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Sandton Convention Centre
Johannesburg

Our Issues, Our Drugs, Our Patients

www.sahivsoc.org
www.sahivsoc2016.co.za
SMOKING IN HIV

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15 April 2016
• Smoking accounts for more life-years lost than HIV infection itself in areas with well-run HIV services

• Mortality rate per 100 person-years
  – HIV negative never smokers  1.76
  – HIV positive never smokers  2.45
  – HIV positive current smokers  5.48

Crothers K et al. AIDS Edu Prev 2009
SMOKING

COMMUNICABLE DISEASES
• Bacterial pneumonia
• Tuberculosis
• Pneumocystis pneumonia

NON-COMMUNICABLE DISEASES
• COPD
• Lung cancer
  • Cardiovascular disease
  • Oral thrush
  • Oral hairy leukoplakia
  • Cognitive and neurological effects, etc.

EFFECTS ON HIV INFECTION
• Faster progression to AIDS?
• Poorer response to ART?

&

SMOKING CESSATION
COMMUNICABLE DISEASES

- Bacterial pneumonia
- Tuberculosis
- Pneumocystis pneumonia
BACTERIAL PNEUMONIA

- Increased risk for pneumonia at all levels of immunosuppression and despite ART

Cigarette smoking was the strongest predictor for development of pneumonia in the viral suppression arm.

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**TABLE 3. BASELINE PREDICTORS FOR BACTERIAL PNEUMONIA BY STUDY ARMS—DRUG CONSERVATION AND VIRAL SUPPRESSION**

<table>
<thead>
<tr>
<th>Predictors</th>
<th>n (% )</th>
<th>Univariate Cox Regression*</th>
<th>Multivariate Cox Regression†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hazard Ratio</td>
<td>95% CI</td>
<td>P Value</td>
</tr>
<tr>
<td>Treatment group</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DC</td>
<td>2,720 (49.7)</td>
<td>1.55</td>
<td>1.07–2.25</td>
</tr>
<tr>
<td>VS</td>
<td>2,752 (50.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cigarette smoking</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>2,215 (40.5)</td>
<td>2.19</td>
<td>1.34–3.60</td>
</tr>
<tr>
<td>Past</td>
<td>1,358 (24.8)</td>
<td>1.80</td>
<td>1.04–3.11</td>
</tr>
<tr>
<td>Never (ref)</td>
<td>1,899 (34.7)</td>
<td>1.00</td>
<td></td>
</tr>
</tbody>
</table>

_Gordin FM et al. Am J Respir Crit Care Med 2008_
TUBERCULOSIS

• “Syndemic” of HIV and TB

• Smoking associated with
  – Increased predisposition to TB infection and TB disease (despite ART)
  – More rapid disease progression of disease
  – Poorer response to treatment
  – Longer duration of infectivity
  – Higher likelihood of recurrence
  – Higher mortality despite appropriate TB treatment

• Estimated that 16% of TB cases preventable with elimination of smoking

TB OUTCOMES IN HIV SMOKERS

• Ever smokers 30% less likely to initiate ART (even though eligible)

• Ever smokers more likely than never smokers to have adverse TB Rx outcomes (lost to follow-up, death, Rx failure): HR 2.15

• Smokers for ≥ 10 years + initiated ART during TB Rx
  – More likely to be lost to follow-up (HR 5.11)
  – Higher mortality (HR 3.81)
PNEUMOCYSTIS JIROVECII PNEUMONIA

Increased risk of PCP in smokers

- 125 patients admitted with PCP
- 78% cigarette smokers
- CD4 < 200 x 10^6/L: OR current vs non-smokers 2.7
- Dose-dependent relationship: 3% risk/cigarette/day
  - One pack/day: OR 1.8
  - Two packs/day: OR 3.35

Miquex-Burbano MJ et al. Int J Inf Dis 2005
COLONIZATION WITH PCP

Prevalence of colonization with PCP
- Healthy subjects: up to 20%
- HIV-infected subjects: 20–69%

Risk of colonization amongst smokers: OR 2.9

PCP prophylaxis does not reduce risk of colonization

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**TABLE 3 Risk factors for *Pneumocystis* colonization**

<table>
<thead>
<tr>
<th>Risk factor</th>
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</thead>
<tbody>
<tr>
<td>Associated medical conditions</td>
<td></td>
</tr>
<tr>
<td>Chronic lung disease, especially COPD</td>
<td></td>
</tr>
<tr>
<td>Pregnancy</td>
<td></td>
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<tr>
<td>HIV infection</td>
<td></td>
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<tr>
<td>Autoimmune disease</td>
<td></td>
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<tr>
<td>Young children, especially during upper respiratory infections</td>
<td></td>
</tr>
<tr>
<td>Malignancy</td>
<td></td>
</tr>
<tr>
<td>Organ transplantation</td>
<td></td>
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<tr>
<td>Medications</td>
<td></td>
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<tr>
<td>Corticosteroids</td>
<td></td>
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<tr>
<td>TNF-α inhibitors</td>
<td></td>
</tr>
<tr>
<td>Other immunosuppressives</td>
<td></td>
</tr>
<tr>
<td>Clinical risk factors</td>
<td></td>
</tr>
<tr>
<td>Low CD4⁺ cell count</td>
<td></td>
</tr>
<tr>
<td>Cigarette smoking</td>
<td></td>
</tr>
<tr>
<td>Geographic location</td>
<td></td>
</tr>
<tr>
<td>History of recent PCP exposure</td>
<td></td>
</tr>
<tr>
<td>Lack of PCP prophylaxis</td>
<td></td>
</tr>
</tbody>
</table>
NON-COMMUNICABLE DISEASES

- COPD
- Lung cancer
COPD

• HIV is independent risk factor for COPD

• Develops over much shorter period of time in HIV infected smokers than in HIV uninfected smokers

• Frequently unrecognized
  – Report of 338 HIV positive smokers (≥ 20 pack years)
    • Prevalence of COPD: 26%
    • Undiagnosed COPD: 74%

• Possible association with PCP

• Acute exacerbations of COPD

  – Rate higher in HIV-infected vs HIV-uninfected (IRR 1.54)

  – HIV-related risk factors
    • Lower CD4 count
    • HIV RNA levels > 500 copies/ml
    • Not on ART
    • Alcohol-related conditions (even after controlling for smoking)
LUNG CANCER

- Increased susceptibility (lower pack-year history)
- Earlier age at presentation
- More advanced disease at presentation
- Worse outcome

- Possible mechanisms
  - High smoking rates in HIV population
  - Decreased immunovigilance (despite ART)
  - Chronic lung damage from infections
  - Enhanced inflammation
  - Increased lifespan due to ART and better healthcare
<table>
<thead>
<tr>
<th>Event</th>
<th>Persons With HIV</th>
<th>Uninfected Persons</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Persons, n</td>
<td>Incidence Rate per 100 000 Person-Years</td>
</tr>
<tr>
<td>Kaposi sarcoma</td>
<td>612</td>
<td>130.4</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>725</td>
<td>153.5</td>
</tr>
<tr>
<td>Lung cancer</td>
<td>614</td>
<td>129.3</td>
</tr>
<tr>
<td>Anal cancer</td>
<td>285</td>
<td>60.1</td>
</tr>
<tr>
<td>Colorectal cancer</td>
<td>173</td>
<td>36.4</td>
</tr>
<tr>
<td>Liver cancer</td>
<td>220</td>
<td>46.3</td>
</tr>
<tr>
<td>Hodgkin lymphoma</td>
<td>159</td>
<td>33.5</td>
</tr>
<tr>
<td>Melanoma</td>
<td>78</td>
<td>16.4</td>
</tr>
<tr>
<td>Oral cavity/pharyngeal cancer</td>
<td>163</td>
<td>34.3</td>
</tr>
<tr>
<td>Death</td>
<td>17 534</td>
<td>3686.0</td>
</tr>
</tbody>
</table>

NA-ACCORD = North American AIDS Cohort Collaboration on Research and Design.
SCREENING FOR LUNG CANCER IN HIV INFECTED POPULATION

• 442 patients underwent LDCT scans
  – Prevalence of lung cancer 2.03%
  – Positive images in 21%
  – 8 cancers occurred in patients < 55 years

• Possible concerns
  – Higher number of false positives due to previous lung infections?
  – Need to lower age at which screening should be performed?

Makinson A et al. AIDS 2016
EFFECTS OF SMOKING ON HIV INFECTION

- Faster progression to AIDS?
- Poorer response to ART?
EFFECT OF SMOKING ON HIV

• Adverse effect on HIV disease progression
  – Conflicting studies

Largest study sample to date examining relationship between smoking and biomarkers of HIV disease progression
• Smokers have poorer response to ART than non-smokers
  – Surrogate marker for non-adherence
  – More side-effects to drugs in smokers
  – Activation of genes by cigarette smoke which promote HIV replication
  – Altered pharmacokinetics
SMOKING CESSATION

• Counselling
• Cognitive therapy (adjustment skills)
• Pharmacotherapy
  – Nicotine replacement therapy
  – Bupropion
  – Varenicline
209 HIV positive smokers

- Face-to-face individual counselling + NRT
- Computer-based Internet smoking intervention + NRT
- Self-help + NRT

Follow-up at 12, 24, 36 and 52 weeks

- No significant difference between 3 groups (abstinence 15-29%)
- Factors associated with achieving abstinence: employment, greater desire to quit, lower mood disturbance score

Humfleet GL et al. Nic Tob Res 2013
VARENICLINE

- Adherence: only 58% at 1 month
- Safety: no difference in adverse effects in patients on ART vs no ART
- Efficacy: OR of abstinence at 3 months for Varenicline vs NRT: 2.75
- Adverse effects: not increased compared to HIV neg
  - Most common adverse effects: nausea, abnormal dreams, change in affect, insomnia
  - No effect on CD4 count or viral load

Shelley D et al. Nicotine & Tobacco Research 2015
Ferketich AK et al. Nicotine & Tobacco Research 2013
Cui Q et al. AIDS Patient Care and STDs 2012
BARRIERS TO SMOKING CESSATION IN HIV PERSONS

• Failure of healthcare providers to
  – screen for smoking
  – promote smoking cessation
• Availability and cost of pharmacological therapy for smoking cessation
• Associated depression in smokers
• High rate of other substance abuse, e.g. alcohol
• Poor social support networks
• Use of tobacco as coping mechanism for HIV-related issues
• Perceived competence
THE WAY FORWARD

• Prioritization and integration of smoking cessation programmes into HIV/TB care programmes
  – Inexpensive
  – Sharing of resources
  – Holistic care