

## Retraction Notice

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# Tuberculosis and Cysticercosis in Brazil: A Review

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## Abstract

Tuberculosis and the taeniasis-cysticercosis complex, typical cases of zoonosis, have great importance for public health, since they cause economic liabilities to the Brazilian beef production chain. They are actually a synonym of technical inadequateness in Good Production Practices. Both diseases have existed since ancient times and their occurrence should be controlled by basic sanitary measures. However, there is a significant neglect attitude by authorities of countries with high occurrence rates, or rather, tropical underdeveloped nations, to focus on public policies for the control and decrease of the prevalence and the occurrence of these diseases. Current review elucidates the epidemiological profile of the diseases and contributes towards the elucidation and establishment of measures ensuring control.

## Keywords

Cysticercosis, Health, Tuberculosis, Medicine, Zoonosis

## 1. Introduction

The World Health Organization (WHO) defines zoonoses as “the interface of diseases and infections between animals and humans”, which may be acquired through contact with animals or by consumption of contaminated food. According to WHO, the main diseases related to the consumption of meat in Brazil are salmonellosis, tuberculosis, cysticercosis and other diseases of the food toxic-infections group (PINTO, 2008). In the main, cysticercosis and tuberculosis are highly relevant in public health since they affect populations with high morbidity rates. In fact, the two diseases are associated to socially and economically

low level populations and to eating customs, hygiene and inadequate handling and the clandestine commerce of products derived from animals.

Clandestine commerce is a constant concern to veterinary inspection services worldwide. Difficulties to eradicate this trade are proportional to the state of development of the country, to economic issues and to cultural standards. The clandestine meat and milk commerce in Brazil (implying the purchase and selling of cattle contaminated by tuberculosis, contaminated dairies, falsification of Sanitary Inspection labels and cattle pens that seem to come directly from the Middle Ages, on the outskirts of big cities) and the lack of reliable statistical data on cattle tuberculosis and cysticercosis in the country are a great threat to public health.

Estimates reveal that the clandestine conditions of beef and milk in Brazil are shocking. Actually it is a source of deep concern to realize that 50% of beef consumed in Brazil come from illegal abattoirs and that 48% of the milk produced in Brazil have shady origins, without any sanitary inspection. What actually occurs in Brazil in the case of tuberculosis boils down to complex social phenomena. As a rule, dairymen ignore the product's sanitary risks. They are small, non-organized farmers, with low schooling, who circumvent the law to survive. If they sell milk to the official dairies, their product becomes commercially non-feasible since they would earn less than when they work within illegal purchase conditions. To make matter worse, most buyers do not have sufficient information on food safety and ignore the risks to which they are exposed. They drink raw milk, considering it healthier. They also have the "advantage" of buying the product by installments. Government authorities should guide the population, give technical assistance to milk and beef producers, and enforce the law on the matter, acknowledging the seriousness of the issue. They often fail in their duty, excusing themselves by saying that financial resources are lacking.

The taeniasis-cysticercosis complex in cattle focuses on the parasite cycle that starts by the ingestion of *Taenia saginata* eggs through the consumption of contaminated water or food. Cysts harbor in the muscles of the intermediate host (cattle) and form cysticerci. The ultimate host (humans) is infected by eating raw or undercook meat, or drink larva-contaminated water. Larvae develop in the small intestine. When they turn adults, they eliminate proglottids with the eggs at the moment of defecation and contaminate the environment.

The taeniasis-cysticercosis cycle ends when a series of preventive measures are taken against human infection by the etiological agent, with the extermination of the parasite from the environment. In several regions, however, few prophylactic measures are taken. In fact, Brazil lacks basic sanitation, especially in the poor, government-abandoned areas where diseases prevail. The establishment of beef inspection in abattoirs is highly relevant to hinder or, at least, to reduce the number of cattle carcasses improper for human consumption.

## 2. Tuberculosis

### 2.1. History

Tuberculosis, caused by a single microbe agent in humans, is one of humanity's

oldest and most serious diseases. It has been the cause of high mortality rates and declared a global emergency by the World Health Organization in 1993 [1]. Tuberculosis has victimized people worldwide since times immemorial. Employing DNA sequencing, researchers have detected traces of a tuberculosis agent in bone samples of an extinct species of bison which lived in North America some seventeen thousand years ago [2] [3]. Similar discoveries were obtained from wild sheep and musk oxen fossils. In fact, it seems that bacteria from the *Mycobacterium tuberculosis* (MTB) complex were widely diffused among bovine species which went over to North America through the Behring Straits by the end of the Pleistocene period. They were the probable vectors and reservoirs for the dispersion that later on would be called the White Plague [2] [4].

Molecular techniques have recently shown that the agent causing tuberculosis infected humans at the time when several animals were domesticated some 10,000 years ago. Reports on human tuberculosis have been described in manuscripts from India hailing from 2000BC [3]; in skeletons from Egypt and Germany, respectively from 5000 and 8000BC [5] [6] and in a mummy from Peru from about 1100BC [6] [7]. The Greeks and the Romans were the first to acknowledge tuberculosis as a dangerous epidemic. Although the Greeks initially thought it was a divine punishment, Hippocrates modified such belief by his clinical description. The disease was renamed *phthisis*, signifying “consumption”, due to the great physical fatigue that people with the disease felt [7]. When the first anatomic dissection of the lungs of human corpses was undertaken in the 17<sup>th</sup> and 18<sup>th</sup> centuries, François de la Boe detected abnormal structures in patients with tuberculosis. It was only in 1839 that Johann Schonheim first called the disease “tuberculosis” [8] [9].

When the English and French started to import European bovines to North America, they became aware that tuberculosis was the most serious bovine disease in the USA during the 19<sup>th</sup> century [3]. Further, in 1819, René Laennec described the lesions caused by the disease and distinguished the productive and exudative tuberculosis types. In 1868, Villemin inoculated rabbits with tuberculosis matter retrieved from humans and bovines and proved that tuberculosis was an infectious disease. However, Robert Koch was the great discoverer of the pathology. In 1882, he identified the tuberculosis bacillus that caused the disease in humans and named it *Mycobacterium tuberculosis*. Koch’s discoveries went further and in 1884 he multiplied the microorganism *in vitro*. In 1891, he developed the tuberculin test which is currently an important diagnosis tool in veterinary medicine [10] [11]. Further, the discovery of different morphological, pathological and *in vitro* culture characteristics between *M. bovis* and *M. tuberculosis* occurred in 1896 and 1898 by Klein and Gibbs [3].

In 1901, several researchers thought that *M. bovis* would be capable of triggering the disease in humans. Ten years later, German and British researchers observed cases of tuberculosis caused by *M. bovis* in children who had taken contaminated milk. They confirmed the high pathogenic potential of the myco-

bacterium for human health. Further, confirmation of aerial transmission only occurred in 1937 [3]. In fact, till the 1970s, *M. bovis* was considered a variant of *M. tuberculosis* and referred to the microorganism as *Mycobacterium tuberculosis* subsp. *bovis* or *Mycobacterium tuberculosis* var. *bovis*. However, Karlson and Lessel recommended change in the classification for a new species [8].

Tuberculosis arrived in Brazil with the Portuguese colonial enterprise and the subsequent contact between the natives and the infected settlers and Jesuits during the Evangelization process. In fact, several natives died of tuberculosis [6] [9]. Letters written in 1555 by Ignatius of Loyola and in 1583 by José de Anchieta to the Portuguese Government report that “several catechized Indians fell ill, most of whom exhibiting phlegm, coughs and fever; many spit blood and died alone in the villages” [6]. In 19<sup>th</sup> century Brazil, an epidemic of tuberculosis, called “paupers’ plague”, became widespread in the towns and cities, killing 700 in every 100,000 inhabitants [6]. High mortality rates occurred up to the 1940s. During this period, approximately 10% of death causes in the city of São Paulo were due to tuberculosis [6] [12].

In the 1960s and 1970s, human tuberculosis was completely under control in most developed and underdeveloped countries. However, population growth in large cities, high poverty rates worldwide, the arrival of Acquired Immunodeficiency Syndrome (AIDS), forest reserves, the persistence of the microorganism in herds and the rise of resistant multidrug strains caused tuberculosis to become a re-emergent health issue [13].

## 2.2. Bovine Tuberculosis

Bovine tuberculosis is a chronic and zoonotic infectious-contagious disease with *Mycobacterium bovis* as its etiological agent [14] [15] [16]. The agent belongs to class *Actinobacteria*, Order *Actinomycetales*, Family *Mycobacteriaceae* and Genus *Mycobacterium*, with approximately 127 species and 11 subspecies, ranging between saprophyte and opportunist microorganisms and obligatory pathogenic organisms [17] [18]. In fact, it is a member of the MTB complex with other six species, namely *Mycobacterium tuberculosis*, *M. microti*, *M. africanum*, *M. canetti*, *M. caprae* and *M. pinnipeddi*. They have a high genetic closeness (99.95%) to DNA and to gene 16S Ribosomal Ribonucleic Acid (rRNA) [19] [20] [21] [22], albeit distinct in phenotype, pathogenicity and tropism among the hosts [20].

The term tuberculosis is employed to characterize the disease caused by microorganisms *M. tuberculosis*, *M. bovis* and *M. avium*, respectively causing illness in humans, bovines and fowls. The other species of the mycobacteria cause mycobacteriosis [23]. Similar to other mycobacteria, the bacillus *M. bovis* is approximately between 0.2 and 0.7  $\mu\text{m}$  wide and between 0.5 and 10  $\mu\text{m}$  long, immobile, aerobic, non-former of spores, alcohol-acid resistant (BAAR), stained by Ziehl-Neelsen method (ZN), slow growth, host-dependent and pyrazinamide-resistant [11] [22] [24] [25] [26].

Its cell wall has singular characteristics and is composed of lipids forming between 20% and 40% of the bacillus's dry weight, most of which are mycolic acids which impair the removal of fuchsin by the alcohol-acid bleacher used in Gram method. They act within the colonies' characteristics and, coupled to wall glycolipids, induce toxicity responses that stimulate the host for a granulomatous inflammatory response [11]. They also contribute towards cell permeability, resistance to several disinfectant agents and enzyme activity of macrophages by inhibiting the formation of phagolysosomes [14].

Although mycobacteria are not spore-forming, the features of the external section of the bacterium wall formed by the mycolicarabinogalactan complex act as a layer of wax that impermeabilizes cells and protects them from hydrophilic substances and from dissection, becoming viable even in extreme environmental conditions, from chlorhexidine and quaternary ammonia-based disinfectants [22] [27] [28]. In favorable temperature, humidity and shade conditions, the viability of *M. bovis* in the environment may last more than two years. However, a host is required so that the agent may multiply [21] [22] [23]. On the other hand, they are destroyed by pasteurization, heat, direct sunlight and by formaldehyde and sodium hypochlorite-based disinfectants [11] [23] [29].

Although *M. bovis* tends to develop in bovines, other species of wild and domestic mammals may be occasionally affected, which also includes humans [23] [30]. The disease generally affects bovines, with prevalence for older and milk-producing animals. The above is due to the production system with greater agglomeration and higher permanence rate on the farm when compared to beef cattle which are slaughtered young [23] [31] [32]. However, greater agglomeration in beef cattle confinement and the permanence of female matrixes for longer periods on farms constitute similar conditions as those infected by tuberculosis [31] [33].

The proximity of infected animals is the main infection source in cattle. Transmission is horizontal and interspecies. It may occur from bovines to bovines, from bovines to wild animals and humans, and from wild animals and humans to bovines, mainly involving the inhalation of particles released by coughs and respiration, or even by the consumption of bacillus-infected milk and meat [23] [34]. Immediately on being infected by the agent and even prior to the formation of lesions in the tissue, the animal may disseminate the disease to the rest of the herd [35]. In fact, the respiration system is the infection's main entrance (80% - 90% of all cases) through the inhalation of aerosols with the bacillus [11] [14] [36]. Although *M. bovis* may also be eliminated in milk, faeces, semen, urine, utero-vaginal secretions, caused by abscedation of lymph nodes, the contagiousness of susceptible animals in contact with contaminated pasture, water and troughs is rare [22] [30] [31]. Consumption of bacillus-contaminated pasture, water and fomites rank second to respiration. However, the mouth is the main entrance of *M. bovis* in the case of young animals and humans [14] [27] [37].

Clinical symptoms depend on the infected organ or system. The main clinical signs comprise progressive slimming, apathy, high fever, dyspnea, dysphagy, noisy respiration and coughing [23] [30]. Live animals are diagnosed by tuberculinization, or rather, intradermal inoculation of tuberculin (simple and comparative intradermal proof), which causes a reaction of type 4 hypersensitiveness in *M. bovis* infections. Post-mortem exams and microbiological and histopathological cultures are also a help in the diagnoses of bovine tuberculosis [38].

Macroscopic findings are characterized by granulomatous nodular lesions, called tubercles, which develop in any type of organ or tissue. They may lie in any lymph node, although usually in bronchial, retropharynx and mediastinal ones [26] [29] [39], and in other organs, such as the liver, spleen and mesenteric lymph nodes [26] [38]. In the case of lesions in the lungs, miliary abscesses occur. They exhibit characteristic colored pus, ranging between cream and orange color, and consistency ranging between thick cream and crumbled cheese. Lesions may be disseminated by the organ causing suppurating bronco-pneumonia, with possible extensions to the pleura and the peritoneum [26] [27] [30]. Further, the formation of fibrous capsule may be triggered as the lesion progresses and the latter may develop in all the tuberculosis lesions [26] [30].

Generalization is featured by miliary tuberculosis defined by spot-shaped lesions in several organs or by caseified and badly encapsulated lesions in the lungs. Chronic lesions are generally calcified or surrounded by a thick fiber capsule and by nodules with yellowish-orange thick caseous material [26] [30] [40].

The treatment of tuberculosis in bovines is not recommended. The most adequate means for reducing the negative impact of the disease is the control and the eradication of the disease [38]. Since 2001, the control and eradication of bovine tuberculosis in Brazil have been undertaken by the Brazilian National Plan for the Control and Eradication of Animal Brucellosis and Tuberculosis (PNCEBT) of the Ministry of Agriculture, Broodstock and Supply (MAPA) [41] [42]. PNCEBT's main role comprises the elimination of tuberculosis and brucellosis through prophylactic activities involving diagnosis and sanitation of bovine breeding sites, active sanitary vigilance, reduction of the prevalence and occurrence of the disease and the decrease of impacts on human and animal life. The above also includes totally free and monitored homesteads and, consequently, the competitiveness of Brazilian beef cattle herds through the production of animal-derived products with low sanitary risks for the public health [41].

Joint work between PNCEBT and official government inspection service and agricultural-broodstock defense service by slaughtering positive bovines, coupled to notification of lesions suggesting tuberculosis in carcasses and viscera during post-mortem inspections, should improve sanitary vigilance activities and the monitoring of the efficaciousness of the program in Brazil [43].

### 2.3. Economic Impact of Tuberculosis on Cattle

Mean prevalence percentage of tuberculosis-infected cattle in Brazil between

1989 and 1998 reached 1.3% [41] [44]. A survey comprising 1600 homesteads and 23,000 animals, undertaken in the central and southern regions of the state of Minas Gerais, Brazil, in 1999, revealed a prevalence of 0.8% of infected animals. Approximately 5% of homesteads featured tuberculization-test-reagent animals. Further, 2019 bovines from 278 homesteads in the Federal District, Brazil, in 2004, revealed a 0.0305% and 0.419% prevalence of animals and farms, respectively [41].

Bovine tuberculosis has been included in the list of diseases with mandatory notification. Notifications reach MAPA through information produced by services of sanitary defense of each municipality and by government inspection organs. Information is transmitted to the World Organization for Animal Health (OIE) which dictates which control and eradication activities should be implemented after analyzing disease prevalence obtained from epidemiological surveys [43].

Economic impacts caused by *M. bovis* on beef cattle have been estimated at three million dollars a year [45]. Losses are due to 10% - 25% decrease in production efficiency, in weight gain, laying down of infected animals, devaluation and total or partial discarding of carcasses of infected animals and restriction in the international beef trade, with significant economic losses for Brazilian beef cattle herds [29] [32] [46] [47]. Liabilities caused by bovine tuberculosis may occur not only on the homestead due to the death of the animal, to the destruction of test-positive tuberculine reagents and to decrease in production rates, but also at the slaughtering point, precisely at the sanitary post-mortem inspection. This is due to the reduction of the price paid to the producer according to carcass degradation by the disease-causing lesions [35].

According to Rulings for Industrial and Sanitary Inspection of Animal-Derived Products (RIISPOA), the carcasses with tuberculosis-suggestive lesions in the muscles, bones, intramuscle tissues, thorax and abdomen organs, multiple or generalized miliary lesions should be forwarded for the rendering process. In the case of localized and discrete lesions, restricted to lymph nodes and organs, the removal of the affected parts and sterilization by heat become mandatory [48]. There is a 50% decrease in total price rate when diseased carcasses are heat sterilized, whereas no payment is due in the case of rendering [35].

Several studies [42] [47] [49] [50] have assessed the prevalence of tuberculosis-suggesting lesions in bovine carcasses during sanitary inspection. Needless to say, prevalence varied according to region and period of the year. In south-western region of the state of Bahia, Brazil, 0.12% of carcasses in 58,268 beef cattle showed tuberculosis-suggestive lesions [49]; in the state of Mato Grosso, percentage reached 0.48% over 41,193 [42]; in the north-eastern region of the state of São Paulo, percentage was 0.27% over 38,172 [47]; in the central-western region of the state of São Paulo, percentage reached 0.81% over 95,655 [50].

## 2.4. Human Tuberculosis

Tuberculosis is evidently hazardous to public health. Almost one third of world population is affected by *Mycobacterium* spp. Although less than half the number of new cases of tuberculosis estimated by the World Health Organization (WHO) is notified, there are nearly nine million new cases worldwide and 1.5 million people die yearly from the disease [51]. Among the twenty-two countries involving 80% of tuberculosis cases worldwide [52] [53], India ranks first, with 1,856,000 new cases a year. Brazil ranks 16<sup>th</sup> in the number of new cases and 22<sup>nd</sup> with regard to disease occurrence coefficient [35] [54].

There is an estimated prevalence of about 50 million people with tuberculosis in Brazil, with an annual occurrence of 43:100,000 inhabitants; mortality rate at 2.6:100,000 inhabitants and an incidence rate of 26:100,000 inhabitants for lung tuberculosis. Further, the disease ranks 9<sup>th</sup> in hospitalization and 4<sup>th</sup> in mortality rate by infectious agents [17] [55].

There were 87,233 cases, or rather, 41.9:100,000 inhabitants [17] in 2005, registered by the Disease Notification Information System of the Brazilian Health Ministry (SINAN/MS). In 2009, world estimates of new tuberculosis cases in humans reached 9.4 million, or rather, 137:100,000 inhabitants, with 4.1 million (62:100,000 inhabitants), featuring the lung type confirmed by bacilloscopy [9]. Further, in 2010, the Brazilian Nation Program for the Control of Tuberculosis (PNCT) informed approximately 72,000 (38:100,000 inhabitants) new cases: 35,000 were lung tuberculosis and almost 48,000 died from the disease. According to WHO, detection rate reached 88% [55].

In 2012, approximately 8.6 million people became committed by tuberculosis worldwide. However, recently there has been a decrease in the number of cases and deaths caused by the disease. There was a 45% decrease in the number of deaths worldwide between 1990 and 2012: estimates reached 1.3 million in 1990, whereas the number decreased to 940,000 in 2012. The same decrease has also been reported in Brazil: there was a 20.4% reduction between 2003 and 2013 [54]. Decrease may be attributed to control and eradication programs, to milk pasteurization and strict beef inspection norms [23] [56]. Within the context of 181 priority municipalities listed by PNCT, underscored municipalities lie in the south-eastern region of the country, followed by those in the northeastern and southern regions of Brazil. The states of São Paulo and Rio de Janeiro are the south-eastern states forming 76.5% of priority municipalities with the highest notification rates in human tuberculosis in the country [55] [57].

Although *M. bovis* was pinpointed as the cause of tuberculosis in humans and animals only in the late 19<sup>th</sup> century, it was only in the 20<sup>th</sup> century that the negative impacts of the microorganism on animal productivity and on human health were acknowledged [56]. Pathogenesis of bacteria *M. bovis* and *M. tuberculosis* is similar for humans since the two agents develop similar clinical and anatomic-pathological types [23] [58]. It has been estimated that in developed countries 1% to 2% of tuberculosis cases in humans are caused by *M. bovis*,

whilst estimates range between 10% to 20% (if not more) in underdeveloped ones [59].

People in contact with infected cattle or with products derived from these animals, such as veterinarians, abattoir workers, animal handlers and butchers are prone to be affected by the disease, especially those recovering from other diseases or immunodeficient persons [42] [44] [60]. Moreover, physiological and immunological factors linked to children, elderly people and AIDS patients raise infection risks in these people. The most common is the extrapulmonary form of tuberculosis [56].

Pet animals, such as cats and dogs inhabiting a rural environment, may also be infected through an aerogenic mode and by the ingestion of milk, meat and raw offal. They become vectors of the disease and transmit it to humans and other animals [23]. Moreover, bovine abattoirs are the most critical environments due to the exposure of workers in direct or indirect contact with the animals and their secretion which may be contaminated by *M. bovis*. The pulmonary mode is the disease's main manifestation [35] [61].

The clinical forms of the disease in humans are 1) primary pulmonary tuberculosis mainly affecting children; irritation, lack of appetite, low fever and night sweating constitute the main symptoms; 2) post-primary tuberculosis affecting people of all ages, but mainly young adults and adolescents; dry or productive cough is the main symptom; 3) extra-pulmonary tuberculosis, classified as peripheral ganglionic, bone, meningo-encephalic, miliary, pleural, genital-urinary or pericardial tuberculosis [34].

Human mortality caused by tuberculosis is unjustified since the disease is curable, diagnosis is relatively straightforward and treatment with rifampicin, isoniazid, pyrazinamide, ethambutol, streptomycin and ethionamide is totally efficacious. The Brazilian National Health System (SUS) provides free drugs for its treatment [35] [53] [62].

### **3. Cysticercosis Caused by *Cysticercus bovis***

#### **3.1. Historical Review**

Parasitism by the genus *Taenia* in humans predates history. Several investigations have revealed that such interrelationships occurred prior to the domestication of animals and the introduction of agriculture [63]. The conviction that eating the flesh of certain animals may cause illnesses is a concept hailing from 3000BC. For example, Jewish ancient laws prohibited the consumption of meat of certain animals (pork, for instance) due to their awareness of the transmission of cysticercosis [64]. Taxonomy of the larval form, called *Cysticercus bovis*, originates from the Greek terms “*kystic*” and “*kerkos*”, respectively meaning gallbladder and appendix [65]. However, the relationship between the adult and larval forms of *Taenia saginata* in bovines was only discovered by Levckart in 1861 after observing the development of cysticerco in calf tissues artificially infected by *Taenia saginata* proglottids [63]. A revision of Levckart's observations

by Oliver in 1969 revealed that the disease was actually a zoonosis due to the possibility of the development of tapeworms in humans through the consumption of cysticerci from infected cattle [65].

### 3.2. Bovine Cysticercosis

Bovine cysticercosis is a powerful zoonotic parasite disease causing great economic and health liabilities. Its etiological agent is *Cysticercus bovis*, the infecting larval form of *Taenia saginata* [66] [67] [68]. *Taenia saginata* is the adult cestode which, coupled to the larval form *Cysticercus bovis* forms the tapeworm-cysticercosis complex with different diseases triggered by the same parasite at different stages of development [69]. Cestodes belong to the class *Cestoi-dea*, order *Cyclophillidea*, family *Taeniidae* and genus *Taenia* [70]. They have a flat body similar to a tape, full of segments called proglottids, with approximately 80,000 eggs each. Measuring between 4 and 12 meters long, they may reach 25 m and may live in humans for nearly 30 years [63].

Although *Taenia saginata* exists worldwide, its occurrence is mainly restricted to less developed countries and regions with low socio-economic and cultural features, poor hygiene conditions, lack of septic cesspools and sewage treatment, causing the dissemination of the parasite in the environment [68] [71]. In fact, humans are the sole hosts of the parasite adult, whereas cattle are the intermediate hosts of *Cysticercus bovis*, the infecting larva [35] [72] [73]. Taeniasis in humans occurs on the ingestion of the larval forms living in the muscle tissues of bovines. After 90 days in the small intestine, the tapeworm turns adult even though egg release with excretion is possible after 60 - 70 days after infection [66] [74]. The final host may eliminate daily some 250,000 in the free mode and through pregnant proglottids. The latter may be found on the hands, clothes and perianal region of humans [73].

The parasite's evolution cycle is directly linked to the interrelationships between cattle and humans [75] [76]. Adult parasite-bearing humans are the main vectors in the contamination of the environment when they excrete parasite eggs in non-adequate places. Pastures and water sources for the consumption of animals and humans are thus contaminated. In fact, the accidental ingestion of human faeces together with pasture and water by bovines is a common event [72] [75].

Human excreta deposited in the open air and dried in the sun cause the eggs to become lighter. They are air-borne to long distancing, contaminating pastures, crops, kitchen gardens and water sources [15] [71]. Eggs present in the environment remain viable for weeks and months if the best humidity and temperature rates are available [73] [77]. Bovines ingest *T. saginata* eggs together with food and water. The eggs hatch in the small intestine due to the pancreatic juice. The released cysticerci penetrate the intestine mucus and reach the great blood-supplying tissues through the blood circulation [69] [78] [79]. Heart muscles, skeleton striate, masseter and pterygoid muscles, diaphragm, tongue and

esophagus are the main sites for the formation of cysts in cattle [80]. Cysticerci remain in these tissues till they develop into cysts. They become visible 15 days after egg ingestion. They are seen under the microscope as a solid transparent or a semi-transparent spot with approximately 1 mm diameter [35] [71].

Cysticerci mature within 84 days and reach a diameter of approximately 1 cm. They have a white-ashy color and are filled with liquid enveloped by a thin fibrous capsule that reveals a single movable scolex. They remain viable for several weeks and months. Dead cysts contain friable to calcified caseous mass, exhibiting live and dead cysts within a single carcass [15] [70]. However, cysticercosis in cattle is generally asymptomatic. Consequently, diagnose is difficult during the development period. On the other hand, intense infestations may generate myocardial conditions, heart insufficiency, non-specific clinical factors, such as high fever, hypersalivation, muscle stiffness and anorexia [73] [81].

Human taeniasis manifests itself clinically and sub-clinically. Symptoms comprise belly aches, nausea, headache, fatigue, slimming, constipation, increase in appetite and diarrhea. In some cases symptoms may be almost imperceptible, except for slight discomfort caused by the evacuation of the proglottids [63]. Further, cestodes in the small intestine damage the mucus and alter intestine motility. Appendicitis may occur due to the penetration of the proglottids in the appendix or even bronchial obstruction when the proglottids are regurgitated and inhaled [63]. Due to low toxicity, a 90% cure rate is usual. Niclosamida is the most efficient drug in the treatment of taeniasis. However, other drugs, such as Praziquantel, Paramomicina and Mebendazol, are also efficient [35]. In the case of cattle, Albendazole is the main anti-helminth for the treatment of cysticercosis with 86.7% efficiency for the degeneration of cysts [81].

### 3.3. Economic Impact and Control against Bovine Cysticercosis

In Brazil cysticercosis has a very high occurrence rate, with enzootic characteristics. Even though its prevalence is underestimated, it varies between 1.74 and 6.90% according to the region under analysis. Percentages may be higher in places where the finishing of confined cattle predominates [35] [78] [75] [82]. Taking into consideration that the Brazilian cattle herd amounts to more than 215.20 million [83], the liabilities caused by cysticercosis may be estimated at R\$ 24.5 million, with a mean prevalence of 5%. Further, the occurrence of the disease is a relevant indirect indicator of the herd's sanitary conditions in a determined farmstead or region. It also demonstrates the occurrence of the adult parasite in human populations close to the sites on which the animals pasture [84].

Southeastern Brazil has the highest occurrence rate in bovine cysticercosis [71], perhaps due to greater sanitary control in abattoirs. A survey in abattoir with sanitary control for 1980-2001 in the state of São Paulo, Brazil, gave a mean prevalence of 4.28%. Further, animals from the same state had the highest prevalence (5.80%) when compared to those from the states of Minas Gerais

(5.02%) and Goiás (1.88%), Brazil [85]. Cattle from the Araçatuba region in the state of São Paulo, Brazil, featured 4.18% prevalence between January 1990 and June 2000. In fact, all the municipalities which exported cattle from the region had cysticercosis-positive cattle [86]. In fact, several studies have shown that prevalence indexes in bovine cysticercosis continued high in the state, with rates close to 9.37% for the 1999-2001 period [87] and 2.9% for the period between 2000 and 2002 [88].

Liabilities caused by bovine cysticercosis within the beef chain are a great concern to abattoirs, beef industries and stock breeders. Since diagnosis is impractical throughout the breeding process, the detection of the disease occurs during the post-mortem examination and the economic losses caused by total or partial destruction of the diseased carcasses are high [66] [73] [78] [79]. According to RIISPOA, carcasses with tarnished flesh or having a watery aspect, with one or more cysts in cuts on several muscle parts or in the hoof area revealed high and generalized infestation, making total destruction mandatory<sup>48</sup>. If examination of heart, tongue, masseters, diaphragm and easily-accessed muscles reveal discrete to moderate infection, rejection of the carcass is partial. In other words, only the parts with cysts are removed and destroyed. The carcass is taken to the cold chamber or de-boned and the flesh cured with brine during 21 days or cold-treated at  $-10^{\circ}\text{C}$  for 15 days. This period may be reduced to 10 days if chamber temperature does not oscillate. If the number of cysts is above the amount mentioned above but generalization fails to occur, the carcass is heat sterilized. Carcasses with a single calcified cyst may be consumed *in natura* by humans after removal and destruction of the infected parts [48] [71]. Liabilities in abattoirs involve costs with carcass treatment, generating quality and price depreciation around 10% - 15% [89].

On the other hand, the producer suffers losses due to the price paid for the carcass and to lower beef yield, with a devaluation of up to 65% when the carcass contains live cysts, a reduction of up to 30% when cold treated, and up to 50% when heat sterilized [35] [75]. Approximately 29,708,550 kg of beef were destroyed due to cysticercosis in the state of Paraná, Brazil, during 2004-2008. At a mean price of R\$ 60.40 per 12 kg in the same state at the time, liabilities reached R\$ 120 million [90].

Several measures for the interruption of the parasite's evolution cycle and avoidance of the dissemination of infection by parasites may be found in the Good Practices for Agriculture and Stock Breeding and in the *Codex Alimentarius* of Brazilian beef production chain [91].

Training workers involved in the production in process makes them aware of the need to adopt basic hygiene habits, such as washing hands after going to the toilette, proper hygiene of fruits and vegetables prior to ingestion, the use of proper sites for human sanitary necessities, correct disposal of excreta, ingestion of cooked beef and supply of food and water to animals in places distant from human dejects-contaminated areas [92].

Although albendazole sulfoxide is an important alternative for the control and treatment of bovine cysticercosis during development, due to 89% - 100% therapeutic efficiency and for the decrease of the occurrence of taeniasis in humans, it is not an easy method. Cysticercosis does not produce any symptoms in bovines and thus diagnosis and decision-taking are difficult. Further, anti-parasite activities do not hinder economic liabilities and carcass discarding since the calcification of cysts is enhanced, leading towards the removal and destruction of the affected parts [71].

Needless to say, sanitary inspection in abattoirs is perhaps one of the most efficient types of control against the tuberculosis parasite. In fact, information retrieved during the post-mortem examination is necessarily transmitted to health and production departments, making possible the implementation of corrective and prevention measures for better sanitary conditions of cattle herds and workers involved. These measures will surely interrupt the parasite life cycle and, consequently, there will be fewer disease cases involving humans and animals [77] [90].

Veterinary inspection should inspect, on a permanent level, all abattoirs and related industries to warrant healthy products of animal origin, the hygiene of the premises and of workers and the maintenance of technological level that would ensure quality for consumers. Abattoirs would actively participate in the war against clandestine products. However, Brazil workers in abattoirs and related industries have low schooling level and low social and cultural upbringing. Such conditions make mandatory special attention to these professionals so that the most common hygiene habits may be complied with. These include washing of hands after toilette, taking a bath on rising, keeping hair short and covered, protecting cuts and wounds with proper dressings, keeping nails short and clean, working in white uniforms and without adornments (bracelets, rings, earrings, watches and others). In fact, hygiene guarantees the products' qualities. Consequently, medical care to workers in food industries is the best strategy to prevent the contamination of products by pathogenic microorganisms, by infected people or vectors of infectious diseases [64] [65] [66] [67] [77] [90].

Further, public health laboratories should control the quality of beef, milk and tinned products commercialized in Brazil to prevent the commercialization of bad products and exercise an educational stance in small- and medium-size industries. In fact, only big industries can afford to have the required control. Quality control should not be restricted to research on microbial agents but should be extended to the detection of chemical additives in amounts above those permitted by law. Unfortunately, Brazilian sanitary authorities undertake control of additives every 10 years on the revalidation of the product [67] [77] [90].

The war on clandestine animal-derived products makes mandatory a politically coercive attitude, even though such policy would be considered unpopular to people who prefer the product in natura and purchased by installments. If

development programs vis-à-vis small producers are not forthcoming to reallocate them within the market, if educational and consciousness-raising activities remain lacking among consumers, if sanitary supervision and inspection fail to warrant food safety to the population, the issue of clandestine commerce of animal-derived products will not be eliminated in Brazil. In the wake of current paradigms, it may be concluded that the magnitude of clandestine beef commerce in Brazil makes mandatory urgent sanitary measures to protect the population exposed not merely to infections with bovine tuberculosis but also with several other diseases vectored by contaminated milk and beef.

#### 4. Future Research

Neglected diseases are a worldwide issue in public health. Since the pharmaceutical industries' Research and Development program is exclusively run for profit, the private industrial sector focuses on global diseases and the production and commercialization of products for the generation of profit. Due to their low buying power and lacking political influence, poor patients and ill-equipped health systems fail to generate financial returns required by most profit-minded firms.

Tuberculosis and the taeniasis-cysticercosis complex partake of the group of neglected diseases which affect in a disproportionate way developing countries and with less relative development. Future research on these diseases should give priority to global activities and strategies to enhance innovation in treatments. Activities should aim at giving priority and enhancement of R&D, establishment and improvement of innovating capacities, promote transference of technology, enable countries to manage and enhance access to intellectual property, ensure mechanisms for sustainable financing, and establish monitoring systems. More attention should be given to funding institutions for medicines involving parasitology since neglected diseases, such as tuberculosis, receive less than 3% of laboratory funds.

One may expect that future research enhances the establishment of a national network which is capable of organizing international integrated R&D projects, including the production of medicines. Brazil has great importance in this field due to the fact that it features several neglected diseases and has a considerable infrastructure for research and production of medicines for these morbidities.

#### 5. Final Considerations

Sanitation in the slaughter line is one of the most effective ways of assistance in the control and prevention of diseases of public health interest, for taking away what you drive, viscera and footers with the warning signs of illnesses commercialized. The importance of cysticercosis and tuberculosis in acts as for the economic sector and the adoption of control measures become indispensable.

One point that tends to be favorable for the even greater reduction in the occurrence diseases, especially cysticercosis, in the next few years are the updates

observed in the new RIISPOA of March 29, 2017, which have become more stringent from a health point of view compared to the previous one, which producers are more concerned about the measures of control and prevention of their herds in order to obtain lower penalties Refrigerators.

Some studies have also been found in the literature that also retrospective evaluation of the evolution of the occurrence of tuberculosis and cysticercosis in certain states and establishments of slaughter, but these were composed of maximum of five years of evaluations. In this study, the long period of 21 years of monitoring of the data provided a greater insight into the behavior of occurrence of both diseases.

New studies, like this one, will be extremely important in order to be evaluated the epidemiological behavior of both tuberculosis and cysticercosis, in the prophylactic and corrective measures, not ruling out the need for intensification of prophylactic and corrective measures implemented by public agencies, in order to reduce even more these problems. It is also expected that this work will contribute to studies aimed at reducing tuberculosis cases caused by *M. bovis* and the increased awareness of the influence of man's role in cysticercosis bovine.

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