

Major impact of massive migration on spread of epidemic *Mycobacterium tuberculosis* strains

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Introduction. *Mycobacterium tuberculosis* has clonal population structure whereas its different lineages are marked with different evolutionary pathways, and some of them have undergone a dramatic global dissemination. Furthermore, clinically/epidemiologically significant compact clusters have been identified by high-resolution genotyping. I will review *M. tuberculosis* clones from different genotype families (Beijing, Latin-American Mediterranean, NEW-1/Iran) that emerge in Russia and some neighboring countries and have impact on health situation on more global scale due to particular migration flows.

Methods. The present study combined the original research, data-mining and systematic and critical review. Molecular data on *M. tuberculosis* strains were obtained by both classical genotyping and WGS/NGS analysis. The published literature and available databases were searched to retrieve information about *M. tuberculosis* genotypes.

Results. A strong association with multi/extensively drug-resistant tuberculosis (TB) has been shown for Beijing B0/W148 strain that I termed a successful Russian clone. It likely originated in Siberia and its primary dispersal was likely driven by a massive population outflow from Siberia to European Russia in the 1960-80s. Its successful dissemination was triggered by an advent and wide use of the modern anti-TB drugs in the same years and was due to its remarkable capacity to acquire drug resistance. However, B0/W148 strains brought to Europe with immigrants from Russia and other FSU countries, do not necessarily spread in the new autochthonous population.

For another significant genetic family of *M. tuberculosis*, LAM (Latin American Mediterranean), we also found an emerging epidemic sublineage, that is actively spread within the European part of Russia and Eastern Europe. In contrast, Ibero-American sublineage LAM RD-Rio is not so widespread as claimed and its dispersal is shaped by global migration flows rather than its special properties. LAM RD-Rio strains are found in South America (area of primary circulation) and North America and Western Europe (due to immigration) but only sporadically in Russia (tourism only).

Finally, the NEW-1 family is an intriguing under-estimated *M. tuberculosis* genotype prevalent in Iran. It was highly prevalent in the South Iran and north-east decreasing gradient towards Central Asia could be observed. Its historical primary dispersal towards North India and China likely took place via the Silk Road. This family has re-attracted attention very recently: due to the significantly growing circulation in Iran (including emergence in North Iran) and neighbors and a capacity to rapidly acquire drug resistance. Particular migration flows in this part of Asia (especially, Afghan refugees) make these strains of special concern.

Conclusions. Mass immigration and a high prevalence in the initial population present decisive factors that define the spread of *M. tuberculosis* strains. On the other hand, manifestation of the strains's pathobiology can be changed (counteracted) by genetic factors of the human host population. New emerging strain becomes emerging in its area of origin, where its parental strain was circulating. But not necessarily it will be emerging/epidemic elsewhere. Mass migration is required to visibly increase prevalence rate of imported *M. tuberculosis* strain in new location. Human exchange/travel is not enough to bring and settle down new *M. tuberculosis* strain in an indigenous population: speculatively, a kind of human resistance is developed in local population through its co-existence with historical local clones, and acting against imported clones.

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References

- Mokrousov I. 2016. Emerging resistant clone of *Mycobacterium tuberculosis* in West Asia. *Lancet Infectious Diseases* 16: 1326-1327.
- Mokrousov I, Vyazovaya A, Iwamoto T, Skiba Y, Pole I, Zhdanova S, Arikawa K, Sinkov V, Umpeleva T, Valcheva V, Alvarez Figueroa M, Ranka R, Jansone I, Ogarkov O, Zhuravlev V, Narvskaya O. 2016. Latin-American-Mediterranean lineage of *Mycobacterium tuberculosis*: Human traces across pathogen's phylogeography. *Molecular Phylogenetics and Evolution* 99:133-143.
- Mokrousov I. 2013. Insights into the origin, emergence, and current spread of a successful Russian clone of *Mycobacterium tuberculosis*. *Clinical Microbiology Reviews* 26:342-360.