

Human Virology

Fourth Edition

Leslie Collier, University of London, Paul Kellam, Sanger Institute, Cambridge and John Oxford, St Bartholomew's and the Royal London Hospital School of Medicine and Dentistry

NEW EDITION

- Carefully tailored in terms of breadth and depth to the needs of medicine and biomedicine students: covers all the essential concepts without extraneous details.

New to this edition

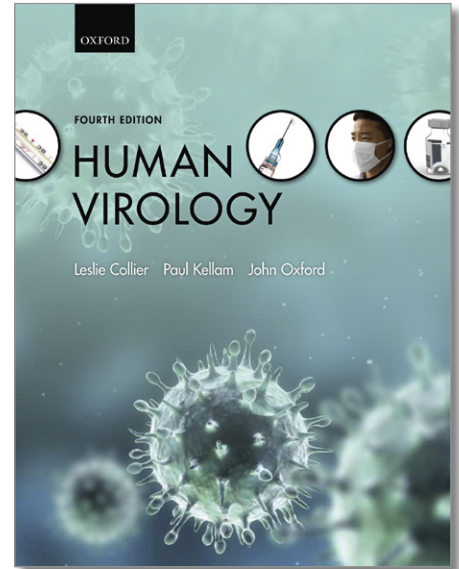
- Greater explanation of virology at the molecular level, supported by new figures.
- Many chapters introduced by new 'Fundamental Concepts' panels, including viral lifecycle boxes, and timelines to show significant landmarks following the discovery of a virus, to give an at-a-glance overview of the topic.
- Case studies throughout illustrate the clinical relevance of the subject.

Human Virology is the perfect introduction to the subject for anyone who needs to understand the general principles of viral biology, how viruses impact on human health, and how they can be managed in a clinical context.

Capturing this complex and rapidly-evolving subject with remarkable clarity, Human Virology describes the general principles of viral biology - the properties of viruses, their replication and genetics - along with disease and resistance, before introducing the infections caused by key groups of viruses. It concludes with an overview of the management of viral disease, including diagnosis and immunization.

Readership: Medical, dental and biomedical students studying virology, microbiology students; and students studying immunology and biomedical sciences.

352 pages February 2011 978-0-19-957088-1 Paperback £34.99



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- Oxford NewsNow - the latest news relevant to human virology from a variety of publications, brought direct to this Online Resource Centre

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CONTENTS

- Virology: How it all began
- General properties of viruses
- Viral replication and genetics
- How viruses cause disease
- Resistance of the human body to virus infections
- Viruses and cancer in humans
- Viruses and the community
- Upper respiratory tract and eye infections due to adenoviruses, coronaviruses (including SARS CoV), and rhinoviruses
- Infections caused by paramyxoviruses: measles, RSV, mumps, parainfluenza, meta-pneumovirus and the henipaviruses
- Orthomyxoviruses and influenza
- Gastroenteritis viruses
- Rubella: postnatal infections
- Parvoviruses
- Poxviruses
- Papilloma and polyomavirus
- Poliomyelitis and other picornavirus infections
- The herpesviruses: general properties
- The alphaherpesviruses: herpes simplex and varicella-zoster
- The betaherpesviruses: cytomegalovirus and human herpesviruses 6 and 7
- The gammaherpesviruses: Epstein-Barr virus and Kaposi's sarcoma-associated herpesvirus
- Introduction to the hepatitis viruses
- The blood-borne hepatitis viruses B and D
- The blood-borne hepatitis C
- The enteric hepatitis viruses A and E
- Rotaviruses and AIDS
- Reynovirus and rabies
- Arthropod-borne viruses
- Exotic and dangerous infections: filoviruses, arenaviruses and hantaviruses
- Prions and the spongiform encephalopathies
- Viral diseases of the central nervous system
- Intrauterine and perinatal infections
- Viral infections in patients with defective immunity
- Respiratory Infections
- Sexually transmitted viral infections
- Resurgent and emergent viral infections
- The laboratory diagnosis of viral infections
- Control of viral diseases by immunization
- Antiviral chemotherapy

Timeline

Year	Event
1892	Discovery of tobacco mosaic virus
1916	Discovery of poliovirus
1930	Discovery of influenza virus
1935	Discovery of adenovirus
1942	Discovery of herpesvirus
1949	Discovery of hepatitis B virus
1952	Discovery of poliovirus vaccine
1953	Discovery of hepatitis A virus
1968	Discovery of HIV
1976	Discovery of SARS
1981	Discovery of AIDS
1982	Discovery of hepatitis C virus
1989	Discovery of hepatitis E virus
1996	Discovery of SARS
2002	Discovery of SARS
2009	Discovery of H1N1
2011	Discovery of MERS-CoV
2012	Discovery of EBOV
2013	Discovery of MERS-CoV
2014	Discovery of EBOV
2015	Discovery of Zika
2016	Discovery of Zika
2017	Discovery of Zika
2018	Discovery of Zika
2019	Discovery of SARS-CoV-2
2020	Discovery of SARS-CoV-2
2021	Discovery of SARS-CoV-2
2022	Discovery of SARS-CoV-2

1 Introduction

In a book of this size there is a great temptation to omit material that is no longer directly relevant to current practice; however, it would be unwise to discuss the past without an account, albeit briefly, of the great success story in the fight against infectious disease and one that provides many valuable lessons. This epic provides at least three 'firsts': the first vaccine, the first disease to be readily eradicated by vaccination, and the first virus infection against which chemotherapy was clinically effective. Although smallpox is now extinct, other poxviruses infect humans, and as we shall see in Chapter 37 some of them may be used in a further surprising way to generate resistance against different diseases. Because of the threat of bioterrorism, some countries are developing vaccine against smallpox and other vaccines are being developed to be held in strategic reserves.

In many ways smallpox would be a poor choice for a human virus because of its relatively low infectivity and long incubation period, during which a population could be immunized. A more suitable or amenable different virus could, in theory, be genetically engineered, but only with great difficulty.

2 Properties of the viruses

2.1 Classification

The family Herpesviridae contains two subfamilies: the *Chloerivirinae*, with eight genera infecting a wide range of mammals and birds; and the *Herpesvirinae*, with three genera that affect insects only. Most of these viruses do not infect humans. Others are pathogenic both for animals and humans, and two, smallpox and measles, only for humans (Table 14.1). The genera are distinguished on the basis of morphology, genome structure, growth characteristics, and serological reactions; there is close serological relationship between the viruses within each genus and good cross-protection between genera.

2.2 Morphology

These are the largest viruses of all; the orthopoxviruses are brick-shaped, those of the *Herpesvirinae* are spherical (Fig. 14.1). The outer membrane shows the virus to be held about 200 × 200–200 nm in size with a single lipid membrane bilayer and a complex internal structure of a double-helical core and two non-enveloping inner shells, as viewed after their location in the virus.

2.3 Genome

The nucleic acid is a linear double-stranded DNA ranging in size from 124 kb (herpesvirus) to 200 kb (poxviruses). The DNA has inverted repeats at each end of the genome and terminal repeats that control the new DNA synthesis in the genome ends. This large genome codes for over 100 polypeptides, including a DNA-dependent RNA polymerase and four enzymes. Genetically located genes are conserved and are essential for virus replication, whereas genes near the two termini affect host range and virulence.

Table 14.1 Poxviruses that infect humans

Genus	Virus	Primary host(s)	Clinical features in humans
Orthopoxvirinae	Variola	Man	Smallpox
	Monkeypox	Man	Monkeypox infection
	Camelpox	Cattle, camels, rodents	Lesions on hands
	Molluscipoxvirus	Monkeys, apes	Resembles mollusc
Parapoxvirinae	Pseudotuberculosis	Primate (e.g. H5N1), cattle	Localized nodules (milky 'cystoid')
	Orf	Sheep, goats	Localized cutaneous/dermatitis lesions
Herpesvirinae	Varicella	Man	Varicella (chickenpox) and shingles

Fig. 14.1 Electron micrographs of poxvirus. (A) Vaccinia (B) orf. (C) molluscipoxvirus. (D) model of poxvirus showing internal bodies, ribonucleic DNA, and double-strand core structure. Scale bar = 100 nm.

2.4 Replication

Unlike most DNA viruses, the poxviruses replicate only in the cytoplasm, and can replicate in cells without a nucleus. Virus entry into cells is a complex process and involves the low-affinity interaction with general cell-surface molecules, such as glycoproteins and specific interactions between groups of viral and cellular proteins. Indeed, a genuine entry complex of eight proteins has been identified in recent years. The virus core enters the cytoplasm of the cell and acts as scaffolding for many virus-coded essential enzymes, such as viral transcription, replication factors, capping and methylating enzymes, and a poly(A) polymerase into the cell. Transcription of viral DNA is initiated immediately and approximately 100 early viral genes are activated, particularly gene coding for enzymes which control DNA replication. All poxvirus genes contain a single ORF and there is no evidence of virus subunit

splicing. Virus genes are expressed in three distinct phases, 'early genes' whose transcription peaks after 1–2 h of infection, 'intermediate genes' with a peak transcription around 2–3 h and 'late genes' peaking at 4 h post-infection. The early genes encode proteins required for virus DNA synthesis, which is initiated at the centre of the genome. Late genes encode the major structural and the factors required to start early gene expression that is packaged into the maturing virion.

Poxviruses encode multiple proteins that interfere with both the innate and adaptive immune response, ensuring that the virus is able to replicate in the face of such a massive response. These include: inhibitors of interferon and chemokine signalling; complement production and co-factor restriction to B cells; inhibitors of viral DNA replication; cell signalling pathway, or apoptosis.

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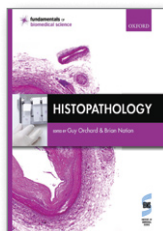
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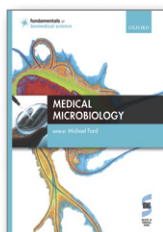
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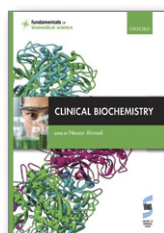
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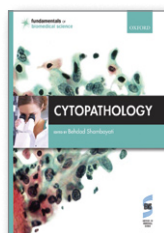
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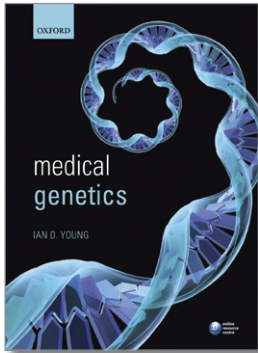
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Readership: Aimed primarily at undergraduate medical and biomedical science students, this book should also appeal to genetic counsellors, and specialist nurses working in clinical genetics.

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Ian D Young, Leicester Royal Infirmary

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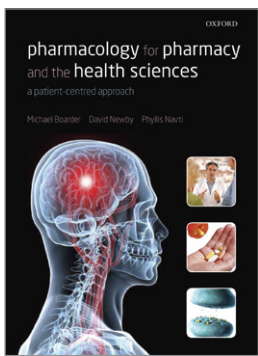
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Readership: Undergraduates studying pharmacology as part of a broader pharmacy or health care science programme. Medical professionals who wish to extend and update their understanding of drug action within a clinical context

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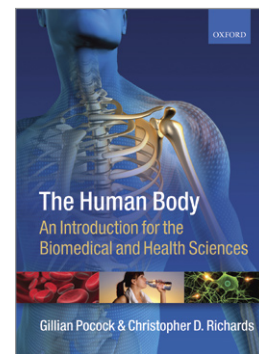
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This volume is an excellent choice for any introductory course in the human health professions. Its tight organization and superb style should give it legs for future editions, much to the benefit of both students and professors.

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John Lackie, Yamanouchi Research Institute, Oxford

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