

Viral Diagnostic Tests

1. HEPATITIS

What defines hepatitis?

- Increased ALT
- The three most common causes of hepatitis are prescription drugs, obesity, and alcohol.

Hepatitis A Virus (HAV)

Test	Result	Interpretation
HAV IgM	Positive	Active Infection
HAV IgM	Negative	Not Infected
HAV Ab total	Positive	Exposure to HAV (immune)
HAV Ab total	Negative	Indeterminate; does not preclude prior exposure (existing Ab may be undetectable)

Hepatitis B Virus (HBV)

HBsAg	HBsAb	HBeAg	HBeAb	Interpretation	Notes	Follow-up
+	-	±	-	Acute or chronic HBV infection	A positive surface antigen means HBV is present and can spread to others. A positive HBeAg confirms actively replicating virus. If HBeAg is positive, this is considered wild type HBV. If HBeAg is negative and the patient is still replicating virus, this is considered mutant HBV. Approximately 2% of acute infections in adults will progress to chronicity.	Check HBV DNA. Repeat serology for clearance of HBsAg and/or resolution of chronicity; serum ALT to monitor disease activity
+	-	-	+	Carrier or early seroconversion	A positive surface antigen means HBV is present and can spread to others. A positive HBeAb usually means no replication is occurring.	Check HBV DNA. If negative, patient is a "carrier".
+	-	+	+	Decreasing infectivity	Very rare results	Repeat serology for resolution; serum ALT to monitor disease activity
NA	+	NA	NA	Immune	Presence of HBsAb indicates immunity, which can occur via vaccination or prior acute infection. NOTE: If both HBsAg (+) and HBsAb (+), the patient is infected with two or more strains of HBV.	
-	-	-	-	Not immune/not infected	At risk for infection	Recommend vaccination series

HBV DNA assay should be performed in any patient with a positive HBsAg to determine whether active replication is occurring.

HBcAb is only relevant when dealing with acute HBV infection because HBcAb may be positive during serologic gap/window between seroconversion from HBsAg positivity to HBsAb positivity. With chronic HBV infection, HBsAg remains positive; thus, no serologic gap/window occurs.

Hepatitis C Virus (HCV)

HCV Ab Test *	HCV RNA	Interpretation
Positive	Positive	Active infection
Positive	Negative	If risk factors exist, cleared acute viremia (15%) or a sustained viral response after antiviral therapy; no risk for reactivation
Negative	Not needed	Not infected

*Enzyme immunoassay (EIA) or enhanced chemiluminescence immunoassay (CIA)

Occupational Exposure (Needlestick Injuries)

Time	Tests
Immediately post-exposure	ALT, AST, HBsAg, HBsAb, HCVAb*, HCV RNA
1 month post-exposure	Repeat
3 months post-exposure	Repeat

*Becomes positive eight weeks after acute infection

3. HERPES SIMPLEX VIRUS (HSV)

Test	Result	Interpretation	Recommendation/Notes
Culture of vesicles or ulcers	Positive	Active infection	Confirm by staining w/ specific monoclonal antibodies establishes the diagnosis. Culture from recurrent late disease is much less sensitive.
ELISA	Positive	Prior exposure or active infection	Distinguishes HSV-1 and HSV-2
Direct Cytologic Exam	Positive	Active infection	Use Wright-Giemsa stain followed by Tzanck smear=see multinucleated giant cells. Negative test does not rule out diagnosis. Does not differentiate HSV-1, HSV-2, and zoster.
PCR	Positive	Active infection	Detects HSV in tissue, CSF, or cell samples. Sensitive, specific and rapid. Distinguishes HSV-1 and HSV-2.
Western blot or Immunoblot	Positive Negative	Prior exposure No prior exposure	Detects glycoprotein G; distinguishes HSV-1 and HSV-2. Western blot is gold standard for antibody detection (IgM and IgG).

4. VARICELLA ZOSTER VIRUS (VZV)

Test	Result	Interpretation	Recommendation/Notes
PCR	Positive	Active infection	88% sensitive in stained smears and 97% sensitive in unstained smears
Wright-Giemsa stain followed by Tzanck smear	Positive	Active infection	75% sensitive but also positive in herpes simplex
Immunofluorescent Staining	Positive	Acute Infection	Diagnostic of acute infection; more sensitive than culture
In situ hybridization	Positive	Primary Infection	Can demonstrate virus in peripheral blood mononuclear cells in primary infection in 24 hours
ELISA	Positive	Prior exposure or active infection	A negative test does not rule out VZV infection because sample may have been collected prior to appearance of detectable IgG. Thus, if negative, repeat in 2-3 weeks.

5. CYTOMEGALOVIRUS (CMV)

Test	Result	Interpretation	Recommendation/Notes
Shell-vial culture (Gold Standard)	Positive	Active CMV replication	Presence of true CMV infection is determined by active replication PLUS clinical correlation.
CMV IgM	Positive	Indicates exposure	Usually detected in primary infection except in immunocompromised patients. However, false positives are not uncommon. Should be confirmed by culture. Can also see false negatives in immunocompromised patients.
CMV IgG	Positive	Indicates exposure	Produced early in infection and persists life-long.
Intranuclear Inclusions	Positive	Active CMV replication	Inclusions in epithelial cells in urine sediment and liver biopsy are diagnostic. More useful in infants than adults. Presence of true CMV infection is determined by active replication PLUS clinical correlation.
PCR for CMV DNA in urine, CSF or serum	Positive	Active CMV replication	Presence of true CMV infection is determined by active replication PLUS clinical correlation. The higher the number of viral copies in serum, the higher the probability of true infection.
DNA & RNA hybridization	Positive	Active CMV replication	Presence of true CMV infection is determined by active replication PLUS clinical correlation.

6. EPSTEIN-BARR VIRUS (EBV)

Test	Result	Interpretation	Recommendation/Notes
Heterophile Agglutination (Paul-Bunnell test)	Positive	EBV infection	"Spot" tests are now performed at the initial test. False positives may occur in leukemia, malignant lymphoma, malaria, rubella, hepatitis & pancreatic carcinoma
Titers, in situ hybridization	Positive	EBV infection	EBV can be confirmed in liver biopsy by in situ hybridization. Titers $\leq 1:56$ may occur in normal persons and in pts w/ other illnesses. A titer of $\geq 1:224$ is presumptive evidence of Infectious Mononucleosis (IM). Therefore, a differential absorption test should be performed using guinea pig kidney and beef cell antigens.
PCR	Positive	EBV replication	Presence of true EBV infection is determined by active replication PLUS clinical correlation. The higher the number of viral copies in serum, the higher the probability of true infection.

IgG-VCA	IgM-VCA	IgD (EA)	EBNA	Interpretation	Notes
-	-	-	-	No evidence of infection	At risk for infection
+	-	-	+	Consistent with prior infection	Immune
±	+	±	-	Consistent with primary infection	IgG becomes positive later. EA decreases later. Repeat in 2-3 weeks for IgG.
±	-	±	±	Potential lack of true Abs	If patient is less than 15 months old, serology may be due to the presence of maternal antibodies
+	±	+	+	Consistent with convalescence of primary infection or reactivation of latent infection	If patient is less than 20-25 years old
				or reactivation of latent infection	If patient is greater than 20-25 years old
+	+	-	+	Consistent with convalescence of primary infection	
-	-	+	-	Unknown	Repeat 2-4 wks.

7. HUMAN HERPESVIRUS-6 (HHV-6)

Test	Result	Interpretation	Recommendations/Notes
IgM Immunofluorescence Assay	Positive	Primary infection or reactivation	
IgG Immunofluorescence Assay	Positive	Primary infection or reactivation	
PCR	Positive	Primary Infection	
Blood Mononuclear Cells Culture	Positive	Infection	Has a sensitivity of 86% and a specificity of 100%
Anticomplement Immunofluorescence Assay (ACIF)	Positive	Infection	Subjective results, less accurate than EIA
Enzyme Immunoassay (EIA)	Positive	Infection	More objective results

NOTE: Nearly 100% of Americans are seropositive. PCR is commonly positive, indicating low-level replication (occurs in ~50% of stem cell transplant patients and ~25% of young healthy adults).

Abbreviations and Notes:

Abbreviation/Symbol	Definition
EBNA	Epstein-Barr nuclear antigen
ELISA	Enzyme-linked immunosorbent assay
HBsAg	Hepatitis B surface antigen
HBsAb	Hepatitis B surface antibody
HBcAb	Hepatitis B core antibody
HBeAg	Hepatitis e antigen; if present indicates high infectivity
HBeAb	Hepatitis e antibody; if present indicates low/no infectivity
IgD (EA)	Anti-D antibody; Early antigen antibody
IM	Infectious mononucleosis
NA	Not applicable
PCR	Polymerase chain reaction
VCA	Viral capsid antigen

References:

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3. <http://www.cdc.gov/hepatitis/HBV/PDFs/SerologicChartv8.pdf>
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6. http://www.cdc.gov/Hepatitis/HCV/PDFs/hcv_graph.pdf
7. <http://virology-online.com/viruses/CMV4.htm>

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