HCV Diagnostic Testing

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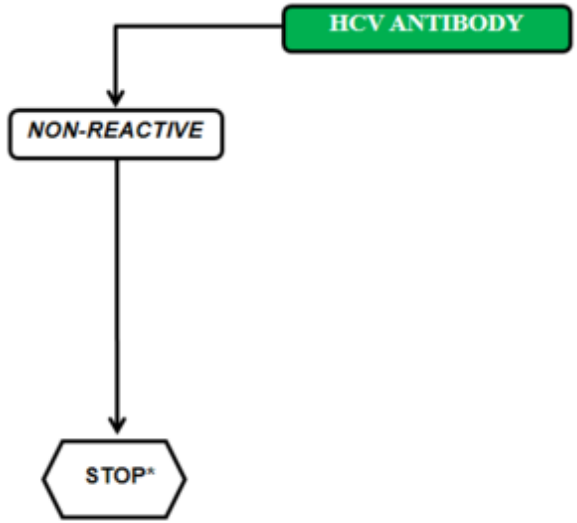
Recorded on March 29, 2013

IAS–USA
International AIDS Society–USA

Recommended Testing Sequence for Identifying Current HCV infection



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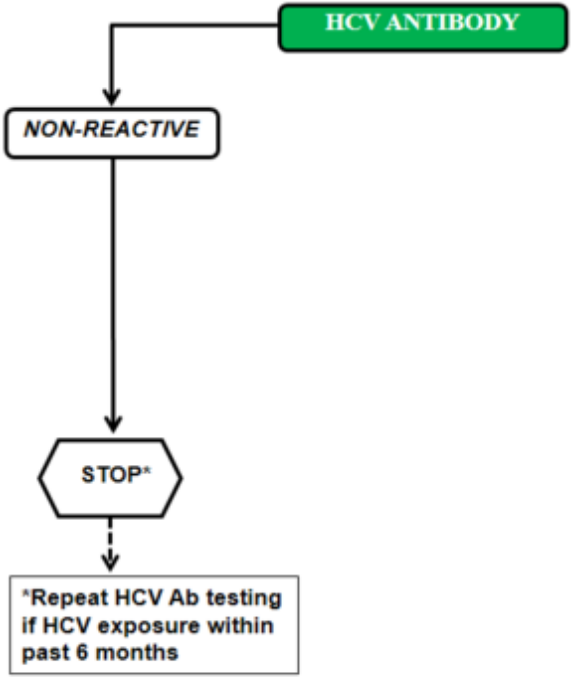

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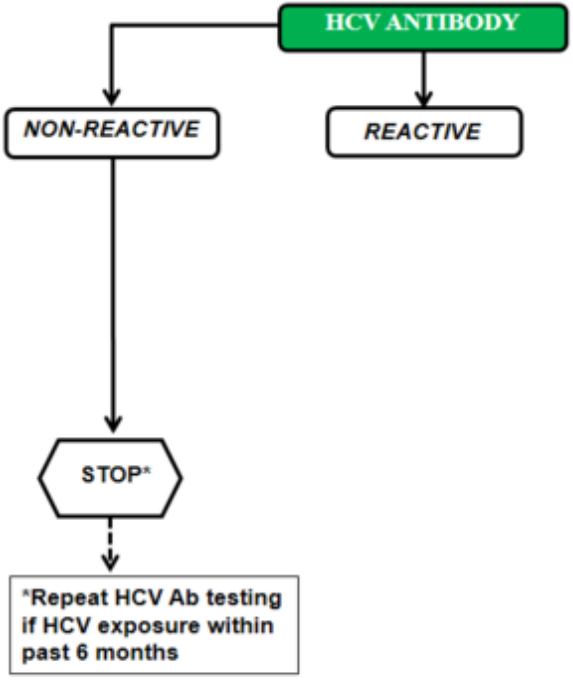
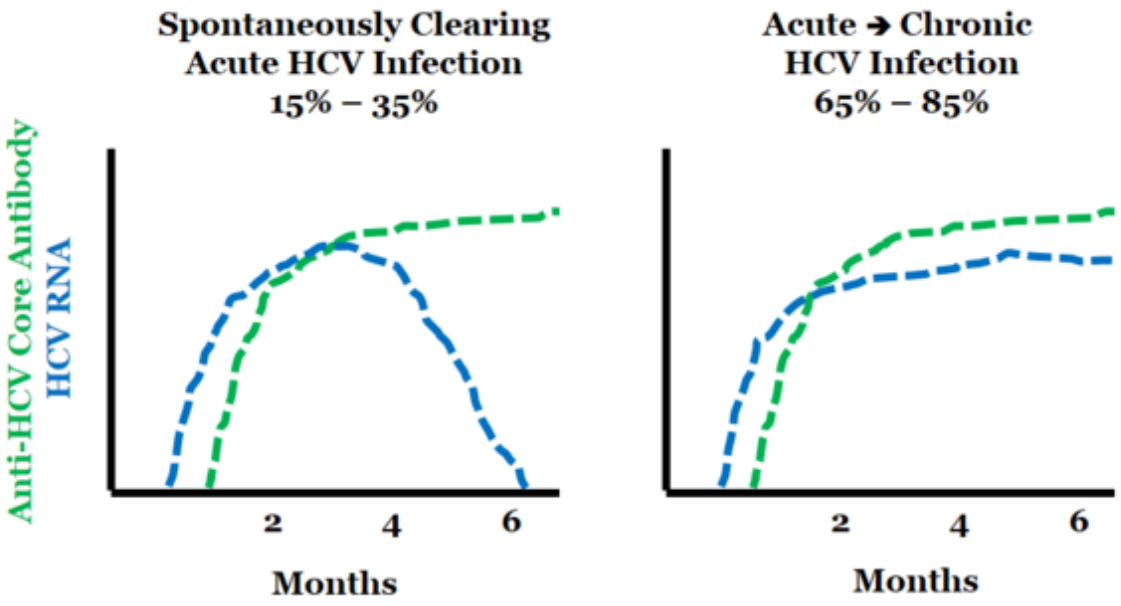


Acute HCV Infection: Viral Clearance or Chronic Infection



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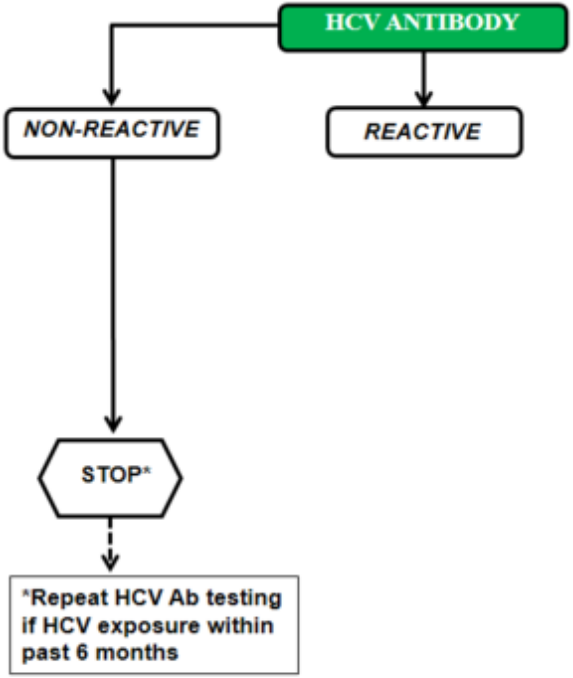

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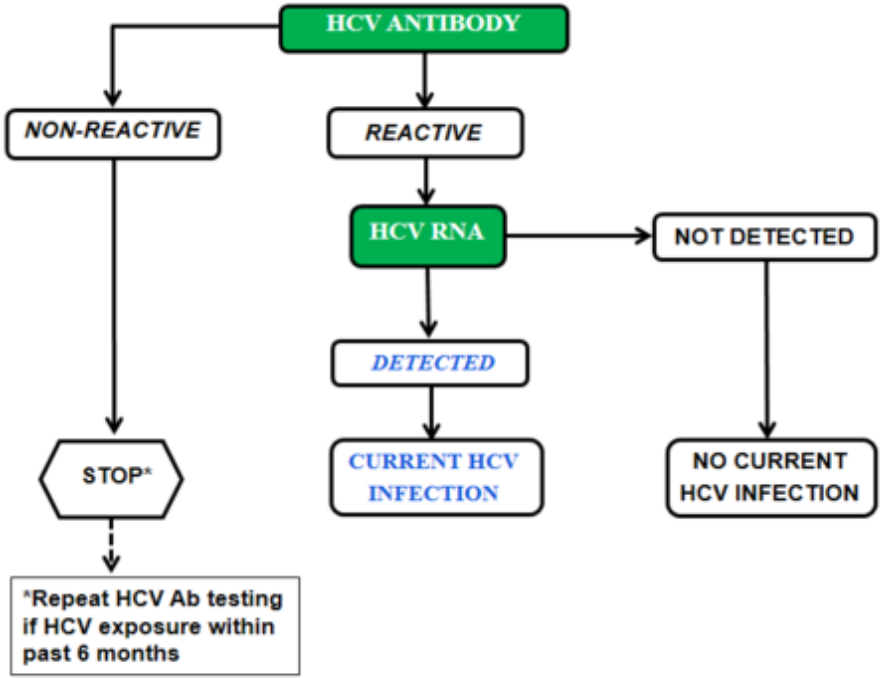

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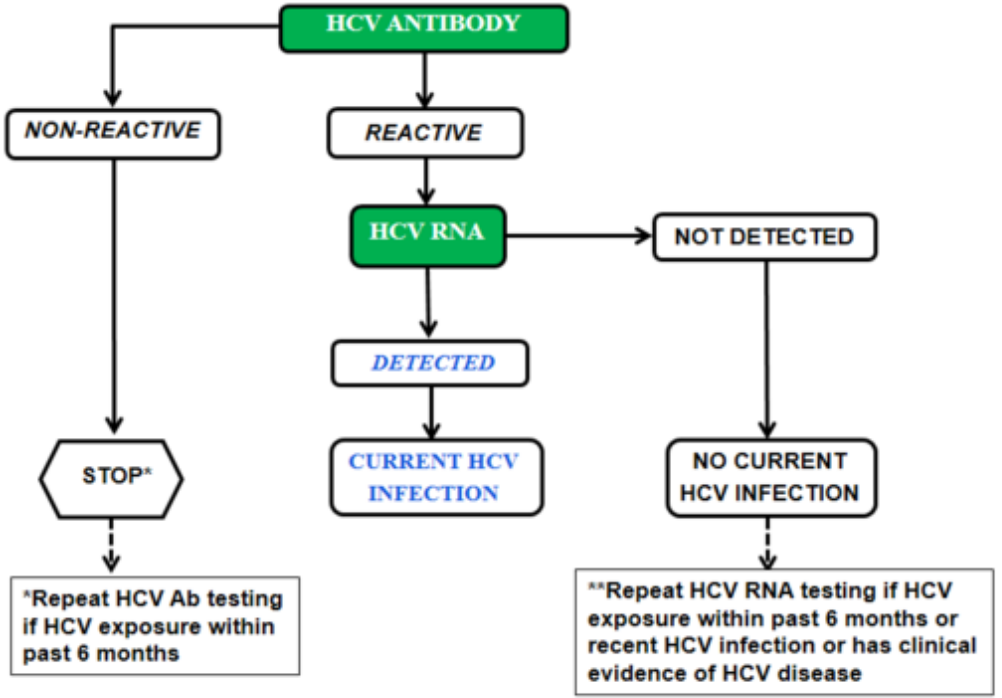

Serologic Diagnosis of Chronic HCV Infection

Primary screening test

	Core	NS3	NS4a	NS5b
EIA 1.0			■	
EIA 2.0	■	■	■	
EIA/CIA 3.0	■	■	■	■

Nucleic Acid (RNA) Test

MMWR 1998 and MMWR 2003; Adapted from Kamili et al, Clin Infect Dis, 2012, S1

Serologic Diagnosis of Chronic HCV Infection

Primary screening test

	Core	NS3	NS4a	NS5b
EIA 1.0			■	
EIA 2.0	■	■	■	
EIA/CIA 3.0	■	■	■	■

Confirmatory test

	Core	NS3	NS4a	NS5b
RIBA 2.0	■	■	■	
RIBA 3.0	■	■	■	■

Nucleic Acid (RNA) Test

MMWR 1998 and MMWR 2003; Adapted from Kamili et al, Clin Infect Dis, 2012, S1

Commercially Available Qualitative HCV RNA Assays

Assay	Manufacturer	Lower Limit of Detection (LLD), IU/mL
Versant HCV RNA	Gen-Probe	10
Procleix HIV/HCV*	Gen-Probe	<50
UltraQual HCV RT-PCR	National Genetics	10
Amplicor HCV v2.0	Roche	50
COBAS Amplicor HCV v2.0	Roche	50
AmpliScreen*	Roche	<50

* Blood screening only

Adapted from Kamili, et. al, Clin Infect Dis 2012, S1

Disclosure Information

- Scientific advisory board member: Gilead Sciences, Inc, Monogram Biosciences, GlobeImmune, Inc
- Grant support: Boehringer Ingelheim, Bristol-Myers Squibb
- Scientific collaborator: MBio Diagnostics
- Consultant: Santaris Pharma A/S, Merck & Co, Inc
- Stockholder: GlobeImmune, Inc

Commercially Available Quantitative HCV RNA Assays

Assay	Manufacturer	LLD, (Dynamic Range) IU/mL
LCx HCV RNA Quantitative*	Abbott	25 (25-2,630,000)
RealTime HCV/m2000sp/m2000rt	Abbott	12 (12 – 100,000,000)
HCV SuperQuant	National Genetics	20 (20 – 1,000,000)
Amplicor HCV Monitor	Roche	50 (600 - 700,000)
COBAS Amplicor HCV Monitor v2.0	Roche	50 (600 - 700,000)
COBAS Ampliprep/TaqMan	Roche	18 (43-69,000,000)
Versant HCV RNA 3.0	Siemens	615 (615 – 7,700,000)

* Blood screening only

Adapted from Kamili, et. al, Clin Infect Dis 2012, S1

Communicating the Results to the Patient

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Implications of a Negative Anti-HCV Antibody Test and a Negative HCV RNA Test

- Your patient is not currently infected with HCV or is in the early “window period” between infection and the appearance of anti-HCV antibodies or RNA.

Implications of a Positive Anti-HCV Antibody Test and a Negative HCV RNA Test

- Your patient is not currently infected with HCV
  - Message for the patient:
    - You previously had an HCV infection that was cleared
      - Spontaneous clearance during acute HCV infection
        - More common in patients with the IL28B CC genotype and those not also infected with HIV
      - Clearance as the result of successful HCV treatment
    - If you engaged in activities that put you at risk for HCV infection in the past 6 months, you should be tested again for HCV RNA at least 6 months after your last potential exposure
    - You can be reinfected with HCV if you engage in risk behaviors that are associated with HCV transmission; if you are engaging in these behaviors, HCV RNA testing should be repeated at regulars intervals. You will continue to have HCV antibodies for a prolonged period of time and repeat antibody testing will not be of benefit to you

Implications of a Positive Anti-HCV Antibody Test and a Positive HCV RNA Test

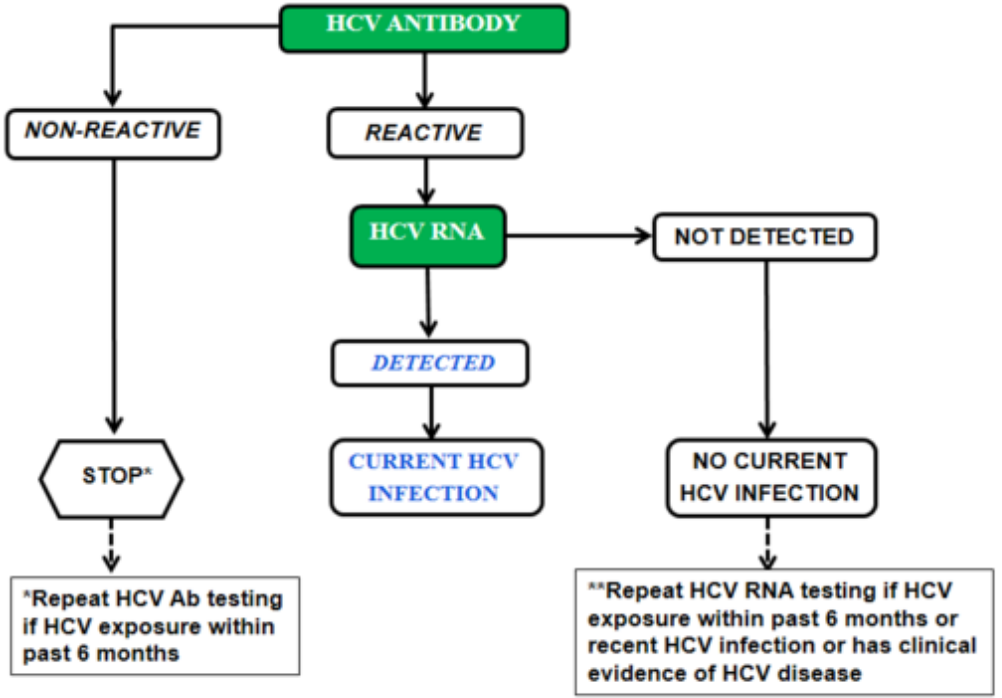
- Your patient is currently infected with HCV
  - Message for the patient:
    - You are currently infected with HCV
      - You need to be evaluated to understand the severity of your liver disease and to be counseled about how not to accelerate the damage the virus may be doing to your liver
      - You should be tested for other infections like HBV and HIV that may be transmitted in the same ways as HCV
      - You may benefit from certain vaccinations such as those for HBV and HAV
      - You can transmit the virus to other people
      - HCV can be successfully treated with HCV medications
        - With successful treatment, your viral infection will be cured
        - Your liver disease will stop progressing although you may need to be followed for certain complications of HCV infection

Implications of a Negative Anti-HCV Antibody Test and a Positive HCV RNA Test

- Possibilities
  - Your patient is in the "window period" in the first 6–12 weeks of HCV infection. HCV RNA appears in the blood before HCV antibodies develop
    - If acute HCV infection is suspected, an urgent referral to a practitioner with expertise in treating HCV infection is appropriate because the virus is particularly responsive to therapy within the first 6 months of infection
  - Your patient is immunocompromised and is not making detectable antibodies to HCV despite an active HCV infection
    - This is much less common with second and third generation anti-HCV antibody tests but it can occasionally occur in immunocompromised patients, including those with advanced HIV infection or those on dialysis

Linkage to Care

Recommended Testing Sequence for Identifying Current HCV infection



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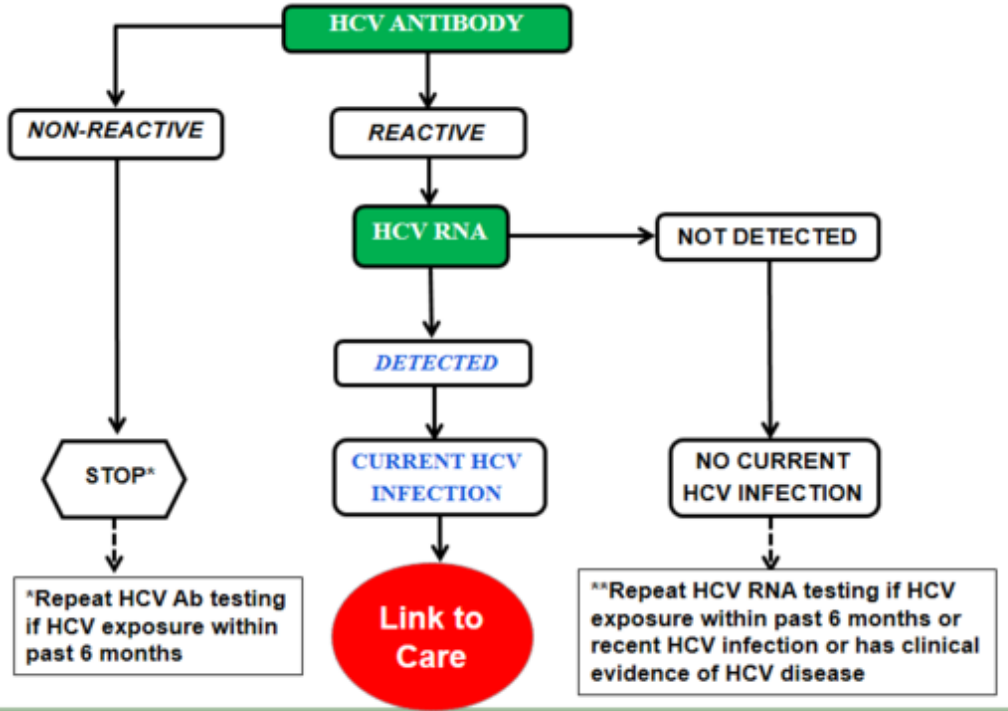

Linkage to Care

- The primary reason to offer testing for HCV infection is to identify those who are candidates for anti-HCV therapy
- Newer anti-HCV regimens (and those in development) are
  - Associated with substantially higher treatment success rates
  - Much better tolerated
  - Increasingly all-oral and interferon-free
  - Usually shorter in duration

Laboratory Diagnostics in HCV Infection

- Diagnosis of HCV infection
- Communicating the results to the patient
- Linkage to care

Summary

- Contemporary diagnosis and management of HCV infection requires an understanding of the proper use of serological and molecular tools for the detection of HCV infection and for monitoring the response to therapy
- HCV antibody tests are useful for the diagnosis of a prior or current HCV infection
- HCV RNA assays are useful in the diagnosis of current infection and in monitoring the success of HCV therapy
- Detection of HCV infection and linkage of those who are infected to medical care has the potential to substantially improve quality and quantity of life, and to reduce the risk that HCV will be transmitted to others

End

This presentation is brought to you by the International Antiviral Society-USA (IAS-USA)
in collaboration with Hepatitis Web Study & the Hepatitis C Online Course

Funded by a grant from the Centers for Disease Control and Prevention

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Diagnosis of HCV Infection

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Recommended Testing Sequence for Identifying Current HCV infection

Serologic Diagnosis of Current HCV Infection

Primary screening test

	Core	NS3	NS4a	NS5b
EIA 1.0				
EIA 2.0				
EIA/CIA 3.0				

EIA = enzyme immunoassay
CIA = chemiluminescence assay

MMWR 1998 and MMWR 2003; Adapted from Kamili et al, Clin Infect Dis, 2012, S1

Serologic Diagnosis of Current HCV Infection

Primary screening test

	Core	NS3	NS4a	NS5b
EIA 1.0				
EIA 2.0				
EIA/CIA 3.0				

Confirmatory test*

	Core	NS3	NS4a	NS5b
RIBA 2.0				
RIBA 3.0				

RIBA = recombinant immunoblot assay

MMWR 1998 and MMWR 2003; Adapted from Kamili et al, Clin Infect Dis, 2012, S1

Serologic Diagnosis of Current HCV Infection

Primary screening test

	Core	NS3	NS4a	NS5b
EIA 1.0				
EIA 2.0				
EIA/CIA 3.0				

Confirmatory test*

***Not required in 2013 revision**

	Core	NS3	NS4a	NS5b
RIBA 2.0				
RIBA 3.0				

MMWR 1998 and MMWR 2003; Adapted from Kamili et al, Clin Infect Dis, 2012, S1

Confirmatory Test Substitution by Sample-to-Cutoff (S/Co) Ratio

Assay	Manufacturer	S/Co for >95% specificity
Abbott HCV EIA 2.0	Abbott	≥3.8
AxSYM Anti-HCV	Abbott	≥10.0
Architect Anti-HCV	Abbott	≥5.0
Ortho EIA 3.0	Ortho	≥3.8
Vitros Anti-HCV	Ortho	≥8.0
Advia Centaur HCV	Siemens	≥11.0

MMWR, 2003; Adapted from Kamili et al, Clin Infect Dis 2012, S1