

## Review of Lobomycosis and Lobomycosis-like disease (LLD) in Cetacea from South America

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### ABSTRACT

Caused by a yeast-like organism known as *Lacazia loboi*, Lobomycosis (or lacaziosis) naturally affects humans, common bottlenose dolphins (*Tursiops truncatus*) inhabiting coastal waters from southern Brazil to Gulf of Mexico and Atlantic coast of Florida, as well as botos-cinza (*Sotalia guianensis*). These species are usually found in coastal waters, subject to runoff provided by large rivers and a considerable burden of associated contaminants. Histological and morphological studies demonstrated that the etiological agent of *L. Loboi* infecting humans is different from the one found to infected dolphins. Moreover, it likely that dolphin-human infections do not occur although infected bottlenose dolphins were from populations engaged in cooperative fishing that involve a relative small number of dolphins and humans. The records of Lobomycosis and Lobomycosis-like disease (LLD) in Tramandaí estuary (29°58'S), Rio Grande do Sul, Brazil, represent the southernmost distribution of *L. loboi*. On the other hand, the northernmost distribution of this disease is reported in the southern portion of Indian River Lagoon (27°25'N), Florida, USA. LLD seems to be more widespread, infecting both toothed small cetaceans and baleen whales, from the tropical Atlantic to the Pacific. Future studies should evaluate the association with impaired immune function in affected dolphins and the emergency of Lobomycosis. It may be associated with an immunosuppressive factor of environmental origin, such as exposure to pesticides or other agricultural or industrial contaminants, introduced through runoff or point sources of pollution, altering conditions to favour disease emergence. Lobomycosis should be assigned as neglected tropical disease, as should be the case of LLD, if future investigations indicate their connection as an emerging pathogen, its pathogenicity and environment requirements.

### INTRODUCTION

Caused by a yeast-like organism known as *Lacazia loboi* (Taborda *et al.*, 1999) (syn. *Loboa loboi*; Caldwell *et al.*, 1975), Lobomycosis (or lacaziosis) naturally affects humans, common bottlenose dolphins (*Tursiops truncatus*) and botos-cinza (*Sotalia guianensis*) (de Vries and Laarman, 1973; Caldwell *et al.*, 1975; Simões-Lopes *et al.*, 1993; Reif *et al.*, 2006; Van Bresse<sup>2</sup> *et al.*, 2007). *L. loboi* infecting *T. truncatus* from North and South America may be different from the one found in humans (Haubold *et al.*, 2000). Until recently it was believed that the same species (fungus) was the etiologic agent for the Lobomycosis in humans and dolphins but a morphological study showed significant differences in size and potential differences in host/organism interaction between the two agents (Haubold *et al.* 2000). The authors point some factors that could influence in the divergence of the two Lobomycosis “forms” (e.g. different environments occupation between the dolphins and humans and different core body temperature). In other hand, a recently study suggest that humans are infected with

similar *L. loboi* strains to those infecting dolphins (Mendoza et al. 2008), showing that this issue remain to be satisfactory described and interpreted. Instead some evidences of contamination exist in the literature (Symmers 1983) there is some controversy (Norton 2006). The possible existence of two different organisms as well the distribution characteristic of the Lobomycosis in human and dolphins could explain the low or inexistent risk of contamination between humans and dolphins. In humans, Lobomycosis is a self-limited, chronic fungal infection of the skin endemic in rural regions in South and Central America. The natural reservoir of *L. loboi* is unknown but soil and vegetation seem to be likely sources of infection for humans (Honda et al., 2007). Patients with Lobomycosis may have immunoregulatory disturbances possibly responsible for the lack of pathogen containment (Vilani-Moreno et al., 2005; Honda et al., 2007). Lobomycosis in dolphins is characterized by whitish to slightly pink, verrucous lesions, often in pronounced relief that may ulcerate (Migaki et al., 1971). In *T. truncatus* from the southern part of the Indian Lagoon, Florida, the disease was associated with an impaired immune function possibly caused by anthropogenic factors. Variation in salinity and water temperature may also play a role (Reif et al., 2006). The apparent emergence of Lobomycosis and Lobomycosis-like disease (LLD) in coastal *T. truncatus* from Colombia, Ecuador, Peru and Brazil was recently reported (Van Bresseem et al., 2007). At least two *T. truncatus* from Brazil have died with extensive Lobomycosis (Simões-Lopes et al., 1993; Van Bresseem et al., 2007). Lobomycosis needs to be recognized as a public health problem in coastal South America and other similar endemic areas. We propose the recognition of Lobomycosis as a neglected tropical disease such as leishmaniasis (kala-azar), onchocerciasis (river blindness), Chagas disease, leprosy, tuberculosis, schistosomiasis (bilharzias), lymphatic filariasis, African trypanosomiasis (sleeping sickness), and dengue.

## MATERIAL AND METHODS

We reviewed the available information on Lobomycosis published in scientific journals since its original description by Brazilian dermatologist Jorge de Oliveira Lôbo in 1931 (Lacaz et al. 1986). At least 12 articles on peer-reviewed publications have diagnosed Lobomycosis in bottlenose dolphins ranging from Florida to Texas, in the United States, south to Santa Catarina, in southern Brazil. More recently there is one confirmed new case for Rio Grande do Sul, south Brazil (see Moreno et al. 2008, this workshop). The emergency of an apparently similar to Lobomycosis mycotic disease, evidencing probable unconfirmed cases of such pathology in cetaceans from South America, so far called Lobomycosis-like disease (LLD) (Van Bresseem et al. 2007), has been pointed out in the literature. Since then, several new cases of LLD have been indicated in cetaceans, mostly Odontoceti (*T. truncatus* and *S. guianensis*) but also Mysticeti (*Balaenoptera brydei*), in the Atlantic and Pacific Oceans.

## RESULTS AND DISCUSSION

### *Geographic distribution of Lobomycosis and LLD*

In dolphins, Lobomycosis is widely distributed occurring from southern Brazil (Tramandaí River) to Gulf of Mexico and Atlantic coast of Florida (Reif et al. 2006, Van Bresseem et al. 2007). In South western Atlantic Ocean the Lobomycosis was first reported from a bottlenose dolphin beached in 1990 in Laguna (28°30'S, 48°45'W), Santa Catarina State, in southern Brazil (Simões-lobes et al. 1993). This was the only known case until recently where the apparent re-emergence of Lobomycosis and Lobomycosis-like disease (LLD) in coastal dolphins from Brazil, Colombia, Ecuador and Peru was reported (Bermúdez-Villapol et al. 2008, Van Bresseem et al. 2007). At least eight new cases of undetermined mycotic diseases, including LLD, in *T. truncatus* from coastal populations in southern Brazil, were reported (Moreno et al. 2008, this paper). Figure 1 shows reported cases of Lobomycosis and LLD in cetaceans from South and North America.

### *Pathogenesis*

The pathogenesis of Lobomycosis is unknown. This is caused primarily because the fungus cannot be cultured in the laboratory. *L. loboi* lives in the soil, water and vegetables, in a saprophytic way, acting as a pathogenic agent when it is able to infect vertebrates, as humans and dolphins. The agent is able to penetrate through the skin, depending of the cutaneous traumatism. It has been referred that previous small wounds in humans has preceded the mycotic lesions (Lacaz et al. 1986). However, in stranded dolphins, Lobomycosis has been associated with immunologic compromise and mutisystemic disease (Bossart, 1984).

### *Etiological aspects of Lobomycosis in dolphins*

Lacaz et al. (1986) have called the attention that Lobomycosis is spontaneously found in dolphins as ulcerated crusts lesions in the skin, usually located in the flukes or the back of the animals. Those authors also provided a first collection of reported cases in dolphins. Until recently it was believed that the same species (fungus) was the etiologic agent for the Lobomycosis in humans and dolphins but a morphological study showed significant differences in size and potential differences in host/organism interaction between the two agents (Haubold et al. 2000). The authors point some factors that could influence in the divergence of the two Lobomycosis “forms” (e.g. different environments occupation between the dolphins and humans and different core body temperature). In other hand, a recently study suggest that humans are infected with similar *L. loboi* strains to those infecting dolphins (Mendoza et al. 2008), showing that this issue remain to be satisfactory described and interpreted. Instead some evidences of contamination exist in the literature (Symmers 1983) there is some controversy (Norton 2006). The possible existence of two different organisms as well the distribution characteristic of the Lobomycosis in human and dolphins could explain the low or inexistent risk of contamination between humans and dolphins. In humans, Lobomycosis is a self-limited, chronic fungal infection of the skin endemic in rural regions in South and Central America.

In fact, the distribution of dolphins’ cases of Lobomycosis and LLD and in humans seems to be parapatric. More intriguing is the apparent lack of reported cases of Lobomycosis and LLD for freshwater mammals, like the Amazonian manatee (*Trichechus inunguis*), tucuxis (*Sotalia fluviatilis*) and botos (*Inia geoffrensis*). It should be noted that Da Silva et al. (2008, this workshop) have not indicated the presence of Lobomycosis or LLD in 385 botos examined in central Amazonia from 1994 to 2007. In addition, no evidence of such mycotic pathologies was found in coastal populations of *S. guianensis* studied in coastal Pará state waters since 2004 (N.R. Emin-Lima and S. Siciliano, pers. observ.), as well as over 90 botos-cinza incidentally captured off Amapá, or in *I. geoffrensis* observed in the vicinities of Belém, Para’s capital and coastal Marajó Isl., northern Brazil. It should be emphasized that other pathologies were noticed in *S. guianensis* from the Marajó bay area and off Amapá, as reported in this workshop.

### *Epidemiology of Lobomycosis*

In humans, Lobomycosis is most common in farmers, rubber workers, hunters, and prospectors, but some travellers are also affected. The natural reservoir of the fungus is unknown but soil and vegetation seem to be likely sources of infection for humans (Honda et al. 2007). All human cases in Brazil are distributed almost exclusively in the tropical zone in North and North-eastern regions where the high temperature (mean 24°C) and humidity favours the occurrence of mycosis (Brito and Quaresma 2007). Conversely, in dolphins all cases are concentrated in Southern region in the estuarine/marine environment under the influence of the Subtropical Convergence (Simões-lobes et al. 1993; Van Bressemer et al. in press) showing a likely parapatric distribution. The same pattern occurs in Venezuela where all human cases are described in inland zones generally at 200-250m over the sea level heights with high temperature, precipitation and humidity (Paniz-Mondolfi et al. 2007) and the recent case described in literature is present in marine environment (Bermúdez-Villapol et al. 2008, this workshop).

In dolphins, especially *T. truncatus*, Lobomycosis is likely to be lethal in older dolphins, subject to severe ulcerative and crosstie lesions, widespread over the flanks, ventral body, jaws, flippers and tailstock (Simões-Lopes et al. 1993, Moreno et al. 2008). Both sexes seem to be equally affected. Lobomycosis seems to be epidemic in small coastal populations of dolphins, with highly social structure and affective bonds. This could explain the prevalence of such pathology in several small dolphin populations confined to coastal habitats along North and South America.

### *The epidemic re-emergency of Lobomycosis and LLD along southern and south-eastern Brazil*

As pointed out by Van Bressemer et al. (2007), naïve populations are more susceptible to develop Lobomycosis and LLD, as might be the case of the *T. truncatus* of Baía Norte and *S. guianensis* of Guaraqueçaba. In *T. truncatus* from the southern part of the Indian Lagoon, Florida, the disease was associated with an impaired immune function possibly caused by anthropogenic factors. Variation in salinity and water temperature may also play a role (Reif *et al.*, 2006). Alternatively, the marked gradient in the distribution of Lobomycosis from the southern to the northern portion of the Indian River Lagoon

may reflect variations in water temperature, salinity, or vegetation and enhanced survival of the organism in the marine environment (Reif et al 2006). Probably the lower water temperatures in southern Rio Grande do Sul State during winter (around 10°C) may constrain the survival of *L. lobo*.

As Lobomycosis and LLD diseases have only been recently reported in bottlenose dolphins from Bafa Norte, Santa Catarina state, and botos-cinza in Guaraqueçaba, Paraná state, Brazil (Flach et al. 2008, this workshop, Van Bresseem et al. 2008, this workshop), it seems to be the re-emergence of the etiologic agent of Lobomycosis among coastal Brazilian dolphins. Moller et al. (1994) have shown that *T. truncatus* photo-identified in Tramandaí were resighted in Mampituba and Laguna, over 200km north of its original site. It is though possible that transient *T. truncatus* and *S. guianensis* are getting contact with infected populations from different sites along southern Brazil, providing the opportunity to infect naïve populations. Evidence of LLD in baleen whales also requires more in-depth investigation for confirming the agent involved in such pathologies.

#### *Lobomycosis like-disease (LLD), a newly reported disease in dolphins and whales from South America?*

Van Bresseem et al. (2007) reported a variety of cases of dolphins with possible Lobomycosis-like diseases (LLD) in different areas of South America. New evidence is provided for southern Brazil, Gulf of Guayaquil (Ecuador), Bahia Malaga and surroundings (Colombia), Callao (Peru) and Isla Margarita (Venezuela). It is thus indicated a widespreading of LLD from the tropical-subtropical Atlantic to the Pacific coast. It seems that LLD, as a disease previously known only to the Atlantic coast may be present in the Pacific coast or represents a new mycotic disease in dolphins and whales yet to be described.

More intriguing is the fact that *Sotalia guianensis* from the Cananéia estuary, in southern São Paulo state coast, does not show any evidence of LLD. Conversely, the *S. guianensis* population in Guaraqueçaba, adjacent to Cananéia, has presented a large proportion of dolphins with skin disorders, most likely LLD (Van Bresseem et al, 2008).

#### *Lobomycosis as a neglected tropical disease*

International attention is currently mainly focused on the “big three” of HIV/AIDS, malaria and tuberculosis, but attention to other infectious diseases, which have a very strong negative impact on poor human populations, is neglected. Neglected diseases are neither perceived as priorities by the health systems of developing countries nor by sponsoring international agencies and philanthropic organizations and they escape especially the attention of the pharmaceutical industry. Therefore they require special attention when the research agendas are set and development of new tools discussed. So far, there is no generally accepted definition of neglected diseases (WHO, 2007). There are several attempts which look at the problem from different angles. A valid approach from the research point of view is to define neglected diseases as those for which there is an insufficient market or political status to drive adequate private sector and public sector research and development (R&D). Depending on the source a quite large number of diseases may fall into this category, like human African trypanosomiasis, buruli ulcer, Chagas disease, dengue fever, filariasis, guinea worm, leishmaniasis, leprosy, malaria, onchocerciasis, rabies, schistosomiasis and tuberculosis.

According to WHO definitions, Lobomycosis should be assigned as a tropical neglected disease affecting both humans and dolphins. Further investigation should provide light into the epidemiology of Lobomycosis-like disease, whether it represents a mycotic agent yet to be described or a widespread “form” of Lobomycosis. The role of environmental factors should also be addressed, as coastal environments are changing dramatically in the last decades.

## **CONCLUSIONS**

In cetaceans, Lobomycosis is reported in only two dolphin species (*T. truncatus* and *S. guianensis*) inhabiting coastal waters from southern Brazil (Tramandaí River) to Gulf of Mexico and Atlantic coast of Florida. These species are usually found in coastal waters, subject to runoff provided by large rivers and a considerable burden of associated contaminants.

Histological and morphological studies demonstrated that the etiological agent of *L. Lobo* infecting humans is different from the one found to infected dolphins. Moreover, it is likely that dolphin-human

infections do not occur although infected dolphins were from populations engaged in cooperative fishing that involve a relative small number of dolphins and humans.

The records of Lobomycosis in Tramandaí estuary (29°58'S) represent the southernmost distribution of *L. loboi*. On the other hand, the northernmost distribution of this disease is reported in the southern portion of Indian River Lagoon (27°25'N), Florida, USA. LLD seems to be more widely diffused, infecting both toothed small cetaceans and baleen whales, from the tropical Atlantic to the Pacific.

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Figure 1. Known distribution of reported cases of Lobomycosis and Lobomycosis-like disease (LLD) in cetaceans in the Americas.

