Rabies
Summary

Introduction

1. This note provides a brief summary of an analysis undertaken by a DISCONTOOLS group of experts on Rabies. They reviewed the current knowledge on the disease, considered the existing disease control tools, identified current gaps in the availability and quality of the control tools and finally outlined the steps necessary to develop new or improved research tools. Full details can be downloaded from the web site at http://www.discontools.eu/ by selecting Disease Database, then the specific disease and highlighting the variables of interest. This is completed by selecting "create a report" which can then be downloaded as either a PDF or Excel spread sheet.

Disease profile

2. Rabies is widely distributed across the globe. There is no accurate surveillance system for the number of rabies deaths globally but it is estimated that more than 59,000 people die of rabies each year. About 95% of human deaths occur in Asia and Africa, where dogs continue to be the main carriers of the disease. Rabies is under reported in many countries due to the lack of appropriate legal and operational infrastructures, including diagnostic facilities and a well-suited surveillance system in the field. In developed countries, massive vaccination and animal control programmes might be effective in reducing the incidence of the disease in man to sporadic cases, as demonstrated in several countries of Latin America.

3. There are several strains of the rabies virus (RABV) which are generally maintained in particular reservoir hosts. Hosts for RABV include bats and non-flying mammals, mainly carnivores. Other animals do not play a role in the maintenance of the disease, but are victims of the disease. Once symptoms appear, rabies is always fatal in terrestrial animals. Dogs are responsible for rabies virus transmission to humans; the disease is spread in most parts of Africa, in Asia, and to a lesser extent in Latin America, where the proportion of unvaccinated and semi-owned or stray dogs is high.

4. In addition to RABV there are other neurotropic viruses in the genus *Lyssavirus* that can cause rabies. In total, 17 lyssaviruses have been described so far among classified and putative ones, most of them associated to specific bat species.

Risk

5. Failure to control rabies in dogs in developing countries will result in continued high mortality each year and will create possibilities for spills-over into wildlife. In general, better surveillance and field diagnostic tools are required. Decreasing the exposure rate between wildlife species and rabies vectors is essential and understanding the efficacy of rabies vaccines in wildlife species is critical, including whether the vaccine is safe to be used in endangered species.

Diagnostics

6. Rabies diagnosis is only possible post-mortem and the target sample is the central nervous system of a symptomatic animal. Agent identification using the fluorescent antibody test (FAT) provides a reliable diagnosis in 98–100% of cases for all serotypes if a potent conjugate is used. Nowadays, rapid immunochromatographic test kits (dRIT) as well as molecular based methods are generally accepted as alternative to FAT to diagnose rabies in animals. Lateral Flow Devices (LFD) are commercially available. However, the specificity and sensitivity of LFDs is still debated. Routine based genetic typing of field rabies cases could help to elucidate the epidemiology of rabies. Virus neutralisation (VN) assays in cell cultures are the prescribed tests for post-vaccinal antibodies for international trade. Alternatively, use may be made of a test that is known to correlate with VN assays, notably an enzyme-linked immunosorbent assay using antibody to the G protein.

7. New, less expensive assays and field tests need to be further validated and made available.

Vaccines

8. There are cheap and safe RABV vaccines, which are effective and give solid immunity. A wide range of vaccines are authorised globally for use in humans, cats, ferrets, horses, sheep, cattle, and dogs. The development of oral vaccines has enabled the eradication of rabies from the red fox population throughout most of Europe. In addition, programmes for oral vaccination of wildlife such as raccoons, coyotes, foxes, and skunks are being undertaken in North America. Oral vaccination programmes use either modified live-virus or live recombinant vaccines. Oral vaccination of stray dogs could lead to the eradication of rabies in countries where dog rabies is the sole source of human exposure and further evidence is needed on the use of such vaccines.

9. There is a need for longer lasting (perhaps lifelong) rabies vaccines. Additionally, a combination of rabies and contraceptive vaccines would provide a valuable tool in the fight against rabies in dogs. New vaccines for lyssaviruses not covered by current vaccines are also needed. There is the necessity to replace all nervous tissue vaccines with more modern and less reactogenic vaccines.

10. The current in vivo assay (NIH) for vaccine potency testing is highly variable and needs to be replaced by a combination of in-vitro testing and consistency monitoring. This is an urgent need for adjuvanted vaccines *ad usum veterinarium*.

Pharmaceuticals

11. Antiviral agents, interferon and massive doses of rabies immunoglobulin have been used to treat human cases, but they only seem to prolong the clinical course without affecting fatality. The replacement of RIG by monoclonal antibodies has been investigated in the last decade with encouraging results. However, to date only one product (based on a single monoclonal antibody) has been developed and is commercially available in India. More research into modifying treatments and determining the most effective anti-viral is needed.

Knowledge

12. Epidemiological data on new and existing lyssaviruses are lacking; what bat species are involved? Why does there appear to be a species barrier for some bat lyssaviruses? Why are there limited spill-over infections even when bats co-roost with other species of bats or other mammals?

13. It is not known why some animals shed virus for longer periods. Some animals, bats in particular, survive rabies after challenge and the reasons need to be investigated. Why does the virus sometimes stay in an ‘eclipse’ phase for weeks, months or even years? More needs to be understood about the disease mechanisms, which allow the virus to be maintained for long periods during hibernation.

14. Cost benefit models and analyses need to be developed to assess the effectiveness and financial savings of strategic control plans.

Conclusions

15. Aspects of the pathogenesis, epidemiology and control of rabies, particularly relating to the more recently identified lyssaviruses, are not fully understood.

16. Although cheap and safe RABV vaccines for animals as well as humans have been developed, there is still room for further developments and improvements.

17. A range of diagnostic and surveillance tools is available, although field tests need to be validated to allow a rapid follow-up of biting and suspect animal cases particularly in the developing world.