

Brucellosis: Treatment and prevention

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INTRODUCTION

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Brucellosis (also known as "undulant fever," "Mediterranean fever," or "Malta fever") is a zoonotic infection transmitted to humans from infected animals (cattle, sheep, goats, camels, pigs, or other animals) by ingestion of food products (such as unpasteurized dairy products) or by contact with tissue or fluids. It is an important public health problem in many resource-limited countries [1-4].

The treatment and prevention of brucellosis will be reviewed here. The epidemiology, microbiology, clinical manifestations, and diagnosis of brucellosis are discussed separately. (See "Brucellosis: Epidemiology, microbiology, clinical manifestations, and diagnosis".)

TREATMENT

General approach

— The goal of brucellosis therapy is to control the illness and prevent complications, relapses, sequelae, and mortality [5-7]. (See 'Outcome' below.)

General principles of brucellosis treatment include use of antibiotics with activity in acidic intracellular environments (such as **doxycycline** and **rifampin**), use of combination therapy (given high relapse rates with monotherapy), and prolonged duration of treatment [8-10].

Issues related to treatment of brucellosis in the absence of focal disease due to spondylitis, neurobrucellosis, or endocarditis are discussed in the section below. These regimens are used for treatment of osteoarticular disease in the absence of spondylitis (such as sacroiliitis, peripheral arthritis), as well as for treatment of other forms of focal disease (such as genitourinary involvement, pulmonary involvement, etc). (See "Brucellosis: Epidemiology, microbiology, clinical manifestations, and diagnosis", section on 'Complications'.)

Nonpregnant adults

Clinical approach

— Regimens for the treatment of adults with brucellosis (in the absence of focal disease due to spondylitis, neurobrucellosis, or endocarditis) include (table 1) [2,11]:

- **Doxycycline** (oral) for 6 weeks PLUS **streptomycin** (parenteral) for the first 14 to 21 days
- **Doxycycline** (oral) for 6 weeks PLUS **gentamicin** (parenteral) for the first 7 to 10 days
- **Doxycycline** (oral) PLUS **rifampin** (oral), both for 6 weeks

The preferred regimen is **doxycycline** combined with an aminoglycoside; data from several meta-analyses demonstrate that this regimen is somewhat more effective than doxycycline-rifampin [2,6,12-18]. In a 2012 meta-analysis including nine studies and 930 patients with brucellosis treated with doxycycline-rifampin or doxycycline-streptomycin, doxycycline-rifampin was associated with a higher combined rate of treatment failure and relapse (18.2 versus 6.7 percent; odds ratio [OR] 3.17, 95% CI 2.05-4.91) [12]. Comparable outcomes have been observed with doxycycline-streptomycin and doxycycline-gentamicin [12,18-20]; in the above meta-analysis, no significant difference between these regimens was observed (OR 1.89, 95% CI 0.81-4.39) [12]. Treatment differences for other outcomes (such as complications or long-term morbidity) have not been observed.

However, many favor doxycycline-rifampin since it is more convenient than parenteral therapy, may be better tolerated than aminoglycosides (which are associated with nephrotoxicity and ototoxicity) and is less costly [2,9]. Further study of oral regimens for treatment of brucellosis is needed.

Monotherapy regimens and regimens shorter than six weeks are not accepted treatment strategies for brucellosis, given high relapse rates with these approaches [2,9,10,18].

Some studies have suggested that triple-drug therapy might improve the illness outcome without increasing the incidence of drug side effects [20-26]. However, this is not regarded as a routine approach [2,10,12]; it may be considered on an individual basis [2,27]. In one systematic review, triple therapy with **doxycycline** and rifampicin plus **streptomycin** or **levofloxacin** was superior to dual combination of doxycycline and rifampicin for initial cure and relapse prevention [20].

Alternative agents

— Alternative agents include fluoroquinolones and TMP-SMX, used in combination regimens:

- Fluoroquinolones may be used as alternative second or third agents in combination regimens containing **doxycycline** or **rifampin** [26,28-30]. They are not appropriate first-line agents (given decreased activity in acidic environments, as well as cost), but may be beneficial in the setting of drug resistance, antimicrobial toxicity, and some cases of relapse [28]. Options include **ciprofloxacin** (500 mg orally twice daily for six weeks), **ofloxacin** (200 to 400 mg orally twice daily for six weeks), or **levofloxacin** (500 mg orally once a day for six weeks). In a randomized trial including 61 patients with brucellosis treated with doxycycline-rifampin or ofloxacin-rifampin for 6 weeks, relapse rates were similar between the groups (3.2 versus 3.3 percent) and there was one case of treatment failure in the ofloxacin-rifampin group [29]. In a subsequent study including 118 patients with brucellosis treated with ofloxacin-rifampin, doxycycline-rifampin, or doxycycline-streptomycin, relapse rates were similar (12.8, 14.3, and 9.7 percent, respectively) [31].
- TMP-SMX may be used as an alternative second or third agent in combination regimens containing **doxycycline** or **rifampin** for treatment of patients with relapse or refractory disease [2]. Dosing consists of one double-strength tablet (160 mg TMP and 800 mg SMX) orally twice daily for six weeks. Based on limited data, the efficacy of doxycycline-TMP-SMX is similar to that of doxycycline-rifampin [14]; however, comparative randomized studies are limited. In addition, TMP-SMX should be used with caution for prolonged treatment of brucellosis given its broad spectrum of activity and potential for development of antimicrobial resistance.

Children

— The approach to treatment of uncomplicated brucellosis in children is based on studies in adults, observational data, and a randomized trial; cure rates are similar to those seen in adults [22,32-40].

- **Children ≥8 years of age** – Regimens for treatment of children ≥8 years with brucellosis (in the absence of spondylitis, neurobrucellosis, or endocarditis) include (table 1):
 - **Doxycycline** (oral) PLUS **rifampin** (oral), both for 6 weeks
 - **Doxycycline** (oral) for 6 weeks PLUS **streptomycin** (parenteral) for the first 14 to 21 days
 - **Doxycycline** (oral) for 6 weeks PLUS **gentamicin** (parenteral) for the first 7 to 10 days

Many favor doxycycline-rifampin for treatment of children ≥8 years with brucellosis since it is more convenient than parenteral therapy.

- **Children <8 years of age** – **Doxycycline** is not recommended for children <8 years of age given risk for dental staining with prolonged duration of therapy.

Treatment of children <8 years with uncomplicated brucellosis consists of **trimethoprim-sulfamethoxazole** (TMP-SMX) PLUS **rifampin**, both for 6 weeks (table 1) [1,2]. Other acceptable regimens include either TMP-SMX or rifampin, in combination with an aminoglycoside [37,41].

In a systematic review of 11 observational studies including 1156 children up to 10 years of age in Brazil, the commonly used therapeutic agents for brucellosis were TMP-SMX PLUS **rifampin** or an aminoglycoside; failure rates were 13 and 2 percent, respectively [42].

Pregnant women

— The optimal approach to management of pregnant women with brucellosis (in the absence of focal disease due to spondylitis, neurobrucellosis, or endocarditis) is uncertain. Tetracyclines are contraindicated in pregnancy; data regarding the efficacy of alternative agents are limited to observational studies [10,43-45].

For pregnant women <36 weeks gestation, we treat with **rifampin** plus TMP-SMX (with folate supplementation), both for six weeks (table 1) [46]. Some studies have suggested an association between use of TMP/SMX during the first trimester of pregnancy and increased risk of neural tube defects (due to interference with folate metabolism) [47]; however, one meta-analysis failed to identify significant adverse effects associated with the use of TMP/SMX during pregnancy [48].

For pregnant women ≥36 weeks gestation, we administer **rifampin** monotherapy until delivery, given risk of neonatal kernicterus with the use of TMP-SMX in the last month of pregnancy.

After delivery, we continue combination therapy as in nonpregnant adults and advise that breastfeeding be postponed until after completion of treatment [46]. The total duration of treatment is six weeks. (See "**Trimethoprim-sulfamethoxazole: An overview**", section on 'Pregnancy and breastfeeding' and 'Nonpregnant adults' above.)

Other regimens described in the literature as effective for treatment of brucellosis in pregnancy include **rifampin** or TMP-SMX monotherapy or combination therapy with rifampin and an aminoglycoside, combination therapy with rifampin and **ceftriaxone**, and combination therapy with rifampin and TMP-SMX and ceftriaxone [10,43-46,49].

In the setting of postpartum relapse, a standard treatment regimen may be used [2]. (See 'Nonpregnant adults' above.)

In one study including 92 pregnant women with brucellosis, antepartum antimicrobial therapy with TMP-SMX or TMP-SMX-rifampin was protective against spontaneous abortion (relative risk 0.14, 95% CI 0.06-0.37) [44]

Kidney or liver failure

— In patients with hepatic failure, we treat with an aminoglycoside in combination with either **doxycycline** or a fluoroquinolone. In patients with kidney failure, we treat with doxycycline plus **rifampin** [27].

Treatment of specific complications

Spondylitis

— Issues related to treatment of *Brucella* spondylitis are discussed here; the approach to treatment of osteoarticular disease (such as peripheral arthritis and sacroiliitis) in the absence of spondylitis is described above. (See '**General approach**' above.)

The optimal approach to treatment of *Brucella* spondylitis is uncertain; data are limited to observational studies [9,50-55]. A number of combination regimens have been used [54].

For adults and children ≥ 8 years with spondylitis, we favor treatment with streptomycin (for the first 14 to 21 days) or gentamicin (for the first 7 to 14 days) PLUS doxycycline (for at least 12 weeks) PLUS rifampin (for at least 12 weeks) (table 2) [50-53,56]. Spondylitis in children is rare; in such cases, we substitute TMP-SMX for doxycycline for children < 8 years.

For pregnant women with spondylitis, we favor treatment with ceftriaxone for 4 to 6 weeks PLUS rifampin and TMP-SMX for 12 weeks (table 2). For pregnant women ≥ 36 weeks gestation, we administer ceftriaxone and rifampin until delivery, given risk of neonatal kernicterus with the use of TMP-SMX in the last month of pregnancy. After delivery, we continue combination therapy as in nonpregnant adults; the total duration of treatment is at least 12 weeks. (See 'Pregnant women' above.)

Other regimens described in the literature for treatment of spondylitis include doxycycline-rifampin, doxycycline-streptomycin, ciprofloxacin-rifampin, doxycycline-rifampin-cotrimoxazole, and doxycycline-rifampin-ciprofloxacin [50,52,54,57].

The duration of therapy may be at least as important as the choice of antimicrobial agents; treatment for *Brucella* spondylitis for adults should consist of antibiotic therapy for at least 12 weeks [53]. In a meta-analysis including 32 observational studies and 303 patients, the failure rate was lower for patients treated ≥ 12 weeks than for patients treated ≤ 6 weeks (17 versus 43 percent) [53].

For patients with persistent symptoms and/or radiographic findings, the duration of treatment should be extended beyond 12 weeks, based on individual patient circumstances.

The above approach is supported by an observational study including 18 patients with *Brucella* spondylitis treated with a combination of at least three antibiotics (doxycycline-rifampin plus streptomycin or TMP-SMX or ciprofloxacin) for a median duration of therapy of 48 weeks (range 24 to 72 weeks); no relapses were observed (median follow-up 36.5 months) [55].

Surgery may be warranted in the setting of spinal instability, persistence or progression of neurologic deficit, vertebral collapse, or localized abscess (epidural or paravertebral) [8,58].

Neurobrucellosis

— The optimal approach to treatment of neurobrucellosis is uncertain; data are limited to retrospective and observational studies [59-62].

For adults and children ≥ 8 with neurobrucellosis, we favor treatment with ceftriaxone for the first 4 to 6 weeks, PLUS rifampin and doxycycline, both for at least 12 weeks; the duration of therapy is often extended to 4 to 6 months (table 3) [59-62]. For children < 8 years, we substitute TMP-SMX for doxycycline [63-65]. An alternative regimen consists of doxycycline-rifampin-TMP-SMX, all administered for at least 12 weeks [61,62].

For pregnant women with neurobrucellosis, we favor treatment with ceftriaxone for the first 4 to 6 weeks, PLUS rifampin and TMP-SMX both for at least 12 weeks (table 3). For pregnant women ≥ 36 weeks gestation, we administer ceftriaxone and rifampin until delivery, given the risk of neonatal kernicterus with the use of TMP-SMX in the last month of pregnancy. After delivery, we continue combination therapy as in nonpregnant adults; the total duration of treatment is at least 12 weeks. (See 'Pregnant women' above.)

The total duration of treatment is at least three months and may be up to six months or longer. The duration of therapy should be tailored to individual patient circumstances including clinical assessment, cerebrospinal fluid findings, and follow-up radiographic imaging [60,61,66].

The above approach is supported by a retrospective study including 215 patients with neurobrucellosis treated with rifampin, doxycycline, and either ceftriaxone or TMP-SMX; patients treated with ceftriaxone-based therapy had a lower rate of the combined outcome of relapse and treatment failure (3.6 versus 14.3 percent) [62].

There is no role for routine use of corticosteroids for treatment of neurobrucellosis [67]. Use of steroids may be appropriate in the setting of neurobrucellosis complicated by iritis, papilledema, myelopathy, polyneuropathy, radiculopathy, encephalitis, and/or cranial nerve palsies [27,68].

Endocarditis

— The optimal approach to treatment of *Brucella* endocarditis is uncertain; data are limited to small case series. In general, most patients with *Brucella* endocarditis require a combination of antimicrobial therapy and surgery for the best chance of cure [3,69,70]. Surgical consultation is warranted for all patients with *Brucella* endocarditis.

In one retrospective study including 308 cases of brucellar endocarditis, combined surgical plus medical treatment (compared with medical treatment only) was associated with reduced mortality (33 versus 7 percent) [71]. A small number of cases treated successfully with antimicrobial therapy alone have been reported; in some circumstances, this may be an acceptable approach in the absence of heart failure, large vegetations, valvular destruction, abscess, or a prosthetic valve [27,72,73].

For adults and children ≥ 8 years with *Brucella* endocarditis, we favor treatment with a triple-combination antibiotic regimen including an aminoglycoside (streptomycin or gentamicin) for the first month, PLUS rifampin and doxycycline both for at least 12 weeks (table 4). An alternative approach consists of substituting a third-generation cephalosporin for the aminoglycoside [69]. For children < 8 years, we substitute TMP-SMX for doxycycline.

For pregnant women with *Brucella* endocarditis, we favor treatment with ceftriaxone for the first four to six weeks, PLUS rifampin and TMP-SMX, both for at least 12 weeks (table 4). For pregnant women ≥ 36 weeks gestation, we administer ceftriaxone and rifampin until delivery, given the risk of neonatal kernicterus with the use of TMP-SMX in the last month of pregnancy. After delivery, we continue combination therapy as in nonpregnant adults; the total duration of treatment is at least 12 weeks. (See 'Pregnant women' above.)

The minimum duration of therapy is 12 weeks; the duration of therapy is often extended for four to six months. The duration of therapy should be tailored to individual patient circumstances, including clinical assessment and follow-up echocardiography. For patients with a prosthetic valve or abscess who do not undergo surgery, a

prolonged duration of therapy is warranted.

In one study including 53 adults with *Brucella* endocarditis treated with ceftriaxone-streptomycin-rifampin, gentamicin (or streptomycin)-doxycycline-rifampin, ceftriaxone-doxycycline-rifampin, or oral agents only, mortality rates were 0, 5, 15, and 25 percent, respectively; however, the sample size was too small for statistical analysis [74].

General issues related to management of endocarditis are discussed separately. (See "Overview of management of infective endocarditis in adults".)

Relapse

— Relapse usually occurs within the first six months following completion of treatment, but may occur up to 12 months later [8,75-77]. Relapse of symptoms should prompt assessment for focal disease. Relapse due to antibiotic resistance is rare; nonetheless, antimicrobial susceptibility should be performed on all culture isolates. (See "Brucellosis: Epidemiology, microbiology, clinical manifestations, and diagnosis", section on 'Relapse'.)

Most relapses can be treated successfully with a repeat course of a standard regimen [2,4,8,75,78]. Patients with a second or third relapse should be treated with an alternative regimen, guided by antimicrobial susceptibility testing. (See 'Alternative agents' above.)

Disease due to vaccine strain RB51

— *Brucella* RB51 is a live attenuated cattle vaccine strain which can be shed in milk and can cause infection in humans who drink the milk without pasteurization; the strain is resistant to rifampin [79].

Uncomplicated brucellosis associated with exposure to *Brucella* RB51 may be treated as follows [79]:

- Adults and children ≥ 8 years: Doxycycline and TMP-SMX for 6 weeks
- Children < 8 years: TMP-SMX for 6 weeks PLUS gentamicin for 7 to 10 days
- Pregnant women: TMP-SMX (monotherapy for 6 weeks), or TMP-SMX in combination with gentamicin (7 to 10 days) or ceftriaxone (4 to 6 weeks)

The dosing is as summarized above. (See 'General approach' above.)

LIMITED ROLE OF FOLLOW-UP SEROLOGY

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In general, routine follow-up serologic testing is not useful for guiding duration of therapy; it is not always possible to distinguish serologically between persistent (active) and past (inactive) infection [80-82].

Given lack of reliable laboratory criteria for definitive cure [83], periodic clinical assessment in combination with serologic follow-up is advisable; and the interpretation of serologic tests should be correlated with clinical history, including presenting clinical manifestations and treatment history [84-86]. In such cases, the most useful laboratory tools include the Coombs test, the immunocapture agglutination (Brucellacapt) test, enzyme-linked immunosorbent assay (ELISA) immunoglobulin (Ig)G, and the 2-mercaptoethanol (2-ME) agglutination test [86-88]. (See "Brucellosis: Epidemiology, microbiology, clinical manifestations, and diagnosis", section on 'Serologic tests'.)

Decline in IgG titer has been suggested as an indicator of successful response to treatment, whereas a failure to decline or a subsequent rise in IgG titer suggests a possibility of relapse or progression to chronic focal disease [89-91]; however, negative serology does not definitively exclude persistence of active *Brucella* infection [87,92]. Some patients may have persistent symptoms (which may be attributable to persistent infection or another cause) after completing treatment, even in the setting of declining or negative serology [93,94]. Conversely, elevated levels of IgG antibodies may persist for years in fully treated individuals with no clinical signs of infection [80].

The above assays (if available) are preferred over the following assays (which are generally not appropriate for monitoring response to treatment):

- Anti-*Brucella* cytoplasmic or periplasmic protein antibodies (detected by ELISA) — These antibodies are elevated only in active brucellosis [82,95].
- Molecular techniques — Molecular techniques are inappropriate to establish the success of treatment or to predict relapse. *Brucella* DNA can be detected using real-time polymerase chain reaction (PCR) techniques in the majority of treated patients throughout the follow-up period, despite apparent clinical recovery. In a significant number of patients, *Brucella* DNA can remain detectable for months or years after clinical cure and in the absence of any symptoms indicative of chronic disease or relapse [96,97]. Conversely, relapses have been observed in PCR-negative patients [96].

OUTCOME

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Unfavorable outcomes (defined by relapses and therapeutic failures) are usually a result of failure to eradicate intracellular bacteria. Therapeutic failures are usually associated with *Brucella* spondylitis and have been reported in up to 15 percent of cases [98]. Rarely, moderate to severe sequelae occur in the setting of spondylitis and neurobrucellosis [50,56,67].

The prognosis of neurobrucellosis is variable; in one report of 18 patients, complete recovery of neurologic function was observed in 60 percent of cases [67]. With appropriate antimicrobial treatment, the mortality rate of brucellosis is <1 percent [58,98,99]. Endocarditis is the main cause of death attributable to brucellosis [58,100-102].

PREVENTION

General principles

— Thus far, there are no vaccines for prevention of brucellosis in humans; improved understanding of disease pathogenesis may facilitate identification of vaccine targets [3,4].

Tools for prevention include treatment of dairy products, precautions for individuals at risk for occupational exposure, precautions to prevent person-to-person transmission, and control of the disease in animals [100] (see "Brucellosis: Epidemiology, microbiology, clinical manifestations, and diagnosis", section on "Transmission"):

- Raw milk should be boiled or pasteurized; consumption of dairy products made from raw milk should be avoided.
- Contact of skin or mucous membranes with infected tissue (such as placenta or miscarriage products) or infected fluids (such as blood, urine, or milk) should be avoided. In addition, inhalation of infected aerosolized particles should be avoided.
 - In clinical settings:
 - Standard infection control precautions are warranted. (See "Infection prevention: Precautions for preventing transmission of infection".)
 - In the setting of obstetrical procedures for pregnant women with brucellosis, health care personnel should wear standard surgical attire (gown, gloves, face mask, and eye protection). (See "Overview of control measures for prevention of surgical site infection in adults".)
 - Manipulation of *Brucella* cultures should be performed with biosafety level 3 practices and containment equipment (table 5).
 - In slaughterhouses, protective measures include separation of the killing floor from other processing areas, using designated spaces for known infected animals, use of protective clothing and disinfectants, and control of air circulation.
- To reduce the likelihood of person-to-person transmission, patients should be counseled to wait until completion of treatment before unprotected sexual contact; *Brucella* organisms have been detected in semen and it is unknown how long the risk of sexual transmission persists following initiating of treatment [103]. Lactating women with brucellosis should be counseled to discontinue breastfeeding until completion of treatment. In highly endemic regions, we recommend serologic testing for blood and organ donors.
- Vaccination of domestic livestock – Available vaccines for prevention of brucellosis in animals include *Brucella abortus* B19 and RB51 (for cattle) and *Brucella melitensis* Rev 1 (for small ruminants such as sheep and goats). A sustained vaccination program over several years is required. These are live attenuated vaccines that are also known to cause disease in humans during preparation or by accidental inoculation; inadvertent exposure requires careful follow-up [3,104-108]. (See 'Postexposure prophylaxis' below.)

There are no suitable vaccines for prevention of *B. melitensis* in cattle or prevention of *Brucella suis* in swine [104,109].

Screening contacts

— Screening household members of an index case enables detection of unrecognized cases, facilitating early treatment and prevention of complications [98,100]. Household members of an index case should undergo clinical evaluation for signs and symptoms of brucellosis serologic testing (with repeat testing at 6 and 12 weeks); they should be instructed to seek medical attention if they develop relevant clinical manifestations. Symptomatic individuals should undergo additional diagnostic evaluation as discussed separately. (See "Brucellosis: Epidemiology, microbiology, clinical manifestations, and diagnosis", section on 'Diagnosis'.)

Postexposure prophylaxis

— Microbiology laboratory workers may be at risk for brucellosis after laboratory exposure. We are in agreement with the United States Centers for Disease Control and Prevention's approach to identification of high-risk exposures, recommendations for serologic testing, and postexposures prophylaxis; these are outlined in the table (table 6) [110,111].

SUMMARY AND RECOMMENDATIONS

- **General treatment principles** – General principles of brucellosis treatment include use of antibiotics with activity in acidic intracellular environments (such as doxycycline and rifampin), use of combination therapy (given high relapse rates with monotherapy), and prolonged duration of treatment. (See 'General approach' above.)
- **Clinical approach** – For treatment of patients with brucellosis (in the absence of focal disease due to spondylitis, neurobrucellosis, or endocarditis), our approach is as follows (table 1):
 - **Nonpregnant adults** – For nonpregnant adults, we suggest combination therapy with doxycycline plus an aminoglycoside (streptomycin or gentamicin) over oral combination therapy (Grade 2B). The aminoglycoside-based regimen has been associated with lower rates of treatment failure and relapse; oral

combination therapy is an acceptable alternative for circumstances in which avoidance of parenteral therapy is preferred. The duration of therapy is six weeks. (See '[Nonpregnant adults](#)' above.)

- **Children** – For children, we suggest oral combination therapy (**Grade 2C**), since administration is more convenient than parenteral therapy. Treatment of children ≥ 8 years consists of **doxycycline** plus **rifampin**; for children < 8 years, we substitute **trimethoprim-sulfamethoxazole** (TMP-SMX) for doxycycline. The duration of therapy is 6 weeks. (See '[Children](#)' above.)
- **Pregnant patients** – For pregnant patients < 36 weeks gestation, we suggest treatment with **rifampin** plus TMP-SMX compared with alternative regimens (**Grade 2C**). For pregnant patients ≥ 36 weeks gestation, we administer rifampin monotherapy until delivery (given the risk of neonatal kernicterus with the use of TMP-SMX in the last month of pregnancy). After delivery, we continue combination therapy as in nonpregnant adults and advise that breastfeeding be postponed until after completion of treatment. The total duration of treatment is six weeks. (See '[Pregnant women](#)' above.)
- **Treatment of specific complications** – For treatment of focal disease due to spondylitis, neurobrucellosis, or endocarditis, our approach is as follows:
 - **Nonpregnant adults and children ≥ 8 years**
 - **Spondylitis** – For nonpregnant adults and children ≥ 8 years with spondylitis, we suggest treatment with **doxycycline** plus **rifampin** plus an aminoglycoside (**streptomycin** or **gentamicin**) compared with alternative regimens ([table 2](#)) (**Grade 2C**). For children < 8 years, we substitute TMP-SMX for doxycycline. The total duration of treatment is at least 12 weeks; it is tailored to individual patient circumstances including clinical assessment and follow-up radiographic imaging. (See '[Spondylitis](#)' above.)
 - **Neurobrucellosis** – For nonpregnant adults and children ≥ 8 years with neurobrucellosis, we suggest treatment with **ceftriaxone**, **rifampin**, and **doxycycline** compared with alternative regimens ([table 3](#)) (**Grade 2C**). For children < 8 years, we substitute TMP-SMX for doxycycline. The total duration of treatment is at least 12 weeks and may be up to 6 months or longer; it is tailored to individual patient circumstances, including clinical assessment, cerebrospinal fluid findings, and follow-up radiographic imaging. (See '[Neurobrucellosis](#)' above.)
 - **Endocarditis** – For nonpregnant adults and children ≥ 8 years with *Brucella* endocarditis, we suggest treatment with a triple-combination antibiotic regimen including an aminoglycoside (**streptomycin** or **gentamicin**) for the first month, PLUS **rifampin** and **doxycycline** compared with alternative regimens both for at least 12 weeks ([table 4](#)) (**Grade 2C**). For children < 8 years, we substitute TMP-SMX for doxycycline. The duration of therapy is often extended for 4 to 6 months, tailored to individual patient circumstances, including clinical assessment and follow-up echocardiography. In general, most patients with *Brucella* endocarditis require a combination of antimicrobial therapy and surgery for the best chance of cure; surgical consultation is warranted for all patients with *Brucella* endocarditis. (See '[Endocarditis](#)' above.)
 - **Pregnant patients** – For treatment of pregnant patients with focal disease due to spondylitis, neurobrucellosis, or endocarditis, we suggest treatment with a triple-combination antibiotic regimen including **ceftriaxone**, **rifampin**, and TMP-SMX compared with alternative regimens (**Grade 2C**). We avoid use of TMP-SMX during the last month of pregnancy. The duration of therapy is as summarized above. (See '[Treatment of specific complications](#)' above.)
- **Prevention** – Tools for prevention of brucellosis include avoiding consumption of raw milk, precautions for individuals at risk for occupational exposure, precautions to prevent person-to-person transmission, and control of the disease in animals. Contact of skin or mucous membranes with infected tissue (such as placenta or miscarriage products) or infected fluids should be avoided. Patients should be counseled to wait until completion of treatment before unprotected sexual contact, and lactating women should be advised to discontinue breastfeeding until completion of treatment. (See '[Prevention](#)' above.)

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