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A multicenter retrospective study of childhood brucellosis in Chicago, Illinois from 1986 to 2008☆

Latania K. Logan [a,b,*], Norman M. Jacobs [b], James B. McAuley [a,b], Robert A. Weinstein [a,b], Evan J. Anderson [c]

[a] Rush University Medical Center, 1653 West Congress Parkway, Suite 736 Murdock, Chicago, IL 60612, USA
[b] John H. Stroger, Jr. Hospital of Cook County, Chicago, Illinois, USA
[c] Northwestern University Feinberg School of Medicine, Northwestern Memorial Hospital, Children's Memorial Hospital, Chicago, Illinois, USA

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SUMMARY

Objectives: To determine risk factors in children for the acquisition of Brucella, clinical presentation, treatment, and disease outcomes.
Methods: A retrospective multicenter chart review was undertaken of children identified with brucellosis from 1986 to 2008 at three tertiary care centers in Chicago, Illinois, USA. The charts were reviewed for data regarding risk factors for acquisition, clinical presentation, and outcomes.
Results: Twenty-one charts were available for review. The median age was 6.5 years (range 2–14 years); 62% were female. Ethnic background was 67% Hispanic and 24% Arabic. Risk factors included travel to an endemic area (86%), particularly Mexico, and consumption of unpasteurized milk products (76%). Common findings included fever (95%), bacteremia (86%), elevated liver transaminases (80%), constitutional symptoms (76%), splenomegaly (60%), and hepatomegaly (55%). Relapse occurred in three of six subjects started on single drug treatment, but in only one of 15 subjects who started on two or more drugs ($p = 0.053$). No relapses occurred in children whose initial therapy included rifampin or those administered three-drug regimens.
Conclusions: Brucella is an infrequent pathogen but should be considered in children with compatible epidemiologic and clinical characteristics. Blood cultures should be obtained, and initial therapy with two or more drugs may decrease the risk of relapse.

1. Introduction

Brucellosis is a zoonotic disease of wild and domestic animals caused by bacteria of the genus *Brucella*. Humans typically contract disease by accidentally ingesting contaminated food, such as unpasteurized milk products, but can also acquire it through inoculation via direct contact with infected animals or animal parts and occasionally through occupational exposure in microbiology laboratories.[1–3]

Brucella remains a rare disease in the USA, with approximately 100–200 cases reported per year, generally found in travellers returning from high-risk areas.[4–7] Surveillance data suggest that brucellosis occurs at a rate eight-fold higher in counties within ~100 km of the border with Mexico than in states that do not border Mexico.[8] Of the 121 individual cases of brucellosis reported in 2006, 43% occurred in Texas or California, while 6.7% occurred in Illinois.[9] Studies from Texas and California suggest that 79–95% of disease occurs among Hispanics in these states.[4–6]

Also known as undulant fever, the recurrent fever episodes in brucellosis characteristically rise and fall in waves, with high spikes often accompanied by rigors or chills.[10] In humans, the manifestations are protean and include myalgias, arthralgias, hepatitis, lymphadenopathy, hepatomegaly, splenomegaly, osteoarticular involvement such as sacroiliitis, peripheral arthritis, or spondylitis, and less commonly uveitis, central nervous system disease, or endocarditis, and is most commonly due to *Brucella melitensis*.[11–14] The disease left untreated can be severely debilitating and is associated with long-term morbidity.

Recent large series data about brucellosis in the USA are restricted to states neighboring Mexico.[4–6,15] Our understanding of pediatric brucellosis in the USA is particularly limited, prompting us to review our experiences at multiple different academic institutions in Chicago over the past 23 years.

2. Methods

A multicenter retrospective chart review was conducted at three large tertiary care centers in Chicago, Illinois: Rush University Medical Center, John H. Stroger Jr. Hospital of Cook

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* Corresponding author. Tel.: +1 312 942 8928; fax: +1 312 563 4159.
E-mail address: latania_logan@rush.edu (L.K. Logan).

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Table 1
Demographics and epidemiological risk factors of children with brucellosis

Patient	Age (years)	Sex	Race/ethnicity	Region of travel outside USA/residence prior to illness	Presumed exposure source	Time to symptom onset after exposure (months)[a]
1	10	Female	Hispanic	Mexico	Unpasteurized milk products	9
2	4.5	Female	Caucasian	None	Direct animal contact (goats)	2
3	4.5	Male	Arabic	Lebanon	Unpasteurized milk products	<1
4	5	Male	Arabic	Jordan, Israel	Unpasteurized milk products	<1
5	6.5	Male	Arabic	Jordan, Israel	Unpasteurized milk products	<1
6	3	Male	Arabic	Jordan, Israel	Unpasteurized milk products	<1
7	4.5	Female	Arabic	Jordan, Israel	Unpasteurized milk products	<1
8	6.5	Male	Hispanic	Mexico	Unpasteurized milk products	1
9	10	Female	Hispanic	Peru	Unpasteurized milk products	1
10	14	Male	Hispanic	Mexico	Unpasteurized milk products	3
11	12	Female	Hispanic	Mexico	Unpasteurized milk products	3
12	3.5	Female	Hispanic	Mexico	Unknown	NA
13	3.5	Female	Hispanic	Mexico	Unpasteurized milk products	4
14	8	Female	Hispanic	Mexico	Unknown	NA
15	6.5	Male	Hispanic	Mexico	Unpasteurized milk products	<1
16	12	Female	Hispanic	None	Unpasteurized milk products	3
17	2	Female	Hispanic	None	Unpasteurized milk products	1
18	14	Female	Hispanic	Mexico	Direct animal contact (goats)	<1
19	13	Female	Hispanic	Mexico	Unpasteurized milk products	<1
20	5	Male	Hispanic	Mexico	Unpasteurized milk products	<1
21	10.5	Female	Asian	Pakistan	Unknown	NA

[a] NA, not applicable; <1, symptom onset within 4 weeks after exposure.

County, and Children's Memorial Hospital. This study was approved by the institutional review boards of the three institutions. Cases of Brucella occurring in children <18 years of age during the period of January 1, 1986 to December 31, 2008 were identified by searchable electronic inpatient and outpatient databases of International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) code 023 (023.0–023.9). A case was defined based on verification of clinical and laboratory supported evidence of brucellosis. Confirmed diagnosis was based on isolation of *Brucella* species on cultures of blood, bone marrow, cerebrospinal fluid, other sterile sites, or in tissue samples. The Illinois Department of Public Health and/or Centers for Disease Control and Prevention were sent all positive cultures for confirmation and speciation. A single positive Brucella serum agglutination titer (SAT) of ≥1:160 was also considered definite evidence of infection when accompanied by compatible clinical evidence of disease in the absence of a positive culture.

Length of bacteremia was defined by number of days between first and last positive blood culture during therapy. Treatment failures were defined as persistent positive blood cultures or persistence of symptoms after 10 days of therapy.[16] Relapse was defined as recurrence of symptoms or blood culture positivity after completion of therapy. *p*-Values were determined using the Fisher's exact test in comparing those who had a relapse with those who did not have a relapse. Charts were reviewed for evidence of a relapse of brucellosis for at least 2 years after initial hospital discharge.

3. Results

3.1. Patient demographics

Twenty-one charts were available for review of the 22 confirmed cases (95%) of childhood brucellosis from 1986 to 2008 (Table 1). Of the subjects available for analysis, the median age was 6.5 years (range 2–14 years); 13 (62%) were female and eight (38%) were male. Fourteen (67%) were Hispanic, while five (24%) were Arabic. Eighteen (86%) reported recent travel or residence in an endemic country, with 11 (52%) having been in Mexico. Sixteen (76%) had a history of consumption of raw or unpasteurized milk products, two (10%) had had direct contact with goats, and in three (14%) no exposure history was described. Eight (38%) subjects had another family member with brucellosis, including four subjects (Table 1, Subjects 4–7) who were all identified from the same family.

3.2. Clinical signs and symptoms

The median time to symptom onset after the presumed exposure was 0.5 months (range 0–9 months). Clinical symptoms on presentation were widely variable in children (Table 2). Subjective fever, present in 20 (95%) children was the most common presenting symptom. The one child without fever was on corticosteroids at the time of presentation. Seventy-six percent had constitutional symptoms, 24% reported abdominal pain, and 24% vomiting and/or diarrhea.

Records of clinical signs on presentation were available for 20 of the children (Table 2). Clinical findings included splenomegaly in 60%, hepatomegaly in 55%, arthritis in 35%, central nervous system (CNS) in 15%, osteomyelitis in 10%, and cardiac in 10%. The arthritis was typically monoarticular, and most commonly involved the sacroiliac, knee, and hip joints. The two cases of osteomyelitis occurred in the iliac bone and femoral head. Two children with CNS symptoms had cerebrospinal fluid pleocytosis with negative cultures, one of whom also had left-sided weakness, facial droop, left upgoing toes, and a normal contrast enhanced computerized tomography scan. A third child had uveitis. Serology of spinal fluid was not performed. Cardiac findings included a right bundle branch block in one child associated with bradycardia. A small pericardial effusion and mild mitral regurgitation associated with mild left atrial dilatation was observed in a second child. No children were identified as having endocarditis.

3.3. Laboratory findings

Twenty children had laboratory records available for review (Table 3). The most common finding was elevated transaminases in 16 (80%). Anemia occurred in 13 (65%). Seventeen initial platelet counts were available; the median platelet count was normal at 224×10^9/l (range $35–530 \times 10^9$/l), however five (29%) had platelet counts $<150 \times 10^9$/l, two of which were $<100 \times 10^9$/l. Two patients had pancytopenia. The erythrocyte sedimentation rate was available on presentation in 15 children, with a median of 46 mm/h (range 8–82 mm/h).

Table 2
Clinical symptoms and signs in children with brucellosis

Symptoms (data available for 21 patients)	No. (%)
Fever	20 (95)
Constitutional symptoms[a]	16 (76)
Anorexia	10 (48)
Fatigue	7 (33)
Chills	5 (24)
Weight loss	5 (24)
Myalgias/arthralgias	5 (24)
Abdominal pain	5 (24)
Vomiting and/or diarrhea	5 (24)
Sore throat	4 (19)
Neuropsychiatric[b]	2 (10)
Other[c]	6 (29)
Physical signs (data available for 20 patients)	**No. (%)**
Splenomegaly	12 (60)
Hepatomegaly	11 (55)
Arthritis	7 (35)
Sacroiliac	3 (15)
Knee	2 (10)
Hip	2 (10)
Central nervous system	3 (15)
Osteomyelitis	2 (10)
Cardiac	2 (10)
Mesenteric adenitis	1 (5)

[a] Constitutional symptoms include anorexia, fatigue, chills, weight loss, myalgias/arthralgias.
[b] Neuropsychiatric symptoms include withdrawn, sad, or depressed.
[c] Other includes headache, rash, epistaxis, constipation.

The majority of children were bacteremic with positive blood cultures in 18 (86%), however the initial diagnosis was made by blood or bone marrow culture in 11 (52%) and by serology in 10 (48%). The median length of bacteremia was 2.5 days (range 1–67 days) and the median number of positive blood cultures was two (range 1–5). In three children (14%), the diagnosis was dependent on serology because of negative blood cultures. Brucella SAT was available in 15 children and the median was 1:320 (range 1:160–1:2580). Confirmation of *Brucella* species was available in six of the cases and all were identified as *B. melitensis*.

Table 3
Laboratory findings in children with brucellosis[a]

Laboratory finding	No. (%)	Median (range)
Elevated transaminases	16 (80)	
White blood count		
Normal	13 (65)	7150 (2600–14500)
Low	6 (30)	
High	1 (5)	
Hemoglobin (g/dl)		10 (6.8–13.6)
Anemia	13 (65)	
Platelets ($\times 10^9$/l)[a]		224 (35–530)
Thrombocytopenia	5 (29)	
<100	2 (12)	
Pancytopenia	2 (10)	
Elevated ESR (mm/h)[a]	13 (87)	46 (8–82)
Positive blood or bone marrow cultures	18 (86)	
Length of bacteremia (days)		2.5 (1–67)
Positive blood cultures per patient		2 (1–5)
Brucella melitensis	6 (100)	
Brucella serum agglutination test (SAT)[b]	15 (71)	1:320 (1:160–1:2580)

ESR, erythrocyte sedimentation rate.
[a] Data were available for 20 patients, except platelet counts available for 17 and ESR available for 15.
[b] Fifteen (71%) children had a SAT performed; 100% had a positive test result.

3.4. Treatment and outcomes

The initial treatment regimens varied considerably and are listed in Table 4 along with relapse rates and outcomes. The median length of antibiotic therapy was 6 weeks (range 2–22 weeks). The most commonly used initial antibiotic therapy was trimethoprim–sulfamethoxazole (TMP–SMX) in five (24%) as single drug therapy, though it was also included in seven (33%) combination regimens. A tetracycline derivative (tetracycline or doxycycline) was used as single drug therapy in one (4.8%) patient and was included in seven (33%) combination regimens. Combination regimens consisted of two- or three-drug therapy, which included rifampin in 10 (48%) and an aminoglycoside (streptomycin or gentamicin) in 11 (52%). One patient had a significant complication of antibiotic therapy, which was a secondarily infected peripherally inserted central catheter.

Relapse occurred in four (19%) children with recurrence of presenting symptoms and/or positive blood cultures after completion of therapy. Treatment failure occurred in two (10%) children with recurrence of symptoms while on therapy and/or persistent positive blood cultures. Three of six subjects started on a single drug for Brucella relapsed, but only one of 15 subjects who were started on two or more drugs ($p = 0.053$). All children experiencing treatment failure or relapse were on single or two-drug combination regimens that did not initially include rifampin. All such children were rehospitalized and retreated with two- or three-drug combinations that included rifampin and were cured. All relapses occurred within the first 4 months after therapy was completed, and treatment failure occurred within 2 weeks of initiation of therapy. Two additional children who were labeled as chronic brucellosis (arthritis) on presentation were initially treated in Mexico, but had had no symptom-free interval between presentations. The outcome of children was good, with 15% requiring initial intensive care monitoring, successful cure in all cases of relapse, and no mortality within 2 years of presentation.

4. Discussion

Brucellosis is the most common zoonotic disease worldwide, accounting for over 500 000 infections each year.[17] Worldwide, *B. melitensis* is the most common cause of infection, and in endemic areas such as the Middle East, is associated with direct contact with infected animal parts and the consumption of unpasteurized milk products; several animal species may be sources, including camels, goats, and sheep.[18] In the USA only 100–200 cases occur annually due to the pasteurization of milk products and vaccine eradication campaigns in livestock; the disease is most commonly seen in states that border Mexico.[4–7,15,19] In recent studies, most brucellosis has been observed in the Hispanic population and has been associated with travel to and/or consumption of unpasteurized milk products from Mexico.[4–6] However, endemic brucellosis still remains in the USA; *Brucella abortus*-affected cattle herds, associated with free ranging elk and bison, continue to be reported in the state of Montana, and *Brucella suis* disease has been associated with feral swine hunting.[20,21]

Most epidemiologic studies have come from endemic countries where prevalence is highest in the 15–35 years age group.[14] In the USA, recent Centers for Disease Control and Prevention (CDC) data demonstrate brucellosis to be associated with male and Hispanic predominance, with 57% of cases occurring in the 25–64 years age group, and only 17% occurring in children aged 0–14 years.[22] In California and Texas where reports of brucellosis are most common, the age distribution is similar to endemic countries, predominating in the 20–49 years age group.[4,15]

A brief summary of 2005 Illinois brucellosis cases found the median age of brucellosis patients to be 44 years.[23,24] The last prior

Table 4
Therapeutic regimens and outcomes in children with brucellosis

Patient	Initial antibiotic regimen	Duration of therapy (weeks)	Relapse or treatment failure
1	TMP–SMX	3	Relapse
2	TMP–SMX	2	Relapse
3	TMP–SMX	3	No
4	TMP–SMX	3	No
5	TMP–SMX	2	No
6	TET	6	Relapse
7	TMP–SMX + G	22	Treatment failure and relapse
8	TMP–SMX + G	6	Treatment failure
9	TET + G	3	No
10	DOXY + G	3	No
11	TET + S	4.5	No
12	TMP–SMX + RIF	8	No
13	TMP–SMX + RIF	6	No
14	TMP–SMX + RIF	6	No
15	TET + RIF	6	No
16	TMP–SMX + G + RIF	6	No
17	TMP–SMX + G + RIF	6	No
18	TMP–SMX + G + RIF	6	No
19	DOXY + G + RIF	6	No
20	DOXY + G + RIF	6	No
21	DOXY + G + RIF	6	No

TMP–SMX, trimethoprim–sulfamethoxazole; R, rifampin; S, streptomycin; G, gentamicin; TET, tetracycline; DOXY, doxycycline.

large study of brucellosis in the Midwest (published in 1951) found that brucellosis was primarily an endemic disease of livestock handlers; now, it is primarily a disease of immigrants or travelers to endemic areas.[23,24] Consistent also in most recent US reports is an overwhelming predominance of disease within Hispanic immigrants from Mexico.[4,15] Illinois has consistently been the state with the third highest number of cases in the USA, but a recent large review of cases from the Midwest has not been published.[9,23] Similarly, US data regarding brucellosis in children are very limited. A Medline search of child and brucellosis, limited to the English language between the years of 1950 and 2010 produced 576 articles, 31 of which were from the USA and having some reference to children, and of which the largest prior pediatric brucellosis series was 20 cases from Texas.[6]

Data from the 2010 US Census of metropolitan Chicago reveal a racial/ethnic distribution of 42% White, 37% Black, 26% Hispanic/Latino (of any race), and 4% Asian.[25] The foreign-born population in Illinois has dramatically increased, rising 86% between 1990 and 2006, and Illinois ranks among the top six states for new immigrants. Of these immigrant populations, approximately half of all immigrants to metropolitan Chicago were from Latin America, nearly a quarter from Asia, and approximately 10% from Poland.[26] Additionally, the most recent data from the 2000 US Census show that 24% of people who reported Arab ancestry lived in the Midwest.[27] In our study of pediatric brucellosis, 67% were Hispanic, similar to other studies,[4–6,15] however approximately one-quarter of our population were immigrants of Middle-eastern descent, which reflects the diversity of our local population and a single family cluster. Imported infectious disease processes often reflect immigration patterns and, as these are constantly evolving, new diseases may emerge or old diseases reemerge based on these local patterns. Clinicians therefore need to be aware of local human migration patterns and these often forgotten diseases.

Once Brucella invades the mucosa, it internalizes and evades killing within phagocytes, allowing bacteria to replicate and spread through the blood and reticuloendothelial system.[28,29] The incubation period is highly variable and can range from less than 1 week to several months, with symptom onset generally 2–4 weeks after exposure.[7,30] The finding of bacteremia in the majority (86%) of our patients is consistent with other reviews of childhood brucellosis, and is particularly associated with *B. melitensis*.[31,32] Prior to the advent of automated continuous monitoring blood culture systems such as the BACTEC system (Becton Dickinson, Franklin Lakes, NJ, USA), Brucella could take several weeks to grow in culture and most cases were diagnosed with serology. Though we were unable to determine time to positivity in our retrospective review, other studies have suggested that the diagnosis can now be made utilizing this system in less than 7 days.[33] The finding of a relatively short median incubation period of 0.5 months is consistent with a history of travel to endemic areas. The nature of the variation in range of incubation of 0–9 months in our population is difficult to assess due to the retrospective nature of the study, however reexposure in those residing in endemic areas prior to relocating to the USA could explain prolonged incubations.[22]

Signs and symptoms in our patients are consistent with other pediatric reviews. Fever and constitutional symptoms consisting of chills, sweating, fatigue, malaise, anorexia, weight loss, abdominal pain, headaches, myalgias, and arthralgias, are amongst the most common complaints in children.[31,34] In the present study, fever and constitutional symptoms were exhibited in 95% and 76% of children, respectively. The hematologic findings of brucellosis often reveal a normal white cell count, with mild anemia and decreased platelets, though pancytopenia in the epidemiologic context should raise suspicion of this diagnosis.[35] Liver involvement of hepatomegaly and splenomegaly with mild to moderate liver transaminase elevations are also common complaints of children with brucellosis, with rates of organomegaly of between 6% and 51% reported in recent studies from endemic areas[31,34,36,37] and 40% in recent US studies.[6] We found even higher rates of organomegaly in our population, of 55% hepatomegaly and 60% splenomegaly.

Complications were also typical in our children, consistent with previous reviews in which monoarticular arthritis of the knee, sacroiliac, and hip joints are most commonly described.[6,31,34,36–38] The largest prior US pediatric review found 50% of children with arthritis on initial presentation, which is higher than, but consistent with our finding of arthritis in 35% of cases.[6] The presentation of fever and arthritis, particularly of the knee and hip, could be confused with more common causes of pyogenic arthritis in children, however the prolonged length of fever, subacute presentation, and lower median leukocyte counts in synovial fluid may be useful for distinguishing Brucella from acute pyogenic organisms.[39]

The protean manifestations of brucellosis can be highlighted in children. Some of the less common but noteworthy complications of brucellosis are CNS and cardiac disease. Two of the children in our

population were described as depressed or withdrawn, consistent with neuropsychiatric symptoms of brucellosis previously described in the literature.[12,40] Common cardiac complications are endocarditis followed by myocarditis.[13,41] We had two children in our study with cardiac complications, one of whom had bradycardia associated with a right bundle branch block without evidence of valvular disease, which is an uncommon finding. Cardiac findings were presumed to be related to brucellosis as none of the children had a prior history of cardiac disease, symptom onset appeared to be temporally related to infection, and resolution of symptoms occurred in all cases once Brucella active treatment was initiated.

Changes have occurred in the antibiotic management of Brucella over time. The treatment regimens in our pediatric population were highly variable, which likely reflects the long study duration and conflicting evidence for ideal therapy in children. In adults, tetracyclines are recommended for therapy, but this antibiotic class is typically avoided in children aged $\leq$8 years due to the risk of dental staining. The two largest prospective trials of therapy in children showed that combination therapy with trimethoprim–sulfamethoxazole and rifampin, with or without aminoglycoside therapy, can be associated with high cure rates and outcomes.[42,43] The optimal duration of therapy remains unclear, though treatment of less than 45 days may be associated with higher relapse rates.[42,44–46]

Our study had a relapse rate of 19%, which is similar to that of other recent reported relapse rates in children of 0–25%.[6,31,34–38] Early antibiotic regimens utilizing single drug therapy have been found to be less efficacious than the current recommendations of combination therapy involving two or more medications active against Brucella.[7,28] Our data would support this in that relapse occurred in three of six subjects started on a single drug for Brucella but in only one of 15 subjects who started on two or more drugs ($p = 0.053$). Notably, no relapses occurred in children whose initial therapy included rifampin or those administered three-drug regimens (which always included an aminoglycoside), but the numbers were small. All children in our study with relapses were cured upon retreatment and all children recovered.

Our study has several limitations. Methodological limitations include a retrospective study design and a small cohort of patients which allows for potential selection bias; however, because the study was multicenter, it potentially lessens this bias. Second, our definition of treatment failure was arbitrary as there is no evidence-based definition in the literature, but was quite similar to another study.[16] Third, information on risk factors may potentially be incomplete as this was a retrospective chart review, however potential risk factors were found in all but three children. Finally, since we were comparing treatment and outcomes over different time periods, which can be prejudiced by confounding factors, we can only postulate that the use of two- or three-drug combination therapy may result in better outcomes for children with brucellosis.

In conclusion, childhood brucellosis in the USA is associated with travel or residence in endemic regions and the consumption of unpasteurized milk products. Most children are bacteremic, presenting with prolonged fever, constitutional symptoms, monoarticular arthritis, hepatomegaly and/or splenomegaly. Common laboratory findings include mild anemia and mild to moderate elevations in liver transaminases. In the Midwestern USA, ethnic demographics of children with Brucella may represent the diversity of immigrants to the region. The use of two- or three-drug combination regimens for treatment in children may result in lower relapse rates.

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References

1. Ergönül O, Celikbaş A, Tezeren D, Güvener E, Dokuzoğuz B. Analysis of risk factors for laboratory-acquired Brucella infections. *J Hosp Infect* 2004;**56**:223–7.
[2] Hall GS, Woods GL. Brucella spp.. In: McPherson RA, Pincus MR, editors. *Henry's clinical diagnosis and management by laboratory methods*. 21st ed., Philadelphia, PA: Elsevier; 2007. p. 1209-1210.
3. Chusid MJ, Russler SK, Mohr BA, Margolis DA, Hillery CA, Kehl KC. Unsuspected brucellosis diagnosed in a child as a result of an outbreak of laboratory-acquired brucellosis. *Pediatr Infect Dis J* 1993;**12**:1031–3.
4. Chomel BB, DeBess EE, Mangiamele DM, et al. Changing trends in the epidemiology of human brucellosis in California from 1973 to 1992: a shift toward foodborne transmission. *J Infect Dis* 1994;**170**:1216–23.
5. Troy SB, Rickman LS, Davis CE. Brucellosis in San Diego: epidemiology and species-related differences in acute clinical presentations. *Medicine (Baltimore)* 2005;**84**:174–87.
6. Shen MW. Diagnostic and therapeutic challenges of childhood brucellosis in a nonendemic country. *Pediatrics* 2008;**121**:e1178–83.
7. Young EJ. Brucella species (brucellosis). In: Long SS, Pickering LK, Prober CG, editors. *Principles and practice of pediatric infectious diseases*.. 3rd rev reprint ed., Philadelphia, PA: Churchill Livingston Elsevier; 2009. p. 855–8.
8. Doyle TJ, Bryan RT. Infectious disease morbidity in the US region bordering Mexico, 1990-1998. *J Infect Dis* 2000;**182**:1503–10.
9. McNabb SJ, Jajosky RA, Hall-Baker PA, Adams DA, Sharp P, Worshams C, et al. Centers for Disease Control and Prevention (CDC). Summary of notifiable diseases—United States, 2006. *MMWR Morb Mortal Wkly Rep* 2008;**55**:1–92.
10. Cutler SJ, Whatmore AM, Commander NJ. Brucellosis—new aspects of an old disease. *J Appl Microbiol* 2005;**98**:1270–81.
11. Güngür K, Bekir NA, Namiduru M. Ocular complications associated with brucellosis in an endemic area. *Eur J Ophthalmol* 2002;**12**:232–7.
12. Bahemuka M, Shemena AR, Panayiotopoulos CP, al-Aska AK, Obeid T, Daif AK. Neurological syndromes of brucellosis. *J Neurol Neurosurg Psychiatry* 1988;**51**:1017–21.
13. Karagiannis SS, Mavrogiannaki AM, Chrissos DN, Papatheodoridis GV. Cardiac tamponade in Brucella infection. *Hellenic J Cardiol* 2003;**44**:222.
14. Buzgan T, Karahocagil MK, Irmak H, et al. Clinical manifestations and complications in 1028 cases of brucellosis: a retrospective evaluation and review of the literature. *Int J Infect Dis* 2010;**14**:e469–78.
15. Taylor JP, Perdue JN. The changing epidemiology of human brucellosis in Texas, 1977-1986. *Am J Epidemiol* 1989;**130**:160–5.
16. Lang R, Dagan R, Potasman I, Einhorn M, Raz R. Failure of ceftriaxone in the treatment of acute brucellosis. *Clin Infect Dis* 1992;**14**:506–9.
17. Pappas G, Papadimitriou P, Akritidis N, et al. The new global map of human brucellosis. *Lancet Infect Dis* 2006;**6**:91–9.
18. Pappas G, Akritidis N, Bosilkovski M, et al. Brucellosis. *N Engl J Med* 2005;**352**:2325–36.
19. Centers for Disease Control and Prevention (CDC). Summary of notifiable diseases—United States 2008. *MMWR Morb Mortal Wkly Rep* 2010;**57**:1.
20. Centers for Disease Control and Prevention (CDC). *Brucella suis* infection associated with feral swine hunting—three states, 2007–2008. *MMWR Morb Mortal Wkly Rep* 2009;**58**:618–21.
21. Donch DA, Gertonson AA. Status report—fiscal year 2008. Riverdale, MD: Cooperative State–Federal Brucellosis Eradication Program; 2008, p. 1–7.
22. Chang MH, Glynn MK, Groseclose SL, Chang M, Glynn MK, Groseclose SL. Endemic, notifiable bioterrorism-related diseases, United States, 1992–1999. *Emerg Infect Dis* 2003;**9**:556–64.
23. The epidemiology of infectious diseases in Illinois, 2005. Chicago, IL: Department of Public Health; 2009, p. 15–7.
24. Feig M. Some epidemiologic aspects of brucellosis in the Midwest. *Am J Public Health* 1951;**42**:1253.
25. US Census Bureau state and county quickfacts. Chicago, IL: US Census Bureau Chicago Regional Office; 2010. Available at: http://quickfacts.census.gov/qfd/states/17/1714000.html (accessed April 25, 2011).
26. Metro Chicago immigration fact book 2009. Chicago, IL: Illinois Coalition for Immigrant and Refugee Rights; 2009. Available at: http://icirr.org/en/node/2082 (accessed April 25, 2011).
27. de la Cruz G, Brittingham A. Census 2000 brief. The Arab population: 2000: US. Washington D.C.: Census Bureau; 2003, p. 1–9. Available at: http://www.census.gov/prod/2003pubs/c2kbr-23.pdf (accessed April 25, 2011).
28. Liautard JP, Gross A, Dornand J, Kohler S. Interactions between professional phagocytes and *Brucella spp*. *Microbiologica* 1996;**12**:197–206.
29. Arenas GN, Staskevich AS, Aballay A, Mayorga LS. Intracellular trafficking of *Brucella abortus* in J774 macrophages. *Infect Immun* 2000;**68**:4255–63.
30. Young EJ. *Brucella* species. In: Mandell GL, Bennett JE, Dolin R, editors. *Principles and practice of infectious diseases*. 7th ed., Philadelphia, PA: Elsevier Churchill Livingstone; 2010. p. 257–62.
31. Shaalan MA, Memish ZA, Mahmoud SA, et al. Brucellosis in children: clinical observations in 115 cases. *Int J Infect Dis* 2002;**6**:182–6.
32. Almuneef M, Memish ZA, Al Shaalan M, Al Banyan E, Al-Alola S, Balkhy HH. *Brucella melitensis* bacteremia in children: review of 62 cases. *J Chemother* 2003;**15**:76–80.

33. Ruiz J, Lorente I, Pérez J, Simarro E, Martínez-Campos L. Diagnosis of brucellosis by using blood cultures. *J Clin Microbiol* 1997;**35**:2417–8.
34. Tsolia M, Drakonaki S, Messaritaki A, et al. Clinical features, complications and treatment outcome of childhood brucellosis in central Greece. *J Infect* 2002;**44**:257–62.
35. Shalev H, Abramson O, Levy J. Hematologic manifestations of brucellosis in children. *Pediatr Infect Dis J* 1994;**13**:543–5.
36. Mantur BG, Akki AS, Mangalgi SS, et al. Childhood brucellosis—a microbiological, epidemiological and clinical study. *J Trop Pediatr* 2004;**50**:153–7.
37. Tanir G, Tufekci SB, Tuygun N. Presentation, complications, and treatment outcome of brucellosis in Turkish children. *Pediatr Int* 2009;**51**:114–9.
38. Benjamin B, Annobil SH, Khan MR. Osteoarticular complications of childhood brucellosis: a study of 57 cases in Saudi Arabia. *J Pediatr Orthop* 1992;**12**:801–5.
39. Press J, Peled N, Buskila D, Yagupsky P. Leukocyte count in the synovial fluid of children with culture-proven brucellar arthritis. *Clin Rheumatol* 2002;**21**:191–3.
40. Omar FZ, Zuberi S, Minns RA. Neurobrucellosis in childhood: six new cases and a review of the literature. *Dev Med Child Neurol* 1997;**39**:762–5.
41. Lubani M, Sharda D, Helin I. Cardiac manifestations in brucellosis. *Arch Dis Child* 1986;**61**:569–72.
42. Khuri-Bulos NA, Daoud AH, Azab SM. Treatment of childhood brucellosis: results of a prospective trial on 113 children. *Pediatr Infect Dis J* 1993;**12**:377–81.
43. Lubani MM, Dudin KI, Sharda DC, et al. A multicenter therapeutic study of 1100 children with brucellosis. *Pediatr Infect Dis J* 1989;**8**:75–8.
44. Ariza J, Corredoira J, Pallares R, et al. Characteristics of and risk factors for relapse of brucellosis in humans. *Clin Infect Dis* 1995;**20**:1241–9.
45. Sánchez-Tamayo T, Colmenero JD, Martínez-Cortés F, Moreiras A, Ramos-Díaz JC, García-Martín FJ, Martínez Valverde A. Failure of short-term antimicrobial therapy in childhood brucellosis. *Pediatr Infect Dis J* 1997;**16**:323–4.
46. Abramson O, Abu-Rashid M, Gorodischer R, Yagupsky P. Failure of short antimicrobial treatments for human brucellosis. *Antimicrob Agents Chemother* 1997;**41**:1621–2.