Minimizing transmission of Transfusion Transmitted infections

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National Blood Transfusion Service
National Cancer Institute of Sri Lanka
Overview

– Introduction of TTI
– NBTS Sri Lanka
– Preventive strategies
– Strengthening the blood safety
Transfusion Transmitted Infection

– A Transfusion transmitted infection (TTI) is a virus, parasite, or other potential pathogen that can be transmitted in donated blood through a transfusion to a recipient.

– The term is usually limited to known pathogens, but ?
Pathogens

– Pathogens – Known and screened by testing

– Pathogens – Known but not screened by testing

– Pathogens- Emerging and re-emerging

– Bacterial Contamination
Pathogens – Known and screened by testing

– Mandatory: WHO recommendation
  • HIV 1 & 2
  • HBV
  • HCV
  • Treponema pallidum,

– Depend on local epidemiological evidence
  • HTLV 1 & 11
  • Malaria
  • West Nile virus
  • Chagas Disease etc......
Pathogens – Known but not screened by testing

– Pathogens of
  • Low prevalence
  • Unknown transmission by transfusion
  • Lack of readily available test

– Known pathogens
  • Viruses – DENV1, DENV4, Chikungunya, EBV, HHV6,7,8
  • Protozoa- Babesia, Leishmania, Toxoplasma
  • Infectious Proteins- -vCJD
Pathogens- Emerging and re-emerging

Defined as pathogens whose incidence of infectivity and disease burden in humans has increased within past 2 decades or threatens to increase in near future.
Pathogens- Emerging and re-emerging

Mechanism of evolution

– Previously unrecognized human agents, emerged by adaptations from animal to human hosts, e.g. HIV, vCJD

– Long recognized pathogens but emerged as new disease threats due to changing population dynamics E.g. West Nile virus, Chaga’s disease

– Existing agents with little or no human disease emerged with mutational adaptations. E.g. Avian flu, strain H1N1.

– Established agents, emerged as problems with changes of the environment that foster growth of the agent or its vector. E.g. Bacteria sepsis in platelets
Factors Contributing to Emergence of Infectious Disease

– Human demographics and behavior
– Technology and industry
– Economic development and land use
– International travel and commerce
– Microbial adaptation and change
– Breakdown of public health measures

Institute of Medicine Report, 1992
Proven or Suspected TTI

<table>
<thead>
<tr>
<th>Organism (disease)</th>
<th>Normal Transmission Route</th>
<th>Transmissibility by Transfusion/Transfusion Risk</th>
<th>Transfusion Cases in US</th>
<th>Treatment for Disease</th>
<th>Intervention for Transfusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parasites</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Babesia</td>
<td>Ticks</td>
<td>Known/moderate</td>
<td>&gt;50</td>
<td>Yes</td>
<td>NA</td>
</tr>
<tr>
<td>Leishmania</td>
<td>Sandflies</td>
<td>Anecdotal</td>
<td>0</td>
<td>Partial</td>
<td>Q</td>
</tr>
<tr>
<td>Malaria</td>
<td>Mosquitoes</td>
<td>Known/low</td>
<td>1–2 per year</td>
<td>Yes</td>
<td>Q, T (unlicensed)</td>
</tr>
<tr>
<td>T cruzi (Chagas)</td>
<td>Reduvid bugs</td>
<td>Known/low</td>
<td>5</td>
<td>Partial</td>
<td>T (unlicensed)</td>
</tr>
<tr>
<td>Bacteria</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anaplasma (ehrlichiosis)</td>
<td>Ticks</td>
<td>Probable/infrequent</td>
<td>1 (presumed)</td>
<td>Yes</td>
<td>NA</td>
</tr>
<tr>
<td>Gram+ &amp; gram- species</td>
<td>Multiple</td>
<td>Known/High</td>
<td>1:75,000 apheresis platelets</td>
<td>Partial</td>
<td>T</td>
</tr>
<tr>
<td>Spirochetes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Borrelia burgdorferi (Lyme disease)</td>
<td>Ticks</td>
<td>Theoretical</td>
<td>0</td>
<td>Yes</td>
<td>NA</td>
</tr>
<tr>
<td>Viruses</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Avian influenza</td>
<td>Respiratory, droplet</td>
<td>Theoretical</td>
<td>0</td>
<td>Partial</td>
<td>NA</td>
</tr>
<tr>
<td>Dengue (dengue fever)</td>
<td>Mosquitoes</td>
<td>Known/low</td>
<td>0 (1 in Hong Kong)</td>
<td>No</td>
<td>NA</td>
</tr>
<tr>
<td>HHV-8 (Kaposi’s sarcoma)</td>
<td>Saliva, sexual contact</td>
<td>Probable/low</td>
<td>0</td>
<td>No</td>
<td>NA, (LR?)</td>
</tr>
</tbody>
</table>
## Proven or Suspected TTI

<table>
<thead>
<tr>
<th>Organism (disease)</th>
<th>Normal Transmission Route</th>
<th>Transmissibility by Transfusion/Transfusion Risk</th>
<th>Transfusion Cases in US</th>
<th>Treatment for Disease</th>
<th>Treatment for Disease Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parvovirus B19</td>
<td>Respiratory</td>
<td>Known/low</td>
<td>3-6</td>
<td>Yes</td>
<td>(T)</td>
</tr>
<tr>
<td>SARS-coronavirus</td>
<td>Respiratory, fecal-oral</td>
<td>Theoretical</td>
<td>0</td>
<td>No</td>
<td>Q</td>
</tr>
<tr>
<td>Simian foamy virus (No known disease)</td>
<td>Primate contact</td>
<td>Theoretical</td>
<td>0</td>
<td>No</td>
<td>Q, (LR)</td>
</tr>
<tr>
<td>TTV/SEN-V (circoviruses) (No known disease)</td>
<td>Parenteral</td>
<td>Known/high</td>
<td>Very frequent (up to 25% of recipients)</td>
<td>None required</td>
<td>NA</td>
</tr>
<tr>
<td>GBV-C/HGV (flaviviruses) (No known disease)</td>
<td>Parenteral</td>
<td>Known/high</td>
<td>Very frequent (up to 7% of recipients)</td>
<td>None required</td>
<td>NA</td>
</tr>
<tr>
<td>New variants of established agents (e.g., HBV, HIV)</td>
<td>Parenteral</td>
<td>Known/low</td>
<td>Rare</td>
<td>Partial</td>
<td>Q, (T)</td>
</tr>
<tr>
<td>Prions</td>
<td>Oral</td>
<td>Known</td>
<td>0 (3 in England)</td>
<td>No</td>
<td>(F)</td>
</tr>
<tr>
<td>vCJD</td>
<td>? oral</td>
<td>Unknown</td>
<td>0</td>
<td>No</td>
<td>NA</td>
</tr>
<tr>
<td>Chronic wasting disease</td>
<td>? oral</td>
<td>Unknown</td>
<td>0</td>
<td>No</td>
<td>NA</td>
</tr>
</tbody>
</table>

Abbreviations: NA, not available; Q, donor questioning; T, laboratory test; (T), test may be partially effective; (LR), leukoreduction thought to reduce infectivity; (F), affinity filters under development.
What makes a good non-bacterial TTI?

Potential for transfusion transmission

– Asymptomatic carriage
– Survival in blood components
– Infectious by IV route
– Susceptible population
What constitutes a TTI: SHOT definition

A report is classified as TTI if, following investigation:

- The recipient had evidence of infection post-transfusion, and there was no evidence of infection prior to transfusion or of an alternative source of infection;

either:

- At least one component received by the infected recipient was donated by a donor who had evidence of the same transmissible infection,

or:

- At least one component received by the infected recipient was shown to contain the agent of infection.
Strategies & Steps
Sri Lankan Experience
NBTS Sri Lanka

- Is under the purview and funding of Ministry of Health
- Consists of
  - National Blood Center
  - 20 cluster centers
  - 94 HBBS
National Blood Center

Services

– Administration
– Staff training (minimum of 1 month) and allocation
– Reference laboratories of the country
– Equipment/reagents/consumables procurement, supply & related services
– Quality management of NBTS
Cluster Blood Centres

- Based in main hospitals
- Under the supervision of Consultant Transfusion Physicians
- Several hospital based blood banks are affiliated to each cluster blood centre
- Collection, testing & processing of blood
- Provide clinical, technical & blood component support to main hospital & affiliated hospitals
• NBTS is the sole supplier of blood and blood products, laboratory, clinical and educational services related to transfusion
• 100% of the collection is from voluntary non remunerated donors
• Components are produced from total whole blood donations
Preventive strategies

- Pre donation
- Testing
- Post Transfusion
Strategies to reduce risk of transfusion-transmitted infections

Transfusion-transmitted infections (Review), Journal of Transfusion Medicine 2007
Preventive strategies - Pre donation

• Donor/Organizer awareness
  – Leaflets
  – Banners
  – Video clips
  – Mass media programs
  – Pre donation awareness programs
    Mobile organizer
    Donors
Donor Selection

- Donor Declaration Form
- Donor Identification details

<table>
<thead>
<tr>
<th>Donor's Name:</th>
<th>Sex: M / F</th>
</tr>
</thead>
<tbody>
<tr>
<td>National ID card No:</td>
<td>Date Of Birth:</td>
</tr>
<tr>
<td>Address (Home):</td>
<td>Age:</td>
</tr>
<tr>
<td>Address (Office):</td>
<td>Blood Group (if known)</td>
</tr>
<tr>
<td>Contact Numbers: Ph. (Home). (Office). (Mobile):</td>
<td>e mail</td>
</tr>
</tbody>
</table>

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National Blood Transfusion Service
Sri Lanka

4th Annual Conference of Indian Society of Transfusion Medicine

Transmedic

ISTM
3. During past 12 months, have you had any of the following:
   A) received blood or blood products?
   B) had tattooing, ear/body piercing or acupuncture treatment?
   C) received any vaccinations?
   D) been imprisoned for any reason?
   E) travelled abroad?

4. A) Have you had Jaundice in the past?
   B) During last 2 years: Have you had tuberculosis?
   C) During last 3 months: Have you had malaria or taken treatment for malaria?
   D) During last one month: Have you had chicken pox, measles, mumps, rubella, dengue fever or any other long-standing (more than one week) fever?
   E) During last 1 week: Have you had a dental extraction or have you taken any medicine (esp. Aspirin or Antibiotics)?
5 A) Do you know that you should not give blood in following conditions? ................. Yes □ No □

- If you were found to be positive for HIV, Hepatitis B, C or Syphilis infections at any time
- If you have ever injected any drug (esp. Narcotics) not prescribed by a qualified medical practitioner
- If you have ever worked as a sex worker?
- If you have ever engaged in male to male sexual activity?
- If you have had sex with a sex worker or unknown partner during last 1 year
- If you have had multiple sex partners during last 1 year
- If you suspect that you or your partner may have got HIV or any other sexually transmitted infection

Please Remember
Unsafe Blood
Can Destroy Lives

B) Do you or your sexual partner belong to one of the above categories? ................. Yes □ No □

C) Are you having persistent fever, multiple swollen glands or unintentional weight loss? ........ Yes □ No □
Donor Counselling

By a trained medical officer

- Confidential Interview
- Health check
- Decide eligibility for donation
WHO Recommendation for TTI testing

4. Screening should be performed using highly sensitive and specific assays that have been specifically evaluated and validated for blood screening.
5. Quality-assured screening of all donations using serology should be in place before additional technologies such as nucleic acid testing are considered.
6. Only blood and blood components from donations that are nonreactive in all screening tests for all markers should be released for clinical or manufacturing use.
7. All screen reactive units should be clearly marked, removed from the quarantined stock and stored separately and securely until they are disposed of safely or kept for quality assurance or research purposes, in accordance with national policies.
8. Confirmatory testing of screen reactive donations should be undertaken for donor notification, counselling and referral for treatment, deferral or recall for future donation, and look-back on previous donations.
Milestones of TTI screening in donation

- **1943** The first cases of transmission of a viral illness through blood transfusion
- **1969** HBsAg Laboratory testing viral transfusion-transmitted viruses
- **1980s** ALT & anti-HBc
- **1980s/1990s** HIV antibody /antigen testing & anti-Hepatitis C virus
- **1999** NAT
Testing

• Selection of sensitive techniques
  – Rapid test: ?sensitivity
  – ELISA- 3\textsuperscript{rd} generation Ab testing
  – 4\textsuperscript{th} Generation ELISA (Ag-Ab) from 2014
  – Chemiluminescence
  – \textbf{N}ucleic acid \textbf{A}mplification \textbf{T}esting Pilot study 2014
Selection of test kits

– Validate with current test kits
– Evaluated by WHO or other recognized bodies such as FDA etc.
– Registered in developed countries
– Used by other transfusion services
– Collaboration with other reference centers
Window Periods Days for HIV, HCV & HBV

- **HIV**
  - 1 copy/20 mls: 9.0 days
  - ID-NAT: 5.6 days
  - MP-NAT: 3.4 days
  - WB: 11.3 days

- **HCV**
  - 1 copy/20 mL: 7.4 days
  - ID-NAT: 4.9 days
  - MP-NAT: 2.5 days
  - WB: 50.9 days

- **HBV**
  - 1 copy/20 mL: 38.3 days
  - ID NAT: 19 days
  - 1:8 - NAT: 15 days
  - Prism HBsAg (1,664 copy/mL): 4 days
  - Auszyme HBsAg (6,800 copy/mL): 5.3 days

*Source: Busch, AABB, 2006, & Kleinman and Busch, J Clin Virol. 2006;36:S23-S29, Assai ISBT & AABB*
Comparison of TTI Prevalence

Year

HIV (scr.+ve) Prevalence
HIV (Conf.+ve) Prevalence
Hepatitis B (rpt.+ve) Prevalence
Hepatitis C (rpt.+ve) Prevalence
VDRL +ve Prevalence
TPPA +ve Prevalence
Comparison of Residual Risks

Transmission risk, per unit
- HIV
- HBV
- HCV

Bacterial Contamination (platelets)
- 1:1000

Clinical Sepsis (platelets)
- 1:10 000

Septic Fatalities (platelets)
- 1:100 000

1:1 000 000


Updated from: Goodnough LT et al. NEJM 1999;341:126-7
Prevention of Bacterial transmission

- Donor counseling
- Cleansing of venipuncture site
- Diversion pouch
- Leucodepletion
- Blood cold chain
- GMP
- Bacterial Detection techniques
- Quarantine of components & treatments
Positive donors

– Tracing of donor & contacts
– Counselling and re-testing
– Deferrals & referrals
– Look back
A look back is the process of identifying previous donations of a donor who currently is testing positive for a transmissible disease marker.

Automatically initiated on each Repeat Reactive & Confirmed positive blood donation.
Post Transfusion
Haemovigilance in Sri Lanka

- Establishment of National Haemovigilance unit in 2009 headed by a Consultant Transfusion Physician
- Incorporated module on haemovigilance for blood bank staff training
- Publication of annual haemovigilance reports & annual update of NBTS staff
- Periodic discussions at quaternary review meeting of NBTS
Supporting background

- Established Centrally coordinated Transfusion Service
- Recognition of Transfusion Medicine as a clinical subspecialty & availability of well established post graduate Diploma & MD in TM
- Functional Hospital Transfusion Committees in majority of hospitals
- Blood safety identified as a priority area of the quality free health care services of MoH
Haemovigilance Scheme in Sri Lanka

Recipient’s Adverse Events at Clinical Areas

Donor Adverse Events

Hospital Blood Bank

In charge consultant

National Haemovigilance Unit

Serious events to be informed immediately

Other events to be informed monthly

IHN

Reporting & Analysis

Feedback
Haemovigilance Data in Sri Lanka

- Recipient adverse events are mandatory to report
- Increased awareness resulted in increased reporting
- Donor adverse events published since 2013
Haemovigilance in Sri Lanka

Haemovigilance Report - 2011
National Blood Transfusion Service
Sri Lanka

Message from the Consultant in-charge

Haemovigilance Report - 2012
National Blood Transfusion Service (NBTS)
Sri Lanka
Volume 03

Haemovigilance Report 2013

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Message from the Director (NBTS)

It is with great pleasure that I write this message to the 4th annual haemovigilance report published by the National Haemovigilance Unit (NHU) of National Blood Transfusion Service (NBTS). During the past few years we have observed a remarkable progress in the national haemovigilance system which is one of the key components in the success of the blood transfusion service. With this positive trend, reporting of unwanted events of transfusion has been improved. Reporting near misses have contributed tremendously to take corrective measures to prevent such further events in future. A series of workshops have been organized by the NHU to discuss and take remedial actions in addition to their involvement in individual cases. We have further stepped to obtain the annual membership of International Haemovigilance Network. Hence, I would like to appreciate all the hard work done by the national haemovigilance team with great gratitude. I wish them the best for their future activities.

Dr. Anil Dissanayake

Message from the Consultant Incharge - NHU

I am extremely happy to release the fourth annual haemovigilance report of the citizens of Sri Lanka NBTS.
## Haemovigilance data in Sri Lanka

<table>
<thead>
<tr>
<th>Transfusion related adverse events in patients</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
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</thead>
<tbody>
<tr>
<td><strong>Major Events</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute Haemolytic Transfusion Reactions (AHTR)</td>
<td>15</td>
<td>11</td>
<td>27</td>
<td>27</td>
<td>17</td>
</tr>
<tr>
<td>Transfusion Related Acute Lung Injury (TRALI)*</td>
<td>12</td>
<td>13</td>
<td>29</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>Transfusion Associated Circulatory Overload (TACO)</td>
<td>28</td>
<td>21</td>
<td>17</td>
<td>17</td>
<td>17</td>
</tr>
<tr>
<td>Transfusion Associated Dyspnoea (TAD)</td>
<td></td>
<td>52</td>
<td>122</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute Pain Transfusion Reaction (APTR)</td>
<td></td>
<td>19</td>
<td>37</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transfusion transmitted Infections*</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Delayed Haemolytic Transfusion Reactions (DHTR)</td>
<td>3</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td><strong>Minor Events</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Febrile Non-Haemolytic Transfusion Reactions (FNHTR)</td>
<td>615</td>
<td>482</td>
<td>507</td>
<td>1095</td>
<td>1102</td>
</tr>
<tr>
<td>Allergic Reactions</td>
<td>849</td>
<td>522</td>
<td>614</td>
<td>1054</td>
<td>998</td>
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<tr>
<td><strong>Total events</strong></td>
<td>1510</td>
<td>1053</td>
<td>1179</td>
<td>2295</td>
<td>2316</td>
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<tr>
<td><strong>Unclassified</strong></td>
<td>76</td>
<td>15</td>
<td>27</td>
<td>241</td>
<td>231</td>
</tr>
<tr>
<td><strong>Total reactions reported</strong></td>
<td>1586</td>
<td>1068</td>
<td>1206</td>
<td>2536</td>
<td>2547</td>
</tr>
<tr>
<td>Transfusion reaction percentage (per transfusion)</td>
<td>0.18</td>
<td>0.17</td>
<td>0.29</td>
<td>0.30</td>
<td>0.18</td>
</tr>
</tbody>
</table>
Trace Back

- A trace back is the process of identifying, locating and testing the donors of products that have been transfused to a patient, who now is testing positive for a transmissible disease to determine the potential source for the transmission of disease.

- Request to initiate a TB can come from internal/external sources

- “Claimant” must be ‘positive’ (antibody) for the infectious marker in question (and provide positive test results)
Strengthening the blood safety further......

- Identified strategies

- Future Prospects
Pathogen Inactivation

• Intercept
  – FDA approved
  – Widely used
  – For platelets & plasma

• Mirasol
  – EU approved
  – Commonly in European countries
  – Applicable to whole blood & Inactivate HAV
  – Risk reduction in alloimmunization: study in Sanquin
## Advantages of PI

<table>
<thead>
<tr>
<th>Testing</th>
<th>Platelets</th>
<th>Inactivation of WBC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Close the window period of testing</td>
<td>Release PC on the day of collection thus transfuse younger platelets</td>
<td>Replace gamma irradiation</td>
</tr>
<tr>
<td>Eliminate ID-NAT</td>
<td>Eliminate release of contaminated PC</td>
<td>Achieve single inventory Reduce rate of transfusion reaction</td>
</tr>
<tr>
<td>Avoid new testing for emerging pathogens</td>
<td>Eliminate recall of PC and associated RBC and plasma</td>
<td>Increase safety for regions that have not introduced universal LR</td>
</tr>
<tr>
<td>Replace CMV testing</td>
<td>Replace bacterial screening</td>
<td></td>
</tr>
<tr>
<td>Change donor referral practice &amp; increase donor availability</td>
<td>Extend platelet storage to 7 days</td>
<td></td>
</tr>
<tr>
<td>Achieve single inventory</td>
<td>Increase availability</td>
<td></td>
</tr>
</tbody>
</table>
Pathogen Inactivation in Sri Lanka

– Started as a pilot project at National Blood Center for buffy-coat derived pooled platelets
– Amotosalen + UVA (INTERCEPT) is used
– Most of the production is used for cancer patients who get multiple platelet transfusions at National Cancer Institute SL
– Each recipient is closely monitored for any adverse events
– Recipients transfusion data are regularly being collected
### Adverse events following PI platelet

#### Summary of adverse events

<table>
<thead>
<tr>
<th></th>
<th>% ATR / Patients</th>
<th>% ATR / Transfusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non PI Platelets</td>
<td>16</td>
<td>11.2</td>
</tr>
<tr>
<td>PI Platelets</td>
<td>5</td>
<td>2.2</td>
</tr>
</tbody>
</table>
Strengthening the blood safety

- Identified strategies
  - Pre-testing of new donors
  - Additional testing of new donors
  - Quarantine of previous donation (plasma)
  - Legally bound to divulge true information
  - Increase Donor awareness
  - Confidential unit exclusion
Strengthening the blood safety

• Identified strategies
  – TTI testing
    • Expansion of NAT
    • Centralization of testing
    • Accreditation of testing centers
  – Computerization of NBTS
    • Computerized donor data base (donor details and previous test results)
    • Unique donor identity
    • Improved donor deferral system (temporary/ permanent)
    • Facilitate look back & trace back
Strengthening the blood safety

• Awareness among blood users
  – Awareness programs for clinicians
  – Improve appropriate clinical use of blood
  – Guidelines & Audits on blood usage
  – Strengthening Hospital transfusion committees
  – Informed written consent for transfusion
  – Patient blood management system
Blood cannot be made 100% safe only by the introduction of state of the art techniques.

It is the responsibility of all stakeholders of the transfusion chain to contribute by adhering to good practices from blood donor awareness to transfusion and beyond....
Thank you

Together We can Save lives