EDITORIAL

New horizons in the bacteriology, antimicrobial susceptibility and therapy of animal bite wounds

In the UK approximately 200 000 persons suffer dog bites each year [1]; in the USA 4.7 million persons, or 1.8% of the population, are bitten annually and 800 000 of these people seek medical attention [2, 3]. The 20% of patients who seek medical attention are often those that are more seriously affected, have some complication such as infection and are the focus of published reports. In addition, 400 000 persons in the USA annually are bitten by cats, 45 000 by snakes and an unknown number by other domestic small pet mammals, feral and wild animals, and other human beings, the most aggressive animal of all. Most bite victims do not need, nor do they seek, medical attention. Relatively few large-scale, systematic studies address any of the various issues concerning the full spectrum of bacteriology of these wounds or the various elements of therapy [4, 5]. Most data come from small studies or anecdotal case reports.

Dog bites occur more frequently in males <20 years old, whereas cat bites are more common in 30–40-year-old women. More bites occur in the warm weather months and during middle afternoon around 4 pm. Most animal bite wounds are provoked and the biting animal is usually owned by, or known to, the victim. Bite wounds may be lacerations, evulsions, or punctures and may be accompanied by extensive trauma and crush injury. Infectious complications occur in 15–20% of injuries and include cellulitis, abscess, septic arthritis, osteomyelitis, and bacteraemia. From 1979 to 1994, dog attacks resulted in 279 deaths in the USA [6], one-third of which were associated with pit bull terriers or rottweilers. Children account for c. 75% of fatalities and may also suffer more severe bite injuries, such as skull fractures, dural tears and blood vessel perforation [6, 7].

The bacteriology of paediatric and adult animal bite wounds has been the focus of several studies [4, 5] that noted aerobes in 85% of wounds and anaerobes in c. 50–65%. Older studies classified isolates according to the available schemata, but new molecular methods have resulted in taxonomic changes that have revolutionised aerobic and anaerobic bacteriology, adding many new genera and species that were not previously recognised. Animal bite wounds in man are problematic, as the isolates are veterinary species that may be difficult to identify by colonial morphology and biochemical tests; they may not match descrip-

tions of species usually causing human infection (some may be new species) and are often quite slow growing. Consequently, many laboratories may recognise and isolate only the predominant and familiar strains and miss some of the new and emerging pathogens.

In 1978, a study of 26 dog bite wounds noted that 23 (88%) grew aerobes and 10 (38%) grew anaerobes [5]. Brook [4] reported a series of 21 children bitten by animals (17 dog and four cat bites) with an average of one anaerobe and 1.8 aerobe isolates/specimen. He found *Staphylococcus aureus*, *Pasteurella multocida* and anaerobic cocci to be the most common isolates, together with four '*Bacteroides*' species (now *Prevotella melaninogenica*, *Pr. intermedia* and an unnamed species) and five fusobacteria. A research group from 18 Emergency Departments in academic centres in the USA has been formed to study infected dog and cat bite wounds in man, including the aerobic and anaerobic bacteriology of these wounds. A preliminary report on the first 50 cases in this study [8] found that 92% of wounds grew a total of 232 isolates – 155 aerobes and 77 anaerobes. Aerobes were isolated from all culture-positive wounds and anaerobes from 46% of dog bites (1–9 isolates/wound) and 62% of cat bites (1–6 isolates/wound). The bacteriology of these wounds generally reflected the oral flora of the biting animal.

Among aerobes, *Pasteurella* spp. are recognised as common isolates from feline and canine bite wounds, but most studies have not differentiated them into the newly described species and *P. multocida* subspecies. Mutters *et al.* [9] recognised 13 taxa in DNA hybridisation studies. Subsequently, Holst *et al.* [10], in describing 159 human clinical isolates, noted various ecological differences and tropisms between certain species. *P. multocida* subsp. *multocida* and subsp. *septica* were often isolated from more serious infections, with the latter having a tropism for the central nervous system. Furthermore, *P. canis* was isolated only from dog bites while the other species were isolated routinely from cat bite wounds and scratches.

In early studies of anaerobes isolated from bite wounds, '*Bacteroides*' (including many species since renamed) were the most common isolates, followed by fusobac-

teria and peptostreptococci. These isolates did not produce β -lactamases. In our recent study [8] we identified the presence of many new genera and species. In addition, we have previously isolated 40 strains of *Porphyromonas*: 26 from 54 cat bites and 14 strains from 48 dog bites. When further characterised by biochemical tests and arbitrarily primed PCR [11], *Por. salivosa* (11 isolates), *Por. gingivalis* (10) and *Por. canoris* (8) were most frequent; other isolates included *Por. cangingivalis* (3), *Por. circumdentaria* (2), *Por. cansulci* (1), *Por. levii*-like strains (1) and some unidentified species (4). Supplemented brucella agar supports growth of all these species, but 66% failed to grow on unsupplemented brucella blood agar, 38% on Columbia blood agar and 30% on tryptic soy blood agar without haemin or vitamin K1 supplementation [12]. In a comparison of the Rapid ID ANA II system, An-Ident panels and API ZYM strips, it was found that the latter performed best because of the presence of tests for trypsin and chymotrypsin; however, detection of glycosidase activity by the API ZYM strips was less sensitive than in the other systems. None of the three test systems was able to identify all the isolates or species [13]. The WEE-TAB system, a single tube, triple substrate system to detect certain pre-formed enzymes (N-acetyl- β -D-glucosaminidase, α -D-galactosidase, β -D-galactosidase, α -fucosidase, trypsin-like activity and chymotrypsin) was recently evaluated and compared with the API ZYM and Rapid-ANA II systems and was found to be useful and accurate in identification of most of these *Porphyromonas* spp. *Por. circumdentaria* and *Por. cansulci* could not be identified by any of the three systems because they are enzymically inert [12].

Several saccharolytic *Bacteroides* and *Prevotella* spp. are often isolated from dog and cat bite wounds. *B. tectum* is a frequent isolate and may be mistaken for *Pr. bivia* by colonial morphology and by test kit identification numbers; it may be differentiated by its growth in bile 20% and by aesculin hydrolysis [13]. PCR fingerprinting suggests as many as four subgroups in this heterogeneous species. *Pr. heparinolytica*, also a common animal bite wound isolate, may be confused with *B. uniformis* because of a positive indole test, but is sensitive to bile and easily distinguished from *Bacteroides sensu stricto* (the *B. fragilis* group). *Pr. zoogloformans* is an occasional bite wound isolate that may also resemble *Pr. heparinolytica* except for its negative indole test. *Pr. buccae* and *Pr. oris*, which are also biochemically similar to *Pr. zoogloformans* and are indole negative, may be distinguished as they do not form a zooglear mass in PRAS (pre-reduced anaerobically sterilised) broth media; also *Pr. buccae* does not produce α -L-fucosidase and *Pr. oris* isolates are positive for α -L-arabinosidase [13]. Because of the slow growth of some of these bite isolates, microbiologists are advised to keep the plates for 7 days to ensure their isolation and accurate culture results.

The principles of therapy consist of irrigation, cautious debridement, elevation, recognition of and monitoring for common complications and appropriate antimicrobial therapy [14]. In-vitro studies with several newer antimicrobial agents have been published [15–18], but few clinical trials involving bite wound infections have been reported.

The new fluoroquinolones, levofloxacin, trovafloxacin, DU-6859a and Bay 12-8039, have excellent activity against almost all gram-positive and gram-negative aerobic isolates including all species and subspecies of *Pasteurella*, *Actinobacillus* and *Haemophilus*, *Weeksella zoohelcum*, EF-4a, *Capnocytophaga* spp., *Eikenella corrodens*, *Neisseria weaveri*, *S. aureus*, *S. epidermidis* and streptococci [15–17]. The older fluoroquinolones, ciprofloxacin and ofloxacin, are less active against streptococci. All fluoroquinolones have limited or poor in-vitro activity against *F. nucleatum* and other *Fusobacterium* spp., but good activity against *B. tectum*, *Por. salivosa* and *Por. gingivalis*. Trovafloxacin, Bay 12-8039 and DU 6859a exhibit good activity against peptostreptococci and other *Porphyromonas* spp. (levofloxacin, ofloxacin and ciprofloxacin are relatively less active), *Pr. heparinolytica* and other *Prevotella* spp. (ofloxacin and ciprofloxacin are less active).

Azithromycin is more active than erythromycin against many aerobes including *P. multocida* and *E. corrodens*. It is also two–four-fold more active than clarithromycin against aerobes such as *Actinobacillus* spp., *Haemophilus* spp., *Moraxella* spp. and *Pasteurella* spp., including all *P. multocida* subspp. For some isolates of *P. canis*, *P. dagmatis*, *P. stomatis* and *P. testudinis*, MICs of clarithromycin are 4–8 mg/L. Clarithromycin is more active than azithromycin against some anaerobes such as *B. tectum*, *Porphyromonas* and *Prevotella* spp. [16]. It is unclear whether this difference in anaerobic activity is related to the presence of CO₂ in the atmosphere of incubation, which lowers the agar surface pH and would have a greater effect on the activity of the dibasic azithromycin.

HMR 3004 is a new ketolide with a 3-keto group on a 14-membered erythronolide ring. It has greater activity against bite wound pathogens than its macrolide relatives. Almost all fastidious and aerobic isolates, including *P. multocida*, *B. tectum*, *Prevotella* spp., *Porphyromonas* spp. and peptostreptococci are inhibited at a concentration of 0.5 mg/L, but *F. nucleatum* and other fusobacteria are more resistant (MIC₉₀ 16 mg/L).

Cefuroxime and cefpodoxime have modest activity against gram-positive aerobes and limited activity against *Prevotella* spp. (other than *Pr. heparinolytica*), fusobacteria and some *B. tectum* strains [16]. Cefprozil has modest to poor activity against gram-positive

aerobes and, like loracarbef, poor activity against peptostreptococci [18].

The choice of antimicrobial therapy favours an agent that is active against all the *Pasteurella* spp., *S. aureus*, streptococci and the anaerobic species such as *B. tectum*, *Pr. heparinolytica*, *Por. salivosa*, fusobacteria and peptostreptococci. Other considerations include the patient's allergy history as well as possible side-effects, drug interactions and other contra-indications.

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