The threat of drug resistant tuberculosis in eastern Europe

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XII EACS conference
Cologne, Germany
Distribution of multidrug-resistant tuberculosis among new TB cases, 1994–2007
Incidence of TB in the countries of former USSR, 2006

- Latvia 57
- Lithuania 62
- Ukraine 83
- Kazakhstan 134

WHO Global Tuberculosis Control 2009
Incidence of TB in Russia 1992-2008 per 100,000 population

Ministry of Health, Russia, 2008
# Tuberculosis in Russia in 2008

<table>
<thead>
<tr>
<th>Category</th>
<th>Per 100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence, general population</td>
<td>84</td>
</tr>
<tr>
<td>Incidence, penitentiary system</td>
<td>1308</td>
</tr>
<tr>
<td>Prevalence, general population</td>
<td>194</td>
</tr>
</tbody>
</table>

Ministry of health Russia, 2008
TB incidence in Russian prisons per 100,000 population

Ministry of health Russia, 2008
TB mortality in Russia
1994 - 2008

% who died among all TB cases

Ministry of health Russia, 2008
Prognoses of TB development in Russia

Cases per 100,000 population

Ministry of health Russia, 2008
<table>
<thead>
<tr>
<th>Country</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azerbaijan</td>
<td>36</td>
</tr>
<tr>
<td>Kazakhstan</td>
<td>32</td>
</tr>
<tr>
<td>Republic of Moldova</td>
<td>29</td>
</tr>
<tr>
<td>Uzbekistan</td>
<td>24</td>
</tr>
<tr>
<td>Russian Federation</td>
<td>21</td>
</tr>
<tr>
<td>Estonia</td>
<td>20</td>
</tr>
<tr>
<td>Ukraine</td>
<td>19</td>
</tr>
<tr>
<td>Lithuania</td>
<td>17</td>
</tr>
<tr>
<td>Belarus</td>
<td>16</td>
</tr>
<tr>
<td>Latvia</td>
<td>14</td>
</tr>
</tbody>
</table>

WHO Global Tuberculosis Control 2009
Causes of MDR-TB

- High proportion of chronically-ill patients
  - TB disease > 1 year

- Among all TB cases, high frequency of chronic forms
  - E.g. 2008: 120,000 new TB cases + >100,000 chronic cases

- “Old” drugs and limited options of new drugs on the market
  - E.g. Isoniazid used > 40 years

- Low living standards
- Migration
- Prisons
Example of chronically-ill TB patient
Causes of MDR-TB

- Deterioration of health care system
- Using of inadequate treatment regimens
- Impossible to complete isolation of patients and the absence of compulsory treatment
- Low patients’ compliance
  - Low education
  - IDU and alcohol
- HIV epidemic
New cases of HIV and TB in Russia 1999-2007, per 100,000 population

O. Frolova 2009 Russian Federal Centre of TB/HIV Surveillance
Transmission of HIV infection
1987-2008 St-Petersburg, Russia

% 100
96 70 97 97 72 54 65 67 89 81 81
0 3 1 7 13 16 10 8 17 17

St. Petersburg City AIDS Centre
Two epidemics in Russia

TB

HIV

TB

HIV
Stages of HIV/TB epidemic development in St. Petersburg

- **1 stage (1999 - 2001)** – first cases of HIV infection in TB patients
- **2 stage (2002 - 2004)** – increase in the number of HIV/TB patients - the appearance of cases with simultaneous detection of tuberculosis and HIV-infection
- **3 stage (2005 - 2007)** – increase in the cumulative number of HIV/TB patients, increasing of TB cases among patients with established HIV-infection
- **4 stage (from 2008)** – extensive spread of TB among HIV-patients associated with the increasing number of patients with advanced HIV infection
Frequency of recording of HIV-infected patients at a late stage in Russia 1999 - 2008

CD4 < 200 cells/mm³

O. Frolova 2009 Russian Federal Centre of TB/HIV Surveillance
TB mortality among overall mortality of HIV-patients
2000-2008 St-Petersburg, Russia

TB mortality among overall mortality of HIV-patients
2000-2008 St-Petersburg, Russia

N of HIV patients died

St. Petersburg City AIDS Centre
Proportion of HIV/TB patients with CD4 < 200 and CD4 < 350 cells/mm³ at TB diagnosis
TB hospital #2 St-Petersburg, Russia

A. Panteleev et al 2009
Incidence of HIV and TB in general population and incidence of TB in HIV-population
2000-2008 St.-Petersburg, Russia

A. Panteleev et al 2009
Proportion of HIV cases among newly diagnosed TB cases
TB hospital #2 St-Petersburg, Russia

%
Frequency of drug resistance in HIV/TB patients
TB hospital #2 St-Petersburg, Russia

<table>
<thead>
<tr>
<th>Drug</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streptomycin</td>
<td>70%</td>
</tr>
<tr>
<td>Isoniazid</td>
<td>69%</td>
</tr>
<tr>
<td>Rifamycin</td>
<td>60%</td>
</tr>
<tr>
<td>Ethambutol</td>
<td>34%</td>
</tr>
<tr>
<td>Ofloxacin</td>
<td>13%</td>
</tr>
</tbody>
</table>
Frequency of MBT-positive tuberculosis in HIV-infected patients according to the CD4 cells level

TB hospital #2 St-Petersburg, Russia

N=1244

MBT-positive – *Mycobacteria tuberculosis* detected by microscopy and/or culture
Detection of MBT in HIV/TB patients
TB hospital #2 St-Petersburg, Russia

MBT was detected in 827 patients (67%) out of total 1244 HIV/TB patients.

- Culture: 53
- Microscopy: 27
- Culture + Micro: 20
Drug resistance in HIV/TB patients
TB hospital #2 St-Petersburg, Russia

N culture positive = 604

- Sensitive: 25%
- Primary DR: 42%
- Secondary DR: 33%
Drug resistance in HIV/TB patients
TB hospital #2 St-Petersburg, Russia

MDR
N tested 604
56%

XDR
N tested 284
10%
XDR-TB in HIV/TB patients
TB hospital #2 St-Petersburg, Russia

N with XDR-TB = 29

Primary DR: 72%
Secondary DR: 28%
Proportion of HIV/TB patients with MDR-TB
TB hospital #2 St-Petersburg, Russia

<table>
<thead>
<tr>
<th>Year</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>2001</td>
<td>59</td>
</tr>
<tr>
<td>2002</td>
<td>49</td>
</tr>
<tr>
<td>2003</td>
<td>61</td>
</tr>
<tr>
<td>2004</td>
<td>64</td>
</tr>
<tr>
<td>2005</td>
<td>64</td>
</tr>
<tr>
<td>2006</td>
<td>63</td>
</tr>
<tr>
<td>2007</td>
<td>56</td>
</tr>
<tr>
<td>2008</td>
<td>46</td>
</tr>
</tbody>
</table>
Proportion of IDUs among HIV/TB patients

TB hospital #2 St-Petersburg, Russia

%
Proportion of patients with prison anamnesis
TB hospital #2 St-Petersburg, Russia

%
Clinical aspects of MDR-TB among HIV/TB patients

- Problems with rapid detection of drug resistance, therefore drug choice relays on:
  - Presence of MDR-TB depends on prison anamnesis
  - The more lung tissue involved, the more chances to have MDR-TB
  - Lack of treatment effect
### Outcomes of TB treatment in HIV-infected patients according to MDR

TB hospital #2 St-Petersburg, Russia

<table>
<thead>
<tr>
<th>Outcome</th>
<th>MDR+ N = 347</th>
<th>MDR- N = 257</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cured and/or treatment completed</td>
<td>2</td>
<td>9</td>
</tr>
<tr>
<td>Relapse</td>
<td>32</td>
<td>19</td>
</tr>
<tr>
<td>Chronically forms</td>
<td>28</td>
<td>21</td>
</tr>
<tr>
<td>Death within 1(^{st}) year of treatment</td>
<td>26</td>
<td>22</td>
</tr>
<tr>
<td>Death after 1(^{st}) year of treatment</td>
<td>38</td>
<td>16</td>
</tr>
<tr>
<td>Lost to follow-up</td>
<td>12</td>
<td>29</td>
</tr>
</tbody>
</table>
Forms of TB relapses HIV/TB infected patients according to MDR
TB hospital #2 St-Petersburg, Russia

<table>
<thead>
<tr>
<th>MDR in the initial TB case</th>
<th>Relapse</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pulmonary</td>
</tr>
<tr>
<td>MDR + N = 347</td>
<td>34 %</td>
</tr>
<tr>
<td>MDR − N = 257</td>
<td>63 %</td>
</tr>
</tbody>
</table>
Cumulative mortality of HIV/TB patients according to drug resistance
2001 - 2009 TB hospital #2 St-Petersburg, Russia

<table>
<thead>
<tr>
<th></th>
<th>MDR +</th>
<th>MDR -</th>
<th>XDR+</th>
<th>XDR-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality, %</td>
<td>65</td>
<td>39</td>
<td>63</td>
<td>38</td>
</tr>
</tbody>
</table>
Treatment of tuberculosis in HIV-infected patients
St-Petersburg, Russia

• Start TB treatment as soon as possible
• Use of adequate treatment regimens
  – using parenteral drugs
• Use of pathogenetic methods of treatment
  – Collapsotherapy
• Timely start of HAART
HAART in patients with HIV/TB

TB hospital #2 St-Petersburg, Russia

**HAART +**
- Cure: 39%
- Chronical forms: 29%
- Without dynamics: 10%

**HAART -**
- Death: 78%
- Without dynamics: 13%
- Chronical forms: 5%
- Curable: 4%
# Efficacy of anti-TB treatment and HAART according to drug resistance

**TB hospital #2 St-Petersburg, Russia**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>MDR + HAART- %</th>
<th>MDR + HAART+ %</th>
<th>MDR - HAART- %</th>
<th>MDR - HAART+ %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cured</td>
<td>1,2</td>
<td>4,4</td>
<td>2,6</td>
<td>22,6</td>
</tr>
<tr>
<td>Relapses</td>
<td>31,0</td>
<td>33,8</td>
<td>19,7</td>
<td>24,5</td>
</tr>
<tr>
<td>Chronical forms</td>
<td>21,7</td>
<td>14,7</td>
<td>20,5</td>
<td>11,3</td>
</tr>
<tr>
<td>Death within the 1\textsuperscript st year of treatment</td>
<td>37,7</td>
<td>33,8</td>
<td>33,3</td>
<td>18,7</td>
</tr>
<tr>
<td>Death after the 1\textsuperscript st year of treatment</td>
<td>35,5</td>
<td>29,9</td>
<td>16,1</td>
<td>10,3</td>
</tr>
<tr>
<td>Lost to follow-up</td>
<td>14,3</td>
<td>13,2</td>
<td>23,9</td>
<td>22,6</td>
</tr>
</tbody>
</table>
Conclusions

• Problem of tuberculosis is extremely actual in the countries of eastern Europe

• Prevalence of MDR-TB (and XDR-TB) is rapidly increasing

• The rapid spread of HIV infection and overlapping risk groups lead to the worsening of TB situation
Conclusions

• Access to HAART is the key to a better prognosis

• Concurrent use of adequate TB treatment and HAART is the way to limit HIV/TB epidemic
For more information please check:

www.tb-hiv.ru
Thank you!