Intervirology 5: 76–82 (1975)

Coronaviridae[1]

D. A. J. Tyrrell, J. D. Almeida, C. H. Cunningham, W. R. Dowdle, M. S. Hofstad, K. McIntosh, M. Tajima, L. Ya. Zakstelskaya, B. C. Easterday, A. Kapikian and R. W. Bingham

An informal proposal has been made to group together a number of recently recognized viruses under the head of coronaviruses [1]. They affect a variety of hosts causing a diversity of diseases, but they are grouped together mainly because they have similar electron microscopic appearances, are ether-labile, and probably contain RNA. However, remembering that influenza and parainfluenza viruses were once thought to be quite closely related on similar grounds, much of the grouping should be regarded as tentative. Nevertheless, murine strains (MHV) are antigenically related to some human strains and, morphologically, human, avian, and murine viruses replicate in a similar way; it is therefore likely that at least some of the groupings will be confirmed by further investigation. There is now some more detailed information on the structure of the prototype virus IBV (avian infectious bronchitis virus), the striking features being the large number of peptides and the large single RNA strand. Some strains possess hemagglutinin and there seems to be a hemagglutinin receptor-destroying enzyme which is not a neuraminidase; also there is evidence of a viral RNA polymerase. These features confirm that IBV is quite distinct from other viruses. We still have no detailed information about the biochemical characteristics of its nucleic acid, the process

[1] Report of the Study Group on Coronavirus, Vertebrate Virus Subcommittee, International Committee on the Taxonomy of Viruses (ICTV). Before the proposals become official, they require approval of the ICTV at its next meeting to be held in Madrid, 10 September 1975. In the meantime, the report has been approved by Dr. H.G. Pereira, Chairman, Vertebrate Virus Subcommittee; by Dr. P. Wildy, Chairman, Coordination Subcommittee; and by Dr. F. Fenner, President, ICTV.

Received: May 13, 1975.

of replication or the lipid composition of the envelope. All in all, the time is now ripe for completing these basic studies of IBV and checking whether the same characteristics are found in the other viruses at present included in the group. It may take years to reach certainty on these points, but we believe this early attempt at taxonomy can be valuable in indicating which facts should be sought first, in order to clarify as soon as possible our understanding of this interesting and superficially diverse group.

The Study Group believes that the coronaviruses are sufficiently distinct from other viruses to constitute a family, **Coronaviridae;** at present, it will have to be considered a monogeneric family.

To save space, references included in the review by MCINTOSH [2] will not be repeated.

1 Taxonomy [2]
1.1 **Coronaviridae**
1.3 Family with only one genus, *Coronavirus*
2 The virion
2.1 Chemical composition
2.1.1 Nucleic acid
2.1.1.1 RNA
2.1.1.2 IBV[2]: single-stranded [5, 6]. HCV: single-stranded [7]
2.1.1.4 Number of pieces: IBV, one [5]
2.1.1.5 Sedimentation coefficients: IBV, 50S [5]
2.1.1.6 Molecular weight: IBV, 9×10^6 [5]
2.1.1.11 Infectivity: Not demonstrated for any member.
2.1.2 Proteins
2.1.2.2 Number of polypeptides: HCV: 6–8 polypeptides [8]; IBV: 16 polypeptides [9]
2.1.2.3 Molecular weight of polypeptides: HCV, 13,000–210,000 [8]. IBV, 14,000–180,000 [9]
2.1.2.5 Enzymes: IBV: possible receptor-destroying enzyme activity [10], possible RNA polymerase [10, 11]. HCV: RNA-dependent RNA polymerase [12].
2.1.2.6 Other functional proteins: hemagglutinin (HCV: some strains; HEV; IBV: some strains [13]).
2.1.3 Lipids: Present
2.1.4 Carbohydrates: IBV, HCV, TGEV: glycopeptides present.
2.2 Physicochemical properties
2.2.1 Density: 1.16–1.23 g/cm^3 in sucrose; 1.23–1.24 g/cm^3 in CsCl.
2.2.2 Sedimentation coefficient: HCV: 374–416S, strain OC43; 378–400S, strain 229E [8]. IBV: 330S.
2.2.4 Stability of infectivity
2.2.4.1 pH: TGEV: optimum stability at pH 6.5 [14]. IBV: optimum stability between pH 6.0 and 6.5 [11]. Conflicting or no evidence for other viruses.
2.2.4.2 Heat: Rapidly inactivated at 56°; slow inactivation at 37°; moderately stable at 4°, assuming optimal suspending medium.
2.2.4.5 Other agents: Unstable with common disinfectants and detergents.
2.3 Structure
2.3.1 Nucleocapsid: See 2.3.3.

[2] See 10.3 for abbreviations of species.

2.3.2 Envelope: Lipid envelope present, containing peptides and glycopeptides.

2.3.3 Cores: Electron-dense inner shell visible in thin section. HCV: ribonucleoprotein (RNP) core, density 1.31 g/cm^3 (CsCl), sedimentation 180S [15]; linear appearance by negative staining [12].

2.3.3.1 Dimensions: 55-nm diameter in thin section.

2.4 Morphology

2.4.1 Overall shape: Round, non-rigid, some elongated forms.

2.4.2 Dimensions: 60–220 nm

2.4.3 Surface projections: Characteristic bulbous projections, 12–24 nm long, widely spaced.

2.4.4 Special features in thin sections: Inner and outer shells, sometimes separated by electron-lucent space. Some reports of internal thread-like structure.

2.4.5 Other features: Fragile attachment of projections to surface of virion. Inner tongue-shaped membrane sometimes visible by negative staining.

3 Replication

3.1 Site of accumulation of viral proteins: Cytoplasm.

3.2 Nonstructural proteins: Probably present.

3.3 Mode of nucleic acid replication

3.3.2 Effect of inhibitors: Sensitive to 6-azauracil, virazole [10]. Insensitive to 5′-iododeoxyuridine, 5′-bromodeoxyuridine, 5′-fluorodeoxyuridine, cytosine arabinoside, aminopterin and actinomycin D.

3.4 Site and mechanism of maturation: Matures in cytoplasm by budding through endoplasmic reticulum.

3.5 Other features: No budding at plasma membrane.

4 Cooperative interactions: No information available.

5 Host range

5.1 Natural: Generally restricted to normal host species.

5.2 Experimental

5.2.1 *In vivo:* Generally specific for species of origin: chicken embryos (IBV), suckling mice (MHV, some strains of IBV[3] and HCV), newborn rabbits (IBV[3]), suckling white rats (IBV[3]), suckling hamsters (HCV), hamsters (MHV).

5.2.2 *In vitro:* HCV: 1°[4] and 2° human embryonic cells, 1° monkey kidney cells, human embryonic tracheal organ cultures. IBV[3]: 1°

[3] Isolation in chicken embryos is essential before adaptation to hosts or cells indicated.

[4] 1° = First passage.

chicken and chicken embryonic cells, 1° monkey kidney, chicken tracheal organ cultures, VERO cells. MHV: L cells, WI-38 cells, 1° mouse and mouse embryonic cells, mouse macrophages, NCTC-1469 cells. TGEV and HEV: 1° porcine cells. TGEV: 1° canine kidney cells. RCV and SDAV: 1° rat kidney cells.

6 Pathogenicity

6.1 Association with diseases: IBV: acute respiratory disease and nephritis in chickens. HCV: common colds in humans. MHV: hepatitis and encephalitis in mice (most strains cause primarily one or the other). TGEV: gastroenteritis in pigs. HEV: encephalitis in pigs. RCV: pulmonary infections of rats. SDAV: sialodacryoadenitis in rats.

6.2 Tissue tropisms: IBV: respiratory and reproductive tract. HCV: upper respiratory tract. TGEV: small intestine, lung. HEV: intestine, brain. MHV: brain, liver, spleen. RCV: lung. SDV: salivary gland.

6.3 Cytopathology: Cellular vacuolation and syncytium formation.

7 Geographic distribution: Probably worldwide.

8 Transmission

8.1 Vertical: HCV: no. IBV: yes. No data available for other strains.

8.2 Horizontal: Yes.

8.3 Vectors

8.3.1 Biological: Not known.

8.3.2 Mechanical: IBV: contaminated equipment, personnel, etc. TGEV: fecal-oral route. HCV: presumed airborne. No data for other strains.

9 Antigenic properties

9.1 Number of distinct antigenic molecules in virion: IBV: up to 3. HCV: 3, possibly 4. MHV: 2.

9.2 Antigens involved in virus neutralization: No adequate information.

9.3 Number of distinct nonstructural antigens: No adequate information.

9.4 Specificity of different antigens: No information.

10 Classification

10.1 Definition of family **Coronaviridae:** Pleomorphic enveloped particles, averaging 100 nm diameter, containing RNA and essential lipid. Bear unique definitive projections. Multiply in cytoplasm, mature by budding through endoplasmic reticulum. No defined subgroups, but a tentative grouping may be made on basis of serology. IBV, many recognized serotypes, however, all seem to be interrelated, possibly by a common antigen. No interrelationship demonstrated

with any of the other coronaviruses. HCV, several serotypes, two main groups – those isolated in tissue culture and those isolated in organ culture. Serologically related to MHV. The three rodent coronaviruses, MHV, RCV and SDAV, are interrelated serologically, and also related to HCV. No adequate information on relationship or diversity between individual strains of MHV. TGEV, no antigenic diversity between strains, possible relationship to HEV. HEV, no antigenic diversity between strains, possible relationship to TGEV. TBDV, only one report available, no relationship shown to other coronaviruses.

10.2 Only one Genus, *Coronavirus*. Type species: IBV.

10.3 Species: Avian infectious bronchitis virus (IBV)
Human coronavirus (HCV)
Murine hepatitis virus (MHV)
Porcine transmissible gastroenteritis virus (TGEV)
Porcine hemagglutinating encephalitis virus (HEV)
Rat coronavirus (RCV)
Sialodacryoadenitis virus of rats (SDAV)
Turkey bluecomb disease virus (TBDV) [3]
Neonatal calf diarrhea coronavirus (NCDCV) [4]

Selected References

1 Tyrrell, D.A.J.; Almeida, J.D.; Berry, D.M.; Cunningham, C.H.; Hamre, D.; Hofstad, M.S.; Mallucci, L., and McIntosh, K.: Coronaviruses. Nature, Lond. *220:* 650 (1968).

2 McIntosh, K.: Coronaviruses: a comparative review. Curr. Topics Microbiol. Immunol. *63:* 85–129 (1974).

3 Ritchie, A.E.; Desmukh, D.R.; Larsen, C.T., and Pomeroy, B.S.: Electron microscopy of coronavirus-like particles characteristic of turkey bluecomb disease. Avian Dis. *17:* 546–558 (1973).

4 Mebus, C.A.; Stair, E.L.; Rhodes, M.B., and Twiehaus, M.J.: Neonatal calf diarrhea: propagation, attenuation, and characteristics of a coronavirus-like agent. Am.J.vet. Res. *34:* 145–150 (1973).

5 Watkins, H.; Reeve, P., and Alexander, D.J.: The ribonucleic acid of infectious bronchitis virus. Archs Virol. *47:* 279–286 (1975).

6 Tannock, G.A.: The nucleic acid of infectious bronchitis virus. Arch. ges. Virusforsch. *43:* 259–271 (1973).

7 Hierholzer, J.C.: Personal commun. (1973).

8 Hierholzer, J.C.: Personal commun. (1975).

9 BINGHAM, R.W.: The polypeptide composition of avian infectious bronchitis virus. (Submitted for publication.)
10 MADGE, M.H. and BINGHAM, R.W.: Personal commun. (1975).
11 ALEXANDER, D.J.: Personal commun. (1975).
12 JOHNSON-LUSSENBERG, C.M.: Personal commun. (1975).
13 BINGHAM, R.W.; MADGE, M.H., and TYRRELL, D.A.J.: Haemagglutination by avian infectious bronchitis virus – a coronavirus. J. gen. Virol. (in press).
14 POCOCK, D.H. and GARWES, D.J.: The influence of pH on the growth and stability of transmissible gastroenteritis virus *in vitro*. (Submitted for publication.)
15 ZAKSTELSKAYA, L.YA.: Personal commun. (1973).

Dr. D.A.J. TYRRELL, Clinical Research Centre, Watford Road, *Harrow, Middlesex HA1 3UJ* (England)