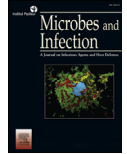




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Highlight

Reservoir rats[☆]

Keywords: *Leptospira*; Leptospirosis; Animal reservoir; Rats; Ecotourism

Don't you go where the husky's go, don't you eat that yellow snow, is the advice the Eskimo Nanook gets from his mother in the “Don't Eat The Yellow Snow Suite” from 1974, a delirious musical product of the insane and brilliant mind of the satirical, anti-mainstream composer and performer Frank Zappa. Later, Nanook clashes with a “strictly from commercial” fur trapper, and husky urine-soaked snow turns out to be a dangerous weapon. Zappa got this actually right, even if maybe not for this reason, as *Leptospira*, the causative agent of leptospirosis is transmitted *via* the urine of animal reservoirs, rats in pole position, which carry the bacteria in their renal tubules and shed them continuously into water and soil [2,3].

The first time I remember having heard about leptospirosis was under Paris. Not in, but under, literally, in the ancient quarries, exaggeratedly generalized as the catacombs, in order to increase their shiver factor [4]. Of course we are not talking about the legal tourist trip to visit some bone wall, but about the forbidden labyrinth of galleries and caves stretching out under a huge part of Southern Paris – maintained, sculpted, painted and expanded on a regular basis by hundreds of “cataphils”. Upon nightfall, dark figures wearing boots and headlamps appear, quickly check the surroundings and swiftly open some metal cover in the pavement, an access to an electrical gallery, and disappear into another world, a humid world without light or time, where the motionless air is at 18 °C all the year, with small stalactites over your head, leftovers of German bunkers at your feet and squeaking rodents in the dark. They gather in a huge room and take the wine and sound system out of their backpacks. There are countless candelabra on the ceiling, candles, plastic flowers, curtains, fake skulls, accumulated over time, the walls are covered in graffiti and psychedelic artwork, someone has painted the notes of Chopin's funeral march on the stone. Eventually, they will cook some sausages on a camping stove or roam the tunnels with garbage bags, cleaning up after the

weekend's party visitors, who only come once. Around 5 am, they re-emerge in front of a bakery diffusing the smell of fresh *croissants*, discretely close the manhole cover and quickly disperse, returning to their other lives as a mobile phone customer consultant, rope access technician or biologist. Only a couple of faint muddy footprints remain on the asphalt.

Going underground has become a *must have been there* of the young Parisian intellectuals. Pseudo-adventurers, I fully assume being part of, filled with pre-historical nostalgia, take an irrational pleasure in walking kilometers in ankle-deep water, crossing the fog of smoke-bombs and compensating the sleep deprivation by liters of coffee. It seems that when the living standard crosses a certain level, the neglected reward system triggers the sudden urge for artificial hardships and dangers, and in the comfortable era of Roombas and pizza delivery services, some fans of Bear Grylls absolutely want to cross snow fields and Piranha-filled rivers.

So, during one of my first descents into the catacombs, a regular told me casually about the possibility to contract leptospirosis. Indeed, there are rats, the natural needs of the rats, water and the skin of one's feet rendered all wet and permeable [3]. And of course I just had a quick look at my wrecked sneakers and shrugged, a certain disrespect, allowedly, for a discrete genus that should be nominated for a range of categories of the prize of successful pathogenic bacteria. For being the world's most spread zoonosis, for example, as *Leptospira* are everywhere, on all continents and in all mammalian species [2,5]. For their survival and cooperation skills in various environmental conditions in soil or water, maybe in form of aggregates or biofilms [3]. And on top of all, for being quite a pain at bench and bedside: growing slowly, demanding in medium conditions [6], they tend to lose their virulence in subcultures [5]. The next difficulty resides in determining the lipopolysaccharide mosaic on the bacterial surface among 24 serogroups and over 260 pathogenic serovars, which actually have nothing to do with a Russian device for tea making [5,7].

[☆] Article highlight based on “*Leptospira*-rat-human relationship in Luzon, Philippines” by Sharon Yvette Angelina M. Villanueva et al. [1].

The gold standard, the microscopic agglutination test (MAT), requires all the things that are rare in tropical and subtropical countries, where leptospirosis is endemic [8] – time, money and material like panels of local *Leptospira* serovars kept in culture [5,6] – and is only slowly replaced by easier detection methods based on qPCR and sequencing [5,6,8]. Due to the diversity of clinical signs, diagnosis is equally difficult for physicians. Vaccines have been developed for nearly a century [5], but they require an annual revaccination, are serovar-restricted [5,6] and tend to upset animal welfare companies for the sake of Golden Syrian Hamsters [9].

But *Leptospira* excel most in the art of mystery keeping. A huge part of reviews in their honor is about the things we do not know, and compared to other bacterial pathogens, this is a lot [2,5]. The cellular and molecular basis for pathogenesis are barely understood, virulence, adhesion factors and membrane topology not identified [5] and potential gene transfer and eventual regulatory small RNA mechanisms not elucidated [2,5]. The recent use of comparative genomics between pathogenic and saprophytic species has added more questions than answers: over 900 genes are proper to pathogenic *Leptospira* species *interrogans* and *borgpetersenii*, but 80% and 60% respectively of those are genes of unknown function and *vice versa*, among the proteins of known functions are no homologs of other bacterial virulence factors [2]. In a nutshell, *Leptospira* displays a high degree of genome plasticity and possesses unique, unknown virulence determinants. Even more recent application of mutagenesis directed against potential virulence factors turned out likewise frustrating and mainly proved the high degree of redundancy in leptospiral proteins [2,5] and the inadequacies of current simulations of *in vivo* conditions [2].

Part of the lack of knowledge is certainly due to a certain lack of interest [7]. As a consequence, genetic tools were applied late and there are no high throughput screening methods available yet [2,5].

The challenge of the peculiarities of *Leptospira* alone is apparently not motivating enough. Maybe, leptospirosis is not deadly enough, and for sure, it will be tricky to arouse much interest in it right now, in the shadows of the current outbreak of Ebola in Western Africa. Maybe it usually happens far away, in some filipino rice fields.

However, maybe the catalyst to promote research on *Leptospira* & Co. will be the adventurers of the 21st century, for whose the curious concept of “recreational exposure” had to be created, which incidence is increasing in the western world while the one of occupational exposure decreases [3]. Ecotourism, adventure races and outdoors sports involving fresh water activities such as triathlons, rowing, bathing in rivers, canoeing and fishing have become the local rice fields [3,6,7]. And while mosquitoes travel to the Europeans thanks to climate change, Europeans travel to the mosquitoes thanks to countless adventure agencies [10]. Leptospirosis is not an individual case, the same goes for leishmaniasis [11,12] or tick-borne diseases [13,14] for example and

several studies deemed necessary to point out that washing contact lenses in rivers is a bad idea and going “Kitty!” when spotting a tiger, even in private zoo, not an adequate reaction [15].

There are largely broadcasted cases like the death of the Olympic rower Andy Holmes [7] in 2010 from leptospirosis and anecdotal ones like the family father who became ill after his vengeful daughter had cleaned the pet-mouse cage with his toothbrush after an argument [3] – they may, as a side effect, direct attention to regions like the Philippines and disadvantaged inner-city environments even in Europe [6], where little is officially known concerning the incidence, prevalence and geographical distribution of animal reservoirs and serovars, thus severely hampering vaccination programs [5,6,8]. In parallel to deciphering the molecular mechanisms of *Leptospira* virulence, much work has to be done in terms of surveillance, reporting and generating the big picture of connections between humans, animal reservoirs and environmental data such as flooding [1,7].

Nota bene, after crossing the Corsican mountains with a hammock, several kilos of pasta and a Nutella jar – drinking directly from any river is not a good idea either.

Biosketch

Dr. Villanueva finished her Science Bachelor in Public Health in 1997 at the University of the Philippines in Manila and got her Master of Medical Sciences in Bacteriology in 2006 and her PhD in Medical Sciences in 2010 both at the Kyushu University of Fukuoka (Japan). Currently, she is completing a postdoctoral fellowship there at the Department of Bacteriology. Dr. Villanueva has been working on *Leptospira* and leptospirosis since 1998. Her research interests include serological and molecular epidemiology, pathogenesis and immunology of *Leptospira*, leptospirosis and other infectious diseases.



Interview with Sharon Y.A.M. Villanueva

What triggered your interest in the link between Leptospira, humans and rats?

As it is common knowledge, leptospirosis is one of the zoonoses that is widely spread around the world. Our country, Philippines, is known to be endemic for this zoonosis. Rodents, especially rats, are known to be the most important

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