

# 8.6.19 Pasteurella 1088

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section 8 Infectious diseases 1088 herds. This has been accomplished for a small number of herds in Norway, removing *Yersinia*, *Salmonella*, and *Campylobacter* carriage, but is not yet widespread. Sequencing of more strains of *Y. enterocolitica* (including *Y. enterocolitica* phylogroup PG1, biovar 1A strains) and *Y. pseudotuberculosis* will shed more light on pathogenic mechanisms and organism evolution. FURTHER READING Guern ASL, et al. (2016). Yersiniosis in France: overview and potential sources of infection. *Int J Infect Dis*, 46, 1-7. Hall M, et al. (2015). Use of whole-genus genome sequence data to develop a multilocus sequence typing tool that accurately identifies *Yersinia* isolates to the species and subspecies levels. *J Clin Microbiol*, 53, 35-42. Huovinen E, et al. (2010). Symptoms and sources of *Yersinia enterocolitica*-infection: a case-control study. *BMC Infect Dis*, 10, 122. Kolstoe EM, et al. (2015). Specific pathogen-free pig herds also free from *Campylobacter*. *Zoonoses Public Health*, 62, 125-30. Reuter S, et al. (2014). Parallel independent evolution of pathogen-icity within the genus *Yersinia*. *Proc Natl Acad Sci U S A*, 111, 6768-73. Rimhanen-Finne R, et al. (2009). *Yersinia pseudotuberculosis* causing a large outbreak associated with carrots in Finland, 2006. *Epidemiology and Infection*, 137 (Special Issue 03), 342-7. Vincent P, et al. (2007). Similarities of Kawasaki disease and *Yersinia pseudotuberculosis* infection epidemiology. *Pediatr Infect Dis J*, 26, 629-31.

### 8.6.19 Pasteurella

Marina S. Morgan ESSENTIALS *Pasteurella multocida* is an important human Gram-negative pathogen residing primarily in the oropharynx of mammals and transmitted through bites and scratches. Presentation is typically within 12 h of the injury with rapidly spreading cellulitis or sepsis, leading to serious morbidity and mortality (up to 40%) if untreated. Diagnosis is clinical: fresh bite wound cultures are unhelpful, but the organism is usually cultured in cases with established infection, especially if presenting within 24 hours of the injury. Treatment requires thorough wound debridement, with delayed closure if possible, along with antimicrobials to provide empirical cover against pasteurellae and all the other expected pathogens (e.g. amoxicillin-clavulanate plus ciprofloxacin, or meropenem plus clindamycin). Prevention is by avoidance of animal bites or scratches and prompt hygienic management of wounds: antibiotic prophylaxis (amoxicillin-clavulanate or—for the penicillin allergic—doxycycline or azithromycin) should be reserved for high-risk bites (e.g. cat bites) or high-risk wounds that are difficult to debride adequately.

### Introduction *Pasteurella multocida*

(literally 'killer of many species') is a major human pathogen and causes severe morbidity. *Pasteurella septicaemia* is associated with a mortality of 40% and a propensity for metastatic infection. Infection usually follows close animal contact or bites. The organism is part of the colonizing oral flora in virtually every species from birds to elephants, water buffalo and Tasmanian devils, but found especially in cats.

### Historical perspective

The genus *Pasteurella* was named in honour of Pasteur who, in 1880, discovered *P. multocida* to be the cause of fowl cholera. *Pasteurella* spp.

cause haemorrhagic septicaemia, 'shipping fever' in cattle, and respiratory infections in goats, sheep, and rabbits. Aetiology, genetics, pathogenesis, and pathology Nearly all infected patients have a history of animal exposure. *Pasteurella* spp. such as *P. dagmatis*, *P. pneumotropica*, *P. bettyae*, *P. haemolytica*, and *P. caballi* rarely cause human infection although *P. bettyae* has caused infection after hamster bites. *Pasteurella* spp. are small, Gram-negative coccobacilli, often with bipolar staining. Unusually for a Gram-negative rod, *P. multocida* is sensitive to penicillin and fails to grow on MacConkey's agar. Potential virulence factors include capsule lipopolysaccharide, a cytotoxin, iron acquisition proteins, and other surface structures including homologues of the *Bordetella pertussis* filamentous haemagglutinin. An aggressive and opportunistic pathogen, *P. multocida* infection can colonize the oropharynx in those working with animals, causing invasive infection in those with underlying pathology such as liver cirrhosis or bronchiectasis. *P. multocida* is particularly associated with infection following animal bites, licks, or scratches. Metastatic infection of bones, joints, and brain following bacteraemia is not uncommon, whereas endocarditis and mycotic aneurysms are very rare. Cat-related trauma is particularly likely to result in *Pasteurella* infection, especially septic arthritis and osteomyelitis following hand bites. Small, sharp cat teeth leave a septic focus in deeper tissues, under an apparently innocuous puncture wound. There are increasing numbers of reports of prosthetic joint infection following cat bites, with a propensity for knee replacements in females with rheumatoid arthritis. Necrotizing soft tissue infections such as tenosynovitis, septicaemia, and liver and brain abscesses are the more common manifestations, with very rare reports of epiglottitis, chorioamnionitis, and neonatal sepsis. *Pasteurella* tenosynovitis is especially severe, often resulting in amputation of digits. Epidemiology Infection can be occupationally related (e.g. in veterinary surgeons, farmers, and postmen), but more commonly follows bites from

8.6.19 *Pasteurella* 1089 companion animals. Animal bites account for roughly 2% of attendances at emergency departments in the United Kingdom, and nearly 60% of cat bites are infected with *P. multocida*, usually with anaerobes. Prevention Avoidance of animal bites or scratches and prompt hygienic management of wounds are key to preventing infection. Antibiotic prophylaxis should be reserved for high-risk bites (e.g. cat bites) or high-risk wounds that are difficult to debride adequately. Oral co-amoxiclav, 625 mg three times daily for 3 to 5 days will cover *Pasteurella* spp. as well as the hundreds of possible oral commensals present. Patients who have undergone mastectomy and those with diabetes, immunosuppression, cirrhosis, steroid therapy, splenectomy, or prosthetic joints are 'high-risk patients' for whom prophylaxis should be seriously considered. 'High-risk wounds' include puncture wounds, particularly to the hand or wrist, and crush wounds with devitalized tissue. Erythromycin, clindamycin, and flucloxacillin are ineffective against *Pasteurella* spp. and should not be used for prophylaxis or treatment in the absence of sensitivity information. Numerous reports of breakthrough *P. multocida* septicaemia and meningitis have occurred during erythromycin or flucloxacillin therapy. Alternative prophylaxis for penicillin-allergic patients includes doxycycline, azithromycin, aztreonam, or linezolid. Metronidazole can be added for deep, penetrating wounds such as cat bites that cannot be debrided easily. Clinical features of *Pasteurella* infection The most common presentation of *Pasteurella* infection is soft tissue infection but septic arthritis, osteomyelitis, osteomyelitis, septicaemia, and meningitis can occur, particularly in infants and immunocompromised individuals. Soft tissue infections are usually cat or dog bites, or cat scratches, but might occur if an animal licks broken skin. Since *Pasteurella* spp. are extremely pyogenic, bite-related or scratch-related infections usually present 8–12 h after the incident and rapidly spreading cellulitis is typical (Fig.

8.6.19.1). Purulent discharge occurs in 40%, lymphangitis in 20%, and regional lymphadenopathy in 10%. *P. multocida* can cause bone and joint infections such as septic arthritis (usually monoarticular and involving the knee joint) or osteomyelitis. Most cases of septic arthritis occur after an animal bite distal to the joint. Osteomyelitis results either from extension of soft tissue infection or via direct inoculation of bacteria into the periosteum by the animal bite; osteomyelitis is more frequently associated with cat bites than dog bites, presumably because of cats' small, sharp teeth. Patients presenting with sepsis and positive blood cultures for *Pasteurella* spp. are less likely to have a history of a bite and are more likely to have comorbidities and need intensive care support. These patients, however, usually also have a history of contact with animals. Respiratory tract *Pasteurella* spp. can be commensals or cause infections such as glossitis, pharyngitis, sinusitis, otitis media, epiglottitis, bronchitis, pneumonia, and empyema. In one study of 108 patients with pleuropulmonary *P. multocida* infections, an underlying disease was found in 90% and mortality was 29%. *P. multocida* can also cause several other serious invasive infections such as meningitis, bacteraemia, endocarditis, and peritonitis. Intra-abdominal infections include peritonitis and appendicitis. Chorioamnionitis is associated with neonatal sepsis. Differential diagnosis Of the hundreds of bacterial species contaminating animal bites, other major pathogens to consider include streptococci, staphylococci, and especially anaerobes; the latter more common in deep penetrating wounds. Clinical investigation A history of animal bite or scratch preceding any presentation of sepsis should alert the clinician to the possibility of *Pasteurella* infection. Established infections necessitate the taking of blood cultures and culture of any discharge. The microbiology laboratory should be alerted to the possibility of *Pasteurella* so that specimens can be cultured appropriately. Unlike most Gram-negative rods it does not grow on MacConkey's agar and is susceptible to penicillin. Selective media containing vancomycin, clindamycin, and amikacin have been used to isolate *Pasteurella*. Most strains are catalase, oxidase, indole, sucrose, and decarboxylate ornithine positive. Antibiotic susceptibility testing is warranted for isolates cultured from normally sterile sites and respiratory specimens, particularly in the immunocompromised. *Pasteurella* is usually susceptible to penicillin, amoxicillin-clavulanate, piperacillin-tazobactam, doxycycline, fluoroquinolones, extended spectrum cephalosporins (e.g. ceftriaxone, cefpodoxime, and cefixime), and carbapenems (imipenem, meropenem, and doripenem). Fig. 8.6.19.1 *Pasteurella multocida* hand infection, preoperative.

section 8 Infectious diseases 1090 Typing of *P. multocida* has traditionally been done serologically. There are 5 capsular serogroups and 16 somatic serotypes; most human infections are caused by serotypes A, D, and F. New typing methods rely on molecular methods. Subspecies of *P. multocida* can be identified by polymerase chain reaction fingerprinting. Human infections have been reported with *P. multocida* subsp. *multocida*, *P. multocida* subsp. *septica*, *P. multocida* subsp. *gallicida*, *P. canis*, *P. dagmatis*, and *P. stomatis*. Treatment Indications for hospital admission after animal bites include systemic sepsis, involvement of joint or tendon, immunocompromise, bites requiring reconstructive surgery, severe cellulitis, and infection refractory to oral therapy. Hands are especially prone to infection because of the numerous small compartments and lack of soft tissues separating the skin from bone and joint. Inadequate debridement and incorrect antibiotic prophylaxis are major contributors to the excessive morbidity of *P. multocida* infection. Where adequate debridement of deep wounds, especially cat bites, is not possible, irrigation with 250 ml saline, using a 19- or 20-gauge needle or plastic intravenous catheter on a 30-ml syringe, followed by prophylactic antibiotics might be effective (Fig. 8.6.19.2). Thorough irrigation and debridement of the wound, and, where possible, delayed closure of limb bites maximizes salvage. Limbs should be elevated and immobilized. Tenosynovitis can be so advanced on presentation that amputation

is the only option. Pus must be drained and affected joints washed out, and the wound left open where possible. Facial bites can be closed primarily since bleeding is profuse and wounds are easily cleaned. While most pasteuriae are susceptible to penicillin,  $\beta$ -lactamase producing strains are increasingly reported, so penicillin monotherapy is not advised until susceptibility is confirmed. Broad-spectrum empiric antimicrobial therapy should be directed at polymicrobial infection that occurs after bite infections and a combination of a penicillin and a  $\beta$ -lactamase inhibitor (e.g. amoxicillin-clavulanate) recommended in patients without penicillin allergy. Definitive treatment is based on the result of wound cultures and should be continued for 7–10 days. Alternative treatments for established pasteuriae infections for patients allergic to penicillins, or infected with  $\beta$ -lactamase producing strains, include oral doxycycline or intravenous aztreonam, or ciprofloxacin. Patients without a history of anaphylaxis to penicillins can be treated with ceftriaxone. For established soft tissue infection, 10–14 days of therapy is usual, compared with 3 weeks for tenosynovitis, 4 weeks for septic arthritis, and 6 weeks for osteomyelitis. In practice, intravenous therapy until the C-reactive protein falls to less than 50 mg/litre is a useful objective guideline for switching to oral therapy. Prognosis The prognosis of *P. multocida* infections depends on the site of infection and comorbidities. Soft tissue infections usually resolve with adequate debridement, drainage, and antibiotics. Established bite-related hand infection unfortunately often results in permanent impairment of function. Factors particularly associated with poor outcome include inadequate initial antimicrobials and inadequate debridement. Pasteurella septicemia, metastatic infection, and death been reported following inappropriate therapy with erythromycin or flucloxacillin. *P. multocida* prosthetic joint infection, usually associated with rheumatoid arthritis and female gender, results in loss of the prosthesis in 70% of patients, even with early appropriate antibiotic therapy. Areas of controversy The role of antimicrobial prophylaxis following animal bites, in the absence of any other risk factor for infection, is debatable. One meta-analysis of eight randomized trials concluded that the relative risk for infection in patients given antibiotics compared with controls was 0.56 (95% confidence interval, 0.38–0.82), whereas another meta-analysis included trials with few cat bites, resulting in no evidence for the benefit of prophylaxis. While there may be cause for careful consideration of prophylaxis for other animal bites, antimicrobial prophylaxis for cat bites is usually indicated. FURTHER READING Adlam C, Rutter JM (1989). Pasteurella and pasteurellosis. Academic Press, London. Cummings P (1993). Antibiotics to prevent infection in patients with dog-bite wounds: a meta-analysis of randomised trials. Ann Emerg Med, 23, 535–40. Giardino A, et al. (2015). Clinical features and outcomes of Pasteurella multocida infection. Medicine (Baltimore), 94, e1285. Heydemann J, Heydemann J, Antony S (2010). Acute infection of a total knee arthroplasty caused by Pasteurella multocida: a comprehensive

Fig. 8.6.19.2 The same patient: infected area being incised and drained.

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