Current HIV Issues in the US: Case Studies in Managing Long-Term Non-AIDS Co-Morbidities

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Maricopa Integrated Health Systems
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Case: Eduardo R.

- 51 y/o Hispanic MSM hair dresser
- HIV+ since 1993 on multiple ARVs
  - Pre-2007: VL >100K, CD4 08/2%, on TVD-TPVr
  - 2007 salvage: DRV/rtv-RLT-ETR-TVD
- Co-Morbidities:
  - Diabetes, hyperlipidemia and hypertension
  - Hypothyroidism, hypogonadism
Soon after the start of his salvage regimen he develops an elevated serum creatinine. Which tests should be ordered to evaluate this?

1. Spot urine protein:creatinine ratio
2. Serum and urine phosphorous
3. Serum and urine glucose
4. 24 hour urine creatinine clearance
5. 1, 2 and 3
6. 1 through 4
Soon after the start of his salvage regimen he develops an elevated serum creatinine. **Which tests should be ordered to evaluate this?**

1. Spot urine protein:creatinine ratio
2. Serum and urine phosphorous
3. Serum and urine glucose
4. 24 hour urine creatinine clearance
5. 1, 2 and 3
6. 1 through 4
**Case: Eduardo R.**

**Question #1 - Data**

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine spot prt:creat ratio</td>
<td>625 mg/g</td>
<td>&lt;200 mg/g creat</td>
</tr>
<tr>
<td>Urine spot creatinine</td>
<td>145 mg/dL</td>
<td>N/A</td>
</tr>
<tr>
<td>Urine random phosphorous</td>
<td>116 mg/dL</td>
<td>N/A</td>
</tr>
<tr>
<td>Serum creatinine</td>
<td>1.9 mg/dL</td>
<td>~&lt; 1.5 mg/dL</td>
</tr>
<tr>
<td>Serum phosphate</td>
<td>2.1 ng/dL</td>
<td>2.5-4.5 mg/dL</td>
</tr>
</tbody>
</table>

**Fractional Excretion of Phosphorous (FE PO4):**

\[
\left( \frac{\text{Ur PO4} \times \text{Ser Cr}}{\text{Ser PO4} \times \text{Ur Cr}} \right) \times 100 = 72\%
\]

**INTERPRETATION:**

\(\downarrow\text{Serum PO4} \quad \uparrow\text{FEPO4}:
\)

= Proximal Tubulopathy

Fanconi’s Syndrome
Case: Eduardo R.  
Question #2

Which of the following are important steps in the management of his CKD?

1. Consideration of non-TDF antiretroviral regimen
2. Optimize ACE / ARB inhibitor therapy to control blood pressure and proteinuria
3. Evaluate for other contributing factors potentially underlying his CKD
4. Phosphate replacement
5. All of the above
Which of the following are important steps in the management of his CKD?

1. Consideration of non-TDF antiretroviral regimen
2. Optimize ACE / ARB inhibitor therapy to control blood pressure and proteinuria
3. Evaluate for other contributing factors potentially underlying his CKD
4. Phosphate replacement
5. **All of the above**
Kidney Disease in HIV
Contributing Factors

- **Acute Kidney Injury**
  - Example *hospitalization complication* (IRIS, DIC)
  - Infections, medications, liver failure

- **ARV Nephrotoxicity**
  - **TDF**: proximal tubulopathy
  - IDV, ATV: crystalluria, nephrolithiasis

- **HIV Associated (HIVAN)**
  - Advanced HIV, blacks (MYH9 gene)

- **Comorbid Disease**
  - HBV, HCV, **DM, HTN**
Case: Eduardo R.
Question #3

Which factors in his history place him at increased risk for osteoporosis?

1. Chronic kidney disease
2. Phosphate wasting
3. Hypothyroidism, Hypogonadism
4. History of Tenofovir usage, History of Protease usage
5. Long duration of HIV disease, Low CD4 nadir
6. All
Which factors in his history place him at increased risk for osteoporosis?

1. Chronic kidney disease
2. Phosphate wasting
3. Hypothyroidism, Hypogonadism
4. History of Tenofovir and Protease usage
5. Long duration of HIV disease, Low CD4 nadir
6. All
Due to his increased risk for osteoporosis which tests should be done?

1. Serum 25-OH Vitamin D
2. Serum 1,25-OH Vitamin D
3. Lumbar and hip DEXA scan
4. Lumbar and hip x-rays
5. 1 and 3
6. 2 and 4
Tests to evaluate osteoporosis:

1. Serum 25-OH Vitamin D
2. Serum 1,25-OH Vitamin D → Inaccurate in HIV
3. Lumbar and hip DEXA scan
4. Lumbar and hip x-rays → Not specific for osteoporosis
5. 1 and 3
6. 2 and 4
### Case: Eduardo R.

#### Question #4 - Data

**Bone Mineral Density (BMD)**

**Dual Energy X-ray Absorptiometry (DEXA) Scores**

<table>
<thead>
<tr>
<th>Location</th>
<th>T-Score</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>AP Spine (L1-4)</td>
<td>-1.8</td>
<td>Osteopenia</td>
</tr>
<tr>
<td>Femoral Neck</td>
<td>-2.7</td>
<td>Osteoporosis</td>
</tr>
<tr>
<td>Total Hip</td>
<td>-1.5</td>
<td>Osteopenia</td>
</tr>
</tbody>
</table>

**Vitamin D Level**

<table>
<thead>
<tr>
<th>Vitamin D</th>
<th>Result</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>25-OH Vitamin D</td>
<td>14 ng/ml</td>
<td>Deficiency</td>
</tr>
</tbody>
</table>
What treatment would you use?

1. Oral bisphosphonate therapy
2. Daily calcium supplementation
3. Weekly high dose vitamin D therapy
4. Daily recombinant PTH therapy
5. 1, 2 and 3
6. All
Osteoporosis therapy:
1. Oral bisphosphonate therapy
2. Daily calcium supplementation
3. Weekly high dose vitamin D therapy
4. Daily recombinant PTH therapy
5. 1, 2 and 3
6. All

In addition he needs treatment optimization of his hypogonadism, hypothyroidism, diabetes, and chronic kidney disease.
Vitamin D Deficiency
Definitions and Treatment

- **Definitions**
  - Deficiency: 25 OH Vit D < 20 ng/ml
  - Insufficiency: 25 OH Vit D 20-30 ng/ml

- **Vitamin D Replacement**
  - Ergocalciferol 50,000 units orally twice weekly for 6-12 weeks (≥ 600,000 units total)

- **Vitamin D Maintenance**
  - Cholecalciferol ≥ 800-2000 IU daily
  - Ergocalciferol 50,000 units every 2-4 weeks
# Osteoporosis Treatment Options

## BISPHOSPHONATES

<table>
<thead>
<tr>
<th></th>
<th>Alendronate</th>
<th>Risedronate</th>
<th>Ibandronate</th>
<th>Zolendronate</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dose</strong></td>
<td>Daily</td>
<td>Daily</td>
<td>Daily</td>
<td>Annually (IV)</td>
</tr>
<tr>
<td><strong>Frequency</strong></td>
<td>Weekly</td>
<td>Weekly</td>
<td>Monthly</td>
<td>Quarterly (IV)</td>
</tr>
</tbody>
</table>

**Adverse Effects**
- GI: Dyspepsia, pain, nausea
- Jaw osteonecrosis (oversuppression of osteoclasts ?)
  - Consider 2 year cycles on and off treatment

## RECOMBINANT PARATHYROID HORMONE

**Teriparatide**
- Stimulates osteoblastic bone formation
- Dose: daily subcutaneous injection for up to 2 years
- Reserved for patients on bisphosphonates with fractures or continued bone loss
Case: Eduardo R.
Question #5 – Follow-Up

- **Additional Interventions:**
  - Stop smoking
  - Reduce alcohol intake
  - Increase weight-bearing exercise
  - Minimize corticosteroid usage
  - Consider hypogonadaism / menopause treatment
  - Consider non-TDF or non-PI-based ARV regimen
  - Calcium intake 1000-1500 mg/day
  - Vit D routine supplementation: ≥ 800 IU/day

- **Repeat BMD DEXA after 1 yr**
  - Consider Teriparatide if no improvement
Case Examples - Karla and Miguel

**Karla:** 26 y/o Mexican female, HIV+ from infancy transfusion
- Multi-drug resistant on salvage regimen:
  - VL = 10,000, CD4 = 21
- Sustained wrist fracture while blocking 7 year old son’s practice karate kick
  - T-score -3.1, 25-OH Vit D3 = 9

**Miguel:** 38 y/o Mexican hetero male, HIV+ x 15 years
- Stable on 2NRTI + PI-rtv regimen
  - VL <48, CD4 = 328
- Sustained clavicle fracture when tripped off curb
  - Z-score -2.7, 25-OH Vit D3 = 15
Case: Jose U.

- 38 y/o Hispanic MSM, HIV Dx 1995
  - 2005-2010 PI/rtv + TVD, 2010 CD4 >400, VL <48
- HBV+ @ Dx, HCV- @ Dx
  - HBV: eAg+ → eAg- after 2 yrs TVD (2007)
  - 2004 partner HCV+ → URAI, HCV+ 2006
- PMH: hypothyroid stable on Tx, psych. negative
- PSH: Ex-wife HIV-, EtOH quit after HCV
Case: Jose U.

Question #1

Which tests should be ordered to evaluate whether he needs HCV treatment?

1. HCV quantitative RNA
2. HCV genotype
3. Liver biopsy
4. Serum transaminases
5. 1 and 3
6. 1, 2, 3 and 4
Case: Jose U.

Question #1

- Which tests should be ordered to evaluate whether he needs HCV treatment?

1. HCV quantitative RNA
2. HCV genotype
3. Liver biopsy
4. Serum transaminases
5. 1 and 3
6. 1, 2, 3 and 4
Case: Jose U.

Question #1 - Data

**HCV EVALUATION:**

- **HCV VL 3.7 million**
- **ALT 140/147** *(doesn’t determine need for treatment)*
- **Liver biopsy** *(not available)*
- **HCV Genotype 1a** *(doesn’t determine need for treatment)*

**“Active” HCV Disease Treatment Candidate**

**Risk of progression**

**Urgency of treatment**

**Likelihood of treatment response**
Case: Jose U.

Question #2

In the absence of a liver biopsy what other information would be indicative of the stage of his liver disease?

1. Serum albumin
2. Serum total bilirubin
3. Protime / INR
4. Serum marker scores
5. All of the above
Case: Jose U.

Question #2

In the absence of a liver biopsy what other information would be indicative of the stage of his liver disease?

1. Serum albumin
2. Serum total bilirubin
3. Protime / INR
4. Serum marker scores
5. All of the above
Case: Jose U.

Question #2 - Data

- **HCV EVALUATION:**
  - Serum albumin: 4.2
  - Serum bilirubin: 0.8
  - Protime / INR: normal
  - Ascites: negative
  - Encephalopathy: negative
  - Serum markers scores: not available
    (Future Biopsy Replacement)
    - Example: HepaScore, FibroTest, etc.
      - Haptoglobin, α-2-macroglobulin, total bilirubin, ALT, apolipoprotein A1, etc.

Child-Pugh Score:
5 = MILD

Correlation with mild or severe disease
What other tests need to be done prior to starting HCV treatment?

1. Hemoglobin, WBC, platelets
2. Serum cretinine
3. Thyroid stimulating hormone
4. Depression score
5. 1 and 4
6. 1, 2, 3 and 4
What other tests need to be done prior to starting HCV treatment?

1. Hemoglobin, WBC, platelets
2. Serum creatinine
3. Thyroid stimulating hormone
4. Depression score
5. 1 and 4
6. 1, 2, 3 and 4
Case: Jose U.
Question #3 - Data

**HCV EVALUATION:**

- Hemoglobin: 15.5
- Absolute neutrophil count: 1.2 K
- Platelet count: 109 K
- Serum creatinine: 1.05
- Thyroid stimulating hormone: 1.5
- Depression score (CES-D): 5
- *Pregnancy*: N/A

*Teratogenicity

**Safe**
For HCV Treatment
Case: Jose U.
Predictors of Treatment Success

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Yes/No</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCV genotype 2 or 3</td>
<td>NO</td>
<td>Genotype 1a</td>
</tr>
<tr>
<td>Low HCV RNA viral load</td>
<td>NO</td>
<td>3.7 million</td>
</tr>
<tr>
<td>No or minimal fibrosis</td>
<td>YES</td>
<td>“Mild”</td>
</tr>
<tr>
<td>Younger age (&lt;40)</td>
<td>YES</td>
<td>38 years</td>
</tr>
<tr>
<td>Low body mass index (BMI)</td>
<td>YES</td>
<td></td>
</tr>
<tr>
<td>No insulin resistance</td>
<td>YES</td>
<td></td>
</tr>
<tr>
<td>Higher CD4 (&gt;350)</td>
<td>YES</td>
<td>&gt;400</td>
</tr>
<tr>
<td>Lower HIV VL</td>
<td>YES</td>
<td>U/D</td>
</tr>
<tr>
<td>Lack of current EtOH</td>
<td>YES</td>
<td></td>
</tr>
<tr>
<td>Lack of current psychiatric</td>
<td>YES</td>
<td></td>
</tr>
</tbody>
</table>
Given his HCV genotype, what treatment regimen would you advise?

1. Fixed dose ribavirin plus PegIFN for $\geq 24$ weeks
2. Fixed dose ribavirin plus PegIFN for 48 weeks
3. Weight-based dose ribavirin plus PegIFN for $\geq 24$ weeks
4. Weight-based dose ribavirin plus PegIFN for 48 weeks
Given his HCV genotype what treatment regimen would you advise?

1. Fixed dose ribavirin plus PegIFN for ≥24 weeks
2. Fixed dose ribavirin plus PegIFN for 48 weeks
3. Weight-based dose ribavirin plus PegIFN for ≥24 weeks
4. Weight-based dose ribavirin plus PegIFN for 48 weeks
Case: Jose U.

Question #4 - Data

SVR Rates for Genotype 1 (mono-infected)

<table>
<thead>
<tr>
<th></th>
<th>Fixed Dose Ribavirin</th>
<th>Weight-Based Ribavirin</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>High VL</td>
<td>Low VL</td>
</tr>
<tr>
<td>≥ 24 Weeks</td>
<td>16%</td>
<td>41%</td>
</tr>
<tr>
<td>48 Weeks</td>
<td>35%</td>
<td>53%</td>
</tr>
</tbody>
</table>

HIV-HCV dual infected
# Case: Jose U.
## Treatment Course

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Week 4</th>
<th>Week 8</th>
<th>Week 12</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>VL</strong></td>
<td>3.7 mill</td>
<td>--</td>
<td>--</td>
<td>5.0 mill</td>
</tr>
<tr>
<td><strong>ALT/AST</strong></td>
<td>140/147</td>
<td>117/129</td>
<td>91/100</td>
<td>80/89</td>
</tr>
<tr>
<td><strong>Hgb</strong></td>
<td>15.4</td>
<td>13.8</td>
<td>13.0</td>
<td>13.4</td>
</tr>
<tr>
<td><strong>ANC</strong></td>
<td>1.2</td>
<td>0.9</td>
<td>1.1</td>
<td>0.7</td>
</tr>
<tr>
<td><strong>Wt (kg)</strong></td>
<td>78.5</td>
<td>-</td>
<td>75</td>
<td></td>
</tr>
<tr>
<td><strong>Depression</strong></td>
<td>2</td>
<td>-</td>
<td>-</td>
<td>23</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td></td>
<td></td>
<td></td>
<td>Null VR D/C</td>
</tr>
</tbody>
</table>

* Depression CES-D: (≤ 9, mild ≤16, mod ≤24, severe >24)
Given his treatment failure, what would you monitor in the future?

1. Serum alpha fetoprotein
2. Liver ultrasound
3. Serum transaminases
4. Serum albumin and PT / INR
5. All of the above
Given his treatment failure, what would you monitor in the future?

1. Serum alpha fetoprotein
2. Liver ultrasound
3. Serum transaminases
4. Serum albumin and PT / INR
5. All of the above
Case: Jose U.

Question #5 - Data

- **HCV EVALUATION:**
  - Bi/annual serum alpha fetoprotein
  - Bi/annual liver ultrasound
  - Serum transaminases (non-specific)
  - Serum albumin
  - PT / INR

  **Hepatocellular Cancer Screening**

  **Liver Fibrosis Monitoring**
Case: Jose U.

Question #6

- If his liver disease progresses and/or he wishes to undergo treatment again, what treatment strategy would advise?

1. Retry same regimen of Peg-IFN + RBV for same 48 weeks

2. Retry same regimen of Peg-IFN + RBV for 72 weeks

3. Wait for future availability of protease inhibitor

4. 2 or 3
Case: Jose U.

Question #6

If his liver disease progresses and/or he wishes to undergo treatment again, what treatment strategy would advise?

1. Retry same regimen of Peg-IFN + RBV for same 48 weeks
2. Retry same regimen of Peg-IFN + RBV for 72 weeks
3. Wait for future availability of protease inhibitor
4. 2 or 3
Case: Aaron F.
Question #6 - Data

1. Wait for future availability of protease inhibitor
2. Peg-IFN + RBV for 72 weeks
3. Peg-IFN + RBV for 48 weeks

72 Week PegIFN-RBV in GT-1 Mono-Infected Prior Relapsers:

- N = 107
- Overall SVR = 51%:
  - 97% of 27% who had RVR
  - 93% of 43% who had EVR
- Total Relapse 36%
  (48wk relapse rate 20-30%)

S Kaiser AASLD 2008
**Case: Aaron F.**
**Question #6 - Data**

**Future HCV Therapy:**
3-4 drug combination antiviral treatment (~ HIV)

<table>
<thead>
<tr>
<th>Drug (GT 1 mono-infected)</th>
<th>Status</th>
<th>RVR</th>
<th>SVR</th>
<th>Relapse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Std. PegIFN + RBV</td>
<td>SOC</td>
<td>10-13%</td>
<td>41-48%</td>
<td>20-23%</td>
</tr>
<tr>
<td>PI: Teleprevir</td>
<td>II. B</td>
<td>69-81%</td>
<td>61-68%</td>
<td>2-14%</td>
</tr>
<tr>
<td>PI: Boceprevir</td>
<td>II. B</td>
<td>39-60%</td>
<td>55-57%</td>
<td>--</td>
</tr>
<tr>
<td>Pol: Nucs: R7128, R1626</td>
<td>II. A</td>
<td>85%</td>
<td>84%</td>
<td>--</td>
</tr>
<tr>
<td>Thiazolide: NTZ</td>
<td>II</td>
<td>64%</td>
<td>79%</td>
<td>--</td>
</tr>
</tbody>
</table>
Case: Ernesto R.

- 40 year old Hispanic MSM
- HIV Diagnosed 2004, CD4 min 290’s
  - Kaletra + Turvada since Dx, VL U/D, CD4 600+
- PMH: Negative, no HPV disease
- PSH: Mild prior depression
- HCV: Diagnosed 2004
  - Genotype 3e, VL 900K
  - Elevated ALT
  - Normal CBC, albumin (4.3), bili (0.9)
### Case: Ernesto R.  
**Predictors of Treatment Success**

<table>
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</tr>
</thead>
<tbody>
<tr>
<td>HCV genotype 2 or 3</td>
<td><strong>YES: 3e</strong></td>
</tr>
<tr>
<td>Low HCV RNA viral load</td>
<td><strong>YES: &lt;1 million</strong></td>
</tr>
<tr>
<td>No or minimal fibrosis</td>
<td><strong>YES: “Mild”</strong></td>
</tr>
<tr>
<td>Younger age (&lt;40)</td>
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</tr>
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<tr>
<td>No insulin resistance</td>
<td><strong>YES</strong></td>
</tr>
<tr>
<td>Higher CD4 (&gt;350)</td>
<td><strong>YES: ~600</strong></td>
</tr>
<tr>
<td>Lower HIV VL</td>
<td><strong>YES: U/D</strong></td>
</tr>
<tr>
<td>Lack of current EtOH</td>
<td><strong>YES</strong></td>
</tr>
<tr>
<td>Lack of current psychiatric</td>
<td>None now</td>
</tr>
</tbody>
</table>
Case: Ernesto R.

Question #1

- Given his HCV genotype, what treatment regimen would you advise?

1. Standard dose ribavirin plus PegIFN for ≥ 24 weeks
2. Standard dose ribavirin plus PegIFN for 48 weeks
3. Weight-based dose ribavirin plus PegIFN for ≥ 24 weeks
4. Weight-based dose ribavirin plus PegIFN for 48 weeks
Given his HCV genotype, what treatment regimen would you advise?

1. Standard dose ribavirin plus PegIFN for $\geq 24$ weeks
2. Standard dose ribavirin plus PegIFN for 48 weeks
3. Weight-based dose ribavirin plus PegIFN for $\geq 24$ weeks
4. Weight-based dose ribavirin plus PegIFN for 48 weeks
SVR Rates for Genotypes 2 and 3 in Mono-Infected

<table>
<thead>
<tr>
<th></th>
<th>Standard Dose Ribavirin</th>
<th>Weight-Based Ribavirin</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥24 Weeks</td>
<td>78%</td>
<td>78%</td>
</tr>
<tr>
<td>48 Weeks</td>
<td>73%</td>
<td>77%</td>
</tr>
</tbody>
</table>

- High rates of relapse in co-infected patients have been seen following only 24 weeks of treatment in GT 2/3
- Many advocate for 48 weeks routinely
- Others focus on having at least 24 weeks undetectable
## Case: Ernesto R.
### Treatment Course

<table>
<thead>
<tr>
<th>Time:</th>
<th>BL</th>
<th>Wk 4</th>
<th>Wk 8</th>
<th>Wk 12</th>
<th>Wk 18</th>
<th>Wk 48</th>
<th>Yr 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>VL</td>
<td>900K</td>
<td>--</td>
<td>--</td>
<td>&lt;10</td>
<td>--</td>
<td>&lt;10</td>
<td>&lt;10</td>
</tr>
<tr>
<td>LFT</td>
<td>73/183</td>
<td>30/42</td>
<td>36/64</td>
<td>40/49</td>
<td>31/41</td>
<td>23/23</td>
<td>35/23</td>
</tr>
<tr>
<td>Hgb</td>
<td>16.5</td>
<td>13.2</td>
<td>14.2</td>
<td>13.5</td>
<td>12.8</td>
<td>12.6</td>
<td>15.4</td>
</tr>
<tr>
<td>ANC</td>
<td>1.1</td>
<td>0.4</td>
<td>2.2</td>
<td>1.7</td>
<td>2.0</td>
<td>1.6</td>
<td>--</td>
</tr>
<tr>
<td>Wt (kg)</td>
<td>82</td>
<td>78</td>
<td>77</td>
<td>75</td>
<td>71</td>
<td>69</td>
<td>83</td>
</tr>
<tr>
<td>Deprs</td>
<td>8</td>
<td>7</td>
<td>12</td>
<td>13</td>
<td>6</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>Other</td>
<td>Neu-pogen</td>
<td>Early VR</td>
<td>D/C Tx</td>
<td>SVR</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Deprsn CES-D: (≤ 9, mild ≤16, mod ≤24, severe >24)
Case: Ernesto R.
Question #2

Ernesto has no history of HPV disease and no anal symptoms of lesions on exam. However his routine annual screening anal Pap smear comes back as “ASCUS”. What should you do next?

1. Repeat the Pap smear in 1 year
2. Refer for high resolution anoscopy with directed biopsies
3. Refer for colonoscopy
4. Refer for anal mapping with random biopsies
Case: Ernesto R.

Question #2

Ernesto has no history of HPV disease and no anal symptoms of lesions on exam. However, his routine annual screening anal Pap smear comes back as “ASCUS”. **What should you do next?**

1. Repeat the Pap smear in 1 year
2. **Refer for high resolution anoscopy with directed biopsies**
3. Refer for colonoscopy
4. Refer for anal mapping with random biopsies
Schematic Representation of SIL

ASCUS

<table>
<thead>
<tr>
<th>Condition</th>
<th>AIN grade 1</th>
<th>AIN grade 2</th>
<th>AIN grade 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>LSIL</td>
<td>HSIL</td>
<td>HSIL</td>
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<tr>
<td>Koilocyes</td>
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<tr>
<td>Microinvasive Carcinoma</td>
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Source: Joel Palefsky, MD, FRCP(C)
Case: Ernesto R.
Question #2 - Data

1. Repeat the Pap smear
   *(Primary care)*
   Insensitive for degree of dysplasia

2. High resolution anoscopy with directed biopsies
   *(Gynecology)*
   **Standard of care recommendation**

3. Colonoscopy
   *(Gastroenterology)*
   Insensitive for pre-cancer at anal verge

4. Anal mapping with random biopsies
   *(Colorectal Surgery)*
   Biopsies should be targeted to HRA-visualized abnormal areas
Case: Ernesto R.

Question #2 – Data continued

- His HRA exam reveals multiple acetowhite areas with coarse punctation. His biopsy is AIN III.
For AIN III what should you do next?

1. Treat with cryotherapy
2. Treat with electrofulguration
3. Treat with 80% trichloroacetic acid
4. Treat with infrared coagulation
5. 1 or 3
6. 2 or 4
1. Treat with cryotherapy
2. Treat with electrofulguration
3. Treat with 80% trichloroacetic acid
4. Treat with infrared coagulation
5. 1 or 3
6. 2 or 4
“InfraRed Coagulation” (IRC)

- 2-4 treatments 2-4 months apart
- 65% disease-free at 1 year
Case: Ernesto R.
Follow-Up

- **Follow-up of AIN II-III:**
  1. Repeat the Pap smear in 6 months
  2. Repeat Pap smear in 1 year
  3. Repeat for high resolution anoscopy with directed biopsies in 4-6 months
  4. Refer for colonoscopy
46 y/o Mexican MSM, with advanced AIDS
(Multidrug resistance, CD4 <50, VL >1 million)

- Treated by outside physician (unsuccessfully) for “anal HSV”
- Initial Pap and biopsy positive for invasive SCC
- Poor tolerance of chemo therapy due to underlying chronic anemia & neutropenia
- High morbidity following radiation (atrophic scarring with incontinence)
- Recurrence after 2 years
Case Example - Gloria

49 y/o Mexican female, HIV+ x23yrs, CD4 400, VL U/D

- History of recurrent condyloma & CIN III
  - Treated with cryotherapy then
  - Loop Electrical Excision Procedure, then
  - Total abdominal hysterectomy

- Subsequently:
  - Vaginal Pap: ASCUS rule out high grade (VAIN III)
  - Anal Pap: AIN III
Case Example - Christopher

38 y/o white MSM, asymptomatic HIV

- No history condyloma, no anal symptoms
- Smooth nontender bulge palpated on lateral wall
- Routine screening Pap = ASCUS, HR HPV+
- HRA: acetowhite with coarse punctation at location of bulge
- Biopsy positive for microinvasive well-differentiated SCC
- Treated successfully by local excision: 2mm micro invasion, no metastases
Co-Morbidities in Long-Term HIV

Case Studies

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McDowell (HIV/AIDS) Healthcare Center
Maricopa Integrated Health Systems
Arizona AIDS Education and Training Center