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

Ann M. Khalsa, MD, MSEd, AAHIVS
Kidney Disease in HIV

- **Increasing Prevalence:**
  - Proteinuria
  - Diminished creatinine clearance

- **Increased Rates of Contributing Factors:**
  - ARV-Associated Nephrotoxicity (TDF, RTV, ATV, IDV)
  - Hypertension
  - Diabetes
  - Hepatitis B and C
Kidney Disease
Increasing CKD Prevalance in HIV Cohort

Johns Hopkins HIV Clinical Cohort: (1990-2004)

HR 1.9, 95% CI (1.2-2.8)  
*P* = .002, log rank test

Lucas G et al. 15th CROI; 2008; Boston. Abstract 972.
Kidney Disease
Contributing Risk Factors

Modifiable risk factors
- Medication nephrotoxicity
  - Antiretrovirals
  - Analgesics
- Medication allergy
  - Antibiotics
- Diabetes mellitus
- High blood pressure
- Drug abuse
- Kidney stones
- Inflammation
  - Glomerulonephritis

Non-modifiable factors
- Age
- Trauma or accident
- Family history of kidney disease
- Presence of other diseases
  - HIV/AIDS,
  - Hepatitis C
  - Lupus
  - Cancer
  - Congestive heart failure
## Tenofovir Toxicity
### Proximal Renal Tubulopathy

<table>
<thead>
<tr>
<th>Finding</th>
<th>Classic</th>
<th>Swiss</th>
<th>Evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proteinuria</td>
<td>X</td>
<td>X</td>
<td>Urine protein:creat ratio</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Urine protein and creatinine</td>
</tr>
<tr>
<td>Phosphate Wasting</td>
<td>X</td>
<td>X</td>
<td>FE-PO4: Urine and serum phosphate and creatinine</td>
</tr>
<tr>
<td>Euglycemic Glucosuria</td>
<td>X</td>
<td>X</td>
<td>Urine and serum glucose</td>
</tr>
<tr>
<td>Metabolic Acidosis</td>
<td>X</td>
<td>--</td>
<td>Serum bicarbonate</td>
</tr>
<tr>
<td>↓ Creatinine Clearance</td>
<td>X</td>
<td>--</td>
<td>MDRD or CG GFR</td>
</tr>
<tr>
<td>Uric Acid Wasting</td>
<td>--</td>
<td>X</td>
<td>FE-Uric Acid: Urine and serum uric acid and creatinine</td>
</tr>
</tbody>
</table>
Osteoporosis
Proximal Renal Tubulopathy (PRT)

Cross-sectional analysis of Swiss HIV Cohort Study (N = 1202)

- **PRT Definition:** ≥ 3 of the following:
  - ↑ fractional excretion (FE) of phosphate
  - ↑ Urine protein/creatinine ratio
  - ↑ fractional excretion (FE) of uric acid,
  - Euglycemic glucosuria

- **Incidence:**

<table>
<thead>
<tr>
<th></th>
<th>TDF+ PI+</th>
<th>TDF+ PI-</th>
<th>TDF- PI-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prox. Renal Tubulopathy</td>
<td>12%**</td>
<td>5%</td>
<td>2%**</td>
</tr>
<tr>
<td>FE PO4 &gt;20%</td>
<td>18%</td>
<td>17%</td>
<td>11%</td>
</tr>
<tr>
<td>FE PO4 &gt;10% + low serumPO4</td>
<td>20%</td>
<td>20%</td>
<td>9%</td>
</tr>
<tr>
<td>Normal</td>
<td>50%</td>
<td>58%</td>
<td>78%</td>
</tr>
</tbody>
</table>

** OR: 7.1 (95% CI: 2.5-19.8; P < .001)

Osteoporosis in HIV

- **Increased Prevalence:**
  - Osteoporosis
  - Low trauma fractures

- **Increased Contributing Factors:**
  - Vit D deficiency
  - Phosphate wasting
  - Hypogonadism
  - Hepatitis C
  - Diabetes
Meta-Analysis of Bone Density in HIV+ Compared to HIV-

Overall prevalence in HIV+:  
- Osteoporosis: 15%  
- Osteopenia: 67%

Osteoporosis
Increased Prevalence of Fractures

A clinical care data registry from the Partners HealthCare System, which consists primarily of Brigham and Women’s Hospital and Massachusetts General Hospital. 8525 HIV-positive and 2,208,792 HIV-negative patients from 1996-2008.

Osteoporosis
Contributing Factors in HIV

Non-modifiable
- Female sex
- Decreased bone acquisition
- White race
- Family history
- Increasing age
- Amenorrhea/premature menopause

Modifiable
- Smoking
- Decreased physical activity
- Alcohol

Secondary causes of osteoporosis
- Chronic disease (e.g., hyperthyroidism, hyperparathyroidism, liver disease, rheumatological conditions, eating disorders, etc.)
- Hypogonadism
- Renal dysfunction
- Malnutrition/low BMI
- Medications (e.g., corticosteroids, anticonvulsants, anticoagulants)

HIV infection-related
- Cytokines (e.g., TNFα, IL6)
- Decreased muscle mass
- Decreased fat mass
- Fat deposition in marrow

HAART-related
- Nucleoside analogues/mitochondrial dysfunction
- Protease inhibitors
- Lipodystrophy

Osteoporosis
Decreases in BMD with PI vs NNRTI

48 Week Trial in Naïve Patients (ANRS 121)

# Osteoporosis Screening Indications

<table>
<thead>
<tr>
<th>Standard</th>
<th>HIV-Associated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low Body Mass Index</td>
<td>Low CD4-nadir</td>
</tr>
<tr>
<td><strong>Low “peak bone mineralization”</strong></td>
<td>Hepatitis C chronic infection</td>
</tr>
<tr>
<td>(low childhood Ca++ intake)</td>
<td></td>
</tr>
<tr>
<td>Hypogonadism / postmenopausal</td>
<td>Exposure to Tenofovir or PI</td>
</tr>
<tr>
<td>Corticosteroid exposure</td>
<td>Phosphate wasting</td>
</tr>
<tr>
<td></td>
<td>(Proximal Renal Tubulopathy)</td>
</tr>
<tr>
<td>High alcohol intake (≥3 units daily)</td>
<td>Vitamin D Deficiency</td>
</tr>
<tr>
<td>Smoking (dose-dependent)</td>
<td>Chronic Kidney Disease</td>
</tr>
<tr>
<td>Family history of osteoporosis</td>
<td><em>Other seconday causes</em></td>
</tr>
<tr>
<td>Corticosteroid exposure</td>
<td></td>
</tr>
<tr>
<td>Aging (W: ≥65 yrs, M: ≥70 yrs; 50-70 yrs if risks)</td>
<td></td>
</tr>
</tbody>
</table>
Osteoporosis Diagnosis

- **WHO Definition (DEXA):**
  - Osteoporosis: T-Score $\leq -2.5$ Std.Dev.
  - Osteopenia: T-Score -1.0 to -2.5 SD
  - Normal: T-Score $\geq -1.0$ SD

- **Risk of fracture:**
  - $\uparrow$ 2-fold for each 1.0 SD $\downarrow$ BMD

- **Z-Score:**
  - Used in men <50 yrs, and premenopausal women
Osteoporosis Evaluation

- DEXA Bone Mineral Density Scan
- Serum Vitamin D level
  - Deficiency: 25 OH Vit D <20 ng/ml
  - Insufficiency: 25 OH Vit D 20-30 ng/ml
- Serum and urine phosphate and creatinine
- Urine protein:creatinine ratio
- Serum Thyroid Stimulating Hormone
- Morning testosterone level or evaluation of menopause
# Osteoporosis

## Treatment - 1

<table>
<thead>
<tr>
<th>Condition</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin D deficiency</td>
<td><strong>Vitamin D replacement:</strong></td>
</tr>
<tr>
<td></td>
<td>Ergocalciferol 50,000 units orally once to twice weekly for 6-12 weeks (≥ 600,000 units total)</td>
</tr>
<tr>
<td></td>
<td><strong>Vitamin D Maintenance</strong></td>
</tr>
<tr>
<td></td>
<td>Cholecalciferol ≥ 800-2000 IU daily</td>
</tr>
<tr>
<td></td>
<td>Ergocalciferol 50,000 units every 2-4 weeks</td>
</tr>
<tr>
<td>Hypogonadism</td>
<td>Testosterone replacement</td>
</tr>
<tr>
<td>Phosphate wasting</td>
<td>Phosphate replacement (K-PO4) Discontinue tenofovir</td>
</tr>
<tr>
<td>Low BMD</td>
<td>Bisphosphonates <em>(above must be first corrected)</em></td>
</tr>
<tr>
<td>Proteinuria CKD</td>
<td>ACE Inhibitor</td>
</tr>
</tbody>
</table>
# Osteoporosis Treatment - 2

## 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 Frequency</strong></td>
<td>Daily</td>
<td>Daily</td>
<td>Daily</td>
<td>Annually (IV)</td>
</tr>
<tr>
<td></td>
<td>Weekly</td>
<td>Weekly</td>
<td>Monthly</td>
<td>Quarterly (IV)</td>
</tr>
<tr>
<td><strong>Adverse Effects</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>GI: Dyspepsia, pain, nausea</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Jaw osteonecrosis (oversuppression of osteoclasts?)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## RECOMBINANT PARATHYROID HORMONE

| Teriparatide         | Stimulates osteoblastic bone formation | Dose: daily subcutaneous injection | Reserved for patients with fractures on bisphosphonates or continued bone loss |
Osteoporosis
Vitamin D Levels and Treatment in HIV

25(OH)D3 levels

1,25(OH)2D3 levels

Levels accurate in HIV

Osteoporosis

Bisphosphonate BMD Improvement in HIV

- Percent change in lumbar BMD, N=31 HIV+ patients on HAART
- Treatment: alendronate 70mg weekly + Calcium + Vitamin D

Hepatitis C Infection in HIV

- HIV worsens HCV disease:
  - ↑ HCV viremia
  - ↑ inflammatory grade
  - ↑ progression to fibrosis & cirrhosis
  - ↑ hepatocellular carcinoma (1-4% annual incidence)
  - ↑ extra-hepatic manifestations

- HCV worsens HIV disease:
  - ↑ Liver toxicity from HIV ARV medications
  - ↑ HIV disease progression
Hepatitis C: Sequence of Events After Infection

- Acute HCV Infection: 100%
  - 55-85% of Adults
- Chronic Infection: 15-45%
  - Spontaneous Viral Clearance
- Compensated Cirrhosis
- Decompensated Cirrhosis
- Transplantation or Death

Time:
- Less than 1 year
- 20-25 years for monoinfected
  - and as little as 5 years or less in co-infected patients

Source: Substance Abuse and Mental Health Services Administration, Unpublished data; 2005.
Hepatitis C
Relative Treatment Contra-Indications

- Ongoing hepato-toxins (alcohol, etc)
- Inability to adhere to treatment
  - Drug abuse,
  - Psycho-social factors, etc.
- Uncontrolled depression or other psychiatric disease
- Co-morbid illnesses:
  - Transplant patient (kidney, heart, lung)
  - Autoimmune condition (RBV exacerbation)
  - Unstable HTN, CHF, CAD, DM, COPD, hyperthyroidism
Hepatitis C
Pre-Treatment Management

- **HIV Treatment:**
  - HAART (to slow HCV disease progression)
    - Option: If high CD4 defer HAART after HCV treatment
  - Monitor for ARV hepatotoxicity
    - Avoid nevirapine and full-dose ritonavir
  - Goal: CD4 >350 (Defer HCV treatment if CD4 <200)
  - Goal: HIV VL undetectable

- **Liver Disease Prevention:**
  - Reduce alcohol intake
  - Vaccinate against Hepatitis A and B

- **Hepatocellular Carcinoma Screening:**
  - Liver ultrasound, serum alpha fetoprotein
Hepatitis C
Pre-Treatment Evaluation - 1

- **HCV quantitative RNA viral load (VL)**
  - If negative: HCV is resolved ⇒ no need for treatment
- **HCV Genotype (GT):**
  - Prognostic of treatment responses
- **Fibrosis and Inflammation Assessment**
  - High degrees are predictive of progressive disease and indicative of greater need for treatment
  - Liver Biopsy: “Gold Standard”
    - false-negatives and invasive
  - Bedside Elastography
  - Lab Interpretation Scores (Metavir, Ishak)
    - Distinguish only between mild and severe stages
Hepatitis C
Pre-Treatment Evaluation - 2

- **Serum Transaminases, Anti-tissue Antibodies, Alkaline Phosphatase:**
  - Not correlated with disease severity nor predictive of treatment outcome in HCV
  - Better tolerance of treatment with “compensated” liver disease

- **HCV Treatment Preparation:**
  - ANC >1.5, Creat <1.5 (caution with nephrotoxic drugs)
  - Hemoglobin >12-13 (Avoid AZT)
  - Reduce weight loss and insulin resistance
  - Stabilization of depression and hyperthyroidism
Hepatitis C
Positive Predictors of Treatment Success

- HCV genotype 2 or 3
- Low HCV RNA viral load (esp GT 1)
- No fibrosis, or just portal fibrosis
- Younger age (<40)
- Low body mass index (BMI), <75kg
- No insulin resistance

Higher CD4 (>350, ~ defer HCV Tx if CD4 <200)
Lower HIV viral load (<10,000)
Lack of current substance abuse (esp EtOH)
Lack of current psychiatric co-morbidity
Hepatitis C
Standard Medication Regimens

- **Ribavirin** (daily oral)
  - GT 1,4,5 or 6: Weight Based Dose:
    - <75kg: 1000mg daily
    - >75kg: 1200mg daily
  - GT 2 or 3: 800mg daily

- **Pegylated Interferon** (weekly subcutaneous injection)
  - α2b (Peg-Intron): 1.5 mcg/kg once weekly
  - α2a (Pegasys): 180 mcg once weekly
Hepatitis C
Ribavirin Dose and Duration Based on HCV GT

HCV Treatment Response Rates (Mono-Infected; Dual-Infected)

SVR (%)

GT 2/3: Standard Dose
GT 1: Weight-Based Dose

- GT 1 - hi VL
- GT 1 - lo VL
- GT 2/3

800 mg x 24 wks
1.0-1.5g x 24 wks
800 mg x 48 wks
1.0-1.2g x 48 wks

SVR (%)

GT 1:

Weight-Based Dose

SVR (%)

GT 2/3:
Standard Dose

SVR (%)

800 mg x 24 wks
1.0-1.5g x 24 wks
800 mg x 48 wks
1.0-1.2g x 48 wks

62%
29%

27%
## Hepatitis C
### Treatment Duration Based on VR

<table>
<thead>
<tr>
<th>VR Type</th>
<th>Virological Response</th>
<th>Treatment Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Rapid VR:</strong></td>
<td>Undetectable @ 4wks</td>
<td>“Endure” Tx / Best prognosis (Optional treatment completion @ 24 weeks for GT 2/3)</td>
</tr>
<tr>
<td><strong>Early VR:</strong></td>
<td>Undetectable at 12 wks</td>
<td>“Endure” Tx / Good Prognosis</td>
</tr>
<tr>
<td><strong>Slow VR:</strong></td>
<td>Undetectable at 24 wks</td>
<td>Consider treatment extension to 72 weeks for GT 1</td>
</tr>
<tr>
<td><strong>Inadequate VR:</strong></td>
<td>&lt;2 log ↓ by 12 weeks or positive VL @ 24 weeks</td>
<td>94-100% predictive of treatment failure ⇒ Discontinue treatment</td>
</tr>
</tbody>
</table>
# Hepatitis C

## Reasons for Lack of Response

<table>
<thead>
<tr>
<th>Virus</th>
<th>Patient</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genotype 1</td>
<td>Cirrhosis</td>
<td>Underdosing</td>
</tr>
<tr>
<td>High viral load</td>
<td>African-American</td>
<td>Nonadherence</td>
</tr>
<tr>
<td>HIV coinfection</td>
<td>Obesity</td>
<td>Interfering agent</td>
</tr>
<tr>
<td></td>
<td>Insulin Resistance</td>
<td>(alcohol)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Insufficient Duration</td>
</tr>
</tbody>
</table>

**Correctable Factors**
## Hepatitis C
### Managing Treatment Adverse Effects

Here is a table outlining the RBV side effects and their respective management:

<table>
<thead>
<tr>
<th>RBV Side Effects</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemolytic anemia</td>
<td><strong>Erythropoietin</strong>, Iron and Folate</td>
</tr>
<tr>
<td>Gout</td>
<td>Regular treatment</td>
</tr>
<tr>
<td>Insomnia</td>
<td>Symptom treatment</td>
</tr>
<tr>
<td>Cough, dyspnea</td>
<td></td>
</tr>
<tr>
<td>Rash, pruritis</td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td></td>
</tr>
<tr>
<td>Teratogenicity</td>
<td>Contraception</td>
</tr>
</tbody>
</table>

**RBV dose-dependent ↑ SVR and ↓ relapse**

*Don’t under dose – manage aggressively*
### Hepatitis C
### Managing Treatment Adverse Effects

<table>
<thead>
<tr>
<th>IFN Side Effects</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression, Irritability, Insomnia, Anxiety</td>
<td>Psychiatric medications</td>
</tr>
<tr>
<td>Neutopenia (↓ CD4 # / no ↓ CD4%)</td>
<td>Granulocyte Growth Factor</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>Bleeding precautions</td>
</tr>
<tr>
<td>Hyperthyroidism</td>
<td>Standard treatment</td>
</tr>
<tr>
<td>“Flu”: fever, chills, fatigue, body aches, H/A, N/V,</td>
<td>Symptom treatment</td>
</tr>
<tr>
<td>Anorexia, wt loss, alopecia</td>
<td>Symptom treatment</td>
</tr>
<tr>
<td>Retinopathy, exacerbation of autoimmune disorders</td>
<td>Monitoring and treatment as indicated</td>
</tr>
</tbody>
</table>

*Don’t under dose – manage aggressively*
**Hepatitis C**  
**Treatment Monitoring**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Monitoring Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight, diabetes, depression</td>
<td>Baseline and every visit</td>
</tr>
<tr>
<td>HCV RNA</td>
<td>Baseline and weeks: 4, 12, 24, 48, 72</td>
</tr>
<tr>
<td>TSH</td>
<td>Baseline and weeks: 12, 24, 36, 48, 72</td>
</tr>
<tr>
<td>CBC w/ diff, Uric Acid, Serum Transaminases*</td>
<td>Baseline and weeks: 2, 4, 8, 12, then every 6 weeks</td>
</tr>
</tbody>
</table>

*ALT: normalization is marker of antiviral treatment efficacy*
Anal Cancer in HIV

- HPV worse in HIV-Infected patients:
  - ↑ HPV infection incidence, persistence and prevalence
  - ↑ HPV-related ano-genital dysplasia prevalence, persistence and disease progression
    - ↓ Interval to from infection to dysplasia: 10 years vs 20+

- Contributing Factors:
  - ↑ activation of oncogenes, inhibition of tumor suppressor genes, increased angiogenic factors
  - ↑ smoking prevalence
  - Anal dysplasia associated with:
    - High risk HPV infection
    - HIV infection
    - Increased numbers of unprotected anal sexual encounters
Anal Cancer
Epidemiology - 1

- HPV Prevalence:
  - HIV-: 42% 60%
  - HIV+: 76% 93%

- Dysplasia Relative Risk
  - HIV+ (vs HIV-): 6.8x↑ 40-80x↑
  (Women: No history anal sex)

Anal Cancer
Epidemiology - 2

- **Multicenter AIDS Cohort Study**
  1984-2006

- **Anal Cancer:**
  Total Cases
  28 / 6972

- **Incidence Rate:**
  HIV+ vs HIV-
  (per 100,000 person-years)
  69 vs 14

- **Incidence Rate:**
  HAART vs PreHAART
  (per 100,000 person-years)
  137 vs 30

- **Multivariate**
  Associated Risks:
  HIV Infection
  RR = 4.7
  (95% CI 1.3-17)

*Not decreased with HAART use*
Anal Cancer
Comparative Anatomy

Cervix

Anus

SCJ: Squamo-Columnar Junction: Active cell turnover: mutation-prone
Anal Cancer
Pap Cytology Dysplasia Stages

Cervical Pap Smear Stages

- NORMAL
- MILD
- MODERATE
- SEVERE

Anal Pap: Severe (3)
Anal Cancer
Screening & Diagnosis

- Normal
- Nodule
- Atypia
- LSIL
- HSIL

**Screening Pap Smear & Digital Rectal Exam**

- **No Lesion**
  - Repeat Pap & DRE
    - 12 months (HIV+)
    - 2-3 years (HIV-)

- **AIN 2-3**
  - Treat

- **AIN 1**
  - Repeat HRA in 4-6 months

**High Resolution Anoscopy w/ Biopsy**

Anal Cancer
Populations to be Screened

- **Immunocompromised Patients:**
  - All HIV+ (M or F, MSM or not)
  - Organ transplant, auto-immune

- **High Risk Histories (HIV- or HIV+):**
  - Any genital HPV disease (warts, cervical dysplasia, etc.)
    - Smokers (↑ HPV disease progression)
  - Receptive anal intercourse
Anal Cancer
Pap Smear Technique

- Blind swabbing of ano-rectal junction and canal walls
  - Water-moistened polyester swabs
  - Inserted 8 cm into anal canal
- Liquid-based ThinPrep® specimen collection with commercial laboratory evaluation for:
  - Anal (rectal) cytology
  - No HPV testing (high false negative rate, no change in management)
Anal Cancer
Digital Examination

External visual inspection

Thorough digital examination: 360° “RADIAL-SPOKE”
Magnified visual inspection with:
- 3-5% Acetic Acid and
- Lugol’s solution

Anal Cancer
High Resolution Anoscopy

Anoscopy: rotated to visualize all areas
Anal Cancer
San Francisco Referral Center 4-Year Data

<table>
<thead>
<tr>
<th>Pap Smears</th>
<th>HRA Biopsies</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 417 total HIV+ MSM</td>
<td>N = 163 of 417</td>
</tr>
<tr>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>46% (189)</td>
<td>19% (31)</td>
</tr>
<tr>
<td>ASCUS</td>
<td>Atypia</td>
</tr>
<tr>
<td>29% (121)</td>
<td>2% (3)</td>
</tr>
<tr>
<td>LSIL</td>
<td>AIN 1</td>
</tr>
<tr>
<td>20% (85)</td>
<td>48% (79)</td>
</tr>
<tr>
<td>HSIL</td>
<td>AIN 2</td>
</tr>
<tr>
<td>4% (18)</td>
<td>17% (28)</td>
</tr>
<tr>
<td>AIN 3</td>
<td>2% (3)</td>
</tr>
<tr>
<td>Squamous Cell Carcinoma</td>
<td>- CA in Situ</td>
</tr>
<tr>
<td>0.9% (4)</td>
<td>8% (13)</td>
</tr>
<tr>
<td></td>
<td>- Carcinoma</td>
</tr>
<tr>
<td></td>
<td>4% (6)</td>
</tr>
</tbody>
</table>

Pap Sensitivity = 95%

## Anal Cancer
### HPV and AIN Treatment

<table>
<thead>
<tr>
<th>Condition</th>
<th>Treatment Type</th>
<th>Treatment Modalities</th>
<th>Follow-Up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Condyloma</td>
<td>Topical Ablation</td>
<td>- Cryotherapy&lt;br&gt;- Podophyllin&lt;br&gt;- Imiquimod&lt;br&gt;- 80% Tricholoacetic Acid&lt;br&gt;- Laser Ablation&lt;br&gt;- InfraRed Coagulation</td>
<td>Repeated treatment: every 2-4 weeks</td>
</tr>
<tr>
<td>AIN I</td>
<td>Observation</td>
<td>- Close monitoring</td>
<td>Biannual screening: Pap, digital exam, HRA</td>
</tr>
<tr>
<td>AIN II-III</td>
<td>Ablation</td>
<td>- Electrofulguration&lt;br&gt;- Laser Ablation&lt;br&gt;- InfraRed Coagulation</td>
<td>Repeat HRA: after 2-4 mo&lt;br&gt;Repeat Treatment: after 4-6 mo</td>
</tr>
<tr>
<td>MicroInvasive Carcinoma</td>
<td>Excision</td>
<td>- Under HRA visualization in O.R.</td>
<td>Biannual monitoring: HRA &amp; CT Scan</td>
</tr>
<tr>
<td>Invasive Carcinoma</td>
<td>Radiation &amp; Chemo</td>
<td>- Oncology referral</td>
<td>Biannual monitoring: HRA &amp; CT Scan</td>
</tr>
</tbody>
</table>