Fowl cholera

J.P. Christensen & M. Bisgaard

Department of Veterinary Microbiology, The Royal Veterinary and Agricultural University, Stigbøljen 4, 1870 Frederiksberg C, Denmark

Summary

*Pasteurella multocida* subspecies *multocida* is the most common cause of fowl cholera, although *P. multocida* subspecies *septica* and *gallicida* may also cause fowl cholera-like disease to some extent. However, the virulence properties of the different subspecies for various hosts have not been elucidated.

The severity and incidence of *P. multocida* infections may vary considerably depending on several factors associated with the host (including species and age of infected birds), the environment and the bacterial strain. No single virulence factor has been associated with the observed variation in virulence among strains. Possible virulence factors include the following: the capsule, endotoxin, outer membrane proteins, iron binding systems, heat shock proteins, neuraminidase production and antibody cleaving enzymes. No RTX toxins (repeats in toxin) appear to be produced by *P. multocida*, but *P. multocida* exotoxin (PMT) could contribute to virulence in some avian infections.

The epidemiology of fowl cholera appears complex. Traditional serotyping systems are only of limited use in epidemiological studies. In recent years, molecular typing methods have been applied to avian strains of *P. multocida* of different origin. The results obtained using these newer methods indicate that wild birds may be a source of infection to commercial poultry. Documentation suggesting that mammals play a similar role is not as comprehensive, but the possibility cannot be excluded. Carrier birds seem to play a major role in the transmission of cholera. Surviving birds from diseased flocks appear to represent a risk, but more recent investigations indicate that carriers of *P. multocida* may exist within poultry flocks with no history of previous outbreaks of fowl cholera. The significance of this awaits further investigation.

The site of infection for *P. multocida* is generally believed to be the respiratory tract. The outcome of infections may range from peracute/acute infections to chronic infections. In the former type of infections, few clinical signs are observed before death and the lesions will be dominated by general septicaemic lesions. In chronic forms of *P. multocida* infections, suppurative lesions may be widely distributed, often involving the respiratory tract, the conjunctiva and adjacent tissues of the head.

Diagnosis is always dependent upon isolation of the organism. For the detection of subclinical infections, mouse passage of relevant samples is recommended, but polymerase chain reaction and isolation attempts on selective media may represent alternatives.

Confinement is probably the most effective way to prevent introduction of *P. multocida*. However, extensive management systems dominate in many parts of the world, and under such circumstances vaccination is recommended as a preventive measure. Unfortunately, the development of safe and efficient live vaccines still poses problems. As a result, control remains dependent on bacterins which exhibit significant disadvantages compared to live vaccines.

Keywords

Introduction

For decades, the term ‘avian pasteurellosis’ has been used to refer to a group of diseases caused by Pasteurellae and Pasteurellae-like organisms. Important poultry pathogens such as *Yersinia pseudotuberculosis* (86), *Riemerella anatipestifer* (84) and *Ornithobacterium rhinotracheale* (94) have all been excluded from the family *Pasteurellaceae sensu stricto* (15) and will consequently not be described. The genus *Pasteurella sensu stricto* presently includes at least eleven species, but only seven species (*P. multocida* with its three subspecies, *P. gallinarum*, *P. avium*, *P. volantium*, *P. anatis*, *P. langaa* and *P. sp. A*) have been associated with avian hosts (6). Among these, *P. multocida* is considered the causative agent of fowl cholera (81). Apart from *P. multocida*, none of the above species appear to be involved as aetiological agents in acute cholerlike disease or to be of any major economic importance in birds (6), and will therefore not be covered by this review.

The taxonomy of organisms previously reported as *P. haemolytica* remained unsolved for many years. Recent investigations have reclassified mammalian isolates as *Mannheimia*, a new genus containing at least five species (2), while avian isolates belong to another new genus within the family *Pasteurellaceae* which has not yet been named (14). These investigations have confirmed that host specificity seems to exist for many species of the family *Pasteurellaceae*. Similar taxonomic investigations are in progress for the *P. multocida* complex, but results are not yet available. Consequently, the following text will be based on published data only.

Description of the aetiological agent

Three subspecies of *P. multocida* (*P. multocida* subspecies *multocida*, *septica* and *gallicida*) are recognised (65). *Pasteurella multocida* subspecies *multocida* is the most common cause of disease, but subspecies *septica* and *gallicida* may also cause fowl cholera-like disease to some extent (43). *Pasteurella multocida* subspecies *gallicida* is mainly associated with web-footed birds (35; J.P. Christensen and M. Bisgaard, unpublished observations), but has also been reported in pigs (10). The relationship between subspecies and serovars of *P. multocida* obtained by published serotyping systems has not been elucidated. For many years, passive haemagglutination tests have formed the basis for a serogrouping system based on specific capsule antigens (13, 67), whereas tube agglutination and gel diffusion precipitin tests have been used to detect somatic antigens (40, 66, 67). Five capsular (A, B, D, E and F) and sixteen somatic (1-16) serovars of *P. multocida* are currently recognised (80). All but serotypes 8 and 13 have been isolated from avian hosts (67), as have capsular types A, B, D and F (80, 81). However, subspecies *multocida* and serovar A appear to be the most frequently isolated subspecies and serogroup from cases of the most severe form of fowl cholera (78, 80). Several of the sixteen somatic serovars have been demonstrated among serovar A isolates, just as somatic serotype variation has been shown to occur within serovars B, D and F (78). Isolates that have multiple somatic antigens are often encountered and are considered distinct serotypes (97). Although the somatic serovars 1,3 and 3,4 within serovar A apparently dominate among strains isolated from fowl cholera in England and the United States of America (21, 79), no particular serovar appears to be more or less virulent than others. Lee et al. demonstrated that different isolates of the common serovar A:3,4 vary greatly in virulence (55). Virulence properties of the different subspecies for different avian hosts are unclear.

No single factor has been associated with the strain variation in virulence observed (56). The capsule is regarded as a major virulence factor of avian *P. multocida* (37, 38, 87, 93), but other factors probably influence the outcome of infections. Other virulence factors suggested include the following:

- endotoxin (20, 25, 26, 57, 76)
- outer membrane proteins (92)
- iron binding systems (34, 49, 69, 100)
- heat shock proteins (59)
- neuraminidase production (51, 58)
- antibody cleaving enzymes (72).

Toxins other than endotoxin may also play a role in the pathogenesis of fowl cholera. *Pasteurella multocida* toxin, which is at least partly responsible for the lesions observed in atrophic rhinitis in pigs (27), cannot be excluded as a possible virulence factor in some of the lesions observed in avian infections with *P. multocida* (15). Production of RTX toxins (repeats in toxin), which is of major importance in the pathogenesis of some members of the family *Pasteurellaceae* (24), has not been observed in *P. multocida*. One of the few factors which may be of practical value as a virulence marker is the ability of *P. multocida* to resist killing by serum components (56). Very little is known about the molecular basis of diseases caused by *P. multocida* in avian species (15), and genetic evidence for the role of virulence factors is lacking, even for some of the factors currently considered to have the most influence over virulence (e.g. the capsule) (1).

Factors other than those associated with the bacteria may influence the outcome of *P. multocida* infections. Although most species of birds are considered susceptible to infection with *P. multocida* (*P. multocida* has been isolated from more than 100 different species of birds [9]), different species of birds differ significantly in susceptibility to infection. Among domestic fowl, turkeys are probably the most susceptible species. Web-footed birds also seem highly sensitive to infection, since outbreaks regularly cause massive losses among waterfowl (9), whereas chickens are considered relatively resistant (81). This was clearly demonstrated by
experimental infections of several species of birds using an outbreak clone of \textit{P. multocida} ssp. \textit{multocida} originally isolated from eiders (16). Intratracheal challenge of seventeen-week-old chickens with $10^4$ colony-forming units did not result in mortality. The organism could not be detected in either the liver or the spleen 48 h after infection, although typical lesions of the lungs were observed in the majority of the birds. In contrast, partridges of the same age all died within 24 h of infection. Infection of three-week-old turkeys also resulted in 100% mortality within 24 h. Pheasants appeared to be of intermediate susceptibility to infection, with approximately 50% mortality observed after 24 h (71). Other factors which have been reported to affect the severity and incidence of the disease include environmental factors (e.g. crowding), climate (85), concurrent disease (19), nutritional stress (23) and age of the host (50). Age markedly influences the outcome of infection, at least in chickens, where birds less than sixteen weeks old are relatively resistant. Under natural conditions, mortality may range from only a few percent to close to 100%, depending on the factors mentioned above (81).

**Epidemiology**

Although fowl cholera probably occurs world-wide (81) and has been studied extensively for many years, the epidemiology of the disease remains controversial, and many aspects are not yet fully understood. Basic knowledge, such as the route of introduction of fowl cholera into a flock, is still lacking. Due to genotypic variation within serotypes, serotyping in many cases does not provide sufficient detailed information to determine the epidemiology of infections (12, 16, 53, 89, 97). Within the last ten years, DNA (deoxyribonucleic acid) fingerprinting in the form of restriction endonuclease analysis and ribotyping has been applied to avian strains of \textit{P. multocida} from different origins, including strains obtained from wild birds (16, 17, 63, 98, 99), and has also been shown to be of value in studying the epidemiology of fowl cholera in turkeys (12, 18, 90). The restriction endonucleases \textit{Hpall} and \textit{Hhal} are reported to be among the most suitable for epidemiological studies (16, 98, 99).

\textit{Pasteurella multocida} is a fairly delicate organism which is easily inactivated by common disinfectants, sunlight, drying or heat, and experiments suggest that \textit{P. multocida} will survive for a maximum of thirty days in the environment (e.g. water or soil) (4, 81, 82). Consequently, contaminated environments are not thought to serve as reservoirs for periods of more than thirty days, although as yet unknown factors could have a protective role.

As the habitat of \textit{P. multocida} is broad, including mucosal surfaces of mammals, birds and humans, many sources could act as a potential reservoir (6). An exchange of \textit{P. multocida} ssp. \textit{multocida} between wild birds and domestic poultry is reported to be possible, and wild birds are capable of spreading the disease to new areas (16, 17, 90). The extent to which the agent is introduced into susceptible flocks by this route of transmission is difficult to estimate and will probably be highly influenced by the form of production. A recent study demonstrated that more than 80% of the diagnosed cases of \textit{P. multocida} infections in poultry in Denmark during the years 1995 to 1997 included poultry which had been in contact with wild fauna (17). This included contact with mammals, but the role of these as a reservoir has not yet been thoroughly investigated by more recent molecular typing methods. The virulence properties for poultry of mammalian isolates of \textit{P. multocida} also remain to be investigated, whereas the clones isolated from wild birds have been found to be identical or closely related to those isolated from domestic poultry. These clones have also been demonstrated to be virulent for poultry in experimental infections (16, 17, 71). However, dogs, cats and pigs, in particular, may act as reservoirs for strains of \textit{P. multocida} which are virulent for poultry (54, 81, 88, 95). Carrier birds are generally believed to play a major role in spreading the disease (11, 81). Many studies suggest that survivors within a diseased flock may act as reservoirs of infection, but until recently, limited information has been available concerning the possibility of carriers in flocks of poultry with no history of previous outbreaks of fowl cholera. However, an investigation by Muhairwa et al. has indicated that a high carrier rate of \textit{P. multocida} ssp. \textit{multocida} and \textit{septica} may exist in apparently healthy poultry flocks (including chickens and ducks) (64). Surprisingly, many birds carried \textit{P. multocida} on the cloacal mucosae. The importance of this finding in explaining the spread of the infection is unclear, as excretions from the mouth, nose and conjunctiva of diseased birds are generally believed to be the primary source of contamination of the environment; transmission by aerosol has been reported to be less important (5). Other potential sources of infection are carcasses of birds which have died of the infection, and equipment or insects which have been in contact with infected birds. Transmission of \textit{P. multocida} through the egg is not believed to represent a risk (81), although contamination of eggshells could theoretically occur during passage through the cloaca. However, given the delicate nature of the micro-organism, contamination of this type is likely to be insignificant.

To minimise the risk of importing the disease through trade of hatching eggs, day-old chicks, point of lay pullets, etc., the guidelines indicated in the \textit{International Animal Health Code} (68) should be followed. However, it should be noted that to further reduce the risk of introducing the disease through imported stock, all imported birds should originate from establishments with a high level of biosecurity, and which follow all-in/all-out principles. Imported eggs and birds should originate from confined flocks only. Mouse inoculations of pooled swabs from mucosal membranes of imported birds must be negative (sampling level to be defined).
Disease
The site of infection for *P. multocida* is generally believed to be the respiratory tract (60, 81). However, inoculation through oculo-nasal-oral routes may also generate typical lung lesions and a progressive bacteraemia (73), indicating that other mucosal membranes may serve as portals of entry. The ability of *P. multocida* to survive passage of the gastro-intestinal tract appears to be limited (81), but the presence of *P. multocida* on the cloacal surface of carrier birds indicates that some organisms may survive passage (64). The observation that some strains of *P. multocida* can be virulent and immunogenic following oral administration also suggests that intestinal invasion or interaction with the intestinal mucosae occurs to some degree (32, 55). Localisation of *P. multocida* in the bursa may occur following a bacteraemia, since *P. multocida* has been detected in the bursa of intratraehically infected chickens (J.P. Christensen and M. Bisgaard, unpublished data). *Pasteurella multocida* may also enter the tissues through cutaneous lesions and result in septicaemia (80) or localised cutaneous lesions (28, 33). Following an upper respiratory tract infection, *P. multocida* may subsequently spread to the lungs and multiply before entering the bloodstream (61). Once in the bloodstream, *P. multocida* either multiply rapidly (87) or localise in the liver and spleen where initial multiplication occurs before a massive bacteraemia (70, 93). Death is presumed to be due to the effects of endotoxin (19, 39, 76), as signs of acute fowl cholera have been reproduced by injection of endotoxin from *P. multocida* (41, 77).

A wide range of signs may be observed in infections with *P. multocida*, depending on the nature of the infection. Few signs may be observed in peracute and acute infections (often referred to as choler). In these cases, death is often the only sign of disease in the flock. In more protracted cases, mucous discharges from the mouth, nose and ears, cyanosis, general depression, ruffled feathers and diarrhoea may be observed. In chronic infections, signs are principally due to localised infections of leg or wing joints, comb, wattles and subcutaneous tissue of the head (36, 81), oviduct (7) and the respiratory tract (81). Severe forms of dermal necrosis in turkeys have also been reported (28, 33).

Lesions
In the case of peracute or acute forms of the disease, the post-mortem findings are dominated by general septicaemic lesions including vascular disturbances, as reflected by general passive hyperaemia and congestion throughout the carcass. Petechial and ecchymotic haemorrhages are often present in the abdominal and coronary fat, and haemorrhages may be observed in the intestinal mucosae and on subserosal surfaces in the thoracic and abdominal cavities. The liver and spleen are often swollen and may contain multiple small focal areas of coagulative necrosis or the organs may undergo more generalised necrosis. The lungs are often involved, especially in turkeys, where the lesions may be very characteristic. In the most acute forms of infection, the lung lesions are dominated by haemorrhages, but this is soon followed by necrosis and fibrinous pleuro-pneumonia where affected areas are clearly marked from unaffected tissue. A unilateral or bilateral productive inflammation of pleura and lungs with extensive exudation of fibrin is common. Histologically, the lesions are mainly associated with heterophilic infiltrations (80, 81).

In chronic forms of *P. multocida* infections, suppurative lesions may be widely distributed, often involving the respiratory tract, the conjunctiva and adjacent tissues of the head (81). Caseous arthritis and productive inflammation of the peritoneal cavity and the oviduct are common in chronic infections. A fibrino-necrotic dermatitis including caudal parts of dorsum, the abdomen and breast, and involving cutis, subcutis and the underlying muscle, has been observed in turkeys and broilers (28, 33).

Diagnostic methods
The history of the disease, clinical signs and gross lesions may be helpful in diagnosis, but are insufficient to allow a definite diagnosis of the disease. The final diagnosis depends on isolation of the organism.

Primary isolation is usually accomplished using media such as blood agar, dextrose starch agar or trypticase soy agar. Isolation may be improved by the addition of 5% heat inactivated serum (67). *Pasteurella multocida* can be readily isolated from viscera of birds dying from peracute/acute fowl cholera and often from suppurative lesions of chronic cases. In cases of acute fowl cholera, bipolar organisms can be demonstrated in liver imprints using Wright’s or Giemsa stain (67, 81). Immunofluorescent microscopy has been used to identify *P. multocida* in tissue and exudate (81).

More recently, the polymerase chain reaction technique has been used with success to detect carrier animals within turkey flocks (52). However, the specificity and sensitivity of this test need to be reinvestigated considering the present uncertain taxonomy of the *P. multocida* complex. Consequently, for surveillance purposes and to investigate for carrier animals, the most sensitive method still appears to be mouse inoculation (52, 64). However, differences in pathogenicity of different clones of *P. multocida* for mice remain to be investigated (64). Swabs should be taken from the cloaca and pharynx. Following inoculation of the swabs in broth medium and thorough shaking, 0.2 ml to 0.5 ml of the contents is injected into mice by the intraperitoneal route. If *P. multocida* is present, the mice usually die within 24 h to 48 h and the organisms can be isolated in pure culture from heart, blood, liver and spleen (81). Isolation attempts on selective media or blood agar may represent an alternative (62), but this method appears to be less sensitive than mouse inoculation (64).
Following isolation, identification is based on the results of biochemical tests. The most valuable characteristics for differentiation of Pasteurella multocida from other relevant organisms are shown in Table I. However, simple diagnostic keys do not allow a firm diagnosis within the family Pasteurellaceae. For this reason, extended characterisation, including the use of reference strains, is recommended (6). For further delineation of P. multocida into subspecies multocida, septica and gallicida, the characteristics to be used are shown in Table II.

Serological tests for the presence of specific antibodies are not used for diagnosis of fowl cholera, but have been used in order to test immunity in vaccinated poultry (67).

Public health implications

Disease in humans caused by P. multocida is not uncommon, and P. multocida may be considered a zoonotic organism (8). This is substantiated by the observation that the disease apparently occurs predominantly among the farming population (8). No reports exist of direct transmission from poultry to man or vice versa, but the possibility for such infections cannot be excluded. The organism is a common cause of infection following animal bites or scratches which are mostly caused by dogs or cats (including large cats) (3). Bite wound infections caused by pigs have also been reported (30, 31). A severe cellulitis may develop which may progress to osteomyelitis and subsequently to sepsis (29).

Pasteurella multocida may also be involved in respiratory tract infections, either as a primary or secondary infectious agent (96). In patients with dysfunction of the liver in particular (74, 96), P. multocida is known to cause bacteraemia which may localise in joints, respiratory tract or progress and cause sepsis. In addition to these principal types of infections, P. multocida has been isolated from a variety of infections, including peritonitis, puerperal sepsis, neonatal sepsis, brain abscesses and urinary tract infections (8). The significance of the different subspecies of P. multocida in relation to diseases reported has not yet been elucidated.

Methods of prevention and control

Control of fowl cholera throughout the world depends principally on vaccination. Extensive management systems still dominate in many parts of the world and under these conditions, control of P. multocida infections is almost impossible, because of the wildlife reservoir. Animal welfare concerns have also increased the use of non-confined production farms in the industrialised world, resulting in a significant risk of introducing the infections to commercial flocks.

Many live and inactivated (bacterins) fowl cholera vaccines have been developed and tested in attempts to control the disease (81). As modified live vaccine strains can revert to

### Table I

<table>
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<th>Characteristic</th>
<th>Pasteurella multocida</th>
<th>Pasteurella gallinarum</th>
<th>Pasteurella avium</th>
<th>Pasteurella volantium</th>
<th>Haemophilus paragallinarum</th>
<th>Pasteurella langa</th>
<th>Ornithobacterium rhinotracheale</th>
<th>Riemerella anatipestifer</th>
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+ : >90% of strains positive within one to two days
- : >90% of strains negative
H: >90% of strains positive within three to fourteen days
D : different
* : character used for separation of subspecies of P. multocida
Table II
Characteristics used for identification of subspecies of Pasteurella multocida

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Pasteurella multocida</th>
<th>ssp. multocida</th>
<th>ssp. septica</th>
<th>ssp. gallicida</th>
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<td>L(+) arabinose</td>
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<td>D(-) arabinose</td>
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<td>Dulcitol</td>
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<td>D(-) sorbitol</td>
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<td>+</td>
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<td>L(-) fucose</td>
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<td>Trehalose</td>
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<td>α-glucosidase</td>
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+: ≥90% of strains positive within one to two days
-: ≥50% of strains negative
D: different

Their pathogenic phenotypes and tend to cause disease in immunocompromised birds, most commercial vaccines are of the bacterin type. The vaccines normally contain P. multocida of serotypes A:1, A:3 and A:4 which has been grown in vitro, emulsified in an oil adjuvant or aluminium hydroxide (47). Bacterins are inexpensive to produce and provide some degree of protection, consequently limiting the incidence and severity of clinical disease (83). The principal disadvantages of the bacterins are that these vaccines have to be injected, often resulting in tissue reactions (22), and only induce immunity to homologous serotypes (75). As a result, the development of safe live vaccines is highly desirable to allow the use of a less laborious route of administration and to obtain cross-immunity. The principal live attenuated vaccines currently used, primarily in North America, are the Clemson University strain and the M-9 strain, both of which are of serotype A:3,4. Both strains have been implicated in outbreaks of fowl cholera (44, 91), and as a consequence, several attempts have been made to further modify these strains. Temperature sensitive mutants of both strains have been constructed which are not capable of growth at 42°C (42, 45). Although some protection has been obtained with these mutants, some mortality was still observed (46). More recently, emphasis has been placed on creating non-reverting auxotrophic mutants of P. multocida by mutating the aro-A gene (47, 48, 83) and on selection of clones with a reduced growth rate (32). Promising results have been obtained in preliminary vaccination trials with some of these strains.

Guidelines for the production and use of bacterins are outlined in the Manual of Standards for Diagnostic Tests and Vaccines (67).

Perceived risks of importing the disease

No country can be considered free of fowl cholera, primarily because the causative agent, P. multocida, has a broad habitat, including mucosal surfaces of a wide range of domestic and wild birds and mammals. Consequently, control of the disease on a national basis should focus on the application of appropriate biosecurity measures at the site of production, rather than import restrictions. However, to ensure that imported stock are free of the infection, the guidelines mentioned earlier should be followed (see section entitled ‘Epidemiology’). Further processed poultry products are not considered to present a major risk for transmission of the infection, due to the delicate nature of P. multocida.

Choléra aviaire

J.P. Christensen & M. Bisgaard

Résumé
Pasteurella multocida, sous-espèce multocida, est l'agent le plus fréquent du choléra aviaire, bien que les sous-espèces septica et gallicida de P. multocida puissent également provoquer, dans une certaine mesure, des maladies apparentées au choléra aviaire. Cependant, les propriétés virulentes de ces diverses sous-espèces pour différents hôtes n'ont pas été éclaircies.

La gravité et l'incidence des infections dues à P. multocida peuvent varier considérablement en fonction de plusieurs facteurs liés à l'hôte (dont l'espèce et l'âge des volailles infectées), à l'environnement et aux souches bactériennes en cause. Aucun facteur unique n'a été associé à une différence de virulence entre souches. Les facteurs de virulence possibles sont notamment les suivants : la capsule, l'endotoxine, les protéines de la membrane extérieure, les systèmes de
fixation du fer, les protéines de choc thermique, la production de neuraminidase, les enzymes de clivage des anticorps. Les toxines RTX (repeats in toxin) ne semblent pas produites par *P. multocida*, mais l'exotoxine de *P. multocida* (PMT) pourrait contribuer à la virulence dans certaines infections aviaires.

L'épidémiologie du choléra aviaire est complexe. Les systèmes de sérotypage traditionnels ne sont guère utilisés dans les études épidémiologiques. Ces dernières années, des méthodes de typage moléculaire ont été appliquées à des souches aviaires de *P. multocida* d'origines diverses. Selon les résultats obtenus avec ces nouvelles méthodes, les oiseaux sauvages pourraient être à l'origine de l'infection des volailles d'élevage. Il n'est pas exclu que les mammifères jouent un rôle similaire, mais cela n'a pas encore été confirmé. Les oiseaux porteurs de l'agent pathogène pourraient jouer un rôle déterminant dans la transmission du choléra. Les survivants semblent représenter un risque, mais des enquêtes plus récentes indiquent que des porteurs de *P. multocida* peuvent exister sans risque dans des élevages de volailles, en l'absence de foyers antérieurs de choléra aviaire. Il faudra attendre des recherches plus poussées pour mesurer l'importance de ce phénomène.

L'infection due à *P. multocida* est généralement localisée dans l'appareil respiratoire. Elle peut évoluer en infections suraiguës/aiguës ou en infections chroniques. Dans le premier type d'infection, les signes cliniques sont rares et on observe principalement des lésions de septicémie généralisée. Dans les formes chroniques d'infections dues à *P. multocida*, des lésions suppuratives peuvent être largement répandues, souvent localisées dans l'appareil respiratoire, la conjonctive et les tissus péri-céphaliques.

Le diagnostic dépend, dans tous les cas, de l'isolement du bacille responsable. Pour déceler les infections infracliniques, il est recommandé d'inoculer à la souris des prélèvements choisis, mais l'amplification en chaîne par polymerase et l'isolement sur certains milieux de culture peuvent également constituer des alternatives.

L'élevage en claustration est probablement le moyen le plus efficace de prévenir l'introduction de *P. multocida*. Cependant, les systèmes d'élevage extensif sont prédominants dans de nombreuses régions du monde et, dans ces systèmes, la mesure prophylactique recommandée est celle de la vaccination. Malheureusement, les problèmes liés à la production de vaccins à bactéries vivantes qui soient à la fois efficaces et sans danger ne sont toujours pas résolus. Par conséquent, la prophylaxie dépend toujours des bactérines, qui présentent des inconvénients significatifs par rapport aux vaccins à germes vivants.

**Mots-clés**

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**Cólera aviar**

J.P. Christensen & M. Bisgaard

**Resumen**
*Pasteurella multocida* subespecie *multocida* es la causa más común de cólera aviar, aunque *P. multocida* subespecies *septica* y *gallicida* pueden también en cierta medida provocar enfermedades afines. Comoquiera que sea, hasta el momento no se han dilucidado las propiedades de las distintas subespecies por lo que respecto a su virulencia para distintos huéspedes.
La gravedad e incidencia de las infecciones causadas por *P. multocida* pueden variar notablemente en función de diversos factores ligados al huésped (especie y edad de las aves afectadas), al entorno o a la cepa bacteriana de que se trate. No habiéndose determinado ningún factor único que explique las variaciones de virulencia observadas entre distintas cepas, cabe suponer que éstas obedecen a un conjunto de factores, entre ellos los siguientes: la cápsula, la producción de endotoxinas, las proteínas de membrana externa, los sistemas de fijación del hierro, las proteínas de choque térmico, la producción de neuraminidasa y los enzimas que degradan anticuerpos. Aunque *P. multocida* no parece elaborar toxinas de tipo RTX (*repeats in toxin*), es posible que su exotoxina (PMT) contribuya a su virulencia en algunas infecciones aviares.

La epidemiología del cólera aviar parece compleja. Los sistemas tradicionales de caracterización de serotipos son de poca utilidad para los estudios epidemiológicos. En los últimos años se han ensayado métodos de tipificación molecular en cepas aviares de *P. multocida* de distinto origen. Los resultados obtenidos con estos nuevos métodos llevan a pensar que las aves salvajes pueden constituir un foco de infección para las explotaciones avícolas industriales. Aunque hay menos pruebas al respecto, tampoco cabe excluir la posibilidad de que los mamíferos desempeñen un papel similar. Las aves portadoras parecen intervenir decisivamente en la transmisión del cólera aviar. En este sentido, los ejemplares supervivientes de bandadas afectadas parecen constituir un peligro, aunque investigaciones más recientes han revelado que pueden existir portadores de *P. multocida* en bandadas sin ningún antecedente de brotes de cólera aviar. En cualquier caso, conviene esperar nuevas investigaciones para valorar el verdadero alcance de esta observación.

La infección por *P. multocida* se instala, según opinión generalizada, en el tracto respiratorio. El proceso infeccioso puede tomar formas diversas, desde la peraguda/aguda hasta la crónica. En el primer caso se observan pocos signos clínicos antes de que sobrevenga la muerte del animal, y entre las lesiones observadas predominan las propias de una septicemia generalizada. En las formas crónicas puede observarse la presencia generalizada de lesiones supurativas, que suelen afectar el tracto respiratorio, la conjuntiva y los tejidos encefálicos adyacentes.

El diagnóstico está condicionado siempre al aislamiento del microorganismo. Para detectar infecciones subclínicas se recomienda inocular ratones con las muestras sospechosas, aunque la amplificación en cadena por la polimerasa o la eventual posibilidad de aislar la bacteria en medios selectivos constituyen posibles métodos alternativos.

El medio más eficaz de impedir la introducción de *P. multocida* es seguramente la segregación de los ejemplares infectados. Sin embargo, en muchas partes del mundo predominan los sistemas de producción extensivos, en cuyo caso se recomienda la vacunación como medida preventiva. Lamentablemente, y dadas las dificultades que todavía plantea la elaboración de vacunas vivas eficaces y seguras, la lucha contra la enfermedad sigue dependiendo de vacunas preparadas con bacterinas, que presentan notables desventajas en comparación con las vacunas vivas.

**Palabras clave**

References


