enterococcus [created by Paul Young 02/10/07]

general:

- Enterococci are enteric Gram-positive cocci originally included in the genus Streptococcus.
- Although over a dozen species have been identified, only two are responsible for the majority of human infections, Enterococcus faecalis and Enterococcus faecium. They account for 85–90% and 5–15% of clinical isolates, respectively, although infections caused by the latter are on the increase.
- Other species (E. gallinarum, E. casseliflavus, E. durans, E. avium and E. raffinosis) account for less than 5% of isolates

epidemiology & resistance

- Vancomycin has been used widely for the treatment of E. faecium and E. faecalis infections since the 1980s.
- Enterococci were the first bacteria to develop vancomycin resistance. Vancomycin-resistant Enterococci have now been identified world-wide.
- The appearance of resistance coincides with an increase in the use of cephalosporins, to which Enterococci are naturally resistant.
- Also implicated is the oral use of vancomycin in the treatment of Clostridium difficile, and its parenteral use in the treatment of methicillin-resistant S. aureus infections.
- Vancomycin resistance is mediated through a complex interplay of many genetic elements found on the van gene clusters

Intrinsic resistance
Beta-lactam (cephalosporins and pencillinase-resistant penicillins)
Low concentrations of aminoglycosides
Clindamycin
Fluoroquinolones
Co-trimoxazole
Acquired resistance
High concentrations of beta-lactams, through penicillin-binding proteins or beta-lactamase
High concentrations of aminoglycosides
Glycopeptides (vancomycin and teicoplanin)
Tetracycline
Fluoroquinolones
Rifampicin
Chloramphenicol
Fusidic acid
Nitrofurantoin

- The resistances that cause the most severe therapeutic problems include high level ampicillin resistance, which is seen in some isolates of E. faecium, high level resistance to aminoglycosides, seen in both E. faecium and E. faecalis, and vancomycin resistance, which has developed preferentially in E. faecium

colonisation & infection

- Enterococci are a part of the normal enteral flora of both humans and animals
- Although vancomycin-resistant Enterococci are most commonly isolated from the gastrointestinal tract, they have also been recovered from the groin, intact skin of the upper arm, oropharynx and gastric and tracheal aspirates in hospitalised patients.
- Enterococci have low pathogenic potential except in patients who are severely ill or immunocompromised. Hence reports of vancomycin resistant enterococcal infections are mainly from ICUs, organ transplant and renal units and oncology wards.
- Colonisation of healthy individuals with vancomycin resistant Enterococci, unlike methicillin-resistant S. aureus, does not necessarily increase the risk of subsequent infection with these organisms.
- In many affected institutions, most vancomycin-resistant Enterococci are isolated from colonised rather than infected patients and are found in association with other more virulent organisms.
- There is an association between colonisation with VRE and the oral or parenteral use of vancomycin, cephalosporins and anti-anaerobic drugs (metronidazole, clindamycin and imipenem).
- Eradication of species which normally compete with Enterococci produces a selective environment where small numbers of vancomycin-resistant Enterococci may multiply.
- However, exposure to antibiotics alone will not select for VRE if resistant bacteria are not already present therefore need to be exposed to VRE to become colonised with it

transmission

- Hand-washing with soap and water is ineffective in removing VRE and aqueous chlorhexidine and povidone-iodine solutions are unreliable.
- Only alcoholic chlorhexidine and alcohol have been found to be effective
- The extent to which environment surfaces act as a source from which VRE are able to spread is still uncertain. However, it is known that VRE may remain viable on surfaces for weeks because they are resistant to desiccation and to extreme temperatures
- At present, there is no evidence that VRE are spread by the airborne route

infections

- Enterococci are the second or third most common pathogen identified in urinary tract infections, bacteraemia and wound infections.
- They are rarely responsible for respiratory tract infections, cellulitis or osteomyelitis.
- Although unusual, endocarditis is well-described. Enterococci are responsible for 5–15% of all cases of endocarditis and are associated with considerable morbidity and mortality. Endocarditis is a potential complication of enterococcal bacteraemia and is becoming increasingly difficult to treat because of multiple antibiotic resistances.
- Enterococcal meningitis is also rare and is usually associated with surgery and other instrumentation

antimicrobial therapy

- The treatment of sensitive enterococcal infections is difficult for several reasons:
  (i) Enterococci are intrinsically resistant to many commonly used antimicrobials.
  (ii) Many useful agents are only inhibitory at clinically unachievable concentrations, which limits the effectiveness of therapy.
  (iii) Where bactericidal action is required, dual or triple therapy becomes necessary. It is often unclear if an enterococcal isolate requires treatment, especially if isolates are recovered from polymicrobial bacteraemias or mixed wound infections
  (iv) Enterococci easily acquire resistance to available antibiotics, either by mutation or by receipt of foreign genetic material through plasmids and transposons.
- The optimum antibiotic for documented infection with VRE is not established
- Although E. faecalis and particularly E. faecium are intrinsically resistant to penicillin, nearly all E. faecalis isolates are at least moderately susceptible to ampicillin Thus, most vancomycin-resistant E. faecalis isolates can be treated with ampicillin.
- bactericidal combination of a cell wall inhibiting agent plus an aminoglycoside is considered standard treatment for deep-seated infections. However, this synergistic action may not always be suitable because of high-level gentamicin resistance, which also confers resistance to tobramycin, netilmicin, amikacin and kanamycin, though not to streptomycin, which may remain useful.
- Quinupristin / dalfopristin is approved for use against serious or life-threatening infections caused by E. faecium. It is inactive against E. faecalis and is bacteriostatic against E. faecium; the lack of bactericidal activity may compromise its clinical and bacteriological activity.
- Linezolid shows excellent inhibitory activity against most vancomycin-resistant isolates. There are reports of the successful use of linezolid in the treatment of E. faecium meningitis and bacteraemia
- Chloramphenicol is one of the few agents to retain in vitro activity against many strains of multiply resistant E. faecium. It has been used with moderate success in the treatment of VRE bacteraemia and remains a reasonable choice for the treatment of meningitis. However, two factors may limit its clinical use. Firstly, resistance is increasing and secondly, there is a risk the drug may cause fatal bone marrow suppression
- Nitrofurantoin is active against most Enterococci regardless of vancomycin resistance, and it remains useful for the treatment of urinary tract infections