ACTHIV 2018: A State-of-the-Science Conference for Frontline Health Professionals
Breakfast with the Experts: Cases in HIV Primary Care

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Learning Objectives

Upon completion of this presentation, learners should be better able to:

• Identify key challenges in diagnosis of at-risk individuals
• Address key management issues as a care team, including:
  – Common and relevant drug-drug interactions
  – Side effects
  – Regimen selection
• Identifying relevant co-morbidities which can negatively impact patient outcomes
Faculty and Planning Committee Disclosures
Please consult your program book.

Off-Label Disclosure
There will be no off-label/investigational uses discussed in this presentation.
Case: 17 year old with fever & sore throat

• Previously healthy (physical 8/2017)
• 2 day history of fever and sore throat
  – Diagnosed with viral syndrome, prescribed azithromycin
• Continued fever, muscle aches, and fatigue (1 month)
What would you like to know?
17 year old (continued)

- JHU ED
  - Febrile (T103)
  - Rhabdomyolysis (CK 8,000)
  - Acute renal failure (Cr 2.0)
  - Transaminitis (AST 265)
  - Leukopenia (1,700)
  - Neutropenia (<500)
  - Thrombocytopenia (63,000)

Other questions? Thoughts?
Differential diagnosis & work-up

- Extensive infectious disease, rheumatology, oncology work-up
- Hospital day #5
Diagnoses of HIV Infection among Adults and Adolescents by Age at Diagnosis, 2016—United States

N = 39,660

Adolescents and Young Adults Aged 13–24 Years Living with Diagnosed HIV Infection by Sex and Transmission Category, Year-end 2015—United States and 6 Dependent Areas

Note. Data have been statistically adjusted to account for missing transmission category. “Other” transmission category not displayed as it comprises 1% or less of cases.

- Heterosexual contact with a person known to have, or to be at high risk for, HIV infection.
- Injection drug use (IDU)
- Male-to-male sexual contact & IDU
- Perinatal
- Other

Adolescents and Young Adults Aged 13–24 Years Living with Diagnosed HIV Infection, by Sex and Race/Ethnicity, Year-end 2015—United States and 6 Dependent Areas

[Bar chart for Male: N = 28,467]
- American Indian/Alaska Native: <1%
- Asian: 1%
- Black/African American: 57%
- Hispanic/Latino: 23%
- Native Hawaiian/Other Pacific Islander: <1%
- White: 14%
- Multiple races: 4%

[Bar chart for Female: N = 8,494]
- American Indian/Alaska Native: <1%
- Asian: 1%
- Black/African American: 63%
- Hispanic/Latino: 19%
- White: 12%
- Multiple races: 5%

a Includes Asian/Pacific Islander legacy cases.
b Hispanics/Latinos can be of any race.

Medical challenges for adolescents at-risk\(^\dagger\) of & living with HIV

<table>
<thead>
<tr>
<th>Disease</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advanced disease/immunosuppression</td>
<td>Treatment experienced</td>
</tr>
<tr>
<td>Co-morbidities(^\dagger)</td>
<td>More complicated cART</td>
</tr>
<tr>
<td>Neurocognitive delay and dysfunction</td>
<td>Treatment fatigue</td>
</tr>
<tr>
<td>(^\dagger)Mental health (anxiety, depression, PTSD), substance use</td>
<td>Drug-resistant virus</td>
</tr>
<tr>
<td>Delayed puberty and short stature</td>
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<tr>
<td>Suboptimal responses to vaccines</td>
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Agwu JIAS 2013; Lee JIAS 2013
# Psychosocial challenges for adolescents at risk of living with HIV

<table>
<thead>
<tr>
<th>Challenge</th>
<th>Source</th>
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<tbody>
<tr>
<td>Stigma (HIV, sexuality, other)</td>
<td>Murphy JAMA 2003; Martinez Pediatrics 2014; Mofenson JIAS 2015; Rudy AIDS Pt Care 2009 &amp; 2010; Lee &amp; Hazra JIAS 2015</td>
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<tr>
<td>Disclosure (HIV, sexuality, other)</td>
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<tr>
<td>Limited support systems</td>
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<tr>
<td>Clinical staff may be only reliable support</td>
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<tr>
<td>Poor adjustment to illness/status, self efficacy, outcome expectancy</td>
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<tr>
<td>Denial/guilt</td>
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<tr>
<td>Limited health literacy</td>
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<td>Logistic barriers: insurance, childcare, transportation</td>
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<tr>
<td>Attempting to be “normal”</td>
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</tbody>
</table>
Know minor testing/counseling laws & research

All 50 states & District of Columbia explicitly allow minor consent to STI services

- Minors ≤17 years of age
- 11 states require minors be (12 or 14) before being allowed to consent
- 32 states explicitly include HIV testing & treatment among STI services to which minors may consent; some laws only apply to HIV testing.
- No state requires that providers notify parents about STI services.
- States and jurisdictions have variably interpreted local law
  - prevention research +/- parental consent

Guttmacher Institute (https://www.guttmacher.org/state-policy/explore/minors-access-sti-services);
https://www.cdc.gov/hiv/policies/law/states/index.html;
Questions raised by case

- Parental disclosure?
- When to start?
- What to start?
- What would happen if he were negative?
- Other questions?
PrEP anyone???
When transgender women choose to take PrEP

How do you do it?

PrEP

CONDOMS

UVL

Prevention...

PrEP is a safe, daily pill that helps prevent HIV.

Find yours at PrEPForHer.com
PrEP for younger individuals

ATN 113:
- safety of TDF/FTC among HIV- YMSM ages 15-17
- acceptability, use, adherence, & drug exposure
- patterns of sexual behavior
- Approached >2800, enrolled 79
- High STI rates during the 48 week study
- HIV incidence: 6.4 per 100 person years

<table>
<thead>
<tr>
<th>Characteristics of enrolled</th>
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<tbody>
<tr>
<td>Mean age</td>
<td>16.5</td>
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</tbody>
</table>
| Sexual Identity             | Gay – 58%  
Bisexual – 28%  
Questioning – 6% |
| Completed high school       | 18.4% |
| Currently living with parents/family | 88.5% |
| Received public aid         | 76.9% |
| Kicked out of house for being gay | 15% |
| Ever been paid for sex      | 17% |
| Partners in past mo         | 2 |
| CRAI w/last partner         | 60% |
| Any positive STI test       | 15.4% |

Case #2: 50 year old

- 50 y/o old AA man with HIV (remote IDU) on tenofovir disoproxil fumarate/emtricitabine plus boosted atazanavir for follow-up visit.
- Concerns: ↓ number of pills. Renal risk? Brother with diabetes & ESRD on HD
- Other medical problems:
  - HTN (145/85 mmHg on meds)
  - elevated cholesterol (lifestyle modification)
  - 20 pk year tobacco (currently 5 cigs per day)
- Would like to know how to optimize his health
  - Minimize risk of adverse effects of HIV and medication

Adapted from eHIV review volume 6
Case #2: 50 year old

Thoughts? Questions?

- Creatinine 1.1, GFR estimated is 74 mL/min, no proteinuria on urinalysis
- CD4=600 (60 at diagnosis)
- HIV-1 RNA <20 (initial difficult adherence with development of resistance (K103N, M184V, minor PI mutations), no failure on current regimen; initial 150,000 copies/mL)
- Recent cholesterol 220 mg/dL (total); LDL 160 mg/dL

Adapted from eHIV review volume 6
Case #2 continued

- Any concerns about his potential for renal disease?
- How to assess risk?
- Recommendations to address? Modifiable risk factors?
- Screening?
- Regimen change?

Data on comorbidities in HIV

Comorbidities Among US Patients With Prevalent HIV Infection—A Trend Analysis
Data on comorbidities in HIV

Case #2 continued

- Regimen simplification? Pros? Cons?
- Would you simplify? How would you simplify?
- Specific agents?
- Number of agents? 2 vs. 3?
Simplifying treatment: fewer agents better?

- Fewer drugs
- NRTI-sparing regimens
- Decreased drug interactions
  - Dolutegravir/rilpivirine (Juluca)
    - Non-inferior to 3-drug regimen
  - Dolutegravir/lamivudine
    - 94 people (78% M, significant pretreatment, lots of co-morbidities with VS x >= 6 months), switch to 3TC/DTG → no VF, improved CD4, reduced cost

Maggiolo et al. BMC 2017
Simplifying treatment: even for experienced individuals?

- More options to craft fully suppressive regimens without ↑ pill burden and ↓ quality of life
- Treatment experienced individuals (n=135) (5 pills average) randomized to EVG/FTC/TAF + DRV (2 tablet)(n=89) vs. baseline regimen (N=46)
- Resistance to ≥2 drug classes, failure of ≥ 2 regimens previously
  - Improved renal markers (protein in urine)
  - No confirmed resistance in the rebound group on E/C/F/TAF
  - ↑ adherence & quality of life

Population: 75% men, 50% white, median age=49
Case #3: “I’m just so tired and weak....”

32 year woman with HIV presents for routine follow up and reports fatigue to the point that she is unable to engage in her usual routine

PMH: obesity, Type 2 diabetes diagnosed about 3 months ago, seizure disorder

Social history: sexually active

Any questions?
Case #3: “I’m just so tired and weak....”

Other HPI: decreased polydipsia, polyphagia. +weight loss due to diet modification
Meds: abacavir, 3TC, dolutegravir, levetiracetam, metformin and long-acting insulin
FH: noncontributory
SH: smokes MJ, no other substances, no condoms (same gender-loving couple)
Labs: viral load 700 copies/mL

Thoughts? Differential?
Case #3: “I’m just so tired and weak....”

Physical exam: unremarkable

Lab results:

Remember 😊 Normal Anion gap = sodium - (chloride + bicarbonate) 8-12;
hers was 18 mmol/L
Lactate 3 mmol/L, repeat 4 mmol/L

Thoughts? Differential? Why?
Lactic acidosis—increased risk with dolutegravir and metformin

- Early signs of lactic acidosis can include **fatigue, nausea and vomiting, stomach pain, decreased appetite, and weight loss**. Although these symptoms may not seem serious, they can be the first signs of life-threatening lactic acidosis.

- Signs of life-threatening lactic acidosis can include **tachycardia, tachypnea, jaundice**.

HIV-Related Risk Factors for Lactic Acidosis

- Taking NRTIs
- Being Female
- Pregnancy
- Obesity
- Poor Liver Function
- Low CD4 Count

AIDSinfo
How would you manage her antiretroviral treatment?

A) Stop her antiretroviral therapy until you address the lactic acidosis
B) Keep the same regimen (dolutegravir, abacavir, lamivudine)
C) Stop the metformin now and change her diabetes regimen
D) Change the ART regimen to a drug regimen that avoids dolutegravir
E) None of the above, I have my own suggestion
Insert Web Page

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Please enter the URL below.

https://api.cvent.com/polling/v1/api/polls/sp774dbe

Note: Many popular websites allow secure access. Please click on the preview button to ensure the web page is accessible.
Case #3: “I’m just so tired and weak....”

**Outcome:** metformin discontinued immediately, worked with endocrine to find alternative regimen
Opted to not change her ART as she had prior nonadherence and was now adherent.
Lactic acidosis resolved, VL undetectable.
Questions raised by case #3

- Assumptions about sexuality?
- Knowledge of drug interactions critical?
- Multidisciplinary teams needed?
- Adherence and psychosocial and behavioral also important?
- Other questions?
CASE #4: “My chest hurts”

- 24 y/o old man with perinatally acquired human immunodeficiency virus (PHIV)
- Chief complaint: fatigue, worsening shortness of breath over the preceding 2 weeks, severe wasting, and oh by the way .......... new chest pain in waiting room.
- Past medical history:
  - Diagnosed shortly after birth
  - First combination antiretroviral therapy (cART) at 5 y/o
  - Treatment-experienced with multiple cART regimens and significant resistance
Case #4: “My chest hurts”

PMH: Chronic, longstanding, nonadherence; multiple OIs (PCP, cryptococcal meningitis)

Modified from Griffith et al. OFID 2017
What would you like to know?
Case #4: “My chest hurts”

• Past medical history (continued):
  – Transitioned to adult care at 19
  – One month prior hospitalized for weakness, chronic diarrhea, and hypokalemia.
  – Upon discharge prescribed cART (abacavir/lamivudine/dolutegravir), nonadherent

• Social history: 5 pack-year smoking; occasional marijuana unemployed

• Family history: negative per his report
“My chest hurts”

• Physical examination:
  • Afebrile, 90/64 mmHg, 80 beats/minute, 18 breaths/minute, 90 pounds (BMI 12.9 kg/m²)
  • Pertinent positives:
    • cachectic and frail, no oral thrush, flat affect, slightly diaphoretic

• Labs:
  – CD4 1 cu mm, HIV1 RNA 43,642 copies/mL
  – Chest x-ray: normal
What is your differential?

What do you want to do next?
Case #4: “My chest hurts”

- Anterior wall ST elevation myocardial infarction (STEMI).
- The STEMI team activated and standard acute coronary syndrome treatment initiated.
- Transthoracic echocardiogram: ejection fraction of 30-35% with severe hypokinesis of the mid anteroseptal, apical septal, mid to apical anterior, apical lateral, and apical inferior walls as well as hypokinesis of the apex consistent with ischemia in the left anterior descending (LAD) supply territory.
- Troponin I levels: 0.76 ng/mL (normal < 0.04 ng/mL). Peak: 9.85 ng/mL
“My chest hurts”

• Post-MI course
  – ST elevations resolved
  – Peak Troponin I level: 9.85 ng/mL (17h after chest pain onset)
  – Total cholesterol 52 mg/dL, triglycerides 48 mg/dL, high-density lipoprotein cholesterol (calculated) 27 mg/dL, low-density lipoprotein cholesterol (calculated) 17 mg/dL, lipoprotein (a) levels < 10 nmol/L and C-reactive protein < 0.1 mg/dL

• Discharged days later with cardiac meds and ART............intermittently adherent to all meds and care
Case #4 continued

• What are his risk factors?
• Recommendations to address? Modifiable risk factors?
• Does he need to be treated differently than other MI patients?
  – Lipid lowering agents
  – Anti-arrhythmics
## Drug interactions with CV meds

**• LOTS!!!**

<table>
<thead>
<tr>
<th>Antiretroviral (ARV)</th>
<th>Dose of ARV</th>
<th>Dose of Amiodarone</th>
<th>Effect on ARV Levels</th>
<th>Effect on Amiodarone Levels</th>
<th>Potential Clinical Effects</th>
<th>Mechanism of Interaction</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elvitegravir/ritonavir-boosted protease inhibitor⁹⁹⁹</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>Not studied; may increase amiodarone levels</td>
<td>Possible increased amiodarone effects (eg, hypotension, bradycardia, cardiac arrhythmias)</td>
<td>Inhibition of CYP3A4 by ritonavir</td>
<td>Do not coadminister with saquinavir/ritonavir or tipranavir/ritonavir. Others use with caution; monitor amiodarone adverse effects. Consider obtaining ECG and monitoring amiodarone levels.</td>
</tr>
</tbody>
</table>

http://hivinsite.ucsf.edu/insite?page=ar-00-02&post=10&param=18
How would you manage his antiretroviral treatment?

A) Stop his antiretroviral therapy until you address his heart condition
B) Keep the same regimen (dolutegravir, abacavir, lamivudine)
C) Change regimens to a 2 drug regimen that avoids the NRTIs
D) Change regimens to a drug regimen that avoids abacavir
E) None of the above, I have my own suggestion
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https://api.cvent.com/polling/v1/api/polls/sp-bkb9k8

Note: Many popular websites allow secure access. Please click on the preview button to ensure the web page is accessible.
Current epidemiology of Perinatally-Infected Children

- Perinatally-acquired HIV+ population in the U.S. (~8500)
- Median age ≈ 18 years

Long-term Morbidity of HIV and/or ART

- Cardiovascular disease
- Malignancy
- Medication side effects:
  - Kidney, bone
- Metabolic abnormalities:
  - Mitochondrial toxicity
  - Lipodystrophy
  - Lipoatrophy
- Longstanding inflammation
- CNS abnormalities
  - Strokes, cognitive effects
- Unknown?
  - Consequences of lifelong ART?
  - Consequences of lifelong HIV?

Hazra R et al. 2010; Griffith D et al. 2017
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Upon completion of this presentation, learners should be better able to:

• To identify key challenges in diagnosis of at-risk individuals
• Key management issues
  – Common and relevant drug-drug interactions
  – Side effects
  – Regimen selection
• Identifying relevant co-morbidities
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