Brucellosis is a global and zoonotic bacterial disease (animals to man and not man to man) soliciting attention world-wide not only occupational but as a public health and economic problem to dairy and animal industries. It has many synonyms such as Malta, Mediterranean, undulant, Gibraltar, and Neopolitan fever. The infection is by a bacteria, Brucella is directly or indirectly harboured in farm animals. Their keepers and animal product consumers’ suffer economic loss by way of abortion, low milk yield and infertility because of this bacterial disease. Symptoms of human brucellosis are fever, sweat, headache, back pain, physical weakness and even severe infection of the central nervous system or lining of the heart. Chronic symptoms could be recurrent fevers, joint pain and fatigue. In USA during the 1950’s, timely attention to bovine brucellosis enabled saving annually 50 million dollars, which continued almost to eradication of brucellosis (Venkatakrishna-Bhatt 1998a). About 200 cases/year are reported in America and the trend in California was found to be more on the food-borne transmission (Chomel et al, 1994). The rural population suffering a low economic profile who make their liveli-hood from farm animals (goat, cattle, poultry, pigs, deer, elk, dog, horse, sheep, etc.) by more returns and less to spend on them. The infected animals brucella germs on contact and in their products (milk, pork and beef) even to remote population. These two aspects of brucella i.e. pocket areas and monetary loss, in addition to health impairment in the agricultural sector focus the problems universally and compels monitoring, prevention and remedial measures. Thus brucellosis is a world-wide major zoonosis.

Keywords: Brucellosis Density Causes Prevention Cure
The WHO is adequately drawing attention to the gravity of brucellosis especially in developing countries (Venkatakrishna-Bhatt 1999a) like India where it incurs a loss of Rs. 35/- crores and 30 million man-days a year and is widely known in many parts of India. The Federation of Obstetrics and Gynaecology of India cited 35 to 40% premature delivery and baby deaths due to brucella out of abortions. Enquiry of aborted cases in urban, rural hospitals help location of pocket areas for diagnosis and to implement remedial measures. High risk population are cited in the Mediterranean basin (Portugal, Spain, Southern France, Italy, Argentina, Egypt, Lebanon, Greece, Turkey, North Africa) South and Central America, Canada, Scotland, Eastern Europe, Asia, Africa, the Caribbean and the Middle East. Unpasteurized “village cheeses” and spread brucellosis among tourists further veterinarians help inevitably a focus on bovine brucellosis (Venkatakrishna-Bhatt et al. 1985a).

Historical and Epidemiological

Historical events date back to B.C. 450, since Hippocrates, disease implication by fetal loss was left, but only in 1860, a British doctor David Bruce identified as Malta fever which is later named after him as brucellosis and as Bang’s disease (ILO 1983, 1998). The disease attracted wide attention by a plethora of synonyms based on symptomatic and geographical locations (Christie 1980). Abortion due to brucella infection in women was first reported in 1913. Economic loss caused by brucellosis was estimated as 500,000 cases/year (WHO 1995) spreading from infected animals, their products, their confined places to man in many countries (Table 1). About 90% of people in developing countries are open to zoonoses due to occupational exposure. Recently in Americas (Mexico, Argentina, Peru) many often suffered from brucellosis.

The frequency has been 2699 in 1995 and 3362 in 1996 (rise by 120%) through food in Mexico alone. Argentina had 496 in 1995 and 569 in 1996 infections mainly from goats. In general, USA has focal areas of 140 herds, though 45 of them underwent quarantine in 1996 (World Health 1998). Thus in USA $25 million, $60 million in Latin America (Seghal 1987) and in India Rs.250 million/year in respect of animal food, 30 million man-days of economic loss were reported (Kunen 1994). Brucellosis is on the rise in Mediterranean, West Asia, Africa, Eastern Europe and Latin America. Latest in Mediterranean countries transmission is by sheep and goats to humans ranging 78/lac in non endemic areas <550/lac population in endemic areas. In Saudi Arabia, 20% people were diagnosed for brucellosis and of them 2% were confirmed among milk and meat, and veterinary workers (Radwan 1998). Sporadic cases through imported food occur even though Canada and UK are reported to be a free zone since 1985 (World Health 1998). Cases of human brucellosis from B. melitensis among microbiology laboratory workers have been reported (Martin-Mazuelos et al. 1994). In Uttar Pradesh, 8.06% dairy workers (including 41.35% milk handlers) 68.95% and 28.5% animal handlers and veterinarians respectively suffered from brucellosis (Bacchi 1998).

Brucellosis is reported to be 18.1% in Haryana among animal handlers (Kulashreshtha et al. 1978). In Madhya Pradesh more women (3.2%) than man (1.86%) suffered from brucellosis (Soni 1976). In Karnataka, 5.9% (Desai et al. 1995) and 3% in Kheda (Patel et al. 1988) and other focal points in Gujarat were reported (Venkatakrishna-Bhatt 1985a). Thus, brucellosis has been widely reported in and out of the country (Venkatakrishna-Bhatt 1998).

Ethiological and Source of Infection

Brucellosis is a bacterial disease i.e. infection by Brucella, a genus with six well identified species and species subtypes. Three of the species melitensis (3 subspecies), abortus (9 subtypes), suis (4 subtypes) are highly infections to man i.e. not only occupational but also a public health hazard. The other three species ovis, canis and neotomae are generally non-infective. The species are host specific i.e. B. melitensis infects only sheep, goat and camel; B. abortus can be traced only in cattle and buffalo and B. suis is found only in pigs, hares, carrabao and reindeers. However; seldom B. ovis infects rams causing epididymits. Similarly, B. canis infects man but precipitates in a mild form. B. suis biovar are predominantly found in pigs but are also known to occur in cattle. In many countries, cattle is a major source of infection to man than pigs. Though scarce, Brucellae species were also known to be isolated from marine mammals, thus widening its ecological biosphere. Other non-viable species are known in poultry, dogs, cats, horse and rats. Human exposure may be direct while handling the infected placenta (bovine aborted fetuses), vaginal discharges, semen (Ox, Bull) or remote when they work in infected places, aerosols or by the infected food (water, milk (raw), aborted cheese, yogurt, meat). The infection of germs can also be through skin abrasions, conjunctive, mucous membranes and respiratory tract. In our country, the highest infection is noted in cattle whereas in USA among sheep and goats. Thus, the entry points are by contact, consumption, through skin abrasions, conjunctive, mucous membrane and respiratory and breeders meat, dairy, laboratory, transport, tanning, hide-goat-wool workers, veterinary surgeons, vaccine industry, knockermen, abattoirs, butchers and meat sellers (Venkatakrishna-Bhatt 1999a).

Pathogenesis and Clinical Signs
Brucellosis manifests in three stages such as acute, subacute and chronic stages. Fever with rigors, headache, lymphadenopathy, hepatomegaly, IgG and IgM mark the acute phase. Subacute phase show signs of insidious fever, malaise with increased IgM.

In the chronic phase, fatigue, weakness, headache, depression, orchitis, meningitis. (Raymond-Parkes 1994) Laboratory and field symptomatic diagnosis are well documented. At the source level, symptoms apparently are retention placenta, abortion, hygroma of limbs and low yield of products mark bovine brucellosis (Steele 1979). The infected animals, their aborted fetuses, placenta, vaginal discharges, semen (ox, bull) and aerosols are a permanent source throughout their life to spread infection to other animals or man whereas in sheep brucella germs becomes dormant after six months. The excreted germs from the carriers survive in the soil for 70 to 80 days (Raymond-Parkes 1994). It is not only entry of brucella by infected food in man, but also enters through skin abrasions, conjunctive, mucous membranes and respiratory tract (FAO/WHO 1986).

Clinical diagnosis

The prognosis of brucellosis is case-wise as per the occupational history and infected area, signs and symptoms, haemoculture examination and field diagnosis by serology wherein a cross immunity to species of Brucella is ascertained. Besides diagnostic tests, medical investigations such as IgM, IgA, IgG, liver biopsy for non-creating granulomata, skin test, milk, blood, placenta and urine culture, CT scan, MRI, brucella typing, CSF analysis, membrane biopsy test and cross reactive determination are being done. Incubation period for brucella organisms is two to three weeks and then it spreads to the lymphatic vessels with development of glandular focus. In acute state (Uwaydah et al. 1998), there is septicemic dissemination (fever with rigors, headache, pain, lymphadenophathy and hepatomegaly).

Secondary infection (joints, bowels, genitals, meninges) causes insidious fever, malaise, pain in joints and increased IgM. Brucellosis can be hepatic (Villar et al. 2002), endocardiotic (Shariyker et al. 2001), glomerulonephritic osteoariculartic (Kubler & Klesto 2001) and material B. abortus causes poorn-perinatal outcome (Malone et al. 1997). Differential diagnosis helps a long way in the recovery of patients. Repeated exposure develops hypersensitivity for Brucella antigens with allergic reactions joints, skin, respiratory tract, thus disrupts occupations, though prognosis is not serious (Venkatakrishna-Bhatt 1998b). During the chronic stage, fatigue physical and mental weakness, depression and orchitis (Saimeron et al. 1998) become apparent. Brucella causes paravertebral abscess (Ozgocmen et al. 2001). In neurobrucellosis, (meningocephalitis, polyreticuloneuritis, myelitis as in cranial nerve palsy) the cerebrospinal fluid of patients show increased proteins, IgG levels, lymphocytosis and low glucose concentration (Akdeniz et al. 1998). Other effects are epididymoorchitis, neuroencephalopathy by way of pituitary supraseller mass (Ciftel et al. 1988). Radiographic symptoms in acute cases are soft miliary mottling, hilar and paratracheal, lymphadenopathy, parenchymal nodules, consolidation that may caviate with chronic diffused changes, pneumothorax and plural effusion (Patel et al. 1988). Chronic patients show sarcoid type of granulomas in lungs, spleen, liver and bone marrow with chest radiography presenting scattered irregular opacities and bone destruction. Radioisotope bone scans present early symptoms of brucellosis (Raymond-Parkes 1994). Besides respiratory symptoms (Elberg and Henderson 1984), ESR goes high and seldom followed by hepatitis. In acute brucellosis high IgM Levels and in the chronic stage IgG and IgA are elevated (1:160). The agglutinin test depend on IgG and IgM antibodies which can be identified by 2-mercaptopethanol, a week after Brucella infection (Madkour 1989). Clinically diagnosed cases show 35% positive blood culture for Brucella in acute cases, 18% in subacute cases and 5% in chronic cases (Lulu et al. 1988). In severe lung and plural biopsies (Garcia et al. 1989) help diagnosis. Other symptoms are synovities of knee joints, sacroiliac joint and show more polymorphonuclear leucocyte. Synovial biopsy shows no case eating granulomata. Serum transaminases are elevated even if there is no overt hepatitis (Hunter’s diseases 1994).

Laboratory and field studies

The US Department of Agriculture has specified several laboratory and field methods such as brucella card test, rapid automated preventive test, Mexican rivanol test or French rose Bengal plate test or buffered acidified plate agglutination test, Standard tube test (for melitensis), cold fixation or complement fixation test (for melitensis) serum or milk ELISA test, milk ring test, brucella antigen specific gamma interferon test or plate antigen test. Conventional general methods are gel diffusion, agar gel precipitation, bacterial haem-agglutination, standard tube agglutination rose Bengal agglutination serum plate compliment fixation, VDRL tests.

Certain studies do reflect focal points of human brucellosis in many places in India. The field investigations in Gujarat present that veterinarians in spite of knowledge of brucellosis are handicapped by occupational exposure and vulnerable to germ infection because of social environment (Venkatakrishna-Bhatt 1998a). Relevant criteria enabled ethiological and epidemiological approach when studied not only the disease susceptibility but also endemically in Gujarat (Venkatakrishna-Bhatt et al. 1985b). Well coordinated
veterinary doctors were later confirmed brucella positive by brucella during this survey four suspected cases of animal contact or consumption of raw products infected foci transmitting the disease in the natives either by tests revealed 12 contaminated zones and endemic bovine and milk samples for STAT, RBPT, SBT, MRT (Bhatt 1990). Animals and veterinary personnel (Venkatakrishna-Bhatt 1990) found to be relatively free of brucellosis as regards to veterinarians who suffered from brucellosis showed high titre of brucella agglutinins with no symptoms of infection. The source of infection was found among doctors treating farm animals, field and laboratory diagnosis. Gujarat (Venkatakrishna-Bhatt 1999b), the focus has been on veterinarians, farm animals, field and laboratory diagnosis. Gujarat state is 195,984 sq.km in area of 25 districts with taluks ranging from 1/1 (Dang-Ahwa) to 15/1 (Surat). Screening was through a programmed brucellosis medical questionnaire (650 cases) and personal visits to the site and meeting animal handlers and farm doctors which revealed well identified carriers such as cattle, buffaloes, sheep, goats, dogs, cats, camels, poultry and horses. Main emphasis was on human brucellosis among veterinary personnel (544 graduates, 94 postgraduates) in Gujarat State covering 203 veterinary hospitals, their 21 branches, 511 first aid centers, 40 motile units, practitioners, 4 dairies. The occupational (suspected brucellosis), personal medical histories including their age and type of animals they handled were considered. The major source of infection was found among doctors treating brucella-infected cattle and buffaloes (39.3%). Seldom veterinarians who suffered from brucellosis showed high titre of brucella agglutinins with no symptoms of disease. The infection was found to have been more common among the veterinary doctors of the age group of 30-39 years. Recovery was significant among graduate doctors and maximum with post-graduate doctors. In the Mehsana, Vadodhara and Banaskantha districts, many veterinary officers as well as animals were known to have suffered from brucellosis. Gandhinagar and Surendranagar districts were found to be relatively free of brucellosis as regards to animals and veterinary personnel (Venkatakrishna-Bhatt 1990).

Further analysis and proper investigations (human, bovine and milk samples for STAT, RBPT, SBT, MRT tests) revealed 12 contaminated zones and endemic foci transmitting the disease in the natives either by animal contact or consumption of raw products infected by brucella during this survey four suspected cases of veterinary doctors were later confirmed brucella positive (Dholakia et al. 1987). An in situ study for a Kheda and Banaskantha districts, established zoonoses of brucella in farm animals passing to humans. A site specific transmission of brucella abortus was found in 12 cases as confirmed by STAT values ranging from 1:80 to 1:320 titres. The endemic brucella titre values were from 1:160 to 1:1280 among 15 cattle. The elimination and vaccination of infected herds, sterilization of containers and instruments, prevention of infection by quarantine, publicity of safety measures in handling farm animals and creating public health awareness by imparting education on the pasteurization of milk, slaughter of infected animals, hygiene measures were suggested to check and spread of brucellosis in the affected areas (Venkatakrishna-Bhatt 1990). In addition, hospital data showed abortion in women native and endemic rural areas. Among hospital patients, brucellosis can be sorted out from 1) febrile and syphilitic cases; 2) brucella exposed subjects; and 3) aborted patients (Venkatakrishna-Bhatt 1989; Panjaratnam 1981).

A local study in Gujarat

In a novel study in Gujarat (Venkatakrishna-Bhatt 1999b), the focus has been on veterinarians, farm animals, field and laboratory diagnosis. Gujarat state is 195,984 sq.km in area of 25 districts with taluks ranging from 1/1 (Dang-Ahwa) to 15/1 (Surat). Screening was through a programmed brucellosis medical questionnaire (650 cases) and personal visits to the site and meeting animal handlers and farm doctors which revealed well identified carriers such as cattle, buffaloes, sheep, goats, dogs, cats, camels, poultry and horses. Main emphasis was on human brucellosis among veterinary personnel (544 graduates, 94 postgraduates) in Gujarat State covering 203 veterinary hospitals, their 21 branches, 511 first aid centers, 40 motile units, practitioners, 4 dairies. The occupational (suspected brucellosis), personal medical histories including their age and type of animals they handled were considered. The major source of infection was found among doctors treating brucella-infected cattle and buffaloes (39.3%). Seldom veterinarians who suffered from brucellosis showed high titre of brucella agglutinins with no symptoms of disease. The infection was found to have been more common among the veterinary doctors of the age group of 30-39 years. Recovery was significant among graduate doctors and maximum with post-graduate doctors. In the Mehsana, Vadodhara and Banaskantha districts, many veterinary officers as well as animals were known to have suffered from brucellosis. Gandhinagar and Surendranagar districts were found to be relatively free of brucellosis as regards to animals and veterinary personnel (Venkatakrishna-Bhatt 1990).

Therapeutic regimens

The treatment varies on the type of brucellosis. Initially supportive therapy, recommending a dose of tetracycline (1.2 g/PO/day) and streptomycin (1 g/PO/day), Vit. B for 2 weeks in acute phase. In chronic brucellosis, WHO advocates (1) a treatment of doxycycline (200 mg/day) and rifampicin (600 mg/day) orally for 6 weeks (Hunter’s Disease 1994). At the sub-acute stage, treatment is by supportive, symptomatic therapy with tetracyclines. Sometimes 40% relapses are observed even after recovery (Ariza et al. 1985). Desensitization by antigenic therapy followed by physiotherapy and if necessary surgical intervention is being done. In case of neurobrucellosis, additional drugs, such as streptomycin and steroids are prescribed (WHO/FAO 1986). It is also recommended doxycycline and rifampin for B-19 and REV-1 of doxycycline for RB-51 for 3 weeks. Same treatment could be given for spraying vaccine in the eyes (6 weeks) or spraying onto open wounds on the skin. In localized severe infections, surgical intervention helps recovery by physiotherapy and desensitization by antigenic therapy (Venkatakrishna-Bhatt et al. 1989).

Areas of research

Brucellosis though reported world-wide, man to man infection is not known. However, mothers transmit the disease to infants during breast feeding. Sexual transmission has also been reported. Uncommon infection could be via contaminated tissue transplantation. At present, there is no vaccine available for human brucellosis. Certain cases though present high brucella antigenic titres, yet show no symptoms. Even six months treatment do not prevent
a relapse. The relapses are not the result of drug resistance as they respond again to chronic course of antibiotics. Optimal treatment for neurobrucellosis is not known, though an effective CSF (cerebrospinal fluid) drug concentration is noted (Hunter’s Diseases 1994).

Prevention

The prevention of brucellosis is to clear contamination and infection by the following methods: 1) slaughter of infected animals, 2) pasteurization of milk, 3) sterilization of contaminated materials, 4) adopting safety measures while handling animals, 5) periodical screening of animals and area for brucella, 6) vaccination of calves, lambs and goats (Alton 1986). Live vaccines (19 BA – brucella antigen) are highly successful in man. A B. abortus antigen L7/L12 in lactococcus lactics as a first step towards food-grade live vaccines against brucellosis was recently reported (Ribeiro et al. 2002). Dean vaccines with additives can be used in animals but it is ineffective in man. Antigenic extract of brucella (glycopeptidic complexes) provide short lived immunity. In France, a phenolic insoluble fraction known as “P” was found better than live attenuated ones. Side effects are observed in the form of stomatitis, dehydration and therefore supportive and replacement therapy is advised. Thus, brucellosis is a disease inviting world-wide attention for sustained multi-focal research to prevent infection and spread of the disease.

Acknowledgement

I thank the director, the National Institute of Occupational Health (NIOH) for support and encouragement during this study.

References


