Transfusion Medicine - Update

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Emerging Pathogens

The risk of spreading pathogens – Dengue, Zika, Yellow Fever

Yellow fever outbreak in Brazil worries U.S. officials

Chagas and chikungunya diseases spread in Texas

Chikungunya and Chagas disease are prevalent in Latin America. Visitors to those areas may be bringing it to the U.S. Dogs are a prime factor in spreading fatal Chagas.

New York City issues Tickborne Disease Advisory

Officials with the New York City Department of Health and Mental Hygiene issued a call for city clinicians to be on the alert for patients with tickborne diseases.

Dengue Fever Makes Inroads into the U.S.

The mosquito-borne infection is cropping up in Florida, but mysteriously not in similar regions in the nation.

Florida Blood Bank, OneBlood, Temporarily Suspends Blood Donations From Martin And St. Lucie Counties Due To Dengue Fever
Infectious Disease Testing

Doc, how safe is this blood? I heard people can get AIDS and hepatitis from blood transfusion.

I am going to order some blood for you. Everything is going to be fine.

Ooch! Does it hurt?
Donor Screen

► Questionnaire
  ► Symptoms of diseases
  ► Risky behavior
  ► Exposure to risk factors
    ► Travel history
    ► Medication

► Physical Exam
Blood Product Screen

- Infectious disease testing
  - HIV
  - HBV
  - HCV
  - HTLV
  - Syphilis

- QC on blood component content
Risk of Transfusion Transmitted Diseases

- Window period
- Immunosilent infection
- Species diversity of infectious agent
- New uncharacterized viruses
- Laboratory error
HIV Window Period

Days post-infectiousness (calculated)

Infectious

22 days
11 days

6 days

3rd generation EIAs

HIV RNA

p24 antigen

HCV Window Period

- 82 days (70 days)
- 59 days (47 days)

Transfusion

Days post-infection

Risk of Viral Infections

Risk of transfusion-transmitted virus

Hepatitis C Virus

HepatitisB Virus

HIV

??? Emerging pathogens

Year

1970 '83 '85 '87 '89 '91 '93 '95 '97 '99
# Transfusion Risks

<table>
<thead>
<tr>
<th>Agent</th>
<th>Risk/Million</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV</td>
<td>0.5</td>
</tr>
<tr>
<td>HCV</td>
<td>0.5</td>
</tr>
<tr>
<td>HBV</td>
<td>7 - 32</td>
</tr>
<tr>
<td>HTLV</td>
<td>0.5 - 4</td>
</tr>
<tr>
<td>Bacteria</td>
<td></td>
</tr>
<tr>
<td>- platelets</td>
<td>83</td>
</tr>
<tr>
<td>- red cells</td>
<td>2</td>
</tr>
<tr>
<td>Acute Hemolytic Rxn</td>
<td>1 –4</td>
</tr>
<tr>
<td>Delayed Hemolytic Rxn</td>
<td>1000</td>
</tr>
<tr>
<td>Transfusion-Related Acute Lung Injury (TRALI)</td>
<td>200</td>
</tr>
</tbody>
</table>

Goodnough et al. 1999, NEJM: 340(6) p438-47
The INTERCEPT® Blood System Solution

- Nucleic acid targeting without reactive oxygen species.
- Separate technologies to:
  - Optimize pathogen inactivation
  - Conserve functional activity
The Problem:
Blood carries residual leukocytes, plasma proteins and the commensal and pathogenic microbial flora of the donor.

Ideal State:

- Enveloped viruses
- Non-enveloped viruses
- Gram-negative bacteria
- Gram-positive bacteria
- Spirochetes
- Protozoa
- Leukocytes

Blood Donor
## Robust Pathogen Inactivation

<table>
<thead>
<tr>
<th>Organism</th>
<th>$\text{Log}_{10}$ Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cell associated-HIV</td>
<td>$&gt;5.4$</td>
</tr>
<tr>
<td>DHBV</td>
<td>$&gt;5.1$</td>
</tr>
<tr>
<td>BVDV</td>
<td>$&gt;4.8$</td>
</tr>
<tr>
<td>Cell associated-CMV</td>
<td>$&gt;3.9$</td>
</tr>
<tr>
<td>Chikungunya (CHIKV)</td>
<td>$&gt;7.1$</td>
</tr>
<tr>
<td>Dengue virus (DENV)</td>
<td>$&gt;4.4^1$</td>
</tr>
<tr>
<td>Zika virus (ZIKV)</td>
<td>$\geq 5.8^2$</td>
</tr>
<tr>
<td>Bluetongue (non-env.)</td>
<td>$\geq 4.4$</td>
</tr>
<tr>
<td>Feline Calicivirus (non-env.)</td>
<td>$&gt;6.8$</td>
</tr>
<tr>
<td>Human Adenovirus 5</td>
<td>$&gt;5.9$</td>
</tr>
<tr>
<td>Plasmodium falciparum</td>
<td>$&gt;7.9$</td>
</tr>
<tr>
<td>Babesia microti</td>
<td>$&gt;4.9^3$</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>4.4</td>
</tr>
<tr>
<td>Pseudomonas fluorescens</td>
<td>$&gt;4.1$</td>
</tr>
</tbody>
</table>

1 Santa Maria et al. Transfusion, 56, S4, 11A. 2 Laughhunn et al. Transfusion epub 2017. 3 Tonetti et al. Transfusion 56, S4, 195A.
INTERCEPT Inactivates T-Cells
Feasibility Study: Inactivation of T-Cells to lower the risk of TA-GVHD

- AABB (2013) hospitals reported 20.6% of all RBC & 58.3% of pediatric RBC were irradiated.
- Selective irradiation vs. Universal PR.
- INTERCEPT RBC have a 35-day shelf-life.

<table>
<thead>
<tr>
<th>Day 28</th>
<th>INTERCEPT RBC</th>
<th>Irradiated RBC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemolysis</td>
<td>0.17%</td>
<td>0.68%</td>
</tr>
<tr>
<td>Plasma Hb (mmol/L)</td>
<td>39</td>
<td>188</td>
</tr>
<tr>
<td>Extracellular K⁺ (mmol/L)</td>
<td>38.8</td>
<td>68.7</td>
</tr>
</tbody>
</table>

Knutson et al. ISBT 2013; Castro et al. ISBT Dubai 2016
It is in the Blood

Abba C Zubair MD., PhD, Human Cell Therapy Lab
Parabiosis – young and old

Aging
- Decreased neurogenesis
- Impaired synaptic plasticity
- Impaired cognition

Rejuvenation
- Increased neurogenesis
- Unknown effect on synaptic plasticity?
- Unknown effect on cognition?
It is in the BLOOD

The elements of blood
It is in the BLOOD

Three Young Females
Three Young Males

Three Old Females
Three Old Males
It is in the BLOOD

- Proteomic and Micro-RNA Analysis of Age Related Plasma Derived Exosomes

- The plasma samples were collected from 6 young (18 – 30 years) and 6 old (>50 years) donors with equal male and female representation.

- Exosomes were isolated from each samples and there microRNA and protein content were isolated.

- The exosomes microRNA content from young and old was compared and some statistically significant differences were discovered.
It is in the BLOOD
It is in the BLOOD

Plasmapheresis versus plasma infusion from young APOE3 homozygotes into MCI APOE4 homozygotes to slow disease progression: An unblinded phase 1 safety, methodological and exploratory biomarkers study.

1.1 SCHEMA

Screening

Screen MCI patients in the Mayo MCI Registry for APOE genotype. Patients that are interested will sign consent and complete screening assessments.

Enrollment

Baseline assessments

Distribute  N = 9

Month 0-6

Plasma Exchange  N=3

Plasma Infusion  N=3

No intervention  N=3

Neuropsychology testing, lumbar puncture, PET, apoE measurement, biomarker measurement, and MRI will be completed according to the table of events in section 1.3.

Month 12

Final Assessments
It is in the BLOOD
It is in the BLOOD – young vs old PLT
It is in the BLOOD

The elements of blood

Plasma (about 55%)
Platelets (0.01)
Red blood cells (about 41%)

White blood cells (about 4%): Lymphocyte, Basophil, Eosinophil, Monocyte, Neutrophil
It is in the BLOOD
RBC Nitrosylation
Effect of Nitric Oxide

- Anti-ageing effects
- Increases energy production
- Increases blood flow to vital organs
- Boosts exercise performance & endurance
- Manages diabetes by regulating insulin
- Prevents diabetic complications
- Lowers blood pressure & LDL (bad) cholesterol
- Reverses atherosclerotic plaque formation
- Reverses kidney disease/failure
- Improves sexual performance
- Offsets damage from tobacco use
- Enhances memory & cognitive function
RBC nitrosylation decreases in storage
Impact of Donor Age on RBC Nitrosylation
Hypothesis

RBC from older donor (>50 yrs) have low nitrosylation capacity compared to the young donor.

Also RBC from older donors lose their nitrosylated Hb faster than young donors during storage.
Impact and Significants

- Change transfusion medicine practice by requiring the RBC from younger donor should be used to treat critically ill patients e.g. ICU, CVS, severely hypoxic patients.
- Put limit on storage of RBC units from older donors.
- Use of young RBC donors to treat patients with neurodegenerative diseases such as Alzheimer's and Parkinson disease.
- The use of RBC transfusion therapy as a measure to contract aging.
It is in the BLOOD

Questions