Table 8-5 Special Techniques for Diagnosing Infectious Agents

Techniques	Infectious Agents
Gram stain	Most bacteria
Acid-fast stain	Mycobacteria, nocardiae (modified)
Silver stains	Fungi, legionellae, *Pneumocystis*
Periodic acid-Schiff	Fungi, amebae
Mucicarmine	Cryptococci
Giemsa	*Campylobacter*, leishmaniae, malaria parasites
Antibody stains	All classes
Culture	All classes
DNA probes	All classes

sections (e.g., the inclusion bodies formed by CMV and herpes simplex virus [HSV]; bacterial clumps, which usually stain blue; *Candida* and *Mucor* among the fungi; most protozoans; and all helminths). Many infectious agents, however, are best visualized by special stains that identify organisms on the basis of particular characteristics of their cell wall or coat—Gram, acid-fast, silver, mucicarmine, and Giemsa stains—or by staining with specific antibodies (Table 8-5). Regardless of the staining technique, organisms are typically easiest to identify at the advancing edge of a lesion rather than at its center, particularly if there is necrosis. Acute infections can be diagnosed serologically by detecting pathogen-specific antibodies in the serum. The presence of specific IgM antibody shortly after the onset of symptoms is often diagnostic. Alternatively, specific antibody titers can be measured during the early, acute infection and again 4-6 weeks later during the convalescent period; a four-fold rise in titer is usually considered diagnostic.

Nucleic acid amplification tests, such as polymerase chain reaction (PCR) and transcription-mediated amplification, are increasingly being used for rapid identification of microbes. These molecular diagnostic assays have become routine for diagnosis of gonorrhea, chlamydial infection, tuberculosis, and herpes encephalitis. In some cases, molecular assays are much more sensitive than conventional testing. PCR testing of cerebrospinal fluid (CSF) for HSV encephalitis has a sensitivity of about 80%, while viral culture of CSF has a sensitivity of less than 10%. Similarly, nucleic acid testing for genital *Chlamydia* detects 10% to 30% more infections than does conventional *Chlamydia* culture. In other cases, such as gonorrhea, the sensitivity of nucleic acid testing is similar to that of culture. In people infected with HIV, quantification of HIV RNA is an important guide to management of antiretroviral therapy. The management of HBV and HCV infections is similarly guided by nucleic acid–based viral quantification or typing to predict resistance to antiviral drugs. Mass spectroscopy is another technique that identifies specific components of an infectious agent by size and charge distribution and can allow for the rapid identification of cultured bacteria.

This concludes our discussion of the general principles of the pathogenesis and pathology of infectious disease. We now turn to specific infections caused by viruses, bacteria, fungi, and parasites, and focuses on their *pathogenic mechanisms* and *pathologic changes* rather than details of clinical features, which are available in clinical textbooks. Infections that typically involve a specific organ are discussed in other chapters.

Viral Infections

Viruses are the cause of many clinically important acute and chronic infections, which may affect virtually every organ system (Table 8-6).

Acute (Transient) Infections

The viruses that cause transient infections are structurally heterogeneous, but all elicit effective immune responses that eliminate the pathogens, limiting the durations of the infections. However, specific viruses exhibit widely differing degrees of genetic diversity, a variable that has an important impact on the susceptibility of the host to re-infection by viruses of the same type. The mumps virus, for example, has only one genetic subtype and infects people only once, whereas other viruses, such as influenza viruses, can repeatedly infect the same individual because

Table 8-6 Selected Human Viruses and Viral Diseases

Organ System	Species	Disease
Respiratory	Adenovirus	Upper and lower respiratory tract infections, conjunctivitis, diarrhea
	Rhinovirus	Upper respiratory tract infection
	Influenza viruses A, B	Influenza
	Respiratory syncytial virus	Bronchiolitis, pneumonia
Digestive	Mumps virus	Mumps, pancreatitis, orchitis
	Rotavirus	Childhood gastroenteritis
	Norovirus	Gastroenteritis
	Hepatitis A virus	Acute viral hepatitis
	Hepatitis B virus	Acute or chronic hepatitis
	Hepatitis D virus	With HBV, acute or chronic hepatitis
	Hepatitis C virus	Acute or chronic hepatitis
	Hepatitis E virus	Enterically transmitted hepatitis
Systemic with skin eruptions	Measles virus	Measles (rubeola)
	Rubella virus	German measles (rubella)
	Varicella-zoster virus	Chickenpox, shingles
	Herpes simplex virus 1	Oral herpes ("cold sore")
	Herpes simplex virus 2	Genital herpes
Systemic with hematopoietic disorders	Cytomegalovirus	Cytomegalic inclusion disease
	Epstein-Barr virus	Infectious mononucleosis
	HIV-1 and HIV-2	AIDS
Arboviral and hemorrhagic fevers	Dengue virus 1-4	Dengue hemorrhagic fever
	Yellow fever virus	Yellow fever
Skin/genital warts	Papillomavirus	Condyloma; cervical carcinoma
Central nervous system	Poliovirus	Poliomyelitis
	JC virus	Progressive multifocal leukoencephalopathy (opportunistic)