Adult Infectious Disease Review

Saroj Misra, DO, FACOFP

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Name of CME Activity: ACOFP Intensive Update & Board Review in Family Medicine
Dates and Location of CME Activity: August 24-26, 2018, Loews Chicago O’Hare Hotel, Rosemont, IL, United States

Name of Faculty/Moderator: Saroj Misra, DO, FACOFP

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<table>
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<tr>
<th>Organization With Which Relationship Exists</th>
<th>Clinical Area Involved</th>
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</table>

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ACOFP 2018
Intensive Update & Board Review
Adult Infections
Saroj Misra, DO, FACOFP
Goals & Objectives

- Review 5 infectious diseases of adults in 4 systems
  - Hepatobiliary System
    - Hepatitis C
  - Genitourinary System
    - Gonorrhea/Chlamydia
    - UTI
  - Integumentary System
    - MRSA/VRE
  - Cardiac
    - Bacterial Endocarditis
- Provide ‘Quick Hit’ information on Hep A
- A splash of Lime
How do these topics compare?

- Harvard Medical School Review - ID in Adults
  - HIV, Hep C, Endocarditis, UTI, C. diff colitis
  - STI, Pneumonia, Lyme, Vaccinations, Zika & Ebola
- IDSA Infectious Disease Review Course
  - Pneumonia, Lyme, Fungal Disease (Immunocompromise)
  - Ticks, Mites, Lice
  - Group A Strep, Influenza, CMV, EBV, HHV
- STIs, Endocarditis, HIV, Hepatitis
Format for Today

• Case
• Epidemiology/Statistics
• Diagnosis/Treatment
• Prophylaxis
Case #1

- 57 Y/O WM - annual well
- Good health; obese, drinker
- Remote history of IVDA
- Physical Exam WNL

<table>
<thead>
<tr>
<th>Test</th>
<th>Results</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1C</td>
<td>5.8%</td>
<td>&lt;5.0%</td>
</tr>
<tr>
<td>AST/ALT</td>
<td>115/190</td>
<td>5-40/5-35</td>
</tr>
<tr>
<td>Anti-HAV IgM</td>
<td>Neg</td>
<td>Neg</td>
</tr>
<tr>
<td>HBsAb</td>
<td>Neg</td>
<td>Immunized</td>
</tr>
<tr>
<td>HBsAg</td>
<td>Neg</td>
<td>Neg</td>
</tr>
<tr>
<td>Anti-HCV-Ab</td>
<td>Pos</td>
<td>Neg</td>
</tr>
</tbody>
</table>

Image Source: Isaiah Alfaro
Case #1

Based on history & labs, the next best step would be:

A. Liver biopsy to determine degree of fibrosis
B. Repeat anti-HCV antibody in 12 months
C. Antiviral therapy for acute Hepatitis C infection

D. Perform qualitative HCV RNA testing
E. Evaluate for possible liver transplant
# Hepatitis C - Testing Results

<table>
<thead>
<tr>
<th>TEST OUTCOME</th>
<th>INTERPRETATION</th>
<th>FURTHER ACTIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCV antibody nonreactive</td>
<td>No HCV antibody detected</td>
<td>Sample can be reported as nonreactive for HCV antibody. If recent exposure in person tested is suspected, test for HCV RNA.†</td>
</tr>
<tr>
<td>HCV antibody reactive</td>
<td>Presumptive HCV infection</td>
<td>A repeatedly reactive result is consistent with current HCV infection, or past HCV infection that has resolved, or biologic false positivity for HCV antibody. Test for HCV RNA to identify current infection.</td>
</tr>
<tr>
<td>HCV antibody reactive, HCV RNA detected</td>
<td>Current HCV infection</td>
<td>Provide person tested with appropriate counseling and link person tested to care and treatment.</td>
</tr>
<tr>
<td>HCV antibody reactive, HCV RNA not detected</td>
<td>No current HCV infection</td>
<td>No further action required in most cases. If distinction between true positivity and biologic false positivity for HCV antibody is desired, and if sample is repeatedly reactive in the initial test, test with another HCV antibody assay. In certain situations, follow up with HCV RNA testing and appropriate counseling.</td>
</tr>
</tbody>
</table>

Source: CDC (https://www.cdc.gov/hepatitis/hcv/pdfs/hcv_graph.pdf)
Hepatitis C

A viral infection of the liver transmitted through blood or body fluid, presenting with nonspecific symptoms and usually progressing to a chronic state which can increase the risk for hepatocellular cancer.
Hepatitis C - Epidemiology

- RNA virus (picornavirus)
- Transmission: body fluids, blood, maternal-fetal
- Leading reason for liver transplantation worldwide
- Incidence
  - Over 41,000 cases in US in 2016 (CDC)
  - 185 million cases worldwide
  - 3.5 million chronic cases in US
- Mortality
  - 1-5 deaths per 100 cases (liver cancer or cirrhosis)
Hepatitis C - Acute vs Chronic

- **Acute** cases are rare - 15-25%
  - Mild/vague symptoms: appetite, fatigue, nausea, myalgia
  - No jaundice
- **Chronic** cases are common - 75-85%
  - Viral replication for at least 6 months
  - May be asymptomatic for decades
  - Fatty liver - 50% of patients
  - Cirrhosis - 10-20% of patients; HCC 20x more likely with cirrhosis
Progression of Hepatitis C

- **Acute Infection**
  - Recovery: 15-25%
  - Chronic HCV: 75-85%

- **Chronic HCV**
  - Stable: 80-90%
  - Cirrhosis: 10-20%
  - Mortality: 25%

- **Mortality**
  - 75%

- **20-30 years**
Hepatitis C - Screening

- Screening
  - American Association for the Study of Liver Disease
    - Annual screening for IVDA, HIV (+) and MSM
  - USPSTF
    - Blood transfusion (1992), multiple sex partners, tattoos, incarceration
    - 1 time screen if born between 1945-1965
Screen with anti-HCV antibody testing

Nonreactive

Acute HCV infection suspected?

No

No further workup required

Yes

Perform HCV RNA testing

Not detected

No current HCV infection

Detected

Current HCV infection

Use Metavir score to determine the need for treatment

Image Source: 'Diagnosis and Management of Hepatitis C' Am Fam Physician. 2015 Jun 15;91(12):835-842.
# Metavir Scoring System for the Assessment of Liver Fibrosis and Cirrhosis

<table>
<thead>
<tr>
<th>LEVEL OF FIBROSIS</th>
<th>SCORE</th>
</tr>
</thead>
<tbody>
<tr>
<td>No fibrosis</td>
<td>0</td>
</tr>
<tr>
<td>Minimal scarring</td>
<td>1</td>
</tr>
<tr>
<td>Positive scarring with extension beyond area containing blood vessels</td>
<td>2</td>
</tr>
<tr>
<td>Bridging fibrosis with connection to other areas of fibrosis</td>
<td>3</td>
</tr>
<tr>
<td>Cirrhosis or advanced liver scarring</td>
<td>4</td>
</tr>
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</table>

**Note:** Treatment should be considered in patients with a score ≥ 2.6.
Hepatitis C - **Treatment**  
It’s All About the **Genotype**

- Recommendations for treatment change rapidly
- Current recommendations are based on *genotype*
- Possible choices include:
  - Pegylated Interferon
  - Ribavirin
  - NS3/4A Inhibitors
  - NS5B Inhibitors
Hepatitis C - Monitoring & Cure

- Baseline tests: TSH, CBC, BUN/Cr/GFR, AST/ALT, Alk Phos
- Check for **pregnancy**; monitor **depression**
- Stop **drinking**, **immunize** for Hep A & B
- Check Quantitative HCV viral load at 4, 12 and 24 weeks
  - **Goal**: (-) HCV 24 weeks post-treatment (SVR24)
  - SVR12 - SVR after 12 weeks (Genotype 1)
  - SVR is best in Genotype 2 or 3
  - Repeat viral at 6 & 12 months for longer SVR
  - US every 6 months if advanced fibrosis
Case #2

- 21 year-old female with concerns about ‘STD’ because of abnormal discharge
- Denies F/C or pelvic pain
- Has boyfriend who was treated for STD; doesn’t use condoms
- Exam reveals non-tender, friable os with mucopurulent cervical discharge (MPD)

Image source: CDC
Given the likelihood that this patient has gonorrhea or chlamydia a reasonable approach to treatment might include any of these medications:

1. Ceftriaxone
2. Doxycycline
3. Clindamycin
4. Azithromycin
5. Gentamicin

A. 1, 2, 3
B. 2, 3, 4
C. 1, 2, 4, 5
D. 3, 4, 5
E. 1, 3, 5
Urethritis/Cervicitis

- Numerous Causes
  - Cervicitis
    - *N. gonorrhea*/*C. trachomatis*
    - Others (*M. genitalium*, BV, HSV-2)
  - Urethritis
    - *N. gonorrhea*
    - Nongonococcal urethritis
      - *C. trachomatis, M. genitalium*
      - Others (*T. vaginalis*, HSV, adenovirus)
Gonorrhea

- Bacteria responsible for:

- **Urethritis**
  - Incubation period: 1-14 days
  - Symptoms: dysuria and purulent discharge

- **Cervicitis**
  - Often asymptomatic, may have associated urethritis
  - Mucopurulent discharge present, but may be seen as normal

Image source: CDC
Gonorrhea

Image source: CDC
Gonorrhea

- **Diagnosis**
  - Gram stain showing: *gram (-) intracellular diplococci (GNID)*
  - Culture from swab (urethral, endocervical, vaginal, rectal and/or pharyngeal)
  - **Nucleic Acid Amplification Test (NAAT)**
    - Can be done off urine
  - If (+), should test for chlamydia, syphilis, HIV
Gonorrhea

- **Treatment**
  - Ceftriaxone **and** Azithromycin or Doxycycline
  - No longer recommend Cefixime as 1st line (2012)
    - If used as alternative, 1 week retest for cure
  - If allergic to ceftriaxone
    - Consider Azithromycin + gentamicin (IM) or gemifloxacin (PO)
  - Test for *C. trachomatis* and treat if (+)
    - If not tested, treat empirically (Azithromycin or Doxycycline)

- **Partners**
  - Evaluate & treat partners if they have been in contact contact **60 days** prior to signs
Gonorrhea

- Other Considerations
  - Disseminated Gonococcal Infection
    - Common cause of **acute septic arthritis**
    - Young adults who are sexually active
    - Dermatitis, tenosynovitis, asymmetrical arthralgias
    - Complications - meningitis, endocarditis
    - Hospitalize-treat (Ceftriaxone IV)-manage complications
Chlamydia

• **Most frequently reported** bacterial STI in US
• Highest prevalence in people ≤ 25 years old
• Sequelae: PID, ectopic pregnancy, infertility
• Annual screen for **all** sexually active women
  • ≤ 25 (CDC) or ≤ 24 (USPSTF)
  • Older women with **risk factors** (new/multiple partners)
  • **Pregnant** women (1st and 3rd trimesters if at risk)
Chlamydia

- Urethritis
  - Incubation is 7-21 days
  - Often asymptomatic
  - Symptoms
    - mild dysuria, meatal itching & mucopurulent discharge (MPD)

- Cervicitis
  - Often asymptomatic
  - Mucopurulent cervical or vaginal discharge
Chlamydia

**Diagnosis**
- Culture is possible - but difficult, long & expensive

**DNA**
- **NAAT** - highly sensitive (swab or urine)
- Nucleic acid hybridization test (DNA probe)

**Antigen**
- Enzyme-linked immunoabsorbent assay (EIA)
- Direct fluorescent antibody test (DFA)
Chlamydia

• Treatment
  • **Azithromycin or Doxycycline**
  • Single dose Azithromycin for compliance concern
  • Alternatives: Levofloxacin, Ofloxacin or Erythromycin

• Follow Up
  • Retest at approximately 3 months (no sooner) or next visit
  • If pregnant, test-of-cure at 3 weeks post-therapy
Chlamydia

- **Partners and Special Cases**
  - Evaluate, test & treat partners if they have had contact **60 days** prior to signs
  - Evaluate and treat the most recent partner if contact was longer than 60 days prior to signs
  - Pregnant - Use Azithromycin or Amoxicillin
  - Infants - Worry about ophthalmia neonatorum or infant pneumonia and treat with Erythromycin
Case #3

- 28 Y/O diabetic WF presents with 3 day history of dysuria
- Seen by PCP
  - History: Recently started new relationship - very active sexually
  - Vitals are normal; patient is afebrile
  - PE reveals no adnexal tenderness, cervical motion tenderness
  - UA shows WBCs, (-) nitrites
  - Specific gravity is normal, microscopic hematuria is present
- Microscopy reveals the following:
Case #3

Image source: commons.wikimedia.org
Case #3

Based on the testing done in office, you make a tentative diagnosis of urinary tract infection. What is the MOST LIKELY causative organism for this patient’s infection, based on the findings given?

A. *Escherichia coli*
B. *Staphylococcus aureus*
C. *Proteus mirabilis*
D. *Klebsiella pneumoniae*
E. *Staphylococcus saprophyticus*
UTI/Pyelonephritis - Epidemiology

- UTIs have a high incidence
  - 50% of women will have one during lifetime
  - Most commonly due to *E. coli* (86%)
    - Other causative organisms:
      - S. saprophyticus, Klebsiella sp., Proteus sp. (10% total)

- Pyelonephritis less common, but potential complication
  - 250,000 office visits; 200,000 admissions yearly

- Highest incidence in healthy women 15-29 years of age

- Complications for untreated infection
  - Sepsis/Permanent structural damage to kidney & function
UTI/Pyelonephritis - Diagnosis

- History of dysuria, frequency and urgency/hesitancy
- Rarely gross hematuria; vaginal discharge not present
- For pyelonephritis
  - Presence of fever (>100.4 F) and flank pain
  - Physical exam demonstrates CVA tenderness (Lloyd’s)
- Initial testing: Urinalysis
  - (+) leukocyte esterase and or (+) nitrites
  - Presence of WBCs, RBCs, bacteria (rods, diplococci)
- Follow-up testing: Urine Culture
  - Grows out > 10^5 colony-forming units; get sensitivities
Pyelonephritis - Imaging

- Options include: US and CT
- Usually reserved for patients who are failing conventional therapy and/or are admitted
- US - low sensitivity for detection of pyelonephritis
  - Potential value - looking at bladder for outflow obstruction
- CT - only moderately better
- Imaging more useful for patients failing to respond
  - Widened differential diagnosis
    - Acute bacterial nephritis, abscess, interstitial nephritis
    - Chronic/emphysematous/xanthogranulomatous pyelonephritis
UTI/Pyelonephritis - Treatment

- No single agent is best for everyone
- IDSA 2011
  - Uncomplicated:
    - **Nitrofurantoin** 100 mg BID x 5-7 days
    - **TMP-SMX DS** BID x 3 days
    - **Fosfomycin** (Monurol) 3 gm single dose x 1
  - If cannot take or for 2nd line:
    - fluoroquinolones
    - beta-lactams or amox/clav
    - 3rd or 4th generation cephalosporins
UTI/Pyelonephritis - Treatment

- Complicated UTI/Pyelonephritis
  - **If stable:**
    - Outpatient treatment
      - Cipro 500 mg PO BID or ER 1000 mg daily x 7 days
      - Levo 750 mg PO daily x 5 days
      - TMP/SMX DS BID x 10-14 days
  - **If unstable** or failed outpatient therapy
    - Inpatient treatment
      - 24 hour IV therapy - FQ, rocephin, AG, imipenem/cilastatin
      - Step down - FQ or TMP/SMX as per outpatient
Case #4

- A 65 Y/O WF with bump on her knee x 2 days
- Bump is swollen and warm to touch; has been draining
- Works as a caregiver for a woman who was diagnosed with an infection 2 weeks ago; given an unknown antibiotic
- PMHx: includes previous MRSA diagnosis/treatment
- Physical exam:
  - Vitals WNL; stable
  - Knee was slightly valgus with patellar crepitus & pain
  - Skin shows 2 mm erythematous tender papule on knee
Case #4

- Assuming this is a case of community-acquired methicillin-resistant *Staphylococcus aureus*, an initial approach should incorporate these elements:

  A. Treatment with trimethoprim/sulfamethoxazole, hand washing and environmental sterilization

  B. Treatment with mupirocin, hand washing and environmental sterilization

  C. Avoidance of work until lesion resolves

  D. Treatment with cephalexin, hand washing and avoidance of work until lesion resolves

  E. Quit the job and stay at home until the CDC arrives to ‘assess’ you.
Community-Associated MRSA

- All MRSA strains are resistant to penicillins/cephalosporins by definition.
- CA-MRSA has become more of a problem over the last decade.
- Risk factors for development include:
  - Weakened immune system
  - Diabetics, frequent UTIs
  - Elderly, healthcare workers & caregivers
  - People who work/live around others in confined spaces
CA-MRSA - Diagnosis

- **Diagnosis** is usually based on *clinical suspicion*
  - **History** consistent with *MRSA exposure*
  - **Physical exam indicating** *skin infection*
  - History of failed penicillin/cephalosporin use
- Can also be done via culture, quantitative PCR and latex agglutination tests
CA-MRSA - Treatment

- Previously, all MRSA was treated with IV vancomycin
- **CA-MRSA** may be treated with **oral antibiotics**
  - Sulfa drugs (TMP/SMX)
  - Tetracyclines (doxycycline and minocycline)
  - Clindamycin
- Newer agents include oxazolidinone and daptomycin
CDC recommends environmental controls:

- Regular **hand washing** with soap/water or alcohol sanitizer
- **Covering wounds** and keeping them clean
- **Avoid sharing** razors and towels
- **Showering** after using pools or gym equipment
Case #5

- 43 Y/O WM with acute onset of fatigue, night sweats
- Goes to see physician and who elicits that patient has history of congenital cardiac abnormality (VSD)
- Patient also states had bronchitis approximately two weeks before onset of fatigue
- Fatigue is noted to be worsening and occurs with exertion and at rest
Case #5

- **PE:**
  - Temp 102 Fahrenheit
  - Grade 3 diastolic murmur
  - Petechiae on mucous mem.
  - Unusual lesions on hand
  - NO cyanosis

- **Treatment plan:**
  - Admit to hospital
  - Draw blood cultures
  - (+) *S. aureus*
Case #5

Based on the previous findings, you make a presumptive diagnosis of acute bacterial endocarditis. Which test is MOST appropriate as a next step in evaluation of the disease?

A. Order ESR and CRP
B. Order a transthoracic echo
C. Set patient up for cardiac transplant
D. Order a transesophageal echo
E. Discharge patient and set up outpatient stress test
Acute Bacterial Endocarditis
Bacterial Endocarditis

- Infection of the endocardium, usually valves & adjacent structures
- 5-8 cases per 100,000 in US annually
- Highest risk (Valves and Vessels):
  - Pre-existing valvular disease; artificial valves
  - IVDA
  - Hemodialysis/other lines
Endocarditis - Diagnosis

- Fevers, night sweats, fatigue, constitutional symptoms
- Concern if pre-existing risk factors exist (Valves/Vessels)
- Signs/symptoms - Janeway lesions/Osler nodes/petechiae
- **Duke Criteria**
  - Developed in 1994 and revised in 2000
  - Includes major and minor criteria
  - Distinguishes between ‘definite’ and ‘possible’ diagnosis
Duke Criteria

• **Major Criteria**
  • (+) blood cultures
    • S. aureus
    • S. viridans/S. bovi
    • Enterococcus
    • HACEK group
  • **Echocardiographic findings**
    • Vegetations
    • Abscesses

• **Minor Criteria**
  • Valvular heart disease
  • IVDA
  • Fever (>100.4 F)
  • Vasculitis or skin lesions
  • (+) single blood culture

• **Definite**
  • 2 major criteria
  • 1 major + 3 minor criteria
  • 5 minor criteria

• **Possible**
  • 1 major + 1 or 2 minor criteria
  • 3 minor criteria
Endocarditis - Treatment

• Choice of treatment based on causative organism

• Empiric therapy
  • Vancomycin or ampicillin/sulbactam + aminoglycoside
  • Add rifampin if patient has prosthetic valve

• First day of therapy is considered the first day that cultures are negative

• Blood cultures x 2 every 24-48 hours until clear

• Most regimens are 2-6 weeks in duration

• Surgery if valves are damaged

• Anticoagulation is controversial; skip for first two weeks
Hepatitis A - Fast Facts

- Picornavirus with 3 genotypes and six subtypes
- Transmitted via fecal-oral routes (shellfish); infectious for 2 weeks
- Often asymptomatic; usually flu-like symptoms
- Kids mild, adults severe
- Diagnosis via serum IgM, ALT elevations (peak - 4 weeks)
- Prevent by hygiene, sanitation and vaccination
- Vaccinate kids at 1-2 years of age; 2 doses 6 mo apart
- High co-infection rate with Hep C
Lyme Disease

- Caused by *B. Burgdorferi* transmitted by *Ixodes scapularis*
- Symptoms: fever, headache, fatigue
- Rash: *erythema migrans*
- Diagnose:
  - Exposure/Symptoms/Rash
  - Immunoassay + Western blot
- Treat:
  - Remove tick
  - Consider antibiotics (Doxycycline)
Summary

- **Hep C** - Viral & chronic, anti-HCV ab/HCV RNA, treatment based on genotype (1 is common and harder to treat); goal is SVR at 24 weeks post treatment

- **GC/Chlamydia** - Bacterial (GNID), NAAT, Rocephin + Azithromycin or Doxycycline

- **UTI/Pyelonephritis** - Bacterial, common, complicated vs. uncomplicated, progress to pyelonephritis

- **MRSA** - Community-associated, oral antibiotics, hand washing and environmental control

- **Endocarditis** - Bacterial, Valves & Vessels, echo, treat the right bug

- **Lyme** - Diagnose by exposure/symptoms/rash; treat with Doxycycline
Resources

- Diagnosis and Management of Hepatitis C. *Am Fam Physician.* 2015 Jun 15;91(12):835-842

- CDC: Hepatitis C FAQs for Health Professionals, http://www.cdc.gov/hepatitis/hcv/hcvfaq.htm#section1

- CDC: Sexually Transmitted Diseases – Treatment Guidelines, 2010. MMWR 2010; 59 (No. RR-12)

- ‘Drugs for Sexually Transmitted Infections’ - Treatment Guidelines from The Medical Letter, July 1, 2010; Issue 95


- Diagnosis and Treatment of Acute Pyelonephritis in Women. *Am Fam Physician.* 2011 Sep 1;84(5):519-526

- Diagnosis and Treatment of Acute Uncomplicated Cystitis. *Am Fam Physician.* 2011 Oct 1;84(7):771-776
Resources

- Infective Endocarditis - http://www.clevelandclinicmeded.com
- CDC Lyme Disease - https://www.cdc.gov/lyme/index.html
- All images from the CDC Public Health Information Library (PHIL) except as noted