Hepatitis C Virus Diagnostics

Case Studies and Updates

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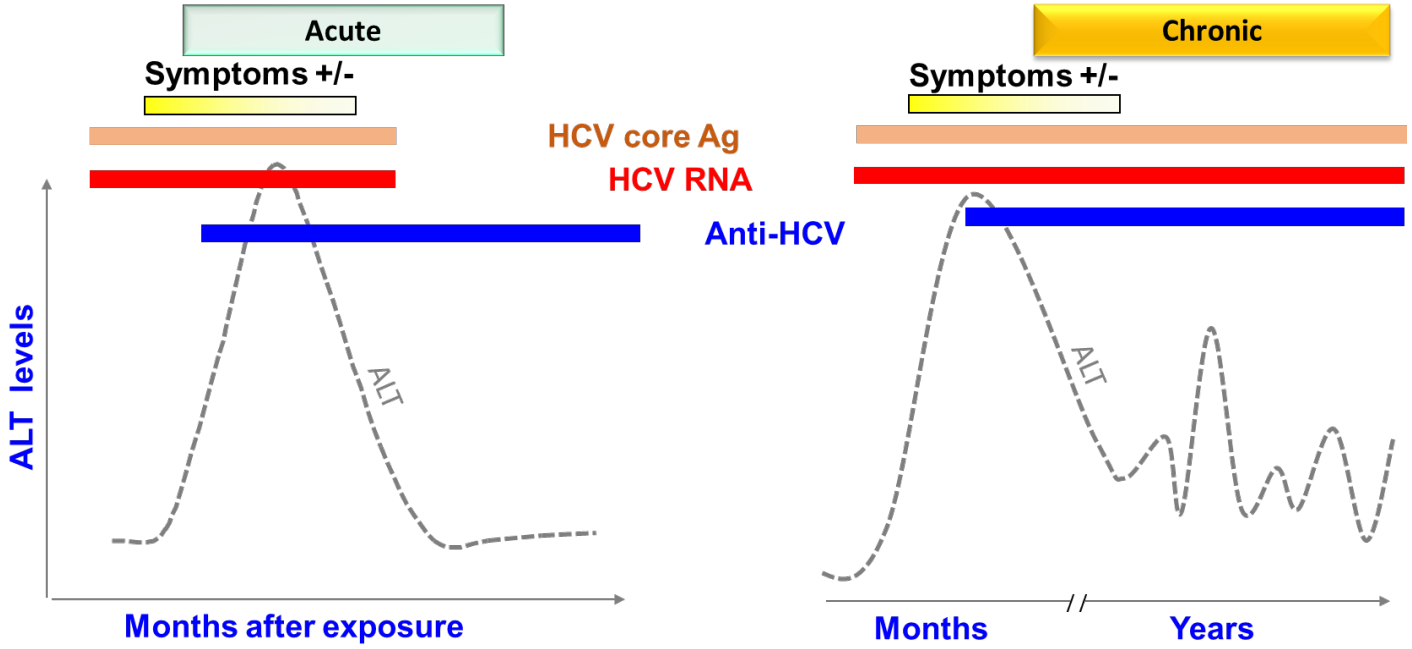
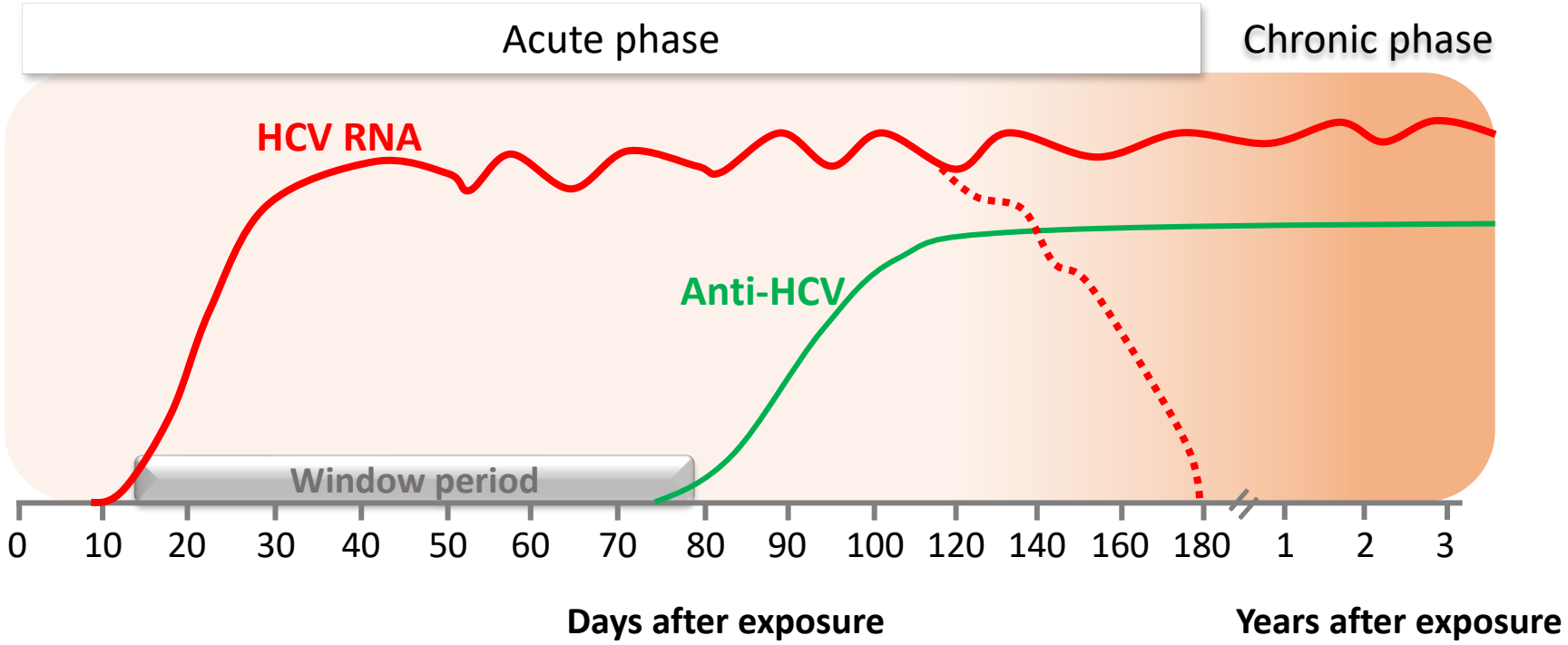
2023 HIV, HCV, and Syphilis Diagnostic Testing Workshop
12 March 2023

Natural History of HCV Infection



Markers of HCV Infection



FDA-approved HCV RNA Tests

Manufacturer	Assay	LoD[a] serum IU/mL	% Sensitivity [95% CI]	% Specificity [95% CI]
Hologic	Aptima HCV Quant Dx Assay	**3.4**	**98.8** [96.7-99.6]	**100** [95.4-100]
Roche Molecular	COBA-HCV	**13.7**	**100.0** [97.5-100]	**98.8** [93.3-99.8]
Abbott Molecular	Abbott RealTime HCV[b]	**12**	**N/A[b]**	**N/A[b]**
Roche Molecular	COBAS AmpliPrep/ COBAS TaqMan HCV Test	**18**	**100** [97.3-100]	**100** [95.5-100]
Hologic (Gen-Probe)	VERSANT TM HCV RNA Qualitative Assay	**7.5**	**99.7 [d]**	**97.9 [d]**

[a] LoD as assessed with the WHO IS for HCV RNA (Genotype 1a); LoDs can vary by genotype
[b] Performance metrics were related to the ability of the test result to predict SRV (PPV/NPV)
[c] Diagnostic claim added to P060030 per PMA supplement
[d] Performance against another PCR assay

Courtesy: Silke Schlottmann (FDA)

Case Study I

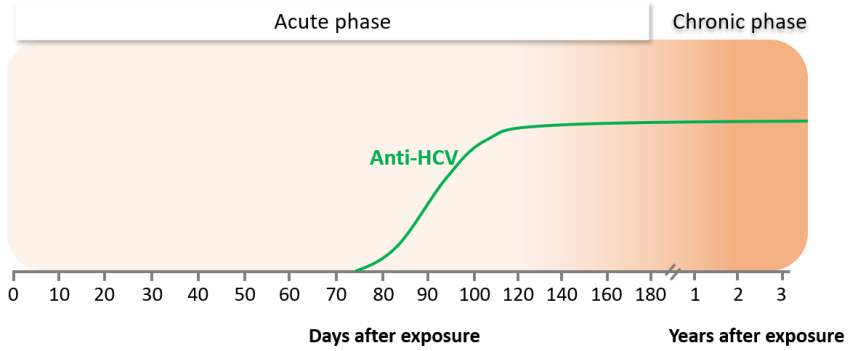
HCV NAT Results

- **HCV RNA <3.4 IU/mL** (Hologic Aptima HCV Quant Dx Assay)
- **HCV RNA <13.7 IU/mL** (Roche Molecular)
- **HCV RNA <12 IU/mL** (Abbott RealTime HCV)
- **HCV RNA <18 IU/mL** (COBAS AmpliPrep/ COBAS TaqMan HCV Test)
- **HCV RNA <7.5 IU/mL** (VERSANT TM HCV RNA Qualitative Assay

Problem: When HCV RNA levels are at the lowest limit of quantitation and are not quantifiable, results can be misinterpreted as if the patient is HCV RNA negative

Antibodies to HCV

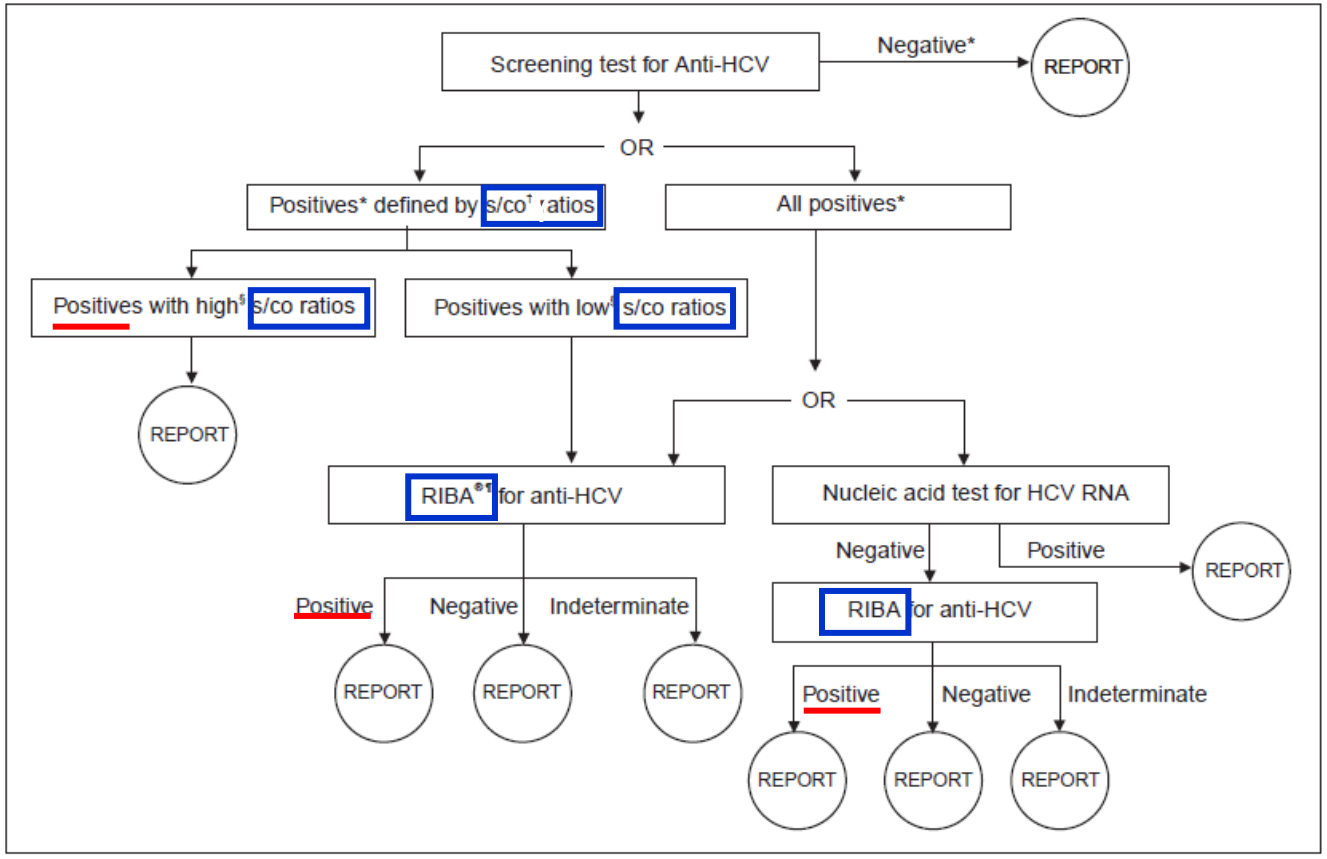
- Indicates exposure to HCV
- Present throughout acute, resolved and chronic phases of infection
- Laboratory tests
  - Enzyme immunoassays (EIAs) and Chemiluminescence assays (CIAs)
    - Serum, plasma, dried blood spot
  - Rapid diagnostic assays (RDTs)
    - Whole blood, serum, plasma
  - Confirmatory Immunoblot assays
    - Serum, plasma



Case Study II

Confirmation of anti-HCV screening test results performed by using incorrect signal-to-cutoff ratio thresholds

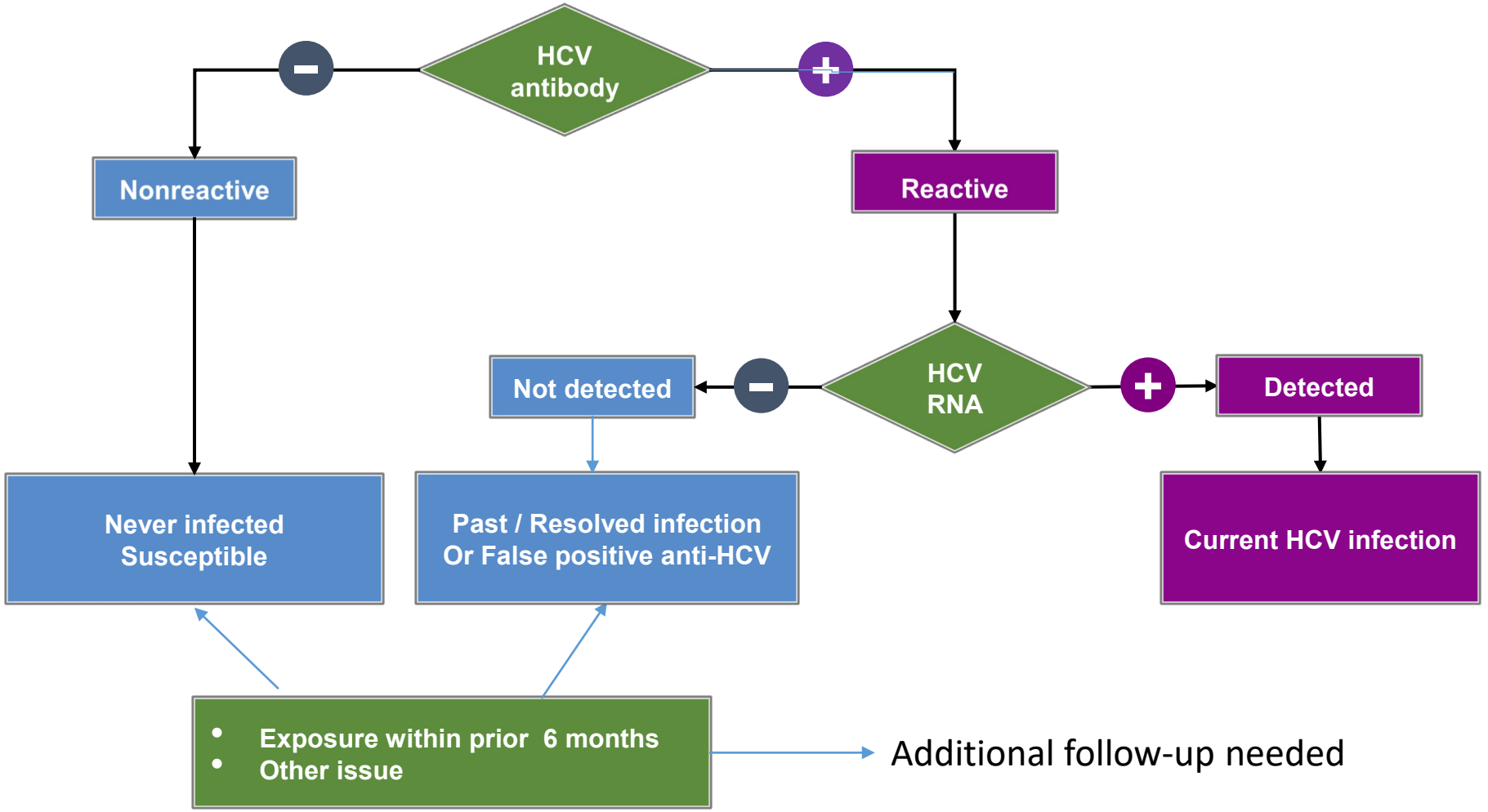
CDC's HCV Testing Guidelines - 2003



Screening Test Kit	S/CO
Ortho HCV V3.0 ELISA	≥3.8
Abbott HCV EIA 2.0	≥3.8
Ortho VITROS Anti-HCV CIA	≥8.0
Abbott AxSYM Anti-HCV MEIA	≥10.0
Abbott Architect Anti-HCV CIA	≥5.0
Bayer Advia Centaur HCV CIA	≥11.0

Guidelines for Laboratory Testing and Result Reporting of Antibody to Hepatitis C Virus. MMWR. 2003 /52 / RR-33

CDC's Updated HCV Testing Guidelines - 2013



MMWR. 2013;62(18)

Case Study II

Manufacturer	Assay	% Sensitivity [95% CI]	% Specificity [95% CI]
OraSure Technologies	**OraQuick HCV Rapid Antibody Test**	**99.5** [98.4-99.9]	**99.0** [98.0-99.6]
Roche	Elecsys Anti-HCV II	**99.6** [98.7-99.96]	**98.8** (98.2-99.3)
	Elecsys Anti-HCV	**99.6** [98.5-99.5]	**96.9** [95.9-97.7]
	Elecsys Anti-HCV	**99.6** [98.5-99.95]	**97.1** [96.2-97.9]
	Elecsys Anti-HCV	**99.4** [98.1-99.9]	**97.2** [96.3-98.0]
Abbott Laboratories	ARCHITECT anti-HCV	**99.53** [97.4-99.99]	**97.6** [96.5-99.8]
Siemens Healthcare	ADVIA Centaur HCV	**99.9** [99.5-100]	**97.5** [96.4-98.3]
Ortho Clinical Diagnostics	Vitros Anti-HCV	**99.5** [98.7-99.9]	**98.2** [97.5-98.8]

Courtesy: Maria Garcia (FDA)

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Ortho HCV V3.0 ELISA	≥3.8
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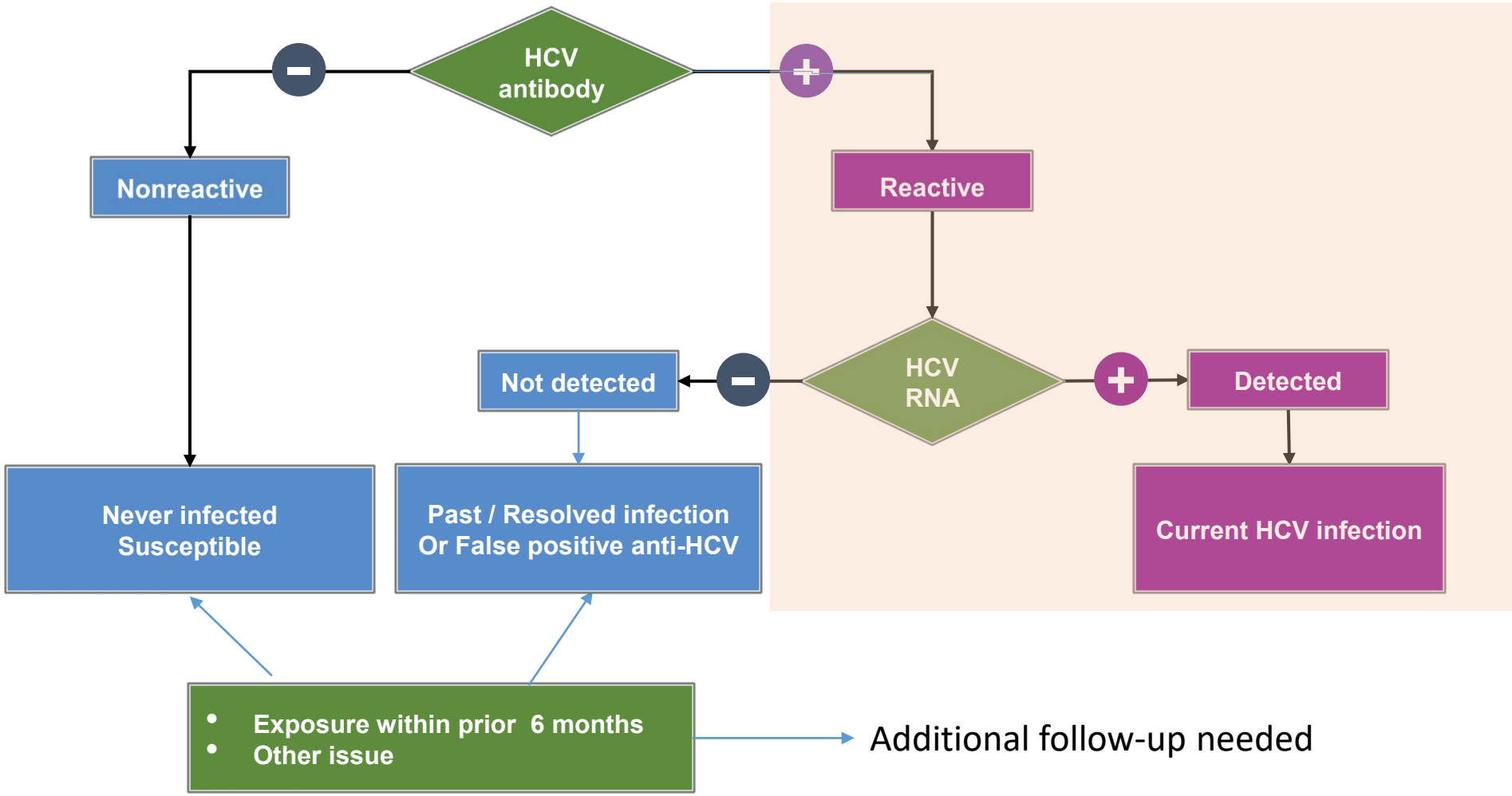
MMWR. 2003 /52 / RR-33

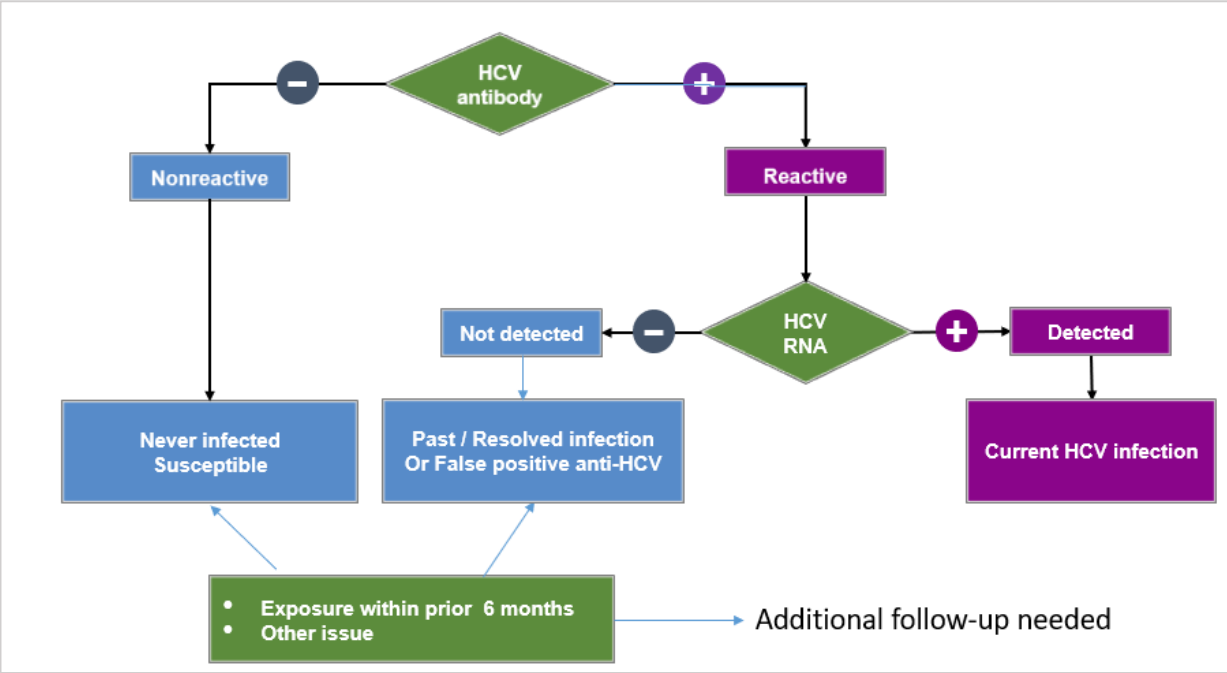
CDC's Updated HCV Testing Guidelines - 2013



MMWR. 2013;62(18)

Hepatitis Testing Guidelines - Updates

Updated Operational Guidance for Implementing CDC's Recommendations on Testing for HCV Infection



Four possible **operational strategies** to accomplish the two-step testing sequence to diagnose current HCV infection:

1. Blood from a subsequent venipuncture is submitted for HCV RNA testing if the blood sample collected is reactive for HCV antibody during initial testing;

2. From a single venipuncture, two specimens are collected in separate tubes, one tube for initial HCV antibody testing, and a second tube for HCV RNA testing if the HCV antibody test is reactive;

3. The same sample of venipuncture blood used for initial HCV antibody testing, if reactive, is reflexed for HCV RNA testing without another blood draw;

4. A separate blood sample is submitted for HCV RNA testing if the initial testing of HCV antibody has used fingerstick blood.

Operational strategy 1 should no longer be used as it can lead to incomplete HCV testing and gaps in the HCV care cascade.

Emily Cartwright et al. unpublished

Draft hepatitis C virus (HCV) testing recommendations for perinatally exposed infants and children

- **Perinatally exposed infants should receive a nucleic acid test (NAT) for HCV ribonucleic acid (RNA) at age 2-6 months to identify children who might go on to develop chronic HCV infection**
  - **Infants and children aged 7-17 months** who are perinatally exposed to HCV and have not previously been tested should receive a NAT for HCV RNA
  - **Children aged ≥ 18 months** who are perinatally exposed to HCV and have not previously been tested should receive an anti-HCV test with reflex* to NAT for HCV RNA

Courtesy: Carolyn Wester, DVH

*A NAT for HCV RNA performed on specimens that are anti-HCV reactive

Status: perinatal HCV testing recommendations

- **External peer review**
  - Completed November 16, 2022
  - https://www.cdc.gov/hepatitis/policy/ISIreview/HepCScreeningAndTesting.htm

- **Public webinar**
  - Held on December 6, 2022
  - https://www.cdc.gov/hepatitis/policy/pdfs/CDC_perinatal_hep_c_testing_508.pdf

- **Federal Register Notice:**
  - Public comment period closed January 27, 2023
  - https://www.regulations.gov/docket/CDC-2022-0116/document

Courtesy: Carolyn Wester, DVH

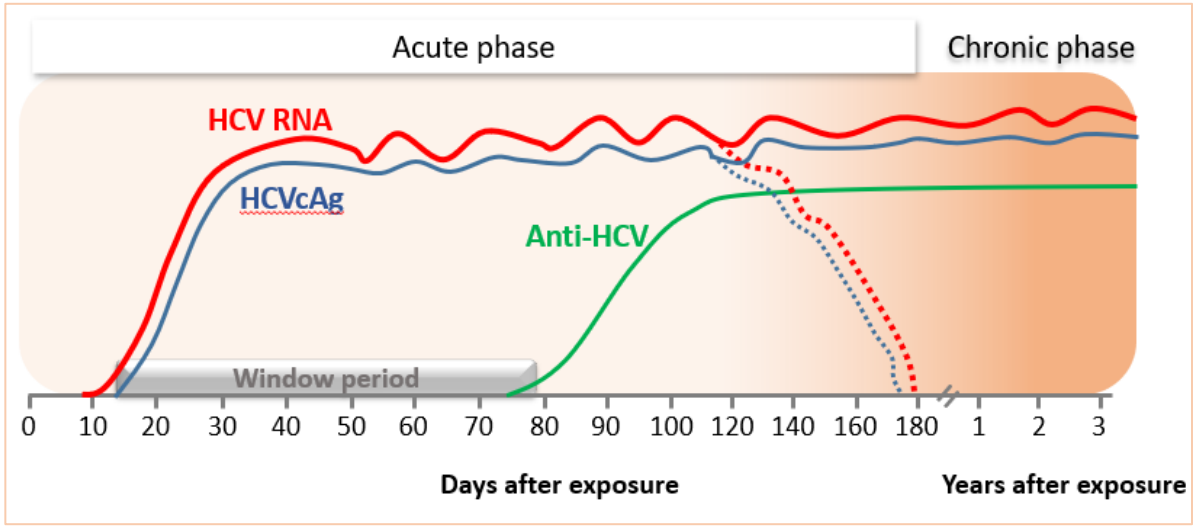
Next steps: perinatal HCV testing recommendations

- **Winter 2022/23: Review and respond to external peer review and FRN comments**
- **Winter/Spring 2023: Supplemental literature review**
- **Summer 2023: Submit revised guidelines to CDC clearance**
- **Fall 2023: MMWR publication (tentative)**

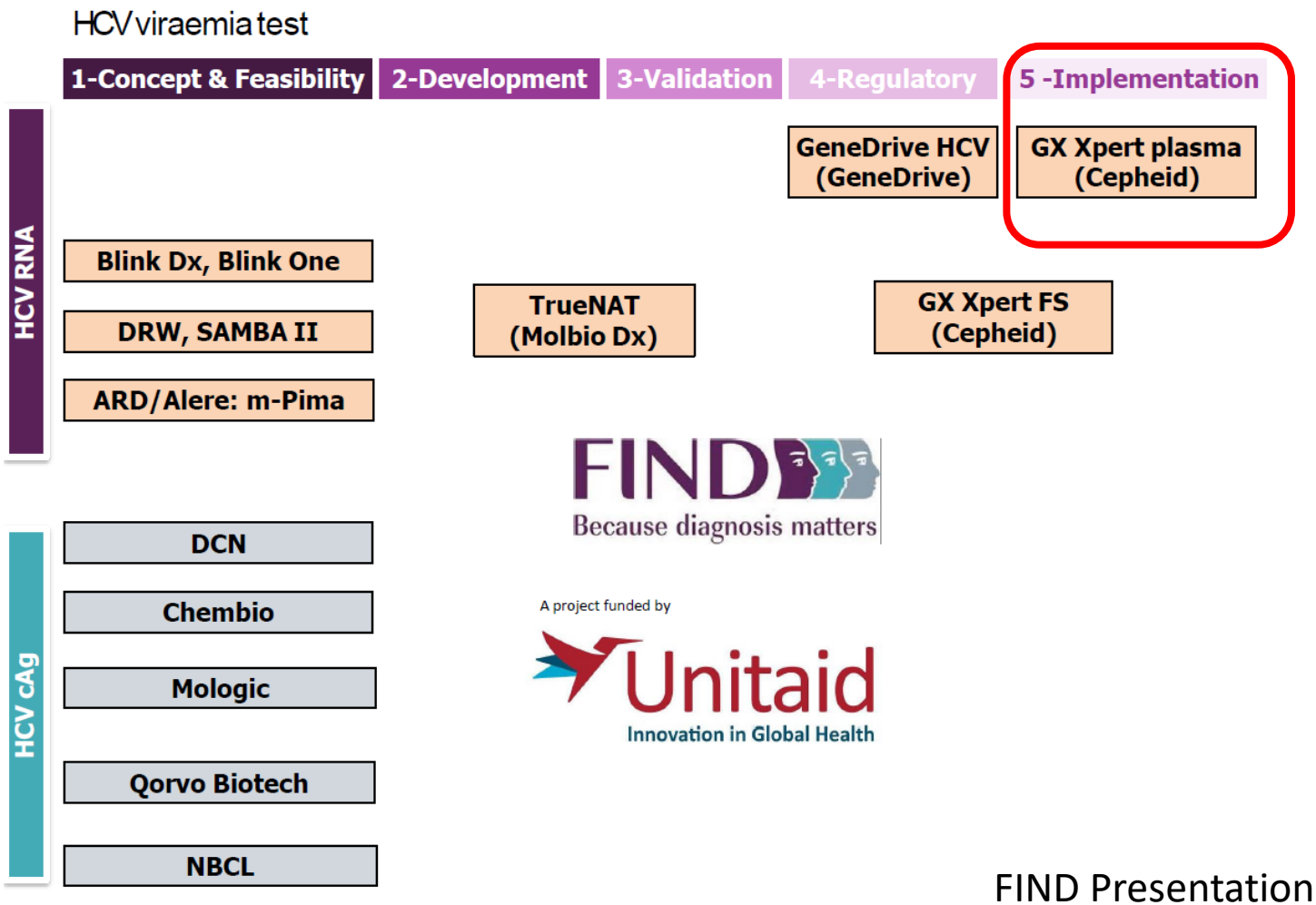
Courtesy: Carolyn Wester, DVH

HCV Core Antigen

- Detectable within 1-2 weeks after exposure to HCV
- Test samples
  - Serum, plasma, dried blood spots
  - Lower sample volume than NAT
  - No pristine sample needed
- Undetectable when HCV RNA <2000 IU/ml
- Abbott and Roche

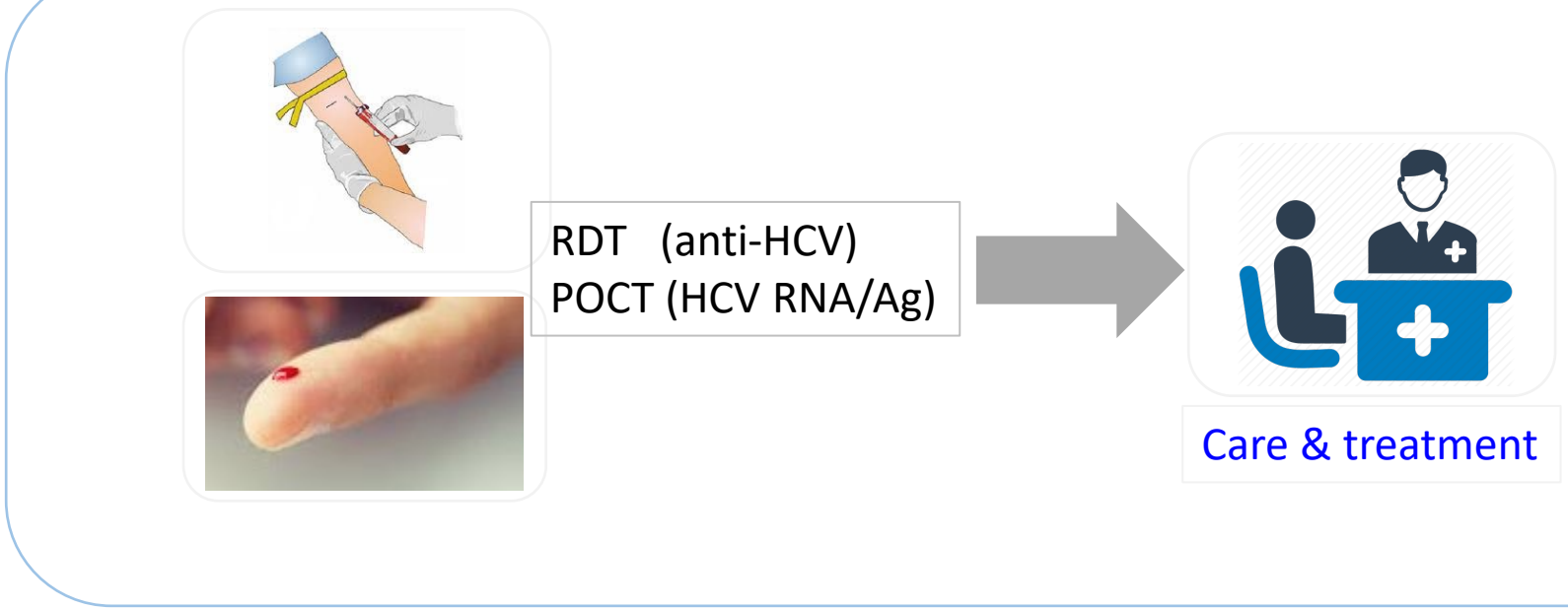


POCTs for HCV RNA and HCV core Antigen



FIND Presentation at EASL 2019, Vienna


Anti-HCV
Anti-HCV +
HCV RNA
Care & treatment


RDT (anti-HCV)
POCT (HCV RNA/Ag)
Care & treatment

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.