

<http://tinyurl.com/stopsmallpox>

## Should we keep researching smallpox?

Humanity has not known a case of smallpox for the last 36 years, since 1978. In 1980, the World Health Organization (WHO) certified the success of the vaccination campaign that cleared one of the worst diseases ever known. Smallpox, caused by the virus *variola*, killed 30 to 80 % of its victims, and afflicted the survivors with crippling disabilities, often blind.

Complete elimination of *variola*, however, has not yet been achieved: stocks remain in 2 laboratories, legacy of the cold war climate, in Russia (former USSR), and the USA. These stocks were destined to destruction, in order to completely rule out a re-emergence of the disease, but the date of their actual destruction has not yet been reached. In the time since eradication, limited and controlled research was permitted with the aim of developing better diagnostics, vaccines and drugs. A small group of virologists directly involved with smallpox research has recently published an opinion article (Inger K. Damon, Clarissa R. Damaso, Grant McFadden, PLoS Pathogens, Vol 10, 5. 2014) asking to postpone once more destruction of stocks and for further research to be allowed. The article was widely reported in the general press (29 reports, from all over the world, see here), which assumed and passed the notion that it was the opinion of the scientific community (articles titled, e.g. The Washington Post: "Scientists urge delay in destroying last smallpox", ABC News: "Scientists Urge Delay in Destroying Last Smallpox").

The Pugwash Conference was held at the call of a group of scientists in the aftermath of nuclear bomb explosions. In that case, it was not until after the fact that scientists came to consider their responsibility in the creation of the most potent weapon ever. At that time the Conference, inspired by the Russel-Einstein Manifesto, assumed the purpose "to bring together, from around the world, influential scholars and public figures concerned with reducing the danger of armed conflict and seeking cooperative solutions for global problems", by calling scientists onto their responsibilities. I think that the bio-science community should also go through a similar process of thinking about the results of our work, but this time before, not after the fact.

There are several reasons to stop all smallpox research now.

Accidents happen. Even the best equipped laboratories cannot prevent or foresee all possibilities of failure, due to human mistakes or external factors. The precedent of the accident at the Fukushima nuclear power plant here should serve as lesson: earthquakes were considered, but not enough. Work in Level 4 safety labs is not easy, and even the most expert researcher can have a bad day, a moment of distraction, a minor difficulty in a complex experiment. It is impossible to prevent every single action that might start a chain of events leading to viral escape. This risk would easily be eliminated if no research with live *variola* virus was to be allowed.

Sociopathic individuals, or a single person with extreme ideals are possibly the most likely, and at the same time the most difficult to detect source of an epidemics. Here, the Anthrax precedent of 2001 should serve as lesson. The best way to make it impossible for such a person to get hold of viral sample would be the total destruction of all stocks.

If an epidemics should start, it would most likely be the worst health problem ever faced. The amount of susceptible hosts, their concentration (> 50% of people live in urban areas), the speed of transport and universal communication would facilitate the spread of the disease, and also cause a world panic capable of a damage comparable to the actual viral disease. It is worth reminding that

people under 35 years old have not been vaccinated, and the rest of us, that still hold a mark on the upper arm may not be protected anyway. However, the only reliable origin of a new smallpox epidemic is held in the freezer and the laboratories of just 2 military research centres in the world. If they were closed, and stocks destroyed the scenario above would be just fantasy.

If an epidemic was ever to be started, the available amount of antiviral drugs and vaccines would be insufficient for the 7 billions people at risk. Distribution of this scarce resource would have to be made according to some criteria, that, at present, have not been finalized; it is easy to foresee that the wealthier would get easier access, widening the gap between the have and have not. Rather than investing in stocking drugs that have not (and cannot be) tested, it seems much more sensible to eliminate the risk of epidemics, by eliminating the viral stocks.

The fact that deliberate use of smallpox as a bioweapon cannot be ruled out (despite all international agreements) makes the destruction even more pressing. In this perspective, the elaboration of vaccines and drugs could be interpreted as a means to protect one's own, while using the virus as an attacking weapon. Once again, a good reason to destroy all samples and stop research, which will lead to increasing distrust among the nations that still hold stocks of virus.

The Authors of the PLoS article play a very dangerous game using the rhetoric trick of repeating many times the threat of 'future epidemics' thus making it appear as a real possibility. However, as explained before, the only threat comes from the continuing existence of viral stocks, and from increasing the number of researchers that have both access to the stocks and the knowledge necessary for keeping it alive. They argue that 'the research agenda with live variola virus is not yet finished and that significant gaps remain'. Gaps of knowledge are huge in many fields (arguably all), and research efforts could be better aimed at subjects that constitute a real (not hypothetical) threat to human health. The 'uniqueness' of variola also seems pretextuous argument: any organism, bacterium or virus is unique in some way. The question is whether or not knowledge in the subject is going to make our future better or worse. In this respect, we consider that all work done from 1999 on smallpox is dangerous, useless or both, because it can only increase the possibility that the disease is revived. The availability of viral genome sequence info makes it possible (although, luckily very difficult) to create synthetic virus. Vaccines and drugs cannot be tested, since no perfect animal model exist. At the same time, practical knowledge on the details of virus cultivation and expansion in the laboratory is spreading, thanks to allowed research. Finally, the claim that smallpox research has produced some benefits relative to other diseases due to different members of the pox family is untenable: if the aim is to cure monkeypox or vaccinia, then the relevant virus type should be studied, and it makes little sense to use variola for these aims.

Altogether, we consider that the 'threat of future epidemics' is a self fulfilling prophecy, but one that can and must be prevented. The decision on the fate of smallpox is rightly on the shoulders of the WHA, in representation of all citizens of all Countries, and must not be stirred by a small group of scientists with a direct interest. We urge the bio-research community to engage in a reflection on their (our) responsibility: are we ready to take upon ourselves the burden of a new smallpox epidemics? We also urge the WHA to finally conclude the job of smallpox eradication by mandating the complete and controlled destruction of remaining stock, while prohibiting any further research and new knowledge acquisition.

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