THE MEDICAL WORK-UP OF THE RED EYE

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Obtaining Samples and Methods of Evaluating Ocular Surface disease by laboratory methods:
- Conjunctival or corneal scrapings
- Impression cytology
- Conjunctival and corneal cultures
- Sensitivity testing

An excellent overview of these topics is available at: http://eyemicrobiology.upmc.com/Cytology.htm

What we will not cover -

The problem directed eye exam
- Systems review – even if it is only a checklist case history.
- Know the ophthalmic manifestations of the patient’s known systemic problems.
- Know the ocular side effects of the patient’s medications.
- Look for them specifically.
- Note their absence in the chart. Always chart SIGNIFICANT NEGATIVES.
- Ordering labs is NOT a substitute for a thorough, DIRECTED case history. Labs are to confirm suspicions based upon history and clinical findings.

What we will cover -
- Episcleritis
- Scleritis
- Anterior uveitis
  - Non-granulomatous
  - Granulomatous

NO FISHING
Most cases are idiopathic occurring more often in women than men and usually in their 30’s or 40’s.
A preliminary work-up is worth considering only if your directed case history leads to suspicion of an underlying systemic association.
Systemic associations found primarily through history in 1/3 of patients. Labs are to confirm.
No correlation between type, laterality or recurrences and presence of associated systemic disease.

Virtual any infectious disease can be associated with episcleritis – CBC with differential, looking for leukocytosis/eosinophilia.
- Bacteria, including tuberculosis, Lyme disease, and syphilis
- Viruses, including herpes
- Fungi
- Parasites

Miscellaneous:
- Atopy: rule out by history and skin appearance
- Foreign Body: rule out by history and exam
- Chemicals: rule out by history, measuring tear pH and exam

Do you understand the need to measure pH when EITHER liquid or powder gets into the eye?

<table>
<thead>
<tr>
<th>Average pH</th>
<th>Hay</th>
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<tr>
<td>1</td>
<td>vinegar (2-3)</td>
<td>6</td>
<td>white sugar</td>
</tr>
<tr>
<td>2</td>
<td>lime juice</td>
<td>6</td>
<td>salt</td>
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<tr>
<td>3</td>
<td>lemon juice</td>
<td>6</td>
<td>well water</td>
</tr>
<tr>
<td>4</td>
<td>vinegar</td>
<td>6</td>
<td>dish detergent</td>
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<tr>
<td>5</td>
<td>mustard</td>
<td>7.2</td>
<td>water, mucosal</td>
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<tr>
<td>6</td>
<td>Coke/orange</td>
<td>8</td>
<td>baking soda</td>
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<tr>
<td>7</td>
<td>Pepsi-Root</td>
<td>8.5</td>
<td>egg white protein (heal)</td>
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<tr>
<td>8</td>
<td>water, and</td>
<td>9</td>
<td>long relief</td>
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<td>9</td>
<td>bleach</td>
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<td>mustard</td>
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<td>11</td>
<td>cream</td>
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<td>12</td>
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<td>9.5</td>
<td>meal</td>
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<td>milk</td>
<td>11.5</td>
<td>[specific test]</td>
</tr>
<tr>
<td>14</td>
<td>water, tap</td>
<td>12</td>
<td>normal saline (0.9%)</td>
</tr>
<tr>
<td>15</td>
<td>water, distilled</td>
<td>12</td>
<td>dish detergent</td>
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</tbody>
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Tear off one inch strip, put one end in inferior cul-de sac until wet. Compare color to standards.
WebMD advice to the public regarding care for chemical burns to the eye

- Chemical Eye Burn Treatment
- 1. Flush the Eye
- Have the person put the eye or eyes under a faucet, shower, or clean container of water.
- Flush with lukewarm water for 15 to 30 minutes. The person should keep the eye open as wide as possible.
- Flush the eye to remove contact lenses. Do not try to remove them with hands.
- Do not place a bandage over the eye.
- 2. Get Help Immediately
- If you seek medical care, the health care provider will continue flushing the eye with saline solution, checking periodically until pH is normal.
- The health care provider may place anesthetic drops in the eye to decrease discomfort with flushing.
- BEFORE PASSAGE OF TPA THE OPTOMETRIST WAS LIMITED TO DOING NO MORE THAN ANY LAY PERSON. SINCE PASSAGE OF TPA YOU ARE EXPECTED TO FULFILL THE ROLE OF HEALTH CARE PROVIDER. NOTE THAT IRRIGATING TO NEUTRAL pH IS THE EXPECTED STANDARD OF CARE BEFORE CLINICAL ASSESSMENT.
- THIS IS TRUE WHETHER YOU ARE COMFORTABLE MANAGING THE CASE THEREAFTER OR YOU ARE REFERRING THE CASE IMMEDIATELY.
- A $20 roll will last a lifetime. Available many places including:
  http://kayesrecipesandremedies.com/products-page/health-supplements/ph-testing-paper-roll/

White blood cell count (WBC)
Total of all white blood cells of all types
Elevation of white count = leukocytosis
Elevation of eosinophils = eosinophilia
Depression of white count = leukopenia
Elevation of red count = erythrocytosis
Depression of red cell count = erythropenia
Elevation of platelets = thrombocytosis
Depression of platelets = thrombocytopenia
Left shift = increase in percentage of immature white cells (aka "bands or blasts") in circulation = usually indication of infection.

CBC - Components
- White blood cell count (WBC) Total of all white blood cells of all types
- White blood cell differential This test counts the various types of WBCs.
- Red blood cell count (RBC) Number of red blood cells present/volume
- Red cell distribution width Variation in the size of red blood cells.
- Hemoglobin How much of that oxygen-carrying protein is in the blood.
- Mean corpuscular hemoglobin Tells how much hemoglobin is inside a red blood cell.
- Hematocrit The percentage of red blood cells in whole blood.
- Platelet count The number of platelets in the blood.
- Mean platelet volume Measures the size of platelets and can give information about platelet production in bone marrow.

Gout—acute attacks of foot or lower joint pain especially in great toe but any synovial joint can be involved. Elevated uric acid level as a result of a defect in purine metabolism. Results in deposition of crystallized uric acid as "tophi." Homeopathic remedy is oxalate. Get urine sample for uric acid level. In acute attacks white count elevated with left shift and ESR may be elevated. Diet.

EPISCLERITIS
Differential Diagnosis
- Removal of stone
Differential Diagnosis

- AUTOIMMUNE DISEASES
  - Adult rheumatoid arthritis
  - Seronegative spondyloarthropathies
    - Ankylosing spondylitis
    - Inflammatory bowel disease
    - Psoriatic arthritis
    - Reactive arthritis (Reiter’s syndrome)

- Other rare causes/associations
  - Systemic Lupus erythematosus
  - Polyarteritis nodosa
  - T-cell leukemia
  - Paraproteinemia
  - Paraneoplastic syndromes: Sweet syndrome, dermatomyositis
  - Wiskott-Aldrich syndrome
  - Adrenal cortical insufficiency
  - Necrobiotic xanthogranuloma
  - Progressive hemifacial atrophy
  - Following transcleral fixation of posterior chamber intraocular lens
  - Insect bite granuloma
  - Malpositioned Jones tube

If the patient is unresponsive to treatment and a referral to an ophthalmology specialist is prudent in order to explore the more rare causes including:

- Episcleritis
- Scleritis

EPISCLERITIS VS SCLERITIS:
Use 2.5% phenylephrine. Generally, it will whiten an episcleritis, not a deep scleritis

Scleritis

- Most common
  4th-6th decade
- In 15% of cases, scleritis is the presenting sign of collagen vascular disease.
- More in females 1.6:1
- One-third are recurrent
Rheumatoid arthritis is the underlying disease for approximately one sixth of patients suffering from scleritis.

Other connective tissue and autoimmune diseases seen with scleritis include the following:
- Systemic lupus erythematosus (SLE)
- Polyarteritis nodosa
- Seronegative spondyloarthropathies
  - Ankylosing spondylitis
  - Psoriatic arthritis
  - Reactive arthritis
  - Inflammatory bowel disease
- Sarcoidosis
- Tuberculosis
- Syphilis
- Lyme

*List is almost identical to anterior uveitis

Any case unrelated to trauma in a child.
- Bilateral presentation at any age.
- Granulomatous presentation at any age.
- Recurrent or treatment-resistant unilateral presentation at any age.

R/O masquerades that can give pseudo cell and flare responses such as:
- Pigment dispersion
- Pseudoexfoliation
- Retinal detachment
- Retinoblastoma
- Melanoma
- Leukemia
- JXG

If not infectious disease revealed through questioning or through CBC with diff, remaining diagnostic possibilities would most likely include:
- HLA-B27 uveitis (HLA-B27+ with only uveitis)
- The seronegative spondyloarthropathies
- Adult rheumatoid arthritis?
- JRA (JIA)
- Behçets Disease
- Tubulointerstitial nephritis and uveitis syndrome (TINU)
Tubulointerstitial nephritis and uveitis syndrome (TINU)

- Mostly young women (average age 15 years)
- Constitutional Signs and Symptoms
  - Lower back pain from kidney disease (retroperitoneal)
  - Pain on urination
  - Muscle weakness
  - Fever
  - Rash
  - Nausea
  - Vomiting

R/O via directed case history and basic kidney function tests including urine creatinine and β₂ microglobulin levels. A creatine anhydride, C₆H₇N₃O, formed by the metabolism of creatine, that is found in muscle tissue and blood and normally excreted in the urine as a metabolic waste creatinine.

- Elevated ESR
- Eosinophilia on CBC

TINU

- HLA-B27 uveitis
- The seronegative spondyloarthropathies
- Adult rheumatoid arthritis?
- JRA (JIA)

Behçets = very rare in N. America
- Occurs in 3rd-4th decades
- Mouth ulcers, genital ulcers, joint pain, sores and pustules especially on legs
- More common in men in Japan and Medi-countries but more common in women in N. America
- Associated with HLA-B5
- Uveitis often presents with hypopyon

Remaining diagnostic possibilities would then most likely include:

- HLA-B27 uveitis
- The seronegative spondyloarthropathies
- Adult rheumatoid arthritis?
- JRA (JIA)

ADULT Rheumatoid Arthritis

  Ocular complications of ADULT rheumatoid arthritis
  Rheumatology International 16, #2/June, 1996.

- In a prospective study of 325 patients with ADULT rheumatoid arthritis, ocular complications were seen in 73 patients (22.4%).
  - Keratoconjunctivitis sicca was the most common ocular finding.
  - Episcleritis
  - Scleritis
  - Marginal thinning of the cornea with peripheral vascularization.
  - The mean duration of the arthritis and the mean duration of seropositivity were found to be significantly higher in patients with ocular complications.

So adult RA is a consideration in work-up of episcleritis/scleritis.

Key tests are rheumatoid factor, sed rate (ESR) and if necessary citrulline antibody.
Rheumatoid Factor

- In patients with symptoms and clinical signs of rheumatoid arthritis, the presence of significant concentrations of RF indicates that it is likely that they have RA.
- A negative RF test does not rule out RA. About 20% of patients with RA persistently negative for RF and/or may have very low levels of RF.
- The RF test is not used to monitor these conditions. Levels rarely correlate with severity of disease.
- There are adult and juvenile forms of rheumatoid arthritis, and they have very different eye findings!
- While a positive RF is found in a majority of ADULT RA, RF is present in only 30% of children with juvenile RA.
- An RF test may be repeated when the first test is negative and symptoms persist.

The Tests for RF

- Agglutination tests. One method mixes the blood being tested with tiny rubber (latex) beads that are covered with human antibodies. If rheumatoid factor (RF) is present, the latex beads clump (agglutinate). This method is best used as a first-time screening test for RA.
- Nephelometry test. This method mixes the blood being tested with sheep red blood cells that have been covered with rabbit antibodies. If RF is present, the red blood cells agglutinate. While a laser light passes through the tube containing the mixture, an instrument measures how much light is blocked by the sample in the tube (optical density). As levels of RF increase, more clumping occurs, causing a cloudier sample and less light to pass through the tube. This method is often used to confirm the presence of RF.

The Results

- Agglutination tests are reported as a titer: A titer is a measure of how much the agglutination test blood sample can be diluted before RF can no longer be detected. A titer of 1 to 20 (1:20) means that RF can be detected when 1 part of the blood sample is diluted by up to 20 parts of saline. A larger second number means there is more RF in the blood. What is reported is the greatest serial dilution that still gives discernable agglutination. So, a 1:50 is more significant than 1:20.
- Normal usually 1:20 or less

- Nephelometry tests are reported in units: Nephelometry is a measure of optical density; units indicate how much light is blocked by the blood sample in the tube. A high level of RF causes the sample to be cloudy, so less light passes through the tube than when the RF level is low. Therefore, an RF level of 100 units is higher than one of 40 units. If persistently negative and strong clinical suspicion remains, citrulline antibody test is a consideration.

Citrulline Antibody (Anti-CCP)

- Citrulline is a non-essential amino acid that when added to proteins by the body, especially in joints, causes a configuration that the immune system can misinterpret as foreign, prompting formation of an active antibody and subsequent autoimmune response.
- This may be because citrulline (Latin for watermelon) is not coded for by DNA directly, but results from a posttranslational modification of arginine.
- Some suspect that citrullination may be the actual instigator of the pattern of inflammation we know as RA.
- Citrulline antibody is a marker of inflammation in those who are RF positive in previously undiagnosed inflammatory arthritis in those who are RF positive.
- Citrulline antibodies are felt to occur in the earlier stages of rheumatoid arthritis.
Erythrocyte Sedimentation Rate
A general indicator of systemic inflammation

Measures the degree to which red blood cells settle out of anti-
coagulated blood in 1 hr in diln. As inflammatory activity increases, more
fibrinogen is present in the blood, causing RBCs to clump more readily
and fall faster.

Normal ESR for men = (age in years) / 2
Normal ESR for women = (age in years + 10) / 2

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<tr>
<th>Normal</th>
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<tr>
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<td>0-15</td>
<td>0-9</td>
</tr>
<tr>
<td>Women</td>
<td>0-20</td>
<td>0-15</td>
</tr>
<tr>
<td>Children</td>
<td>0-10</td>
<td>0-13</td>
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Values increase with age but values above 30 usually of concern.

C-reactive Protein

- C-reactive protein is produced by the liver
- A non-specific indicator of SYSTEMIC inflammation
- Under normal circumstances CRP should be nearly undetectable.
- CRP levels can be elevated in the later stages of pregnancy as well as with use of birth control pills or hormone replacement therapy.

Non-Granulomatous Anterior Uveitis

Remaining diagnostic possibilities would then most likely include:

- HLA-B27 uveitis
- The seronegative spondyloarthropathies
- Adult rheumatoid arthritis
- JRA (JIA)
- Behçets — very rare in N. America

JUVENILE Rheumatoid (Idiopathic) Arthritis

- Juvenile rheumatoid arthritis (JRA) is arthritis that causes joint inflammation and stiffness for more than 6 weeks in a child of 16 years of age or less.
- Inflammation causes redness, swelling, warmth, and soreness in the joints, although many children with JRA do not complain of joint pain.
- Any joint can be affected and inflammation may limit the mobility of affected joints.
- Key elements for the optometrist are type of JIA, and results of rheumatoid factor and ANA.
**JUVENILE Rheumatoid Arthritis**

**Three Types of JRA**

1. **Pauciarticular** = four or fewer joints affected. Usually larger joints, such as knees or ankles are affected by this type of JRA.
2. **Polyarticular** = five or more joints. Although this kind of JRA usually involves large joints, such as knees, wrists, elbows, and ankles, small joints of the hands and feet are also often involved. Additionally, the joints of the neck (cervical spine) and jaw (temporomandibular joint) may also be affected. Polyarticular JRA is often symmetrical.
3. **Systemic JRA**. In this type of JRA there may be joint swelling, pain, and limited motion in joints, as well as other symptoms, including rashes and high fevers that come and go for weeks at a time.

**How does JRA show up in the Optometrist’s Office?**

- If you elicit that the child has JRA but has had no eye problems, ask which of the three types of JIA. Especially if pauciarticular, ask if the parent knows the results of RF and ANA.
- If they don’t know – you have to find out in order to counsel the parent. And regardless of the lab results, you have to warn that the slightest red eye needs attention of an eyecare specialist. Do not bring a red eye to a general practitioner in these cases.
- Just as joint pain may underestimate the severity of the joint inflammation, there maybe little or no eye pain or redness and yet the child presents with synechiae. Eye involvement can be chronic, leading to complications of glaucoma, cataract and calcific band keratopathy.
- JRA shows a positive RF in only about 30% of cases but it is important to also get an ANA done. Positive ANA is the best predictor of eye involvement in JRA.
- Children, especially girls, who are RF- and ANA+, should be seen q 3 months for quiescent but aggressive anterior uveitis.

**ANA in JRA**

- These days ANA is an ELISA test looking for an IgM against nuclear antigens.
- Normal values may vary from lab to lab.
- Antinuclear antibody titer usually undetectable or below 1:20 or 1:40, depending on the test method used.

**Spondyloarthropathies vs. RA**

- The spondyloarthropathies are a diverse group of inflammatory arthritides that share certain genetic predisposing factors and clinical features, which, as a group, distinguish them from rheumatoid arthritis.
- The most characteristic unifying symptom of the spondyloarthropathies is inflammatory back pain as opposed to knee, hip, finger and/or shoulder pain in RA.
- Pattern of joint involvement in RA is more often symmetric and rheumatoid nodules are occasionally found over joints.
- The most characteristic sign of the spondyloarthropathies is enthesitis, as opposed to synovitis in rheumatoid arthritis.
- Enthesitis involves inflammation at sites where tendons, ligaments, or joint capsules attach to bone.
- Synovitis involves inflammation within the synovial joint and its capsule.
Rheumatoid Factor as it relates to the term Seronegative
Spondyloarthropathies

- Seronegative = Means that the patient tests negatively for the presence of "rheumatoid factor".
- Spondyloarthropathies
  - Spondylo = vertebrae
  - arthro = joint
  - pathy = suffering (disease)

The Spondyloarthropathies

- ankylosing spondylitis
- reactive arthritis (including Reiter's syndrome)
- psoriatic arthritis
- inflammatory bowel disease-associated spondyloarthropathy

OVERVIEW: www.aafp.org/afp/20040615/2853.html

What Makes Them a Group?

- Association with the HLA-B27 gene
  - Haida Indians of Queen Charlotte Islands
    - 50% are HLA-B27+
- The presence of enthesitis as the basic pathologic lesion
- Additional clinical features:
  - Inflammatory back pain
  - Dactylitis
  - Uveitis
  - Skin rash

Enthesitis

- Inflammation at the interface of tendons and bones, leads to bony erosion, pain and swelling.
HLA Human Leukocyte Antigen

- HLA class I antigens (A, B & C) present peptides from inside the cell (including viral peptides if present). Foreign antigens attract killer T-cells (also called CD8 positive or cytotoxic T-cells) that destroy cells.
- HLA class II antigens (DP, DQ, DOA, DOB, DQ & DR) present antigens from outside of the cell to T-lymphocytes. These particular antigens stimulate T-helper cells to multiply, and these T-helper cells then stimulate antibody-producing B-cells to produce antibodies to that specific antigen.
- Self-antigens are suppressed by suppressor T-cells.

Major Antigens
- HLA A - 349
- HLA B - 627
- HLA C - 182

HLA-B27:
- 5-8% of normals
- 85% of those with ankylosing spondylitis
- 75-80% of patients with Reiter's syndrome
- 75% of patients with psoriatic arthritis
- 40-45% of patients with acute anterior uveitis NOT due to juvenile rheumatoid arthritis

HLA B5:
- Positive in 30% of normal Japanese
- Positive in 70% with Behcet’s disease
- Positive in smaller percentages of people from other Behcet’s prone regions (e.g. the Mediterranean basin).

Presentation in the office: Acute anterior uveitis.
*Note that this is the diagnosis in most young men presenting with a acute anterior uveitis that ultimately involves both eyes.

History and Physical Exam:
- Any history of low back pain?
- Does it wake you from sleep?
- Any difficulty breathing? (decreased chest extensibility)
- Examine hands for dactylitis (sausage fingers)
- Inspect mouth or ask about frequent canker sore (aka aphthous ulcer)

LAB WORK-UP: RF (-) HLA-B27 (+) Sed Rate (variable) CBC (mild leukocytosis)

RADIOLOGICAL: SI Joint X-ray or CT to R/O Sacroiliitis/Enthesitis

www.emedicine.com/RADIO/topic41.htm
When inflammation is limited to joints the diagnosis is reactive arthritis. If it additionally involves any of the areas below, this is a form of reactive arthritis called Reiter’s syndrome.

- "Sterile" urethritis
- Aphthous ulcers in the mouth
- Anterior uveitis/conjunctivitis

Reiter’s Syndrome

- Presentation in the office: Acute anterior uveitis or Conjunctivitis (50%)
- History and Physical Exam:
  - Any history of recent infection? Febrile episode?
  - Any diarrhea, especially bloody diarrhea in past few months?
  - Any pain/burning on urination?
  - Any joint pain? (Knees, ankles, and feet most likely)
  - Ask if any lesion in genital area (circinate balanitis on penis)
  - Examine hands for keratoderma blennorrhagicum
  - Inspect mouth or ask about frequent canker sore (aka aphthous ulcers)
- LAB WORK-UP: RF (-) HLA-B27 (+) Sed Rate, CBC, Urine culture
- RADIOLOGICAL: None

www.emedicine.com/EMERG/topic498.htm
medind.nic.in/jac/100/3/jact00i3p233.pdf

Psoriatic Arthritis

- After having psoriasis for an average of 10 years, 10-30% of patients develop a complication called psoriatic arthritis
- Symptoms include:
  - joint discomfort, swelling, stiffness
  - throbbing, swelling in the toes and ankles
  - Swelling of DIP joint
  - pitting of nails, loss of nails

Psoriatic Arthritis

- Presentation in the office: Acute anterior uveitis.
- History and Physical Exam:
  - How long have you had psoriasis? (Arthritis rare before 10 yrs)
  - Which joints hurt? Symmetric or Unilateral?
  - Examine hands for dactylitis (sausage fingers)
  - Examine nails for pitting/oncholysis/oil droplet sign
  - Inspect mouth or ask about frequent canker sore (aka aphthous ulcers)
- LAB WORK-UP: RF (-) HLA-B27 (+) Sed Rate (variable)
- RADIOLOGICAL: Affected Joint X-ray
Inflammatory Bowel Disease-associated Spondyloarthropathy

- Presentation in the office: Anterior uveitis or Episcleritis

- History and Physical Exam:
  - Any diarrhea, especially bloody diarrhea in past few months?
  - Any joint pain? High incidence of asymptomatic sacroiliitis (varying from 10% to 52%) and on the other hand the equally high incidence (about 50%) of characteristic inflammatory low back pain in the absence of radiological findings in IBD patients
  - Have you had any red discolored areas on your shins or calves?
  - Inspect mouth or ask about frequent canker sore (aka aphthous ulcers) (10%)
  - Inspect fingers for clubbing/oncholysis (nails falling off)

- LAB WORK-UP: RF (-) HLA-B27 (+) HLA B58 (+), Sed Rate

- RADIOLOGICAL: None


Granulomatous vs Non-granulomatous inflammation

Chronic, non-granulomatous inflammation is characterized by the presence of lymphocytes and antibody-producing plasma cells.

Granulomatous reactions (e.g. fungal, foreign body, TB, sarcoid) are a subset of chronic inflammation due to a persistent antigen of low virulence that is poorly cleared by the immune system leading to a chronic T helper cell (Th1) subtype response. In addition to lymphocytes and plasma cells, a modified macrophage called an epithelioid cell is present. These macrophages can merge together to form giant cells.

Caseating vs Non-caseating granulomas

- Tuberculosis
- Syphilis
- Sarcoidosis
- Lyme

Initial Work-up if TB suspected

- CXR
- PPD
The tuberculin skin test is based on the fact that infection with *M. tuberculosis* produces a delayed-type hypersensitivity skin reaction to certain components of the bacterium. The active protein principle of *Mycobacterium tuberculosis*. An intradermal injection of 0.1 ml of PPD is given and injection site is checked 48-72 hrs later. Induration and erythema 10 mm or greater measured perpendicular to the long axis of the arm is positive.

**PPD - Purified Protein Derivative**

- The tuberculin skin test is based on the fact that infection with *M. tuberculosis* produces a delayed-type hypersensitivity skin reaction to certain components of the bacterium.
- The active protein principle of *Mycobacterium tuberculosis*. An intradermal injection of 0.1 ml of PPD is given and injection site is checked 48-72 hrs later. Induration and erythema 10 mm or greater measured perpendicular to the long axis of the arm is positive.

**Bacille Calmette-Guerin (BCG)**

- BCG, or Bacille Calmette-Guerin, is a vaccine used in many countries to protect children against severe forms of TB disease. However, its efficacy in preventing TB in adults is variable and controversial. BCG vaccination complicates the interpretation of TST results because it can produce a false-positive reaction to the TST. There is no way to distinguish a positive reaction to BCG vaccination and one due to TB infection although reactions of >20 mm of induration are not likely caused by BCG.
- Sensitivity to tuberculin in BCG vaccinated persons is highly variable and tends to wane over time.
- BCG vaccination is not a contraindication for tuberculin skin testing and any BCG vaccinated person who is a recent arrival from a high incidence country is a high priority for testing.
- A positive TST in a BCG vaccinated person originating from a high incidence country is considered indication of tuberculosis infection. After active TB has been ruled out, the person should be evaluated for treatment of latent TB infection.

**Interferon Gamma Release Assay**

- Like PPD it does NOT distinguish latent TB from active disease.
- This test run on whole blood assesses ability of WBCs to produce and release cytokines when mixed with TB-related antigens.
- These cells will release interferon gamma if they have previously encountered *M. tuberculosis*.
- Prior BCG vaccination does NOT cause a false positive test result, nor does anergy interfere.

**Initial Work-up if Syphilis suspected - Luetic serology**

- **CMIA/TPPA/FTA.Abs** - does the patient have or have they ever had syphilis?
- **VDRL/RPR** - what is the current level of activity of the disease?
Chemiluminescent Microparticle Immunoassay (CMIA) (Used by Health Canada)

- Screens clotted blood and serum specimens for evidence of syphilis infection.
- Detects both IgG and IgM antibodies to T. pallidum.
- High sensitivity and specificity for syphilis infection during all stages of disease.
- May give false negative in early infection.
- If positive, in most cases, the CMIA will remain positive for life.
- When CMIA is positive, other confirmatory tests are done.

Fluorescent Treponemal Antibody /Absorbed

- A treponemal test using indirect immunofluorescence to detect antibodies to T. Pallidum.
- Can’t be titrated so results are read as reactive, borderline or non-reactive.
- Patients who are FTA/Abs positive remain so for life.
- False positives in pregnancy and some CT diseases.

Direct and Indirect Immunofluorescence Assays

Direct: A specific antibody to which fluorescein has been attached is put onto the specimen to detect an antigen.

Indirect: An antibody to which fluorescein has been attached is put onto the specimen to detect a specific antibody.

Venereal Disease Research Lab or Reactive Plasma Reagin

A non-treponemal test that detects REAGINS. Reagins are non-protective antibodies produced by patients infected with T. Pallidum.
Active, luetic serum causes flocculation of a beef heart extract.
Provides information on level of disease activity. Successfully treated patients are VDRI/RPR negative.
**Initial Work-up if Sarcoidosis suspected**
- CXR - Chest CT if CXR equivocal or negative and suspicion is high.

**ACE (Angiotensin converting enzyme)**
- ACE catalyzes conversion of angiotensin I to angiotensin II - a very potent vasoconstrictor that elevates BP. This process has been targeted by the development of drugs called ACE inhibitors that are commonly used to decrease vasoconstriction as a means of treating systemic hypertension.
- ACE levels are increased in an array of diseases but the test is used especially in a work-up for sarcoidosis. Increasing ACE does not increase BP since there is not an unlimited source of substrate.
- Serum ACE activity, expressed in units/L, in normal subjects 10-70.

**Anergy Panel**
- The presence of skin anergy is typical of but not diagnostic for sarcoidosis. Replacement of normal lymph node tissue with granulomatous tissue suppresses the normal skin response to antigens such as the PPD. An anergy panel is therefore run to control for false negatives.

**Limited Gallium Scan**
- Injection of citrated gallium followed by nuclear scan 48 hours later.
The clinical manifestations of untreated Lyme disease occur in 3 stages.

Stage 1 is the localized bull’s eye skin rash. This pathognomonic skin rash begins 3-30 days after the tick bite, however, as many as 18% of patients can present without the skin rash.

In stage 1 Lyme disease, the ocular manifestations are conjunctivitis and photophobia.

Conjunctivitis may be the SOLE PRESENTING SIGN of Stage 1 Lyme Disease. It is self-limited and then there is a period of quiescence prior to emergence of Stage 2.

Lyme disease is rarely life threatening but chronicity can produce permanent disability.

Resiliency (therefore chronicity) comes from ability to exist in 3 forms – spirochete, cell-wall deficient and cyst – and all require different treatments due to different susceptibilities.

Intermediate uveitis (pars planitis) with papillitis is more commonly associated with Lyme. Granulomatous anterior uveitis is less common and may occur with a papillitis. Such a combination should call to mind Lyme.

Testing is done for both IgM and IgG antibodies but is best handled by someone who is really familiar with diagnosing Lyme disease.

You can’t do a Lyme work-up on every Conjunctivitis

- If you are presented with a conjunctivitis, ask about circumstances that would cause exposure to Lyme and ask about or look for the rash. If present, get them worked up.
- If they have been in an area of exposure risk but have no rash, tell them conjunctivitis will go away but educate them about signs and symptoms of second stage of Lyme, urging them to get care right away of they surface.

Signs and Symptoms of Secondary Lyme Disease

- Being tired.
- Additional skin rashes as the infection spreads.
- Pain, weakness, or numbness in the arms or legs.
- Facial nerve palsy.
- Recurring headaches or fainting.
- Poor memory and reduced ability to concentrate.
- Occasional rapid heartbeats (palpitations).