

Capstone

Unpasteurized Milk

Consumption and Brucella

Infection and Prevention

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IMPH

Table of Contents

1. The Title.....	1
2. Table of Contents.....	2
3. History and Etiology.....	4
4. The Disease.....	6
5. Symptoms of Brucellosis.....	7
6. Complications.....	7
7. Brucellosis - Treatment.....	10
8. Brucella Vaccine.....	11
9. The Consumption of Unpasteurized Products.....	11
10. Laboratory Exposure to Brucella. Spp.....	14
11. Prevention.....	17
12. Summary.....	19
13. References.....	21

Table of Figures

1. Brucella Morphology	5
2. A Map of Annual Incidence of Brucellosis per 1000,000 populations.....	6

Abstract

Our world became more and more advanced in the medical field and we can see it in different areas like medical technology, drugs, complex surgeries, nutrition et.al. Unfortunately, some of our norms and beliefs changed because people forgot the past. The deadly infections and disease can be barely seen around the world, maybe only in developing countries. The Ministry of Health trying to avoid spending money on cases like unvaccinated cattle, to protect people from Brucella infection and make pasteurized milk safer for consumption. This all happened because our world population convinced that diseases like Brucella or Cholera have no influence on our modern lifestyle anymore.

The reality of natural food products, life with zero medical interventions and drugs became a new trend. This trend brought unexpected consequences on children with a poor immune system and parent's choices on the best treatment.

This paper concentrated on Brucellosis, the ways of contracting the disease and the potential complications. This data collection was very important in order to emphasis and prove that our world and health organizations should never take Brucella infection for granted. We always have to fight new diseases and infections, but never forget about the ones which waiting for a chance to attack us again.

History and Etiology

Brucellosis is a zoonotic disease. This bacterial disease is also called "Undulant fever", Mediterranean fever" and "Malta fever" and it caused by different types of Brucella species (M.J. Corbel. 2006).

The most common Brucella infections are caused by *B. abortus* and *B. melitensis*, *B. suis* and *B. canis*. The history of Brucella and the first discovery started with a great Scottish pathologist and microbiologist, Major - General Sir David Bruce, who was born on May 29, 1855, in Melbourne, Australia. In 1886 David Bruce was the first man who isolated Brucella melitensis from the spleen of a British soldier in Malta. That is why the origin of the name "melitensis" was derived from the Roman name for "Malta" and Brucella was named in honor of David Bruce Stuart D, 2010). The morphology of these bacteria is a small gram-negative coccobacillus with no capsules, endospores or native plasmids (Edward J. Young 2006). Brucella can mainly infect goats, cattle, dogs, camels, and sheep as well as rare cases of humans. The human cases caused by a direct contact with infected animal, consumption of unpasteurized dairy products and meat, open skin wounds or mucous membrane, and tissue transplantation or blood transfusion. (World Health Organization). But the most interesting fact is the ability of Brucella spp. to remain present in dust, dung, water, slurry aborted fetuses and soil for a long period of time and people can get infected by just inhalation of aerosols. The survival of Brucella organisms in these cases depends on a number of organism present, temperature, pH, sunlight and the presence of other microbial organisms (M.J. Corbel, 2006).

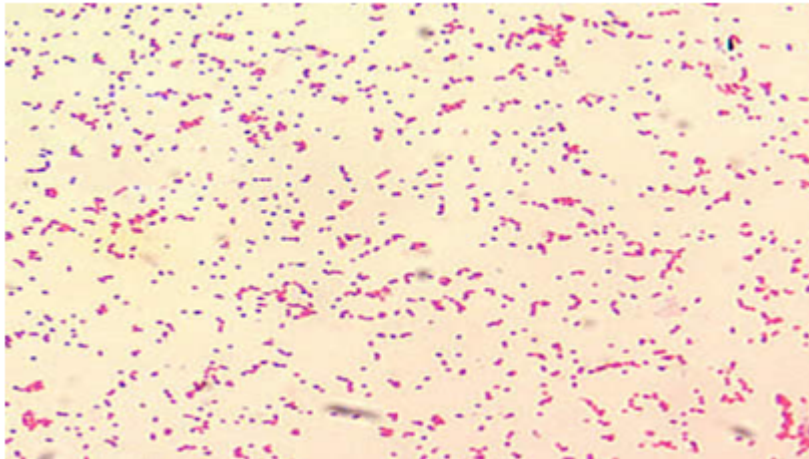


Figure 1. Gram – Negative Coccobacillus smear, *Brucella* spp.

Human Brucellosis is a very common zoonotic disease among the Mediterranean countries of Europe, North and East Africa, the Middle East, South and Central Asia and Central and South Africa. The especial high incidence rate was reported by Eastern Mediterranean countries with 100 cases per 100,000 person/ year, where Syria, Lebanon, Iraq, Saudi Arabia and Sudan are among the highest Brucellosis reporters (Humberto G. Garcell 2016).

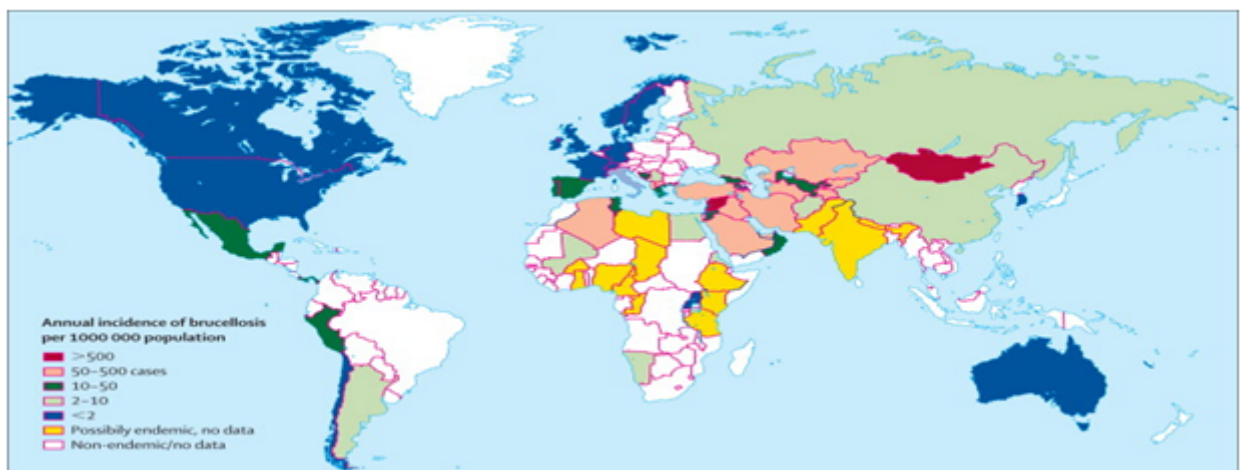


Figure 2, Annual incidence of Brucellosis per 1000,000 populations.

The epidemiology of Human Brucellosis has been changed over the past decades. The reasons for this change were advanced biotechnology, medicine

development, the expansion of animal industries and urbanization. The decrease in Brucella cases was mostly reported from industrial countries, where the infection was endemic. However, the same changes in technology and urbanization led to a greater spread of Brucella infection among previously Brucella free regions and becoming a great concern of international tourism. Mostly the exotic dairy goods like fresh cheeses created a global spread of Brucella infection.

The main concern of Brucella infection still remains in low socioeconomic countries, where people economy is based on the health of their livestock. Farmers who financial status mainly based on livestock, not necessarily kill the infected animals, but continue to get revenue from the sick livestock, that way increase and contribute to the human spread of infection. This financial concern of the farmers can be a potential reason why human Brucella cases globally occur in the estimation of 500, 00 cases annually in low – middle socioeconomic countries (Shengjie Lai, 2017).

In general, the human Brucellosis epidemic is a big concern among global health professionals because of its high initial treatment failure and high relapse rate. Moreover, Brucella spp are highly infectious and as was mentioned before can spread through aerosol route, which makes them a potential agent of biological weapons and bioterrorism (Shengjie Lai, 2017). In order to emphasize the importance of Brucellosis eradication and prevention programs globally, it is necessary to explain the symptoms, treatment and complication of human Brucellosis as well as ways of contracting the infectious pathogen.

The Disease:

Brucellosis is an acute febrile illness which can be accompanied by anorexia, prostration, sweats, back pain and malaise. Important to mention that in the morning the patients can feel better, however, the symptoms worsening as the day progress.

The signs and symptoms developed only over a period of weeks to months from the actual infection, which makes the diagnosis very difficult and requires investigation of patient past actions.

Usually, there are two main signs when body infected by Brucella, the first one is the liver or spleen enlargement and the second is the appearance of the lymph nodes. These two signs are not helpful in accurate diagnosis since they present mostly in any other infection which invades the human body, meaning that only accurate medical laboratory diagnosis needed. Also, there is a possibility for acute phase which might progress to chronic illness and have a potential to occur in about half of the cases with an incubation period of two to three weeks. This chronic illness usually leads to “chronic fatigue syndrome” (M.J. Corbel, 2006).

Symptoms of Brucellosis:

There are common symptoms in human Brucellosis: Fever, chills, sweats, aches, lack of energy, joints and back pain, Arthritis, spinal tenderness, headache, loss of appetite, weight loss, abdominal pain and diarrhea.

Disease Complications:

Osteoarticular problems occur up to 40 % of cases and involve bones and joints complications. Very common for patients to present symptoms of fever and back pain, often radiating down the legs. When the complication occurs in children, they may refuse to walk and extremely bear weight. (M.J. Corbel, 2006).

Gastrointestinal problems usually occur from Brucella melitensis which is a foodborne bacterial infection. This complication causes typhoid fever, nausea, vomiting and abdominal discomfort. Also, there is a presence of rare cases with ileitis, colitis and spontaneous bacterial peritonitis. (M.J. Corbel, 2006)

Hepatobiliary complications, the liver function is usually influenced by Brucellosis, it can be mildly elevated in the liver test, but can also show histological changes as epithelioid granulomas which are hard to distinguish from sarcoidosis lesions. (M.J. Corbel, 2006)

Respiratory complications are paratracheal lymphadenopathy, interstitial pneumonitis, and bronchopneumonia and lung nodules. (M.J. Corbel, 2006).

Genitourinary complications- the most frequent complication of Brucellosis in men are Orchitis and Epididymitis. The Orchitis, when caused by Brucella, can mimic testicular cancer or tuberculosis. Moreover, some Brucella organism has been recovered from banked human spermatozoa, but only a few reports were found about the ability of Brucella being sexually transmitted. In a woman, the complications can be seen as pelvic abscesses and salpingitis.

Pregnancy and Breastfeeding- caused by B. Abortus and increase the risk of abortions in pregnant women as well as infected animals. The ability to infect the baby during the breastfeeding is very low. (M.J. Corbel, 2006)

Cardiovascular complications- the most common cause of death from Brucellosis which reported in about 2% of cases is Endocarditis. Also, this infection might target the middle cerebral artery and lead to neurological complications. The treatment is very complicated and heavy, involves a combination of antimicrobial therapy and even a valve replacement surgery. (M.J. Corbel, 2006).

Chronic Brucellosis- defined as clinical symptoms experienced by patients which last 12 months or more from the time they were first diagnosed. There are three phases to consider when diagnosing Brucella infection: relapse and chronic localized infection.

The relapse occurs after the completion of the treatment and defines as recurrence of signs and symptoms of Brucellosis, but is not obligated to be detected as a positive blood culture. The relapse characterized by fever and elevated IgG antibodies in the serum. It can be treated by the same course of antibiotics as the first antimicrobial treatment.

The localized chronic Brucellosis is very similar in its signs and symptoms to the relapse phase, but the treatment of this condition requires a surgical intervention in addition to antimicrobial treatment.

Brucellosis Treatment

Brucella infection has a very complex treatment since it requires several antibiotics together in order to fight the infection.

Simple Infection – usually doctors use Doxycycline (100 mg PO twice daily for 6 weeks), however, the relapse rate in this type of therapy might reach 40% and in order to minimize the relapse rate, Rifampin (600 – 900 mg/day) should be added to the therapy. Also, when patients have a resistance to rifampin the combination of Fluoroquinolones and Doxycycline can be used as well (Wafa Al –Nassir, 2017).

Acute Brucellosis Therapy - can be the same as during the simple infection, but much more effective with 100 mg PO twice of Doxycycline daily for 6 weeks and 1 g/day for 2-3 weeks of Streptomycin or to use the Gentamicin as an equal efficacy substitute. (Wafa Al –Nassir, 2017).

Pregnant Woman Therapy- this therapy is one of the most challenging therapies, as every other treatment related to the pregnant woman. The reason for the challenge is the limited data available regarding the treatment of Brucellosis in a pregnant

woman. Usually, for this treatment doctors are advised to use TMP –SMZ (Trimethoprim/ Sulfamethoxazole) either as monotherapy or a combination with Rifampin or Gentamicin. Unfortunately, the treatment with TMP – SMZ by the end of the pregnancy is related to kernicterus. (Wafa Al –Nassir, 2017).

Brucella Meningitis Therapy – usually treated by the third – generation cephalosporins. The duration of the therapy can vary depends on the cases from 1-19 months and can last till the cerebrospinal fluid (CSF) is clean from Brucella infection. (Wafa Al –Nassir, 2017).

Endocarditis Treatment from Brucellosis- this therapy is one of the most aggressive therapies in comparison to other Brucellosis treatments. The treatment involves Aminoglycoside therapy in conjunction with Doxycycline, TMP-SMZ and Rifampin for at least four weeks, as well as additional treatment with at least 2 -3 active agents for another 8 – 12 weeks. (Wafa Al –Nassir, 2017).

Brucella Vaccine

Unfortunately, there is no licensed vaccine for Brucellosis in humans. The only existent vaccine is available for livestock only (Xinghong Yang, 2013).

There are only three live attenuated vaccines for immunization of the livestock. The cattle are usually vaccinated by B. abortus RB51, which serves as indicators for serological testing to figure out if the cattle were naturally infected or was vaccinated.

Also, there are additional vaccines as B. abortus S19 which used for cattle as well and B. melitensis Rev – 1, which usually used for goats and sheep. However, human exposure to these animals, like direct contact with eyes and wounds splashes or needle sticks, can lead to an infection with Brucella (CDC – Cattle Vaccination).

There are two most popular ways of Brucella contraction. The first one is unpasteurized milk products and raw meat consumption which can target everyone around the globe and the second method is laboratory contraction, which mostly infects laboratory technicians.

The Consumption of Unpasteurized Products

Natural food products and healthy lifestyle became one of the leading brands around the world. Mostly, there are two main consumers of the natural food products. The first type is the consumers who belong to low socioeconomic status, which grows and raise natural food sources in farms and villages like fruits, vegetables and cattle. Often, farmers who raise the cattle also consume milk, eggs and meat in order to save money. The second type of consumers are people who believe in organic, healthy and natural food sources as a cultural belief, social norm or a brand. Unfortunately, unpasteurized milk consumption is a part of normative and accepted natural treatments which can be reached mostly by every individual.

There is a list of natural products and unconventional treatments which people accept as much safer and efficient than antibiotics, vaccinations and basically any treatment prescribed by a doctor. The examples of these products are unpasteurized milk, organic fruits and vegetables, essential oil therapy, acupuncture (traditional Chinese medicine) et al.

Lately, everything that labeled as natural is accepted as the best and healthier to our body. Unfortunately, not everyone aware of the danger and risk these natural sources can hide. For example, essential oil therapy can cause very bad allergy reactions and acupuncture can lead to infections. Moreover, the unpasteurized milk which was always the first aid for immunization boost by our grandparent's generation was discovered to be one of the main sources of bacterial infection spread

as *Brucella* spp, *Escherichia coli*, *Salmonella* spp, *Listeria monocytogenes* and *Campylobacter* spp (Solenne Costard, 2017).

The concern about unpasteurized milk consumption is very high since this is one of the major ways *Brucella* spp. can be spread to humans. In order to create a solution to the problem of *Brucella* spread, we have to understand the true reason why and in what conditions people think and use unpasteurized milk as a part of their diet. There are multiple reasons why people consume unpasteurized milk. The first myth about the advantages of unpasteurized milk consumption is lactose intolerance. People who experience this condition suffer from bloating, gas and diarrhea when consuming any milk product. This is caused by the inability of human's body to digest lactose, in particular dysfunction of an enzyme, β -galactosidase which hydrolyzes sugar lactose to glucose and galactose. Interestingly, it was found that raw milk does not contain a β -galactosidase enzyme that is why there is no logical reason why it is able to reduce the lactose intolerance in people. Moreover, there are some yogurts, which contain β -galactosidase enzyme and are able actually to tolerate lactose and reduce this condition among individuals who suffer from lactose intolerance. (John A. Lucey, 2015).

Nutrition is another important fact why people choose unpasteurized milk over the pasteurized dairy products. Usually, the unpasteurized milk represents natural product which contains a big amount of proteins, minerals and vitamins, in contrast to pasteurized products which are less natural and have a small amount of nutritional quality and value. However, none of these claims were proven scientifically. Instead, it was reported, that milk pasteurization does not cause any significant level of protein denaturation and changes to the nutritional quality of the milk. Also, very important to mention that minerals are heat stable, and pasteurization does not cause any harm to

their concentration in the milk. Regarding the vitamins, people should pay more attention to storage and time/temperature and packing of the milk products, which has much more influence on the milk composition, than pasteurization. The vitamin B12 B1, B2 and fat-soluble vitamin A and E always present in the milk and do not undergo any sufficient changes during pasteurization. The only way which can potentially influence the nutritional quality of milk is ultra-pasteurization and ultra-high temperature milk processing (John A. Lucey, 2015).

The additional reason for unpasteurized milk consumption which requires more scientific research is allergy and asthma reduction. Parents believe that children who grew up on the farms and been introduced to natural products as raw milk in their first years of life in result have a better immune system. However, they do not consider the fact that the robust immune system of children who grew up in the farm actually caused by a wider range of exposures to bacteria and allergens from the environment than children who were raised in the big cities. This misconception by uneducated parents can become a potential threat to infant's health and become one of the reasons why babies usually get infected by *Brucella*. spp (John A. Lucey, 2015).

Unpasteurized milk consumption became a major concern in health and well-being of infants and children. For example, in endemic areas like Saudi Arabia was reported 18/100,000 population /year with Brucellosis in 2011, which is 10% of the cases included children 0 - 14 years old (Mohammad A. Alshaalana, 2014). Usually, the main source of the problem are grandparents and uneducated parents who believe that unpasteurized milk can treat all sorts of health problems in children, like mouth and foot disease, autoimmune disorders and even cancer.

When a sick child, who already suffers from low immune system consume unpasteurized milk, he or she increases the risk of complication in already existing

health problem. Especially, when we are dealing with case of cancer or autoimmune disorder, additional infection like Brucella which requires a very intense antibiotic treatment can increase the complications and be a potential life threat to the child.

Laboratory exposure to Brucella spp.

Brucella is considered class 3 organism and it is strongly recommended that live Brucella culture should be handled in biological safety cabinet class 2. Brucellosis is the most commonly recognized cause of laboratory - transmitted infection. Because Brucella has relatively rare outbreaks among the industrialized countries, technicians in clinical microbiology laboratories are often unfamiliar with the genus, which leads to misidentification of the organism and 2 % of laboratory-acquired disease. (Pablo Yagupsky 2005).

Between 1982- 2007 was reported 18% cases of laboratory infections with Brucella due to laboratory accidents and 88% cases due to aerosolization of organisms and 2 % cases of exposure were unknown (Rita M. Traxler, 2013).

There are several ways of Brucella transmission in the laboratory facilities. The first one is the aerosol - generating procedures while working on an open bench, which might be very dangerous not just for the individual who violates the rules, but also includes the coworkers who located in the same room, not to mention that aerosol spread might target the whole facility through common ventilation. Laboratory accidents as blood - culture vials, and breakage of centrifuge tubes are responsible for 20 % of cases. The unsafe laboratory practices, which are the core responsibilities of laboratory technicians are often violated as well. For example, no use of protective equipment such as gloves, masks and goggles, sniffing plates, ingestion of living Brucella during mouth pipetting, which was actually prohibited long time ago, but

some old school technicians still too stubborn to switch old techniques into innovative technology. Some unexpected incidence might occur as well during the routine work, like self- inoculation of Brucella by syringes loaded with a big amount of living organism or injury to the conjunctiva by the broken tube which contained a living culture. Technical issues can also play a major role in the fast identification of Brucella organism, for example, in the gram - stain procedure a particular case of Brucella isolates can resist the decoloration and to appear as a gram - positive or gram - variable coccobacillus under the microscope examination. In this point, inexperienced technician who did not receive any health suspicion or diagnosis from the physician regarding the particular patients might misidentify the organism. (Pablo Yagupsky 2005)

There is a couple of biological characteristics which make Brucella so easily transmitted to humans. First of all, the infection dose of Brucella. spp is relatively low for human infection. The organism can enter the body in many ways, for instance, respiratory mucosa, conjunctivae, gastrointestinal tract and abraded skin. It is very important to mention that right after the body invasion, Brucella is ingested by mononuclear and polymorphonuclear phagocytes. After that, the Brucella organism can escape phagocytic killing by their ability to inhibit the phagosome - lysosome fusion and reproductive skills inside of the macrophages. After the incubation period of approximately several months, patients are usually bacteremic, and Brucella can be detected much more easily by blood culture testing. (Pablo Yagupsky 2005)

Brucellosis in Israel

Brucella melitensis is an endemic disease in Israel as well as other Mediterranean countries. In Israel, Brucella. spp can be found in infected goats, sheep, humans,

cattle, and camels. Almost 72% of Brucella cases reported through April and August. In 2006 - 2011, 252 children were hospitalized with Brucellosis in the South of Israel and 50% of those cases had bacteremia. Also, in 2016 several cases of Brucella infection were reported from the ingestion of unpasteurized camel milk (Dr. Stephen Berger 2017). The main body who controls Brucellosis in Israel is Veterinary Services which use Rev 1 vaccination of the young females and annual testing for serology the unvaccinated males. However, a big portion of this information is just a theory. There is a huge problem with veterinary control over the disease in the northern and in the southern region of Israel due to serious logistic difficulties like lack of shepherd's incentive to participate, budgetary constraints and illegal trade in infected animals(Ari A Shemesh, 2013).Most of the infected livestock owned by Bedouins and Arabs who underreport or not reporting at all regarding the infected animals continue to spread Brucella infection between the family members who own the livestock and the customers who buy the dairy products (Armon, L.2015).

According to Israeli Dairy Board, private marketing of unpasteurized dairy products is prohibited, in order to keep track on the quality of the dairy products which consumed by Israeli population and prevent people from contracting infections.

The Kimron Veterinary Institute was designed in the early 1980s in Rishon Lezion, and later was recognized as OIE reference laboratory for Brucellosis, it is also a small section of veterinary services in the Ministry of Agriculture, where Israeli human isolates are sent in order to get diagnosed and confirmed by biotyping. Also, it serves as a record keeper of epidemiological reports of the disease in Israel. Also, this laboratory works closely with partner institutions from Egypt, Jordan, the Palestinian Authority, Kazakhstan, Germany, USA, Italy, and Greece (Ministry of Agriculture and Rural Development, Israel).

Prevention

In order to prevent Brucellosis and to come up with eradication campaigns, we have to increase the awareness around this issue among all ages and cultures. There is no reason why preventable infection like Brucella will endanger our children and influence our well-being. Also, it is very important to understand that we have to take care of our animals and keep them healthy.

In order to make a successful Brucella prevention and eradication program, we should target different types of ethnic groups, age groups, and cultures, since all of them have their own reasons and beliefs behind the action which results in Brucella infection. However, before changing any habits of the target population we have to consider the norms, values and cultural beliefs in order to engage people for changes.

- The first and very basic step is to vaccinate the livestock and make veterinary checkups to home pets owned by families with children. This should be controlled by a representative body which includes members from Ministry of Agriculture and The Ministry of Health. The vaccination has to be financed by The Ministry of Agriculture only and have to be a mandatory process for each person who owns any livestock, even privately in his yard. The vaccination of the livestock should not be a farmer responsibility since populations as Bedouins in Israel cannot financially afford the vaccination or kill their only source of dairy products, even if infected.
- Farmers should avoid mixing different herds of livestock together, in order to reduce the transmission of disease if one of the animals get infected.
- Increase and financing of animal screening by Ministry of Agriculture. Also, it is very important to educate the owners of the livestock about the benefits of

the vaccination, and what disease and infection humans are exposed to by consumption of unpasteurized dairy products from the infected animal.

- The second important step is to protect young children from Brucella infection. This prevention should target young parents with children under age 9, who is at risk of getting foot and mouth disease. Pediatricians should find time during routine visits to consulting young parents about common disease and viruses their children might experience and how to deal with it using conventional treatments. Also, it is very important mentioning to parents that children should not consume any unpasteurized products.
- Kindergarten is a perfect place to spread information about foot and mouth disease and ways to treat it avoiding the unconventional treatments, like unpasteurized milk consumption.
- The workers at the kindergarten should be aware of the foot and mouth disease symptoms in small children. In case of infection, they must inform the parents as soon as possible, in order to avoid the spread of infection to other children.
- Regarding the families who raise cattle in the villages. If an infected animal was detected in the farm or village, screening family members who own the cattle and village population is much recommended in order to control the outbreak.
- Media is playing a huge role in our health and life trends. The Ministry of Health should use the power of media in order to increase the awareness about the danger in unconventional treatments or natural treatments as unpasteurized dairy product. Also, media can be used in order to guide people on how to self - manage your health. For example, make a health tip page in the local and available for free newspaper and include guidance for healthier and protected

from parasites and bacteria life. One of the tips can be a guide for how long an individual should cook the meat in order to reach a safe meal level for consumption, for instance, the internal temperature of meat should be from 145 to 165 F or 63 to 74 C, and people should order beef and pork at least medium - well, when visiting a restaurant.

- The Ministry of Health should shut down factories and fine families who sell unpasteurized dairy products.
- Laboratory workers should self-manage their safety from Brucella infections by using gloves and protective equipment.
- Laboratory technicians should always work with Brucella cultures in protective hood, BSL-2 laboratory setting.
- In blood culture, while preparing a blood smear, laboratory technician should make a fixation by covering the slide with Methanol, before the slide leaves the protective hood.
- In case, the technician identified tiny gram- negative coccobacillus under the microscope, he or she should seal the petri dish by using parafilm before the incubation. This step of precaution will reduce the risk of petri dish accidentally to open up and mark the plate as “dangerous” for the rest of technicians and workers.

Summary:

The technological innovations and well -developed medicine reduced many of infections and deadly diseases. Moreover, some of the infections and symptoms became unfamiliar to modern doctors and to The Ministry of Health and Agriculture worldwide, who are no longer preoccupied with the issue of rare infections.

Unvaccinated animals and human's new lifestyle, as well as distrust in public health contributed to reemerging of Brucella infection, which became a serious public health threat to the world, especially children and elderly.

Brucellosis is highly pathogenic for humans and it became a very serious problem not just for the farmers who are at risk of losing their only source of trade and food, but also for the country's economy, since the duration of the human illness and a very high relapse rate damages the normal activities of individuals, as well as the time off work which resulted due to medical condition.

The world health leaders have to use media and policies in order to increase the awareness about the importance of livestock vaccination and humans' medical education. Also, more resources have to be invested in medical laboratory equipment and annual safety updates for medical technicians. The World Health Organization have to come up with one universal protocol, which states that every blood smear has to be treated with methanol in order to fix the bacteria on the slide for future procedures.

The most important issues related to Brucellosis is the health of our children. Public health educators have to develop a program, that includes pediatricians and kindergarten teachers and guide the young parents on how properly react and be prepared to infections us Brucellosis and ignore the internet bias.

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