The Strange World of Viruses

Not annotated

Introduction

It was the 15th of March when I first read the six points of advice for how to survive a lockdown. They were: 1) Plan your days ahead; 2) Turn down the stream of news; 3) Stop your train of thought when the negative stream start free-wheeling; 4) Avoid isolation and use the social media to keep in touch with the wider world; 5) Sleep well and for long enough during the night; 6) Talk about *that* – and then about something else. My plan for this day and the next few days is to write this essay.

However, long before that I have been shocked by the speed by which the powers that be have been able to introduce policies, which we the freewheeling, freedom loving generation of the post WWII, thought would never see the light of day at least not in countries with such impeccable credentials as for example the Netherlands, Scandinavia and also the United Kingdom.

I had to ask myself what could possibly justify introducing these policies, which we previously would have associated only with totalitarian regimes. Fear had begun to spread around the world about a virus which had now been dubbed GOVID-19. It was therefore at that point I decided to look into the world of viruses. The essay is therefore not an attempt to create a scholarly work of scientific research, but rather to describe a journey of discovery through the world of viruses; and what a journey it has been.

In the first instance the definitions of viruses vary:

“A **virus** is a submicroscopic infectious agent that replicates only inside the living cells of an organism” is suggested by Wikipedia. A Scientist might say: “Viruses are important microbial predators that influence global biogeochemical cycles and drive microbial evolution …”

Chambers Twentieth Century Dictionary, 1977 edition, defines viruses as: “A pathogenic agent, a combination of chemicals, but capable of increasing rapidly inside a living cell.”

And the experts seem to find it difficult to describe whether viruses can be considered alive or without life.

It is common to distinguish between living and dead matter by the ability to synthesize proteins and replicate autonomously. The giant viruses may be considered as a missing link between the two, because they harbor “almost” the protein synthesis apparatus. The transition from living to the non-living world is continuous, not separated by a sharp borderline.

Viruses are not considered alive by most of the scientific community and as written in textbooks, because they cannot replicate autonomously. Yet some of the giant viruses are equipped with almost all components of the protein synthesis machinery close to bacteria suggesting that they belong to the living matter.

Furthermore viruses, by mutation and in other ways, constantly change shape and traits almost like a Scarlet Pimpernel. In one incarnation a virus can be immobile and easy to describe in another it may be highly mobile and variable. Most baffling of all is perhaps that they are variably described as parasitic predators as well as most important drivers of evolution, as transmitters of genetic material, as innovative agents. In other words as agents of both good and bad.

Viruses supplied the syncytin genes that are essential for the development of the mammalian placenta, and allowed the growth of embryos without its rejection by the maternal immune system. Thus, the same property which causes immunodeficiency in HIV-infected patients and leads to AIDS causes syncytia formation.

Most of this essay is based on data and other information copied from or downloaded from Wikipedia supplemented likewise with data, information and comments from scientific journals and other publications also downloaded or copied from the internet.

Viruses and Virions

According to Racaniello (2010) "viruses are distinct biological entities with the following five properties: a) they are infectious, obligate intracellular parasites; b) their genetic material is DNA or RNA; c) the genetic material enters a host cell and directs the production of the building blocks of new virus particles called virions; d) new virions are made in the host cell by assembly of these building blocks; e) the new virions transport their viral genetic material to another host cell or organism to carry out another round of infection.

The infected cell is the virus, while the virus particles are 'spores' or reproductive forms. The viral factory corresponds to the organism, whereas the virion is used to spread from cell to cell. To confuse the virion with the virus would be the same as to confuse a sperm cell with a human being.

In the introduction we referred to the dilemma virologists faces when considering whether viruses are a dead or living matter. It seems to be solved by referring to the hypothesis that the infected cell is the virus, while the virus particles are 'spores' or reproductive forms. It is suggested that the viral factory corresponds to the organism, whereas the virion is used to spread from cell to cell.

The infected cell is considered to be an organism and as such a living entity. The virions are akin to sperm cells or eggs in the animal world, or pollen or the ovules of a flower. If fertilization or pollination is unsuccessful, all of these agents will perish. Similarly, if a virion does not reach a cell on which to attach itself, that too will perish.

Human viruses

Human viruses are defined as viruses for which there is evidence of natural infection of humans.

We are interested in all stages of the process by which a virus shifts from not infecting humans at all to becoming a major human pathogen. As experiences with HIV-1 and new variants of influenza A (and also with novel animal pathogens such as canine parvovirus) show, this shift can occur rapidly, over time scales of decades, years or even months." – or even weeks as we have experienced with the emergence of COVID-19.

After BSE's emergence in the 1980s, well before it was found to infect humans (as vCJD), it rapidly became apparent that it could infect a wide range of hosts, including carnivores. This was in marked contrast to a much more familiar prion disease, scrapie, which was naturally restricted to sheep and goats.

Humans are constantly exposed to a huge diversity of viruses, though those of others mammals (and perhaps birds) are of greatest importance. Moreover, these viruses are very genetically diverse and new genotypes, strains and species evolve rapidly.

There is a hint, from the slower accumulation of new virus families found in humans, that virus diversity may be bounded, but that does not preclude there being a much larger number of virus species 'out there' than we are currently aware of.

The ease with which viruses can disperse, potentially worldwide within days, coupled with the very wide geographical distribution of emergence events, means that a coordinated, global surveillance network is essential if we are to ensure rapid detection of novel viruses.

Reporting of unusual disease events is patchy, even once detected, reflecting both governance issues and lack of incentives.

We need to consider extending the surveillance effort to other mammal populations as well as humans, because these are the most likely source of new human viruses.

Coronaviruses

Coronaviruses are a group of related viruses that cause diseases in mammals and birds. In humans, coronaviruses cause respiratory tract infections that can range from mild to lethal. Mild illnesses include some cases of the common cold (which has other possible causes, predominantly rhinoviruses), while more lethal varieties can cause SARS, MERS, and COVID-19.

The ‘Center for Disease Control and Prevention’ group them together as ‘Human Coronaviruses’ of which Coronavirus 2019 (COVID-19) is one.

There are 219 (+1!) virus species that are known to be able to infect humans. The first of these to be discovered was yellow fever virus in 1901. Three to four new species are still being found every year and for the year 2019 we can add COVID-19.

New human viruses will continue to emerge, mainly from other mammals and birds, for the foreseeable future. There is a clear implication that the emergence of new human viruses is a long-standing and ongoing biological process.

It seems the emergence of COVID-19 will not be the last such virus to emerge.

Distribution

Viruses seem to be ubiquitous and have been reported from any environment where life is present, from freshwaters to the sands of the Sahara desert. In soils, potentially the biggest biosphere on the planet, most viral studies have concentrated on estimating their abundance and taxonomy. Viruses are associated with the rhizosphere of plants and are also common in some of the harshest environments on the planet, ranging from hot springs to hypersaline waters. In many of these extreme ecosystems, viruses are the only known microbial predators.

Analyses of natural communities and man-created niches have shown that viruses are extremely diverse and novel. For example, 1 kg of marine sediment may contain over a million different viral types and 200 litres of seawater may contain about 5000 viral types. And there may be at least 1000 different viruses living in the human gut. The vast majority (>70%) of genetic material carried by these viruses is completely uncharacterized and natural viral communities probably represent the largest unexplored area of genetic information space left on the planet. Analyses of blood have also shown that healthy humans carry a number of novel, unknown viruses, including phage to known human pathogens.*)

Viruses can infect all types of life forms, from animals and plants to microorganisms, including bacteria and archaea. Viruses are found in almost every ecosystem on Earth and are the most numerous type of biological entity.

Viruses are the most abundant biological entities on Earth. They are present everywhere, in our surrounding, the oceans, the soil and in every living being.

The virosphere is the most successful reservoir of biological entities on our planet in terms of numbers of particles, speed of replication, growth rates, and sequence space. There are about 10^{33} viruses on our planet and they are present in every single existing species.

*) On the 3rd of June 2020 ‘Reuters’ reported from Holland that studies had shown coronavirus antibodies in 5.5% of Dutch blood donors, an increase from 3% shown in a similar study the previous April.

There is no living species without viruses! Viruses also occur freely in the oceans, in the soil, in clouds up to the stratosphere and higher, to at least 300 km in altitude. They populate the human intestine, birth canal, and the outside of the body as protective layer against microbial populations. Microbes contain phages that are activated during stress conditions such as lack of nutrients, change in temperatures, lack of space and other changes of environmental conditions.

Transmission

That viruses have become so widely present in the natural and man-made environments is not surprising when we consider the multitude of means of transmission and pathways they are able follow.

One transmission pathway is through disease-bearing organisms known as vectors: for example, viruses are often transmitted from plant to plant by insects that feed on plant sap, such as aphids; and viruses in animals can be carried by blood-sucking insects. Influenza viruses are spread by coughing and sneezing.

In the modern world humans live in close proximity to each other and each individual is actively engaged with numerous other individuals and all of them are part of the global biosphere, making for unlimited opportunities of exposure to alien viruses. The source of human viruses is most likely to be other mammals or birds and 'exposure' implies any transmission route by which a particular viral infection might be acquired, whether by contact with blood, saliva or faeces, contamination of food and water or via an arthropod vector.

COVID-19 appears to have originated from a Wuhan seafood market where wild animals, including marmots, birds, rabbits, bats and snakes, are traded illegally. Coronaviruses are known to jump from animals to humans, so it's thought that the first people infected with the disease – a group primarily made up of stallholders from the seafood market – contracted it from contact with animals.

Airborne spread of the disease *'foot and* mouth' that affects cattle can take place and under favourable climatic conditions the disease may be spread considerable distances by this route. For example, circumstantial evidence strongly suggests that the outbreak on the Isle of Wight in 1981 resulted from the airborne spread of the virus from Brittany in northern France.

The coronavirus mainly spreads face to face via infected droplets expelled in a cough or sneeze. There is also evidence it is transmitted in faeces.

Viruses not only move genes from one organism to another, they are also able to move genetic material between ecosystems. Some viral sequences have been found to be ubiquitously spread through the biosphere. There is also evidence that viruses from one environment can successfully infect and replicate on microbes from unrelated environments. These results provide support that viruses can move throughout the world and move genes between ecosystems. Similarly a recent study of RNA viruses in human stool samples showed that plant viruses are efficiently passing through the human gut and are disseminated with the seeds. In this way, viruses can use animals to move from place to place.

Most disturbing in the present state of the world is perhaps the notion that there is evidence that the virus that causes COVID-19 (as well as a number of other disease causing viruses) can be transmitted by socalled ‘silent spreaders’ - people who are infected, yet feel generally OK and go about their daily lives, giving the virus to friends, family members and strangers without knowing that they themselves have it.

Silent spreaders can be divided into three categories:

Asymptomatic: people who carry the active virus in their body but never develop any symptoms.

Presymptomatic: people who have been infected and are incubating the virus but don't yet show symptoms.

Very mildly symptomatic: people who feel a little unwell from a COVID-19 infection but continue to come in close contact with others.

As you might imagine, it is hard to figure out when someone has a disease but shows no signs of it. For that reason these cases present a particular problem for the powers that be, those who are charged with devising strategies and policies to combat viral infections, in particular COVID-19. Should tests be carried out only on people with clear signs and symptoms of the disease or on the whole population?

Survival

In the absence of host cells, viral populations in the environment may only decrease or remain stable.

A higher temperature means a faster reduction of the viral population, as do increased sunlight, higher antimicrobial concentration, or higher oxygen levels. Another documented impact is linked to the presence of indigenous microbial populations: virus survival is higher in sterile water.

Temperature has been the most studied factor, and is indeed often recognized as the most influential one. It has been universally demonstrated that higher temperatures mean faster viral inactivation. At low temperatures above freezing, viruses may survive for extended periods of time and sometimes for several years.

Solar light is another important factor producing viral inactivation, through the action of UV radiation. Viruses survive better in the dark than when exposed to sunlight.

Dried virus on smooth surfaces retain its viability for over 5 days at temperatures of 22–25°C and relative humidity of 40–50%, that is, typical air-conditioned environments. However, virus viability was rapidly lost (>3 $\log_{10}$) at higher temperatures and higher relative humidity (e.g., 38°C, and relative humidity of

>95%). The better stability of SARS coronavirus at low temperature and low humidity environment may facilitate its transmission in community in subtropical area (such as Hong Kong) during the spring and in air-conditioned environments. It may also explain why some Asian countries in tropical area (such as Malaysia, Indonesia or Thailand) with high temperature and high relative humidity environment did not have major community outbreaks of SARS.

High temperature at high relative humidity has a synergistic effect on inactivation of SARS CoV viability while lower temperatures and low humidity support prolonged survival of virus on contaminated surfaces.

Human-to-human transmissions have been described with incubation times between 2-10 days, facilitating its spread via droplets, contaminated hands or surfaces.

The analysis of 22 studies reveals that human coronaviruses such as Severe Acute Respiratory Syndrome (SARS) coronavirus, … (etc.) can persist on inanimate surfaces like metal, glass or plastic for up to 9 days, but can be efficiently inactivated by surface disinfection procedures.

As no specific therapies are available for SARS-CoV-2, early containment and prevention of further spread will be crucial to stop the ongoing outbreak and to control this novel infectious thread.

Western and Southern Europe have experienced a sunny and relatively warm spring with recorded number of sunshine hours the highest for almost a century which may have contributed to the progressive reduction in daily diagnoses of COVID-19 cases.

For the same reason it seems to me that the authorities in particular and the population in general have limited reason to worry about new outbreaks at the time of writing this (May-June, 2020). The really dangerous time will come with onset of winter, especially a mild winter as we have seen in recent years.

Perhaps in the future large auditoria such as cinemas, concert halls, theatres, clubs, pubs and restaurants could be fitted with devices for disinfection by exposure to excessive heat and humidity and UV lighting for short periods while not in use. It may also be preferable to excessive use of chemicals. New therapies making use of these means may also be considered.

Mutations

On the 24th of March it was reported that “Scientists in Iceland claim they have found 40 mutations of the coronavirus” which had enabled them to trace the pathway of the virus from a country of origin back to Iceland.

A month later it was reported from China that researchers there “have discovered more than 30 mutations of the new coronavirus, which they say may partly explain why it has been more deadly in certain parts of the world. The researchers said the findings indicate "the true diversity of the viral strains is still largely underappreciated" and they warned that “vaccine developers need to consider the impact of these accumulating mutations... to avoid potential pitfalls".

However, Dr Gatherer, an infectious disease specialist at Lancaster University, commenting on the Icelandic research, was not surprised with the findings. “This is much as we would expect. All viruses accumulate mutations, but few of them are of much medical consequence. They are valuable in tracing the origins of infection chains. It looks like Iceland has imported quite a few infections from other European countries.”

Professor Thomsen, a virologist at the University of Copenhagen, said: 'It is interesting with the 40 specific variants that fall into three clusters that can be traced back to specific sources of infection. As a virologist, it is very exciting that you can start to see which pathways are infected.”

Coronavirus is known as a virus that can mutate reasonably violently. We have seen reports of variants from China already. That way, it fits well with what one expects.

Writing for Yahoo News Alexandra Thompson takes a broad overview: “It seems like every couple of days new research is released revealing the coronavirus has mutated. Fears have been raised the ever-evolving pathogen could become more contagious or deadly. Some have also flagged whether a virus that changes almost constantly can be controlled by a vaccine, with immunisation being hailed the way out of lockdown.”

Hundreds of mutations have been identified since the virus was discovered at the end of 2019, but scientists are yet to pinpoint exactly how this could impact the pandemic.

Fears were raised when scientists from Peking University, Beijing, claimed two major types of the coronavirus have evolved, with the more “aggressive” strain being the most widespread.

To learn more, a team from the University of Glasgow “examined in detail” the data presented by the Beijing scientists, concluding it “cannot be substantiated”. “By analysing the extensive genetic sequence variation present in the genomes of the virus, the evolutionary analysis shows why these claims that multiple types of the virus are currently circulating are unfounded”, said Dr Oscar MacLean from the University of Glasgow. “It is important people are not concerned about virus mutations; these are normal and expected as a virus passes through a population.”

Writing in Twitter, Professor Andrew Rambaut from the University of Edinburgh said these genetic variations are “entirely expected” and added that it is a “flawed inference” to suggest the mutations could make the virus behave differently.

It is clear that mutations are part and parcel of the virus existence. However, these changes must make it difficult ‘pin it down’ so to speak and must make it difficult if not impossible to find a formula for a vaccine not to mention manufacture a vaccine with a lasting impact.

Complexity < = > variability

In whatever form life first appeared on planet Earth (and some scientists believe that viruses were the first life form) it must be a plausible assumption, that life started simple with high genetic variability and then became more complex.

However, the complexity of genomes depends on the environment: poor conditions lead to increased complexity and rich environments to reduced complexity. It may therefore also be accepted that as the new life experienced deteriorating environmental conditions, and became more complex.

It is speculated that viruses may have been autonomous entities initially, but at some point in their evolution autonomous viruses gave up independence for an obligatory intracellular life. To what extent have viruses been autonomous and independent of cellular metabolisms originally – and contributed to the origin of cells? Could they only later have lost their autonomy and become parasitic? At what point did they give up complexity for a less energy consuming lifestyle with small genomes and high speed of replication.

We have noticed that there are at least 1000 different viruses living in the human gut and even healthy humans carry a number of novel, unknown viruses, including phage to known human pathogens. The description of obesity by Moelling & Broecker may therefore be of particular interest:

Nutrition under affluent conditions with sugar-rich food contributes to obesity, which results in a significant reduction of the complexity of the microbiome. This reduction is difficult to revert. The gut microbiome in human patients with obesity is reminiscent of the gene reduction described in the Spiegelman's experiment: reduction of genes in a rich environment.

The obesity-associated microbiota that survive are fitter and more difficult to counteract. Urbanization and westernization of the diet is associated with a loss of microbial biodiversity, loss of microbial organisms and genes.

The role of viruses ~ drivers of evolution

Viruses can be pathogens, but their recognition as primarily causing diseases is wrong. This notion is based on the history of viruses in medicine.

Only a minority of viruses are in fact pathogens; most of them do not cause diseases. On the contrary, they are most important as drivers of evolution, as transmitters of genetic material, as innovative agents. In particular, the RNA viruses are the most innovative ones. Some of them are pathogenic and dangerous, such as HIV or influenza virus, or viroids in plants. RNA viruses are able to change so rapidly that the host immune system is unable to counteract the infection. Pathogenicity arises when environmental conditions change, for instance, when a virus enters a new organism or species.

That viral-mediated mortality increases net respiration, the release of CO2 and nutrient recycling in the world's oceans. Viruses and their microbial prey are also extremely diverse, abundant and active in marine sediments. Moreover, viruses affect primary productivity by killing diatoms, dino flagellates and cyano bacteria, as well as by releasing nutrients. In this way viruses account for a very significant part of the ocean's carbon cycling.

In addition to their influences on biogeochemical cycles, viruses drive microbial evolution by natural selection for microbes resistant to infection and via lateral gene transfer. Many viruses are strain-specific predators. Therefore as a particular microbial strain becomes dominate in a system, its viral predators will expand exponentially and kill it off. This will leave a niche for another microbial strain to grow into.

Viruses are important exchangers of genetic information between hosts, because they inject their genomes into the host cells. They move ecologically important genes from host to host. They move genes from one organism to another, they move genetic material between ecosystems and viruses from one environment can successfully infect and replicate on microbes from unrelated environments.

These results support the notion that viruses can move throughout the world and move genes between ecosystems.

Viruses have been proven to be drivers of evolution, including the human genome, which by at least 45% is composed of sequences related to retroviruses. Retroviruses supplied the syncytin genes that are essential for the development of the mammalian placenta, and allowed the growth of embryos without its rejection by the maternal immune system. Thus, the same property which causes immunodeficiency in HIV-infected patients and leads to AIDS causes syncytia formation, cell fusion after infection by a retrovirus.

There are numerous other examples of the contribution of viruses to the evolution of life since at least as long as 550 MYA. But genetic noise through random mutations does not allow us to go back to the origin of life. It may not be impossible that the earliest compartment was indistinguishable, either a pre-cell or a pre-virus.

Conclusion

Human viruses are defined as viruses for which there is evidence of natural infection of humans. New human viruses will continue to emerge, mainly from other mammals and birds, for the foreseeable future.

There are about 10^{33} viruses and they are the most abundant biological entities on Earth. They are present everywhere, in our surrounding, in the oceans, in the soil, in clouds up to the stratosphere and higher, to at least 300 km in altitude. They populate the human intestine, birth canal, and the outside of the body as protective layer against microbial populations.

Viruses are transmitted across space by a multitude of different means.

One **transmission** pathway is through disease-bearing organisms known as vectors: for example, viruses are often transmitted from plant to plant by insects that feed on plant sap, such as aphids; and viruses in animals can be carried by blood-sucking insects. Influenza viruses are spread by coughing and sneezing and may be it is transmitted in faeces.

Humans are constantly **exposed** to a huge diversity of viruses, though those of others mammals (and perhaps birds) are of greatest importance. Moreover, these viruses are very genetically diverse and new genotypes, strains and species evolve rapidly. It is thought that COVID-19 originated in bats and ‘jumped’ to humans possibly via pangolins in a socalled ‘wet’ foodmarket in China.

Survival: A higher temperature means a faster reduction of the viral population, as do increased sunlight, higher antimicrobial concentration, or higher oxygen levels. Another documented impact may be the presence of indigenous microbial populations: virus survival is higher in sterile water.

Temperature is often recognized as the most influential factor. It has been demonstrated that higher temperatures mean faster viral inactivation. At low temperatures above freezing, viruses may survive for extended periods of time and sometimes for several years.

Solar light is another important factor producing viral inactivation, through the action of UV radiation. Viruses survive better in the dark than when exposed to sunlight.

Mutations

All viruses produce variations, but the precise numbers and the importance of this varies.

However, it seems sensible to warn that vaccine developers need to consider the impact of these accumulating mutations to avoid potential pitfalls.

Complexity v variability

The development of viruses from being autonomous entities to become dependent on an intracellular lifestyle and being parasitic is explained and the implications for humans assessed.

The role of viruses - drivers of evolution

From a layman’s perspective it would seem that viruses have no other role in the natural world than being transmitters of disease and destroyers of other living entities. Viruses can obviously be pathogens, but this recognition as primarily causing diseases is wrong and is most likely based on the history of viruses in medicine.

They have a role in the cycling of carbon and recycling of nutrients in the world’s oceans. They have a role in mammal reproduction by supplying the syncytin genes that are essential for the development of the mammalian placenta, and allowing the growth of embryos without being rejected by the maternal immune system. As well as the inside of the human body viruses populate the outside of the body where they form a protective layer.

It is, however, as drivers of evolution viruses have achieved their most important role. Through their many faceted ways of transmission they have ensured effective and speedily spreading throughout the natural world. By injecting their genomes into host cells they facilitate exchange of genes between organisms, between ecosystems and even between separate environments. They are in effect acting as enablers and catalysts of change, unfortunately (from the point of view of existing life forms including homo sapiens!) killing the host cells in the process.

Post Scriptum

Through this trawl though the conditions for the existence of life we have discovered how supple viruses are as physical entities being able to mutate and change as well as move from organism to organism, move between different types of organisms as well as between ecosystems.

It therefore seems pointless to base any policies or strategies on the idea that we may be able to control viruses and it seems equally pointless to put any faith in the belief that a vaccine may be developed anytime soon. Even if it is possible to develop a vaccine it seems more than likely to be against a variant that is known about now, but also likely that an active virus will be able to bypass the vaccine by jumping to a new unknown type of host or take on a new form through mutation

To my way of thinking it would be more fruitful to accept that COVID-19 is here now and is likely to remain with us for some time and that we therefore have to think in terms of ways of co-exist alongside it. We need to think in terms of suitable therapies and in terms of widening the opportunities for limiting the scope for the virus to spread.

In the section “Survival” we found that increased sunshine through UV radiation, higher temperature and increased relative humidity would lead to “faster deactivation” of viruses in general.

New forms of disinfection

I am therefore suggesting that in the future large auditoria such as cinemas, concert halls etc. could be fitted with devices for disinfection that would expose the venue to excessive heat and humidity and UV lighting for short periods while not in use. I would envisage it could be done by some electrical installation and would not involve excessive use of chemicals.

It is possible that this idea could be applied to family homes or even as therapy for individual people.

More surveillance

The ease with which viruses can disperse, potentially worldwide within days, coupled with the very wide geographical distribution of emergence events, means that a coordinated, global surveillance network*) is essential if we are to ensure rapid detection of novel viruses.

We need to consider extending the surveillance effort to other mammal populations as well as humans, because these are the most likely source of new human viruses.

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*) I do not know if such a network exists, but if it does not an organisation along those lines needs to be created forthwith.

Completed 5th of June, 2020.

Readings

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