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THE BIOMEDICAL SKILLS LABORATORY | MANAGEMENT SYMPOSIUM



Tissue Donor Screening and Laboratory Testing

A Basic Review

ViroMed Laboratories

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 **LabCorp**
Laboratory Corporation of America

Introduction

- Laboratory role in donor testing
- Tissue donor screening
 - Relevant communicable diseases
 - Screening process
- Laboratory testing
 - Laboratory and test requirements
 - Testing for relevant diseases
 - Serology testing
 - Molecular testing
 - Test Performance Characteristics

Laboratory Testing Regulations

- Testing for organ, eye, and tissue donors is regulated by different entities within the government.
- Food and Drug Administration (FDA) regulates testing for tissue donors (including bone, skin, ligament, dura mater, heart valve, and cornea).
- United States Department of Health and Human Services (DHS) regulates organ donor testing (including kidney, pancreas, liver, heart, lung and intestine).

Tissue Donor Screening

- Code of Federal Regulations 21 CFR 1271
- Relevant communicable diseases
 - HIV types 1 and 2
 - Hepatitis B
 - Hepatitis C
 - Human transmissible spongiform encephalopathy (TSE), including CJD
 - Treponema pallidum (syphilis)
 - Other: West Nile Virus, Sepsis, Vaccinia

Tissue Donor Screening

- Screening to include:
 - Medical and social behavior history interview (29 questions: past diagnosis of viral hepatitis, MSM, injected drugs, prison...)
 - Physical assessment for clinical evidence
 - Other available records (e.g., medical records, laboratory test results, autopsy report, police report)

Tissue Donor Testing

- Laboratory testing requirements
- Must be FDA registered for testing human cells, tissues, and cellular and tissue-based products (HCT/Ps).
 - <http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/EstablishmentRegistration/TissueEstablishmentRegistration/FindaTissueEstablishment/ucm110270.htm>
- Must use FDA-licensed donor screening kits
 - <http://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/TissueSafety/ucm095440.htm>
- Must follow package inserts

Relevant Diseases

Infectious Agent	Serology	NAT
HIV (Type 1/O/2)	X	X
HBV (HBsAg, HBcore Total)	X	
HCV	X	X
Treponema pallidum (syphilis)	X	

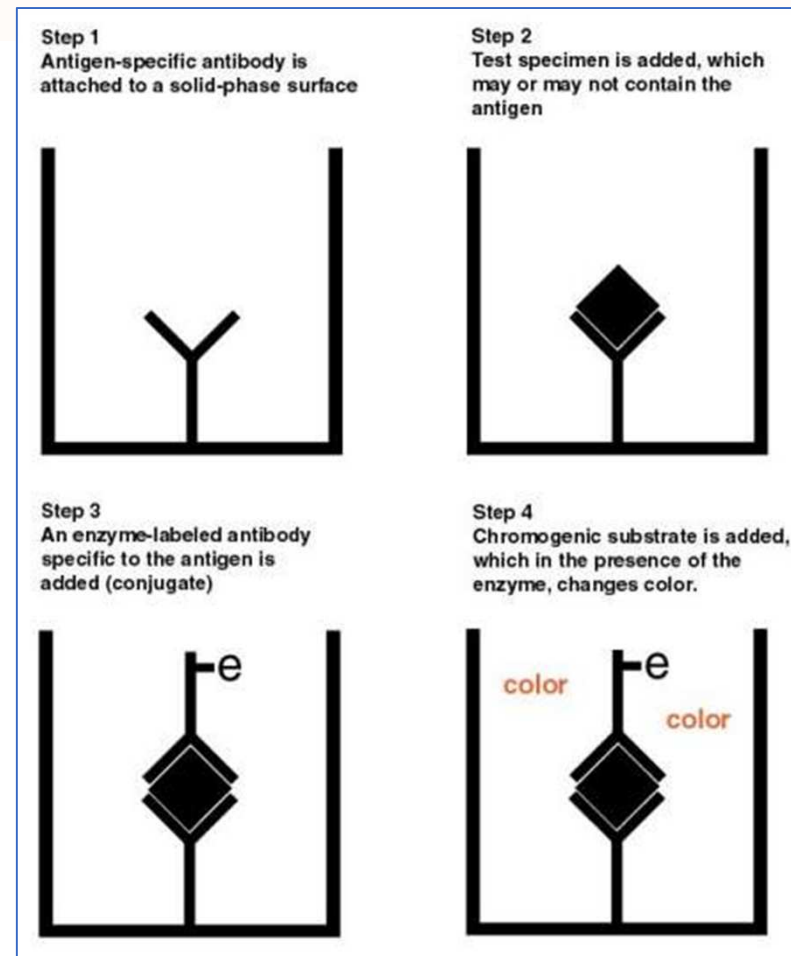
Additional testing needed for leukocyte-rich and reproductive tissue.

Serology Testing

- Serology is a blood test to detect the presence of antibodies against a microorganism.
- Detection of antibodies can be used to either diagnose an active or previous infection, or used to determine immunity.
- IgG and IgM antibodies \neq 'Total antibody'.

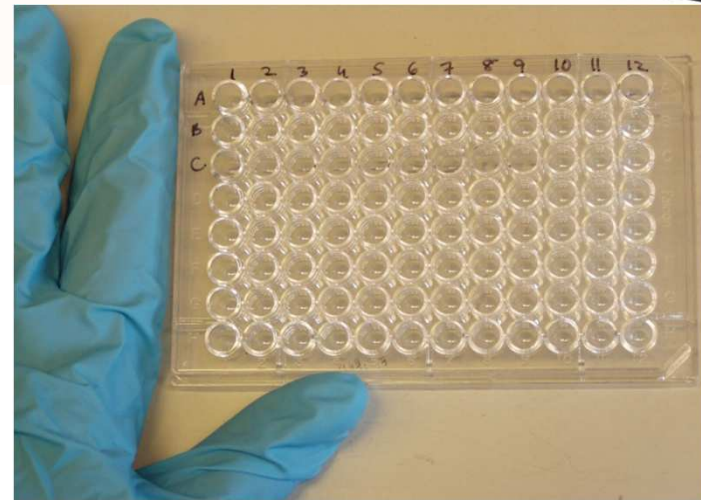
Serology Method

- Immunoassays test for specific antigen (HBsAg) or antigen-specific antibodies (HCV, HIV).
- Enzyme linked immunosorbent assays (ELISA), also known as enzyme immunoassays (EIA).
- Tests designed to detect antigens or antibodies by producing an enzyme triggered color change.



Serology Assays

- Solid-phase assays require the immobilization of antigens or antibodies on solid surfaces such as plastic beads or the wells of microtiter plates.
- Results usually reported as 'Positive' or 'Negative'.



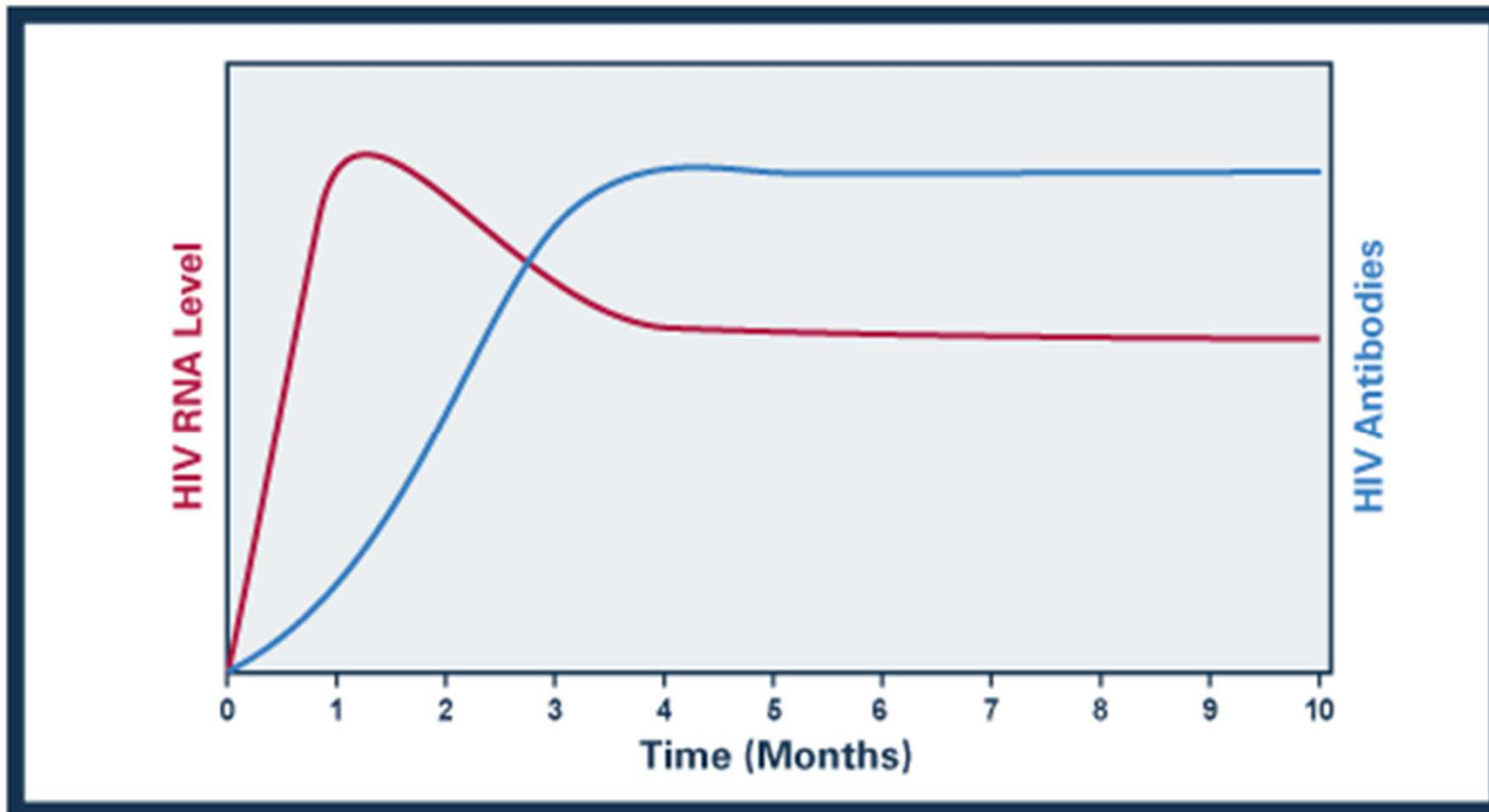
Confirmatory Testing

Infectious Agent	Confirmatory/ Additional Test
HIV (Type 1/O/2)	HIV-1 Western Blot
HBV - HBsAg - HBcore Total	HBsAg Neutralization HBcore IgM
HCV	RIBA
Treponema pallidum (syphilis)	Clinical RPR

Molecular Testing

- Molecular testing is based on the detection of the viral genome
- NAT (Nucleic Acid Testing) or NAA (Nucleic Acid Amplification)
- NAT shortens the window period
- HIV-1/HCV NAT

Serology vs. Molecular



HIV Web Study (www.HIVwebstudy.org)

Supported by HRSA

Test Performance Characteristics

- Clinical Characteristics
 - Analyte presence
 - Analyte concentration
- Test Characteristics
 - Sensitivity
 - Specificity
- Population Characteristics
 - Disease prevalence
 - Positive Predictive Value
 - Negative Predictive Value

Clinical Characteristics

- Analyte presence and concentration determines the detection, precision and accuracy of the test.
 - Low concentrations need tests with higher sensitivity

Test Characteristics

Sensitivity

- Analytical - Ability of test to detect very small amounts of a substance
- Clinical - Ability of test to give a positive result if the patient has the disease (no false negatives)
- 95% sensitive = 5% false negative

Test Characteristics

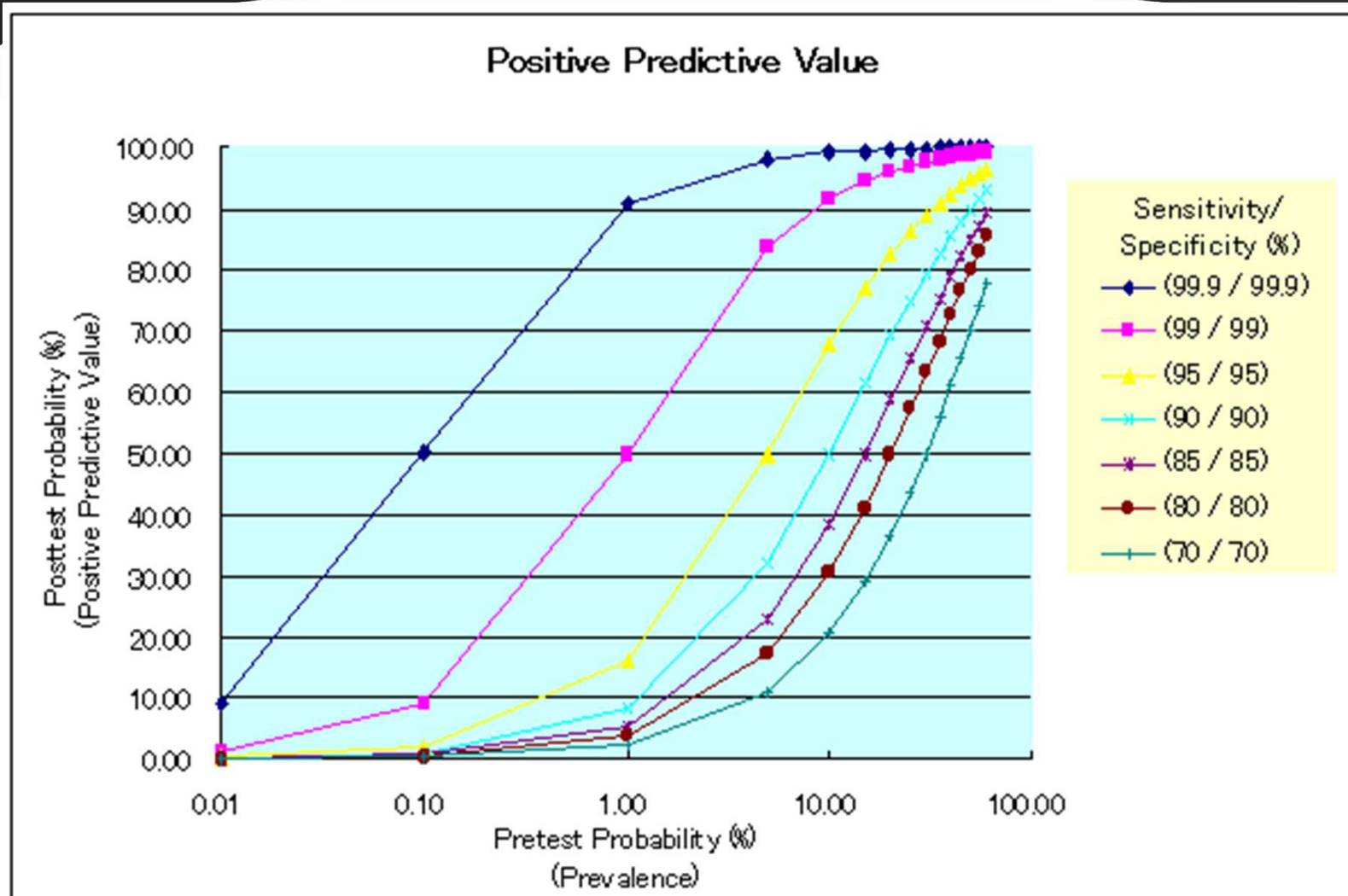
Specificity

- Analytical - Ability of test to detect a substance without interference from cross-reacting substances
- Clinical - Ability of test to give a negative result if the person does not have the disease (no false positives)
- 95% specific = 5% false positives

Population Characteristics

- Disease prevalence: measure of disease that allows us to determine a person's likelihood of having a disease
 - Positive Predictive Value (PPV) – chance that a positive result is correct
 - Negative Predictive Value (NPV) – chance that a negative result is correct

Disease Prevalence and Test Accuracy



Source: www.kdcnet.ac.jp

Summary

- Assay characteristics affect test performance
- Disease course affects test performance
 - Time to detection: serology vs. molecular
- Population differences (prevalence) affects test performance

Questions

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