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Original Contribution

Effects of Waning Maternal Immunity on Infection Dynamics in Seasonally Breeding Wildlife

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Abstract: Increasing outbreaks of emerging infectious diseases originating from wildlife have intensified interests in understanding their dynamics in reservoir hosts. The effect of waning maternally derived antibodies on epidemics in a seasonally breeding wild mammal population is unclear. We examined how the population structure, influenced by seasonal breeding and maternally derived immunity, affects viral invasion and persistence using a hypothetical system based on Hendra virus infection in black flying foxes (*Pteropus alecto*). A deterministic Hendra virus epidemic model with uncertainty in parameter values was used to simulate transient epidemics following viral introduction into an infection-free population, including various timings within a year and differences in pre-existing seroprevalence. Additionally, we applied different modelling methods of waning maternal immunity to examine whether different models notably affected modelling outputs. The waning of maternally derived immunity temporally dispersed the supply of susceptible individuals in seasonally breeding populations, diminishing the effect of birth pulses generating the temporally synchronised supply of susceptible newborns. Thus, even in a population with seasonal births, a considerable level of probabilities of viral invasion and persistence could occur no matter when infectious individuals were introduced into the population. Viral invasion and persistence were substantially influenced by the modelling method of maternally derived immunity, emphasising the need to select an appropriate method and further investigate the waning pattern of maternally derived antibodies.

Keywords: Black flying foxes, Epidemic model, Hendra virus, Maternal immunity, Seasonal birth, Viral dynamics

Introduction

Bats (Order: *Chiroptera*) have been identified as natural reservoirs of many emerging infectious diseases of public health concern (Calisher et al. 2006; Luis et al. 2013). Although the bats do not appear to suffer from many of these infections, the fatality rates attributable to bat viral diseases are often quite high in other mammalian species including

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humans (Calisher et al. 2006). Hendra virus, for example, has been detected in four species of flying foxes (*Pteropus alecto*, *P. conspicillatus*, *P. poliocephalus*, and *P. scapulatus*) in Australia (Halpin et al. 2000). Spillover from *P. alecto* and *P. conspicillatus* (Edson et al. 2015; Field et al. 2015; Burroughs et al. 2016) to horses, and thereafter to humans, causes serious clinical symptoms and even death in both horses and humans (Field et al. 2007). Surveillance of the Hendra virus has revealed that spillover events temporally concentrate between June and September in the southern subtropics of eastern Australia (Plowright et al. 2015). This temporal pattern implies that the seasonal behaviour of reservoir hosts, such as seasonal breeding, can be considerably implicated with Hendra virus dynamics in bat populations. Although seasonal factors such as birth pulses are not the only drivers of Hendra virus dynamics and other factors (*Eucalyptus* phenology, bat movement, temperature, and nutrition) can also markedly influence Hendra virus spillover (Giles et al. 2016; Paez et al. 2017; Martin et al. 2018), it would be valuable to understand the underlying mechanism of this influence, as Hendra virus spillover is known to result from various processes involving many interacting factors (Plowright et al. 2017).

Births from susceptible mothers and immigration of susceptible bats are not the only sources of Hendra virus-susceptible bats. While newborns of immune mothers can obtain protection against infection via maternally derived antibodies (MatAbs), this protection wanes over a certain period (Epstein et al. 2013), causing these individuals to enter the susceptible pool as juveniles. The proportion of immune mothers that confer waning passive immunity to newborns could, therefore, markedly modify the supply of susceptible bats. The supply of susceptible bats from these two sources (from births to susceptible mothers and via loss of MatAb (Hayman et al. 2018)) interacts to determine whether viral introduction into a population results in epidemics or viral persistence. The presence of MatAbs in seasonally breeding wildlife delays recurrent epidemics over a multi-year timescale (Garnier et al. 2014). However, the mechanism underlying the effect of this delay on the timing of epidemics within a year requires further investigation.

Profiles of Hendra virus prevalence and seroprevalence in flying foxes may be generated by at least three different underlying mechanisms: susceptible–infectious–recovered (SIR), susceptible–infectious–recovered–susceptible (SIRS), and susceptible–infectious–latent–infectious (SILI) (Plowright et al. 2016). Later, two modelling studies, which both investigated henipavirus in *Eidolon helvum* bats in Africa, did not support lifelong immunity. One study suggested long-lasting immunity (mean four years) (Peel et al. 2018), while another study suggested about 1–2 years of immune period that followed by recurring latent infection (Glennon et al. 2019).

A modelling approach was established to describe the infectious period based on an exponential distribution, which is a classical method for transferring individuals across infection stages (Anderson and May 1991) and is implicit in a simple differential equation susceptible–infectious–immune (SIR) model with constant rate parameters (Keeling and Rohani 2008). Although exponential distributions are used widely for computational ease, efforts towards finding more realistic methods to model the infectious period resulted in the development of gamma-distributed infectious periods, which divides a compartment of the infectious stage into multiple compartments (Lloyd 2001). Wearing et al. (2005) examined the implication of modelling infectious and latency periods in predicting the impact of infectious diseases. Like the infectious period, the recovery period has been modelled with an exponential distribution in modelling studies; the impact of different approach of modelling the recovery period has not been widely studied. Modelling studies about bat viruses treated the period of maternally derived immunity as the exponential distribution (Hayman et al. 2018; Peel et al. 2018). In particular, when hosts seasonally breed, the supply of susceptible hosts into a population through births and loss of maternally derived immunity would be seasonally concentrated in a narrow window, which emphasises the importance of accurate modelling of loss of maternally derived immunity for exact prediction of the epidemic impact. Therefore, the exploration of different epidemic modelling outcomes using an exponential and gamma distribution would help to determine whether the method for modelling waning maternal immunity is an important influence on model behaviour.

Studies found that maternally derived antibody facilitates the viral persistence in bat populations (Hayman et al. 2018; Peel et al. 2018). Unlike Peel et al. (2018) in which infectious individuals were introduced three months prior to the birth pulse peak, we applied various timings of the introduction of infectious individuals, focusing on the timing gap between the introduction of infectious individuals into a population and a seasonal birth pulse. The focus on the timing gap makes the modelling method of the waning of maternal immunity critical in that the waning timing depends on the modelling methods. Thus, we ex-

plore the effects of the modelling method on differences in decaying MatAbs between an exponential distribution and gamma distribution to assess how important the effect of decaying MatAbs on viral dynamics can be affected by modelling methods. To this end, we set up a hypothetical population of *P. alecto* with two age groups.

Methods

Model Structure

We simulated Hendra virus dynamics in *P. alecto* using compartmental deterministic models with uncertainty in parameter values, which were framed using ordinary differential equations and numerically integrated using the *deSolve* package (Soetaert et al. 2010) in R (R Core Team 2018). An MSIRS model was built by adding a maternally immune (M) compartment to an SIRS model. Maternally immune (M) newborns become susceptible at a rate δ. Susceptible (S) bats become infected at the rate βSI (assuming density-dependent transmission). Plowright et al. (2011) estimated the mean values of a Hendra virus transmission rate (β) and recovery rate (γ), which we used in our models. Bats are infectious (I) before recovery at a rate γ. Based on the SIRS model, we assumed that once recovered (R), bats lost their immunity at a rate (ω). The uncertainty in parameter values is shown in Table 1. Hendra virus infection is known to not cause clinical disease in its reservoir hosts (flying foxes) (Halpin et al. 2001); therefore, infected bats are considered to have the same mortality rate as susceptible and recovered bats. The models were simulated with annual birth pulses and run with a daily time step. As viral extinction is likely to occur in the first few post-epidemic troughs (King et al. 2009), the simulation period was limited to five years, which was considered as long enough to include the first few epidemics and following troughs.

Simulation of seasonal birth pulses and MatAbs required an age-structured model of the bat population. The age structure consisted of sexually immature juvenile bats (denoted by the subscript i) and sexually mature adult bats (subscript m). In the MSIRS model, juveniles became adults, which could breed at the timing of two years after birth (at rate ε) (Wang et al. 2013). The proportion of juveniles in the total population (η) was, on average, 0.24 (McIlwee and Martin 2002). Four epidemic compartments for the two age groups led to a total of eight stages (see Appendix A). Although maternally immune adults are not expected to exist in nature, we included this stage for modelling consistency. The exponential distribution of periods of MatAbs means that some individuals remained in the maternally immune compartment for longer than in

Table 1. Model parameters. Three numbers in brackets following PERT indicate minimum, mode, and maximum values of the PERT distribution

Parameter	Symbol	Value	Unit	Reference
Transmission rate	β	PERT(2E-5, 0.0000476, 5E-5)	Per day	(Plowright et al. 2011)
Recovery rate	γ	PERT (1/10, 1/7, 1/4)	Per day	(Plowright et al. 2011)
Acquired immunity losing rate	ω	PERT(1/7.2, 1/4.1, 1/2.7)	Per day	(Peel et al. 2018)
Mortality rate	μ	PERT (1/15, 1/10, 1/7)	Per year	(McIlwee and Martin 2002)
Maternally derived immunity losing rate	δ	PERT (1/223, 1/ 250, 1/277)	Per day	(Epstein et al. 2013; Baker et al. 2014)
Ageing rate	α	PERT (1/18, 1/24, 1/30)	Per month	(McIlwee and Martin 2002)
Scalar to control birth rate	κ	0.00159	Per day	This study
Birth pulse synchrony	s	130	–	(Peel et al. 2014)
Timing of birth pulse	φ	1/2	–	(McIlwee and Martin 2002)
Colony size	N	10,000	Capita	(Plowright et al. 2011)
Average proportion of juvenile bats in total bats	η	0.23	–	(McIlwee and Martin 2002)

any period between birth and adulthood. With the parameters used, few maternally immune adults remained, which minimally affected the results. We assumed an age-independent annual mortality rate (μ) of 16% (McIlwee and Martin 2002). The mortality rate (μ) and birth rate were independent of population density and were chosen such that the population size remained constant. Bats born to immune female adults (R_m) and maternally immune female adults (M_m) were assumed to be maternally immune (M_i) in the MSIRS model, whereas all newborns were assumed to be susceptible (S_i) in the SIRS model. The initial numbers in each compartment are shown in Appendix B.

Seasonally pulsed births were modelled with a periodic Gaussian function (Peel et al. 2014; Hayman 2015): $b(t) = \kappa\sqrt{s/\pi}e^{-s\cos^2(\pi t-\varphi)}$, where κ controls the magnitude, s determines synchrony, and φ determines the timing of birth pulse. This function allows births to occur exclusively in a certain period within a year, with none outside this period (Peel et al. 2014; Hayman 2015). The scaling parameter (κ) was used to ensure that the total population size was stable inter-annually. *Pteropus alecto* shows different seasonal birth patterns depending on latitude (McIlwee and Martin 2002). In southeast Queensland and Northern NSW, where most Hendra virus spillover events have occurred, the offspring of *P. alecto* are born in October and November, which is closely aligned to that of *P. poliocephalus* (Vardon and Tidemann 1998; McIlwee and Martin 2002). With reference to the seasonal birth pulse of *P. poliocephalus*, we set s = 130, so that 95% of annual births were concentrated within one month (Peel et al. 2014).

Flying fox colonies are patchily distributed and individuals move among colonies. This movement may introduce the Hendra virus into infection-free colonies, triggering transient epidemics (causing metapopulation dynamics of the virus within the host populations (Plowright et al. 2011)). As natural reservoir hosts of Hendra virus, flying fox colonies are highly likely to have been previously exposed to the virus (Plowright et al. 2011), and so colonies are not necessarily immunologically naïve at the timing of viral introduction. Partial immunity of a population affects the duration and size of an epidemic caused by the viral introduction (Pulliam et al. 2007). We, therefore, designed models to simulate Hendra virus dynamics in a colony of flying foxes within this broader context of a metapopulation in eastern Australia, assuming a proportion of bats in a colony had previously been exposed to Hendra virus and thus was partially immune.

Uncertainty in parameter values was included in the models by using PERT distributions in R package 'mc2d' (Pouillot and Delignette-Muller 2010). The minimum, mode, and maximum values of parameters are displayed in Table 1. After 1,000 iterations were simulated, the proportion of viral invasion and viral persistence were recorded. We predicted that viral invasion occurred when the maximum of the sum of infectious juveniles (I_i) and infectious adults (I_m) surpassed ten, whereas viral persistence was defined as occurring when the sum of infectious juveniles (I_i) and infectious adults (I_m) did not drop below one over the entire simulation period of five years.

In addition to the uncertainty in parameter values, we applied varying conditions of seroprevalence and days from birth pulse to viral introduction, as seroprevalence can be an important factor in determining the viral invasion and persistence (Plowright et al. 2011). Nevertheless, multiple studies that collected samples from pteropid bats to investigate Hendra virus seroprevalence showed spatiotemporally varying levels of seroprevalence (Breed et al. 2006, 2010, 2011; Field et al. 2015). Additionally, the days from birth pulse to viral introduction may affect viral invasion and persistence in seasonally breeding wildlife (Peel et al. 2014). Considering the frequent migration of flying foxes among colonies (Roberts et al. 2012), it is likely that viral introduction into a colony can occur any time of the year. Because Hendra virus infection has not found to be pathogenic to *P. alecto*, we assumed that the infective stage of bats did not affect the migration of bats and thereby the migration did not change the proportion of susceptible bats in the population. Also, the seasonal migration pattern of *P. alecto* has not been investigated enough to include our models, and we assumed that seasonality did not affect the migration pattern of bats. Therefore, we simulated the models with combinations of various levels of seroprevalence and days from birth pulse to viral introduction.

Modelling of Waning Maternally Derived Immunity

The half-life of anti-Hendra virus MatAbs was markedly similarly estimated as 52.24 days in *P. alecto* (Epstein et al. 2013) and 61 days in *Eidolon helvum* (Baker et al. 2014). By using dilutions of 1:16 as the negative cut-off, the immune duration of the MatAb was 255.13 days (95% CI: 221.0–289.3) (Epstein et al. 2013) and 244 days (95% CI: 224–

264) (Baker et al. 2014). The mean of the two durations, 250, was used in this study. The MSIRS model with exponentially distributed waning periods of MatAb (hereafter referred to as exponential MSIRS model) assumed that the number of maternally immune hosts decreased exponentially from birth. In addition to the exponential MSIRS model, an MSIRS model with gamma-distributed waning periods of MatAb (hereafter referred to as gamma MSIRS model) was simulated. This model used a gamma distribution in transferring maternally immune juveniles to susceptible juveniles. Gamma-distributed waning periods of MatAb were modelled by dividing the maternally immune stage into multiple (g) sub-stages, where gamma-distributed waning periods of MatAb had a mean of g and variance of 1/g (Wearing et al. 2005). As the gamma distribution parameter (g) increased, the rate of loss of maternally immune individuals shifted from exponential decay to a fixed duration of maternal immunity (Fig. 1). We then modelled the gamma-distributed maternally immune durations using various gamma distribution parameters. By using Pearson's Chi-squared test of the experimental data (Epstein et al. 2013) with various gamma distribution parameters, we found that g = 8 showed the smallest Chi-squared value. Thus, we used this value in our models. This study included the three different modelling methods in terms of the waning of MatAb: SIRS model, exponential MSIRS model, and gamma MSIRS model.

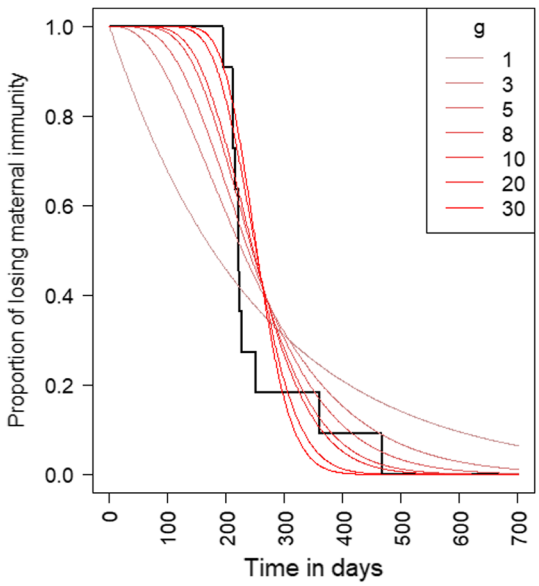

Figure 1. Gamma-distributed maternally immune periods. Gamma-distributed maternally immune periods and histogram of duration of maternal antibodies in fruit bats. The decreasing proportion of maternally immune pups as a function of time is shown with an increasing number of subdivisions within the compartment of maternally immune pups. The gamma parameter in gamma distribution increases from g = 1 to 30. Gamma distribution of g = 1 corresponds to the exponential distribution, while increasing g becomes close to a constant length. The black line shows the decreasing proportion of maternally immune *P. alecto* pups, in which the data in Epstein et al. (2013) were used.

Results

Viral Invasion

The effect of seroprevalence on epidemics was predominant compared to the effect of days from viral introduction to birth pulse in all three models (Fig. 2). A seroprevalence as low as 0.5 generated a nearly 100% probability of viral invasion, whereas a value as high as 0.9 seroprevalence generated a nearly 0% probability. In the SIRS model, viral

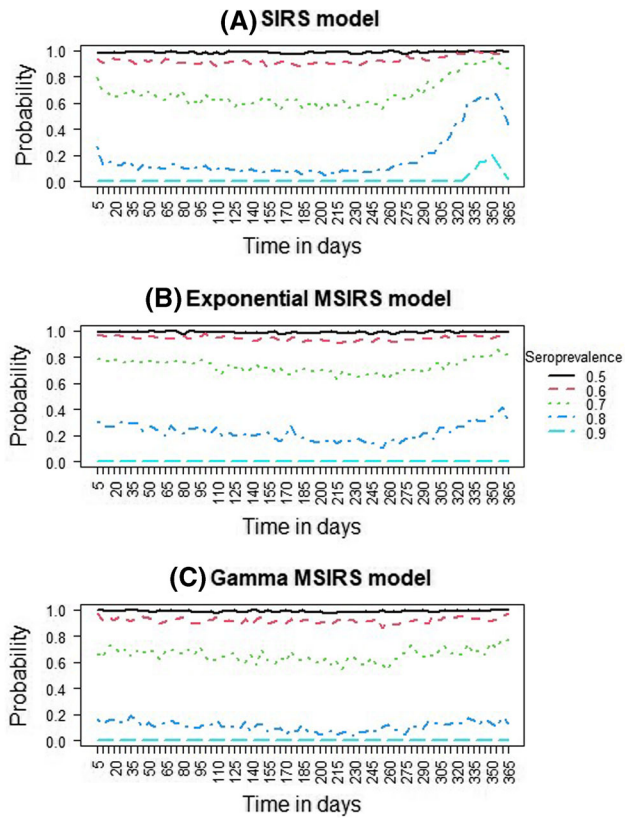

Figure 2. Probabilities of viral invasion. The likelihood of viral invasion was simulated with five levels of seroprevalence across varying days from viral introduction to a seasonal birth pulse in the (A) SIRS model, (B) exponential MSIRS model, and (C) gamma MSIRS model. Time in days represents the days from viral introduction to a birth pulse.

introduction shortly before a birth pulse (e.g. about 345 days after a birth pulse) resulted in the highest likelihood of viral invasion. However, in the exponential MSIRS model, the characteristic was weakened and even more weakened in the gamma MSIRS model. Compared to the SIRS model, the addition of MatAb resulted in a more uniform steady probability of viral invasion across the timings of viral introduction by dispersing the timing of supply of susceptible bats into the population. Therefore, waning MatAbs appeared to reduce the effect of a highly seasonal birth pulse, and the reduction was most pronounced in the gamma MSIRS model compared to in the exponential MSIRS model.

Viral Persistence

The introduction of infected individuals did not strongly maintain infections in the population with the SIRS model in all combinations of seroprevalence and days from birth pulse to viral introduction (Fig. 3). If an infected bat was introduced into a population with a high proportion of susceptible bats, high-magnitude epidemics were followed by deep troughs. Otherwise, if viral introduction occurred into a population with a low proportion of susceptible bats, epidemics and viral persistence were not triggered. The three mechanisms of viral fadeout (initial fadeout, epidemic fadeout, or endemic fadeout) are described in Appendix C. In the MSIRS models, the simulation results showed conditions for the determination of viral persistence. Seroprevalence should be intermediate. Seroprevalences of 0.6 and 0.7 were found to have higher probabilities than the low (0.5) and high (0.8 and 0.9) seroprevalence. Too low seroprevalence led to epidemic fadeout, while too high seroprevalence caused initial fadeout. Regarding the timing of viral introduction, with low seroprevalence (i.e. 0.5) the timing was critical in determining viral persistence, whereas the timing had little impact with higher seroprevalence. This is because viral introduction into a population with low seroprevalence resulted in a high-impact epidemic that was followed by a deep trough and fadeout of infectious bats, and this phenomenon was accelerated by the birth pulses. Gamma MSIRS model showed more flatten probabilities of viral persistence across time than the exponential MSIRS model. This was because the gamma MSIRS model generated a relatively steady supply of susceptible hosts throughout the year.

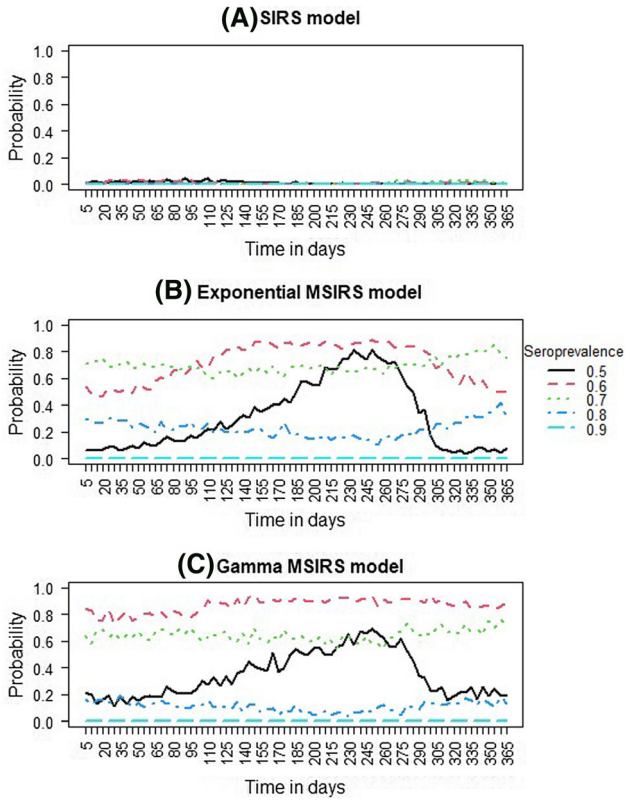

Figure 3. Probabilities of viral persistence. The likelihood of viral persistence was simulated with five levels of seroprevalence across varying days from viral introduction to a seasonal birth pulse in the (A) SIRS model, (B) exponential MSIRS model, and (C) gamma MSIRS model. Time in days represents the days from viral introduction to a birth pulse.

Exponential and Gamma MSIRS Models

The epidemic patterns appeared to be more affected by seasonal birth pulses than by maternally derived immunity in the exponential MSIRS model than in the gamma MSIRS model (Fig. 4A). In the exponential MSIRS model, we modelled the number of maternally immune bats to decrease by on average as much as 1/250 of the remaining maternally immune bats every day. As a result, most juvenile bats lost their MatAbs soon after birth, rather than 250 days after birth. When seroprevalence was high and maternally immune newborns were more common than susceptible newborns, the temporal trend of epidemics was expected to change noticeably at approximately 250 days after a birth pulse (period of maternally derived immunity) rather than at the birth pulse. However, the number of infected individuals began increasing at the time of birth pulses, likely because of the exponential method used to model the loss of MatAbs.

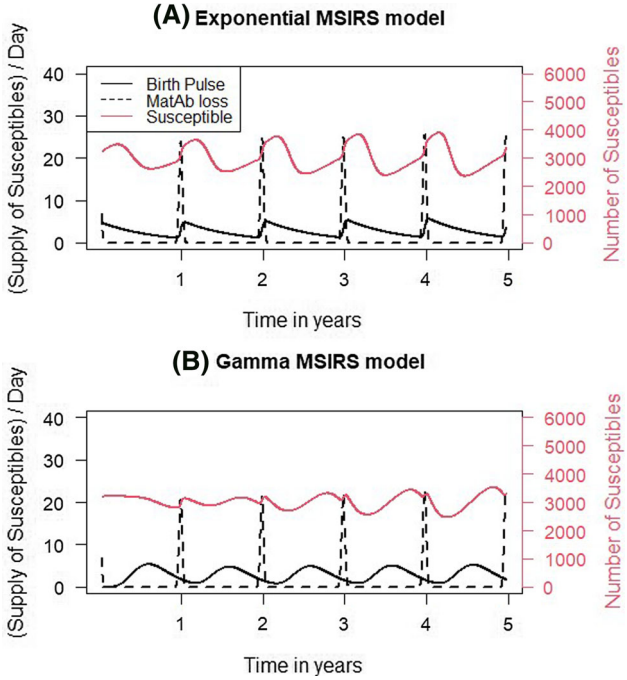

Figure 4. Supply of susceptible individuals from birth pulses and waning maternal immunity in (A) exponential MSIRS and (B) gamma MSIRS models. This is an example of simulation results that were generated by using the mean value of parameters. The number of days since the last birth pulse before viral introduction until viral introduction into a colony was 1, and seroprevalence of the population was 0.7. Black sold lines and black dashed lines represent the daily supply of susceptible individuals from newborn pups from birth pulses and juvenile bats who lost their maternally derived immunity, respectively. Red solid lines represent the number of susceptible. In both simulations, viral invasion and persistence occurred.

In comparison, the gamma MSIRS model showed a more enhanced effect of MatAb than the exponential MSIRS model (Fig. 4B). In the gamma MSIRS model, loss of MatAb appeared to occur mainly at 250 days after birth. Therefore, the impact of MatAb in determining the epidemic pattern was much higher than in the exponential MSIRS model. Moreover, the two relatively separate timings ensured a steady supply of susceptible individuals throughout the year. Another reason for birth pulses with a stronger impact on epidemics compared to the loss of MatAb was that the temporal synchrony of birth pulses was higher than that of MatAb loss. Although more susceptible hosts were supplied from the loss of MatAb than from birth pulses, the tighter span of the latter relative to the former had a high impact on epidemic patterns.

Discussion

This study suggests that the effect of MatAb in seasonal breeding species is not negligible and should be considered to improve the understanding of viral invasion and persistence in wildlife host populations. The existence of MatAb dilutes the effect of the temporally concentrated supply of susceptible individuals and contributes to making viral invasion and persistence possible whenever infectious individuals were introduced even into a seasonally breeding population. However, these conclusions should be interpreted with caution, as the modelling results are contingent on the assumptions made. This study identified the relative importance of births and waning MatAb as sources of susceptible hosts and the implication of modelling methods for waning MatAb. In addition, the methods to model waning MatAb should be emphasised, as we demonstrated that the modelling results can considerably differ depending on the methods.

As flying foxes are natural reservoir hosts of the Hendra virus (Halpin et al. 2000), the virus must be maintained within flying fox populations. However, seasonal birth pulses make it more difficult for the virus to persist compared to in a population with a constant birth rate (Altizer et al. 2006). Furthermore, when the annual birth pulse is tight, the disadvantage is further intensified (Peel et al. 2014). For seasonally breeding flying foxes, other mechanisms are required to overcome or offset the disadvantageous conditions for viral persistence. Our modelling results support that MatAbs can play a role in mitigating adverse conditions to maintain a non-pathogenic virus by dispersing the timing of the supply of susceptible hosts into the population (Peel et al. 2018). This is consistent with recent stochastic models showing that MatAb supports the maintenance of a henipavirus and lyssavirus in seasonally breeding African fruit bats (*Eidolon helvum*) (Hayman et al. 2018; Peel et al. 2018).

Wearing et al. (2005) demonstrated that infectious disease modelling-based predictions are markedly affected by whether the infectious and latent periods are modelled using an exponential distribution or gamma distribution. Heterogeneity in the longevity of protective immunity in different individuals requires mechanisms to deal with the distribution of immune periods of individuals in a model structure (Antia et al. 2018). Here, we showed that gamma-distributed periods of MatAbs could generate substantially different modelling results compared to exponentially dis-

tributed periods. Because the functional form of loss of MatAbs against Hendra virus or other viruses is unknown, we set g = 8 to illustrate the effect of reducing the coefficient of variation in the duration of immunity by a third, from 100% (exponential distribution) to approximately 35% ($1/\sqrt{g}$), to realistically imitate waning MatAbs. The results of the gamma MSIRS model do not show more accurate predictions than the exponential MSIRS model but rather show that substantially different modelling results can be generated depending on whether the loss of maternally derived immunity is exponentially or gamma-distributed. Therefore, appropriate modelling of when maternally immune newborns lose their passive immunity, depending on the species and pathogens against emerging infectious diseases, is expected to improve the prediction of disease outbreaks.

Although this study modelled epidemics in a single population, the results should be considered in the context of metapopulation structure, as we assumed SIRS dynamics in which metapopulations are expected to play an important role in Hendra virus maintenance (Plowright et al. 2011, 2016). An effect of the seasonality of epidemics in metapopulations is that seasonal forcing of transmission may synchronise epidemics in each population (Grassly and Fraser 2006). Synchronised epidemics are likely to increase the likelihood of viral fadeout in a metapopulation. The viral introduction would be less probable if epidemics in populations become extinct at similar times. Therefore, it is necessary to examine the effects of the seasonality of viruses on the synchrony of epidemics in metapopulation seasonal clustering.

The addition of waning MatAb on birth pulses affects not only viral invasion and persistence but also the timing of epidemic peaks, although the timing was not described in this study. Dispersion of timing of the supply of susceptible individuals into a population delayed the timing of epidemic peaks. The timing should be explored to prevent Hendra virus spillover, as spillover events are seasonally clustered in austral winter in southeast Queensland and Northern NSW (Plowright et al. 2015). In contrast, *P. alecto* in southeast Queensland and Northern NSW has high birth synchrony (McIlwee and Martin 2002). High birth synchrony results in temporal clustering of epidemic peaks (Hirsch et al. 2016), although other climatic or ecological factors may also contribute to the different timing of spillover events (Paez et al. 2017; Plowright et al. 2017).

This study used deterministic models with uncertainty in parameter values. Deterministic models are easier to analyse and interpret the modelling results, while stochastic models are more appropriate to reflect the world realistically (Keeling and Rohani 2008). We used deterministic models because one of the primary goals of this study was to understand how Hendra virus dynamics were affected by seasonal breeding when it is combined with waning MatAb rather than to assess the accurate probability of Hendra virus persistence. Instead, we applied uncertainty in the parameter values by using the PERT distribution (Xue et al. 2013). Thus, we were able to estimate the probabilities of epidemic occurrence and viral persistence to compare the effects of different conditions of waning MatAb and seasonal breeding on viral dynamics.

Conclusion

Given the growing interest in emerging zoonotic diseases from wildlife (Rhyan and Spraker 2010), empirical studies of zoonotic reservoir ecology should be combined with mathematical models to develop a mechanistic understanding of virus persistence and spillover. By incorporating MatAbs into generic epidemic models, we provide a framework for studying epidemics in seasonally breeding wildlife species. Complex effects of demographic and virus-related parameters were previously reported in other systems (Begon et al. 2009). We explored a range of plausible assumptions to complement the limited empirical data available for the dynamics of the Hendra virus in flying fox populations. The results showed the effects of MatAb on viral invasion and persistence, rather than predicting actual viral invasion and persistence. Caution must be used, however, when making conclusions on the effect of MatAb, given the specific circumstances associated with each disease and host population structure.

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Declarations

Conflict of interest None.

References

Altizer S, Dobson A, Hosseini P, Hudson P, Pascual M, Rohani P (2006) Seasonality and the dynamics of infectious diseases. *Ecology Letters* 9:467–484

Anderson RM, May RM (1991) *Infectious diseases of humans : dynamics and control*, Oxford: Oxford University Press

Antia A, Ahmed H, Handel A, Carlson NE, Amanna IJ, Antia R, Slifka M (2018) Heterogeneity and longevity of antibody memory to viruses and vaccines. *PLoS biology* 16:e2006601

Baker KS, Suu-Ire R, Barr J, Hayman DT, Broder CC, Horton DL, Durrant C, Murcia PR, Cunningham AA, Wood JL (2014) Viral antibody dynamics in a chiropteran host. *Journal of Animal Ecology* 83:415–428

Begon M, Telfer S, Smith MJ, Burthe S, Paterson S, Lambin X (2009) Seasonal host dynamics drive the timing of recurrent epidemics in a wildlife population. *Proceedings of the Royal Society B-Biological Sciences* 276:1603–1610

Breed AC, Breed MF, Meers J, Field HE (2011) Evidence of Endemic Hendra Virus Infection in Flying-Foxes (Pteropus conspicillatus)-Implications for Disease Risk Management. *PLoS one* 6

Breed AC, Field HE, Epstein JH, Daszak P (2006) Emerging henipaviruses and flying foxes - Conservation and management perspectives. *Biological Conservation* 131:211–220

Breed AC, Yu M, Barr JA, Crameri G, Thalmann CM, Wang LF (2010) Prevalence of henipavirus and rubulavirus antibodies in pteropid bats, Papua New Guinea. *Emerging infectious diseases*. Dec;16(12):1997

Burroughs AL, Durr PA, Boyd V, Graham K, White JR, Todd S, et al. (2016) Hendra Virus Infection Dynamics in the Grey-Headed Flying Fox (Pteropus poliocephalus) at the Southern-Most Extent of Its Range: Further Evidence This Species Does Not Readily Transmit the Virus to Horses. *Plos One* 11(6)

Calisher CH, Childs JE, Field HE, Holmes KV, Schountz T (2006) Bats: Important reservoir hosts of emerging viruses. *Clinical Microbiology Reviews* 19(3):531

Edson D, Field H, McMichael L, Vidgen M, Goldspink L, Broos A, et al. (2015) Routes of Hendra Virus Excretion in Naturally-Infected Flying-Foxes: Implications for Viral Transmission and Spillover Risk. *Plos One* 10(10)

Epstein JH, Baker ML, Zambrana-Torrelio C, Middleton D, Barr JA, DuBovi E, et al. (2013) Duration of Maternal Antibodies against Canine Distemper Virus and Hendra Virus in Pteropid Bats. *Plos One* 8(6)

Field H, Jordan D, Edson D, Morris S, Melville D, Parry-Jones K, et al. (2015) Spatiotemporal Aspects of Hendra Virus Infection in Pteropid Bats (Flying-Foxes) in Eastern Australia. *Plos One* 10(12)

Field HE, Breed AC, Shield J, Hedlefs RM, Pittard K, Pott B, et al. (2007) Epidemiological perspectives on Hendra virus infection in horses and flying foxes. *Australian Veterinary Journal* 85(7):268–270

Garnier R, Gandon S, Harding KC, Boulinier T (2014) Length of intervals between epidemics: evaluating the influence of maternal transfer of immunity. *Ecology and Evolution* 4(5):568–575

Giles JR, Plowright RK, Eby P, Peel AJ, McCallum H (2016) Models of Eucalypt phenology predict bat population flux. *Ecology and Evolution* 6(20):7230–7245

Glennon EE, Becker DJ, Peel AJ, Garnier R, Suu-Ire RD, Gibson L, et al. (2019) What is stirring in the reservoir? Modelling mechanisms of henipavirus circulation in fruit bat hosts *Philosophical Transactions of the Royal Society B* 374(1782):20190021

Grassly NC, Fraser C (2006) Seasonal infectious disease epidemiology. *Proceedings of the Royal Society of London b: Biological Sciences* 273(1600):2541–2550

Halpin K, Young P, Field H, Mackenzie J (2000) Isolation of Hendra virus from pteropid bats: a natural reservoir of Hendra virus. *Journal of General Virology* 81(8):1927–1932

Halpin K, Young P, Mackenzie JS (2001) Bats and viruses-a long association. *American Journal of Tropical Medicine & Hygiene* 65:249

Hayman DT (2015) Biannual birth pulses allow filoviruses to persist in bat populations. *Proceedings of the Royal Society of London b: Biological Sciences* 282(1803):2014259

Hayman DT, Luis AD, Restif O, Baker KS, Fooks AR, Leach C, et al. (2018) Maternal antibody and the maintenance of a lyssavirus in populations of seasonally breeding African bats. *PloS one* 13(6):e0198563

Hirsch BT, Reynolds JJ, Gehrt SD, Craft ME (2016) Which mechanisms drive seasonal rabies outbreaks in raccoons? A test using dynamic social network models *Journal of Applied Ecology* 53(3):804–813

Keeling MJ, Rohani P (2008) *Modeling infectious diseases in humans and animals*, Princeton: Princeton University Press

King AA, Shrestha S, Harvill ET, Bjornstad ON (2009) Evolution of Acute Infections and the Invasion-Persistence Trade-Off. *American Naturalist.* 173(4):446–455

Lloyd AL (2001) Realistic distributions of infectious periods in epidemic models: changing patterns of persistence and dynamics. *Theoretical Population Biology* 60(1):59–71

Luis AD, Hayman DTS, O'Shea TJ, Cryan PM, Gilbert AT, Pulliam JRC, et al. (2013) A comparison of bats and rodents as reservoirs of zoonotic viruses: are bats special? *Proceedings of the Royal Society B-Biological Sciences* 280(1756)

Martin G, Yanez-Arenas C, Plowright RK, Chen C, Roberts B, Skerratt LF. (2018) Hendra Virus Spillover is a Bimodal System Driven by Climatic Factors. *EcoHealth.*:1–17

McIlwee A, Martin L (2002) On the intrinsic capacity for increase of Australian flying-foxes (Pteropus spp., Megachiroptera). *Australian Zoologist* 32(1):76–100

Paez DJ, Giles J, McCallum H, Field H, Jordan D, Peel AJ, et al. (2017) Conditions affecting the timing and magnitude of Hendra virus shedding across pteropodid bat populations in Australia. *Epidemiology & Infection* 145(15):3143–3153

Peel AJ, Baker KS, Hayman DT, Broder CC, Cunningham AA, Fooks AR, et al. (2018) Support for viral persistence in bats from age-specific serology and models of maternal immunity. *Scientific Reports* 8(1):3859

Peel AJ, Pulliam JRC, Luis AD, Plowright RK, O'Shea TJ, Hayman DTS, et al. (2014) The effect of seasonal birth pulses on pathogen persistence in wild mammal populations. *Proceedings of the Royal Society B-Biological Sciences* 281(1786)

Plowright R, Foley P, Field H, Dobson A, Foley J, Eby P, et al. (2011) Urban Habituation, Connectivity, and Stress Synchrony: Hendra Virus Emergence from Flying Foxes (Pteropus spp.). *Ecohealth* 7:S36–S37

Plowright RK, Eby P, Hudson PJ, Smith IL, Westcott D, Bryden WL, et al. (2015) Ecological dynamics of emerging bat virus spillover. *Proceedings of the Royal Society B-Biological Sciences* 282(1798)

Plowright RK, Parrish CR, McCallum H, Hudson PJ, Ko AI, Graham AL, et al. (2017) Pathways to zoonotic spillover. *Nature Reviews Microbiology* 15(8):502–510

Plowright RK, Peel AJ, Streicker DG, Gilbert AT, McCallum H, Wood J, et al. (2016) Transmission or Within-Host Dynamics Driving Pulses of Zoonotic Viruses in Reservoir-Host Populations. *Plos Neglected Tropical Diseases* 10(8)

Pouillot R, Delignette-Muller ML (2010) Evaluating variability and uncertainty separately in microbial quantitative risk assessment using two R packages. *International Journal of Food Microbiology* 142(3):330–340

Pulliam JRC, Dushoff JG, Levin SA, Dobson AP (2007) Epidemic Enhancement in Partially Immune Populations. *Plos One* 2(1)

R Core Team (2018) R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/

Rhyan J, Spraker T (2010) Emergence of diseases from wildlife reservoirs. *Veterinary Pathology* 47(1):34–39

Roberts BJ, Catterall CP, Eby P, Kanowski J (2012) Long-Distance and Frequent Movements of the Flying-Fox Pteropus poliocephalus: Implications for Management. *Plos One* 7(8)

Soetaert K, Petzoldt T, Setzer RW (2010) Solving differential equations in R: package deSolve. *Journal of Statistical Software* 33(9):1–25

Vardon MJ, Tidemann CR (1998) Reproduction, growth and maturity in the black flying-fox, Pteropus alecto (Megachiroptera : Pteropodidae). *Australian Journal of Zoology* 46(4):329–344

Wang HH, Kung NY, Grant WE, Scanlan JC, Field HE (2013) Recrudescent Infection Supports Hendra Virus Persistence in Australian Flying-Fox Populations. *Plos One* 8(11)

Wearing HJ, Rohani P, Keeling MJ (2005) Appropriate models for the management of infectious diseases. *Plos Medicine* 2(7):621–627

Xue L, Cohnstaedt LW, Scott HM, Scoglio C (2013) A Hierarchical Network Approach for Modeling Rift Valley Fever Epidemics with Applications in North America. *PLoS ONE* 8(5): e62049