Textbook of Medical Virology

Edited by

Erik Lycke

and

Erling Norrby

Textbook of Medical Virology

Edited by

Erik Lycke
Professor of Clinical Virology; Chairman, Department of Virology, University of Gothenburg, Sweden

and

Erling Norrby
Professor of Virology; Chairman, Department of Virology, Karolinska Institute, School of Medicine, Stockholm, Sweden

Butterworths
London Boston Durban Singapore Sydney Toronto Wellington

Swedish edition first published 1981

English edition 1983

British Library Cataloguing in Publication Data

Textbook of medical virology.
1. Virus diseases
I. Lycke, Erik II. Norrby, Erling
III. Medicinsk virologi. *English*
616'.0194 RC114.5

ISBN 0-407-00253-7

Photoset by Butterworths Litho Preparation Department
Printed in England by Mackays of Chatham Ltd, Kent

Preface

Virus infections have influenced the life of man throughout history, but knowledge about viruses and the diseases they cause is of relatively recent origin. The expansion of virological knowledge has been markedly determined by the availability of methods for growing viruses under laboratory conditions and for the biochemical characterization of virus particles and molecular events in infected cells. Thus advents such as the introduction of cell culture techniques, the development of techniques for polypeptide analyses and detailed nucleic acid characterization have been of major importance.

It has become increasingly possible to describe pathogenic events in molecular terms although a great deal still remains to be discovered. The comprehensive knowledge available about virus replication now allows a rational approach to the design of antiviral drugs. It can be foreseen that a number of antiviral compounds will be introduced during the forthcoming decade. These drugs will be an important supplement to the currently used immunoprophylactic measures which have already provided some of the major advances in biomedicine. Vaccines also will be used more extensively in the future and new products will be developed.

This book encompasses the whole field of medical virology. The first part of the book describes the structure and chemical composition of virus particles and the biological and immunological activity of individual virus components. The next section analyses the interaction between viruses and cells. The capacity of viruses to enter cells, the modes of replication of DNA and RNA viruses and the mechanism of release of viruses are discussed separately. Before the subsequent section of the book which presents the pathogenesis of virus infections, the effect of viruses on cellular functions and the genetics of viruses are reviewed. The pathogenesis of virus infections include chapters on acute, congenital, persistent, 'slow' and tumorigenic infections and on defence mechanisms against virus infections. Hereafter, separate chapters discuss laboratory diagnosis of virus infections, their epidemiology, and prevention by use of immune prophylaxis and antiviral drugs. The last section of the book concentrates on special virology, focusing in separate chapters on the major virus groups and summarizing the information on viral syndromes in a concluding chapter.

It is our hope that this book will enable the reader to comprehend the disease process in virus infections in man and to understand the methods currently available for diagnosis and prevention.

Gothenburg and Stockholm — Erik Lycke
June 1982 — Erling Norrby

List of contributors

Böttiger, Margareta, M. D., Professor, Department of Epidemiology, The National Bacteriological Laboratory, Stockholm, Sweden

Espmark, Åke, M.D., Professor, Department of Virology, The National Bacteriological Laboratory, Stockholm, Sweden

Fenyö, Eva-Maria, M.D., Reader, Department of Virology, Karolinska Institute, School of Medicine, Stockholm, Sweden

Forsgren, Marianne, M.D., Assistant Professor, Department of Virology, The Stockholm Central Microbiological Laboratory, Stockholm, Sweden

Grandien, Monica, M.D., Assistant Professor, Department of Virology, The National Bacteriological Laboratory, Stockholm, Sweden

Hermodsson, Svante, M.D., Assistant Professor, Department of Clinical Virology, Institute of Medical Microbiology, University of Gothenburg, Sweden

Lycke, Erik, M.D., Professor, Department of Clinical Virology, Institute of Medical Microbiology, University of Gothenburg, Sweden

Mårdh, Per-Anders, M. D., Assistant Professor, Department of Medical Microbiology, University of Lund, Sweden

Nordenfelt, Erik, M.D., Assistant Professor, Department of Clinical Virology, Malmö General Hospital, Malmö, Sweden

Norrby, Erling, M.D., Professor, Department of Virology, Karolinska Institute, School of Medicine, Stockholm, Sweden

Öberg, Bo, Ph.D., Assistant Professor, Division of Antiviral Chemotherapy, Astra Pharmaceutical Co., Södertälje, Sweden

Pettersson, Ulf, M.D., Professor, Department of Medical Genetics, University of Uppsala, Sweden

Philipson, Lennart, M.D., Professor, Director, European Molecular Biology Organization, Heidelberg, West Germany

Strannegård, Örjan, M.D., Associate Professor, Department of Virology, Institute of Medical Microbiology, University of Gothenburg, Sweden

Svedmyr, Arne, M.D., Assistant Professor, Department of Virology, The Stockholm Central Microbiological Laboratory, Stockholm, Sweden

Wadell, Göran, M.D., Professor, Department of Virology, University of Umeå, Sweden

Wahren, Britta, M.D., Associate Professor, Department of Virology, The National Bacteriological Laboratory, Stockholm, Sweden

von Zeipel, Gerolf, M.D., Department of Virology, The Stockholm Central Microbiological Laboratory, Stockholm, Sweden

Contents

1 Viruses – a unique kind of infectious agent **1**
Erik Lycke and Erling Norrby

2 The morphology of virus particles. Classification of viruses **4**
Erling Norrby
Infectious nucleic acid 4
Principal aspects of virus particle structure 4
Live or dead materia? 5
Structural proteins – symmetry arrangements 5
The virus envelope 8
Classification of viruses 9
Introduction to different families of animal viruses 12

3 The biochemistry of virus particles **17**
Ulf Pettersson
Virus-DNA 17
Virus-RNA 20
Virus proteins 23
Additional components in virions 27

4 Viral gene products; their immunological properties and biological activities **28**
Erling Norrby
Viral antigens 28
Haemagglutination 32
Cell fusion and haemolysis 35
Enzymatic activities of viral gene products 36

5 Cultivation of viruses **38**
Göran Wadell
Identification and propagation of viruses in tissue and cell cultures 38
Identification and propagation of viruses in embryonated hen's eggs 42
Identification and cultivation of viruses in experimental animals 43

6 General views on virus replication **45**
Erling Norrby
Morphological methods for analysis of virus replication 45
Molecular methods for characterization of virus replication 46
Quantitative determination of virus infectivity 46
Quantitative determination of other biological properties of viral products 48
The different phases of virus replication 48

7 Attachment of viruses to cell receptors and penetration of viruses into cells **51**
Lennart Philipson
Virus and receptors 52
Penetration 53

8 Replication, transcription and translation of RNA viruses **57**
Lennart Philipson
Classes of RNA viruses 57
Reoviruses 59
Picornaviruses 60
Togaviruses 63
Rhabdoviruses and paramyxoviruses 64
Orthomyxoviruses 66
Retroviruses 68

9 Replication, transcription and translation of DNA viruses **72**
Ulf Pettersson
Parvoviruses 72
Papovaviruses 74
Adenoviruses 76
Herpesviruses 79
Poxviruses 81

10 The morphogenesis of virions **84**
Erling Norrby
The maturation and release of non-enveloped viruses 84
The morphogenesis of enveloped viruses 84

11 Virus-induced changes of cell structures and functions **93**
Erik Lycke and Erling Norrby
Cytopathic changes 93
Inclusions in virus-infected cells 97
The effect of integration of viral antigens in cellular membranes 98
Effects of viruses on functions of highly specialized cells 98
Chromosomal changes 100
Virus-induced cell transformation 100
Interferon 104

12 Virus genetics **105**
Lennart Philipson
Mutations 105
Recombination 108
Phenotypic mixing and complementation 109

13 General aspects of pathogenesis of virus infections **112**
Erik Lycke
Modes of transmission of virus diseases 114
The importance of cellular and viral receptor functions 116
The spread of virus infections within the body 117
The importance of barrier systems in limiting the spread of the infection 119
Influence of immune reactions on the pathogenesis 120
Influence of constitution, age, sex and genetic background 122

14 Pathogenesis of acute virus infections **125**
Erik Lycke
Respiratory infections 125
Infections of visceral organs 126
Infections of the skin and mucous membranes 128
Infections of the nervous system 131

15 The pathogenesis of congenital infections **135**
Marianne Forsgren
Different ways by which a virus may cause fetal damage 136
Spread of virus in congenital infections 137
Direct effects of fetal infections 138
Indirect fetal-damaging effects in connection with infections of pregnant women 142

16 The pathogenesis of persistent infections **144**
Erling Norrby
Chronic subclinical infections with immune pathological reactions 146
Latent infections 148
Slow virus infections caused by conventional viruses 151

17 Slow infections caused by non-immunogenic infectious agents **155**
Erling Norrby
Different forms of infectious encephalopathy 155
Biological and physical-chemical properties of atypical infectious agents 159
How do atypical infectious agents spread? 160

18 Viruses and tumours **163**
Eva-Maria Fenyö and Britta Wahren
Tumour viruses in animals 167
Human tumour viruses 174
Human tumour virus candidates 175

19 Mechanisms of defence against virus infections **178**
Örjan Strannegård
Non-specific immunity 178
Humoral immunity 180
Cell-mediated immunity 183
Immunopathological effects of virus infections 184
Virus infections in connection with malignant diseases and immune suppression 187
Immunological defence against congenital virus infections 187

20 Laboratory techniques for diagnosis of virus infections **189**
Monica Grandien and Arne Svedmyr
Isolation of viruses 189
Direct identification of virus or viral antigens in samples from patients 193
Analysis of antibody response in patients 195
Evaluation of laboratory results 200

21 The epidemiology of virus diseases **202**
Margareta Böttiger and Erling Norrby
Methods of surveillance of the epidemiological occurrence of infectious diseases 202
The dissemination mechanisms of virus infections 204
Epidemiological patterns of virus infections 206
Examples of the epidemiology of some virus diseases 206

22 Inactivation of viral infectivity and disinfection **212**
Erik Lycke

23 Immune prophylaxis **216**
Erling Norrby
Passive immunization 216
Active immunization 218

24 Antiviral drugs **230**
Örjan Strannegård and Bo Öberg
Mechanisms of action of antiviral drugs 230
Antiviral drugs used for clinical chemotherapy 232
Antiviral drugs with a potential clinical usefulness 235
Interferon 236

25 Picornaviruses **242**
Gerolf von Zeipel
Properties of picornaviruses 243
Enteroviruses 243
Rhinoviruses 248

26 Togaviruses **251**
Marianne Forsgren and Gerolf von Zeipel
Alphaviruses 253
Flaviviruses 253
Rubellavirus (Rubivirus) 256

27 Orthomyxoviruses (influenza viruses) **262**
Svante Hermodsson
Properties of the virus 262
Clinical features 264
Pathogenesis 265
Epidemiology 268
Laboratory diagnosis 269
Prophylaxis 270

28 Paramyxoviruses **272**
Svante Hermodsson
Parainfluenza virus 273
Mumps virus 276
Measles virus 279
Respiratory syncytial (RS) virus 282

29 Adenoviruses **286**
Göran Wadell
Properties of the virus 287
Clinical features 289
Epidemiology 291
Prophylaxis 292

30 Hepatitis viruses **293**
Erik Nordenfelt
Properties of the virus 293
Clinical features 295
Pathogenesis 297
Immunity 298
Laboratory diagnosis 298
Epidemiology 300
Prophylaxis 302

31 Herpesviruses **304**
Erik Lycke
Properties of the virus 304
Latency and transformation 306
Herpes simplex virus (HSV) infections 308
Varicella zoster virus (VZV) infections 314
Cytomegalovirus (CMV) infections 316
Epstein–Barr virus (EBV) infections 318

32 Poxviruses **323**
Åke Espmark
Classification 323
Properties of the virus 324
Variola (smallpox) 325
Smallpox vaccine (vaccinia virus) 325
The WHO smallpox eradication programme 326
Clinical features of variola 326
Laboratory diagnosis 327
Other medically important poxviruses 328

33 Other viruses **331**
Åke Espmark and Monica Grandien
Reoviruses 331
Retroviruses 331
Bunyaviruses 332
Arenaviruses 334
Coronaviruses 335
Rhabdoviruses (rabies virus) 336
Marburg/Ebola virus 338
Parvoviruses 339
Papovaviruses 339

34 Viral syndromes **341**
Erik Lycke
Respiratory tract infections 341
Infections of the pharynx 343
Infections with exanthemas 344
Hepatitis 345
Gastrointestinal infections 345
Urogenital infections 346
Infections of the nervous system 347
Infections of the sensory organs 349
Neonatal infections 350

Appendix. Chlamydia **353**
Erik Lycke and Per-Anders Mårdh
Microbiology of chlamydiae 353
Chlamydia psittaci infections 354
Chlamydia trachomatis infections 354
Laboratory diagnosis 356
Susceptibility of chlamydiae to antibiotics 360

Index **361**

1

Viruses – a unique kind of infectious agent

Erik Lycke and Erling Norrby

Our first awareness of the infectious agents which later became known as virus (L. poison) dates back to the turn of the century. It had been observed that there were infectious diseases which were caused by agents lacking the capacity to replicate on artificial substrates and that these agents were smaller than all previously known infectious agents. Unicellular organisms, arranged according to decreasing size and complexity, include protozoas, fungi, bacteria, mycoplasmas, rickettsia and chlamydia. These groups of cellular microorganisms differ distinctly from viruses with regard to many basic properties.

Viruses can only replicate in living cells. As a consequence two separate phases can be distinguished in the life-cycle of a virus. During one of these phases the virus occurs outside cells in the form of a virus particle. This particle is a passive transport vehicle which provides opportunities for a spread of infection both from cell-to-cell within the multicellular organism and between individuals. During the other phase the virus resides inside the infected cell where replication may occur. This replication includes a synthesis of new virus-genetic material and new virus-specific proteins. Other building materials for virus particles as well as the necessary energy and main machinery for the assembly of a virus are provided by the infected cell. Certain unicellular organisms, e.g. rickettsia and chlamydia, replicate in cells but in contrast to the replication of viruses this occurs through a growth and division of the organisms. Furthermore, both rickettsia and chlamydia like other cellular organisms contain both DNA and RNA whereas the genetic material of a virus is represented by either one of these nucleic acids. As a consequence a virus displays a relatively more advanced form of cellular parasitism. Concerning certain intracellular functions of a virus there are similarities with functions carried by some extrachromosomal genetic elements in cells, i.e. episomes and plasmids. However, as distinct from these kinds of cellular genetic material, a virus has an independent extracellular form of transmission.

Viruses occur not only in mammals but also in insects, plants and prokaryotes, e.g. bacteria. From a practical point of view one therefore refers to animal, insect, plant and bacterial viruses. The latter viruses are usually called bacteriophages (Gk. *phagein* = to eat). Certain viruses have a capacity to replicate in completely different hosts, for example both in mammalian cells and in insect cells. Bacteriophages, however, are limited to replication in prokaryotic cells only.

Replication of an animal virus in cells can lead to their destruction. If the replication of a virus in a particular organ is widespread this may lead to such extensive destruction that symptoms of disease appear. Thus, viruses may cause acute degenerative diseases. Such diseases are common. In industrial societies children in the pre-school age usually have 5–7 virus infections per year. About half of all absenteeism from work and school is considered to be caused by virus diseases. Most often these diseases are of a rather trivial nature such as the uncomplicated common cold.

Every year new variants of known viruses and often completely new viruses are discovered. In the case of some of these newly discovered agents methods for laboratory cultivation are not available and frequently it is not known whether the agent has the capacity to cause disease. In spite of our increasing knowledge of the complex capacity of virus infections to influence cellular and organ functions we still do not have an overall view of the total medical importance of virus infections.

The possibilities of specific treatment of virus diseases are still rather limited but developments concerning preventive treatment, i.e. immune prophylaxis have been a major advance in modern medicine. Smallpox has disappeared from our world. Poliomyelitis has become a very rare disease in many industrial countries. Yellow fever has been brought under control. Vaccines against measles, mumps and rubella provide an opportunity for effective control of these infections and in the foreseeable future there could be effective vaccination against other childhood diseases and against the two major forms of virus-induced hepatitis. In principle it is possible today to produce vaccines against all cultivatable viruses.

During the last few decades it has been found that many viruses can give not only acute infections but also have the capacity to remain in the body and give chronic diseases or dormant infections. A special property of certain viruses is their ability to change the growth characteristics of normal cells into those of tumour cells. The importance of this phenomenon for the emergence of tumours in man and animals is currently subject to intensive studies. It should be emphasized that a majority of all virus infections contracted by man or animals are not apparent, i.e. they do not produce any symptoms. From a biological viewpoint there obviously is no reason for a virus to cause severe disease. Concerning the possible spread of infection it is an advantage if the infected individual does not contract incapacitating disease.

Viruses have been the focus of attention not only because of their importance as disease-causing agents but also because they are interesting subjects for general biological study. Viruses represent the most simplified self-replicating and genetically active elements. The possible evolutionary origin of viruses has been extensively debated. In the absence of hard facts these discussions are usually more speculative than informative. Viruses have been referred to as the 'selfish' gene which during its evolution has acquired capacity to a restricted cell-independent existence and an ability to transfer its genetic information to another cell. It does not seem unlikely that the evolution of viruses has been advantageous also for the evolution of cells and cellular organisms. Genetic material which is important for cells can be transported by use of virus-genetic material as a vehicle within and between genomes of cells. Studies of viruses therefore provide opportunities for an analysis of the basic cellular mechanisms of life.

Our knowledge about viruses has increased dramatically during the last three decades. This is due to the development of practical methods for the cultivation of viruses in cell cultures in the laboratory and to the development of new methods for biochemical characterization of virus products. The total chemical composition of certain viruses is now known and much detailed information concerning the interaction between viruses and cells has been obtained. A continued rapid accumulation of knowledge concerning both the theoretical and the applied aspects of virology can be predicted. Today we stand on the threshold to an age in which the practical application of antiviral substances in medicine will be seen. Diagnostic knowledge of viral diseases will therefore become of increasing importance and the study of virology will be essential for both practising and trainee medical doctors and other personnel engaged in biomedicine.

Bibliography

General handbooks in virology

ANDREWES, C. H. and PEREIRA, H. G. (1972). *Viruses of Vertebrates*. 3rd edn. London: Balliere

DEBRÉ, R. and CELERS, J. (1970). *Clinical Virology*. Philadelphia: W. B. Saunders Co.

EVANS, A. S. (Ed.) (1976). *Viral Infections of Humans*. London: John Wiley and Sons

FENNER, F. and WHITE, D. O. (1976). *Medical Virology*. 2nd edn. New York: Academic Press Inc.

FENNER, F., AUSLAN, B. R., MIMS, C. A., SAMBROOK, J. and WHITE, D. O. (1974). *The Biology of Animal Viruses*. 2nd edn. New York: Academic Press Inc.

HORSFALL, F. L. and TAMM, I. (1972). *Viral and Rickettsial Infections of Man*. Philadelphia: J. B. Lipincott

LENNETTE, E. H. and SCHMIDT, J. (Ed.) (1979). *Diagnostic Procedures for Viral, Rickettsial and Chlamydial Infections*. 5th edn. Washington: American Public Health Association

LURIA, S. E., DARNELL, J. E. Jr., BALTIMORE, D. and CAMPBELL, A. (1978). *General Virology*, 3rd edn. New York: John Wiley & Sons, Inc.

2

The morphology of virus particles. Classification of viruses

Erling Norrby

The survival of organic life is dependent on its capacity to replicate genetic material. The most simplified natural form of a viral infectious agent therefore would comprise a limited amount of nucleic acid with capacity to direct its own replication. This form of infectious agent exists in plants but has not been identified so far in other host organisms. It is called *viroid*. Viroids are composed of a circular form of single-stranded RNA with a molecular weight of about 100 000. It is not known how this nucleic acid can be replicated nor has it been clarified how this kind of agent can cause disease in the plants on which it forms a parasite.

Infectious nucleic acid

All known animal, insect and bacterial viruses have an extracellular transport form which includes nucleic acid and a protein shell in which this nucleic acid is enclosed. In some cases the particles also include additional structures. Isolated virus nucleic acid, DNA or RNA, may cause infection and initiate a synthesis of complete virus particles. The nucleic acid is infectious, however, only in cases when the complete virus particle does not contain any enzyme(s) needed to initiate replication (*see* Chapter 3). Free isolated *infectious nucleic acid* is an ineffective contagious entity. One single break in the nucleic acid molecule induced by physical or chemical factors will lead to the loss of its infectious capacity. It is therefore of importance to their survival that viral infectious agents have their nucleic acid packed into a protective protein shell during the transport between cells.

Principal aspects of virus particle structure

The composition of a conventional virus can schematically be described as follows. Centrally the particle contains nucleic acid of varying quantity. This nucleic acid is either RNA or DNA, but never both kinds simultaneously. The nucleic acid is surrounded by a protein shell, called *capsid* (from L. *capsa* = box). In the case of many viruses the nucleoprotein complex represents the whole virus particle. The virus particle is referred to as the *virion*. In more complex viruses further (one or more) enclosing structure(s) occur. This component is structurally similar to cellular membranes and is referred to as the *envelope*. An envelope is composed of proteins specific to the virus and lipids and carbohydrates which are taken preformed from the infected cell. Even the more complex virus particles do not contain organelle structures equivalent to, for example, mitochondria and lysosomes of cells. If strict definitions were applied, a virus should not be called a microorganism. However, for practical reasons, viruses are included in the group of microorganisms.

Virions thus have a relatively simple compostion and, as a consequence, they are small. The largest virions have dimensions of 320 × 270 × 120 nm, a size corresponding to that of certain forms of the smallest bacteria (mycoplasmas), whereas the diameter of the smallest virions is about 20 nm. The difference in volume is 5000-fold. In spite of this variation in dimensions, viruses have common features which motivates their classification as one common category of infectious agent. The limited size of virions allowed a distinction to be made between bacteria and viruses as cellular infectious agents in early studies. Virions were found to be capable of passing through filters which retained bacteria and they were therefore classed as being ultrafiltrable. Furthermore, bacteria were characterized by light microscopy whereas virus particles, because of their limited size, could not be detected. Information about the morphology and dimensions of virions could be clarified firstly through electron-microscopic analysis. Originally it was possible to get only a rough impression of the size and form of virus particles. In 1956 the negative contrast technique for electron microscopy was introduced. Instead of being stained with electron-dense substances, the particles were suspended in a contrast solution. With this technique new possibilities for detailed characterization of virus morphology became available.

Live or dead materia?

During the 1930s it was shown that purified virions of a plant virus could be crystallized. The fact that virus particles were giant molecules with a capacity to crystallize caused extensive discussion about whether a virus should be considered as live or dead materia. The extracellular virus particle which lacks energy-providing systems and has no capacity, or only a limited capacity, for independent metabolism obviously must be considered as a lifeless unit. Since it also lacks capacity for active movement, the transport of virions in time and space from cell to cell is a chance event. If a virion comes into contact with a susceptible cell, however, a sequence of events is initiated which fulfils all definitions of life, i.e. the reproduction of genetic material which is incorporated into new transport particles. The question about live or dead material becomes more complicated when we are dealing with defective viruses which have a capacity to replicate only in cells which concomitantly are infected with another virus (*see* Chapter 12).

Only certain non-enveloped virions can be crystallized. The availability of viral crystals has facilitated three-dimensional analyses by aid of x-ray diffraction. Through these studies it has been possible to shed light upon the interaction between virus nucleic acid and capsid protein.

Structural proteins – symmetry arrangements

A single-stranded nucleic acid can direct the synthesis of a protein which has a size corresponding to about 1/7 of its molecular weight. This fact caused Watson and

Crick, well known for their description of the double helix nature of DNA, to postulate two important principles for the structuring of virus particles. The first principle was that the virus capsid must be built up of repetitive units; the second, that the structure of the capsid should be symmetrical. By use of the two above-mentioned methods of analyses – electron microscopy and x-ray crystallography – and chemical analyses, the correctness of these postulates has been verified. The number and character of the chemical units, *structural proteins*, which are the building stones in virions, have been described for the majority of animal viruses.

Nature generally utilizes symmetrical building principles in the construction of more comprehensive three-dimensional structures. Hereby, information can be spared since the design of the individual building stones can decide their mutual

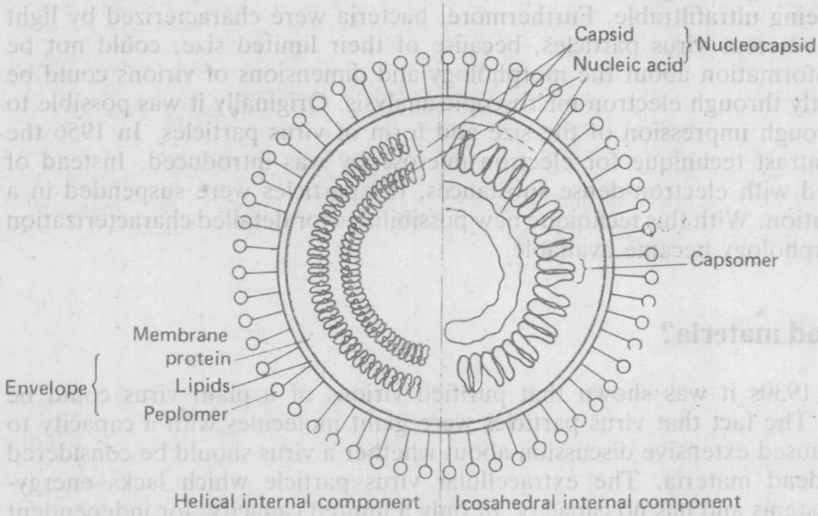

Figure 2.1. Schematic description of the structure of a virus with a helical (left part of the picture) or icosahedral (right part of the picture) internal component (nucleocapsid). The particle in the figure is surrounded by an envelope but many viruses lack this structure. A capsid represents the outermost protective structure in such non-enveloped viruses

relationships and therefore allow a spontaneous assembly via crystallization-like processes. It is characteristic of nature that it alternates unique design and symmetrical arrangements on different levels of the organized biological hierarchy in both plants and animals.

The principle of symmetrical constructions is well illustrated by the design of virus particles. Two different forms of symmetry, *helical* and *icosahedral* have been used for the construction of virus capsids (*Figure 2.1*).

Helical symmetry

Helical (screw-formed) capsid symmetry is used in the construction of rod-shaped plant virions and bacteriophages and the internal structure of some enveloped animal viruses. Among the rod-shaped viruses tobacco mosaic virus (TMV) has