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BACHELOR THESIS

Incidence and Prevalence of *Mycobacterium bovis* in SADC countries

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Study program: Tropical and Subtropical Agriculture

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1. Introduction
2. Background
3. Aim of the thesis
4. Methodology
5. Results
6. Discussion
7. Conclusions

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Thesis supervisor

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Head of DASFPTS CULS in Prague Director of ITS CULS in Prague

I hereby declare, that I wrote this bachelor thesis by myself and I used only mentioned literature.

Prague, 15th May, 2008 ____________________________

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I would like to express my thanks to my thesis supervisor, Mr. Holejšovský, DVM, PhD, for valued advices, professional recommendations and guidance, time, ispirations and immense help with my bachelor thesis.

My thanks also belong to my family and to my friends for their support and patience.

ABSTRAKT

Mycobacterium bovis, druh patřící mezi Mycobacterie, způsobuje tuberkulózu skotu a jiných savců včetně člověka.

Rozšíření je celosvětové, nicméně dosud existují země, kde bovinní tuberkulóza nebyla nikdy zaznamenána. Je to onemocnění, které postihuje zvířata a člověka od pradávna, a nyní, na počátku 21.století, bovinní tuberkulóza stále způsobuje velké zdravotní problémy, jak u zvířat, tak u lidí, a dále způsobuje značné ekonomické ztráty.

V Africe, a zejména v zemích Jihoafrického Rozvojového Společenství, je výskyt bovinní tuberkulózy stále relativně vysoký, ačkoliv některé země byli prohlášeny za bovinní tuberkulózy prosté. Rozšíření HIV infekce v lidsképopulaci je velice závažné, neboť pacient stižený infekcí HIV patří do nejrizikovější skupiny z hlediska vnímavosti k infekci *Mycobacterium bovis*. Bylo dokázáno, že stejně jako skot může být zdrojem infekce pro člověka, může být i člověk zdrojem infekce pro skot. Výrok MD. Philipa LoBue (*Associate director for Science, Division for Tuberculosis Elimination, CDC*), který zní "*Humánní tuberkulóza způsobená Mycobacterium bovis: Zapomenutá, ale stále přítomná*", výstižně vyjadřuje stávající situaci a dožaduje se pozornosti. Nutno dodat, že snaha veterinárních lékařů o eradikaci bovinní tuberkulózy bez spolupráce s lékaři humánními nezaručí úspěch.

Úloha volně žijící zvěře v šíření nákazy způsobované zárodky *Mycobacterium bovis* v Africe zaujímá významné místo. Snaha o vymícení bovinní tuberkulózy z populace volně žijící zvěře neustále pokračuje i ve vyspělých zemích, jako jsou například Spojené Státy Americké nebo Velká Británie, což znamená, že někrté africké státy mají před sebou ještě velmi dlouhou cestu do prohlášení za státy tuberkulózy prosté.

Klíčová slova: Skot, tuberkulóza, mycobacterie, Afrika, SADC, rozvojové země

ABSTRACT

Mycobacterium bovis, species of *Mycobacteria,* cause bovine tuberculosis in cattle and other mammals, including man. Bovine tuberculosis occurs worldwide, however some countries where bovine tuberculosis has never been reported exists still. It is a disease, which infects animals and human since antiquity and now, at the beggining of 21th Century, bovine tuberculosis continue inducing major public, both veterinarian and human, health problems and economical losts.

In Africa and especially in countries of Southern African Development Community, bovine tuberculosis incidence is relatively high, however, some countries have been declared as bovine tuberculosis free. The spread of HIV infection in human is of big importance, as HIV infected man is at the highest risk group who is susceptible to *Mycobacterium bovis* infection. It was proved, that the same as cattle can be the source of infection for human, can human be the source of infection for cattle. Therefore, the statement of Philip LoBue,MD (*Associate director for Science, Division for Tuberculosis Elimination, CDC*): "*Human tuberculosis caused by Mycobacterium bovis: Forgotten, but Not Gone*", express exactly the current situation and call for attention.
Thus, any effort of veterinarians to eradicate bovine tuberculosis without co-operation with physicians would not quarantee the success.

The role of wildlife within *Mycobacterium bovis* infection is in Africa of great importance. Eradication of bovine tuberculosis from wildlife continue even in developed countries, such as USA or Great Britain, which mean that some African countries have still long way to achieve bovine tuberculosis free status.

Key words: Cattle, tuberculosis, mycobacteria, Africa, SADC, developing countries

METHODOLOGY

Objectives of the study

The objective of my bachelor thesis is to introduce and describe problematics within incidence and prevalence of *Mycobacterium bovis* and therefore bovine tuberculosis in Africa, notably Southern African Development Community countries.

My main objective was to find out whether there is incidence and prevalence of *Mycobacterium bovis* in individual countries of SADC, and if so, how heavy there is the impact on that country and if there is any eradication program which deal with this problem.

My secondary objectives were to present the problematics within *Mycobacteria bovis* infection in general and outline incidence and prevalence of *Mycobacterium bovis* in other world continents to compare the differences. The role of international organization was also mentioned.

In detail, to describe this problematics accurtely, the thesis was divided into introduction and 5 chapters.

The introduction is dedicated to history of bacteria, mycobacteria and later on of *Mycobacteria bovis* infection, for better understanding, why this disease calls for attention. Seeming eradication of bovine tuberculosis and following lost of interest in this disease lead to re-emerge *Mycobacterium bovis* infections. Therefore, looking back into history might give clearly imagination what is happening right now and what the future of *Mycobacterium bovis* infection might be. In the following chapter, microbiology, pathology and epidemiology of *Mycobacterium bovis* was decribed.

After brief description of international organization engaged in agriculture, veterinary and public health, namely FAO, OIE and WHO, followed by description of SADC, the most important part of the thesis comes. Incidence and prevalence of *Mycobacterium bovis* infection in the world and SADC was mainly find out from WAHID Interface, database of OIE. Final chapter was dedicated to economic impact of BTB in SADC.

Materials

For complementing this bachelor thesis I used both bibliographical and internet sources. Main source of information and data are from 4 bibliographical sources (*Thoen et.al, 2006*; *Grange, 1996; Rev.sci.tech.Off.int.Epiz., Vol. 20 (1), 2001; Quinn et.al, 2002*) and WAHID Interface, database of OIE.
(http://www.oie.int/wahid-prod/public.php?page=home)

Webpages of the National Institute of Public Health (Czech Republic)
(http://www.szu.cz), webpages of SADC *(http://www.sadc.int/)*, CDC *(www.cdc.gov)*, FAO *(http://www.fao.org)* and WHO *(http://www.who.int/en/)* are important to noticed too.

The rest of informations and data were find in another bibliography or in scientific electronic databases, such as ScienceDirect Journals *(http://www.sciencedirect.com)* and/or PubMed Central *(http://www.pubmedcentral.nih.gov/index.html)* and others.

From all the literature listed I took important data, selected them and later on complited from them this bachelor thesis.

TABLE OF CONTENTS

INTRODUCTION

PAST, PRESENT AND FUTURE OF MYCOBACTERIAL DISEASE

Mycobacterial diseases are caused by some subspecies of Mycobacteria species, which belongs to genus Mycobacterium, family Mycobacteriaceae, order Actinomycetales, phylum Actinobacteria and kingdom Eubacteria.[1]

BACTERIA

Bacteria, which belong to prokaryotes organism, have always been the dominant form of life on earth. Prokaryotes were the first cellular life to involve about 3500 million years ago. It may seem surprisingly that a fossil of bacteria has been preserved. The oldest fossils currently known are nearly 3500 million years old (far back into the Precambrian era) and belong to group of cyanobacteria (cyanobacteria-like fossils). This earliest fossil is a cell without organelles. Fossil record suggests that organized cellular mats (probably of filamentous photosynthesising bacteria) existed about 3000 million years ago.[1, 2, 3]

Bacteria aren´t only really old widespread organism of unimaginable variety, prodigious number with spectacular adaptability to diverse enviroments, but they also represent the greatest success story amongst living organisms.[1]

When eucaryotes appeared about 1500 million years ago, bacteria found in them useful host to colonize. An estimated 10% of the dry body weight of humans consists of bacteria.[3] Bacteria can be the same really useful and vitally important as pathogenic (host-microbe relationships) for humans and animals (and not only for them), depending on variety scale of circumstances.

In 1967, an interesting Lynn Margulis´s endosymbiotic theory was postulated. This theory is based on similarities between prokaryotic cells and the organelles of eukaryotic cells. Thus, this theory says that the earliest Eukarya, anaerobic mastigotes, hypothetically originated from permanent whole-cell fusion between members of

Archaea (e.g., Thermoplasma-like organisms) and of Eubacteria.[4] The eucaryotic cell according to this theory has its origin in Archaeal--Eubacterial cells.[4, 5]

Bacteria, the most numerous prokaryotes, are single celled organisms, commonly 1-2 µm in size. Bacteria are critical to the earth´s ecology, but some cause major diseases, including tuberculosis from some *Mycobacterium* species.[6] Bacteria can exist both as independent and as parasites. They can be find in the environment, soil, water and also many vertebrate and invertebrate animals contain dense populations of prokaryotes, icluding bacteria.[7] For the first time bacteria were recognized by Antony van Leewenhoek (1632-1723) by the microscopic animalcules and in the 19th century categorized by Ferdinand Cohn (1828-1898). [8, 9]

MYCOBACTERIA

Mycobacteria represent a thriving and ingenious family in the microbial domain. Many mycobacterial species have selected as "home" the very cell dispatched by the host to defeat them: the macrophage. Having thus defused a key weapon in the immune arsenal, the bacilli flourish for years prior to killing or debilitating the host.[1] The genus Mycobacterium consists of more then 80 species, from which mainly *Mycobacterium tuberculosis, Mycobacterium leprae and Mycobacterium bovis* call for special attention because of diseases that they induce. Those diseases are called tuberculosis and leprosy.[10]

Nevertheless, other subspecies of Mycobacterium, namely *Mycobacterium avium* may play very important role in poultry and pig pathology as well. *Mycobacterium avium subsp. paratuberculosis* causes Johne´s diseases, known as paratuberculosis.[11, 12]

At present, it is of big economic importance, because in poultry, swine, cattle farms and farmed deer avian tuberculosis imposes the highest financial losses. It is not only disease of animals, but it can be also transmitted to human. Within spread of human immunodeficiency virus (HIV) infection, the incidence of mycobacterium infection caused by *Mycobacterium avium* complex is increasing.[13]

Paratuberculosis is chronic, progressive and incurable infection of gastrointestinal tract.[14] There is suspicion, that infection caused by *Mycobacterium avium* complex in human has some impact on incidence of human Crohne´s diseases [14, 15, 16, 17] however more investigation is still needed. *Mycobacterium avium* subsp. paratuberculosis is commonly detected from the faeces and tissues of infected animals and there are also detections in milk samples.[18]

To sum up, infection in dairy cattle and other domestic animals (pig, poultry) affects animal health and productivity and is also a potential public health concern.[19]

Tuberculosis, caused by *Mycobacterium tuberculosis*, and leprosy, caused by *Mycobacterium leprae* are diseases known since the time immemorial. Those two diseases have ranked amongst the most feared and dreaded of numerous diseases that afflict mankind. The evangelist John Bunyan dubbed tuberculosis as the "Captain of all of these men of Death" and in India it was known as the King of Diseases. Leprosy may be termed the Disease of Kings, as Robert Bruce, King of Scotland, and Emperor Constantine are numbered amongst its victims.[20]

There are also older mentiones about tuberculosis and leprosy. Mention about leprosy can be find in Bible (*Leviticus*, Chapter 13th) nevertheless it is supposed that the disease designated as "tsara´at" in Hebrew, which had been translated into English as "leprosy" isn´t the same as the modern technical meaning of the term "leprosy" (comprehended as disease caused by *Mycobacterium leprae*). It is assumed that in *Leviticus* "leprosy" was in general term for contagious skin disease of various origins.[21, 22]

Despite this fact, we can´t eliminate the suspicion that *Mycobacterium leprae* didn´t have any role between contagious skin disease in antiquity.

Nowadays, tuberculosis has been suspected as a cause of death in some of the Egyptian mummies 3,000 years ago.[10, 23] According to Zink *et al.*, evidence has been proved by modern science investigation when bone and soft tissue samples from 85 ancient Egyptian mummies (from different tomb complexes in Upper Egypt and from different time period- since ca. 2050 BC until 500 BC) were analyzed for the presence of *Mycobacterium tuberculosis* complex DNA and further analyzed by spoligotyping.

A total of 25 samples provided a specific positive signal for the amplification (exactly signal for the amplification of a 123-bp fragment of the repetitive element IS*6110*) which indicates the presence of *M. tuberculosis* DNA. Only 12 of this 25 possitive samples could be succesfully characterized by spoligotyping (the other failed due to lack of specific amplification products in the historic tissue samples). The result was that all of these samples showed either *M. tuberculosis* or an *M. africanum* pattern and none revealed to *M. bovis* specific pattern. Moreover, the study says, that their results do not support the theory that *M. tuberculosis* originated from the *M. bovis* type but, rather, suggest that human *M. tuberculosis* may have originated from a precursor complex probably related to *M. africanum*.[23]

Evidence for pulmonary tuberculosis was also detected in New World mummy from Peru, dated 700 AD. First piece of medical knowledge about tuberculosis was reported by Hipocrates, Celsus and Galen, as they found out, that rest and fresh air is essential for patients. Tuberculosis was recognized as a contagious disease in 16th century and later on, in 1679 anatomical and pathological characteristics were reported in Opera Medica by Sylvius. It that time tuberculosis was innitially termed as phthisis. Despite all those facts, up to 1881 the non-communicability of tuberculosis was a general belief. [10]

According to John M. Grange, the description of isolation of organism causing tuberculosis was firstly described at the meeting of the Berlin Physiologycal Society on the evening of 24th March 1882 by Robert Koch *(see pictures 1.a and 1.b in annexes)*. However, the generic name *Mycobacterium* was first introduces by Lehmann and Neumann in 1896. [20, 24]

The name *Mycobacterum* is not related to the fungi altought it´s name means "fungus-bacterium". It is only because of its way of growing on liquid media like mould-like pellicles. Later on apellation, four types of "tubercle bacilli" were recognized, namely: human, bovine, avian and "cold blooded". The biggest problem was tuberculosis in man and catle. It was discovered, that human tuberculosis causes *Mycobacterium tuberculosis* and bovine one *Mycobacterium bovis*. [24]

Nevertheless it was big mistake, when Robert Koch thought that *Mycobacterium bovis* is of no danger for man and said this statement at the British Congress on Tuberculosis in 1901. This claim has outraged veterinary surgeons that persuated Minister of Agriculture to convene a Royal commision and put effort to investigate this issue. After ten years of investigation, Arthur Stanley Griffith and Louis Cobbett, scientist employed by the commisisoners, have presented irrefutable evidence that bovine tuberculosis is of danger for man. This counclusion was based on enourmous information of the epidemiology, bacteriology and pathology of bovine tuberculosis and had also impact on state-sponsored medical research as a great idea and was not only the foreruner of British Medical Research Council but also laid the foundations for the bovine tuberculosis eradication programmes. [20, 25] According to John M. Grange in his book Mycobacteria and human disease this foundation for the bovine tuberculosis eradication programmes must be hailed as the most effective control measures ever mounted against bacterial disease. [20]

Thus, it is sad fact, that almost 100 years after first effort to eradicate tuberculosis by eradication programmes and 84 years after first use of vacinne in 1921, produced by Calmette and Guérin and called Bacille Calmete- Guérin (BCG), the World Health Organization had declare tuberculosis as one of three major global emergency health problem (together with AIDS and malaria) in 2005. [26]

Therefore, WHO created strategy which is described in The Global Plant to Stop TB, 2006-2015. Its effort is also included in Millenium Development Goal (MDG), where TB prevalence and death rates should be reduced by 50% relative to 1990 by year 2015, and by 2050 TB should be eliminate as a public health problem. The 20th century is remarkable not only for the effort for eradication TB, times of great fascination, interest and confidence in tuberculosis and vacinne research, but also of times mainly during 70s and 80s, when health scientific interest convert its orientation to the other diseases, for example AIDS, and times, when the Internation Union Against Tuberculosis was appended “And Lung Disease” and later on, the British Medical Research Council´s Tuberculosis and Chest diseases Unit was closed. [20, 27]

Probably, if tuberculosis hadn´t be underestimated the WHO would not need to re-call it world healt problem at the beginning of 21st century. What is more, in developing countries it is the leading cause of mortality due to an infectious disease. [10, 28, 29]

This is valuable especially for *Mycobacterium tuberculosis*; however, *Mycobacterium bovis* has also its role in human tuberculosis as it is one of three species of the *Mycobacterium tuberculosis* complex that causes tuberculosis in humans and nowadays is of big importance within people who suffer from HIV. [25, 28, 30]

And what about veterinary medicine and *Mycobacterium bovis*? *Mycobacterium bovis* cause mainly (but not only) disease in animals, the main host is cattle and species occasionally infected are deer, badgers, possums, cats and other mammalian species. [31, 32, 33, 34]

As mentioned above, the existance of *Mycobacterium bovis* was known since the end of 19th century and during 20th centrury a lot of eradication programmes have been made.[20, 35, 36, 37] Nevertheless, sporadic outbreaks continue to occur in many countries in which disease was almost eliminated and what is more, in some developing countries it is still big issue within livestock health. [20, 28, 36, 38]

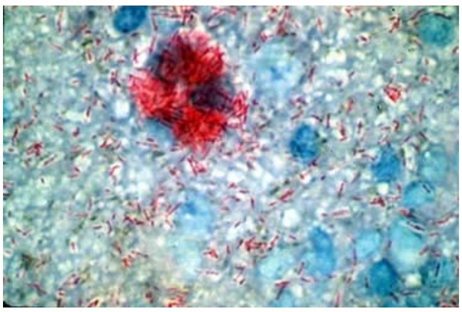
Wildlife can be also reservoir of *Mycobacterium bovis* of big importance. [28, 32, and 38]

Therefore, there is still what to study, what to improve and we might find inspiration of eradication programmes in past, improve them and try to reduce *Mycobacterium bovis* infection in animals and man once again.

CHAPTER 1 MYCOBACTERIA

1.1. General characteristics

Mycobacteria are aerobic, cytochemically Grampositive, non-motile, non-spore-forming, slowly growing with colonies visible aftre several weeks, rod shaped, acid fast (ZN- positive) bacilli. Some mycobacteria produce carotenoid pigments. As for the size, Mycobacteria can be from less than 2 um up to 4 um in legnth, depending on species. The biggest ones are *Mycobacterium bovis* and *Mycobacterium avium*. Cells are strainght shaped or moderately incurvate shaped rods, which can form ramified filaments. Cell walls are rich in lipids, waxes and mycolic acids content that prevents uptake of the dyes employed in the Gram stain. Lipid-rich walls render mycobacteria hydrophobic and resistant to adverse environmental influences. The cell wall lipids bind carbol fuchsin which is not removed by the acid- alcohol decolourizer used in the Ziehl-Neelsen (ZN) staining method. Therefore, bacillli, which stain red by this method, are called acid- fast or ZN- positive. The ZN staining method is used to differentiate mycobacteria from other bacteria. [10, 11, 24]



1. Mycobacterium bovis, tissue smear, acid-fast stain, high power.

Addapted from: .merckvetmanual.com/mvm/img/tn/tn_gentb02.jpg

1.2. Mycobacterium species

Mycobacteria species include not only strict, opportunistic and obligate pathogens, but also environmental saprophytes. Environmental mycobacteria are found in soil, on vegetation and in water. Obligate pathogens, shed by infected animals, can also survive in the environment for extended periods. [10, 11]

1.2.1. Differentation of pathogenic mycobacteria

Differentiation of pathogenic mycobacteria relies on cultural characteristics, biochemical tests, animal inoculation, chromatographic analyses and molecular techniques. In addition, mycobacteria associated with opportunistic infections can be differentiated on the basis of pigment production, optimal incubation temperature and growth rate. [11]

For better understanding, below are some examples, how exactly can be pathogenic mycobacteria differentiate.

1.2.1.1. By biochemical tests:

Biochemical differentiation based on specific test methods aids in the identification of M. tuberculosis, M. bovis and M. avium. Some mycobacterial isolates cannot be assigned to a given species using biochemical differentiation as their biochemical profiles are difficult to interpret. [11]

Chromatographic analyses of the lipid composition of some mycobacterial species are used in specialized laboratories. [11]

- Pigment production and photoreactivity for opportunistic mycobacteria:
    - Non- chromogens produce colonies devoid of orange, carotenoid pigments.
    - Photochromogens, when cultured in the dark, produces non-pigmented colonies which become pigmented after a period of exposure to light.
    - Scotochromogens produce pigment when cultured in the dark or in light. [11]

- Molecular techniques:
    - DNA probes, complementary to species-specific sequences of rRNA, are commercially available for the *M. tuberculosis* complex, the *M. avium* complex and *M. kansasii*.

- Nucleic acid amplification procedures, including the polymerase chain reaction, are being developed as sensitive and rapid methods for the detection of mycobacteria in tissue samples
- DNA restriction endonuclease analyses (DNA fingerprinting) are used in epidemiological studies. [11]

1.2.1.2. By animal inoculation:

Guinea-pig and rabbit inoculation was used in the past to differentiate *M. tuberculosis* from *M. bovis* and *M. avium*. Guinea-pigs are highly susceptible to infection with *M. tuberculosis* and *M. bovis*. Rabbits are highly susceptible to infections with *M. bovis* and *M. avium*. [11]

1.2.1.3. By optimal incubation temperature:

Mycobacterium bovis, *M. tuberculosis* and *M. avium* subsp. paratuberculosis have an optimal incubation temperature of 37° C. Mycobacteria belonging to the *M. avium* complex grow in the temperature range of 37 to 43° C. [11]

1.2.1.4. By growth rate:

Pathogenic species grow slowly and colonies are visible after several (at least three) weeks after incubation. For growth of pathogenic species is required complex egg-enriched media. In comparison, the colonies of rapidly growing saprophytes are visible within days. [11]

1.2.1.5. Other possible differentiation:

Supplementation of media with mycobactin is required for *M. avium* subs. paratuberculosis. Mycobactin is extracted from laboratory- maintained, rare, non-mycobactin-dependent isolated of *M. avium* subsp. paratuberculosis. [11]

Anyway, while working with material containing mycobacteria, safety precautions including use of biohazard cabinet are needed. [11]

Pathogenic Mycobacterial species induce serious, chronic, progressive and granulomatous diseases like tuberculosis in avian and mammalian species, paratuberculosis in ruminants or feline leprosy. Two other clinical conditions, skin tuberculosis and bovine farcy are associated with the presence of acid-fast bacteria in lesions. In skin tuberculosis of cattle, nodular lesions are located along the course of lymphatics in the limbs. Unspecified acid- fast bacilli have been demonstrated in these lesions. *Mycobacterium senegalense* and *M. farcinogenes* have been isolated from the lesions of bovine farcy. Their aetiological role in this condition, however, is uncertain.[11]

Granulomatous lesions which develop following opportunistic infections with environmental saprophytic mycobacteria are encountered occasionally in domestic animals. These saprophytic mycobacteria are grouped on the basis of pigment production and growth rate. Members of the *M. avium* complex are grouped with those which produce opportunistic infection because they are occasionally involved in mammalian infections. [11]

The major pathogenic *Mycobacterium* species which affect domestic animals exhibit a considerable degree of host specificity although they can produce sporadic disease in a number of other hosts. [11]

The following members of *Mycobacterium tuberculosis* complex, i.e. *M. tuberculosis, M. bovis* and *M. africanum* cause tuberculosis in human. Concerning their susceptibility and resistance, the species of *Mycobacterium* are resistant to chemical disinfectants and environmental influences, but on the other hand they are susceptible to heat treatment (pasteurization). Therefore, pasteurization of milk is of big importance in reducing mainly *Mycobacterium bovis* infection in man. [28, 29]

Other species, *Mycobacterium avium,* is of public health importance too. [13, 19]

1.2.2. Mycobacterium bovis

1.2.2.1. Characteristics, epidemiology and prevalence in domestic animals:

Mycobacterium bovis, one of Mycobacterium species, cause bovine tuberculosis, a disease, which has been detected in cattle worldwide and which is characterized by the progressive development of characteristic granulomas (or tubercles) in the lungs, lymph nodes and other organs. This affects the health of individual animal and has a destructive effect on animal production. The disease is infectious and can spread within a herd before any sign of disease are obvious. In some cases the infection lies dormant for many years, spreading only when the animal is subjected to addition stress, like overstocking, drought or just simply when the immune system deteriorates in old age. [31]

Despite *M. bovis* can survive for several months in the environment, transmission is mainly through aerosols generated by infected cattle. The mode of transmission in cattle is principally horizontal, but not all infected animals transmit the disease. However, most cattle suffering from pulmonary tuberculosis and tuberculous mastitis are infectious, and in some infected individuals, urine, vaginal secretion, semen of faeces may also contain tubercle bacilli and act as a means of disease transmission between animals. [31]

The most important factors determining the occurence and spread of tuberculosis within a herd of cattle are the number of infected individuals, the number of young stock exposed to these infected animals, and the measures taken to prevent spread. [31]

The primary mode of spread of bovine tuberculosis between herds is by the introduction of infected animal into non-infected herds, when health animal inhals infectious aerosols from coughing or sneezing animal with open tuberculosis or from infected particles. Because of this fact, infection is spread more rapidly in intensive animal husbandry than in extensive or rangeland conditions. Moreover, aerosol transmission is effective only over short distaces (about 1 or 2m) and therefore cattle density is other significant factor in the rate of transmission.[31] Prevention from close contact between animals during milking or when housed during winter month (or during unfavourable season) are many times difficult, so dairy cattle are in particulary risk anyway because of husbandry methods. [31]

To summarize, on dairy farms with a high density of cattle, or in production systems which house animals together for extended periods, the transmission rate between susceptible animals may be very high.

When there is positive diagnosis on bovine tuberculosis in cattle, infected animal must be placed into a special, separated stable or barn for tuberculous cattle. Nevertheless, in such as stables and barns used to house tuberculous cattle, infected droplets and particles may be constantly present in the air, which still presents a hazard to susceptible animals and farm workers. [31]

Calves can become infected by ingesting contaminated milk and ingestion is the probable route of transmission to pigs and cats. Rout of infection to other domestic animals, such as goats, farmed or domesticated camelids (camels, alpacas and llamas) is usually the respiratory tract. Infection in horses is uncommon and in sheep rare. Dogs suffer mainly from infection of *Mycobacterium tuberculosis*; infection of *Mycobacterium bovis* is rare too. [31]

1.2.2.2. Prevalence in wildlife

In general, infection in wildlife is of big significance. Wildlife reservoirs of *Mycobacterium bovis* are major sources of infection for grazing cattle in some countries. [32, 38, 39, 40]

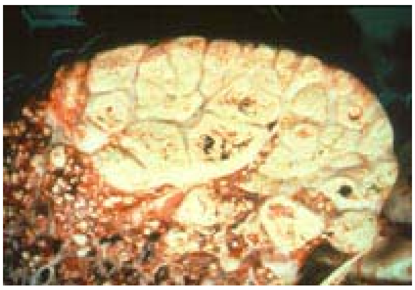
Wildlife reservoirs include the badger (*Meles meles*) in Europe, the brush-tailed possum (*Trichosurus vulpecula*) in New Zealand and the African buffalo (*Syncerus caffer*) and other ruminants in Africa. Deer, both wild and farmed, are particularly susceptible and may act as reservoirs of infection for cattle, as mentioned above. Susceptible are also primates, hares, and antelopes etc. [32, 38, 39]

What is more, wildlife reservoirs are major obstacles to disease eradication in some countries. [32, 36, 38, 39, 40] Furhter reduction of incidence in the presence of a wildlife host should be possible through application of ecologically designed management procedures at farm level, but greater gains could be made if new control measures could be developed, especially vaccines. [41]

As for Africa in detail, bovine TB continues to be a major problem within wildlife in South Africa, Uganda and Zambia. The disease has been confirmed in buffalo, lechwe (*Kobus leche*), greater kudu, warthog (*Phacochoerus africanus*), bushpig (*Potamochoerus larvatus*), baboon (*Papio ursinus*), lion (*Panthera leo*), leopard (*Panthera pardus*), cheetah (*Acinonyx jubatus*) and spotted hyaena. Of these species, only buffalo, lechwe and kudu appear to be maintenance hosts.[42]

Bovine TB was for the first time diagnosed in African buffalo in the Hluhluwe-Umfolodzi complex (1986) and in the Kruger National Park (1990), South Africa. Since the first diagnostic, epidemic proportion reached with the infection rates up to 92% in some herds in the Southern region of the Kruger National Park (KNP) [43, 44]

In the KNP, the disease was also diagnosed for the first time in a honey badger (Mellivora capensis) and a common genet (Genetta genetta) in 2001. Bovine TB was also cultured from two wildebeest (Connochaetes taurinus), a topi (Damaliscus lunatus) and a baboon (Papio anubis) in the Serengeti ecosystem in Tanzania. A buffalo TB vaccination trial using BCG was completed in 2001. [42, 43]



2. Lung lesions in an African buffalo with bovine tuberculosis

3. Lymph node abscess due to infection with Mycobacterium bovis in a kudu

(Addapted from: http://www.arc.agric.za/home.asp?pid=605 online on 2008-05-08)

1.2.2.3. Clinical signs and pathology

Quite complication in taking notice about bovine tuberculosis in cattle is the fact that clinical signs are evident only in advanced disease so even cattle with extensive lesions can still appear to be in good health. As the disease progress, loss of condition may become evident. Later on, in advanced pulmonary tuberculosis, animals may eventually develop a cough and intermittent pyrexia. Involvement of mammary tissue may result in marked induration of affected quarters, often accompanied by supramammary lymph node enlargement. In the early stages of the disease, lesions may be difficult to detect at postmortem examination. These small lesions are composed of aggregates of macrophages, termed epithelioid cells. Multinucleate Langhan´s giant cells, formed from the fusion of macrophages, may also be present. In older lesions, fibroplasias produces early detectable grossly as yellowish cheesy material. Tuberculous mastitis facilitates spread of infection to calves and cats, and it is of major public health importance. [11]

The virulence of *M. bovis* relates to its ability to survive and multiply in host macrophages. Specific toxic factors, contributing to virulence, have not been identified. The macrophage accumulation at the primary site of infection is initially a response to the foreign body effect of waxes and lipids in the mycobacterial cell wall. Survival within the cytoplasm of macrophages is promoted by interference with phagosome-lysosome fusion and failure of lysosomal digestion. Bacilli released from dead macrophages are engulfed by surrounding viable phagocytes. Migration of macrophages containing viable mycobacteria can disseminate infection.[11]

The complex lipid and waxy composition of the mycobacterial cell wall contributed not only to virulence but also, in association with tuberculoproteins, to the immunogenicity on which the development of the host responses and the lesions depends. With the development of cell-mediated immunity some weeks after infection, macrophage recruitment accelerates under the influence of cytokines produced by T lymphocytes sensitized to tuberculoprotein. In addition, these macrophages become activated through cytokine stimulation and proliferate. The gradual accumulation of macrophages in the lesion and the formation of a granulomatous response lead to the development of a tubercle, the typical host response in the delayed-type hypersensitivity to mycobacterial infections. [11]

1.2.2.4. Diagnostic procedures

The tuberculin test, based on a delayed- type hypersensitivity to mycobacterial tuberculoprotein, is the standard antemortem test in cattle. The test can be adapted for use in pigs and farmed deer. Reactivity in cattle is usually detectable 30-50 days after infection. Tuberculin, prepared from mycobacteria and called purified protein derivative (PPD), is injected intradermally to detect sensitization. Two main methods of tuberculin testing are employed: [11]

- In the single intradermal (caudal fold) test, 0.1 ml of bovine PPD is injected intradermally into the caudal fold of the tail. The injection site is examined 72 hours later and a positive reaction is characterized by a hard or oedematous swelling. [11]
- In the comparative intradermal test, 0.1 ml of avian PPD and 0.1 ml of bovine PPD are injected intradermally into separate clipped sites on the side of the neck about 12cm apart. Skin thickness at the injection sites is measured with calipers before injection of tuberculins and after 72 hours. An increase in skin thickness at the injection site of bovine PPD which exceeds that at the avian PPD injection site by 4mm or more is interpreted as evidence of infection and the animal is termed a reactor. [11]

False positive reactions which occur in the tuberculin test may be attributed to sensitization to mycobacteria other than *M. bovis.* [11]

False negative test results may be recorded:

- Cattle tested before delayed- type hypersensitivity to tuberculoproteins develops (at about 30 days post-infection) do not react.
- In some cattle an unresponsive state, referred to as anergy, may accompany advanced tuberculosis. The mechanisms involved are incompletely understood.

- A transient desensitization may follow injection of tuberculin. Reactivity usually returns within 60 days.
- Cows may be unresponsive to the tuberculin test during the early postpartum period. [11]

Blood-based tests which have been developed for use in conjunction with the tuberculin test include:

- Gamma interferon assay
- ELISA for detecting circulating antibodies
- Lymphocyte transformation and related assays [11]

Specimens suitable for laboratory examination include lymph nodes, tissue lesions, aspirates and milk. [11]

The low numbers of mycobacteria present in bovine lesions can render visual confirmation difficult using the ZN stain. In contrast, large numbers of acid-fast bacilli are usually present in smears of specimens from deer and badgers.[11]

Stained tissue sections usually reveal typical patterns of tubercle formation.

Isolation of *M. bovis* requires:

- Decontamination of specimens to eliminate fast-growing contaminating bacteria. Ground-up specimens are treated for up to 30 minutes with 24 % sodium hydroxide or 5% oxalic acid, followed by neutralization of the alkali or acid. Centrifugation is used to concentrate the mycobacteria and the supernatant fluid is discarded.
- Slants of Lowenstein- Jensen medium, without glycerol and containing 0, 4% sodium pyruvate are inoculated aerobically at 37° C for up to 8 weeks. [11]

Identification criteria for isolates:

- Growth rate and colonial appearance
- Positive ZN- staining of bacilli in smears from colonies
- Biochemical profile
- Analytical and molecular techniques [11]

Commercially- available, rapid, automated systems can be used for isolating pathogenic mycobacteria of the M. tuberculosis complex. [11]

Control of bovine tuberculosis, relies on early diagnosis, removal of infected animals and tracing and containment of contact exposed cases. [11]

Treatment and vaccination are inappropriate in control programmes for cattle. In many countries, tuberculin testing followed by isolation and slaughter of reactors has been implemented as the basis of national eradication schemes. Routine meat inspection forms part of the surveillance programme for bovine tuberculosis in many countries. [11]

1.2.2.5. Impact of *Mycobacterium bovis* infection on human health

Mycobacterium bovis is a zoonosis and as already mentioned people could be infected too. While looking on the published data which describes tuberculosis in Europe in the 1930s and 1940s, they show that bovine tuberculosis was considered to be a significant zoonosis: *M. bovis* was responsible for more than 50% of cervical lymphadenitis cases in children. By now, it was considered, that the situation within epidemiological conditions for the spread of *Mycobacterium bovis* infection between animals and humans in Africa is likely to be the same as in Europe in 1930s. Due to lack of laboratories for diagnostic and culture of *Mycobacterium bovis* in developing countries, including Africa, there is still little information about human cases of nonpulmonary *Mycobacterium bovis* infection. [45, 46]

However, despite the lack of informations, it was considered, that *Mycobacterium bovis* infection in Africa is probably widely distributed and has been found at significantly high prevalence in some populations of animals. [28, 46]

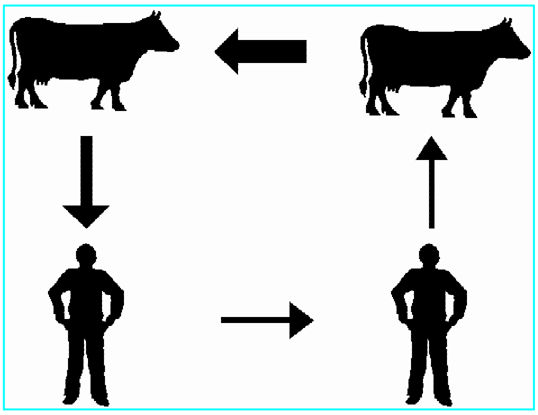
According to Ashford *et al*, in Europe and North America, 0.5% to 1% of human tuberculosis cases were estimated to be result of *Mycobacterium bovis* infection. Before eradication programmes which started in 1960s, the incidence was between 5% and 20%. In countries, where bovine tuberculosis is still common, and pasterizaution of milk rare, an estimated 10% to 15% of human cases of tuberculosis were caused by *Mycobacterium bovis* in 2001. [29]

To discribe human tuberculosis in detail, some more information has been found out. It was proved, that TB caused by *M. bovis* is clinically indistinguishable from TB caused by *M. tuberculosis.* In countries where bovine TB is uncontrolled, most human cases occur in young persons and result from drinking or handling contaminated milk; cervical lymphadenopathy, intestinal lesions, chronic skin TB (lupus vulgaris), and other nonpulmonary forms are particularly common. Nevertheless, some published data says, that such cases can also be caused by *M. tuberculosis*. Differentiation of mycobacteria species is therefore necessary. [10, 24, 46]

Nevertheless, while already confirmed that the disease in human was caused by *Mycobacterium bovis*, epidemiological precautions are necessary. The inner danger within bovine tuberculosis infections is the fact, that there are animal reservoirs of tuberculosis that pose a serious threat to the human population. The most important reservoir is cattle and therefore, no tuberculosis programme is complete without serious consideration of bovine infection. Tuberculosis in cattle is principally pulmonary and is spread from animal to animal by the aerogenous route. Although milk is the usual vector of transmission to humans, the udder is involved in only about 1 % of infected cows. The practice of bulking milk from many animals and herds to facilitate transport allows one tuberculous cow to infect many humans. [30]

While these people, most of the time agricultural workers, are infected, their desease usually develops to typical pulmonary TB. These patients may infect cattle; however the evidence for human-to-human transmission is rare. [30]

For the ilustration a picture describing the probability within cattle-human-cattle transmission was added.



Cycle of *Mycobacterium bovis* transmission between cattle and humans. The thickness of the arrows suggests probability. Addapted from *LoBue, CDC.*

In Africa, there is another big issue connecting to *Mycobacterium bovis* infection in human. That is HIV infection, widely spread in most of African countries. The study of Jonh M. Grange says that some cases of HIV-related tuberculosis due to M. bovis had been reported and in one case human-to-human transmission with rapid progression to overt disease was demonstrated. This raised the serious possibility that, in pastoralist comunities, HIV infection could cause the dissemination of *M. bovis* in the human population with increased transmission back to the cattle. [30]

For all these facts, it is evident, that bovine tuberculosis eradication programmes are necessary. John M. Grange in his study wrote that in countries where bovine tuberculosis eradication programmes have been completed, a few cases continue to occur in humans, mostly in elderly people. Studies of CDC published that these are fewer that 1% of all TB cases. According to John M. Grange it was assumed that these were due to endogenous reactivation of infections acquired in the days when cattle tuberculosis was prevalent, but the possibility of human-to-human spread could not be ruled out. Unlike primary human tuberculosis due to *M. bovis* which is usually non-pulmonary, the lung is involved in about half the cases of post-primary disease. There have been several instances of cattle being infected by such patients. The kidney is involved in about a quarter of cases of post-primary disease and cattle have been infected by farm workers urinating in cowsheds. [30, 46]

CHAPTER 2

INTERNATIONAL ORGANIZATION

There are 3 really important International organizations that have something to do with incidence and prevalence of disease or potentially infections caused by Mycobacteria species. Hopefully brief description of each of them will outline what role they play.

2.1. FAO

The Food and Agriculture Organization of the United Nations. Established in 1945, FAO had to improve the world situation within food supply and agricultural situation around the world. [47]

In 1962, FAO and WHO established Codex Alimentarius Commission to set international food standards which becomes operational. The main purposes of this Programme are protecting health of the consumers and ensuring fair trade practices in the food trade, and promoting coordination of all food standards work undertaken by international governmental and non-governmental organizations. [47]

In 1974 UN World Food Conference in Rome recommended the adoption of an International Undertaking on World Food Security. [47]

In 1994, the Special Programme for Foof Security (SPFS), targeting low- income food-deficit countries and the Emergency Prevention System for Transboundary Animal and Plant Pests and Diseases (EMPRES) strengthening the Organization´s existing contribution to prevention, control and, when possible, eradication of diseases and pests, were established. [47]

Indeed, there are more roles that FAO has, however these points are the most important while speaking about FAO and Mycobacterial diseases.

The veterinary public health group in FAO contributes to research, consulting and training on veterinary public health and feed/ food safety issues. That is the FAO point of view on Mycobacterial diseases. FAO cooperates with OIE and WHO.

2.2. OIE

The Office International des Epizooties (OIE) or World organisation for animal health is the intergovernmental organisation responsible for improving animal health worldwide.[48]

The need to fight animal diseases at global level led to the creation of the Office International des Epizooties through the international Agreement signed on January 25th 1924 by 28 countries including Czechoslovakia. [48]

When FAO and WHO were established by United Nations, their aims partially covered those of the office. Fortunatelly, the functions of OIE were kept alive. In 1952 official agreement between the OIE and the Food and Agriculture Organization was signed and 8 years later, in 1960, official agreement between the OIE and the World Health Organization (WHO) was signed too. [48]

Later on, agreements with other organization were signed, for example with the Inter-American Institute for Cooperation on Agriculture (IICA), WTO (World Trade Organization), Organismo Internacional Regional de Sanidad Agropecuaria (OIRSA), Pan American health Organization/World Health Organization (PAHO/WHO), the World Bank, the Organization of African Unity - Interafrican Bureau for Animal Resources (OUA-IBAR), the World Veterinary Association (WVA), the International Federation for Animal Health (IFAH) and others. [48]

In 2003 The International Office of Epizootics becomes the World Organisation for Animal health, but keeps its historical acronym OIE. [48]

By January 2008, OIE has a total of 172 Member Countries and Territories and maintains pernament relation with 36 other international and regional organizations. [48]

As for diseases, OIE has its own animal disease data, control world animal healt situation, status etc. Bovine tuberculosis or avian tuberculosis, diseases caused by Mycobacteria species, belongs to diseases monitoring by OIE.

2.3. <u>WHO</u>

The World Health Organization is organization under the United Nations. First idea of setting global health organization was in 1945, when the UN was established. Finally, on 7 April 1948 WHO came into force. WHO is responsible for providing leadership on global (human) health matters, shaping the health research agenda, setting norms and standards, articulating evidence-based policy options, providing technical support to countries and monitoring and assessing health trends. [49]

WHO and its point of view to Mycobacterial disease:

WHO is not only involved in human public health issues, but has also its systems for surveillance, alert and response to communicable diseases including zoonoses.

Data which WHO puts together are mainly about *Mycobacterium tuberculosis*, as WHO is organization for human health issues. However, also other subspecies of *Mycobacteria* might cause infections disease in human (for example *Mycobacterium bovis* as one of the Mycobacterium tuberculosis complex or subsp.of *Mycobacterium avium* etc.). [49]

Nevertheless, in 1950 the public health importance of *Mycobacterium bovis* was recognized by WHO. It was said, that there is a seriousness of human infection with bovine tuberculosis in countries where the disease is prevalent in cattle. The danger of transmission of infection consists in direct contact between infected cattle, farm workers and their families, as well as from infected food products. Since that time, bovine TB was almost eliminated in several industrialized countries, however, only in very few developing countries. [49]

More recently, WHO has been involved in zoonotic TB control and activities through Division of Emerging and other Communicable disease Surveillance and Control and Veterinary Public Health program of the WHO Regional Office for the American, Pan American Health Organization etc. and has organized and coordinated a working group of experts from countries worldwide. Their subjects are epidemiology, public health aspects, control, and research on zoonotic TB. [49, 50]

CHAPTER 3

SADC- South African Development Community

3.1. SADC general characteristic and history

The Southern African Development Community was formed as The Southern African Development Coordination Conference (SADCC) by Governments of the nine Southern African countries, namely Angola, Botswana, Lesotho, Malawi, Mozambique, Swaziland, Tanzania, Zambia and Zimbabwe in Lusaka, Zambia, in April 1st , 1980 and "Lusaka Declaration- Southern Africa: Towards Economic Liberation" was adopted. The main aim of SADCC was to coordinating development projects in order to lessen economic dependence on the then apartheid South Africa. [51]

Nevetheless, there were also other objectives, namely:

- to implement programmes and projects with national and regional impact
- to mobilise Member States' resources, in the quest for collective self-reliance
- to secure international understanding and support [51]

The idea of establishing SADC was the result of long process of consultations of leaders of Southern Africa. From 1977 active consultations were undertaken by representatives of the Frontline States, culminating in a meeting of Foreign Ministries of the Frontline States in Gaborone, in May 1979, which called for a meeting of ministers responsible for economic development. The meeting was then convened in Arusha, Tanzania, in 1979 and led to the birth to the Southern African Development Co-ordination Conference a year later. [51]

The transformation from SADCC to SADC happened in Windhoek, Namibia on August 17, 1992. The Declaration and Treaty establishing Development Community (SADC) from the Coordinating Conference (SADCC) was signed at the Summit of Heads of State and Government. [51]

Within the change of SADCC to SADC, there was need to shift the focus of the organisation from co-ordination of development projects to a more complex task of integrating the economies of member States. [51]

SADC and its member States are expected to act according to the following principles: [51]

- Sovereign equality of all member States;
- Solidarity, peace and security;
- Human rights, democracy, and the rule of law;
- Equity, balance and mutual benefit;
- Peaceful settlement of disputes

The objectives of SADC are to: [51]

- Achieve development and economic growth, alleviate poverty, enhance the standard and quality of life of the people of Southern Africa and support the socially disadvantaged through regional integration;
- Evolve common political values, systems and institutions;
- Promote and defend peace and security;
- Promote self-sustaining development on the basis of collective self-reliance, and the interdependence of Member States;
- Achieve complementarity between national and regional strategies and programmes;
- Promote and maximise productive employment and utilisation of resources of the Region;
- Achieve sustainable utilisation of natural resources and effective protection of the environment;
- Strengthen and consolidate the long standing historical, social and cultural affinities and links among the people of the Region.

The ultimate objective of SADC, the Community is, therefore, to build a Region in which there will be a high degree of harmonisation and rationalisation to enable the pooling of resources to achieve collective self-reliance in order to improve the living standards of the people of the region. [51]

Nowadays, SADC has 14 Member States, namely Angola, Botswana, the Democratic Republic of Congo, Lesotho, Madagascar, Malawi, Mauritius, Mozambique, Namibia, South Africa, Swaziland, United Republic of Tanzania, Zambia and Zimbabwe. [51]

SADC headquarters are located in Gaborone, Botswana. The Chairperson of SADC is His Excellency Mr. Levy Patrick Mwanawasa, President of the Republic of Zambia and the Executive Secretary for the SADC is Mr. Tomaz Augusto Salomão. [51]

3.2. SADC Institutions, FANR

3.2.1. The Institutions of SADC

The Institutions of SADC are: [51]

- Summit, the ultimate policy-making institution of SADC. It is responsible for the overall policy direction and control of functions of the Community
- The TROIKA, the Extra-Ordinary Summit decided to formalise the practice of a Troika system consisting of the Chair, Incoming Chair and the Outgoing Chair of SADC. This system has enabled the Organisation to execute tasks and implement decisions expeditiously as well as provide policy direction to SADC Institutions in period between regular SADC meetings.
- Organ on Politics, Defence and Security, beside other terms; the structure, operations and functions of the Organ shall be regulated by the Protocol on Politics, Defence and Security Cooperation
- Council of Ministers, this Council is responsible for overseeing the functioning and development of SADC and ensuring that policies are properly implemented.
- Integrated Committee of Ministers, aimed at ensuring proper policy guidance, coordination and harmonization of cross-sectoral activities
- Tribunal, will ensure adherence to, and proper interpretation of the provisions of the SADC Treaty and subsidiary instruments, and to adjudicate upon disputes, referred to it.

- SADC National Committees, shall be composed of key stakeholders notably government, private sector and civil society in member States. Their main functions will be to provide inputs at the national level in the formulation of regional policies, strategies, SPA as well as coordinate and oversee the implementation of the these programmes at the national level. The Committees shall also be responsible for the initiation of projects and issue papers as an input to the preparation of the Regional Indicative Development Plan.
- Standing Committee of Senior Officials, this Committee is a technical advisory committee to the Council.
- Secretariat, is the principal executive institution of SADC responsible for strategic planning, co-ordination and management of SADC programmes. It is headed by an Executive Secretary and has its headquarters in Gaborone, Botswana.
- Commissions and Sector Coordinating Units (SCUS), the Extra-Ordinary Summit agreed that SCUs and Commissions should be phased out within a period not exceeding two years.

3.2.2. FANR

At the Secretariat, SADC has four Directorates, namely: [51]

- Food, Agriculture and Natural Resources (FANR)
- Trade, Industry, Finance and Investment (TIFI)
- Infrastructure and Services (I&S)
- Social and Human Development & Special Programmes (SHD&SP)

Because of the theme of this bachelor thesis, "*Incidence and prevalence of Mycobacterium bovis in SADC countries*", and therefore agricultural topic, special attention will be given to the Food, Agriculture and Natural Resources (FANR) Directorate.

The main function of FANR is the coordination and harmonization of agricultural policies and programmes in the SADC region, in line with priorities in the RISDP. The main focus of FANR is to ensure food availability, access, safety and nutritional value; disaster preparedness for food security; equitable and sustainable use of the environment and natural resources; and strengthening institutional framework and capacity building.[51]

Within the incidence and prevalence of *Mycobacterium bovis* in SADC, are two areas on which FANR focus, namely: ensurance of sustainable food security policies and programmes; and trade in agricultural products. [51]

The FANR programmes are coordinated through the following technical units: [51]

- Agricultural Research and Development
- Agricultural Information Management (AIMS)
- Crop Development
- Environment and Sustainable Development
- Livestock Development
- Natural Resources Management (NRM)

Special attention will be given to Livestock Development, as livestock constitutes an important natural resource of the Southern African Region, with over 60% of the region´s total land area suitable for livestock farming.[51] What is more, livestock, especially cattle, is susceptible to bovine tuberculosis and can be the source of the disease. [10] For this reason, further information about the livestock in SADC is presented.

According to information published on the SADC webpages; the farm animal resources of SADC are rich and immensely diverse. The livestock population in SADC is estimated at 64 million cattle, 39 million sheep, 38 million goats, 7 million pigs, 1 million equines and 380 million poultry. An estimated 75% out of the above livestock population is kept under smallholder traditional systems. Traditionally, farm animals are a source of food, skins, fertilizer, traction power, medicine and other raw materials. [51]

The information on SADC webpages also show that despite the livestock sector offers the region an opportunity for accelerated economic growth, diversification and increased trade; poor animal disease control and husbandry, lack of marketing infrastructure and information, lack of harmonised policy and strategy and inadequate capacity for coordination are hindering achieving those goals. [51]

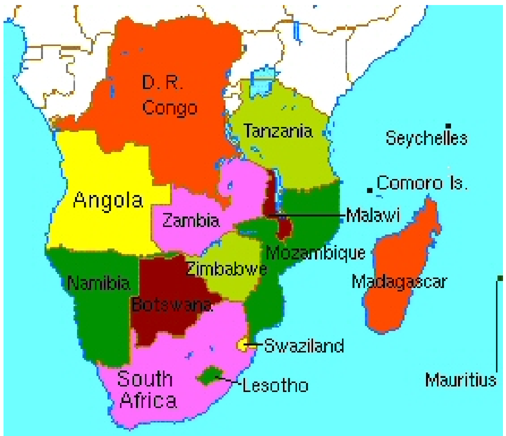
The Livestock Sector Unit (LSU) of the FANR Directorate is the focal point for the coordination of livestock development related activities. [51]

There are many programmes and projects within SADC in the livestock sector, for example Promotion of Regional Integration (PRINT), SADC foot and mouth disease (FMD Programme) and Trans-boundary Animal Diseases (TADs) project. [51]

According to SADC webpages; with these projects and programmes and in close collaboration with the Livestock Technical Committee (LTC) and its sub-committees, the LSU is in a better position to coordinate the livestock sector of the region. [51]

4. Logo of SADC

(Addapted from: http://bp2.blogger.com/_OuY663KPrjY/RgzFPdqX3UI/AAAAAAAAAHE/1KKf0olMhbE/s1600-h/sadc_logo.gif)



5. Map of SADC countries

(Addapted from: http://www.eia.doe.gov/emeu/cabs/images/SADC.jpg)

CHAPTER 4

INCIDENCE AND PREVALENCE OF *MYCOBACTERIUM BOVIS*

4.1. Incidence and prevalence of *Mycobacterium bovis* in the world and its eradication programs and monitoring as paradigm for SADC countries

4.1.1. World situation

Bovine tuberculosis, caused by *Mycobacterium bovis*, is a well – known zoonotis disease which occurs worldwide. Since discovery that *Mycobacterium bovis* is of danger for human (by the end of 19th century, British Royal Commission) and therefore state of public health risk, most developed nations have embarked on campaigns to eradicate *M. bovis* from cattle population or at least to control the spread of infection. [20, 25, 28]

It was shown, that humans could be infected by drinking contaminated milk, with the resulting disease commonly manifesting as lymphadenitis in children, or via inhalation of droplet nuclei produced by sick cattle, which could result in pulmonary disease. Therefore, *Mycobacterium bovis* eradication programmes were begun in cattle herds, along with the widespread pasteurization of dairy products. [25, 31]

The incidence of human infection with *M. bovis* has been reduced to low levels in countries where tuberculosis eradication programmes have been implemented in cattle. The measures produced a sharp decline in the incidence of human *M. bovis* infection. By the 1990s less than 1% of human tuberculosis cases in industrialized countries were caused by this organism. In addition, pasteurization of milk has eliminated exposure of humans to infection from dairy products. [25]

This shows, that pasteurization of milk and other veterinary precautions are of big importance, not only for human health, but what is really important, veterinary precautions are neccesary also for cattle health (or others susceptible animals), as infection of *Mycobacterium bovis* can spread in herds easily and the disease continues to cause production losses when poorly controled. Quite important is the fact, that not only human can get this disease from animals, but human can be also carrier of this infection and can transmit this disease to animals. [25, 31]

Infection of *Mycobacterium bovis* in cattle not only affects health of the individual animal and significantly reduces their productivity, but, according to veterinary legislative (of EU, OIE etc.), infected animal or any animal from infected herd can´t be used for food product or for trade purposes (food product- for example milk for human comsumption- see directive of EU number 64/432/EHS- terms for trade with livestock and hygienic standard for milk products).

Bovine tuberculosis was classified by the Office International des Epizootes as a List B disease, a disease which is considered to be of socio-economic or public health importance within countries and of significance to the international trade of animals and animal products. This mean that infection of *Mycobacterium bovis* has also big economic impact on economic lost and is barrier within international trade for countries or areas where Bovine tuberculosis is widely spread. [28, 48, 52]

Consequently, the production losses due to bovine tuberculosis chronic progressive nature were other motive, why eradication programmes were necessary and why they have been introduced in many countries. Nevertheless, the success of eradication and control programmes has been mixed, as *Mycobacterium bovis* infects not only cattle, but also other animal species, both domesticated and wild and this range of hosts may complicate (and complicates) attempts to control or eradicate the disease in cattle. [10, 31, 32, 35, 36]

What is more, when eradication programmes are successful, infections in cattle caused by other subspecies, namely by members of the *M. avium* complex and by other saprophytic mycobacteria are occasionally encountered. [10]

However, in some countries of the world bovine tuberculosis has been eradicated (for example in the Czech Republic, and thus state as bovine tuberculosis free country), and in some countries of the world bovine tuberculosis have never been reported (French Guiana, Greenland, New Caledonia, Sri Lanka, St. Kitts and Nevis, St. Vincent and the Grenadines, Wallis and Futuna Islands). Nevertheless, in some of developed countries, such as Great Britain, bovine tuberculosis is still major problem. There was “fall and rise” of bovine tuberculosis in Great Britain, due to lack of consistent eradication programmes and problems with bovine tuberculosis in wildlife, especially badger. [36, 53] The same problem may happen while eradicating bovine tuberculosis from other countries, such as USA, where deer may be of wildlife source importance, and the same brushtail possums for Australia as buffalo for Africa. [32, 37, 46,] What is more, in most developing countries the surveillance and control activities within bovine TB are often inadequate or unavailable. Many epidemiologic and public health aspect of infection therefore remain largely unknown. [28, 46]

Thus, the major difference between developed and developing countries is the financial and other resources that the country has for eradicating bovine tuberculosis. According this, needless to say, the incidence and prevalence of *Mycobacterium bovis* infections occurs.

Description of the incidence and prevalence of bovine tuberculosis in selected countries of the world and their eradication or other programs that were run are described below. Some of them show great success while eradicating bovine tuberculosis, which may encouraged SADC countries to run these programs too. However, as already mentioned above, wildlife reservoir of *Mycobacterium bovis* might be, and somewhere already is, barrier in eradication of bovine tuberculosis. Other fact, which will be described later, is the incidence of HIV/AIDS infection in Africa, which complicates the *Mycobacterium bovis* infection in man.

For the overview, map showing incidence of bovine tuberculosis in the world from 2005 until 2007 is added (*see annexes 2.1.-2.6.)*.

4.1.2. Incidence and prevalence of bovine tuberculosis in selected areas

4.1.2.1. NORTH AMERICA:

4.1.2.1.1. UNITED STATES OF AMERICA

USA is the coutry, where bovine tuberculosis eradication programmes have been already made. Important to say, The National Tuberculosis (TB, *Mycobacterium bovis*) eradication campaign in the United States is of an economic and animal health success. This success is manifest in the low occurrence of TB in U.S. cattle, bison, captive cervids and swine today. The reduction or elimination of TB´s burden is a perpetual benefit that all subsequent generations realize. [37]

The U.S eradication program has improved the welfare of consumers and producers alike. When the program began in 1917, bovine tuberculosis occurred within a substantial proportion of cattle. [37] Firstly not only of big economical losts and veterinary health problems within cattle herds and cattle industry in general, but also of inflicting terrible consequences on humans via unpasterized milk, the bovine tuberculosis eradication program decline these facts and finally, the benefit of reducing of the occurrence of TB among cattle is a reduction in losses caused by the TB bacterium. The true economic return of the TB program is estimated to be between $ 13 and $ 55 billion (from 1917 to 2003). [37]

As for the prevalence; since 1917 the estimated prevalence of infected U.S. cattle has declined from about 5% to about 0.001%. Early estimates of prevalence were primarily based on individual-animal testing results. The program was focused on individual-animal testing from 1917 through 1959, and prevalence was estimated as the number of reactors detected divided by the number of cattle tested in a given year. Since 1959, TB surveillance has shifted to a much greater reliance on slaughter inspection of carcasses. [37]

The prevalence of TB-infected cattle has decreased by 90% for each 20 years of the program. For example, between 20th year of the program (1937) and the 40th year of the program (1957), the prevalence decreased by 90%, from approximately 1% to 0.1%. However, recent estimates for the 84th –86th years of the program (2001-2003) suggest dramatically lower prevalence levels than the trend predict. [37] Despite this fact, it was shown, that bovine tuberculosis eradication programs are of big importance and have its purpose.

Incidence of bovine tuberculosis (*by number of animals*) in USA 2005-2007:

Species and Year	Susceptible	Cases	Deaths	Destroyed	Slaughtered
2007 cattle	13 984	9		1630	11 827
2006 cattle	5867	6		2112	
2005 cattle	14 110	9		8550	

(by OIE, WAHID, online on 18.4.2008)

4.1.2.1.2. CANADA

Koller-Johnes *et.al*. in the recent study described, that after almost 100 years of effort and financial investment by Canadian taxpayers and livestock owners, all livestock herds in Canada, except those in small area of Manitoba surrounding Riding Mountain National Park, are now officially free from bovine tuberculosis. [35]

As for the Riding Mountain Area, it was said, that the problem with eradication of bovine tuberculosis is also due to infection in wildlife. The prevalence of bovine tuberculosis in the free-roaming elk population, when the capture-test-removal program was carried in the area between years 2003-2005, was estimated to be between 1% and 5%. [35]

Incidence of bovine tuberculosis in Canada 2005-2007:

Disease absent *(by OIE, WAHID, online on 18.4.2008)*

4.1.2.2. LATIN AMERICA AND CARRIBEAN:

In this part of the world, *Mycobacterium bovis* is spread significantly too. Nowadays, in most of Latin America countries, pasterization of milk is common, but the quality control of this process is not always complete and realiable, and what is more, the coverage is rather low in certain areas, meaning that a part of the population continues consuming unpasterized milk. Aerogenic infection is till quite frequent among cattle industries and slaughterhouse workers in areas where TB infection in cattle continues to be prevalent. [54]

Incidence and prevalence of the *Mycobacterium bovis* infection between countries differ, in most industrialized of them, human tuberculosis (TB) incidence ranges between 2 and 10 / 100,000 and TB in cattle has been either controlled or totally eradicated. Nevertheless, in less developed countries, bovine TB infection in cattle continues being prevalent and human TB incidence rates are relatively high (30 to > 100 /100,000). In these conditions, the relation ship between *M. bovis/ M. tuberculosis* human TB cases can be also steadily maintained, but not because of a decrease in the denminator. [54]

Reported bovine TB cases in humans are either person more than 70 years of age, whose disease is a result of endogenous reactivation of ancient infections, or immigrants from developing countries. A steady relationship between the number of *Mycobacterium bovis* and *Mycobacterium tuberculosis* human TB cases (0.5-1.0%) is observed, mostly because of a constant decrease in the denominator. [54]

According to data collected in a survey in 2003; at least 7% of the total population in 15 Latin America and Caribbean countries that answered the questionare (Mexico, Panama, Costa Rica, Nicaragua, Honduras, Argentina, Chile, Uruguay, Brazil, Paraguay, Peru, Ecuador, Surinam, Cuba and Jamaica) were in close contact with cattle, including meat processing and veterinary services workers, as well as cattle breeders and farmers. This 7% represented some 21 million people. However, the estimated percentage for these 15 countries would be significantly higher if the peasant population were also considered at risk, as a result of their sporadic or frequent contact with bovines and the habit of drinking raw milk. [54]

4.1.2.2.1. <u>ARGENTINA</u>

Infection of *Mycobacterium bovis* is prevalent both in animal and human. According to study performed in 1982-1984, it was shown, that *M. bovis* was the origin of human disease in 0,5% of all TB cases diagnosed by culture, ranging between 2% in Santa Fe and 0,04% in the northwest of the country, where cattle breeding is not frequent. [54]

In the period 1977-2001, nearly 150,000 persons were investigated for TB. The average percentage of cases caused by *M. bovis* versus the total cases caused by any mycobacterial species was 2,3% (97 of 4243 cases, range: 0.0-6.0). There was not any trend in the incidence of *M. bovis*. Eighty-three percent of patients who had *M. bovis* isolated were man, in 65% of these cases, a direct working relationship with cattle was proved (rural or slaughterhouse workers, veterinary professionals, and other related activities). All cases presented pulmonary localization. No extrapulmonary TB case caused by *M. bovis* was detected during this period. The mean age of *M. bovis* TB patients was 45 years. The youngest patient diagnosed with bovine TB was a 14-year-old girl. In the period 1980-2001, the incidence rate of TB in Santa Fe decreased from 48.1 to 20.3 / 100,000. Although the total incidence cases in the province showed a clear decreasing trend, the number of cases caused by *M. bovis* or MAC (*Mycobacterium avium complex*) did not present any clear trend, either increasing or decreasing. [54]

The percentage of cases caused by MAC in the same period was 1, 8% (range: 0.8-5.0). In the case of *Mycobacterium bovis*, the random variatio here found could be related to a rather constant risk of infection (endemic TB in cattle, maintained risk for rural and slaughterhouse workers). The infection risk for MAC seems to be also quite constant, possibly as a result of contact with birds and poultry in a population predominantly residing in small towns with a rural enviroment. [54]

In population from big cities, two studies were published in the last decade in Argentina. In La Plata, Ferreyra and Poggio found in 1997 that 1.7% of TB cases were caused by *M. bovis*. In Buenos Aires, among 10,000 patients not suspected of being HIV infected who were studied over an 11-year period, 1981-1991, *Mycobacterium bovis* was the cause of disease in 0.95% of them, and MAC in another 0.32%. Among 240 HIV- positive patients examined in the same laboratory in the period 1985-1991, with mycobacteria isolated by culture, in 0.8% of the patients, the disease was caused by *M. bovis*, and by MAC in another 5.8%. All cases caused by *M. bovis*, either in HIV-infected patients or not, presented pulmonary localization. [54]

Incidence of bovine tuberculosis in Argentina 2005-2007:

Disease present but without quantitative data *(by OIE, WAHID, online on 18.4.2008)*

4.1.2.2.2. MEXICO

According to Ritacco, Sequeira and de Kantor, a study on human case of bovine tuberculosis in San Diego, California, which is conected to rates of TB infection and lesion found predominantly in dairy cattle in Mexico, was made. This study shows that in San diego, 3% of TB cases diagnosed between 1980 and 1991 were caused by *M. bovis*. Of these cases, more than 90% occured in Hispanic persons, about 25% of patients were children, the main site of disease was extrapulmonary, and 54,3% of the patients were born in Mexico. Of all adults with *M. bovis* disease, 30% tested positive to HIV infection. The authors suggest that the relatively high percentage of extrapulmonary *M. bovis* disease-and particularly abdominal disease, which occured nine times more frequently in *M. bovis* than in *M. tuberculosis* cases- could be caused by transmission via ingestion of unpasteurized dairy products. As almost all cases were confined to Hispanic persons born in the United States or Mexico, and a large proportion of them were children, it appears that Mexican dairy herds could be the primary source of *M. bovis* in San Diego County. This combination of HIV and contaminated dairy products was considered a very probable origin for the continuing presence of HIV-associated M. bovis disease in young adults and children. [54]

Moreover, according to LoBue, there was one report which found that 17% of cattle in meat processing plants in Mexico were infected with *Mycobacterium bovis*, up to 30% of milk was not pasterized and the percent of human case of bovine tuberculosis was unknown, however likely to be higher than in USA or Canada. [39]

<u>Icidence of bovine tuberculosis (*by number of animals*) in Mexico 2005-2007</u>:

Species and Year	Susceptible	Cases	Deaths	Destroyed	Slaughtered
2007					
cattle		290			290
2006					
cattle		159			159
2005					
cattle		124			59

(by OIE, WAHID, online on 18.4.2008)

6. Cattle in a private ranch in Coahuila. Mexico

(Addapted from www.profimedia.cz)

4.1.2.3. ASIA

This continent is specialized by its variabibity within bovine tuberculosis incidence and prevalence. In Sri Lanka bovine tuberculosis has never been reported, however, in India, only few kilometres far from Sri Lanka, bovine tuberculosis is spread since 1916. Thus, there are countries of all OIE status, from “bovine tuberculose free” to “confirmed clinical disease” or “disease spread to certain zones”. [53]

4.1.2.3.1. INDIA

As mentioned above, bovine tuberculosis in cattle was considered rare disease until 1916. In the province Punjab, 17.54 per cent from examinated cattle on bovine tuberculosis were positive in 1917. Incidences of bovine tuberculosis in other species were also of significance. In Bombay, 13.3% of 120 examinated buffaloes were bovine tuberculosis positive in 1944. Swine and bullock also show positive results for TB. According to Thoen et.al., from the published reports, the highest occurrence of bovine tuberculosis in cattle was 59.57% from 141 examinated animals in Uttar Pradesh, 1998. Other tested animal, which showed positive TB diagnostic were sheep, goat and horse, despite the fact, that this infection was firstly supposed as rare. Until 1932, not a single case of caprin or ovine TB was reported, nevertheless, from 0.64% to 0.87% incidence in goat and from 3.7% to 6.3% incidence in sheep was later find. The incidence of TB in camels in Bikaner was reported as 2.6% by the years 1966-1967. Also infection in slaughtered pigs was find. Bombay, Jullunder and Rawalpindi reported 17.7%, 5.3%, 7.4% TB infections in slaughtered pigs. [55]

Incidence of bovine tuberculosis in India 2005-2007:

Disease present but without quantitative data *(by OIE, WAHID, online on 18.4.2008)*

4.1.2.4. OCEANIA

New Caledonia and Wallis and Futuna Islands are states from Oceania where bovine tuberculosis has never been reported. On the other hand, in Australia bovine tuberculosis was common since the cattle breeding until succesful eradication and in New Zealand the incidence of bovine tuberculosis is present still. [53, 56]

4.1.2.4.1. AUSTRALIA AND NEW ZEALAND

Cattle were introduced about 200 years ago, early in the British settlement of Australia and New Zealand. There are approximately 23 million cattle in 159 000 herds in Australia. The cattle are mostly British breeds but there are substantial infusions of Zebu type blood in northern Australia. There are 47 000 herds in New Zealand with 8.36 million cattle of which 45% are dairy breeds and 55% are beef (mostly British) breeds. There are several other animals susceptible to bovine tuberculosis, such as water buffalo, banteng, red deer, elk, red crossed and fallow deer. By the 20th century, bovine TB was well established and a serious public health problem, especially in children through ingestion of tuberculous milk. Therefore, bovine tuberculosis testing and later on eradication programs had started. Testing programs were introduced in the various States of Australia progressively from the early 1900s. From the 1940s compulsory testing of raw milk supplying dairy herds was required. During the 1960s, the State and Commonwealth governments negotiated the Australian National Brucellosis and Tuberculosis Eradication Campaign (BTEC) which commenced on 1 July 1970. Both countries by 1970 had launched national TB eradication campaigns for cattle. The driving force for the compulsory national TB cattle eradication campaigns in both countries was similar: public health, by then a minor concern, productivity loss and the maintenance of access to export markets as the major issue. The successful Australian campaign was based on a sound technical program, with good cattle control and strong industry support. Australia has been declared Impending Free with "No Known Tuberculosis" and a vision of being confirmed biologically free of *M. bovis* by 2008. In contrast, the presence of a significant wildlife reservoir (brushtail possum) of *Mycobacterium bovis* in New Zealand has hindered the eradication of bovine tuberculosis, which show how big problem wildlife reservoir could be. [56]

Incidence of bovine tuberculosis (*by number of animals*) in Australia 2005-2007:

Disease absent *(by OIE, WAHID, online on 18.4.2008)*

Incidence of bovine tuberculosis (*by number of animals*) in New Zealand 2005-2007:

Species and Year	Susceptible	Cases	Deaths	Destroyed	Slaughtered
2007					
cattle	234.777	695			1039
cervidae	12.018	240			635
2006					
cattle	167.916	282			623
cervidae	25.597	88			584
2005					
cattle	234.237	441			915
cervidae	61.817	199			1030

(by OIE, WAHID, online on 18.4.2008)

4.1.2.5. EUROPE

4.1.2.5.1. EUROPEAN UNION

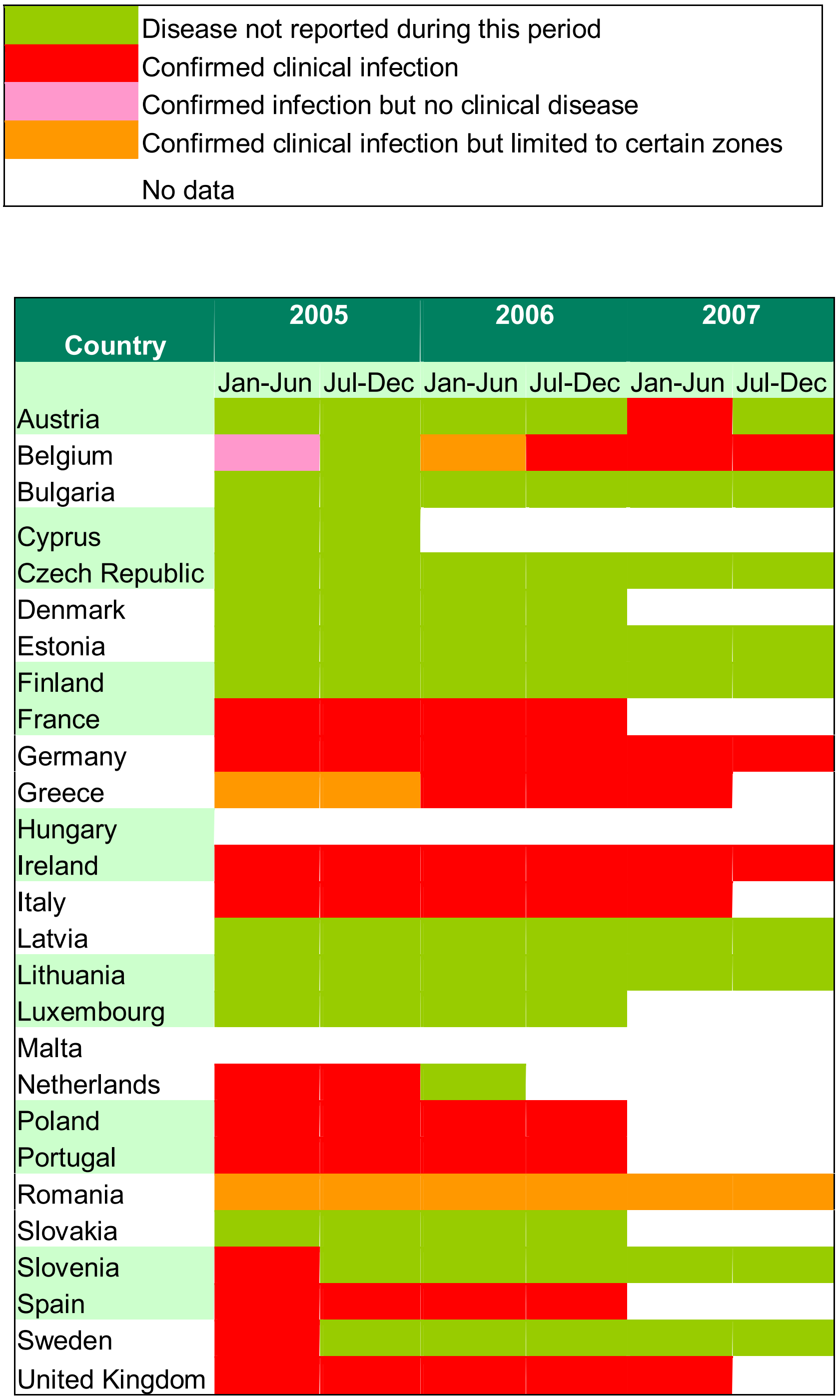
According to Pavlik, bovine tuberculosis has been controled or eliminated in all economically developed countries of Europe. In 1991 high prevalence of bovine tuberculosis was only found in five European Union (EU) States: Spain (herd prevalence 10.8%), France (0.37%), Greece (0.31%), Ireland (8.8%), and Italy (3.71%). According to the definition of the International Animal Health Code of the Office of International Des Epizooties (OIE), a region or state or country is considered free of bovine tuberculosis in cattle provided the herd prevalence does not exceed 0.2%. [57]

Futhermore, within the European Union (based on a Commission decision on 17 December 1996); Member States, and regions of Member States, are considered free of bovine tuberculosis if at least 99.9% of bovine herds have been declared officially tuberculosis-free for at least 10 years, and where bovine tuberculosis has not been detected in each of the last 6 years in more than 1 herd per 10.000 herds in that Member State. These requirements were met by six EU States prior to 11 March 1999: Denmark, Finland, Sweden, the Netherlands, Luxembourg, and Germany. [57]

Next, on 1 May 2004, 10 new European States joined the European Union, with a human population of approximately 72 million people, a land area of 735 090 km^2, and 10.439 million cattle in 1.318 million establishments. Based on geographical and historical aspects, these 10 States can be subdivided into three groups: the three Baltic States (Estonia, Latvia, and Lithuania), the five Central European States (the Czech Republic, Hungary, Poland, Slovakia, and Slovenia) and the two Mediterranean island States (Cyprus and Malta). [57]

By 2008, European Union has 27 members, namely Austria, Belgium, Bulgaria, Cyprus Czech Republic, Denmark, Estonia, Finland, France, Germany, Great Britain, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Lucembourg, Malta, Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, and Sweden. [58]

The incidence of bovine tuberculosis in EU from the year 2005 until 2007 explains following table (1.) *(Addapted from WAHID Interface, OIE)*



European Union has its own legislatives connected to Agriculture, Food Safety, Veterinary Checks, Animal Health, Food Hygiene, Animal Nutrition etc.[58]

For example, the objective of the European Union´s food safety policy is to protect consummer health and interests while guaranteeing the smooth operation of the single market. In order to achieve this objective, the EU ensures that control standards are established and adhered to as regards food and food product hygiene, animal health and welfare, plant health and preventing the risk of contamination from external substances. It also lays down rules on appropriate labelling for these foodstuffs and food products. [58]

There is European Safety Authoority (EFSA), which provides scientific advice and scientific and technical support in all areas impacting on food safety.[59]

Food safety is also connected within international trade. According to EU legislatives; food and feed imported with a view to being placed on the market or exported to a third country must comply with the relevant requirements of EU food law. The European Union and its Member States must contribute to the development of international technical standards for food and feed, as well as for animal health and plant protection.[58, 59]

Council Directive 64/432/EEC of 26 June 1964 on animal health problems affecting intra-Community trade in bovine and swine, besides concerns about bovine animals and swine breeding, production and slaughter, among others definates "tuberculosis-free bovine animal“, "officially tuberculosis-free bovine herd", "epizootic free area", "compulsorily notifiable diseases", "official veterinarian", "exporting country", "country of destination", "region" etc. [58]

This directive besides says, that EU Member States have the option of refusing entry into their territory cattle and pigs that have, or are suspected to have, a contagious disease.[58]

For example, this directive definate, that within trade and slaughter:

Bovine animals and pigs, on the day of loading:

- must not display any clinical sign of disease;
- must not have been obtained from a holding subject to prohibition for animal health reasons;
- must come from a bovine herd officially free of tuberculosis or brucellosis.[58]

Within EU, there are also legislatives and directives, focused on monitoring of zoonoses and zoonotic agents. Bovine tuberculosis is one of the priority disease. [58]

Namely, it is Directive 2003/99/EC of the European Parliament and of the Council of 17 November 2003 on the monitoring of zoonoses and zoonotic agents, amending Council Decision 90/424/EEC and repealing Council Directive 92/117/EEC.[58]

Commission Decision 2006/875/EC of 30 November 2006 approving programmes for the eradication and monitoring of animal diseases, of certain TSEs, and for the prevention of zoonoses presented by the Member States for the year 2007 is also related to bovine tuberculosis in EU. [60]

4.1.2.5.1.1. Detailed characteristic for selected countries

4.1.2.5.1.1.1. GREAT BRITAIN

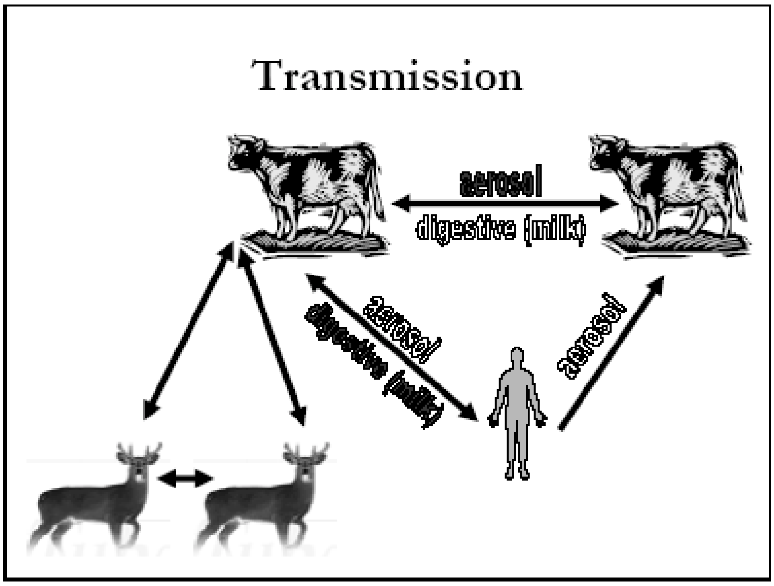
There are many studies on bovine tuberculosis in Great Britain. Bovine tuberculosis in Great Britain continue to be a major economic problem. Despite eradication programmes, disease is still present in livestock, especially cattle and wildlife species, especially badger. [32, 36]

According to Goodchild et al, there was a steady decrease in the prevalence of bovine tuberculosis between 1935 and 1980 (the number of cattle slaughtered annually decreased from 23,000 to less than 1000) nevertheless since then there has been a many-fold increase, with 24,000 head being slaughtered annually between 2002 and 2004, of which 19,700 a year were reactors to the skin test. The role of the badger in the epidemiology of BTB was not acted on until 1975. Despite badger control program halving the incidence of BTB in cattle in 4 years, a further 18 years of control did not prevent a rise in incidence. Since 1990, the number of BTB-lesioned or BTB-infected animals has doubled every 4 years. The cost of control has parallely increased with the incidence of BTB. [36]

According to LoBue, there was a case of badger-cattle-human-human transmission of *Mycobacterium bovis* infection reported in Great Britain. This happenned in the farm diagnosed with *Mycobacterium bovis*. Brother who assisted at veterinary examinations of cattle got infected via airborne (became covered in cow mucus and saliva) from cattle and was diagnosed as AFB smear negative cavitary disease. His sister had no contact with cattle. Despite this was diagnosed as AFB smear negative pulmonary disease. Anybody of them drank unpasteurized milk. Six years prior this incident, there were 5 cattle of 15 that had *Mycobacterium bovis* and were slaughtered. In that time 5 badgers were trapped. Four of them were infected with *Mycobacterium bovis*. Tree years later, 3 of 8 cattle had *Mycobacterium bovis* and herd was slaughtered. One badger with *Mycobacterium bovis* infection was trapped. The transmission was explained as following: badger to cattle via indirect digestion, cattle to human via airborne and human to human via airborne. [39]

According this, the role of wildlife in *Mycobacterium bovis* infection is evident. Beside badger, also role of deer (*Cervidae*) in *Mycobacterium bovis* infection in Great Britain is important. According to Goodchild deer may enhance the role of badgers in the geographical spread of BTB by acting as the longer-distance links in "small-world" networks. The estimate prevalence of *Mycobacterium bovis* in deer is about 1%, however this report is from limited areas of the Southwest of England, where prevalence in cattle and badger is high. Variation in prevalence between species of deer and areas of Great Britain was reported. [36]

The possible transmision of deer-cattle-human infection of Mycobacterium bovis shows the picture number 7.



7. Deer-cattle-human transmission of *Mycobacterium bovis* (Addapted from LoBue, 2008 (citation 39))

OIE reported 22 human cases of bovine tuberculosis on 11th rank in Great Britain in 2005 within zoonoses in humans. This 11th rank represents 0.0369 rates per 100.000 population of bovine tuberculosis in Great Britain in 2005. Same data are for the year 2006; however bovine tuberculosis is on 10th rate. [53] According to Jalava *et al*, between 1993 and 2003 culture-positive human *Mycobacterium bovis* cases identified 315 *Mycobacterium bovis* infections, the mean anual number of cases was 28 (range 12-41). The main reason of infection was consumption of unpasteurized dairy products (49% of the cases) and exposure to the cattle (37% of the cases).[64]

As for the cattle (according to Goodchild) the extent and zoonotic efect of BTB in cattle was recognized in the 1930s, when as many as 40% of cattle in Great Britain were infected. It led to the program of progressively skin-testing herds, slaughtering animals that reacted to the test, and accrediting herds which the disease had been controlled. Within this control, the incidence of bovine tuberculosis was decreasing up to 1970s, stayed constant until the mid of 1980s and then commenced the present pattern of doubling every 4 years.[36]

The average annual costs of the bovine tuberculosis control program in Great Britain, were in total 24.45 millions of pounds in 1996-2000, 30.48 millions of pounds in 2001 and 81.05 millions of pounds in 2002 and 2003. In response to the inceasing incidence of BTB a new control strategy for Great Britain has been planned. [36]

According this it is evident that control of bovine tuberculosis is very expensive and that eradication of bovine tuberculosis isn´t only of public health interest, but also of economic interest. [36]

Incidence of bovine tuberculosis (*by number of animals*) in United Kingdom in 2005-2007:

Species and Year	Susceptible	Cases	Deaths	Destroyed	Slaughtered
2007 cattle		12.802			13.972
2006 cattle					
2005 cattle		25.773			30.099

(by OIE, WAHID, online on 18.4.2008)

Note:

Data from 2007 represents only data from January-June

In 2006 disease was present however no quantitative data were find

4.1.2.5.1.1.2. CZECH REPUBLIC

Czech Republic is important country to noticed, because according to Commision Decision 2004/320/EC of the European Union, Czech Republic was declared as bovine tuberculosis-free country on 31 March 2004. [57]

Bovine tuberculosis was succesfuly eliminated in the Czech Republic in 1968. [61]

According to Pavlik et al, during the postelimination period the incidence of bovine tuberculosis decreased. The rate of bovine tuberculosis incidence in cattle reached 12-16 outbreaks per year during the years 1969-1978. In the next decade, from 1979 to 1988, the incidence of bovine tuberculosis decreased. There were zero outbreaks in the years 1981, 1987 and 1988. Bovine tuberculosis of cattle was observed sporadically (from one to two infected herds per year), and the last reported outbreaks was from 1995. In the years 1989, 1990, 1993 and 1996-2003 no bovine tuberculosis was reported in cattle at all. [57]

Despite this fact, infection in human caused by *Mycobacterium bovis* was repeatedly noticed. The reports from The National Institute of Public Health (NIPH) from 2001 to 2007 in the bulletin „Acta Hygienica, epidemiologica et microbiologica" show the precise data. The information which has been found shows that the incidence was mainly within eldery people. The detailed information is recorded in table (2.).

According to personal written comunication with Mrs.Havelkova, MD (NIPH), about the nationality of patient who were infected with *Mycobacterium bovis* Mrs. Havelkova, MD, said, that "*It is probable that due to small incidence of Mycobacterium bovis in the Czech Republic, all patients were Czech*".

According to Pavlik, within the study on bovine tuberculosis in the human population between the years 1990 and 1999 in the Czech Republic, none patients were under 30 years of age and 83% of the patients were either inhabitants of the rural area or had at least lived in the countryside and worked in farms in their young. [57]

To compare, in the studies between 2001-2007, one case of bovine tuberculosis in patient under 30 years was find.

(2.) <u>Incidence of Mycobacterium bovis in the Czech Republic 2000-2006:</u>

(Addapted from „Acta hygienica, microbiologica et epidemiologica")

Year	M.b. incidence	M.b. isolation	Region and number of cases	Gender and age groups			
				male		female	
2006	1	1	Zlínský - 1	1	60-69	0	
2005	7	2	Karlovarský - 6 Zlínský - 1	0		2	1x 0-9 1x 80-89
2004	3	1	Karlovarský - 2 Liberecký - 1	1	40-49	0	
2003	7	2	Středočeský - 3 Plzeňský - 4	1	60-69	1	40-49
2002	21	4	Praha - 11 Středočeský - 10	1	60-69	3	1x 30-39 2x 80-89
2001	12	5	Středočeský - 10 Moravskoslezský - 2	2	1x 60-69 1x 70-79	3	1x 50-59 2x 70-79
2000	24	5	Středočeský - 22 Severomoravský - 1 Jihomoravský - 1	no data		no data	

Although bovine tuberculosis has been succesfuly eradicated from the cattle population in the Czech Republic, considerable attention should be given to risk factors, such as: infected wild animals manifesting clinical signs of weakness and loss of timidity which may become a source of causal agent of bovine tuberculosis for their self-sacrificing rescuers; wild animals kept in captivity at zoological gardens, and domestic animals like cats, horses, dogs, and other, that may pose the risk of infection for humans; refugees from Third World countries infected with a causal agent of bovine tuberculosis and working on farms may also represent the risk of spreading the infection; and products from infected animals, such as milk and milk products processed from unpasteurized milk, and the total absence of or inconsistent meat inspections in slaughterhouses, as well as inadequate laboratory examination of organs with tuberculous alterations, may leave a dangerous window of infection for humans. [57]

<u>Incidence of bovine tuberculosis in the Czech Republic 2005-2007:</u>

Disease absent (*OIE, WAHID, online on 18.4.2008*)

4.2. Incidence and prevalence of *Mycobacterium bovis* in Africa

4.2.1. Situation in general

Tuberculosis ranks seconds position (after HIV/AIDS) within infectious diseases which are responsible for people deaths worldwide each year. There are more then 7 million new cases and 2 million deaths caused by tuberculosis yearly. What is more, the spread of HIV infection in human is of big importance, as HIV infected man is at the highest risk group who is susceptible to *Mycobacterium bovis* and other Mycobacterium species infection. According to Zinsstag *et.al*, clinical disease caused by TB remains the largest attributable cause of death in HIV-infected individuals who are also infected with TB. TB is responsible for one-third of all deaths of HIV-infected individuals in Africa. [62]

As for sub-Saharan Africa, there are almost 2 million cases of tuberculosis which occur yeach year. Despite this, the role of cattle-derived *Mycobacterium bovis* in rising epidemic of tuberculosis in Africa, fostered by HIV/AIDS, is unknown. Moreover, studies made in Malawi have shown, that areas of high bovine tuberculosis prevalence are not necessarily matched by a contamitant high prevalence of tuberculosis in man. Nevertheless, substantive evidence for significant transmission of *Mycobacterium bovis* in pastoralist communities with close human-to-livestock contact have been made. [62]

Because of considerable and continuing public health significance of *Mycobacterium bovis* infection in humans, meeting on zoonotic tuberculosis was convened by WHO in Geneva in November 1993 and the project protocol to investigate the zoonotic aspects of bovine tuberculosis was elaborated. [62]

However there is still lack of information on *Mycobacterium bo*vis infection in Africa, there is sufficient evidence to indicate that it is widely distributed and is found at high prevalences in some animal population. [62]

Also Bonsu *et al*, said, that although bovine tuberculosis is widespread in African countries, little is known about the actual prevalence and the risk posed to humans. An investigation of cattle in Tanzania indicated a low prevalence rate of tuberculosis but the rate in cattle in nearby Zambia was much higher. There was no information available on the prevalence of bovine tuberculosis and the risk of human infection in Ghana. [63]

According to Zinsstag *et al*, the public health threat of tuberculosis in Africa requires urgent investigation through collaborative veterinary/medical research programs. The available literature on *Mycobacterium bovis* in Africa is focused on Bacille Calmette-Guerin (BCG) vaccination, public health, milk, livestock, game, or biological aspects, but very few reports mention isolation from humans and animals in the same setting. In addition, very little is known about the antibiotic resistance of *Mycobacterium bovis* and mycobacteria in general in African countries. [62]

It was shown, that among other reasons for the relatively little attention paid to *Mycobacterium bovis* in Africa is the limited diagnostic capacity. [62]

According to Zinsstag *et al*, in most countries, the diagnosis of tuberculosis relies on sputum microscopy alone. If strains were isolated, they grown on media that are not suitable for *Mycobacterium bovis*, and methods for molecular characterization are rarely available. Only very few veterinary mycobacteriology laboratories exist on the continent.[62]

According to Zinsstag *et.al*; Njanpop-Lafourcade *et al*, for example, reported on molecular strain were identified recently in Chad. In Tanzania, similar spoligotype patterns of *Mycobacterium bovis* could be demonstrated in livestock and humans. At present, the variable number of tandem repeats method is being examinated for its use in Africa and is further compared to microarray and the the analysis of genomic deletions.[62]

In general, it was prove, that extensive pastoral systems may be less favorable for *Mycobacterium bovis* transmission between animals than intensive industrial agricultural systems. Nevertheless, studies in Chad show that there was relatively high prevalence of tuberculin-positive animals in pastoral nomadic settings. [62] This show, that Africa needs special attention, as some general presumptive facts are not always true in case of Africa.

Nowadays, a lot of people in Africa are migrating from rural areas to peri-urban areas of larger cities and intensive dairy production is a livelihod for thousands of people. According to Zinsstag *et al*, cross breeding with exotic breeds is more and more widely practiced. Milk production systes are still mostly tradictional, with little disease control in live animals and the milk. Milk is usually consumed after spontaneous fermentation, but raw milk consumption occurs frequently too, and isolation of *M. bovis* has been reported in raw milk. [62]

Although cattle is the main host for bovine tuberculosis in Africa, *Mycobacterium bovis* was also isolated from small ruminants, camels, and many different wildlife species. [32, 62]

Therefore, while eradicating bovine tuberculosis in Africa, programmes to eliminate or control bovine tuberculosis should be oriented not only to cattle.

What is more, according to Zinsstag *et al*, countries with endemic bovine tuberculosis implement various control efforts, but in most cases they are unable to compensate farmers for culled livestock. Attempts to protect cattle against tuberculosis by BCG vaccination in the 1970s had no success, but new trials are ongoing in Madagascar and are planned in Etiopia. [62]

For the overview, map showing incidence of bovine tuberculosis in Africa between 2005-2007 is added (see annexes 3.1.-3.6.)

4.2.2. West and central Africa

According to Zinsstag et.al, in West and Central Africa, bovine tuberculosis in humans seems to be specially prevalent among the nomadic Fulani tribe, who herd their cattle across the country borders of nations. They use milk, which they do not usually boil, from their cattle for food. Cross-border migration of livestock is allowed under the treaty of the Economic Community of West African States. [62]

4.2.2.1. Chad

According to Zinsstag *et.al*, there is only very little information on *Mycobacterium bovis* prevalece in chadian livestock. What is more, they consist mostly of unpublished reports.[62]

Nevertheless, according to Zinsstag *et.al.*, a prevalence of 17 % using the *Mycobacterium bovis* PPD tuberculin test was find. These *Mycobacterium bovis* estimates are differentiated against *Mycobacterium avium*, but it is not clear to what extent *Mycobacterium farcinogenes* cross reacts. Accordig this, Zinsstag *et.al* wrote, that the quantification of *Mycobacterium bovis* in livestock is thus even more important. Chad reported 949 cases of human tuberculosis, for a total population of nearly 7 million in 1996, and is suspected to have an incidence of tuberculosis ranging from 100 to 250 per 100,000. In this situation, we expect an incidence rate of *Mycobacterium bovis*- derived tuberculosis of 4-25 per 100,000, depending on exposure to livestock and milk. [62]

Futhermore, there was an report of 10% smear positive cases from 1400 cases registered at the General Hospital in N´Djaména. This was find out after the Directly Observed Treatment Short Course (the World Health Organization-recommended control strategy).[62]

What is more bovine tuberculosis was one of the main causes for carcass condemnation at the largest slaughterhouse (Société Moderne des Abattoirs) in N´Djaména, Chad. During a prospective study from July to August 2002 at the slaughterhouse, meat inspectors condemned 727 of 10,000 cattle carcasses because of tuberculosis-like lesions. Microbiological examination of 201 lesions from 75 Mbororo zebu and 124 Arab zebu carcasses confirmed bovine tuberculosis by strain isolation. A significantly higher proportion of Mbororo than Arab carcasses were declared entirely unfit for consumption in comparison to partial condemnation. *Mycobacterium bovis* was more often cultured from specimens of Mbororo cattle than of Arab cattle. Spoligotyping of 56 *Mycobacterium bovis* isolated showed a lack of the direct repeat in 30 of the isolates.[62]

<u>Incidence of bovine tuberculosis in Chad 2005-2007:</u>

No information available for this disease *(by OIE, WAHID, online on 18.4.2008)*

4.2.2.2. Ghana

According to Zinsstag *et.al*, Ghana continues to make dramatic progress in the reduction of tuberculosis in both human and livestock populations, however, the advent of HIV/AIDS in the country has led to the county´s disproportionate share of bovine TB in man. [62]

In 1984 and 1985, the prevalence of human cases of tuberculosis was 3%. Between 1983 and 1986, single bovine caudal fold tests were conducted in several ranches in northern Ghana, using PPD (purified protein derivate) tuberculin imported from Weybridge, England, the TB prevalence obtained was between 0% and 2%. [62]

According to Bonsu *et al*, the Ghanaian Government, through its peri-urban dairy cattle development project was promoting the use of milk and dairy products from local cows in selected districts of the country, including the Dangme-West district of the Greater Accra region. [63]

This survey was undertaken to determine the prevalence of tuberculosis infection in cattle and to assess the level of awareness with regard to the risks through milk consumption. The standard single intradermal comparative tuberculin test (SCITT) using purified protein derivative (PPD) of *M. bovis* and *M. avium* was used to detect cattle infected with *M. bovis*. [63]

According to Zinsstag *et al*, on over 2860 animals were tested in this study and the prevalence was find between 10.8% and 19%. [62]

According to Bonsu *et.al.* the study established the prevalence of a 13.8% infection in cattle in the district although the prevalence was as high as 50% in some kraals. Prevalence was highest in the Ningo sub-district (19.0%), followed by Dodowa, the district capital (14.0%), while the other two sub-districts, Prampram and Osudoku had lower rates of 11.3 and 10.8%, respectively. [63]

In detail, according to Bonsu *et al*; cattle of all ages and both sexes were affected, but the prevalence in cows was twice as high as that in heifers or bulls. The study also established that there is a considerable lack of knowledge about bovine tuberculosis among cattle owners and herdsmen in the community and that milk is often used untreated, thus increasing the risk of human infection. [63]

As for the lack of knowledge about bovine tuberculosis in Dangme-West district of Ghana in detail, according to Bonsu *et al.,* all the 30 herdsmen interviewed said they did not know that tuberculosis could be transmitted from cattle to man. None of them knew that cattle with tuberculosis could serve as sources of infection for man. Out of the 30 herdsmen interviewed, 25 said they do not boil their milk before use, five of them said they boil the milk simply because they have been told to do so. Most cattle owners interviewed said they knew or had heard about tuberculosis, six knew the clinical signs of the disease, and eight said they knew that tuberculosis can be transmitted from cattle to man. Despite this none of them, however, boiled milk before use. [63]

This show, how important is survey on bovine tuberculosis awareness within herdsmen and cattle owners not only in Ghana, but probably anywhere in LDC. Before starting any eradication project, questionnaire on general public awareness about bovine tuberculosis would be definetely usefull. Nevertheless later on it is necessary to compare it with real situation what herdsmen or cattle owners really do. According this, precautions or educational campaig on bovine tuberculosis should be made before starting any eradication program or project.

Zinsstag *et.al.* in the study said, that though the cattle owners and herdsmen in the communities often consume unpasterized milk, the prevalence of bovine tuberculosis in human populations is not know. [62]

Incidence of bovine tuberculosis in Ghana 2005-2007: *(by OIE, WAHID, online on 12.5.2008)*

Species and Year	Susceptible	Cases	Deaths	Destroyed	Slaughtered
2007					
cattle	62	18			18
2006					
cattle	585	46			46
2005					
cattle	243	11			11

4.2.3. Easter and Southern Africa

Bovine tuberculosis in known to be endemic in most Eastern and Southern Africa. There is general awareness that the disease is found in various mammalian species ranging from domesticated animals to wildlife. There are many studies about the mechanism of disease transmission from animals hosts to human population made in this region. Despite this the exact incidence of human *Mycobacterium bovis* infection in this region is not known. This is mainly because of lack of diagnostic facilities to determine species of mycobacteria involved in human tuberculosis cases. According to Zinsstag *et.al*, this scenario has led to the underreporting of cases of *M. bovis* in humans. The lack of disease control measures allows for unrestricted progression of the disease and potential transmision to humans through consumption of raw milk, undercooked and sometimes raw blood and meat (reported in Tanzania), nonpasteurized milk and products from uninspected and informally (privately) slaughtered cattle, or directly through close animal-human contact. This currently unacknowledged risk to human health, locally, is of great concern to researches in the Southern and Eastern African countries. [62]

Moreover the occurence of *Mycobacterium bovis* in humans, against the background of the rising HIV/AIDS incidence in the region, implies that the risk of spillover of zoonotic tuberculosis to rural communities is rapidly increasing. Various researches have reported on scientific evidendce for acceleration of pathogen replication during coinfection of *Mycobacterium tuberculosis* and HIV and because of the close relationship among *Mycobacterium tuberculosis* complex mycobacteria, the same can be assumed for *Mycobacterium bovis*. At present, 50% of new TB cases can be attributed to HIV infection. For example, in the Hlabisa hospital, situated in the district where *Mycobacterium bovis* is endemic, Hluhluwe-Umfolozi Park, in Kwazulu/Natal South Africa, is surrounded by more than 100,000 head of communal cattle, and the number of HIV-positive patients with tuberculosis increased from six in 1989 to 451 as early as in 1993. Similarly, in Tanzania between 1991 and 1998, up to 44% of tuberculosis cases were coinfected with HIV. [62]

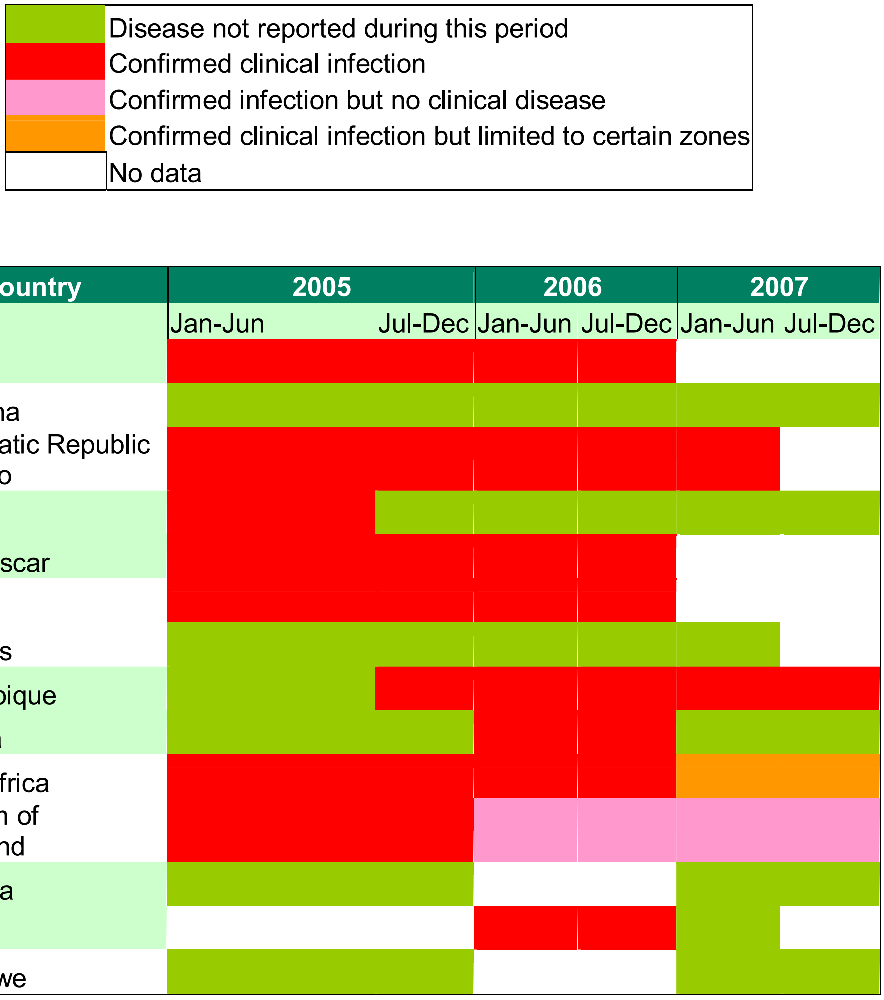
As this bachelor thesis is oriented to the incidence and prevalence of *Mycobacterium bovis* in SADC, which belong to Southern Africa, coutry reports are in next subhead.

4.2.3.1. Situation in the coutries of SADC

SADC countries are situated, as the name already says, in the Southern Africa. Therefore, the general situation about incidence and prevalence of *Mycobacterium bovis* was described in the previous subhead.

The following table presents the disease timelines of bovine tuberculosis in SADC countries from the year 2005 until 2007.

Disease timelines: Bovine tuberculosis (*addapted from WAHID Interface, OIE)*



4.2.3.1.1. ANGOLA

Last reported cattle population in Angola was 4.525.000 with the density (units per square kilometre) of 3.63 in 2005. *(WAHID, OIE, online on 8.5.2008)*

Last report for bovine tuberculosis in Angola was in July-December 2005 and clinical disease was demonstrated. *(Disease situation, WAHID, OIE, online on 8.5.2008)*

Incidence of bovine tuberculosis (*by number of animals*) in Angola 2005-2007:

Species and Year	Susceptible	Cases	Deaths	Destroyed	Slaughtered
2007					
cattle					
2006					
cattle	1355	100	1	2	884
2005					
cattle	1983	34		2	1370

(by OIE, WAHID, online on 18.4.2008)

4.2.3.1.2. BOTSWANA

Cattle population in Botswana in 2005 was 1.815.365 with the density (units per square kilometre) of 3.02. *(WAHID, OIE, online on 8.5.2008)*

Last report for bovine tuberculosis in Botswana was in July-December 2007. No surveillance was specified. *(Disease situation, WAHID, OIE, online on 8.5.2008)*

Incidence of bovine tuberculosis (*by number of animals*) in Botswana 2005-2007:

Disease absent *(by OIE, WAHID, online on 18.4.2008)*

4.2.3.1.3. DEMOCRATIC REPUBLIC OF CONGO

Cattle population in the Democratic Republic of Congo in 2005 was 756.940 with the density (units per square kilometre) of 0.32. *(WAHID, OIE, online on 8.5.2008)*

Last report for bovine tuberculosis in Democratic Republic of Congo was in January-June 2007 and clinical disease was demonstrated. *(Disease situation, WAHID, OIE, online on 8.5.2008)*

Incidence of bovine tuberculosis (*by number of animals*) in Democratic Republic of Congo 2005-2007:

Disease present but without quantitative data *(by OIE, WAHID, online on 18.4.2008)*

4.2.3.1.4. LESOTHO

Cattle population in Lesotho in 2005 was 675.504 with the density (units per square kilometre) of 22.25. *(WAHID, OIE, online on 8.5.2008)*

Last report for bovine tuberculosis in Lesotho was in July-December 2007. No surveillance was specified. Last occurrence of bovine tuberculosis was in 2005. *(Disease situation, WAHID, OIE, online on 8.5.2008)*

Incidence of bovine tuberculosis (*by number of animals*) in Lesotho 2005-2007:

General status was of "Disease absent", however, there was one oubreak on bovine tuberculosis from May, 2005:

Species and Year	Susceptible	Cases	Deaths	Destroyed	Slaughtered
2007 cattle					
2006 cattle					
2005 cattle	6	1	1		

(by OIE, WAHID, online on 18.4.2008)

4.2.3.1.5. MADAGASCAR

Cattle population in Madagascar in 2005 was 8.105.000 with the density (units per square kilometre) of 13.81. *(WAHID, OIE, online on 8.5.2008)*

Last report for bovine tuberculosis in Madagascar was in July-December 2006 and clinical disease was demonstrated. *(Disease situation, WAHID, OIE, online on 8.5.2008)*

Incidence of bovine tuberculosis (*by number of animals*) in Madagascar 2005-2007:

Disease present but without quantitative data *(by OIE, WAHID, online on 18.4.2008)*

4.2.3.1.6. MALAWI

Cattle population in Malawi in 2005 was 777.846 with the density (units per square kilometre) of 6.57. *(WAHID, OIE, online on 8.5.2008)*

Last report for bovine tuberculosis in Malawi was in July-December 2006 and clinical disease was demonstrated. *(Disease situation, WAHID, OIE, online on 8.5.2008)*

Incidence of bovine tuberculosis (*by number of animals*) in Malawi 2005-2007:

Species and Year	Susceptible	Cases	Deaths	Destroyed	Slaughtered
2007					
cattle					
goat					
2006					
cattle		79			
goat		25			
2005					
cattle		563	1		
goat					

(by OIE, WAHID, online on 18.4.2008)

4.2.3.1.7. MAURITIUS

Cattle population in Mauritius in 2006 (*no data for the year 2005 were available*) was 7000 with the density (units per square kilometre) of 3.43. *(WAHID, OIE, online on 8.5.2008)*

Last report for bovine tuberculosis in Mauritius was in January-June 2007. No surveillance was specified. Last occurrence of bovine tuberculosis was in 2000. *(Disease situation, WAHID, OIE, online on 8.5.2008)*

Incidence of bovine tuberculosis in Mauritius 2005-2007:

Disease absent *(by OIE, WAHID, online on 18.4.2008)*

4.2.3.1.8. MOZAMBIQUE

Cattle population in Mozambique in 2005 was 1.363.854 with the density (units per square kilometre) of 1.70. *(WAHID, OIE, online on 8.5.2008)*

Last report for bovine tuberculosis in Mozambique was in July-December 2007 and clinical disease was demonstrated. *(Disease situation, WAHID, OIE, online on 8.5.2008)*

Incidence of bovine tuberculosis (*by number of animals*) in Mozambique 2005-2007:

The whole country is considered as bovine tuberculosis absent, however, in some districts of the country there is still incidence as following (*total by country*):

Species and Year	Susceptible	Cases	Deaths	Destroyed	Slaughtered
2007					
cattle	80.183	40	2	1	102
2006					
cattle	1712	412	1		411
2005					
cattle	475	4			4

(by OIE, WAHID, online on 18.4.2008)

4.2.3.1.9. <u>NAMIBIA</u>

Cattle population in Namibia in 2005 was 2.148.543 with the density (units per square kilometre) of 2.60. *(WAHID, OIE, online on 8.5.2008)*

Last report for bovine tuberculosis in Mauritius was in July-December 2007. General and targeted surveillance. Last occurrence of bovine tuberculosis was in 1995. *(Disease situation, WAHID, OIE, online on 8.5.2008)*

<u>Incidence of bovine tuberculosis in Namibia 2005-2007:</u>

<u>2005</u>: Disease absent *(by OIE, WAHID, online on 18.4.2008)*

<u>2006</u>: Disease present but without quantitative data *(by OIE, WAHID, online on 18.4.2008)*

<u>2007</u>: Disease absent *(by OIE, WAHID, online on 18.4.2008)*

4.2.3.1.10. <u>SOUTH AFRICA</u>

Cattle population in South Africa in 2005 was 11.547.278 with the density (units per square kilometre) of 9.47. *(WAHID, OIE, online on 8.5.2008)*

Last report for bovine tuberculosis in South Africa was in July-December 2007 with disease restricted to certain zone(s) / region(s) of the country *(Disease situation, WAHID, OIE, online on 8.5.2008)*

<u>Incidence of bovine tuberculosis (*by number of animals*) in South Africa 2005-2007:</u>

Species and Year	Susceptible	Cases	Deaths	Destroyed	Slaughtered
2007					
cattle		47		21	
buffalo		62		62	
wildlife		3		3	
2006					
cattle		19	2	17	
buffalo					
wildlife		1		1	
2005					
cattle		747		2659	
buffalo		2			
wildlife		57	1	38	

4.2.3.1.11. KINGDOM OF SWAZILAND

Cattle population in the Kingdom of Swaziland in 2005 was 600.252 with the density (units per square kilometre) of 34.57. *(WAHID, OIE, online on 8.5.2008)*

Last report for bovine tuberculosis in the Kingdom of Swaziland was in July-December 2007 with infection present (however no clinical disease) *(Disease situation, WAHID, OIE, online on 8.5.2008)*

Incidence of bovine tuberculosis in Kingdom of Swaziland 2005-2007:

2005: Disease present but without quantitative data. *(by OIE, WAHID, online on 19.4.2008)*
2006: Confirmed infection / infestation (without clinical signs) *(by OIE, WAHID)*
2007: Confirmed infection / infestation (without clinical signs) *(by OIE, WAHID)*

4.2.3.1.12. TANZANIA

Many of the recent studies carried out in Tanzania have centered on determining the involvement of *M. bovis* in the incidence of tuberculosis in the human population, particularly in communities involved in livestock keeping. [62]

One of the published studies, namely "Bovine tuberculosis in the Lake Victoria zone of Tanzania and its possible consequences for human health in the HIV/AIDS era" reported 0.2% prevalence of bovine tuberculosis in the Lake Victoria zone. These 0.2% were diagnosed within 8190 cattle from 42 well-managed herds by a single comparative intradermal test (SCITT) using avian and bovine purified protein derivate (PPD) antigens. Significal variation among the herds tested in the four regions of the Lake Victoria zone, namely Kagera, Mara, Mwanza and Shinyanga was find. According to Jiwa et al, the highest prevalence (2.12%) was in a herd of 566 cattle which had recently arrived in Kagera region from Dar-es-Salaam. None of the 915 cattle tested in Shinyanga or of the 254 resident cattle in the Kagera region were positive by SCITT. [65]

Moreover, the role of HIV/AIDS in these regions was mentioned. According to Jiwa *et al*, the Shinyanga area, and particularly the Kagera region, has the highest human morbidity and mortality due to the acquired immunodeficiency syndrome in Tanzania. Therefore, the presence of bovine tuberculosis in cattle necessitates further investigations on the role of animal-derived tuberculosis in human health. [65]

According to Zinsstag *et al*, the tuberculosis in man resulting from *M. bovis* generally occurs in the extrapulmonary form, and in particular, as cervical lymphadenitis. In Tanzania, the proportion of extrapulmonary TB among all forms of tuberculosis stands at around 16%. The major part of these cases has been recorded in the Arusha region in the north of Tanzania, where regional data indicate that up to 30% of total tuberculosis cases are the extrapulmonary form. In this region, the main ethnic groups comprise the Maasai Iraqws, and Barbaigs tribes, who form the majority of patients diagnosed as having extrapulmonary forms of tuberculosis. The predisposing factors for this condition in the aforementioned ethnic groups include the close contact between humans and cattle, as some of the groups keep their animals indoors, and the custom of drinking raw milk and blood. [62]

The custom of drinking raw milk and blood in Tanzania as the preposition factor for the bovine tuberculosis infection also reported LoBue in his study. [39]

According to Zinsstag *et al*, in a more recent study, differences in local knowledge and practices that might influence tuberculosis control were assessed among 27 villages in Tanzania. In each vilage, a general and a livestock-keeping group were selected at random. The households were home visited, and 426 family members were interwied. The finding from this study revealed that on average, 40% of respondents practiced habits that migh expose them to both bovine and human tuberculosis. The Barbaig tribe had a significantly higher number of respondents (P= .024) who did not boil milk. Eating uncooked meat or meat products was practiced by 17.9% of all respondents. The habit was practiced more by Iraqw (P= .008) and Barabaig (P= .016) tribes than by other tribes. The study also found about 75% of the respondents had a poor knowledge of tuberculosis.[62]

Moreover, in Tanzania, the increasing cases of extrapulmonary tuberculosis paralleled the increasing total cases of tuberculosis reported each year between 1983 and 2001. A positive correlation ($r = 0.67$) between the proportion of extrapulmonary tuberculosis and the cattle-to-human population ratio was found. In Tanzania, molecular epidemiology studies were conducted to ascertain the genetically relatedness of strains of *Mycobacterium bovis* recovered from humans and those from cattle. It was shown that *Mycobacterium bovis* from cattle has infected man. [62]

The data published by CDC, notably the study "Zoonotic tuberculosis due to *Mycobacterium bovis* in Developing countries" , by Cosivi *et al*, report that in a recent investigation in Tanzania, seven of 19 lymph node biopsies from suspected extrapulmonary TB patients were infected with *Mycobacterium tuberculosis* and four with *Mycobacterium bovis.* No mycobacteria were cultured from the remaining eight. Although the number of samples was low, the high proportion (36%) of *Mycobacterium bovis* isolates is of serious concern. [46]

According to Zinsstag, the increase in bovine tuberculosis could be associated to a certain extent with the following factors: declining living standards in villages, increased urban and peri-urban cattle keeping/raising, increased size and density of the urban population, improved detection, and most notably, emergence of the HIV/AIDS virus among people living in urban and peri-urban areas. Some of these factors have also been found to be confounding factors for the national efort toward the eradication of tuberculosis in the human population.[62]

According to Cleaveland *et al*, *M. bovis* is the cause of approximately 800–1,000 human cases of TB annually in Tanzania. Its prevalence in cattle was relatively low (0.9%), but the infection was widespread and occurred in 12% of cattle herds. [66]

In Tanzania there were some projects relative to bovine tuberculosis already run, for example the Project "R7357 – Quantifying the costs and risks of bovine tuberculosis in Tanzania", Cleaveland *et al* (*Centre for Tropical Veterinary Medicine, University of Edinburgh, UK*) or the Project "R7229 – *Mycobacterium bovis* infection of cattle and man in Tanzania", Mike Sharp (*Moredun Research Institute, Edinburgh, UK*) [66, 67]

Beside the *Mycobacterium bovis* incidence of tuberculosis in the human population, *Mycobacterium bovis* infection has been also reported in wildlife. According to OIE, bovine tuberculosis was detected in 11.1% wildebeest (*Connochaetes taurinus)* and 11.1% of topi (*Damaliscus lunatus)* culled during local meat cropping programmes in the Serengeti ecosystem.There is also serological evidence of infection in buffalo and lions in the Serengeti. *M. bovis* was also isolated from wildebeest and kudu (*Tragelaphus strepsiceros*) from the Mdori hunting block adjacent toTarangire National Park in Tanzania. [48]

Cattle population:

Cattle population in Tanzania in 2005 was 16.578.953 with the density (units per square kilometre) of 17.54. *(WAHID, OIE, online on 8.5.2008)*

Disease situation:

Last report for bovine tuberculosis in Tanzania was in July-December 2007. No surveillance was specified. *(Disease situation, WAHID, OIE, online on 8.5.2008)*

Incidence of bovine tuberculosis (*by number of animals*) in Tanzania 2005-2007:

2005: Disease absent. *(by OIE, WAHID, online on 19.4.2008)*

2006: No information available *(by OIE, WAHID, online on 19.4.2008)*

2007: Disease absent. *(by OIE, WAHID, online on 19.4.2008)*

4.2.3.1.13. ZAMBIA

There are many reports about bovine tuberculosis in the wildlife in Zambia. The occurrence of *Mycobacterium bovis* was confirmed in free-living Kafue lechwe (*Kobus leche kafuensis*) in the Kafue River Valley. Nevetheless, Mycobacterium bovis was also reported in other species, for example bushbuck (*T. scriptus*). According to OIE, bovine tuberculosis contiues to be a major problem in wildlife in Zambia. [48]

Acccording to Zinsstag *et. al*, in 1996, Cook and coworkers performed a cross-sectional survey on 176 randomly selected rural households in the Monze District of Zambia, 103 of these presented cattle for tuberculin testing. Of the 2226 cattle tested, 165 (7.4%) were positive reactors, 33% of herds contained positive animals. Risk of a positive reaction varied with an animal´s age and body condition. Cattle in larger herds were more likely to give positive reactions. Ten households reported a human case of TB during the preceding 12 months, the herds or these households were 6 times more likely to have a tuberculin-positive animal than were herds in households without a reported human TB case. [62]

According to Cooke *at el*, between 1992 and 1993 the project on bovine tuberculosis in Zambia was run. Specifically, it was project R5408- Tuberculosis in Zambia- A cross sectorial study of bovine and human TB in Monze district of Zambia. The objective was to investigate the potential link between bovine and human TB among traditional cattle keepers in the southern Zambia. [68]

According to Cooke, the survey was completed in Monze district using random sample of more than 200 rural households. All households had owned cattle at some time and all used milk in their diet. Each household completed a questionnaire which included questions on the incidence of human TB, and cattle were subjected to a standard comparative intradermal tuberculin test. Human TB cases were positively associated with the ownership of cattle and significantly with the use of milk in the household. Humans in households with at least 1 reactor animal were 7 times more likely to have TB. Of the 2,226 cattle tested, 7.4% gave positive tests with a third of the herds having at least one reactor. It was found that older cattle, pregnant cows and animals in good condition were more likely to have TB. [68]

According to Cooke, the study provided sufficient evidence to conclude that there was a likely positive link between TB in cattle and humans, which should cause concern to both medical and veterinary authorities in Zambia. What is more, those results triggered further DFID-sponsored research to validate the tuberculin tests for cattle and investigate the actual link between cattle and human TB. [68]

According to Cooke et al, further research was undertaken in Project R5498- Bovine tuberculosis in the tropics. [68]

Cattle population:

No information available *(WAHID, OIE, online on 8.5.2008)*

Disease situation:

Last report for bovine tuberculosis in Zambia was in January-June 2007. General surveillance. Last occurrence of bovine tuberculosis was in 2006. *(Disease situation, WAHID, OIE, online on 8.5.2008)*

Incidence of bovine tuberculosis in Zambia 2005-2007:

2005: No information available *(by OIE, WAHID, online on 19.4.2008)*
2006: Disease present but withou quantitative data. *(by OIE, WAHID, online on 19.4.2008)*
2007: Disease absent (Jan-Jun), No information available (Jul-Dec). *(by OIE, WAHID, online on 19.4.2008)*

4.2.3.1.14. ZIMBABWE

Cattle population:

No information available. *(WAHID, OIE, online on 8.5.2008)*

Last report for bovine tuberculosis in Zimbabwe was in July-December 2007. General surveillance. Last occurrence of bovine tuberculosis was in 1996. *(Disease situation, WAHID, OIE, online on 8.5.2008)*

Incidence of bovine tuberculosis in Zimbabwe 2005-2007:

2005: Disease absent. *(by OIE, WAHID, online on 19.4.2008)*

2006: No information available. *(by OIE, WAHID, online on 19.4.2008)*

2007: Disease absent. *(by OIE, WAHID, online on 19.4.2008)*

CHAPTER 5

ECONOMIC ASPECT OF BOVINE TUBERCULOSIS IN SADC

Bovine tuberculosis as zoonosis not only afect public and animal health and has impact on agriculture but also plays significant role within international trade from economical point of view.

The economic aspect of bovine tuberculosis could be divided into two areas, direct and indirect costs. Direct cost are these that are visible immediately such as medical care for patients infected with *Mycobacterium bovis*; and within livestock expenses for vaccination, control or slaughter of livestock infected with *Mycobacterium bovis*.
Indirect costs are loss of money because of restrictions within trade, especially international.

Therefore, there is big economic impact on countries, where bovine tuberculosis is present.

5.1. *Mycobacterium bovis* infection in animals of economic interest

One study reported that the need to focus international attention on the continuing problem of tuberculosis in animals of economic interest can hardly be over-emphasized. *Mycobacterium bovis*, is the most universal pathogen among the mycobacteria and produces progressive disease in most domestic animals (especially those of economic interest) and in humans. The prevalence of animal tuberculosis therefore, has relevance for both human and veterinary medical practitioners and decision makers on the strategic approach to be adopted in the control of the disease. There is the tendency to underestimate the ability of *Mycobacterium bovis* to produce tuberculosis or to assume that it has been totally eliminated and that potential exposure to this pathogen may be a remote occurrence. This perception could have a direct implication for the control of the disease at source that is in domestic animals. The current epidemic of human immunodeficiency virus (HIV) infection raises the issue of what future impact this epidemic may have if the incidence of *Mycobacterium bovis* infection in humans increases, when control in livestock especially cattle, is neglected by both developed and developing countries. [69]

Because of the high prevalence of HIV/AIDS in Africa and thus in the countries of SADC with lack of control and epidemiological precautions within *Mycobacterium bovis* infection especially in rural areas, the impact of *Mycobacterium bovis* on economic is immense. [28, 69]

5.2. Internation trade and restriction of food products trade (export and import) due to *Mycobacterium bovis* infection

Many countries of the world, including countries of SADC, have their own policies and legislatives related to the food security and international trade. [70]

Beside that, the Terrestial Animal Health Code of OIE make the requirements relevant to the bovine tuberculosis within import or export of live animals, semen, meat and meat products and milk and milk products. [48]

As for the trade restriction, according to WAHID Interface we can easilly find more than one example within SADC countries.

If we compare for example Angola and Botswana and their current disease incidence and the situation within international trade- import and export of food and other agricultural products and animals, we can find out that Angola is of possible trade hazard for Botswana. [53, 70]

In detail, as already mentioned in the previous chapter, Angola is a country where bovine tuberculosis is present. Botswana is a country, where bovine tuberculosis is absent. Despite the fact, that Angola has Food Control Inspection within food import and export trade, and moreover there is an agent tested for *Mycobacterium bovis*, according to OIE, export from Angola where bovine tuberculosis is present and import to Botswana where the disease is absent should be probably considered as hazard trade. (*WAHID Interface, OIE*)

The same could be valid for any other SADC countries where bovine tuberculosis is present in comparison with bovine tuberculosis free country.

5.3. Eradication programmes and monitoring from economic point of view

There are big differences between developed and developing countries in the field of eradicatin bovine tuberculosis, as eradicatiol and control programmes are expensive to run and require professional approach. The financial and other aspects of countries differ, the same as the the needs of the individual country.

The reason of starting up with these programmes is not only the public health both of animals and humans, but most of the times it is economic interest within international trade, as mentioned in previous subhead. This is valuable mostly for countries, which produces milk and meat. Any restriction within meat and milk product could mean great financial lost. Therefore, the economic impact is a big incentive to run eradication and control programmes.

However, according to Cosivi et al, of all nations in Africa, only seven apply disease control measures as part of a test-and-slaughter policy and consider bovine TB a notifiable disease; the remaining 48 control the disease inadequately or not at all. Almost 15% of the cattle population are found in countries where bovine TB is notifiable and a test-and-slaughter policy is used. Thus, approximately 85% of the cattle and 82% of the human population of Africa are in areas where bovine TB is either partly controlled or not controlled at all. [46] Nevertheless, this study was reported in the year 1998, so the current situation may differ.

The project which was run in the years 1999-2001 in Tanzania, oriented on the cost and risks of bovine tuberculosis didn´t show the exactly *Mycobacterium bovis* economic burden as it was required because it was difficult to quantify due to the relatively low number of reactors detected. Nevertheless, this project show that for example milk yields for some herds – often the first indicator of a production problem – were significantly lower in infected than non-infected cattle. This suggests that *M. bovis* infection may have an impact on cattle production. To be sure, a more detailed, long-term study is required to tease out the impact of *M. bovis* from other contributing factors to production losses. [66]

The project also quantified the contribution of *M. bovis* to the human TB epidemic in Tanzania. Its public health burden was compared with *M. tuberculosis* and other zoonotic diseases to help identify priorities for disease control, both for Tanzania and other developing countries. [66]

Moreover the study highlighted the importance of atypical *Mycobacterium* in both human and livestock TB. Strategy development for controlling bovine TB and control of extrapulmonary TB in humans was set up. [66]

To summarize, any project on bovine tuberculosis in both developed and developing countries bring new outcomes and is really important. The economic impact is evident, eventhough not in all countries could be quantified the exact data.

There are many strategies within *Mycobacterium bovis* control and eradication in the world. For example, in the study of Livingstone *et al*, oriented on a strategy which will assist with bovine tuberculosis control and facilitate trade was written that it is expected that the revised chapter on bovine tuberculosis in the Terrestrial Animal Health Code of the Office Internationale des Épizooties (OIE) will embrace regionalisation as a functional means of assisting countries, states or regions to meet the requirements for freedom from tuberculosis and to facilitate trade. The benefits and applications of regionalisation, which comprises zoning and compartmentalisation, are discussed. Regionalisation requires that a country's veterinary administration is able to implement transparent and auditable biosecurity measures that will ensure that the tuberculosis-free status of a subpopulation of cattle is maintained despite the presence of infection in another cattle subpopulation, or in other domestic or wild animal species. Zoning, which requires cattle subpopulations to be separated by geographic boundaries, provides a practical basis whereby countries, states or regions, can progress towards freedom from tuberculosis, regardless of the source of infection for defined cattle subpopulations. Compartmentalisation however, requires that husbandry or management practices will be used to prevent a tuberculosis-free cattle subpopulation from contacting interspecific and intraspecific sources of infection. This will be difficult to achieve except for specialised cases such as artificial breeding centers. [71]

CONCLUSION

It was shown, that bovine tuberculosis is widespread all over the world and thus it isn't disease which occurs only in the countries of SADC. Among all of the SADC countries the incidence and prevalence of bovine tuberculosis differ. For example Botswana is reported as bovine tuberculosis free country however Angola and South Africa are countries with relatively high bovine tuberculosis incidence. In comparison with other non-SADC African states, the situation is similar. The problem within SADC or other African countries is the high prevalence of HIV/AIDS because HIV infected man is at the highest risk group who is susceptible to *Mycobacterium bovis* infection. From given examples from other world countries such as Great Britain it was shown that even though the human-human transmission of *Mycobacterium bovis* is rare it can happen still. Moreover, it was proved, that the same as cattle can be the source of infection for man, can man be the source of infection for cattle. This might be threat for countries, where bovine tuberculosis from cattle was sucessfuly eradicated but is still present within human infection. The role of people who imigrate from countries where bovine tuberculosis is still present and thus who may suffer from *Mycobacterium bovis infection* to the bovine tuberculosis free countries should be also considered. The role of wildlife was also described and should be note, that wildlife could be the threat even to the countries where bovine tuberculosis was sucessfuly eradicated. This can happen through the captive wildlife sent from country where bovine tuberculosis is present to the other country´s zoological gardens where bovine tuberculosis wasn´t reported. The re-emerge of the disease is also possible as it was reported in the United Kingdom. The projects on eradication and control of bovine tuberculosis are essential, nevertheless, co-operation with both physician and veterinarians is necessary.

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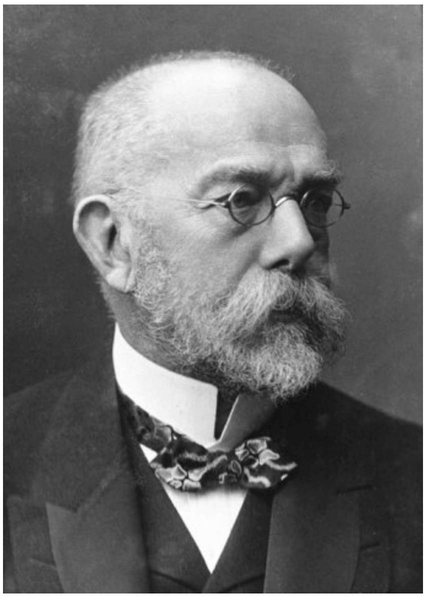
Annexes:

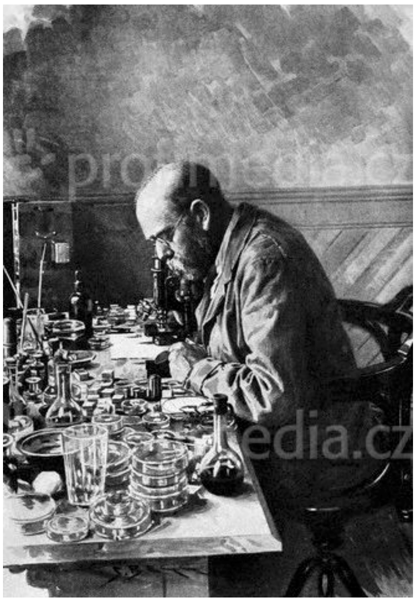
1. www.profimedia.cz (pictures 1.1. and 1.2.)
2. www.oie.int (pictures 2.1.-3.6.)

ANNEXES

1. Robert Koch



1.a



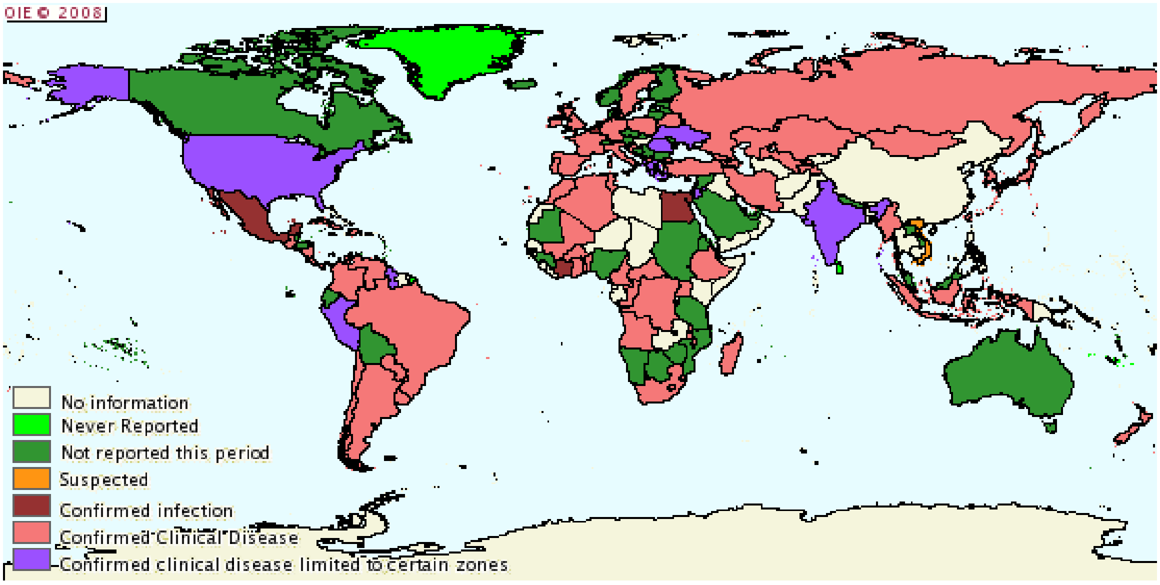
1.b

1.a, 1.b. Pictures of Robert Koch, German physician who described isolation of organism causing tuberculosis

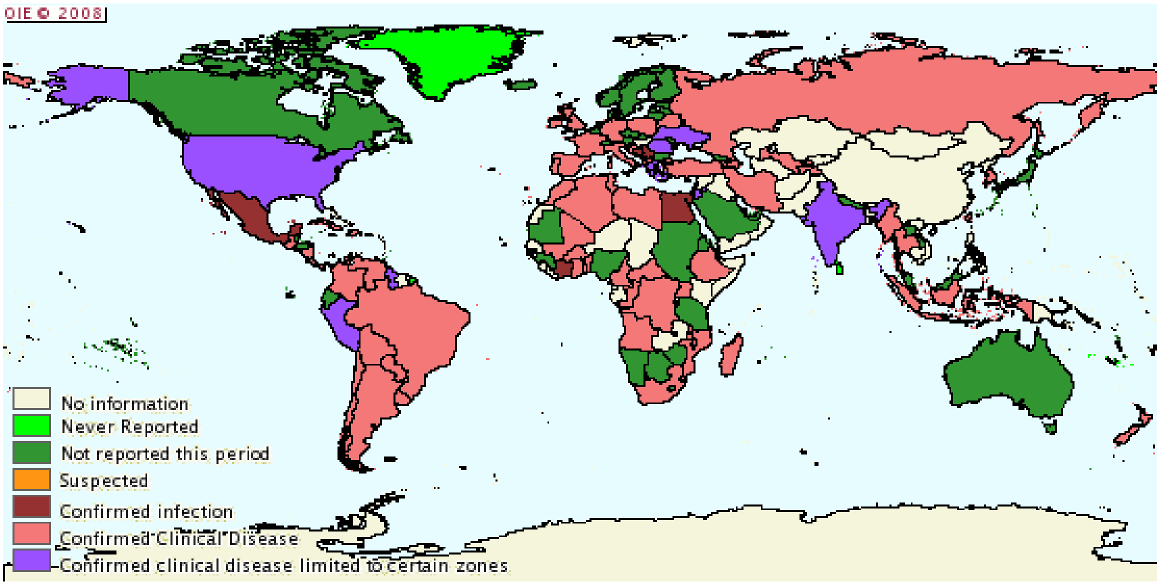
(Addapted from http://www.profimedia.cz)

2. BOVINE TUBERCULOSIS IN WORLD- DISTRIBUTION MAPS

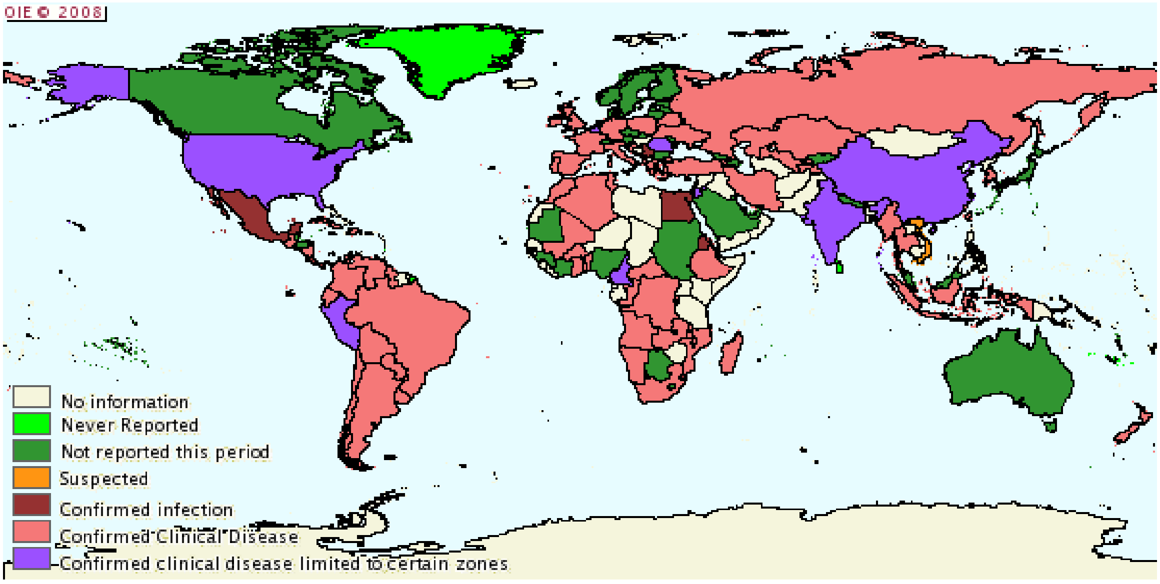
2.1. Disease distribution maps-World, Bovine tuberculosis, Jan-Jun 2005



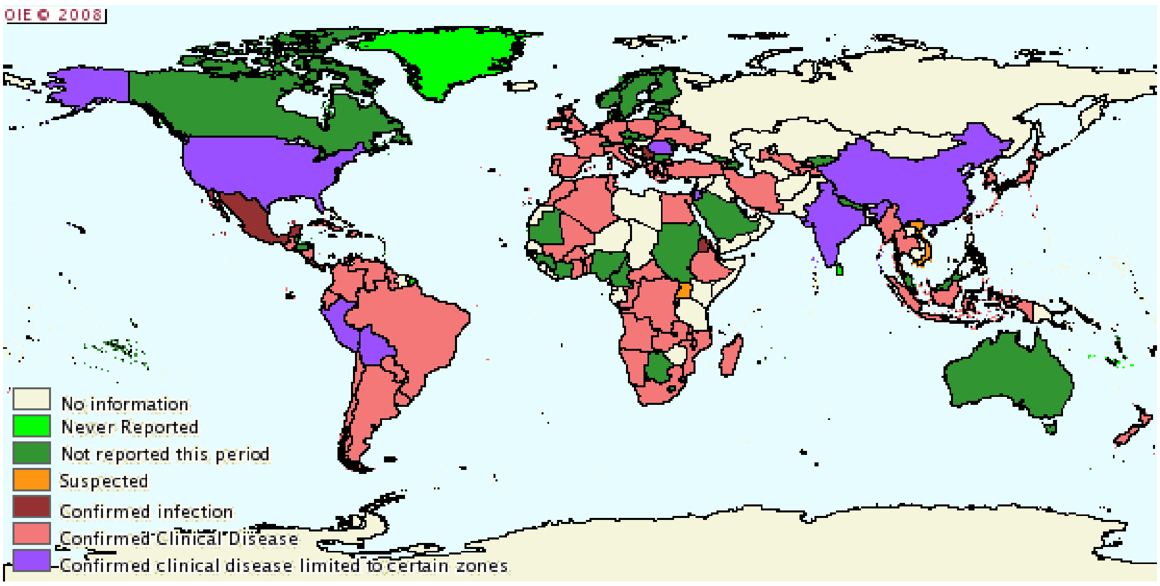
2.2. Disease distribution maps-World, Bovine tuberculosis, Jul-Dec 2005



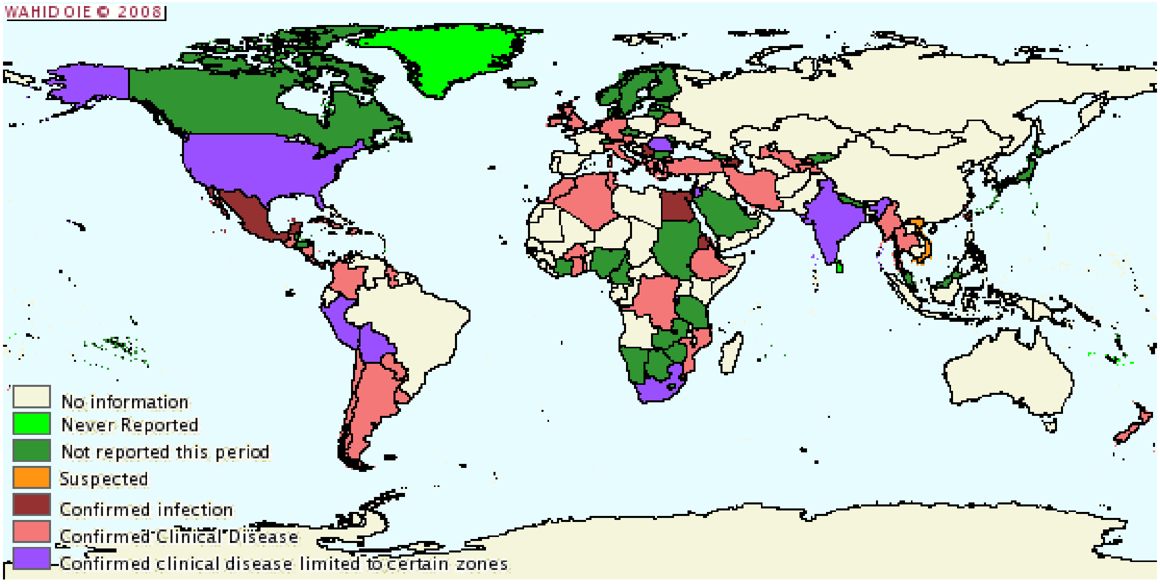
2.3. Disease distribution maps-World, Bovine tuberculosis, Jan-Jun 2006



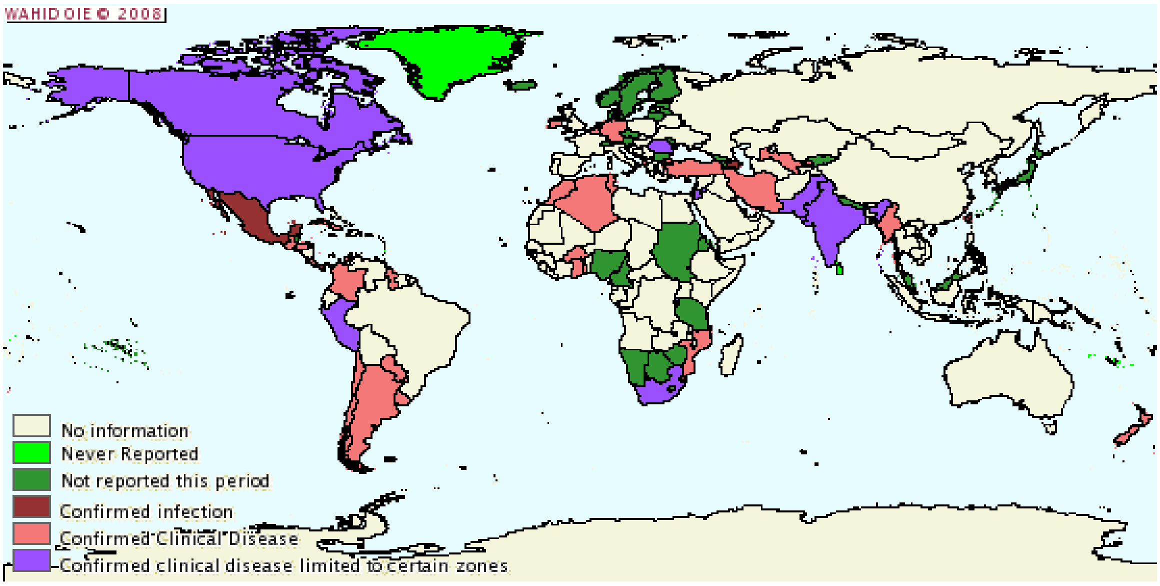
2.4. Disease distribution maps-World, Bovine tuberculosis, Jul-Dec 2006



2.5. Disease distribution maps-World, Bovine tuberculosis, Jan-Jun 2007

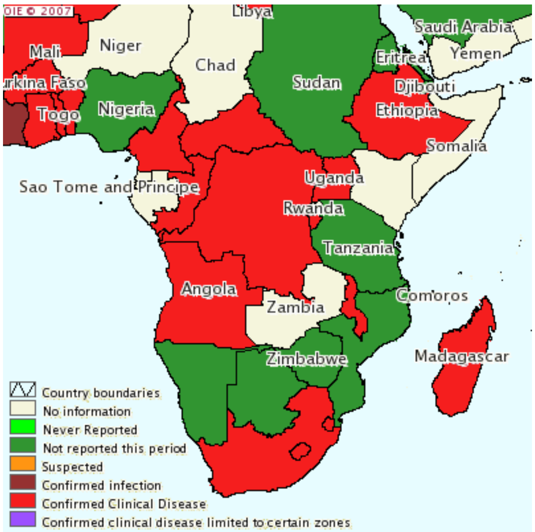


2.6. Disease distribution maps-World, Bovine tuberculosis, Jul-Dec 2007

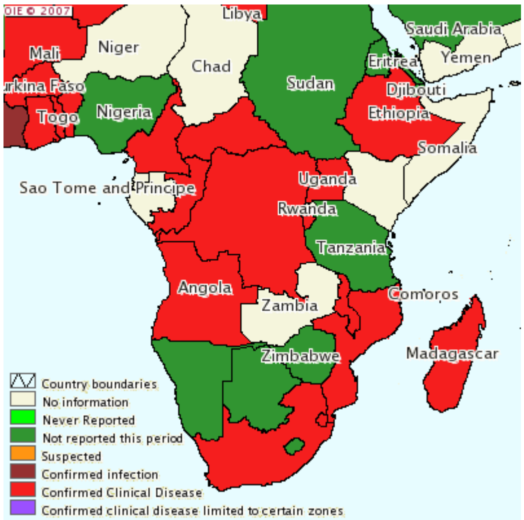


3. BOVINE TUBERCULOSIS IN SADC- DISTRIBUTION MAPS

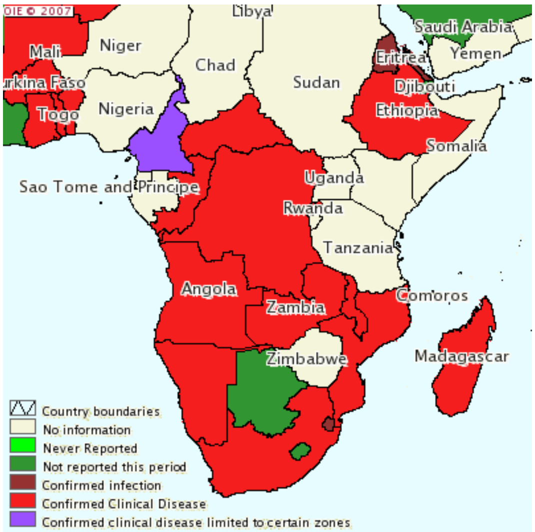
3.1. Disease distribution maps-SADC Bovine tuberculosis, Jan-Jun 2005



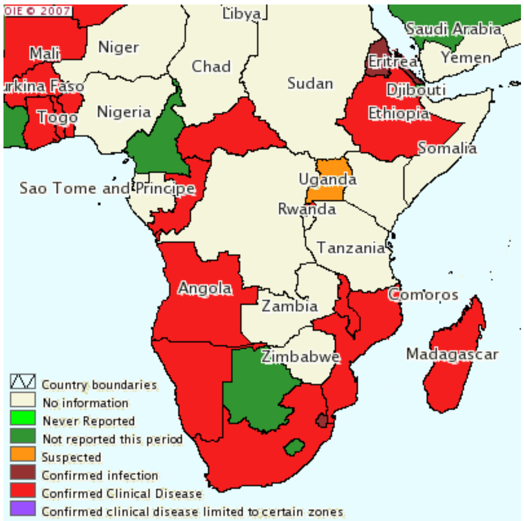
3.2. Disease distribution maps-SADC Bovine tuberculosis, Jul-Dec 2005



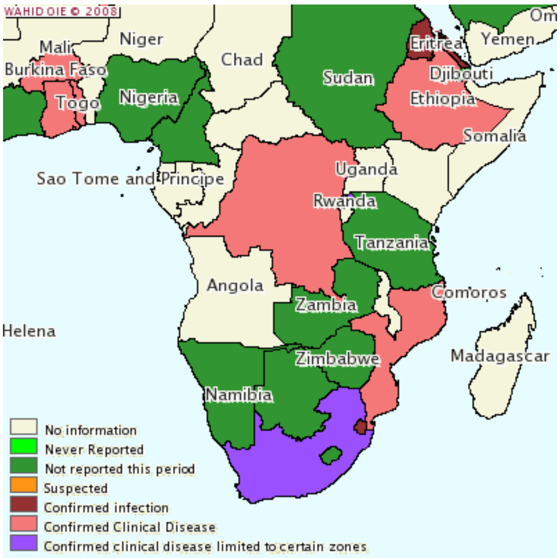
3.3. Disease distribution maps-SADC Bovine tuberculosis, Jan-Jun 2006



3.4.Disease distribution maps-SADC Bovine tuberculosis, Jul-Dec 2006



3.5. Disease distribution maps-SADC Bovine tuberculosis, Jan-Jun 2007



3.6.Disease distribution maps-SADC Bovine tuberculosis, Jul-Dec 2007