LEARNING OBJECTIVES:

Medical Knowledge: Students should be able to define, describe, & discuss:
1. The way to approach a patient with a potential rheumatic disease & order appropriate diagnostic tests based on pre-test probability of disease
2. The various auto-antibodies and what their presence signifies in disease pathogenesis
3. The utility of synovial fluid recovery and the interpretation of the fluid.
4. The basic role of genetics in autoimmune disorders

Patient Care: Students should be able to demonstrate specific skills, including:
1. How the patient’s history & physical lead one to choose subsequent diagnostic tests rather than performing a “shot-gun” approach to rheumatic disease
2. Understanding how the tests results help to rule in, rule out, or qualify the severity or classification of rheumatic disease
3. Appropriate ordering of radiologic tests
4. Suggest appropriate initial therapy for patients with rheumatic disease based on the diagnosis & symptoms.

Professionalism:
1. Be sensitive to risk-benefit, cost-benefit & evidence-based considerations in the selection of diagnostic and therapeutic interventions for rheumatologic problems
2. Recognize the importance of patient preferences when selecting among diagnostic and therapeutic options for rheumatologic problems.
3. Demonstrate ongoing commitment to self-directed learning regarding rheumatologic problems.
4. Appreciate the impact rheumatologic problems have on a patient’s quality of life, well-being, ability to work, & the family.

CASE I: (10 min)

Medical History: A 46 y/o woman with a history of hypothyroidism, acne & chronic hepatitis C (but no cirrhosis) presents with a 5 year history of diffuse arthralgia that are poorly localized & 10/10 in severity. The pain is constant, dull/aching in nature with no exacerbating or alleviating factors. She also reports some b/l knee pain that is worse with standing, walking & improved with rest. She reports associated poor, non-restorative sleep & depression. She denies associated morning stiffness, swelling, rashes, ulcers, fevers, weight loss. ROS (review of systems) is otherwise negative. Her past history is otherwise significant for a history of 3 normal pregnancies & a mother with SLE (systemic lupus erythematosus). She takes synthroid for her hypothyroidism & minocycline for her acne.

Physical Exam: WDWN (well-developed, well-nourished) woman with a BMI of 35. VSS (vital signs stable).
Positive Findings: Multiple tender points over her upper & lower back, anterior chest, arms & legs. Flattened affect. Bilateral knees have palpable crepitis with passive ROM
Negative Findings: No hair loss, skin rash, oral ulcers, joint swelling or deformity, or neurologic deficit.
Laboratory Data:
ANA (anti-nuclear antibody): 1:40
RF (rheumatoid factor): 50 (normal is < 20)
CCP (cyclic citrullinated peptide antibody): pending
ESR (erythrocyte sedimentation rate): 3 (normal <10)
CRP (C-Reactive Protein): <0.1

DISCUSSION

1. Formulate 3 differential diagnoses listed in order from more likely to less likely. Support your list with medical knowledge & exam skills of rheumatic disease learned in the previous lecture.

2. What are some reasons for this woman’s positive ANA?

3. What are some reasons for this woman’s positive RF?

4. Predict the result of this woman’s CCP antibody

5. Explain the significance of this woman’s ESR & CRP levels. Be able to draw what her sedimentation rate (in a test tube) would look like compared to someone’s ESR with severe rheumatoid arthritis might look like.

6. What additional lab tests, if any, would you like to order?

7. What radiologic tests, if any, would you like to order?

8. What treatments (general, e.g.: analgesics, NSAIDs, steroids, DMARDs, chemotherapy, anticoagulation, antidepressants (SSRI/SNRI), anti-neuropathic (eg: gabapentin)) would you offer her?

Notes:
CASE II: (10-15 min)

Medical History: A 30 y/o woman without prior medical history presents with 6 weeks of pain & swelling in her bilateral elbows, wrists, & ankles. The pain is 6/10, dull/achy, intermittent & worse in the morning when she wakes up. She notices improvement as the day progresses. She also takes about 800 mg of ibuprofen at least 4 times daily with moderate relief. She reports associated stiffness in the AM for at least 1 hour that improves with use, & some warmth over her painful joints. Aside from the joint symptoms, she notes severe fatigue that limits her daily activities, ulcers in her mouth, some hair thinning, and a rash over her cheeks in the shape of a butterfly that seems to worsen in the sun and lasts for about 1 week at a time. Her past history is otherwise significant for a history of 3-second trimester spontaneous abortions & a mother with SLE (systemic lupus erythematosus)

Physical Exam: WDWN (well-developed, well-nourished) woman with a BMI of 20. Her vital signs are remarkable for a BP of 160/90
Positive Findings: Temporal hair thinning, palpable malar rash, prominent cervical & axillary lymph nodes, ulcers on the upper hard palate, swelling/tenderness/warmth (aka “synovitis”) of her joints, & 1+ edema of her lower legs.
Negative Findings: No tachycardia, murmurs or rubs, abnormal breath sounds, eye abnormalities, or neurologic abnormalities

Laboratory Data:
ANA: 1:1280
RF: 10 (normal is < 20)
CCP: negative
ESR: 88 (normal <10)
CRP: 10 (normal < 0.8)
C3: 60 (normal > 85)
C4: 2 (normal > 20)
CBC w/ diff: WBC 2.5, Hgb 8, PLT 80

Nuclear antibodies (also known as ENA-extractable nuclear antigen panel at Loyola): All are normally < 1.0
RNP: >8.0
Sm (Smith)/RNP: >8.0
Smith (alone): 3.5
SSA: 3
SSB: <1.0
SCL-70: <1.0
ds (double stranded, or “native”) DNA: >300 (normal <10)

DISCUSSION

1. Formulate 3 differential diagnoses listed in order from more likely to less likely. Support your list with medical knowledge & exam skills of rheumatic disease learned in the previous lecture.
2. Compare & contrast the ANA screening test and the ENA tests in terms of specificity and sensitivity, & how this relates to their clinical utility.

3. This patient has multiple signs & symptoms, prioritize the next step in work-up. What clinical features led to this priority?

4. Her ESR is almost 100. What is the most likely explanation?

5. How might her past history of recurrent miscarriages relate to her diagnosis? What additional labs should you order?

6. You later find out that her fingers turn white, then blue in the cold weather with intense redness upon rewarming. Given her serologies (antibody profile), what other clinical syndromes/diseases should you be on the look-out for?

7. What treatments (general, e.g.: analgesics, NSAIDs, steroids, DMARDs, chemotherapy) would you offer her?

8. What “lupus activity monitoring” tests would you check at follow up?

Notes:

**CASE III:** (10 min)

**Medical History:** A 41 y/o man without prior medical history presents with 6 months of insidious skin changes. He first noticed his fingers turning white, then blue in the cold weather with intense redness upon rewarming about 6 months ago. Thereafter, he started getting intense pruritus over his fingers & slightly over his face with erythema, followed by tightening of the skin. He also noticed tiny ulcers at his fingertips. ROS is positive for very mild increased dyspnea on exertion. His past medical history is otherwise unremarkable, and he is on no meds.

**Physical Exam:** WDWN (well-developed, well-nourished) man with a BMI of 24. VSS Positive Findings: Decreased oral aperture; Erythema & thickening over all of the fingers & slightly over the hands with mild contractures of the fingers. Several pits at the finger pads just
below the nails with thin brittle nails. Extremities are cool with slightly decreased capillary refill and some visible capillary dilation at the cuticles.

Negative Findings: No tachycardia, murmurs or rubs, abnormal breath sounds, eye abnormalities, or neurologic abnormalities

Laboratory Data:
ANA: 1:1280  
ESR: 30 (normal <10)  
CRP: 0.5 (normal < 0.8)

Nuclear antibodies:  
RNP: < 1.0  
Sm/RNP: < 1.0  
Sm: < 1.0  
SSA: < 1.0  
SSB: <1.0  
SCL-70: pending  
dsDNA: <10

DISCUSSION

1. Formulate 3 differential diagnoses listed in order from more likely to less likely. Support your list with medical knowledge & exam skills of rheumatic disease learned in the previous lecture.

2. You visit the immunology laboratory to discuss the ANA & learn that the ANA immunofluorescence pattern is centromere. What screening tests, if any, do you want to do?

3. You see a similar patient in clinic with skin thickening extending over her wrists/elbows & chest as well as upper thighs. She also has shortness of breath & is found to have a positive SCL-70 antibody. What tests, if any, do you want to do?

4. This same patient is later admitted to the hospital with headaches & found to have a blood pressure of 180/100. She has new renal dysfunction with a creatinine of 2.0. What is happening, & what should you do? Bonus: what iatrogenic cause could have precipitated this?

Notes:
CASE IV: (5 min)

Medical History: A 50 y/o woman presents with severe fatigue & gradual onset of weakness in her shoulders and hips/thighs. She denies pain, but notices that it is difficult to get up from the couch or off of the toilet. Additionally, she has noticed purplish discoloration around her eyes and a red, scaly rash over her shoulders, her chest and her bilateral knuckles. ROS is positive for a 15 lb. weight loss in the past 1 month.

Physical Exam: Thin woman with a BMI of 19. VSS
Positive Findings: Rash noted around the eyes, shoulders, chest & knuckles; She has full aROM of her shoulders & hips, but she is unable to stand from a chair without using her arms, and her proximal muscle strength is 3+/5. She has faint crackles at her lung bases. She has very mild synovitis of several joints. Her nailbed have visible capillary dilatation
Negative Findings: Neurologic exam is normal & distal muscle strength is intact. No sclerodactyly.

Laboratory Data: ANA: negative
ESR: 85 (normal <10)
CRP: 20 (normal < 0.8)
CBC w/ diff: normal except for normocytic anemia
BMP: normal
ALT: 100
AST: 80
Alk Phos: normal

Radiologic Data: CXR: Mild basilar ground-glass opacities, otherwise normal

DISCUSSION

1. Formulate 3 differential diagnoses listed in order from more likely to less likely. Support your list with medical knowledge & exam skills of rheumatic disease learned in the previous lecture.

2. What further studies are likely to be helpful in confirming the suspected diagnosis?

3. In light of her weight loss & diagnosis, what additional counseling should you give her?

4. What treatments (general, e.g.: analgesics, NSAIDs, steroids, DMARDs, chemotherapy) would you offer her?

Notes:
Case V: (5 min)

Medical History: A 63-year-old man with a history of hyperlipidemia & chronic sinusitis is transferred from an outside hospital with a 2-month long history of general malaise, fevers, unintentional weight loss of twenty pounds, and cough. He noted bloody nasal discharge for the week prior to admission to the hospital. Chest CT done at the outside facility revealed two cavitating lung lesions bilaterally.

Physical Exam: Ill-appearing man, mildly labored breathing. Vitals: 100.3, 22, 144/80, 120. BMI 17
Positive Findings: Slight saddle-nose deformity; Coarse breath sounds bilaterally, Non-blanching, non-tender rash on his lower extremities with rough feel; and oozing crusts in his nose bilaterally
Negative Findings: No oral lesions, no eye abnormalities, or neurologic abnormalities

Laboratory Data:
ANA: negative
ESR: 110
CRP: 50
CBC w/ diff: WBC 15, Hgb 8, PLT 200
BMP: BUN 50, creatinine 5 (GFR is now in the 20's)
Urinalysis: 3+ protein, >30 RBCs, (+) RBC casts

DISCUSSION

1. Formulate 3 differential diagnoses listed in order from more likely to less likely. Support your list with medical knowledge & exam skills of rheumatic disease learned in the previous lecture.

2. The patient is found to have a high titer of c-ANCA (cytoplasmic-antineutrophilic cytoplasmic antibodies) on immunofluorescence with high titer follow up specificity for PR-3 (proteinase-3) on ELISA. Speculate how this may confirm the diagnosis, and how these antibodies may be pathogenic (HINT: reach back to host defense or MHD!)

3. If the immunofluorescence had been a different pattern or had been negative, what may that have suggested as a diagnosis? What if he had a history of asthma?

4. What treatments (general, e.g.: analgesics, NSAIDs, steroids, DMARDs, chemotherapy) would you offer him?
**CASE VI**: (5 min)

**Medical History:** A 30 y/o woman without prior medical history presents with 3 months of pain & swelling in her bilateral elbows, wrists, knuckles, & ankles. The pain is 6/10, dull/aching, intermittent & worse in the morning when she wakes up. She notices improvement as the day progresses. She also takes about 800 mg of ibuprofen at least 4 times daily with moderate relief. She reports associated stiffness in the AM for at least 3 hours that improves with use, & some warmth over her painful joints. Aside from the joint symptoms, she notes severe fatigue that limits her daily activities as well as dry, gritty eyes and feelings of cotton in her mouth. ROS is negative for ulcers in her mouth, hair thinning, rash, photosensitivity, chest pain or respiratory symptoms. She denies recent cold or flu illness. Her past history is otherwise significant for a mother with RA. She quit smoking about 1 year ago.

**Physical Exam:** WDWN (well-developed, well-nourished) woman with a BMI of 23. VSS
Positive Findings: Synovitis of her PIP, MCP, wrist, elbow, & ankle joints. Slight ulnar deviation of her fingers from her MCP joints with swan neck & boutinierre’s deformity of her fingers. Her sublingual salivary pooling is decreased & her conjunctivae b/l are slightly irritated. There are shotty cervical & axillary lymph nodes palpable.
Negative Findings: No oral or nasal ulcers, rash, nodules, edema, tachycardia, murmurs or rubs, abnormal breath sounds, or neurologic abnormalities.

**Laboratory Data:**
- ANA: 1:320
- RF: 200 (normal is < 20)
- CCP: pending
- ESR: 50 (normal <10)
- CRP: 5 (normal < 0.8)
- CBC: WBC 15, Hgb 10, Platelets 550

Nuclear antibodies:
- RNP: <1.0
- Sm (Smith)/RNP: <1.0
- Smith (alone): <1.0
- SSA: pending
- SSB: pending
- SCL-70: <1.0
- ds (double stranded, or “native”) DNA: <10

**DISCUSSION**

1. Formulate 3 differential diagnoses listed in order from more likely to less likely. Support your list with medical knowledge & exam skills of rheumatic disease learned in the previous lecture.
2. Can you make a diagnosis of RA?

3. Suppose the anti-CCP antibody returned negative, & SSA/SSB antibodies were high positive? What would be another likely diagnosis?

4. What additional tests, if any would you like to order?

5. What treatments (general, e.g.: analgesics, NSAIDs, steroids, DMARDs, chemotherapy) would you offer her?

Notes:

**CASE VII:** (5 minutes-if there is time. Synovial fluid takes priority)

**Medical History:** A 30 y/o man without prior medical history presents with 3 months of low back pain. The pain is 6/10, dull/achy, intermittent & worse in the morning when he wakes up. He notices improvement as the day progresses. He also takes about 800 mg of ibuprofen at least 4 times daily with moderate relief. He reports associated stiffness in the AM for at least 3 hours that improves with use. Aside from the joint symptoms, he has been having recurrent photophobia with eye discomfort. He denies GI symptoms or dysuria. He is a non-smoker and drinks only on occasion. He has been in a steady relationship for the past 5 yrs and denies a history of STIs.

**Physical Exam:** WDWN (well-developed, well-nourished) man with a BMI of 25. VSS

**Positive Findings:** Right eye with slight pain when light is shone into the pupil, mild erythema noted. TTP of the b/l sacroiliac joints, worse on the right.

**Negative Findings:** No skin rashes, no nail changes, no arthritis in peripheral joints

**Laboratory Data:**
ANA: negative
RF: 10 (normal is < 20)
CCP: negative
ESR: 25 (normal <10)
CRP: 1.5 (normal < 0.8)
CBC: WBC 8, Hgb 12, Platelets 400

**Radiologic Data:**
X-ray bilateral sacroiliac joints: negative for changes

**DISCUSSION**
1. Formulate 3 differential diagnoses listed in order from more likely to less likely. Support your list with medical knowledge & exam skills of rheumatic disease learned in the previous lecture.

2. Given that the plain film was negative, but your clinical suspicion is high, what genetic marker can help you make the diagnosis?

3. What radiologic tests, if any, would you like to order? And what do you expect to find?

4. What treatments (general, e.g.: analgesics, NSAIDs, steroids, DMARDs, chemotherapy) would you offer?

Notes:
MATCH THE SCENARIO WITH THE SYNOVIAL FLUID

<table>
<thead>
<tr>
<th>Case VIII:</th>
<th>Color</th>
<th>Yellow</th>
</tr>
</thead>
<tbody>
<tr>
<td>50 y/o obese man with pain on standing, ambulation. Exam reveals minimal warmth &amp; slight effusion of the left knee with crepitus, but good PROM</td>
<td>WBC/mm3</td>
<td>2000-50,000</td>
</tr>
<tr>
<td>% Neutrophils</td>
<td>&gt;50%</td>
<td></td>
</tr>
<tr>
<td>Case IX:</td>
<td>Color</td>
<td>Yellow</td>
</tr>
<tr>
<td>50 y/o obese diabetic man with a history of gout &amp; sudden onset of severe swelling of his left knee, exquisite pain with any motion, &amp; erythema over the joint. He has a low-grade fever. Exam reveals a red, hot, swollen joint; no active or passive range of motion allowed by patient. Bland tophi are noted over the elbows &amp; ears. His WBC count is 20.</td>
<td>WBC/mm3</td>
<td>200-2000</td>
</tr>
<tr>
<td>% Neutrophils</td>
<td>&lt;25%</td>
<td></td>
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<tr>
<td>Case X:</td>
<td>Color</td>
<td>Opaque</td>
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<tr>
<td>50 y/o obese diabetic man with a history of gout &amp; sudden onset of severe swelling of his left knee, right wrist &amp; left ankle. He complains of exquisite pain with any motion, &amp; erythema over the joint. He has a low-grade fever. Exam reveals 3 red, hot, swollen joints; no active or passive range of motion allowed by patient. Bland tophi are noted over the elbows &amp; ears. His WBC count is 20.</td>
<td>WBC/mm3</td>
<td>&gt;80,000</td>
</tr>
<tr>
<td>% Neutrophils</td>
<td>95%</td>
<td></td>
</tr>
<tr>
<td>Case XI:</td>
<td>Color</td>
<td>Yellow/Turbid</td>
</tr>
<tr>
<td>40 y/o woman with a h/o RA who recently stopped all her medications. She complains of a flare in her b/l wrists &amp; left knee. Exam reveals b/l wrist swelling &amp; moderate synovitis and effusion of the left knee with warmth, but no erythema.</td>
<td>WBC/mm3</td>
<td>&gt;80,000</td>
</tr>
<tr>
<td>% Neutrophils</td>
<td>85%</td>
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<tr>
<td>Case XII:</td>
<td>Color</td>
<td>bloody</td>
</tr>
<tr>
<td>The same guy from case VIII, but it is your first time tapping a knee &amp; the fluid come out dark red</td>
<td>WBC/mm3</td>
<td>5000</td>
</tr>
<tr>
<td>% Neutrophils</td>
<td>80%</td>
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