



The Pathophysiology of Long COVID-19 Illness and Acyclovir

Robert M Beatty*, Shelley Smith Beatty and Beatty LLC

3800 West 57th Terrace, Fairway, KS 66205, USA

***Corresponding Author:** Robert M Beatty, 3800 West 57th Terrace, Fairway, KS 66205, USA.

DOI: 10.31080/ASMI.2026.09.1637

Received: September 24, 2026

Published: October 12, 2026

© All rights are reserved by **Robert M Beatty., et al.**

Abstract

A theory of the mechanism of long COVID-19 is presented. Even though long COVID-19 can present a variety of symptoms, a universal mechanism is involved in each case and is discussed in this paper. Also presented is the role of acyclovir and how it can alleviate the diverse symptoms of long COVID-19. Although long COVID-19 is multifaceted, meaning it affects many organ systems, the mechanism is universal based upon the immune response seen in wound healing.

Keywords: COVID-19; Long COVID-19; Immune Response; Fibrin Net; Foreign Body; Acyclovir

Introduction

Long COVID-19 illness can present in a variety of ways [1]. Some patients develop pulmonary issues. For others, the brain is the organ most affected. Additionally, joints, muscles, and the gastrointestinal tract can be affected by long COVID-19.

Even though long COVID-19 syndrome is varied, the symptoms of long COVID-19 are created by the same mechanism. This mechanism is the universal wound healing pathway.

Infection with COVID-19 virus causes inflammation. This inflammation invokes the immune system. Many processes in the body react to this inflammation. The processes occur concurrently; however, these processes are synchronized. Fibroblasts are attracted and multiply. These fibroblasts synthesize collagen. A fibrin net is formed by platelet activation.

Inflammatory cells, such as neutrophils, monocytes, and endothelial cells, adhere to a fibrin scaffold [2]. The COVID-19 virus is trapped in the fibrin net.

Normally, the neutrophils enable phagocytosis of cellular debris and bacteria caught in the net. However, when COVID-19 is trapped in the net, phagocytosis does not eliminate it. The trapped virus acts like a foreign body, continually triggering a low-level immune response. This immune response is responsible for the symptoms of long COVID-19.

Acyclovir treatment can reach the trapped COVID-19 virus through the limited vascularity created by angiogenesis. The angiogenesis is limited in this fibrin net, but eventually acyclovir blocks viral replication and allows eradication of the virus.

Discussion

The COVID-19 virus is virulent and has a capacity to create a worldwide pandemic [3]. Long COVID-19 syndrome is unique in the variety of organ systems in which the syndrome can involve. When the COVID-19 virus enters the body the immune system response is immediate as well as the wound healing process.

There already exists a mechanism to fight viral illness in our bodies. This mechanism is the immune system and the cascade of wound healing. The process of wound healing is universal, whether activated by COVID-19 virus or a wood splinter in a finger. In the healing process of all wounds, a fibrin net is formed (Figure 1).

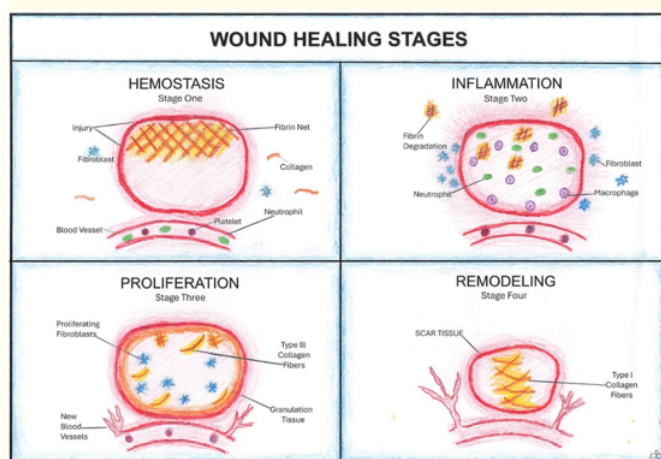


Figure 1: Wound Healing Process. Stage One Hemostasis: Early cellular injury, early fibrin net. Stage Two Inflammation: Response to injury, increase cellular immune response. Stage Three Proliferation: Proliferation of fibroblasts, white blood cells, and platelets. Collagen fibers increase. Stage Four Remodeling: Encapsulation with collagen.

When the COVID-19 virus enters the body the immune system response is immediate. The mechanism by which the body counteracts COVID-19 is universal. It is the universal mechanism of wound healing. The COVID-19 virus initiates the wound healing cascade [4]. In this cascade of wound healing a delicate interplay occurs involving white blood cells, macrophages, fibroblasts, platelets, cytokines, collagen and an array of chemicals and a fibrin net/collagen scar is formed.

Unfortunately, the elimination part of the immune/wound healing process stalls. Wherein the COVID-19 virus remains active in the fibrin net only to become an encapsulated foreign body. Enough virus is able to maintain low level activity to incite a continued immune response. This continued low-level immune response is seen as long COVID-19. Whether COVID-19 strikes the brain, lungs or GI tract the pathophysiology is the same. The

elimination phase of wound healing stalls and a prolonged immune response is activated against the COVID-19 virus seen as a retained foreign body.

There may be something unique to COVID-19 viral protein capsule that allows it to be caught in the fibrin net. It is then possible for the COVID-19 virus to act like a foreign body [5].

The sequestered virus elicits an ongoing immune response. This ongoing immune response is the illness we recognize as long COVID-19. Depending upon the organ in which the virus is sequestered, that organ reflects long COVID-19 symptoms and physical findings.

For example, if a long COVID-19 patient presents with significant chronic respiratory illness, it is likely there is sequestered COVID-19 virus in the tissue. Because the COVID-19 virus is protected from the full advances of the immune system, the virus remains active at a low level. There are insufficient viral particles to be detected on a routine COVID-19 test. However, the presence of virus and virus particles keep the immune system active. The virus is sequestered and acts like a foreign body similar to a foreign body in a non-healing wound anywhere in the body.

The process of virus sequestration begins in seconds to hours with infiltration with neutrophils and macrophages. Cytokine, histamine, serotonin and platelet derived growth factor are released to form a fibrin net. Platelets release signals to activate the intrinsic and extrinsic clotting pathways, which activate fibrinogen to form the fibrin net. COVID-19 virus becomes ensnared in the fibrin net. This is why we see vascular emboli early on in COVID-19 patients. The activation of the clotting pathways forms a fibrin embolus. Hence, early on in the COVID-19 treatment protocol, heparin was used to combat these fibrin emboli [5].

A granulation phase operates during the first three weeks of the immune response. Neutrophils rebuild the tissue. Angiogenesis brings fibroblasts with immune growth factor, forming a fibrin matrix/fibrin net. Macrophages signal cytokine release as well as histamine and serotonin to initiate reparative process.

After the third week of COVID-19 infection, collagen reinforces the fibrin net encapsulating the virus. Normally, the inflammatory process would resolve at this stage. Because the sequestered virus acts like a retained foreign body, low-grade inflammation

continues. This low level of inflammation is what we term long COVID-19. The organ that sustains the greatest injury due to the inflammatory response is the organ system associated with the patient's presentation of long COVID-19. This addresses the variety of symptoms with which long COVID-19 presents. Pre-existing factors in a patient, such as smoking, may predispose the patient to long COVID-19. Diabetes, malnutrition, older age, steroids, obesity, vascular disease and anemia are some of these pre-existing factors. In addition, previous injury can elicit long COVID-19 at the site of previous injuries.

To illustrate this, a patient underwent microvascular decompression of the trigeminal nerve years before the COVID-19 infection. The surgery involved placing a Teflon pledget between the trigeminal nerve and the superior cerebellar artery.

The woman contracted COVID-19, and within two weeks post recovery of COVID-19, she experienced the return of the pain suffered fifteen years earlier with the trigeminal neuralgia. MRI was performed and was negative.

Acyclovir was prescribed, 800 mg four times daily. Facial pain lessened within 24 hours and resolved in 48 hours. She finished her 5-day course.

Within a few days of completion of acyclovir treatment her facial pain returned.

Acyclovir was restarted. With the second course of acyclovir the facial pain resolved for 10 days.

Facial pain returned.

The acyclovir was restarted. Her pain resolved once again. The acyclovir was continued for 4 months. It was then gradually tapered off over ten days.

Facial pain did not return and she has been pain-free.

The COVID-19 virus had circulated to the Teflon scar at the operative site and remained there inciting an inflammatory response, namely long COVID-19.

For further examples of patients who developed long COVID-19 in an area of previous scar formation, refer to the paper presented in the American Journal of Infectious Diseases [6].

We know acyclovir works by blocking virus replication. Viral replication must be associated with the development of long COVID-19 patients post infection. Viral replication must be very low since most long haulers test negative for COVID-19. Even though the virus is not detected in the bloodstream, the trapped COVID-19 virus in the fibrin net is sufficient to maintain a chronic immune response. The sequestered COVID-19 virus acts like a foreign body, eliciting the low-level chronic immune activity creating long COVID-19 symptoms.

Depending on the viral variant at the time of infection it can affect patients differently. The patient's individual genetics, physiology and past medical history affect the severity and has influence on long COVID-19 syndrome.

Acyclovir works by substituting a guanine-like base in the viral replication. Acyclovir even though it works on double-stranded DNA viruses it will work on COVID-19 viruses, which are RNA viruses, because of reverse transcriptase. For further details reference [6] (See Figures 2-4).

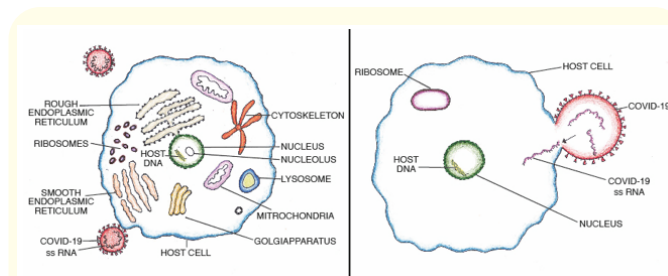


Figure 2: Left: Normal cell. Right: Covid-19 infecting cell.

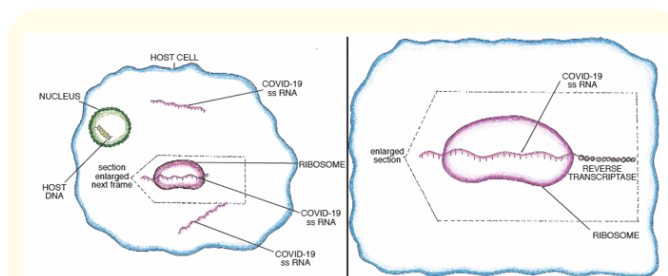
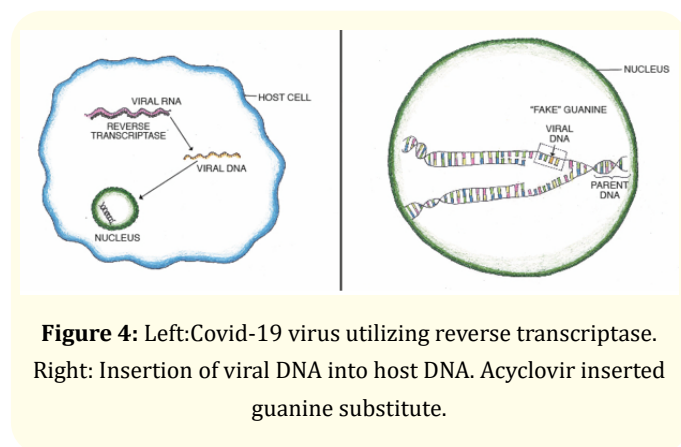


Figure 3: Left: Covid-19 translation in ribosome. Right: Enlargement of Covid-19 in post ribosome.



Conclusion

The importance of this paper is the long COVID-19 syndrome is not a unique disease process. Rather long COVID-19 represents the natural conclusion associated with COVID-19 acted upon by our immune system's wound healing pathway. We encourage investigation such as electron microscopy of long COVID-19 scar formation.

Funding Information

Author received no funding or financial support.

Acknowledgement

Authors have not received any outside support. This article is the sole work of the authors. Diagrams by Shelley Smith Beatty.

Author Contribution

Both authors take full responsibility of the content of this manuscript.

Conflict of Interest

None.

Ethics

This article is original and contains unpublished material. The corresponding author confirms all of the other authors have read and approved the manuscript and no ethical issues involved.

Bibliography

1. Davis HE., *et al.* "Long COVID: major findings, mechanisms and recommendations". *Nature Reviews Microbiology* 21.3 (2023): 133-146.
2. Almadani YH., *et al.* "Wound Healing: A Comprehensive Review". *Seminars in Plastic Surgery* 35.3 (2021): 141-144.
3. Alizon S and Sofonea MT. "SARS-CoV-2 virulence evolution: Avirulence theory, immunity and trade-offs". *Journal of Evolutionary Biology* 34.12 (2021): 1867-1877.
4. Sinno H and Prakash S. "Complements and the wound healing cascade: an updated review". *Plastic Surgery International* 2013 (2013): 146764.
5. Ryu JK., *et al.* "Fibrin drives thromboinflammation and neuropathology in COVID-19". *Nature* 633 (2024): 905-913.
6. Beatty RM. "Long COVID-19 Symptoms Remedied by Anti-Viral Treatment in Neurosurgical Patients". *American Journal of Infectious Diseases* 19.3 (2023): 39-44.