Live Donor Infectious Diseases Testing Workgroup

Michael G. Ison, MD MS
Divisions of Infectious Diseases & Organ Transplantation
Transplant Infectious Diseases Service
Northwestern University
Comprehensive Transplant Center

Optimal Testing of Live Donors to Prevent Transmission of Infectious Diseases Consensus Conference

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Testing WG Objectives

- To determine which tests are appropriate for live donors and
- To determine the appropriate time frame for testing to avoid transmission of blood-borne pathogens
  - Focused on HIV, HCV, and HBV

Testing WG Membership

Name	Employer	Expertise
Michael Ison, MD MS (Chair)	Northwestern	Transplant ID
Shandie Covington	UNOS*	DTAC
Melissa Greenwald, MD	FDA*	Donor Testing
Atul Humar, MD	U Alberta	Transplant ID
Bernie Kozlovsky, MD	HRSA*	Div. of Transplantation
Matt Kuehnert, MD	CDC*	Office of Blood, Organ, and Other Tissue Safety
Diane Lapointe-Rudow, DNP	Mt. Sinai (NY)	Transplant Admin
Brigitte Sullivan	Johns Hopkins	Transplant Admin

*Employed by the US Government; non-voting members of WG.

Key Questions WG Considered

- What are the available assays for assessing current and prior donor infections?
- What are the test characteristics of available assays (i.e. sensitivity, specificity, turn-around-time)?
- What is the availability of assays in living donor ID assessment?
- Are there substantive differences between assays that have specific screening approval vs. those that do not?
- What is the residual window period by each assay method?
- What specific testing should be done of living donors to screen for organ transplantation?
- What time frame should this testing be done?
- Should the approach to donor screening be different if the donor has identified risk factors for HIV, HBV, and HCV?
- What assays are currently being used by TCs for screening?
- Is NAT being utilized by TCs performing living donation?
- What are current challenges recognized by TCs in live donor screening?

Approach

- Review transmission events that have been identified
  - Understand errors that were made to attempt to avoid in the future
- Review available guidelines for living donor screening
  - CDC and NY Department of Health Recommendations
  - OPTN Deceased Donor Policy & LD Evaluation Guidance Document
  - Global guidance documents on LD screening: Australia, UK, US
- Review current guidelines by US PHS for screening healthy patients for HIV, HBV, and HCV
  - Review epidemiology as well
- Survey the US transplant centers conducting living donation
  - Assess the current status of donor screening (assays, timing)
  - Assess challenges to live donor screening policy
- Review available assays that could be used to screen donors
  - Serologic and NAT
  - Understand limitations and challenges with each assay
- Understand the window period for each assay and its potential impact on live donor screening

Key Findings

- Existing Guidelines/Policies
  - Suggest that HIV, HBV, and HCV should be screened for
    - Do not recommend specific assays
    - Do not outline timeline for conduct relative to transplant
  - Current US PHS Guidelines for Screening
    - HIV: All patients should be screened for HIV
    - HBV: Screening is recommended as follows:
      - Previously or currently pregnant women
      - Infants born to HBsAg-positive mothers
      - Household contacts and sex partners of HBV-infected pt
      - Persons born in countries with HBsAg prevalence of ≥2%
      - Persons who may come in contact with blood or needles
      - Persons infected with human immunodeficiency virus
      - Men who have sex with men
      - Injection-drug users
      - All blood, plasma, tissue, deceased organ and semen donors

Key Findings

- Existing Guidelines/Policies
  - Current US PHS Guidelines for Screening
    - HCV: Screening is recommended as follows:
      - Prior illicit injected drugs use
      - Persons with the following risk factors:
        - » Persons with HIV infection
        - » Persons with hemophilia who received clotting factor concentrates prior to 1987
        - » Persons who have ever been on hemodialysis
        - » Persons with unexplained abnormal LFT levels
      - Prior recipients of transfusions or organ tx prior to July 1992
      - Children born to HCV-infected mothers
      - Health care, emergency medical and public safety workers after a needle stick injury or mucosal exposure to HCV-positive blood
      - Current sexual partners of HCV-infected persons
      - All blood, plasma, tissue, deceased organ and semen donors

Survey of US Tx Administrators

- Obtained the e-mail of all TAs from US TCs that conduct live donor procurement from OPTN/UNOS
- Used Survey Monkey to query all TAs about:
  - Awareness of change CDC recommendations for LD screening after the recent HIV transmission event
  - Assess if local practice has changed based on these recommendations
  - Current LD screening practices
    - Specific assay used for HIV, HBV, and HCV serology & NAT
    - Assess if NAT is utilized for LD screening
      - If so, what viruses are tested, in what patients, and when are assays run relative to transplant
    - Assessed ability to comply with a 14 or 7 day test window requirement
  - Open ended option for other comments

Survey Results: *Demographics*

- 504 e-mail addresses obtained from UNOS
  - Represents 237 LD Kidney and 73 LD Liver Centers
  - 9 e-mails failed, 3 opted out of the survey and 359 didn't respond
- 155 (31.3%) responded to the survey
  - Most (85 – 54.8%) completed the entire survey
  - Many (70) did not proceeded beyond questions about assay type
- Knowledge of recent CDC screening recommendations
  - 129/150 (86%) were aware of the CDC recommendations
  - 78 (52%) have changed their LD screening practices as a result
- Assays used for LD screening
  - Approximately 35% of overall respondents completed the answers for specific assay type
    - Suggests that education may be needed
  - Most respondents are testing for HIV, HBV, and HCV
    - All are doing serology for HIV, HBV, and HCV
    - 46.8 – 38.2% use FDA-approved screening serologic assays

Survey Results: *Donor Screening*

- Assays used for LD screening
  - Overall, 43 (55.8%) of respondents said their TC used NAT for LD screening
    - Of those that do use NAT92.3% do HIV NAT, 87.2% do HCV NAT, and 61.5% do HBV NAT
    - NAT is done on:
      - All donors at 78.6% of LD Centers that responded
      - Increased Risk Donors Only in 16.7% of LD Centers that responded
  - NAT for HIV
    - 33 (21.3%) are using HIV NAT to screen LDs
    - 42 % are quantitative vial load measurements*
  - NAT for HBV
    - Assays are generally quantitative vial load measurements*
  - NAT for HCV
    - 32 (53.3%) are using are using HCV NAT to screen LDs
    - 60% are quantitative vial load measurements*

*Although many are FDA-approved assays, they are not approved for donor screening.

Survey Results: *Timing of Screening*

- At what point is donor screening for risk factors done
  - Initial Evaluation Only: 32.8%
  - Initial Evaluation & within 2 weeks of surgery: 23.9%
  - Initial Evaluation & within 1 week of surgery: 35.8%
  - Initial evaluation & close to surgery for HR only: 7.5%
- At what point is donor serology done
  - Initial Evaluation Only: 38.2%
  - Initial Evaluation & within 2 weeks of surgery: 27.9%
  - Initial Evaluation & within 1 week of surgery: 22.1%
  - Initial evaluation & close to surgery for HR only: 11.7%
- 73.9% of respondents screen donors with identified risk factors the same as those without

Survey Results: *Screening Challenges*

Question	Yes	No
Capacity to perform FDA-approved screening serology & NAT within 7 days of transplant	41 (60.3%)	27 (39.7%)
Capacity to perform non-FDA-approved screening serology & NAT within 7 days of transplant	22 (36.7%)	38 (63.3%)
Capacity to perform FDA-approved screening serology & NAT within 14 days of transplant	43 (66.2%)	22 (33.8%)
Capacity to perform non-FDA-approved screening serology & NAT within 14 days of transplant	26 (43.3%)	34 (56.7%)

Open Ended Response to Challenges (43 comments):

- •Turn-around time
- •Cost
- • Availability of test (esp NAT)
- • False positive results
- •Assays require send out and frequently associated with errors
- •Inconvenient for donors if they live far away
- •No patient education materials for why tests are being done

Available Serologic Assays

- HIV-1/2 Serology
  - Detect the presence of anti-HIV-1/-2 antibodies
  - Window period: 17 – 90 days
    - Genetic System HIV-1/HIV-2 Plus O EIA
    - Abbott PRISM HIV O Plus
    - HIVAB HIV-1/HIV-2 (rDNA) EIA
    - ARCHITECT HIV Ag/Ab Combo
      - Not approved for blood donor screening
- HCV Serology
  - Detect the presence of anti-HCV antibodies
  - Window period: 40 – 70 days
    - Abbott HCV EIA 2.0
    - ORTHO® HCV Version 3.0 ELISA
    - VITROS® Anti-HCV assay
    - Confirmation with a RIBA is recommended

Available Serologic Assays

- Hepatitis B Serology
  - Window period: 35-44 days for HBsAg
  - Hepatitis B Surface Antigen (HBsAg)
    - Genetic Systems HBsAg EIA 3.0
    - Auszyme Monoclolnal*
    - Abbott PRISM HBsAg Assay
    - Ortho Antibody to HBsAg ELISA Test System 3
  - Hepatitis B Surface Antibody (HBsAb)
    - All assays are diagnostic (none approved for donor screening)
  - Hepatitis B Core Antibody (HBcAb)
    - Corzyme Monoclolnal*
    - Abbott PRISM HBcore Assay
    - Ortho Antibody to HBcAb ELISA Test System

*No longer commercially available.

Available HIV NAT Assays

- Detects the presence of HIV-1 RNA only (not HIV-2)
- Window Period: 7 – 10 days
- Approved for donor screening
  - COBAS AmpliScreen HIV-1 Test (v 1.5) – LOD: 10 – 100 c/mL
  - COBAS TaqScreen MPX Test – LOD: 10 c/mL
  - Procleix HIV-1/HCV – LOD: 100 c/mL
  - Procleix Ultrio – LOD: 100 c/mL
- Approved for viral load assessment
  - AMPLICOR HIV Monitor Test – LOD: 400 or 50 c/mL
  - Versant HIV-1 RNA 3.0 assay – LOD: 75 c/mL
  - NucliSens HIV RNA QT – LOD: 176 c/mL
  - COBAS AmpliPrep/COBAS TaqMan HIV-1 Test – LOD: 48 c/mL
  - RealTime HIV-1 – LOD: 40 to 10,000,000 c/mL

Available HBV NAT Assays

- Detects the presence of HBV DNA
- Window Period: 20 – 22 days
- Approved for donor screening
  - COBAS AmpliScreen HBV Test – LOD: 10 – 100 c/mL
  - COBAS TaqScreen MPX Test – LOD: 10 c/mL
  - Procleix Ultrio – LOD: 100 c/mL
- Approved for viral load assessment
  - HBV Digene Hybrid Capture I – LOD: ~10^6 c/mL
  - HBV Digene Hybrid Capture II – LOD: ~10^5 c/mL
  - Ultra-sensitive Digene Hybrid Capture II – LOD: ~$10^{3.5}$ c/mL
  - Amplicor HBV Monitor – LOD: ~10^3 c/mL
  - Cobas Amplicor HBV Monitor – LOD: ~10^2 c/mL
  - Cobas Taqman 48 HBV – LOD: ~10 c/mL
  - Versant HBV DNA 1.0 – LOD: ~$10^{5.5}$ c/mL
  - Versant HBV DNA 3.0 – LOD: ~10^2 c/mL

Available HCV NAT Assays

- Detects the presence of HCV RNA
- Window Period: 7 – 10 days
- Approved for donor screening
  - COBAS AmpliScreen HCV Test (v 2.0) – LOD: 10 – 100 c/mL
  - COBAS TaqScreen MPX Test – LOD: 10 c/mL
  - Procleix HIV-1/HCV – LOD: 100 c/mL
  - Procleix Ultrio – LOD: 100 c/mL
- Approved for viral load assessment
  - Amplicor HCV Monitor – LOD: 600-500,000 IU/mL.
  - Cobas Amplicor HCV Monitor V2.0 – LOD: 600-500,000 IU/mL.
  - Versant HCV RNA 3.0 Assay (bDNA) – LOD: 615-7,700,000 IU/mL.
  - LCx HCV RNA-Quantitative Assay – LOD: 25-2,630,000 IU/mL.
  - SuperQuant – LOD: 30-1,470,000.
  - Cobas Taqman HCV Test – LOD: 49-69,00,000 IU/mL.
  - Abbott RealTime – LOD: 12-100,000,000 IU/mL
  - Cobas Amplicor Hepatitis C Virus Test, version 2.0 – LOD: 50 IU/mL
  - Versant HCV RNA Qualitative Assay – LOD: 10 IU/mL

Cost Factors

Assay	Median Allowable Cost	Facility Fee
HIV Serology	$78.75	$12.50
HIV NAT	$302.94	$119.75
HBsAb	$73.01	$15.12
HBsAg	$71.95	$16.96
HBcAb	$73.01	$15.12
HBV NAT	$226.00	$60.28
HCV Serology	$93.40	$20.08
HCV NAT	$289.00	$60.28
Serology	$390.12	$79.78
Serology + NAT[1]	$982.06	$259.81
Serology + NAT[2]	$1,208.06	$320.09

[1]HIV, HCV only; [2]HIV, HBV, and HCV

Considerations for Making Recs

- Serology is generally available at all TCs
  - FDA-approved screening assays are preferred
  - If they are not available in the lab, the TC should discuss with their Laboratory Director to ensure that the LOD is similar for the available assay to FDA-approved assays
    - Sensitivity and specificity is dependent on the study population and therefore should not be used to compare assays
- For Hepatitis B
  - We are recommending that all live donors have HBsAb drawn
    - If negative, the donor should be offered HBV vaccine series
    - We felt that this was important because:
      - All patients with liver disease should receive HBV vaccine if they are not immune (for liver donors)
      - Since HBV is a potential blood-borne pathogens and donors may require blood products, the donors should be offered HBV vaccine if they are not previously immune
      - HBV vaccination series should be initiated pre-donation and completed post-donation for HBsAb negative donors

Considerations for Making Recs

- NAT is generally available for HIV & HCV
  - Most TCs have access to HIV & HCV NAT
  - Most TCs have quantitative VL studies, not qualitative PCRs approved for donor screening
    - Assays for HIV should have a lower LOD of 50 c/mL
    - Assays for HCV should have a lower LOD of 50 IU/mL
    - Some centers may not have access to assays with cutoffs as above; higher cut-offs (typically 1 log higher) are typically available and can be used
      - Consider informing recipients that the assay utilized may not detect HIV or HCV at the same level as FDA-approved screening assays
  - HBV NAT is not recommended for all donors because:
    - Higher false positive rate with assays with low limits of detection
    - HBsAg provides significant screening power (difference in window period is only ~10 day benefit

WG Live Donor Screening Recs

- All live donors
  - HIV: HIV Serology and NAT
  - HBV: HBsAg, HBsAb, HBcAb
  - HCV: HCV Serology and NAT
  - Timing Pre-Transplant: 14 days Pre-Tx
- Donors with identified risk factors
  - Screening as above PLUS HBV NAT
  - Timing Pre-Transplant: 7 days Pre-Tx

Questions?

Michael G. Ison, MD MS
312-695-5085
mgison@northwestern.edu