Immune Study Guide Part 2- SLE and RA

Systemic Lupus Erythematous (SLE)

- SLE is a multisystem inflammatory autoimmune disease.
- Unpredictable course with alternating periods of remission and worsening disease
- Unknown cause of abnormal immune response
    - Most probable causes
        - Genetic influence: high prevalence among family members
        - Hormones: menses, oral contraceptives, pregnancy
        - Infections: Epstein Barr virus
        - Environment factors: sun, UV light, stress, chemicals, toxins
        - Drugs: occurs months to years after continuous therapy with a causative drug
- 90% are women.
- Most develop disease between ages 15 to 45 years.
- Autoantibodies are made against bodies own cells.
- Circulating immune complexes deposited in basement capillary membranes of kidneys, heart, skin, brain, and joints.
- Severity of SLE varies widely.
- **Ranges from a relatively mild disorder to rapidly progressive disease affecting many bodily systems.**
    - No characteristic pattern occurs with progression.
    - Most commonly affects skin, muscles, lining of lungs, heart, nervous tissue, and kidneys.
    - General: fever, weight loss, joint pain, and excessive fatigue precede worsening disease activity
- **Integumentary**-Vascular skin lesions(discord), Malar butterfly rash, oral or nasopharyngeal ulcers, and alopecia is common.
- **Musculoskeletal/Joints**-Polyarthralgia with morning stiffness, muscle pain, diffuse swelling that is often nonerosive, swan neck deformity in fingers, ulnar deviation, hypermobile and double jointed. *Increased risk of bone loss and fracture
- **Cardiopulmonary**-Raynaud's Phenomenon, dysrhythmias, pericarditis, myocarditis, and endocarditis.
- *Risk of coagulation disorder, stroke, gangrene and heart attack.
- **Renal-– 40% of SLE patients develop kidney problems that need medical evaluation and treatment. Usually present within 5 years after diagnosis.**
    - Proteinuria, glomerulonephritis, end stage renal disease (ESRD)
    - Treatment: Corticosteroids and immunosuppressive agents

- **Hematologic systems**-Antibodies against blood cells, Anemia, Leukopenia, Thrombocytopenia Coagulation disorders
    - *People with SLE are likely to be resistant to the blood thinning effects of aspirin
    - *Hydroxychloroquine may decrease risk of clots
- **Neurologic systems-** Headache, seizures, stroke, aseptic meningitis, peripheral neuropathy, disordered thinking, disorientation, depression, anxiety, and psychosis.
- **Reproductive system**-Menstrual irregularity is common.
    - **Increased susceptibility for infections**
    - Impaired ability to destroy invading bacteria, deficient production of antibodies, and immunosuppressive effect of many anti-inflammatory drugs.
    - Pneumonia is most common infection.
        - Vaccinations are generally safe for lupus patients. Must be cautious receiving because of immunosuppressant medications.
        - Patients receiving corticosteroids or cytotoxic drugs **must avoid live virus vaccines.** (Measles, mumps, and rubella, Chickenpox, and Nasal flu mist.)
        - **Influenza vaccine injection, pneumonia, and hepatitis are NOT LIVE Vaccines**
- No specific test is diagnostic.
- Variety of abnormalities in blood
    - **Antibodies: ANA is present in 97%**
    - Testing for anti-DNA antibodies, anti-Smith antibodies, antiphospholipid antibodies
        - Expected to identify immunologic disorders typical of SLE.
    - Increased ESR, CRP indicate inflammation.
        - May help monitor disease activity, treatment effectiveness.

Increased ESR and CRP indicate inflammation but are not diagnostic of SLE

- **CBC**
- **Urinalysis**
- **X-rays of affected joints and chest x-ray**
- **ECG to assess cardiac involvement.**

If at least FOUR of the criteria on the list, either at the present time or at some time in the past, there is a strong chance of lupus.

Mnemonic = SOAP BRAIN MD

Remember lupus related problems relate to systemic inflammation or redness from attacking its own cells

1. **S**erositis – inflammation of the lining around the lungs (pleuritis) or inflammation of the lining around the heart that causes chest pain which is worse with deep breathing (pericarditis).
2. **O**ral ulcers – sores appearing in the mouth.
3. **A**rthritis – joint pain and swelling of two or more joints in which the bones around the joints do not become destroyed.
4. **P**hotosensitivity – a reaction to sun or light that causes a skin rash to appear or get worse.
5. **B**lood disorder – anemia (low red blood cell count), leukopenia (low white blood cell count), lymphopenia (low level of specific white blood cells), or thrombocytopenia (low platelet count)
6. **R**enal disorder – persistent protein or cellular casts in the urine
7. **A**bnormal antinuclear antibody (ANA-+) ANA is present in 97% of lupus patients.
8. **I**mmunologic disorder –anti-DNA or anti-Sm or positive antiphospholipid antibodies
9. **N**eurological disorder – seizures or psychosis
10. **M**alar rash – a rash over the cheeks and nose, often in the shape of a butterfly
11. **D**iscoid rash – a rash that appears as red, raised, disk-shaped patches.

Medication management:

NSAIDS- Used to treat mild pain and inflammation. Mild joint pain – monitor for GI and renal impact.

May need to try multiple different NSAIDs to find the most effective one.

*Warfarin or low dose heparin may be prescribed for blood clots related to SLE

Steroid- Sparing drugs (Helps keep steroid dosing low)- Methotrexate works by decreasing inflammation, which can reduce pain and prevent long-term injury to the joints and skin.

Antimalarial drugs – Hydroxychloroquine *** Should have eye exams every 6-12 months because retinopathy can develop over time with high doses. Generally, reverses when medication is stopped. ***

Repress the immune system but do not cause immunosuppression. Fatigue, skin and joint problems; reduce flares. Reduces thromboembolic complications.

Corticosteroids

High dose may be appropriate for severe cutaneous SLE flares. Short term use preferred should be limited to the lowest does for the shortest possible time. Taper dose slowly and do not abruptly stop.

Immunosuppressive drugs

Suppress immune system and decrease end-organ damage. May help decrease need for steroids.

Topical immunomodulators

Used for serious skin conditions.

Suppress immune activity of the skin.

Can be used instead of corticosteroids to treat serious skin conditions (Useful in treating malar rash and discoid lesions.)

***Hydroxychloroquine (Plaquenil) *TAKES 1-3 months to be effective*

Antimalarial/antirheumatic

Use: SLE, RA, Malaria

Monitor- CBC, Liver function test (LFT), glucose, assess for decreased deep tendon reflexes, and rash.

Side effects: Hepatotoxicity, Dysrhythmia, retinal damage.

EDUCATION: Eye exam every 6-12 months* Call HCP -fever, bleeding, bruising, or visual changes.

- Assess- Pain and fatigue; ability to perform ADLs, renal function, tissue perfusion and psychological status.
- Disease flare symptoms
    - Fever patterns, joint inflammation, limitation of motion, location and degree of discomfort, fatigue
    - Monitor weight, fluid intake and output.
    - 24-hour urine samples for protein, creatinine clearance
    - Observe for signs of bleeding (drug therapy)
- Psychosocial issues- **Provide the patient a safe space to express what stressors they are experiencing.**
    - Supportive therapies important to cope with the disease.
        - Emotional support, especially during a flare-up
        - Stress importance of planning recreational and work activities
        - Assist patient in developing reasonable goals.
        - Patient concerns about marriage, careers, plan.

Pregnancy with SLE

- For best outcomes pregnancy should be planned when disease activity is minimal.
  Some drugs should be stopped such as methotrexate or switched up to 3 months before the patient tries to become pregnant.
- Mothers are at increased risk for thrombosis and flares during the postpartum period.

Flares are common during postpartum period. Therapeutic abortion offers the same risk for postdelivery exacerbation as carrying fetus to term.

- **Women with <u>serious SLE</u> - Counsel against pregnancy**

- **Expected Outcomes**
    - Use energy conservation techniques.

    - Adapt lifestyle to current energy-schedule rest period/days.
    - Adherence to medication regimen-Educate if medication takes weeks to months to work/help.
    - Maintain skin integrity with use of topical treatments.
    - Prevent disease flare with use of sunscreens and limited sun exposure-cover with clothing.
    - Maintain positive self-image.
- **Goal: prevent exacerbation**
- **Maintain good nutrition-Eat fatty fish- Mackerel, sardines, salmon, or tuna. Increase Omega3. Increase calcium (beans, dark green vegetables, cheese, low-fat milk, plant milks fortified with calcium, tofu, and yogurt.)**
- **Avoid exposure to infections. Seek medical attention if contract infection or acute illness because it will cause an exacerbation/ flare.**
- **Teach client about medications.**
- **Avoid sunlight exposure.**
- **Call HCP before taking immunizations- Avoid live vaccine if on immunosuppressant medication.**
- **Avoid pregnancy if show serious effects in systems-**
    - **Educate on postpartum flares and infertility.**

Rheumatoid Arthritis (RA)

Rheumatoid Arthritis (RA) is a chronic systemic autoimmune disease characterized by inflammation of connective tissue in the diarthrodial (synovial) joints. RA is typically marked by periods of remission and exacerbation.

RA most often begins in women between ages 30-60years. It is rare in men under age 45 years of age. Almost 3 times as many women have RA than men.

The cause of RA is unknown but is thought to be caused by a combination of genetics and environmental triggers.

Without adequate treatment more than 60% of patients with RA may develop marked functional impairment within 20 years of diagnosis. Includes need for mobility aids, loss of self-care ability & need for joint reconstruction.

- RA is marked by the presence of autoantibodies to this abnormal IgG. The autoantibodies are known as rheumatoid factor (RF).
- Activated CD4 cells cause monocytes, macrophages, & synovial fibroblasts to secrete the proinflammatory cytokines interleukin-1 (IL-1), interleukin-6 (IL-6), & tumor necrosis factor (TNF).
- These cytokines drive the inflammatory response in RA.
- Some patients report precipitating stressful event.
    - Research has not correlated such events with RA onset.
- Genetic link
    - Genetic predisposition important in RA development
        - Role of human leukocyte antigens (HLA)
        - HLA-DR4 and HLA-DR1 antigens
- Smoking increases risk in patients genetically predisposed and may interfere with treatment.
    - Smoking cessation can reduce risk of developing RA.

Onset is often subtle.

Nonspecific manifestations:

Fatigue, anorexia, weight loss, and general stiffness

Specific joint involvement is marked by:

Pain, stiffness, limited motion, and signs of inflammation (warmth, swelling, and pain.)

Stiffness becomes more localized in the following weeks to months.

******Morning stiffness lasting longer than 60 minutes. Joint stiffness after periods of inactivity*****

- Pain increases with motion, intensity varies.
    - May not be related to degree of inflammation.
- Joint symptoms occur symmetrically.
- Affect the small joints of hand (PIP, MCP) and feet (MTP)

- Affect larger joints such as:
    - Wrists, elbows, shoulders, knees, hips, ankles, cervical spine and jaw.
- Tenosynovitis affects wrists.
- Carpal Tunnel Syndrome symptoms, difficulty grasping objects.
- With progression, inflammation and fibrosis may cause deformity and disability.
- Subluxation—muscle atrophy and tendon destruction
- Walking disability
    - **Hallux valgus (Bunion formation)**
- Deformities in the hands
- **Ulnar deviation/drift, swan neck, and boutonnière's deformity**
- Can affect everybody system.
    - More likely in persons with high levels of biomarkers, such as RF
        - Atherosclerosis – chronic inflammation that damages endothelial cells within blood vessels.
        - More cholesterol plaques form
        - Lead to heart attack or stroke when they break loose.
        - Risk of heart attack 60% higher than persons without RA
- Rheumatoid nodules-develop in about half the patients with RA. These nodules appear subcutaneously as firm, nontender, granuloma-type masses.
- Nodular myositis & muscle fiber degeneration can cause pain like that of vascular insufficiency.
- Sjogren's syndrome can occur by itself or in conjunction with other arthritic disorders such as RA & SLE. Affected patients have diminished lacrimal & salivary gland secretion, leading to a dry mouth, burning, itchy eyes with decreased tearing, & photosensitivity.
- Felty syndrome is rare but can occur in patients with long-standing RA. Felty syndrome is an enlarged spleen & low white blood cell (WBC) count. Patients with Felty syndrome are at increased risk of infection & lymphoma.
- Flexion contractures & hand deformities cause diminished grasp strength and affect the patient's ability to perform self-care tasks.
- Depression also may occur. However, it is unclear if people become depressed from struggling with chronic pain & disability, or if depression is part of the autoimmune disease process.
    - Levels of CRP, a marker of inflammation, are higher in patients with depression compared to those with no symptoms of depression.
- Raynaud's phenomenon- a problem that causes decreased blood flow to the fingers. In some cases, it also causes less blood flow to the ears, toes, nipples, knees, or nose. This happens because of spasms of blood vessels in those areas. The spasms happen in response to cold, stress, or emotional upset.

- **Positive RF occurs in about 80% of adults with RA.**
    - **Positive RF does not guarantee diagnosis.**
    - **Negative RF does not exclude disease.**
    - **Titers may rise during active disease.**
    - **Anti-CCP: antibody specific to RA**
    - **ANA: autoimmune reaction/activity, not diagnostic of RA**
    - **ESR, CRP: general indicators of active inflammation**
- **Tissue biopsy to confirm early inflammatory changes.**
- **X-Rays alone not diagnostic of RA**
    - **May show soft tissue swelling, bone demineralization in early disease.**
    - **Baseline for monitoring disease progression**
- **Bone scans more useful in detecting early changes.**
- **Progression**
- **Stage I**
    - Synovitis
    - X-ray: soft tissue swelling, possible osteoporosis, no joint destruction
- **Stage II**
    - Increased joint inflammation.
    - Gradual destruction in joint cartilage
    - Narrowing joint space from loss of cartilage
- **Stage III**
    - Formation of synovial pannus
    - X-ray: extensive cartilage loss, erosion at joint margins, possible deformity
- **Stage IV**
    - Inflammatory process subsides.
    - Loss of joint function
    - Formation of subcutaneous nodules
- Treatment advances have improved prognosis.
    - Aggressive early treatment
    - Caring, long-term relationship with health care team
- **Goals of drug Therapy for RA**

- Relieve symptoms such as pain and inflammation.
- Maintain joint function & ROM.
- Manage systemic involvement Delay disease progression.
- Because irreversible joint changes can occur as early as the first year of RA, HCPs aggressively prescribe DMARDs. These drugs may slow disease progression and decrease the risk for joint erosion and deformity. The choice of drug is based on disease activity, the patient's functional level, and lifestyle considerations, such as the wish to become pregnant.
- **Classes of Antiarthritic Drugs**
- - NSAIDs - **Nonsteroidal anti-inflammatory drugs** (Help with pain and inflammation)
    - **NSAIDs and salicylates**
    - Treat pain and inflammation
    - Do not delay progression of RA.
    - May take 2 to 3 weeks for full effectiveness.
    - Check Salicylate levels if taking more than 3600 mg daily.
    - Celecoxib (Celebrex): COX-2 inhibitor
        - May be more manageable.
        - Can be taken only 1-2X/day.
- **- Disease-modifying anti-rheumatic drugs (DMARDs) act by altering the underlying disease rather than treating symptoms. They are not painkillers, but they will reduce pain, swelling and stiffness over a period of weeks or months by slowing down the disease and its effects on the joints. (2 types) Monitor for liver toxicity and bone marrow suppression.**
- - Nonbiologic DMARDs (traditional DMARDs) "shotgun approach" not as specific
- Methotrexate is preferred for early treatment and can help delay joint degeneration and systemic effect. It has a lower risk for toxicity than other drugs. Rare but serious side effects include bone marrow suppression and liver toxicity.
- Therapy requires frequent lab monitoring, including CBC and blood chemistry. The patient will begin to see therapeutic effects within 4-6 weeks.
- However, not everyone gets adequate relief from methotrexate alone.
- It can be given with other DMARDs or BRMs.
- Avoid use during pregnancy.
- Use adequate contraception.
- May require prophylactic use of PPI.
- Sulfasalazine (Azulfidine) and hydroxychloroquine (Plaquenil)
    - Used for mild to moderate disease.

    - Rapidly absorbed, relatively safe, well-tolerated
- Leflunomide (Arava)
    - Blocks immune cell overproduction.
    - Not used during pregnancy; teratogenic
- - Biologic DMARDs “sniper approach” – target certain steps / factors in the inflammatory process

BRMs. (Biologic Response Modifiers)

******Biologic therapies drug alert******

- **TB test and chest x-ray before start of therapy**
- **Monitor for infection and therapy may be temporarily stopped.**
- **Notify HCP if acute infection develops.**
- **Avoid live vaccinations for 4 weeks before starting drug.**
- **Report bruising, bleeding.**
- BRMs are used to slow disease progression. They can be used alone or in combination therapy with a DMARD, such as methotrexate. BRMs can be used to treat patients with moderate to severe RA who have not responded to DMARDs.
- We classify BRMs by their mechanism of action. These drugs all inhibit the inflammatory response.
- Biologic response modifiers (BRMs) target molecules or immune cells that are involved in the inflammatory process. ‘sniper’ approach. EXPENSIVE!

- - **Glucocorticoids**
- Adrenal corticosteroids
- **During disease flare-ups**
    - Corticosteroid therapy
        - Intraarticular injections
        - Low-dose oral for limited time to help treat acute flare-ups in addition to other primary medication regimen (not for long term treatment)

Synovectomy – remove all or part of synovium of a joint. Done only if pt does not respond to medication. Can be done by radiation and chemical injection however this is not widely available.

Total joint replacement (arthroplasty)

Overall goals

- Acceptable pain management and anti-inflammatory methods.
- Utilize medication regimen to slow disease progression and maintain joint function and range of motion.
- Take part in planning and implementing treatment plan.

- Maintain positive self-image.
- Perform self-care to maximum amount possible.
- Nondrug management may include the use of therapeutic heat and cold, rest relaxation techniques, joint protection, biofeedback, transcutaneous electrical nerve stimulation, and hypnosis.

    Energy conservation requires careful planning.

    - Alternate rest periods with activity (pacing)
        - Helps relieve pain and fatigue.
    - Amount of rest varies.
        - Based on disease severity, patient limitations
        - Avoid total bed rest.
        - 8 to 10 hours of sleep plus daytime rest
    - Modify activities to avoid overexertion and fatigue.
        - Can worsen disease activity.
- Good body alignment during rest
    - Firm mattress or bed board
    - Encourage positions of extension
    - Avoid flexion positions because of possibility of contractures forming.
    - No pillows under knees
        - Decrease risk for joint contracture.
    - Small, flat pillow under head and shoulders- Fluffy pillows can cause cervical deformity.
- Modify tasks for less stress on joints-Avoid repetitive motions.
- Work simplification techniques.
    - Organizing activities
    - Use of carts instead of caring
    - Convenient, easy-to-reach storage
    - Joint protective devices
    - Delegation
- Occupational therapy
    - Helps maintain upper extremity function.
    - Splinting and assistive devices for joint protection
    - Assistive devices such as Velcro, built up utensils, button hooks, push pull knobs.

- **Maintain joint in neutral position to minimize deformity.**
- **Use strongest joint available for any task.**
- **Distribute weight over many joints instead of stressing a few.**
- **Change positions often.**
- **Avoid repetitious movements.**
- **Modify chores to avoid stress of joints.**
- Relieve pain, stiffness, and muscle spasm.
- **Cold-Don't apply ice directly to skin.**
    - Especially beneficial during periods of increased disease activity
    - Application should not exceed 10 to 15 minutes.
    - Can be used several times a day.
    - Bags of frozen vegetables, ice
- **Moist heat- We want warm not hot!**
    - Relieve chronic stiffness.
    - Should not exceed 20 minutes at a time.
    - Heating pads, moist hot packs, paraffin baths, warm baths, or showers
        - Do not use with topical heat-producing cream (ICY HOT)
    - Be alert for burn potential.
- Balanced nutrition important
- Weight loss
    - Loss of appetite from fatigue, pain, depression
    - Food shopping, preparation impacted from limited endurance and mobility.
    - OT for assistance in home environment
- Weight gain
    - Corticosteroid therapy
    - The patient taking corticosteroids may become distressed as signs and symptoms of Cushing syndrome (moon face and redistribution of fatty tissue to trunk) changes their appearance. Encourage the patient to not change the dose or stop therapy abruptly.
    - Weight will return to normal several months after treatment ends.
- Decreased mobility
- Meals on Wheels type program may be helpful for progressed RA or family/ friends preparing food. Patient may need to live in an assisted facility if financially able.

- Chronic pain or loss of function may make the patient vulnerable to claims of false advertising about unproven.
- Chronic pain or loss of function may make the patient vulnerable to claims of false advertising about unproven or even dangerous remedies.
- Help the patient recognize fears and concerns faced by all people who live with chronic illness.
- Allow the patient to express their concerns and what barriers they have related to RA.
- Allow the patient to describe their stressors and try to assist find resources to assist them.
- Living with chronic pain may lead to depression. To decrease depressive symptoms, suggest activities such as Music, reading, exercise, counseling, hypnosis, biofeedback, etc.
- Polypharmacy can affect lab values Polypharmacy can cause increased interactions.
- Need simple drug regimen to improve adherence.
- Need collaboration among providers.
- Musculoskeletal pain and weakness could be related to depression and inactivity.