Ocular Manifestations in Autoimmune Diseases

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Disclosures and Special Request

Paid consultant for:
Alcon Pharmaceuticals, Bausch and Lomb, Carl Zeiss Meditec, Shire Pharmaceuticals, Valeant

Commitment to change:
- write down three things that you “learned” from this presentation that you can incorporate into your practice to improve patient care
Autoimmune Diseases

• Group of acquired diseases in which genetic factors appear to play a role
• They have in common widespread immunologic and inflammatory alterations of connective tissue
• The illnesses share certain clinical features and differentiation between them is often difficult because of this.
• Although thought to be acquired diseases, often their causes cannot be determined.
CASE
Case

• 55 yr white female complains of fluctuating vision
  – Worse at near
  – Spends 8-10 hours/day on the computer
• Medical Hx:
  – Hypertension for 10 years
  – Joint pain
• Medications:
  – HCTZ for HTN
  – Celebrex for her joint pain
Exam Data

- VA (corrected): OD: 20/25, OS: 20/25
- PERRL
- EOM’s: FROM
- CVF: FTFC
- SLE:
  - TBUT 5 sec OD, OS
  - Positive NaFl staining and Lissamine green staining of conj and cornea
  - Decreased tear prism
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Additional Testing/Questions

• Schirmer: < 5 mm of wetting in 5 minutes OD, OS
• RF and ANA: normal for patients age
• SS-A: 2.0 (normal < 1.0), SS-B: 1.9 (normal <1.0)
• Additional symptoms reported:  
  – Patient experiences dry mouth and taking Salagen

• **Diagnosis: Sjogren’s Syndrome**
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Differential Diagnosis of Dry Eye

- Deficient Aqueous Tear Production
  - Sjögren Syndrome
  - Non-Sjögren Syndrome
- Increased Evaporative Loss
  - Blepharitis/Mebomian Gland Dysfunction
  - Exposure
  - Other factors
    1. Contact lenses
    2. Blink abnormality
    3. Environmental
Signs and Symptoms of Dry Eye

**Signs:**
- Ocular Surface Damage
  - Corneal Staining (Fluorescein and/or Rose Bengal)
  - Conjunctival Staining (Lissamine Green)
- Decreased Tear Quantity
  - Schirmer Score
  - Phenol Red Thread Test
  - Tear Meniscus Height
- Decreased Tear Quality
  - Tear Break Up Time (TBUT)
  - Tear Osmolarity

**Symptoms:**
- Grittiness
- Burning
- Irritation
- Stringy discharge
- Blurring of vision
- Ocular Surface Disease Index (OSDI)
InflammaDry

• Point of care testing to measure MMP-9 levels
  – MMP-9 is an inflammatory biomarker found to be elevated in patients with dry eye
• Marketed by RPS
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Treatment

• We initiated:
  – Omega-3 supplements (2 grams per day)
  – Recommended warm compresses and lid washes qhs
  – Testosterone cream 3% applied to upper lid bid

• Patient had significant improvement in symptoms with the use of the topical testosterone cream.
  – However, she was still symptomatic at the end of the day and she still had significant staining on her cornea and conjunctiva
  – Initiated FML tid for 1 month, Restasis bid after 2 weeks
    • 2 months later patient reported further improvement in her symptoms
    • No conjunctival staining was noted and only slight SPK
    • Schirmer values improved to OD: 9 mm, OS: 10 mm
Role of Androgens?

• Recent studies have suggested that androgen deficiency may be the main cause of the meibomian gland dysfunction, tear-film instability and evaporative dry eye seen in Sjogren patients.

• Transdermal testosterone 3% promotes increased tear production and meibomian gland secretion, thereby reducing dry eye symptoms (Dr. Charles Connor).

• Progesterone 0.05%/Testosterone 0.05% Ophthalmic Solution BID (available from Leiter’s Pharmacy).
Sjogrens

• Chronic AI disease that involves diffuse exocrine gland dysfunction and lymphocytic infiltration throughout the body
• Decreased lacrimal gland secretion results in K sicca
• Decreased salivary gland secretion results in sicca complex
• Emotional tearing is not affected
SJOGREN’S SYNDROME: OLD/NEW CLASSIFICATION

• Old:
  – 1° Sjogrens: occurs when sicca complex manifests by itself
    • no systemic disease present
  – 2° Sjogrens: occurs in association with collagen vascular disease such as
    • RA and SLE
    • significant ocular/systemic manifestations

• New:
  – The diagnosis of SS should be given to all who fulfill the new criteria while also diagnosing any concurrent organ-specific or multiorgan autoimmune diseases, without distinguishing as primary or secondary.
Diagnosis: New Criteria

- Sjogren’s International Collaborative Clinical Alliance (SICCA) was funded by the National Institutes of Health to develop new classification criteria for SS
- New diagnostic criteria requires at least 2 of the following 3:
  - 1) positive serum anti-SSA and/or anti-SSB or (positive rheumatoid factor and antinuclear antibody titer >1:320),
  - 2) ocular staining score >3, or
  - 3) presence of focal lymphocytic sialadenitis with a focus score >1 focus/4 mm² in labial salivary gland biopsy samples
Ocular Surface Score (OSS)

• The ocular surface score (OSS) is the sum of:
  – 0-6 score for fluorescein staining of the cornea and
  – 0-3 score for lissamine green staining of both the nasal and temporal bulbar conjunctiva,
  – yielding a total score ranging from 0-12.
Antibodies to SS-A and SS-B

• Sjogren’s syndrome A and B
• Typically tested by ELISA and immunoblot
• Associated Conditions:
  – Uncommon in the normal population and in patients with rheumatic diseases other than Sjogren’s syndrome and SLE
  – Present in 75% of patients with “primary” Sjogren’s but only 10-15% of patients with RA and secondary Sjogren’s syndrome
Antibodies to SS-A and SS-B

• Indications:
  – Should be measured in patients with a clinical suspicion of Sjogren’s or SLE

• Interpretation:
  – Presence of AB’s is a strong argument for the diagnosis of Sjogren’s Syndrome in a patient with sicca syndrome
Uncover a potential systemic cause of dry eye before it takes hold

Introducing Sjö™ for the early detection of Sjögren’s Syndrome

- High sensitivity and specificity
- First panel to incorporate traditional and novel proprietary biomarkers that help detect Sjögren’s Syndrome in early stages of disease
- Simple in-office test for patients with dry eye

Additional support is always available by calling 1.855.MYNICOX (1.855.696.4269).

**Sjö Diagnostic Test**

*Sjö™—Early detection of Sjögren's Syndrome for patients with dry eye*

Introducing novel biomarkers in an advanced diagnostic panel for the early identification of Sjögren's Syndrome

- Significantly higher sensitivity and specificity than with traditional screening methods³
- Includes traditional biomarkers plus 3 novel, proprietary biomarkers to support earlier detection of Sjögren's Syndrome

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Type</th>
<th>Diagnostic Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>SS-A (Ro)</td>
<td>Traditional</td>
<td>Expressed in approximately 70% of patients and typically appears later in the course of the disease than novel biomarkers¹⁷</td>
</tr>
<tr>
<td>SS-B (La)</td>
<td>Traditional</td>
<td>Expressed less frequently than Ro and typically appears later in course of disease than novel biomarkers¹⁷</td>
</tr>
<tr>
<td>Antinuclear Antibody (ANA) by HEP-2</td>
<td>Traditional</td>
<td>Expressed in about 70% of Sjögren's Syndrome patients¹</td>
</tr>
<tr>
<td>Rheumatoid Factor (RF) Levels (IgA, IgG, IgM)</td>
<td>Traditional</td>
<td>Found in many rheumatic conditions but is not unique to Sjögren's Syndrome⁸</td>
</tr>
<tr>
<td>Salivary Protein-1 (SP-1, IgA, IgG, IgM)</td>
<td>Novel, proprietary</td>
<td>Provides high specificity and sensitivity for early Sjögren's Syndrome²</td>
</tr>
<tr>
<td>Carbonic Anhydrase (CA-6, IgA, IgG, IgM)</td>
<td>Novel, proprietary</td>
<td>Offers additional sensitivity for an early diagnosis⁷</td>
</tr>
<tr>
<td>Parotid Secretory Protein (PSP, IgA, IgG, IgM)</td>
<td>Novel, proprietary</td>
<td>Expressed early in disease course⁷</td>
</tr>
</tbody>
</table>
Sjo: new diagnostic test for Sjogrens

• SP-1 (salivary gland protein-1), CA-6 (carbonic anhydrase-6) and PSP (parotid secretory protein).

• Traditional tests use ANA, SS-A and SS-B and RF antibodies which have significant limitations of sensitivity and/or specificity and are associated with later-stage disease.

• During studies, these novel antibodies were found in 45% of patients meeting the criteria for Sjögren’s Syndrome who lacked the traditional antibodies for SS-A and SS-B.
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Sjogren’s Ocular and Systemic

- Recently published article comments:
  - One or more extraglandular ocular manifestations (e.g. corneal scarring/melts, uveitis) were present in 35% of patients
  - 13% had vision threatening findings
  - Approximately 55% with a vision threatening ocular finding did not have an established diagnosis of primary SS at the time of presentation
Sjogren’s Ocular and Systemic

• Recently published article comments:
  – all patients had dry eye symptoms for approximately 10.4 years before presentation
  – 42% of the patients had systemic manifestations resulting from primary SS
  – SS has been shown to be an independent risk factor for the development of non-Hodgkin’s lymphoma.
Sjogren’s Ocular and Systemic

• Authors recommendation:
  – primary SS is associated with vision- and life-threatening complications
  – presence of SS needs to be explored in patients with clinically significant dry eye because dry eye precedes the occurrence of the systemic manifestations
Dry Eye Summit

• Held in December 2014
  – Combination of optometrists, an ophthalmologist and industry

• Goal:
  – to find a way to encourage optometrists to look for, diagnose and manage dry eye in their patients
  – Come to a consensus on the minimum:
    • 3 questions that should be asked to identify dry eye patients
    • 3 diagnostic tests
    • 3 initial treatments
Consensus on Screening Questions

1. Do your eyes ever feel dry or uncomfortable?
2. Are you bothered by changes in your vision throughout the day?
3. Are you ever bothered by red eyes?
4. Do you ever use or feel the need to use drops?

Recommendations from the *Dry Eye Summit 2014*
Consensus on Baseline Diagnostic Options for Entry Level Dry Eye Disease

1. The lid
2. Staining
3. Tear stability

Recommendations from the *Dry Eye Summit 2014*
Consensus on Baseline Management

1. For all patients:
   A. Ocular lubrication
   B. Lid hygiene
   C. Nutrition

2. Topical anti-inflammatories

Recommendations from the *Dry Eye Summit 2014*
Dry Eye and Lid Disease?

• It is estimated that 67-75% of patients who have dry eye have some form of lid disease
  — it is often the most overlooked cause for dry eye symptoms

• Important to address the lids in any treatment plans for patients with dry eye
Treatment of MGD

At Home Therapy
  – Warm compresses (recommend commercially available compresses such as Bruder)
  – Eyelid Scrubs/washes
  – Self expression

In-Office Therapy
  – Manual Expression
  – Off-Label Pharmacotherapy
    – Oral tetracycline/doxycycline
    – Topical Antibiotics – erythromycin, tobramycin
    – Topical Steroids – dexamethasone
Treatment of MGD

At Home Therapy
- Warm compresses
- Eyelid Scrubs
- Self expression

In-Office Therapy
- Manual Expression
- Off-Label Pharmacotherapy
  - Oral tetracycline/doxycycline - *systemic side effects*
  - Topical Antibiotics – erythro., tobra. - *antibiotic resistance, poor gland penetrance*
  - Topical Steroids – dexamethasone - *risk of cataract, glaucoma, poor gland penetrance*
LIPIFLOW® THERMAL PULSATION SYSTEM

The Lid Warmer: Comprised of a precision heater, eye insulation & vaulted shape

The Eye Cup: Comprised of an inflatable bladder & rigid eye cup

Caution: Investigational device. The LipiFlow Auto Console pictured (inset) is not approved for use in the U.S. Limited by United States law to investigational use.
LIPIFLOW® THERMAL PULSATILE PRESSURE SYSTEM

- Heat applied to the palpebral surfaces of the upper and lower eyelids directly over the meibomian glands.

- Graded pulsatile pressure delivered to the outer eyelid.
Therapeutic Goal of Heat Therapy

- Liquefy the meibomian gland contents
- Facilitates release of secretion from the meibomian gland
- Increase likelihood that the glands can resume normal function
Lifitegrast (Xiidra)

• Lifitegrast 5% (Xiidra) from Shire Pharmaceuticals approved by the FDA on July 11th, 2016
• indicated for the treatment of both signs and symptoms of dry eye disease
• Lifitegrast inhibits T-cell mediated inflammation associated with dry eye disease at several different points in the inflammatory cascade
• The most common side effects included irritation at the instillation site, dysgeusia and reduced visual acuity, reported in 5% to 25% of patients.
30 YR WM

• Patient calls from his PCP office asking if we can see him today because he has had red/painful eyes for over a week and has not resolved

• Medical history:
  – Past week has been experiencing painful urination and discharge
  – New sexual partner approx 10 days ago, who also had developed a red eye
  – Chlamydia and gonorrhea testing were negative
  – Has tested positive for HSV2 but no current flare up
30 YO WM

• Medications:
  – In the past week patient:
    • 2 courses of azythromycin (1 gram each)
    • Injection of rocephin
    • Injection of penicillin G
    • Currently taking doxycycline 100 mg bid
    • Valtrex 1 gram 3 times per day for 7 days (d/c 1 day ago)
    • Was on Vigamox qid for 7 days (d/c 1 day ago)

• VA: 6/7.5 (20/25) OD, OS

• Entrance skills unremarkable though some pain on eye movement
30 YO WM

• SLE:
  – 2+ injection conjunctival both eyes
  – 1-2+ lid edema
  – Mixed papillary and follicular response
  – 1-2+ diffuse SPK (no staining noted above infiltrates)
  – No cells or flare noted
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30 YO WM

- AdenoPlus:
  - Performed on the right eye (patient felt that was the worst eye)
  - Negative
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30 YO WM

• Started patient on the miracle drop
  – Tobradex 4 times per day and scheduled patient to come back the next day

• 1 day f/u
  – Patient was feeling better
  – Less redness and much reduced photophobia and discomfort
  – No improvement on painful urination or discharge and is now seeing blood in his urine
  – Continue tobradex 4 times per day and RTC in 4 days for f/u with dilation and told to contact PCP to update on the blood in the urine
30 YO WM

• 4 day f/u:
  – Patient says his eyes are doing great and that all of his urogenital problems abruptly stopped on Saturday
  – Discussion with PCP: Kidney stone
  – What was going on with the eye?
    • Viral conjunctivitis likely EKC

What did we learn from this?
I ROCK!!
RHEUMATOID ARTHRITIS
Rheumatoid Arthritis

- Collagen vascular disorders:
  - most common form of inflammatory joint disease
  - lead to most common form of physical disability in the US
- Average onset between 35-50
- Familial predisposition
- 3x more females
- Predominately Caucasian

Figure 3. Joint frequently affected by rheumatoid arthritis. Less commonly affected are elbows, hips and the neck.
Rheumatoid Arthritis

• Rheumatoid Arthritis (RA) is not a benign disease.
• RA is associated with decreased life expectancy.
  – The risk of cardiovascular mortality is twice that of the general population.
• Affecting approximately 1% of the adult population, RA is associated with considerable disability.
• It is now well recognized that there is a "window of opportunity" early in the disease process to initiate treatment which will fundamentally change the course of the disease.
Rheumatoid Arthritis
Epidemiology-Systemic

• Primary sites of infl’n are centered around musculoskeletal tissues
  – small joints with synovial linings are most commonly affected ie hands/feet early in disease

• RA joint characterized by hypertrophic, inflamed synovial tissue with fluid accumulation and adjacent soft tissue swelling
  – this is responsible for hot, swollen, tender joints that are hallmark of RA

Figure 3. Joint frequently affected by rheumatoid arthritis. Less commonly affected are elbows, hips and the neck.
Other Diagnostic Criteria for RA

<table>
<thead>
<tr>
<th>Cutaneous</th>
<th>Ocular</th>
<th>Pulmonary</th>
<th>Cardiac</th>
<th>Neurological</th>
<th>Hematological</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nodules</td>
<td>Sicca</td>
<td>Pleuritis</td>
<td>Pericarditis</td>
<td>Peripheral neuropathy</td>
<td>Leukopenia</td>
</tr>
<tr>
<td>Vasculitis</td>
<td>Episcleritis</td>
<td>Nodules</td>
<td>Atherosclerosis</td>
<td>Cervical myelopathy</td>
<td>Anemia of chronic disease</td>
</tr>
<tr>
<td>Scleritis</td>
<td>Interstitial lung disease</td>
<td>Myocardial infarction</td>
<td></td>
<td></td>
<td>Lymphadenopathy</td>
</tr>
</tbody>
</table>

Fibrosis
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Osteoarthritis (OA) vs. RA

- Etiology of RA is inflammatory which improves with activity while osteo is mechanical and worsens with activity.
- Inflammation is secondary to mechanical insults in osteo while no previous insult required in RA.
- Joint cartilage is primary site of articular involvement in osteo while its the bony surfaces of the joints in RA.
Diagnosis

• Many patients have symptoms that are not exclusive to RA making diagnosis difficult
  – prodromal systemic symptoms of malaise, fever, weight loss, and morning stiffness

• Lab tests and radiographic studies are necessary for initial diagnosis and are helpful in monitoring progression
  – no one single test is confirmatory of disease
Criteria for Diagnosis of RA

RA likely if:

- Morning stiffness > 30 minutes
- Painful swelling of 3 or more joints
- Involvement of hands and feet (especially MCP and MTP joints)
- Duration of 4 or more weeks
- Differential diagnoses include: crystal arthropathy, psoriatic arthritis, lupus, reactive arthritis, spondyloarthropathies.
# Lab Testing for RA

<table>
<thead>
<tr>
<th>Tests</th>
<th>Diagnostic Value</th>
<th>Disease Activity Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESR or CRP</td>
<td>Indicate only inflammatory process - Very low specificity</td>
<td>ESR elevated in many but not all active inflammation. Maybe useful in monitoring disease activity and response to treatment</td>
</tr>
<tr>
<td>RF</td>
<td>RF has a low sensitivity and specificity for RA. Seropositive RA has worse prognosis.</td>
<td>No value</td>
</tr>
<tr>
<td>ANA</td>
<td>Positive in severe RA, SLE, or other connective tissue disorders (CTD)</td>
<td>No value-do not repeat</td>
</tr>
<tr>
<td>X-rays</td>
<td>Diagnostic erosions rarely seen in disease of &lt;3 mo’s duration</td>
<td>Serial x-rays over many years may show disease progression and indicate med change</td>
</tr>
<tr>
<td>Joint aspiration</td>
<td>Indicated if infection suspected</td>
<td></td>
</tr>
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Erythrocyte Sedimentation Rate

This measures the height of RBC’s settling out of plasma per hour

<table>
<thead>
<tr>
<th>ESR</th>
<th>Males: Age/2</th>
<th>Good sensitivity but poor specificity. Takes time for the levels to become detectable</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Females: (Age + 10)/2</td>
<td>High: Indicative of giant cell arteritis but normal levels do not exclude GCA as a diagnosis</td>
</tr>
</tbody>
</table>

Giant Cell Arteritis

- vessels most often involved are the arteries over the temples,
  - GCA = "temporal arteritis."
- symptoms, such as fatigue, loss of appetite, weight loss or a flu-like feeling
  - pain in the jaw with chewing (jaw claudication).
  - Sometimes the only sign of GCA is unexplained fever.
  - Less common symptoms include pains in the face, tongue or throat.

Giant Cell Arteritis

- GCA is a clinical diagnosis!
- If patient meets criteria of clinical symptoms then treatment will be started regardless of whether lab test or biopsy are positive
- Treatment should be started before lab results are back.

Rheumatoid Factor (RF)

• RF is an autoantibody directed against IgG
• Most common lab testing are latex fixation and nephelometry
• RF present in 70-90% of patients with RA
  – However RF is not specific for RA
  – Occurs in a wide range of autoimmune disorders
  – Prevalence of positive RF increases with age
    • As many as 25% of persons over age of 65 may test positive
  – High titer for RF almost always reflects an underlying disease
Rheumatoid Factor (RF)

• Indication:
  – RF should be ordered when there is clinical suspicion of RA
• Interpretation
  – Positive test depends on pretest probability of the disease
    • If other clinical signs present can provide strong support for diagnosis of RA
    • Keep in mind that the combination of a positive test is not specific for RA
  – Negative test should not completely rule out possibility of RA
    • From 10-30% of patients with long-standing disease are seronegative
    • The sensitivity of the test is lowest when the diagnosis is most likely to be in doubt
Antibodies to Cyclic Citrullinated Peptides (anti-CCP)

- Proteins that contain citrulline are the target of an AB response that is highly specific for RA
- Anti-CCP detected using ELISA
- Associated conditions:
  - Appears to be quite specific for RA
    - Specificity as high as 97%
  - Sensitivity in the range of 70-80% for established RA and 50% for early-onset
  - Has superior specificity and comparable sensitivity for diagnosis of RA as compared to RF
Antibodies to Cyclic Citrullinated Peptides (anti-CCP)

Indication:

– Should be ordered when there is a clinical suspicion of RA

Interpretation:

– Presence provides strong support for the diagnosis of RA
– In patients with early onset, undifferentiated, inflammatory arthritis positive results are a strong predictor of progression to RA and the development of joint erosion
– Negative test does not exclude possibility of RA particularly at the time of initial presentation (apprx 50% of patients lack detectable antibodies)
Diagnosis

- Joint x-ray and radionucleotide evaluation of suspected inflamed joints are indicated
Rheumatoid Arthritis: Treatment

• Treatment must be started early to maximize the benefits of medications and prevent joint damage.

• The use of traditional medications in combination and the new biologic therapies has revolutionized the paradigm of RA treatment in recent years.

• There is no curative treatment for RA
  – treatment is to minimize inflammation
  – minimize damage and
  – maximize patient functioning
Treatment and Management-Systemic

• Current Tx regimens utilize a step-down approach with initiation of one or more DMARD’s at time of diagnosis.
• RA most destructive early in disease
• “Easier” and more effective if Tx initiated early.
• DMARD-disease modifying antirheumatic drug
  – these drugs not only reduce inflammation but also change the immune response in a long-term and more dramatically than NSAID’s
  – give chance of permanent remission
Treatment and Management: Aspirin and NSAID’s

- block infl’ n by inhibition of prostaglandin release in response to cell trauma
- arachadonic acid converted by COX (1&2) enzymes into inflammatory mediators including:
  - Thromboxanes
  - Prostaglandins
  - Leukotrienes
Treatment and Management:
Aspirin and NSAID’s

- aspirin and NSAID’s inhibit both and used in initial Tx for pain but don’t inhibit progression of disease
- newer selective COX 2 inhibitors avoid GI upset
  - COX 1 needed for GI protective PG’s but have CV toxicity
Propionic Acids

• Most commonly used and largest class of NSAIDs.

• MOA is similar to ASA.
  – Metabolized in the liver and excreted in the urine.

• Superior analgesic efficacy over ASA with less incidence of side effects.

• Includes: Ibuprofen, Naproxen, Ketoprofen, Oxaprozin, and Fenoprofen.
Ibuprofen

- Adult analgesic dose: 200-400mg q4hours
  - Maximum Dosage: 2400 mg/day for pain (approved for 3200 mg/day in arthritis treatment)

- OTC: 200 mg tabs
- Rx: 300, 400, 600, 800mg tabs
  - Can prescribe 800 mg q8hrs

- Peak levels 1-2 hours

- Most renal toxic of all the NSAID’s

- Brand Names: Motrin, Advil, and Nuprin
Naproxen and Naproxen Sodium

– Sodium speeds up the absorption over Naproxen (Naprosyn) alone causing it to be used more frequently.
Naproxen Sodium

- Type of Medication Determines Dosage (This is for Naproxen Sodium):
  - OTC: 220mg tablets (Aleve)
  - Rx: 275 and 550 mg tablets (Anaprox and Anaprox DS)

• Adult Dose:
  - OTC: 220 or 440 initial dose followed by 220 mg q 8 – 12 hours.
  - Rx: 550 initial dose, followed by 275mg q6-8h or 550mg q12hours.
  • Maximum Dose: 1375mg/day.
Ketoprofen

• Adult dose:
  – 50 mg q 6-8 hours for pain
  – 50 – 100 mg TID for inflammation

• Maximum Dose: 300 mg/day
  – Limited to 7-14 days

• Rx: 50, 75, 200ER mg capsules
Indole Acetic Acids: Indomethacin

- Rx Only
- Available as 25, 50, 75 ER, and IV
- Adult Dosage: 25 - 50 mg TID

- Mainly used as a short term anti-inflammatory especially for conditions that do not respond to less toxic NSAID's.
  - Indomethacin has a very high level of intolerance compared to other NSAID’s.

- Available in Canada as a topical Ophthalmic Suspension (Indocid).
Side Effects of Oral NSAID’s

• Very similar to the side effect profile of ASA.
  
  – GI Effects
    • Profile is dependent on COX selectivity.
    • Consider using PPI’s while treating with NSAID or ASA.
  
  – CNS problems such as headache, confusion in the elderly, and loss of short-term memory.
  
  – Inhibit platelet function
    • Only while a high concentration exists in the body.
  
  – Risk of triggering asthma attacks is less with NSAID’s than what is found with ASA.
Side Effects of Oral NSAID’s

• NSAID’s are excreted from the body via urine. Must monitor kidney function.

• NSAID’s block prostaglandins to the kidney which causes renal blood flow to decrease and increases the retention of sodium and fluid.
  – Risk factors for kidney damage include:
    • Dehydration
    • Hypertension
    • Congestive Heart Failure
    • Use of ACE Inhibitors
    • Advanced Age
  – This will effect Cardiovascular homeostasis – can exacerbate heart failure.
    • NSAID’s can cause hyperkalemia and have been linked to cardiac arrest in patients at risk.
NSAIDS Black Box Warning

•  BLACK BOX WARNING:
  – May increase the risk of serious thrombotic events, MI, and stroke.
  – Increase risk of serious GI adverse effects such as bleeding, ulcer, and perforation.
Treatment and Management: Steroids

- steroids interfere with all facets of the inflammatory process and effectively shut it down
- rapidly bring down joint infl’n and increase physical function and reduce progression of joint damage
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## Anti-Inflammatory Efficacy

<table>
<thead>
<tr>
<th>Generic Name of Medication</th>
<th>Anti-Inflammatory Activity</th>
<th>Equivalent Dose (mg)</th>
<th>Relative Sodium Retaining Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrocortisone</td>
<td>1.0</td>
<td>20 mg</td>
<td>1.0</td>
</tr>
<tr>
<td>Prednisone</td>
<td>4.0</td>
<td>5 mg</td>
<td>0.8</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>4.0</td>
<td>5 mg</td>
<td>0.8</td>
</tr>
<tr>
<td>Triamcinolone</td>
<td>5.0</td>
<td>4 mg</td>
<td>0.0</td>
</tr>
<tr>
<td>Methylprednisolone</td>
<td>5.0</td>
<td>4 mg</td>
<td>0.0</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>25.0</td>
<td>0.75 mg</td>
<td>0.0</td>
</tr>
<tr>
<td>Betamethasone</td>
<td>25.0</td>
<td>0.75 mg</td>
<td>0.0</td>
</tr>
</tbody>
</table>
Systemic Corticosteroids

- Often grouped based on duration of action:
  - **Short acting**: Hydrocortisone and Cortisone
  - **Intermediate acting**: Prednisone, Prednisolone, Methylprednisolone, and Triamcinolone
  - **Long acting**: Dexamethasone

- Most commonly used oral steroid by Optometrists: **Prednisone**

- Most commonly used IV steroid by Optometrists: **Methylprednisolone**
Side Effects of Systemic Corticosteroids

- Incidence increases with long-term high-dose therapy.
- Length of use has greater link to developing side effects than dosage amount.
Corticosteroids Side Effects

- Decreased growth in children
- Glaucoma
- Centripetal distribution of body fat
- Negative calcium balance
- Impaired wound healing
- Increased risk of infection
- Hirsutism
- Increased appetite
- Emotional disturbances
- Peptic ulcer
- Hypertension
- Peripheral edema
- Hypokalemia
Treatment and Management: Steroids

- usually used in short-term pulse dosages (e.g. 7.5 mg/day in combination with DMARD to reduce joint damage in early disease Tx).
Treatment and Management: Antimalarials

- hydroxychloroquine more common and less toxic than more effective chloroquine
- usual dose is 200-400 mg/d @night with onset of action after a period of 2-4 months
- has mild DMARD effect, does not slow radiographic progression and has relatively slow onset of action, useful with other DMARD’s
Treatment and Management: Antimalarial Ocular Complications

• Have affinity for pigmented structures such as iris, choroid and RPE
• Toxic affect on the RPE and photoreceptors leading to rod and cone loss.
• Have slow excretion rate out of body with toxicity and functional loss continuing to occur despite drug discontinuation.
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Question

Which of the following depicts a retina undergoing hydroxychloroquine toxicity?
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Treatment and Management: Antimalarial Ocular Complications

- Toxicity can lead to whorl keratopathy, “bulls eye” maculopathy, retinal vessel attenuation, and optic disc pallor.
- Early stages of maculopathy are seen as mild stippling or mottling and reversible loss of foveal light reflex
- “Classic” maculopathy is in form of a “bulls eye” and is seen in later stages of toxicity
  - this is an irreversible damage to the retina despite discontinuation of medication
Treatment and Management: Antimalarials

Bulls Eye Maculopathy

Whorl Keratopathy
Fabry Disease

- alpha-galactosidase-A deficiency.
  - insufficient breakdown of lipids, which build up to harmful levels in the eyes, kidneys, autonomic nervous system, and cardiovascular system.
- Fabry disease is one of several lipid storage disorders and the only X-linked lipid storage disease.
- Lipid storage may lead to impaired arterial circulation and increased risk of heart attack or stroke.
  - The heart may also become enlarged and the kidneys may become progressively involved.
- Other signs include decreased sweating, fever, and gastrointestinal difficulties.
Revised Recommendations on Screening for Retinopathy

• 2002 recommendations for screening were published by Ophthalmology

• Revised recommendations on screening published in Ophthalmology 2011;118:415-42
  – Significant changes in light of new data on the prevalence of retinal toxicity and sensitivity of new diagnostic techniques
  – Risk of toxicity after years of use is higher than previously believed
    • Risk of toxicity approaches 1% for patients who exceed 5 years of exposure
Revised Recommendations on Screening for Retinopathy

• Amsler grid testing removed as an acceptable screening technique
  – NOT equivalent to threshold VF testing
• Strongly advised that 10-2 VF screening be supplemented with sensitive objective tests such as:
  – Multifocal ERG
  – Spectral domain OCT
  – Fundus autofluorescence
• “Ideal” body weight versus “real weight” recommended for dosing and at <6.5 mg/kg
Ideal vs Real Weight

• Ideal body weight calculation:
  – Women: 100 pounds for the first 5 feet of height
  – Men: 110 pounds for the first 5 feet of height
    • Add 5 pounds for every additional inch

• Overdose at typical dosage of 400 mg/day
  – Any woman < 5’7”
  – Any man < 5’5”
    • (135 lbs=61.2 kg, 400/61.2=6.5 mg/kg/day)
Ideal vs Real Weight

• Our patient:
  – 5’8” and 135 pounds and taking 400 mg/day
  – Ideal weight = 140 pounds (6.3 mg/kg/day)
  – Real weight = 135 pounds (6.5 mg/kg/day)
“New” New Recommendations

- Recommendations on Screening for Chloroquine and Hydroxychloroquine Retinopathy – Ophthalmology 2016; 123:1386-1394
  - Released March 2016 from American Academy of Ophthalmology
  - revised in light of new information about the prevalence of toxicity, risk factors, fundus distribution, and effectiveness of screening tools.
2016 Recommendations

• maximum daily HCQ use of 5.0 mg/kg real weight, which correlates better with risk than ideal weight.

• risk of toxicity is dependent on daily dose and duration of use.
  – at recommended doses:
    • risk of toxicity up to 5 years is under 1%
    • up to 10 years is under 2%
    • rises to almost 20% after 20 years. However, even after 20 years, a patient without toxicity has only a 4% risk of converting in the subsequent year.
2016 Recommendations

• High dose and long duration of use are the most significant risks.
  – Other major factors are concomitant renal disease, or use of tamoxifen
• A baseline fundus examination should be performed to rule out preexisting maculopathy.
• Begin annual screening after 5 years for patients on acceptable doses and without major risk factors.
2016 Recommendations

• primary screening tests are automated visual fields plus spectral-domain optical coherence tomography (SD OCT)

• most patients of Asian descent will show initial damage in a more peripheral extramacular distribution near the arcades
Revised Recommendations on Screening for Retinopathy

• Parafoveal loss of visual sensitivity may appear before changes are seen on fundus evaluation
  • Many instances where retinopathy was unrecognized for years as field changes were dismissed as “non-specific” until the damage was severe
  • 10-2 VF should always be repeated promptly when central or parafoveal changes are observed to determine if they are repeatable
  • Advanced toxicity shows well-developed paracentral scotoma
Paracentral Scotomas
Normal Retina: VF/OCT/ERG


PIL=PR Integrity Line
Mild Maculopathy


- Normal Foveal Peak
- Thinned Outer Nuclear Layer
- PIL
- Paracentral Scotomas
- Loss of Photoreceptor Inner Segment/Outer Segment Junction

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Bull’s Eye Maculopathy

- Flattened Foveal Peak
- Dense Para/Central Defects
- RPE Atrophy
- Remnant of PIL

# Major Risk Factors

<table>
<thead>
<tr>
<th>Factor</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily dosage</td>
<td></td>
</tr>
<tr>
<td>HCQ</td>
<td>$&gt;5.0 \text{ mg/kg real weight}$</td>
</tr>
<tr>
<td>CQ</td>
<td>$&gt;2.3 \text{ mg/kg real weight}$</td>
</tr>
<tr>
<td>Duration of use</td>
<td>$&gt;5 \text{ Yrs, assuming no other risk factors}$</td>
</tr>
<tr>
<td>Renal disease</td>
<td>Subnormal glomerular filtration rate</td>
</tr>
<tr>
<td>Concomitant drugs</td>
<td>Tamoxifen use</td>
</tr>
<tr>
<td>Macular disease</td>
<td>May affect screening and susceptibility to HCQ/CQ</td>
</tr>
</tbody>
</table>

\[CQ = \text{chloroquine}; \ HCQ = \text{hydroxychloroquine.}\]
Screening Recommendations

Table 2. Screening Frequency

<table>
<thead>
<tr>
<th>Screening Type</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline Screening</td>
<td>Fundus examination within first year of use</td>
</tr>
<tr>
<td></td>
<td>Add visual fields and SD OCT if maculopathy is present</td>
</tr>
<tr>
<td>Annual Screening</td>
<td>Begin after 5 yrs of use</td>
</tr>
<tr>
<td></td>
<td>Sooner in the presence of major risk factors</td>
</tr>
</tbody>
</table>

SD OCT = spectral-domain optical coherence tomography.
Treatment and Management: Methotrexate

- now considered as part of mainstay treatment
- antimetabolite used in cancer therapy that inhibits DNA synthesis (thought to cause suppression of lymphocyte proliferation)
- low dose in RA (7.5-25mg) once weekly orally or injection with onset of action 6-8 weeks
Treatment and Management: Methotrexate

- toxicity not uncommon but adverse events tend to be minor and can be managed by cessation of drug.
- supplement of folic acid prevents common SE of oral ulceration and nausea.
- serious complications of lung disease and fibrosis with incidence of 3-15% and fatality of 17%.
Treatment and Management: Biological Therapies-TNF Inhibitor

- High concentration of TNF-alpha in synovial fluid in RA and increased in areas of bone erosions
- TNF-alpha released in cell damage and binds to receptors that increase the inflammatory process and cell death
Treatment and Management: Biological Therapies-TNF Inhibitor

- inhibitors bind TNF before it can be bound to the receptor (infliximab [Remicade], etanercept [Enbrel], adalimumab [Humira]) and newest golimumab (Simponi)
- quicker onset of action (several weeks)
- new studies indicate use as first line therapy, potentially combined with methotrexate
Treatment and Management: Biological Therapies-TNF Inhibitor

- Remicade: 3 mg/kg as IV infusion followed by similar doses at 2 and 6 weeks and then every 8 weeks after.
- Enbrel and Humira are SC injections every 2 weeks.
- Newest is Simponi which is once a month injection.
- Adverse affects include increased risk of opportunistic infections (TB most common), malignancies (lymphoma) and neurological disease.
- Common SE’s include nausea and vomiting.
Case: Gonzalez

- 33 HF presents with a painful, red right eye
  - Started a couple of days ago, deep boring pain
  - Has tried Visine but hasn’t helped the redness
- PMHx: patient reports she has been diagnosed with rheumatoid arthritis 3 years ago
  - Takes Celebrex for the joint pain
  - Patient reports she occasionally gets a skin rash when she is outdoors in the sun
- POHx: unremarkable
- PMHx: mother has rheumatoid arthritis
Case: Gonzalez

- VA: 6/9 (20/30) OD, 6/6/ (20/20) OS
- Pupils: PERRL – APD
- VF: FTFC OH
- EOM’s: FROM OU
- BP: 130/85 mm Hg RAS
- SLE: see picture
  - 2+ cells, mild flare
- IOP’s: 16, 16 mm HG
- DFE: see fundus photo
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# Etiologies of Cotton Wool Spots

<table>
<thead>
<tr>
<th>Vascular Occlusive Disease</th>
<th>Hypertension</th>
<th>Ocular Ischemic Syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autoimmune Disease e.g.</td>
<td>Hyperviscosity syndromes</td>
<td>Trauma</td>
</tr>
<tr>
<td>SLE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-eclampsia</td>
<td>Radiation Retinopathy</td>
<td>Toxic e.g. interferon</td>
</tr>
<tr>
<td>Neoplastic e.g. leukemia</td>
<td>Anterior Ischemic Syndrome</td>
<td>Infectious e.g. HIV</td>
</tr>
</tbody>
</table>
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Patient Update

• Patient was worked up for lupus and diagnosed with lupus.
• Patient was already taking Celebrex which was not effective in treating the scleritis she presented with
  – upon referral to rheumatology it was discovered that she had several organs already being affected by the lupus
  – she was put on immunosuppressive agents to treat the systemic and ocular manifestations
• Patient was taken off of Celebrex and put on plaquenil (hydroxychloroquine) 400 mg po qd
Ocular Manifestations: Dry Eye

- Most common ocular complication is dry eye
- >95% of patients suffer from dry eye signs and symptoms
- Compromised cornea can lead to bacterial keratitis
Differential Diagnosis of Dry Eye

DRY EYE

Deficient Aqueous Tear Production
- Sjögren Syndrome
- Non-Sjögren Syndrome

Increased Evaporative Loss
- Blepharitis/Meibomian Gland Dysfunction
- Exposure
- Other factors
  1. Contact lenses
  2. Blink abnormality
  3. Environmental
## Treatment/Management

<table>
<thead>
<tr>
<th>DTS Severity</th>
<th>Treatment Recommendation</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Tier 1</td>
<td>No treatment</td>
<td>Use of hypoallergenic products</td>
</tr>
<tr>
<td></td>
<td>Preserved tears</td>
<td>Water intake</td>
</tr>
<tr>
<td></td>
<td>Environmental management</td>
<td>Psychological support</td>
</tr>
<tr>
<td></td>
<td>Allergy drops</td>
<td>Avoidance of drugs contributing to dry eye</td>
</tr>
<tr>
<td>Tier 2</td>
<td>Unpreserved tears</td>
<td>Secretagogues</td>
</tr>
<tr>
<td></td>
<td>Gels</td>
<td>Topical steroids</td>
</tr>
<tr>
<td></td>
<td>Ointments</td>
<td>Topical cyclosporine</td>
</tr>
<tr>
<td></td>
<td>Nutrient support (fatty acids)</td>
<td></td>
</tr>
<tr>
<td>Tier 3</td>
<td>Tetracyclines</td>
<td>Punctual plugs</td>
</tr>
<tr>
<td>Tier 4</td>
<td>Surgery</td>
<td>Punctal cauterity</td>
</tr>
<tr>
<td></td>
<td>Systemic anti-inflammatory therapy</td>
<td>Acetylcysteine</td>
</tr>
<tr>
<td></td>
<td>Oral cyclosporine</td>
<td>Contact lenses</td>
</tr>
<tr>
<td></td>
<td>Moisture goggle</td>
<td></td>
</tr>
</tbody>
</table>
Episcleritis

• self-limiting, recurring, idiopathic inflammation of the episcleral tissue that does not threaten vision
• Symptoms are a localized area of hyperemia of the globe, irritation, and lacrimation. Diagnosis is clinical. Treatment is symptomatic
• Unilateral (bilateral possible but rarely simultaneously)
Episcleritis

- occurs in young adults, more commonly among women. It is usually idiopathic; it can be associated with connective tissue diseases and rarely with serious systemic diseases.
- Recurrent episodes of episcleritis usually manifest prior to active periods of arthritis and a better indicator than dry eye.
- Episcleritis will recur despite systemic treatment.
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Treatment and Management: Episcleritis

• Treatment of episcleritis is dependent upon severity and chronicity.
• Palliative care maybe considered for mild cases (ocular lubrication).
• Utilization of vasoconstrictors, NSAIDs and steroid (Pred mild, Lotemax) use for more severe or chronic cases.
Scleritis

- chronic, painful, and potentially blinding inflammatory disease that is characterized by edema and cellular infiltration of the scleral and episcleral tissues
- Symptoms of scleritis can include pain, tearing or photophobia, tenderness, and decreased visual acuity. The primary sign is redness.
Ocular Manifestations-Scleritis

- classified into anterior and posterior.
- Anterior:
  - Diffuse and nodular forms
  - Necrotizing (with/without inflammation) less frequent
    - Have the most serious systemic implications
    - Scleromalacia perforans
- Posterior:
  - characterized by flattening of the posterior aspect of the globe, thickening of the posterior coats of the eye (choroid and sclera), and retrobulbar edema.
Treatment and Management: Scleritis

• Scleritis treatment depends on both the type and severity.
• Aggressive treatment is necessary in order to prevent structural damage.
• Topical steroids (e.g. Pred Forte) have ease of use and relatively minimal side effect profile when compared to systemic therapy are advantageous, scleritis does not usually respond to topical corticosteroids alone.
• Subconjunctival/subtenon’s triamcinolone:
  – A multicenter retrospective case series of 68 eyes with either diffuse or nodular scleritis showed that 89.7% of eyes had complete resolution after a single injection
  – Only indicated in non-necrotizing forms
Treatment and Management: Scleritis

• Oral NSAIDs:
  – considered first-line therapy for scleritis for their ease of use, cost, and relatively mild side effect profile for both anterior and posterior scleritis
  – E.g. Ibuprofen 400-600 mg QID, Naproxen 250-500 mg BID, or Indomethacin 25-50 mg TID
  – short term use of an NSAID is often well tolerated, NSAIDs can cause adverse effects which include peptic ulcer disease, hypertension, increased heart disease, bleeding, fluid retention, renal disease, and mood change
Treatment and Management: Scleritis

- **Oral Prednisone:**
  - considered to be the first line therapy for the treatment of non-necrotizing scleritis in the setting of poor control on oral NSAIDs, or as a first line agent for necrotizing scleritis.
  - Typically start at between 40-60 mg until resolution with a slow taper
Treatment and Management: Scleritis

- If necrotizing present patient needs to receive aggressive medical therapy by rheumatologist
  - patients have better prognosis when immunosuppressive therapy is instituted
SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)
Systemic Lupus Erythematosus (SLE)

- Idiopathic, multisystemic inflammation disorder characterized by hyperactivity of immune system and prominent auto-antibody production
  - against components of cell membranes and nuclear material
- Acute periods followed by periods of remission are common
  - gives disease an unpredictable course
Systemic Lupus Erythematosus (SLE)

- Definite genetic predisposition has been demonstrated
  - environmental factors also play a role especially as triggers
- Clinical course varies from mild episodic disorder to rapidly developing fatal disease
Epidemiology

• SLE is not uncommon with prevalence exceeding 1:2000 persons with 85% being female

• Disease may occur at any age though most patients are b/w ages 20-40
  – AA being affected 3x more than any other race (and more severely)
Epidemiology

• Have to ensure that condition is not secondary to a drug response (several drugs produce lupus-like syndrome)

  – Agents strongly associated include:

    • Procainamide (cardiac arrhythmias), hydralazine (high blood pressure) and isoniazid (anti-tuberculosis)
    • Others include: phenytoin, quinidine, tetracyclines and TNF inhibitors.
Diagnosis

• Based on clinical presentation and lab results
• Systemic features include
  – fever
  – anorexia
  – malaise and
  – weight loss.
• Most patients have skin lesions at some time with the characteristic “butterfly” rash (occurs approx 50%) and often precedes disease manifestations
Diagnosis

- Joint symptoms (with/without active synovitis) occur in >90% of patients and are often the earliest manifestation.
- Other organs affected include heart, kidney, lungs, CNS.
- American Rheumatology Association established 11 criteria for diagnosis (8 clinical manifestations and 3 lab).
  - Minimum of 4 needed serially or simultaneously.
Lab Tests:
Antinuclear Antibodies (ANA)

- AB’s directed against nuclear material:
- Detection is via indirect immunofluorescence
  - ANA with titers $\geq 1:40$ considered positive
- Associated conditions:
  - Positive tests occur in a wide variety of conditions
    - Low-titer ANA are relatively common among healthy adults
# Conditions Associated with Positive ANA

<table>
<thead>
<tr>
<th>Rheumatic Diseases</th>
<th>Organ-Specific AI Diseases</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>SLE</td>
<td>AI thyroid disease</td>
<td>Drug-induced lupus</td>
</tr>
<tr>
<td>Mixed connective tissue disease</td>
<td>AI hepatitis</td>
<td>Asymptomatic drug-induced ANA</td>
</tr>
<tr>
<td>Scleroderma</td>
<td>Primary biliary cirrhosis</td>
<td>Chronic infections</td>
</tr>
<tr>
<td>Sjogren syndrome</td>
<td>AI cholangitis</td>
<td>Idiopathic pulmonary fibrosis</td>
</tr>
<tr>
<td>RA</td>
<td></td>
<td>Primary pulmonary hypertension</td>
</tr>
<tr>
<td>Polymysositis</td>
<td></td>
<td>Lymphoproliferative disorders</td>
</tr>
<tr>
<td>Dermatomyositis</td>
<td></td>
<td>Type 1 diabetes (ketoacidosis)</td>
</tr>
<tr>
<td>Discoid Lupus</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Lab Tests:
Antinuclear Antibodies (ANA)

• Indications:
  – Very useful initial test when there is clinical suspicion of:
    • SLE,
    • drug induced lupus
    • Mixed connective tissue disease
    • Scleroderma

• Interpretation:
  – Sensitivity of ANA for SLE is very high (>95%)
    • Negative result is very strong evidence against the diagnosis and usually precludes the need to pursue further testing
Lab Tests:
Antinuclear Antibodies (ANA)

• Interpretation:
  – Probability of an underlying AI disease increases with the titer of the ANA
  – In an unselected population:
    • Positive test has a predictive value for SLE of 30-40%
    • Negative predictive value for SLE is >99%
  – In proper clinical context a positive ANA provides support for further testing for SLE
ANA Staining Patterns

- **Peripheral (rim)**
  - anti-DNA (not seen on HEp-2)
  - SLE

- **Homogeneous (diffuse)**
  - anti-DNA
  - anti-histone
  - anti-DNP (nucleosomes)
  - RA & SLE
  - Misc. Disorders (anti-ssDNA)

- **Speckled**
  - anti-Sm & RNP
  - anti-Ro & La
  - anti-Jo-1 & Mi-2
  - anti-Scl-70
  - SLE & SS
  - PM/DM
  - PSS (Systemic)

- **Centromere**
  - anti-centromere
  - PSS (CREST)

- **Nucleolar**
  - anti-nucleolar
  - SLE & PSS
Lab Tests: Antibodies to Double-Stranded DNA

• ELISA is most commonly used
• Associated conditions:
  – Occurs in SLE and is rare in other diseases and in healthy persons
• Indications:
  – Should be measured when there is clinical suspicion of SLE and the ANA is positive
• Interpretation:
  – Specificity for SLE is 97% and approaches 100% when titer is high
  – AB’s occur in 60-80% of patients with SLE
Lab Tests

• Decreased serum complement C1 level is 90% predictive for SLE and C4 is 75%
  – simultaneous presence of both a decreased C1 level and native DNA Ab’s has been reported to be virtually 100% predictive

• Decreased serum complement levels result from activation and consumption of complement components
“New” Lab Tests

• Anti Sm is found almost exclusively in people with lupus.
  – It is present in 20% of people with the disease
  – rarely found in people with other rheumatic diseases and its incidence in healthy individuals is less than 1%
• Anti-RNP antibodies are commonly found along with anti-Sm antibodies in people with SLE.
  – The incidence in lupus is approximately 25%, while less than 1% of healthy individuals possess this antibody.
• Anti-Ro/SSA and Anti-La/SSB are antibodies found mostly in people with systemic lupus (30-40%) and primary Sjogren’s syndrome.
  – They are also commonly found in people with lupus who have tested negative for anti-nuclear antibodies.
Treatment and Management

• No cure for SLE (rest, reduce stress and avoid UV exposure)

• Medical management includes:
  – Salicylates and NSAIDs employed to treat arthralgias, arthritis, myalgias and fever in 20-30% of Px with mild disease
  – Antimalarials (Plaquinil) used to treat discoid lesions and joint disease
  – High dose, short-acting steroids are used in life-threatening and severely disabling cases. Prolonged maintenance at low dosages needed after.
  – Cytotoxic controversial-used when steroids ineffective
  – Exp therapy: high dose immunoglobulin injections
Ocular Manifestations

- SLE produces various ocular complications which tend to manifest in more acutely ill patients.
- Retinal vasculopathy is believed to be due to autoimmune reactions to Ab/Ag complexes deposited in the retinal/choroidal vessel walls.
- Common retinal finding include:
  - Cotton wool spots (CWS)
  - Retinal hemes
Ocular Manifestations

- Occlusions are uncommon but occur more frequently in arteries and can result in nonperfusion and hypoxia.
- Optic nerve and retinal neo may arise.
- Vitreous heme and RD may also occur.
- Optic atrophy and blindness may result in severe occlusions.
Ocular Manifestations

- SPK most common corneal change
- In patients with uncontrolled systemic disease sicca syndrome is common
- Occasional corneal manifestations may include infiltrates, ulcers and neo.
Ocular Manifestations

- Scleritis is usually diffuse and nodular and is fairly common. It may be the presenting feature of SLE.
- Non-granulomatous uveitis is sometimes found.
- Diplopia and pupillary abnormalities secondary to cranial nerve palsies also arise.