Viral infection and autoimmune disease

Marie Chansuphan (Year 2 Biomedical Engineering)

We often think of viral infections as short-lived; fevers that pass, sore throats that heal, and bodies that return to normal. But what if they don't? A year ago, I experienced a viral infection that did not end with recovery. Instead, it left me with chronic symptoms that affected my muscles, joints, and nerves. It felt as if my body was no longer mine. As I've come to learn, the virus may have done more than just make me sick; it might have triggered my immune system to turn against itself. This essay explores how viruses, some of the most fascinating and disruptive microbes in history, can initiate autoimmune diseases. Through my own experience and the science behind these tiny invaders, I hope to shed light on a less-discussed consequence of infection: what happens when the microbe leaves, but the body doesn't stop fighting.

My Experience With a Mysterious Viral Infection

It began with a sharp pain in the center of my chest. Not the kind of pain linked to a heart attack, but one that worsened with sneezing, coughing, or even turning from side to side. I also developed a high fever that lasted for a few days, followed by persistent low-grade fever for almost a month. Medical tests, including electrocardiogram, X-ray, and blood work, showed no major abnormalities, except for elevated markers of inflammation. The diagnosis was simple: a viral infection. No one could tell me what virus I had contracted, only that it was likely self-limiting.

But the infection was only the beginning.

About a month later, I started experiencing severe muscle pain, especially in my triceps and calves. Even light touch or movement became painful. Then came recurring chest pain that mimicked cardiac symptoms: pain radiating to my left arm and jaw. My joints began to ache. Numbness and tingling in my hands became frequent, sometimes extending to my legs. At times, my left arm felt weaker than my right. These symptoms, especially the chest inflammation and referred pain, would appear without warning.

Now, more than a year later, some symptoms have eased, but others still linger, particularly the sharp chest sensations, nerve-related numbness, and weakness in my arm. I've come to suspect that my viral infection might have triggered something deeper, an autoimmune response.

Viruses: Tiny Microbes, Massive Impact

Viruses are among the most influential microbes in human history. Unlike bacteria, they are not alive in the traditional sense; they rely entirely on host cells to replicate [1]. Yet their small size belies their power. They have shaped entire civilizations; smallpox, influenza, HIV, SARS-CoV-2 and most recently, COVID, have left indelible marks on the world. But beyond pandemics and epidemics, viruses can profoundly affect individuals, invading cells and triggering long-term health consequences."

One of the lesser-known consequences of viral infection is autoimmunity, when the immune system begins attacking the body's own cells [2]. This misdirected response can lead to chronic diseases such as lupus, rheumatoid arthritis, type 1 diabetes, and multiple sclerosis [2]. What I experienced might be part of this growing list.

How Viruses Trigger Autoimmune Disease

The human immune system is a highly sophisticated defense mechanism, finely tuned to identify and eliminate invading microbes such as bacteria and viruses. However, this system is not infallible. Under certain conditions, it can misidentify the body's own cells as threats, resulting in autoimmunity. Increasingly, research suggests that viral infections may act as significant environmental triggers for autoimmune diseases, particularly in genetically predisposed individuals [3], [4].

One of the most studied mechanisms by which viruses can induce autoimmunity is molecular mimicry. This occurs when viral antigens closely resemble human proteins in structure. As the immune system mounts a response against the invading virus, it may mistakenly attack similar-looking host tissues [3], [5] . This misdirected immune response has been implicated in a number of autoimmune diseases. For instance, Guillain-Barré syndrome is frequently preceded by infections such as influenza or Zika virus, where the resulting antibodies cross-react with components of the peripheral nervous system [6]. Similarly, multiple sclerosis has been associated with Epstein-Barr virus (EBV), and type 1 diabetes has been linked to enteroviruses like Coxsackie B, both of which may involve molecular mimicry mechanisms [5]. Notably, these autoimmune reactions often persist long after the viral infection has resolved.

Another proposed mechanism is bystander activation, wherein the immune system becomes broadly hyperactive during a viral infection. In the course of responding to the virus, non-specific immune cells, especially T-cells, may become inadvertently activated. These cells can attack nearby healthy tissues that were not initially involved in the infection [7]. Over time, this collateral damage can lead to chronic inflammation and autoimmune symptoms such as joint pain, muscle aches, or neuropathy. In cases where inflammation is not adequately resolved, the immune system's heightened state may evolve into sustained tissue damage [8].

A third pathway is known as epitope spreading. As infected or inflamed cells become damaged, they may release intracellular proteins that were previously concealed from immune surveillance. These newly exposed self-antigens can become unintended targets of the immune system. What begins as a focused antiviral response may thus escalate into a broader autoimmune reaction [9], [10]. This process has been documented in diseases such as systemic lupus erythematosus, where autoantibody profiles become increasingly diverse over time [11]. Epitope spreading may help explain why some patients experience expanding and evolving symptoms months after their initial illness.

In some cases, persistent viral infections may be responsible for prolonged immune dysregulation [3]. Certain viruses, such as human herpesvirus 6 (HHV-6), Epstein-Barr virus, and SARS-CoV-2, have been known to remain latent within the body or reactivate intermittently. These viral remnants or reactivations can maintain a state of low-grade inflammation, continuously

stimulating the immune system [12]. As a result, chronic immune activation could develop. This phenomenon is particularly relevant in conditions like long COVID, where symptoms such as fatigue, joint pain, and cognitive disturbances may linger for months beyond the initial infection [13]. In such cases, even though the acute phase of the viral illness has ended, the immune system can continue to behave as if the threat remains.

These processes can explain what happened in my case: my body initially fought off a virus, but the immune system didn't switch off afterward. Instead, it kept attacking my muscles, joints, and possibly even my nerves, leading to symptoms of inflammation, pain, and weakness.

Biomedical Innovations in Diagnosing and Managing Post-Viral Autoimmune Conditions

My experience with post-viral autoimmune symptoms, ranging from chest pain and inflammation to nerve dysfunction, has highlighted the challenges of diagnosing and monitoring autoimmune conditions that emerge after infection. Despite undergoing numerous tests and consultations, no single diagnostic tool could fully explain my condition. This diagnostic ambiguity reveals a critical gap in healthcare, one that biomedical engineering is well-positioned to address through innovative solutions in diagnostics, monitoring, and therapy.

One promising area is the development of diagnostic biosensors. Researchers and engineers are designing sensors capable of detecting disease markers at extremely low concentrations in bodily fluids such as blood or saliva [14]. These include cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), as well as the autoantibodies such as anti-nuclear antibodies (ANA) and anti-double-stranded DNA (anti-dsDNA) [15]. Advanced biosensors that can distinguish between active viral inflammation and autoimmune activation could significantly shorten the diagnostic timeline. Utilizing technologies such as microfluidics, nanomaterials, and smartphone-compatible platforms, these biosensors can offer real-time insights from just a single drop of blood [16], [17], [18]. If such tools had been available during my illness, they might have provided greater clarity in distinguishing between residual viral activity and an autoimmune response.

In parallel, the rise of wearable monitoring devices is revolutionizing how autoimmune symptoms are tracked. These wearables continuously monitor physiological signals relevant to inflammation and autonomic function, such as body temperature fluctuations, skin conductance, heart rate variability, and electromyographic activity from muscles [19]. In my case, a device capable of identifying fluctuations in chest pain, muscle spasms, or nerve-related symptoms would have offered valuable data for clinicians to understand and interpret seemingly inconsistent complaints. When paired with machine learning algorithms, these wearables could facilitate predictive modeling, forecasting disease flare-ups and evaluating treatment efficacy in real time.

Another transformative area is targeted drug delivery, which seeks to overcome the limitations of traditional systemic immunosuppressants used in autoimmune disease treatment. While such drugs are effective, they carry the risk of compromising the body's ability to fight infections [20]. This can be addressed through the design of nanocarriers that release drugs specifically at sites of inflammation, thereby minimizing systemic exposure and side effects [21]. These "smart" delivery systems can be triggered by environmental cues such as pH changes or specific enzymes associated

with inflammation. Although I have not required medication myself, it is reassuring to know that more precise and safer treatment options are becoming a reality.

Finally, our understanding of post-viral autoimmunity is being advanced through lab-on-a-chip and organ-on-chip technologies. These microengineered systems replicate human tissues and immune interactions, allowing researchers to model how specific viruses can trigger autoimmune responses in various organs [22], [23]. By simulating complex immune-pathogen interactions outside the human body, these tools provide an alternative to animal testing and offer new opportunities for drug discovery. Moreover, they may help answer elusive questions such as why some individuals, like myself, go on to develop chronic symptoms after infection, while others recover completely.

Reflection

Viral infections are often seen as fleeting illnesses, but for some, they can leave behind lasting, invisible battles. My journey with post-viral autoimmune symptoms has shown me that the real challenge sometimes begins after the infection ends. As I've explored in this essay, viruses have the potential to mislead the immune system, causing it to turn against the very body it is meant to protect. Through mechanisms like molecular mimicry, bystander activation, and epitope spreading, viruses can spark a cascade of autoimmune reactions, leading to chronic pain, inflammation, and neurological symptoms that are difficult to diagnose and treat.

This experience has also deepened my appreciation for the role of biomedical engineering in addressing these challenges. From biosensors that can detect immune markers in real time, to wearable devices that monitor symptom fluctuations, to nanotechnology that delivers drugs precisely where they are needed, these innovations offer not just clinical value, but hope. Organ-on-chip technologies, in particular, stand out as tools that could revolutionize how we study and understand post-viral autoimmune diseases without relying solely on animal models or trial-and-error treatments.

From a personal perspective, writing this essay has been both intellectually and emotionally meaningful. It allowed me to make sense of a confusing and difficult year, and to reframe my experience through the lens of science and innovation. This process has not only deepened my understanding of the biological mechanisms at play, but also clarified my sense of purpose. In the future, I hope to contribute to innovations that make autoimmune conditions easier to detect, understand, and treat, especially those triggered by infections. My own journey may have begun with a virus, but I want the next chapter to be about solutions.

Word Count : 1851 words

Reference

[1] Milstein & Randal L. (2024). *Viral Genetics*. EBSCO Research Starters. https://www.ebsco.com/research-starters/health-and-medicine/viral-genetics

[2] Kris Martins. (2023, October 3). *What is autoimmune disease?.* WebMD. https://www.webmd.com/a-to-z-guides/autoimmune-diseases

[3] Sundaresan, B., Shirafkan, F., Ripperger, K., & Rattay, K. (2023). *The Role of Viral Infections in the Onset of Autoimmune Diseases*. *Viruses*, *15*(3), 782. https://doi.org/10.3390/v15030782

[4] Cooper, G. S., Miller, F. W., & Pandey, J. P. (1999). The role of genetic factors in autoimmune disease: implications for environmental research. *Environmental health perspectives*, *107 Suppl 5*(Suppl 5), 693–700. https://doi.org/10.1289/ehp.99107s5693

[5] Cusick, M. F., Libbey, J. E., & Fujinami, R. S. (2012). Molecular mimicry as a mechanism of autoimmune disease. *Clinical reviews in allergy & immunology*, *42*(1), 102–111. https://doi.org/10.1007/s12016-011-8294-7

[6] Laman, J. D., Huizinga, R., Boons, G. J., & Jacobs, B. C. (2022). Guillain-Barré syndrome: expanding the concept of molecular mimicry. *Trends in immunology*, *43*(4), 296–308. https://doi.org/10.1016/j.it.2022.02.003

[7] Shim, C. H., Cho, S., Shin, Y. M., & Choi, J. M. (2022). Emerging role of bystander T cell activation in autoimmune diseases. *BMB reports*, *55*(2), 57–64. https://doi.org/10.5483/BMBRep.2022.55.2.183

[8] Xiang, Y., Zhang, M., Jiang, D., Su, Q., & Shi, J. (2023). The role of inflammation autoimmune disease: a therapeutic target. *Frontiers in immunology*, *14*, 1267091. https://doi.org/10.3389/fimmu.2023.1267091

[9] Tuohy, V. K., & Kinkel, R. P. (2000). Epitope spreading: a mechanism for progression of autoimmune disease. *Archivum immunologiae et therapiae experimentalis*, *48*(5), 347–351.

[10] Vanderlugt, C., Miller, S. Epitope spreading in immune-mediated diseases: implications for immunotherapy. *Nat Rev Immunol* **2**, 85–95 (2002). https://doi.org/10.1038/nri724

[11] Pan, Q., Liu, Z., Liao, S., Ye, L., Lu, X., Chen, X., ... & Liu, H. (2019). Current mechanistic insights into the role of infection in systemic lupus erythematosus. *Biomedicine & Pharmacotherapy*, *117*, 109122. https://doi.org/10.1016/j.biopha.2019.109122

[12] Vojdani, A., Vojdani, E., Saidara, E., & Maes, M. (2023). Persistent SARS-CoV-2 Infection, EBV, HHV-6 and Other Factors May Contribute to Inflammation and Autoimmunity in Long COVID. *Viruses*, *15*(2), 400. https://doi.org/10.3390/v15020400

[13] Brooks, B., Tancredi, C., Song, Y., Mogus, A. T., Huang, M. W., Zhu, H., Phan, T. L., Zhu, H., Kadl, A., Woodfolk, J., Jerome, K. R., & Zeichner, S. L. (2022). Epstein-Barr Virus and Human Herpesvirus-6 Reactivation in Acute COVID-19 Patients. *Viruses*, *14*(9), 1872. https://doi.org/10.3390/v14091872

[14] Broza, Y. Y., Zhou, X., Yuan, M., Qu, D., Zheng, Y., Vishinkin, R., ... & Haick, H. (2019). Disease detection with molecular biomarkers: from chemistry of body fluids to nature-inspired chemical sensors. *Chemical reviews*, *119*(22), 11761-11817. https://doi.org/10.1021/acs.chemrev.9b00437

[15] Teniou, A., Rhouati, A., & Marty, J. L. (2024). Recent Advances in Biosensors for Diagnosis of Autoimmune Diseases. *Sensors (Basel, Switzerland)*, *24*(5), 1510. https://doi.org/10.3390/s24051510

[16] Sekhwama, M., Mpofu, K., Sivarasu, S. *et al.* Applications of microfluidics in biosensing. *Discov Appl Sci* **6**, 303 (2024). https://doi.org/10.1007/s42452-024-05981-4

[17] Fu, Y., Liu, T., Wang, H., Wang, Z., Hou, L., Jiang, J., & Xu, T. (2024). Applications of nanomaterial technology in biosensing. *Journal of Science: Advanced Materials and Devices*. https://doi.org/10.1016/j.jsamd.2024.100694

[18] Baker, D. V., Bernal-Escalante, J., Traaseth, C., Wang, Y., Tran, M. V., Keenan, S., & Algar, W. R. (2025). Smartphones as a platform for molecular analysis: concepts, methods, devices and future potential. *Lab on a Chip*. DOI: 10.1039/D4LC00966E

[19] Ortet, C., & Vale Costa, L. (2022). "Listen to Your Immune System When It's Calling for You": Monitoring Autoimmune Diseases Using the iShU App. *Sensors (Basel,Switzerland)*, *22*(10), 3834. https://doi.org/10.3390/s22103834

[20] Cleveland Clinic (2023).Immunosuppresants: Definition, Uses & Side Effects. https://my.clevelandclinic.org/health/treatments/10418-immunosuppressants

[21] Prosperi, D., Colombo, M., Zanoni, I., & Granucci, F. (2017). Drug nanocarriers to treat autoimmunity and chronic inflammatory diseases. *Seminars in immunology*, *34*, 61–67. https://doi.org/10.1016/j.smim.2017.08.010

[22] Farhang Doost, N., & Srivastava, S. K. (2024). A Comprehensive Review of Organ-on-a Chip Technology and Its Applications. *Biosensors*, *14*(5), 225. https://doi.org/10.3390/bios14050225

[23] Morsink, M. A. J., Willemen, N. G. A., Leijten, J., Bansal, R., & Shin, S. R. (2020). Immune Organs and Immune Cells on a Chip: An Overview of Biomedical Applications. *Micromachines*, *11*(9), 849. https://doi.org/10.3390/mi11090849