VIRUSES, THE UNKNOWN PATHOGENS

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INTRODUCTION

Viruses form a group of pathogens that most people are not very familiar with, However whether we like it or not, viruses are familiar with us and there is probably nobody in this world that does not have personal experience with them. We all have had a simple cold, the flu or measles, each of them caused by a (different) virus. Not only humans are susceptible to viruses, almost every living organism in this world is affected by them. There are viruses that infect plants, viruses specific for fungi or for bacteria and animal viruses. Even snakes have their specific viruses.

The fact that viruses are relative unknown to most people is one of the reasons why sometimes strange ideas on the cause and treatment of virus diseases surface. In this article I want to give some limited background information of what viruses are, how they infect snakes (and other organisms) and how one can deal with and, maybe most important, can try to prevent virus infections.

WHAT IS A VIRUS?

The word virus is Latin and means 'poison'. This word gives an indication of the association of these organisms with diseases and plagues that mankind has suffered over the centuries. The actual concept of viruses however, is only just over 100 years old.

At the end of the nineteenth century the theory that diseases are caused by 'germs' became established. This may seem obvious to us now but it was long believed that diseases arose from the organism itself or were caused by the hand of some god. Following the 'germ theory', the causative agents of many diseases were isolated, observed under the microscope, cultured

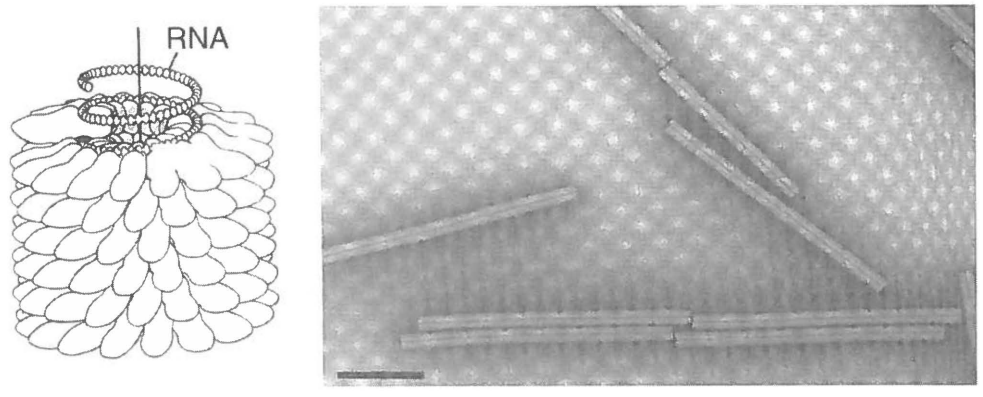

Figure 1. Left: model of a particle of tobacco mosaic virus (TMV) with the coat protein forming a protective structure around the RNA structure. Right: electron micrograph of tobacco mosaic virus (TMV) particles. The bar represent 100 nm, (reprinted from Van Regenmortel et al, 2000).

on artificial media and demonstrated to cause their particular pathologies. Some diseases however, sometimes called 'virus', could not be studied in this way since they did not follow the rules. So in what aspects are viruses different from other pathogens?

CHARACTERISTICS OF VIRUSES

First of all viruses are very small. It was soon discovered that the disease agents that did not follow the rules could not be seen under the microscope, this in contrast to bacteria and fungi. Viruses were also able to pass through porcelain filters that were used to remove bacteria and fungi and sterilize solutions, another indication of their (much) smaller size. The first virus, a plant virus called tobacco mosaic virus or TMV, was described in 1898 by Beyerinck in Wageningen in the Netherlands. However it took until 1939, when the first electron microscope was constructed, before TMV could actually be seen (Figure 1). Since 1939 many plant and animal viruses have been visualized and we now know that on average a virus is about 1000x smaller then a bacterium.

A second characteristic of viruses is that they can not be cultured on artificial media. Although this is not an exclusive property of viruses we now know that they require a host organism. To be more precise viruses require a host cell since they can only grow inside a living cell.

When science further developed it became possible to study viruses in more detail both in their structure as well as in their, biochemical, composition. Viruses proved to be simple structures composed only of protein(s) and one single type of genetic material (nucleic acid called DNA or RNA). Bacteria and fungi are far more complex and are composed of at least two types of genetic material (DNA and RNA), proteins, lipids, sugars and many more small molecules.

All of the characteristics above now make it possible to formulate a definition of what a virus is: *Viruses are entities whose genomes are elements of nucleic acid that replicate inside living cells using the cellular synthetic machinery and causing the synthesis of specialized elements that can transfer the virus genome to other cells* (Luria et al, 1978). In more simple words: 'Viruses are relative simple structures that depend on the machinery of a living cell for their survival, replication and spread'. Whether viruses can be regarded as living organisms is more a philosophical question. Not being able to replicate on their own viruses are, technically speaking, non-living organism, and by some people regarded as simple, dead, biochemical structures.

VIRUS ARCHITECTURE

So if viruses consist only of protein(s) and one type of genetic material, what do viruses then look like? The basis arrangement of a virus is that the protein forms a protective shell around the genetic material (RNA or DNA). This results in either a rod-shaped (Like TMV, figure 1) or a spherical configuration. Figure 2 gives an overview of the diversity of shapes and sizes of the different viruses that can infect vertebrates. The shell or coat consists of one or more proteins that are encoded by the genetic material, or genome, of the virus. Some viruses also have an envelope around them, derived from their host, which is formed around the virus upon release from the infected cell.

Despite this basically simple architecture there is still an amazing variety and complexity in shape and some viruses are simply beautiful as is demonstrated by bacteriophage T4 (figure 3).

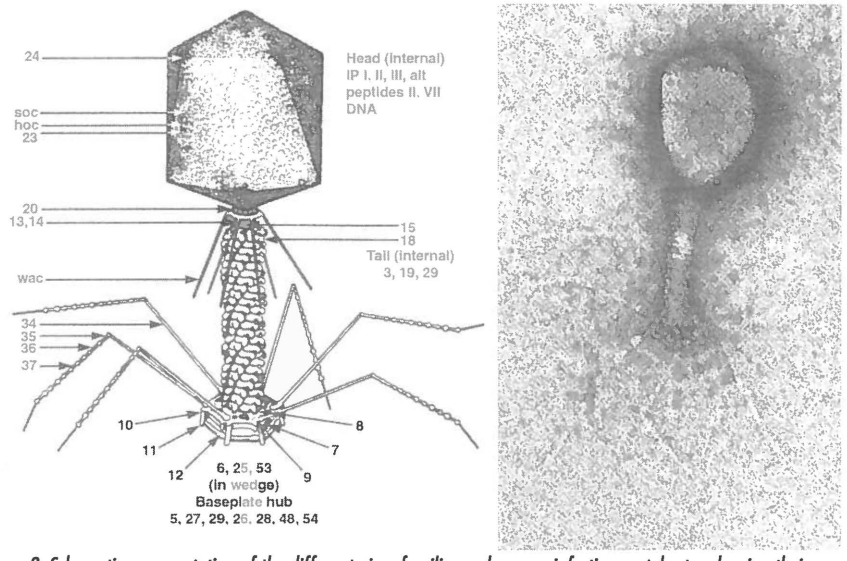

Figure 2. Schematic representation of the different virus families and genera infecting vertebrates showing their variety in shape and size (reprinted from Van Regenmortel et al, 2000).

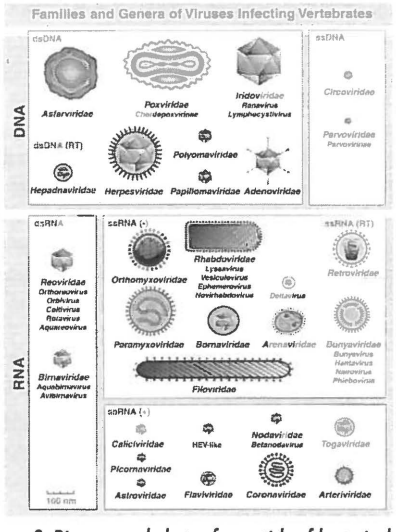

Figure 3. Diagram and photo of a particle of bacteriophage T4 showing the head, tail and base of this complex virus particle (reprinted from Van Regenmortel et al, 2000).

VIRUS INFECTION

We now know that viruses are basically simple structures that consist of genetic material protected by protein(s). How then can these simple structures infect cells and cause such serious diseases? The answer is that the virus more or less takes over the machinery of the cell in order to produce as much progeny virus as possible. This progeny is then released from the infected cell and will in turn infect other adjacent cells where the whole process is repeated.

In the case of snake and other animal viruses the infection starts when the virus attaches itself to the cell surface. This attachment can be very specific and depend on the specific recognition of the virus of the cell surface. This specific recognition is the main reason why specific viruses are only capable of infecting very specific types of cells cells. The AIDS virus only infects a particular type of blood cell.

Upon attachment the virus penetrates the host cell, falls apart and its genetic material is released. This ge-

netic material (either DNA or RNA) then starts using the cell machinery with only one purpose: replicate as may copies of itself as possible. Clearly this interferes with the normal cellular processes. In a relative short time a huge number of copies of the DNA or RNA of the virus is produced. At the same time the virus starts to use another part of the cell machinery to synthesize viral proteins encoded on its genetic material.

Maturation of new viruses starts as new genetic material and virus proteins become available and are assembled into new virus particles. Large number of newly formed virus particles are released from the infected cell. Each new virus particle is itself capable of starting a new infection of surrounding cells thereby starting the whole process again. In a relative short time an infection of one initial cell can lead to large number of infected cells.

EFFECTS OF VIRUS INFECTIONS

In the case of a successful virus infection a large number of cells will become infected. Since the virus takes over part of the cell machinery this, as one can imagine, will inevitable interfere with the normal processes within the cell. In result, cells will often show cytopathic effects upon virus infection. Some effects are localized alterations within infected cells and the most common of these are the so-called inclusion bodies (Figure 4, see also Jacobson and Schumacher, 1998) Virus infection however, can also lead to structural changes in cell morphology.

Cells in return have evolved methods of combating virus infections. By producing and secreting very specific proteins (e.g. interferons), infected cells are able to warn adjacent cells for the oncoming virus attack. These cells can then prepare themselves to combat the viral infection. In quit some cases a situation may develop in which nobody wins. Completely destroying its host is usually not in the best interest of the virus. When the host dies, the virus dies with it since it depends on the living cells of the host.

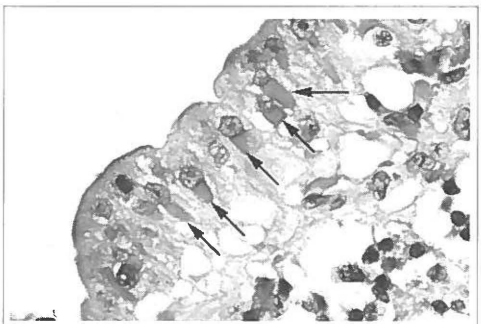

Figure 4. Photomicrograph of lung of boa constrictor with Inclusion Body Disease (IBD). Inclusions are indicated by the arrows.

IS THERE A TREATMENT FOR VIRUS DISEASES?

As outlined above there are two important characteristics of a virus infection. The first is that most of the viruses in an infected animal will be inside the cells. Secondly, once inside a cell the virus will take over and use the normal machinery of the cell.

Since the majority of the virus particles will be inside the cells they are unreachable for the snake's immune system. Normally capable of recognizing and destroying any foreign molecules and pathogens, the cells of the immune system are helpless because they can not get inside the cells. Only a limited number of virus particles released from infected cells, are recognized and destroyed. However, viruses have the ability to change themselves so as to make it harder for the immune system to recognize them. This way the virus tries to stay one step ahead of the immune system.

Fighting or prohibiting virus replication inside the cell is very difficult. It generally means interfering in the normal cellular processes and when employing such drugs these will inevitably also affect uninfected cells. Basically this means that virus infections can not be treated with drugs (except for a few very specific exceptions). Antibiotics will not work against virus infections since viruses are no 'biotics'. Antibiotics however

can help in fighting secondary (bacterial) infections that may result from the general weakened state of the infected animal.

CONTROL

So when active treatment is either very difficult or simply impossible what can one do? One of the best strategies seems to be to simply prevent infection. But, this is often not as simple as it seems. We are all aware of the benefits of good and strict hygiene. This includes quarantine of newly acquired snakes, regular cleaning and disinfecting cages and enclosures as well as being careful who you give access to your snakes. In the case of inclusion body disease virus snake mites (*Ophionyssus natricis*) are suspected to transmit the virus. Cruel as it may seem the best (long-term) solution is to euthanatize any animal in which a virus infection is diagnosed or strongly suspected.

Effective control measures however depend on the ability to recognize what you are up against. With viruses of snakes this can be difficult. Not always a virus infection is obvious and infection can be latent which means that virus is present but it does not cause symptoms. Clinical signs can be very subtle or non-specific like off-feed for only a short period. Virus can have an effect on different cell types, thereby causing completely different clinical symptoms. Virus infections cause an immune response so theoretically a simple blood test for the presence of virus-specific antibodies would give an indication of exposure to this virus. Unfortunately these tests are either not (widely) available or too expensive. Development of such tests requires a fair amount of scientific research, which is expensive. Given the fact that snakes (either in the wild or as pets) are not likely to be a profitable market progress in this field is slow.

Viruses of snakes are likely to be around for some time to come. I hope that through this article I have made some of you more aware of the nature of these pathogens and it will to prevent and control the serious problems they can cause for our beloved snakes.

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