The origin of immunity by means of prior infection and vaccination with implications for the origin of species

Paul Ola¹

¹Institute of Theoretical Biology and Medicine

July 11, 2022

Abstract

Reality has failed to agree with the expectation that vaccines will solve the COVID-19 problem by preventing onward transmission of the coronavirus known as SARS-CoV-2, which followed logical deductions from inflammatory phenomena in which Mechnikov and his contemporaries described immunity as originating from the elimination of pathogens by a system of cells and substances that has since been named the immune system. But upon illustrating the reality in which we are protected from the pathological manifestations that occur in response to the pathogen in immunological phenomena, it was found to be that in which the pathogen does not cause such pathological manifestations through effects that are due to its mere presence but rather through effects that are due to its influence on pathological mechanisms so that immune mechanisms do not protect us from such pathological manifestations by eliminating the pathogen but rather by making asymptomatic hosting of the pathogen possible. And such protection, which occurs in spite of the presence of the pathogen when the conditions from which it originates are present, is obtained by means of infection with the same pathogen through the attenuation of its The origin of immunity by means of prior infection and vaccination with implications for the origin of species

Paul Ola

Institute of Theoretical Biology and Medicine, Lagos, Nigeria

Email: paulolatheorist@gmail.com

Abstract

Reality has failed to agree with the expectation that vaccines will solve the COVID-19 problem by preventing onward transmission of the coronavirus known as SARS-CoV-2, which followed logical deductions from inflammatory phenomena in which Mechnikov and his contemporaries described immunity as originating from the elimination of pathogens by a system of cells and substances that has since been named the immune system. But upon illustrating the reality in which we are protected from the pathological manifestations that occur in response to the pathogen in immunological phenomena, it was found to be that in which the pathogen does not cause such pathological manifestations through effects that are due to its mere presence but rather through effects that are due to its influence on pathological mechanisms so that immune mechanisms do not protect us from such pathological manifestations by eliminating the pathogen but rather by making asymptomatic hosting of the pathogen possible. And such protection, which occurs in spite of the presence of the pathogen when the conditions from which it originates are present, is obtained by means of infection with the same pathogen through the attenuation of its causative influence and by means of vaccination through the attenuation of the causative influence of the entity in the vaccine, such as the cowpox virus in Jenner's vaccine, since it is through the same pathway that pathological mechanisms respond to the causative influences of the pathogen and such an immunologically-linked entity. And it follows from the reality thus illustrated that symptoms fail to appear in spite of infection with the pathogen for as long as either or both of the conditions that give rise to both different but connected paths to the immunity obtained by means of infection with the pathogen and vaccination persist. COVID-19 hospitalizations and death therefore do not surge because variants and sub variants of the coronavirus become capable of being transmitted faster after becoming masters in the art of escaping the system which was logically described as the origin of immunity by the theory Mechnikov and his contemporaries formulated in the absence of such an illustration of reality. Rather, such surges occur because the protective conditions that give rise to immunity by enabling us to host pathogens without symptoms disappear in so many people at about the same time. And the higher likelihood of such conditions that give rise to the single asymptomatic infection pathway in the unvaccinated disappearing than those that give rise to the two asymptomatic infection pathways in the vaccinated explains why the unvaccinated are at greater risk of such unfortunate events. If we will put an end to the severe pathological manifestations which have already claimed the lives of millions prematurely during this pandemic and prevent those such as Ebola and those malignancies that appeared catastrophically in Tasmanian devils and decimated their populations within a short period, an understanding of the immunological nature of the pathological effects of the pathogens that are linked with these manifestations, which will enable us to understand both conditions and keep them stable, must be our topmost research priority now.

Keywords: Public health; SARS-CoV-2; COVID-19; Omicron; Evolutionary origins; Monkeypox; Smallpox; Eradication; Epidemiology; Vaccines; infectious diseases; pathogen

Introduction

After the last surge in the incidence of COVID-19 cases, which was attributed, through logical deductions from data, to the appearance of the Omicron variant surge, daily cases began to decline in the United States and globally to their lowest levels in over 6 months but in May 2022, the reported number of cases began rising again.^{1,2} And this surge is being attributed, again through logical deductions from data, to the emergence of Omicron's sub variants, progressive waning of the immunity obtained by means of prior infection and vaccination^{1,3,4} as well as the lifting of mandates such as mask use and other restriction aimed at reducing transmission.¹

Given the fact that the mechanisms by which vaccines protect us against pathological manifestations that appear in response to pathogens are so poorly understood that it has been impossible to develop vaccines that are effective against major killers of humankind, from ancient Tuberculosis and malaria to old HIV/AIDS,^{5,6} and that the development of effective vaccines to control outbreaks of pathological manifestations that have the capacity to threaten global health security such as Ebola and COVID-19 is currently facing challenges, an understanding of the immunological basis for vaccination has been considered urgently needed.⁶

An investigation which has the capacity to lead us to an understanding of the mechanisms by which prior infection and vaccination protect us from outbreaks of pathological manifestations such as COVID-19 and Ebola must begin with a justifiable explanation of two important phenomena in which such immunity is brought about. The results from an illustration of reality, which enabled us to account for monkeypox cases with no established travel links to Africa which have emerged in multiple countries in unlinked clusters⁷ in a recent paper,⁸ yielded these two phenomena through which immune mechanisms protect humans from pathological manifestations that appear in those who are infected with pathogens by means of prior infection with such pathogens and vaccination as consequences in an earlier paper.⁹ And the correspondence of these results with experience demonstrates their source as knowledge of reality which is capable of leading us to the origin of these phenomena in this paper.

The phenomenon in which immunity is brought about by means of vaccination ought to be the most important to humankind among phenomena and therefore the most understood because in less than 200 years after Edward Jenner began bringing about this phenomenon in humankind by inoculating material from cowpox lesions in 1796, cases of the terrible pathological manifestations of smallpox, which devastated humankind and left death, blindness and disfigurement in their wake for thousands of years, disappeared and were declared eradicated¹⁰

From the beginning, it was clear that this most important among phenomena that Jenner recognized was effectively brought about by his vaccine. But instead of the question, "How did

Jenner's vaccine bring about immunity in the vaccinated?" which we must answer justifiably if we will understand the origin of immunity by means of vaccination, another question became important. It was observed that smallpox cases disappeared in West and Central Africa after the vaccination of the individuals around smallpox cases which occurred during the rainy season when the number of outbreaks and cases were lowest, even when the entire population was not vaccinated.^{11,12,13}

And a logical deduction was made without understanding why smallpox cases were so low during the rainy season that such unvaccinated individuals around smallpox cases were not affected despite the fact that cases of infectious diseases have been attributed to the spread of pathogens in the population at about the time of their appearance until this paper was written. This logical deduction which was made without an understanding of the reality in which smallpox cases declined during the rainy season in this region of the world is that such "selective ring vaccination" contained smallpox by preventing the spread of the smallpox virus and that smallpox eradication was the consequence of the application of such method of vaccination.¹¹

After all, immunity had been logically deduced to be brought about by mechanisms that eliminate pathogens when Mechnikov and his contemporaries observed inflammatory phenomena in which cells and substances target foreign entities¹⁴ when the knowledge of the true nature of the immune mechanisms that protect humans from the pathological manifestations that appear in the presence of pathogens could only emerge from an illustration of the reality in

which the severity of such pathological manifestations is reduced in immunological phenomena such as the one that inspired Jenner to begin vaccinating humans.

If follows from such logical deductions that proceeded from inflammatory phenomena that whatever brings about immunity in a sufficiently large proportion of the population by eliminating pathogens must eradicate the pathological manifestations that appear in the infected by preventing transmission since infected individuals are likely to be surrounded by individuals who are unable to transmit the pathogen because they are immune. And the answer to the question, "How did Jenner's vaccine eliminate smallpox from those populations which were selectively rather entirely vaccinated?", which became important when smallpox cases disappeared in West and Central Africa in the 1970's¹¹ was supplied by the consequence of such logical deductions which is the protection of individuals who lack vaccine-induced immunity against an infection in a population where a sufficiently large proportion of individuals with such immunity exist. This indirect protection which was expected on the basis of such logical conclusions has since become known as herd immunity, community immunity, community protection.^{15,16} And the eradication of smallpox has since been considered to be the consequence of vaccine-induced herd immunity.^{15,17}

Given the fact that transmission of the coronavirus in spite of vaccination represents a failure of these logically derived hypotheses to find representation in reality, and that such failure suggests that it is not through herd immunity that vaccines will solve the COVID-19 problem^{15,16,17} or problems that are connected with infection with other pathogens but rather by reducing the

severity of pathological manifestations that appear in the infected as Jenner's vaccine did, we must now return to the question begged by that important phenomenon that inspired Jenner to begin vaccinating humans against smallpox so that we may understand how COVID-19 vaccination will put an end to the millions of premature deaths which have occurred since the pandemic began.

The phenomenon in which immunity was brought about by means of Jenner's vaccination is one in which immune mechanisms prevent the generally terrible pathological manifestations of smallpox from appearing in an individual after the generally mild pathological manifestations of cowpox have appeared in the same individual.¹⁰ The occurrence of this phenomenon in milkmaids after inoculating themselves with material from the cowpox lesions on cows in the process of milking them explained why their faces had none of the pockmarks that smallpox left on the faces of survivors.¹⁰ And Jenner began inoculating the people with such material from cowpox lesions which he named vaccine because he was convinced that smallpox would be annihilated if the phenomenon could be produced in every human.¹⁰

Things have however been much more difficult for Jenner's heroic successors who did not have a vaccine placed in their hands by nature like he was. And these individuals, who ought to be no less celebrated than Jenner, have had to develop vaccines without understanding the mechanisms by which Jenner's vaccination protected humans from smallpox.^{5,6}

In order to investigate the origin of immunity by means of vaccination, we ought to ask the following question: "How did immune mechanisms bring about the phenomenon in which milkmaids became protected from the terrible pathological manifestations that appear in those who were infected with the smallpox virus during smallpox outbreaks after they became infected with the cowpox virus while milking cows that had cowpox lesions on them?" And in order to ensure that the answer to this question leads us to the understanding of the mechanisms by which vaccination protects us against the pathological manifestations that appear in the presence of pathogens, we must ensure that it agrees with what we know through our sense experiences to be true before it is accepted as knowledge of reality.

Methods

The method which we ought to employ is that which illustrates reality and makes logical deductions only for the purpose of deriving consequences which must correspond perfectly with what we know through our experiences if what has indeed been obtained through the method is, indeed, knowledge of reality.¹⁸ And the following are the conditions that permit such illustration from which the results that give us the capacity to justifiably explain the origin of immunity by means of prior infection and vaccination have emerged.

Let the dog in the porous house B from our earlier illustration⁹ be familiar with one of the cats which our old friends, the aliens, saw entering the house without provoking the dog to their surprise, because the pathway through which the dog's disturbing rage is brought about in response to the presence of this cat was blocked by the attenuation of its influence on the dog. We shall refer to this cat as cat 1. Let the dog be familiar with the other cats because their influences have the same rage-provoking nature as the influence of cat 1 so that the dog fails to respond aggressively to their presence because it is through the pathway that was blocked upon the attenuation of the influence of cat 1 that such an aggressive response is produced in response to the presence of these cats.

Let the dog suddenly begin to produce a disturbing rage in response to the presence of these different cats and let the aliens, despite having observed the unexpected asymptomatic entry of these feline variants in our earlier illustration, continue to hold on to their old logical deduction because, without the aid of a thought experiment, they cannot know the reality in which the mechanisms of aggression bring about a disturbing rage in response to the presence of such cats from their location outside the porous house. And this old deduction is that the influence of a cat causes a disturbing rage through effects that depend on a destructive nature that the cat uniquely possesses, which requires the feline to be eliminated from the house for the occupants to be exempted from disturbance, a deduction which disagrees with the experience that a thought experiment that illustrates the reality in which such disturbance is brought about would enable them to predict. This experience, which would demonstrate the knowledge obtained through such a thought experiment to be knowledge of reality is that the nature of cats is that which makes them prefer to ignore or escape at the sight of the true source of the disturbing rage, the dog,

which could either be sociable or aggressive in its response to the presence of the cat¹⁹ depending on whether or not immune mechanisms, which serve the purpose of exempting the occupants of the house from the dog's disturbing rage, are exposed to conditions that permit them to block the pathway through which such rage is brought about by the mechanisms of aggression in response to the harmless presence of the cat.

Let the aliens conclude logically that the sudden appearance of the disturbing rage in porous house B is a consequence of the failure of an immune system within the porous house to eliminate the cats and that the changes that made different variants out of the cats in the house has turned them into experts at evading this system. And let them conclude, when they see cats that are similar to the cats in porous house B happily going in and out of nearby porous houses that some of the changes that made different variants out of the cats in porous houses B have made some of them so transmissible that they have become able to move from house to house so quickly when in reality, the cats had been in such houses long before the attention of the aliens was called to their presence by the disturbance in the neighborhood that followed the disappearance of conditions that permit immune mechanisms to block the pathway through which the dog responds to cats with a disturbing rage that makes their influence on the dog harmful to the occupants of porous houses in spite of their harmless nature of their presence in such houses.

Results

1. The response to the vaccine is not an immune response but rather a response in which pathological manifestations are brought about through the same pathway as the response to infection with the pathogen and when immune mechanisms block this shared pathway through the opportunity presented by the occurrence of the response to the vaccine at a time when protective conditions that permit such obstruction to be brought about by the attenuation of the causative influence of the immunologically-linked entity in the vaccine are present, infection with the pathogen is asymptomatic even when conditions that attenuate the influence of the pathogen disappear.

The first among the two phenomena in which immune mechanisms protect us from the pathological manifestations that occur in response to the presence of the pathogen is the phenomenon in which humans, who are infected with a pathogen such as the smallpox virus and yet have the severity of the pathological manifestations that occur in response to the pathogen reduced so much that they survive while others who are infected with the same pathogen are killed by severe manifestations, become so protected by immune mechanisms that such manifestations fail to appear in them during subsequent outbreaks. Smallpox survivors were called upon to nurse the afflicted and variolation, the inoculation of material from smallpox lesions, was employed by different civilizations for the goal of preventing smallpox when this phenomenon became recognized.¹⁰

The knowledge of reality that predicted this phenomenon reveals it to be a consequence of the obstruction of the pathway through which pathological manifestations appear in response to the

causative influence of the pathogen which immune mechanisms bring about when such a pathological response coincides with the presence of conditions that make asymptomatic hosting of the pathogen possible by permitting the attenuation of the causative influence of the pathogen. This is illustrated by the protection of the occupants of porous house B from the disturbance caused by the aggression with which the dog responds to the presence of cats when conditions, such as those that are present when dogs are yet puppies, permit the attenuation of the influence through which cat 1 causes the dog's aggression by obstructing the pathway through which such aggression is provoked by such causative influence. It follows that when such a pathway through which pathological manifestations (such as smallpox and COVID-19) occur in response to a pathogen (such as the smallpox virus and the coronavirus known as SARS-CoV-2 respectively) is obstructed by immune mechanisms in an individual A, the pathological manifestations that occur in response to the pathogen become reduced in severity so that survival occurs. And it follows that when the conditions that make asymptomatic hosting of the pathogen possible by permitting immune mechanisms to obstruct the pathway through which pathological manifestations occur in response to the causative influence of the pathogen persist in A until the next outbreak when such protective conditions disappear in individuals in A's locality that are similarly exposed to certain factors that cause their disappearance and pathological manifestations appear in such unprotected individuals, A hosts the pathogen asymptomatically during such an outbreak in spite of the harmful nature of the pathogen's causative influence.

It follows therefore that by virtue of the first phenomenon, the pathogen is capable of being hosted asymptomatically by unvaccinated individuals in A's locality at times when the conditions that permit immune mechanisms to attenuate the causative influence of the smallpox virus are present so that outbreaks are absent in such a locality at such times in spite of the presence and spread of the smallpox virus in the population. The consequence of this result is that the number of cases of pathological manifestations (such as smallpox and COVID-19)) must rise suddenly at a time when the population is exposed to factors that cause the disappearance of the conditions that make it possible for the pathogens that are etiologically linked with them (such as the smallpox virus and the coronavirus) to be hosted asymptomatically by permitting immune mechanisms to attenuate the causative influence of such pathogens and cases of such manifestations must necessarily begin to decline as such protection-eliminating factors begin to disappear and exposure to them reduces.

This consequence finds representation in the periodic surge in the incidence of pathological manifestations that occur in response to person-to-person transmitted pathogens which corresponds to seasons.²⁰ Although seasonal patterns of the incidence of such pathological manifestations, which were reported for smallpox even before Edward Jenner began vaccinating the people²¹ and which have imposed substantial strain on healthcare systems during the COVID-19 pandemic, ^{3,22} have been recognized since the Hippocratic era, the mechanisms underlying such seasonal patterns were not understood^{20,23} because such patterns were logically concluded to be due to the influence of variation in environmental factors on pathogen transmission^{13,23} in the absence of the knowledge of reality that predicts them.

It has been concluded that such understanding will elucidate host-pathogen interactions and improve the accuracy of public health surveillance and forecasting systems²⁰ and the clarification

of the seasonal pattern of smallpox incidence has been described as pressing given its relevance to bioterrorism preparedness.²⁴ And indeed, it is an understanding of the seasonal appearance of protection-eliminating factors which should be the topmost priority in public health if surveillance and forecasting will be accurate. The complete understanding of such seasonality must necessarily begin with the investigation of the immunological nature of the effects of important pathogens (such as the smallpox virus) which permits the different diseases which are brought about in response to different causes with effects of the same immunological nature (such as the smallpox virus and the cowpox virus) to be rendered asymptomatic when the conditions permit immune mechanisms to attenuate the causative influence of any one of them are present. And such an investigation which has the capacity to elucidate such protective conditions that give rise to immunity must necessarily lead us to such complete understanding of the factors that cause their seasonal disappearance and the surge in cases and deaths that accompanies increased exposure to these protection-eliminating factors.

The second phenomenon is that in which the same individual A (a milkmaid in Jenner's day), who is infected with an "untargeted" pathogen (the cowpox virus) in response to which pathological manifestations (cowpox) appear through the same pathway as those that appear in response to the "targeted" pathogen (smallpox), is made able to host such a targeted pathogen asymptomatically in spite of the disappearance of the conditions that made such asymptomatic hosting of the targeted pathogen possible in the first phenomenon by permitting immune mechanisms to obstruct the shared pathway through their attenuation of the causative influence of such a targeted pathogen. This is illustrated by the protection of the occupants of porous house B from the disturbance caused by the aggression with which the dog responds to the presence of

cats even when conditions, such as those that are present when dogs are yet puppies, have already disappeared but the cats still coexists with the dog asymptomatically (without the rage that disturbs the occupants of the house) because the pathway through which the dog's aggression is brought about in response to them is already blocked by virtue of the presence of conditions that attenuate the influence of another thing which may not be similar to cats in appearance or genetic constitution but which provokes the dog's aggression through the same pathway as cats.

Why should the milkmaid continue to host the targeted pathogen (the smallpox virus) asymptomatically in this phenomenon when her immune mechanisms could no longer block the pathway through which smallpox is brought about in response to the pathogen through the attenuation of the causative influence of the same pathogen? The answer could be no other than the persistence of the conditions that permitted immune mechanisms to obstruct the single pathway through which both smallpox and cowpox are brought about in response to their causes by attenuating the causative influence of the cowpox virus which she was infected with while milking cows so that the cowpox that occurred in response to that infection could be reduced in severity.

It follows that the response to the vaccine that "targets" a pathogen (such as the smallpox virus), which we have assumed to be an immune response is a response in which pathological manifestations are brought about through the same pathway as the response to infection with the pathogen. And it follows as a consequence that when immune mechanisms block this shared

pathway through the opportunity presented by the occurrence of the response to the vaccine at a time when protective conditions that permit such obstruction to be brought about by the attenuation of the causative influence of the immunologically-linked entity in the vaccine (such as the cowpox virus) are present, infection with the targeted pathogen (the smallpox virus) is asymptomatic even when conditions that attenuate the influence of this pathogen disappear. The severe pathological manifestations and deaths that follow vaccination in rare cases are therefore not adverse effects of vaccines which must necessarily occur in certain individuals²⁵ as logically deduced in the absence of the knowledge of reality that predicts the phenomenon that inspired vaccination. Rather, they are effects of the absence of such protective conditions at the time of vaccination or their coincidental disappearance after vaccination in rare cases which we can prevent if such protective conditions are understood.

And it follows that it is possible to make vaccinations safe in every single case and implement programmes which would protect humankind from bioterrorism, such as that with which the United States justifiably aimed to mitigate a possible release of the smallpox virus by terrorists after the September 2001 airplane attacks on the World Trade Center and the anthrax spore attacks using the US mail²⁶ without the risk of the severe manifestations and death which have been attributed to adverse effects of vaccines. All we need to do is to understand and ensure that the conditions that permit immune mechanisms to reduce the severity of pathological manifestations that occur in response to vaccines, which we have assumed to be an immune response in the absence of the knowledge of the reality in which such manifestations are brought about, are present in every single one of the vaccinated and kept stable for as long as they live.

2. Vaccination does not protect the population by preventing onward transmission of the pathogen but rather by increasing the likelihood that, even in the face of widespread infection, a surge in deaths will not accompany the periodic surges in the incidence of pathological manifestations that occur in response to the pathogen and those that are present among etiological factors that are immunologically linked with it such as its new variants or sub variants.

Since infection with the pathogen (such as the smallpox virus) and vaccination, which inoculates entities with effects that share the same immunological nature with the effects of the pathogen (such as the cowpox virus), both bring about immunity by presenting immune mechanisms with the opportunity to block the pathway through which pathological manifestations occur in response to the pathogen and immunologically-linked entities, then it is by making asymptomatic hosting of the pathogen and its undetected spread in the population possible that prior infection and vaccination bring about immunity and not by reducing onward transmission as we logically concluded in the absence of the knowledge of reality that yielded this result.

The first consequence of this result finds representation in facts that indicate that transmission of circulating variants of the coronavirus occurs in spite of vaccination^{26,27,28} as well as in those that indicate that despite such transmission that occurs in spite of vaccination, COVID-19 vaccines continue to do what they should, to prevent severe COVID-19 and the hospitalization and death that follows its appearance,¹ when those protective conditions, which are the origin of the immunity they bring about, are present.

It also follows as a consequence of this result that, until vaccination wields the powerful tool by which it eradicates the pathological manifestations that occur in response to pathogen without preventing infection and transmission, severe illness, including hospitalization and death, must necessarily occur even in the vaccinated when such protective conditions disappear in them. But the likelihood that the vaccinated will be simultaneously exposed to the factors that cause the disappearance of the two conditions that protect them, those that permit asymptomatic hosting of the pathogen to be brought about by means of vaccination and those that permit the same to be brought about by means of prior infection, must necessarily be lower than the likelihood that the unvaccinated will be exposed to the factors that cause the disappearance of the only conditions that protect them, those that permit asymptomatic hosting of the pathogen to be brought about by means of prior infection. This consequence finds representation in the fact that the great majority of smallpox cases occurred in persons who did not have a smallpox vaccination scar with a small minority of cases reporting having been vaccinated at some time in their lives¹³ as well as the fact that COVID-19 continues to kill unvaccinated people at much higher rates than the vaccinated despite the immunity that the unvaccinated obtain by means of prior infection with an ultimate result of this consequence during the present pandemic being the observed association between higher vaccination coverage and lower rates of COVID-19 deaths.²⁹

Finally, it follows that if, as the reality we have illustrated enables us to predict, the powerful tool by which vaccination eradicates the pathological manifestations that occur in response to the pathogen is not one that blocks transmission of the pathogen but rather one that causes the disappearance of such manifestations in spite of transmission and widespread infection by

stabilizing the conditions that permit asymptomatic hosting of the pathogen through the attenuation of its causative influence, smallpox cases must have continued to appear even in the most vaccinated populations before the tool was wielded and must have disappeared even from the least vaccinated populations when the tool was completely wielded. This consequence corresponds perfectly with the endemicity of smallpox in populations even when vaccination numbers exceeded the estimated population, an observation which, in the absence of the result that predicted its occurrence, resulted in the attribution of the eventual disappearance of cases in the less vaccinated populations of West and Central Africa in 1969 to an interruption of smallpox transmission as a result of a method of intelligent use of vaccination that is based on knowledge of where the disease is and when, where and to whom the disease is likely to spread than blind mass vaccination.^{12,13}

These facts that justify the result which has emerged from knowledge of reality demonstrates as unnecessary, the ad hoc hypothesis of evasion of both the immunity obtained by means of vaccination and prior infection by variants and sub variants of the coronavirus^{1,2,4} which was posited to account for the unexpected result that coronavirus transmission in spite of vaccination constitutes for the logical deductions which emerged from those of Mechnikov and his contemporaries, that immune mechanisms will bring about immunity to COVID-19 in the vaccinated by eliminating the coronavirus and interrupting its transmission.

3. Pathogens that are considered to be of a single clade, strain, variant or sub variant on the basis of their genetic similarities are not descendants of a single biological entity but rather

are biological entities which have evolved such genetic similarities independently as a result of exposure to similar conditions according to the evolutionary law that governs all biological entities and therefore do not become widespread in a population within a short period of time because such genetic similarities have made them more transmissible but rather because such convergent independent changes occurred at about the same time in so many members of the population.

On the basis of the inference he made from the similarities that exist between animals and plants, Charles Darwin concluded that the evolutionary law that governs the appearance of endless forms from previously existing forms is the biological law according to which species appeared on the planet and therefore that all such species must necessarily be descendants of a single biological entity.³⁰ "Analogy would lead me one step further, namely, to the belief that all animals and plants have descended from some one prototype. But analogy may be a deceitful guide. Nevertheless, all living things have much in common…" he wrote.³⁰

On the basis of this deduction that has its origin in analogy, inferences from genomes have suggested that certain genetic similarities which distinguish pathogens, such as coronaviruses of the Omicron variant and the monkeypox viruses detected in the current multi-country monkepox outbreak from pathogens of their kind, are consequences of their single origin from a common ancestor.^{31,32} And the explanations which were proposed to explain how such a single origin of the genetic similarities that distinguish coronaviruses of the Omicron variant could have occurred include a jump of their common ancestor from a human to a nonhuman host only to find its way

back into humans, the acquisition of such mutations that distinguish them in a patient with compromised immunity (an immunocompromised patient),³¹ who from the logical deductions that follow those of Mechnikov and his contemporaries, would be someone in whom immune mechanisms are unable to eliminate such a common ancestor and therefore would have provided conditions necessary for such mutations to occur.

And on the basis of such inferences that suggest their single origin outside of humans who are immune, in whom their common ancestor is seen as unable to survive and therefore unable to acquire the mutations that brought about the genetic similarities that distinguish them, the coronaviruses of the Omicron variant and the monkeypox viruses detected in the current multi-country monkeypox outbreak were assumed to have found their way into the individuals in whom they are detected through the spread of such a common ancestor. Such an unexpected rapid spread would require the mutations that cause such genetic similarities that distinguish these viruses from others of their kind to have conferred greater transmissibility on their common ancestor.^{31,32}

But the absence of established travel links to Africa or links between clusters in the current multi-country monkeypox outbreak ⁷ demonstrates that the disagreement between reality and the inference that the monkeypox viruses detected in so many countries of the world within a short period originated from a fast spreading common ancestor from Africa³³ and by extension, all such inferences which have been made from genomes in the absence of the knowledge of reality.

But the earlier illustrated reality in which such outbreaks occur reveals the evolutionary law to be different from the biological law according to which the species appeared so that the changes of evolution are not those that bring about the common ancestor of a species but rather those which are capable of making even biological entities of different species similar within a short period of time if they are exposed to the same conditions at about the same time let alone biological entities of the same species. The sudden appearance of skeletal remains of diverse animals in the lowest known fossiliferous rocks which Darwin admitted to be a grave objection to his theory of the origin of species³⁰ is the oldest among the facts that demonstrates the source of this evolutionary law as knowledge of reality.

Such sudden appearance of forms which are as complex as the animals that exist today,³⁴ has since been referred to as the Cambrian Explosion³⁵ and Evolution's big bang.^{36,37} And for as long as the Cambrian Explosion has been seen as a consequence of rapid manner of animal diversification in the light of Darwin's inference that the evolutionary law and the biological law according to which the species appeared on the planet are one and the same, the event has appeared to be one that is far more complicated than any historical event³⁸ and therefore incapable of being accounted for by any single cause which can be easily tested.^{38,39,}

But the results that predict the event enable us to see that it is not one of rapid diversification at all as we have assumed since the time of Darwin but rather one in which the diverse species of animals, which originated independently of one another long before the Cambrian, according to a biological law which is different from the evolutionary law, were changed from forms which could not be preserved in rocks into mineralized forms which could be preserved within a short period so that their fossils appeared suddenly in the rocks of the Cambrian as though they had just appeared on the planet during the period.

And it follows as a consequence of the results which have enabled us to justifiably account for the rapid convergence of animal forms during the Cambrian that biological entities such as the coronaviruses of the Omicron and those which have been detected in the current multi-country monkeypox outbreaks are not seen in so many cases because the genetic similarities that distinguish them from other viruses of their kind have made them capable of spreading faster but rather because they were already being asymptomatically hosted by so many individuals before the mutations that brought about such genetic similarities occurred by convergent evolution as a result of their exposure to similar conditions in such different humans. Such convergence that distinguishes some biological entities from other members of their species to create diversity within the species, rather than the origin of species is the consequence of the evolutionary law. And all living things have much in common³⁰ because the convergent changes that distinguish some biological entities from other members of their species to create diversity within the species also make them similar to members of other species in which the same changes occur because of exposure to the conditions that bring about such changes and not because all species descended from one prototype as Darwin believed.

To avoid delaying the publication of this paper, which calls for prompt investigation of the conditions that permit asymptomatic hosting through a single pathway in the unvaccinated and

through two pathways in the vaccinated so that the likelihood that infection will become symptomatic is lower in the vaccinated for as long as the conditions that ensure that protection occurs through both pathways are kept stable, we shall delay the presentation of the illustration of reality which has the capacity to lead us to the solution of what Professor Philip Sharp described as the central problem in Biology, the origin of life and its evolution, an illustration which is of utmost importance given the fact that it must necessarily give us the capacity to investigate what he described as the most challenging central questions, those that concern an integrated model of the processes that constitute and maintain the state of the cell in a dynamic fashion.⁴⁰

4. Vaccination eradicates the pathological manifestations that appear in the presence of a pathogen by increasing the likelihood that the pathogen remains asymptomatically hosted until it is able to change into a form that is necessary for the conditions that permit the attenuation of the pathogen's causative influence to become stable even in the presence of the factors that cause the surge in cases of the pathological manifestations that appear in the presence of the pathogen during certain seasons

An important question which we must ask now is, "How does vaccination bring about eradication if immune mechanisms do not bring about immunity by eliminating pathogens but rather by making asymptomatic hosting of the pathogen possible when conditions permit such protection and the evolutionary law is one according to which the convergent evolution brings about the differentiation of asymptomatically hosted pathogens from other members of their species when they are exposed to similar conditions in different immune individuals?

It follows from the reality we have illustrated that vaccination could only bring about eradication under such conditions by increasing the likelihood that the pathogen remains asymptomatically hosted until it is able to change into another form that is necessary for the stabilization of the conditions that permit the attenuation of the pathogen's causative influence even in the presence of the factors that cause the disappearance of such conditions and the surge in cases of the pathological manifestations that appear in the presence of the pathogen during certain seasons.

And it follows as a consequence that as convergent evolution changes the pathogen into such a form that is necessary for the stabilization of the conditions that permit the attenuation of the causative influence of the pathogen in different individuals in different regions of the world, only factors that cause the destabilization of such protective conditions will be able to cause the appearance of pathological manifestations and since such factors are not external factors to which the population is generally exposed during certain seasons, such pathological manifestations that are due to destabilization must necessarily appear haphazardly in the population. It therefore ultimately follows as a consequence that the haphazard appearance of such pathological manifestations must necessarily give the impression that the spread of the pathogen has become slower to anyone who views the appearance of such manifestations in the presence of such a pathogen as a result of its current spread when in reality it has already spread undetected in the population because it is asymptomatically hosted.

This consequence terminates in the observation of epidemiologists as the eradication of smallpox drew nearer that smallpox cases involved only a small percentage of villages in endemic districts and only few of the unvaccinated individuals in the households of smallpox cases and that smallpox had sometimes been absent from smallpox-infected villages for 20-30 or more years. In the absence of the knowledge of reality that predicted their observations, they logically deduced from such field observations that the spread of smallpox is slow when it had already been described as one of the most highly contagious of the infectious diseases, even by textbooks at that time.^{12,13}

And as soon as we realize that smallpox cases did not disappear because the smallpox virus disappeared but rather because the virus changed and the conditions that permit the attenuation of its causative influence changed into conditions that disappear haphazardly in the population so that cases of pathological manifestations that occur in response to the new form of the smallpox virus must ultimately become isolated as eradication progresses, then we can conclude that the monkeypox virus is the product of the convergent evolution that changed the smallpox virus from one form into another. If the monkeypox virus, in the presence of which pathological manifestations, which were indistinguishable from smallpox and could only be diagnosed by laboratory examination, appeared in the decade that ended with the declaration of smallpox eradication,^{13,41} is the outcome of convergent evolution that changed the smallpox virus and differentiated the members of the group from others hence the different clades of the monekeypox virus which have since been detected, what should be observed? What epidemiologists ought to observe is the consequence of the haphazard appearance of the factors

that cause the destabilization of the conditions that permit the attenuation of the causative influence of the smallpox virus which is the isolation of cases of the pathological manifestations that occur in response to the virus at about the time when smallpox cases disappear so that the virus will appear to be incapable of human-to-human transmission to anyone who views the occurrence of such cases to be a consequence of its current spread when such a spread had already occurred undetected in populations before the smallpox virus changed form.

And indeed, in the decade leading to the declaration of smallpox eradication, the consequence of the haphazard appearance of the factors that cause the destabilization of the conditions that permit the attenuation of the causative influence of the virus terminated in the observation of only 1 monkeypox case in a Nigerian family of 12 unvaccinated individuals and only 2 monkeypox cases out of 30 unvaccinated household contacts upon a review of all known outbreaks. But such observations were assumed to have been made because the monkeypox virus finds it difficult to spread even among unvaccinated close contacts and, therefore, that it is not sufficiently transmissible to permit continuing infection to become established in humankind because it spreads from animals to humans even though such animals were unknown^{41,42} and could never be known because such isolated monkeypox cases and clusters of few cases are not consequences of current spread of the monkeypox virus.

In the light of the results which have emerged from our illustration of reality, we are able to see that what epidemiologists were being told is that the absence of vaccination increases the likelihood of exposure to internal factors that destabilize the conditions that permit the

attenuation of the causative influence of the smallpox virus which vaccination stabilizes by providing an environment that is favorable for the asymptomatic hosting of the virus and its evolution into a form that permits such stabilization. And in the same light, we are able to see that infection with the monkeypox virus, the new form that emerged from the smallpox virus after its members were differentiated by convergent evolution, was already established in humankind at the time when smallpox cases disappeared even though such stabilization of protective conditions that vaccination caused prevented pathological manifestations from appearing in its presence even during those seasons when factors that cause their disappearance appear.

The widespread stabilization of such protective conditions through mass vaccinations is therefore the powerful tool by which vaccination eradicated smallpox and not the interruption of transmission by selective vaccination as epidemiologists assumed at the time. Such stabilization of protective condition through which vaccination should eradicate smallpox by changing its form into the monkeypox form is not maintained in the unvaccinated so that protection disappears as new destabilizing factors appear without vaccination to create an environment that favors the evolution of the monkeypox virus into the necessary form as smallpox was.

It was assumed that children and women comprised most of the monkeypox cases that occurred from 1970 to 1979 in West and Central Africa because they play with carcasses of wild animals that host the monkeypox virus and cook the animals hunters brought to the village respectively and, therefore, were both at greater risk of infection than other individuals in their zones because

of such activities.⁴¹ And it is presently being assumed that men who have sex with men (MSM) constitute the majority of cases in the current multi-country outbreaks because they are at greater risk of transmission.^{43,44}

But in reality, children and women comprised most of the monkeypox cases that occurred from 1970 to 1979 in West and Central Africa and men who have sex with men (MSM) constitute the majority of cases in the current multi-country outbreaks because individuals in such groups constituted the majority of those in whom such destabilizing factors first appeared in the inadequately vaccinated populations to which they all belong. And if we do not get the population vaccinated against the smallpox virus, such destabilizing factors may eventually appear in everyone even within a short period as in the current outbreaks thereby causing a monkeypox pandemic which is in reality a smallpox pandemic.

And how virulent such pathological manifestations that appear in such a pandemic will be must necessarily depend on what has become of the monkeypox form of the smallpox virus at such a time so that they may be milder than monkeypox manifestations are presently or even worse than smallpox manifestations were before vaccination brought about the circumstances that protected us by stabilizing the conditions that permit asymptomatic hosting of the smallpox virus by changing its form into the monkeypox virus form.

Pathological manifestations do not appear because of mere infection but rather because conditions that make asymptomatic hosting of the pathogen possible through prior infection or both prior infection and vaccination are absent. The solution to the problems that pathological manifestations that appear in the presence of pathogens constitute therefore lies in ensuring that we give all humans the opportunity to protect themselves through both paths and ensuring that the sources of both paths, the protective conditions that permit the attenuation of the causative influence of the pathogen and those that permit the attenuation of the causative influence of the pathogen and those that permit the attenuation of the causative influence of the before vaccine which is immunologically linked with the pathogen, are stabilized even before vaccination wields its powerful tool.

Discussion

While many questions about the future of the pandemic remain, it has been concluded that the coronavirus will not be eradicated.¹ And indeed, the facts that led to this conclusion are consequences of the reality that the means by which vaccination brings about immunity and eradication is asymptomatic hosting of the pathogen and not its elimination by a system that the logical deductions of Mechnikov and his contemporaries made from inflammatory phenomena described as immune.

The results of the current investigation have led us to the realization that the great power of vaccination does not lie in the interruption of pathogen transmission but rather in two effects. The first is the reduction of the severity of the pathological manifestations that occur in response to the pathogen even when the conditions that permit such reduction in severity by means of prior infection have disappeared so that seasonal surges in the incidence of cases are no longer

coupled with surges in severe manifestations, hospitalizations and death. And the second, which it was only able to achieve close to two centuries after smallpox vaccination began, is eradication, the disappearance of cases of such pathological manifestations in spite of pathogen transmission by increasing the likelihood that the conditions that permit the attenuation of the causative influence of the pathogen change into conditions that are stable in the face of the external factors that cause seasonal surges.

Given that COVID-19 continues to cause deaths even in some of the vaccinated,⁴⁵ the conditions that make asymptomatic hosting of the coronavirus possible by means of vaccination must be made stable in every single one of the vaccinated until vaccination is able to wield the tool by which it will eradicate the pathological manifestations that appear in response to infection with the coronavirus even in the vaccinated when such conditions disappear. The results of such stability will be the absence, in every single one of the vaccinated, the severe manifestations that cause hospitalization and death which were attributed to waning immunity in the absence of knowledge that immunity has its origin in such protective conditions as well as the absence of those rare unfortunate events which were considered to be adverse effects of the vaccines when they do not have their origin in the nature of the vaccine at all but in the absence of the same conditions at about the time of vaccination. And such unprecedented results in the history of vaccination will erase the doubts on the minds of the skeptical subset of the public, which has been growing.⁶

Armed with the knowledge that will enable us to ensure the stability of such conditions that permit immune mechanisms to bring about immunity by means of vaccination, never again will the transmission of pathogens inspire fear in us or will global health security be threatened by such transmission. By making our topmost research priority the understanding of the protective condition which are the origin of immunity by means of prior infection and vaccination, we must necessarily become able to ensure their presence and stability in every single one of the vaccinated even before vaccination wields the powerful tool by which it brings about eradication. And our world will become that grand environment most astutely described by Sir Andrew Pollard, one in which immunization is normal and access to vaccination is a right and expectation.⁶

Declaration of Competing Interest

I declare that there are no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgement

I am grateful to Priscillia for her assistance throughout the process of preparing this manuscript.

References

1. Del Rio C, Malani PN. COVID-19 in 2022-The Beginning of the End or the End of the Beginning? JAMA. 2022. doi: 10.1001/jama.2022.9655.

Wise J. Covid-19: Omicron sub variants driving new wave of infections in UK. BMJ.
 2022;377:o1506. doi: 10.1136/bmj.o1506.

3. Chen, LL., Abdullah, S.M.U., Chan, WM. et al. Contribution of low population immunity to the severe Omicron BA.2 outbreak in Hong Kong. Nat Commun 2022;13:3618. https://doi.org/10.1038/s41467-022-31395-0

4. Cai J, Deng X, Yang J et al. Modeling transmission of SARS-CoV-2 Omicron in China. Nat Med 2022. https://doi.org/10.1038/s41591-022-01855-7

 Pulendran B, Ahmed R. Immunological mechanisms of vaccination. Nat Immunol. 2011 Jun;12:509-17. doi: 10.1038/ni.2039.

6. Pollard AJ, Bijker EM. A guide to vaccinology: from basic principles to new developments. Nat Rev Immunol. 2021;21:83-100. doi: 10.1038/s41577-020-00479-7.

7. World Health Organization. Disease Outbreak News: Multi-country monkeypox outbreak in non-endemic countries. 2022 May 21. <u>https://www.who.int/emergencies/disease-outbreak-news/item/2022-DON385</u>

8. Ola, P. The origin of the mysterious multi-country monkeypox outbreak in non-endemic countries. OSF Preprints 2022. doi: 10.31219/osf.io/c4q8d

9. Ola, P. The immunological nature of the pathological effects of SARS-CoV-2 and other pathogens. OSF Preprints 2022. doi: 10.31219/osf.io/reh2t.

10. Riedel S. Edward Jenner and the history of smallpox and vaccination. Proc (Bayl Univ Med Cent) 2005;18:21-25. doi: 10.1080/08998280.2005.11928028.

11. Breman JG. Smallpox Eradication: African Origin, African Solutions, and Relevance for COVID-19. Am J Trop Med Hyg. 2021;104:416-421. doi: 10.4269/ajtmh.20-1557.

Foege WH, Millar JD, Lane JM. Selective epidemiologic control in smallpox eradication.
 Am J Epidemiol. 1971;94:311-5. doi: 10.1093/oxfordjournals.aje.a121325.

13. Foege WH, Millar JD, Henderson DA. Smallpox eradication in West and Central Africa.Bull World Health Organ. 1975;52:209-22.

Mechnikov, I. Nobel Lecture. NobelPrize.org. Nobel Prize Outreach AB 2022. Sun. 13 Mar
 2022. https://www.nobelprize.org/prizes/medicine/1908/mechnikov/lecture/

15. Omer SB, Yildirim I, Forman HP. Herd Immunity and Implications for SARS-CoV-2 Control. JAMA. 2020;324:2095-2096. doi: 10.1001/jama.2020.20892.

16. Morens DM, Folkers GK, Fauci AS. The Concept of Classical Herd Immunity May Not Apply to COVID-19. J Infect Dis. 2022:jiac109. doi: 10.1093/infdis/jiac109.

17. Fine P, Eames K, Heymann DL. "Herd immunity": a rough guide. Clin Infect Dis.2011;52:911-6. doi: 10.1093/cid/cir007.

18. Einstein A. On the method of theoretical physics. Philosophy of Science. 1934;1:163-169.

19. Menchetti L, Calipari S, Mariti C, Gazzano A, Diverio S. Cats and dogs: Best friends or deadly enemies? What the owners of cats and dogs living in the same household think about their relationship with people and other pets. PLoS One 2020;15:e0237822. doi:

10.1371/journal.pone.0237822.

20. Fisman DN. Seasonality of infectious diseases. Annu Rev Public Health. 2007;28:127-43. doi: 10.1146/annurev.publhealth.28.021406.144128.

21. Hillary W. 1740 a practical essay on the smallpox. London. C. Hitch/J, Leake

22. Ebinger, JE, Lan R, Driver M et al. Seasonal COVID-19 surge related hospital volumes and case fatality rates. BMC Infect Dis 2022;22:178. https://doi.org/10.1186/s12879-022-07139-2

23. Liu X, Huang J, Li C, Zhao Y, Wang D, Huang Z, Yang K. The role of seasonality in the spread of COVID-19 pandemic. Environ Res. 2021;195:110874. doi:

10.1016/j.envres.2021.110874.

24. Nishiura H, Kashiwagi T. Smallpox and season: reanalysis of historical data. Interdiscip Perspect Infect Dis. 2009;2009:591935. doi: 10.1155/2009/591935.

25. Aragón TJ, Ulrich S, Fernyak S et al. Risks of serious complications and death from smallpox vaccination: A systematic review of the United States experience, 1963–1968. BMC Public Health 2003;3:26. https://doi.org/10.1186/1471-2458-3-26

26. Singanayagam A, Hakki S, Dunning J, Madon KJ, Crone MA, Koycheva A, Derqui-Fernandez N, Barnett JL, Whitfield MG, Varro R, Charlett A, Kundu R, Fenn J, Cutajar J, Quinn V, Conibear E, Barclay W, Freemont PS, Taylor GP, Ahmad S, Zambon M, Ferguson NM, Lalvani A; ATACCC Study Investigators. Community transmission and viral load kinetics of the SARS-CoV-2 delta (B.1.617.2) variant in vaccinated and unvaccinated individuals in the UK: a prospective, longitudinal, cohort study. Lancet Infect Dis. 2022;22:183-195. doi: 10.1016/S1473-3099(21)00648-4. 27. Wilder-Smith A. What is the vaccine effect on reducing transmission in the context of the SARS-CoV-2 delta variant? Lancet Infect Dis. 2022;22:152-153. doi: 10.1016/S1473-3099(21)00690-3.

Franco-Paredes C. Transmissibility of SARS-CoV-2 among fully vaccinated individuals.
 Lancet Infect Dis. 2022; 22: 16. doi: 10.1016/S1473-3099(21)00768-4

29. Suthar AB, Wang J, Seffren V, Wiegand RE, Griffing S, Zell E. Public health impact of covid-19 vaccines in the US: observational study. BMJ. 2022;377:e069317. doi: 10.1136/bmj-2021-069317.

30. Darwin, C.R. 1859. On the origin of species by means of natural selection, 1st ed. London:John Murray

31. Wei C, Shan KJ, Wang W, Zhang S, Huan Q, Qian W. Evidence for a mouse origin of the SARS-CoV-2 Omicron variant. J Genet Genomics. 2021 Dec;48(12):1111-1121. doi: 10.1016/j.jgg.2021.12.003.

32. Isidro, J., Borges, V., Pinto, M. et al. Phylogenomic characterization and signs of microevolution in the 2022 multi-country outbreak of monkeypox virus. Nat Med 2022. https://doi.org/10.1038/s41591-022-01907-y

33. Bisanzio D, Reithinger R. Projected burden and duration of the 2022 Monkeypox outbreaks in non-endemic countries. Lancet Microbe. 2022 doi:https://doi.org/10.1016/S2666-5247(22)00183-5

34. Fortey, RA. "Harry Blackmore Whittington. 24 March 1916 – 20 June 2010. Biographical Memoirs of Fellows of the Royal Society. 2012;58:299–325. doi:10.1098/rsbm.2012.0033

35. Daley AC. A treasure trove of Cambrian fossils. Science. 2019 March 22;363:1284-1285. doi:10.1126/science.aaw8644.

36. Levington JS. The big bang of animal evolution. Scientific American 1992;267:84

37. Nash, JM. When life exploded. Time Magazine 1995;146:23

38. Zhang X, Shu D. Current understanding on the Cambrian Explosion: questions and answers.
PalZ 2021;956:41–660. <u>https://doi.org/10.1007/s12542-021-00568-5</u>

39. Erwin and Valentine, 2013 The Cambrian explosion, the construction of animal biodiversity.Greenwood Village, Colorado: Roberts and Company.

40. Dev SB. Unsolved problems in biology--The state of current thinking. Prog Biophys Mol Biol. 2015;117:232-239. doi: 10.1016/j.pbiomolbio.2015.02.001.

41. Breman JG, Kalisa-Ruti, Steniowski MV, Zanotto E, Gromyko AI, Arita I. Human monkeypox, 1970-79. Bull World Health Organ. 1980;58:165-82.

42. Arita I, Henderson DA. Monkeypox and whitepox viruses in West and Central Africa. Bull World Health Organ. 1976;53(4):347-53.

43. Velavan TP, Meyer CG. Monkeypox 2022 outbreak: An update. Trop Med Int Health. 2022. doi: 10.1111/tmi.13785.

44. Guarner J, Del Rio C, Malani PN. Monkeypox in 2022-What Clinicians Need to Know. JAMA. 2022. doi: 10.1001/jama.2022.10802.

45. Hippisley-Cox J, Coupland CA, Mehta N, Keogh RH, Diaz-Ordaz K, Khunti K, Lyons RA, Kee F, Sheikh A, Rahman S, Valabhji J, Harrison EM, Sellen P, Haq N, Semple MG, Johnson PWM, Hayward A, Nguyen-Van-Tam JS. Risk prediction of covid-19 related death and hospital

admission in adults after covid-19 vaccination: national prospective cohort study. BMJ. 2021;374:n2244. doi: 10.1136/bmj.n2244.