

Essential veterinary education in the virology of domestic animals, wild animals and birds: diagnosis and pathogenesis of viral infections

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Summary

An education in veterinary virology should establish a basis for life-long learning and enable veterinary graduates to address professionally the control and eradication of viral diseases, both locally and globally. It is therefore more important that the curriculum focuses on a sound understanding of the nature and behaviour of viruses and their interactions with animal hosts, rather than imparting detailed information on an ever-increasing number of individual viral diseases in a widening range of animal species. Graduate veterinarians should be prepared with a comprehensive knowledge of the nature of viruses and their close dependence on the hosts that they infect, as well as a good understanding of pathogenesis, immunology, epidemiology, diagnostic approaches and control options. All these are necessary if the profession is successfully to meet familiar and new challenges in viral diseases in a wide range of host species, under different management conditions, in various geographic areas of the world.

Keywords

Curriculum – Diagnosis – Epidemiology – Immunology – Pathogenesis – Replication – Taxonomy – Transmission – Vaccination – Virology.

Introduction

Veterinary education aims to prepare graduate veterinarians to prevent, treat, control and eradicate animal diseases, and to apply their veterinary knowledge and skills to the protection and promotion of human and environmental health. Although a large component of veterinary education is focused on ensuring that certain abilities and skills are possessed by graduates from their first day of entering the profession, it is also clear that veterinary education must form the basis for life-long learning.

If those statements are accepted for veterinary education in general, then it is possible to apply them to education in virology in particular, and to develop rationally the content

and emphases of a virology programme appropriate to the overall veterinary curriculum. It is recognised that different virology programmes may vary in content, emphasis, format and location. Often this reflects particular interests of the individual school, the geographical context in which it is located and the communities in which its graduates are expected to work. Sometimes it may simply be a reflection of the personal interests of the instructor charged with developing the course.

A common point of tension within veterinary schools is whether virology should be taught from the perspective of a virologist, usually perceived as a laboratory researcher, or from the perspective of clinical relevance, with an emphasis on clinical signs, epidemiology, diagnostic tests, recommended treatments and control options. Such tensions can be healthy and the discussions provoked can

result in courses that encompass the best elements of both extremes, so that students achieve both synergy and breadth of understanding while their interest is stimulated.

While education in veterinary virology must be integrated with other courses in the veterinary curriculum, which also contain much of the information needed to understand and respond to viral diseases, a virology programme also needs to address a number of specific elements of viral infection, if it is to meet the educational objectives stated above. The authors argue that these essential elements comprise:

- the nature of viruses
- viral replication and antiviral therapies
- methods of transmission, routes of infection and pathogenesis of viral diseases
- the immune response to viral infections
- epidemiology
- diagnostic methods
- control options, including vaccination.

The nature of viruses

It is probably safe to assume that few students enter professional veterinary training so that they can become virologists. However, it is important that they understand enough about the nature of viruses so that they can apply that knowledge in what might be considered the more clinical or applied components of the veterinary course. If this is kept in mind by teachers, then links can be made from knowledge of the nature of viruses, and the value of taxonomic approaches when thinking about them, to practical applications in the field.

Understanding the basics of viral taxonomy and nomenclature provides a framework for grouping viruses, revealing features about them that are invaluable in practical applications. Examples include their common appearance under the electron microscope or the structure and organisation of their genome. It is also clearly of practical value to know which families:

- are enveloped, and hence less robust in the external environment
- persist for long periods after being shed into the environment
- are characterised by life-long infection of their hosts
- are transmitted by arthropod vectors
- have segmented RNA genomes
- are characterised by frequent genetic drift and reassortment.

A concise but solid appreciation of all these issues provides a good basis for understanding and predicting the likely behaviour of newly discovered viruses, many of which will appear during the working lifetimes of the veterinary students of today, just as they have over the past few decades.

Viral replication and antiviral therapies

Viruses are totally dependent on the living cells of their host species to replicate. An understanding of the general model of viral replication, and the major variations, is essential for at least two reasons.

First, such an understanding provides the information necessary to appreciate where a virus and virus-infected cells may initiate an immune response and be either susceptible to or protected from that response. Understanding that viruses have surface molecules that enable them to become attached to specific receptors on cells before they are internalised indicates at which point they may be susceptible to the action of specific antiviral antibodies. Virus-infected cells expressing 'foreign' virus-coded molecules on their surface are important in interactions with other components of the immune system.

Secondly, understanding viral replication allows an appreciation of how the infecting virus uses host cell enzymes and other components for its own replication, thus presenting a challenge for the development of antiviral therapies. Since a number of antiviral therapies have been developed, and are being increasingly used in veterinary medicine, it is important that veterinary graduates understand their modes of action. In short, virus-specific steps or enzymes have been identified for some viruses, so that therapeutic agents can be produced that are selective for the virus and not the host cell. These agents include, for example:

- those that interfere with reverse transcriptase activity to inhibit retroviral replication
- those that interfere with the attachment and release of influenza viruses
- nucleoside analogues that interfere with deoxyribonucleic acid (DNA) replication in herpesviral infections.

Methods of transmission, routes of infection and pathogenesis

An understanding of the nature of viruses and their replication in host species provides an appropriate

foundation for considering:

- virus survival
- methods of transmission between hosts
- modes of entry into hosts
- mechanisms for producing disease.

Since viruses require living cells in which to replicate, there are a limited number of portals of entry into susceptible hosts. The oro-nasal, ocular, venereal, transplacental and percutaneous (e.g. by biting vectors) routes are the most common ways in which viruses can enter a new susceptible host and commence replication.

For example, viruses with fragile envelopes, such as herpesviruses and influenza viruses, survive poorly in the external environment and often rely on close juxtaposition between the mucosal surfaces of infected and susceptible individuals in a population, or prompt transmission by aerosol droplets or on food. Non-enveloped viruses, such as parvoviruses, may be robust in the environment, surviving for months under appropriate conditions until they are introduced into the next susceptible host, often via the mouth. Still other viruses rely on vector transmission, for example, by insects, in which they may replicate or simply be transmitted mechanically by contaminated mouth parts. Vertical transmission from the pregnant mother to the foetus is used by some viruses; others are transmitted in germplasm, with their DNA provirus inserted into the host genome.

The pathogenesis of a particular viral infection depends on:

- the route of entry into the host
- the cells which are first infected and the nature of that infection (lytic or not)
- the means by which the virus spreads within the body to reach the target organs
- the specific cells within those organs that are infected.

The immune response of the host to the infection, which may be beneficial to the host or contribute to the nature and severity of the disease, is an added and important dimension. If one considers the example of canine parvovirus, much of the clinical appearance of the enteric disease produced, as well as many of the physiological mechanisms disturbed and treatments and actions required to prevent spread and protect susceptible animals, can be reasoned from a knowledge of:

- the nature of the virus (long persistence in the environment)
- the route of entry (oral)
- the site of primary replication (tonsillar cells)
- the spread through the body (viraemia)
- the target organ (intestine)

- the specific target cells (epithelial cells in the crypts of intestinal villi, because the virus is only able to replicate in cells that are already rapidly replicating themselves)
- the disturbance in fluid and electrolyte balance due to intestinal damage (loss of the villus epithelium)
- the shedding of virus in the diarrhoeic faeces, and so on.

One could reasonably expect that a veterinary graduate, armed with a sound knowledge of the nature of viruses, their replication strategies, their methods of spread and entry into hosts, and their pathogenesis, could intelligently deal with even a 'new' viral infection in an unfamiliar host species, if they were given an indication of which family the 'new' virus belonged to, and what clinical signs had been observed.

Immune response

It is common for veterinary students to have already completed a course in immunology by the time they begin to study veterinary virology. In applying their existing knowledge to veterinary virology they need to focus on three key areas:

- protective immunity against viral infections (vaccination and recovery from infection)
- immunopathology
- diagnostic immunology (usually serology).

When considering protective immunity, whether induced by vaccination or during recovery from infection, it is again helpful to draw on what has already been mentioned above, i.e. viral structure and replication, routes of entry, sites of initiation of infection, and pathogenesis of viral infection. Issues to be covered include:

- the antigenic structure of viruses
- the location of key immunogens on the viral particle
- the site of the desired immune response (mucosal surface, blood or tissue fluids)
- the type of immune response (humoral response for cell-free virus in serum versus cell-mediated response for the detection and destruction of virus-infected cells)
- inactivated versus live vaccines
- the antigenic variation of virus strains (and why this occurs commonly with some viruses yet not with others)
- the transfer of passive immunity from mother to offspring.

The authors have commonly found that students who have completed a course in immunology have a good appreciation of the components of the immune system and

its interactions in bringing about an immune response. Yet, they have little appreciation of the time over which this typically occurs in the whole animal or the duration of protection. This appears a simple point but it is vitally important in understanding how soon protective immunity can be expected after the administration of a vaccine, how long this immunity lasts, and in the interpretation of serological tests for evidence of infection.

There are numerous examples of viral diseases in which the immune response is harmful to the host and, in some cases, this may be exacerbated by vaccination. There are instances where antibody may lead to antigen-antibody complexes, which precipitate and cause damage to organs such as the eyes or kidneys; where the exuberant activation of macrophages leads to tissue destruction, and where cytokine storms lead to haemorrhage and fluid leakage in organs such as the lungs.

A good understanding of viral immunology is an important basis for understanding vaccine development and usage, viral immunopathology, and the use of the immune response in tests for diagnosis and surveillance of viral diseases.

Epidemiology

An appreciation of epidemiology, as applied to viral diseases, can be readily built on a sound knowledge of:

- the nature of viruses
- their restriction to replication in living cells
- varying durations of survival outside the host
- modes of transmission
- routes of entry and shedding from infected hosts.

It is also essential to understand the role played by host factors, such as:

- individual or herd susceptibility
- population size and behaviour
- the presence and behaviour of vectors, when these are required for transmission
- factors that may affect the susceptibility of a population to infection, such as nutrition, concurrent disease or overcrowding.

Graduates should appreciate that disease is not simply the result of the presence of the relevant virus plus the susceptible host. Many other factors are important when trying to reduce the risk of outbreaks. Practical examples of taking an epidemiological approach to prevent and control viral diseases may include such actions as:

- bringing animals into insect-proof housing at the end of the day, to avoid them being bitten by insect vectors that are only active after dark

- monitoring climate and vegetation coverage, to predict when outbreaks of certain diseases, such as Rift Valley fever, are likely to occur.

An epidemiological approach, and hence the need to understand epidemiological principles when applied to viral diseases, is also necessary when developing surveillance programmes to either detect viral disease and estimate its prevalence or to obtain evidence of freedom from infection, for trade purposes.

Diagnosis of viral diseases

In practice, many viral diseases are diagnosed by the presenting clinical signs and the knowledge of the veterinarian about commonly occurring conditions in their particular geographic area. Many veterinarians become extremely skilled at this approach. They recognise subtle clinical signs or other factors, such as the time or circumstances leading to the disease occurrence, to reach their diagnosis and select their treatment or control option. However, this is hardly a sufficient basis to diagnose diseases that may occur less frequently, or have clinical signs that closely resemble those of other infectious diseases, or which are new to the area or occurring in unfamiliar species.

The basic approaches to conducting a disease investigation also need to be covered, although it is expected that this subject will be dealt with in greater detail in pathology and the clinical courses that often follow on from virology at most veterinary schools. Graduate veterinarians should be familiar with the different types of laboratory tests that are available (including serological tests for antibody or antigen detection, virus isolation and the detection of viral nucleic acid) and the appropriate samples for each test. Thus, by the time of graduation, a veterinarian should, for any viral disease in any species, be able to:

- collect a thorough, relevant history
- conduct a clinical examination
- perform a necropsy
- detect visible abnormalities
- select suitable samples
- collect and store these samples properly for submission to a laboratory, for further specialist examination.

It is to be hoped that, by the time students graduate, they will have had an opportunity to conduct a disease investigation, following samples that they have collected through to the laboratory and conducting some of the tests themselves. In the experience of the authors, the greatest challenge for students, and many graduate veterinarians, is

in interpreting the results of laboratory tests and knowing what information can be expected from particular tests.

Understanding the correct generic approach and being able to conduct a diagnostic investigation is far more important than learning lists of diagnostic features of an ever-increasing number of viral diseases.

Vaccination and other control options

If all the components of a veterinary virology course discussed above have been covered, then control of viral diseases, including the use of vaccination, becomes an exercise in applying the principles that have been learned. Once a diagnosis is achieved, and the causative virus identified, then knowledge of the environmental survival of the virus, its mode of transmission, the carrier state, routes of shedding, involvement of vectors, availability of vaccines and antigenic variability of the virus involved, as well as the other factors mentioned, can be used to develop a rational control or prevention programme and to conduct efficient surveillance.

Students should be reminded of the survival properties of viruses when considering how vaccines should be stored before use and how diagnostic samples should be packaged and stored to provide the best opportunity for the laboratory to conduct meaningful tests.

At the point of graduation, all veterinarians should be able to understand the rationale behind particular control programmes, including strategic vaccine usage, even if they do not have the experience, at that stage, to develop from scratch such programmes themselves.

Conclusions

In presenting what the authors consider to be the essential elements of veterinary education in virology, they have not attempted to address the structure, format, style or methods of presenting this information to students, nor the challenge of actively involving them in the educational process. This will vary widely in different schools and with the particular preferences of the programme co-ordinator.

Experience suggests that veterinary virology is an exciting subject to teach. Students are motivated by the fact that so many of the important veterinary diseases that they will have an opportunity to address are caused by viruses, and more and more tools are becoming readily available for diagnosis and control. Further, since more high-profile emerging diseases are recognised as being caused by viruses originating from animals, the subject is topical and dynamic. There remains much to be learned as the profession becomes more involved with a wider range of animal species, including new species of farmed animals, wildlife, domestic and wild birds and aquatic animals, all of which have their own concerns with viruses, many of which are just being discovered.

A generic approach that includes sound principles and an understanding of the nature and behaviour of viruses, combined with a case-based treatment of each viral family to reveal the generic properties of that family, is a sound way of preparing veterinarians to deal with the known and unknown challenges of viral animal diseases in the future. Such an approach has the added advantage of avoiding a parochial treatment of local diseases and promotes global awareness and education.



Les fondamentaux de l'enseignement vétérinaire dans le domaine de la virologie des animaux domestiques, des animaux sauvages et des espèces aviaires : diagnostic et pathogénie des infections virales

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Résumé

L'enseignement de la virologie vétérinaire doit offrir aux futurs diplômés les bases qui leur permettront de continuer à se former tout au long de la vie et d'intervenir avec professionnalisme dans la lutte et l'éradication des maladies virales, aussi bien au plan local que mondial. Par conséquent, l'objectif des programmes de formation consistera à élucider la nature et le comportement des virus et leurs interactions avec leur hôte animal, plutôt qu'à accumuler des informations détaillées sur les maladies virales particulières, dont le nombre ne cesse de croître chez de plus en plus d'espèces animales. Les vétérinaires diplômés doivent posséder une connaissance étendue sur la nature des virus et sur leur étroite dépendance à l'égard des hôtes qu'ils infectent, ainsi que des notions solides de pathogénie, d'immunologie et d'épidémiologie ; ils doivent également connaître parfaitement les méthodes diagnostiques disponibles et les différentes possibilités de prophylaxie. Toutes ces compétences sont nécessaires pour que la profession puisse faire face aux défis connus et inédits associés aux maladies virales chez une grande variété d'espèces hôtes, dans différentes conditions de gestion et en diverses régions du monde.

Mots-clés

Diagnostic – Épidémiologie – Immunologie – Pathogénie – Programme d'enseignement – Réplication – Taxonomie – Transmission – Vaccination – Virologie.



Enseñanza veterinaria básica sobre virología de aves y animales domésticos y salvajes: diagnóstico y patogénesis de las infecciones víricas

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Resumen

La enseñanza de la virología veterinaria debe servir para sentar las bases de un proceso de aprendizaje permanente y para que los titulados sepan abordar con profesionalidad el control y la erradicación de enfermedades víricas, tanto en el plano local como en el mundial. Por ello no es tan importante transmitir información muy detallada sobre un número creciente de enfermedades víricas

que afectan a un número creciente de especies animales como lograr que los planes de estudios confieran una sólida comprensión de la naturaleza y el comportamiento de los virus y sus interacciones con el animal anfitrión. La preparación de los futuros veterinarios pasa por adquirir un conocimiento global de la naturaleza de los virus y su estrecha dependencia del anfitrión y por entender cabalmente la patogénesis, inmunología y epidemiología de las enfermedades víricas y los métodos para diagnosticarlas y controlarlas. Todo ello es indispensable para que los profesionales resuelvan con éxito los problemas, tanto conocidos como inéditos, que van a plantearles las enfermedades víricas de muy diversas especies anfitrionas, en muy diversas condiciones de gestión y en distintas zonas geográficas del mundo.

Palabras clave

Diagnóstico – Epidemiología – Inmunología – Patogénesis – Plan de estudios – Replicación – Taxonomía – Transmisión – Vacunación – Virología.
