Lupus, Rheumatoid & Autoimmune disorders

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United Healthcare

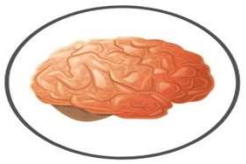
Disclosure

I have no actual or potential conflict of interest in relation to any product or service mentioned in this program or presentation.

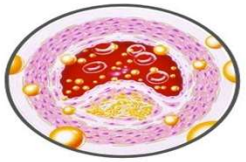
Learning Objectives

1. Describe the autoimmune (AI) process and what factors influence the pathogenesis of autoimmune diseases.
2. State the demographics of those most commonly affected by AI.
3. Identify the connection between AI and Diabetes Type 1.
4. Discuss the basics of Systemic Lupus Erythematosus including the diagnosis and prognosis.
5. Compare Rheumatoid Arthritis to Osteoarthritis including their different characteristics and laboratory findings.
6. List other less common AI disorders.
7. Determine common diseases that are NOT autoimmune.

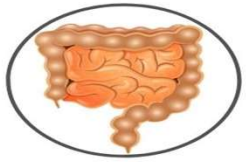
18 COMMON AUTOIMMUNE DISEASES



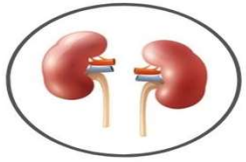
MULTIPLE SCLEROSIS (MS)



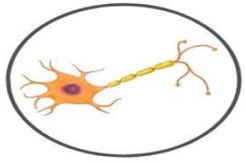
TYPE 1 DIABETES
HEMOLYTIC ANEMIA
PERNICIOUS ANEMIA
AUTOIMMUNE VASCULITIS



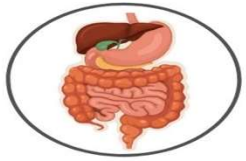
CELIAC DISEASE



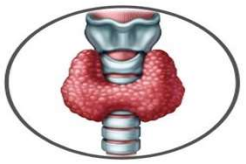
ADDISON'S DISEASE



GUILLAIN-BARRE
MYASTHENIA GRAVIS
CIDP



INFLAMMATORY BOWEL DISEASES (IBD)
CROHN'S DISEASE
ULCERATIVE COLITIS



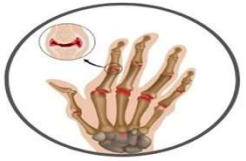
GRAVES' DISEASE
HASHIMOTO'S DISEASE

VITILIGO

LUPUS

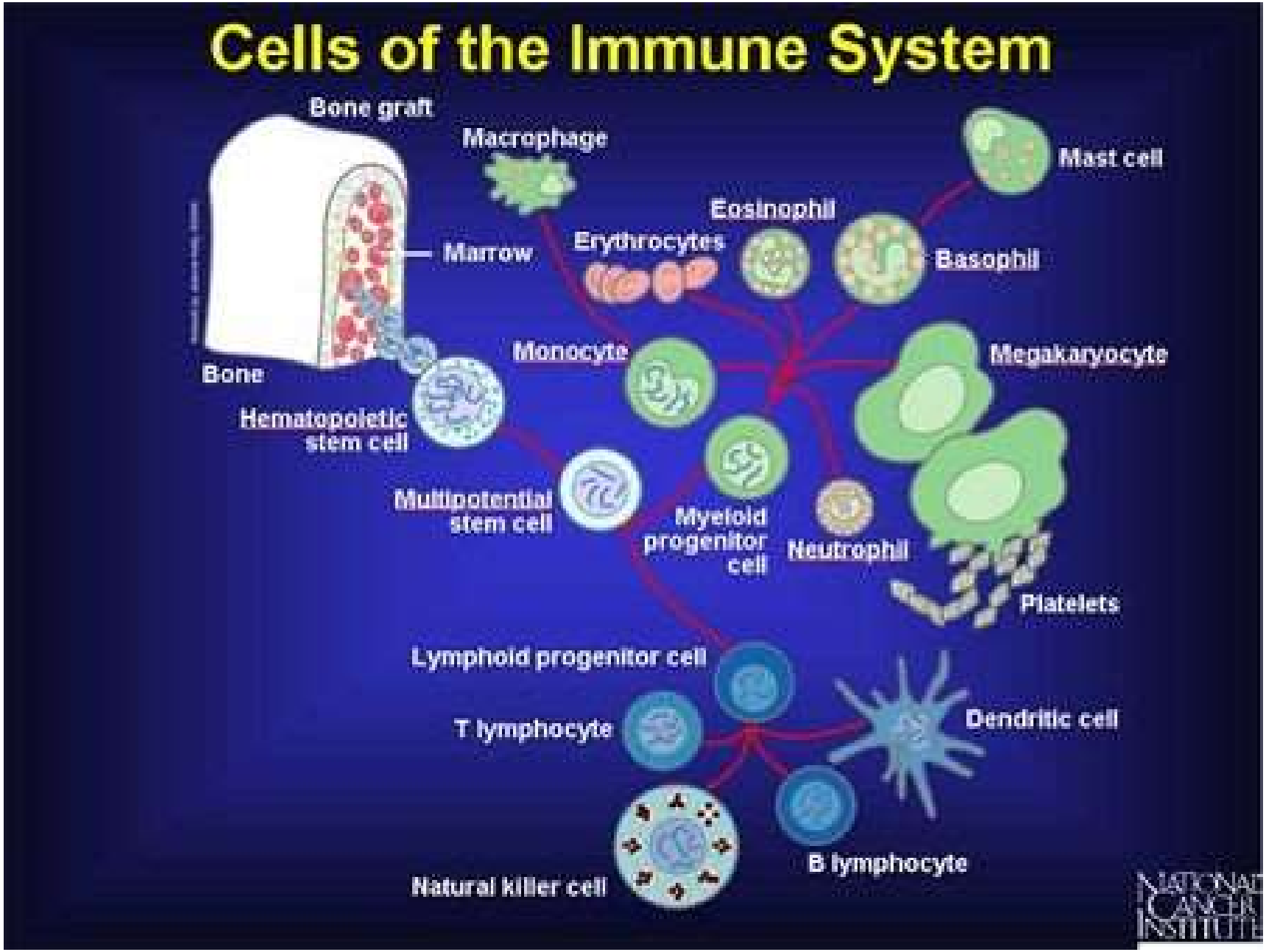
SJÖGREN'S SYNDROME

PSORIASIS



RHEUMATOID ARTHRITIS (RA)

Definition of Autoimmune


Cells of the Immune System
Bone graft
Macrophage
Mast cell
Eosinophil
Erythrocytes
Marrow
Basophil
Monocyte
Megakaryocyte
Bone
Hematopoietic stem cell
Multipotential stem cell
Myeloid progenitor cell
Neutrophil
Platelets
Lymphoid progenitor cell
T lymphocyte
Dendritic cell
B lymphocyte
Natural killer cell
NATIONAL CANCER INSTITUTE

What is Autoimmunity?

- Autoimmune diseases are characterized by a pathologic state in which an aberrant immune response directed at a normal bodily constituent leads to inflammation, cell injury, or a functional disturbance with clinical manifestations
- An autoimmune disease usually involves both a T and B cell response and can be generalized or tissue- or organ-specific and either acute or chronic.
- derives *from the same mechanisms* that underlie the *normal i*mmune response to foreign antigens
- The molecular constituent (ie, protein, carbohydrate, nucleic acid) that is targeted in autoimmunity is called a "self"-antigen or an autoantigen; by contrast, a molecule from an infecting organism that stimulates an immune response is called a foreign antigen or "non-self. ie - An autoimmune response can be initiated by an autologous (self) or foreign (non-self) antigen;
- Immune responses can be divided into two broad categories: innate and adaptive.
  - The innate immune response is a rapid and nonspecific response to a challenge, whether it arises from infection, trauma, or stress.
  - By contrast, an adaptive immune response is slow (days to weeks) and involves the production of antigen-specific B or T cells to overcome a foreign challenge

What is Autoimmunity?

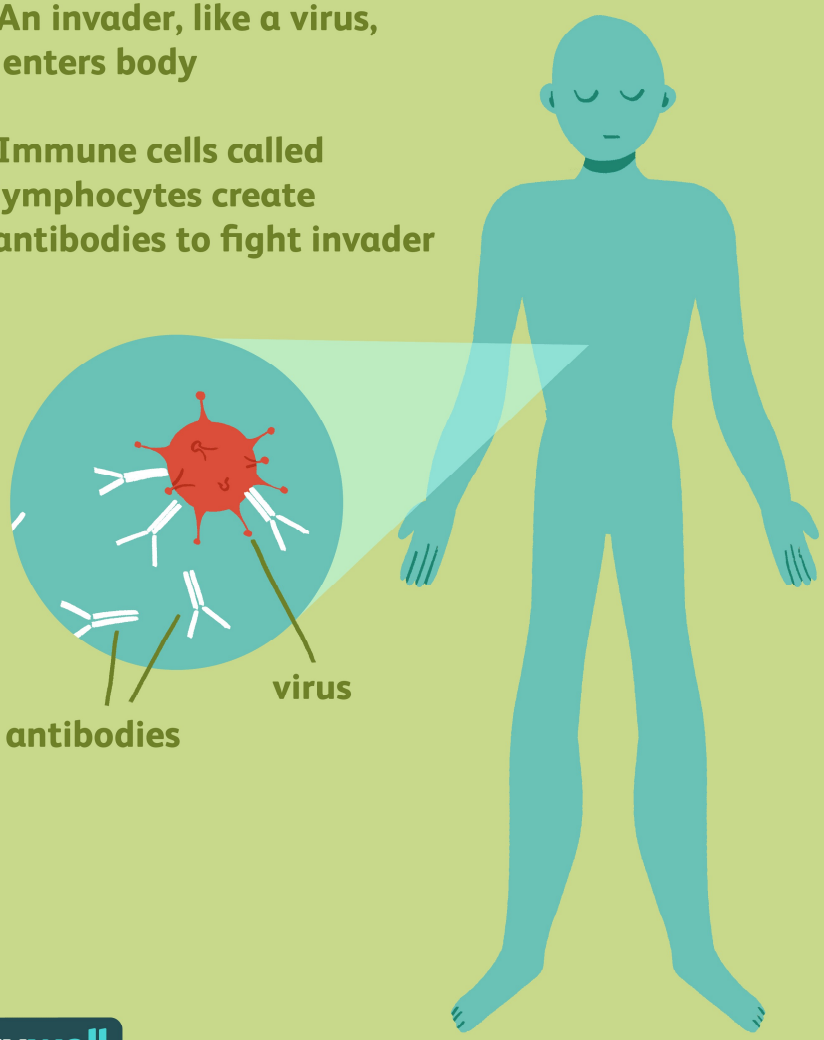
So, in sum..

- An autoimmune disease results from a specific adaptive autoimmune response to an autoantigen; this response is in violation of the normal function of the immune system in which mechanisms of tolerance prevent "hyper-reactive" autoimmune responses to self-antigens.

Normal Immune Response:

1. An invader, like a virus, enters body

2. Immune cells called lymphocytes create antibodies to fight invader



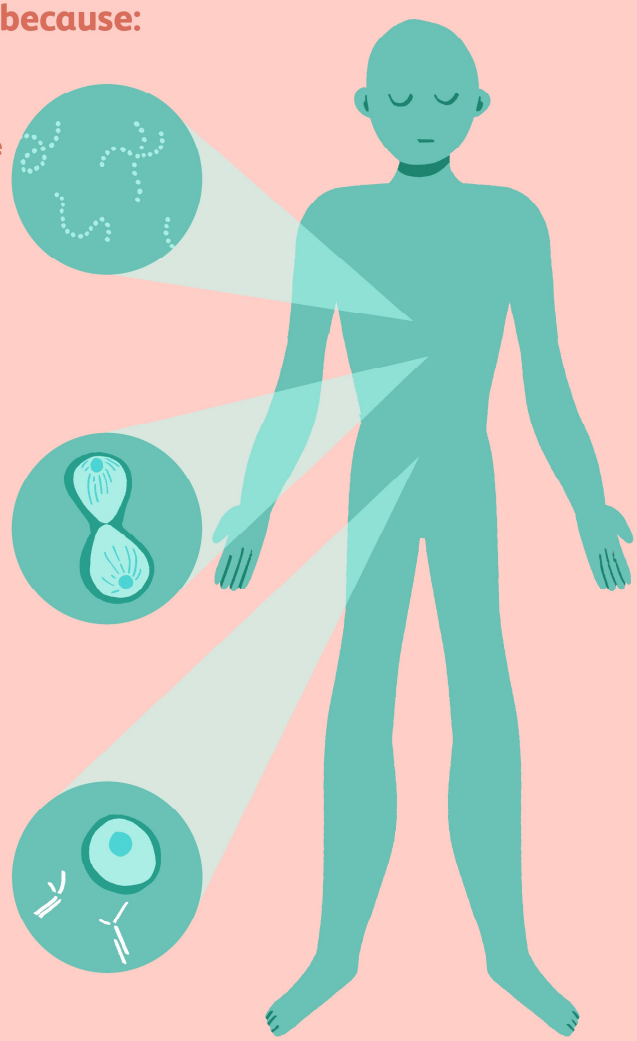
Autoimmune Disease:

Immune system creates antibodies that attack it. This happens because:

A foreign substance resembles bodily substances

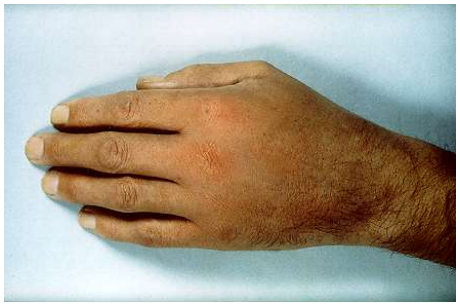
Normal body cells become altered

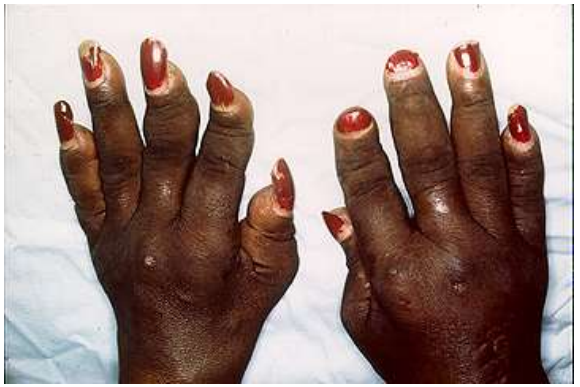
Lymphocytes malfunction and make abnormal antibodies

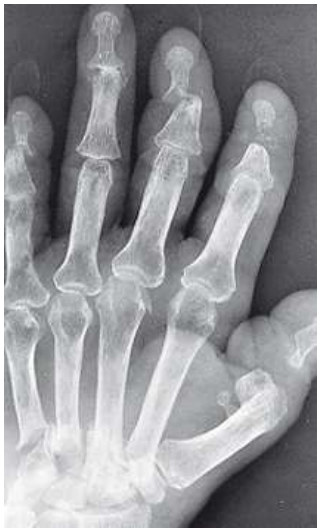


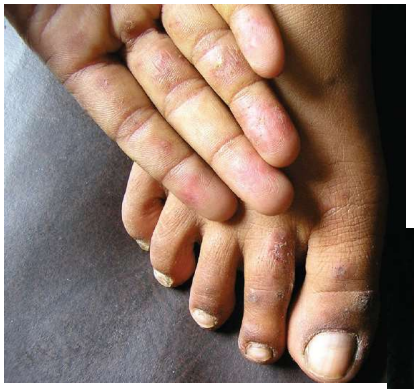
verywell

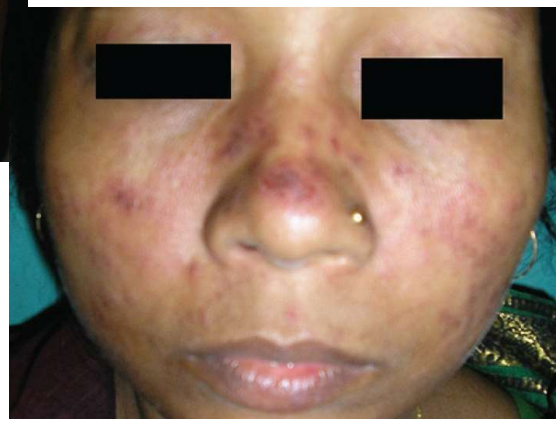
A few pictures of the destructive nature of the AI diseases.

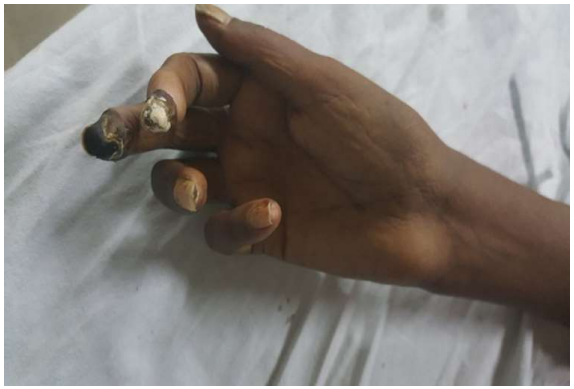












Who is more likely to develop AI?

Who is more likely to develop AI?

- **Genetic studies** of families and of large populations of patients have demonstrated the role of inherited susceptibility factors in many autoimmune diseases but the genetics of disease in humans are complex
- **Direct evidence** - genetic factors may affect the balance of the immune system, predisposing an affected individual to generating an autoimmune response to an antigenic challenge that would be without consequence in other individuals - *typically demonstrated experimentally*.
  - Antibody transfer from human patient to animal model
  - Transplacental human-to-human autoantibody transfer - Most of the clinical manifestations in transplacental transfer to the offspring are temporary because the autoantibody in these cases is provided through passive transfer of serum from the mother
    - Eg. been well documented in cases of Graves' disease ,myasthenia gravis ,and the complete heart block and other cardiac abnormalities in neonatal lupus associated with maternal lupus and Sjögren's syndrome

Who is more likely to develop AI?

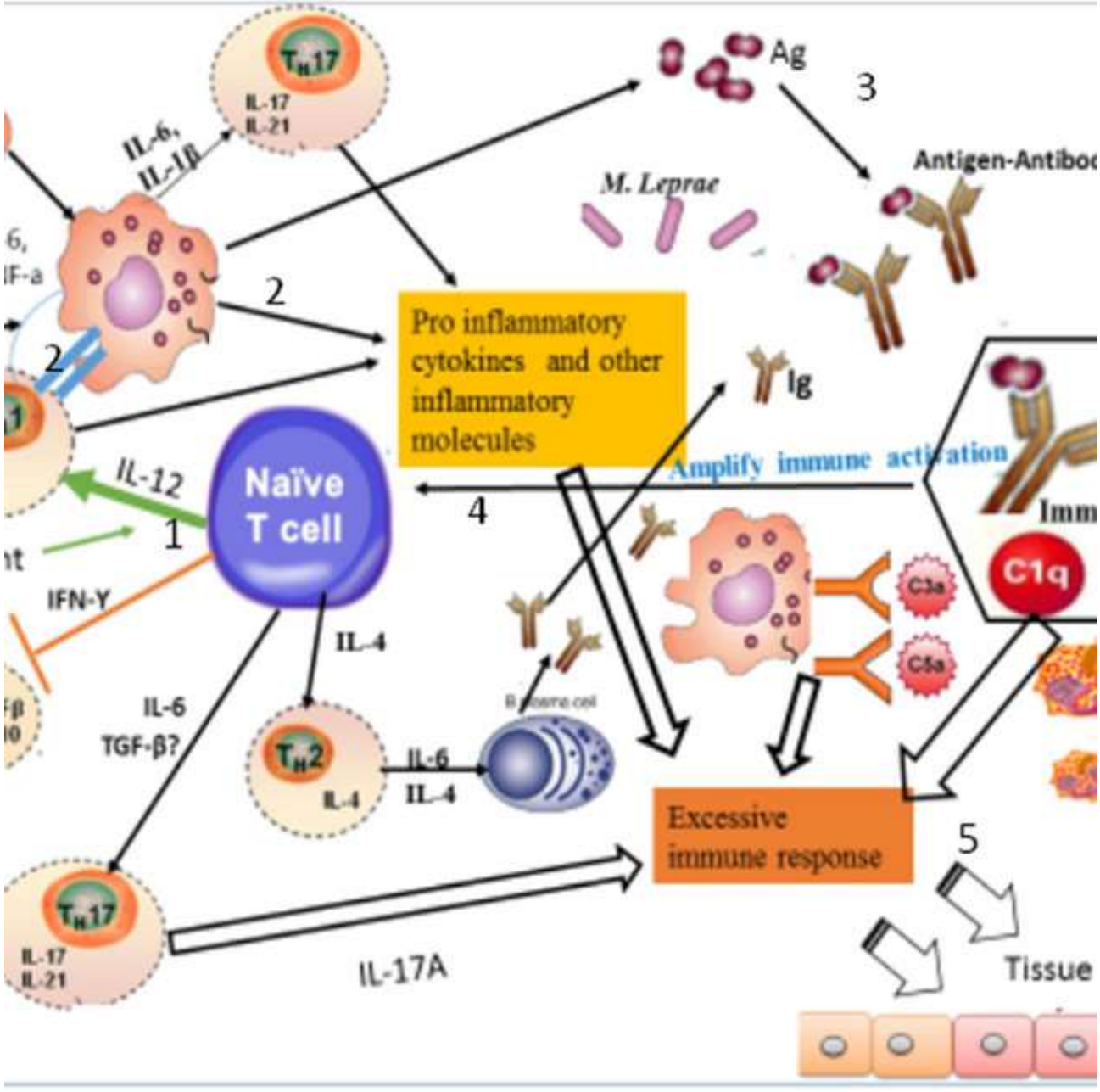
- **Trends** –

  - frequent evidence of systemic inflammation (eg, increased ESR, increased levels of CRP), along with findings of immune activation such as increased levels of immunoglobulins

  - autoimmune diseases tend to cluster
    - single individual may have more than one autoimmune disease
    - members of the family share the same or other, related autoimmune diseases however, *the majority of patients with an autoimmune disease present without a clear family history (the paradox)*
    - key role of environmental factors as triggers of autoimmune disease in genetically more susceptible individuals
    - Most, but not all, autoimmune diseases are more common in women than men.
    - the favorable response of a disease to immunosuppressive treatment is often an initial clinical hint of a possible autoimmune etiology.

What is the body's way of protection?

- **The following regulatory and pathogenic factors contribute to the pathogenesis of autoimmune disease.**
  - Breakdown or defects in immune tolerance – Autoimmune disease represents a breakdown in the normal mechanisms that prevent autoreactivity of both T and B cells
  - Defects in active regulation and control of autoreactivity - the autoimmune response can be kept in check by active regulation .Regulatory T cells (Tregs) are diverse
  - Defects in regulation of autoimmune B cell responses - autoreactive cells are eliminated at various steps, called checkpoints, by mechanisms that include deletion, anergy, and receptor editing.
    - *Whether clinical manifestations of autoimmune disease will follow from the presence of B or T cell autoreactivity depends upon both the quality of the immune response and the availability of the corresponding antigen.*
  - Immune complexes –the formation of immune complexes between autoantibodies and the corresponding autoantigen present in the circulation and/or on cell surfaces.
    - eg. for systemic lupus erythematosus, immune complexes of anti-DNA antibodies with DNA can deposit in the kidney and activate complement to produce nephritis
  - Effector T cell-mediated injury – While many other autoimmune diseases result from direct effects of autoantibodies, some diseases are associated with T cell-mediated immune responses
    - eg. rheumatoid arthritis, systemic lupus erythematosus, Graves' disease, and type 1 diabetes mellitus
  - Innate immune mechanisms – The innate immune system uses sets of molecules known as pattern-recognition receptors that have been selected through evolution to recognize molecular patterns found in microorganisms.
    - eg. autoimmune disorders that cluster with vitiligo (eg, autoimmune thyroid disease, latent autoimmune diabetes mellitus in adults, rheumatoid arthritis, psoriasis, pernicious anemia, and Addison disease)


Ag
3
Antigen-Antibo
M. Leprae
IL-6,
IL-1β
IL-17
IL-21
2
2
Pro inflammatory
cytokines and other
inflammatory
molecules
Ig
Amplify immune activation
4
IL-12
1
Naïve
T cell
IFN-Y
IL-4
IL-6
TGF-β?
IL-6
IL-4
IL-4
C1q
C3a
C5a
Excessive
immune response
5
IL-17A
Tissue

About Diabetes mellitus Type I

Diabetes Mellitus Type I (T1DM) & other AI disorders – Thyroid disorders

- one of the most common chronic diseases in childhood
- is caused by insulin deficiency resulting from the destruction of insulin-producing pancreatic beta cells.
- As with autoimmunity in general, females are at greater risk for multiple autoantibodies.
- clinical care includes screening protocols for the more common endocrinopathies associated with T1DM
- Children and adolescents with T1DM are at increased risk for developing other autoimmune diseases, most commonly:
  - **Autoimmune thyroiditis** –
    - Up to 25 % have positive antithyroid antibodies (antithyroid peroxidase [TPO-Ab] and/or antithyroglobulin [Tg-Ab]
    - Autoimmune hypothyroidism develops before adulthood in up to 10 % , Hypothyroidism is less common before adolescence;
    - Other patients have subclinical hypothyroidism, defined as normal serum free thyroxine (fT4) concentration with elevated thyroid-stimulating hormone (TSH).- might be associated with an increased risk of symptomatic hypoglycemia [18] and reduced linear growth
    - Rarely, children with T1DM may be hyperthyroid, with a reported prevalence of approximately 0.2 to 1 % which is significantly higher than in the age-matched general population – Graves and Hashimoto'sthyroiditis
    - Children with T1DM and hyperthyroidism are more likely to have a history of diabetic ketoacidosis, hypoglycemia, and high blood pressure
    - All children with T1DM should have regular surveillance for thyroid disease by measuring TSH (table 1) [7,22]. Autoimmune thyroiditis is common in this population and can affect the clinical course
  - celiac disease

Diabetes Mellitus Type I (T1DM) & other AI disorders – Celiac disease

Celiac disease

- @ 5 to 10 percent of patients with T1DM have serologic evidence of celiac disease (anti-endomysial antibodies or tissue transglutaminase [tTG] antibodies)

- @5 percent have celiac disease confirmed by small bowel biopsy

- Most cases of celiac disease (up to 79% in one study) are diagnosed within five years of diabetes onset

- Risk factors for celiac disease include female sex, younger age of onset and longer duration of T1DM, and presence of thyroid disease

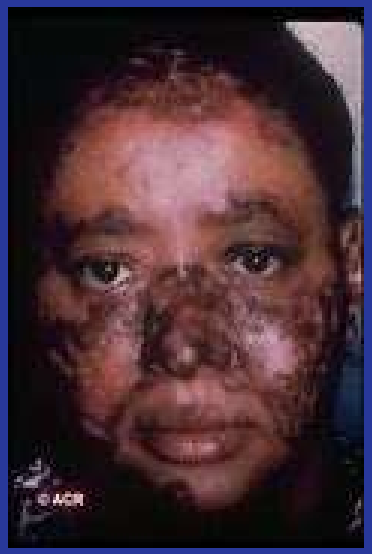
- Only a minority of children with T1DM and celiac disease present with gastrointestinal symptoms of food intolerance, food avoidance, gastrointestinal discomfort, and diarrhea.

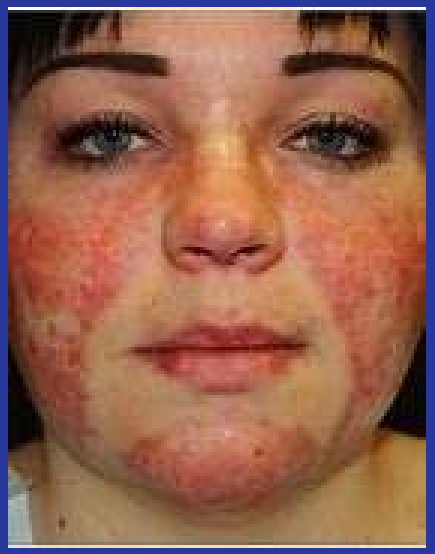
- More common initial findings include unpredictable blood glucose measurements, recurrent episodes of hypoglycemia, poor glycemic control, and growth failure because of erratic intestinal absorption of nutrients . In addition, bone mineralization may be reduced

- Because of the prevalence of celiac disease and its potential clinical impact on patients with T1DM, all children with T1DM should have regular surveillance for celiac disease .

Serologic testing for celiac disease is valid only when the child is being exposed to dietary gluten; false negative results may occur if the test is performed while on a gluten-free diet.

What is Lupus?





The many faces of SLE

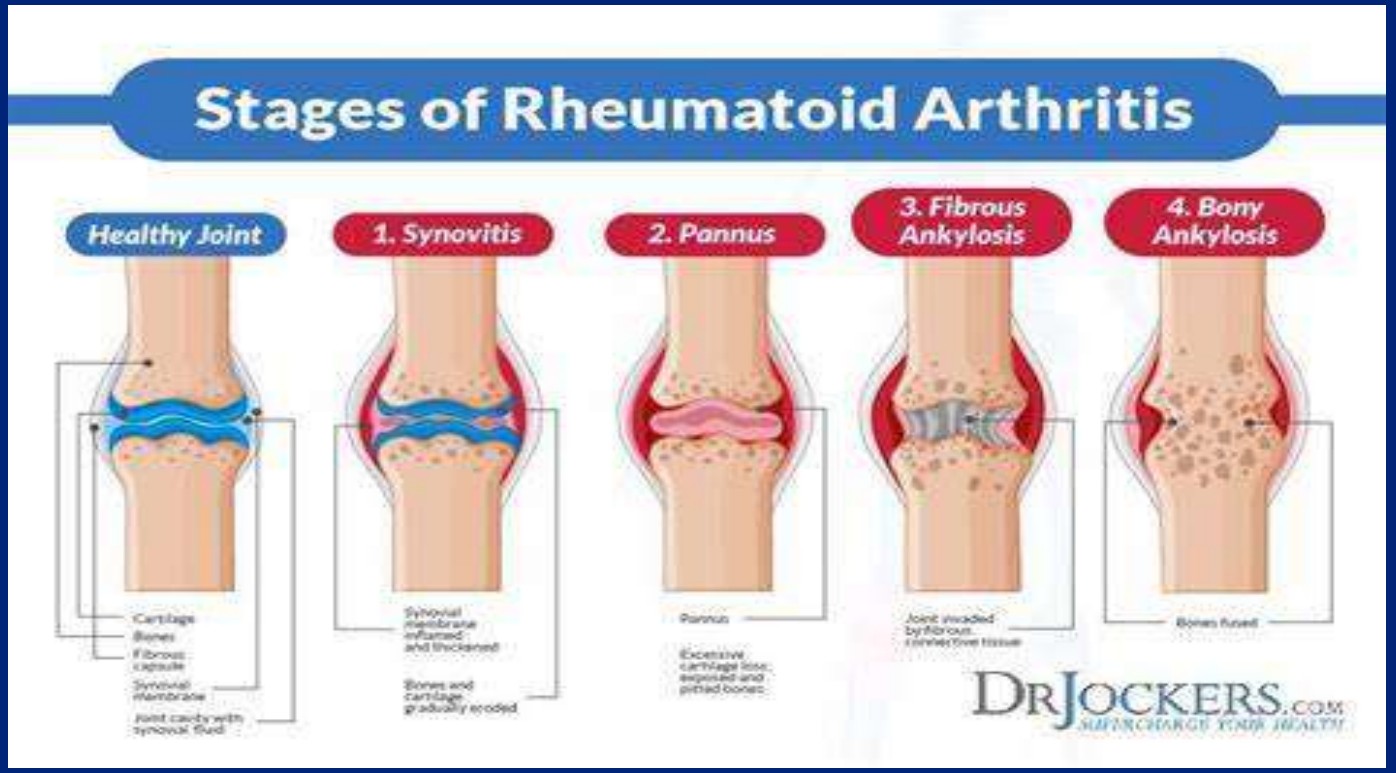
Systemic lupus erythematosus

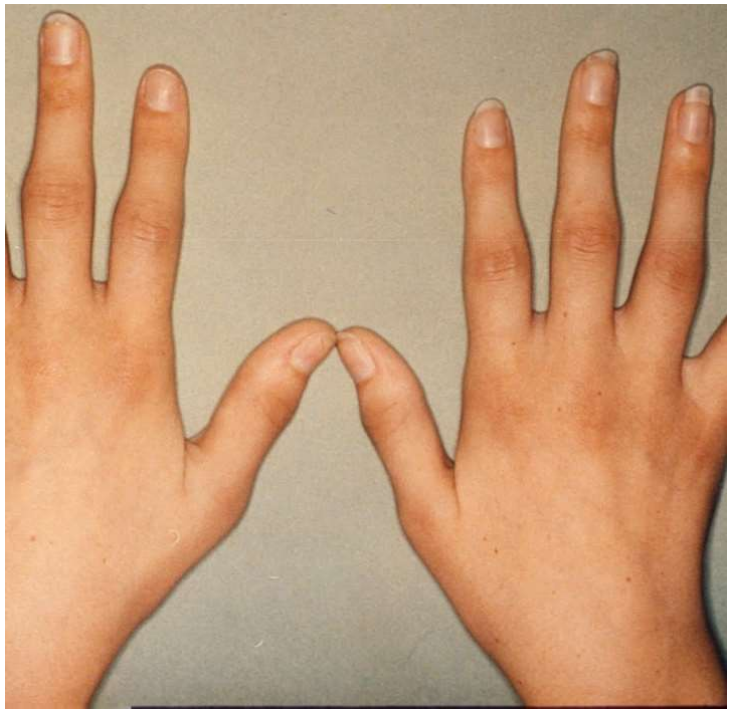
- a chronic autoimmune disease of unknown cause that can affect virtually any organ of the body. Immunologic abnormalities, especially the production of a number of antinuclear antibodies (ANA), are a prominent feature of the disease.
- occurs primarily in young women of childbearing age & more commonly in Black, Asian, and Hispanic populations
- variable clinical features ranging from mild joint and skin involvement to life-threatening kidney, hematologic, or central nervous system involvement
- clinical heterogeneity of SLE and the lack of pathognomonic features or tests pose a diagnostic challenge - To complicate matters, patients may present with only a few clinical features of SLE, which can resemble other autoimmune, infectious, or hematologic diseases.
- **The diagnosis** of SLE is generally based on clinical and laboratory findings after *excluding alternative diagnoses*.- Serologic findings are important *in suggesting* the possibility of SLE, with some antibodies (eg. anti-dsDNA, Anti-Smith)
- **Prognosis**- Causes of death in the first few years of illness are active disease (eg, central nervous system [CNS] and renal disease) or infection due to immunosuppression,. Causes of late death include complications of SLE (eg, end stage renal disease), treatment complications, and cardiovascular disease . *remission is uncommon, and, when it is achieved, it is often not sustained.*
  - among the top 20 leading causes of death in females ages of 5 to 64 (CDC)
  - higher among women, African Americans, and residents of the South
- ***Prognostic indicators****: Renal disease esp diffuse proliferative glomerulonephritis, HTN, male , young age, Older age, low SE status, Black race, Anti PL Ab (+), high overall disease activity*

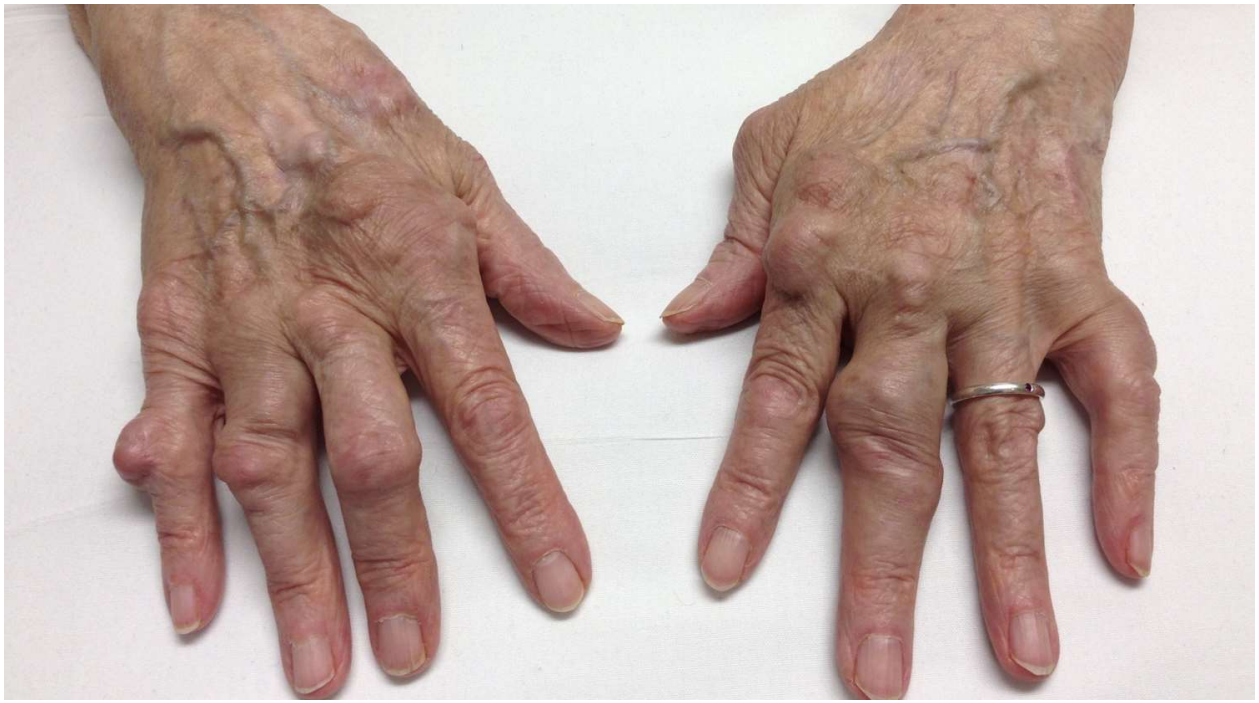
Systemic lupus erythematosus - Sx

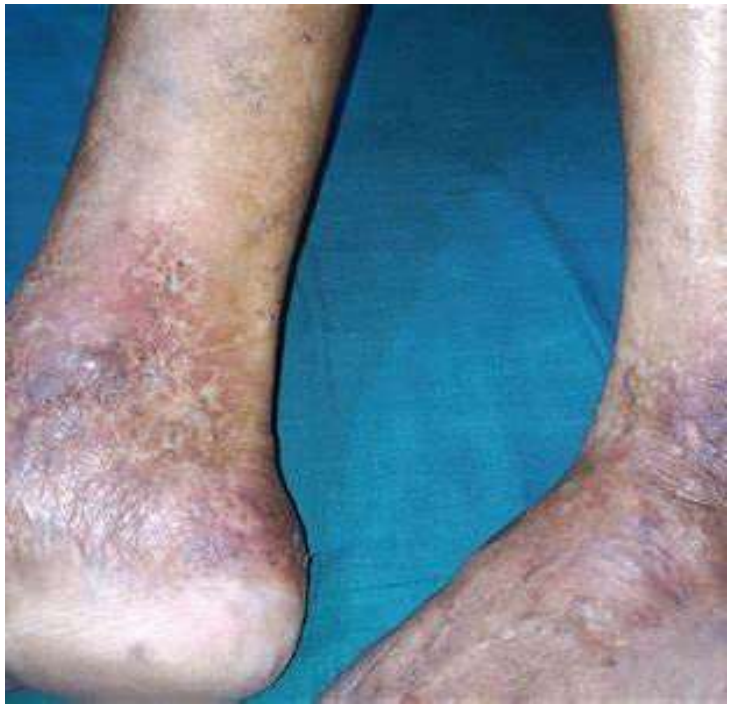
- **Constitutional symptoms** – fatigue**, Fever – unresponsive to NSAIDS,- Acetaminophen or Steroids, Myalgia, Weight change: Loss – poor appetite, meds, GI sx. Gain – salt/water retention, hypoalb, steroids induced increased appetite
- **Arthritis and arthralgias** – presents in >90%
- **Mucocutaneous involvement -** facial eruption that characterizes acute cutaneous lupus erythema (also known as "the butterfly rash") after sun exposure, discoid lesions, which are more inflammatory & tend to scar , painless oral and/or nasal ulcers, in contrast to herpetic chancre blisters, Scarring alopecia
- **Cardiovascular manifestations** - pericardium, myocardium, valves & thromboembolic ds (esp w Anti PL Ab) , conduction system, and coronary arteries
- **Kidney involvement** - >50% involvement, Several forms of glomerulonephritis- clinical presentation of lupus nephritis is highly variable,
- **Gastrointestinal involvement -** majority of GI sx are caused by Rx SE reactions and viral / bacterial infection. SLE-related GI abnormalities can involve almost any organ along the GI tract
- **Pulmonary involvement** - pleuritis (with or without effusion), pneumonitis, interstitial lung disease, pulmonary hypertension, shrinking lung syndrome, and alveolar hemorrhage
- **Neurologic and neuropsychiatric involvement** - broad range of neurologic /psychiatric manifestations eg stroke, seizures, cognitive dysfunction, delirium, psychosis, and/or peripheral neuropathies.
- **Hematologic abnormalities -** all three blood cell lines can be affected, Lymph node enlargement :cervical, axillary, and inguinal regions.; Splenomegaly
- **Ophthalmologic involvement** - keratoconjunctivitis sicca (Sjogren's), retinal vasculopathy. Less common: optic neuropathy, choroidopathy, episcleritis, scleritis, and anterior uveitis
- **Other associated conditions and complications**
  - Infection - risk for infection was increased in Black Americans and for male, skin, respiratory, and urinary systems in >50% of SLE patients
  - Other autoimmune disease, Antiphospholipid syndrome, Fibromyalgia, Osteonecrosis , Osteoporosis , Immunodeficiencies – eg. Hereditary Angioedema

What is Rheumatoid Arthritis?







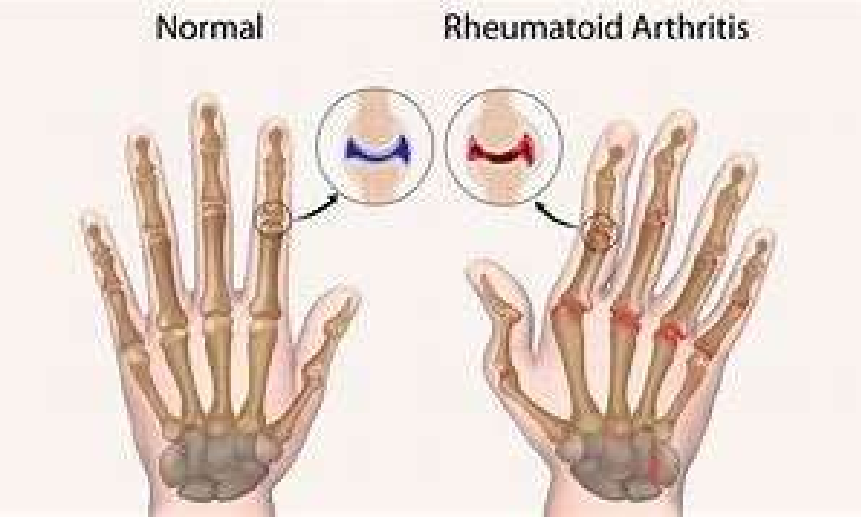


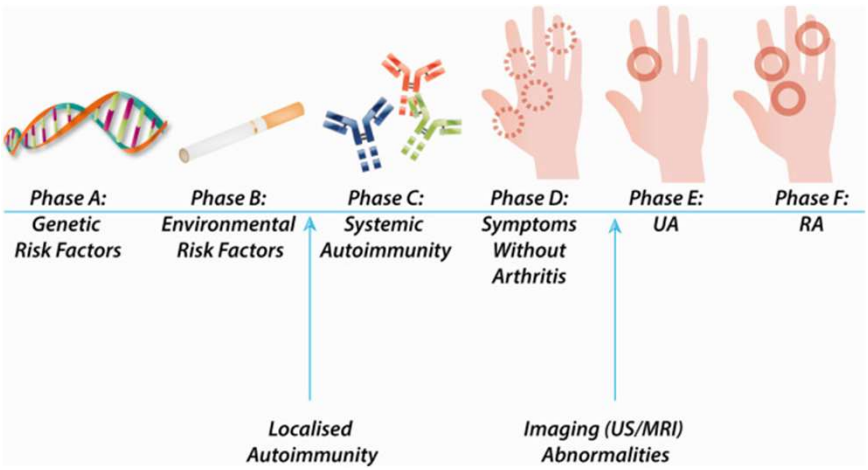
Effects of Rheumatoid Arthritis

Rheumatoid Arthritis

- Should be suspected in the adult patient who presents with inflammatory polyarthritis
- The pathogenesis of rheumatoid arthritis (RA) is complex, with multiple genetic, environmental, immunologic, and other factors contributing to the development and expression of disease.
- environmental and genetic influences can interact and trigger adaptive responses associated with autoimmunity long before the onset of clinical symptoms.
- Disease initiation results from a combination of predetermined (genetic) and stochastic (random environmental) events. . "pre-RA" or preclinical RA. -" ACPAs and autoantibodies, including rheumatoid factors (RFs), can appear more than 10 years before clinical arthritis
- the precise etiology of RA remains uncertain - bc ACPAs and other antibodies against altered peptides are not true autoantibodies, since they recognize modified proteins - These antibodies may contribute to the initiation or exacerbation of synovitis but do not necessarily cause RA by themselves
- The diagnosis of RA with inflammatory arthritis involving >/= 3 joints, (+) RF and/or ACPA, disease duration of >6wks, and elevated CRP or ESR, but without evidence of alternative diagnoses with similar clinical features. Also - patients with seronegative RA, those with clinically quiescent disease, and those with recent onset RA . While diagnostic uncertainty in early RA is expected, the diagnosis should become clearer with time. ***
- Implications for RA treatment – many advancements have been made, but individual patients vary in their therapeutic response to these agents, which usually must be maintained indefinitely to sustain disease control. Therefore, these highly effective therapies are not a cure for the disease.

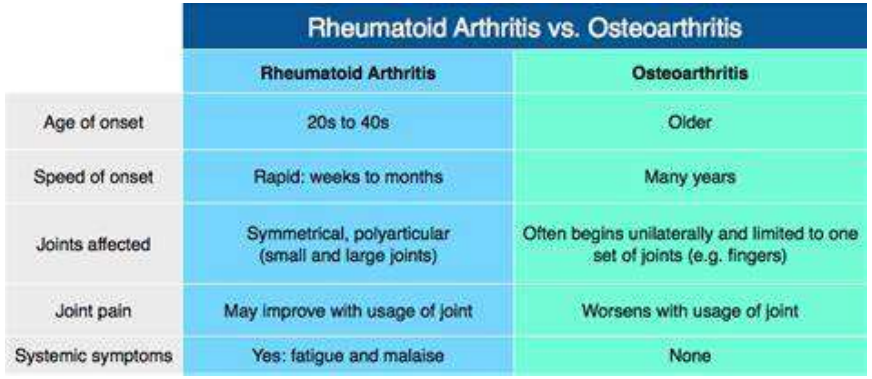
Rheumatoid Arthritis progression





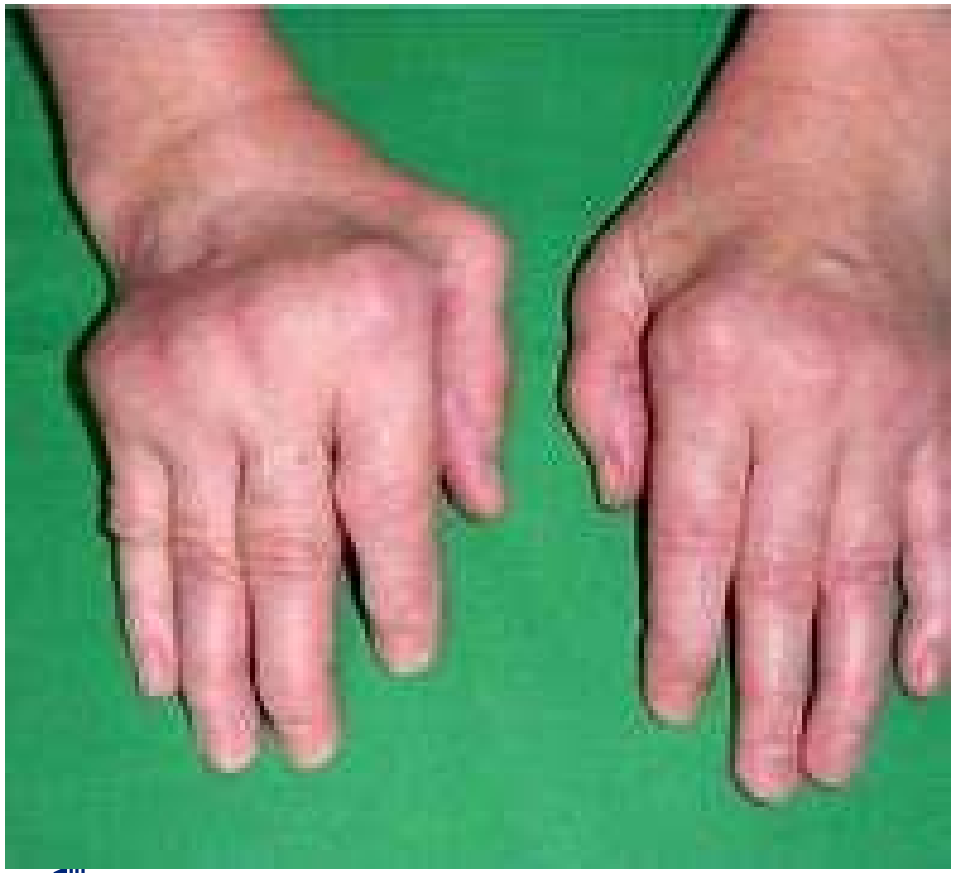
Rheumatoid Arthritis vs Osteoarthritis

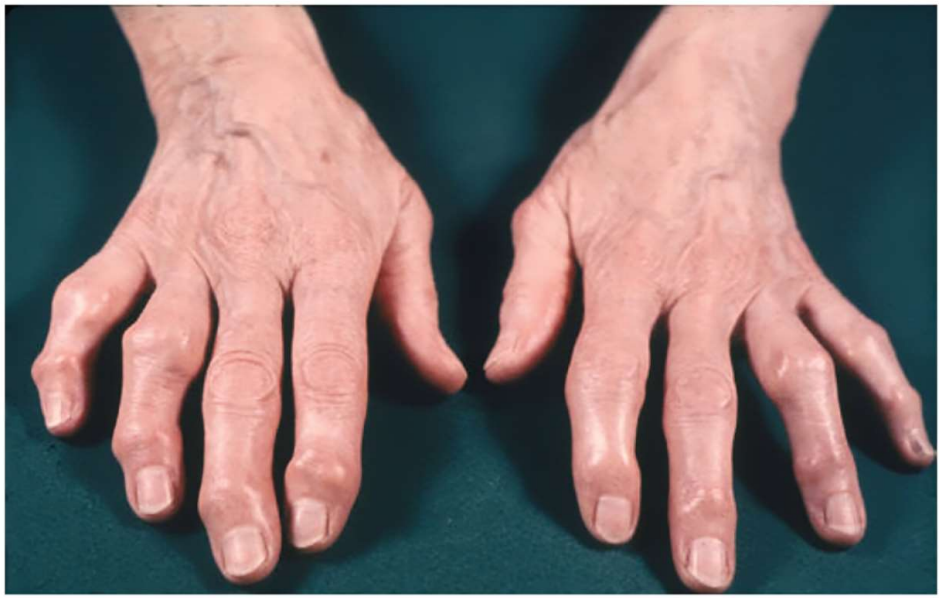
Feature	Rheumatoid arthritis	Osteoarthritis
Primary joints affected	Metacarpophalangeal	Distal interphalangeal
	Proximal interphalangeal	Carpometacarpal
Heberden's nodes	Absent	Frequently present
Joint characteristics	Soft, warm, and tender	Hard and bony
Stiffness	Worse after resting (eg, morning stiffness)	If present, worse after effort, may be described as evening stiffness
Laboratory findings	Positive rheumatoid factor	Rheumatoid factor negative
	Positive anti-CCP antibody	Anti-CCP antibody negative
	Elevated ESR and CRP	Normal ESR and CRP



	Rheumatoid Arthritis vs. Osteoarthritis	
	Rheumatoid Arthritis	**Osteoarthritis**
Age of onset	20s to 40s	Older
Speed of onset	Rapid: weeks to months	Many years
Joints affected	Symmetrical, polyarticular (small and large joints)	Often begins unilaterally and limited to one set of joints (e.g. fingers)
Joint pain	May improve with usage of joint	Worsens with usage of joint
Systemic symptoms	Yes: fatigue and malaise	None

Rheumatoid vs Osteoarthritis





Other AI disorders

Mixed connective Tissue Disease (MCTD)

- 1. **Mixed connective Tissue Disease (MCTD)**
  - defined as a systemic rheumatic disease characterized by the presence of high titer anti-U1 ribonucleoprotein (U1 RNP) antibodies in *combination with clinical features commonly seen in systemic lupus erythematosus (SLE), systemic sclerosis (SSc), rheumatoid arthritis (RA), and polymyositis (PM).*
  - *All organs can be involved*;
    - skin,
    - joint,
    - pulmonary (ILD, PAH**),
    - vascular (Raynaud's)
    - muscle (Polymyositis),
    - cardiac(heart blocks/Abn EKG, Pericarditis, MVP/pericardial effusion),
    - kidney (proteinuria, MN, GN but rarely CKD4-5),
    - GI,
    - CNS (mild only – no cerebritis, psychosis, Sz)
  - It often takes several years before enough overlapping features have appeared to be confident that MCTD is the most appropriate diagnosis. – *they usually have 3+ of these Sx: :●Swollen hands ●Synovitis ●Myositis ●Raynaud phenomenon ●Acrosclerosis*
  - The distinctive overlap features of SLE, SSc, inflammatory arthritis, and PM commonly appear sequentially over time.

Pediatric autoimmune neuropsychiatric disorder associated with group A streptococci (PANDAS)

- a subset of children whose sx of obsessive-compulsive disorder, tic disorders, or other neuropsychiatric symptoms (eg, anxiety) are exacerbated by GAS infection*. The hypothesized association between PANDAS and GAS is controversial,*
- Support for a role of autoimmunity is provided by reports of response to treatment with immune-modifying therapies, such as glucocorticoids, intravenous immune globulin, and plasma exchange The response to plasma exchange appears to be specific to children with OCD/tic disorders and preceding GAS infection
- **Working diagnostic criteria** — PANDAS is characterized by 5 working criteria
  - Obsessive-compulsive disorder (OCD) and/or tic disorder (Tourette syndrome, chronic motor or vocal tic disorder that meets the Diagnostic and Statistical Manual of Mental Disorders,
  - Pediatric onset (between three years and onset of puberty)
  - Abrupt onset and episodic course of symptoms
  - Temporal relation between GAS infection and onset and/or exacerbation.
  - Neurologic abnormalities, such as motoric hyperactivity (eg, fidgeting, difficulty remaining seated), choreiform movements (elicited through stressed postures [eg, standing upright with the feet together and the eyes closed, holding the arms outstretched with the hands extended] but not present at rest), or tics during exacerbations. Frank chorea (rapid, irregular, and nonstereotypic jerks that are continuous while the patient is awake but improve with sleep) suggests Sydenham chorea.

Prognosis: The long-term outcome is not known. Unrecognized PANDAS and untreated PANDAS may result in an increased risk of progression to lifelong obsessive-compulsive disorder and tic disorders that show the more typical waxing and waning pattern and are not associated with GAS infections

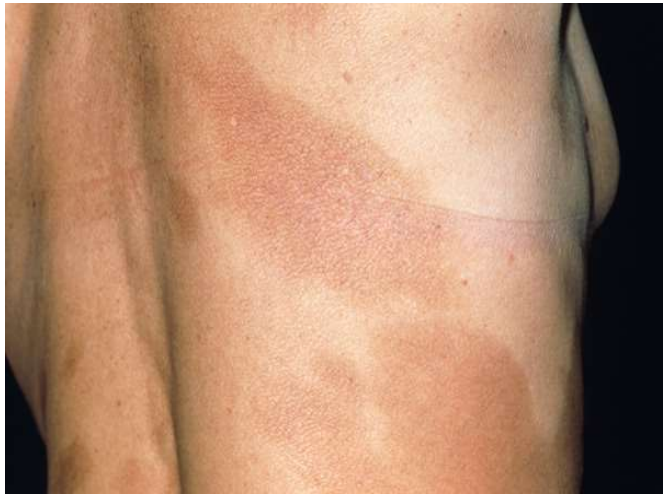
Autoimmune Hepatitis – Other names: Lupoid hepatitis, plasma cell hepatitis, and autoimmune chronic active hepatitis

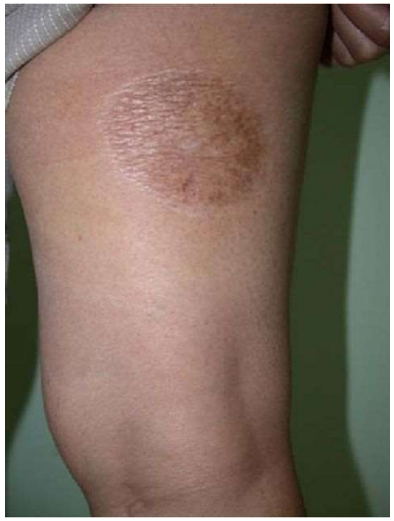
- a chronic, inflammatory disease of the liver that is characterized by circulating autoantibodies and elevated serum globulin levels.
- may start as acute hepatitis and progress to chronic liver disease and cirrhosis.
- can present at any age(Age of presentation is bimodal, with a peak in the 2nd decade and another peak between the 5th and 6th decade) and in all ethnic groups,
- occurs predominantly in women : For type 1 autoimmune hepatitis, the female to male ratio is 4:1, but for type 2 autoimmune hepatitis, the ratio is 10:1
- Alanine aminotransferase [ALT] & aspartate aminotransferase [AST]elevated 10-20x upper limit; AlK Phos:AST ratio <1:5
- Pathogenesis One theory is that the disease is *caused by an environmental trigger* in a *genetically predisposed individual*. The exact relationships between genes and the autoimmune process remain largely undefined, but at the molecular level, they are thought to involve the autoantigen, the major histocompatibility complex, and the T-cell receptor.
- Presentations- variety of clinical phenotypes include: ;
  - patients with abnormal liver biochemical tests, acute hepatitis, cirrhosis, or acute liver failure
  - an acute or chronic disease with a fluctuating pattern
  - asymptomatic patients
  - with debilitating symptoms (eg, anorexia, fatigue, weight loss).
  - Associated extrahepatic disorders: AI disorders:- autoimmune thyroiditis, rheumatoid arthritis, type 1 diabetes mellitus, ulcerative colitis, celiac disease, and systemic lupus erythematosus and Skin conditions - as a transient and nonspecific maculopapular rash, particularly over the face, trunk, and upper arms

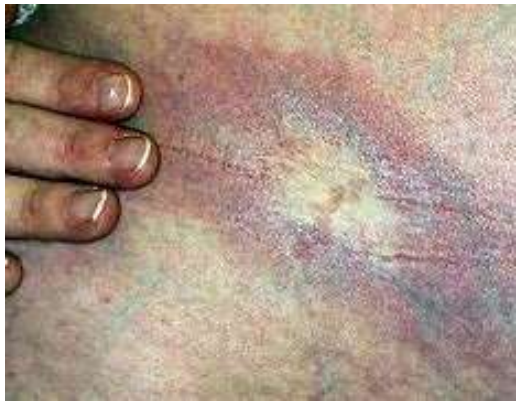
What is NOT autoimmune?

Morphea (localized Scleroderma)

- **What is it?-** is an idiopathic, inflammatory disorder that causes sclerotic changes in the skin, pathogenesis of *morphea is poorly understood* - likely to have an autoimmune basis; genetic and environmental factors may also play a role in the development of this disease. routine testing for autoantibodies is not indicated in adults with morphea.
- relatively uncommon disorder that affects adults and children, >50% develops in Adulthood, Females are more susceptible to morphea than males
- **How it presents-** typically begin as inflammatory patches or plaques that evolve into firm, sclerotic plaques. Involvement may be limited to the dermis, or may extend to underlying subcutaneous fat, muscle, or bone. Atrophic changes often remain after lesion resolution.
- **Prognosis -** Disease activity typically persists for three to six years; some patients develop more persistent or recurring involvement.- Cosmetic disfigurement or functional impairments due to atrophy or contractures often remain after the resolution of active disease.







Drug-induced Lupus

- The mechanism or mechanisms involved in drug-induced lupus remain uncertain
- Certain drugs may trigger an autoimmune response eg. Common Drugs: Isoniazid, Hydralazine, Procainamide, Minocyline, Quinidine, TNF inhibitors (etanercept, infliximab, adalimumab). Less common: anti-Sz meds, Methyldopa, Sulfasalazine,
- the relative incidence of drug-induced lupus from each of these agents will depend upon the extent to which they are prescribed. Onset months to years of exposure, may be abrupt
- most often, these drugs induce autoantibodies, (which may occur in a significant number of patients,) but most of these patients do not develop signs of an autoantibody-associated disease. In some patients, a clinical syndrome with features similar to systemic lupus erythematosus (SLE) may develop
  - most common symptoms of drug-induced lupus include fever, arthralgias/arthritis, myalgias, rash, and/or serositis. More severe manifestations, such as kidney disease and central nervous system involvement, are uncommon
- Drug-induced lupus has similarities to spontaneous SLE, but there are some differences in clinical and immunologic features and in the frequency of such features. The clinical and serologic pattern of disease is also often drug-specific, and a single pattern is not seen across all agents.
- Generally, equally common in males and females, and more common in older adults and White populations - An exception is minocycline-induced lupus, which is mostly observed in young women treated for acne.
- **prognosis** is generally quite favorable in most cases. Typically resolving after drug withdrawal, even though management of specific manifestations (eg, with NSAIDs or hydroxychloroquine) may be needed for up to several months in some patient. Occasional patients require glucocorticoid therapy, *but life-threatening disease is infrequent* and may suggest idiopathic systemic lupus erythematosus (SLE)-like presentation

Drugs you need to know that can cause DIL

Table 3. Common Agents That Cause DIL[a]

Drug	Risk
Acebutolol	Low
Carbamazepine	Low
Chlorpromazine	Low
Hydralazine	High
Isoniazid	Low
Methyldopa	Low
Minocycline	Low
Penicillamine	Low
Procainamide	High
Quinidine	Moderate
Sulfasalazine	Low

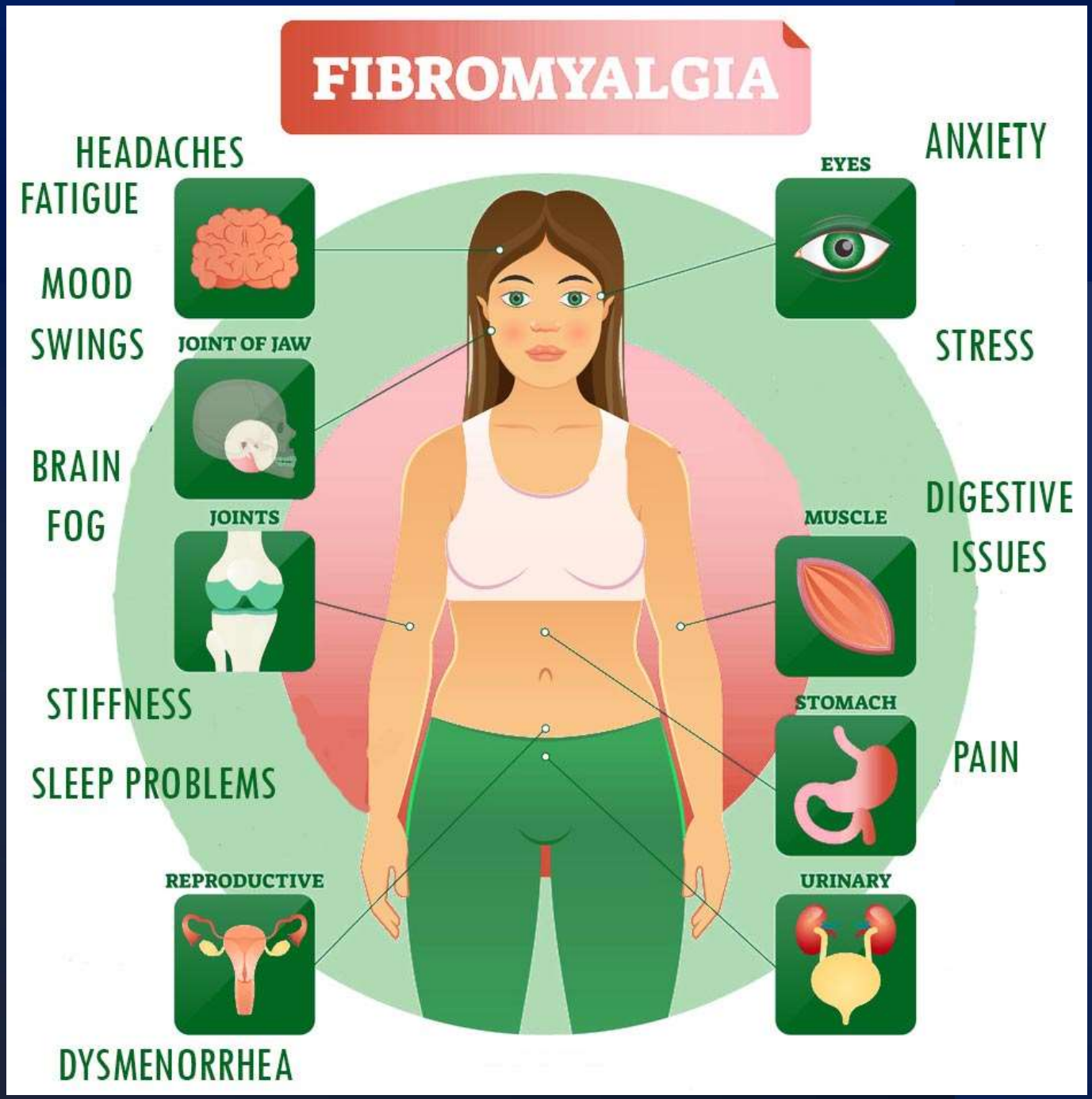
[a] Insufficient data at this time to assess the risk for anti-TNF-alpha agents.
DIL: drug-induced lupus; TNF: tumor necrosis factor.
Source: References 1, 2, 7, 8, 11.

Inborn errors of immunity (IEIs) or Primary immunodeficiency

- People with primary immunodeficiency (PI) have an immune system that does not work correctly.
- range in severity from life-threatening disorders presenting in infancy to less severe disorders diagnosed in adulthood.
- Most patients with IEIs present with recurrent or chronic infections
- A significant number of patients with IEIs do not initially present with infections but rather with failure to thrive, severe atopy, autoinflammatory disease, or autoimmune disease. Others may develop such complications in the course of the disease'
- The diverse immunological abnomalities along with the compensatory and excessive sustained inflammatory response result in tissue damage and finally in manifestation of organ-, cell-specific or systemic autoimmune diseases.
- Several forms of primary immunodeficiency disorders are characterized by a variety of specific autoimmune phenomena.
- The concomitant appearance of primary immunodeficiency and autoimmunity appears to be rather paradoxical, therefore making the diagnosis of immunodeficiency patients with autoimmune complications challenging.

Fibromyalgia (FM) – what is it?

- a common cause of chronic widespread musculoskeletal pain,
- often accompanied by fatigue, cognitive disturbance, psychiatric symptoms, and multiple somatic symptoms and soft tissue pain affecting the muscles, ligaments, and tendons,
- FM itself is not associated with evidence of tissue inflammation, and a cardinal feature of FM is that the pain is not explained by another rheumatic or systemic disorder.
- *Explicit in the definition of FM is the exclusion of other conditions that can present with widespread pain*
- FM is often associated with other conditions that may cause musculoskeletal pain, disruption of sleep, or psychiatric symptoms; features of these conditions may also mimic FM, and the presence of such disorders should be considered in the diagnostic evaluation.
- There are no "objective" physical findings or specific laboratory or radiograph abnormalities that characterize FM,



Fibromyalgia (FM) - diagnosis of exclusion

- A careful history and physical examination, rather than serologic testing, should be sufficient to differentiate (FM) from most rheumatic diseases,:
  - including rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), and Sjögren's syndrome (SS).
- Selected laboratory or imaging findings, in addition to the history and physical examination, may be useful in distinguishing FM from:
  - ankylosing spondylitis, polymyalgia rheumatica (PMR), inflammatory or metabolic myopathies, hypothyroidism, and other endocrine disorders in patients in whom one of these conditions is suspected clinically.
- Peripheral neuropathies, entrapment syndromes (such as carpal tunnel syndrome), and neurologic disorders (such as multiple sclerosis [MS] and myasthenia gravis) may mimic FM.
- Myofascial pain syndrome causes pain in one anatomic region, with tenderness being confined to that area. Some of the confusion lies in the differentiation between trigger points and tender points.
- FM is often present in patients together with other common functional somatic syndromes, including chronic fatigue syndrome (CFS), irritable bowel syndrome (IBS), migraine, and temporomandibular dysfunction, as well as chronic bladder and pelvic pain syndromes.
- Psychiatric disorders (Anxiety, depression) are common in FM and have symptoms that can mimic FM
- Sleep disturbances are common in patients with FM, including primary sleep disturbances, such as sleep apnea, restless leg syndrome, and repetitive leg movement disorders. These conditions have symptoms that can mimic FM, including nonrestorative sleep and fatigue
- Routine autoimmune serologic testing or creatine kinase or thyroid-stimulating hormone (TSH) are not useful.

Differential diagnosis of fibromyalgia

Disease	Features not present in fibromyalgia	Pitfalls in diagnosis
Rheumatoid arthritis	Joint swelling, elevated ESR and CRP	"False positive" rheumatoid factor in FM occasionally
Systemic lupus erythematosus	Rash and renal, cardiac, pulmonary, and neurologic features	"False positive" antinuclear antibody in some with FM and many symptoms
Polymyalgia rheumatica	Severe stiffness in the morning and when sedentary, elevated ESR and CRP, usual onset >60 years, rapid response to glucocorticoids	Like FM, often no abnormal physical findings in polymyalgia rheumatica
Polymyositis	Muscle weakness, elevated muscle enzymes, abnormal EMG/NCV	FM patients often feel weak (but have normal strength)
Spondyloarthritis	Restricted spinal motion, elevated ESR or CRP	May be no peripheral joint abnormality in spondyloarthritis
Lyme disease	Characteristic rash, joint swelling, serologic tests confirmatory	"Post-Lyme" FM symptoms, false positive serologic tests, early flu-like symptoms
Hypothyroidism	Abnormal thyroid function tests, pain not prominent	Hypothyroidism may present with a myopathy/mild myalgia
Neuropathy	Sensory or motor deficits, abnormal EMG/NCV	Subtle neurologic disorders, small fiber neuropathy in some with FM

ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; FM: fibromyalgia; EMG: electromyogram; NCV: nerve conduction velocity.

QUESTIONS

Question –T or F

Cigarette smoking can lead to RA and other AI diseases?

Question

Which drugs cause drug – induced Lupus?

Question –T or F

Men and Women are affected equally?

Question

What does MCTD mean?

Is it an AI disease?

Question –T or F

You can have more than one AI disease?

Question

Is Fibromyalgia an AI disease?

Question –T or F

The environment has nothing to do with AI disease?


Thank you
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