CLINICAL SYMPTOMS AND INFECTION DYNAMICS: IMPLICATIONS FOR DISEASE AND INFECTION MANAGEMENT

De Jong MCM[1], Janss LLG[2]

[1]Quantitative Veterinary Epidemiology, ID-Lelystad & Wageningen Institute Animal Science Wageningen University, P.O. Box 65, 8200 AB Lelystad, The Netherlands
[2]Breeding and Reproduction, ID-Lelystad

The manifestation of disease, i.e. clinical symptoms, especially in its epidemic manifestation has long interested scientists. In fact this interest was what started the development of veterinary science in the form of European veterinary schools. One important aspect of these epidemics is that after a period of clinical manifest outbreaks there can be a period where the disease disappears but the infection is still present. Seemingly, there has then been a change in virulence.

Biologists have been studying the evolutionary changes in virulence of disease-causing agents using mathematical modelling (e.g. Bremerman & Thieme, 1989, Johnson, 1986). In veterinary epidemiology we can also contribute to solving questions around changes in virulence because we can not only model but we can also do experiments and make observations.

Changes in virulence are of interest to veterinary epidemiology because it may provide tools to:

(i) stop disease by making conditions favourable for the selection and maintenance of less virulent micro-organisms (disease management),
(ii) understand how programmes of infection management (Classical Swine Fever, Foot & Mouth Disease) based partly on clinical detection may be influenced adversely by changes in virulence.

Models

- one bag

The simplest model of virulence evolution leads to the conclusion that micro-organisms will develop into strains with maximum virulence that would still allow the strain to spread. As a consequence conditions that enhance transmission (e.g. high-density animal keeping) will select for higher virulence. The well-studied example of myxomatosis in rabbits (Fenner & Kerr, 1994) seems to comply with this model. The description of the model is as follows: more replication of the agent in the host leads to more disease and more replication leads also to more transmission. Then there are two levels of selection. The first level of selection is within the individual host where the fastest replicator wins and hence such selection leads to much disease. However, this is counteracted by selection at the between host level where each strain can only exist when each infected host infects more than one other host. The combination of the two selection processes could lead to intermediate virulence. Note that the

assumptions of the model imply that the host is seen as one bag of cells (or growth medium). An example where this applies are immune tolerant cattle caused by Bovine Virus Diarrhoea Virus. All cells in these cattle replicate the virus and sure enough these virus populations within a single host are invaded by virulent BVDV (cytopathogenic strains).

- More bags

A more realistic model could be a model of at least two bags:

(i) a first compartment in which the agent can replicate and spread but where replication does not cause much damage and hence virulence is limited when the agent is constrained to that compartment

(ii) a second compartment where replication does cause damage resulting in (severe) clinical disease.

This model applies to most infections. For example it applies to BVDV in its transient manifestation. Other clear-cut examples are infections that cause meningitis: the replication of the agent that causes disease does not contribute to the transmission of the infection (Levin & Bull, 1994). In the conceptual model there are again two selection processes one selection process for the host that leads to less disease and one selection process in the agent to leads to more replication. A typical outcome would therefore be that there is effective replication of the agent but normally this would occur without disease. Occasionally, in the weak individuals severe disease will still occur as selection on the host as a population will in the case of rare events be very weak.

Conclusions

Depending on the type of agent-host relationship the interaction may be either be of the one-bag type or it may be of the multi-bag type. Especially when the immune apparatus does not work the one-bag applies. In other cases of agent-host association the immune system will contain the replication of the infection to the less vital organs. Insight which of the two models applies can only be obtained by taking into account the host-parasite characteristics and/or studies of previous outcomes of the selection process (e.g. avian influenza).

references

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