

Clinical Laboratory Perspective

CDC Townhall: Medical Device Design- Incorporating Safety and Biosafety

Sheldon Campbell M.D., Ph.D.

Professor of Laboratory Medicine, Yale School of Medicine
Associate Chief for Laboratory Medicine, VA Connecticut Health Care



Emerging infections in Context

- Plagues have been a part of human existence during recorded history; and have had a deep impact on societies.
- *Four Horsemen of the Apocalypse*, by Viktor Vasnetsov. Painted in 1887. From left to right, they are Death/Plague on the pale horse, Famine on the black, War on the red, and a rider whose identity is unclear in the Revelation text on the white.

Learning Objectives

- Recognize the potential routes of spread of emerging (or endemic, for that matter) pathogens within the laboratory.
- Recognize the modes of laboratory activities where biosafety concerns arise related to instrumentation.
- Analyze different levels of instrument biosafety and how they may impact laboratory operations and care.

Laboratory- Acquired Infections Are Still Infections (duh!)

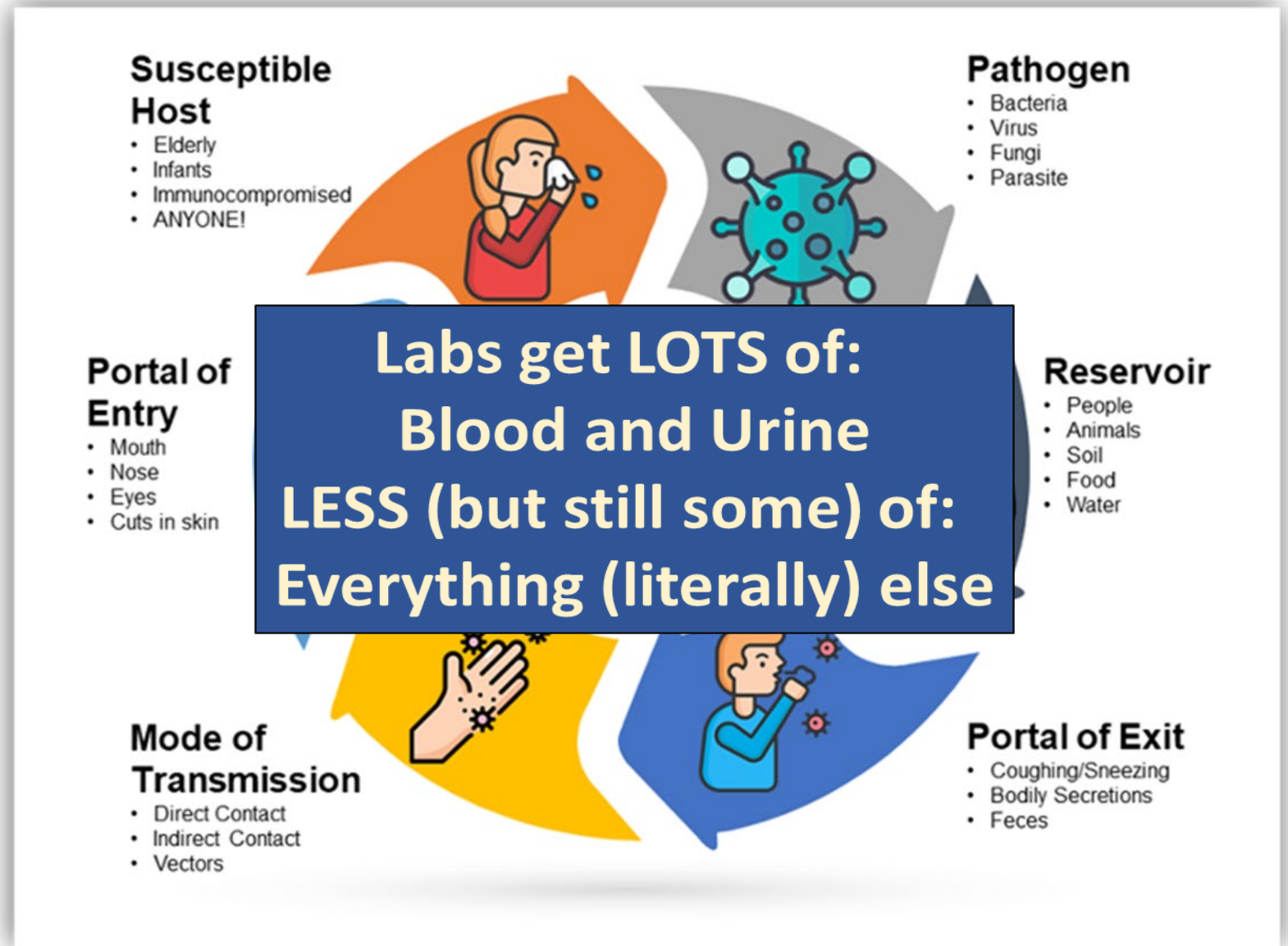


Image from: <https://apps.hhs.texas.gov/providers/NF/credentialing/cna/infection-control/module2/Module 2 Chain of Infection print.html>

Instrumentation and Processes

Pre-analytic

Sample collection

Transport

Reception and Unpacking

Centrifugation

Uncapping

Aliquoting

Transport within the Lab

Transport to Reference Labs

Analytic

Chemistries

Blood Gases

Hematology

Bacteriology

Virology

Molecular Testing

Transfusion Medicine

Post-Analytic

Waste Management

Sample Storage - Retrieval

Risks In the Analytic Phase 1

Chemistry

- Complex analyzers with multiple sampling stations, aliquoting events, and waste pathways.
- Many cannot perform closed-tube sampling
- Require frequent periodic maintenance, service.
- Extremely expensive; critical for care of large numbers of patients.
- Large-scale automation has multiple interaction points both with sample and users.

Blood Gases

- Sample submitted in syringe
- Extremely labile sample requires rapid handling

Hematology

- Complex analyzers as above
- Manual or automated slide-making; glass slides.

Risks In the Analytic Phase 2

Bacteriology

- Survival of emerging viruses in culture media generally unknown, but likely (old studies show HIV does)
- Much manual handling of samples and cultures
- Complex analyzers as above

Virology

- Growth of emerging pathogens in viral culture (waning in importance as labs abandon viral culture)

Molecular diagnostics

- Complex analyzers as above.
- Many manual or semi-manual methods in some laboratories.
- How to validate EUA tests for dangerous, rare pathogens?

Transfusion Medicine

Risks In the Analytic Phase 3

- Tube-based methods likely generate droplets
- No sealed-rotor blood bank centrifuge is currently available, per my local colleague.
- Risks associated with gel or instrumented methods unknown.

Risks Associated With Laboratory Automation

Clinical Chemistry 62:7
973-981 (2016)

Infectious Disease

Bloodborne Viral Pathogen Contamination in the Era of Laboratory Automation

Andrew Bryan,^{1*} Linda Cook,¹ Ederlyn E. Atienza,¹ Jane Kuypers,¹ Anne Cent,¹ Geoffrey S. Baird,¹
Robert W. Coombs,^{1,2} Keith R. Jerome,^{1,3} Mark H. Wener,^{1,2} and Susan M. Butler-Wu⁴

- Study of contamination in a large, automated clinical chemistry laboratory.
- Swabbed parts of the TLA system at baseline, and after running high-titer HCV samples.
- Placed glass slides in places where droplets might go.

Positive swab for HBV, "B," or HCV, "C"

Negative swab for both HBV and HCV

Contamination after running high-positive HCV samples

Positive clean glass slide placed during experiment (far right image)

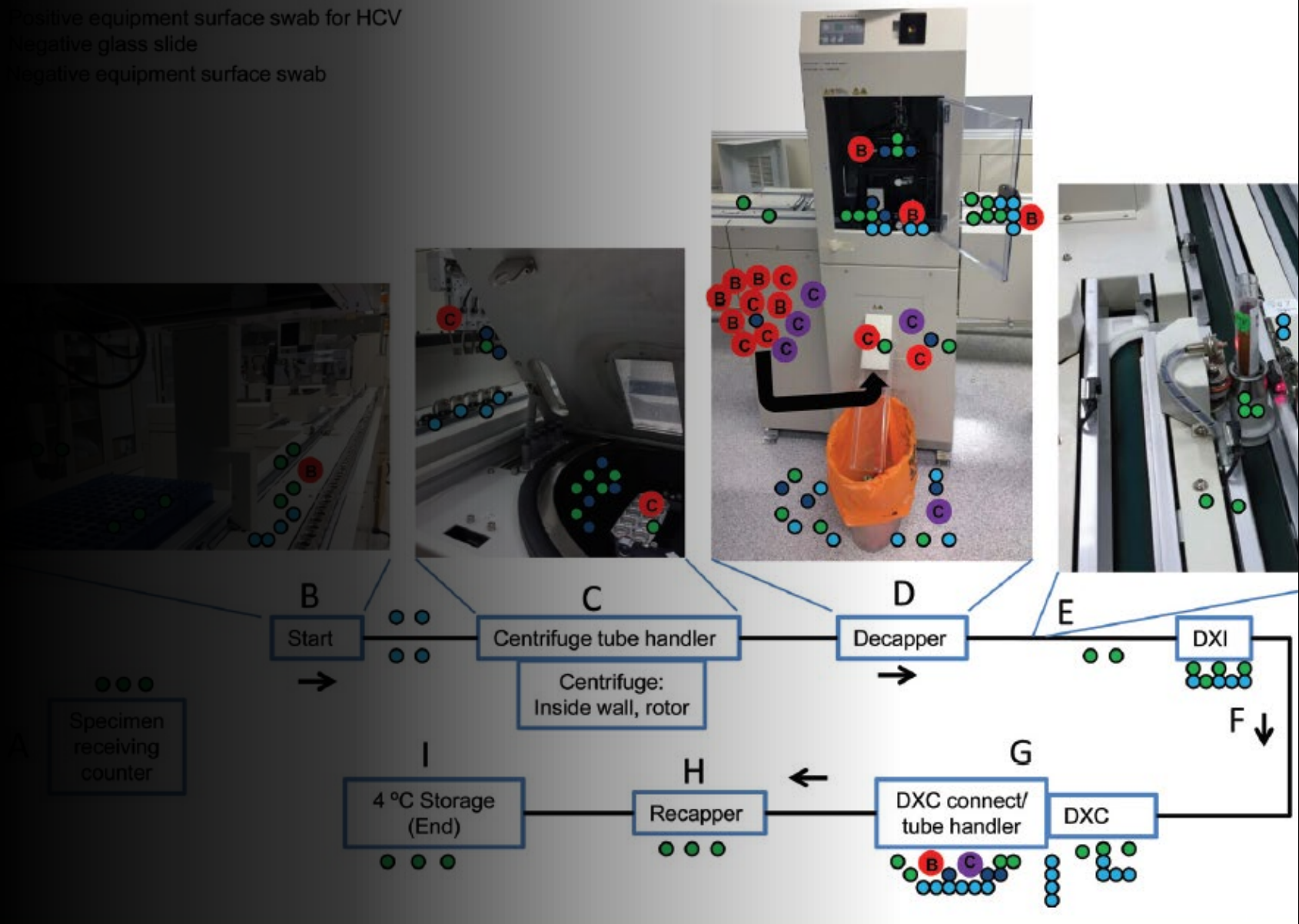
Positive equipment surface swab for HCV

Negative glass slide

Negative equipment surface swab

Virus in the Lab?

- HBV and HCV nucleic acid found both at baseline (during routine usage), and in additional sites after processing of high-titer HCV
- Unknown whether this represents infectious virus; but different pathogens will have different environmental stability and infectiousness



Hazard Modes

- During Use
 - Samples from patients with known high-consequence pathogen.
 - Samples from Patients Under Investigation.
 - Samples from patients not under investigation (who still might have X)
- After Use
 - Decontamination...
 - Before more use
 - Before servicing
 - End of life



Partnership Pathway Toward More Biosafety

Current: Risks are unknown

- Lack of study of clinical laboratory safety.
- Lack of documentation of risks related to instrumentation.

Improvement: Risks Described

- What elements of instruments are associated with what risk(s)?
- What degree of risk/contamination occurs?

More Improvement: Risks Mitigated

- Identified risks addressed with clever engineering.
- Other identified risks mitigated by laboratory practices

Unattainable: Risks Eliminated