Emerging Infections and Their Impact on Transfusion Safety

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Outline

► Blood safety
► Emerging infections
► West Nile virus
► Chagas’ Disease
► BSE/cCJD
► Others
► Summary and conclusions
Current Safety Estimates for the U.S. (Risk of Infection per unit)

- HBV: 1:205,000-488,000
- HCV: 1:1,935,000
  - Pre-NAT: 1:276,000
- HIV: 1:2,135,000
  - Pre-NAT: 1:1,468,000
- HTLV: 1:514,000-2,993,000

Based on data from ARC repeat donations, 2000-2001, representing 4.2 million person-years of observation (not corrected for rates among 1st time donors) Dodd et al, Transfusion, 2002

Emerging Infections

“Clinically distinct conditions whose frequency in humans has increased over the past two decades”
Speed of Global Travel in Relation to World Population Growth

From: Murphy and Nathanson Sems. Virol. 5, 87, 1994

Infectious Disease Mortality in the United States, 1980-1996

Source: JAMA 1996;275:189-193 and unpublished CDC data

Reported Cases (Thousands)

Unpublished data: Pan American Health Organization, March 1999

Emerging Infections

- New Agent
- Expanding Range
- Imported
- Reemergent
- Newly recognized
- Patient changes

- HIV, BSE/vCJD, SARS
- Babesia/Ehrlichia
- Chagas’, WNV
- Malaria
- HHV-6, 8, TTV….
- CMV, B19?
Elements of an Emerging Infections Program

- Surveillance/Intelligence
- Assessment for relevance
  - Public health
  - Public concern
- Measures of risk
- Investigation of intervention(s)
- Recommendations
- Implementation
- Evaluation

Concern high, Action favored

Benefit High, Action favored

- vCJD
- CJD
- CJD
- Ebola etc
- HHV 8
- CJD
- Babesia
- HGV, etc
- T.cruzi
- HAV
- B19
- Malaria
- RMSF
- CTF
- Chlamydia, HHV, JC, Leptospira, Bartonella, etc

vCJD

(HIV)
West Nile Virus: Background

► First isolated in 1937 in Uganda from blood of a febrile woman.
► Family: Flaviviridae
  ▪ Genus: Flavivirus
  ▪ Japanese Encephalitis Antigenic Complex
  ▪ Complex includes: Alfuy, Japanese encephalitis, Kokobera, Koutango, Kunjin, Murray Valley encephalitis, St. Louis encephalitis, Stratford, Usutu, and West Nile viruses.
► All are transmissible by mosquitoes, many can cause febrile, sometimes fatal, illnesses in humans.
West Nile Fever: Human Disease

- Febrile, influenza-like illness with abrupt onset
- Moderate to high fever
- Headache, sore throat, backache, myalgia, arthralgia, fatigue
- Rash, lymphadenopathy
- Acute aseptic meningitis or encephalitis
- Most fatal cases >50 years old.
**WNV surveillance, 1999-2001**

- 1999: Human cases: 66, 2 deaths
- 2000: Human cases: 21, 2 deaths
  - Conn, NJ, NY
- Infected birds: 4323
  - 12 States, VT to NC
- 483 infected mosquito pools
- 60 horses
- (Infected area larger than ‘99)
- 2001: Human cases: 66, 9 deaths

**West Nile, ’02 cases reported to March 3rd, 2003**

- United States
  - 39 States, plus D.C.
  - 4156 cases, 284 deaths
  - 23 confirmed transfusion cases
- Canada (as of Nov 26, 2002)
  - 3 provinces
  - 73 cases, 2 deaths
  - 1 possible transfusion case
2002 WNV transmission

- 23 cases reported
- 16 donors
- Primary cases recognized by symptoms
- Only 1/7 cocomponent cases symptomatic
- 9/14 donors symptomatic (3 before donation)
- 11/12 implicated donations detectable by pooled testing (one variably so)

Donor NAT for WNV RNA

- Two methods (Roche, Chiron/Gen-Probe)
- Small pools (6 or 16)
- Implementation started June 03
  - All civilian centers by 7/14, military somewhat later
- First positive reported July 3rd, 2003 (TX)
- By September 18: 2.5 million tested, 601 presumed positives, many States
  - Compare likely 380 viremic donations in 2000
  - 489 rep to ArboNet, mean age 45, (15-83), 54% male, 11% subsequent symptoms, 0.7% (2) meningoencephalitis.
- Limited, resource-based ID testing in place
- 2 transfusion-associated cases reported (ID+, pool-)
West Nile Virus Genome

Sequencing target

WNV Phylogenetic Tree
Envelope gene: 1721 - 2514
Other issues

► Size of 2004 epidemic
► Significance of low titer RNA
► Significance of IgM positive
► Future of epidemic
► Other flaviviruses?

JE infection in Hong Kong?

The Department of Health (DH) is investigating a case of Japanese encephalitis in a 38 year old local woman living in Fairview Park, Yuen Long. Serology tests on her blood samples yielded positive result for Japanese encephalitis virus infection. A DH spokesman stated today (Wed 5 Nov 2003) that: "Japanese encephalitis virus is transmitted by the bite of infective mosquitoes. Person to person transmission does not occur."

(From 1992 to 2002, there have been a total of 5 sporadic cases reported in Hong Kong, including one local case in 1996, one imported case in 1997, one imported case in 2001, and 2 imported cases in 2002. Japanese encephalitis virus is transmitted by culicine mosquitoes living mainly in rural areas.) From: ProMed-mail
During investigation of a confirmed case involving a Ma Wan resident, it was found that he donated blood one day before onset of symptoms. A 72-year-old lady, who received transfusion of his blood on 24 August, developed fever on 27 August which resolved three days later. Anti-dengue IgM antibodies were demonstrated in her blood specimen taken on 7 October. Subsequently, her serum samples taken before and after blood transfusion were retrieved and seroconversion was demonstrated. Thus, it was confirmed that she had contracted dengue fever through blood transfusion. Transmission of dengue fever through blood or blood products is extremely rare. There was no previous report on transfusion-induced dengue case found in the literature.
Trypanosoma cruzi

- small parasite: outside and inside cells
- found in Latin America
- causes life-long, untreatable infections, usually without symptoms
- transmission:
  - by vector/bug
  - mother to unborn child
  - organ transplant
  - blood transfusion

U.S./Canadian Transfusion Cases:

1987: California - Mexican donor
1989: New York City - Bolivian donor
       Manitoba - Paraguayan donor
1993: Houston - unknown donor
1999: Miami - Chilean donor
2000: Manitoba - German/Paraguayan donor
2002: Rhode Island – Bolivian donor
U.S. Residents Born in Latin America*

Mexico 4,447,000
Central America 1,482,000
South America 1,107,000
7,036,000

* 1990 Census Data

Seroprevalence Data:

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<thead>
<tr>
<th></th>
<th>Los Angeles</th>
<th>Miami</th>
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<tbody>
<tr>
<td>Total no. donations</td>
<td>1,104,030</td>
<td>181,139</td>
</tr>
<tr>
<td>“Yes” to risk question</td>
<td>78,736 (7.1%)</td>
<td>25,908 (14.3%)</td>
</tr>
<tr>
<td>Number tested</td>
<td>77,967</td>
<td>25,352</td>
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<tr>
<td>EIA repeat reactive</td>
<td>329</td>
<td>75</td>
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<tr>
<td>Confirmed by RIPA</td>
<td>147 (0.2%)</td>
<td>20 (0.1%)</td>
</tr>
<tr>
<td>Seropositivity rate</td>
<td>1 in 7,500</td>
<td>1 in 9,000</td>
</tr>
</tbody>
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Cumulative Parasitemia Testing:

<table>
<thead>
<tr>
<th>Test</th>
<th>n</th>
<th>positive (%)</th>
<th>negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCR</td>
<td>52</td>
<td>33 (63)</td>
<td>19</td>
</tr>
<tr>
<td>Hemoculture</td>
<td>52</td>
<td>3* (6)</td>
<td>49</td>
</tr>
</tbody>
</table>

* also PCR positive

T. cruzi Summary

- seropositive donors nationwide
- no reliable risk factors
- infections are:
  - asymptomatic, chronic, & untreatable
  - congenitally transmitted
- infectious donors demonstrable
- blood screening?
  - lack of available tests
  - universal screening
  - first time donors
Babesia

- Tick-borne, intra-erythrocytic parasite
- Several species
- Global distribution
- Transfusion-transmissible
  - > 50 cases US
  - 1 case from Japan
- Treatable, but can be fatal
Malaria as a re-emerging infection

- Climate change
- Population movement
- Recreational travel
- Transportation
  - Airport malaria
Note: As of 1999, annual cases averaged 20,000

Figure. Imported cases of malaria in Europe (34,35).
TSEs

► “Classical” CJD unlikely to be transmitted by transfusion
  ▪ Epidemiologic studies, animal models
► BSE/vCJD: Insufficient information
  ▪ Some animal models lead to concern
► Protective measures implemented
  ▪ Leukoreduction in some countries
  ▪ Travel deferrals

vCJD

► UK cases as of October 6th:
  ▪ 137 deaths, 7 alive
► Other
  ▪ France 6, Italy 1, Ireland 1
  ▪ US, Canada, Hong Kong (UK exposure)
► Transfusion transmission
  ▪ None observed
  ▪ UK linkage studies
PREDICTING THE SIZE OF THE vCJD EPIDEMIC

SARS (Severe Acute Respiratory Syndrome)

- Global outbreak of a readily transmissible, potentially fatal respiratory disease
- Initial cases in Asia, most serious in China
- As of 31 July, 03, WHO reported 8098 cases, 774 deaths
  - US, 63 cases, no deaths (subject to revision)
- Blood safety concern
  - Disease severity, evidence of viremia
Probable cases of SARS by week of onset
Worldwide* (n=5,910), 1 November 2002 - 10 July 2003

* This graph does not include 2,527 probable cases of SARS (2,521 from Beijing, China), for whom no dates of onset are currently available.

Probable cases of SARS by date of onset
Hong Kong SAR, China, 1 February - 10 July 2003 (n=1,734*)

* As of 10 July 2003, 21 additional probable cases of SARS have been reported from Hong Kong SAR, China, for whom no dates of onset are currently available.
Source: Department of Health, Hong Kong Special Administrative Region of China
SARS

Etiologic agent is a previously unknown coronavirus (30% of common colds)

Donor deferral proposed as interim measure in US, elsewhere
- 14 day deferral after arrive from or transit through an area defined as “affected” by CDC and for contact with a known case
  - Much of mainland China, Hong Kong, Singapore, Hanoi, Toronto, Taiwan
- 28 day deferral for disease

SARS: future concerns

Epidemic returns?
Animal reservoirs
Subclinical infection
Nature, timing of viremic phase
Testing program?
Interventions

- Medical history – pre & post symptoms
  - WNV, SARS
- Risk/geographic deferral
  - SARS, BSE/vCJD, HIV
- Test implementation
  - WNV
- Pathogen reduction?
  - Two different trials for rbc halted

Bacteria

- AABB, CAP Standards
  - Expect guidance on managing AABB standard shortly
- Blood center involvement
- Need to validate 7-day platelets and pre-pooled whole-blood derived platelets
- Significant data from Hong Kong, where testing is routine
Summary

► Blood supply very safe
► New and emerging infections offer risk
► Risk should be analyzed
► Interventions should be evaluated
► Some interventions planned
► Continuing process
► Bacterial detection important, even if not discussed.