Public health relevance of platelet bacterial screening

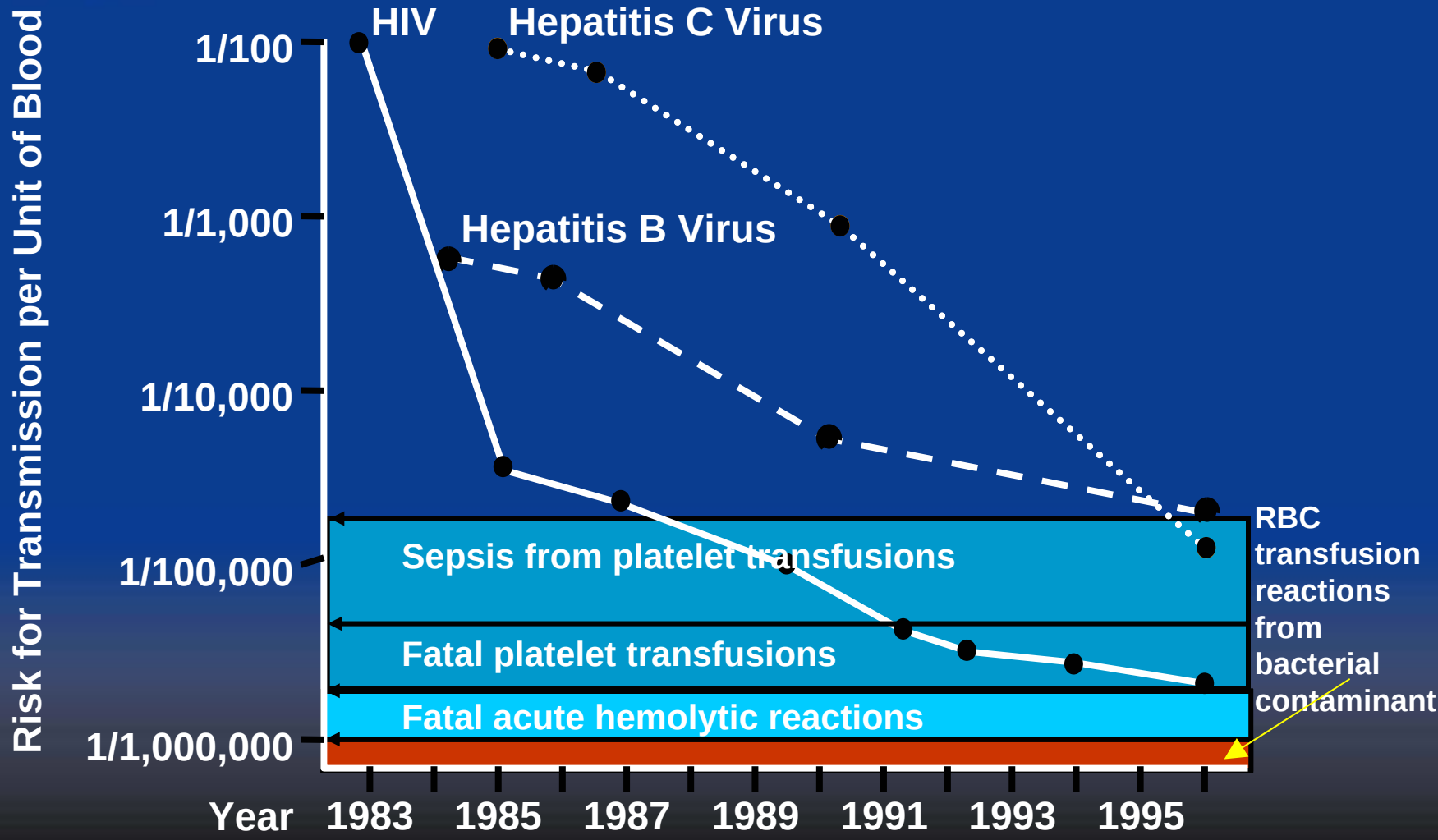
Arjun Srinivasan, MD
Division of Healthcare Quality Promotion
National Center for Infectious Diseases
Centers for Disease Control and Prevention

SAFER • HEALTHIER • PEOPLE™

Outline

- Need for bacterial screening
- Public health considerations:
  - Organism identification
  - Shared data collection and analysis
  - Use of results
  - Impact of screening on platelet supply
- Potential next steps

Comparison of Per-unit Risk for Transmission of Bacterial and Viral Pathogens



Adapted from AuBuchon, et al. Ann Intern Med 1997

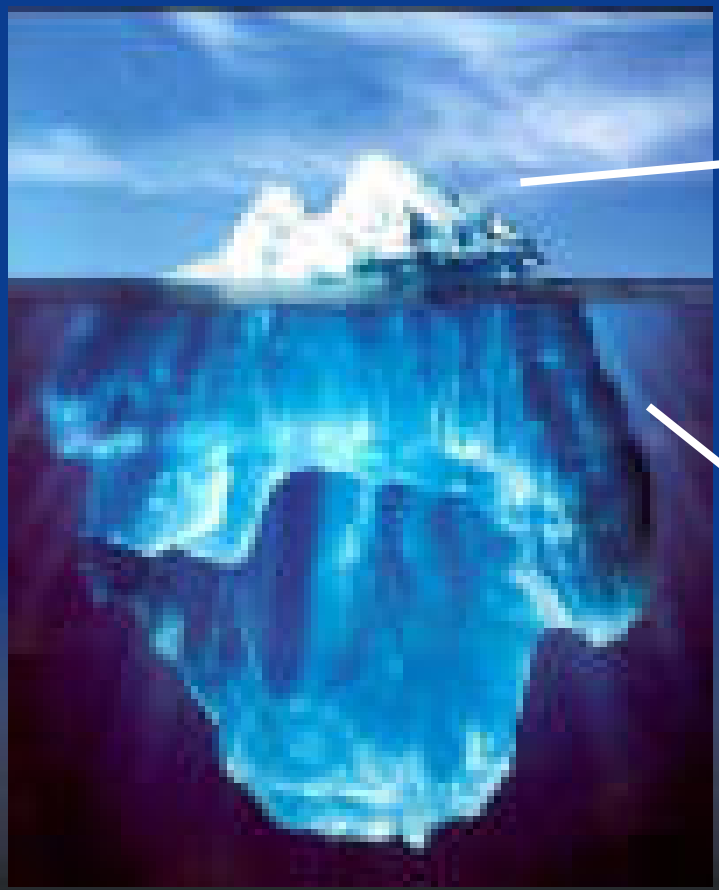
Bacterial contamination of blood (BaCon) study

- Though bacterial contamination is thought to be a serious problem, there had never been a rigorous, prospective, multi-center evaluation of associated adverse events.

Goal of the BaCon study

- To prospectively evaluate the incidence of **septic transfusion reactions** caused by contaminated blood products.

Defining the scope



Fatal reactions

Septic reactions

Febrile and other reactions

Contaminated products

BaCon design

- Collaborative effort involving:
  - American Association of Blood Banks
  - American Red Cross
  - Department of Defense
  - CDC
  - Many hospitals and transfusion centers

Reporting Criteria:
Any of the following that occur within 4 hours of transfusion

- **Fever**
  - **Temperature ≥39° C or ≥ 102° F**
  - **Temperature ≥ 2° C or ≥ 3.5° F rise***
- **Rigors** (shaking chills)
- **Tachycardia**
  - **Heart rate ≥120/min or ≥ 40/min rise***
- **Systolic blood pressure**
  - **Rise ≥ 30 mm Hg***
  - **Drop ≥ 30 mm Hg***

***change from pre-transfusion values**

Case Definition

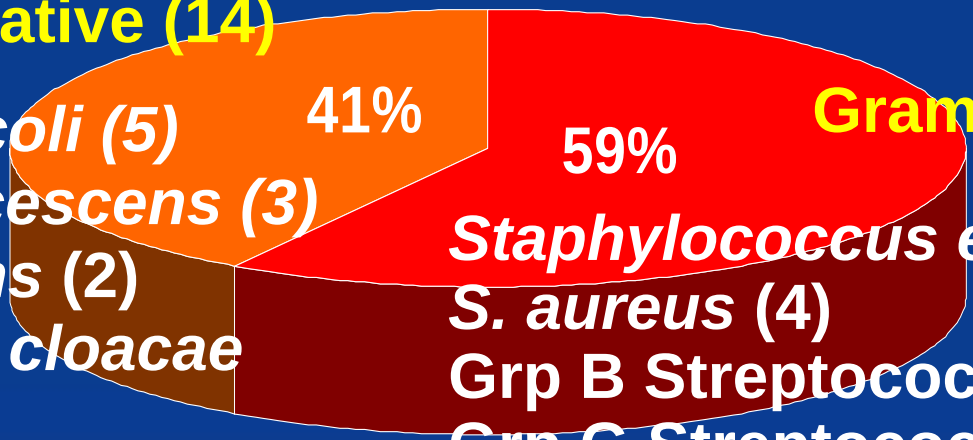
- Confirmed Case
  - One or more clinical criteria for transfusion reaction
  - Culture-positive blood product
  - Recipient blood culture grows the same organism recovered from blood product
  - Organism pair identical by Pulsed-Field Gel Electrophoresis (PFGE)

Results

- 34 septic reactions
- Products
  - 19 Single donor platelets
  - 10 Pooled platelets
  - 5 RBCs
- Recipients
  - 76% with underlying malignancy
  - 9 (27%) had fatal outcome

Kuehnert MJ, Roth VR, Haley NR et al.
Transfusion 2001;41:1493-99

Bacteria Implicated



Gram-negative (14)

***Escherichia coli* (5)**
***Serratia marcescens* (3)**
***S. liquefaciens* (2)**
Enterobacter cloacae
E. aerogenes
Providencia rettgeri
Yersinia enterocolitica

Gram-positive (20)

***Staphylococcus epidermidis* (8)**
***S. aureus* (4)**
Grp B Streptococcus (2)
Grp G Streptococcus
S. lugdunensis
Bacillus cereus
Enterococcus faecalis
Streptococcus pneumoniae

Kuehnert MJ, Roth VR, Haley NR et al.

Transfusion 2001;41:1493-99

Gram negative organisms

- Mortality significantly higher in cases with gram negative organisms:
  - 83% (gram negative) vs. 17% (gram positive) ($p < 0.001$).
- High levels of endotoxin in many units contaminated with gram negative organisms.

Estimated U.S. Rates of sepsis and death related to contaminated blood products 1998-2000

Event	RBC	SDP	PP
Units distributed	23,711,169	1,804,725	1,033,671*
Cases (fatal)	5 (3)	18 (4)	11 (2)
Case Rate (per million)	.21	9.98	10.64
Fatality Case Rate	.13	2.22	1.94

*Average pool assumed to be 6 single-unit concentrates

RBC=Red Blood Cell Unit

SDP=Single-Donor Platelet Unit, PP=Pooled Platelet Unit

Kuehnert MJ, Roth VR, Haley NR et al.
Transfusion 2001;41:1493-99

Limitations of BaCon

- BaCon did:
  - prospectively describe reaction rates and etiologic pathogens for documented septic reactions.
- Bacon did not:
  - Provide information on other, non-septic reactions due to contaminated products
  - Estimate the incidence of bacterial contamination of products

BaCon implications for screening

- Important issues related to gram negative organisms:
  - Less likely to be skin contaminants, more likely related to donor bacteremia- better skin antisepsis will not address
  - Produce endotoxin- complicates therapy

Bacterial screening of platelets

- The question now is not whether, but how!
- Data indicate that screening will save lives, however, implementation of the screening standard raises some important public health issues.

Public health considerations of platelet screening

- Identification of contaminating organisms
- Shared data collection
- Using results for quality assurance and improvement
- Issues with platelet supply

Organism identification

- Identification requires significant investments in resources and time:
  - Microbiology equipment
  - Staff training
  - Certification

Why might identification be useful?

- Organism identification may help improve the health of:
  - Recipients
  - Donors
  - The community

Organism identification: Recipient health

- If the unit has been transfused, knowing the organism can help the treating clinician choose the most appropriate therapy.

Organism identification: Donor health

- The blood banking community has already set the standard for donor notification.
- Findings on blood screening that have important implications for donors, like presence of HIV or hepatitis, are conveyed to the donors so action can be taken.

Organism identification: Donor health

- In most cases, donors with bacterial bloodstream infections will be excluded because they will have symptoms.
- However, there are cases when asymptomatic bacteremia may have important consequences for the donor.

Case: Donor health

- Patient received platelets and subsequently developed a blood stream infection with *Streptococcus agalactiae* (group B streptococcus)-unit found to be contaminated.
- Bacteremia with this organism has been associated with colon cancer.

Stevens, WT et al.

Case: Donor health

- The donor was notified and encouraged to undergo screening for colon cancer.
- A sigmoidoscopy revealed a tumor that was removed.

Organism identification: Community health

- Findings of unexpected clusters of organisms may lead to important discoveries.

Case I: Community health

- An unusual cluster of 2 cases of *Serratia marcescens* bloodstream infections related to transfusions prompted an investigation.
- A national survey found 11/1515 units (0.73%) of blood products were contaminated with *S. marcescens*.

Heltberg et al. Transfusion 1993;33:189

Case I: Community health

- Investigators determined that all of the contaminated units had been collected in bags from a single batch made by one company.
- Cultures taken at the manufacturing plant grew *S. marcescens* that was identical to the patient samples.

Heltberg et al. Transfusion 1993;33:189

Case II: Community health

- Healthy donor who gave regularly- nearly once a month over the last few years.
- Platelets obtained during one apheresis session were transfused into 2 patients.

Jafari et al. NEJM 2002;347:1075

Case II: Community health

- Patient 1 developed septic shock during the transfusion requiring initiation of life support
- Patient 2 developed septic shock 1 hour after the transfusion and later died.
- Blood cultures from both patients grew *Salmonella enterica*

Jafari et al. NEJM 2002;347:1075

Case II: Community health

- Because the organism was so unusual, an investigation was initiated.
- Blood cultures of the donor grew *S. enterica*, though he was asymptomatic.
- It was found that the donor had a pet snake which was colonized with *S. enterica.*

Jafari et al. NEJM 2002;347:1075

Case II: Community health

- Given how often this person donated, the investigation likely prevented transmission to other patients (in addition to helping the donor!).

Organism identification: Community health

- These types of outbreaks are probably extremely rare, but the cases illustrates how serious the consequences can be.
- Bacterial screening provides a powerful method to find and stop such events, but doing so will require identifying the organism.

Shared data collection and analysis

- Bacterial screening will generate a significant amount of data- especially if organisms are identified.
- Keeping track of the information will again require investment of resources.

Why might data collection and sharing be useful?

- Knowing how often units are contaminated and what they are contaminated with can help with:
  - Quality assurance
  - Surveillance for unusual outbreaks

Using microbiology for quality assurance

- Data collection will help establish a baseline or expected rate of contamination.
- Changes in contamination rates can prompt investigation into collection and processing practices.

Using microbiology for quality assurance

- Knowing the identity of the organism can help focus investigations:
  - Increases in skin flora might prompt a review of collection practices.
  - Increases in some gram negatives might prompt investigation into processing and storage issues.

Using microbiology for outbreak surveillance

- Bacterial screening creates an opportunity to link results from separate areas which may help uncover outbreaks.

Issues with supply

- Concerns have been raised about the utility of some of the non-culture methods for screening.
- We err on the side of caution, but too many false positive results may have serious implications for platelet supply.

Unanswered questions

- Though an important step forward, bacterial screening raises some important issues:
  - How should we compile and track results?
  - How can results best be used for QA?
  - How sensitive and specific are the non-culture methods and what impact might false positive results have on supply?

Collaboration is key: West Nile Virus and Blood Safety

- By June 1, 2003 testing in place (with FDA approval via IND).
- Weekly meetings with AABB WNV task force to coordinate data monitoring

West Nile Virus and Blood Safety: A public health success in 2003

- Of approximately 4.5 million donations screened, nearly 1,000 units of presumed WNV-infected blood detected and removed.
- Multiple units from each infected donation likely would otherwise have been transfused

Collaboration is key

- The WNV Task Force and the BaCon study were great examples of how public health and the blood banking community can work together to address important issues.
- Bacterial screening provides another opportunity to collaborate for public health benefit.

Potential collaborative efforts

- Establishing procedures to collect information in a standard format.
- Projects to demonstrate the use and value of screening as part of QA.
- Projects to prospectively evaluate the performance of screening methods.

Conclusion

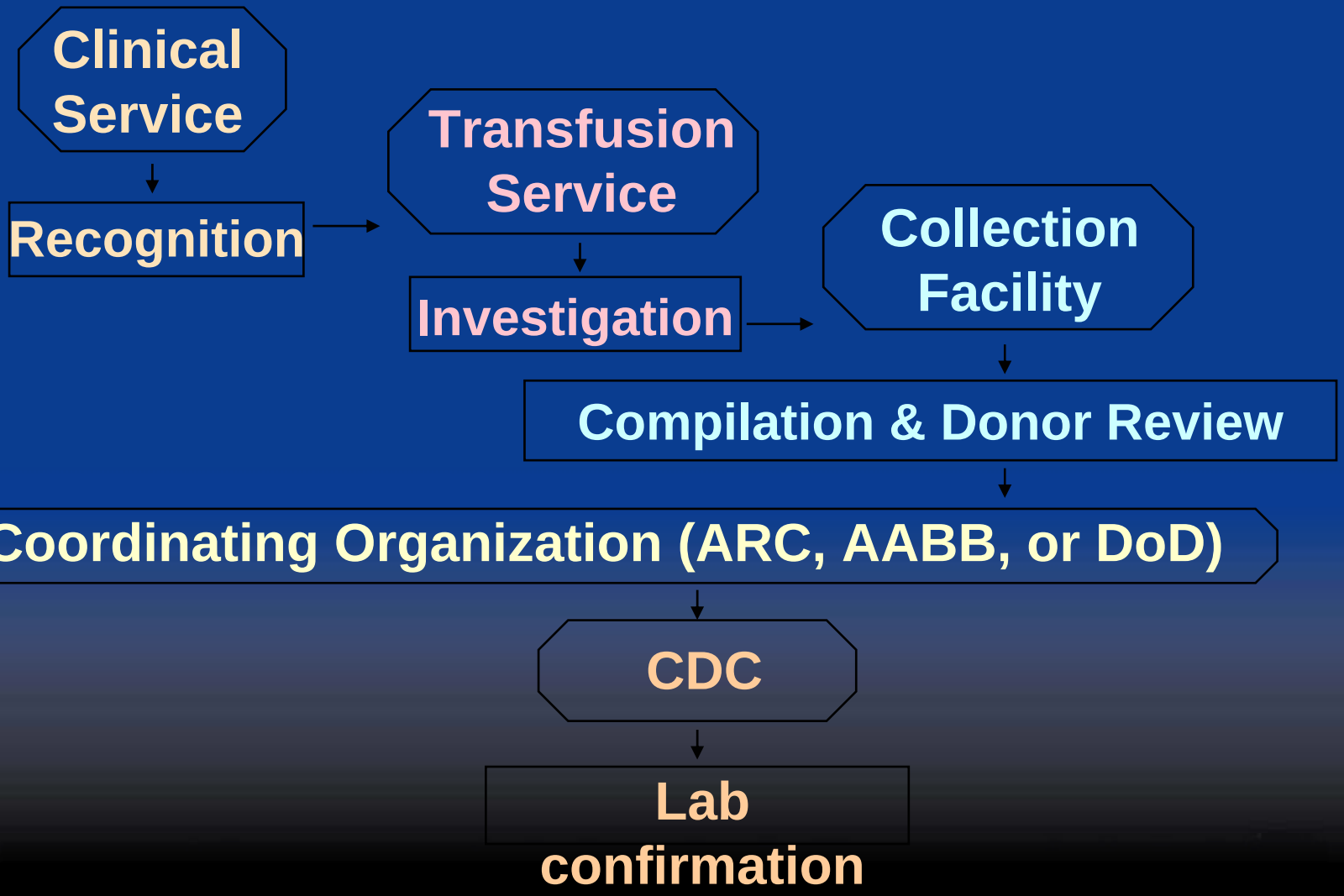
- Bacterial screening of platelets is an important step forward.
- Like any new measure, it does raise some important questions.
- As we have in the past, the blood banking and public health communities can and should work together to answer those questions.

Organism identification and community health

- There are some organisms that may prompt investigations, with useful results.

BaCon reporting

In addition to established Standard Operating Procedures



Results:
January 1998 - December 2000

56 evaluable episodes

↓

44 (79%) met clinical criteria

↓

34 (61%) confirmed by molecular typing

Tip of the iceberg- example of an excluded case

- Patient with leukemia got platelets and developed fever 22 hours after transfusion. Blood cultures and cultures of the transfused unit grew *S. aureus* but the case was not included because the reaction occurred more than 4 hours after transfusion.