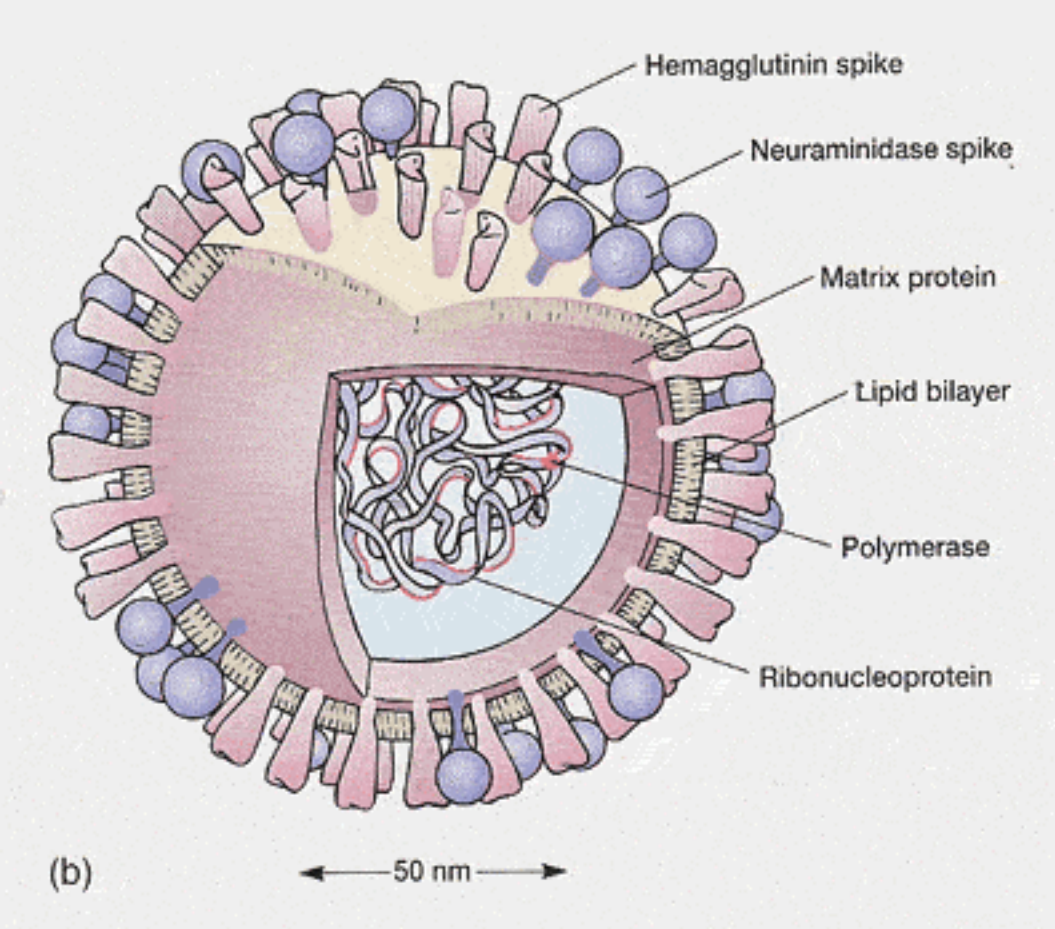
Table 39–2. Differences between orthomyxoviruses and paramyxoviruses.

Property	Orthomyxo-viruses	Paramyxo-viruses
Diseases caused in humans	Influenza types A, B, and C	Parainfluenza 1–4 infections, respiratory syncytial disease, mumps, measles
Genome organization	Single-stranded RNA in eight pieces	Single-stranded RNA in a single piece
Inner ribonucleoprotein helix	9 nm in diameter	18 nm in diameter
RNA in nucleocapsid	RNase-sensitive	RNase-resistant
Fusion of virus with cell	Endosome	Plasma membrane
Transcription of viral RNA	Host cell nucleus	Host cell cytoplasm
Genetic reassortment	Frequent	Rare
Rate of antigenic change	High	Low

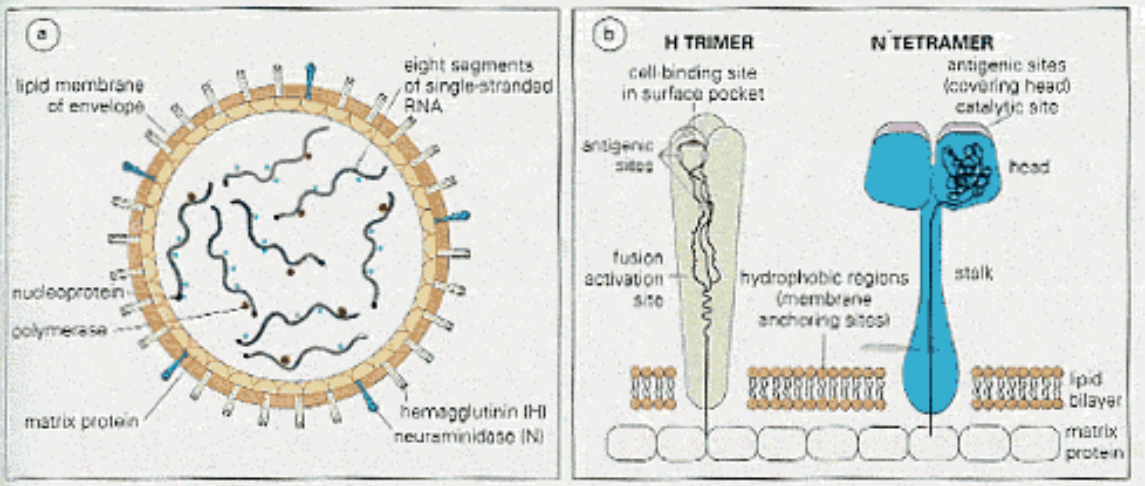
Table 39–1. Important properties of orthomyxoviruses.

Virion: Spherical, pleomorphic, 80–120 nm in diameter (helical nucleocapsid, 9 nm)
Composition: RNA (1%), protein (73%), lipid (20%), carbohydrate (6%)
Genome: Single-stranded RNA, segmented (eight molecules), negative-sense, total 13.6 kb overall size
Proteins: Nine structural proteins
Envelope: Contains viral hemagglutinin (HA) and neuraminidase (NA) proteins
Replication: Nuclear transcription; capped 5′ termini of cellular RNA scavenged as primers; particles mature by budding from plasma membrane
Outstanding characteristics:
Genetic reassortment is common
Influenza viruses cause worldwide epidemics

20b



20c



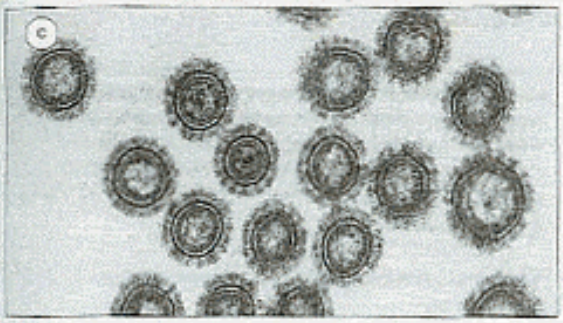


Fig. 17.14 The influenza A virus particle (a), with detail enlarged (b) to show surface haemagglutinin (H) and neuraminidase (N). Each particle has approximately 500 H spikes, which bind to the host cell and fuse the viral envelope to the cell's plasma membrane to initiate infection, and approximately 100 N spikes, which release the virus from the cell surface. Nucleoprotein and polymerase proteins are closely associated with RNA segments to form ribonucleoprotein (RNP). The N tetramer is propeller-shaped as viewed from the end. Detail of only one unit of H trimer and N tetramer is shown. The three-dimensional structure is known from X-ray crystallographic analysis. Electron micrograph (c) shows sectioned influenza virus particles. ×300 000. (Courtesy of D Hockley.)

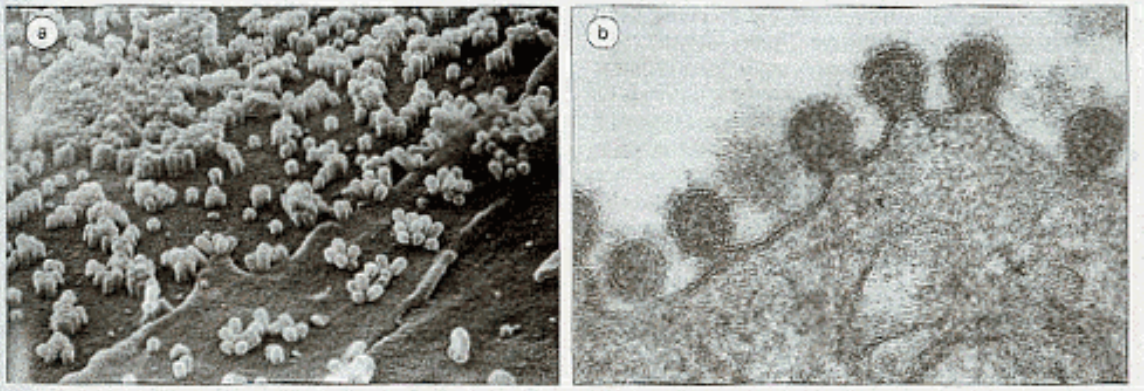


Fig. 17.15 Influenza virus budding from the surface of an infected cell. (a) Scanning electron micrograph. ×27 000. (b) In section. ×350 000. (Courtesy of D Hockley.)

20d

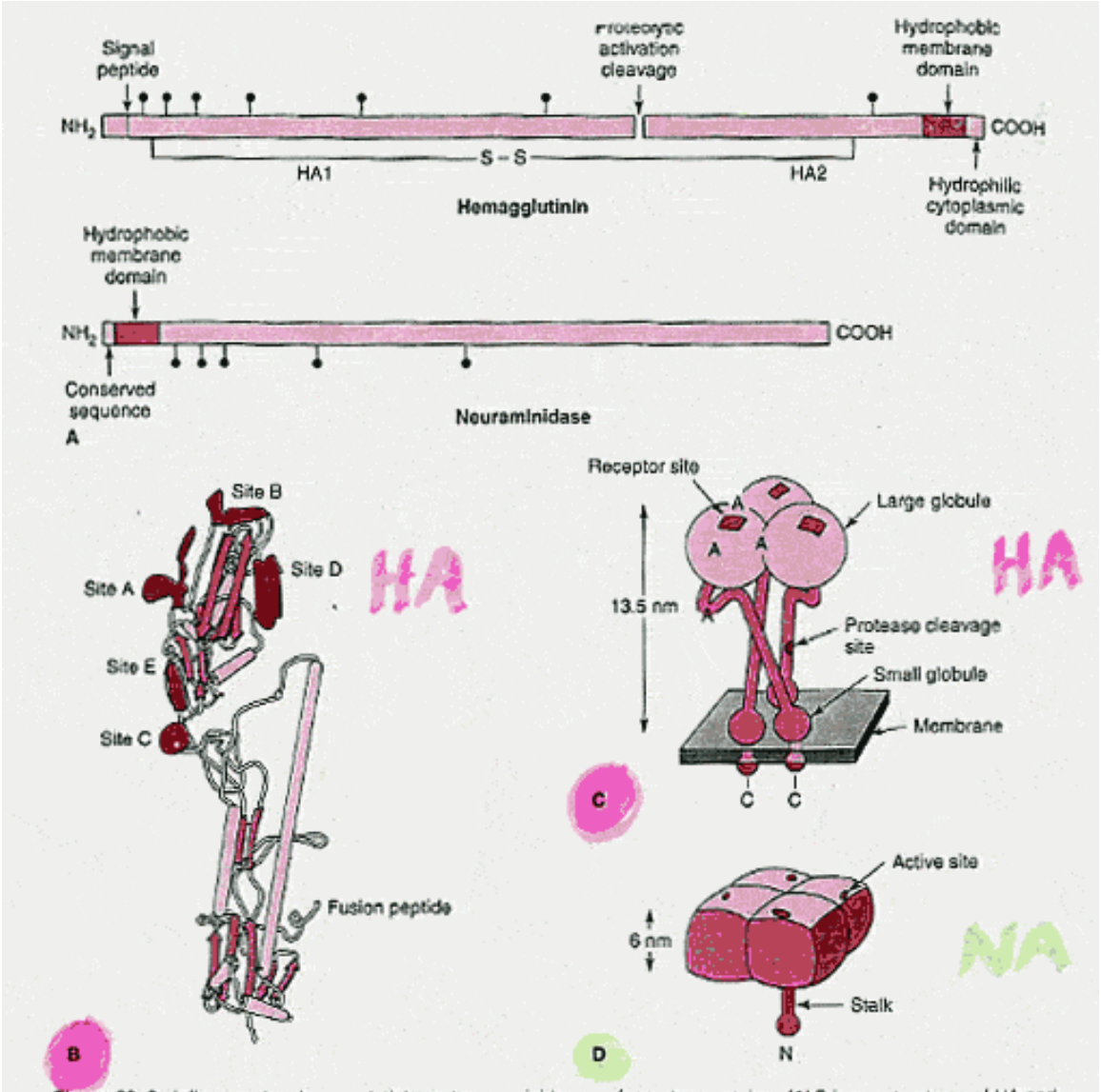
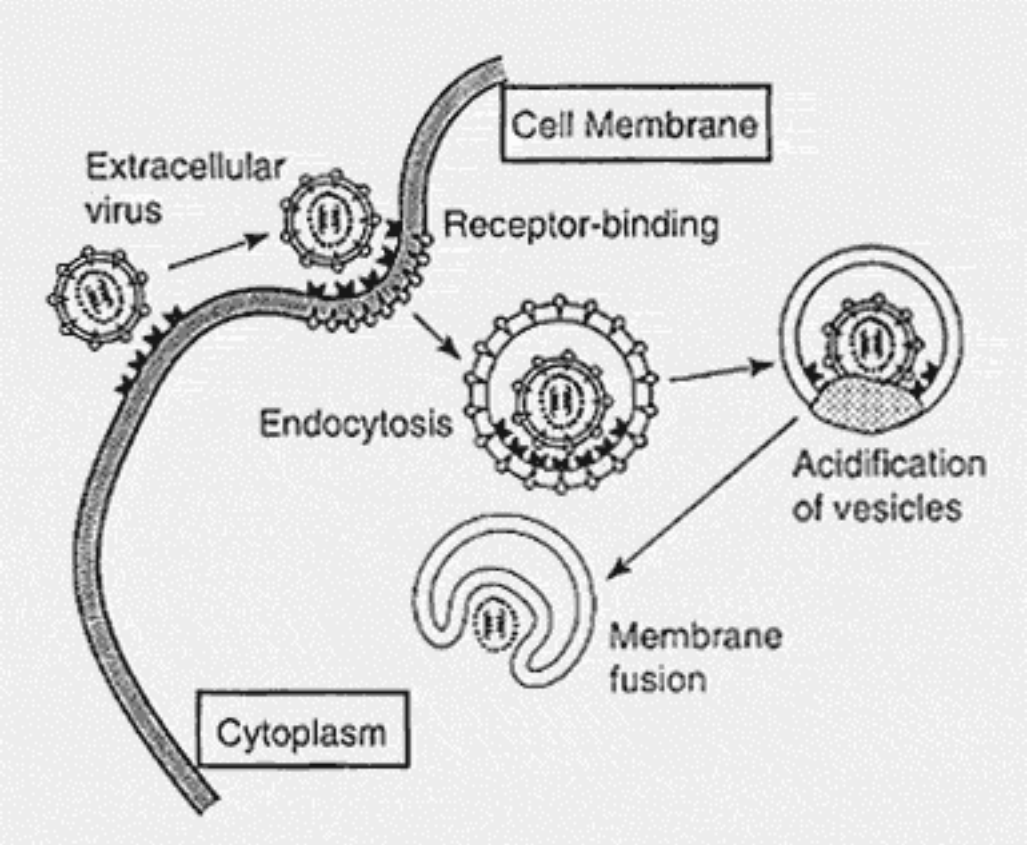
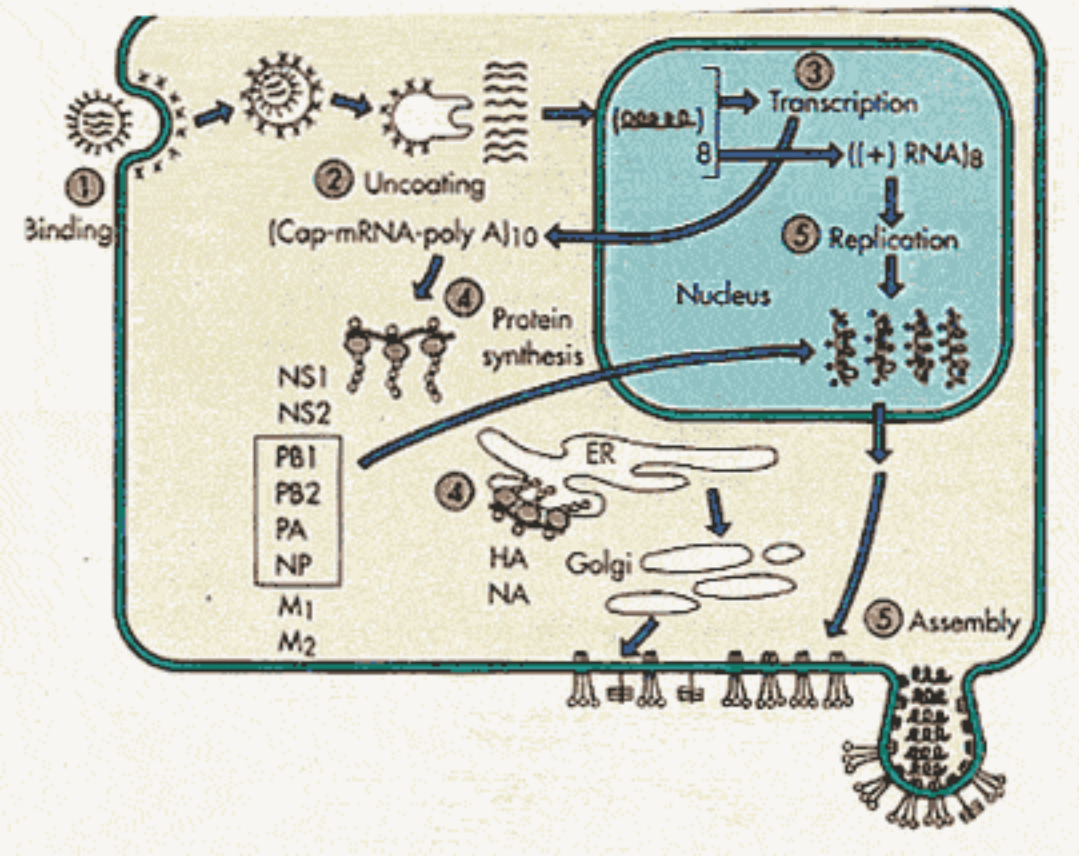


Figure 39–2. Influenza virus hemagglutinin and neuraminidase surface glycoproteins. ***(A)*** Primary structures of HA and NA polypeptides. The cleavage of HA into HA1 and HA2 is necessary for virus to be infectious. HA1 and HA2 remain linked by a disulfide bond (S–S). No posttranslational cleavage occurs with NA. Carbohydrate attachment sites (🍴) are shown. The hydrophobic amino acids that anchor the proteins in the viral membrane are located near the carboxyl terminal of HA and the amino terminal of NA. ***(B)*** Folding of the HA1 and HA2 polypeptides in an HA monomer. Five major antigenic sites (sites A–E) that undergo change are shown as shaded areas. The amino terminal of HA2 provides fusion activity (fusion peptide). The fusion particle is buried in the molecule until it is exposed by a conformational change induced by low pH. ***(C)*** Structure of the HA trimer as it occurs on a virus particle or the surface of infected cells. Some of the sites involved in antigenic variation are shown (A). Carboxyl terminal residues (C) protrude through the membrane. ***(D)*** Structure of the NA tetramer. Each NA molecule has an active site on its upper surface. The amino terminal region (N) of the polypeptides anchors the complex in the membrane. (Redrawn, with permission, from ***[A, B]*** Murphy BR, Webster RG: Influenza viruses, p 1179, and ***[C, D]*** Kingsbury DW: Orthomyxo- and paramyxoviruses and their replication, p 1157. In: *Virology*. Fields BN et al [editors]. Raven Press, 1985.)

20e


Cell Membrane
Extracellular virus
Receptor-binding
Endocytosis
Acidification of vesicles
Membrane fusion
Cytoplasm
20f


1
Binding
2 Uncoating
(Cap-mRNA-poly A)10
3 Transcription
8
((+) RNA)8
5 Replication
Nucleus
4 Protein synthesis
NS1
NS2
PB1
PB2
PA
NP
M1
M2
4
ER
HA
NA
Golgi
5 Assembly
20g

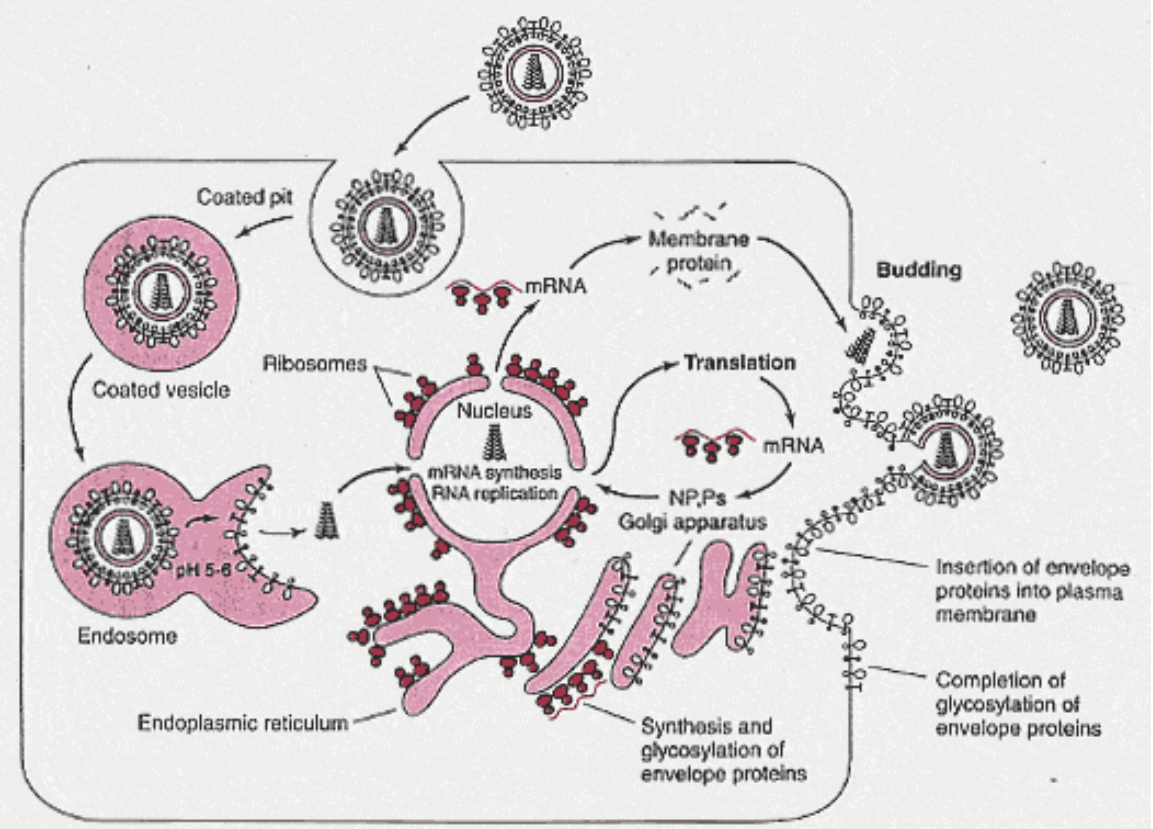


Figure 39–4. Schematic diagram of the life cycle of influenza virus. (Reproduced, with permission, from Lamb RA, Krug RM: Orthomyxoviridae: The viruses and their replication. In: *Fields Virology*, 3rd ed. Fields BN et al [editors]. Lippincott-Raven, 1996.)

20h

DESIGNATION OF VIRAL SUBTYPES

A/Texas/1/77(H3N2)

A = virus type

Texas = city, state, or country of first isolation

1 = Strain

77 = year of recovery (1977)

(H3N2) = Hemagglutinin & Neuraminidase subtypes

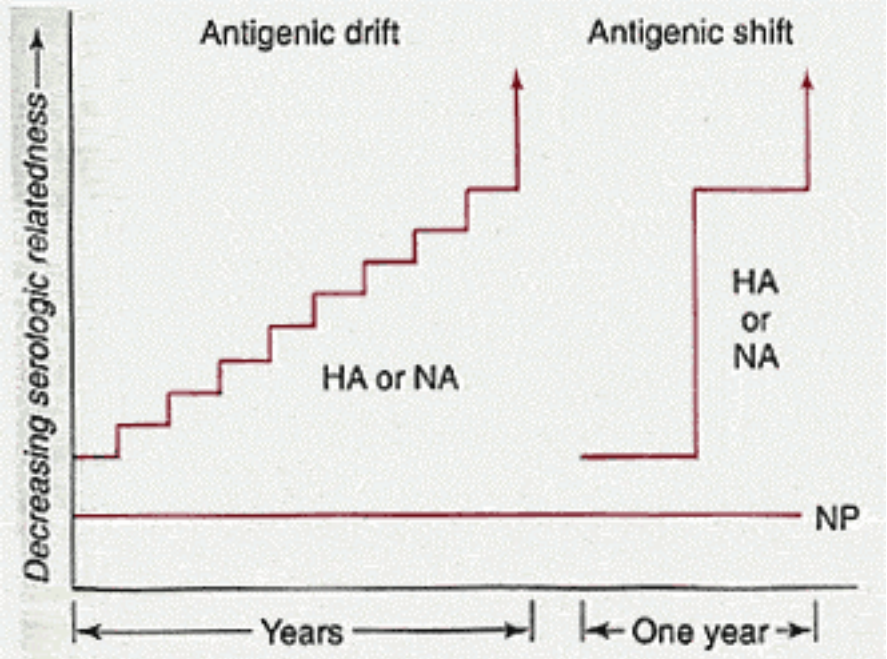
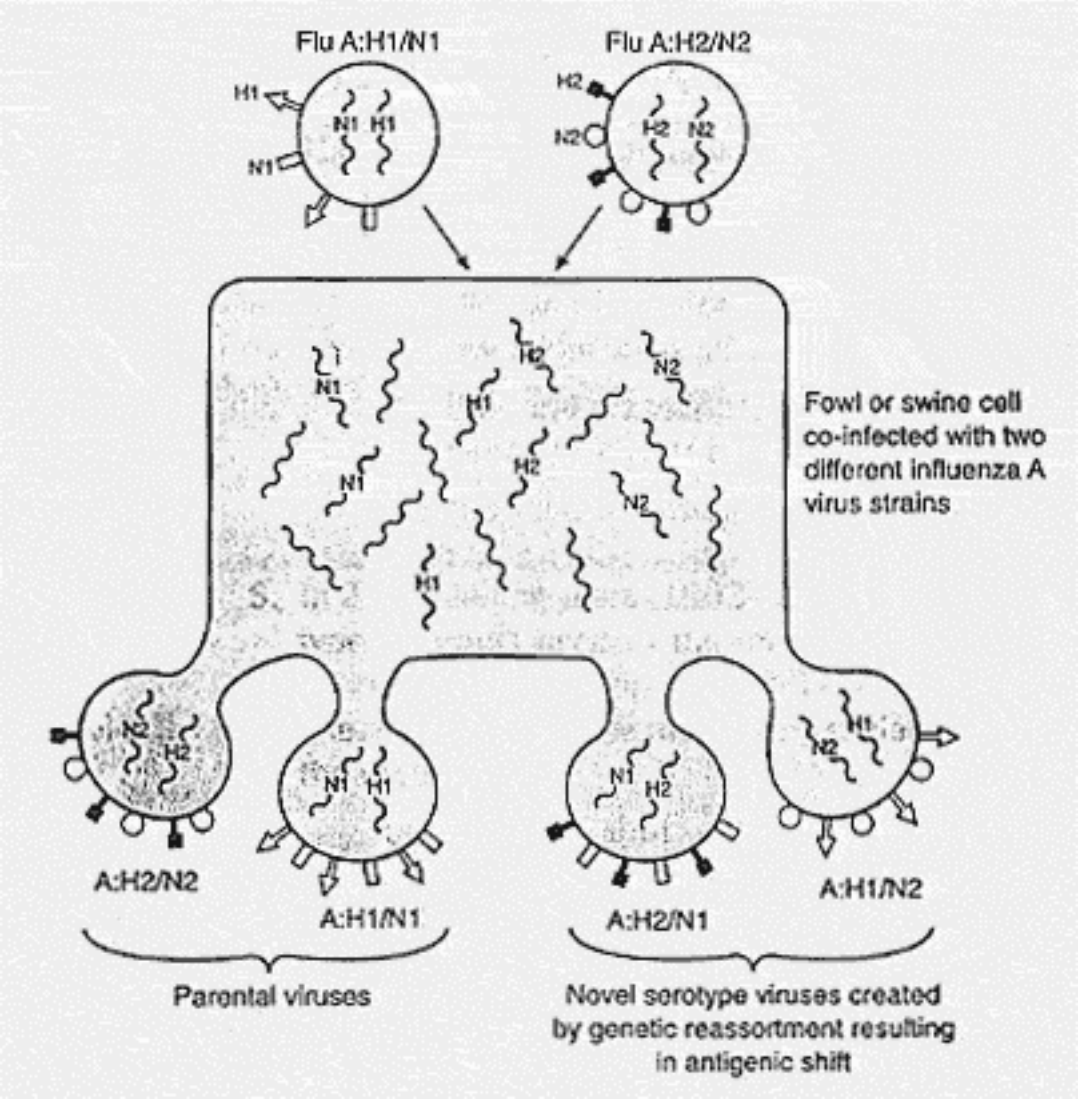
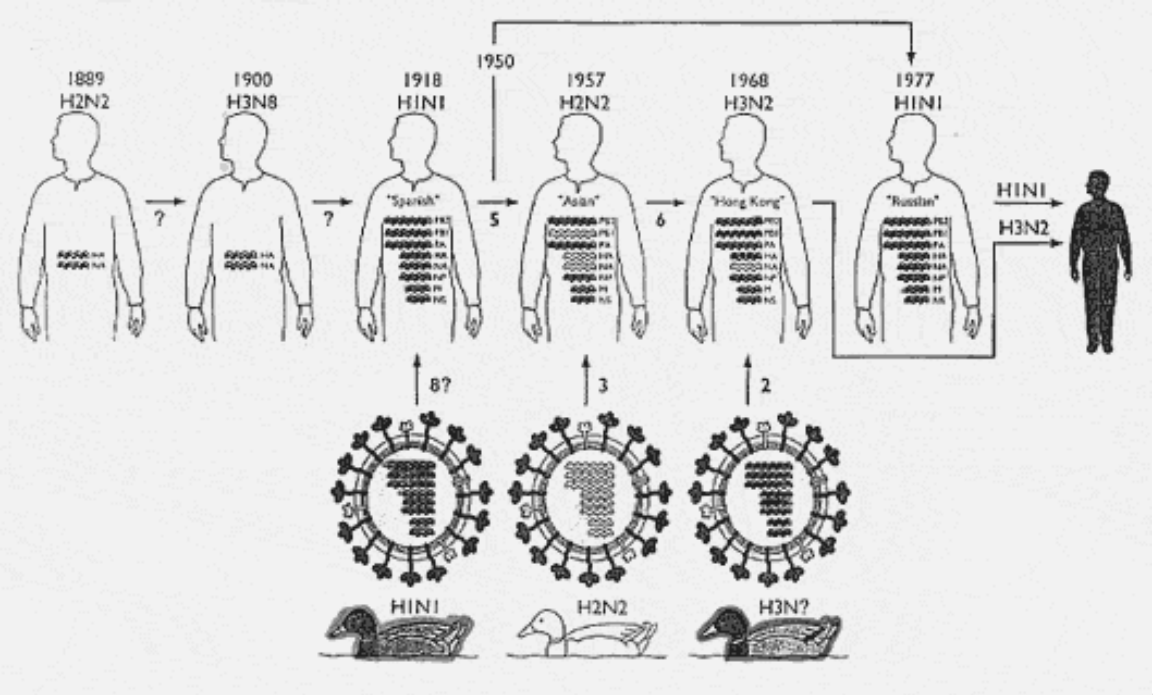


Figure 39–3. Principles of antigenic drift and antigenic shift that account for antigenic changes in the two surface glycoproteins (HA and NA) of influenza virus. Antigenic drift is a gradual change in antigenicity due to point mutations that affect major antigenic sites on the glycoprotein. Antigenic shift is an abrupt change due to genetic reassortment with an unrelated strain. Changes in HA and NA occur independently. Internal proteins of the virus, such as the nucleoprotein (NP), do not undergo such antigenic changes.


Flu A:H1/N1
Flu A:H2/N2
H1
N1
N1 H1
H2
N2
H2 N2
Fowl or swine cell co-infected with two different influenza A virus strains
A:H2/N2
A:H1/N1
A:H2/N1
A:H1/N2
Parental viruses
Novel serotype viruses created by genetic reassortment resulting in antigenic shift
20k



20l

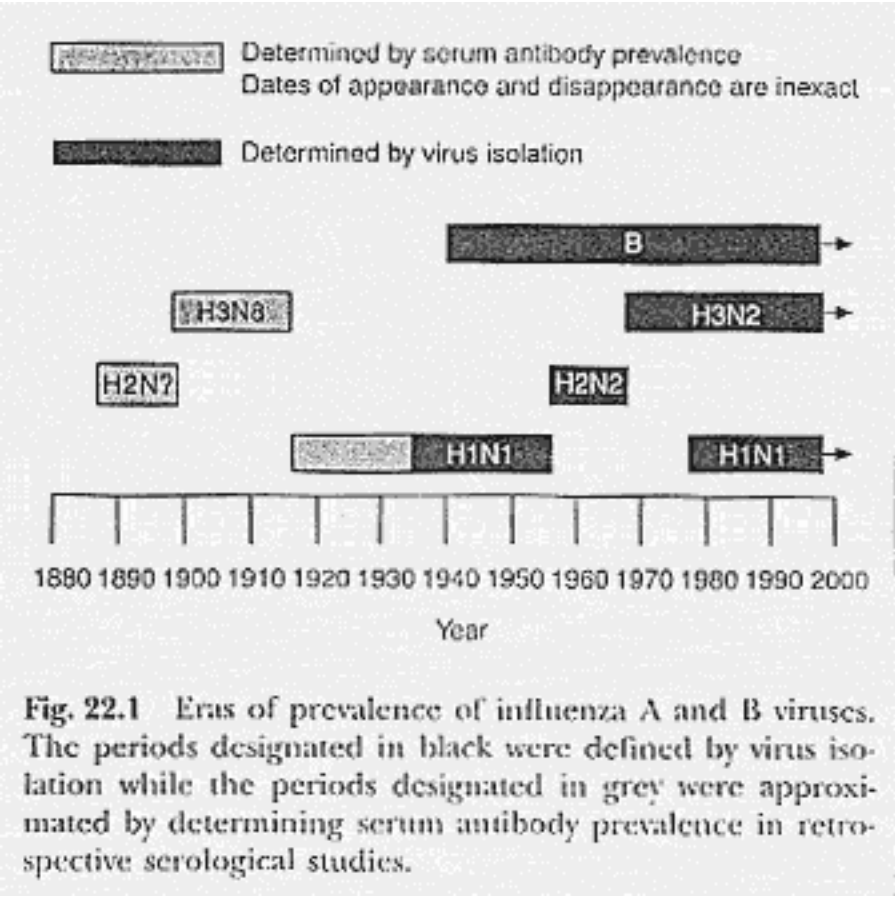
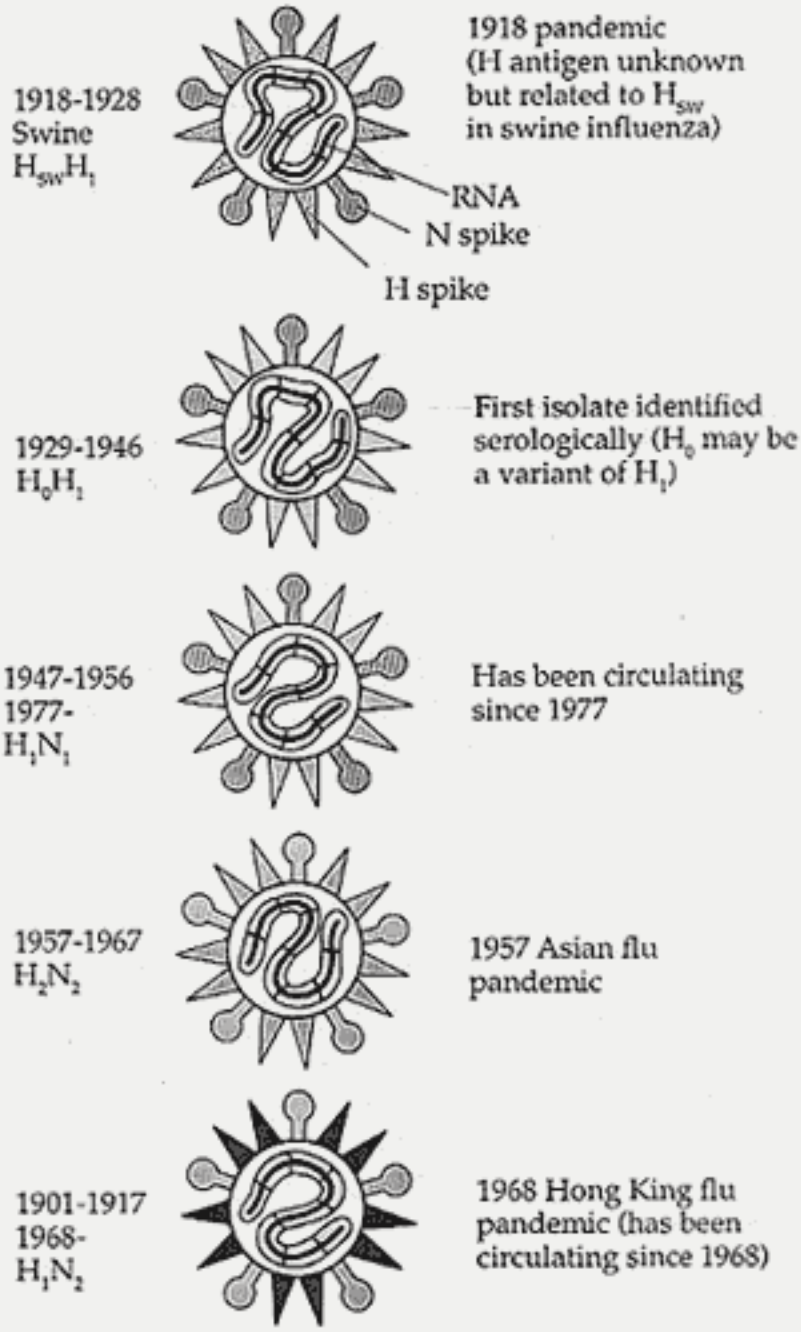


Fig. 22.1 Eras of prevalence of influenza A and B viruses. The periods designated in black were defined by virus isolation while the periods designated in grey were approximated by determining serum antibody prevalence in retrospective serological studies.

20m

Differences among influenza viruses (Figure 24.12)



20n

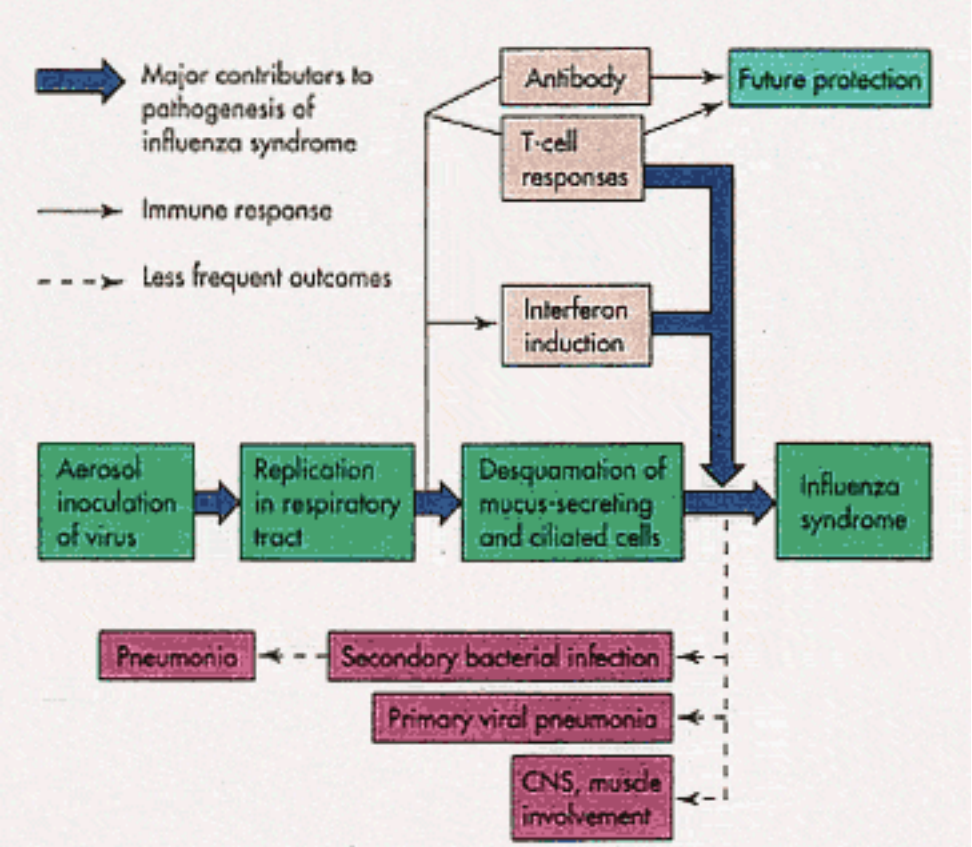
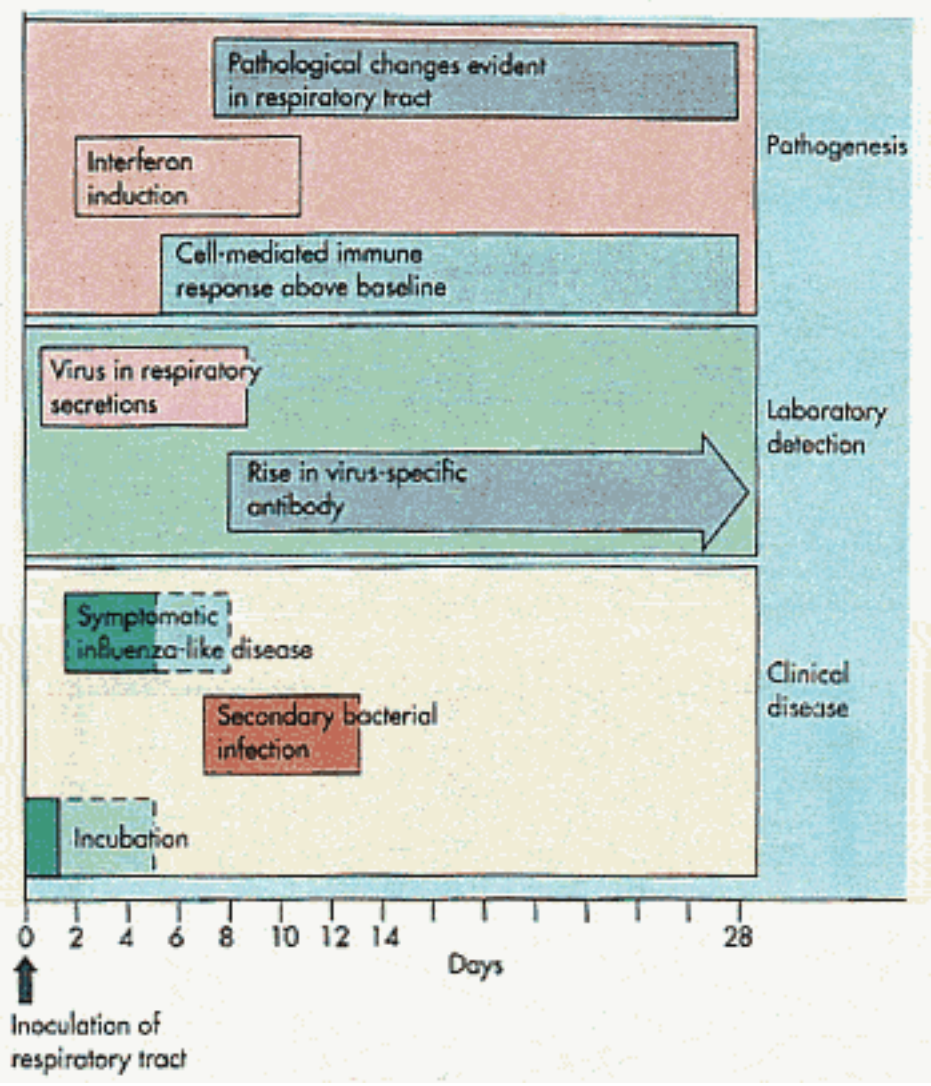


FIGURE 56-3 Pathogenesis of influenza A virus. The symptoms of influenza are caused by viral pathology and immunopathology, but the infection may promote secondary bacterial infection. *CNS*, Central nervous system.

20o


Pathological changes evident in respiratory tract
Interferon induction
Cell-mediated immune response above baseline
Pathogenesis
Virus in respiratory secretions
Rise in virus-specific antibody
Laboratory detection
Symptomatic influenza-like disease
Secondary bacterial infection
Incubation
Clinical disease
0 2 4 6 8 10 12 14 28
Days
Inoculation of respiratory tract

20p