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Short communication

Ecological and taxonomic variation among human RNA viruses

Mark E.J. Woolhouse*, Kyle Adair

Centre for Immunology, Infection & Evolution, Ashworth Laboratories, University of Edinburgh, Kings Buildings, West Mains Road, Edinburgh EH9 3JT, UK

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ABSTRACT

Only a minority of RNA viruses that can infect humans are capable of spreading in human populations independently of a zoonotic reservoir. This is especially true of vector-borne RNA viruses; the majority of these are not transmissible (via the vector) between humans at all. Understanding the biology underlying this observation will help us evaluate the public health risk associated with novel vector-borne RNA viruses.

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1. Introduction

The realisation that many newly discovered and/or emerging pathogens have zoonotic origins has prompted much interest in the nature of the non-human reservoirs and biological characteristics that enable pathogens to jump between host species.¹ Here, we focus on an important group of pathogens – RNA viruses – and consider how taxonomic diversity and various aspects of ecological diversity – host range, route of infection and transmissibility – are related to one another. Comparative biology is routinely used on a case by case basis to assess the threat to public health posed by newly discovered pathogens – Schmallenberg virus being a recent example. Here we aspire to a more systematic approach to answering the question ‘which kinds of viruses should we be most worried about?’

2. Virus survey

In surveying human viruses we follow the nomenclature and taxonomy set out by the International Committee for the Taxonomy of Viruses (ICTV).² We catalogue ICTV-recognised RNA virus species for which we can find convincing evidence of natural human infection in the peer-reviewed scientific literature (see Ref. 3 for more methodological details). Whilst having a number of limitations (discussed elsewhere⁴), the use of virus species as our unit of study is a natural starting point. Our procedure reveals a total of 158 human infective RNA virus species from 47 genera and 17 families (with one genus unassigned to a family).

This inventory is almost certainly incomplete: we are still discovering or recognising new human infective RNA viruses at an

average rate of more than 2 species per year (data from Ref. 5). Statistical analysis of rates of discovery confirms that there are still many more species yet to be discovered.⁵ However, most of these new viruses are not that different, in terms of their taxonomy or ecology, from previously recognised viruses, implying that studying known viruses should provide insights as to what to expect in the future.

3. Host range

Among the human RNA viruses 22% (34 species) infect *only* humans. The remaining 78% are zoonotic, i.e. they naturally infect vertebrate hosts other than humans. Breaking this down we find that these “other” hosts are usually mammals (84 species) and sometimes other mammals or birds (40 species). Humans do not share their RNA viruses with any other kinds of vertebrate.

At higher taxonomic levels the overlap between RNA viruses of humans and of other mammals is even more striking: all but three species (hepatitis C, hepatitis delta and rubella) have close relatives, usually congeners, which infect other mammals. The overlap is also illustrated in that 47 out of 60 recognised mammal virus genera contain human infective species, as do 17 out of 19 families. The overlap with avian viruses is less marked, although influenza A is an important instance.

These observations give the strong impression that human infectivity evolves relatively easily among mammal RNA viruses. This is supported by phylogenetic analyses suggesting that many human RNA viruses have evolved by host switching from other mammals,⁶ with HIV-1 as an obvious example.⁷

4. Route of infection

Humans may be infected by RNA viruses via any of several possible routes including inhalation, ingestion, bites or broken skin,

* Corresponding author. Tel.: +44 1316505456.
E-mail address: mark.woolhouse@ed.ac.uk (M.E.J. Woolhouse).

sexual contact, in utero, iatrogenic and arthropod vectors. Some viruses can infect by multiple routes. Here we focus on the distinction between viruses which are vector-borne and those which are not. There are 68 species of vector-borne RNA virus that can infect humans. This is >40% of the total but they are confined to just 10 genera from 6 families.

We have previously reported that there is a strong positive association between vector-borne transmission and a broad host range, which is likely due to the need for a pathogen to be able to infect whatever host its vector may bite.⁸ For human RNA viruses this tendency is very marked: there are none that are vector-borne and infect only humans, and just two (dengue and yellow fever) that are primarily viruses of primates; all the remainder have (or are believed to have) reservoirs in non-primate mammals or birds.

5. Transmissibility

We can distinguish three categories of human RNA viruses based on their basic reproduction number in human populations (R_0). First, there are viruses for which R_0 may exceed 1, which implies that they are sufficiently transmissible between humans (via any natural route of infection, which may involve a vector) to cause major epidemics and/or persist endemically in human populations. There is a total of 52 species (including some zoonotic species, e.g. influenza A) in this category. Other viruses always have R_0 less than 1. Some of these are transmissible between humans but not sufficiently so that they can cause major epidemics and/or persist endemically; they are restricted to self-limiting outbreaks. We estimate that there are 28 species of this kind. The remainder – comprising almost half the total of human RNA virus species – is not known to be transmissible between humans at all. This generally reflects their inability to replicate in tissues that permit release from the body (notably the upper respiratory tract, lower gastrointestinal tract, urogenital tract or possibly blood).

Of particular interest are characteristics of the $R_0 > 1$ RNA viruses. Here, we consider just one of many possibilities: whether such viruses are more or less likely to be vector-borne. We find a very strong and statistically significant tendency for human infective vector-borne RNA viruses (in comparison to those transmitted

by other routes) to be much less likely to have $R_0 > 1$ – dengue virus and yellow fever virus are the only examples. There is a similar pattern for being transmissible at all – just 14 of the 68 vector-borne species are that category. These results are illustrated in Fig. 1.

6. Conclusions

Here, we both confirm that the great majority of human RNA viruses are zoonotic and highlight the considerable taxonomic overlap between those found in humans and those found in other mammals (and sometimes birds). We also find that few vector-borne human RNA viruses spread efficiently through human populations, and the ones that can are primate specialists. The reasons for this remain unclear. However, patterns of this kind suggest that it may be possible to identify characteristics of novel viruses that predict their propensity to become significant public health problems, although we stress that we are describing trends not absolute rules.

We offer two observations. First, RNA viruses show little respect for any distinction we might make between ourselves and other mammals (or birds), and the study of their emergence in human populations is a classic “One Health” problem. Reflecting this, several important virus taxa – including the retro-, rota- and corona viruses – were known as animal pathogens before they were found in humans and, at least initially, there was greater knowledge of them in the veterinary community than the medical community. Second, we cannot hope to understand the characteristics that make some viruses serious threats to public health if we do not also study those that are not. So we end with a plea not to neglect the more obscure and unregarded human RNA viruses; they too have something to teach us.

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Conflict of interest statement

None.

Ethical approval

No ethical approvals were required for this work.

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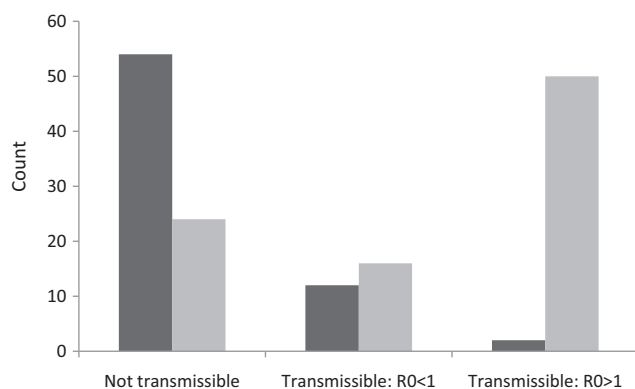


Fig. 1. Comparison of the transmissibility (in human populations) of RNA viruses that are vector-borne (dark grey) and those that are not (light grey). Three categories of transmissibility are shown: (1) not transmissible at all in humans, (2) transmissible but only capable of causing sporadic cases or self-limiting outbreaks ($R_0 < 1$), and (3) transmissible and capable of causing epidemics and/or persisting as endemic human viruses ($R_0 > 1$) (see main text for more detail). Statistical analysis (that allows for taxonomic relatedness by including genus and family as random effects) using a generalised linear mixed model confirms significant differences when comparing category 3 vs categories 1 + 2 ($p = 0.006$) or categories 2 + 3 vs category 1 ($p < 0.001$).