30. SUMMARY

CHAPTER 1 STEPS IN THE DEVELOPMENT OF VIRUS RESEARCH

Viruses as disease-causing agents.
Viruses existed even before the dawn of human history.
Attempts to immunize humans against smallpox and measles as early as the eighteenth century.
The concept *virus*, meaning poison, was initiated by Edward Jenner in 1798.
The concept of virus during the period of Pasteur (end of nineteenth century) was that of a filterable agent not visible in the light microscope.
Discovery in 1887 that the mosaic disease of tobacco plants is caused by a virus.
Discovery in 1898 that foot-and-mouth disease in cattle is caused by a virus.
Investigations on filtration of homogenates of tumors revealed that viruses cause cancer.
Viruses infect bacteria: the discovery of the bacteriophages.
Viruses cause diseases in test animals.
Yellow fever virus (YFV) was attenuated by passage in chick embryos: development of the vaccine.
Viruses replicate in the infected host in selected tissues.
Animal viruses can replicate in isolated tissues in culture.
Plaque assay for animal viruses allowed quantitative analysis of viruses.
The electron microscope made possible the visualization of virus structure.
Viruses cause mouse leukemia.

Y. Becker, *Molecular Virology*

The molecular basis of virology is that the viral nucleic acids are the carriers of the viral genes.
Tobacco mosaic virus (TMV) genes are present in viral RNA.
Experimental evidence provided the proof that viral DNA genomes contain the viral genes.
The viral DNA is the template for mRNA for the synthesis of viral proteins.
Virus defined as a particle containing either DNA or RNA that carries all the viral genetic information.
Subviruses that include viroids are infectious agents.
Genetic engineering technology makes it possible to isolate and study individual genes.

CHAPTER 2 VIRUS CLASSIFICATION

The classification of viruses is an ongoing process.

CHAPTER 3 MOLECULAR CONSIDERATIONS OF VIRUS REPLICATION AND VIRUS-CELL INTERACTIONS.

Viruses are obligate parasites of cells.
Viral genes code for different groups of functional proteins.
The viral capsomeres assemble into capsids.
Virion formation requires capsid-nucleic acid interactions.
Cells can be transfected with naked viral nucleic acids.
Virions must be released from cells to initiate new infections.
Viruses are transferred from one host to another.
An infection starts with the attachment of virions to receptors in the cell membrane.
RNA viral genomes can serve as plus or minus nucleic acids.
The one-step growth cycle in vitro requires spontaneous infection of all cells.
Enzymes are contained in virions of some virus families.
The mechanisms utilized for virus replication in infected cells depend on the viral nucleic acid.
Cells respond differently to different viruses.

CHAPTER 4 GENES IN HUMAN CELLS DETERMINING VIRUS SUSCEPTIBILITY

Different genes in the human chromosomes determine the sensitivity of human cells to virus infection.

CHAPTER 5 THE POXVIRUS FAMILY

Relatedness between poxviruses can be determined by DNA-DNA reassociation techniques.
The DNA genome of the orthopoxviruses contains more than 150 genes.
Poxvirions contain structural proteins and enzymes.
The mechanism of cell infection with a poxvirus is a multistage process.

The virions are phagocytized by infected cells.
Uncoating of the virions leads to release of the viral cores.
Virus infection inhibits nuclear processes.
Expression of early viral genes leads to the synthesis of early viral mRNA molecules.
The biosynthesis of viral DNA takes place in discrete cytoplasmic sites.
Expression of late viral genes in infected cells takes place after viral DNA synthesis.
Morphogenesis of the poxvirions: the final step in virus infection of a cell.
Specific antipoxvirus agents inhibit or prevent virus infection.
Marboran is the prophylactic drug against smallpox.
Rifampicin and distamycin inhibit poxviruses.
Interferon inhibits virus replication.
Smallpox, a disease in humans, starts with a respiratory infection.
Differential diagnosis of the disease is important.
Virulent smallpox viruses in research laboratories constitute a danger around the world.
Humans are infected by monkeypox virus.
Animal poxviruses are yabavirus of monkeys and myxomatosis in rabbits.

CHAPTER 6 THE IRIDOVIRUS FAMILY

Iridoviruses include African swine fever virus, frog viruses, and lymphocystis virus in fish.

CHAPTER 7 THE HERPESVIRUS FAMILY

Viruses belonging to the herpesvirus family occur in numerous hosts.
The icosahedral virus capsid is made of 162 capsomeres.
The viral DNA is double-stranded.
DNAs of different members of the herpesvirus group differ in density.
The viral DNA contains repetitive sequences.
The virions contain subpopulations of viral DNA.
Viral DNA is infectious for permissive cells by transfection.
Partial homology exists between DNAs of different herpesviruses.
Virion proteins are antigenic.
Cloning of HSV-DNA restriction fragments in bacterial plasmids allows analysis of viral genes.
Herpesvirus replication in cells is controlled by the cell and the virus.
The viral DNA is uncoated by cellular enzymes.
Early transcription of viral DNA is carried out by the host cell RNA polymerase II.
Viral mRNA is transcribed from a particular group of genes in the viral DNA.
Virus infection causes the disaggregation of the nucleoli.
Synthesis of viral proteins is a process regulated by virus-coded proteins.
DNA binding proteins are involved in the synthesis of viral DNA.
A cellular gene function determines the initiation of viral DNA synthesis.

Synthesis of HSV DNA is semiconservative and initiates at three possible sites.
Replication of a viral DNA molecule takes 20 min.
Mutants of HSV defective in DNA synthesis are used to characterize the viral enzymes.
Recombinants between HSV-1 and HSV-2 were developed.
Defective HSV is due to an error in viral DNA biosynthesis.
HSV causes latent infections in humans and animals.
Inactivated HSV transforms cells in vitro.
Herpesviruses affect humans and animals and spread in the blood and along nerve axons.
HSV-2 is connected with cervical carcinoma.
HSV-coded thymidine kinase gene biochemically transforms TK^- cells.
Chemotherapy of herpesvirus infections with phosphonoacetic acid, IUdR, Ara-A, and acyclovir.
Herpesviruses like varicella-zoster and cytomegalovirus cause diseases in humans.
Epstein-Barr virus (EBV) is a ubiquitous virus associated with Burkitt's lymphoma (BL) and causes infectious mononucleosis in humans.
EBV receptors are found on human B lymphocytes.
EBV might have a role in human cancer.
Herpesvirus papio is a monkey virus related to EBV.
Herpesvirus saimiri and H. ateles cause malignant lymphomas in monkeys.
Herpes B virus is a latent monkey virus but causes fatal infections in man.
Pseudorabies is a herpesvirus that causes Aujesky's disease in pigs.
Herpesviruses infect cattle, horses, and dogs.
Herpesvirus in frogs causes Lucké renal carcinoma.
A herpesvirus from turkeys immunizes chickens against a herpesvirus that causes Marek's diseases (lymphoma and neural damage).

CHAPTER 8 THE ADENOVIRUS FAMILY

Human and mammalian adenoviruses belong to the genus mastadenovirus.
Adenoviruses of birds belong to the genus aviadenovirus.
The adenovirions are made up of 252 capsomeres.
The virions attach to the cell membrane and are incorporated into the cytoplasm by pinocytosis.
Adenovirus DNA is $20–25 \times 10^6$ daltons and is infectious.
There are at least five separate transcription units for early mRNA in the viral genome.
Intermediate and late mRNA synthesis are coupled to the onset of DNA replication.
Viral DNA synthesis marks the late phase of virus replication.
Virions assemble in the nuclei of infected cells.
Removal of arginine from the medium of infected cells results in abortion of virus replication.

Adenoviruses are divided into four subgroups on the basis of their oncogenicity for newborn hamsters.
Cells can be transformed by adenovirus DNA.
No evidence is available for specific integration sites for adenovirus DNA in the cell chromosomes.
Adenovirus-SV40 hybrid viruses appear when the two viruses infect the same cell.
Adenovirus type 7 can cause epidemic outbreaks of respiratory disease in different parts of the world.

CHAPTER 9 THE PAPOVAVIRUSES

Genus papillomavirus infects vertebrates and causes benign papillomas
Genus polyomavirus includes polyoma virus of mice, SV40 of monkeys, BK and JC viruses of man, and other related viruses.
The host cell determines the type of virus infection.
Viral DNA is superhelical and is a minichromosome.
The nucleotide sequence of SV40 was reported.
Under certain conditions of infection, SV40 DNA might contain cellular DNA.
Structural viral proteins and DNA-bound histones constitute the proteins of the virions.
The viral DNA contains two strands: one coding for early and the other for late functions.
Products of the early (E) genes are the T and t antigens.
Transcription of SV40 late (L) genes starts immediately after the initiation of DNA replication.
The transcription of polyoma virus DNA resembles that of SV40.
The initiation sequence for DNA replication is mapped in 0.67 map units and contains 27 base pairs that form a palindrome.
The synthesis of viral DNA is semiconservative and bidirectional.
Cells are transformed by SV40 as a result of viral DNA integration into chromosomal DNA.
SV40 is released from transformed cells by fusion with permissive cells.
SV40 mutants were isolated.
Polyoma viruses were isolated from brains of progressive multifocal leukoencephalopathy (PML) patients.
Papilloma virus causes human warts.

CHAPTER 10 HEPATITIS B VIRUS

The discovery of Australia antigen led to the discovery of hepatitis B virus in humans and related viruses in vertebrates.
The surface antigen of hepatitis B virus (HBsAg) is present in the blood of hepatitis patients.

The virion-like Dane particles in the patient's blood contain a circular DNA genome.
Primary hepatic carcinoma cells in humans contain integrated viral DNA in the cell chromosomes.

CHAPTER 11 THE PARVOVIRUS FAMILY

The genus parvovirus contains animal parvoviruses that are able to replicate without a helper virus.
The adeno-associated viruses require human or simian adenoviruses for their replication.
The genus densovirus contains insect viruses.
The genome of parvoviruses is a single-stranded DNA molecule.

CHAPTER 12 THE REOVIRUSES

The virions contain a fragmented double-stranded RNA genome.
Ten species of mRNA molecules are made in the infected cell by a virion-bound RNA polymerase.
Each mRNA species is translated to a viral protein.
The viral mRNA is the template for the double-stranded genome in the virions.
Rotaviruses cause gastroenteritis in humans.

CHAPTER 13 THE RHABDOVIRUSES

The genus vesiculovirus (vesicular stomatitis virus), genus lyssavirus (rabies virus), and genus sigmavirus (Drosophila σ virus) constitute the rhabdovirus family.
The rabies virions have a bullet-shaped structure.
When humans are bitten by rabid animals, virus is introduced into the wound and migrates to the nervous system.
A rabies vaccine prepared from virus-infected human fibroblasts inactivated by formaldehyde is used to immunize humans.
Vesicular stomatitis virus molecular structure and mode of replication was investigated.

CHAPTER 14 THE PARAMYXOVIRUSES

Genus paramyxovirus contains Newcastle disease virus (NDV) of birds, mumps virus of humans, and parainfluenza viruses.
Genus morbillivirus includes measles virus of humans.
Pneumovirus subgroup contains the respiratory syncytial virus of humans.
Two types of spikes are present on the envelope of paramyxoviruses: neuraminidase acid and hemagglutinin.
The virions attach to the neuraminic acid-containing receptor.
The virion genomic RNA has a sedimentation coefficient of 50S in sucrose gradients, but cytoplasmic viral RNA contains subgenomic information.

Arginine must be present in the medium of cells infected with NDV.
Incomplete virions are formed in the course of virus synthesis.
Paramyxoviruses cause persistent infections.
Several types of paramyxovirus mutants are known.
A number of human diseases are caused by paramyxoviruses.
Subacute sclerosing panencephalitis (SSPE) is associated with the presence of measles virus in the human brain.

CHAPTER 15 THE ORTHOMYXOVIRUSES

Genus influenzavirus contains influenza A, B, and C viruses.
The viral genome is RNA negative and is made up of eight genes—each on a separate, single-stranded RNA molecule.
The virions contain an RNA-dependent RNA polymerase responsible for mRNA synthesis.
The influenza virus hemagglutinin and neuraminidase genes were cloned in bacterial plasmids and their sequence determined.
The initiation of RNA synthesis is dependent on the host cell.
Incomplete defective virions (von Magnus effect) are formed.
Recombinants of influenza virus were constructed.
Influenza in man is a respiratory infection.
Inactivated influenza virus vaccines are available for use in man.
A new approach to the development of a vaccine: cloning of the viral hemagglutinin gene in bacterial plasmids.
Amantadine is a possible prophylactic drug (see chapter 24).

CHAPTER 16 THE ARENAVIRUSES

The virions contain cellular ribosomes.

CHAPTER 17 THE BUNYAVIRUSES

Single-stranded viruses with a circular fragmented genome.
The viral genome is divided into three minus circular molecules (L, M, S); ribonucleoprotein complexes can be isolated.
RNA-dependent RNA polymerase is present in the virions.
Diseases like RVF are transmitted by a mosquito-borne virus.

CHAPTER 18 THE PICORNAVIRUSES

The genus enterovirus includes human pathogens like poliovirus and Coxsackie virus.
The viral genome is RNA plus and serves as mRNA.
A gene in chromosome 19 of the human cell codes for the poliovirus receptor on the cell surface.
Synthesis of viral RNA is done by a virus-coded RNA polymerase.
Viral mRNA is monocistronic and is translated into a long peptide that is processed into structural peptides.

Phenotypic mixing occurs in cells infected with two picornaviruses.
Poliovirus still exists in nature; laboratory diagnosis of attenuated and virulent poliovirus strains is necessary.
Rhinoviruses cause the common cold in humans.
Foot-and-mouth disease virus in cattle and its prevention by vaccination.

CHAPTER 19 THE TOGAVIRUSES

Alphavirus, flavivirus, rubivirus, and pestivirus are the various genera of this family of RNA plus viruses.
Subgenomic mRNA species are found in infected cells.
Togaviruses include viruses like yellow fever, St. Louis encephalitis, and rubella.

CHAPTER 20 THE CORONAVIRUSES

These viruses affect pigs, rats, and mice.

CHAPTER 21 THE RETROVIRUSES

Oncovirinae, spumavirinae, and lentivirinae are the subfamilies.
The viral genome is made up of two hydrogen-bonded RNA^+ molecules.
Each RNA molecule contains four genes (gag-pol-env-onc).
The nucleotide sequence at the 5′ end includes a cap.
The nucleotides at the 3′ end include a unique sequence, a repeat sequence, and a poly(A) sequence.
The primer for the synthesis of viral DNA is $tRNA^{trp}$.
The RNA-dependent DNA polymerase is responsible for the synthesis of the double-stranded viral DNA.
The viral DNA resembles the bacterial transposons.
Viral RNA transcripts from the integrated viral DNA are produced by the cellular DNA-dependent RNA polymerase.
Several species of viral mRNA exist in the infected cell.
The integrated viral DNA can be infectious.
Retrovirus DNA can be incorporated into the germ line.
The H_2 histocompatibility locus might affect leukemogenesis.
Retroviruses have distinct evolutionary pathways.
Porcine retrovirus was acquired from an ancient rodent.
Monkey retrovirus originated from an ancient Asian rodent.
In avian sarcoma viruses (ASVs), the *src* gene is the transforming gene.
Endogenous viruses replicate only in chicken cells.
The viral gene *src* is closely related to the cellular gene *sarc*.
Endogenous retroviruses invaded the germ line of chickens.
The oncogene theory postulated that viral *onc* genes present in normal cells may cause cancer.
Mammalian type C retroviruses have been recognized in mice, hamsters, rats, cats, pigs, in several primates, and in humans.
Mouse genes determine sensitivity to leukemogenic viruses.

Radiation-induced leukemia virus (RadLV) is mouse-associated.
Mammary tumor virus (MTV) in female mice is transferred horizontally.
Feline leukemia virus (FeLV) was isolated from a lymphosarcoma in cats.
Bovine leukosis virus (BLV) was isolated from leukemic cattle.
Viral sequences in the cellular DNA of primates are related to sequences in baboons.
Infectious type C retroviruses were isolated from a gibbon ape and a woolly monkey.
Mason-Pfizer monkey virus was isolated from a breast tumor in a rhesus monkey.
Human retroviruses were isolated from human leukemic cells.
Sarcoma viruses are defective in their ability to replicate in infected cells and require a helper virus.
Human cellular *onc* genes are related to simian sarcoma transforming genes.

CHAPTER 22 UNCLASSIFIED VIRUSES: MARBURG AND EBOLA VIRUSES

The disease in humans takes the form of hemorrhagic fever.

CHAPTER 23 SLOW VIRUS INFECTION OF THE CNS

Kuru and Creutzfeldt-Jakob (C-J) diseases in humans are caused by a virus-like or subviral agent not yet characterized.
Transmissible mink encephalopathy is caused by eating meat from sheep infected with the scrapie agent.

CHAPTER 24 IMMUNIZATION AGAINST VIRUS DISEASES

Viruses are foreign antigens that stimulate the immune system.
Mature T-lymphocytes are required for the production of antiviral antibodies.
The secondary immune response depends on memory cells.
Passive immunization with virus-specific antibodies also protects against disease.
Antibodies have a role in recovery and prevention of virus diseases.
The development of viral vaccines is an ongoing process.
Vaccination against poliomyelitis: achievements and problems.
Immunization of humans with Sabin's vaccine is the method of choice.
Awareness of the dangers of immunization against poliomyelitis.
Immunization against influenza and problems encountered in the production of influenza virus vaccines.
Swine influenza vaccine: immunization in the United States and its shortcomings.
Other virus vaccines in current use.

CHAPTER 25 VIRUSES AS SELECTIVE FORCES IN NATURE: EPIDEMICS

Destruction of civilizations and populations as a result of the introduction of a new pathogenic virus into an unimmunized population.

Viruses are capable of introducing their genes into the chromosomal DNA of the host cell.

CHAPTER 26 ANTIVIRAL DRUGS AND CHEMOTHERAPY OF VIRAL DISEASES OF MAN

The search for antiviral drugs.
Virus-coded enzymes are targets for the development of antiviral drugs.
Mode of action of natural antivirals.
Antivirals against herpesviruses.
Antivirals against RNA viruses.
Antiviral drugs in medical use.
Prophylactic drugs.
Interferon: a cellular protein with antiviral activity.
Interferon acts on cells by binding to cell membrane receptors.
Cloning of human interferon genes in bacterial plasmids.

CHAPTER 27 LABORATORY DIAGNOSIS OF DISEASE-CAUSING VIRUSES

Rapid diagnosis of viruses can be done with the aid of the electron microscope.
Isolation and characterization of viruses from clinical materials.
The immunological response in the patient.
Tests available for the detection of viral antibodies.
Immunofluorescence is used for the detection of viral antigens in infected cells.
Radioimmunoassay (RIA) and enzyme-linked immunosorbent assay (ELISA) are used for the detection of viral antigens and antibodies.
Viral nucleic acids can be detected in infected cells.

CHAPTER 28 VIRUSES AND HUMAN CANCER

Epstein-Barr virus and Burkitt's lymphoma.
Nasopharyngeal carcinoma.
Herpes simplex virus type 2 and cervical cancer.
Hepatocarcinoma and hepatitis B virus.
Retroviruses and human cancer.

CHAPTER 29 SOCIAL, ECONOMIC, AND JURIDICAL ASPECTS OF VIRUS DISEASES

Social aspects: herd immunity to viral diseases.
Environmental aspects: monitoring of viruses in water reservoirs.
International virus diagnosis systems.
Problems in virus vaccine production.
Responsibility for individuals affected by a virus disease or vaccination.
Economic aspects.
Juridical aspects of vaccination of humans.