Avian Chlamydiosis caused by *Chlamydia psittaci*
Summary

Introduction

1. This note provides a brief summary of the Disease and Product analysis prepared by a DISCONTOOLS group of experts on avian chlamydiosis caused by *Chlamydia psittaci*. 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 determined the research necessary to develop new or improved tools. Full details are available on the web site at http://www.discontools.eu/.

Disease profile

2. *C. psittaci* is an obligate intracellular bacterium replicating within a non-acidified vacuole, termed an inclusion. *C. psittaci* undergoes a unique developmental cycle alternating between the elementary body, which guarantees extracellular survival and infection of host cells, and the reticulate body, which is responsible for replication and generation of infectious progenitor bacteria.
3. The pathogenesis starts with primary replication of *C. psittaci* in mucosal epithelial cells and macrophages of the bird's respiratory tract, after which the pathogen causes septicaemia and replication in epithelial cells and parenchymatous tissues throughout the body. The agent is excreted in faeces and nasal discharges. Faecal shedding occurs intermittently and can be activated through stress caused by nutritional deficiencies, prolonged transport, overcrowding, chilling, breeding, egg laying, treatment or handling. Bacterial excretion periods may occur for several months. Many of the birds become chronically infected and show no clinical signs until stressed. These birds serve as a source of infection for humans, livestock and other birds.
4. Depending on the chlamydial strain and the avian host, *C. psittaci* causes pericarditis, air sacculitis, pneumonia, lateral nasal adenitis, peritonitis, hepatitis, and splenitis. Generalized infections result in fever, anorexia, lethargy, diarrhoea and occasionally shock and death.
5. Transmission of *C. psittaci* occurs mainly through inhalation of contaminated material and, sometimes, ingestion. *C. psittaci* can also be transmitted by blood-sucking ectoparasites, such as lice, mites and flies, and, less commonly, through bites or wounds. Vertical transmission can occur and *C. psittaci* can penetrate eggshells. The organism is relatively stable in the environment and can survive for long periods in near-freezing temperatures and for up to 30 days under temperate climatic conditions in faeces and bedding.

Risk

6. *Chlamydia psittaci* infections in humans, often referred to as psittacosis, can result in an asymptomatic infection or an acute symptomatic infection characterized by mild flu-like illness to severe pneumonia and fulminant sepsis which can be lethal. Globally, psittacosis is a notifiable disease in many countries. Infection most commonly occurs in persons with a history of contact with birds. *C. psittaci* are currently divided into different outer membrane protein A (*ompA*) genotypes. Humans can potentially be infected by any *C. psittaci* genotype, but some genotypes (e.g. genotype A, Sequence Type 24) seem to be associated with a higher incidence of serious illness in patients than others. Reports on hospitalized psittacosis patients are predominantly related to zoonotic transfer of genotype A from infected *Psittaciformes* (cockatoos, parrots, parakeets and lories). Genotype B, frequently occurring in pigeons, is also often detected in psittacosis patients. Other genotypes reported to cause severe illness in humans are genotypes C and E/B, which frequently occur in poultry, but also in wild birds.

Diagnostics

7. Few commercial tests exist for the detection of antibodies by ELISA. None of these antibody detection assays are *C. psittaci* specific. Few commercial antigen detection tests, based on immunofluorescence or the use of antibodies for ELISA or immunohistochemistry, are available. These tests can be used for the detection of *C. psittaci* antigens in animal samples but none of these antigen detection tests are *C. psittaci*-specific. Few commercial PCR tests are available for the detection of *C. psittaci* DNA in animal samples. Commercial *C. psittaci*-specific antigen or antibody detection tests are lacking and there is a need for rapid, sensitive and specific point of care (PoC) tests.

8. The current gold standard test is detection of pathogen DNA in pharyngeal, ocular or faecal swab samples and/or tissues/organs using a *C. psittaci*-specific PCR. In humans deep respiratory samples like sputum or broncho-alveolar lavage fluid is preferred.
9. Other confirmatory methods include isolation of *C. psittaci* in embryonated chicken eggs or in cell culture, although these methods require specialist BSL3 facilities.

Vaccines

10. No commercial *C. psittaci* vaccines are available. Because of zoonotic risk, animal welfare and economic loss, there is a requirement for a safe, stable and cheap vaccine for poultry, pigeons and psittacine birds. The vaccine will likely be based on recombinant protein technology, as multi-component subunit vaccines, viral vectored vaccines, DNA or mRNA vaccines.

Pharmaceuticals

11. Tetracyclines are the drugs of choice for treating avian chlamydiosis (medicated feed for 14 to 45 days or injection for individual birds, using 8 to 10 injections in a 45-day period, for instance in psittacine pet birds). Still, there are general concerns with the overuse of antibiotics in farming due to antimicrobial resistance. However, there may be a potential market for anti-bacterial and immunostimulatory pharmaceuticals that could be used in conjunction with vaccines, as vaccine research has shown that sterile immunity is difficult to achieve. In humans, doxycycline or macrolides like azithromycin is used when psittacosis is diagnosed. It is generally assumed that newer quinolones which are often used in severe pneumonia in humans are also effective.

Knowledge

12. Better detection of latently/persistently infected poultry, pigeons, psittacine birds and other wildlife birds is needed.
13. There is a need for sensitive and specific diagnostic point of care tests for both birds and humans.
14. Generation of an immunological toolbox for different bird species would speed up vaccine design.
15. Next generation vaccines (mucosal) for mass application in poultry are needed.
16. Next generation vaccines for pigeons and psittacine birds are also required, as *C. psittaci* in these birds presents a high zoonotic risk.
17. Vaccines should ideally be developed as DIVA compatible, in conjunction with complementary diagnostics for different bird species.
18. There should be stricter regulations on bird trade and bird selling.
19. There is a need for governmental support and regulation in promoting and introducing vaccination and diagnostic monitoring in poultry, pigeons, psittacine birds or birds in captivity in general, through health certification. This will not only improve animal welfare and reduce economic losses but will also positively impact on public health as *C. psittaci* is zoonotic and can be transmitted from birds to humans.

Conclusions

- *C. psittaci* is an important respiratory pathogen of birds. The infection can become systemic and lead to mortality. Birds can remain persistently infected and be carriers of the organism for long periods but without showing clinical disease. A persistent infection is characterized by the presence of intracellular aberrant chlamydia bodies which no longer replicate and are larger than the metabolically active, replicating reticulate bodies. Nevertheless, aberrant bodies can revert to reticulate, replicating bodies.
- *C. psittaci* infection in human is a mandatory notifiable disease in many countries, but the infection in underdiagnosed and underreported.
- Vaccines for poultry, pigeons and psittacine birds are urgently needed.
- Better and DIVA-based diagnostic tools, including PoC tests are required especially to identify persistently infected birds and to differentiate naturally infected from (future) vaccinated birds, but also for rapid source tracing in the case of human infection.