

Experimental adaptation of an influenza H5HA strain confers respiratory droplet transmission to reassortant H5H/H1N1 virus strain in ferrets

Adaptação experimental de uma cepa de influenza H5HA confere transmissão por gotículas aéreas numa cepa recombinante H5Ha/H1N1 do vírus da influenza em furões

Jacyr Pasternak*

ABSTRACT

An evaluation of the role – if any – of censorship in scientific papers, based on the publishing of the article that shows it is possible to modify the genetics of the H5N1 aviary influenza virus, enhancing its transmission among mammals, which was followed by much ado and ethical discussion.

Keywords: Influenza in birds; Influenza vaccines; Science

RESUMO

Analisa-se o papel – se houver algum – da censura a artigos científicos, alicerçada na publicação do trabalho que mostra ser possível a modificação genética do vírus H5N1 da influenza aviária, tornando-o mais transmissível entre mamíferos, que foi seguida de muito alvoroço e muita discussão ética.

Descritores: Influenza aviária; Vacinas contra influenza; Ciência

INTRODUCTION

Censorship is atrocious, in any circumstance and relating to any subject – although this may seem a radical position! In a historic decision, the North American Supreme Court determined that even pornography should be freely released and distributed, as long as it is restricted to adults. After all, adults, by definition, have the capacity, discernment and free choice to decide what they do or do not want to see or read – and there is nothing easier to do, if what they are seeing or reading does not please them, than to use the remote control of the television, of the CD, or to put the book aside.

In science, there have been areas prohibited by ecclesiastical authorities: discussing the course of stars in non-geocentric models, for example. Even today, in Islamic countries, it is very complicated, if not impossible, to discuss the theory of evolution in the terms known here in the Western World; it may even be used for animal evolution, but when it comes to the human species, it is opposed to the Koran. Contrary to the Bible, admitted as inspired by God, but written and interpreted by men, the Koran was dictated by the archangel Gabriel directly to Mohamed, who dictated the text to the people who wrote it, with the supervision of Gabriel so that there would be no imprecisions. In it is the story of Adam and Eve, created directly by God, and so, where do we stand?

Attempts to censure science have existed before. The Nazis considered psychoanalysis a “Jewish” science, and the physics of Einstein a “Jewish physics” and therefore, inadmissible. The Argentinian Neo-Nazi generals considered every psychologist an infidel interested in demolishing the Christian foundation of the Argentine soul, and not only did they persecute and kill many psychologists (and that is why we have in Brazil so many Argentine psychologist who sought refuge here), but they also tried to prohibit the teaching of this heresy. In order to avoid biases, let us remember that Stalin and his cohorts also believed in the existence of Soviet genetics, following the principles of Lyssenko, a perfect charlatan, who delayed the progress of Russian genetics by decades. Vavilov, a classic geneticist, ended up being killed and

* Hospital Israelita Albert Einstein – HIAE, São Paulo (SP), Brazil.

Corresponding author: Jacyr Pasternak – Avenida Albert Einstein, 627, consultório 1.316, 13º andar – Morumbi – Zip code: 05651-901 – São Paulo (SP), Brazil – Phone: (55 11) 2151-2430 – E-mail: jpaster@einstein.br

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his works were prohibited in the old Soviet Union. The results were insignificant. No valuable scientific project, as per the paradigms of science, was kept from being widely known, despite the objection by the guardians of “morals” and “common decency.”

ETHICAL DILEMMAS

Now that we have greater knowledge and better technology with which to modify and understand the genetics of pathogens, ethical dilemmas are created: should projects that would offer malicious people the capacity to do evil be reported? A recent paper, or rather, two recent articles epitomized this dilemma.

Imai et al.⁽¹⁾ published in the May 2nd, 2012 issue of *Nature*, an article in which they evaluate the molecular alterations in HA that would allow a virus possessing the H5HA subtype to become transmissible among mammals. This project – in addition to another one that leads to the same conclusion, authored by Dr. Ron Fouchie and sent to *Science* – almost was not published. A group of scientists and bureaucrats of the National Science Security Advisor Board for Biosecurity requested both from *Nature* and *Science* that they change parts of the articles of these authors, by not revealing the methodology developed to make the H5N1 aviary influenza virus transmissible by respiratory route to ferrets.

This virus is basically aviary, and contrary to other influenza viruses that are not a great bother to birds, it can be lethal⁽²⁾. There are few cases – around 600 known cases – of documented transmission of this virus from chickens and ducks, fundamentally, to humans, and the mortality of this disease has been high – around 50%⁽³⁾. This virus has an antigen that binds to a receptor of the lower respiratory tract, and not of the upper respiratory tract, and for this reason has little potential transmission from human to human. In almost all known cases, there is intimate contact between humans and bird. There are scarce reports of possible transmission between humans, and these cases were in individuals who care for birds seriously ill with influenza by this agent, with a greater quantity of the virus being excreted⁽⁴⁾.

CENSORSHIP IN SCIENCE

This is likely the first attempt of vetoing the publication of an article submitted to scientific journals. In reality, there are studies that analyzed biological agents, such as weapon of war, which were never offered to these journals.

The ancient Soviet Union affectionately studied the use of anthrax – and this led to what was probably the worst accident with this agent, with more than 90 deaths, surpassing in lethality the attempts made with this same anthrax soon after September 11th, in New York⁽⁵⁾; in that case, a “researcher” opened a window that should have never been opened, causing a “plume” of anthrax spores to invade a city in the Urals⁽⁶⁾.

In the United States, it is known of studies conducted at Fort Detrick, which were never published or submitted to publication to scientific journals. The scientists involved in these feats knew perfectly well that what they were doing should remain secret – and this without considering the ethical implications of toying with these things, which could have made them not want to make their projects public⁽⁷⁾...

The claim made by the Board for Biosecurity is that there is a risk of this piece of information going to the wrong people (who would they be?) and being used to produce a biological weapon for which, at the moment, there is no authorized vaccine. In truth, there is a study published that indicates how to produce a vaccine⁽⁸⁾, equally using molecular methodology. And how could such a vaccine be tested, after all, in a disease with this lethality rate? It is necessary to have an experimental model, and this is what these authors were able to develop. It is also important to point out that these viruses are genetically very similar⁽⁹⁾ and that they can be isolated from pigs, in which they coexist. Pigs are the incubators that generated practically all the epidemics of influenza, since they bear the recombination of aviary, swine and human viruses.

The technology used to develop the virus transmissible among ferrets – in which this transmissibility is a marker of possible capacity to transmit among humans – is complex.

All one has to do is read the article: essentially four mutations were induced and seven segments of the H1N1 were introduced into the aviary influenza virus, which then proved transmissible by airborne sneeze droplets among ferrets. The virulence, however, was not great, and the ferrets did not die; they lost weight, coughed, became very unhappy, stopped playing (ferrets play all the time), but they recovered.

The article by Dr. Fouchier has not yet been published in *Science*, but after *Nature* published the article by Dr. Imai, there is no sense in censoring it. The article published in *Nature* hides no technical aspect, but I doubt that anyone in the caves of Afghanistan or in the contiguous regions of Pakistan, where Al Qaeda still survives, would be capable of developing the technology necessary to reach this result, and in

addition, if the disease is attenuated, the only thing worthwhile, from the biological weapon standpoint, is to follow this path to test a vaccine. To use biological weapons without having the vaccine is very unlikely, since the virus and other biological weapon agents are not capable of recognizing the political, religious or national orientation of people. There is, of course, Iran, which has competent scientists, but I do not imagine that they have the resources necessary to reproduce this study, since there is a demand for time, material, instruments, expertise in molecular biology and patience – and the latter is not a hallmark of the local ayatollahs. I also cannot imagine religious leaders producing something of this type, although history shows us that very religious people, such as Torquemada, Luther and Osama bin Laden, to mention only the most prominent, were perfectly capable of great evil.

Fortunately, the recommendations of this Advisory Board were non-binding, i.e., they left the decision to the publishers of the journals as to whether or not they would be accepted. Both meditated on the subject, and Nature took the initiative, publishing the entire article. Science hesitated, but probably will publish now that the knowledge has been reported. Ethical dilemmas may exist, but in my opinion – and this is only a personal opinion, I would like to emphasize, that secrets leak rapidly, and these would certainly leak sooner or later. I believe that no censorship is acceptable for scientific articles, and this one, specifically, is not justifiable, since, on the contrary, it seems to be a pathway for obtaining a vaccine against aviary influenza.

Once again, owing to the similarity between the H1N1 virus and the fact that it can coexist in pigs with H5N1, we always run the risk of a recombination between these two, and hence, a new epidemic of influenza. It is crucial, therefore, to pursue a vaccine, and these studies are a good route towards testing them. Of course it would be possible to test a vaccine in birds, but no one can guarantee that this vaccine would be efficient in mammals, and the ferret is closer to our species than chickens...

The only terrorist group that tried to use biological weapons was in Japan, when a band of crazy people

cultivated the *Bacillus anthracis* and disseminated it in the Tokyo subway system. They forgot that the agent – which can be used as a weapon - is the anthrax spore and spread in the subway the vegetative cell, or the spore not duly transformed into a weapon; absolutely nothing happened. Later, this same group chose to use a neurotoxic gas⁽¹⁰⁾ and this, in fact, did lead to deaths and panic in the same Tokyo subway. Incredible as it may seem, this group had people capable of dealing with the bacillus, but they used nothing more complex than molecular engineering. Within these groups, in which mental health must not be a quality needed for admission, it is fairly unlikely that scientists will emerge. But there is the risk that technology be bought, such as what happened with the atomic bomb from North Korea, acquired by Pakistani scientists.

Finally, once more, censorship has no place in science...

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