BAD BUGS, BAD BUGS, WHATCHA GONNA DO?

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- Drug residues and antibiotic resistance is causing concern over the use of antibiotics in veterinary patients, including horses. Practitioners often choose drugs based on recommendations from scientific papers generated from eastern Canada and the United States. These recommendations are not necessarily valid for cases in western Canada.
- Recently, the author and coworkers analysed five years of bacterial cultures at the Western College of Veterinary Medicine.
- Results of this study show that infections from *Streptococcus zooepidemicus* is the most common cause of infections in horses. Typical infections in horses were from common bacteria that were not resistant to routine antibiotics.
- Veterinarians can use the results of this study as a guide in selecting antibiotics for initial treatment.

In recent years there have been important changes in antibiotic therapy in equine practice. There are new antibiotics available and there is more information available on the antibiotics used in horses. Concerns over drug residues in food animals and antibiotic resistance has lead to the development of the Canadian Veterinary Medical Association's Prudent Use Guidelines. These guidelines stress obtaining a diagnosis and selecting appropriate antibiotic therapy. In practice situations, it is often difficult to submit samples for microbiologic culture and antibiotic susceptibility testing. Practitioners often choose antibiotics selection based on data from university teaching hospitals and veterinary diagnostic laboratories from other parts of Canada, the United States and even Europe. These data do not necessarily reflect the bacteria and their susceptibility to antibiotics for clinical cases in western Canada. Recently, the author and her coworkers gained computer access to Prairie Diagnostics' database of equine bacterial submissions from the Large Animal Clinic of the Western College of Veterinary Medicine (WCVM) for the years 1998-2002. A total of 542 submissions from equine cases were made during this time period. Three hundred and thirty five positive cultures were obtained and 493 bacteria were identified and tested for antibiotic susceptibility (Table 1).

Bacteria associated with infections in horses

Streptococcus zooepidemicus (104 isolates/493) was the most common cause of bacterial infection in horses at the WCVM. This was followed by *E. coli* (53/493), *Actinobacillus suis* (37/493), alpha-streptococci (30/493) and *Actinobacillus equuli* (26/493). These isolates are part of the normal bacterial flora of the skin, gastrointestinal and respiratory tracts of horses. Their role in infection reflects the primary care nature of the equine caseload of WCVM. This distribution of pathogens is likely to be similar to cases seen in private practice in western Canada, but is very different compared to data from United States teaching hospitals with more tertiary care caseloads, where "super bugs" are commonly found. At the WCVM, infections caused by serious bacteria such as *Staphylococcus aureus* and *Pseudomonas species* are relatively uncommon (24/493 and 42/493, respectively) and these infections are associated with severe

disease and repeated antibiotic use. Infections from *S. equi*, the cause of "strangles", are also relatively uncommon, with only 18 isolates identified. *Rhodococcus equi* (4/493) and *Salmonella* species (3/493) appear to be infrequent causes of disease in horses in western Canada.

Respiratory tract infections

Respiratory tract disease is common in horses and the respiratory tract was the most frequently sampled site in the study, with 171 isolates cultured from 107 transtracheal washes, 39 isolates cultured from 24 nasal swabs, and 25 isolates cultured from 19 guttural pouch washes. A few isolates were also obtained from cultures of lung and pleural fluid. From all sites but the guttural pouch, the most common isolate involved was *S. zooepidemicus* (47/218). The next most common pathogens were *A. suis* (27/218), *A. equuli* (16/218) and alpha-streptococci (15/218). From guttural pouch washes, *S. equi* was isolated most often (6/25), followed by *A. suis* (5/25), *S. zooepidemicus* (4/25) and *A. equuli* (3/25). In chronic cases of pleuropneumonia with considerable lung damage, opportunistic bacteria such as *Pseudomonas* spp., *Enterobacter*, *Serratia* spp., and *Staph. aureus* were cultured.

The role of *S. zooepidemicus* and *S. equi* in equine respiratory tract infections has been well documented. *S. zooepidemicus* is considered normal flora of the upper respiratory tract and *S.equi* is known to cause persistent, asymptomatic infection in horses. Penicillin, ceftiofur (Excenel®) and trimethoprim/sulfonamides (TMP/sulfa, Tribrissen®) are the usual first line treatment choices for streptococcal infections in horses. The results of the WCVM study support the use of penicillin and ceftiofur for treatment of bacterial sinusitis and guttural pouch infections, as there was a high degree of susceptibility to these antibiotics. Of the *S. zooepidemicus* isolates, 97% were susceptible to penicillin and 100% were susceptible to ceftiofur. Of the *S. equi* isolates, 100% were susceptible to both penicillin ceftiofur. Only 47% of *S. zooepidemicus* and 72% of *S. equi* isolates were susceptible to TMP/sulfa. The susceptibility of *S. zooepidemicus* to TMP/sulfa is much less at the WCVM than that reported from veterinary teaching hospitals in other countries. Availability and therefore use of TMP/sulfa products in horses varies between countries and influences bacterial susceptibility to these products. Because of availability of injectable formulation and the convenience of oral dosing, TMP/sulfa is frequently and sometimes inappropriately administered to horses in western Canada, and this may explain the high level of resistance documented in the WCVM isolates.

Pneumonia and pleuronpneumonia often involves multiple bacteria in horses. Typically, it starts with initial invasion of the lower respiratory tract with *S. zooepidemicus* followed by invasion by Gram-negative and anaerobic pathogens. The Gram-negative bacteria *A. suis* and *A. equuli* were the most common respiratory tract isolates from the WCVM after *S. zooepidemicus*. This is in contrast to a previous study that found *E coli* and *Pasteurella* spp. to be the most common Gram-negative isolates. More severe pathogens such as *Pseudomonas spp.*, *Serratia* spp. and *Staphylococcus aureus* were isolated from more chronic cases with severe lung damage. Because of the combination of bacteria involved, antibiotic therapy needs to target streptococci, Gram-negative and anaerobic therapy. No single antibiotic product tested provided this coverage, therefore combination therapy is required for effective therapy. Of all isolates tested, the *Actinobacillus* spp. had the greatest susceptibility to TMP/sulfa, with >90% of isolates susceptible. However, susceptibility of the other Gram-negative isolates (*E coli*, *Pseudomonas*, *Enterobacter*, *Serratia*, and *Klebsiella* spp.) to TMP/sulfa varied considerably.

Only 46% of *A. suis* isolates were susceptible to penicillin. The *Pasteurella* spp. isolates were extremely susceptible to all tested antibiotics, with 91% susceptible even to penicillin. Enrofloxacin (Baytril®) or gentamicin (Gentocin®) showed the greatest activity against the respiratory pathogens isolated at the WCVM. Previous studies have reported a high incidence of anaerobic infections in horses with pneumonia or pleuropneumonia (25-46%). While putrid smelling breath indicates the presence of anaerobes, the lack of a putrid odour does not rule out the possibility of an anaerobic infection. In the WCVM study, only 7 anaerobes were isolated from transtracheal washes, and tended to be from cases with advanced disease, and 2 isolates were *Bacteroides* spp. Antibiotic therapy targeted against anaerobes is relatively easy and inexpensive, and a previous study has suggested improved survival rates of horses with pleuropneumonia with attention to treatment of anaerobes.

From the WCVM data, the most logical treatment choice for bacterial pneumonia or pleuropneumonia is a combination of penicillin, ampicillin or ceftiofur with gentamicin or enrofloxacin. Oral metronidazole (Flagyl®) may be added for its ability to penetrate abscessed tissue and its excellent activity against *Bacteriodes fragilis*, which has become increasingly resistant to penicillins and cephalosporins. Culture and susceptibility testing from a transtracheal wash or pleural fluid sample should always be performed because of the variable susceptibilities of the Gram-negative bacteria to antibiotics. The use of gentamicin or enrofloxacin for respiratory infections in horses is extralabel, but consistent with prudent use guidelines. Practitioners should be familiar with the potential side effects of these drugs in horses and should receive appropriate client consent before initiating therapy.

Reproductive tract infections

The second most common site for bacterial culture was the reproductive tract of mares. A total of 43 isolates were cultured from 33 uterine samples and 7 isolates were cultured from 6 vaginal samples. Like the respiratory tract, the majority of isolates were *S. zooepidemicus* (14/39). The next most common pathogen was *E. coli* (11/39). *Pseudomonas* spp. were only cultured from one uterine sample and one vaginal swab. These results agree with previous studies from other teaching hospitals, except for the low prevalence of *Pseudomonas* spp. The majority of reproductive tract infections are limited to the mucosa and superficial endometrium, therefore intrauterine therapy is the preferred method of treatment. Systemic therapy should be limited to cases of postpartum metritis where the mare is systemically ill or where a uterine biopsy suggests deep inflammation and infection. Currently, treatment regimens (including drug, dose, frequency and method of infusion) for endometritis in the mare are based more on convenience and practicality rather than scientific evidence. In Canada, only gentamicin and amikacin (Amiglyde®) are approved for intra-uterine use in mares with endometritis. Based on the results from the WCVM study, gentamicin should be the first choice for intrauterine treatment of endometritis. As only 9% of *S. zooepidemicus* isolates were susceptible to amikacin, it should be reserved for Gram-negative infections with documented resistance to gentamicin.

Urinary tract infections

Infection of the urinary tract in horses typically occurs as an ascending infection from skin and gastrointestinal bacteria. From horses with urinary tract infections, 18 cultures grew 26 isolates and the most common pathogen isolated was *E. coli* (7/26), followed by alpha streptococci (5/26). Although uncommon, isolates of *Pseudmonas* spp. (2/26), *enterococcus* sp.(3/26) and *enterobacter* sp.(2/26) were highly resistant to most antibiotics. The remaining isolates were varying Gram-positive and Gram-negative bacteria. These results emphasize the need for culture and susceptibility testing to determine appropriate therapy for equine urinary tract infections.

Post-surgical infections

From a variety of post-surgical sites, 27 isolates were cultured from 15 submissions. A wide variety of Gram-positive and Gram-negative bacteria were isolated, with the most common isolates being *Staph. aureus* (5/27), *Pseudomonas areuginosa* (4/27) and non-hemolytic *E. coli* (4/27). The staphylococcal and enterobacteriaceae isolates indicate contamination of surgical sites with skin and fecal flora, while *Pseudomonas aeruginosa* is often an environmental opportunist that is given a selection advantage by the routine use of antibiotics. While the antibiotic susceptibility patterns of the Gram-negative isolates were highly variable, the *Staph. aureus* isolates were highly susceptible to most antibiotics. Therefore, culture and susceptibility testing is mandatory for post-surgical infections in order to select appropriate antibiotic therapy and to identify hospital contamination problems.

Abscesses/Wounds/Joints/Tendon Sheaths

Traumatic injuries are common in horses due to the popularity of barbed wire fencing. A variety of isolates were grown from samples identified as abscesses and chronic or acute wounds. *E. coli* and *S. zooepidemicus* were the most common isolates. Eighteen isolates were cultured from 16 joint fluid samples and 3 isolates were cultured from 3 tendon sheath fluid samples. *A. equuli* was the most common isolate (4/21), followed by equal numbers of *S. zooepidemicus* (3/21), *Enterococcus* sp.(3/21) and *Staph. aureus* (3/21). Previous reports from a US veterinary college supported the use of amikacin for musculoskeletal infections in horses because of its efficacy against staphylococci and pseudomonads, and it has been the first choice of surgeons. While the WCVM results support the efficacy of amikacin against the *Staph. aureus* isolates (100% susceptible), its activity against the other common isolates was poor: *A. equuli* (56%), *S. zooepidemicus* (9%) and *Enterococcus* spp. (50%). While gentamicin was poorly effective for musculoskeletal infections in a previous study, it was highly effective against the pathogens from the WCVM: *A. equuli* (92%), *S. zooepidemicus* (93%), *Enterococcus* spp. (94%) and *Staph. aureus* (100%). Therefore, gentamicin should be considered the first choice for antibiotic therapy of equine musculoskeletal infections based on its spectrum activity and reduced cost of therapy as compared to amikacin.

Bacterial Eye Infections

Eight isolates were cultured from eight eyes with infections in the cornea. The most common isolate was S. zooepidemicus (5/8). The other three isolates were alpha streptococci, *Staph. aureus*, and *Actinobacillus* sp. Although only a small number of cultures were submitted from the WCVM, these results are different than a previous report of 63 cases of eye infections in horses, where 58% of cultured isolates were Gram-positive organisms and 48% were Gram-negative, with nearly 50% of the Gram-negative isolates being *Pseudomonas* spp. Because nonresponsive or inadequately treated corneal infections in horses can quickly lead to irreversible damage, it is reasonable to initiate treatment with broad spectrum antibiotic therapy effective against staphylococci and pseudomonads. Gentamicin or triple antibiotic preparations are good initial choices. Triple antibiotic contains neomycin, bacitracin and polymixin. This combination provides broad spectrum antibiotic activity. Neomycin has good activity against *Staphylococcus* spp. and Gram-negative bacteria. Polymixin B is rapidly bactericidal against Gram-negative bacteria including *Pseudomonas* spp. Due to systemic toxicity, polymixin B is only used topically, so it is not typically included on susceptibility reports from microbiology services, but *Pseudomonas aeruginosa* veterinary isolates are routinely susceptible to polymixin B. Polymixin B also binds and inactivates endotoxin, reducing inflammation and tissue destruction. Like polymixin B, bacitracin is a topical product not routinely included on susceptibility reports. Bacitracin is active against Gram-positive bacteria, with a mechanism of action similar to the ß-lactam antibiotics.

Septic Foals

Too few isolates were submitted from septic neonatal foals at the WCVM for any meaningful interpretation. Previously published reports indicate that *E. coli* is the most common pathogen isolated. However, reports from investigators of sepsis in humans indicate the re-emergence of Gram-positive bacteria such as *Enterobacter* spp. and *Enterococcus* spp. as “super bugs”. This is of great concern because of the tendency for these bacteria to be resistant to multiple antibiotics. This trend was recently documented in a study of critically ill neonatal foals from Pennsylvania. These studies emphasize the need for culture and susceptibility testing of samples from septic neonates.

Conclusions

Veterinarians should do culture and susceptibility testing for equine infections when possible, but they can use the results of this study to start therapy while waiting for results. Computerization has made it practical for us to review our lab data at the WCVM, and such reviews need to be conducted periodically, as bacteria change with time or vary on the basis of location or treatment. Final selection of the optimal antibiotic must also consider other factors such as the site of infection, chemical properties of the drug, risks of adverse side effects, cost of therapy and effect of underlying diseases.

Table 1. Antibiotic susceptibilities (% of isolates) from equine infections at the WCVM (1998-2002)

Organism	No. of Isolates	Amp	Pen	Amp/ Sulb	Cef	Ceph	Enro	Amik	Gent	Eryth	Tet	TMS
Actinobacillus equuli	26	92	80	100	100	100	100	56	92	46	96	92
Actinobacillus	16	94	76	91	94	93	100	67	81	12	88	94
Actinobacillus	37	81	46	100	100	97	97	40	73	30	84	97
Actinobacter	6	80	17	100	83	67	100		100	33	67	100
E. coli	4	50	0		100	50	100	100	100	0	100	75
E. coli	53	62	0	85	96	51	92	100	86	4	69	60
Enterobacter	23	36	4	71	91	35	96	80	91	13	52	83
Enterococcus	16	94	94	100	25	31	38	50	81	50	62	56
Klebsiella	5	0	0	100	100	60	100	100	80	0	60	100
Klebsiella pneumonia	5	0	0	75	80	80	60	100	80	0	80	60
Pasturella	11	100	91	100	100	100	100	100	100	100	100	100
Proteus vulgaris	6	17	0	67	100	0	100	100	100	0	17	67
Pseudomonas	21	29	19	63	40	19	67	100	71	10	48	57
Pseudomonas aeuroginosa	21	5	0	12	10	0	21	100	55	0	0	0
Rhodococcus equi	4	75	50	100	75	50	100	100	100	100	75	50
Salmonella	3	100	0		100	100	100	100	100	0	67	100
Serratia	9	22	0	50	89	11	78	100	100	0	11	89
Staphylococcus aureus	24	43	43	94	96	100	95	100	100	78	96	100
Staphylococcus intermedius	5	60	60	100	100	100	100		100	80	100	100
Staphylococcus spp.	22	50	45	93	86	95	95	100	86	86	77	91
Streptococcus equi	18	100	100	100	100	100	93	0	93	100	89	72
alpha-*Streptococcus* spp.	30	87	87	83	100	100	78	33	100	90	90	76
Streptococcus zooepidemicus	104	95	97	87	100	100	91	9	93	92	53	47

Amp: ampicillin; Pen: penicillin; Amp/Sulb: ampicillin/sulbactam; Cef: ceftiofur; Ceph: cephalothin; Enro: enrofloxacin; Amik: amikacin; Gent: gentamicin; Eryth: erythromycin; Tet: tetracycline; TMS: trimethprim/sulfonamide