Autoimmune Diseases

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The immune system represents an interface between a constant everchanging external environment and an internal system that is striving to maintain homeostasis and defend its boundaries from harmful foreign invaders.

Primary Roles of the Immune System

- Identify potentially infectious or injurious substances
- Distinguish self-antigens from non-self-antigens
- Assess the potential level of threat posed by infectious, toxic or non-self-adherents
- Mount an appropriate response
- Repair any damage that ensues

Macrophages

- First cell type to act as a sentinel to detect and report about what it finds in the environment around it.
- Macrophage means "big eater."
- Constantly eating up a little bit of whatever surrounds it, cutting the ingested proteins up into small pieces (the antigens mentioned above), and then displaying these pieces of protein on its surface.

T Cells

- Macrophage presents these antigens to the T cell
- Primary decision maker in the immune process
- Highly specialized • Each are different from every other one.
- On their surface, T cells express a protein called the T cell receptor, which will bind to only one or a few antigens out of the thousands that are possible.
- When a macrophage and a T cell encounter one another, they see whether any of the antigens on the surface of the macrophage fit into the T cell receptor.
- Most of the time the antigens don't fit.
- If the antigens do match the T cell receptor, then the cells stick to one another.
- Through the action of chemical messengers, the T cell becomes turned on, or activated.

B Cells

- Each B cell is unique
- Instead of making specific surface proteins, B cells make proteins called antibodies that are released in the bloodstream
- These antibodies travel until they bind to the antigen that fits
- After an antigen is coated with antibodies, it is tagged for destruction
- Whether autoimmune disease will follow an autoimmune response depends upon both the quality of the immune response and the availability of the corresponding antigen.

B Cells

- Antigens on the surface of circulating cells such as blood cells are readily available to circulating antibody, and therefore such cells may be damaged or eliminated by autoantibody acting with complement, killer T cells, or phagocytes.
- The receptors on cell surfaces such as the TSH receptor on the thyroid cell or on the acetylcholine receptor at neuromuscular junctions may also be directly attacked by autoantibody.
- This interaction may result in stimulating the receptor in Graves' disease or in blocking the neuromuscular transmission as observed in myasthenia gravis

Other Causes of Autoimmunity

- Other autoimmune diseases are not due to the direct effects of autoantibody
- They are associated with T-cell-mediated immune responses
- Cytotoxic T cells may be generated that can damage their respective target cell.
- In other cases, cytokines are produced that are harmful to surrounding tissue cells.

How Common Are Autoimmune Diseases

- Affect more than 23.5 million Americans - 1:7 Americans incidence
- Autoimmune diseases constitute a leading cause of death among young and middle-aged women per NIH.
- Some autoimmune diseases are rare, while others, such as Hashimoto’s thyroiditis, affect many people.
- Some estimate that >50 million people have autoimmune disease as many cases are undiagnosed.
- According to the AADRA (American Autoimmune Disease Related Association), there are @ 80-100 conditions that are autoimmune related.

Who Gets Autoimmune Disease?

- It is also common for different types of autoimmune diseases to affect different members of a single family.
- Inheriting certain genes can make it more likely to get an autoimmune disease.
- A combination of genes and other factors may trigger the disease to start.
- Certain events or environmental exposures may cause some autoimmune diseases, or make them worse.
- Sunlight, chemicals called solvents, and viral and bacterial infections are linked to many autoimmune diseases.
- People of certain races or ethnic backgrounds.
    - For instance, type 1 diabetes is more common in white people.
    - Lupus is most severe for African-American and Hispanic people.
- More women than men have autoimmune diseases, which often start during their childbearing years.
    - The statistics are that women are more prone to autoimmune disease X16 more than men!

Autoimmune (AI) Disorders

- Immune system recognizes and reacts to all foreign substances in the body and tries to destroy them by forming antibodies
- The average adult has specific antibodies to up to 10 million antigens
- Sometimes the immune system works to hard and can attack it's own cells thinking they are foreign.
- The immune system is composed of two major parts.
    - One component, B lymphocytes, produces antibodies, proteins that attack "foreign" substances and cause them to be removed from the body; this is sometimes called the humoral immune system.
    - The other component consists of special white blood cells called T lymphocytes, which can attack "foreign" substances directly; this is sometimes called the cellular immune system.
- Over a lifetime, the immune system develops an extensive library of identified substances and microorganisms that are cataloged as "threat" or "not threat."
- Vaccinations utilize this process to add to the library.
- Normally, the immune system can distinguish between "self" and "not self" and only attacks those tissues that it recognizes as "not self."
- Autoimmune disorders are diseases caused by the body producing an inappropriate immune response against its own tissues.
- Sometimes the immune system will cease to recognize one or more of the body's normal constituents as "self" and will create autoantibodies – antibodies that attack its own cells, tissues, and/or organs. This causes inflammation and damage and it leads to autoimmune disorders.

Autoimmune Causes

- Normal tissue can be altered by a virus, drug, radiation
- Defective programmed cell death may malfunction
- Heredity
- Hormonal changes
- Middle age and elderly

What about diet?

- "Single nutritional components have the capability to potently modulate autoimmune responses and inflammation."
- Avoiding foods such as **red meat, eggs, vegetable oils** fried foods, sugar, dairy products, refined carbs, gluten, alcohol, and caffeine might be necessary to limit such flare-ups.
- Nightshade vegetables, such as tomatoes, potatoes, eggplant, and peppers, can also be problematic.

Autoimmune disorders fall into two general types:

- Systemic autoimmune diseases
  - RA, JRA, SLE, Polymyalgia Rheumatica
  - Guillain-Barre syndrome
- Localized
  - Type 1 Diabetes Mellitus, Hashimoto's thyroiditis, Graves' disease ,Celiac disease, Crohn's disease, Ulcerative colitis, Multiple sclerosis , Addison's disease
- S & S
  - Fever, fatigue, malaise
  - Other symptoms depend on the organ involve
- Diagnosis
  - History
  - Blood tests – ESR, CRP, RF, ANA, ELISA
- Treatment
  - Some drugs suppress the immune system
  - Some drugs reduce the inflammatory response
    - Steroids, NSAIDs
- Prognosis
  - Some AI disorders resolve
  - Most are lifelong chronic diseases needing lifelong care

Here are the top 14 AI Diseases

1. Type 1 diabetes - Pancreas
2. Rheumatoid arthritis (RA) - Joints
3. Psoriasis/psoriatic arthritis - Skin
4. Multiple sclerosis - Nerves
5. Systemic lupus erythematosus (SLE) - Skin and internal organs
6. Inflammatory bowel disease - Colon
7. Addison’s disease - Adrenal gland
8. Graves’ disease - Thyroid
9. Sjögren’s syndrome - Eyes and mouth
10. Hashimoto’s thyroiditis - Thyroid
12. Autoimmune vasculitis - Blood vessels
13. Pernicious anemia - RBC
14. Celiac disease - Colon

Type 1 Diabetes Mellitus

- Genetic susceptibility
  - Failure of beta cells by autoimmune destruction, requires insulin therapy
- Immunologically mediated destruction of beta cells
- Manifestations:
  - Hyperglycemia
  - Polydipsia
  - Polyuria
  - Polyphagia
  - Weight loss
  - Fatigue

Pancreatic Islet Cells

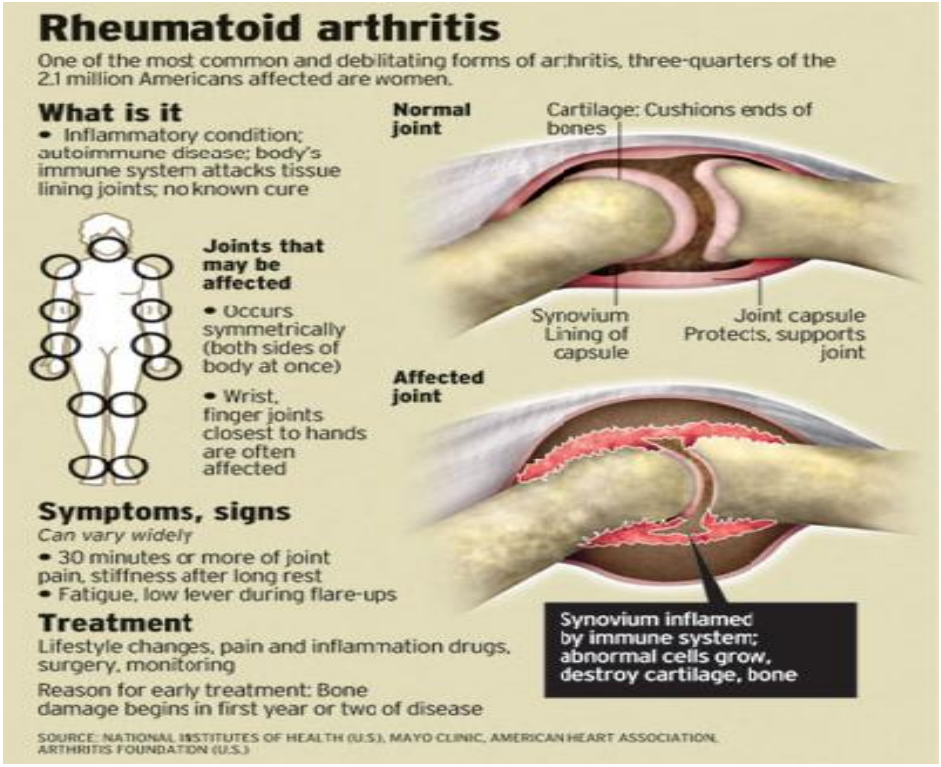
- Function: regulate blood glucose levels through the production of insulin and glucagon
- Diabetes Mellitus: most common endocrine disorder
- Two forms, with differing pathogenesis:
  - Juvenile onset DM, type I DM, insulin-dependent DM
  - Maturity onset DM, type II DM, non-insulin-dependent DM

Rheumatoid Arthritis

- Most common autoimmune disorder
- Inflammatory arthritis affecting 1% population
- An autoimmune disease causing chronic joint inflammation
- A progressive illness that has the potential to cause joint destruction and functional disability
- Affecting approximately 1.3 million people in USA
- Three times more common in women as in men
- It afflicts people of all races equally
- Can begin at any age, but it most often starts after age 40 and before 60
- In some families, multiple members can be affected, suggesting a genetic basis for the disorder
- RA S & S
  - Symmetrical small joint pain with pronounced morning stiffness (morning gel), low grade fever, joints deformed
- RA Diagnosis
  - ESR, RF, ASO titer, HLA (human leukocyte antigen)
  - Joint fluid contains WBC, biopsy rheumatoid nodules
- RA Treatment
  - Supportive – rest, PT, hold and cold packs, DME
  - NSAIDs, Methotrexate, antimalarials
- RA Prognosis
  - 50-75% remission in a few years, the rest have progressive disease process and dies 10-15 years premature

Rheumatoid Arthritis – continued

- What causes rheumatoid arthritis?
  - Cause is largely unknown
  - Has a strong genetic link
  - It is suspected that certain infections or factors in the environment might trigger the immune system to attack the body's own tissues
- RA Symptoms
  - Come and go, depending on the degree of inflammation
  - When body tissues are inflamed, the disease is active
  - The course of rheumatoid arthritis varies from patient to patient, and periods of flares and remissions are typical
  - Inflammation usually symmetrical and of the small joints
    - Pronounced morning stiffness – "morning gel"
  - Rheumatoid arthritis and inflammation of organs - can affect organs and areas of the body other than the joints
    - Sjogren's syndrome is inflammation of the glands of the eyes and mouth and causes dryness of these areas
    - Rheumatoid inflammation of the pleura
    - Pericarditis
    - Can have lowered RBC (anemia) and WBC
    - Felty's Syndrome (lowered WBC and splenomegaly)
- RA Diagnosis
  - Positive RF (rheumatoid factor) and RF titer, ASO titer
  - WBC changes
  - Joint fluid with WBC and proteins
  - X-ray changes
- RA Treatment
  - Supportive and appliance measures
    - Hot and cold packs, walkers, etc.
  - NSAIDs and COX2 inhibitors
  - Steroids are the main treatment
  - Rest and mild ROM exercise



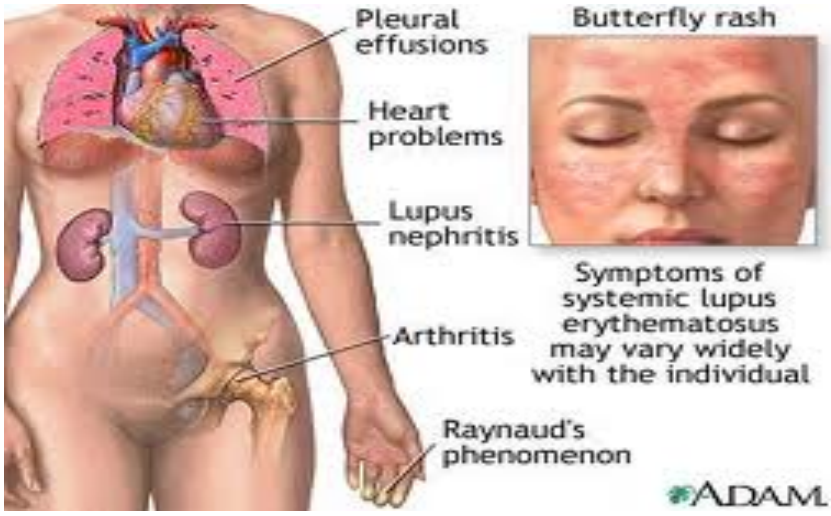
Juvenile Rheumatoid Arthritis (JRA) causes joint inflammation and stiffness for more than six weeks in a child aged 16 or younger – affects 50,000 children

Multiple Sclerosis (MS)

- Possibly caused by an interaction between a viral illness in teen years and a genetic predisposition
- Arises through a single mechanism of lesion
  - Focal, chronic, progressive
- Areas of demyelination are called plaques
- Optic neuritis is often the first symptom
- Chronic exacerbation and remission
- Triggers: infection, medication, stress, fatigue

SLE – Systemic Lupus Erythematosus

- Generalized AI involving joints, skin, brain, mucus membranes, kidneys, bone marrow, vessel walls
- 50,000 new cases per year
- 90% are young women in their late teens to 30s
- Four types:
  - Systemic lupus erythematosus – most common
  - Drug-induced lupus – resolves when drug stopped
  - Discoid lupus – affects skin with the classic butterfly rash
  - Neonatal lupus – transmitted to fetus
- Spontaneous remissions & relapses is the typical course
- S & S
  - Arthralgia (95%), inflammatory arthritis (90%)
  - Fever (90%), fatigue (81%) rashes (74%)
  - Anemia, kidney involvement, chest pain, alopecia
  - Cognitive dysfunction, photophobia, headaches
  - Blood clotting problems, Raynaud's
  - Mucosal ulcers, pericarditis, vasculitis
  - Seizures, psychosis, peripheral neuropathy
- Diagnosis
  - Confirmed by four or more of the above symptoms
- Lab tests
  - ANA (95%), RF usually negative, antibodies (40%)
  - Anemia (60%), proteinuria, hematuria
  - Tissue biopsy of rash

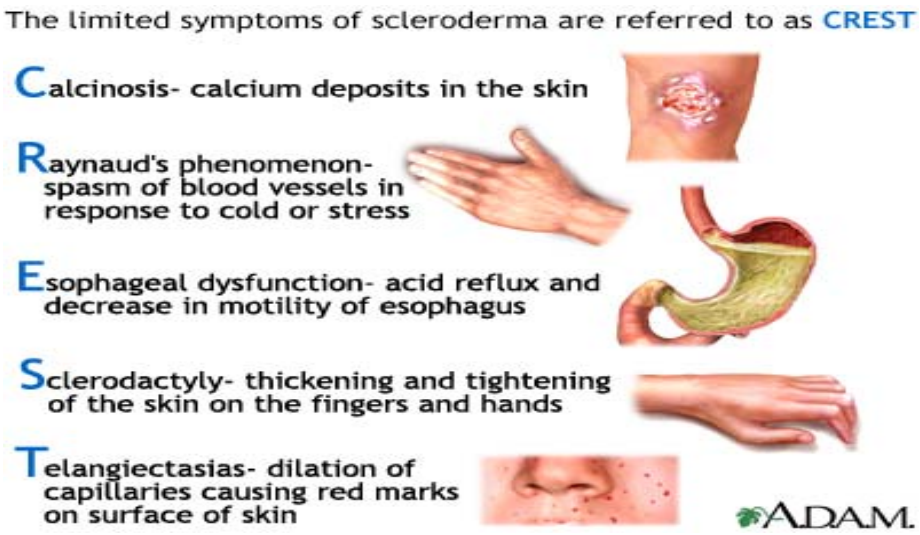


SLE – Systemic Lupus Erythematosus

- Treatment
  - Very little western treatment effective – supportive
  - Avoid sun exposure with rash
  - NSAIDs
  - Hemodialysis is needed
  - Other meds
    - Hydroxycortisone, prednisone, Medrol
    - Decadron
    - Topical corticosteroid creams and ointments
    - Cytoxan, Imuran, Methotrexate
    - Antimalarials
    - DHEA

Scleroderma

- Inflammation and fibroids in connective tissue, skin and supporting tissues around joints
- More in women
- Signs and Symptoms
  - Skin hardening, tendon friction rubs, migratory polyarthritis (90%), low grade fever, spider veins, calcified lumps, dysphagia, heatburn, GI tract fibrosis, pulmonary fibrosis
  - Usually starts with Raynaud's, finger swelling and tightness
- CREST syndrome – less severe form
    - C – calcium deposits
    - R – Raynaud's of fingers and toes
    - E – Esophageal dysfunction
    - S – Sclerodactyly –finger hardening
    - T – Telangiectasia – spider veins
- Diagnosis
  - Suggestive history and physical
  - Positive ANA, ELISA, skin biopsy thickened skin
- Treatment
  - No current effective western care
  - Supportive treatment
  - NSAIDs, corticosteroids
- Prognosis
  - Course varies widely and progresses to rapid decline and death
  - Survival rate averages 9 years



Crohn's Disease

- Chronic lifelong illness thought to be an autoimmune inflammatory disease
- S & S
  - Pain, cramping, fever, malaise, weight loss, frequent bowel movements
  - 50% involve small & large intestine, 35% involve small intestine only, 15% involve only large bowel
- Diagnosis
  - Clinical history with x-ray findings
- Treatment
  - Strict nutritional program with low lactose, low fiber, vitamin and mineral supplements
  - Corticosteroids (Prednisone)
  - Antibiotics (Flagyl)
  - Immunosuppressant drugs (Imuran)

Ulcerative Colitis

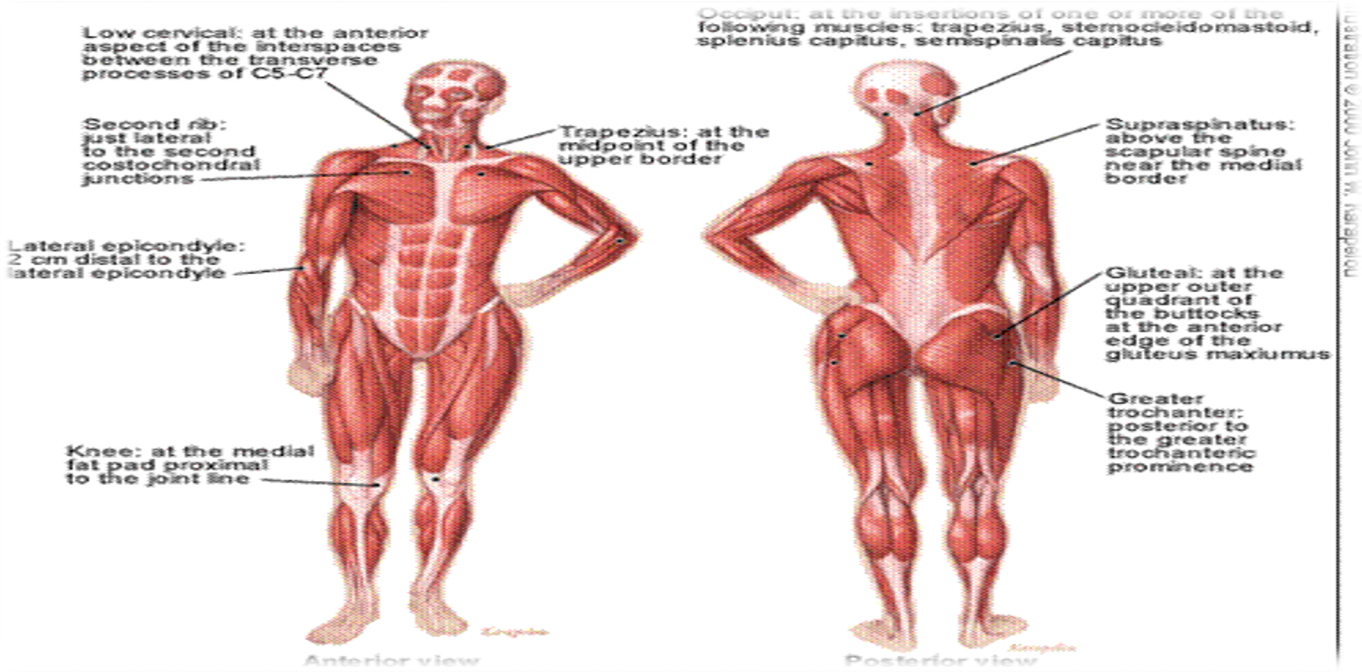
- Lifetime inflammatory auto-immune disorder
- Confined to the colon only
- S & S
  - Severe disorder with bloody diarrhea, cramping, and abdominal pain
  - Fecal urgency 5-10 x per day, with blood & mucus
  - Weight loss, anemia, low-grade fever
- Diagnosis
  - Sigmoidoscopy with mucosal biopsy
- Treatment
  - High fiber diet
  - Imodium
  - Corticosteroids
  - Mesalamine suppositories
- Prognosis - High risk of colon cancer

Hyperthyroidism – Grave's Disease

- Thyroid gland produces thyroxine hormone
- An autoimmune disorder
- Significantly accelerates metabolism
    - Sudden weight loss, a rapid or irregular heartbeat, sweating, nervousness or irritability
    - Fatigue, muscle weakness, difficulty sleeping
    - Tremor, sweating
    - Changes in menstrual patterns
    - Increased sensitivity to heat
- Causes
    - Graves' disease, an autoimmune disorder, is the most common cause of hyperthyroidism
        - Antibodies produced by your immune system stimulate your thyroid to produce too much thyroxine
    - Hyperfunctioning thyroid nodules
    - Thyroiditis
- Diagnosis
    - Radioactive iodine uptake test
    - Thyroid scan
    - Increased T3 & T4
    - Increased ANA titers
- Treatment
    - Beta blockers (atenolol) block increased sympathetic stimulation
    - Thioamides – block production of thyroid enzymes
    - Increased iodine intake
    - Radioactive iodine
    - Lifetime thyroxine replacement if surgery utilized

Fibromyalgia and Chronic Fatigue Syndrome

- The diagnostic criteria are twofold
    - Widespread pain and tenderness in 11 of 18 defined points
    - PMS Symptoms include non-restorative sleep, chronic fatigue, stiffness, and headache, migraine, IBS, TMJ, and mood disorders
- CFS symptoms include
    - Profound fatigue, myalgia, sleep difficulties, low grade fever, pharyngitis, lymphadenopathy



- Fibromyalgia treatment
  - Exercise decreases symptoms, overuse increases symptoms
  - Very light Chiropractic techniques
  - Consider PT with TENS and massage therapy
  - Tai chi – ROM Dance
  - It is best to treat softly and tenderly
  - Remember to not aggravate
- Lifestyle Changes
  - Eliminate consumption of coffee, smoking, and alcohol
  - Consider aggravating factors of body mechanics at work and home

Polymyositis & Dermatomyositis

- Polymyositis – disabling muscle weakness
- Dermatomyositis – hyper-pigmentation rashes
  - Both occur in 40-60 year old's
  - S & S
    - Affects large muscles in shoulders and hips
  - Diagnosis
    - Muscle weakness of shoulders and hips in middle age is suggestive, characteristic skin rash
    - EMG, muscle biopsy
  - Treatment
    - Steroids and immunosuppressive drugs

Vasculitis – Polyarteritis Nodosa

- Inflammation of the walls of blood and lymph vessels
  - Damaged wall, resulting in either
    - aneurysm: thin and weak wall
    - stenosis and occlusion: thickened wall
  - Vasculitis in general
    - there are 20 different types of Vasculitis
    - Vessels can be in any organ; isolated in one (generally the skin) or systemic (multiple organs)
- Pathophysiology
  - Autoimmune of blood vessel walls, disrupting blood supply to the organ, starts at 40-50, more in women
  - Often triggered by hepatitis, streptococcus
- S & S
  - Gradual onset often associated with joint and connective tissue inflammation
  - Fever, paresthesia, weakness, weight loss, extremity pain
  - Kidney damage (75%), liver arteries
  - Mesenteric vessels, coronary arteries
  - Peripheral nerves, rashes and ulcers common
- Diagnosis
  - Typical picture with elevated ESR, antibodies (75%)
  - Biopsy of involved vessels and nerves
  - Angiography occlusion
- Treatment
  - Corticosteroids
  - Immunosuppressive drugs
  - BP meds
- Prognosis
  - Very fatal Autoimmune
  - Without treatment – 67% die with 1 year, 88% in 5 years
    - Worse if renal involvement
  - With treatment – 5-year survival to 60%