

Stern et al. present an easy to read summary of Myxomatosis, the disease caused by the Myxoma virus in European rabbits. The order and flow of the article is good, and in most sections the level of detail provided is sufficient, or nearly sufficient. However, the sections on virulence and the use of the system as an evolutionary model are lacking in detail; many of my major comments are in regards to these two sections. The majority of my line-by-line comments focus on adding a bit of detail to a few overly terse sentences.

Major comments

Virulence

The second paragraph in “Cause” needs to be expanded and terms need to be clarified:

— First, virulence needs to be defined when it is first used. This term can cause confusion for a general readership because it is still used in some sub-fields to describe transmissibility, and can also describe different aspects of host-harm (mortality and/or morbidity). It is important to define what it usually describes in this system, which is case fatality (which I note is not the more common mortality rate that is usually used in evolutionary models for virulence).

— Second, as virulence is fundamentally controlled by the interaction of host and pathogen (and is not an intrinsic trait of a pathogen), it is important to lay out exactly how virulence is measured for a strain of this pathogen (usually case fatality of infected naive strains of rabbit). The last sentence of this second paragraph feels like it was added almost as an afterthought, but it should be central to the discussion of virulence.

Use as an evolutionary model

This system played an extremely important role (was the key player) in the development of the intermediate virulence paradigm / virulence-transmission tradeoff theory that still forms a central component of our understanding of virulence evolution today. At the very least, I would like to see some discussion of Anderson and May’s 1982 work on virulence evolution that focuses on Myxomatosis as its key example. Alizon et al. 2019 J. Evol. Biol. is a good citation for tradeoff theory as a whole.

I would also like to see the authors unpack “came to dominate because they were more readily transmitted” a bit because “more readily transmitted” could easily be interpreted incorrectly. Lower virulence strains had/have higher lifetime transmission potential because rabbits survive longer, in spite of lower transmission success per transmission event because of lower titer (Dwyer et al. 1990 Eco Monographs has some good figures that describe this variation).

Virus release

I feel that the history of the early success and subsequent rebound of the Rabbit population in Australia following the introduction of the virus is not characterized well enough here. For example, two different sections begin with “the long term failure of”.

— I would suggest that prior to “The long-term failure” in the section “Use of a population control agent” it would be nice to see a sentence starting: “Despite initial success...” with an accompanying figure that illustrates this immense early success, possibly the boom and bust cycle shown in Di Giullonardo and Holmes 2015, Trends in Microbiology. This will help to illustrate the extent of the evolution of the pathogen and rabbit population which the focus of subsequent sections

Co-infection

There is a large and ever-expanding literature on the interactions of rabbit hemorrhagic disease and gastrointestinal helminth parasites on the infection dynamics of the myxoma virus in European Rabbits. I feel that a small section (a few sentences should be sufficient) on co-infection would better help link this disease with current research and recent changes in Rabbit population dynamics.

Line-by-line comments

Abstract

— I suggest a slight rephrasing for: “Myxomatosis is an excellent example of what occurs when...”. The current phrasing makes this sentence read to me as if Myxoma emerging in a naive host is what occurs for all emergences. We study it because it is an example of what *can/may* occur, both for the host and for the evolution of the virus.

— Add a sentence about the early success of the purposeful introduction and the subsequent evolution of the virus, which is a key component of what makes this a model system

Cause

P1

— “Large DNA viruses”: Give a length of this virus

P2

— “Different strains exist which vary in their virulence.”: I don’t think this is descriptive enough. Substantial variation exists both across the globe and within a very narrow spatial range (e.g. a single region of Australia). I specifically bring this up because the examples are from locations very distant from one another, but strains spanning the full virulence spectrum have been found to co-circulate

— “Strains present in Europe and Australia have become attenuated”: Where did they start?

Transmission

P1

— “The myxoma virus does not replicate in these insect hosts,”: Rewrite to open with “Transmission is mechanical, meaning...”

— Would like to see a sentence or two about transmission potential of various strains to link back to the virulence discussion. Dwyer et al. 1990 Eco Monographs is a good source.

P2

— “drying” → “desiccation”

Clinical presentation in European rabbits

— “Highly virulent strains, such as those present in North and South America”: Already stated in a previous sentence, feels a bit redundant

Diagnosis

— It makes sense to me to place this section before “Treatment”, but I don’t feel too strongly about this

Vaccination

P1

— “group situations”? Clarify a bit. Are you talking about rabbit farms here?

— Switch the order of the last two sentences

P3

— “cause a great deal of environmental damage”: I would like to see a citation or two here of the severity of this damage (maybe economic burden)

P4

— The second sentence in this paragraph doesn’t feel particularly relevant to me

Other preventative measures

— A decent portion of this material has already been discussed. I suggest removing this section altogether, and adding what details aren’t already provided (which is just a sentence or two) to the end of P1 in “Vaccination”. After the order of the last two sentences in “Vaccination” are flipped (see previous comment), this material will directly flow from the sentence about “not 100% effective”

Population control agent

— “namely the”: remove “namely”

Australia

— Would like to see a sentence about the fence built north-south across Australia as a first line of attack (prior to the release of the virus) against the growing rabbit population. I think it will help to illustrate how big of a problem these rabbits were and just how far the govt. was willing to go — i.e. release an extremely pathogenic virus on population of hundreds of millions.

— “The virus was at first highly lethal, with an estimated case fatality rate of close to 99.8%”
Would like a citation here. Maybe Fenner and Marshal 195X (there are a few) or Dwyer or Kerr