1.1 INTRODUCTION

Brucellosis is a highly contagious zoonosis caused by ingestion of unpasteurized milk or undercooked meat from infected animals, or close contact with their secretions. It is also known as undulant fever, Malta fever and Mediterranean fever.(Di Pierdomenico et al 2011).Brucellosis is a zoonotic infection caused by the bacterial genus Brucella. The bacteria are transmitted from animals to humans by ingestion through infected food products, direct contact with an infected animal, or inhalation of aerosols. Humans are accidental hosts, but brucellosis continues to be a major public health concern worldwide and is the most common zoonotic infection.

Brucellosis is one of the most common zoonotic infections globally (Ariza J et al. 2007). This bacterial disease causes not only a severely debilitating and disabling illness, but it also has major economic ramifications due to time lost by patients from normal daily activities (Roth F et al. 2003) and losses in animal production (Roth F, et al.2003).In a review of 76 diseases and syndromes of animals, brucellosis lies within the top ten in terms of impact on impoverished people (Perry B (2002) . A brucellosis disability weighting of 0.2 has been previously proposed for Disability-Adjusted Life Years (DALY) calculation, based on the pain and impaired productivity known to result from infection (Roth F et al. (2003).

However, a more informed estimate is needed for an accurate assessment of disease burden.

Brucella organisms, which are small aerobic intracellular coccobacilli, localize in the reproductive organs of host animals, causing abortions and sterility. They are shed in large numbers in the animal's urine, milk, placental fluid, and other fluids. To date, 8 species have been identified, named primarily for the source animal or features of infection. Of these, the following 4 have moderate-to-significant human pathogenicity:

Brucella melitensis (from sheep; highest pathogenicity)

Brucella suis (from pigs; high pathogenicity)

Brucella abortus (from cattle; moderate pathogenicity)

Brucella canis (from dogs; moderate pathogenicity)

Although domesticated animals are of particular importance, brucellosis is also found in wild animals that exist in herds (eg, bison or elk in North America and wild boar in Germany). Humans have only a limited risk from wild animals, mainly because of lack of proximity or intimate contact and infrequent use of milk and meat products from these animals. Concerns have been voiced that interaction of wild animals with domesticated ones may lead to infection of agricultural herds, though supportive evidence is quite limited.

1.2 HISTORY

David Bruce Under the name "Malta fever", the disease now called brucellosis first came to the attention of British medical officers in the 1850s in Malta during the Crimean War. Jeffery Allen Marston (1831–1911) described his own case of the disease in 1861. The causal relationship between organism and disease was first established in 1887 by David Bruce.(Colmenero JD,et al, 1991,Crosby E,et al 1984). The agent that Bruce identified was classed as a coccus.In 1897, Danish veterinarian Bernhard Bang isolated a bacillus as the agent of heightened spontaneous abortion in cows, and the name "Bang's disease" was assigned to this condition. At the time, no one knew that this bacillus had anything to do with the causative agent in Malta fever.Maltese scientist and archaeologist Dr Themistocles Zammit identified unpasteurized goat milk as the major etiologic factor of undulant fever in June 1905(Dunea G,et al,1969). In the late 1910s, American bacteriologist Alice C. Evans was studying the Bang bacillus and gradually realized that it was virtually indistinguishable from the Bruce coccus.(Tena D,et al 2006)The short-rod versus oblong-round morphologic borderline explained the leveling of the erstwhile bacillus/coccus distinction (that is, these "two" pathogens were not a coccus versus a bacillus but rather were one coccobacillus).(Dunea G,et al,1969)It was already known that the Bang bacillus was enzootic in American dairy cattle, which showed itself in the regularity with which herds experienced contagious abortion.(Dunea G,et al,1969)Having made the discovery that the bacteria were certainly nearly identical and perhaps totally so, Evans then wondered why Malta fever was not widely diagnosed or reported in the United States.(Dunea G,et al,1969)She began to wonder whether many cases of vaguely defined febrile illnesses were in fact caused by the drinking of raw (unpasteurized) milk.(Dunea G,et al,1969).

1.3 ETIOLOGY

Brucellosis in humans is usually associated with the consumption of unpasteurized milk and soft cheeses made from the milk of infected animals, primarily goats, infected with Brucella melitensis and with occupational exposure

of laboratory workers, veterinarians, and slaughterhouse workers.(Bouza E,et al, 2005). Some vaccines used in livestock, most notably B. abortus strain 19, also cause disease in humans if accidentally injected. Brucellosis induces inconstant fevers, miscarriage, sweating, weakness, anaemia, headaches, depression, and muscular and bodily pain. The other strains, B. suis and B. canis, cause infection in pigs and dogs, respectively.

the 4 Brucella species known to cause disease in humans (*B abortus, B melitensis, B canis, B suis*), *B melitensis* is thought to be the most virulent and causes the most severe and acute cases of brucellosis; it is also the most prevalent worldwide. B melitensis may be acquired via exposure to animals or animal products or, in the case of laboratory technicians, to specimens from animals (including humans) whose tissues are operated upon or submitted for culture or pathologic analysis. (Bouza E et al, 2005)

EPIDEMIOLOGY

Although brucellosis is still a reportable disease, it has become rare as a result of the institution of veterinary control measures (eg, routine screening of domestic livestock and vaccination programs). Currently, fewer than 100 cases are reported annually to the Centers for Disease Control and Prevention (CDC), mostly from California, Florida, Texas, and Virginia. Incidental cases arise as a result of relaxation of surveillance standards or because of the increasing international exchange of foodstuffs and animals that may harbor Brucella organisms.At present, most human cases of brucellosis in the United States are due to *B melitensis.* The B abortus and *B suis* species that have accounted for most brucellosis in North America are less likely to engender clinical disease in humans than B melitensis is. When disease develops in North Americans, it often does so with greater latency to onset and milder manifestations.

INTERNATIONAL STATISTICS

Brucellosis causes more than 500,000 infections per year worldwide. Its geographic distribution is limited by effective public and animal health programs, and the prevalence of the disease varies widely from country to country. (Pappas G et al 2006) Overall, the frequency of brucellosis is higher in more agrarian societies and in places where handling of animal products and dairy products is less stringent.

AGE-RELATED DEMOGRAPHICS

Brucellosis in the Mediterranean, chiefly due to B melitensis, has the highest age/sex-related incidence in males in their mid-20s. A report from northern Saudi Arabia found that 60% of cases of brucellosis occurred in individuals aged 13-40 years, whereas 21% occurred in those younger than 13 years, 16% in those aged 40-60 years, and 2.5% in those older than 60 years. (Fallatah SM,2005 Oct 25)

For unknown reasons, men aged 13-40 years are particularly vulnerable to the manifestation of illness due to B melitensis. Possible explanations include engaging in activities that increase exposure to Brucella organisms (eg, animal husbandry) and less diligent personal hygiene. The predilection is not universal, given that 60% of cases in Jordan occur in individuals younger than 24 years.

Elderly individuals with acute localized brucellosis are particularly likely to manifest destructive localized brucellosis of the spine.(Alp E et al 2008)

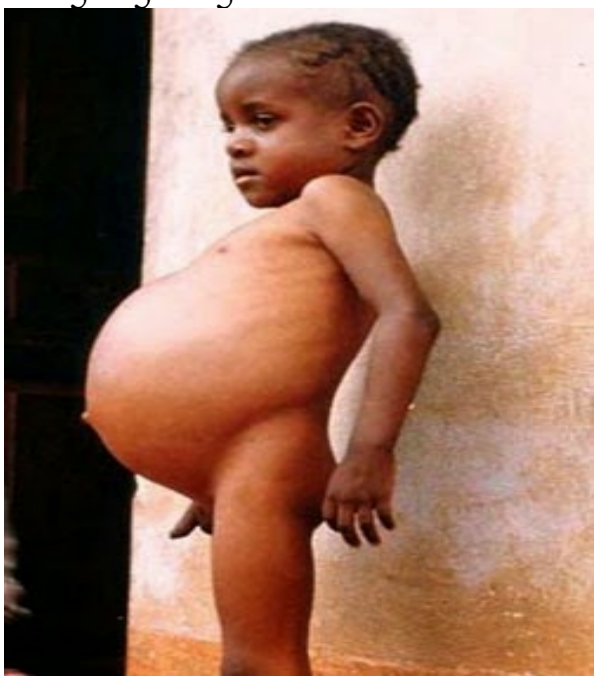
Brucellosis is generally uncommon in infants. The international literature suggests that brucellosis may be more common in children in developing countries because of lack of pasteurization and working in an agrarian society. Transmission to infants may occur through breastfeeding (Celebi G et al 2007) or ingestion of raw milk. Prepubertal children account for less than 2% of all cases of neurobrucellosis; fewer than 50 such cases have been described in the peer-reviewed medical literature over the past 50 years.

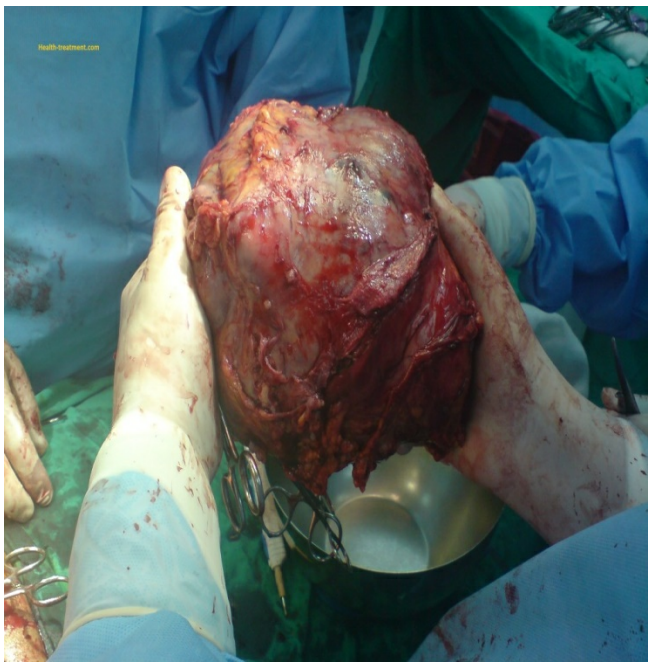
SEX-RELATED DEMOGRAPHICS

Worldwide, brucellosis is more common in males than in females. Young adult males predominate in most series of patients with brucellosis compiled in areas of endemic disease. A report from northern Saudi Arabia found a male-to-female ratio of 1.7:1, chiefly individuals aged 13-40 years. (Fallatah SM,2005 Oct 25) .The cases represented in such series are caused chiefly by Bmelitensis.

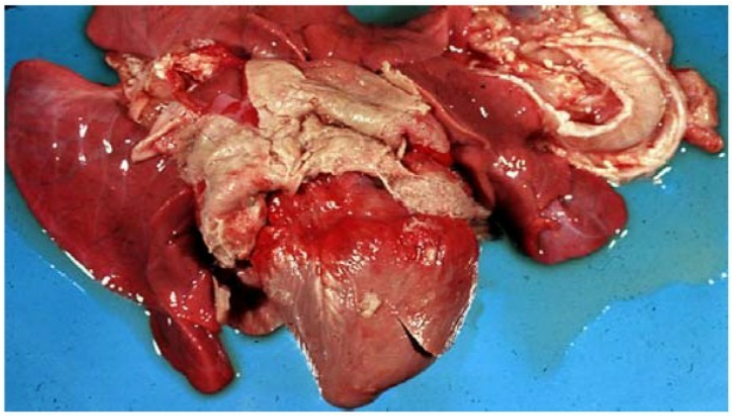
PATHOPHYSIOLOGY

Brucellae are aerobic gram-negative coccobacilli that possess a unique ability to invade both phagocytic and nonphagocytic cells and to survive in the intracellular environment by finding ways to avoid the immune system. This ability helps explain why brucellosis is a systemic disease and can involve almost every organ system.

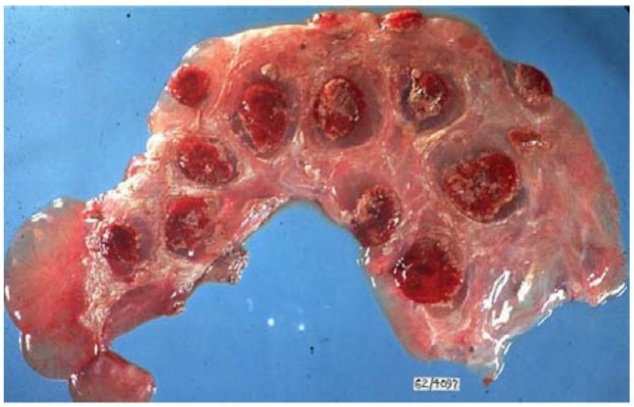




Brucella can gain entry into the human body through breaks in the skin, mucous membranes, conjunctivae, and respiratory and gastrointestinal (GI) tracts. Sexual transmission has not been convincingly documented. Ingestion usually occurs by way of unpasteurized milk; meat products often have a low bacterial load.



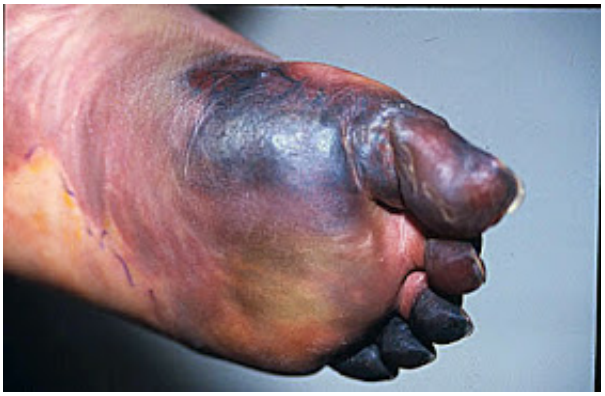
Pericarditis congestiva en abortado.



Placentitis con necrosis cotiledonaria.

Brucellae that survive are transported into the lymphatic system and may replicate there locally; they also may replicate in the kidney, liver, spleen, breast tissue, or joints, causing both localized and systemic infection. Any organ system can be involved (eg, central nervous system [CNS], heart, joints, genitourinary system, pulmonary system, and skin); localization of the process may cause focal symptoms or findings. After replication in the endoplasmic reticulum, the brucellae are released with the help of hemolysins and induced cell necrosis.

Ingestion of unpasteurized goat milk and related dairy products is the main route by which *B melitensis* is transmitted to humans.



Slaughterhouse workers, primarily those in the kill areas, become inoculated with brucellae through aerosolization of fluids, contamination of skin abrasions, and splashing of mucous membranes. Farmers and shepherds have similar exposure risks, and they also have exposure to aborted animals. Veterinarians are usually infected by inadvertent inoculation of animal vaccines against B abortus and B melitensis. Laboratory workers (microbiologists) are exposed by processing specimens (aerosols) without special precautions.

PROGNOSIS

The prognosis is generally excellent. Although initial symptoms of brucellosis may be deb the first few months of of relapse or chronic dise present with congestive h proaches 85%. In some pa with extensive morbidity.

In uncomp many other manifestatic ined physical activity may improvement from the symptoms of the acute phase of illness typically occurs within a few

weeks, with or without treatment. In many cases, this is followed by complete remis ortus infec

Over s of bruce It is usual lt of sever

1.4 D

Diagnosis of brucellosis infection is generally made by carrying out blood tests and detecting antibodies against the causative bacteria. Tests may also be conducted using bone marrow and other body fluids although this is quite rare.

Brucellosis: Blood test

Once diagnosis is done, the treatment of brucellosis is carried out by administering a combination of the antibiotics doxycycline and rifampin for at least 6-8 weeks.

PHARMACOLOGIC THERAPY

ANTIBIOTICS

Although m ella species, clinical resp r of agents. Drugs that following:

- Doxy
- Genta
- Strep
- Rifam
- Trimethoprim-sulfamethoxazole (TMP-SMZ)
- Other agents with potential roles include the following:
- Chloramphenicol
- Imipenem-cilastatin
- Tigecycline
- Fluoroquinolones

SURGICAL INTERVENTION

The main roles of surgery in patients with brucellosis lie in the treatment of endocarditis and in the drainage of pyogenic joint effusions or paraspinal abscesses. [(Roushan MR, et al, 2006 ,Keshtkar-Jahromi M et al, 2006).

Previously healthy native valves, diseased native valves, and prosthetic valvular structures have been involved in brucellosis. (Arslan H,et al 1998). Valvular lesions are typically large and destructive, regardless of the organism involved. Accordingly, valve replacement surgery is often recommended in addition to a prolonged course of antibiotics.

1.5 PREVENTION AND CONTROL

Prevention of brucellosis in humans depends on eradication or control of the disease in animals and on avoiding potential sources of infection. Better handling of infected animals or animal products is paramount. Public awareness and education play major roles in prevention.

Consumption of unpasteurized milk and milk products, as well as of raw or undercooked meats, should be avoided.

Education may be provided to the patient and family concerning risks and should emphasize avoiding anything identified as a specific cause in the case at hand. Should the identified source be a live animal, the herd or flock from which

it came should be investigated. In endemic areas, investigation is warranted for all animals.

Scrupulous hygiene may prevent infection, especially when practiced by individuals likely to have close contact with goats, sheep, cows, camels, pigs, reindeer, rabbits, or hares. Obviously, this contact is of greatest importance in areas of endemic disease.

All persons with an occupational risk for brucellosis should be informed about the use of protective devices (eg, goggles, masks, and gloves) to avoid exposure to aerosols, body fluids, or the brucellosis vaccine. In particular, laboratory personnel should be advised of the potential diagnosis so they will use biosafety level-3 precautions when in contact with suspicious specimens.

CONCLUSION

Brucellosis is a bacterial disease transmitted to humans by consumption of infected, unpasteurised animal milk or through direct contact with infected animals, particularly aborted foetuses. The livestock production losses resulting from these abortions have a major economic impact on individuals and communities. Infected people often suffer from a chronic, debilitating illness. Severe complications of brucellosis infection were not rare, with 1 case of endocarditis and 4 neurological cases per 100 patients. One in 10 men suffered from testicular infection, which can case sterility. Debilitating conditions such as joint, muscle, and back pain affected around half of the patients. Given that most patients had fever, brucellosis poses a diagnostic challenge in malaria-endemic

areas where fever is often assumed to be malaria. More high quality data is needed for a more complete understanding of the clinical manifestations of disease and exposure risks, and to provide further evidence for policy-makers.

RECOMMENDATIONS

Patient education should include efforts to address the following issues:

The nature of the disease and the routes by which it can be transmitted

The symptoms, complications, and treatment of the disease, as well as the risk of relapse if it is not adequately treated

The potential adverse effects of the medications administered

The need for strict compliance with the antibiotic regimen

In soma case, reassurance concerning recurrent symptoms that are not

associated with clinical or laboratory evidence of acute brucellotic disease

The need to avoid potential sources of infection – This may involve avoiding infected animals, using stricter precautions (eg, gloves and mask) when dealing with a potentially infected animal, or avoiding potentially contaminated foods

For farmers and ranchers, immunization of their cattle against the disease as necessary

For laboratory workers, maintenance of the appropriate level of containment

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