

***POLYMERASE CHAIN REACTION
(PCR)
&
infectious disease***

principles

-CLINICAL SAMPLE

-PRIMERS (20-30)

-DNA POLYMERASE

-AMPLIFICATION

-RECOGNITION

-CONFIRMATION

POSITIVE CONTROL

NEGATIVE CONTROL

FALSE POSITIVE

- ***CONTAMINATION***
- ***PRECISE DNA MAP***
- ***AMPLIFICATION OF A NONCAUSATIVE (BYSTANDER) ORGANISM***
- ***AMPLIFICATION OF NUCLEIC ACID FROM A LATENT INFECTION***
- ***BLOODY TAP (CSF)***

FALSE NEGATIVE

- ***FRAGMENTED DNA***
- ***MUTATION IN TARGET SEQUENCE***
- ***INSUFFICIENT SAMPLE***
- ***BLOODY TAP (CSF)***

Molecular tests for encephalitis

Etiology	Availability*	When inclusion of NAAT is indicated	Preferred testing method(s)•
Bacteria			
<i>Coxiella burnetii</i> (Q fever)	Yes	When clinically suspected	NAAT, serology
<i>Listeria</i> spp	Limited	Rarely	Culture +/- NAAT, serology
<i>Mycobacterium tuberculosis</i> Δ	Yes	Potentially	AFB stain, culture, histologic exam
<i>Mycoplasma pneumoniae</i>	Yes	When clinically suspected	Serology +/- NAAT of alternative sites (eg, respiratory)
Viruses			
Adenoviruses	Yes	Rarely	Testing of alternative sites (eg, respiratory) +/- CSF
Arboviruses	Limited	Rarely	Serology
Enteroviruses	Widespread	When clinically suspected	NAAT
Human herpesvirus 6 (HHV-6)	Yes	When clinically suspected	NAAT, preferably quantitative
Herpes simplex virus (HSV)	Widespread	When clinically suspected	NAAT
Influenza	Yes	Rarely	Testing of alternative sites (eg, respiratory) +/- CSF
Lymphocytic choriomeningitis virus (LCM)	Limited	Rarely	Serology
Mumps	Limited	Rarely	History, culture, serology
Rabies◊	Limited (CDC)	When clinically suspected	Combination of serology, biopsy, NAAT
Varicella zoster virus (VZV)	Yes	When clinically suspected	NAAT
West Nile Virus§	Yes	Rarely (unless immunodeficient)	Serology
Fungal			
<i>Cryptococcus</i>	Limited	No	Antigen detection, culture
Other	Limited	No	Culture, serology, histologic exam
Spirochetes			
<i>Rickettsia</i> ¥	Limited	Occasionally	Serology
Parasites			
Microsporidia	Limited	Rarely	Serology, stains, histologic exam

PPV: positive predictive value; CDC: Centers for Disease Control and Prevention; NAAT: nucleic acid amplification testing; CSF: cerebrospinal fluid; AFB: acid fast bacilli.

* Widespread: readily available; Yes: consistently available, but not yet common; Limited: one or two specialized laboratories (eg, Centers for Disease Control and Prevention (CDC) or research groups).

• Test on CSF except where noted.

Δ Limited experience, presumably poor sensitivity, high PPV.

◊ In conjunction with other modalities.

§ Virus is usually cleared from blood and CSF prior to symptom onset.

¥ Limited experience from CSF.

Molecular tests for meningitis

Etiology	Availability*	When inclusion of NAAT is indicated	Preferred testing method(s)•
Bacteria			
Common pathogens (eg, <i>Streptococcus pneumoniae</i> , <i>Haemophilus influenzae</i>)	Limited	Gram's stain positive, culture negative; prior antibacterial therapy	Gram's stain; culture
Fastidious (<i>Mycoplasma</i> spp, <i>Tropheryma</i> spp, <i>Brucella</i> spp)	Yes	When clinically suspected	NAAT +/- culture
<i>Mycobacterium tuberculosis</i> Δ	Yes	Occasionally	AFB stain, culture
Prior antibiotic therapy◊	Investigational	Rarely	Culture prior to antibacterial therapy
Viruses			
Adenoviruses	Yes	Rarely	Testing of alternative sites (eg, respiratory) +/- CSF
Arboviruses	Limited	Rarely	Serology
Cytomegalovirus (CMV)	Yes	When clinically suspected	NAAT, preferably quantitative
Epstein Barr Virus (EBV)	Yes	When clinically suspected	NAAT, preferably quantitative
Enteroviruses	Widespread	When clinically suspected	NAAT
Human herpesvirus 6 (HHV-6)	Yes	When clinically suspected	NAAT, preferably quantitative
Herpes simplex virus (HSV)	Widespread	When clinically suspected	NAAT
Influenza	Yes	Rarely	Testing of alternative sites (eg, respiratory) +/- CSF
Lymphocytic choriomeningitis virus (LCM)	Limited	Rarely	Serology
Mumps	Limited	Rarely	Viral culture, serology
Parechoviruses§	Limited	Rarely	
Varicella zoster virus (VZV)	Yes	When clinically suspected	NAAT
West Nile Virus¥	Yes	Rarely (unless immunodeficient)	Serology
Rickettsia‡	Limited	Occasionally	Serology
Spirochetes			
<i>Leptospira</i>	Limited	Rarely	Serology
<i>Borrelia burgdorferi</i> (Lyme)	Yes	Yes	Serology, NAAT
<i>Treponema pallidum</i> (syphilis)	Limited	No	Serology, CSF VDRL
Fungal			
<i>Cryptococcus</i>	Limited	No	Antigen detection, culture
Other	Limited	Rarely	Culture, serology
Parasites	Limited	Rarely	Serology, histologic exam

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• Test on CSF except where noted.

Δ Poor sensitivity, high PPV, rapid.

◊ 16s rDNA "Universal" PCR.

§ Not detected by most enterovirus assays.

¥ Virus is usually cleared from blood and CSF prior to symptom onset.

‡ Limited experience from CSF.

Molecular tests for infectious causes of transverse myelitis

Etiology	Availability*	When inclusion of NAAT is indicated	Preferred testing method(s)•
Bacteria			
Mycoplasma spp	Yes	When clinically suspected	NAAT, serology
Mycobacterium tuberculosis Δ	Yes	Potentially	AFB stain, culture, histologic exam
Viruses			
Cytomegalovirus (CMV)	Yes	When clinically suspected	NAAT, preferably quantitative
Epstein Barr Virus (EBV)	Yes	When clinically suspected	NAAT, preferably quantitative
Enteroviruses	Widespread	When clinically suspected	NAAT
Herpes simplex virus (HSV)	Widespread	When clinically suspected	NAAT
Mumps	Limited	Rarely	History, viral culture, serology
Varicella zoster virus (VZV)	Yes	When clinically suspected	Molecular
West Nile Virus \diamond	Yes	Rarely (unless immunodeficient)	Serology
Spirochetes			
Treponema pallidum (syphilis)	Limited	No	Serology, CSF VDRL
Parasites			
Schistosomiasis	Limited	Rarely	Serology, histologic exam

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• Test on CSF except where noted.

Δ Limited experience, presumably poor sensitivity, high PPV.

\diamond Virus is usually cleared from blood and CSF prior to symptom onset.

Molecular tests for infectious causes of intracranial mass lesions

Etiology	Availability*	When inclusion of NAAT is indicated	Preferred testing method(s)•
Bacteria			
Abscess Δ	Limited	Gram's stain positive, culture negative; prior antibacterial therapy	Gram's stain, culture prior to antibacterial therapy
Mycobacterium tuberculosis \diamond	Yes	Potentially	AFB stain, culture, histologic exam
Viruses			
Epstein Barr Virus (EBV), primary central nervous system lymphoma (PCNSL)	Yes	Yes	NAAT, preferably quantitative
JC virus, progressive multifocal leukoencephalopathy (PML)	Yes	Yes	NAAT, preferably quantitative
Spirochetes			
Treponema pallidum (syphilis)	Limited	No	Serology, CSF VDRL
Fungal			
Cryptococcus	Limited	No	Antigen detection, culture
Other	Limited	Rarely	Culture, serology, histologic exam
Parasites			
	Limited	Rarely	Stains, Serology, histologic exam

PPV: positive predictive value; PCR: polymerase chain reaction; CDC: Centers for Disease Control and Prevention; NAAT: nucleic acid amplification testing; CSF: cerebrospinal fluid; AFB: acid fast bacilli.

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• Testing on brain mass tissue.

Δ 16s rDNA "Universal" PCR.

\diamond Limited experience, presumably poor sensitivity, high PPV.

Major indication in practice

- *HSV ENCEPHALITIS*
- *TB MENINGITIS*
- *VIRAL LOAD*

HIV

HCV

EBV



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