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Fall of the Rebel Angels: How SARS-Cov-2 Landed on Earth

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Introduction

According to Webster's Dictionary, a guardian angel is "an angel believed to have special care of a particular individual", in a more broadly sense "a protector" and the representation of Good [1]. Not all angels are good, however, because even before Eve accepted the forbidden fruit in the Garden of Eden, a confrontation between Good and Evil took place in Heaven. Lucifer, a mighty angel, no longer accepted the authority of God and started a revolt. The Archangels Michael and Gabriel remained faithful to God and expelled Lucifer and his associates from Heaven [2]. During their fall from Heaven, the rebel angels transformed into demons, and ended in Hell. In the painting of Jheronimus Bosch, Fall of the rebel angels, it can be seen that the transgression of angels into toad-like demons takes place when they are falling from the sky (Figure 1a) [3]. Unlike most other artistic visualizations of the above described biblical scene, the demons of Jheronimus Bosch are not landing in Hell but on Earth. The landscape is barren and the human figures are miserable, some are crippled and/or in obvious pain. Demons in different sizes and shapes are omnipresent. In the middle part of the painting, near the right-hand edge, a demon is holding a weapon, resembling a spike protein in its left hand (Figure 1b) The facial and overall expression of the demon clearly reflects the intention to attack the innocent people on earth. The parallel with the SARS-CoV-2 virus having transformed into a threat (thus acting as a demon virus) is striking. The origin of this virus most probably lies in bats [4]. Whether coronaviruses in bats play a guardian role is unknown, but at least they do not cause severe disease [5,6]. For reasons and by mechanisms also unknown, a change took place in one of the bat coronaviruses, causing it to leave its bat habitat and fall to earth. For the human population living on earth this virus now behaves like a demon virus [7,8]. Could this analogy be extended, and would there as suggested above, apart from demon viruses, also be guardian angel viruses? Not only in bats but also in humans.

Figure 1: The Fall of the Rebel Angels, left panel of the triptych Hell and the Flood by Jheronimus Bosch (approximately 1500) Museum Boijmans Van Beuningen, Rotterdam, The Netherlands. Figure 1a shows the complete panel, the detail shown in 1b is indicated with a hatched rectangle.

https://commons.wikimedia.org/wiki/File:Hieronymus_Bosch_-_The_Fall_of_the_Rebel_Angels_(obverse)_-_WGA2572.jpg Assessed October 18, 2020.

Demon Viruses and Guardian Angel Viruses

The concept of micro-organisms that are beneficial for humans is rather new, but well established [9]. It is known that commensal bacteria in the gastrointestinal tract and elsewhere in and on the body can protect the human host against infections [10]. These commensal bacteria also contribute to maintaining health in a number of different ways, including production of vitamins, digestion of fibers, and so on [11]. Such a guardian role of bacteria can also be executed by viruses. It has been demonstrated that an

enteric animal virus in fact can function in a similar manner as commensal bacteria [12]. Persistent infection of germ-free mice with various different strains of enteric Murine Norovirus (MNV) had beneficial physiological effects such as reversal of otherwise occurring abnormalities in intestinal morphology and lymphoid cells in germ free mice [13]. Moreover, MNV counteracts the negative effects of antibiotic treatment in experimental infections or dextran sodium sulphate induced colitis [13]. It is possible that these or other RNA viruses play similar roles in human hosts. A second category of beneficial viruses are the Human Endogenous Retroviruses (HERV) [14,15]. HERV have played a clear role in the evolution of their hosts. The mammalian gene for syncytin1, encoding an essential protein for establishment of the placenta, in fact is a retroviral env gene. Many other (remnants of) these so-called symbiogenic viruses are integrated into the human genome [16]. It has been argued that this viral symbiosis contributes to the holobiontic nature of the human genome [17] via processes like insertion, deletion and mutation, the retroviruses have become domesticated. By analogy with Lucifer and Gabriel, demon viruses would during evolution of man have transgressed into guardian angel viruses.

A third and final category of beneficial viruses are formed by the bacteriophages. Bacteriophages with a specificity ranging from pathogenic bacteria such as *Yersinia pestis* [18] to the more innocent, but annoying *Propionibacterium acnes* [19] have been described. Despite the common opinion that bacteriophages are all, to some extent, pathogenic, many bacteriophages are not harmful and rather are beneficial to its host. For example, many of the viruses present in the human gut are in fact bacteriophages [20]. Bacteriophages are also known to adhere to mucous membranes in many different metazoan hosts. These bacteriophages are able to attack invading bacterial pathogens, thus contributing to the first line of defense of the metazoan host. [21] Similar mechanisms are found elsewhere in the animal kingdom. *Hamiltonella defensa* protects its host, *Acyrthosiphon pisum*, from its parasitoid predator, *Aphidius ervi*, by killing the developing wasp larvae [22]. Lastly, bacteriophages are known for using bacteria or archaea to replicate, killing them in the process. Due to their specificity and ecological safety, bacteriophages have historically been used to develop phage therapy [23]. Their use declined when antibiotics were discovered, but they may make a revival, as multi-drug-resistant bacteria are emerging. Bacteriophages could offer an effective alternative to antibiotics [24].

Guardians and Devils: Evolution or Creation?

A theological issue that has been debated for centuries was whether demons are inherently evil, and if so, how that could be if they were, like all beings, created by God. It was not until the Fourth Lateran Council in 1215 that it was decided by Pope Innocent III and 400 bishops present that "The devil and other demons were created by God naturally good, but they became evil by their own doing. Man, however, sinned at the prompting of the devil." [25]. In this sense, man would be innocent (=healthy) until infected by a demon virus. The parallel between demons and viruses is that they both are invisible. The difference is that viruses exist in the real world. Faith may make you resistant to demons, the strength of the immune system will determine survival of an infection with a demon virus such as SARS-CoV-2. Whether SARS-CoV-2 could transgress from demon virus into guardian angel virus is a question that can only be speculated about, but let's do that for the sake of argument. The circulating coronaviruses (OC43, NL63, 229E, and HKU1) have been around for hundreds to thousands years [26,27]. All of them most probably have started as demon virus for humans but by now have become domesticated and are rather innocent viruses causing a common cold at best. There are indications that immunity to these common circulating corona viruses would offer some kind of protection against severe COVID-19 [28]. The co-evolution of viruses and humans thus shows that guardian angel viruses can turn into demons and back. We are witnessing a circular history on the interaction between viruses and their human hosts.

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