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THE ECOLOGY AND EVOLUTION OF INSECT BACULOVIRUSES

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■ **Abstract** Baculoviruses occur widely among Lepidoptera, and in some species of forest and agricultural insects, they cause epizootics in outbreak populations. Here we review recent developments in baculovirus ecology and evolution, in particular focusing on emerging areas of interest and studies relating to field populations. The expanding application of molecular techniques has started to reveal the structure of baculovirus populations and has highlighted how variable these pathogens are both genotypically and phenotypically at all levels from within individual hosts to among host populations. In addition, the detailed molecular knowledge available for baculoviruses has allowed the interpretation of gene functions across physiological and population levels in a way rarely possible in parasite-host systems and showed the diverse mechanisms that these viruses use to exploit their hosts. Analysis of the dynamic interactions between insects and baculoviruses, and their compatibility for laboratory and field experiments, has formed a basis for studies that have made a significant contribution to unraveling disease interactions in insect populations. In particular, manipulative studies on baculoviruses have been instrumental in developing an understanding of disease transmission dynamics. The results so far indicate that baculoviruses have the potential to be an excellent model for investigations of changes in virulence and resistance in fluctuating and stable host populations.

INTRODUCTION

The role of disease in host populations is a finely balanced interplay between a pathogen's capacity to exploit a host and host susceptibility. Exploitation includes successful transmission, the potential of a disease organism to successfully infect a host, (infectivity), and virulence, the impact of the disease on host fitness from benign to fatal. Host susceptibility is determined by environmental and condition-dependent factors that influence the sensitivity of the host to infection and the ability of the host to modify susceptibility through resistance mechanisms. These factors

can change over evolutionary as well as ecological time following fluctuating selection pressures. Baculoviruses and their insect hosts provide a model system for exploring pathogen-host interactions. Baculoviruses are DNA viruses that infect arthropods, mainly insects, in particular Lepidoptera, but also hymenopteran sawflies and some Diptera. Some baculoviruses play a role in the population dynamics of their hosts (Myers 1988) and viruses have also been explored as control agents for insect pests (Moscardi 1999). Here we present an overview of the characteristics that influence the ecology and evolution of baculovirus-host interactions, and identify areas that are ripe for further study. We have not covered all issues; we have focused on new data, emerging areas, and particularly field-related studies. For background on baculovirus biology, molecular biology, and other aspects of their ecology, in particular multi-species interactions, readers are referred to Cory et al. (1997), Entwistle & Evans (1985), Miller (1997), and Rothman & Myers (2000).

The Baculovirus Life Cycle and Infection Process

Baculoviruses have several unique features. First, they only infect the larval feeding stages where they form occlusion bodies (OBs). These are proteinaceous structures that contain the virions (virus particles). The OB is the infectious unit of the baculovirus and is critical for spreading infection between hosts. Second, many baculoviruses contain multiple virions (genomes) in each infective OB. Once in the midgut the virions are rapidly released by the combined action of the alkaline gut pH and proteases, and they then pass through the peritrophic membrane lining the gut (Figure 1). Baculoviruses encode various proteins that enhance the infection process (Peng et al. 1999, Popham et al. 2001). The virions released from the OBs fuse with the plasma membranes of the midgut columnar cells and the DNA-containing nucleocapsids move to the nucleus to initiate infection. In all non-Lepidopteran groups, infection is restricted to the midgut (or its equivalent), however in Lepidoptera most baculoviruses spread to other tissues, initially via the tracheoles (Engelhard et al. 1994, Volkman 1997). The baculovirus replication cycle is biphasic; tissue-to-tissue spread is carried out by nonoccluded budded virus whereas host-to-host transmission is carried out by the OBs. For more detail on baculovirus infection and its molecular basis see Miller (1997) and Volkman (1997).

In Lepidoptera by the end of the infection cycle, larval body tissue is converted into millions of OBs that are released into the environment when the host dies. In host species such as sawflies, baculovirus infections are restricted to the midgut, and infective OBs are shed continually with the feces. Occlusion bodies persist in the environment for considerable periods of time, particularly when protected from degradation by UV irradiation (Carruthers et al. 1988, Thompson et al. 1981). Baculoviruses "sit and wait" until they are ingested by another susceptible host or inactivated. Infection, and thus transmission, expose the baculovirus to two very different environments. Characteristics that promote successful invasion and reproduction within the body of the host may not necessarily maximize transmission to new hosts (DeFillippis & Villarreal 2000). The factors that influence these

within and between host processes and shape baculovirus ecology and evolution are discussed in the sections that follow.

THE EVOLUTION OF BACULOVIRUSES

Variation Among Species of Virus

Baculoviruses have been recorded from hundreds of species of insect, however few have been characterized in detail. Baculoviruses are often identified initially by their morphology and their characteristic pathology in their hosts. With the advent of widely available DNA technology, it is now possible to routinely characterize baculoviruses using restriction endonuclease profiles of their DNA, and more recently, DNA sequence data. However, biological characteristics, particularly host range information, are also important for identifying relationships between baculoviruses, but broad-ranging biological data on individual isolates are sparse.

PHYLOGENY Baculoviruses are divided into two groups, the nucleopolyhedroviruses (NPVs) and the granuloviruses (GVs). NPV occlusion bodies are larger (1–5 μm) and contain multiple virions embedded in a protein matrix. Each virion can either contain one nucleocapsid—single NPVs (SNPVs), or many—multiple NPVs (MNPVs) (Figure 1). MNPVs have only been isolated from Lepidoptera and SNPVs from Lepidoptera and non-lepidopteran groups. GVs have only been reported from Lepidoptera and each OB (600–800 nm) contains a single virion enclosing one nucleocapsid. Phylogenetic studies indicate that lepidopteran baculoviruses fall into three groups, the GVs, Group I NPVs, and Group II NPVs,

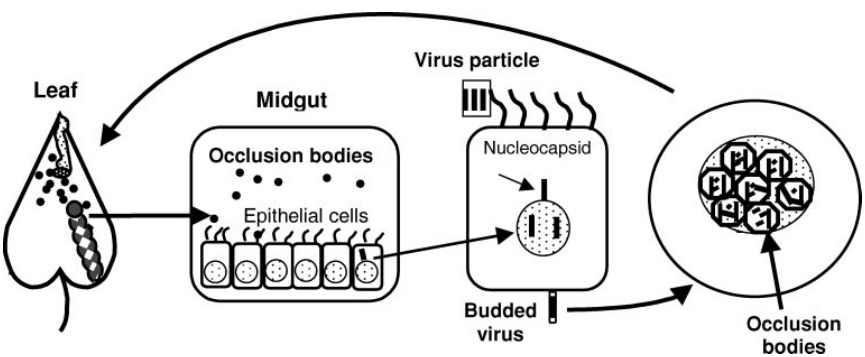

Figure 1 Diagram of the infection cycle of baculoviruses. Caterpillars become infected by ingesting virus that contaminates food plants when an infected larva dies. At the end of the cycle occluded polyhedra are formed, which will eventually be released from the host at death. In NPVs, OBs contain many virions embedded in a protein matrix, each of which may contain one or many nucleocapsids.

with hymenopteran and dipteran NPVs falling outside these clusters (Herniou et al. 2001, 2003; Moser et al. 2001; Zanotto et al. 1993). Analysis of the patterns of gene acquisition and loss among different viruses highlights the very fluid nature of baculovirus genomes (Herniou et al. 2003). A key question is whether baculoviruses have coevolved with insect orders or whether they evolved from one group of hosts. Preliminary indications from wide-ranging sequence analysis indicate that isolates collected from species within an order cluster together, but the relationship between orders is not clear (E.A. Herniou, J.A. Olszewski, D.R. O'Reilly, J.S. Cory, unpublished data).

VIRUS SPECIES Baculoviruses are named after the host from which they were isolated and therefore a virus that infects several host species could be given different names, as is the case with *Anagrapha falcifera* NPV and *Rachiplusia ou* NPV (Harrison & Bonning 1999). Alternatively, isolates from the same host species may represent very different virus species, as has been found with *Orgyia pseudotsugata* MNPVs and SNPVs (Zanotto et al. 1993), *Spodoptera littoralis* NPVs (Kislev & Edelman 1982) and *Mamestra configurata* NPVs (Li et al. 2002a,b). Molecular analysis is helping to clarify this issue but guidelines are needed to determine the criteria for designating different baculovirus isolates as species and the relative importance of molecular and biological data.

HOST RANGE SPECIFICITY The possibility for coevolution between baculoviruses and hosts is closely tied to their host range. Data are limited, but it is clear that different baculovirus species vary in the number of host species they can kill. Some baculovirus species appear to be genuinely host specific, such as the NPVs that infect Lymantriidae (Barber et al. 1993, Cory et al. 2000, Richards et al. 1999a). At the other end of the spectrum, cabbage moth, *Mamestra brassicae* NPV infects species from four families of Lepidoptera (Doyle et al. 1990), and the NPV from the alfalfa looper, *Autographa californica*, (AcMNPV) can infect species within at least 15 families of Lepidoptera (Payne 1986; J.S. Cory, R.D. Possee, M.L. Hirst, unpublished data). Other species of baculovirus (including GVs) have not been studied in such detail, although available evidence suggests that many have narrow host ranges; either monospecific (Gelernter & Federici 1986) or infective within a genus (Allaway & Payne 1984, Carner et al. 1979). Wider host range viruses are not equally infective to all host species. Additionally, studies on AcMNPV indicate that although species closely related to *A. californica* include some of the most highly susceptible species, host range does not closely follow host taxonomy (J.S. Cory, R.D. Possee, M.L. Hirst, unpublished data). This makes host range within the Baculoviridae hard to predict.

All host range data are from laboratory assays. Host usage in the field is likely to be considerably narrower owing to a lack of spatial or temporal synchrony. The trade-offs between generalism and specificity in host range are poorly understood (Woolhouse et al. 2001). Viruses with broader host ranges have the advantage of increased host availability. Specificity may well allow more efficient and less

costly host use, however it carries a greater risk of extinction, particularly in unpredictable and patchy environments (Combes 2001). The wider host range viruses tend to be MNPVs isolated from Noctuidae. The M phenotype has been shown to establish irreversible systemic infections more rapidly than SNPVs, and this may make them more efficient at infecting a wider range of hosts (Washburn et al. 1999). Additionally, the high level of genetic variability in baculoviruses combined with the enhanced opportunities for recombination in the multiply occluded morphotypes may predispose MNPVs to wide host ranges.

Variation Within Species of Virus

The potential for selection to act on baculoviruses is related to their levels of genetic variation. Restriction endonuclease (REN) profiles of baculovirus DNA have shown that baculoviruses are extremely variable. Isolates from the same host species in different geographic regions frequently show differences in REN patterns for lepidopteran NPVs (e.g., Gettig & McCarthy 1982, Shapiro et al. 1991, Takatsuka et al. 2003), GVs (Crook et al. 1985, Parnell et al. 2002, Vickers et al. 1991), and hymenopteran sawflies (Brown 1982). However, we know little about the role and maintenance of this variation.

MOLECULAR (GENOTYPIC) VARIATION From an ecological perspective, an infected larva is the relevant unit of inoculum for initiating transmission. However studies of spatial and temporal variation in baculoviruses isolated directly (without amplification) from individual larvae collected in the field are rare (see review in Cooper et al. 2003b). An exception is a recent study that has shown that variation in the NPV of the western tent caterpillar, *Malacosoma californicum pluviale*, exhibits a hierarchical spatial structure. Isolates from individual larvae from within family groups were more likely to be the same as were isolates from within populations compared to those from different island and mainland populations (Cooper et al. 2003b). An exciting area for future work will be to determine if genetic and phenotypic diversity of the NPV (and its host) changes over time and with host density in forest caterpillars with cyclic population dynamics.

Isolates of NPV rarely contain a single genotype or variant. Variants can be separated by in vitro (e.g., Crozier & Ribeiro 1992, Maruniak et al. 1984, Stiles & Himmerich 1998) or in vivo cloning techniques (Jehle et al. 1995, Muñoz et al. 1998, Smith & Crook 1988). In vivo cloning has also been used to separate at least 24 genotypically distinct variants of NPV from a single infected caterpillar of pine beauty moth, *Panolis flammea* (J.S. Cory, B.M. Green, submitted manuscript). Analysis of *Spodoptera exigua* NPV also revealed that mutants with large deletions occurred naturally in wild-type isolates (Muñoz et al. 1998), but these variants were not capable of initiating oral infection alone. They were, however, abundant in the wild-type virus, and more importantly, reduced the pathogenicity of the virus population, indicating that they may well act as parasitic genotypes (Muñoz

& Caballero 2000). More recently Kikhno et al. (2003) found a naturally occurring, plaque-purified mutant of wild-type *Spodoptera littoralis* NPV with a 4.5-kb deletion that was not infective by ingestion, although it was as pathogenic as the wild-type virus by injection. This difference in phenotype was related to the presence of a specific gene, missing from the deletion mutant, which was named "*per os* infectivity factor" (*pif*). The product of this gene appears to be a structural protein associated with occlusion-derived virus that is required for the initial stages of infection within the midgut (Kikhno et al. 2003).

GENERATION OF GENOTYPIC VARIATION The observed high level of genotypic heterogeneity in baculoviruses could result from infection with multiple genotypes, or could be generated during the infection cycle through point mutations, gene duplications, and DNA deletions or insertions. The frequent generation of so-called few plaque mutants during repeated passage in cell culture originates from the insertion of DNA into the genome (Cary et al. 1989). Naturally occurring mutants of codling moth, *Cydia pomonella*, GV also contain host transposable elements that could increase variation (Arends & Jehle 2002, Jehle et al. 1995). Baculoviruses replicate clonally, but co-infection, or the multiple genome packaging found in NPVs, could allow the exchange of genetic material during infection via recombination between virus genotypes, virus and host, or virus and other co-infecting organisms. Recombination occurs in vivo with high frequency (up to 50%) between closely related virus genotypes (Crozier et al. 1988, Crozier & Ribeiro 1992, Hajós et al. 2000), but its importance and frequency in natural populations is unknown. The patterns of insertions and deletions of intraspecific variants indicate that these might involve a limited number of sites within the genome (Muñoz et al. 1999; Stiles & Himmerich 1998; J.S. Cory, B.M. Green, submitted manuscript). Some of the variable regions include long repeat sequences in homologous regions (Garcia-Maruniak et al. 1996, Muñoz et al. 1999), possibly indicating the presence of recombinational hot spots.

Recombination requires coinfection of the same cell and studies using AcMNPV show that the frequency of multiple infection of single cells in vivo is surprisingly high (Bull et al. 2001, 2003; Godfray et al. 1997). Additionally, studies with a recombinant AcMNPV have shown that genetically distinguishable NPVs can be packaged in a single OB (Bull et al. 2001). Thus recombination in vivo as a major source of variation driving the evolution of virulence and host range is highly feasible. If this were the case, NPVs should be more variable than the singly enveloped GVs. However, high levels of genotypic diversity are also found in GVs, and there is indirect evidence for the generation of recombinants in wild-type GVs (Smith & Crook 1993) as well as NPVs (Muñoz et al. 1997). The mechanisms for generating and maintaining genotypic diversity may be different in the two baculovirus groups, and further studies of the mechanisms that generate genotypic heterogeneity in field populations are needed.

PHENOTYPIC VARIATION Whereas genotypic variation may be ubiquitous in baculoviruses, it is of little relevance unless it translates into differences in virus phenotype. Baculoviruses isolated from the same species in different sites frequently vary in their pathogenicity (e.g., Allaway & Payne 1983, Ebling & Kaupp 1995, Hatfield & Entwistle 1988) and their speed of action (e.g., Hughes et al. 1983). Individual variants from within the same virus population obtained by in vitro (Lynn et al. 1993, Ribeiro et al. 1997) and in vivo cloning (Hodgson et al. 2001) can also vary dramatically in virulence. For example, clones of *Anticarsia gemmatalis* NPV, isolated by plaque purification, differed in LD_{50} (number of OBs required to kill 50% of challenged hosts) by over one-hundredfold (Ribeiro et al. 1997). Comparison of four NPV genotypes from a single *P. flammea* larva differed in LD_{50} by a factor of 7, and also showed significant differences in both infection duration and yield of progeny virus (Hodgson et al. 2001). Virus pathology and OB formation can also vary: plaque-purified variants from *Spodoptera frugiperda* NPV differed in the degree to which the infected larvae liquified at death, as well as in the size of the resultant OBs (Hamm & Styer 1985). Lysis of the host and OB size are likely to influence both transmission and persistence of baculoviruses in the wild.

MAINTENANCE OF VARIATION Potential mechanisms for maintaining baculovirus diversity include, (*a*) trade-offs, (*b*) differential selection, (*c*) multiple infection, (*d*) interspecific competition, and (*e*) frequency dependent selection (for a fuller discussion see Hodgson et al. 2001, 2003). Trade-offs occur when negative genetic correlations exist among beneficial traits. For baculoviruses, the most obvious potential trade-off is between the duration of infection and the production of infective OBs, such that the longer a virus takes to kill its host, the more OBs will be produced. Several within genotype comparisons have demonstrated that this is the case, although yield often plateaus (Hernández-Crespo et al. 2001, Hodgson et al. 2001). Intergenotype comparisons are rare. Hodgson et al. (2001) found no significant relationship between yield and infection duration or between the virulence (LD_{50}) and either yield or speed of kill in *P. flammea* NPV genotypes, although the sample size was small. However, Ribiero et al. (1997) found a strong positive relationship between virulence and yield measured as OB number per unit larval weight rather than the absolute yield per cadaver in *Anticarsia gemmatalis* NPV variants. This essentially measures the efficiency of converting insect tissue to virus rather than total production. Thus it is perhaps not surprising that the two are positively correlated.

Differential selection occurs when particular genotypes perform better under different ecological conditions, for example during infection of different host species. Multiple passage of a mixed virus isolate in alternative hosts can change the genotypic structure and biological activity of the virus (Kolodny-Hirsch & van Beek 1997, Tompkins et al. 1988), and individual variants can perform differentially in different hosts (Paul 1997). When AcMNPV was passaged through the diamondback moth, *Plutella xylostella*, 20 times, infectivity toward *P. xylostella* increased 15-fold (Kolodny-Hirsch & van Beek 1997). The changes were

accompanied by an increase in virion number per OB, as well as a change in DNA restriction endonuclease profile, but whether they resulted from selection for different genotypes or the production of novel variants is unclear. Abiotic factors could also influence the success of variants through selection on different temperature profiles or for improved persistence against UV (Brassel & Benz 1979). As virus persistence is intimately linked with host plant, it is also possible that adaptation to different plant species could occur. Preliminary support for this idea comes from the pine beauty moth, *P. flammea* NPV system. In Scotland, where this virus was collected, *P. flammea* feeds on two host plants, Scots pine and the introduced lodgepole pine. When insects were infected with two *P. flammea* variants on the two host plants they exhibited differential pathogenicity (Hodgson et al. 2002).

An interesting possibility is that infections by more than one genotype might actually be beneficial to the virus. Conventional theory predicts that mixed infections should be more virulent, as multiple genotypes will increase the rate of host exploitation (Frank 1996). Comparison of two equally infective variants of *P. flammea* NPV alone and in combination showed that mortality was significantly higher in the mixed infection (D.J. Hodgson, R.B. Hitchman, A.J. Vanbergen, et al., submitted manuscript). Unexpectedly, this was not accompanied by a more rapid speed of kill and reduction in overall (combined) yield per insect. The mechanism for increased virulence from mixed infections in mouse malaria was suggested to be the cost to the immune system of having to fight multiple strains (Taylor et al. 1998). However, although differential immunity may be involved in insect defense, other mechanisms, such as variable tissue tropisms, seem more likely causes of enhanced virulence. This has implications for host-pathogen dynamics and virulence management, particularly in the application of baculoviruses as pest control agents. Another possibility is that the structure of the virus population is influenced by interactions with competing natural enemies. Preliminary data suggest that REN profiles of *S. frugiperda* NPV vary depending on whether the host is parasitized or not (Escribano et al. 2000, 2001), however there is little information on this issue.

Coevolutionary processes may also be involved in the maintenance of baculovirus polymorphism. Various coevolutionary scenarios have been proposed for the interaction between parasites and their hosts, in particular escalating arms races between host and parasite and the potential for frequency dependent selection. In antagonistic interactions, such as host-parasite relationships, negative frequency dependent selection may operate whereby dominant genotypes are at a selective disadvantage resulting in fluctuating polymorphisms (Lively 2001). This would provide another route for maintaining baculovirus diversity, however, as yet there are insufficient data on the dynamics of baculovirus (or host) strain structure to address this hypothesis. Frequency dependent selection may also be involved in the maintenance of parasitic genotypes, which potentially have a replication advantage within the host but require an occlusion body for host-to-host transmission (Hodgson et al. 2003). There is already evidence that baculovirus populations show hierarchical spatial structure (Cooper et al. 2003b). Adding a spatial component to

all these mechanisms would increase the complexity of the interactions together with the likelihood of increased diversity (Thompson 2001).

Host Manipulation

The manipulation of host behavior by parasites is well studied in vertebrates (Moore 2002), and there is also some information on insect parasitoids (Edwards & Weaver 2001). Pathogens of insects, however, have received considerably less attention, although there is increasing evidence that they may manipulate their hosts in a number of ways both behaviorally and physiologically. Baculoviruses, in particular, offer ideal systems for linking mechanisms of response to underlying genetics.

BEHAVIORAL Some of the earliest descriptions of baculovirus disease mention behavioral changes in infected larvae, in particular, the tendency for infected caterpillars to move up the plant to die, so-called tree-top disease or "wipfelkrankheit" (Steinhaus 1967). However, despite frequent anecdotal observations, this behavior has only recently been quantified. Infection of the cabbage moth, *M. brassicae*, by its NPV produces increased movement (dispersal) and upward migration on cabbage plants (Goulson 1997, Vasconcelos et al. 1996a). It is assumed that this behavior has evolved to enhance the transmission of the virus by either gravity or rainfall (Goulson 1997, D'Amico & Elkinton 1995, Vasconcelos et al. 1996a). Climbing behavior could also make a virus-infected caterpillar more apparent to predators, thus increasing its dispersal rate. A wide range of predators eat infected caterpillars and passively disperse OBs in their feces (Entwistle et al. 1993, Lee & Fuxa 2000, Vasconcelos et al. 1996b). However, although the observed behavioral changes appear to be beneficial for the virus, conclusively demonstrating their adaptive value is more difficult (Moore 2002, Poulin 1998).

From the host's perspective, enhanced mobility may remove infected individuals from the vicinity of their uninfected conspecifics, particularly in gregarious and semigregarious species. In this way, the inclusive fitness of family groups may be increased. Additionally, because baculoviruses are sensitive to sunlight, greater exposure on branch tips may also increase the rate of inactivation. Alternatively, the observed behavioral changes may not be adaptive to either host or virus and may result from pathological changes resulting from virus infection. However, behavioral changes have only been quantified in one species: upward movement may not necessarily enhance virus fitness in all hosts, for example, in cutworms that dwell in the soil, this may not be beneficial. There is thus a need for more studies in host species with diverse life histories.

PHYSIOLOGICAL The function of many baculovirus genes is still not known, but it is evident that not all genes are associated with activities crucial for virus replication or structure. These genes have been termed auxiliary genes (O'Reilly 1997), although when knowledge of their activity increases, it may be more appropriate

to ascribe them to functional groups. Baculoviruses can be genetically modified with precision; this allows the function of these nonessential genes to be assessed at both the individual and population level.

The egt gene The only auxiliary gene that has been studied in any detail is the ecdysteroid UDP-glucosyltransferase (*egt*) gene (Cory et al. 2001, O'Reilly & Miller 1989). This gene produces an enzyme that conjugates ecdysteroids (insect molting hormones) with UDP-glucose or galactose (Kelly et al. 1995, O'Reilly et al. 1992). Comparison of wild-type baculoviruses with those without a functional *egt* gene has clearly shown that EGT expression inhibits the larval-larval or larval-pupal molt (O'Reilly 1997, O'Reilly & Miller 1989) and prolongs larval infection by up to 60% (Cory et al. 2001, O'Reilly & Miller 1991, Slavicek et al. 1999). It was originally hypothesized and subsequently shown that the extended infection period would increase production of viral progeny (Slavicek et al. 1999, Wilson et al. 2000). Insect development (rather than time to death) is crucial in determining virus yield in final instar *Heliothis virescens* larvae infected with AcMNPV. Insects for which molting is arrested early produce more than four times the quantity of OBs than insects that go on to the pharate pupal stage (O'Reilly et al. 1998). Thus the *egt* gene manipulates host development, thereby increasing available resources and the quantity of viral progeny produced. As virus productivity is a crucial component of virus fitness, increases in yield should be highly beneficial to the virus.

The *egt* gene might have other potentially beneficial effects. Indirect evidence suggests that insect ecdysteroids could interfere with virus replication (Keeley & Vinson 1975, O'Reilly et al. 1995). However, deletion of the *egt* gene does not reduce pathogenicity (Cory et al. 2001). EGT expression could also influence virus transmission and persistence. A simplified transmission experiment using larvae confined to cut branches showed that gypsy moth NPV without the *egt* gene had a significantly lower transmission rate than the wild-type virus (Dwyer et al. 2002). However, a cost of the greater yield from insects infected with viruses which express EGT is slower death that delays the release of OBs for further rounds of transmission. Theoretical exploration of the dynamics of *egt* plus and minus viruses indicates that the fitness of viruses lacking the *egt* gene would be less than that of the parent wild-type (Dwyer et al. 2002). Extending this analysis to competition between viruses that differ in speed of kill and transmissibility indicates that the faster killing virus requires relatively high levels of transmission to dominate (Dushoff & Dwyer 2001). However, overwinter survival of virus, about which little is known, is crucial in these simulations. The field situation is considerably more complex and it is plausible that baculoviruses lacking a functional *egt* gene could coexist with wild-type virus by essentially "parasitizing" their expression of EGT in the same host.

The chitinase and cathepsin genes The only other auxiliary genes for which a potential function at an organismal level has been identified are the chitinase and cathepsin (cysteine protease) genes. These genes appear to act together to

facilitate the release of the virus OBs from the insect cadaver after death by breaking down the chitin and protein present in the insect cuticle. When either gene is deleted, the cuticle of the infected insect fails to liquefy (Hawtin et al. 1997, Slack et al. 1995). The ecological implications of these genes have received little attention. Their most likely function is to enhance horizontal transmission: liquefaction of the infected cadaver will spread the OBs over a greater area thereby potentially increasing the likelihood that a susceptible host will encounter them. However, there is likely to be a trade-off with this strategy as more widely disseminated virus may be more rapidly degraded by sunlight.

Not all baculoviruses contain a chitinase or a cathepsin gene (Herniou et al. 2001, 2003), and liquefaction or "melting" of the cadaver, commonly regarded as a characteristic of baculovirus infection, does not always occur. For example, the Indian mealmoth, *Plodia interpunctella*, does not lyse when infected with its GV, and in this system cannibalism is thought to be the major route of virus transmission (Boots 1998). Whether the lack of liquefaction in this host-virus system is due to a change in chitinase or cathepsin expression is not known. However, the study of the role of genes such as chitinase and cathepsin that appear to exert their effects at an organismal level, would benefit from a comparative approach using species with different ecologies and transmission dynamics.

Variation in Susceptibility

The insect host presents different layers of defense that must be breached for the baculovirus to infect and multiply in the host. Each could impose selectivity on the system and this has recently been described as the "defense component model" (Schmid-Hempel & Ebert 2003). We next discuss some of the factors that influence the susceptibility of insect hosts to baculoviruses.

HOST BEHAVIOR There is no evidence to suggest that insects modify their behavior to reduce the ingestion of baculoviruses. Postingestive behavior is also little studied. In other insect-pathogen systems, fatal infection levels may be reduced through behavioral fever (Blanford & Thomas 1999, Boorstein & Ewald 1987). However, although temperature affects life history parameters that may well have consequences for host-pathogen dynamics such as speed of kill and yield (Kelly & Entwistle 1988, van Beek et al. 2000), there is no evidence that altering temperature can influence fatal infection in baculoviruses (Frid & Myers 2002).

DEVELOPMENTAL RESISTANCE It is well established that susceptibility to baculovirus infection decreases with increasing larval age both within and between instars. Originally this was thought to be related to the increasing weight of the larva. However, comparisons of oral with intrahemocoelic inoculation demonstrated that this resistance did not occur when virus was injected (Teakle et al. 1986); which implies that developmental resistance is related to the infection process in the midgut. Detailed investigations on the development of intrastadial

resistance in *Trichoplusia ni* to AcMNPV, showed that fourth instar larvae were most susceptible immediately after molting (Engelhard & Volkman 1995). By using a recombinant AcMNPV that could be tracked in the gut, it was clearly demonstrated that larvae can remove baculovirus infection by sloughing off infected cells lining the midgut (Hoover et al. 2000; Keddie et al. 1989; Washburn et al. 1995, 1998). Thus a decreasingly small window of opportunity exists for the virus to establish infection as the insects age, particularly in later instars.

SYSTEMIC RESISTANCE Although the midgut appears to be the major barrier to baculovirus infection, there is also evidence for systemic resistance in some species. In fourth instar gypsy moth larvae, *Lymantria dispar*, infection levels decreased when the insect was challenged later in the instar and this was not fully reversed when the virus was administered by intrahemocoelic injection, indicating resistance has a systemic component (Hoover et al. 2002). In fifth instar, *H. virescens*, developmental resistance to AcMNPV was partially removed by methoprene, a juvenile hormone analog, suggesting that a component of systemic resistance is mediated by hormones (Hoover et al. 2002, Kirkpatrick et al. 1998).

Insects possess both cellular and humoral mechanisms of immunity and both have been implicated in resistance to baculoviruses. Studies with a recombinant AcMNPV and *Helicoverpa zea* (a less susceptible species) demonstrated that the initial number of infection foci in the midgut was equal to that found in a highly susceptible species (*Heliothis virescens*). However, in *H. zea* the number of infection foci decreased, suggesting that the larvae had somehow removed the infection (Washburn et al. 1996). This was associated with the presence of hemocyte aggregations around infected tracheoles, similar to the type of cellular encapsulation response seen with invading parasitoids. This response was reduced with immunosuppressors confirming the role of the immune system. How systemic resistance is involved between hosts and their homologous viruses is not so clear.

Although links between susceptibility and immunity have received little attention, it has been shown that responses to baculoviruses can vary with rearing density, with insects reared at higher densities less susceptible to infection (Goulson & Cory 1995, Kunimi & Yamada 1990). In the African armyworm, *Spodoptera exempta*, insects reared gregariously were more resistant to NPV infection than those reared solitarily and this was correlated with higher levels of phenoloxidase activity in the hemolymph, indicative of increased immune function (Reeson et al. 1998). Crowding in phase polyphenic Lepidoptera also tends to be related to an increase in melanization. It has been suggested that melanism could indicate enhanced immune activity and disease resistance (Wilson et al. 2001).

FOOD PLANT EFFECTS Herbivorous insects are intimately associated with their food plants and so are their pathogens. Host plant can influence virus interactions in many ways; plant architecture affects virus persistence, palatability modifies host mobility and virus acquisition, plant chemistry modulates infection in the gut and nutrient content determines host survival. The impacts of plant

phytochemicals, such as phenolics, on host susceptibility has received most attention and numerous studies have shown that both mortality (Duffey et al. 1995; Farrar & Ridgway 2000; Forschler et al. 1992; Hoover et al. 1998a,b,c; Raymond et al. 2002) and speed of kill vary depending on plant type or allelochemicals (Farrar & Ridgway 2000, Raymond et al. 2002). However the influence of previous herbivory and induced responses on virus susceptibility is equivocal (Ali et al. 1998, Hoover 1998b, Hunter & Schultz 1993). Intraplant variation can also have significant effects. For example, when *H. zea* was infected with its NPV on cotton, susceptibility was lower when the caterpillars were fed on the reproductive rather than the vegetative structures (Ali et al. 1998) and the resulting virus yield was also lower on reproductive tissues (Ali et al. 2002). As heliothines tend to feed cryptically on cotton buds, they are not only avoiding natural enemies but also apparently further reducing their risk of infection.

Finding a mechanism behind the observed differences in plant mediated effects could provide a better framework for understanding and predicting plant-baculovirus interaction. As most of the studies focus on chemical influences at the time of ingestion, alterations in susceptibility are likely to be related to the midgut. In an elegant study, Hoover et al. (2000) compared the susceptibility of *H. virescens* larvae feeding on cotton to those feeding on lettuce. Insects inoculated with AcMNPV on cotton were less susceptible and this was positively correlated with levels of foliar peroxidase. Previous studies suggested that reactive oxygen species associated with peroxidase activity damage the lining of the midgut and cells are sloughed off at early infection (Hoover et al. 1998c). By administering an optical brightener (thought to enhance the retention of gut cells) the effect of feeding on cotton was reversed (Hoover et al. 2000). Reduced susceptibility to NPV on cotton was not observed if the virus was injected directly into the hemocoel. This provides strong support that differences in susceptibility mediated by host plant relate to the effect of phytochemicals on the rate of sloughing gut cells.

Both pre and postingestion nutritional quality of the diet can play significant roles in infection (Duffey et al. 1995). For some host species, epizootics of virus occur following high population densities and the influence of food quantity and quality is relevant. When the susceptibility of the stored product pest, *P. interpunctella* to its GV was assayed, McVean et al. (2002) found that larvae reared on a lower quality diet were less susceptible to virus infection, but died more quickly than larvae on the high quality diet. Recent data, using *Spodoptera littoralis* and its NPV, has shown that ingestion of a high protein: low carbohydrate diet postingestion reduces fatal baculovirus infection (Lee 2002). Additionally, larvae that survived virus challenge increased their intake of protein-biased food after infection when given a choice. Protein may be important in defense against baculoviruses, either via the immune system or by increasing larval development rate (Hoover et al. 1998d, Lee 2002). An intriguing possibility is that insects could alter their dietary intake in response to pathogen challenge by self-medication (Clayton & Wolfe 1993, Lozano 1998). Karban & English-Loeb (1997) report that

caterpillars parasitized by a tachinid fly parasitoid adjust their host plant choice to enhance survival. Diet can influence immune function in other groups of insects (Suwanchaichinda & Paskewitz 1998, Vass & Napi 1998) and it has recently been shown that starvation can rapidly decrease phenoloxidase activity in the beetle *Tenebrio molitor* (Siva-Jothy & Thompson 2002). The influence of food plant on virus infection is complex and whether these tritrophic interactions significantly influence host-virus dynamics and evolution in natural populations requires studies of transmission, adaptation and host plant usage in the field.

THE ECOLOGICAL IMPACTS OF BACULOVIRUSES ON HOST POPULATIONS

Theoretical Considerations

Infection by baculoviruses is generally lethal and therefore has the potential to influence host population densities particularly if viral transmission increases with host density. The theoretical relationships of host-microparasite dynamics of insects have been widely explored in mathematical models starting with those of Anderson & May (1980, 1981). More recent models have incorporated modifications such as variation in transmission parameters (Getz & Pickering 1983), vertical transmission (Regniere 1984), both density dependence and vertical transmission (Vezina & Peterman 1985), nonlinear transmission (Hochberg 1991), density dependence (Bonsall et al. 1999, Bowers et al. 1993, White et al. 1996), host stage structure (Briggs & Godfray 1996), heterogeneity in susceptibility (Dwyer et al. 1997), discrete generations and seasonal host reproduction (Dwyer et al. 2000), and sublethal infection (Boots & Norman 2000).

Models of virus versus disease of insect hosts have usually been evaluated by whether or not they generate multigenerational, cyclic population dynamics of the hosts. However, many are unrealistic in other characteristics such as levels of infection (Bowers et al. 1993), e.g., almost 100% infection for three generations of peak host density in the model of Dwyer et al. (2000). Prolonged, high levels of infection do not occur in field populations (Woods & Elkinton 1987, Myers 2000). Whether the outcomes of disease models are realistic depends on how disease transmission is simulated.

Transmission

Transmission in baculoviruses is thought to be primarily horizontal via susceptible larvae ingesting OBs persisting in the environment. However, there is also evidence that baculoviruses can be transmitted vertically from adults to their young. These important processes are discussed in the following sections.

HORIZONTAL TRANSMISSION Transmission depends on the interactions between infected and susceptible individuals, and the rate at which contacts result in new

infections. Most models assume that transmission is a mass action process; a density-dependent relationship based on a per capita transmission coefficient, β, the number of susceptible individuals, S, and the number of infected individuals, I, (βSI) although some have argued that this should be related to population size (βSI /N) (reviewed in McCallum et al. 2001).

The transmission process in field populations is unlikely to fit either of these simple representations. For baculoviruses disease transmission depends on susceptible larvae encountering and ingesting a discrete patch of virus that results from the death of an infected individual, and thus depends on the behavior of infected and susceptible larvae. We next consider experimental studies that have estimated the transmission of baculoviruses.

Quantifying transmission In studies that have experimentally estimated the transmission coefficient for baculovirus infection in insect populations, all have found that it declined with increasing inoculum densities (D'Amico et al. 1996, Beisner & Myers 1999, Knell et al. 1998,Vasconcelos 1996). However, the relationship with host density was more variable. Transmission efficiency of NPV increased with increasing density of *M. brassicae* larvae on cabbage (Vasconcelos 1996), and for GV in *P. interpunctella* (Knell et al. 1998). Conversely, in gypsy moth and its NPV, the transmission coefficient declined as the density of susceptible larvae increased (D'Amico et al. 1996). Beisner & Myers (1999) varied both the numbers of susceptible and infected individuals in groups of western tent caterpillar larvae, *M. c. pluviale*, a naturally gregarious species. Again virus transmission was more efficient at lower virus densities, but transmission within groups was not related to density. However, group size did influence infection levels, and increased movement among larger caterpillar groups on individual trees, increased between-group spread of the virus. In a recent analysis, Fenton et al. (2002) explored the influences of transmission functions in a metapopulation model of hosts and microparasites. They suggest that small-scale transmission events can drive large-scale epizootics. This would seem to be the case with the tent caterpillars.

Transmission could vary if the susceptibility of larvae changes at high density, as might result from stress. As mentioned above, crowding has been shown in laboratory studies to reduce the susceptibility of caterpillars to fatal infection. This led Wilson & Reeson (1998) to propose the concept of density-dependent prophylaxis; as the risk of exposure to pathogens increases with density, insects respond physiologically and invest more in resistance. Reeson et al. (2000) compared NPV transmission on maize plants in field cages using *S. exempta* larvae that had been reared either singly or gregariously. Virus transmission was lower in the larvae that had been previously reared gregariously.

These experimental measurements of transmission yield the clear message that simple mass action does not describe baculovirus transmission in the field. More appropriate descriptions of transmission must be found based on a more detailed knowledge of the heterogeneities that influence the infection process.

Spatial distribution and persistence The spatial distribution of virus on the plant, and between plants and the soil, is likely to significantly influence virus transmission at a local scale. Different species of insect, different instars, different host plants, and even different baculovirus-host combinations could influence the pattern of virus distribution. In the first study on the influence of virus distribution on transmission, Dwyer (1991) found that for third instar Douglas fir Tussock moth, *O. pseudotsugata*, transmission was lower when virus distribution was heterogeneous than when it was uniform. For later more mobile instars however, the distribution of the virus was less important. The amount and location of inoculum were varied by Hails et al. (2002) in field experiments with *T. ni*. Whether infected larvae remained on the plant or fell to the ground influenced transmission but not the inoculum (cadaver) size. This suggests that the amount of virus in a patch is less important than the number of patches.

Persistence and thus transmission of virus will also be influenced by the location of the virus OBs. If the virus is on the surface of leaves, it will be exposed to UV and more rapidly inactivated. For example sun exposure is thought to reduce viral infection of forest tent caterpillars, *Malacosoma disstria*, feeding at the edges of forests compared to the interior (Rothman & Roland 1998). The eventual repository for most virus is the soil, where the OBs are protected from exposure to sun but may have reduced opportunity for transmission to new hosts. Hochberg (1989) introduced a pathogen reservoir into a model of host-pathogen dynamics and showed that allowing for translocation of a pathogen from the reservoir to a transmissable surface could result in regulation of the host. A virus reservoir in the soil is crucial to the association between *Wiseana* spp. and baculovirus in New Zealand pastures (Crawford & Kalmakoff 1977). The larvae live in the soil, and grazing animals enhanced the spread of virus, but plowing disrupted the virus reservoir, resulting in outbreaks of the insect. However, Fuxa & Richter (2001) have shown that baculovirus movement from the soil to plants is very low and depends on rainfall. Larval behavior can also have a major impact on virus acquisition from a reservoir. In pine forests in Scotland, early instar larvae of the vapourer moth, *Orygia antiqua*, moved (ballooned) off the trees and into contact with the understory reservoir of NPV where they acquired high levels of infection. When they moved back up to the trees, the virus infection was transmitted to other larvae (Richards et al. 1999b).

Heterogeneity in susceptibility Heterogeneity in host susceptibility related to age structure and variation in resistance within and among populations can also influence transmission. Goulson et al. (1995) investigated the influence of stage-dependent variation in susceptibility on the transmission of NPV among cabbage moth larvae, *M. brassicae*. They predicted that because later instar larvae eat much more leaf material than early instars, transmission should increase for later instars even though they are less susceptible to infection, but this was not supported. In contrast, greater susceptibility of first instar larvae compared to later instars can influence the outcome of models of disease dynamics. Heterogeneity in host

susceptibility causes the relationship between virus density and transmission ($\log_n$ proportion susceptible individuals surviving) to be curvilinear with increasingly efficient transmission at lower virus densities (Dwyer et al. 1997). Incorporating heterogeneity in susceptibility improved the fit of the model to the observed NPV infection in low-density gypsy moth populations within generation (Dwyer & Elkinton 1993, Dwyer et al. 1997). Dwyer et al. (2000) extended the model to multiple generations by including a between season component and concluded that having a combination of highly and less susceptible individuals could drive outbreaks of gypsy moth. In this model, virus infection is initiated early and results from overwintering virus contaminating egg masses so that the highly susceptible first instar larvae become infected at hatching. Although, adding heterogeneity to models generally makes dynamics more stable, cyclic dynamics in this model persisted under some conditions. Frid (2002) showed that adding a random variable to the model based on an observed relationship between high levels of sunshine and increased NPV infection (Frid & Myers 2002), expanded the range of conditions under which cycles occurred.

VERTICAL TRANSMISSION Baculoviruses are generally thought to be transmitted horizontally from host to host via OBs persisting in the environment. However, baculoviruses can also be transmitted vertically from the adult to young (Easwaramoorthy & Jayaraj 1989, Fuxa et al. 2002, Kukan 1999, Melamed-Madjar & Raccah 1979, Myers et al. 2000). Vertical transmission encompasses passage of virus from the adult to their progeny by any means. This can be owing to surface contamination of eggs (transovum transmission) or virus passing within the egg (transovarial transmission), including transfer of latent infections; the latter is dealt with below. Infection levels can be as high as 50% in the progeny of adults that were exposed to virus as larvae (Kukan 1999). Surface sterilization usually reduces the level of infection considerably, but rarely eliminates it (Kukan 1999, Myers et al. 2000). Transovum transmission is harder to detect in the field because the eggs could become contaminated when they are laid onto foliage. They could also become contaminated in more subtle ways, e.g., in sawflies the meconia can be infectious, and this could contribute to adult to egg transmission (Olofsson 1989).

Distinguishing between latent and persistent infections The "spontaneous" generation of baculovirus disease from apparently healthy insects has been observed for over 100 years, and has stimulated discussion on possible latent baculoviruses and what might trigger them. Host crowding, fluctuations in temperature or relative humidity, dietary changes, chemical stress, parasitization, and infection by a second pathogen have all been suggested as possible stressors (Fuxa et al. 1999, Podgwaite & Mazzone 1986). Latent virus is a noninfective and nonreplicating form of virus that can be transformed to an infective state by some stressor (Fuxa et al. 1992). Understanding, or even consistently demonstrating, baculovirus latency has proven to be elusive, and triggering an active infection from a latent virus may be an unpredictable, stochastic process. The polymerase chain reaction

(PCR) was used to demonstrate that NPV infection persisted in all life stages of a laboratory culture of *M. brassicae* (Hughes et al. 1993). However, further studies using reverse transcriptase (RT)-PCR showed that a low level of viral transcripts were produced that implied that the virus was replicating and not truly latent (Hughes et al. 1997). More recent controlled experiments with *P. interpunctella* and its GV, demonstrated that a persistent infection was introduced into a high proportion of the survivors of viral challenge, and that this infection was passed via both sexes to the next generation (Burden et al. 2002). Whether this virus persists in later generations is not known. However, these studies suggest that baculoviruses do not persist in a classic latent form, but by a low-level replicating, persistent infection.

Little is known about whether sublethal, persistent virus infection actually occurs in field populations, the rate at which triggering occurs, what causes it, or whether this has any impact on the development of virus epizootics. In a recent study, cross-inoculation with an NPV from the western tent caterpillar (*M. c. pluviale*) was shown to "stress out" a second virus in field populations of the forest tent caterpillar, *M. disstria* (Cooper et al. 2003a). Interestingly, the virus "stressed out" of the population appeared to be a single genotype that differed from the mixed genotypes of horizontally transmitted virus isolated from the same population. Additionally whereas virus was readily activated from high-density forest tent caterpillar populations, no infection resulted in larvae from low-density western tent caterpillar populations in reciprocal cross-infections. This suggests that levels of sublethal infection or the propensity for a covert infection to be reactivated may be related to the history of viral infection in the host population and host density. Interestingly, recent work on the African armyworm, *S. exempta*, using RT-PCR, demonstrated high levels of persistent NPV infection in adults in field populations in Tanzania (L. Vilaplana, E.M. Redman, K. Wilson, J.S. Cory, unpublished data).

The role that vertical transmission plays in virus-host dynamics in field populations is not clear. Transovum transmission appears common in many species, and the emerging picture indicates that persistent, sublethal infections might also be very common in natural populations. The costs of maintaining these persistent infections must be low if they are widespread; a vertically transmitted virus should maximize its fitness by maintaining high host fecundity. It is not known how baculoviruses persist in hosts that have extended periods of low (and unpredictable) density, in situations where the host is highly mobile, or where the host occurs in environments with low environmental persistence of OBs and under these conditions a persistent virus strain may well be able to out-compete a nonpersistant virus. For example, in cyclic populations of tent caterpillars, populations at some sites only occur when densities are high regionally and thus, are initiated by immigration of moths every six to eight years (Myers 2000). However infection from NPV still characterizes these new populations (Cooper et al. 2003b), and vertical transmission on or in eggs must explain the occurrence of virus in these ephemeral populations. The circumstances in which vertical transmission is

favored, together with the costs and benefits to both pathogen and host are important for understanding the ecology and evolution of baculoviruses.

Sublethal Effects

Surviving baculovirus challenge is often costly and survivors can have altered development times and reduced size, fecundity, egg viability, and vigor (Duan & Otvos 2001, Matthews et al. 2002, Milks et al. 1998, Myers et al. 2000, Rothman & Myers 1996a). Although the impacts varied with study, on average sublethal effects reduced the reproductive potential (R_0) of the host by 22% (Rothman & Myers 1996a). The causes of these effects are not known, but they could result from fighting off infection or from the continued presence of a persistent virus infection. For example, sloughing off infected gut cells might reduce food intake, or the mobilization of an immune response could be physiologically costly. One interpretation is that infection of late instar larvae is terminated by pupation, and survivors show the influence of early infection as reduced size and fecundity. Infection may be removed at pupation, or could remain as a persistent infection (Burden et al. 2002) and be transmitted to the next generation. Thus baculoviruses can influence host population dynamics through direct mortality and also by delayed effects, such as reduced fecundity.

Resistance

Interactions between parasites and hosts provide an arena in which selection can act. For the host, increased resistance has an obvious benefit but is also expected to have costs (but see Rigby et al. 2002). Baculoviruses are transmitted (horizontally) at the death of the host and transmission is based on the number of new occlusion bodies produced. Therefore, selection, for the virus, should favor (*a*) overcoming host resistance, (*b*) maximizing the conversion of host tissue to OBs, and (*c*) optimizing the time of host death to promote transmission to new hosts. These conflicting selection pressures make theoretical predictions complex. The strength of selection will be influenced by the prevalence of infection, and for many host species the levels of infection by baculoviruses are low.

Variation in resistance to baculoviruses has been identified in several host species (reviewed by Watanabe 1987). However, with the exception of the measurement of a 38-fold increase in resistance of larch budmoth following a GV epizootic (cited in Watanabe 1987), the potential for coevolutionary change in hosts and pathogen following strong selection in the field remains little studied. Resistance has been selected for in the laboratory. Fuxa & Richter (1989) increased resistance threefold in a laboratory colony of fall armyworm, *S. frugiperda*, and resistance was rapidly lost when selection was stopped. After 13 to 15 generations of selection with NPV, colonies of velvetbean caterpillar, *A. gemmatalis*, from Brazil became 1000 times more resistant, whereas those from the United States plateaued at five times more resistant after four generations (Abot et al. 1996). In the U.S. population, resistance was associated with reduced production of young and was

rapidly lost (Fuxa & Richter 1998). Milks (1997) compared the susceptibility of 12 lines (8 laboratory strains and 4 wild collections) of *T. ni* and found significant but low (3.5-fold) variation in resistance levels. Females from the most resistant lines laid significantly fewer eggs. Vail & Tebbets (1990) also found variation in resistance among populations of *P. interpunctella* to GV and larval growth was slower in the most resistant populations.

In the only experiment that has selected host resistance and viral virulence, Milks & Myers (2000) increased resistance to *T. ni* SNPV in two laboratory populations of cabbage loopers by 4.4-fold and 22-fold. The virulence of the virus did not change over 26 generations of host selection. Host resistance was stable, and no costs could be identified (Milks et al. 2002). This work agrees with Rigby et al. (2002) who point out that not all mechanisms of resistance are costly. Interestingly, the increased resistance to *T. ni* SNPV in cabbage loopers also conferred resistance to a GV of *Pieris rapae* and a GV of *T. ni* but not to AcMNPV (Milks & Myers 2003). This may indicate more similarity in infection mechanisms between singly embedded viruses and GVs than with (wider host range) multiply embedded NPVs.

The levels of increased host resistance to baculovirus following selection have been low, and the persistence of resistance has varied. Whether the benefits of increased resistance would be sufficiently large to be realized in field populations is impossible to predict. Thus, theoretical considerations assuming patterns of coevolution in regard to baculovirus must remain speculative.

Viral Epizootics

Epizootics are outbreaks of disease in animal populations. An epizootic requires the presence of the pathogen and sufficient numbers of susceptible hosts to allow an increased rate of infection. Mitchell & Fuxa (1990) showed that NPV infection of the fall armyworm, *S. frugiperda*, was only sustainable if host densities averaged one larva per corn plant. Epizootics of baculoviruses occur irregularly in agricultural pests including many species in the genera *Agrotis*, *Feltia*, *Mamestra*, *Plusia*, *Trichoplusia*, *Heliothis*, *Helicoverpa*, *Spodoptera*, and others (Weiser 1987). For example, *Mamestra configurata* periodically outbreaks in canola fields in the prairie provinces of Canada (Mason et al. 1998). NPV infection is widespread among populations (Turnock 1988), and infection of more than 95% of the population has been recorded (Erlandson 1990). Epizootics have been best studied in cyclic species of temperate forest Lepidoptera.

EPIZOOTICS AND FOREST LEPIDOPTERA Baculoviruses infect many species of forest lepidopterans (Cory et al. 1997, Evans & Entwistle 1987, Rothman & Myers 2000, Weiser 1987) and most of the mathematical models of baculovirus-host interactions specifically focus on population outbreaks and cyclic dynamics of forest Lepidoptera. To determine if virus is commonly associated with outbreaks of forest caterpillars, we reviewed information collected by the Forest Insect and Disease Survey of the Canadian Forest Service (Martineau 1984). Of 41 species of native,

outbreaking species of Lepidoptera and sawflies (Hymenoptera) in Canada, NPV was recorded associated with the decline of nine species; less than a quarter. Of eight introduced forest outbreak species, virus infection was associated with the declines of four, two sawflies and two Lymantriids.

Other studies of forest caterpillars indicate that epizootics are not the norm. Species for which the population dynamics have been well studied, but for which viral epizootics do not regularly occur are; spruce needleminer, *Epinotia tedella* (Munster-Swendsen 1991), larch budmoth, *Zeiraphera diniana* (Baltensweiler & Fischlin 1988), pine beauty moth, *Panolis flammea* (Watt & Hicks 2000), winter moth and bruces spanworm, *Operophtera brumata*, (Tenow 1972), and *O. bruceata*, (Roland & Embree 1995), *Epirrita autumnata* (*Oporinia autumnata*) (Ruohomäki et al. 2000), jack pine budworm, *Choristoneura pinus pinus* (McCullough 2000), beech caterpillar, *Syntypistis punctatella*, (Kamata 2000), and fall webworm, *Hyphantria cunea* (Weiser 1987). Viral epizootics are largely limited to the families Lymantriidae (gypsy and nun moth, *Lymantria*, tussock moths, *Orgyia*), Lasiocampidae (tent caterpillars, *Malacosoma*), and Diprionidae (sawflies, *Neodiprion*). What is different about these hosts and their NPVs is not readily apparent.

Field tests of the impact of virus have occurred for three species. Spraying virus on western spruce budworm, *Choristoneura occidentalis*, a tortricid moth for which viral infection is not part of the population dynamics, caused high levels of infection (50%) and some vertical transmission. However, the epizootics were not sufficient to control the outbreak (Otvos et al. 1989). Similarly, spraying NPV on introduced populations of the winter moth, *O. brumata*, a geometrid, caused initial infection, but the virus did not persist (Cunningham et al. 1981). Spraying Douglas fir tussock moth, a lymantriid species for which virus is part of the population dynamics, successfully initiated an early epizootic and controlled the populations (Otvos et al. 1987). Thus for species that normally have epizootics, early initiation may be beneficial for control.

Long-term studies of baculoviruses and their hosts are rare. Patterns of infection with population change have been most closely studied in gypsy moth, *L. dispar* (Dwyer et al. 1997, Dwyer & Elkinton 1993, Woods & Elkinton 1987). Long-term patterns of population change and infection have also been monitored for tent caterpillars (Myers 2000). This shows that infection is not always associated with peak population densities, and that infection falls rapidly with population density after the peak (Figure 2). It has been suggested that sublethal effects might explain the reduced fecundity of moths often observed after epizootics of forest caterpillars (Myers 1988). Most of the evidence gathered on tent caterpillars supports this (Myers 2000, Myers & Kukan 1995, Rothman 1997, Rothman & Myers 1996b). An alternative is the "disease-resistance hypothesis" (Myers 2000) in which reduced fecundity is a cost of resistance of insects surviving the epizootic. Forest insect populations show large changes in population density and are frequently found in disjunct populations. This, combined with their considerable genetic variation at all levels; individuals, families, populations, and location, means that this is likely

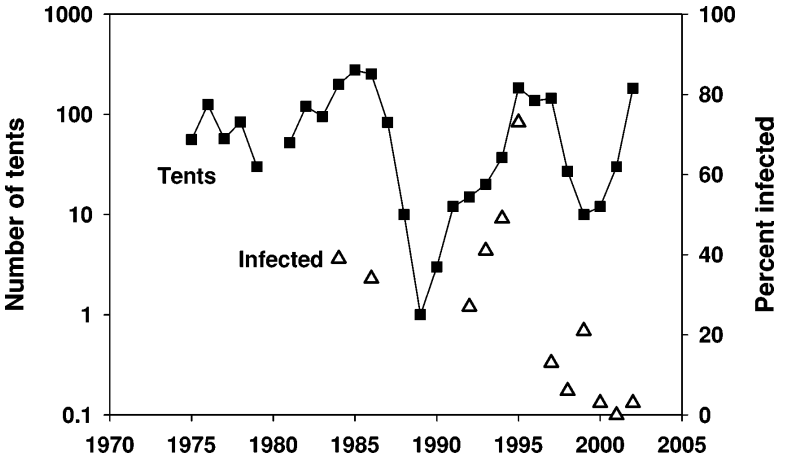

Figure 2 Population trend (number of tents) and proportion infected larvae for western tent caterpillars monitored on Mandarte Island, British Columbia.

to lead to a heterogeneous mixture of host-parasite traits, features underpinning Thompson's (1999) geographic mosaic theory of coevolution. Baculovirus-insect interactions in strongly fluctuating populations have great potential for further field tests of theory of host-parasite interaction.

CONCLUSIONS

Baculoviruses are proving to be a rich source of information on how insects and their pathogens interact, allowing the examination of the relationship from the gene to the population level. The development of increasingly sophisticated molecular tools such as microarray technology, combined with a rapidly expanding database on baculovirus genomes will provide a superb resource for examining issues such as the molecular basis of host range and the genetic basis of persistent infections. They will also provide a framework that will allow the examination of the coevolution of baculoviruses with their hosts and the features that define baculovirus species. A rich theoretical literature exists on the evolution of disease virulence (Day 2001, 2002; Lipsitch & Moxon 1997; Myers & Rothman 1995), and recent studies on baculoviruses have shown they could play a role in furthering our understanding of this key issue. The high level of variation seen in baculovirus populations is particularly fascinating, and it is already contributing to our understanding of what generates and maintains pathogen diversity and the role its plays in disease severity.

Much of the theory on epizootics of baculoviruses and forest Lepidopterans has been in the form of mathematical models that explore the conditions that might yield cyclic host population dynamics. However, many questions still remain about baculoviruses in natural populations. For example, why do baculoviruses occur

widely but generally remain rare in most host populations? How is virus maintained when host densities are low? Can tri-trophic interactions influence disease epizootics? If infection is closely associated with host population fluctuations, do virulence and resistance change temporally and spatially? How are the ecology and evolution of baculoviruses influenced by their interaction with other natural enemies? Do baculoviruses (or any insect pathogen) play a role in determining insect community structure? Without learning more about the interactions between baculoviruses and their hosts in field populations, understanding of the evolutionary changes and ecological impacts of these diseases will remain elusive.

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LITERATURE CITED

Abot AR, Moscardi F, Fuxa JR, Sosa-Gomez DR, Richter AR. 1996. Development of resistance by *Anticarsia gemmatalis* from Brazil and the United States to a nuclear polyhedrosis virus under laboratory selection pressure. *Biol. Control* 7:126–30

Ali MI, Felton GW, Meade T, Young SY. 1998. Influence of interspecific and intraspecific host plant variation on the susceptibility of heliothines to a baculovirus. *Biol. Control* 12:42–49

Ali MI, Young SY, Felton GW, McNew RW. 2002. Influence of the host plant on occluded virus productivity and lethal infectivity of a baculovirus. *Biol. Control* 81:158–65

Allaway GP, Payne CC. 1983. A biochemical and biological comparison of three European isolates of nuclear polyhedrosis viruses from *Agrotis segetum*. *Arch. Virol.* 75:43–54

Allaway GP, Payne CC. 1984. Host range and virulence of five baculoviruses from lepidopterous hosts. *Ann. Appl. Biol.* 105:29–37

Anderson RM, May RM. 1980. Infectious diseases and population cycles of forest insects. *Science* 210:658–61

Anderson RM, May RM. 1981. The population dynamics of microparasites and their invertebrate hosts. *Phil. Trans. R. Soc. London Ser. B* 291:451–524

Arends HM, Jehle JA. 2002. Homologous recombination between the inverted terminal repeats of defective transposon TCp3.2 causes an inversion in the genome of *Cydia pomonella*. *J. Gen. Virol* 83:1573–78

Baltensweiler W, Fischlin A. 1988. The larch budmoth in the Alps. In *Dynamics of Forest Insect Populations: Patterns, Causes, Implications.* ed. A Berryman, pp. 332–53. New York: Plenum

Barber KN, Kaupp WJ, Holmes SB. 1993.

Specificity testing of the nuclear polyhedrosis virus of the gypsy moth, *Lymantria dispar* (L.) (Lepidoptera: Lymantriidae). *Can. Entomol.* 125:1055–66

Beisner BE, Myers JH. 1999. Population density and transmission of virus in experimental populations of the western tent caterpillar (Lepidoptera: Lasiocampidae). *Environ. Entomol.* 28:1107–13

Blanford S, Thomas M. 1999. Host thermal biology: the key to understanding host-pathogen interactions and microbial pest control? *Agric. For. Entomol.* 1:195–202

Bonsall M, Godfray HCJ, Briggs C, Hassell MP. 1999. Does host self-regulation increase the likelihood of insect-pathogen population cycles? *Am. Nat.* 153:228–35

Boorstein SM, Ewald PW. 1987. Costs and benefits of behavioral fever in *Melanoplus sanguinipes* infected by *Nosema acridophagus*. *Physiol. Zool.* 60:586–95

Boots M. 1998. Cannibalism and the stage-dependent transmission of a viral pathogen of the Indian meal moth, *Plodia interpunctella*. *Ecol. Entomol.* 23:118–22

Boots M, Norman R. 2000. Sublethal infection and the population dynamics of host-microparasite interactions. *J. Anim. Ecol.* 69:517–24

Bowers R, Begon M, Hodgkinson D. 1993. Host-pathogen population cycles in forest insects? Lessons from simple models reconsidered. *Oikos* 67:529–38

Brassel J, Benz G. 1979. Selection of a strain of the granulosis virus of the codling moth with improved resistance against artificial ultraviolet radiation and sunlight. *J. Invertebr. Pathol.* 33:358–63

Briggs CJ, Godfray HCJ. 1996. The dynamics of insect-pathogen interactions in seasonal environments. *Theor. Popul. Biol.* 50:149–77

Brown D. 1982. Two naturally occuring nuclear polyhedrosis virus variants of *Neodiprion sertifer* Geoffr. (Hymenoptera; Diprionidae). *Appl. Environ. Micro.* 43:65–69

Bull JC, Godfray HCJ, O'Reilly DR. 2001. Persistence of an occlusion-negative recombinant nucleopolyhedrovirus in *Trichoplusia ni* indicates high multiplicity of cellular infection. *Appl. Environ. Micro.* 67:5204–9

Bull JC, Godfray HCJ, O'Reilly DR. 2003. A few polyhedra (FP) mutant and wild-type nucleopolyhedrovirus remains as a stable polymorphism during serial coinfection in *Trichoplusia ni*. *Appl. Environ. Micro.* 69:2052–57

Burden JP, Griffiths CM, Cory JS, Smith P, Sait SM. 2002. Vertical transmission of sublethal granulovirus infection in the Indian meal moth, *Plodia interpunctella*. *Mol. Ecol.* 11:547–55

Carner GR, Hudson JS, Barnett OW. 1979. The infectivity of a nuclear polyhedrosis virus of the velvetbean caterpillar for eight noctuid hosts. *J. Invertebr. Pathol.* 33:211–16

Carruthers WR, Cory JS, Entwistle PF. 1988. Recovery of pine beauty moth *Panolis flammea* nuclear polyhedrosis virus from pine foliage. *J. Invertebr. Pathol.* 52:27–32

Cary LC, Goebel M, Corsar BG, Wang H, Rosen E, Fraser MJ. 1999. Transposon mutagenesis of baculoviruses: analysis of *Trichoplusia ni* transposon IFP2 insertions within the FP locus of nuclear polyhedrosis viruses. *Virology* 172:156–69

Clayton DH, Wolfe ND. 1993. The adaptive significance of self-medication. *Trends Ecol. Evol.* 8:60–63

Combes C. 2001. *Parasitism, the Ecology and Evolution of Intimate Interactions*. Chicago: Univ. Chicago Press. 728 pp.

Cooper D, Cory JS, Myers JH. 2003b. Hierarchical spatial structure of genetically variable nucleopolyhedroviruses infecting cyclic populations of western tent caterpillars. *Mol. Ecol.* 12:881–90

Cooper D, Cory JS, Theilmann DA, Myers JH. 2003a. Nucleopolyhedroviruses of forest and western tent caterpillars: cross-infectivity and evidence for activation of latent virus in high density field populations. *Ecol. Entomol.* 28:41–50

Cory JS, Hails RS, Sait SM. 1997. Baculovirus ecology. In *The Baculoviridae*, ed. LK Miller, pp. 301–9. New York: Plenum

Cory JS, Hirst ML, Sterling PH, Speight

MR. 2000. Narrow host range nucleopolyhedrovirus for control of the browntail moth (Lepidoptera: Lymantriidae). *Environ. Entomol.* 29:661–67

Cory JS, Wilson KR, Hails RS, O'Reilly DR. 2001. Host manipulation by insect pathogens: the effect of the baculovirus *egt* gene on host-virus interaction. In *Endocrine Interactions of Insect Parasites and Pathogens*, ed. JP Edwards, RJ Weaver, pp. 233–44, Oxford: BIOS

Crawford AM, Kalmakoff J. 1977. A host virus interaction in a pasture habitat *Wiseana* spp. Lepidoptera Hepialidae and its baculoviruses. *J. Invertebr. Pathol.* 29:81–87

Crook NE, Spencer RA, Payne CC, Leisy DJ. 1985. Variation in *Cydia pomonella* granulosis virus isolates and physical maps of the DNA from three variants. *J. Gen. Virol.* 66:2423–30

Crozier G, Crozier L, Quiot JM, Lereclus D. 1988. Recombination of *Autographa californica* and *Rachiplusia ou* nuclear polyhedrosis viruses in *Galleria mellonella* L. *J. Gen. Virol.* 69:179–85

Crozier G, Ribeiro HCT. 1992. Recombination as a possible major cause of genetic heterogeneity in *Anticarsia gemmatalis* nuclear polyhedrosis virus wild populations. *Virus Res.* 26:183–96

Cunningham JC, Tonks NV, Kaupp WJ. 1981. Viruses to control winter moth *Operophtera brumata* Lepidoptera Geometridae. *J. Entomol. Soc. B. C.* 78:17–24

D'Amico V, Elkinton JS. 1995. Rainfall effects on transmission of gypsy moth (Lepidoptera: Lymantriidae) nuclear polyhedrosis virus. *Environ. Entomol.* 24:1144–49

D'Amico V, Elkinton JS, Dwyer G, Burand JP, Buonaccorsi JP. 1996. Virus transmission in gypsy moths is not a simple mass action process. *Ecology* 77:201–6

Day T. 2001. Parasite transmission modes and the evolution of virulence. *Evolution* 55:2389–400

Day T. 2002. The evolution of virulence in vector-borne and directly transmitted parasites. *Theoret. Popul. Biol.* 62:199–213

DeFillippis VR, Villarreal LP. 2000. An introduction to the evolutionary ecology of viruses. See Hurst 2000, pp. 125–208

Doyle CJ, Hirst ML, Cory JS, Entwistle PF. 1990. Risk assessment studies: detailed host range testing of wild-type cabbage moth *Mamestra brassicae* Lepidoptera Noctuidae nuclear polyhedrosis virus. *Appl. Environ. Micro.* 56:2704–10

Duan L, Otvos IS. 2001. Influence of larval age and virus concentration on mortality and sublethal effects of a nucleopolyhedrovirus on the Western spruce budworm (Lepidoptera: Tortricidae). *Environ. Entomol.* 30:136–46

Duffey SS, Hoover K, Bonning BC, Hammock BD. 1995. The impact of host plant on the efficacy of baculoviruses. *Rev. Pest. Toxicol.* 3:137–275

Dushoff J, Dwyer G. 2001. Evaluating the risks of engineered viruses: modeling pathogen competition. *Ecol. Appl.* 11:1602–9

Dwyer G. 1991. The roles of density, stage, and patchiness in the transmission of an insect virus. *Ecology* 72:559–74

Dwyer G, Dushoff J, Elkinton JS, Burand JP, Levin SA. 2002. Host heterogeneity in susceptibility: lessons from an insect virus. In *Adaptive Dynamics of Infectious Diseases*, ed. U Dieckmann, JAJ Metz, MW Sabelis, K Sigmund, pp. 74–84. Cambridge, UK: Cambridge Univ. Press

Dwyer G, Dushoff J, Elkinton JS, Levin SA. 2000. Pathogen-driven outbreaks in forest defoliators revisited: building models from experimental data. *Am. Nat.* 156:105–20

Dwyer G, Elkinton JS. 1993. Using simple models to predict virus epizootics in gypsy moth populations. *J. Anim. Ecol.* 62:1–11

Dwyer G, Elkinton JS, Buonaccorsi JP. 1997. Host heterogeneity in susceptibility and disease dynamics: tests of a mathematical model. *Am. Nat.* 150:685–707

Easwaramoorthy E, Jayaraj S. 1989. Vertical transmission of granulosis virus of sugarcane shoot borer, *Chilo infuscatellus* Snell. *Trop. Pest Manage.* 35:352–53

Ebling PM, Kaupp WJ. 1995. Differentiation and comparative activity of six isolates of

a nuclear polyhedrosis virus from the forest tent caterpillar, *Malacosoma disstria*, Hübner. *J. Invertebr. Pathol.* 66:198–200

Edwards JP, Weaver RJ, eds. 2001. *Endocrine Interactions of Insect Parasites and Pathogens.* Oxford, UK: BIOS

Engelhard EK, Volkman LE. 1995. Developmental resistance in fourth instar *Trichoplusia ni* orally inoculated with *Autographa californica* M nuclear polyhedrosis virus. *Virology* 209:384–89

Engelhard EK, Kam-Morgan LNW, Washburn JO, Volkman LE. 1994. The insect tracheal system: a conduit for the systemic spread of *Autographa californica* M nuclear polyhedrosis virus. *Proc. Natl. Acad. Sci. USA* 91:3224–27

Entwistle PF, Evans HF. 1985. Viral control. In *Comprehensive Insect Physiology, Biochemistry, and Pharmacology*, ed. LI Gilbert, GA Kerkut, 12:347–412. Oxford: Pergamon

Entwistle PF, Forkner AC, Green BM, Cory JS. 1993. Avian dispersal of nuclear polyhedrosis virus after induced epizootics in the pine beauty moth, *Panolis flammea*, (Lepidoptera: Noctuidae). *Biol. Control* 3:61–69

Erlandson MA. 1990. Biological and biochemical comparison of *Mamestra configurata* and *Mamestra brassicae* nuclear polyhedrosis virus isolates pathogenic for the bertha armyworm, *Mamestra configurata* (Lepidoptera: Noctuidae). *J. Invertebr. Pathol.* 56:47–56

Escribano A, Williams T, Goulson D, Cave RD, Chapman JW, Caballero P. 2000. Effect of parasitism on a nucleopolyhedrovirus amplified in *Spodoptera frugiperda* larvae parasitized by *Campoletis sonorensis*. *Entomol. Exp. Appl* 97:257–64

Escribano A, Williams T, Goulson D, Cave RD, Caballero P. 2001. Consequences of interspecific competition on the virulence and genetic composition of a nucleopolyhedrovirus in *Spodoptera frugiperda* larvae parasitized by *Chelonus insularis*. *Biocontrol Sci. Technol.* 11:649–62

Evans HF, Entwistle PF. 1987. Viral diseases. In *Epizootiology of Insect Disease*, ed. JR Fuxa, Y Tanada, pp. 257–322. New York: Wiley & Sons

Farrar RRJ, Ridgway RL. 2000. Host plant effects on the activity of selected nuclear polyhedrosis viruses against the corn earworm and beet armyworm (Lepidoptera: Noctuidae). *Environ. Entomol.* 29:108–15

Fenton A, Fairbairn JP, Norman R, Hudson PJ. 2002. Parasite transmission: reconciling theory and reality. *J. Anim. Ecol.* 71:893–905

Forschler BT, Young SY, Felton GW. 1992. Diet and the susceptibility of *Helicoverpa zea* (Noctuidae: Lepidoptera) to a nuclear polyhedrosis virus. *Environ. Entomol.* 21:1220–23

Fox CW, Roff, DA, Fairbairn DJ, eds. 2001. *Evolutionary Ecology.* Oxford, UK: Oxford Univ. Press

Frank SA. 1996. Models of parasite virulence. *Q. Rev. Biol.* 71:37–78

Frid L. 2002. *Thermal ecology of western tent caterpillars Malacosoma californicum pluviale and infection by nucleopolyhedrovirus.* MSc thesis. Univ. British Columbia, Vancouver. 48 pp.

Frid L, Myers JH. 2002. Thermal ecology of western tent caterpillars *Malacosoma californicum pluviale* and infection by nucleopolyhedrovirus. *Ecol. Entomol.* 27:665–63

Fuxa JR, Richter AR. 1989. Reversion of resistance by *Spodoptera frugiperda* to nuclear polyhedrosis virus. *J. Invertebr. Pathol.* 53:52–56

Fuxa JR, Richter AR. 1998. Repeated reversion of resistance to nucleopolyhedrovirus by *Anticarsia gemmatalis*. *J. Invertebr. Pathol.* 71:159–64

Fuxa JR, Richter AR. 2001. Quantification of soil-to-plant transport of recombinant nucleopolyhedrovirus: effects of soil type and moisture, air currents, and precipitation. *Appl. Environ. Micro.* 67:5166–70

Fuxa JR, Richter AR, Ameen AO, Hammock BD. 2002. Vertical transmission of TnSNPV, TnCPV, AcMNPV, and possibly recombinant NPV in *Trichoplusia ni*. *J. Invertebr. Pathol.* 79:44–50

Fuxa JR, Sun J-Z, Weidner EH, LaMotte LR.

1999. Stressors and rearing diseases of *Trichoplusia ni*: evidence of vertical transmission of NPV and CPV. *J. Invertebr. Pathol.* 74:149–55

Fuxa JR, Weidner EH, Richter AR. 1992. Polyhedra without virions in a vertically transmitted nuclear polyhedrosis virus. *J. Invertebr. Pathol.* 60:53–58

Garcia-Maruniak A, Pavan OHO, Maruniak JE. 1992. A variable region of *Anticarsia gemmatalis* nuclear polyhedrosis virus contains tandemly repeated DNA sequences. *Virus Res.* 41:123–32

Gelernter WD, Federici BA. 1986. Isolation, identification, and determination of virulence of a nuclear polyhedrosis virus from the beet armyworm, *Spodoptera exigua* (Lepidoptera: Noctuidae). *Environ. Entomol.* 15:240–45

Gettig RG, McCarthy WJ. 1982. Genotypic variation among wild isolates of *Heliothis* spp. nuclear polyhedrosis viruses from different geographic regions. *Virology* 117:245–52

Getz W, Pickering J. 1983. Epidemic models: thresholds and population regulation. *Am. Nat.* 121:893–98

Godfray HCJ, O'Reilly DR, Briggs CJ. 1997. A model of nucleopolyhedrovirus (NPV) population genetics applied to co-occlusion and the spread of the few polyhedra (FP) phenotype. *Proc. R. Soc. London Ser. B* 264:315–22

Goulson D. 1997. Wipfelkrankheit: modification of host behavior during baculoviral infection. *Oecologia* 109:219–28

Goulson D, Cory JS. 1995. Responses of *Mamestra brassicae* (Lepidoptera: Noctuidae) to crowding: interactions with disease resistance, color phase and growth. *Oecologia* 104:416–23

Goulson D, Hails RS, Williams T, Hirst ML, Vasconcelos SD, et al. 1995. Transmission dynamics of a virus in a stage-structured insect population. *Ecology* 76:392–401

Hails RS, Hernandez-Crespo P, Sait SM, Donnelly CA, Green BM, Cory JS. 2002. Transmission patterns of natural and recombinant baculoviruses. *Ecology* 83:906–16

Hamm JJ, Styer EL. 1985. Comparative pathology of isolates of *Spodoptera frugiperda* nuclear polyhedrosis virus in *S. frugiperda* and *S. exigua*. *J. Gen. Virol.* 66:1249–62

Harrison RF, Bonning BC. 1999. The nucleopolyhedroviruses of *Rachoplusia ou* and *Anagrapha falcifera* are isolates of the same virus. *J. Gen. Virol.* 80:2793–98

Hajós JP, Pijnenburg J, Usmany M, Zuidema D, Závodszky P, Vlak JM. 2000. High frequency recombination between homologous baculoviruses in cell culture. *Arch. Virol.* 145:159–64

Hatfield PR, Entwistle PF. 1988. Biological and biochemical comparison of nuclear polyhedrosis virus isolates pathogenic for the oriental armyworm, *Mythimna separata* (Lepidoptera: Noctuidae). *J. Invertebr. Pathol.* 52:168–76

Hawtin RE, Zarkowska T, Arnold K, Thomas CJ, Gooday GW, et al. 1997. Liquefaction of *Autographa californica* nucleopolyhedrovirus-infected insects is dependent on the integrity of virus-encoded chitinase and cathepsin genes. *Virology* 238: 243–53

Hernández-Crespo P, Sait SM, Hails RS, Cory JS. 2001. Behavior of a recombinant baculovirus in lepidopteran hosts with different susceptibilities. *Appl. Environ. Micro.* 67: 1140–46

Herniou EA, Luque T, Chen X, Vlak JM, Winstanley D, et al. 2001. Use of whole genome sequence data to infer baculovirus phylogeny. *J. Virol.* 75:8117–26

Herniou EA, Olszewski J, Cory JS, O'Reilly DR. 2003. The genome sequence and evolution of baculoviruses. *Annu. Rev. Entomol.* 48:211–34

Hochberg M. 1991. Nonlinear transmission rates and the dynamics of infectious diseases. *J. Theor. Biol.* 153:301–21

Hochberg ME. 1989. The potential role of pathogens in biological control. *Nature* 337:262–65

Hodgson DJ, Hitchman RB, Vanbergen AJ, Hails RS, Hartley SE, et al. 2003. The existence and persistence of genotypic

variation in nucleopolyhedrovirus populations. In *Genes in the Environment, British Ecological Soc. Symp. 15*, ed. RS Hails, JE Beringer, HCJ Godfray, pp. 258–80. Oxford, UK: Blackwell

Hodgson DJ, Vanbergen AJ, Hartley SE, Hails RS, Cory JS. 2002. Differential selection of baculovirus genotypes mediated by different species of host food plant. *Ecol. Letts.* 5:512–18

Hodgson DJ, Vanbergen AJ, Watt AD, Hails RS, Cory JS. 2001. Phenotypic variation between naturally co-existing genotypes of a Lepidopteran baculovirus. *Evol. Ecol. Res.* 3:687–701

Hoover K, Alaniz SA, Yee JL, Rocke DM, Hammock BD, Duffey SS. 1998d. Dietary protein and chlorogenic acid effect on baculoviral disease of noctuid (Lepidoptera: Noctuidae) larvae. *Environ. Entomol.* 27:1264–72

Hoover K, Grove MJ, Su S. 2002. Systemic component to intrastadial developmental resistance in *Lymantria dispar* to its baculovirus. *Biol. Control* 25:92–98

Hoover K, Kishida KT, Digiorgio LA, Workman J, Alaniz SA, et al. 1998c. Inhibition of baculoviral disease by plant-mediated peroxidase activity and free radical generation. *J. Chem. Ecol.* 24:1949–2001

Hoover K, Stout MJ, Alaniz SA, Hammock BD, Duffey SS. 1998b. Influence of induced plant defenses in cotton and tomato on the efficacy of baculoviruses on noctuid larvae. *J. Chem. Ecol.* 24:253–71

Hoover K, Washburn JO, Volkman LE. 2000. Midgut-based resistance of *Heliothis virescens* to baculovirus infection mediated by phytochemicals in cotton. *J. Insect Physiol.* 46:999–1007

Hoover K, Yee JL, Schultz CM, Rocke DM, Hammock BD, Duffey SS. 1998a. Effects of plant identity and chemical constituents on the efficacy of a baculovirus against (*Heliothis virescens*). *J. Chem. Ecol.* 24:221–52

Hughes D, Possee RD, King LA. 1993. Activation and detection of a latent baculovirus resembling *Mamestra brassicae* nuclear polyhedrosis virus in *M. brassicae* insects. *Virology* 194:600–15

Hughes DS, Possee RD, King LA. 1997. Evidence for the presence of a low level, persistent baculovirus infection of *Mamestra brassicae* insects. *J. Gen. Virol.* 78:1801–5

Hughes PR, Gettig RR, McCarthy WJ. 1983. Comparison of the time-mortality response of *Heliothis zea* to 14 isolates of *Heliothis* nuclear polyhedrosis virus. *J. Invertebr. Pathol.* 41:256–61

Hunter MD, Schultz JC. 1993. Induced plant defenses breached? Phytochemical induction protects an herbivore from disease. *Oecologia* 94:195–203

Hurst CJ, ed. 2000. *Viral Ecology*. San Diego: Academic

Jehle JA, Fritsch E, Nickel A, Huber J, Backhaus H. 1995. TCI4.7: a novel lepidopteran transposon found in *Cydia pomonella* granulosis virus. *Virology* 207:369–79

Kamata N. 2000. Population dynamics of the beech caterpillar, *Syntypistis punctatella*, and biotic and abiotic factors. *Popul. Ecol.* 42:267–78

Karban R, English-Loeb G. 1997. Tachinid parasitoids affect host plant choice by caterpillars to increase caterpillar survival. *Ecology* 78:603–11

Keddie BA, Aponte GW, Volkman LE. 1989. The pathway of infection of *Autographa californica* nuclear polyhedrosis virus in an insect host. *Science* 243:1728–30

Keeley LL, Vinson SB. 1975. β-ecdysone effects on the development of nucleopolyhedrosis in *Heliothis* spp. *J. Invertebr. Pathol.* 26:121–23

Kelly PM, Entwistle PF. 1988. In vivo mass production in the cabbage moth (*Mamestra brassicae*) of a heterologous (*Panolis*) and a homologous (*Mamestra*) nuclear polyhedrosis virus. *J. Virol. Meth.* 19:249–56

Kelly TJ, Park EJ, Masler CA, Burand JP. 1995. Characterization of the glycosylated ecdysteroids in the hemolymph of baculovirus-infected gypsy moth larvae and cells in culture. *Eur. J. Entomol.* 92:51–61

Kikhno I, Gutierrez S, Crozier L, Croizier G,

López-Ferber M. 2002. Characterisation of *pif*, a gene required for the per os infectivity of *Spodoptera littoralis* nucleopolyhedrovirus. *J. Gen. Virol.* 82:3013–22

Kirkpatrick BA, Washburn JO, Volkman LE. 1998. AcMNPV pathogenesis and developmental resistance in fifth instar *Heliothis virescens*. *J. Invertebr. Pathol.* 72:63–72

Kislev N, Edelman M. 1982. DNA restriction-pattern differences from geographic isolates of *Spodoptera littoralis* nuclear polyhedrosis virus. *Virology* 119:219–22

Knell RJ, Begon M, Thompson DJ. 1998. Transmission of *Plodia interpunctella* granulosis virus does not conform to the mass action model. *J. Anim. Ecol.* 67:592–599

Kolodny-Hirsch DM, van Beek NAM. 1997. Selection of a morphological variant of *Autographa californica* nuclear polyhedrosis virus with increased virulence following serial passage in *Plutella xylostella*. *J. Invertebr. Pathol.* 69:205–11

Kukan B. 1999. Vertical transmission of nucleopolyhedrovirus in insects. *J. Invertebr. Pathol.* 74:103–11

Kunimi Y, Yamada E. 1990. Relationship of larval phase and susceptibility of the armyworm, *Pseudoletia separata* Walker (Lepidoptera, Noctuidae) to a nuclear polyhedrosis-virus and a granulosis-virus. *Appl. Entomol. Zool.* 25:289–97

Lee KP. 2002. *Ecological factors impacting on the nutritional biology of a generalist and a specialist caterpillar: effects of pathogen and plant structural compound on macronutrient balancing.* DPhil thesis. Univ. Oxford. 168 pp.

Lee Y, Fuxa JR. 2000. Transport of wild-type and recombinant nucleopolyhedroviruses by scavenging and predatory arthropods. *Micro. Ecol.* 39:301–13

Li Q, Donly C, Li L, Willis LG, Theilmann DA, Erlandson M. 2000a. Sequence organization of the *Mamestra configurata* nucleopolyhedrovirus genome. *Virology* 294:106–21

Li L, Donly C, Li Q, Willis LG, Keddie BA, et al. 2002b. Identification and genomic analysis of a second species of nucleopolyhedrovirus isolated from *Mamestra configurata*. *Virology* 297:226–44

Lipsitch M, Moxon ER. 1997. Virulence and transmissibility of pathogens: what is the relationship? *Trends Microbiol.* 5:31–37

Lively CM. 2001. Parasite-host interactions. See Fox et al. 2001, pp. 290–302

Lozano GA. 1998. Parasitic stress and self-medication in wild animals. *Adv. Stud. Behav.* 27:291–317

Lynn DE, Shapiro M, Dougherty EM. 1993. Selection and screening of clonal isolates of the Abington strain of gypsy moth nuclear polyhedrosis virus. *J. Invertebr. Pathol.* 62:191–95

Martineau R. 1984. *Insects Harmful to Forest Trees.* Montreal: Multiscience

Maruniak JE, Brown SE, Knudson DL. 1984. Physical maps of SfMNPV baculovirus DNA and its genomic variants. *Virology* 136:221–34

Mason PG, Arthur AP, Olfert OO, Erlandson MA. 1998. The bertha armyworm (*Mamestra configurata*) (Lepidoptera: Noctuidae) in western Canada. *Can. Entomol.* 130:321–36

Matthews HJ, Smith I, Edwards JP. 2002. Lethal and sublethal effects of a granulovirus on the tomato moth *Lacanobia oleracea*. *J. Invertebr. Pathol.* 80:73–80

McCallum H, Barlow N, Hone J. 2001. How should pathogen transmission be modelled? *Trends Ecol. Evol.* 16:295–300

McCullough DG. 2000. A review of factors affecting the population dynamics of jack pine budworm (*Choristoneura pinus pinus* Freeman). *Popul. Ecol.* 42:243–56

McVean RIK, Sait SM, Thompson DJ, Begon M. 2002. Dietary stress reduces the susceptibility of *Plodia interpunctella* to infection by a granulovirus. *Biol. Control* 25:81–84

Melamed-Madjar V, Raccah B. 1979. The transstadial and vertical transmission of a granulosis virus from the corn borer *Sesamia nonagrioides*. *J. Invertebr. Pathol.* 33:259–64

Milks ML. 1997. Comparative biology and susceptibility of cabbage looper (Lepidoptera:

Noctuidae) lines to a nuclear polyhedrosis virus. *Environ. Entomol.* 26:839–48

Milks ML, Burnstyn I, Myers JH. 1998. Influence of larval age on the lethal and sublethal effects of the nucleopolyhedrovirus of *Trichoplusia ni* the cabbage looper. *Biol. Control* 12:119–26

Milks ML, Myers JH. 2000. The development of larval resistance to a nucleopolyhedrovirus is not accompanied by an increased virulence in the virus. *Evol. Ecol.* 14:645–64

Milks ML, Myers JH. 2003. Cabbage looper resistance to a nucleopolyhedrovirus confers cross-resistance to two granuloviruses. *Environ. Entomol.* 32:286–89

Milks ML, Myers JH, Leptich MK. 2002. Costs and stability of cabbage looper resistance to a nucleopolyhedrovirus. *Evol. Ecol.* 16:369–85

Miller LK, ed. 1997. *The Baculoviridae*. New York: Plenum

Mitchell FL, Fuxa JR. 1990. Multiple regression analysis of factors influencing a nuclear polyhedrosis virus in populations of fall armyworm Lepidoptera Noctuidae in corn. *Environ. Entomol.* 19:260–67

Moore J. 2002. *Parasites and the Behavior of Animals*. Oxford, UK: Oxford Univ. Press. 315 pp.

Moscardi F. 1999. Assessment of the application of baculoviruses for control of Lepidoptera. *Annu. Rev. Entomol.* 44:257–89

Moser BA, Becnel JJ, White SE, Alfonso C, Kutish G, et al. 2001. Morphological and molecular evidence that *Culex nigripalpus* baculovirus is an unusual member of the family Baculoviridae. *J. Gen. Virol.* 82:283–97

Muñoz D, Caballero P. 2000. Persistence and effects of parasitic genotypes in a mixed population of the *Spodoptera exigua* nucleopolyhedrovirus. *Biol. Control* 19:259–64

Muñoz D, Castillejo J, Caballero P. 1998. Naturally occurring deletion mutants are parasitic genotypes in a wild-type nucleopolyhedrovirus population. *Appl. Environ. Micro.* 64:4372–77

Muñoz D, Murillo R, Krell PJ, Vlak JM, Caballero P. 1999. Four genotypic variants of a *Spodoptera exigua* nucleopolyhedrovirus (Se-SP2) are distinguishable by a hypervariable genomic region. *Virus Res.* 59:61–74

Muñoz D, Vlak JM, Caballero P. 1997. In vivo recombination between two strains of the genus *Nucleopolyhedrovirus* in its natural host *Spodoptera exigua*. *Appl. Environ. Micro.* 63:3025–31

Munster-Swendsen M. 1991. The effect of sublethal neogregarine infections in the spruce needleminer, *Epinotia tedella* (Lepidoptera: Tortricidae). *Ecol. Entomol.* 16:211–19

Myers JH. 1988. Can a general hypothesis explain population cycles of forest Lepidoptera? *Adv. Ecol. Res.* 18:179–242

Myers JH. 2000. Population fluctuations of the western tent caterpillar in southwestern British Columbia. *Popul. Ecol.* 42:231–41

Myers JH, Kukan B. 1995. Changes in the fecundity of tent caterpillars: a correlated character of disease resistance or sublethal effects of disease? *Oecologia* 103:475–80

Myers JH, Malakar R, Cory JS. 2000. Sublethal nucleopolyhedrovirus infection effects on female pupal weight, egg mass size, and vertical transmission in gypsy moth (Lepidoptera: Lymantriidae). *Environ. Entomol.* 29:1268–72

Myers JH, Rothman LE. 1995. Virulence and transmission of infectious diseases in humans and insects: evolutionary and demographic patterns. *Trends Ecol. Evol.* 10:194–98

Olofsson E. 1989. Transmission of the nuclear polyhedrosis virus of the European pine sawfly from adult to offspring. *J. Invertebr. Pathol.* 54:322–30

O'Reilly DR. 1997. Auxiliary genes of baculoviruses. In *The Baculoviruses*, ed. LK Miller, pp. 267–300. New York: Plenum

O'Reilly DR, Brown MR, Miller LK. 1992. Alteration of ecdysteroid metabolism due to baculovirus infection of the fall armyworm *Spodoptera frugiperda* host ecdysteroids are conjugated with galactose. *Insect Biochem. Mol. Biol.* 22:313–20

O'Reilly DR, Hails RS, Kelly TJ. 1998. The impact of host developmental status on

baculovirus replication. *J. Invertebr. Pathol.* 72:269–75

O'Reilly DR, Kelly TJ, Masler EP, Thyagaraja BS, Robson RM, et al. 1995. Overexpression of *Bombyx mori* prothoracicotropic hormone using baculovirus vectors. *Insect Biochem. Mol. Biol* 25:475–85

O'Reilly DR, Miller LK. 1989. A baculovirus blocks insect molting by producing ecdysteroid UDP-glucosyltransferase. *Science* 245:1110–12

O'Reilly DR, Miller LK. 1991. Improvement of a baculovirus pesticide by deletion of the *egt* gene. *Bio/Technology* 9:1086–89

Otvos IS, Cunningham JC, Alfaro RI. 1987. Aerial application of nuclear polyhedrosis virus against Douglas-fir tussock moth *Orgyia pseudotsugata* Mcdunnough Lepidoptera Lymantriidae ii. Impact 1 and 2 years after application. *Can. Entomol.* 119:707–16

Otvos IS, Cunningham JC, Kaupp WJ. 1989. Aerial application of two baculoviruses against the western spruce budworm *Choristoneura occidentalis* Freeman Lepidoptera Tortricidae in British Columbia Canada. *Can. Entomol.* 121:209–18

Parnell M, Grzywacz D, Jones KA, Brown M, Odour G, Ong'aro J. 2002. The strain variation and virulence of granulovirus of diamondback moth (*Plutella xylostella* Linnaeus, Lep., Yponomeutidae) isolated in Kenya. *J. Invertebr. Pathol.* 79:192–96

Paul RK. 1997. *Evolution and interaction of insect pathogens*. PhD thesis. Univ. Reading. 248 pp.

Payne CC. 1986. Insect pathogenic viruses as pest control agents. In *Biological Plant and Health Protection*, ed. JM Franz. pp. 183–200. Stuttgart: Fischer

Peng J, Zhong J, Granados RR. 1999. A baculovirus enhancin alters the permeability of a mucosal midgut peritrophic matrix from lepidopteran larvae. *J. Insect Physiol.* 45:159–66

Podgwaite JD, Mazzone HM. 1986. Latency of insect viruses. *Adv. Virus Res.* 31:293–320

Popham HJR, Bischoff DS, Slavicek JM. 2001. Both *Lymantria dispar* nucleopolyhedrovirus enhancin genes contribute to viral potency. *J. Virol.* 75:8639–48

Poulin R. 1998. *Evolutionary Ecology of Parasites.* Boca Raton, FL.: Chapman and Hall. 212 pp.

Raymond B, Vanbergen A, Pearce I, Hartley SE, Cory JS, Hails RS. 2002. Host plant species can influence the fitness of herbivore pathogens: the winter moth and its nucleopolyhedrovirus. *Oecologia* 131:533–41

Reeson AF, Wilson K, Cory JS, Hankard P, Weeks JM, et al. 2000. Effects of phenotypic plasticity on pathogen transmission in the field in a Lepidoptera-NPV system. *Oecologia* 124:373–80

Reeson AF, Wilson K, Gunn A, Hails RS, Goulson D. 1998. Baculovirus resistance in the noctuid *Spodoptera exempta* is phenotypically plastic and responds to population density. *Proc. R. Soc. London Ser. B* 265:1787–91

Regniere J. 1984. Vertical transmission of diseases and population dynamics of insects with discrete generations: a model. *J. Theor. Biol.* 107:287–301

Ribeiro HCT, Pavan OHO, Muotri AR. 1997. Comparative susceptibility of two different hosts to genotypic variants of the *Anticarsia gemmatalis* nuclear polyhedrosis virus. *Entomol. Exp. Appl.* 83:233–37

Richards A, Cory J, Speight M, Williams T. 1999b. Foraging in a pathogen reservoir can lead to local host population extinction: A case study of a Lepidoptera-virus interaction. *Oecologia* 118:29–38

Richards A, Speight M, Cory J. 1999a. Characterization of a nucleopolyhedrovirus from the vapourer moth, *Orgyia antiqua* (Lepidoptera Lymantriidae). *J. Invertebr. Pathol.* 74:137–42

Rigby MC, Hechinger, RF, Stevens L. 2002. Why should parasite resistance be costly? *Trends Parasitol.* 18:116–20

Roland JH, Embree DG. 1995. Biological control of the winter moth. *Annu. Rev. Entomol.* 40:475–92

Rothman LD. 1997. Immediate and delayed effects of a viral pathogen and density on tent

caterpillar performance. *Ecology* 78:1481–93

Rothman LD, Myers JH. 1996a. Debilitating effects of viral diseases on host Lepidoptera. *J. Invertebr. Pathol.* 67:1–10

Rothman LD, Myers JH. 1996b. Is fecundity correlated with resistance to viral disease in the western tent caterpillar? *Ecol. Entomol.* 21:396–98

Rothman LD, Myers JH. 2000. Ecology of insect viruses. See Hurst 2000, pp. 385–412

Rothman LD, Roland J. 1998. Forest fragmentation and colony performance of forest tent caterpillar. *Ecography* 21:383–91

Ruohomäki K, Tanhuanpää M, Ayres MD, Kaitaniemi P, Tammaru T, Haukioja E. 2000. Causes of cyclicity of *Epirrita autumnata* (Lepidoptera, Geometridae): grandiose theory and tedious practice. *Popul. Ecol.* 42:211–24

Schmid-Hempel P, Ebert D. 2003. On the evolutionary ecology of specific immune defense. *Trends Ecol. Evol.* 18:27–32

Shapiro DI, Fuxa JR, Braymer HD, Pashley DP. 1991. DNA restriction polymorphism in wild isolates of *Spodoptera frugiperda* nuclear polyhedrosis virus. *J. Invertebr. Pathol.* 58:96–105

Siva-Jothy MT, Thompson JJW. 2002. Short-term nutrient deprivation affects immune function. *Physiol. Entomol.* 27:206–12

Slack JM, Kuzio J, Faulkner P. 1995. Characterization of v-cath, a cathepsin L-like proteinase expressed by the baculovirus *Autographa californica* multiple nuclear polyhedrosis virus. *J. Gen. Virol* 76:1091–98

Slavicek JM, Popham HJR, Riegel CI. 1999. Deletion of the *Lymantria dispar* multicapsid nucleopolyhedrosis ecdysteroid UDP-glucosyl transferase gene enhances viral killing speed in the last instar of the gypsy moth. *Biol. Control* 16:91–103

Smith IRL, Crook NE. 1988. In vivo isolation of baculovirus genotypes. *Virology* 166:240–44

Smith IRL, Crook NE. 1993. Characterization of new baculovirus genotypes arising from inoculation of *Pieris brassicae* with granulosis viruses. *J. Gen. Virol.* 74:415–24

Steinhaus EA. 1967. *Principles of Insect Pathology*. New York: McGraw-Hill

Stiles S, Himmerich B. 1998. *Autographa californica* NPV isolates: restriction endonuclease analysis and comparative biological activity. *J. Invertebr. Pathol.* 72:174–77

Suwanchaichinda C, Paskewitz SM. 1998. Effects of larval nutrition, adult body size and adult temperature on the ability of *Anopheles gambiae* (Diptera: Culicidae) to melanise sephadex beads. *J. Med. Entomol.* 35:157–61

Takatsuka J, Okuno S, Nakai M, Kunimi Y. 2003. Genetic and biological comparison of ten geographic isolates of a nucleopolyhedrovirus that infects *Spodoptera litura* (Lepidoptera: Noctuidae). *Biol. Control* 26:32–39

Taylor LH, MacKinnon MJ, Read AF. 1998. Virulence of mixed-clone and single clone infections of the rodent malaria *Plasmodium chabaudi*. *Evolution* 52:583–91

Teakle RE, Jensen JM, Giles JE. 1986. Age-related susceptibility of *Heliothis punctiger* to a commercial formulation of nuclear polyhedrosis virus. *J. Invertebr. Pathol.* 47:82–92

Tenow O. 1972. The outbreaks of *Oporina autumnata* Bkh. and *Operophtera* spp. (Lep. Geometridae) in the Scandinavian mountain chain and northern Finland 1862–1968. *Zool. Bidrag Uppsala, Suppl.* 2:1–107

Thompson CG, Scott DW, Wickman BE. 1981. Long-term persistence of the nuclear polyhedrosis virus of the Douglas-fir tussock moth, *Orgyia pseudotsugata* (Lepidoptera: Lymantriidae), in forest soil. *Environ. Entomol.* 10:254–55

Thompson JN. 1999. Specific hypothesis on the geographic mosaic of coevolution. *Am. Nat.* 153:S1–S14

Thompson JN. 2001. The geographic dynamics of coevolution. See Fox et al. 2001, pp. 331–43

Tompkins GJ, Dougherty EM, Adams JR, Diggs D. 1988. Changes in the virulence of nuclear polyhedrosis viruses when propagated in alternate noctuid (Lepidoptera: Noctuidae) cell lines and hosts. *J. Econ. Entomol.* 81:1027–32

Turnock WJ. 1988. Density, parasitism, and disease incidence of larvae of the bertha armyworm, *Mamestra configurata* Walker (Lepidoptera: Noctuidae), in Manitoba, 1973–86. *Can. Entomol.* 120:401–13

Vail PV, Tebbets JS. 1990. Comparative biology and susceptibility of *Plodia-interpunctella* Lepidoptera Pyralidae populations to a granulosis virus. *Environ. Entomol.* 19:791–94

Van Beek N, Hughes PR, Wood HA. 2000. Effects of incubation temperature on the dose-survival time relationship of Trichoplusia ni larvae infected with *Autographa californica* nucleopolyhedrrovirus. *J. Invertebr. Pathol.* 76:185–90

Vasconcelos SD. 1996. *Studies on the transmission and dispersal of baculoviruses in Lepidopteran populations*. DPhil thesis, Univ. Oxford. 168 pp.

Vasconcelos SD, Cory JS, Wilson KR, Sait SM, Hails RS. 1996a. Modified behavior in baculovirus-infected lepidopteran larvae and its impact on the spatial distribution of inoculum. *Biol. Control* 7:299–306

Vasconcelos SD, Williams T, Hails RS, Cory JS. 1996b. Prey selection and baculovirus dissemination by carabid predators of Lepidoptera. *Ecol. Entomol.* 21:98–104

Vass E, Napi AJ. 1998. The effects of dietary yeast on the cellular immune response of *Drosophila melanogaster* against the larval parasitoid, *Leptopilina boulardi*. *J. Parasitol.* 84:870–72

Vezina A, Peterman R. 1985. Tests of the role of nuclear polyhedrosis virus in the population dynamics of its host, Douglas-fir tussock moth, *Orgyia pseudotsugata* (Lepidpotera: Lymantriidae). *Oecologia* 67:260–66

Vickers JM, Cory JS, Entwistle PF. 1991. DNA characterization of eight geographic isolates of granulosis virus from the potato tuber moth *Phthorimaea operculella* Lepidoptera Gelechiidae. *J. Invertebr. Pathol.* 57:334–42

Volkman LE. 1997. Nucleopolyhedrosis interactions with their insect hosts. *Adv. Virus Res.* 48:313–48

Washburn JO, Kirkpatrick BA, Haas-Stapleton E, Volkman LE. 1998. Evidence that the stilbene-derived optical brightener M2R enhances *Autographa californica* M nucleopolyhedrovirus infection of *Trichoplusia ni* and *Heliothis virescens* by preventing sloughing of infected midgut epithelial cells. *Biol. Control* 11:58–69

Washburn JO, Kirkpatrick BA, Volkman LE. 1995. Comparative pathogenesis of *Autographa californica* M nuclear polyhedrosis virus in larvae of *Trichoplusia ni* and *Heliothis virescens*. *Virology* 209:561–68

Washburn JO, Kirkpatrick BA, Volkman LE. 1996. Insect protection against viruses. *Nature* 383:767

Washburn JO, Lyons EH, Haas-Stapleton EJ, Volkman LE. 1999. Multiple nucleocapsid packaging of *Autographa californica* nucleopolyhedrovirus accelerates the onset of systemic infection in *Trichoplusia ni*. *J. Virol.* 73:411–16

Watanabe H. 1987. The host population. In *Epizootiology of Insect Diseases*, ed. JA Fuxa, Y Tanada, pp. 71–112. New York: Wiley & Sons

Watt AD, Hicks BJ. 2000. A reppraisal of the populations dynamics of the pine beauty moth, *Panolis flammea*, on lodgepole pine, *Pinus contorta*, in Scotland. *Popul. Ecol.* 42:225–30

Weiser J. 1987. Patterns over place and time. In *Epizootiology of Insect Disease*, ed. JR Fuxa, Y Tanada, pp. 215–42. New York: Wiley & Sons

White A, Bowers R, Begon M. 1996. Host-pathogen cycles in self-regulated forest insect systems: resolving conflicting predictions. *Am. Nat.* 148:220–25

Wilson K, Cotter SC, Reeson AF, Pell JK. 2001. Melanism and disease resistance in insects. *Ecol. Letts.* 4:637–49

Wilson K, Reeson AF. 1998. Density-dependent prophylaxis: evidence from Lepidoptera-baculovirus interactions? *Ecol. Entomol.* 23:100–1

Wilson KR, O'Reilly DR, Hails RS, Cory JS. 2000. Age-related effects of the

Autographa californica multiple nucleopolyhedrovirus *egt* gene in the cabbage looper (*Trichoplusia ni*). *Biol. Control* 19:57–63

Woods SA, Elkinton JS. 1987. Bimodal patterns of mortality from nuclear polyhedrosis virus in gypsy moth *Lymantria dispar* populations. *J. Invertebr. Pathol.* 50:151–57

Woolhouse MEJ, Taylor LH, Haydon DT. 2001. Population biology of multihost pathogens. *Science* 292:1109–12

Zanotto PMA, Kessing BD, Maruniak JE. 1993. Phylogenetic interrelationships among baculoviruses: evolutionary rates and host associations. *J. Invertebr. Pathol.* 62:147–62