

## Laboratory diagnosis of viruses

There are five approaches to the diagnosis of viral diseases by the use of clinical specimens:

- (1) identification of the virus in cell culture.
- (2) microscopic identification directly in the specimen.
- (3) serologic procedures to detect a rise in antibody titer or the presence of IgM antibody.
- (4) detection of viral antigens in blood or body fluids.
- (5) detection of viral nucleic acids in blood or the patient's cells.

### Identification in Cell Culture

- The presence of a virus in a patient's specimen can be detected by seeing a "cytopathic effect" (CPE) in cell culture. CPE is not specific (i.e., many viruses cause it). A specific identification of the virus usually involves an antibody-based test such as fluorescent antibody, complement fixation, or enzyme-linked immunosorbent assay (ELISA).

### Microscopic Identification

- **Inclusion bodies**, formed by aggregates of many virus particles, can be seen in either the nucleus or cytoplasm of infected cells. They are not specific. Two important examples are the nuclear inclusions formed by certain herpesviruses and the cytoplasmic inclusions formed by rabies virus (Negri bodies).
- **Multinucleated giant cells** are formed by several viruses, notably certain herpesviruses, respiratory syncytial virus, and measles virus.
- Fluorescent antibody staining of cells obtained from the patient or of cells infected in culture can provide a rapid, specific diagnosis.

- Electron microscopy is not often used in clinical diagnosis but is useful in the diagnosis of certain viruses, such as Ebola virus, that have a characteristic appearance and are dangerous to grow in culture.

### **Serologic Procedures**

- The presence of IgM can be used to diagnose current infection.
- The presence of IgG cannot be used to diagnose current infection because the antibody may be due to an infection in the past. As a result, an acute and convalescent serum sample should be analyzed. An antibody titer that is fourfold or greater in the convalescent serum sample compared with the acute sample can be used to make a diagnosis.

### **Detection of Viral Antigens & Nucleic Acids**

- The presence of viral proteins, such as p24 of HIV and hepatitisB surface antigen, is commonly used in diagnosis.
- The presence of viral DNA or RNA is increasingly becoming the "gold standard" in viral diagnosis. Labeled probes are highly specific, and results are rapidly obtained. Small amounts of viral nucleic acids can be amplified using reverse transcriptase to produce amounts detectable by the probes. An important example is the "viral load" assay of HIV RNA.

### **Clinical viruses**

## **DNA ENVELOPED VIRUSES**

### **Herpesviruses**

These viruses are noted for their ability to cause latent infections. This family includes:

(1) Herpes simplex virus types 1 and 2, which cause painful vesicles on the face and genitals, respectively.

(2) varicella-zoster virus, which causes varicella (chickenpox) typically in children and, when it recurs, zoster (shingles).

(3) cytomegalovirus, an important cause of congenital malformations.

(4) Epstein–Barr virus, which causes infectious mononucleosis.

(5) human herpesvirus 8, which causes Kaposi’s sarcoma.

### **Hepatitis B Virus**

This virus is one of the important causes of viral hepatitis. In contrast to hepatitis A virus (an RNA nucleocapsid virus), hepatitis B virus causes a more severe form of hepatitis, results more frequently in a chronic carrier state, and is implicated in the induction of hepatocellular carcinoma, the most common cancer worldwide.

### **Poxviruses**

Poxviruses are the largest and most complex of the viruses. The disease smallpox has been eradicated by effective use of the vaccine. Molluscum contagiosum virus is the only poxvirus that causes human disease in the United States at this time.

## **DNA NONENVELOPED VIRUSES**

### **Adenoviruses**

These viruses are best known for causing upper and lower respiratory tract infections, including pharyngitis and pneumonia.

### **Papillomaviruses**

These viruses cause papillomas on the skin and mucous membranes of many areas of the body. Some types are implicated as a cause of cancer (e.g., carcinoma of the cervix).

### **Parvovirus B19**

This virus causes “slapped cheeks” syndrome, hydrops fetalis, and severe anemia, especially in those with hereditary anemias such as sickle cell anemia.