THE INCIDENCE OF UNDULANT FEVER IN CHILDREN

BY

PARKER DOOLEY, M.D.

Physician to Kent School, Connecticut, U.S.A.

In the decade since Bevan¹ suggested that the organism responsible for contagious abortion in cattle might be pathogenic for man, innumerable cases of undulant fever have been diagnosed among the populations of most civilized countries. During 1925, there were only 24 cases reported in the United States, but each succeeding year thereafter an increasingly large number was reported until, in 1929, there were more than 1,300. Complete statistics for 1930 are not yet available, but it is safe to assume that there were many thousands of cases. There is every reason to believe that this increase is only apparent, and not real, as cases are being reported now which could not have been recognized before the present methods of laboratory diagnosis came into general use. In the United States at least, the number of cases reported from any given region seems to depend more on the alertness with which the physicians search for the disease than on any other factor.

With the increasing appreciation of the ubiquity and gravity of this disease, it seems advisable for students of children's disease to try to evaluate the importance of undulant fever among the diseases of childhood. Several theoretical considerations suggest that a higher incidence of infection prevails among children than among adults. The *Brucella abortus* causes a low-grade, febrile illness of a type which is frequently undiagnosed unless specific laboratory tests are made. Such low-grade fevers are so much more common in children than in adults that it would seem reasonable to expect a higher incidence of *Brucella* infection among children than among adults when specific tests are generally applied. Also the fact that raw milk customarily constitutes a large part of the diet of infants and little children suggests that infection may be found to be common in childhood. Despite these considerations, it has become the more or less tacit opinion of writers on undulant fever that the disease is relatively uncommon in children. In fact, some authors have gone so far as to argue that *Brucella* infection is not caused by drinking milk because children seem to contract the disease so infrequently in spite of drinking large quantities of milk.

Previous investigations.—In 1913, Larson and Sedgewick² tested 425 children with bone or joint disease for complement fixation, using *Brucella abortus* as antigen. This test was positive in 73 instances. At that time, it was not known that this organism could act as one of the human pathogens. These studies were carried out as a part of a problem relating to the transmission of antibodies through the intestinal wall. Nothing is said about the ages of the children nor about the probable source of the infection. Later these same workers³ used the

same test on 42 new-born babies, with negative results. One baby was taken from the breast on his 7th day, because of high fever, the cause of which was never ascertained. He was then fed on raw cows' milk. On his 21st day his reaction was positive. Another baby, 19 months old, had a positive reaction.

In 1915 Nicoll and Pratt⁴ raised the question of human infection with *Brucella*. They performed agglutination tests on an unstated number of the inmates of a foundling asylum, including cases of marasmus, rickets, enlarged lymph nodes, and hypertrophied tonsils and adenoids, as well as on about 100 supposedly normal infants. Presumably these patients were getting raw milk. One 3 year old child had a positive reaction to 1 : 100 ; one child of 2½ years had a slightly positive reaction to 1 : 10 ; a 5 year old child had a positive reaction to 1 : 10. Otherwise they were all negative. These same writers also found a positive reaction in the 7 months old baby of a woman whose own serum reaction was positive in dilutions up to 1 : 300.

Hardy⁵, in summarizing all cases of undulant fever reported in the United States up to June of 1929, found very few instances in children under 10 years of age. Among 354 cases in Iowa, this author noted only 4 in children under 4 years, and 8 in children between the ages of 5 and 9 years. Of these, 6 were in one family, the diagnosis being made on the basis of dried blood specimens alone. His data were collected chiefly from various State laboratories and consequently are not very useful in an attempt to determine the incidence of the disease among children. Most of the blood specimens submitted to such laboratories come from rural practitioners who rarely take blood specimens from young children. Extensive bacteriological and serological studies of the blood of young children are very infrequently made save in city clinics where, of course, the general use of pasteurized milk precludes the satisfactory study of *Brucella* infection. The same criticism applies to the statistics of Bayne-Jones⁶ who found no positive agglutinations in infants under one year in some 3,700 routine blood specimens on which *Brucella* agglutination tests were made in the New York State laboratory. In similar specimens in the Ohio State laboratory, Ey⁷ found positive agglutination reactions in one child of 19 months, in whose family there were three persons sick with undulant fever ; and in another child of 2 years who was sick with an undiagnosed febrile illness.

In Denmark Kristensen⁸ has made a careful study of 500 cases of undulant fever and concluded that young children are not affected. Guest⁹ carried out agglutination tests on 250 patients in the Children's Hospital of Boston, and found only one who reacted positively in dilutions up to 1 : 40. He does not state whether these children used raw or pasteurized milk. Giordano and Sensenich¹⁰ have reported 35 cases, the youngest being 16 years old. Hartman¹¹ mentions an infection occurring in an 8 year old child. Bonyne¹² had a case in an 11 months old infant who had been using certified milk for 9 months. Three other children in the same family had been using this milk but were not affected. King¹³ noted four cases in children under 6 years of age, including one 2 year old child who had what was believed to be rheumatic fever until a chance agglutination against *Brucella* was found to be positive in dilutions up to 1 : 1280. This child, however, had been transfused with blood from two adults who had agglutinins in their sera. Simpson¹⁴ studied 90 cases of undulant fever, nine of which occurred in children between the ages of 6 and 10 years. Kling¹⁵, in Sweden, found only one case under 10 years, a child of 8 years. Levin¹⁶ made intradermal tests on 33 children between the ages of 6 months and 14 years. Only one child, a 5 year old girl with sinusitis and mastoiditis, gave a positive skin reaction. Her serum did not contain *Brucella* agglutinins. Kohlbry¹⁷ saw the disease in an infant of 1 year. The diagnosis was made on the basis of positive agglutination test done three days after the baby was transfused with its mother's blood. Koschate¹⁸ considers childhood infection to be so rare that he reports the case of a 12 year old boy as a curiosity. Tobler¹⁹ has reported *Brucella* infection in an 8 year old girl.

Present investigations.—Since the literature on the occurrence of undulant fever in childhood is so fragmentary and inconclusive, it seems worth while to record any item which may be helpful in the understanding of it.

In the autumn of 1930 a small epidemic of undulant fever appeared in a school community which uses raw milk from a single dairy. Several moderately severe cases of the disease occurred among the adult milk consumers. Of some

300 adolescent boys and young adults using this milk, 41 per cent. showed serum agglutinins for *Brucella abortus* in dilutions over 1 : 20. Several of the cows in the dairy were found to have positive sera, and some were shedding virulent organisms in their milk. Among the consumers of this heavily infected milk, were fifteen children who had been reared on this raw milk since infancy. The age distribution of these children was as follows :—

Under 1 year	...	...	...	1
1—2 years	...	...	...	3
2—4 ..	...	...	...	4
4—6 ..	...	...	...	4
6—8 ..	...	...	...	2
8—10 ..	...	...	...	1

At least three agglutination tests, each with a different antigen, were done on each one of these children. The first antigen was a stock one made from four strains of *Brucella* of bovine origin ; the second, the so-called Huddleson antigen ; the third, a live antigen prepared from a strain of *Brucella* isolated from the blood of a patient²⁰ who was infected through drinking the same raw milk which the children used. The dilutions in these agglutination tests were from 1 : 10 to 1 : 640. In not one of these children could any *Brucella* agglutinins be demonstrated. All of these children had been under the continuous care of the writer either since their birth, or at least for the two years preceding the testing. In that time, none of them had any illness which could possibly be suspected of being undulant fever. Although this series is very small, the results seem to justify the supposition that young children are less susceptible to infection with *Brucella* than are persons who have passed puberty.

In this connection, it is tempting to speculate on the apparent analogy between *Brucella* infection in young children and in calves. White²¹ states that all calves, regardless of the reaction of the dams, are born non-reactors.. When they are permitted to suck positive dams within the first 24 hours of life, they become reactors in a remarkably short time, but again become negative, almost invariably before the end of the sixth month of age. It is only after sexual maturity that definite infection is established.

Summary.

A review of the literature of undulant fever shows that little is definitely known regarding the infection in childhood.

Study of serum agglutination in young children, who had been drinking infected raw milk, suggests that they are relatively insusceptible to the disease.

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[EDITORIAL NOTE. So far two cases only of Brucella infection in children have been reported in England: the first in a child of 3½ years by W. Broadbent, *Lancet*, Jan. 10th, 1931: the second by B. Williamson and J. Gibson in a child of 1½ years, *B.M.J.*, May 2nd, 1931.]