

Review Article

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Smallpox Eradication and Human Morality in Evolution

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Abstract

Successful WHO smallpox eradication is considered to be the unprecedented event in history of human evolution, namely human species' long struggle with vicious pathogen termed variola or smallpox. The victory resulted from human efforts, firstly recent scientific discovery of vaccine and epidemiological strategy to interrupt the smallpox transmission and secondly the human species' joint effort to eradicate smallpox despite difference in nationality, race, religions and politics worldwide. In this article, specifically the second elements are discussed in view of Charles Darwin's struggle for existence and natural selection and his few followers' opinions that human genome may have an important role in evolution process, for instance, of ethics, morality, as expressed in "Nature via Nurture": Genes, experience, what makes human. Since the time unmemorable human species suffered considerable tragedy of smallpox disaster, themselves as well as their family and friends without knowing how to escape: Perhaps their ancestors sad memories could have influenced the minds of the staff or villagers, how to contribute themselves for rescuing their fellow human species: Please read and think for the future of human species.

Keywords: Smallpox; Human species; Vaccines; Environmental stress

Introduction

In 1980 the World Health Assembly declared that smallpox had been eradicated from the world. With eradication, all participating member states agreed that smallpox vaccination could be discontinued. Almost a half century has passed since that declaration and there has been no smallpox transmission at all. Here immense human efforts were truly successful. Indeed, it would not be an over statement to say that the event of smallpox eradication is an unprecedented historical event in long history of human evolution and human survival on this planet. It was a victory of the human species in its fight against negative forces – in this case a virus called variola of which its sole reservoir was man.

Following eradication, there have been multiple publications describing how, by applying the latest medical technology, the programme succeeded. These publications describe the immense global collaboration that under leadership of the WHO, the technical agency of UN succeeded despite differences between nations, races, religions and inequality. One 1500 page publication, known as the "Red Book" [1], describes this immense effort. In addition, among the many smallpox publications, one, "Princes and Peasants: Smallpox in History" by Donald Hopkins [2], covers the broader historical story of smallpox. The book describes how smallpox virus behaved over the past 2-4000 years and how humans responded to its on slaught before technological advances led to preventative vaccines.

Given the frequency of infection, the human misery caused by smallpox was immense and it caused the fall of some civilizations. The purpose of this essay is to examine how such an immensely negative human experience eventually resulted in positive actions that ended this virus presence in nature.

I am neither an anthropologist nor a molecular biologist, but I strongly suspect that in a Darwinian sense^{*}, our ancestors efforts to confront diseases likely evolved over the generations. And, in the case of smallpox, these efforts likely crystallized over time to eventually lead to a successful worldwide eradication program. I propose to divide the critical elements of this endeavor into two general groups. One, "Group A" may be defined as those that include the technical and managerial elements. Another, "Group B" may be defined as those that

include the social (nature versus nurture) elements that evolved from people's experience dealing with smallpox disasters that occurred since prehistoric time. These involve the intersection of morality and social responsibility that include sympathy, altruism and cooperation among smallpox patients, their families and friends. On the negative side, these also include social defects highlighted by smallpox epidemicsthe parochialism and hostility directed toward smallpox virus and the people affected by it.

The eradication programme had to confront issues from both group A and group B. The more technical group A issues were distinct and frequently discussed in published reports from the time. On the other hand, the group B issues evolved with the evolution of the human species as it repeatedly dealt with smallpox disasters.

Based on these headings, this essay will discuss how smallpox eradication (SME) was ultimately successful.

Darwinism and Human Morality Behavior

Darwin, late in his life, tried hard to understand complex human behaviors such as altruism and parochialism within the greater realm of progressive evolution [3]. At that time he did not have facilities to study the behavior of large mammals like chimpanzees and gorillas. Instead, he based his conclusions on his studies of small animals, flowers and insects. Despite these limits, he believed that large mammals, including the human species, possessed special instincts such as morality, sociality, and mutual assistance. He surmised that such instincts, or nature, would be strengthened as these animals, having developed such instincts or nature, would eventually dominate as their numbers would increase through natural selection and the struggle for existence. The end result would be an evolutionary advantage for their species.

Darwin's idea, in fact, has been promoted by his colleague, Thomas

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Henry Huxley, who wrote "Evolution of Ethics" [4]. Further, in more recent years, Frans de Waal reported that "in chimp, bonobo, macaque group there are morality expressions such as alliance, reciprocal exchange, reconciliation following aggression... and response to environmental stress" [5]. Notably such moral and social behaviors are important elements if a species is to win the battle of natural selection. As Darwin defined it in his book, the Origins of Species, this was the struggle for existence.

The larger implication of these observations is that human morality became distinctly strong and vivid as the human species evolved in the face of disasters. Such strength was very valuable in order to counter the immense misery caused by diseases like smallpox. Those of us working in smallpox eradication witnessed such strength in many, many humans in outbreak after outbreak. It was such an observation that brings the issue to the fore in this essay.

Group A: Technical and Managerial Elements Leading to the Success of Smallpox Eradication

Below is a list of some salient historical events that I believe set the stage for the success of the human endeavor to eradicate smallpox:

- In 1958, the idea of smallpox eradication was first proposed by a Russian delegate during the World Health Assembly (WHA). The rational was based upon the epidemiological facts that humans were the sole reservoir of the virus and an effective vaccine was available to stop its transmission among humans.
- 2) Unfortunately, at that time, it was left to individual endemic countries to implement such a new ambitious programme on a global scale. But the approximately 30 endemic countries had very limited resources over and above the substantial donation of vaccine from Russia (then USSR) a state then governed politically by communism. In most of these 30 countries, there were no teams, no transport, no surveillance and no containment of outbreaks. Indeed, there were no manuals, no budgets and no guidance from supervisory levels. And WHO had virtually no role.
- 3) During the 1960s, the WHA often debated the need for improvement. But no actions were taken.
- 4) Finally, in January 1966, despite many pessimistic opinions of the WHA's Executive Board (EB) members, Marcolino Candou, WHO's Director General from Brazil, proposed a WHO regular budget to intensify SME. The EB approved the proposal with only a two vote margin.
- 5) In May 1966, the WHA approved the proposal with a special note acknowledging that the development of this new programme was due to the extremely supportive efforts made by Marcolino Candou, himself during EB and WHA. Candou left WHO a few years later.
- 6) In 1966, Karel Raska (from the Czech Republic) was Director of the Communicable Disease Division at WHO's headquarters. He flew to the US to discuss smallpox eradication. The result was the commencement of US bilateral assistance for a measles and smallpox eradication programme in 19 countries of West and Central Africa. The US Centers for Disease Control (CDC) set up the operational system with about 50 experts located both at CDC and in the field. The activities started in 1967 and the results were dramatic. By 1970 Nigeria had its last smallpox case (measles eradication remained operative as

of 2013). Notably, the success of this effort resulted from the devoted efforts of the special program staffs - WHO as well as national. It is not possible for me to list all of the remarkable people that made this a success but allow me to note a few. First is Bill Foege from the US. When confronted with a smallpox outbreak in a Nigerian village that his team had recently vaccinated, he developed the ultimately successful strategy of "search and containment". In addition, Rafe Henderson from US and Maximillian Yekper from Benin need special mention. They undertook the valuable epidemiological field research that formed the basis of the strategy that proved successful.

- 7) The success in West and Central Africa greatly encouraged the other African and Asian countries to take on smallpox eradication. It also provided, as mentioned above, the effective epidemiologic strategy for SME operations in the other programmes around the world.
- 8) In October 1975, Asia became the first continent to rid itself of smallpox transmission. It was not easy, especially in Bangladesh where its "Liberation war" from Pakistan disturbed its previous smallpox zero status. The war, during 1970-71, caused massive war refugee movements resulting in smallpox returning to Bangladesh from India. Multiple importations resulted in nationwide epidemics that continued for the next five years after which (in October 1975) Bangladesh again became smallpox free. Six months earlier, in May of 1975, the last Indian smallpox case occurred. This Indian success resulted from the personal support of the strong and popular Prime Minister Indira Gandhi. She was encouraged at the early 1970s World Health Assembly meeting by Ghana's WHA delegate's critical query: "Ghana is already free of smallpox, why India not yet".
- 9) Ethiopia and Somalia, situated in the Horn of Africa, continued to have endemic smallpox transmission. The region posed a special challenge for the eradication operations. First, these countries had large, isolated desert areas where nomadic populations roamed. Second, and most disturbing, were the territorial quarrels and hostilities between Ethiopia and Somalia. In the midst of these conflicts, a few WHO programme staff were captured by Somali guerillas. Fortunately no physical harm resulted. Indeed, the guerrillas were sometimes persuaded to cooperate with the captured teams to improve smallpox vaccination and smallpox reports. These teams included WHO staff from the Netherlands, Brazil, Canada, Egypt, France, Sweden, UK and USA. They worked tirelessly, risking their lives for the programme. The national staff from Ethiopia and Somalia did the same. Instead of driving or flying in helicopters, they often preferred to walk in order to have a better chance of uncovering smallpox outbreaks. For example, in 1972, in order to verify that there was no hidden smallpox, a USA Peace Corps team in South Western Ethiopia walked over 300 KM all the way to the Sudan border. The world's last case of smallpox, the end of natural transmission of smallpox virus, occurred in October 1977 in Somalia. Looking back, one must ask why were humans so strongly motivated to eradicate smallpox in the face of such challenges and risks?
- 10) To financially support SME, a new method of international financing was developed during the programme. It followed the concept of North and South collaboration. This was, in fact, the beginning of the international cooperation where Northern richer countries assisted Southern countries that had

Page 2 of 6

limited resources available. Today this is a common method for international health. But 30 years before, it was new.

11) Throughout the programme, a few scientific discoveries, administrative policies and operational evaluation were essential for the programme's eventual success. These, included the improvement of vaccine quality, the development of rapid laboratory diagnostic tests, the avoidance of bureaucracy, and importantly, the introduction of surveillance and containment strategy that had been remarkably successful in Africa and India. In my experience, such an ideal joint effort, combining ongoing research and operational management, has been rare event. Such constant evaluation and reevaluation demonstrated the programme staff's keen interest for better solutions for ongoing problems. It should be noted that some actions were, in fact contrary to WHO rules. For instance, it was not uncommon for SME staff members, responding to an outbreak in a village, to follow the chain of transmission from that village across a border and into another country. Such an emergency did not allow time to be taken to obtain formal WHO entrance procedures from these countries.

Group B: Broad Moral and Social Elements Such as Social Responsibility, Sympathy, Empathy, Joy, Altruism, Cooperation, Anger, Fear, and Parochialism - All in Relation to Human Evolution and Smallpox Disasters

To start this section, it is important to understand that smallpox was a serious health threat that was often individually fatal and often caused considerable social panic. The disease was usually well known by the people and often given local names. Smallpox outbreaks came in periodic intervals spaced a few years apart. When it arrived, it often attacked a large number of inhabitants in an area. Recovered patients frequently showed ugly pock marks on the face and many lost vision in one or both eyes.

In certain geographical areas, smallpox was a direct threat to human survival. Matt Ridley details this threat in his book, "Nature via Nurture [6]: "Genes not only predetermine the broad structure of the brain, but they also absorb formative experience, react to social causes, and even run memory. They are consequences as well as causes of the will......".

Some illustrations may serve to highlight the long history of human evolution in relation to this specific infection. These explore how the human genome may have enabled us to eventually successfully eradicate smallpox.

History of human contact with smallpox virus

Almost 10,000 years ago humans started their agricultural revolution and lived together with some 500 individuals in tiny hamlets [7]. This new personal proximity no doubt facilitated the transmission of microbes such as the smallpox virus. Unfortunately fossil evidence is not available since smallpox infection did not leave its mark in fossils. Smallpox scars on a mummy of Egyptian king dating to 1163 BC is the oldest sign of disease.

In those early days, there was no medical technology capable of preventing or treating the disease. As a result, it was impossible to suppress or reduce the smallpox threat. But one thing was clear, as Donald Hopkins wrote in his book, "Princes and Peasants" (2). Smallpox infected everyone - both princes and peasants without differentiation of their social status. This meant that, to deal with the onslaught of this disease successfully, it had to be dealt with by both individuals and societies at levels extending from princes down to peasants. All people had to respond regardless of rich or poor, of higher social level or lower social level. For good man or bad man smallpox was the universal threat to everybody.

Hopkins showed that, during the period of since 1000 BC, smallpox travelled along the main gathering places in Egypt, Greece, China and India (Figure 1). Also shown is the proportion of deaths caused by smallpox among all causes of death in London and Geneva during the 16th to 19th centuries. During that time, out of 1000 deaths, smallpox accounted for 80 to 100. As a result, smallpox was the fear and concern of everybody.

Recent statistics recorded the smallpox incidence worldwide from 1920 to 1977 (Figure 2). During those years, smallpox epidemics had cycles with high incidence years reporting about 400,000 cases and low incidence years reporting from 100,000 to 200,000 cases. If the disease was caused by variola major, about one third of the cases would be fatal. "But, as studied in Africa, these reports represented only a fraction of the actual disease occurrence- perhaps less than 1%. This suggests that the world's incidence ranged from 10 million to 40 million cases every year in early 1920s. If we estimate a world population of about 1.8 billion in 1920, smallpox was clearly not a rare occurrence.

I suspect that in ancient times variola major was the only smallpox virus infecting humans. It is scientifically feasible that, as hosts started dying from variola infection, natural selection took root. In this case, a variola virus strain having a lower fatality would have a selective advantage as the human host living longer would have more chance to infect others. In reality, nations did not fight smallpox by differentiating variola minor from major. The clinical manifestations of both minor and major are virtually identical. Thus, to consider the impact of variola infection upon humans in ancient times, I assume the virus was variola major.

Probable modification of human nature via nurture, through their experience with smallpox

Before the development of the smallpox vaccine, there was no public health tool available to prevent or lessen the scourge of smallpox. As a result, the human species suffered from smallpox generation after generation for millennia. Given the immense number of years, the genes of our ancestors may have found some path of how to escape from its wrath. Suppose the life expectancy at birth 4-5000 years ago was somewhere around 20 years^{*}. Thus, many generations of humans would have been "stressed" by the virus and humans may well have





evolved to survive from its on slaught. The experience may have been long enough for humans to have developed significant adjustments to alter the impact of a disease like smallpox.

One could hypothesize that, given the remarkable severity of smallpox, the "pressure" exerted by this type of natural selection would be intense. If true, wouldn't that survival message be present human DNA? If more than one half of the population living in Africa and Eurasia 4-5000 years ago would have experienced smallpox, the evolutionary pressure would, no doubt, be considerable.

If not infected themselves, humans would have observed the suffering of infected individuals nearby. Thus, almost all the population would have faced the scourge of smallpox– an unknown mysterious and ugly threat against which they could do little to escape. Even in the absence of a laboratory to confirm the diagnosis, smallpox would have been clearly recognized as playing a principal human threat at that time. As mentioned above, smallpox was so familiar that it was often named locally, for example, boshonto in Bangladesh, furuka in horn of Africa, and gujappe in Western Japan.

'Parenthetically, the average life span in 18th century London was 18 years. In pre-historical times, between the years of 12,000 and 10,000 it was only 15 years. And some estimate that 5000 years ago it was between 30 to 40 years. For the sake of discussion, 20 years is used as the average life span.

When a mother saw her baby suffering from boshonto with pain, fever and pustules all over the child's body, she, no doubt, felt unbearable hatred towards the diseases that affected her child. Given the mother's helplessness, the horrible experience would likely be deeply cut into her memory and, perhaps, genes. Then with this memory, if she could save the next baby's life, she would do it wholeheartedly. One would suspect that the impact of such immensely tragic experiences would increase dramatically as they stopped their nomadic life styles and began to live in groups of perhaps 500.

As discussed above regarding Charles Darwin's theory, if there were a promising method to avoid this disaster, human instinct would

drive one's behavior to follow such a method with utmost urgency. One can ask whether the desire of the SME staff to work so hard could have resulted from such marked miserable experiences of their forefathers that were now expressed in their genes. Was the desire to conquer smallpox in their genes and inherited from their ancestors? It is certainly true that for all of us, who were involved in the eradication of smallpox, the seriousness of the disease was always directly before us and the drive to stop it was intense.

I will never forget my first-hand experience in 1967. I visited a hospital in Kuwaithad an imported smallpox outbreak of 41 cases. In the isolation ward I saw one young nurse with high fever and fully developed smallpox pustules covering her face and extremities. She actually broke down in tears pleading for me to "help, help!". But there was little I could do to help as there was no effective therapy. I also remember when I was in West Africa for a WHO smallpox surveillance mission. Just a few cases had been reported. But after investigating, I uncovered more than 200 smallpox patients who were staying together away from the village. They camped under the temporary shade at the side of a small stream at the edge of tropical rain forest. When I inquired why they were there, they replied "we came here because there is water available. The disease comes up every 5-6 years, and every time when it comes, we do like this. You are the first doctor we met in our lives". They did this camping away from the village until the outbreak was over. It was their way to handle (and survive) smallpox. Once infected, our human society had little help to offer. These two episodes occurred when both areas were at peace. Luckily there was no war. One can imagine the effect on a smallpox outbreak if wars occurred simultaneously in such areas.

Failed struggles to escape from smallpox in the past

In more recent historical times, perhaps a few thousand years ago, humans created gods or goddesses which were represented by statues (Sapona in Yoruba tribe in West Africa, or Shitla Mata a Hindu goddess in India). These people would to pray before these deities in order to either not get infected or, if infected, to escape from the death caused by the disease. Later, during the medieval period, a new practice was developed. It was the first vaccination called variolation. Here smallpox scab material from one person was inoculated to either prevent or perhaps cure the disease in the next person. It was practiced in some regions of China, Russia, Europe and limited local areas of Africa and the Middle East. It induced some protection from disease, but, at the same time, it also became the source of smallpox infection for others resulting in subsequent epidemics. But the phenomenon was one of many examples of how humans tried to escape from the smallpox disaster, but often vainly.

Invention of effective vaccines.

Finally the true remedy emerged. In the late 1700s, British investigators Benjamin Jesty, John Fewster and, most notably, Edward Jenner made brilliant breakthroughs. They discovered that, by using scabs from a bovine disease known as cowpox as a vaccine, they could prevent smallpox in humans. The resulting effect was dramatic. When vaccination was first introduced into Europe, early in 19th century, it alone prolonged the life span of the European population substantially. Indeed, the average life span of 31 years rose to41 years in two countries. The situation continued into the 20th century as Europe started to enjoy Jenner's vaccine innovation. Gradually the vaccine's use spread to other continents. However, it was a long, slow process. Eventually vaccination was extended worldwide and finally, in 1967, a special global effort for eradication of the disease was launched.

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What happened after the declaration of smallpox eradication?

It is of note that the declaration of the successful eradication of smallpox on 8 May, 1980 at the WHA was historical and resulted in headlines in newspapers around the world. But within WHO's walls, after a few months the situation changed. There was an informal recommendation from the Director General's office that there should not be too much praise given to the successful eradication of smallpox - an example of an excellent WHO project. The logic here was that smallpox (known as a "vertical" programme attacking a single disease) may have been a detrimental project, being contrary to the most important policy of WHO at the time, namely strengthening of basic health service ("horizontal" health programmes). At the time, such strengthening was considered the most important principle and purpose of WHO's global health programmes. Some of this was the direct result of the failure of the another vertical programme - malaria eradication. Many stressed the negative effects that these vertical programmes had on other basic health services. By the time of complete eradication, the programmes that aimed at just a single disease were against WHO's global policy. Even in the WHO headquarters corridors, the Director General's Office advised, not to talk about the success of SME. This situation continued for a few years. But times do change. Today, directly in the front of WHO's main building, a statue proudly commemorates the success of SME.

In March 1997, there was the Dahlem Workshop in Berlin, Germany that was organized to discuss the eradication of infectious diseases. It was chaired by Walt Dowdle, Don Hopkins, and others. William Foege, in his talk "Thoughts on Organization for Disease Eradication", asked, why had SME succeeded? His answer: "Because SME was carried out by a small adhoc organization over 10 years and was free of bureaucracy. It eventually served world peace". In my talk, I suggested that if we take on any other eradication efforts, it should be finished within 10 to 15 years. The audience was impressed with the fact that such a grand eradication programme was done by simple people in a simple organization.

The huge diversities of opinions cited above are not unusual in human history. To me smallpox eradication was a symbolic success resulting from a moral force that has been built up in the human genome. But, as such, it is not surprising that its success would not be accepted by all this stage of human evolution. In fact, these events remind us of a note by Samuel Bowles that he presented in an essay, "Conflict: Altruism's mid wife" on the occasion of Darwin's 200th anniversary celebrating Darwin and his book [8]. Bowles pointed out that many wars had been carried out by human races, as observed in the fossils of the crushed skulls, broken forearms and stone points embedded in the bones of a large number of prehistoric men and women. He then opined that climatic and archeological evidence indicated that 126,000-10,000 years ago, humans continued war with parochialism and altruism synergistically. Stressing the altruism side, he stated that "the inspiring public spiritedness, courage and generosity that are distinctive of humans bear the birth marks of history of conflict".

Summary and Conclusion

Our ancestors, over the past several millennia, generation after generation, had immensely tragic experiences with variola. Then humans created an effective tool for prevention, vaccination. And they began actively fighting the virus. With time, these efforts began to be effective and finally in a 10 year joint, worldwide effort, the WHO Smallpox Eradication Programme succeeded in eliminating the virus from humans forever. It is important to remember, though, that such success was done using tools that emerged from a growing human genetic memory. These tools were accumulated during a long evolutionary period that made success possible. These tools are not just due to a single medical advancement (the vaccine) that was developed in recent times. I believe that other essential "tools" lay far deeper in our genetic heritage – thus the title of this essay, Human Morality in Evolution. In this case, I see the joining of morality with the advancement of the tool called vaccination. This joining led to the successful eradication of a dreaded disease.

Often, when working in the operational field, it was hard for me to understand the immense, even unimaginable, heroic behaviors of the SME programme staff members- both WHO and national. This manuscript tries to highlight their excellent contribution to the programme's success. It then tries to move deeper and understand what drove them to rescue the world from the most disastrous diseases in human history. I believe that it is strongly suggested that their behaviors were rooted in their own evolutionary nature. In other words - in their genes. In no way is this observation meant to undermine the value of their work. Rather it just highlights the lesson that human races are capable of joining together to accomplish noble and valuable things that ultimately improve the chances of the survival of human species.

From the scientific point of view, this conclusion also would suggest that many human behaviors in the future, including ethics and compassion, could be explained as a function of chemicals and physical behaviors driven by our genes. Can today's or tomorrows powerful molecular biology help us understand it? Let us see.

One additional point needs to be stressed – the actions of the public. The smallpox programme staff contributed immensely to the programme's successes. But it was people, individuals in each affected town or village, who collaborated or acted as the programme staff requested that allowed for those successes. These people must also have had their instinct or nature similarly influenced by nurture from their ancestors. They were no doubt "nurtured" by the human tragic experience of smallpox disasters since ancient time. Let's hope that the success of the world's people to eradicate smallpox discussed here will, in time, promote the eradication of other important diseases.

Additional Notes

Professor Henry Bedson

Finally, I must note here with profound respect and regret that Professor Henry Bedson, Medical Virologist, Birmingham University, UK killed himself in 1978. He took personal responsibility for an accident, namely, the occurrence of smallpox cases due to the laboratory associated infection. Prof. Bedson contributed greatly to research on the molecular biology of smallpox virus in his WHO collaborating center during SME. Henry was my respected friend. It was a tragic and symbolic incident in human evolutionary history.

Destruction of smallpox viruses in laboratories

And I cannot finish this discussion without addressing the issue of what to do with the specimens of smallpox virus that still exist in laboratory freezers. WHO's annual report, 2007, entitled a Safer Future, expressed the concern that "the greatest fear is that, in the absence of global capacity to contain an outbreak rapidly, smallpox might reestablish endemicity, undoing one of public health's greatest achievements". No doubt, the destruction of smallpox virus stocks at two centers known to store it would reduce the risk of virus escape. But nobody knows that these two laboratories are the only laboratories in the world keeping the virus. Also it is well known that, with current progress in synthetic science, it may be possible soon to synthesize a smallpox virus if some laboratory would like to do it [9]. While I am writing this report, newspapers are reporting the incidence of terrorist attacks during Boston Marathon, followed by posting of envelopes with a toxic substance to important individuals. Are we prepared for a threat of smallpox bioterrorism? It is believed that such probability would be very low, but the consequences would be considerable. In view of the extremely low immunity now against smallpox, a virus release could risk the survival of human species on this planet. As we have had no smallpox vaccination for over more than three decades, the vast majority of the world's people are now susceptible to infection. To undue the great accomplishments of smallpox eradication discussed in the paper, would run totally contrary to the wishes of all human species over the last few millennia.

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Page 6 of 6