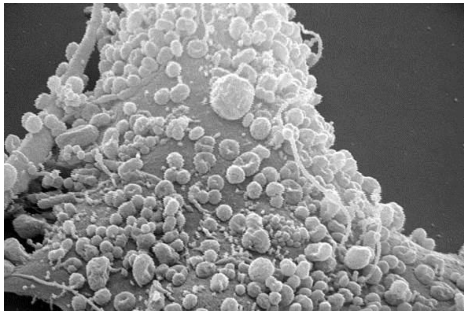
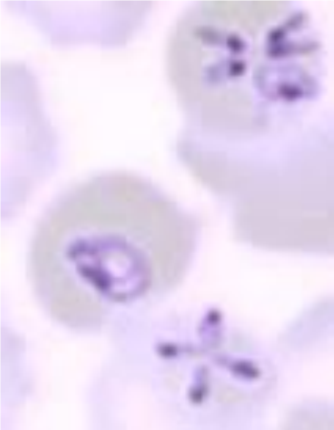




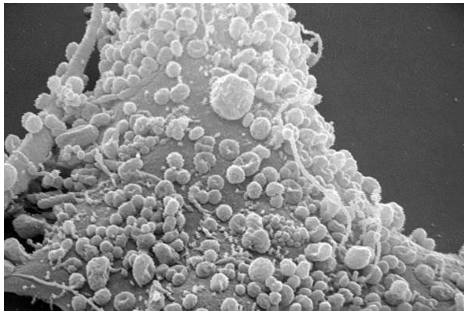
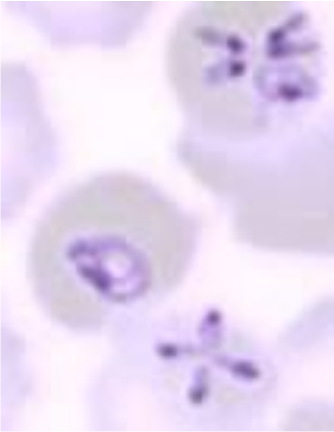

Autoimmunity and the Viral/Bacterial Connection

Armin Schwarzbach MD, PhD
Medical Doctor and
Specialist for Laboratory Medicine

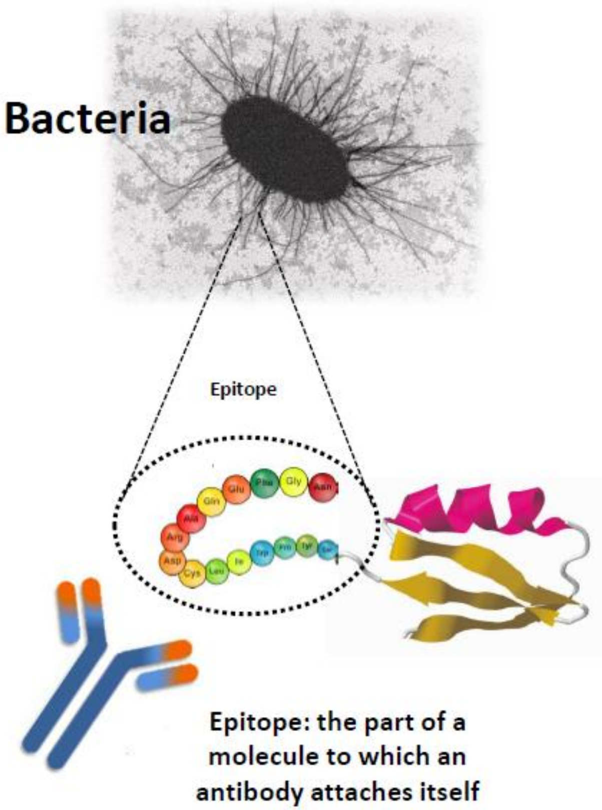
Gilian Crowther MA (Oxon), FBANT, CNHC reg.
AONM Director of Research

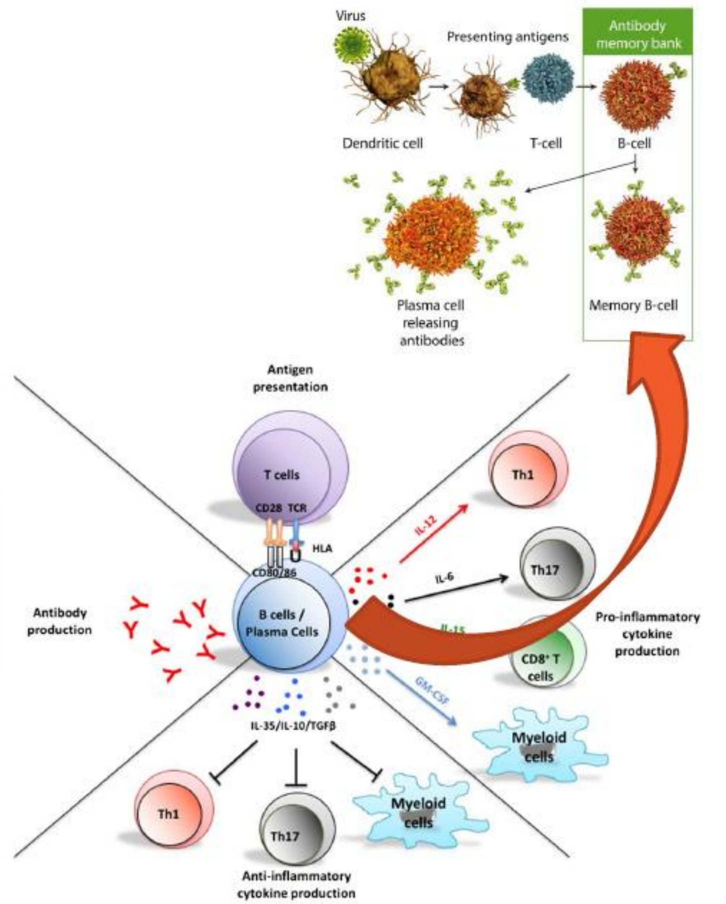
Autoimmunity and the Bacterial/Viral Connection

- **Mechanisms by which pathogens can trigger autoimmunity**
- **Pathogen involvement in specific autoimmune conditions**
  - Type 1 Diabetes and Autoimmune Diabetes insipidus
  - Multiple Sclerosis
  - Rheumatoid arthritis
  - Hashimoto's/Graves'
  - IBD
  - Sjögren's Syndrome
  - Myasthenia Gravis
  - Guillain Barré Syndrome
  - PANS/PANDAS
  - ALS/Motor Neurone Disease
  - Antiphospholipid syndrome


Antibodies recognise epitopes on infectious agents





Source: *Courtesy of Professor C. Shimasaki, CEO of Moleculera Biosciences;* [*https://microbeonline.com/epitope/*](https://microbeonline.com/epitope/)

Illustration of the four key mechanisms

Epitope spreading

Bystander activation

Molecular mimicry

Super-antigens

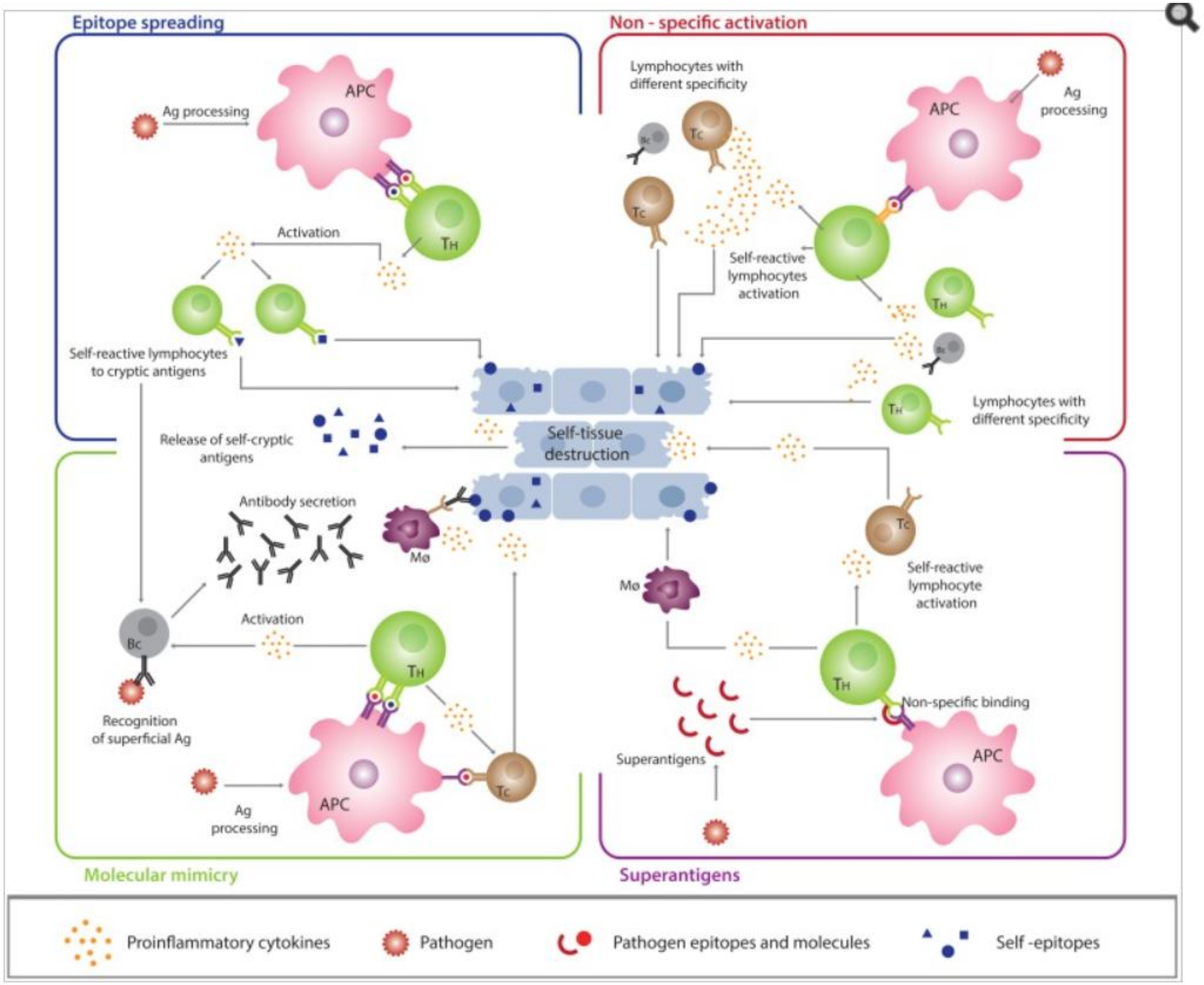
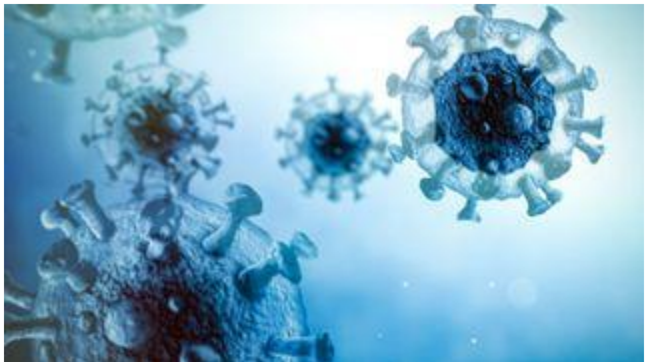
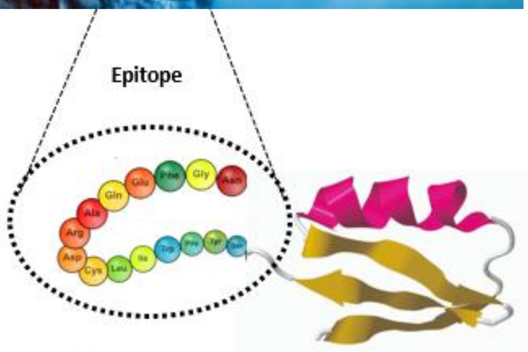


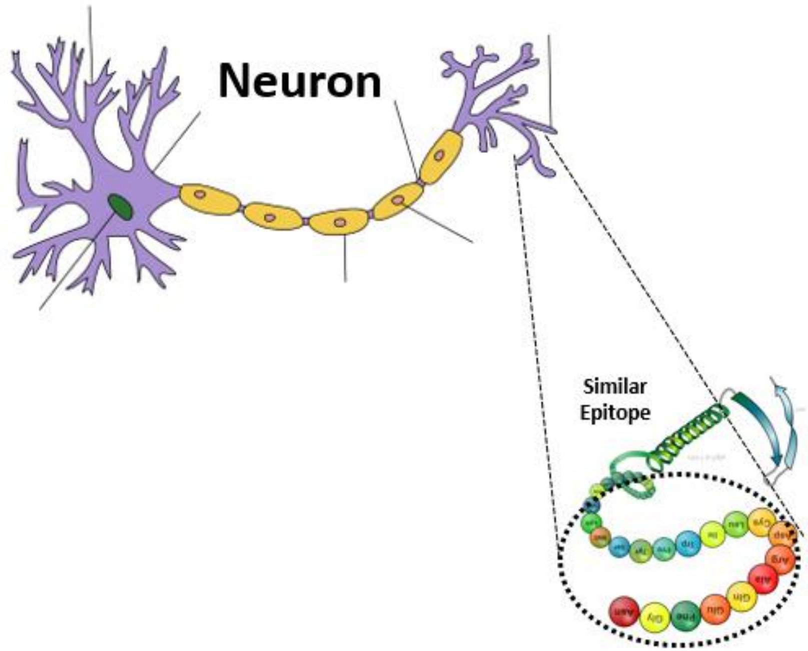
Figure 2 Infectious mechanisms of autoimmune disease.

Source: https://www.ncbi.nlm.nih.gov/books/NBK459437/; Sfriso P, Ghirardello A, Botsios C, et al. Infections and autoimmunity: the multifaceted relationship. J Leukoc Biol. 2010;87:385–95.

Molecular mimicry: Example - viral





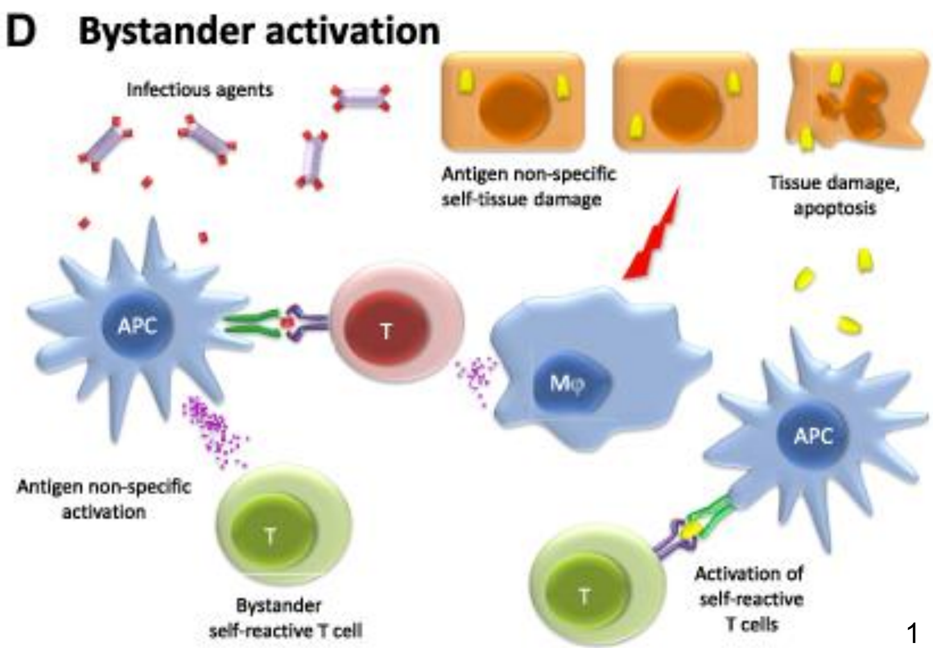


“T-cell receptors can recognise and react towards both viral antigens and self-antigens that have structural or sequential homology”[1]

“Our results demonstrate that human-infecting viruses frequently leverage mimicry in the course of their infection, point to substantial evolutionary pressure for mimicry, and highlight mimicry’s important role in human autoimmunity.”[2]

Source: 1. Sundaresan B, Shirafkan F, Ripperger K, Rattay K. The Role of Viral Infections in the Onset of Autoimmune Diseases. Viruses. 2023 Mar 18;15(3):782, Fig 1; 2. Maguire C et al. Molecular Mimicry as a Mechanism of Viral Immune Evasion and Autoimmunity. bioRxiv [Preprint]. 2024 Mar 9:2024.03.08.583134

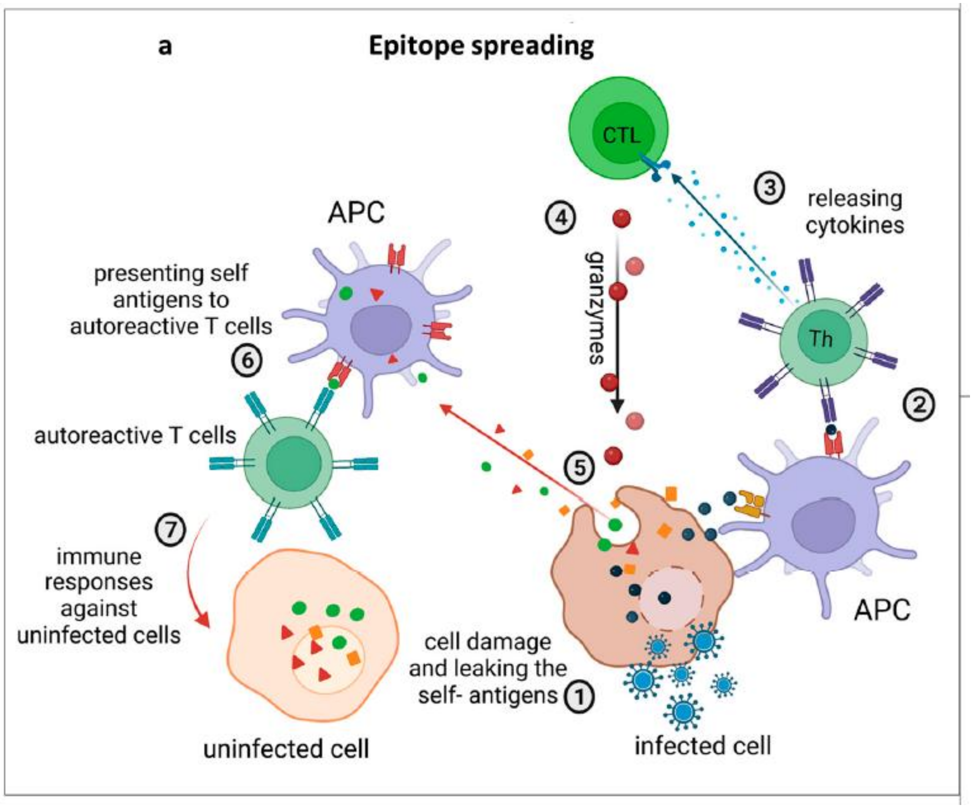
Bystander activation: nearby uninfected cells get caught in the assault in an antigen-unspecific manner: "collateral damage"



"Infected cells present viral antigens to virus-specific T cells. T cells identify infected cells and release cytotoxic granules, causing cell death of infected – but also of nearby uninfected cells …. In contrast to epitope spreading and molecular mimicry, bystander activation is a mechanism by which autoimmune reactions are triggered in an antigen-unspecific manner."[2]

Source: 1. Sfriso P, Ghirardello A, Botsios C, et al. Infections and autoimmunity: the multifaceted relationship. J Leukoc Biol. 2010;87:385–95; 2. Sundaresan B, Shirafkan F, Ripperger K, Rattay K. The Role of Viral Infections in the Onset of Autoimmune Diseases. Viruses. 2023 Mar 18;15(3):782, Fig 1

Epitope spreading



*** Epitope: the part of an antigen that the host's immune system recognizes, eliciting the** immune response to an invading pathogen[2]

In this case, the autoimmune response is due to the spatial proximity and similarities between several self epitopes and epitopes from the microorganism

Source: Sundaresan B, Shirafkan F, Ripperger K, Rattay K. The Role of Viral Infections in the Onset of Autoimmune Diseases. Viruses. 2023 Mar 18;15(3):782, Fig 1;
2. https://www.news-medical.net/life-sciences/What-is-an-Epitope.aspx;
https://www.researchgate.net/publication/276353052_Autoimmunity_From_Bench_to_Bedside, Yehuda Shoenfeld, MD et al.

Superantigens: massive cytokine release

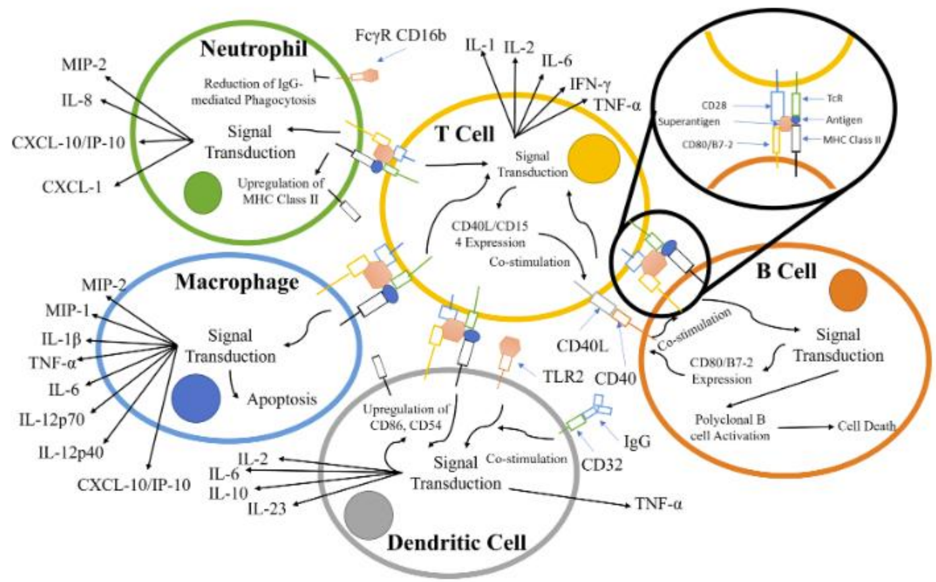


FIGURE 2 | Principal components involved in the superantigen activation of T-cells, B-cells, macrophages, and neutrophils. The interactions displayed are based on material from references (28–49). The responses contribute to and escalate the hyper-activation of T-cells and subsequent cytokine storm.

Superantigens are bacterial, viral, or retroviral proteins that can activate a large quantity of T cells by binding the T cell antigen receptor to molecules expressed on other cells. They produce excessive activation of the immune system, resulting in massive cytokine release. Primarily from bacteria like Staphylococcus aureus and Streptococcus pyogenes that bypass normal antigen recognition to cause massive and non-specific T-cell activation by simultaneously binding to MHC Class II molecules and T-cell receptors outside their usual binding sites.

Source: Deacy AM, Gan SK, Derrick JP. Superantigen Recognition and Interactions: Functions, Mechanisms and Applications. Front Immunol. 2021 Sep 20;12:731845.

Objectives of the following pages

The following are the key autoimmune conditions with high-quality PubMed references for the viruses and bacteria that have been associated with them, to

- Help speed your background research when perhaps preparing to see patients, and

- in case useful when putting together reports

T1D

Diabetes Type 1

Viruses

1. Cytomegalovirus
2. Coxsackie A & B
3. Echovirus
4. SARS-CoV-2

Bacteria

1. Bacterial pneumonia, especially Klebsiella oxytoca
2. Chlamydia pneumoniae
3. Yersinia
4. H pylori

References for bacteria and Type 1 Diabetes

T1D

Selection

Bacteria

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T1D

Selection

CMV virus

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T1D Selection Enteroviruses

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MS

Multiple Sclerosis

Viruses

1. EBV
2. HHV6
3. SARS-CoV-2
4. Coxsackie Virus A & B
5. Echovirus

Bacteria

1. Borrelia
2. Bartonella
3. Chlamydia pneumoniae
4. H pylori Blot
5. Tapeworm

References for bacteria and MS

MS

Selection

Bacteria

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MS

Viruses

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Rheumatoid Arthritis

Bacterial tests

1. Borrelia
2. Mycoplasma pneumoniae
3. Chlamydia pneumoniae/Chlamydia trachomatis
4. H pylori Blot
5. Yersinia enterocolitica

Viral tests

1. EBV
2. CMV
3. HSV1/2
4. SARS-CoV-2

Rheumatoid arthritis and bacterial infections

Selection RA Bacteria

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Selection RA Viruses

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Hashimoto's/Graves'

Hashimoto's/Graves'

Viruses

Hashimoto's

1. EBV
2. HSV 1 & 2
3. CMV
4. Parvovirus B19
5. SARS-CoV-2

Graves'

1. SARS-CoV-2
2. Possibly the Herpes viruses

Bacteria

Hashimoto's

1. Borrelia
2. Yersinia enterocolitica

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Viruses

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Irritable Bowel Disorder (IBD)

Viruses

1. Coxsackievirus
2. Echovirus
3. Norovirus
4. EBV
5. CMV
6. Varicella Zoster Virus

Bacteria

1. Campylobacter jejuni
2. Salmonella
3. Yersinia enterocolitica
4. Shigella
5. Listeria

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SS

Sjögren's Syndrome

Viruses

1. EBV
2. CMV
3. SARS-CoV-2
4. Hepatitis C also mentioned

Bacteria

1. Staphylococcus aureus/saccharolyticus
2. Chlamydia pneumoniae
3. Chlamydia trachomatis
4. Chlamydia psittaci
5. Mycoplasma hominis
6. Ureaplasma urealyticum
7. H pylori

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Myasthenia gravis

1. EBV
2. CMV
3. SARS-CoV-2
4. VZV

Selection MG Viruses

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Guillain-Barré Syndrome

1. Campylobacter jejuni
2. Mycoplasma pneumoniae
3. H pylori

References Guillain-Barré Syndrome and bacteria

GBS

Bacteria

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PANS/PANDAS

PANDAS – Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcus
PANS – Pediatric Acute-onset/Autoimmune Neuropsychiatric Syndrome

1. Streptococcus
2. Borrelia
3. Mycoplasma pneumoniae
4. Coxsackie Virus
5. Babesia
6. Bartonella
7. EBV
8. HSV1
9. VZV

Vast number of microbes associated with neuropsychiatric conditions (1/2)

Box 1. Some microbes associated with mental symptoms & mental illness.

Spirochetes

- *Borrelia afzelii* (Lyme disease in the UK and the rest of Europe)
- *Borrelia burgdorferi sensu stricto* (Lyme disease in the USA, UK and rest of Europe)
- *Borrelia garinii* (Lyme disease in the UK and rest of Europe)
- *Borrelia hermsii* (relapsing fever)
- *Borrelia turicatae* (relapsing fever)
- *Leptospira* (Leptospirosis)
- *Treponema pallidum pallidum* (syphilis)

Bacteria

- *Anaplasmas phagocytophilum* (human granulocytic ehrlichiosis)
- *Bartonella henselae* (cat scratch fever)
- *Bartonella quintana* (trench fever)
- *Bartonella rochalimae* (bartonellosis)
- *Chlamydophilia pneumoniae* (chlamydia)
- *Chlamydophila psittaci* (chlamydia)
- *Coxiella burnetti* (Q-fever and post-Q fever fatigue syndrome)
- *Ehrlichia chaffeensis* (human monocytic ehrlichiosis)
- *Francisella tularensis* (rabit fever or tularemia)
- *Haemophilus influenzae* (haemophilus)
- *Listeria*
- *Meningococcus* (meningococcal meningitis)
- *Mycoplasma fermentans*
- *Mycoplasma pneumoniae*
- *Mycobacterium tuberculosis* (tuberculosis)
- *Rickettsia akari* (rickettsialpox)
- *Rickettsia rickettsii* (rocky mountain spotted fever)
- *Rickettsia* species (eastern tick-borne rickettsiosis)
- *Shigella* (shigellosis)
- *Streptococcus pneumoniae* or pneumococcus (pneumonia)
- *Streptococcus* (pediatric autoimmune diseases associated with *Streptococcus*, Sydenham's chorea and St Vitus dance)

Yeast

- *Candida albicans* (candidiasis)
- *Candida dubliniensis*

Source: Bransfield RC. Preventable cases of autism: relationship between chronic infectious diseases and neurological outcome. Ped Health. 2009;3:125–40.

Vast number of microbes associated with neuropsychiatric conditions (2/2)

Box 1. Some microbes associated with mental symptoms & mental illness (cont.).

Prion

- Variant Creutzfeldt–Jakob

Viruses

- Borna virus
- *Coltivirus* (Colorado tick fever)
- *Coxsackievirus*
- *Cytomegalovirus*
- *Enterovirus*
- *Flaviviridae* virus (Japanese B encephalitis)
- Hepatitis C virus
- Herpes virus family
- Human endogenous retroviruses
- *Human herpesvirus 4* or Epstein–Barr virus
- HIV
- Influenza A virus subtype H3N2 (Hong Kong flu)
- Influenza virus
- Pandemic influenza of 1918
- *Papopavirus*
- *Paramyxovirus* (measles virus)
- *Parvo B19*
- *Poliovirus*
- Rabies virus
- Rubella
- Toga virus
- Varicella zoster virus (chicken pox)
- Viral meningitis
- West Nile virus

Protozoa

- *Plasmodium* (malaria)
- *Babesia microti* (babesiosis)
- *Babesia duncani* (babesiosis)
- Other *Babesia* species (babesiosis)
- *Toxoplasma gondii* (toxoplasmosis)

Parasites

- *Blastocystis* (blastocystosis)
- *Taenia solium* (neurocysticercosis or cysticercosis)

Fungal

- *Cryptocococcus*
- Coccidiomycosis
- Histomycosis

Source: Bransfield RC. Preventable cases of autism: relationship between chronic infectious diseases and neurological outcome. Ped Health. 2009;3:125–40.

Selection PANS

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Lab testing for ALS: Evidence-based suggestions

Viruses

1. Coxsackie
2. Echovirus
3. SARS-CoV-2
4. HIV

Bacteria

1. Borrelia
2. Babesia
3. Mycoplasma pneumoniae

References: Bacteria and ALS/Motor Neurone Disease

Selection ALS Bacteria

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References: ALS/Motor Neurone Disease

Selection | ALS | Viruses

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Antiphospholipid Syndrome

Infections that may be involved

1. CMV
2. EBV
3. Mycoplasma pneumoniae
4. HIV
5. Hepatitis B and C
6. Parvovirus B19
7. H pylori
8. SARS-CoV-2

APS

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Small selection

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