Observations on Difficulties Encountered in the Serological Diagnosis of Brucellosis and Q Fever

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WITH the introduction of the complement-fixation technique in the routine serological diagnosis of Q fever as originally developed by Bengtson (1941), difficulties have arisen regarding the interpretation of the results. The problem becomes particularly evident when the clinical and epidemiological history strongly incriminates exposure of the patients to meat and milk producing animals which may be infected not only with Coxiella, but likewise with Brucella.

In the course of serological studies on persons exposed by means of slaughterhouses or dairy products in California, it was observed that serological reactions of several patients with symptoms and signs indicative of brucellosis, sometimes including strongly positive agglutination and complement-fixation reactions for Brucella, were also positive in the presence of Coxiella antigens. The records of a few such observations are summarized in Table 1.

In Case 1 (Table 1), the presence of Brucella suis infection was proved through cultures and the rise of antibodies for this organism. In addition, however, serum in the same case gave a positive complement-fixation reaction with Q fever antigen (Cox-Lederle antigen, American strain). Whether this reaction expresses the coexistence of Q fever and brucellosis or whether the low complement-fixation titer indicates a response to an antigenic fraction common to both Brucella and Coxiella can only be answered through antigen analysis of the Coxiella.

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TABLE 1.—*Serologic Results Illustrating Diagnostic Difficulties.*

Case	Date	*Brucella Diagnostic Tests* Agglutination	Complement-Fixation	Phagocytic Index	*Q Fever* Complement-Fixation	*Diagnosis**	*Exposure*
1.	3-18-48	1:1280++++	1:256++++	7.72	1:16++++	Brucellosis (Br. suis, blood culture)	Slaughterhouse, 6 months
	4-2-48	1:5120++++	1:2048++++		1:8++++		
					1:16+++		
					a.c. 1:8+		
2.	6-28-48	1:640++++	1:640++++	0.36	0	Brucellosis	Butcher, slaughterhouse, 9 months
	8-18-48	1:2560++++	1:64++++	8.44	1:16++++		
3.	7-11-47	0	1:256++++		1:32++++	(Brucellosis) Q fever	Butcher, slaughterhouse, over 2 yrs.
	3-30-48	0	1:4++++	9.7	1:64++++		
	5-4-48	0	1:4++++	13.36	1:256++++		
4.	9-9-48	0	1:64++++		1:64++++	Q fever	Raw milk mixer, milk plant, over 10 years
	9-16-48	0	1:32++++		1:64++++		
	10-13-48	0	1:16++++		1:64++++		
5.	11-26-47†	0				(Brucellosis) Q fever	Slaughterhouse contact, 3 to 4 yrs.
	12-14-47	1:640++++	1:256++++		1:64++++		
	12-31-47	1:640++++	1:64++++		No serum		
	4-27-48	0	0		1:256++++		
	5-13-48	0	0		1:256++++		
6.	5-17-48	1:640++++	1:256++++	2.0	1:256++++	Q fever	Slaughterhouse, 13 years
	5-27-48	1:40++++	1:256++++		1:1024++++		
	6-24-48	0	1:32++	7.24	1:2048++++		
7.	5-5-48	1:640++++	1:256++++		1:16++++	(Brucellosis) (Virus pneumonia) Q fever	Raw milk
	5-28-48	1:640++++	No serum		1:64++++		
	6-4-48	0	0		1:256++++		
8.	6-15-48	1:1280++++	1:64++++		1:256++++	Q fever	Dairy cattle ranch, 27 yrs.
	6-24-48	1:64++++	0		1:256++++		
	7-12-48	0	0		1:256++++		
					1:512++		
	10-21-48	0	0		1:64++++		

*If the diagnosis was changed, the first is given in parentheses.
†Serologic tests were not made in Hooper Foundation laboratories.

In the future in cases in which this question arises, it will of course be necessary to make every possible effort to demonstrate the presence of Coxiella.

In Case 3, in which the presence of chronic brucellosis was indicated by complement-fixation reactions with Brucella in 1947, the patient continued to have clinical relapses although there was no serological or other evidence to support the diagnosis of chronic brucellosis. When serum from this patient was finally tested following a pronounced relapse in 1948, a progressive rise in titer definitely indicated a Coxiella infection. Thus, the diagnosis was changed to Q fever. Again, an inoculation test for Coxiella would have been valuable.

A similar history concerning the patient in Case 5 emphasizes the necessity for testing the sera of slaughterhouse employees over a period of several months before a diagnosis is made. In this case a diagnosis of brucellosis was made, despite the fact that repeated blood cultures were negative and the agglutination and complement-fixation titer for Brucella gradually declined while, on the other hand, the titer for Coxiella rose. This reversal is an example of an anamnesic reaction; that is, Brucella antibodies increase or reappear in the presence of the nonspecific antigen. The patient in this case had previously been infected with Brucella and the antibody-producing center was stimulated through the infection with Coxiella. The serological findings and histories in Cases 6, 7 and 8 furnish additional evidence in support of the interpretation offered for the findings in Case 5.

These observations are merely presented as additional evidence of the well-known fact that a diversity of antigens stimulate the appearance of Brucella antibodies. On the other hand, Brucella antigens may stimulate, in occupational groups exposed to livestock, the appearance of Q fever antibodies. There is no need to emphasize that in view of these findings the serological diagnosis of undulant or Q fever may be very difficult and that repeated blood cultures for Brucella and now inoculation of guinea pigs for the demonstration of the Coxiella are absolutely essential.

Detailed investigations are indeed indicated before far-reaching conclusions are drawn from epidemiological surveys based on serological tests.