
Invisible Pain
Realities
Within
The World OF
Autoimmune
Diseases
KAREN DAVIS, RDH, BSDH

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How Could You
Be Their Hero?

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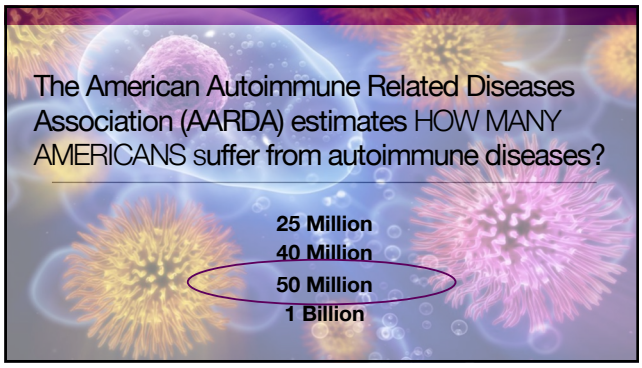
The American Autoimmune Related Diseases Association (AARDA) estimates HOW MANY AMERICANS suffer from autoimmune diseases?
25 Million
40 Million
50 Million
1 Billion

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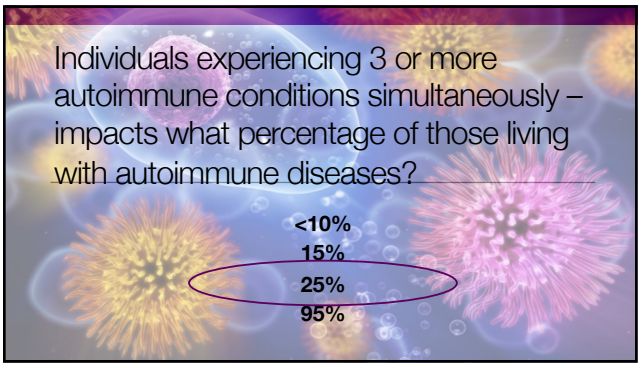
Individuals experiencing 3 or more autoimmune conditions simultaneously – impacts what percentage of those living with autoimmune diseases?
<10%
15%
25%
95%

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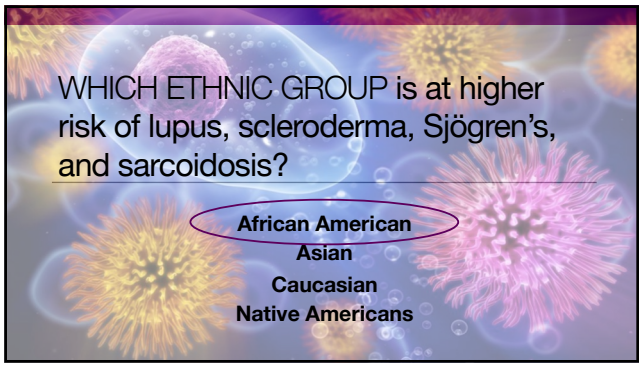
WHICH ETHNIC GROUP is at higher risk of lupus, scleroderma, Sjögren's, and sarcoidosis?
African American
Asian
Caucasian
Native Americans

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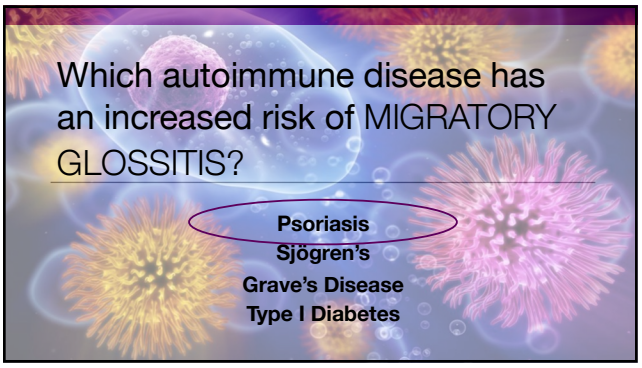
Which autoimmune disease has an increased risk of MIGRATORY GLOSSITIS?
Psoriasis
Sjögren's
Grave's Disease
Type I Diabetes

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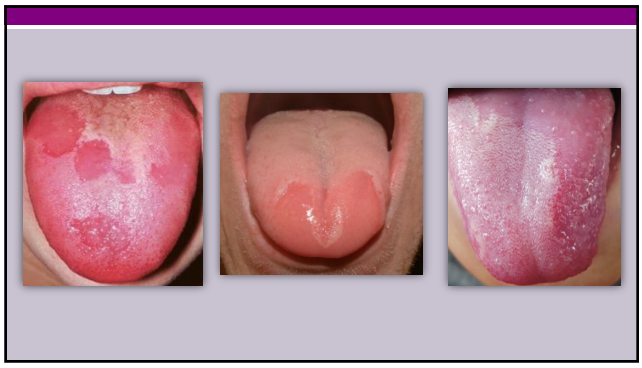

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Which autoimmune disease commonly affects the gingiva with conditions such as DESQUAMATIVE GINGIVITIS, BURNING, AND BLEEDING?

Ulcerative Colitis
Mucous Membrane Pemphigoid
Lupus
Scleroderma

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MULTIPLE ORAL ULCERATIONS are often the earliest presentation for which autoimmune disease?

Behcet's Disease
Psoriasis
Scleroderma
Lupus

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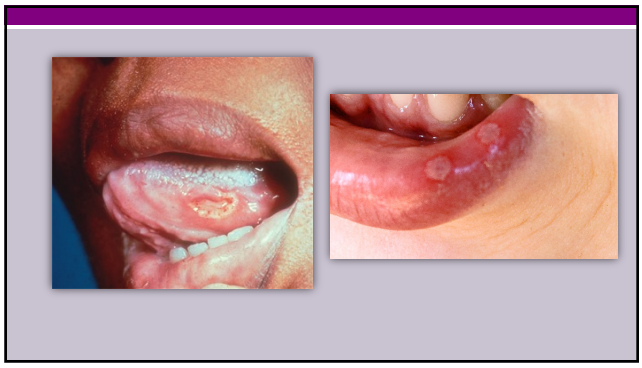

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Women are affected by autoimmune diseases by WHAT GREATER PERCENTAGE than men?

40%
50%
60%
75%

15

Women are at greatest risk of acquiring autoimmune diseases IN WHAT PERIOD OF THEIR LIVES?

**Childhood**
**Childbearing years**
**Post-menopausal**
**Pre-puberty**

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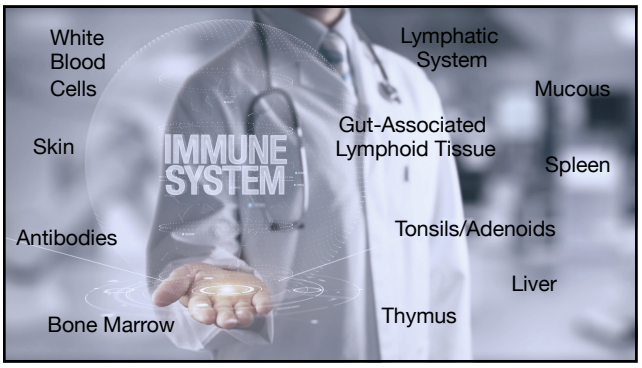


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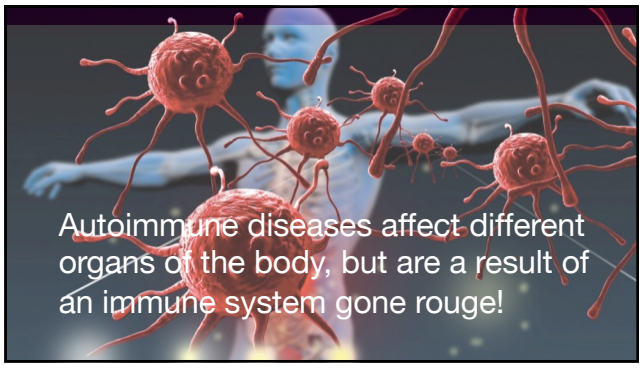


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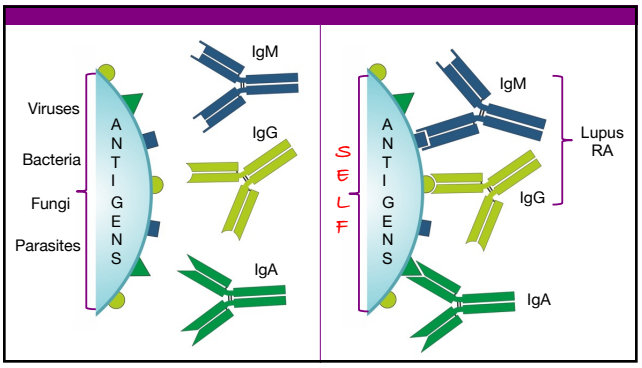


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Autoimmune Diseases
Verus
Autoinflammatory Diseases

El-Shebiny, E.M., Zahran, E.S., Shoeib, S.A. *et al.* Bridging autoinflammatory and autoimmune diseases. *Egypt J Intern Med* **33**, 11 (2021). https://doi.org/10.1186/s43162-021-00040-5

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**Table 1 Summary of monogenic autoinflammatory diseases [7]**

From: Bridging autoinflammatory and autoimmune diseases

| Monogenic auto inflammatory diseases | Mode of inheritance/gene (protein) | Main clinical features | Treatment |
|---|---|---|---|
| **Familial Mediterranean fever** | Recessive MEFV (Pyrin) | Recurrent fever (12–72 h, arthritis, and serositis (abdominal pain and thoracic pain) | Colchicine (IL-1 blockade in refractory cases or colchicine side-effects) |
| **TNF receptor-associated periodic syndrome** | Dominant TNFRSF1A (TNFR1) | Recurrent fever (1–3) weeks arthromyalgia, fasciitis, rash, conjunctivitis periorbital edema, and splenomegaly | IL-1 blockade Corticosteroids/Etanercept/NSAID/Colchicine |
| **Hyperimmunoglobulinemia with periodic fever syndrome** | Recessive (Mevalonate Kinase gene) | Recurrent fever(3–7) days, abdominal pain, diarrhea, hepato-splenomegaly, and lymphadenopathy | IL-1 blockade/NSAID Corticosteroids/TNF blockade |
| **Familial cold auto inflammatory syndrome** | Dominant NLRP3 (Cryopyrin) | Recurrent fever (12 h–2 days), and cold-induced urticaria-like rash, conjunctivitis, and arthralgia | IL-1 blockade |
| **Muckle–Wells syndrome** | Dominant NLRP3 | Recurrent fever (2–3) days if present, urticaria rash, and sensori-neuronal deafness | IL-1 blockade |
| **Neonatal onset multi systemic inflammatory disorder** | Dominant NLRP3 | Subcontinuous fever, rash, neurologic symptoms, and skeletal abnormalities | IL-1 blockade |
| **Pyogenic arthritis pyoderma gangrenosum and acne syndrome** | Dominant (PSTPIP1) | Pyoderma gangrenosum, cystic acne, and sterile pyogenic oligoarthritis | Corticosteroids, anakinra, Infliximab, immunosuppressive agent |
| **Deficit of IL-1 receptor antagonist** | Recessive IL1RN (IL1 receptor antagonist) | Neonatal onset-multifocal osteomyelitis, periostitis, neonatal onset-pustular rash | Anakinra |
| **Majeed's syndrome** | Recessive LPIN2 (LPIN2) | Recurrent multifocal osteomyelitis, dyserythropoietic anemia, and chronic dermatosis | Corticosteroids, Bisphosphonates TNF–inhibitor IL-1 antagonist (anakinra) |

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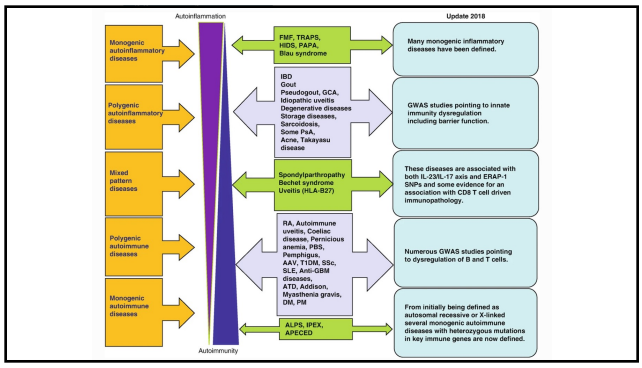


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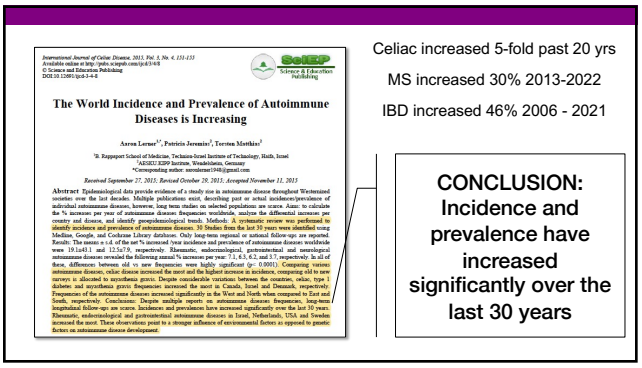


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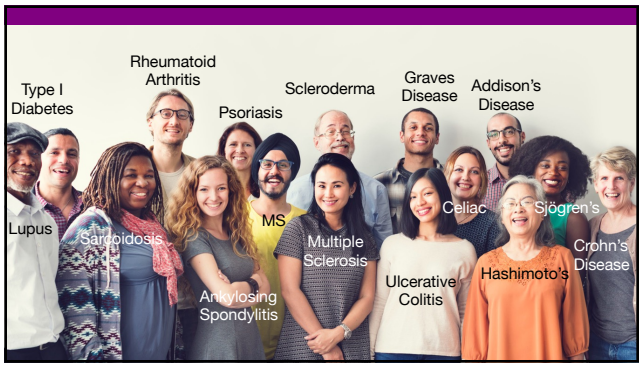


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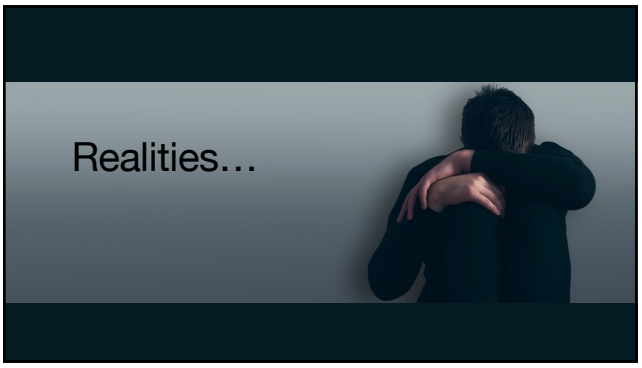


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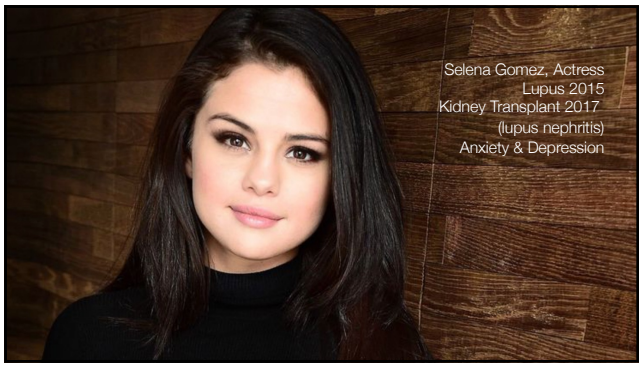


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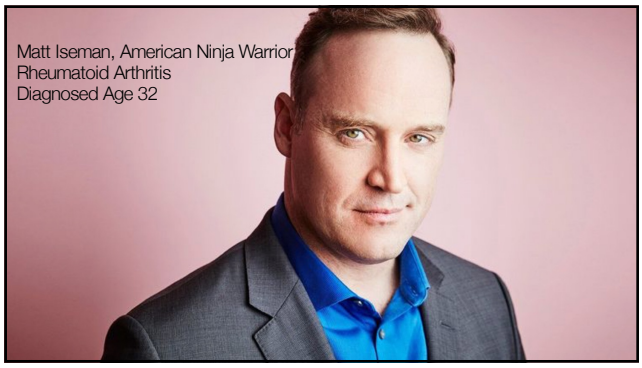


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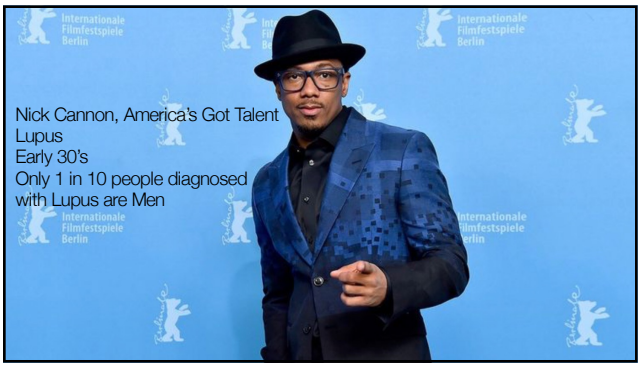


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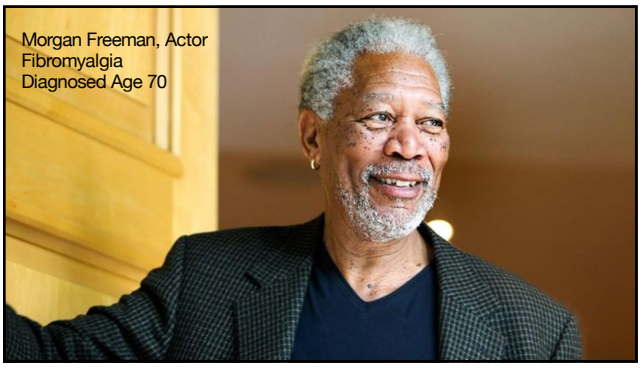


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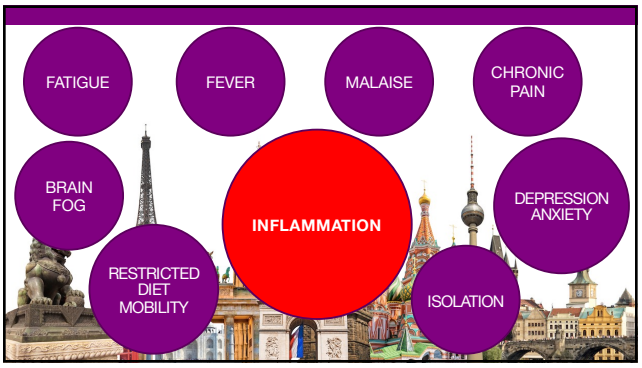


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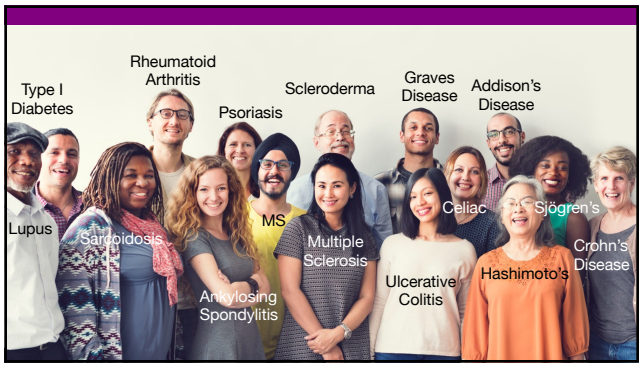


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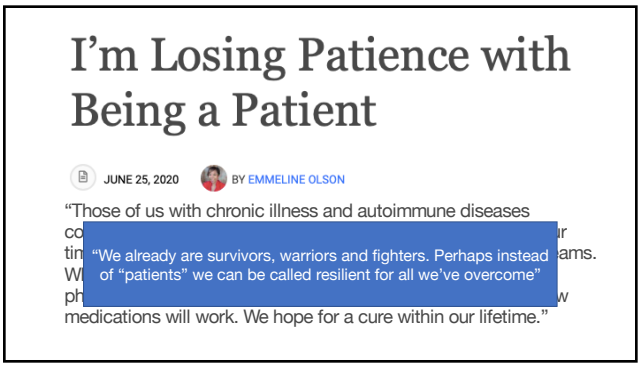

I'm Losing Patience with Being a Patient

JUNE 25, 2020 BY EMMELINE OLSON

"Those of us with chronic illness and autoimmune diseases co ur ti ams. W ph w medications will work. We hope for a cure within our lifetime."

"We already are survivors, warriors and fighters. Perhaps instead of "patients" we can be called resilient for all we've overcome"

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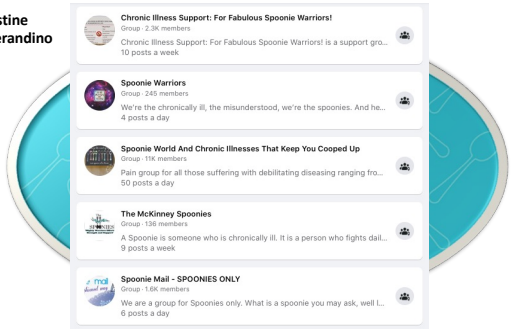
Christine Miserandino

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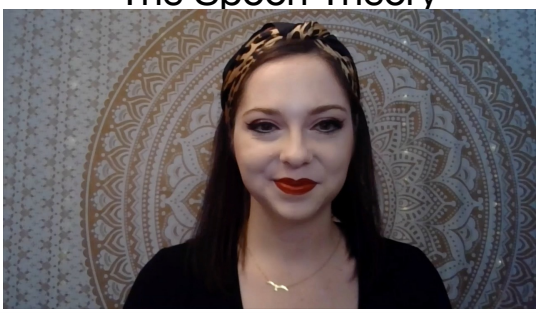
## The Spoon Theory



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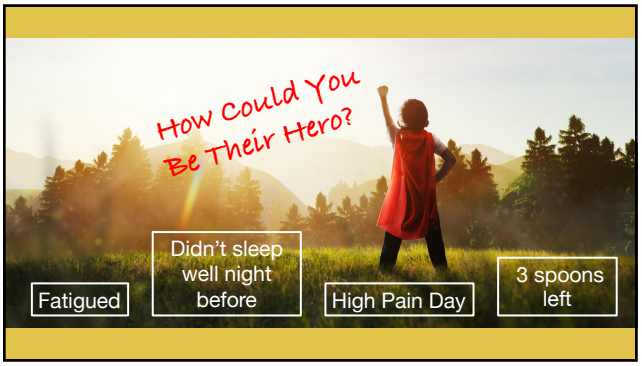


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## Medical Histories – ASK THE RIGHT QUESTIONS

- Do you have an autoimmune disease?
  Please list your diagnosis and date of diagnosis
  - Do you have specific dietary restrictions? If so, what?
  - Are you currently taking Immunosuppressants?
  - Do you often experience increased susceptibility to infections?
  - Do you suffer from chronic fatigue?
  - Do you suffer from chronic pain?
    - Do you use CBD or THC for pain management?
    - Do you use opioids for pain management?

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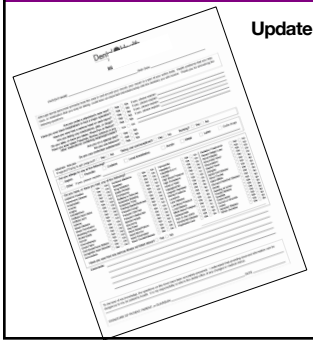

## Update Medical History Prior to Appointment

Stelara
Amitiza
Gabapentin
Wellbutrin
Lo-loestrin
Nexium
Nortriptyline
Dicyclomine
Tylenol
Skelaxin
Zofran
Nitrofurantion Mono-MCR
Clotrimazole

B-12
L-Lysine
Inositol
Turmeric
Grapefruit Seed Extract
Soccharomyces boulardii
Florastor
ProbioraPro

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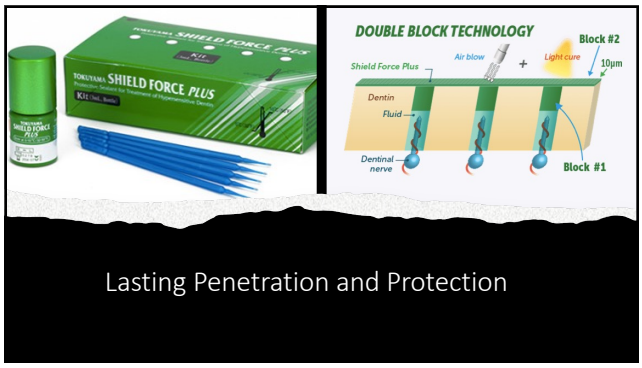


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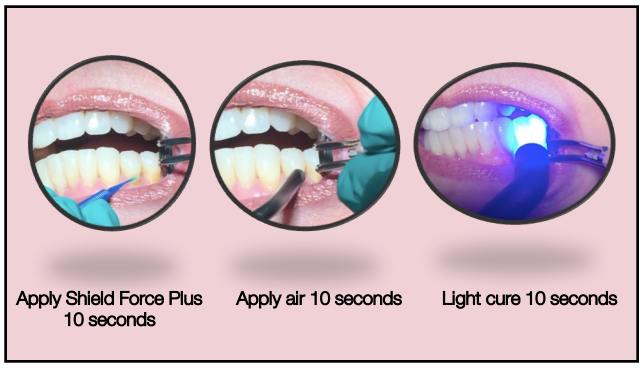


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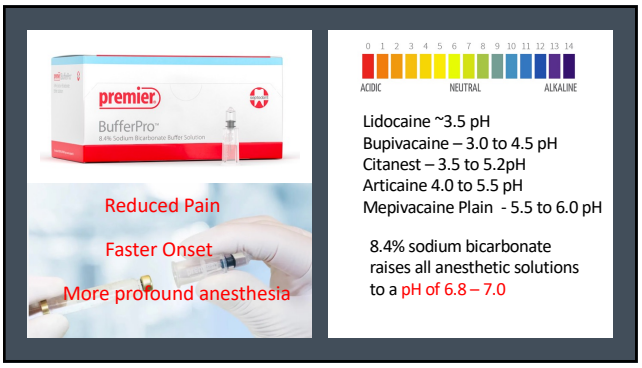


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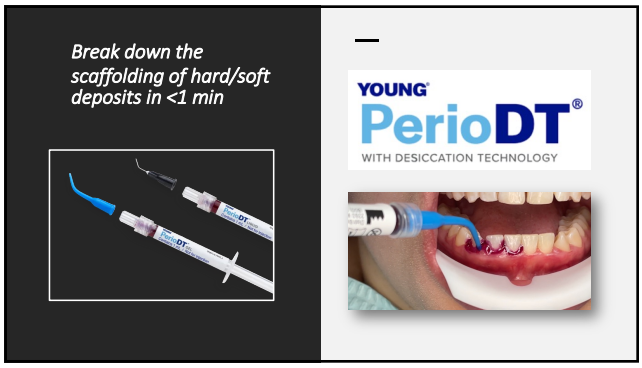


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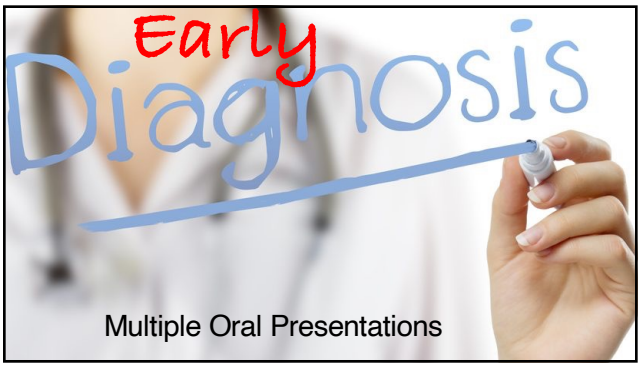


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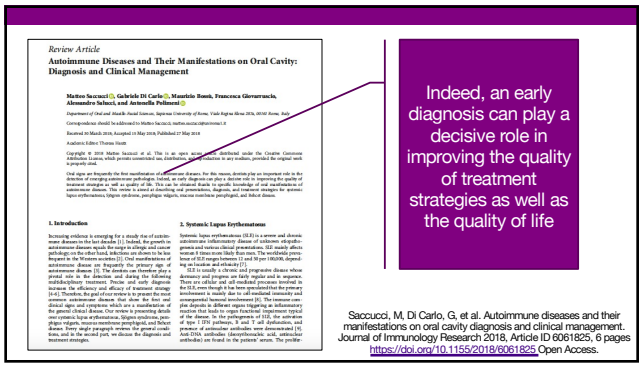


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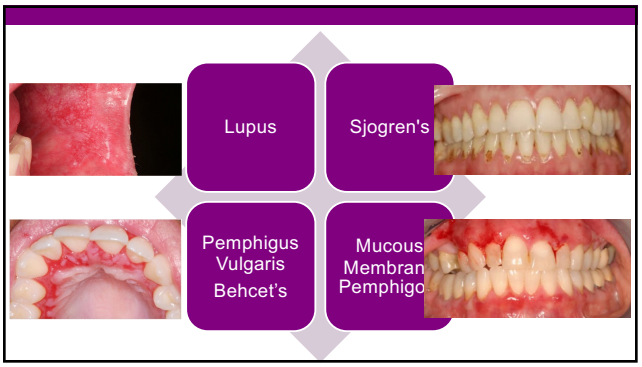


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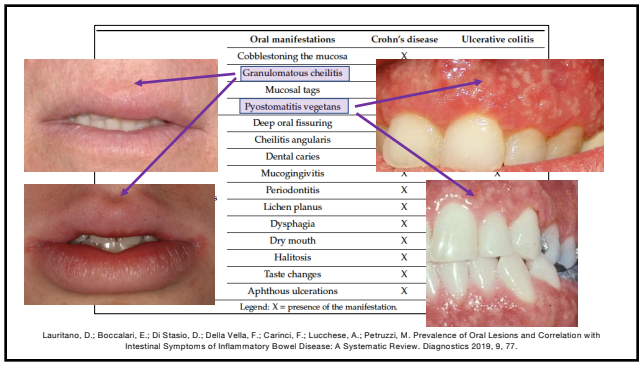


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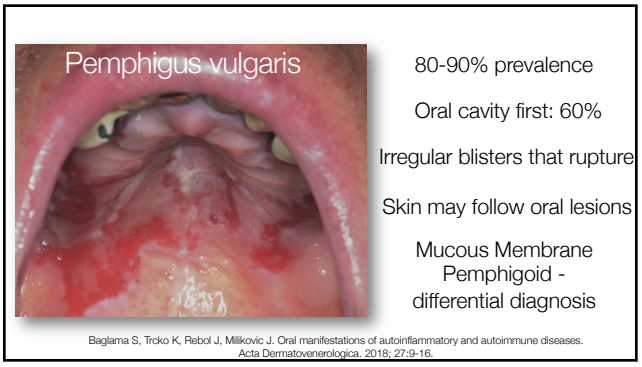


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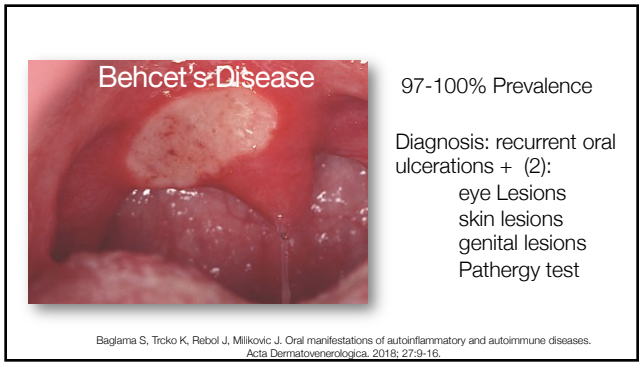


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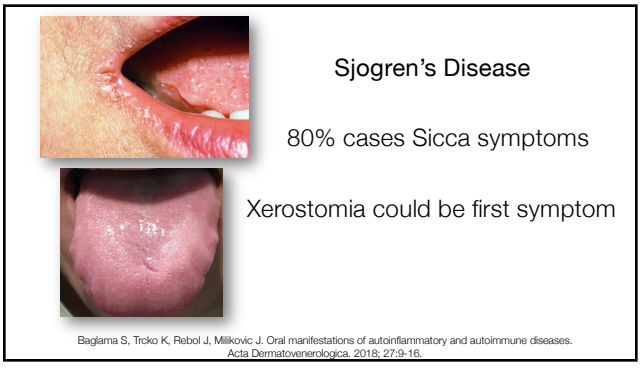


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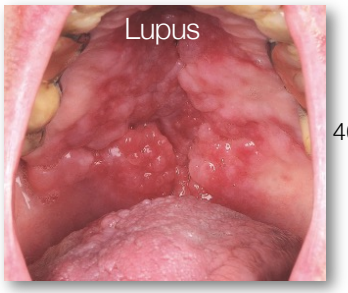


45% oral prevalence

40% erosive painful lesions

Secondary viral, bacterial & fungal infections

Baglama S, Trcko K, Rebol J, Milikovic J. Oral manifestations of autoinflammatory and autoimmune diseases. Acta Dermatovenerologica. 2018; 27:9-16.

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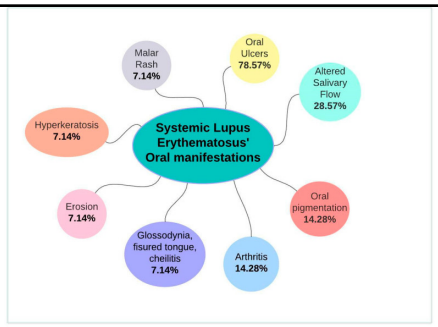
2022 Systematic Review
180 studies
15 accepted




García-Ríos P, Pecci-Lloret MP, Oñate-Sánchez RE. Oral Manifestations of Systemic Lupus Erythematosus: A Systematic Review. Int J Environ Res Public Health. 2022 Sep 21;19(19):11910. doi: 10.3390/ijerph191911910. PMID: 36231212; PMCID: PMC9565705.

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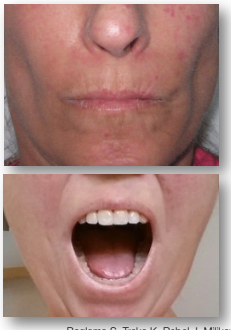

Scleroderma

80% prevalence

Localized or Systemic

Xerostomia common

Baglama S, Trcko K, Rebol J, Milikovic J. Oral manifestations of autoinflammatory and autoimmune diseases. Acta Dermatovenerologica. 2018; 27:9-16.

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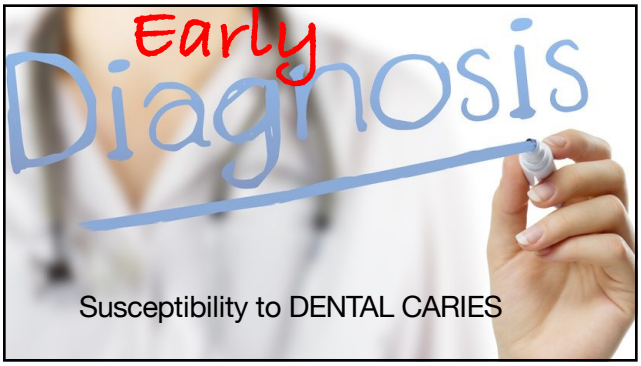


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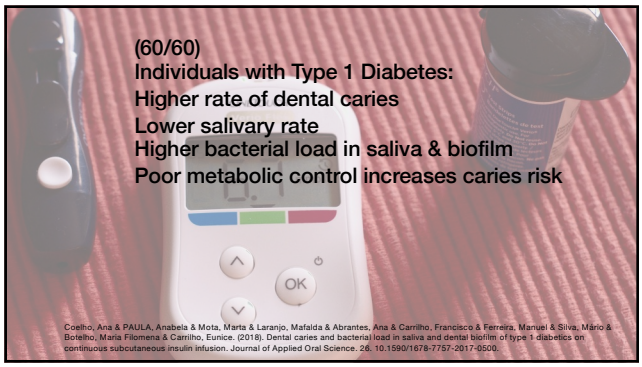


Coelho, Ana & PAULA, Anabela & Mota, Marta & Laranjo, Mafalda & Abrantes, Ana & Carrilho, Francisco & Ferreira, Manuel & Silva, Mário & Botelho, Maria Filomena & Carrilho, Eunice. (2018). Dental caries and bacterial load in saliva and dental biofilm of type 1 diabetics on continuous subcutaneous insulin infusion. Journal of Applied Oral Science. 26. 10.1590/1678-7757-2017-0500.

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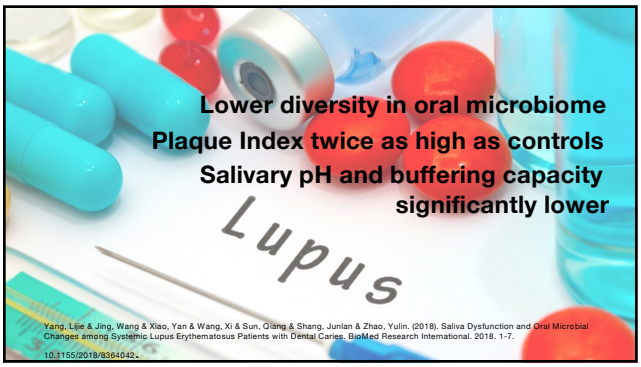


Yang, Lijie & Jing, Wang & Xiao, Yan & Wang, Xi & Sun, Qiang & Shang, Junlan & Zhao, Yulin. (2018). Saliva Dysfunction and Oral Microbial Changes among Systemic Lupus Erythematosus Patients with Dental Caries. BioMed Research International. 2018. 1-7. 10.1155/2018/8364042.

70

(53/53)
78% of patients with Sjogren's Syndrome brushed twice daily

**Arthritis, nephritis, pneumonitis & vasculitis**

Patients with SS had **higher decay rates and required more invasive treatment**

Lisa Bøge Christensen, Poul Erik Petersen, Jens Jørgen Thorn & Morten Schiødt (2001) Dental caries and dental health behavior of patients with primary Sjo¨gren syndrome, Acta Odontologica Scandinavica, 59:3, 116-120, DOI: 10.1080/000163501750266684

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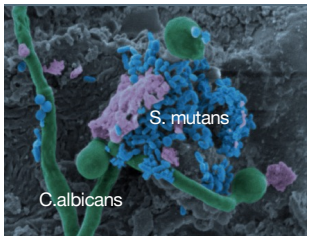
**Do Candida albicans & Strep mutans Co-infections Increase Caries Risk?**




Both produce & tolerate acids

Both thrive on high sugar diet

S. mutans provides C. albicans adhesion sites in the oral cavity

C. albicans lowers oxygen favoring environment for growth of S. mutans

Vila T, Sultan AS, Montelongo-Jauregui D, Jabra-Rizk MA. Oral candidiasis: a disease of opportunity. J. Fungi 2020, 6, 15; doi:10.3390/jof6010015. www.mdpi.com/journal/jof Accessed: August 18, 2020.

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"Collectively, these studies strongly indicate that the presence of Candida albicans in the oral environment could be considered a risk factor for the development of dental caries"

Vila T, Sultan AS, Montelongo-Jauregui D, Jabra-Rizk MA. Oral candidiasis: a disease of opportunity. J. Fungi 2020, 6, 15; doi:10.3390/jof6010015. www.mdpi.com/journal/jof Accessed: August 18, 2020.

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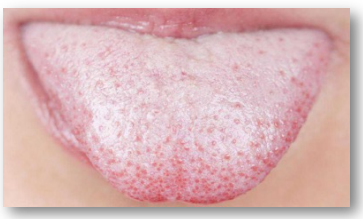

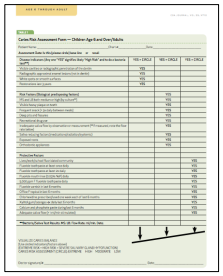

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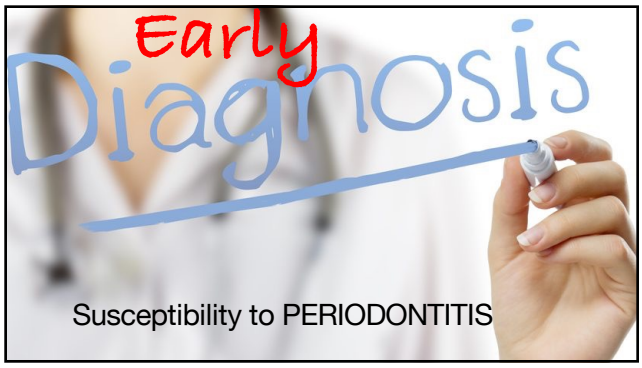


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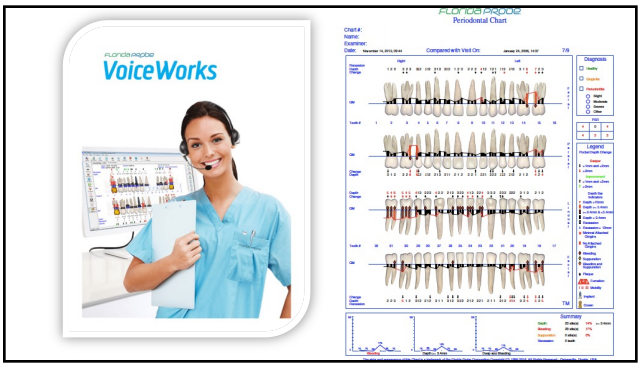


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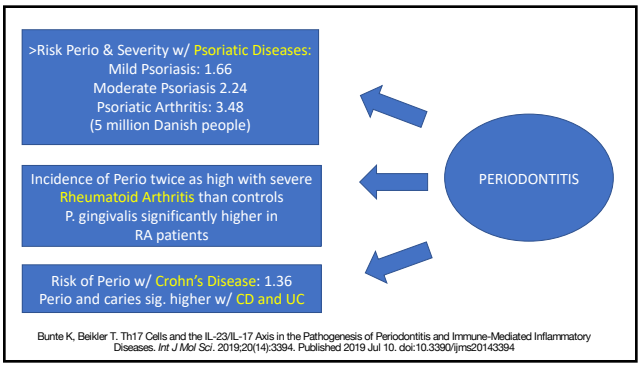


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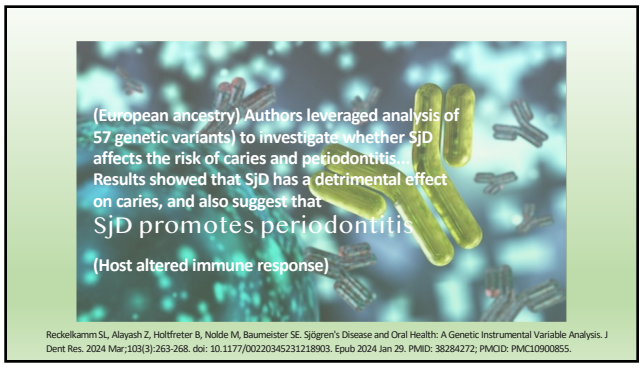


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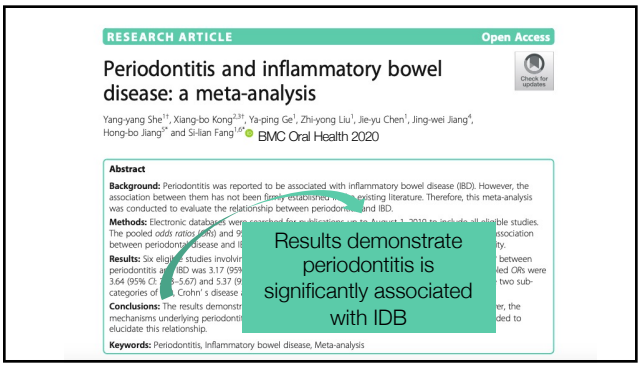


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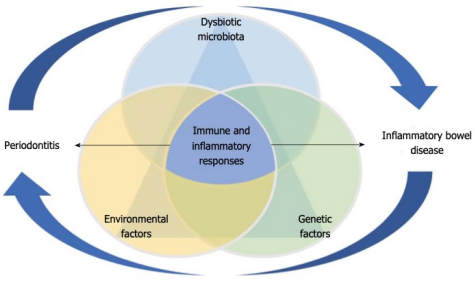


Lira-Junior R, Figueredo CM. Periodontal and inflammatory bowel diseases: Is there evidence of complex pathogenic interactions? World J Gastroenterol 2016 September 21; 22(35):7963-7972

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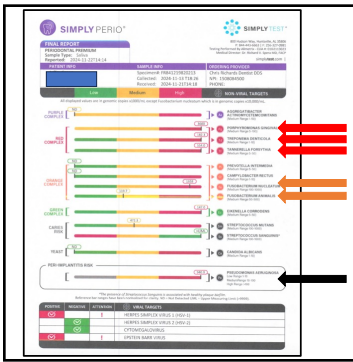

Oral/Gut Microbiota Influencing Outcomes?

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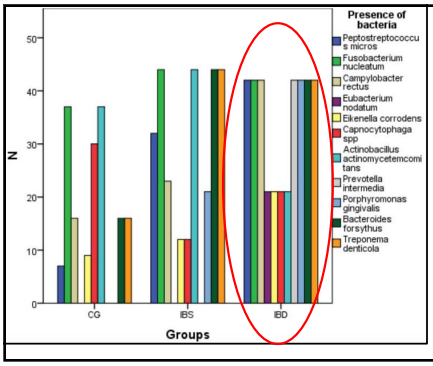


Rat LA, Moldovan AF, Trifan DF, Matiș L, Murvai GF, Maris L, Ghitea TC, Maghiar MA. **Can the Correlation of Periodontopathies with Gastrointestinal Diseases Be Used as Indicators in Severe Colorectal Diseases?** Biomedicines. 2023 Jan 29;11(2):402. doi: 10.3390/biomedicines11020402. PMID: 36830938; PMCID: PMC9953596.

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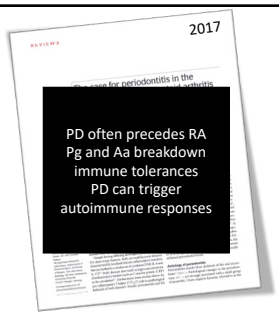


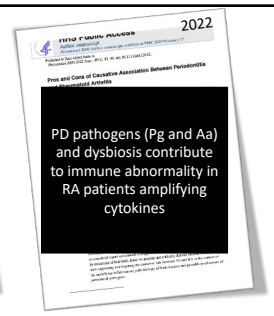


Koziel J, Potempa J. Pros and cons of causative association between periodontitis and rheumatoid arthritis. Periodontol 2000. 2022 Jun;89(1):83-98. doi: 10.1111/prd.12432. Epub 2022 Mar 9. PMID: 35262966; PMCID: PMC9935644

87

A compilation of data showing the pros and cons of causative relationship between periodontitis and rheumatoid arthritis;

| PROS | CONS |
|---|---|
| • PD patients are at greater risk for RA than healthy individuals [81]<br>• Inflammatory nature of both diseases; bidirectional exacerbation through inflammatory mediators without causative relationship [20,25-28]<br>• PD prevalence [illegible] degree relatives a[illegible]<br>• Significantly h[illegible] pathogens in RA [illegible] [31,82–85,87,88]<br>• Association of [illegible] with ACPA in RA [illegible]<br>• Increased preva[illegible] patients and indiv[illegible]<br>• PD treatment a[illegible] while RA treatme[illegible]<br>• Pre-existing pe[illegible]<br>• The inflamed p[illegible] potent stimulator [illegible] [118,130,135]<br>• Citrullinated *P. gingivalis* proteins and peptides reacts with ACPA [135,140,141]<br>• *P. gingivalis* and *P. nigrescens* promote arthritis progression via IL-17 signaling [87,9]<br>• Molecular mimicry of bacterial enolase, Hsp60 and RgpA; bacterial proteins are recognized by antibodies from RA patients [142,148,150] | • RA risk alleles within the HLA (particularly HLA-DRB1) predispose to PD[25]<br>• [illegible] proposed [illegible] een RA and [illegible] *ivalis* [illegible] s of PD [illegible] ecognized<br>• Pre-existing chronic inflammation induced by other than periopathogens factors exacerbates the development of adjuvant arthritis [86]<br>• The spontaneous alveolar bone loss in adjuvant arthritis model [76] |

Initiation and progression of RA likely influenced by unique roll of periopathogens & inflammatory response but not all data is conclusive

PD - periodontitis, RA - rheumatoid arthritis, PTMs - posttranslational modifications, PADs – peptidylarginine deiminases, PPAD - *P. gingivalis* PAD, *A.a* - *Aggregatibacter actinomycetemcomitans*

Koziel J, Potempa J. Pros and cons of causative association between periodontitis and rheumatoid arthritis. Periodontol 2000. 2022 Jun;89(1):83-98. doi: 10.1111/prd.12432. Epub 2022 Mar 9. PMID: 35262966; PMCID: PMC9935644

88


89

Review > Best Pract Res Clin Rheumatol. 2017 Feb;31(1):19-30.
doi: 10.1016/j.berh.2017.08.001. Epub 2017 Sep 1.

**Periodontal disease and periodontal bacteria as triggers for rheumatoid arthritis**

Zijian Cheng [1], Josephine Meade [1], Kulveer Mankia [2], Paul Emery [2], Deirdre A Devine [3]

Affiliations + expand
PMID: 29221594 DOI: 10.1016/j.berh.2017.08.001
Free article

**Abstract**

There is an epidemiological association between periodontitis and rheumatoid arthritis (RA), which is hypothesised to lead to enhanced generation of RA-related autoantibodies that can be detected years before the onset of RA symptoms. Periodontitis is a common dysbiotic disease; tissue damage occurs because the immune system fails to limit both the resident microbial community and the associated local immune response. Certain periodontal bacteria, including Porphyromonas gingivalis and Aggregatibacter actinomycetemcomitans, may contribute to RA autoantibody production through direct post-translational modification of proteins or, indirectly, by influencing neutrophil-mediated neo-epitope generation. Oral bacteria that invade the blood may also contribute to chronic inflammatory responses and generation of autoantibodies. The putative association between periodontitis and the development of RA raises the potential of finding novel predictive markers of disease and disease progression and for periodontitis treatment to be included in the future as an adjunct to conventional RA immunotherapy or as part of a preventive strategy.

RA patients have a significantly increased prevalence of periodontal disease

Future Research Agenda: To determine whether periodontal treatment should be considered as an adjunct to immunotherapy in patients with early RA.

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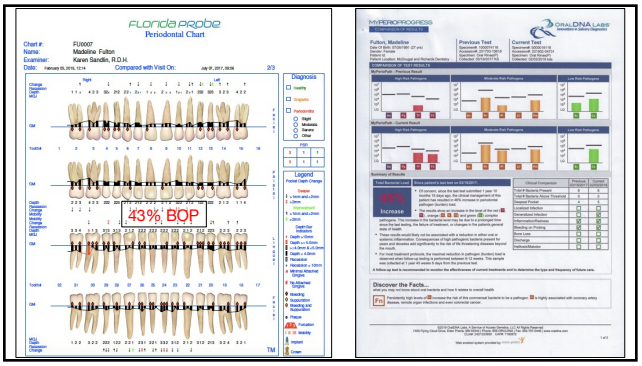


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Dental Caries
Periodontal Disease

Intervene Early

92


93

Become part of their care TEAM

94

Gastroenterologist
Rheumatologist
Physical Medicine Doctor
Gynecologist
Psychiatrist
Therapist
Physical Therapist
Chiropractor
Infectious Disease Doctor
Pain Management Doctor
Dietician
Dentist/Dental Hygienist


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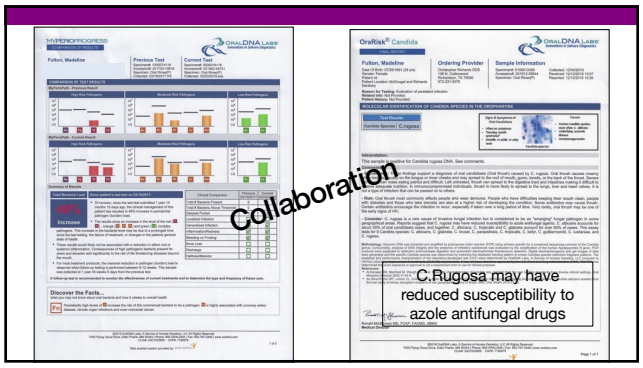


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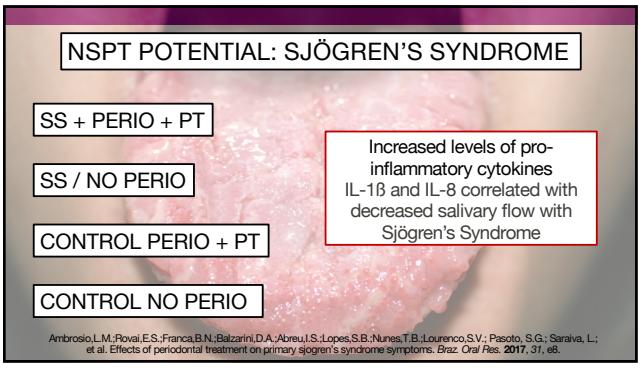


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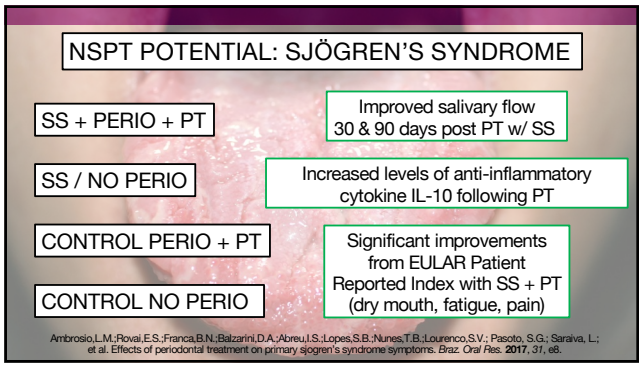


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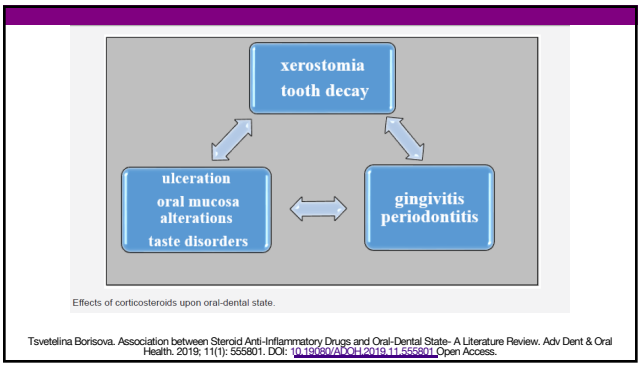


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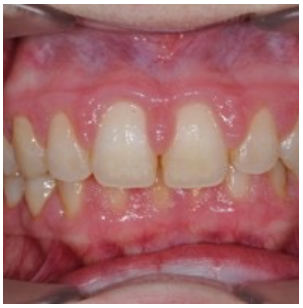
## Treatment challenges

Methotrexate
Hydroxychloroquine
Biologics

Glucocorticoids + Flavonoid-rich diets

Glucocorticoids alone

102



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## Biologics Target Specific Cytokines

TNF-a
Enbrel
Remicade
Humira

IL-12 & 23
Stelara

IL-6
Actemra

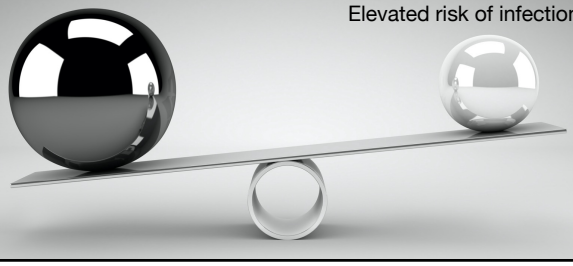
IL-17a
Taltz
Cosentyx

IL-1
Kineret

104

Dampens immune response

Elevated risk of infections



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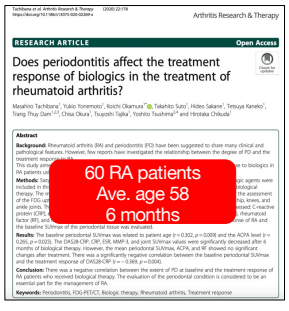

Tachibana et al. Arthritis Research & Therapy (2020) 22:178
https://doi.org/10.1186/s13075-020-02269-x

Arthritis Research & Therapy

RESEARCH ARTICLE Open Access

Does periodontitis affect the treatment response of biologics in the treatment of rheumatoid arthritis?

Masahiro Tachibana[1], Yukio Yonemoto[1], Koichi Okamura[2*], Takahito Suto[1], Hideo Sakane[1], Tetsuya Kaneko[1], Trang Thuy Dam[1,3], Chisa Okura[1], Tsuyoshi Tajika[1], Yoshito Tsushima[2,4] and Hirotaka Chikuda[1]

Abstract

Background: Rheumatoid arthritis (RA) and periodontitis (PD) have been suggested to share many clinical and pathological features. However, few reports have investigated the relationship between the degree of PD and the treatment response in RA.

This study aimed to investigate the relationship between the degree of PD and the response to biologics in RA patients [illegible]

Methods: Sixty RA patients [illegible] biologic agents were included in this study. [illegible] biological therapy. The evaluation of the periodontal condition was performed using the periodontal inflamed surface area/periodontal inflammation surface area (PISA/PISA) [illegible] hip, knees, and ankle joints. [illegible] C-reactive protein (CRP), [illegible] rheumatoid factor (RF), and [illegible] response of RA and the baseline SUVmax of the periodontal tissue was evaluated.

Results: The baseline periodontal SUVmax was related to patient age ($r = 0.322$, $p = 0.006$) and the ACPA level ($r = 0.265$, $p = 0.023$). The DAS28-CRP, CRP, ESR, MMP-3, and joint SUVmax values were significantly decreased after 6 months of biological therapy. However, the mean periodontal SUVmax, ACPA, and RF showed no significant changes after treatment. There was a significantly negative correlation between the baseline periodontal SUVmax and the treatment response of DAS28-CRP ($r = -0.369$, $p = 0.004$).

Conclusion: There was a negative correlation between the extent of PD at baseline and the treatment response of RA patients who received biological therapy. The evaluation of the periodontal condition is considered to be an essential part for the management of RA.

Keywords: Periodontitis, FDG-PET/CT, Biologic therapy, Rheumatoid arthritis, Treatment response

60 RA patients
Ave. age 58
6 months

There was a negative correlation between the extent of PD at baseline and the treatment response of RA patients who received biological therapy.

The evaluation of the periodontal condition is considered to be an essential part for the management of RA.

Tachibana, M., Yonemoto, Y., Okamura, K. *et al.* Does periodontitis affect the treatment response of biologics in the treatment of rheumatoid arthritis?. *Arthritis Res Ther 22*, 178 (2020). https://doi.org/10.1186/s13075-020-02269-x

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## NSPT POTENTIAL

NSPT in lupus/periodontitis subjects was reported to significantly improve the responsiveness to immunosuppressive therapy compared to the control group

Fabbri,C.;Fuller,R.;Bonfa,E.;Guedes,L.K.;D'Alleva,P.S.;Borba,E.F.Periodontitis treatment improves systemic lupus erythematosus response to immunosuppressive therapy. *Clin. Rheumatol.* 2014, *33*, 505–509.

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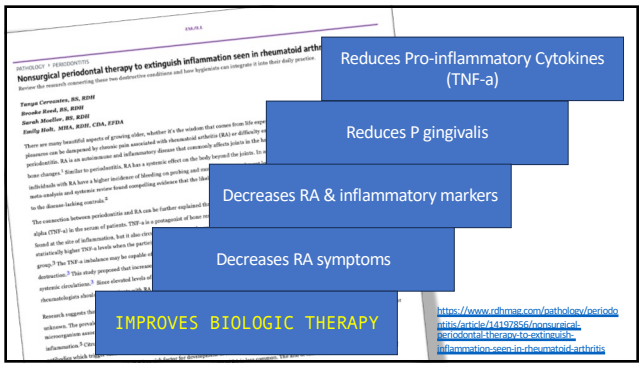


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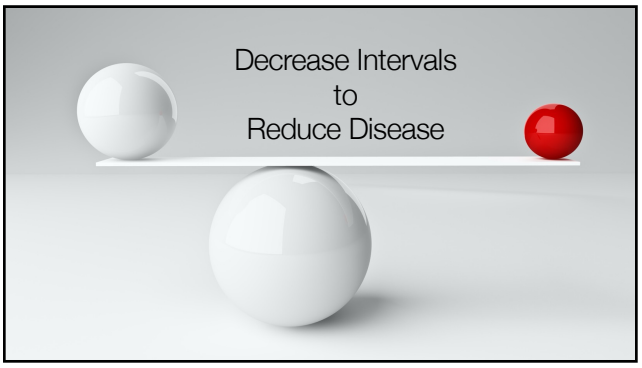


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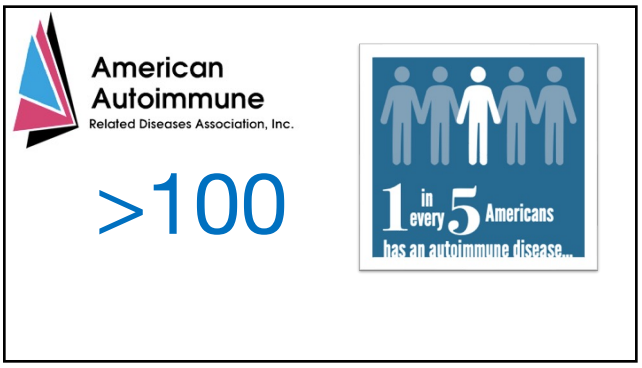


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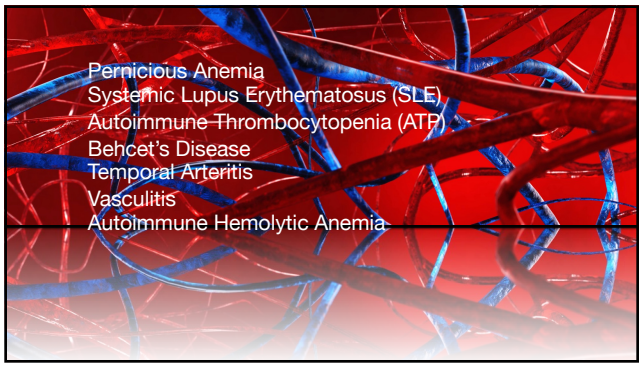


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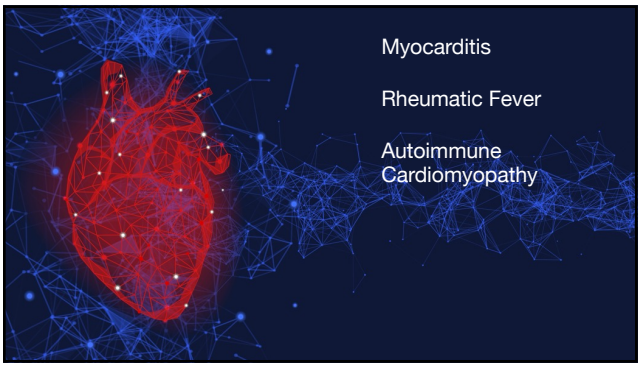


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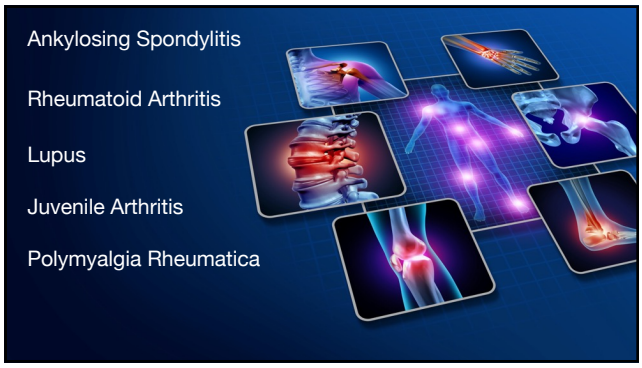


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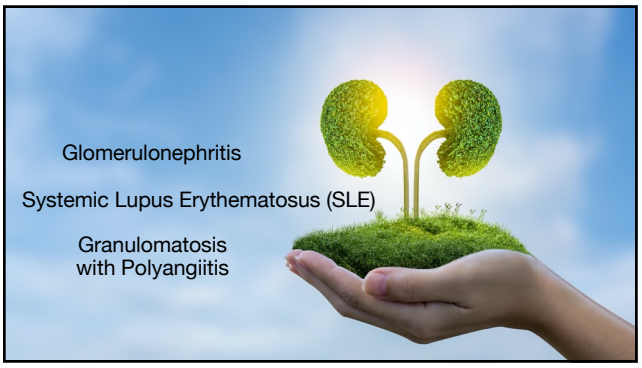


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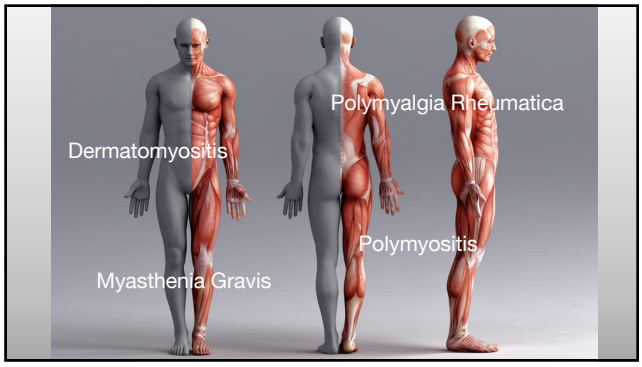


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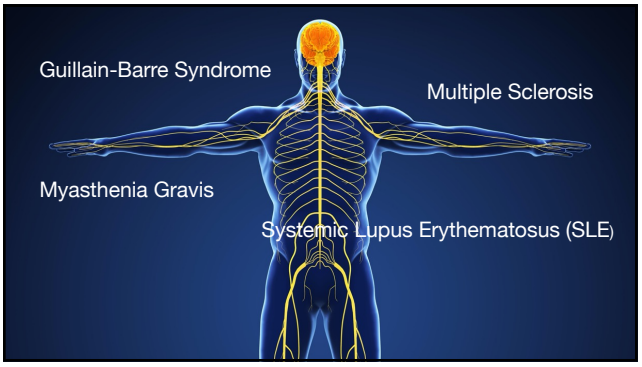


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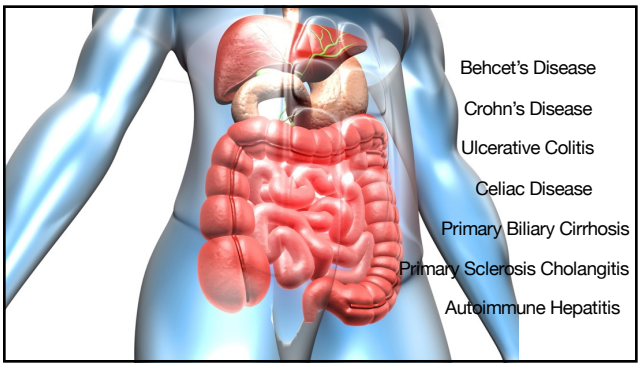


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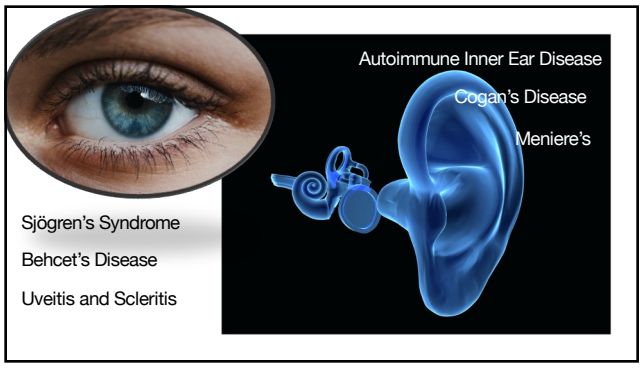


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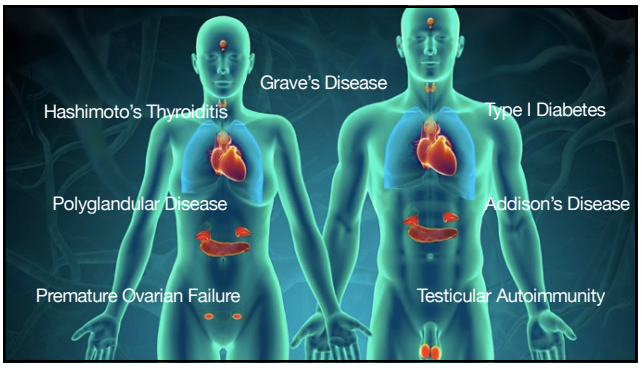


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## Age of Onset of Autoimmune Diseases

Type I Diabetes, Celiac Disease, Vitiligo
CHILDREN

Multiple Sclerosis, Myasthenia Gravis, Vitiligo, Lupus
YOUNG ADULTS

Scleroderma, Sjögren's Syndrome, Rheumatoid Arthritis
MIDDLE AGED ADULTS

Sjögren's Syndrome, Autoimmune Thyroid Disease , Myasthenia Gravis
ELDERLY ADULTS

Castiblanco J, Arcos-Burgos M, Anaya JM. Introduction to Genetics of Autoimmune Diseases. In: Anaya JM, Shoenfeld Y, Rojas-Villarraga A, et al., editors. Autoimmunity: From Bench to Bedside [Internet]. Bogota (Colombia): El Rosario University Press; 2013 Jul 18. Chapter 16. Available from: https://www.ncbi.nlm.nih.gov/books/NBK459433/

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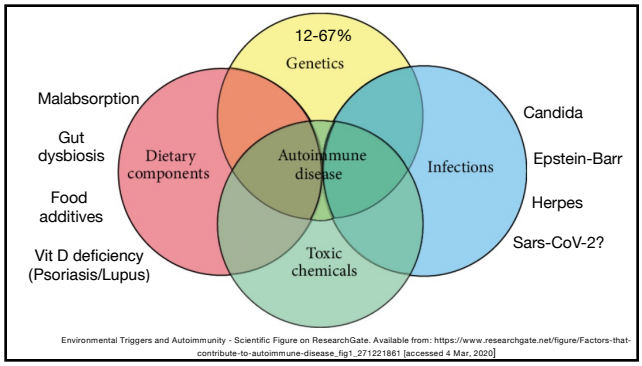


Environmental Triggers and Autoimmunity - Scientific Figure on ResearchGate. Available from: https://www.researchgate.net/figure/Factors-that-contribute-to-autoimmune-disease_fig1_271221861 [accessed 4 Mar, 2020]

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## Risk of autoimmune diseases in patients with COVID-19: a retrospective cohort study

Renin Chang,[a,b,c,m] Thomas Yen-Ting Chen,[d,e] Shiow-Ing Wang,[c,f,m] Yao-Min Hung,[g,h,i,*] Hui-Yuan Chen,[c] and Cheng-Chung James Wei[c,j,k,l,**]

**Summary**

**Background** There are a growing number of case reports of various autoimmune diseases occurring after COVID-19, yet there is no large-scale population-based evidence to support this potential association. This study provides a closer insight into the association between COVID-19 and autoimmune diseases and reveals discrepancies across sex, age, and race of participants.

**Methods** This is a retrospective cohort study based on the TriNetX U.S. Collaborative Network. In the test-negative design, cases were participants with positive polymerase chain reaction (PCR) test results for SARS-CoV-2, while controls were participants who tested negative and were not diagnosed with COVID-19 throughout the follow-up period. Patients with COVID-19 and controls were propensity score-matched (1: 1) for age, sex, race, adverse socioeconomic status, lifestyle-related variables, and comorbidities. The primary endpoint is the incidence of newly recorded autoimmune diseases. Adjusted hazard ratios (aHRs) and 95% confident intervals (CIs) of autoimmune diseases were calculated between propensity score-matched groups with the use of Cox proportional-hazards regression models.

**Findings** Between January 1st, 2020 and December 31st, 2021, 3,814,479 participants were included in the study (888,463 cases and 2,926,016 controls). After matching, the COVID-19 cohort exhibited significantly higher risks of rheumatoid arthritis (aHR:2.98, 95% CI:2.78–3.20), ankylosing spondylitis (aHR:3.21, 95% CI:2.50–4.13), systemic lupus erythematosus (aHR:2.99, 95% CI:2.68–3.34), dermatopolymyositis (aHR:1.96, 95% CI:1.47–2.61), systemic sclerosis (aHR:2.58, 95% CI:2.02–3.28), Sjögren's syndrome (aHR:2.62, 95% CI:2.29–3.00), mixed connective tissue disease (aHR:3.14, 95% CI:2.26–4.36), Behçet's disease (aHR:2.32, 95% CI:1.38–3.89), polymyalgia rheumatica (aHR:2.90, 95% CI:2.36–3.57), vasculitis (aHR:1.96, 95% CI:1.74–2.20), psoriasis (aHR:2.91, 95% CI:2.67–3.17), inflammatory bowel disease (aHR:1.78, 95%CI:1.72–1.84), celiac disease (aHR:2.68, 95% CI:2.51–2.85), type 1 diabetes mellitus (aHR:2.68, 95%CI:2.51–2.85) and mortality (aHR:1.20, 95% CI:1.16–1.24).

**Interpretation** COVID-19 is associated with a different degree of risk for various autoimmune diseases. Given the large sample size and relatively modest effects these findings should be replicated in an independent dataset. Further research is needed to better understand the underlying mechanisms.

1-1-2020 to 12-31-21
888,643 cases with AD
2,926,016 controls

At 6-mo follow-up risk of various AD substantially higher in COVID-19 individuals than controls

Chang, R., Chen, T. Y. T., Wang, S. I., Hung, Y. M., Chen, H. Y., & Wei, C. C. J. (2023). Risk of autoimmune diseases in patients with COVID-19: A retrospective cohort study. EClinicalMedicine, 56.

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**Table S1.** Risk of autoimmune diseases among COVID-19 patients compared to control subjects

| Outcomes | Autoimmune diseases | | Hazard ratio (95%CI) | |
|---|---|---|---|---|
| | COVID-19 | Control | Crude | Adjusted[a] |
| **Inflammatory arthritis** | | | | |
| Rheumatoid arthritis | 2878 | 1044 | **3.01 (2.87-3.16)*** | **2.98 (2.78-3.20)*** |
| Ankylosing spondylitis | 243 | 82 | **3.01 (2.54-3.57)** | **3.21 (2.50-4.13)** |
| **Connective tissue disease** | | | | |
| Systemic lupus erythematosus | 1189 | 429 | **3.26 (3.02-3.53)** | **2.99 (2.68-3.34)** |
| Dermatopolymyositis | 131 | 72 | **2.12 (1.71-2.63)** | **1.96 (1.47-2.61)** |
| Systemic sclerosis | 222 | 93 | **2.74 (2.31-3.26)** | **2.58 (2.02-3.28)** |
| Sjogren's syndrome | 727 | 301 | **2.91 (2.64-3.21)** | **2.62 (2.29-3.00)** |
| Mixed connective tissue disease | 139 | 48 | **3.35 (2.66-4.23)** | **3.14 (2.26-4.36)** |
| Behçet's disease | 45 | 21 | **2.92 (1.97-4.34)** | **2.32 (1.38-3.89)** |
| Polymyalgia rheumatica | 330 | 123 | **2.52 (2.19-2.90)** | **2.90 (2.36-3.57)** |
| Vasculitis | 800 | 444 | **1.99 (1.82-2.17)*** | **1.96 (1.74-2.20)** |
| Psoriasis | 1967 | 734 | **3.09 (2.91-3.28)*** | **2.91 (2.67-3.17)** |
| **Intestinal related autoimmune** | | | | |
| Inflammatory bowel disease | 7945 | 4863 | **1.85 (1.80-1.90)** | **1.78 (1.72-1.84)** |
| Celiac disease | 434 | 254 | **1.96 (1.74-2.20)** | **1.85 (1.59-2.16)** |
| **Type 1 DM** | 3263 | 1318 | **3.42 (3.26-3.59)*** | **2.68 (2.51-2.85)*** |
| **Mortality** | 6385 | 5769 | **1.14 (1.11-1.17)*** | **1.20 (1.16-1.24)*** |

* Proportionality <0.001; CI: Confidence interval.
Crude: before matching; Adjusted: after matching.
a. Propensity score matching was performed based on age at index, sex, race, adverse socioeconomic status (problem related to housing and economic circumstances, problems related to employment and unemployment, problems related to education and literacy, occupational exposure to risk factors), and comorbidities (type 2 diabetes, vitamin D deficiency, hyperlipidemia, asthma, depression, chronic kidney disease, sleep disorder, psychoactive substance use, and BMI).
Abbreviations: DM, diabetes mellitus

https://doi.org/10.1016/j.eclinm.2022.101783

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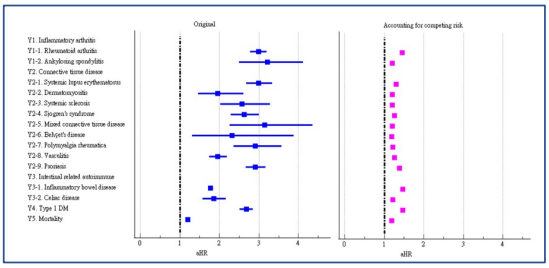


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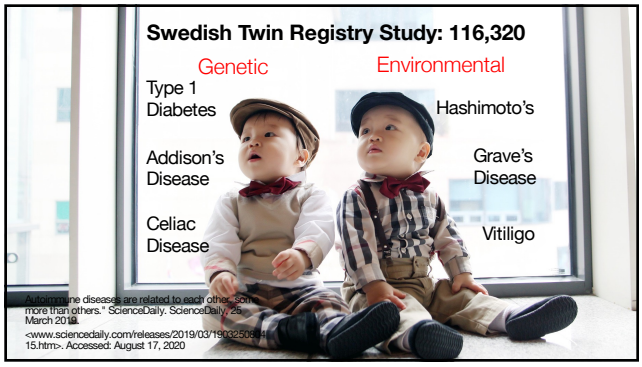


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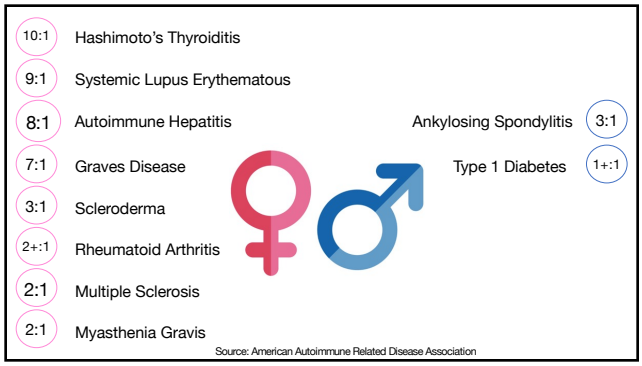


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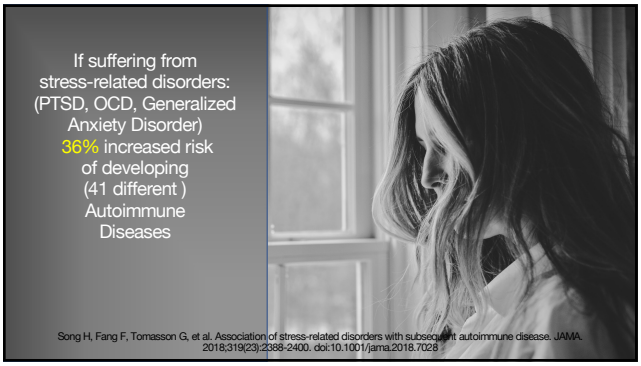


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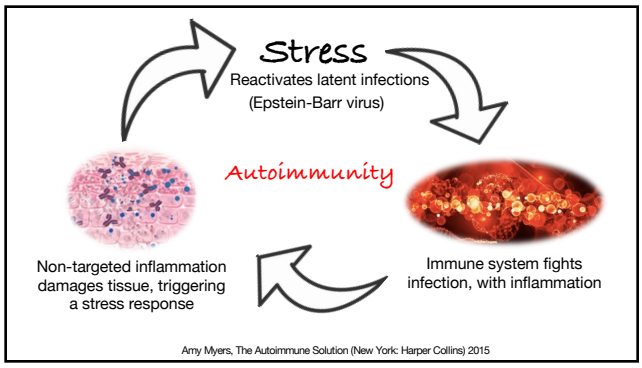


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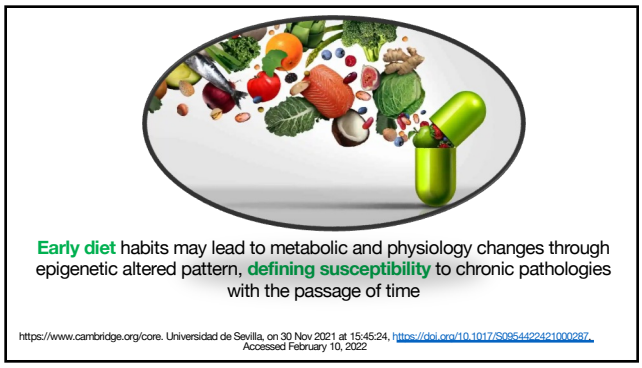


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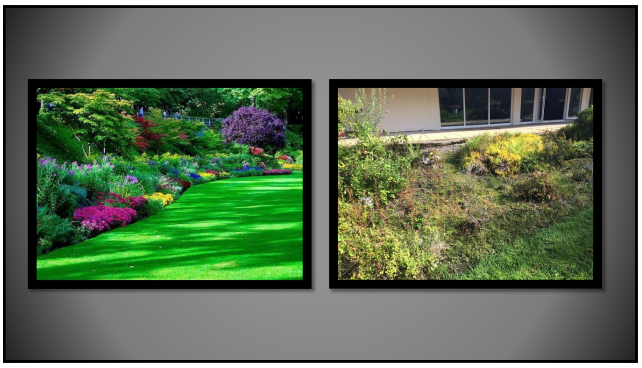

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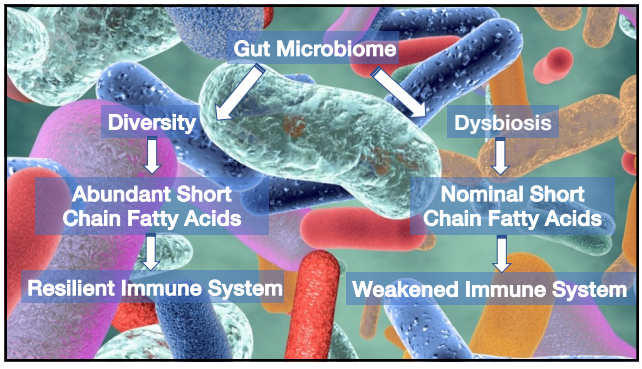


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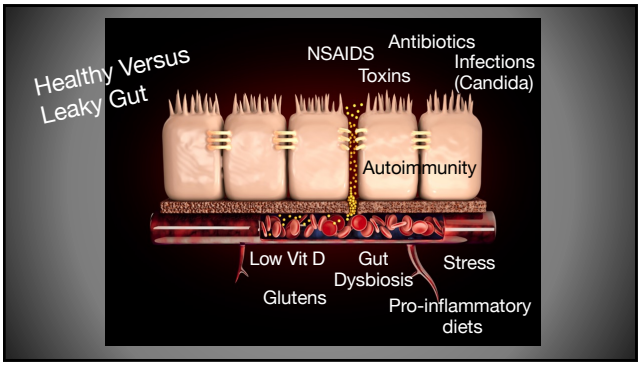


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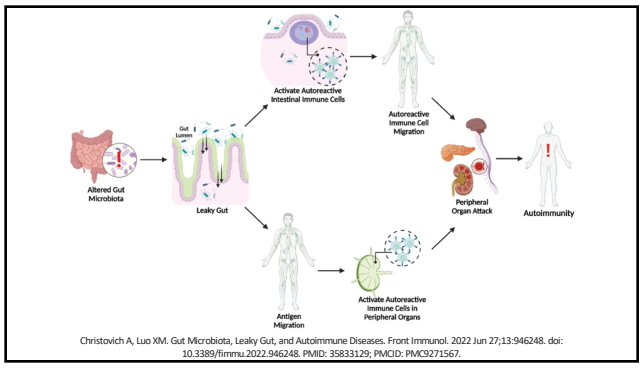


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Autoimmunity Reviews

Changes in intestinal tight junction permeability associated with industrial food additives explain the rising incidence of autoimmune disease

Aaron Lerner, Torsten Matthias

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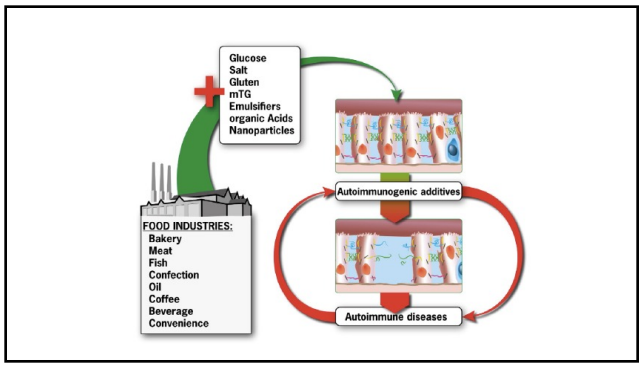


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