Policy briefing

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Infection and autoimmune disease

Key points

- Infections trigger autoimmunity and increase disease risk through mechanisms related to molecular mimicry
- Autoimmune diseases complicate treatment regimens for symptoms of autoimmunity, raising infection risk due to immunosuppressive therapies
- Vaccination can help prevent infection-related autoimmune triggers but requires careful management
- Patient and practitioner education, awareness and further research are essential for improving management and outcomes for patients

Autoimmune diseases are conditions where the immune system mistakenly attacks the body's own tissues, causing inflammation, tissue damage, and other symptoms such as chronic pain, fatigue, and organ dysfunction depending on the specific disease and affected organs. There are over 80 types of autoimmune disease, including rheumatoid arthritis, systemic lupus erythematosus, multiple sclerosis, and type 1 diabetes.

Diagnosis and treatment vary by disease and severity. Typically the aim is to reduce immune activity and manage symptoms with medications like anti-inflammatory drugs, immunosuppressants, and biologics, along with lifestyle changes and supportive therapies.

Autoimmune diseases affect millions of people worldwide, leading to chronic health issues that significantly impact quality of life. In the USA alone, direct costs associated with disease diagnosis, treatment, and management, exceed $100 billion annually.

Globally, incidence of autoimmune diseases is rising. However, the exact causes are multifaceted and often unclear. These are likely to involve genetic, environmental, and hormonal factors, with certain infections, medications, and stress also playing a role. Understanding the role of infections in triggering autoimmunity or exacerbating the symptoms of the disease, is crucial to better disease management.

Multifaceted relationship between autoimmunity and infection[1]

There is an established relationship between infection and increased risk of autoimmune disease, however this is complex and varies between diseases. Infection can trigger autoimmunity by prompting immune responses. Conversely, autoimmune conditions can increase susceptibility to infections due to immune dysregulation and immunosuppressive

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treatments. Balancing treatment to control autoimmunity while managing infection risk is crucial for optimal patient care.

Infections as triggers for autoimmunity

Research on identical twins, where there is a low concordance rate of autoimmune diseases, suggests an important role for environmental factors such as viral, bacterial and other pathogens in triggering autoimmunity. Evidence supporting the role of infections includes correlation of incidence of Epstein Barr virus (EBV) infections during winter with an increase in systemic lupus erythematosus onset, and detection of the viral genomic DNA/RNA in affected tissues.[1,2]

Pathogen infections can trigger autoimmunity through mechanisms like molecular mimicry, where the immune system response to microbial antigens that resemble self-antigens, results in it attacking both. For instance, viruses and bacteria can mimic host proteins, contributing to conditions such as Guillain-Barré syndrome and rheumatic fever. Infections may also cause epitope spreading, where the body's immune attacks expand to target additional self-antigens, or disrupt immune tolerance, activating autoreactive T cells and promoting inflammation.

Autoimmunity increases susceptibility to infection

Patients with autoimmune diseases face a heightened risk of infections compared to the general population due to related factors such, immune dysfunction, and treatments used to manage their conditions.[1]

Infections can be a significant cause of mortality among autoimmune patients, highlighting the importance of understanding how treatments for the autoimmune disease impact infection susceptibility. For instance, treatments targeting inflammatory cytokines crucial for immune function, like TNF-alpha inhibitors used in rheumatoid arthritis and other conditions, can increase susceptibility to bacterial, viral, and fungal infections by impairing pathogen clearance. Cautious use of immunosuppressants in patients with concurrent infections are essential to balance disease management with infection control and optimise patient outcomes.

Implications for clinical practice

The relationship between infection and autoimmune diseases can greatly influence the approach to patient care across diagnosis, treatment, prevention, and management.

Diagnosis: Recording a patient's recent infections can provide crucial insights into autoimmune disease development. Post-infection symptoms can guide diagnostic testing, while identifying infection-related biomarkers, like elevated anti-streptolysin O (ASO) antibodies in rheumatic fever or EBV antibodies in multiple sclerosis (MS), can improve diagnostic precision.

Treatment: Strategies to manage infection-triggered autoimmune diseases often involve targeting inflammation and modulating the immune system. Antiviral treatments, for instance, can be beneficial for MS linked to EBV. Understanding infection-induced autoimmunity pathways can help develop therapies addressing underlying mechanisms without broadly suppressing immune function.[3]

Research and prevention: Identifying biomarkers predicting susceptibility to autoimmune diseases, such as APOC4 protein marker post-infection for type 1 diabetes, could enable earlier intervention and potentially prevent disease onset. Biomarker discovery to support diagnosis and clinical management is an active area of research; work in diverse populations is needed to address challenges affecting their use such as specificity issues, variable sensitivity, interpretation complexity, individual variability, high costs, ethical concerns, and patient factors affecting reliability.

Case study: Acquired Haemophilia A (AHA) in Hong Kong[4]

Acquired Haemophilia A (AHA) is a rare but serious bleeding disorder caused by the development of autoantibodies that inhibit the function of coagulation factor VIII. It is often associated with underlying conditions like autoimmune diseases and viral infections such as acute hepatitis B and C.

Acquired Haemophilia A occurs at an estimated rate of 1.5 cases per million people per year globally, primarily affecting elderly populations. However, a study in Hong Kong found a higher annual incidence of 2.4 per million, which is significantly more than reported rates in European ancestry populations and in the China Acquired Haemophilia Registry (CARE) from Mainland China. This suggests potential demographic differences in susceptibility to the disorder between population groups.

Treatment focuses on two key components: therapy to manage bleeding and immunosuppressive therapy (IST) to eliminate factor VIII autoantibodies. However, immunosuppressive therapy poses significant risks, particularly to elderly patients who are more vulnerable to complications, such as infections. In the Hong Kong cohort study, over 50% of patients died, often due to infections related to immunosuppressive therapy. This mortality rate is notably higher than in other large-scale studies of European ancestry populations. While intensive immunosuppressive therapy aims to achieve faster remission and lower bleeding-related mortality, it increases the risk of sepsis and other infections, especially in elderly patients.

The Hong Kong study also found that the choice of immunosuppressive therapyregimen did not significantly improve survival rates, although more intensive regimens were associated with longer hospital stays. This suggests that more aggressive immunosuppression does not necessarily provide survival benefits but does contribute to higher rates of infection-related mortality. Hence it is crucial to optimise treatment protocols and monitor patients for infections.

Management of autoimmune disease and infection as a public health challenge

Managing autoimmune diseases triggered by infections faces several challenges, including complex diagnosis, limited public and provider awareness, and high diagnostic costs. Treatment is complicated by immunosuppressive therapies that increase infection risk.

Research gaps, vaccine hesitancy, and resource limitations further hinder effective management. A multifaceted approach is needed, with enhanced education, better access to diagnostics, targeted therapies, and improved public health strategies focused on sanitation, hygiene, and infectious disease education. Careful vaccine management for at-risk individuals is also crucial to prevent complications.

Vaccination strategies

Vaccination efforts and guidelines advocate for immunisation against pathogens known to trigger autoimmune diseases. By targeting infectious agents like Coxsackievirus, vaccines aim to prevent immune system dysregulation that can lead to conditions such as type 1 diabetes. This approach protects against infections and potentially lowers the incidence of associated autoimmune disorders, demonstrating the dual benefits of vaccination in public health strategies. However, careful monitoring is crucial, especially in predisposed populations, to ensure vaccines are administered safely. This is evident in the case of COVID-19 and the associated vaccines.

Case study: COVID-19

Research indicates a complex relationship between COVID-19 and autoimmune diseases[5,6], with severe symptoms potentially triggering new autoimmune conditions or worsening existing ones. Diagnosis and treatment complexities arise from overlapping symptoms and the balance needed with immunosuppressive therapies. Long COVID may also involve autoimmune aspects, complicating recovery.

Additionally, COVID-19 vaccination has been linked to increased risks of autoimmune diseases like glomerulitis, rheumatism, and Guillain-Barré syndrome, potentially due to molecular mimicry from vaccine components. However, studies[6] suggest that vaccines are generally safe and may even protect against infection-induced autoimmunity, especially in immunosuppressed patients.

Overall, the benefits of vaccination in controlling COVID-19 and preventing severe complications outweigh the risks of triggering autoimmune diseases, warranting further investigation into the mechanisms underlying immune system activation.

Education, training and future policy considerations

Improving management of infection-linked autoimmune diseases requires enhanced research, robust infection prevention, early detection through better diagnostics, multidisciplinary care, affordable treatments, and public awareness.

Addressing disparities, regulating environmental triggers, and fostering global collaboration are also essential to reduce disease burden and improve outcomes.

Educating patients and healthcare providers on the link between infections and autoimmune diseases promotes earlier diagnosis and better management. Informed patients can recognise symptoms and seek timely care, while well-trained providers can offer personalised treatment by focusing on patient history, biomarkers, and updated protocols. This approach, supported by improved clinical guidelines and advanced diagnostics, enhances outcomes and reduces healthcare burdens.

Future research should integrate global data, experimental models, long-term studies, and clinical trials, while addressing social factors like socioeconomic status and food security to help lower infection risks and prevent outbreaks that may trigger autoimmune diseases. It should also use diverse methods to understand infection-driven autoimmune diseases.

Using global data can reveal population-specific risk factors, while experimental models and long term studies will help investigate disease mechanisms and progression. Clinical trials should focus on treatments aimed at inflammation and immune response. It is also crucial to consider socioeconomic factors that influence infection risk and access to healthcare.

A comprehensive approach - including biological, environmental, and social factors - will improve outcomes and reduce infection-related autoimmune triggers.

Conclusion

The connection between infections and autoimmune diseases is complex and a great deal remains to be understood about underlying mechanisms, pathogen-specific triggers, host genetic interactions, biomarkers, and the role of chronic or latent infections. Improving diagnosis, treatment, and prevention involves balancing the use of immunosuppressive therapies to control autoimmune symptoms while minimising infection risk.

Advances in research - such as identifying specific disease markers and developing targeted treatments and vaccines - offer hope for better care. However, it is essential to educate both patients and healthcare providers about these connections so that symptoms are recognised early, and care can be more personalised. By raising awareness and focusing on safe, informed treatment options, we can improve patient outcomes and reduce the healthcare burden of autoimmune diseases.

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Author: Bhavya Balaji Krishnan

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