of this investigation the original object, which was to explain the apparently low incidence of contamination of ordinary milk with *Br. abortus*, became of subsidiary importance in view of the interest of the information which came to light. It would appear that in guinea-pigs, under suitable circumstances, tubercular infection can interfere with the development of *Br. abortus*. This fact obviously reduces the value of guinea-pig inoculation as a means of identifying *Br. abortus* in milk. It cannot be claimed, however, that the presence of tubercle bacilli fully explains the difference between the incidence of *Brucella* contamination in ordinary and in high grade samples of milk. Even if it were assumed that every sample of milk which appeared to be contaminated with tubercle bacilli only actually contained *Br. abortus* as well, the incidence of this organism in ordinary herd samples would still be much lower than one would expect. But if it is accepted that the presence of tubercle bacilli in the inoculum stimulates a reaction which interferes with the development of *Brucella* infection, it is not unreasonable to suggest that other unidentified organisms or agents, which can occur in ordinary milk, may have a similar effect. The fact that, in Exps. 1 and 2, there was no definite evidence to support this suggestion may have been due to the absence of the correct contaminant. At the same time, the high incidence of contamination of "rail tank" samples might be explained by the presence of a diversity of strains of *Br. abortus* including some of high virulence which could override any inhibitory action. Also, as has been shown to be the case with tubercle bacilli, it is possible that milk in "rail tanks" is uniformly and highly contaminated with *Br. abortus* owing to the admixture of milk from heavily infected herds.

Results recorded in Tables III, IV, V and VI indicate clearly that tuberculosis can interfere with the establishment of a strain of *Br. abortus* of low virulence, whilst with a more virulent strain a similar inhibition exists, though to a smaller degree. This is well demonstrated by the fact that, in Exp. 6, in which the more virulent strain of *Br. abortus* was used, infection was established in 5 of the 26 guinea-pigs to an extent sufficient to stimulate the production of specific agglutinins, but insufficient for successful cultivation of the organism from the spleen.

The immediate mononuclear cellular response in an animal to appropriate stimuli, which has frequently been described, reacts not only against the specific stimulant, but also against other invading organisms normally combated by that type of phagocyte. Such an invader would find unusual difficulty in becoming established as long as mobilization of cells persists. Whether the invader succeeds in overcoming this non-specific resistance depends upon the extent to which the cellular defence is mobilized and the invasive ability of the organism.

Summary and conclusion

1. The difficulty of isolating *Br. abortus* from samples of "dirty" milk by means of guinea-pig inoculation is noted. This has been shown to be due in certain instances to the presence of tubercle bacilli in the inoculum, though this is probably not the full explanation.

2. Following the simultaneous inoculation of virulent tubercle bacilli and *Br. abortus* into guinea-pigs, the latter infection generally failed to become established, whereas control animals inoculated under the same conditions with *Brucella*, but without tubercle bacilli, became infected.

Results of the inoculation of the two organisms into opposite sides of guinea-pigs indicate a generalized as well as a local increase of resistance to *Br. abortus*.

3. It is suggested that the mononuclear cell reaction stimulated by the tubercle bacilli destroyed *Br. abortus*.

I am indebted to the Directors of the United Dairies, Limited, for their interest and financial support. My thanks are due to Dr W. S. Gordon, Moredun, for sending a virulent strain of *Br. abortus*.

References

Beattie, C. P. (1932). *Lancet*, i, 1002.
Dienes, L. (1936). *Arch. Path. Washington*, **21**, 357.
Dienes, L. & Mallory, T. B. (1932). *Amer. J. Path.* **8**, 689.
Gaiger, S. H. & Davies, G. O. (1933). *Veterin. Rec.* **13**, 876.
Gay, F. P., Clark, A. R. & Linton, R. W. (1926). *Arch. Path. Washington*, **1**, 857.
Pullinger, E. J. (1934). *Lancet*, i, 967.
Rowlands, W. T. (1933). *Veterin. Rec.* **13**, 127.
Schoenfeld, A. F. & Cotton, C. M. (1925). *J. Inf. Dis.* **37**, 68.
Schroeder, E. C. & Cotton, W. E. (1911). *28th Ann. Rep. Bureau Animal Industry, Washington*, p. 139.
Smith, J. (1932). *J. Hyg.* **32**, 354.
Wilson, G. S. & Nutt, M. N. (1926). *J. Path. and Bact.* **29**, 141.

(*MS. received for publication* 24. vi. 1936.—Ed.)

CORRECTION SLIPS

to *Journal of Hygiene*, Vol. XXXIV (1934)

Table IV. *Comparison of incidence of cancer in various sites at post-mortem (Leeds)*

Gum annexed tabular matter over the previous table

P. 221

Year	Total cancers	Large intestine		Rectum		Stomach		Oeso-phagus		Brain		Pancreas		Gall bladder		Intra-thoracic	
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
1908–1912	375	64	17·1	34	9·1	54	14·4	24	6·4	20	5·3	20	5·3	13	3·5	31	8·3
1913–1917	401	55	13·7	28	7·0	56	14·0	26	6·5	17	4·2	16	4·0	7	1·7	31	7·7
1918–1922	389	63	16·2	43	11·1	63	16·2	20	5·1	28	7·2	18	4·6	21	5·4	24	6·2
1923–1927	552	102	18·4	90	16·3	88	16·0	21	3·8	36	6·5	27	5·0	17	3·1	44	8·0
1928–1932	670	100	14·9	84	12·5	119	17·8	31	4·6	53	7·9	27	4·0	23	3·4	50	7·5

P. 222

Graph I. Comparison of incidence of cancer of stomach and lung in Berlin and Leeds, 1905–32

In the part dealing with Leeds, the figures for *Ca ventriculi* should read:

1908–12	14·4
1913–17	14·0
1918–22	16·2
1923–27	16·0
1928–32	17·8

https://doi.org/10.1017/S0022172400043783 Published online by Cambridge University Press