SECTION I

AN INTRODUCTION TO THE STRUCTURE AND BEHAVIOR OF VIRUSES
CHAPTER 1

DEFINING THE ECOLOGY OF VIRUSES*

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1.1 INTRODUCTION

The goal of virology is to understand the viruses and their behavior. Virology is an interesting subject and even has contributed to the concepts of what we consider to represent deities and art. Sekhmet, an ancient Egyptian goddess, was for a time considered to be the source of both causation and cure for many of the diseases that we now know to be caused by viruses (Figure 1.1). Influenza, a viral-induced disease of vertebrates, was once assumed to be caused by the influence of the stars, and that is represented by the origin of it’s name which is derived from Italian. The following was a

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rhyme which children in the United States sang while skipping rope during the influenza pandemic of 1918–1919:

I had a little bird
It’s name was Enza

I opened a window
And in-flew-Enza.

And a bit more recently an interesting poem was written about viruses (Source: Michael Newman, 1984):

“The Virus”

Observe this virus: think how small
Its arsenal, and yet how loud its call;
It took my cell, now takes your cell,
And when it leaves will take our genes as well.
Genes that are master keys to growth
That turn it on, or turn it off, or both;
Should it return to me or you
It will own the skeleton keys to do
A number on our tumblers; stage a coup.

But would you kill the us in it,
The sequence that it carries, bit by bit?
The virus was the first to live,
Or lean in that direction; now we give
Attention to its way with locks,
And how its tickings influence our clocks;
Its gears fit in our clockworking,
Its habits of expression have a ring
That makes our carburetors start to ping.

This happens when cells start to choke
As red cells must in monoxic smoke,
When membranes get the guest list wrong
And single-file becomes a teeming throng,
And growth exists for its own sake;
Then soon enough the healthy genes must break;
If we permit this with our cells,
With molecules abet the clanging bells;
Lend our particular tone to our death knells.

The purpose of this book is to define the ecology of viruses and, in so doing, try to approach the question of what life is like from a “virocentric” (as opposed to our normal anthropocentric) point of view. Ecology is defined as the branch of science which addresses the relationships between an organism of interest and the other organisms with which it interacts, the interactions between the organism of interest and its environment, and the geographic distribution of the organism of interest. The objective of this chapter is to introduce the main concepts of viral ecology. The remaining chapters of this book set, Studies in Viral Ecology volumes 1 and 2, will then address those concepts in greater detail and illustrate the way in which those concepts apply to various host systems.

1.1.1 What is a Virus?

Viruses are biological entities which possess a genome composed of either ribonucleic acid (RNA) or deoxyribonucleic acid (DNA). Viruses are infectious agents which do not possess a cellular structure of their own, and hence are “acellular infectious agents”. Furthermore, the viruses are obligate intracellular parasites, meaning that they live (if that can be said of viruses) and replicate within living host cells at the expense of those host cells. Viruses accomplish their replication by usurping control of the host cell’s biomolecular machinery. Those which are termed “classical viruses” will form a physical structure termed a “virion” that consists of their RNA or DNA genome surrounded by a layer of proteins (termed “capsid proteins”) which form a shell or “capsid” that protects the genomic material. Together, this capsid structure and its enclosed genomic material are often referred to as being a “nucleocapsid”. The genetic coding for the capsid proteins generally is carried by the viral genome. Most of the presently known virus types code for their own capsid proteins. However, there are some viruses which are termed as being “satellite viruses”. The satellite viruses encapsidate with proteins that are coded for by the genome of another virus which coinfects (simultaneously infects) that same host cell. That virus which loans its help by
giving its capsid proteins to the satellite virus is termed as being a “helper virus”. The capsid or nucleocapsid is, in the case of some groups of viruses, surrounded in turn by one or more concentric lipid bilayer membranes which are obtained from the host cell. There exist many other types of acellular infectious agents which have commonalities with the classical viruses in terms of their ecology. Two of these other types of acellular infectious agents, the viroids and prions, are included in this book set and are addressed within their own respective chapters (Volume 1, chapters 10 and 12). Viroids are biological entities akin to the classical viruses and likewise can replicate only within host cells. The viroids possess RNA genomes but lack capsid proteins. The agents which we refer to as prions were once considered to be nonclassical viruses. However, we now know that the prions appear to be aberrant cellular protein products which, at least in the case of those afflicting mammals, have acquired the potential to be environmentally transmitted. The natural environmental acquisition of a prion infection occurs when a susceptible host mammal ingests the bodily material of an infected host mammal. The reproduction of prions is not a replication, but rather seems to result from a conversion of a normal host protein into an abnormal form (Volume 1, chapter 10). The Acidianus two-tailed virus, currently the sole member of the viral family Bicaudaviridae, undergoes a morphological maturation following its release from host cells and this is unique among all of the biological entities now considered to be viruses suggesting that this species may represent the initial discovery of an entirely new category of biological entities.

1.1.2 What is Viral Ecology?

Ecology is the study of the relationships between organisms and their surroundings. Viral ecology is, therefore, the relationship between viruses, other organisms, and the environments which a virus must face as it attempts to comply with the basic biological imperatives of genetic survival and replication. As shown in Figure 1.2, interactions between species and their constituent individual organisms (biological entities) occur in the areas where there exist overlaps in the temporal, physical, and biomolecular (or biochemical) aspects of the ecological zones of those different species. Many types of interactions can develop between species as they share an environment. One of the possible types of interactions is predation. When a microorganism is the predator, that predator is referred to as being a pathogen and the prey is referred to as being a host.

When we study viral ecology we can view the two genetic imperatives that every biological entity must face, namely, that it survive and that it reproduce, in the perspective of a biological life cycle. A generalized biological life cycle is presented in Figure 1.3. This type of cycle exists, in its most basic form, at the level of the individual virus or individual cellular being. However, it must be understood that in the case of a multicellular being this biological life cycle exists not only at the level of each individual cell, but also at the tissue or tissue system level, and at the organ level. This biological life cycle likewise exists on even larger scales, where it operates at levels which describe the existence of each species as a whole, at the biological genus level, and also seems to operate further upward to at least the biological family level. Ecologically, the life cycles of those different individuals and respective species which affect one another will become interconnected both temporally, geographically, and biologically. Thus, there will occur an evolution of the entire biological assemblage and, in turn, this process of biotic evolution will be obliged to adapt to any abiotic changes that occur in the environment which those organisms share. While a species physiologic capacities establish the potential limits of the niche which it could occupy within this shared environment, the actual operational boundaries of it’s niche are more restricted and defined by it’s interspecies connections and biological competitions.
1.1.3 Why Study Viral Ecology?

The interplay which occurs between a virus and the living organisms which surround it, while all simultaneously pursue their own biological drive to achieve genetic survival and replication, creates an interest for studying the ecology of viruses (Doyle, 1985; Fuller, 1974; Kuiken et al., 2006; Larson, 1998; Morell, 1997; Zinkernagel, 1996). While examining this topic, we improve our understanding of the behavioral nature of viruses as predatory biological entities. It is important to realize that in nature both the viruses of macroorganisms and the viruses of microorganisms normally

FIGURE 1.2 Interactions between organisms (biological entities) occur in the areas where the physical and chemical ecologies of the involved organisms overlap. Infectious disease is a type of interaction in which a microorganism acts as a parasitic predator. The microorganism is referred to as a pathogen in these instances.
exist in a cycle with their respective hosts. Under normal conditions, the impact of viruses upon their natural hosts may be barely apparent due to factors such as evolutionary coadaptation between the virus and its host (evolutionary coadaptation is the process by which species try to achieve a mutually acceptable coexistence by evolving in ways which enable them to adapt to one another). However, when viruses find access to new types of hosts and alternate transmission cycles, or when they encounter a concentrated population of susceptible genetically similar hosts such as occurs in densely populated human communities, communities of cultivated plants or animals, or algal blooms, then the impact of the virus upon its host population can appear catastrophic (Nathanson, 1997; Subbarao et al., 1998).

As we study viral ecology we come to understand not only those interconnections which exist between the entities of virus and host, but also the interconnections between these two entities and any vectors or vehicles which the virus may utilize. As shown in Figure 1.4, this interplay can be represented by the four vertices of a tetrahedron. The possible routes by which a virus may move from one host organism to another host organism can be illustrated as the interconnecting lines between those vertices which represent two hosts (present and proximate) plus one vertex apiece representing the concepts of vector and vehicle. Figure 1.5, which represents a flattened form of the tetrahedron shown in the previous figure (Figure 1.4) can be considered our point of reference as we move forward in examining viral ecology. The virus must survive when in association with the present host and then successfully move from that (infected) host organism (center of Figure 1.5) to another host organism. This movement, or transmission, may occur via direct contact between the two host organisms or via routes which involve vectors and vehicles (Hurst and Murphy, 1996). Vectors are, by definition, animate (living) objects. Vehicles are, by definition, inanimate (non-living) objects. Any virus which utilizes either vectors or vehicles must possess the means to survive when in association with those vectors and vehicles in order to sustain its cycle of transmission within a population of host organisms. If a virus replicates enough to increase its population while in association with a vector, then that vector is termed to be “biological” in nature. If the virus population does not increase while in association with a vector, then that vector is termed to be “mechanical” in nature. Because viruses are obligate intracellular parasites, and vehicles are by definition non-living, then we must assume that the virus cannot increase its population while in association with a vehicle.
Environmentally, there are several organizational levels at which a virus must function. The first and most basic of those levels is the individual host cell. That one cell may comprise the entire host organism. Elsewise, that host cell may be part of a tissue. If within a tissue, then the tissue will be contained within a larger structure termed either a tissue system (plant terminology) or an organ (plant and animal terminology). That tissue system or organ will be contained within an organism. The host organism is exposed to the open (ambient) environment, where it is but one part of a population of other organisms belonging to its same species. The members of that host species will be surrounded by populations of other types of organisms. Those populations of other types of organisms will be serving as hosts and vectors for either the same or other viruses. Each one of these organizational levels represents a different environment which the virus must successfully confront. A virus’ affects upon it’s hosts and vectors will draw responses against which the virus must defend.
itself if the virus is to survive. Also, the virus must always be ready to do battle with its potential biological competitors. Contrariwise, the virus must be open to considering newly encountered (or reencountered) species as possible hosts or vectors. Because of their acellular nature, when viruses are viewed in the ambiental environments (air, soil and water) they appear to exist in a form that essentially is biologically inert. However, they have a very actively involved behavior when viewed in these many other organismal environments.

Considering the fact that viruses are obligate intracellular parasites, their ecology must be presented in terms which also include aspects of the ecology of their hosts and any vectors which they may utilize. Those factors or aspects of viral ecology which we study, and thus which will be considered in this book set, include the following:

**Host Related Issues**

1. what are the principal and alternate hosts for the viruses;
2. what types of replication strategies do the viruses employ on a host cellular level, host tissue or tissue system level, host organ level, the level of the host as a whole being, and the host population level;
3. what types of survival strategies have the viruses evolved that protect them as they confront and biologically interact with the environments internal to their host (many of those internal environments are actively hostile, as the hosts have developed many powerful defensive mechanisms);
4. what direct effects does a virus in question have upon its hosts, i.e. do the hosts get sick and, if the hosts get sick, then how severe is the disease and does that disease directly threaten the life of the host;
5. what indirect effects does the virus have upon its hosts, i.e., if the virus does not directly cause the death of the hosts or if viral-induced death occurs in a temporaly delayed manner as is the case with slow or inapparent viral infections, then how might that virus affect the fitness of the host to compete for food resources or to avoid the host’s predators;

**General Transmission-Related Issue**

6. what types of transmission strategies do the viruses employ as they move between hosts, including their principal and alternate transmission routes which may include vehicles and vectors; and

**Vector-Related Issues**

7. in reference to biological vectors (during association with a biological vector the virus will replicate and usually is carried within the body of the vector), what types of replication strategies do the viruses employ on a vector cellular level, vector tissue or tissue system level, vector organ level, the level of the vector as a whole being, and also on a vector population level;
8. in reference to biological vectors, what types of survival strategies have the viruses evolved that protect them as they confront and biologically interact with the environments internal to their vectors (those internal environments may be actively hostile, as vectors have developed many powerful defensive mechanisms);
9. in reference to biological vectors, what direct effects does a virus in question have upon its vectors, i.e. do the vectors get sick and, if the vectors get sick, then how severe is the disease and does that disease directly threaten the lives of the vectors;
10. in reference to biological vectors, what indirect effects does the virus have upon its vectors, i.e., if the virus does not directly cause the death of the vectors or if viral-induced death occurs in a temporaly delayed manner as is the case
with slow or inapparent viral infections, then how might that virus affect the fitness of the vectors to compete for food resources or to avoid the vector’s predators;

11. in reference to mechanical vectors, what types of survival strategies have been evolved by those viruses which are transmitted by (and during that event usually carried on the external surfaces of) mechanical vectors, since while in association with a mechanical vector the virus must successfully confront any compounds naturally present on the body surface of the vector plus confront the passively hostile ambiental environments of either air, water or soil through which the vector will be moving; and

Vehicle-Related Issue

12. what types of survival strategies have been evolved by those viruses which are transmitted by way of vehicles and which thereby must successfully confront the passively hostile ambiental environments of either air, water or soil as the virus itself is transferred through those environments.

If biological curiosity alone were not a sufficient reason for studying viral ecology, then perhaps we would study the viruses out of a desire to both understand them as predators and to contemplate the ways in which we might enlist their aid as ecological tools.

1.2 SURVIVING THE GAME: THE VIRUS AND IT’S HOST

Remember that: so long as the virus finds a new host, whether or not the current host survives is unimportant. Although it may be beneficial to not kill a current host until that host has reproduced to help provide a new generation of potential host organisms, if the host to virus ratio is large enough, then even this latter point may be unimportant.

This section presents in general terms the relationship between a virus and host. The generalities of relationships between viruses, vectors, and vehicles will be discussed in section 1.3 of this chapter. The specific subject of the practical limits to viral virulence in association with hosts and vectors will be addressed in section 1.4 of this chapter.

While in association with a host, the virus has only one principle goal. This goal is for the virus to replicate itself to a sufficient level that it can achieve transmission to another host. This goal can be attained by one of two basic strategies. The first of these strategies would be a productive infection, for which five basic patterns can be defined. The second strategy would be a non-productive infection. The goal of a productive infection is for the virus to produce infectious viral particles (those capable of infecting cells) which are termed “virions”, during the virus’ association with the current host. Subsequent spread of the infection to the next host occurs by transfer of these produced virions. Contrastingly, some of those agents which exhibit a non-productive pattern may either seldom or never produce actual virions. Thus, the usual goal of a non-productive strategy of infection is to pass the infection to the next host by directly transferring only the viral genomic sequences (van der Kuyl et al., 1995). The patterns of productive infection are:

“Short term - initial” in which viral production has only a short term initial course, after which the viral infection ends and there no longer is a presence of that virus within the body of the host individual although subsequent reinfection can occur, the outcome from this pattern of infection depends upon the virus type and historical exposure to that type within the host population, the situation being that in otherwise healthy members of a multicellular host population with which the virus has coevolved, these infections are usually mild and by
themselves normally associated with a fairly low incidence of mortality;

“Recurrent” in which repeated episodes of viral production occur, this pattern often has a very pronounced initial period of viral production, after which the virus persists in a latent state within the body of the host with periodic reinitiations of viral production that usually are not life threatening;

“Increasing to end-stage” in which viral infection is normally associated with a slow, almost innoxious start followed by a gradual progression associated with an increasing level of viral production and eventual death of the host, in these instances death of the host may relate to destruction of the host’s immunological defense systems which then results in death by secondary infections;

“Persistent-episodic” is a pattern that represents a prolonged nonfatal infection which may persist for the remainder of the host’s natural lifetime associated with a continuous production of virions within the host, but interestingly the infection only episodically results in symptoms, the viral genome does not become quiescent throughout the course of this associative interaction, and very notably some members of the family Picobirnaviridae often produce this pattern of productive infection;

“Persistent but inapparent” is a pattern that represents a prolonged nonfatal infection which seemingly never results in overt symptoms of illness attributable to that particular virus, the viral genome never becomes quiescent and viral infections that follow this pattern are persistently productive with the host often remaining infectious for the remainder of their natural lifetime, with notable examples of viruses which produce this pattern being members of the family Anelloviridae, and it also occurs in certain rare instances of infection by Human immunodeficiency virus 2 which is a member of the genus Lentivirus of the family Retroviridae.

There are two options to the “short term - initial” pattern. The first option is a very rapid, highly virulent approach which is termed “fulminate” (seemingly explosive) and usually results in the rapid death of the host organism. This first option usually represents the product of an encounter between a virus and a host with which the virus has not coevolved. The second option is for the virus to be less virulent, causing an infection which often progresses more slowly, and appears more benign to the host. The “recurrent” and “increasing to end-stage” patterns incorporate latency into their scheme. Latency is the establishment of a condition in which the virus remains forever associated with that individual host organism and generally shows a slow and possibly only sporadic replication rate that, for some combinations of virus and host, may never be life threatening to the host. The strategy of achieving a non-productive, or virtually non-productive, pattern of infection involves achieving an endogenous state (Terzian et al., 2001). Endogeny implies that the genome of the virus is passed through the host’s germ cells to all offspring of the infected host (van der Kuyl et al., 1995; Villareal, 1997).

The product of interspecies encounters between a virus and it’s natural host will usually lead to a relatively benign (mild, or not directly fatal), statistically predictable, outcome that results from adaptive coevolution between the two species. Still, these normal relationships do not represent a static coexistence between the virus and the natural host, but rather a tenuous equilibrium. Both the virus species and it’s evolved host species will be struggling to get the upper hand during each of their encounters (Moineau et al., 1994. The result will normally be some morbidity and even some mortality among the host population as a result of infection by that virus. Yet, because the virus as a species may not be able to survive without this natural host species
(Alexander, 1981), excessive viral-related mortality in the host population is not in the long term best interest of the virus. Some endogenous viruses have evolved to offer a survival-related benefit to their natural host, and this can give an added measure of stability to their mutual relationship. Two examples of this type of relationship are the hypovirulence element associated with some strains of the Chestnut blight fungus, and the endogenous retroviruses of placental mammals. The hypovirulence (reduced virulence) which the virus-derived genetic elements afford to the fungi that cause Chestnut blight disease reduce the virulence of those fungi (Volume 1, chapter 9). This reduced virulence allows the host tree, and in turn the fungus, to survive. Placental mammals, including humans, permanently have incorporated species of endogenous retroviruses into the chromosomes of their genomes. It has been hypothesized that the incorporation of these viruses has allowed the evolution of the placental mammals by suppressing maternal immunity during pregnancy (Villareal, 1997).

However, the impact of a virus upon what either is, or could become, a natural host population can sometimes appear catastrophic. The most disastrous, from the host’s perspective, are the biological invasions which occur when that host population encounters a virus which appears new to the host (Kuiken et al., 2006). Three categories of events can lead to biological invasions of a virus into a host population. These categories are: first, that this virus species and host species (or sub-population of the host species) may never have previously encountered one another (examples of this occurring in human populations would be the introduction of measles into the Pacific islands and the current introduction of HIV); second, if there have been previous encounters, the virus may have since changed to the point that antigenically it appears new to the host population (an example of this occurring in humans would be the influenza pandemic of 1918–1919); and third, that even if the two species may have had previous encounters, this subpopulation of the host species subsequently may have been geographically isolated for such a length of time that most of the current host population represents a completely new generation of susceptible individuals (examples in humans are outbreaks of viral gastroenteritis found in remotely isolated communities on small islands as related to the occasional arrival of ill passengers by aircraft or watercraft). Sadly, the biological invasion of the HIV viruses into human populations seems to be successful (Caldwell and Caldwell, 1996), and the extreme host death rate associated with this invasion can be assumed to indicate that the two species have not had time to coevolve with one another. The sporadic, but limited, outbreaks in human populations of viruses such as those which cause the hemmorhagic fevers known as Ebola and Lassa represent examples of unsuccessful biological invasions. The limited chain of transmission for these latter two illnesses (for Lassa, see: Fuller, 1974), with their serial transfers often being limited to only two or three hosts in succession, represents what will occur when a virus species appears genetically unable to establish a stable relationship with a host species. The observation of extremely virulent and fulminate symptomatology, as associated with infections by Lassa and Ebola in humans, can generally be assumed to indicate either that the host in which these drastic symptoms are observed is not the natural host for those viruses or, at the very least, that these two species have not had time to coevolve. In fact, the extreme symptomatology and mortality which result in humans from Ebola and Lassa fevers seems to represent an overblown immune response on the part of the host (Spear, 1998). While having the death of a host individual occur as the product of an encounter with a pathogen may seem like a dire outcome, this outcome represents a mechanism of defense operating at the level of the host population. If a particular infectious agent is something against which members of the host population could not easily defend themselves, then it may be better to have that particular host individual die (and die very quickly!) to reduce the possible spread
of the contagion to the other members of the host population.

### 1.2.1 Cell Sweet Cell, and Struggles at Home

As diagramed in Figure 1.6, viruses can arrive at their new host (solid arrows) either directly from the previously infected host, via an intermediate vehicle, or via an intermediate vector. Viral survival in association with that new host depends upon: viral replication within that new host, the effects which the virus has upon that host, and the response of that host to the virus. Successful viral survival in association with this new host will allow a possible subsequent transfer of the virus (open arrows) to its next host either directly, via a vehicle, or via a vector. This represents a segment from Figure 1.5.

Within a multicellular host, the virus may face anatomically associated barriers including membranous tissues in animals. The virus may also face non-specific, non-immune biological defenses (Moffat, 1994), including such chemical factors as the enzymes found in both tears and saliva, and the acid found in gastric secretions. The types of anatomical and non-specific, non-immune defenses encountered can vary depending upon the viral transmission route and the portal by which the virus gains entry into the host’s body. After a virus finds it’s initial host cell and succeeds in beginning it’s replication, the effects which the virus has upon the host can then draw a defensive biological response. The category of non-specific non-immune responses which a virus may encounter at this stage include even such things as changes in host body temperature for mammals. As if in a game of spy versus spy, the virus most importantly must survive the host’s specific immune defenses.
(Beck and Habicht, 1996; Gauntt, 1997; Levin et al., 1999; Litman, 1996; Ploegh, 1998; Zinkernagel, 1996).

The listing and adequate explanation of antiviral defense techniques would by itself be enough to nearly fill a library. But, I will attempt to summarize some of them here and help the reader to track those through this book set.

Molecular antiviral defenses begin at the most basic level which would be non-specific mechanisms. These conceptually include DNA restriction and modification systems (volume 1, chapter 5), progressing upward with greater complexity to the use of post-transcriptional processing (Russev, 2007). Countering these defenses is done by such techniques as using virally-encoded restriction-like systems to chop-up the DNA genome of their host cells to provide a ready source of nucleic acids for the production of progeny viral genomes. There also are viruses which try to shut down the post-transcriptional defenses, most clearly noticed among some viruses infective of plants. Plants in fact heavily rely upon molecular defenses such as post-transcriptional control, (volume 1, chapter 11) and beyond that technique the plants try to wall off an infection, essentially trying to live their lives despite presence of the infectious agent and hoping not to pass the infection along to their offspring through viral contamination of their germ cells.

Antimicrobial peptides are a defensive mechanism found in all classes of life, and represent a main part of the insect defensive system (volume 2, chapter 10). Higher on the scale of defensive responses are things which we term to be immunological in nature (Danilova, 2006). Some of these we term to be innate, others we call adaptive. A good starting point for this discussion of immunological responses is the capacity for distinguishing self versus non-self, accompanied by the capability for biochemically destroying cells that are determined to be non-self. This approach exists from at least the level of fungi (volume 1, chapter 9) upwards for the non-animals, and among the animals this approach begins with at least the corals (volume 2, chapter 5). Determining and acting upon the distinction of self versus non-self likely may have developed as a system that helps to support successful competition for growth in a crowded habitat, but it serves well against pathogenic organisms. As a health issue, this process sadly plays a role in autoimmune diseases and we try to suppress it when hoping to use organ and tissue transplantation to save human lives.

Apoptosis, the targeting of individual cells within the body of the host for selective destruction by the host, commonly exists across the animal kingdom. This mechanism is used by many invertebrates (volume 2, chapters 6 and 7) as well as vertebrates to destroy any virally infected cells which may be present within their bodies. However, apoptosis is a weapon that can be used by both of the combatants. Using apoptosis to destroy virally-infected cells before the virus contained within those cells can assemble progeny virions is an effective approach when used carefully by the host. As might be expected, some viruses therefore defensively try either to shut-down the process of apoptosis, or at least to shut-down that process until the virus is ready to use apoptosis as a mechanism for assisting in the liberation of assembled virions from the infected host cell.

Vertebrates, and some of the invertebrates, have more complex body plans and can use them with good effectiveness in combating infections. With the evolutionary development of more complex body plans, comes the possibility of dedicating cells and even organs to the task of fighting pathogenic invaders. Those invertebrates with more complex body plans are represented in the anti-viral fight by their use of lymphoid organs to actively collect and either sequester or actively assault and destroy the microbial offenders. Some of the aquatic crustaceans (volume 2, chapter 7) tend to rely upon sequestering an infection and must hope to breed a new generation of their own progeny before they, themselves, are killed by the infection which they have sequestered within their
body. At the same time, the infected parents must hope not to pass along the sequestered infection to their offspring through contamination of their eggs and sperm. Such collection and sequestration techniques are found upward through the evolutionary line and likewise used by the vertebrates. Many viruses have found ways around these issues, as is the case with endogenous viruses and retrotransposons that insert and maintain themselves in the genome of their host, passing directly through the germ cell line. Some viruses infect and replicated within the immune cells! Some viruses are shed along with the eggs of invertebrates and thus are ready to await the hatching of those offspring. Still other viruses, as in the case of viviparous mammals, simply cross the placenta to infect the fetus.

Interferons and their homologues are protein systems which vertebrates have developed and use effectively against some viruses, and correspondingly many viral groups contain mechanisms for suppressing interferon production (Muñoz-Jordán and Fredericksen, 2010). Although the “walling-off” of a pathogen still occurs in vertebrates, with an example being the development of tubercules in some mycobacterial infections, active mechanisms for hunting down and destroying pathogens and pathogen-infected cells within their bodies is highly developed. With vertebrates, the end goal can be perceived as ridding the body of the pathogen even if that end goal is not always achieved. The jawed vertebrates possess immune systems which are termed adaptive, and these produce protein antibodies that can be highly specific (volume 2, chapters 8, 9, 11–14).

Options for surviving the immune defenses of the host can include such techniques as:

“**You don’t know me**” (a virus infecting an accidental host, in which case a very rapid proliferation may occur, an example being Lassa fever in humans);

“**Being very, very quiet**” (forming a pattern of latency in association with the virus’ persistence within that host, an example being herpesviruses);

“**Virus of a thousand faces**” (antigen shifting, an example being the lentiviruses);

“**Keep to his left, that’s his blind spot**” (maintaining low antigenicity, an approach used by viroids and prions);

“**Committing the perfect crime**” (infecting the immune system, an approach taken by many retroviruses and herpesviruses); and

“**Finding a permanent home**” (taking up permanent genetic residency within the host and therefore automatically being transmitted to the host’s progeny, an approach taken by viroids, endogenous retroviruses, and LTR retrotransposons).

Each virus must successfully confront its host’s responses while the virus tries to replicate to sufficient numbers that it has a realistic chance of being transmitted to another candidate host. Failure to successfully confront the host’s responses will result in genetic termination of the virus and, on a broader scale, such failure may eventually result in extinction for that viral species.

### 1.2.2 I Want a Niche, Just Like the Niche, That Nurtured Dear Old Mom and Dad

The initial tissue type in which a virus replicates may be linked inextricably with the initial transmission mode and portal (or site) of entry into the body of the host. For example, those viruses of mammals which are acquired by fecal - oral transmission tend to initiate their replication either in the nasopharyngial tissues or else in the gastrointestinal tissues. There then are subsequent host tissue and organ types affected, some of which may be related to the virus’ efforts at trying to reach it’s proper portal of exit. Others of the host tissues affected by the virus may be unrelated to interhost viral transmission, although the affect upon those other tissues may play a strong role in the severity of illness which is associated with that viral infection. An example of the latter would be the
encephalitic infection of brain neurons in association with echoviral conjunctivitis, an infection which initially would be acquired from fomites as part of a fecal-oral transmission pattern. In this case, the encephalitis causes nearly all of the associated morbidity but does not seem to benefit transmission of the virus (personal observation by author C. J. Hurst).

1.2.3 Being Societal

Successful viral survival in association with this new host will allow a possible subsequent transfer of the virus (Figure 1.6, open arrows) to its next host either directly, via a vehicle, or via a vector. The movement of a viral infection through a population of host organisms can be examined and mathematically modeled. An epidemic transmission pattern, characterized by a short term, higher than normal rate of infection within a host population is represented by the compartmental model shown in Figure 1.7 (Hurst and Murphy, 1996). An endemic transmission pattern, characterized by a long term, relatively constant incidence rate of infection within a host population is represented by the compartmental model shown in Figure 1.8 (Hurst and Murphy, 1996).

1.3 STEPPIN' OUT AND TAKING THE A TRAIN: REACHING OUT AND TOUCHING SOMEONE BY VECTOR OR VEHICLE

Remember that: host-vector choices, cycles and vehicle utilizations as they exist today may (and probably do!) reflect evolutionary progression from prior species interactions and ecological relationships.

After a virus has successfully replicated within the body of it’s current (present) host, it must seek successful transmission to it’s next (proximate) host. The resulting chain of transmission usually is the end-all of viral reproduction. These are three basic approaches by which this can be attained: transmission by direct contact between the present and proximate hosts, transmission mediated by a vector (Brogdon and McAllister, 1998; Hurst and Murphy, 1996; Mills and Childs, 1998), and transmission mediated by a vehicle (Hurst and Murphy, 1996). While considering these approaches, it is important to keep in mind that the chains of transmission originate by random chance followed by evolution.

1.3.1 “Down and Dirty” (Just Between Us Hosts)

This heading is one which can be used to describe host to host transmission (transmission by host to host contact). While this is one of the most notorious, it is not the most common route of viral transmission between animals. This route only serves to a limited extent in microbes. Even worse, this route essentially does not seem to function in vascular plants due to the relative immobility of those hosts.

1.3.2 “The Hitchhiker” (Finding a Vector)

Transmission by vectors may be the most prevalent route by which the viruses of plants are spread among their hosts. This route clearly also exists for some viruses of animals. However, this route has not yet been defined in terms of viruses which infect microbes. Vectors are, by definition, animate objects, and more specifically they are live organisms. Being a vector implies, although by definition does not require, that the entity serving as vector has self-mobility. Thus, plants could serve by definition as vectors, although when we consider the topic of viral vectors we usually tend to think in terms of the vectors as being invertebrate animals. Vertebrate animals can also serve as vectors, as likewise can some cellular microbes.

There are two categories of vectors: biological and mechanical. As was stated earlier, if the virus increases it’s numbers while in association with a vector, then that vector is termed
as being biological. Conversely, the vector is termed to be mechanical if the virus does not increase its numbers while in association with that vector. Beyond this there lie some deeper differences between mechanical and biological vectors. These differences include the fact that the acquisition of a virus by a biological vector usually involves a feeding process. Phagic habits of the biological vector result in the virus being acquired from an infected host when the vector ingests virally contaminated host body materials acquired through a bite or sting. Subsequent transfer of the infection from the contaminated biological vector to the virus’ next host occurs when the biological vector wounds and feeds upon the next host. Actual transference of the virus to that next host occurs incidentally when the vector contaminates the wound by discharging viruses contained either in the vector’s saliva, regurgitated stomach or intestinal contents, or else discharged feces and urine. Essentially any animal is capable of serving as a potential biological vector provided that the wound which it inflicts while feeding upon a host plant or animal will not result in the death of that new host until the virus would have had the chance to replicate within and subsequently be transmitted onward from that new host. There are many issues surrounding the question of what makes a good biological vector. These issues include: physical contact between the virus’ host and the potential vector during a feeding event, viral reproduction within that potential vector, and that the infected vector be able to survive long enough to transmit the virus to a new host. It also helps if there is some factor driving the vector to pass along the infection, such as the

![Diagram of epidemic transmission](image-url)
virus finding its way into the vector’s saliva, or the virus increasing the physical aggressiveness of the vector.

The fact that biological vectors usually acquire the viral contaminant while wounding and ingesting tissues from an infected host brings us to another distinguishing difference between biological and mechanical vectors: viral contamination of a biological vector usually is associated with the virus being carried internal to the body of the vector. Replication of the virus then occurs within the body of the biological vector. Contrastingly, viral contamination of a mechanical vector usually occurs on the external surface of the vector and the virus subsequently tends to remain on the external surface of the mechanical vector. One possible example of mechanical vectoring would be the acquisition of plant viruses by pollinating animals such as bees and bats during their feeding process. These pollinators can serve as mechanical vectors if subsequently they are able to passively transfer the virus from their body surface to the next plant from which they will feed. In the case of these pollinators, the acquired virus presumably is carried external to the pollinator’s body. Conversely, it is possible that a plant being visited by a pollinator might become contaminated by viruses afflicting that pollinator, and the plant could then passively serve as a mechanical vector if subsequent pollinators should become infected when they visit that plant. Biting flies can serve as biological vectors if, during feeding, they ingest a pathogen which can replicate in association with that fly and then be passed onward when the fly bites its next victim (Hurst and Murphy, 1996). Non-biting flies can passively serve as mechanical vectors if they feed upon contaminated material and then subsequently transmit those microbial contaminants to the food of a new host without that pathogen having been able to replicate while in association with the non-biting fly (Hurst and Murphy, 1996). Arthropods such as wasps, which repeatedly can sting multiple animals, could serve as mechanical vectors by transporting viruses on the surfaces of their stingers. Also, passive surface contamination of pets that occurs unrelated to a feeding event can result in the pets serving as mechanical vectors (Hurst and Murphy, 1996).

When a virus is transported inside the body of the vector, then that transportation is referred to as being an “internal carriage”. Contrastingly, transportation of a virus on the external body surfaces of a vector is referred to as being an “external carriage”. As will be described in volume 1, chapter 11, there are some plant viruses which are transported through internal carriage by invertebrates that represent mechanical vectors (because the virus does not increase its population level when in association with those invertebrates). Thus, although the biological vectoring of a virus usually involves internal carriage, the fact of internal carriage does not alone always indicate that

**FIGURE 1.8** Endemic transmission of a virus within a host population is represented by this type of compartment model (Hurst and Murphy, 1996). This model is essentially an extension of the model presented in Figure 1.7. This model contains the same three compartments (susceptible, infectious, and immune) representing actively included individuals and the category of individuals removed by infection related mortality as were described for Figure 1.7. This model differs in that it must also consider the various possible categories of live removed individuals which can move into and out from the compartments of actively included individuals. Their removal represents the fact that they do not interact with the actively included individuals in such a way that the virus can reach them, often due to spatial isolation. This model also includes the fact that the immune status of individuals can naturally wane or diminish with time such that immune individuals return to the compartment labeled susceptible; production of host progeny, representing reproductive success of the members of the host species; natural mortality, as a means of removing members of the population; and the possible use of vaccination to circumvent the infectious process plus the associated vaccine-related mortality. Please notice that the progeny of infectious individuals may be susceptible, infectious, or immune at the time of their birth depending upon the type of virus which is involved and whether or not that viral infection is passed to the progeny. Used with permission of the author and Cambridge University Press.
the vectoring is biological. Humans, interestingly, can serve as mechanical vectors via internal carriage for plant viruses that would be consumed with food and later excreted in feces (Zhang et al., 2006).

Because a virus must (by definition!) replicate in association with the biological vector; we can view the viral - vector association (Figure 1.9) in the same manner as was done for that of a virus and it’s host (Figure 1.6). Indeed, it often is difficult to know which species is actually the viral host and which is actually the viral vector; to distinguish which is the victim and which serves as the messenger. Traditionally, we have often taken the view that humans are a high form of life and that there is a decreasing heirarchy down to the microbes. From this traditional, and sadly very anthropo-centric, viewpoint we might assume that any living thing that transmits a virus between humans must be the vector as humans surely must be in the respectable position of serving as the host. Another version of this philosophy would consider a vertebrate to be the host and any invertebrate to be the vector. Still a third version has been based upon relative size, with the largest creature considered as the host and the smaller considered as the vector. Since we stated earlier that this chapter is intended to consider life from a virocentric perspective, we could easily accept the virocentric view which finds that there may be no clear distinction
between host and vector. Rather, any biological vector can likewise be viewed as a host. The argument as to which one, the traditional host or traditional vector, really serves as the host would then become moot.

Because many types of viruses are capable of infecting more than a single species of host, we are also left to ponder about determining which is the principle host versus those which serve as alternate hosts. Settlement of the distinction asked by this latter question is usually done by examining the comparative virulence of the virus in the different types of hosting species. That species for which the virus seems less virulent is assumed to be the more natural, most coevolved, host. It then is assumed that the species for which the virus seems to have greater virulence are alternate hosts. While trying to appreciate this conundrum, it must be understood that from a virocentric perspective both the principle and alternate hosts, as well as any biological vectors utilized by a virus, will all represent hosting species, and thus we may never be able to sort out the answers. Any further discussion of this particular issue is best left to only the most insistent of philosophers! Perhaps the only things left to be said of this issue are that examples of the transmission of a virus by a biological vector are represented in Figure 1.10, and that ecological interactions between a virus and its principle hosts, alternate hosts, and biological vectors can be represented by the example shown in Figure 1.11.
FIGURE 1.11 This figure represents a generalization of the ecological interactions which lead to insect-transmitted viral encephalitis. These infections generally are either enzootic or epizootic, meaning that their natural hosts are animals. Humans normally represent dead-end hosts for these viruses, meaning that the virus is not efficiently transmitted from infected humans to other hosts. The example shown in this figure is of a virus which has evolved ecological cycles both in warm, tropical climates and in cold, temperate climates. The cycle that has evolved in the warm climates can utilize arthropod vectors which do not have to go through the process of overwintering, thus allowing for an active year-round transmission cycle. Migratory birds, which may travel thousands of miles during their seasonal migrations, can shuttle the virus infection to the temperate zones. In the temperate zones, the virus' ecological cycle may need to include strategies for overwintering in insect eggs or larva and the possibility of survival as a prolonged infection in animals which may migrate lesser distances, such as bats.
1.3.3 “In a Dirty Glass” (Going There by Vehicle)

Viruses also can be transmitted by vehicles. Vehicles are, by definition, inanimate objects. More specifically, the term vehicle applies to all objects other than living organisms. There are four general categories of vehicles and these are: foods, water, fomites (pronounced fo mitez, defined as contaminated environmental surfaces which can serve in the transmission of pathogens), and aerosols. Figure 1.12 represents viral association with a vehicle. Transmission of the virus, via a vehicle, to a new host first requires contamination of that vehicle (shown by the filled arrows in Figure 1.12). The virus must then survive while in association with the vehicle. Because viruses are by definition obligate intracellular parasites, and by definition vehicles are non-living, then a virus neither can replicate on nor within a vehicle. Likewise, because vehicles are by definition non-living, we do not expect that any specific antiviral response will be produced by the vehicle. Transference of the virus to its next host can occur either directly or via a vector (open arrows).

FIGURE 1.12 This figure addresses viral association with a vehicle and represents a segment from Figure 1.5. Viral transmission between hosts can occur by means of a vehicle. Vehicles are by definition inanimate objects. Viral contaminants can reach the vehicle (filled arrows) either directly from an infected host or via an intermediate vector. Transmission of the virus, via this vehicle, to a new host requires that the virus survive in association with the vehicle. Transference of the virus to its next host can occur either directly or via a vector (open arrows).
chapter 8). The are even viruses of terrestrial plants, including some carmoviruses of the viral family Tombusviridae, which seem as though they might be transmitted by water. The list of vehicles associated with viral transmission even includes agricultural tools and other work implements. The topic of vehicle-associated transmission of pathogens is discussed at length in the reference by Hurst and Murphy (1996).

1.3.4 Bringing Concepts Together

Biological entities exist over a spectrum of complexities, ranging from the viruses, viroids and prions (yes, even the prions are biological entities!) to multicellular organisms. The process of maintaining the viability of even the largest of organisms is, and perhaps must, be organized at small levels. Biologically, this has been achieved by a highly evolved process of internal compartmentalization of functions with a systemic coordination. If we consider for a moment one of the most enormous of the currently living multicelled organisms, the blue whale (*Balaenoptera musculus*), we notice that this kind of compartmentalization and coordination begins all of the way down at the level of the subcellular structures and organelles within each individual cell. The compartmentalization and coordination then continue upward through a number of levels including the various individual types of cells, the tissues into which those cells are organized, the organs which the tissues comprise, and finally the total internal coordination of all of these through nerve signaling and hormonal regulation. At every one of these biological levels there is a "taking from" and a "leaving behind" exchange of material with respect to the immediate surrounding environment. This results in the existence of dramatic environmental differences at all levels, even down to the many microenvironments which exist within the organizational regions of a single cell.
Every virus must try to comply with the basic biological imperatives of genetic survival and replication. While complying with these imperatives the viruses must, as obligate intracellular parasites, not only face but also survive within and successfully be transported through the various environments which are internal to the host. Those viruses which are transmitted by biological vectors must also have evolved the capability to survive and be transported through internal environments faced within the vector. Viruses which are transmitted by mechanical vectors generally must possess an additional evolved ability to survive on the surface of that vector. Likewise, both those viruses transmitted by mechanical vectors and viruses transmitted by vehicles must possess the ability to survive exposure to natural ambiental environments encountered either in the atmosphere, hydrosphere or lithosphere. These numerous environments are summarized in Figure 1.14. Conditions confronted at the interface zones, as indicated by the dashed lines in Figure 1.14, represent areas of still additional environmental complexity. While viruses appear biologically inert when viewed in the ambiental environments, they display their biology and interact with their surroundings when they reach the environments internal to their hosts and biological vectors.

The adaptability of a species in terms of its biological cycle and biological needs will determine that species’ potential distribution range. This potential distribution range is limited in actuality to a smaller range based upon interspecies relationships and competitions. Ourselves being large multicellular creatures, we humans normally think of a distribution range as being geographical in nature. As microbiologists, many of us have come to understand the concept of distribution range in finer detail; an example being the depth within a body of water where a particular species of microorganism normally will be found. At the level of viral ecology, the concept of species distribution range encompasses everything from tissue and organ tropisms (those tissues and organs which a virus seems to attack preferentially) upwards to the geographical availability of host species, vector species, and the prevailing directional flow of appropriate vehicles such as air and water. The larger, geographical end of this scale is represented in Figure 1.15.

While considering the factors addressed in Figure 1.15, it is important to keep in mind that albeit the virus’ election of hosts, vectors, and routes of transmission would all originate by random chance, the attainment of reliable continued viral success would require that such random selection events be followed and strengthened by evolution. This explains the reason why viruses do not appear suddenly to develop the ability to use a different vehicle. Indeed, it is perhaps likely that in order to use a vehicle such as air or water, the virus must have preadapted itself to the conditions which it will encounter in association with that vehicle. Nearly each individual species of virus which achieves transmission by vehicles, seems invariably to use only one type of vehicle. This trait likewise seems to hold true for all species belonging to any given viral genus. Furthermore, this identification seems to nearly always hold true at the level of viral family. In fact, this is one of the defining characteristics of the ecology of a viral group. The only virus which seems to have evolved the ability to utilize more than a single vehicle is the Hepatitis A virus (Hurst and Murphy, 1996), which has evolved a most remarkable ability to be effectively transmitted both by water and on fomites. Perhaps accordingly, the Hepatitis A virus currently exists in a genus (Hepatovirus) of its own. We should not be surprised if we eventually would discover other members of that viral genus, and subsequently discern those other members to likewise use these same two vehicles. It is for these reasons, that fears expressed in the public press that viruses such as Ebola will suddenly take flight and be transmitted over large distances via aerosol transmission amount to nothing more than frightening speculation. Why is it just speculation? Because that route of transmission is not a part of the
virus’ ecology. Invasive medical devices such as syringes, endoscopes and other surgical implements, plus transplanted animal tissues including transfused blood and blood products, and grafted plant material, represent exceptions to this rule. These devices and transplanted tissues represent unnatural vehicles which, by their nature, allow the virus an abnormal access to the interior of a new host (Hurst and Murphy, 1996). Any virus which would naturally be transmissible by direct contact with either an infected host or any type of

FIGURE 1.14 This figure integrates the concepts of host, vehicle and biological vector by representing the environments potentially faced by a virus. As obligate intracellular parasites, the viruses must face, survive within, and successfully be transported through environments which are internal to the host. Those viruses which are transmitted by biological vectors must also have evolved the capability to survive and be transported through internal environments faced within the vector. Viruses which are transmitted by vehicles and mechanical vectors must additionally possess an evolved ability to survive in natural ambiental environments (atmosphere, hydrosphere and lithosphere). Conditions confronted at the interface zones, as indicated by dashed lines, represent areas of additional environmental complexity.
FIGURE 1.15  This figure presents a hypothetical example of the way in which the ecology of a virus is delineated by the spatial relationships between its potential hosts, vectors, and vehicles. The figure represents a viral infection existing in a watershed basin whose area covers tens of millions of hectares. An assumption is made that the four potential indigenous host populations and three potential indigenous vector populations are terrestrial organisms whose ecological areas are delineated and that these organisms do not migrate outside of their own respective ecological areas. Indigenous host populations 1, 2, and 3 reside in riverine ecological areas within the basin. Indigenous vector population B has a highland ecology, while vector population C has a lowland ecology, and both of these vector populations reside within the basin. Indigenous vector population A and indigenous host population 4 are excluded from participation in the viral infection cycle due to their geographical isolation and, because of their
vector can also be transmitted by one of these unnatural vehicular routes.

Viruses occasionally will appear in association with “apparently new” (unexpected) hosts and biological vectors. These latter occurrences with unexpected hosts or vectors represent the identification of sporadic events which occur when geographical boundaries are breached by the movement of those potential hosts and vectors for which the virus in question already has a preevolved disposition. These preevolved dispositions may represent, at some basic level, the renewal of old acquaintances between a virus, vector, and host. Alternatively, if these particular viral, host, and vector species truely never have met before, then an important aspect which can factor into these encounters is the biological relatedness between these “apparently new” hosts or vectors and those other hosts or vectors which the virus more normally would use.

1.3.5 Is There no Hope?

Many host-related factors do play a role in the transmission of viral-induced illnesses. These include:

“Finding the wrong host” – the “oops” or accidental occurrence factor wherein viruses occasionally will encounter and successfully infect living beings other than their natural hosting species, an event which represents a mistake not only for the host (which often will be fated to die for want of having inherited an evolved capability to mount an effective defense against that virus) but also is a mistake for the virus (which often will not be able to subsequently find one of its natural hosts and hence also loses it’s existence);

“Only the good die young” – culling the herd for communal protection can have some advantage for the host population as a whole if those individuals that demonstrate a lesser ability to resist the virus are weakened enough by the infection that they then are more easily killed by predators (this is an act that both reduces the likelihood that other members of the host population will become infected by that virus strain and also may improve the gene pool of the host species by selectively eliminating it’s most susceptible members);

“Being your own worst enemy” – behavioral opportunities for disease transmission do exist, and ethnic or social customs often play a role in disease transmission (including the probable reality that a lack of male circumcision has spelled disaster for the human population of Africa by facilitating the heterosexual transmission of HIV) (Caldwell and Caldwell, 1996), and in fact most of those vector borne diseases that afflict humans can be avoided by changes in host behavior.

If we view this situation from the human perspective, there does exist a basis for hope in terms of the health of hosts. Our most important

geographical exclusion from the basin, we do not need to be concerned with the nature of their ecological zones. Vector population B is capable of interacting in a cycle of transmission involving host population 2. Vector population C is capable of interacting in a cycle of transmission involving host populations 1 and 2. None of the indigenous vector populations is capable of interacting in a cycle of transmission involving host population 3. A virus capable of being transmitted by surface waters could move from host population 3 to host population 2, since host population 2 is located downstream of host population 3. That same surface waterborne route could not spread the virus to host population 1, because host population 1 is not situated downstream of either host populations 2 or 3. Likewise, neither could the surface waterborne route spread the virus in an upstream direction from host population 1 to host population 2, nor from host population 2 to host population 3. Alternatively, a migratory host or vector population could carry the virus from host population 1 to host populations 2 and 3, as likewise could air flow if the virus is capable of being transmitted as an aerosol.
advantage lies in the use of barriers, which
represent a very effective means by which we
can reduce the transmission of all types of
infectious agents. Barriers can be classified by
their nature as physical (Table 1.1), chemical
(Table 1.2), and biological (Table 1.3). In many
cases, these barriers already exist in nature.
Natural examples of barriers include both high
and low temperatures (thermal, a physical bar-
rier), sunlight (radiation, a physical barrier),
the natural salinity of water (both osmotic, a
physical barrier and also dessicant, a chemical
barrier), and ecological competition (competi-
tive, a biological barrier). The intentional use
of barriers can involve both individual and com-
bined applications. One example of a combined
barrier application is the retorting of canned
products, a process which employs a combina-
tion of elevated temperature and hydrostatic
pressure to achieve either disinfection or ster-
ilization (this process is similar to autoclaving).
Many of these barrier concepts, such as filtra-
tion acting as a physical barrier, can be applied
at different levels. For example: some particle
exclusion filtration devices have pore sizes small
enough that they can act as a filtration barrier
against virus particles themselves; natural latex
condoms and disposable gloves act as filtration
barriers against a liquid vehicle (they contain
pores which are larger than the virus particles yet
smaller than the droplets of liquid in which the
virus is contained); window screens and mos-
quito netting act as filtration barriers against
flying vectors; and walls, fences, doors and gates
can act as filtration barriers against infected
hosts. The ingestion of food and water is asso-
ciated with digestive treatments such as pH
changes and secreted enzymes, both of which
represent chemical barriers. When viewed from
the virocentric perspective, the use of barrier
techniques for preventing viral transmission
would represent cause for despair instead of
hope. There is, however, a notable exception
represented by the idea of some viruses such as
the polyhedrin- forming members of the viral
families Baculoviridae and Reoviridae seem to
require digestive treatment as an aid to their
infectivity for their insect hosts.

<table>
<thead>
<tr>
<th>Table 1.1 Categories of Physical Barriers</th>
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<tbody>
<tr>
<td>Thermal</td>
</tr>
<tr>
<td>Acoustic (usually ultrasonic)</td>
</tr>
<tr>
<td>Pressure</td>
</tr>
<tr>
<td>barometric</td>
</tr>
<tr>
<td>hydrostatic</td>
</tr>
<tr>
<td>osmotic</td>
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<tr>
<td>Radiation</td>
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<tr>
<td>electronic</td>
</tr>
<tr>
<td>neutronic</td>
</tr>
<tr>
<td>photonc</td>
</tr>
<tr>
<td>protonc</td>
</tr>
<tr>
<td>Impaction (includes gravitational)</td>
</tr>
<tr>
<td>Adhesion (adsorption)</td>
</tr>
<tr>
<td>electrostatic</td>
</tr>
<tr>
<td>van der Waals</td>
</tr>
<tr>
<td>Filtration (size exclusion)</td>
</tr>
<tr>
<td>Geographic features</td>
</tr>
</tbody>
</table>
| Atmospheric factors (includes meterolog-
  ical aspects as humidity, precipitation,
  and prevailing winds)                    |

<table>
<thead>
<tr>
<th>Table 1.2 Categories of Chemical Barriers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ionic (includes pH and salinity)</td>
</tr>
<tr>
<td>Surfactant</td>
</tr>
<tr>
<td>Oxidant</td>
</tr>
<tr>
<td>Alkylant</td>
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<tr>
<td>Desiccant</td>
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<td>Denaturant</td>
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<table>
<thead>
<tr>
<th>Table 1.3 Categories of Biological Barriers</th>
</tr>
</thead>
</table>
| Immunological (includes specific as well as
  nonspecific)                             |
| naturally induced (intrinsic response)     |
| naturally transferred (lacteal, transovarian,
  transplacental, etc.)                     |
| artificially transferred (includes injection
  with antiserum and tissue transfers such as
  transfusion and grafting)                 |
| Biomolecular resistance (not immune-relat-
  ed)                                       |
| lack of receptor molecules                 |
| molecular attack mechanisms (includes nucleo-
  tide-based restrictions)                  |
| antibiotic compounds (metabolic inhibitors,
  either intrinsic or artificially supplied) |
| Competitive (other species in ecological
  competition with either the virus, its vectors,
  or its hosts)                             |
1.4 WHY THINGS ARE THE WAY THEY ARE

The ability of a virus to pass on its genetic content is the key consideration of the virus. We now understand how this gets done on a molecular level. What still remains to be understood are how this thing gets done and has come about at the species level.

1.4.1 To Kill or Not to Kill - A Question of Virulence

One of the nagging questions which a virus must face is what should be the extent of its virulence, i.e., whether or not it should kill its hosts and biological vectors as a consequence of their encounters (Ewald, 1993; Lederberg, 1997). When considered in purely evolutionary terms, virulence is the ability of the disease agent to reduce reproductive fitness of that host. The relative virulence of a virus with respect to one of its hosts or biological vectors is generally presumed to be a marker of co-evolution. More specifically stated, it seems that the less virulent is the virus for one of its hosts or vectors, the more greatly coevolved is the relationship. Why should this be so? It should clearly be the case that, were a virus to infect an individual member of a host or biological vector population prior to that individual having reached reproductive age, it would be in the virus’ best interest to not kill that host or vector. Contrariwise, in a very strict sense, death of that host or biological vector should not matter to the virus if that individual host or biological vector has passed the end of the normal reproductive lifespan. The reason for this latter philosophy is that, even if this particular host were to survive, it would not produce more susceptible offspring. Additionally, within each species of potential host or biological vector, there would be a strong genetic drive to enable their infants to mount sufficient immunological defense so as to reach the age of reproductive maturity. That same genetic drive does not, by definition, act upon the preservation of individuals who have passed their reproductive years. One example of the result from interaction of these forces is the fact that infections caused by the Hepatitis A virus can go nearly unnoticed in human infants, yet Hepatitis A virus infections can be disastrous in human adults.

Figure 1.16 represents the question of how the success of a virus relates to its’ virulence. The virus will not be successful if the result of viral infection is too deleterious in terms of affecting the ability of the present host or biological vector to survive before that virus has been able to achieve transmission to its’ next host or biological vector.

1.4.2 Genetic Equilibrium (versus Disequilibrium)

One of the hallmarks of relationships between virus species and their host species is their apparent goal of reaching a mutually acceptable genetically-based equilibrium (Dennehy et al., 2006; Lederberg, 1997; Zinkernagel, 1996). Some viruses also seem to have interchanged genetic material with their hosts while striving to evolutionarily reach a level of mutual coexistence.

There are many considerations associated with an apparent genetic equilibrium. In most instances of endemic viral infection in populations of a coevolved host or biological vector, the infections appear relatively unnoticed or relatively innocuous. This may change when the virus encounters a concentrated population of genetically similar susceptible hosts or biological vectors concentrated within a small radius, perhaps resulting in an epidemic. It also may change when the virus invades a population of novel hosts or vectors (hosts or vectors to which that virus appears to be new); this is termed a “biological invasion”. Excessive virulence may represent reduced genetic fitness with respect to the virus, host, or biological vector. Limited virulence on the part of the virus seems to represent a state of coevolution but with some remaining flux in the virus-host
interaction. This state may have a beneficial effect by acting as a genetic screening upon both the host species and the viral species. In contrast, avirulence may represent a far more evolved steady state, although evolutionarily it may not be the final state, between the viral and host populations. Avirulence is normally acquired by repeated successive passage of the virus through members of a host or biological vector population.

What are the considerations associated with an apparent genetic disequilibrium? If the virus seems to make all of the members of a species extremely sick, then presumably it normally may not be hosted or vectored by that species. If a virus causes a reduction in the genetic fitness of the host (ability of the host to pass on its genetic heritage) then the virus is viewed as being in disequilibrium with the host. Incompatible genetic differences may both fuel the fires of virulence and allow a constant state of genetic disequilibrium to exist. Genetic equilibria need time to establish. Constant disequilibrium may be viewed as a competitive strategy effected via “Evolutionary Cheating” (included in loving memory of Dr. Alex Frasier who taught me to understand evolution). Evolutionary cheating involves finding ways to change the rules of fair competition and thereby tilt the playing field in favor of your species. One good
example of evolutionary cheating would be to eat your competing species. Viruses tend to steal genes from their hosts (Balter, 1998), and this would represent another example of evolutionary cheating.

1.4.3 Uniqueness versus Commonality (There Are Hussies and Floozies in the Virus World)

1.4.3.1 Numbers of Major Viral Groups (Viral Families and Floating Genera) Affecting Different Host Categories:

From examining the list of approved viral taxonomic groups published by the ICTV (International Committee on Taxonomy of Viruses, Master Species list for November 2009, which is available as 2009_SF00_v3 on their website http://www.ictvdb.org/) it was possible to determine the host ranges of the 100 major viral groups (88 families plus 12 unassigned or ‘floating’ genera). These groups are listed alphabetically in Table 1 of Chapter 2 (if you are curious, searching each of those 2,289 viral species on the internet took 8 days of diligence). From that knowledge, the relative specificity of those major viral groups can be ascertained with regard to the host categories for which they are infective. Each of the major viral groups was associated only with either prokaryotic hosts or eukaryotic hosts. As such, none of the major viral groups crossed the imposing biochemical divide between prokaryotes and eukaryotes.

1.4.3.1.1 Prokaryotic Host Categories

There are 18 known major viral groups that are associated with prokaryotic hosts, and summarizing these by category of host the results are:

Archaea - a total of 10 major viral groups contain member species which infect archaea, with 8 of those viral groups being unique to only this host category, and the other 2 viral groups being common which means that they include viral species infective of additional host categories;

Bacteria - a total of 10 major viral groups contain member species which infect bacteria, with 7 of those viral groups being unique to only this host category, and the other 3 viral groups being common which means that they include viral species infective of additional host categories;

Cyanobacteria - a total of 2 major viral groups contain member species which infect cyanobacteria with none of those viral groups being unique to only this host category.

Among those major viral groups associated with prokaryotes, we can assess which groups have commonality as expressed in terms of their possessing a general capacity for association with more than one host category (the hussies!), and those are:

1 viral group is common to Archaea + Bacteria
1 viral group is common to Archaea + Bacteria + Cyanobacteria
1 viral group is common to Bacteria + Cyanobacteria

1.4.3.1.2 Eukaryotic Host Categories

There are 82 known major viral groups that are associated with eukaryotic hosts, and summarizing these by category of host the results are:

Algae – a total of 4 major viral groups contain member species which infect algae, with 1 of those viral groups being unique to only this host category, and the other 3 viral groups being common which means that they include viral species infective of additional host categories;

Fungi – a total of 14 major viral groups contain member species which infect fungi, with 6 of those viral groups being unique to only this host category, and the other 8 viral groups being common which means that they include viral
species infective of additional host categories;

Invertebrates – a total of 22 major viral groups contain member species which infect invertebrates, with 9 of those viral groups being unique to only this host category, and the other 13 viral groups being common which means that they include viral species infective of additional host categories;

Plants – a total of 33 major viral groups contain member species which infect plants, with 25 of those viral groups being unique to only this host category, and the other 8 viral groups being common which means that they include viral species infective of additional host categories;

Protozoa – a total of 3 major viral groups contain member species which infect protozoans, with 1 of those viral groups being unique to only this host category, and the other 2 viral groups being common which means that they include viral species infective of additional host categories; and

Vertebrates – a total of 33 major viral groups contain member species which infect vertebrates, with 22 of those viral groups being unique to only this host category, and the other 11 viral groups being common which means that they include viral species infective of additional host categories.

Among those major viral groups associated with eukaryotes, we can assess which groups have commonality as expressed in terms of the general capacity for association with more than one host category (the hussies!), and those are:

**Viruses Infecting Invertebrate Animal Hosts**

1. viral group is common to Invertebrates + Fungi + Plants
2. viral group is common to Invertebrates + Fungi + Plants + Algae

**Viruses Infecting Vertebrate Animal Hosts**

1. viral group is common to Invertebrates + Vertebrates
2. viral group is common to Invertebrates + Vertebrates + Fungi
3. viral groups are common to Invertebrates + Vertebrates + Plants
4. viral group is common to Invertebrates + Vertebrates + Fungi + Plants + Algae

The absolute floozies were the Reoviridae, a viral family that produces infectious virions and presently is known to have representation in five host categories of eukaryotes excepting only the protozoa; and the Metaviridae and Pseudoviridae which are the two viral families that represent LTR (long terminal repeat) retrotransposons and are known to each be associated with four host categories of eukaryotes.

Table 1.4 gives an assessment of relative specificity in terms of the percentage of major viral groups that were determined associated with (unique to) only a single host category, plus those major viral groups that were associated with only one additional host category. The absolute numbers of viral groups associated with each host category differed, with the greatest numbers of viral groups being known for vertebrates and plants. This relative wealth of information may be an absolute indication that in fact some host categories are more fertile ground for the evolution of new viral groups, but there also is an important associated truth which is that this difference in numbers of identified viral groups likely reflects the far greater amount of time and money that have been spent on researching viruses of vertebrates and plants. Among the eukaryotic host categories, those major viral groups infective for plants and vertebrates tended to be more
unique, ranging from 67–76%, with the extent of uniqueness being either 43% or less for viral groups associated with the other categories of eukaryotes. Among the prokaryotic host categories, those major viral groups infective for archaea and bacteria tended to be more unique, ranging from 70–80%, while the extent of uniqueness was zero for viral groups associated with the only other category of prokaryotes, which was the cyanobacteria. The vast majority of the major viral groups either were unique to a single host category or common to only one additional host category (71–100%) except for the viruses of algae and cyanobacteria (50%).

### 1.4.3.2 What Might be Reflected When We Look at the Concept of Uniqueness versus Commonality for the Major Viral Groups?

Figure 1.17 gives a visual representation for this concept of assessing uniqueness versus commonality. The most obvious separation was observed to be an apparently absolute distinction between those major viral groups associated with eukaryotic host categories (Figure 1.17a) versus prokaryotic host categories (Figure 1.17b). The second most obvious separation is not quite as absolute, but nevertheless represents a clear distinction between viral groups associated with animals versus non-animals. Among those major viral groups associated with animals, the majority of commonalities were limited to the host categories of vertebrates and invertebrates, with only a relatively small percentage of those viral groups extending between the animals and non-animals. Among those major viral groups associated with non-animals, the majority of commonalities were between the host categories of fungi and plants. Half of those viral groups which were common to fungi and plants were able to cross the divide into invertebrates.

Invertebrates often serve as biological vectors for viruses, and this accounts for many, but not all, of the viral group associations which exist between the host categories of invertebrates and either vertebrates, fungi, or plants. It also is very possible that the apparent separations or ‘divides’ visualized as we examine Figures 1.17a. and 1.17b. can give us clues as to when the presently known major viral groups evolved, i.e., that all presently known viral groups may have arisen since the separation of prokaryotes and eukaryotes, with there being a second major point representing the development of animals.

<table>
<thead>
<tr>
<th>Host Category</th>
<th>Viral groups unique to that host category</th>
<th>Viral groups common to one additional host category</th>
<th>Summary of viral groups either unique to that host category or common to just one additional host category</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eukaryotes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Algae</td>
<td>25% (1 of 4)</td>
<td>25% (1 of 4)</td>
<td>50% (2 of 4)</td>
</tr>
<tr>
<td>Fungi</td>
<td>43% (6 of 14)</td>
<td>29% (4 of 14)</td>
<td>71% (10 of 14)</td>
</tr>
<tr>
<td>Invertebrates</td>
<td>41% (9 of 22)</td>
<td>32% (7 of 22)</td>
<td>73% (16 of 22)</td>
</tr>
<tr>
<td>Plants</td>
<td>76% (25 of 33)</td>
<td>9% (3 of 33)</td>
<td>85% (28 of 33)</td>
</tr>
<tr>
<td>Protozoa</td>
<td>33% (1 of 3)</td>
<td>67% (2 of 3)</td>
<td>100% (3 of 3)</td>
</tr>
<tr>
<td>Vertebrates</td>
<td>67% (22 of 33)</td>
<td>21% (7 of 33)</td>
<td>88% (29 of 33)</td>
</tr>
<tr>
<td>Prokaryotes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Archaea</td>
<td>80% (8 of 10)</td>
<td>10% (1 of 10)</td>
<td>90% (9 of 10)</td>
</tr>
<tr>
<td>Bacteria</td>
<td>70% (7 of 10)</td>
<td>20% (2 of 10)</td>
<td>90% (9 of 10)</td>
</tr>
<tr>
<td>Cyanobacteria</td>
<td>0% (0 of 2)</td>
<td>50% (1 of 2)</td>
<td>50% (1 of 2)</td>
</tr>
</tbody>
</table>

The viral taxonomic groups represented in this table are the 88 families and 12 floating genera currently listed by the ICTV (International Committee on Taxonomy of Viruses, Master species list of November 2009 (2009_5F00_v3) which is available on the website http://www.ictvdb.org/) and those groups are listed along with their host ranges in Table 1 of Chapter 2.)
1.4.4 Evolution

As we look at the relationships between viruses and their hosts and vectors, we might ask ourselves that age-old question of “Which came first, the virus or the cell?” (Koonin et al., 2006). It is perhaps more likely that the viruses and cells arose simultaneously. Presumably they have been struggling to come to terms for a long time, (Claverie, 2006; Forterre and Prangishvili, 2009). We do not

Figure 1.17

This figure represents the number of major viral groups, those having the taxonomic classification level of either family or unassigned “floating” genus, know to be associated with eukaryotic host categories (Figure 1.17a) and prokaryotic host categories (Figure 1.17b). The boxes represent host categories. The circles represent interconnections, which are zones that illustrate the fact that many of the major virus groups overlap and are common to more than a single host category. The areas within the boxes and circles are in relative proportion to the numbers of viral families and floating genera being represented, thus giving a visual presentation of viral diversity. The connecting lines represent possibilities for viral-mediated gene flow between host categories. To date, there are no viral families or floating genera known capable of crossing the boundary between eukaryotic and prokaryotic host categories. The names of the virus families and floating genera are listed in Table 1 of chapter 2.
know either to what, or to where, the viruses are leading. Although in a true biological sense it is not necessary for the viruses to “lead” anywhere. From a virocentric view, a perfectly organized virus reproducing from host to host (perhaps with a few vectors included for spice) and transmitting its genetic information over time is a sufficient trend. In considering the evolution of viruses, we must remember the wisdom of Niles Eldredge (1991), that no existing biological entity can be said to represent an end product of evolution. Rather, it is only the extinct biological life forms that clearly can be said to have represented end products of evolution. Likewise, we do not and perhaps never may know if viruses arose only once or else have arisen at many times, with their evolutionary arisal bounded only by the practical limits of some definable adaptive zone. Understanding this comes from the realization that thus far, sabre-toothed cats have evolved at three different times during history and that they evolved from different lineages (Eldredge, 1991). Their evolution at each time would have corresponded to the opening of the appropriate niche, and each of their extinctions would have corresponded to the closing of that niche. For just as it is true that the availability of a niche can drive evolution, so too can the closure of a niche drive extinction.

Although the lack of viral fossils restricts our efforts at following the evolution of viruses, we can draw hypotheses by looking at parallels between a few of the virus groups and their hosts. To begin this process, we have seen that some of the presently existing viral families (we know nothing about those viral families that may be extinct) seem restricted to different host groups. It is likely that as time has gone by, these viruses and their hosts have coevolved and perhaps even undergone phylogenation (the evolution of phylogenetic groupings) in parallel. For example, those viruses which we know as the Myoviridae seem restricted to
infecting prokaryotic cells. This could suggest either that the ancestors of the Myoviridae are relatively new or else relatively ancient. Members of the Siphoviridae, which also infect prokaryotes, have developed a relatively stable mechanism of endogeny (in their case referred to as lysogeny), which may be suggestive of these viruses having had a long period of coevolutionary adaptation with their host cells. We can see that the viroids of plants, which genetically bear a link to the viruses (chapter 2 addresses viral taxonomy, and prions are specifically addressed in chapter 12 of volume 1) seemingly have developed such a highly evolved endogenous state that they never produce anything resembling a virion and indeed may not use or even need a natural route of transmission because they remain internal to their host. Additional examination of the existing viral groups, and the establishment of parallels between these and the known evolution of animal phyla, reveals that virus groups such as the Iridoviridae, which do produce virions, seem restricted to invertebrates and poikilothermic vertebrates. This latter examination could lead to the suggestion that ancestors of the iridoviruses followed the animal phylogenation pathway upward to a point just short of the evolution of euthermia. The retroviruses have gone onward to infect euthermic animals, and it has been hypothesized that at least some retroviruses have coevolved with their hosts to the extent that they allowed development of the placental mammals (Villareal, 1997).

Why are the viruses still around? The viruses might serve as an evolutionary benefit to the cellular organisms by gradually transferring genetic information between different sources and serving as a source for genomic development (de Lima Fávaro et al., 2005; Piskurek and Okada, 2007; Todorovska, 2007; Williams, 1996). Perhaps this is the reason why their hosting species continue allowing the viruses to exist. Perhaps the pure beauty of a virus, when viewed as an evolutionary element, is that it can break free from one host to enter another host. Gradually, that virus could coevolve until at last it might settle upon a permanent home as some endogenous genetic element within a single hosting species. Alternatively, the virus may play the role of eternally being a rebel in search of a cause. Oh, to be so free as a species!

What will the viruses become with time? As stated above, in a strictly evolutionary sense it is not necessary for the viruses to be leading to anywhere. However, if we can draw parallels and make the assumption that the relationship between virus and host moves with time towards avirulence and an eventual genetic equilibrium, then we can make hypotheses. Perhaps some of the viruses will indeed continue the way of being predatory outsiders. Others, however, seem destined for symbiosis and thus to become a part of us. We see at least two clues pointing to the latter type of destiny. One of these lies in Villareal’s hypothesis (Villareal, 1997) that by evolving to have the same biological agenda as their placental mammalian hosts, the endogenous retroviruses have symbiotically joined with their hosts to create a single species. The hypovirulence elements of the fungi which cause Chestnut blight disease are another clue (Volume 1, Chapter 9), these elements apparently evolved from a virus and seemingly have achieved symbiosis. The hypovirulence elements sustain their existence by reducing the virulence of their host fungi, so that in turn the host fungus does not kill the tree upon which the fungus feeds, enabling all to survive.

Alas, it might also be true that the evolution of viruses represents a question which we cannot yet even try to answer.

1.5 SUMMARY (CAN THERE BE CONCLUSIONS?)

The ecology of a virus primarily consists of it’s interactions with the organisms that serve as it’s hosting species (principle hosts, alternate hosts, and vectors. The routes by which viruses achieve transmission between these other organisms represent a second aspect of the ecology of viruses. Furthermore, an
examination of the interactions between a virus and its hosts and biological vectors brings up many questions. Principle among these questions is the reason why the outcome of viral infections sometimes appears to be so disastrous, and yet at other times appears unnoticeable.

One of the founding principles in biology is that natural selection serves as the basis for the population dynamics which produce the many different outcomes that we observe as scientists. When we use this principle as the lens through which to examine interactions between viruses and their host and vector species, we notice that many possible strategies exist, more than can be explained. The strategies which we do find in evidence began at random and exist because selection has not done away with them. While we do not know how the viruses have arisen, or what will be their destiny, we can assume that there may be viruses for as long as there are cells.

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REFERENCES


