

COMPARATIVE MEDICINE

Tackling MRSA in animals and humans

THE emergence of methicillin-resistant *Staphylococcus aureus* (MRSA) as a veterinary disease and the increasing prevalence of MRSA in humans were discussed at a seminar held at the Royal Society of Medicine (RSM) in London on October 26. Entitled 'Killer Staph – just media hype or a real problem?', the aim of the seminar, which was organised by the RSM's Comparative Medicine Section, was to discuss recent research on MRSA and its current status in humans and animals. The presentations, given by speakers from the medical and veterinary fields, highlighted that MRSA was a genuine problem, which could not be dismissed as media hype, and that collaboration between the medical and the veterinary professions was vital to help identify, control and treat infections.

Source of MRSA in animals

The question of where MRSA in animals came from was examined by Dr Andrew Waller of the Animal Health Trust (AHT), who noted that, although its incidence in animals was relatively low compared with the human situation, MRSA could cause serious disease and had been identified in a wide range of species, including poultry, dogs, cats, horses and cattle.

He believed that it was most likely that methicillin resistance had spread from humans to animals, particularly considering the close contact companion animals had with humans. One would therefore expect to see the same strains circulating in humans and in animals.

A number of studies using pulsed-field gel electrophoresis (PFGE) had demonstrated that the same strain of MRSA in an animal could be identified in in-contact humans. One such study

described two dog owners suffering from persistent MRSA infection, who relapsed every time they returned home from hospital. Further investigation revealed that their dog was carrying the same strain of MRSA (F. A. Manian, 2003, *Clinical Infectious Diseases*, vol 36, pp 26-28). He pointed out, however, that these types of studies did not resolve the 'chicken or egg situation': did the dog initially acquire the infection from the humans or was it the other way around?

Other studies had shown that many strains of MRSA found in animals were identical to those in the human population, namely UK epidemic MRSA clone 15 (EMRSA-15) and clone 16 (EMRSA-16). In the UK these were the predominant epidemic clones and caused 96 per cent of serious MRSA infections in humans in hospitals. Preliminary data from a collaborative study between the AHT and the Royal Veterinary College (RVC), funded by the Petplan Charitable Trust, to sequence-type canine strains in the UK, had backed up these findings. The researchers used multilocus sequence typing (MLST) to identify specific MRSA strains in dogs. Of the 14 they had analysed to date, 13 were EMRSA-15 and one was EMRSA-16. It appeared that canine strains were generally similar to human strains, implying the transmission of human MRSA strains to animals.

MRSA in the horse

MRSA in horses was explored by Professor Peter Clegg and Dr Nicola Williams from Liverpool veterinary school. Professor Clegg noted that MRSA was first reported in the horse in 1997 and was associated with wound infections. However, since then, MRSA infections had been reported as a cause of pneumonia, osteomyelitis, catheter site infections, metritis and dermatitis.

He said that MRSA was 'not a major problem' at the Philip Leverhulme Equine Hospital in Liverpool. It was one of the biggest equine hospitals in the UK and, of 2000 cases seen per year, it had identified five cases of MRSA over the past three-and-a-half years. Three cases arose from joint wounds and joint wound infections, another from pastern dermatitis and one case was isolated from a horse with chronic pleuropneumonia.

In a study conducted between late autumn 2003 and spring 2004, samples were taken from 67 horses at the Liverpool hospital and from 41 other horses that were privately owned and from riding schools. At the hospital, 11 horses were found to be carriers of

MRSA; staff were screened but none was found to be positive. All the horses sampled outside the hospital were negative for MRSA. (Details of this study are to be published in *Emerging Infectious Diseases*; the paper is available online at www.cdc.gov/ncidod/EID/vol11no12/05-0241.htm.)

Dr Williams said that three of the clinical cases and all of the carriers identified from the equine hospital were subjected to PFGE and MLST, which showed five distinct strains, the most common being EMRSA-10. None was related to EMRSA-15 or EMRSA-16, which differed markedly from the findings at the small animal hospital at Liverpool where all the isolates that had so far been identified were EMRSA-15.

Describing the uncertainty surrounding how these strains entered hospitals, she noted that many were resistant to gentamicin, an antimicrobial widely used in equine medicine. She suggested that these particular strains were being selected for; in contrast, the EMRSA strains seen generally in small animals were resistant only to ciprofloxacin as well as methicillin.

MRSA in small animals

How a small animal referral hospital coped with MRSA infection was considered by Professor David Lloyd, from the Queen Mother Hospital for Animals at the RVC. The RVC had begun to recognise cases of MRSA in 1997/98 and, after that, had started to see a substantial increase in the number of MRSA infections in referred cases.

So how did the hospital treat MRSA cases? A diverse range of clinical presentations were referred to the hospital, treatments were tailored to individual patients and encompassed medical, financial and ethical concerns. It did not use certain antibiotics, for example, vancomycin, which it believed should be left for use in human medicine. Simply removing implants, such as external fixators, could result in survival and recovery. If antimicrobials were indicated, oxytetracycline or co-trimoxazole could be effective. As well as this, decolonisation procedures were used in most cases, which involved administration of fusidic acid into mucosal sites, and application of chlorhexidine shampoo to the skin.

Professor Lloyd recommended carrying out swab or tissue sampling for culture and antimicrobial susceptibility testing in all non-responsive infections, non-healing wounds, or if MRSA was suspected for any other reason; for



Photograph: Dr Karl Lountraas/Science Photo Library

Coloured transmission electron micrograph of a cluster of methicillin-resistant *Staphylococcus aureus* (MRSA) showing some cells dividing. x 24,000

example, if the owner had a healthcare-related job or had just been in hospital.

He also noted that people should be alerted if laboratory testing revealed a resistance pattern for an isolate that was unusual or just not believable. One finding that raised suspicions at the hospital was the identification of cefalexin-resistant *Staphylococcus intermedius*. *S. intermedius* was very rarely resistant to cefalexin, so it was important to ensure that the organism had been identified correctly.

A survey conducted at the hospital, which had been published recently in the *Journal of Antimicrobial Therapy* (A. Loeffler and others, 2005, vol 56, pp 692-697), aimed to provide more accurate information on its MRSA status. On one day in February 2004, all staff present, all animals (with the owners' consent) and environmental surfaces were sampled for MRSA. The study identified MRSA carriage in 17.9 per cent of veterinary staff, 9 per cent of dogs, and 10 per cent of environmental sites. Most survey isolates were indistinguishable from (56 per cent) or closely related to (26 per cent) EMRSA-15. None was related to EMRSA-16.

Professor Lloyd highlighted the hospital's hygiene and surveillance procedures. It no longer allowed animals with recurring infections to enter the hospital unless they had been tested for MRSA. In emergency cases, they were isolated

until they were tested. If the animals required intensive care treatment, 'barrier nursing' was implemented, which used very strict hygiene procedures. Alcoholic hand scrubs had also been attached to cages in the intensive care unit.

Human experience

Dr Angela Kearns, from the Health Protection Agency, described the difference between 'community-acquired' and 'hospital-acquired' MRSA infections in humans. The community-acquired form tended to be unrelated to the hospital-acquired form and was notably more virulent and transmissible. It tended to occur in previously healthy individuals in the community, with no known risk factors for acquiring MRSA.

A particularly virulent form of MRSA was discussed by Dr Marina Morgan, from the Royal Devon & Exeter Foundation NHS Trust. She described the key clinical features of infections caused by an *S. aureus* that produced an exotoxin called Panton-Valentin leukocidin (PVL). PVL exhibited strong cytotoxic activity towards human leucocytes and had the ability to cause severe inflammation and tissue necrosis. All *S. aureus* strains, not just MRSA, could be infected by PVL-producing phages, and the toxin greatly increased the bacterium's virulence. Most PVL-related infections caused recurrent furunculo-

sis and severe recurrent abscesses, but if the *S. aureus* was carried in the nose and throat, it could descend into the lungs causing necrotising pneumonia. Despite aggressive management, including massive doses of antibiotics, this pneumonia had a mortality rate of more than 75 per cent in young, fit people.

She noted that although only 2 per cent of *S. aureus* produced this exotoxin, the more people looked for the strain, the more they found it; she suggested that PVL positivity in strains isolated from recurring skin infections was as high as 8 per cent, and that probably all the strains that caused necrotising pneumonia produced PVL.

The relationship between cleanliness in hospitals and MRSA infection was explored by Dr Stephanie Dancer, from the Southern General Hospital in Glasgow. She noted there was no way to assess the risk of acquiring MRSA from the clinical environment because there was no way of measuring the effect of cleaning. However, just because there was no direct evidence linking surface hygiene and MRSA acquisition, did not mean there was no link. She suggested that it might be time to introduce microbiological standards for surface hygiene levels in hospitals. This would not only allay concerns over the grading of hygiene by visual assessment, but could help convert cleaning to an evidence-based discipline.

Papers in this week's Veterinary Record

Zoonoses reported in Scotland, 1993 to 2002

ZOONOTIC diseases in people are most commonly food- or waterborne, but contact with infected animals or their faeces and subsequent person-to-person spread are also important routes of infection. On p 697, Mr Cameron Stewart and colleagues analyse the reports of zoonoses in humans and animals submitted to Health Protection Scotland between 1993 and 2002. There were 24,946 reports of zoonotic pathogens in animals, and 94,718 of the 468,214 reports in humans were considered to be zoonotic. *Campylobacter*, *Salmonella* and *Cryptosporidium* species were found commonly in humans and animals; *Giardia* species and *Escherichia coli* O157 were also commonly reported in humans, and *Chlamydia* species and *Mycobacterium avium* subspecies *paratuberculosis* in animals. Most of the areas with a higher than expected incidence of zoonoses in people were rural. New and emerging pathogens considered zoonotic included *Rhodococcus* and *Leishmania* species, *Cyclospora cayetanensis*, *Pneumocystis carinii* (*jiroveci*) and the agent of BSE/variant Creutzfeldt-Jakob disease.

Salmonella serovars on dairy farms in England and Wales

CATTLE are considered to be an important reservoir of salmonellae, and cases of human salmonellosis have been associated with contaminated dairy products or contact with infected herds. On p 703, Dr Helen Davison and colleagues survey the prevalence and incidence of *Salmonella* species infection on dairy farms in England and Wales. A total of 449 farms were visited up to four times. Samples of pooled faeces or slurry were collected from various sites around each farm and cultured for salmonellae. The farm-specific prevalence of *Salmonella* ranged from 12.1 per cent to 24.7 per cent; the three serovars most commonly isolated were *Salmonella* Dublin, *Salmonella* Agama and *Salmonella* Typhimurium. The prevalence of serovars presenting a risk to public health was low. The incidence rate of *Salmonella* infection was 0.43 cases per farm-year at risk. Antimicrobial susceptibility testing of the isolates revealed little resistance except for *S. Typhimurium* DT104, all of which were resistant to at least one of the 16 agents tested, and in which multiresistance was common.

West Nile virus in horses in France

IN October 2003, clinical cases of West Nile virus (WNV) infection in people and horses were reported on the Mediterranean coast of France. In a short communication on p 711, Dr Benoit Durand and colleagues describe a serosurvey of horses in the area, following the outbreak. Up to 30 horses from each of the commercial stables within 30 km of the first equine case were blood sampled, and sera were tested by ELISA for antibodies to WNV. Of samples taken from 906 horses, 305, from 33 of 41 stables, were positive for immunoglobulin (Ig) G to WNV. The seroprevalence in positive stables ranged from 3 to 95 per cent. The IgG seroprevalence was higher in two areas close to 'important bird areas' (IBAs). Twenty-three of the horses, from nine stables, were also IgM positive, indicating recent infection; these were all within 3.5 km of an IBA. The authors note that their findings correspond better to an endemic situation than a sporadic outbreak. They suggest that the biodiversity within IBAs may enable WNV to persist, with mosquito vectors then transmitting the virus to surrounding areas.