RESULTS FROM THE BLOOD BANK SCREENING IN TURKEY

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University Hospital Blood Bank
Content of the presentation

• A short review about the blood bank organization in our country
• Measures taken in blood banks to prevent transmission of HBV / HCV and the current status in Turkey
• Results from blood bank screenings
• What to do more to minimize the risk of transfusion transmitted HBV and HCV infections
Blood Bank Organization in Turkey

• Hospital Blood Banks
  – Public hospitals (State hospitals)
  – University hospitals
  – Private hospitals
  – Military hospitals

• Red Crescent Blood Banks

Donation / year > 5.000  65 blood bank
Donation / year > 10.000  27 blood bank
Donation / year > 20.000  10 blood bank

Total about 400
1.800.000 U of Red Cell Susp / Year
New Blood Law – April 2007

• Regional blood banks
  – Will collect blood, perform screening tests and prepare and store all kind of components. Send them systematically to the transfusion centers.

• Transfusion centers (in hospitals)
  – Will store a amount of blood components how much it needs, perform cross-match testing and antiglobulin tests.

• Blood collection centers
  – Centers where the blood is collected from donors and send to the regional blood bank.
Current status of blood banks

• Now we are in a transition period

• The Red Cresent Blood Banks begins to be organized as regional blood banks
  – The rate of blood which is collected from Turkish Red Cresent arised to 40-44 % in the last year

• All hospital blood banks will transform to “transfusion centers”

• It is foreseen that this transformation will be completed in 2013-2014
Measures taken in blood banks to prevent transmission of HBV and HCV

• Donor assessment

• Screening tests

• Quarantine

• Pathogen inactivation
Donor assessment

• Donor questionnaire and selection to eliminate high-risk donors
• Practiced in all blood banks, standard donor questioning forms are used
• Unknown routes of transmission of HBV /HVC (25-40%)
• Truthfulness of the donor declarations
  – The majority of donors are first-time donors
  – Very few voluntary-regular donors
Quarantine

- Only for fresh frozen plasma
- First screening and collection of blood (donor can be in the seronegative / window period) → quarantine → invitation of the donor for the second test → if nonreactive put the plasma in service
- What about the used red cell suspension?
- Recall of donors is problematic
- Currently not used in Turkey
Pathogen Inactivation

• Used in some developed countries
  – Not in all blood banks
• For fresh frozen plasma since more than 15 years (USA and Europa)
• Recently for platelet suspensions (Europa)
• Studies for red cell suspensions and whole blood
• Cost-effectiveness is under debate
• Not used in Turkey yet
Screening tests

• Mandatory tests
  – HBsAg (minimum sensitivity 0,5 IU/mL)
  – Anti-HCV (± HCVcorAg)
  – Anti-HIV I-II-g0 ± HIV Ag (p24)
  – Screening for Syphilis

• Performed in all blood banks

• High sensitive 3rd generation immunoassays (EIA, ChLIA)

• Quick test only in emergency situations, in a few very small blood banks
Screening results

- The donors are people who “seems to be healthy”

- Seroprevalances of infectious diseases are lower in donor populations compared to the general population because the pre-screening elimination of high-risk donors
The change in our seropositivity rates

- 28 blood banks, n=1.060.087 donors
- HBsAg
  - 1995: 5,6 %
  - 1999: 3,3 %
- Anti-HCV (since 1996)
  - Arised form 0,2 % to 0,6 % in 1999
  - Improvement of the anti-HCV tests

Study of Blood Banks and Transfusion Society of Turkey, 2000
The change in our seropositivity rates

- n= 6,240,130 donors
- HBsAg
  - 1989: 4,19 %
  - 2004: 2,1 %
- Anti-HCV
  - No change: 0,38%

Study of Emekdaş G et all, 2005
## Uludag University, Bursa

<table>
<thead>
<tr>
<th>Year</th>
<th>HBsAg (%)</th>
<th>Anti-HCV (%)</th>
<th>Number of donors (n)</th>
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<td>1998</td>
<td>3,53</td>
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<td><strong>Total (12 years)</strong></td>
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<td>Year</td>
<td>HBsAg (%)</td>
<td>Anti-HCV (%)</td>
<td>Number of donors (n)</td>
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<td>1996</td>
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<td>2004</td>
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<td>2006</td>
<td>0.87</td>
<td>0.01</td>
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<td>Total (11 years)</td>
<td>1.57</td>
<td>0.44</td>
<td>133.915</td>
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## Tepecik Research & Training Hospital, Izmir

<table>
<thead>
<tr>
<th>Year</th>
<th>HBsAg (%)</th>
<th>Anti-HCV (%)</th>
<th>Number of donors (n)</th>
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<tbody>
<tr>
<td>2002</td>
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<td>2006</td>
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<td><strong>Total (5 years)</strong></td>
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<td><strong>0.54</strong></td>
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Istanbul Research & Training Hospital,

<table>
<thead>
<tr>
<th>Year</th>
<th>HBsAg (%)</th>
<th>Anti-HCV (%)</th>
<th>Number of donors (n)</th>
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<tr>
<td>2000</td>
<td>3.69</td>
<td>0.63</td>
<td>6.454</td>
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<tr>
<td>2001</td>
<td>3.91</td>
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<td>2002</td>
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<td>2.75</td>
<td>0.30</td>
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<td>2005</td>
<td>2.36</td>
<td>0.23</td>
<td>5.981</td>
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<td>2006</td>
<td>2.08</td>
<td>0.05</td>
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<td>2007 (first 6 months)</td>
<td>1.81</td>
<td>0.13</td>
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<td>Total (8.5 years)</td>
<td>2.9</td>
<td>0.30</td>
<td>50.495</td>
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### Regional differences

<table>
<thead>
<tr>
<th>Blood Bank / Region</th>
<th>Years</th>
<th>Number of donors (n)</th>
<th>HBsAg (%)</th>
<th>Anti-HCV (%)</th>
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</thead>
<tbody>
<tr>
<td>Research and Teaching State Hospital Blood Bank / Trabzon- Black Sea Region</td>
<td>2004-2007</td>
<td>12,092</td>
<td>1,62</td>
<td>0,2</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Decreased from 1,9 to 1,2</td>
<td>Decreased from 0,31 to 0,15</td>
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<tr>
<td>Süleyman Demirel University Blood Bank / Isparta- Mediterranean Region</td>
<td>2000-2007</td>
<td>51,361</td>
<td>1,09</td>
<td>0,44</td>
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<tr>
<td>Selçuk Meram University Blood Bank / Konya-Middle Anatolia</td>
<td>2006</td>
<td>54,266</td>
<td>0,6</td>
<td>0,1</td>
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<tr>
<td>Turkish Red Crescent Blood Banks / Middle Anatolia</td>
<td>2006</td>
<td>102,359</td>
<td>1,62</td>
<td>0,49</td>
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<tr>
<td>Turkish Red Crescent Blood Banks / Aegean Region</td>
<td>2004-2007</td>
<td>268,578</td>
<td>1,36</td>
<td>0,42</td>
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<td></td>
<td></td>
<td></td>
<td>In Uşak-Kütahya 0,5</td>
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</table>
Possible explanations for the decrease

• Advances in blood banking
  – The effect of intensive and continuous education initiated by The Blood Banks and Transfusion Society of Turkey and supported by the Ministry of Health
  – More attention in donor assessment !!

• Rise in public awareness
  – About transfusion transmitted infections, HBV, HCV, vaccination, prevention etc. Many people are screened and vaccinated through their own wish.

• Vaccinations
  – Adult vaccination
  – The effect of the vaccination program in children which begun in 1998 will be observed in the next decade
What to do more?

• Anti-HBc testing

• NAT (Nucleic acid testing)

• HCV cor Ag testing
Anti-HBc

- Window period and occult HBV infections!!
- Anti-HBc positivity rates in
  - HBsAg negative donors 18 %
  - HBsAg and anti-HBs negative donors 2,7 %

Bal SH et al. Mikrobiol Bul (43), 2007

- Loss of donors (how many of them are infectious?)
- Initially screen for HBsAg, then consecutively for anti-HBs and anti-HBc will not be practical and cost-effective
- The majority of our donors are first time donors
  - This proportion will definitely be decreased in regular voluntary donors
How many of HBsAg negative, but anti-HBc positive donors are infectious?

• 9282 HBsAg non-reactive donors
• Anti-HBc, anti-HBs, HBV-DNA (Real-time PCR)
• HBV-DNA was performed only in isolated anti-HBc reaktive donors
• HBV-DNA positive in one (1 / 8.333 donation)
• HBV-DNA positive in
  – 0,012 % of HBsAg non-reactive donors
  – 0,45 % of isolated anti-HBc reactive donors

Bal SH et all. Mikrobiol Bul (43), 2007
Nucleic acid testing

T = 0

NAT

serology

antigen

antibody

infectivity

T = 0

eclipse

low

high

medium

low

neutralized

relative concentration

antigen detection limit

NAT detection limit

infectivity threshold

antibody

virus

infectivity threshold
eclipse phase

viral load \( \text{geq/ml} \)

day 6  day 15  day 21

\( \cdots \cdots \cdots \rightarrow \text{below infectivity threshold?} \)

\( \text{infectious} \)

day 3

day 8  day 24  day 38

10^3  10^6

\text{RNA}  \text{HIV-Ag}  \text{Anti-HIV}

\text{HCV-RNA}  \text{Anti-HCV}

\text{HBV-DNA}  \text{HBsAg}
NAT in Europa

- HCV-RNA is mandatory in plasma fractionation (1999)

- HIV-RNA is mandatory in France and Holland (2001), Belgium and Switzerland (2002), Poland (2003), Germany (2004)

- HCV-RNA is mandatory in Austria, Germany, Holland, and Switzerland (1999), Finland, Norway and Slovenia (2000), France and Poland (2001), Belgium and Italy (2002), Spain (2003)

- Optionally: England, Ireland, Luxemburg, Portugal, Greece

- HBV-NAT introduced in Austria, Germany, Italy, Lithuania, Poland, Spain, Portugal, Greece
Study of Turkish Red Crescent

- 18,200 donors (February 2007-September 2008)
- Serology + ID-NAT (Cobas-ROCHE and Tigris-CHIRON)

- 314 HBsAg reactive (1.72 %)
- 17,886 HBsAg non-reactive
  - 11 HBV-DNA positive (1 / 1626)

- 62 anti-HCV reactive (0.34 %)
- 18,138 anti-HCV non-reactive
  - 2 HCV-RNA positive (1 / 9069)

Altunay H et all. XIV. KLIMIK Kongresi, 2009
• These results are well-above the calculated estimates

• It may be argued whether or not these cases reflect true positivity and the potential method of confirmation is also another subject of debate

• Further studies are required
False positive?

• 4,484 donors (January 2005 – March 2006)
• Minipools, Real-Time PCR
  – 186 minipools from 24, one minipool from 20 samples
• 3 minipool reactive
• Test repeated (double): 2 minipool reactive
• ID-test in 48: 3 (1+2) reactive
• Test repeated (double): 2 reactive
• Recall of the reactive donors (new blood samples):
  All HBV markers negative

Karakoç AE. II. Ulusal Kan Merkezleri ve Transfüzyon Tıbbı Kongresi, 2007
• Talasemia Center, Antalya
• 388 Talasemia patients, 246 of them needs regular transfusions every 2-4 week
• HCV infection rates in transfused patients
  – 1994 → 25,2 %
  – 1997 → 29,8 %
  – 2006 → 28,4 %
• NAT is cost-effective in this population

Canatan D. II. Ulusal Kan Merkezleri ve Transfüzyon Tıbbı Kongresi, 2007
Yield of NAT

• Transmission through transfusion depends on the viral load, the quantity of the infected product and the immunocompetence of the recipient. Therefore it is not easy to estimate how many transfusion transmitted HBV and HCV infections are reduced by NAT.

• More studies are needed
• Hemovigilans data
• Turkish Red Crescent will initiate the implementation of NAT testing in the regional blood banks
HCV cor Ag test

• Appropriate for blood banks

• Results are compatible with HCV-NAT

• Not used yet in any of our blood banks

• Studies will begin recently
Conclusion

• Seropositivity rates in the donor population is decreasing
  – Advances in blood banking
  – Rise in public awareness
  – Adult vaccination

• We believe that regional blood banks will provide more advances in blood banking
  – Changes in donor profile
  – Hemovigilans
  – Implementation of NAT, HCV cor Ag tests, and also pathogen inactivation