

**Please read this bit first**

The HPCSA and the Med Tech Society have confirmed that this clinical case study, plus your routine review of your EQA reports from Thistle QA, should be documented as a "Journal Club" activity. This means that you must record those attending for CEU purposes. Thistle will **not** issue a certificate to cover these activities, nor send out "correct" answers to the CEU questions at the end of this case study.

The Thistle QA CEU No is: **MT00025**.

Each attendee should claim **THREE** CEU points for completing this Quality Control Journal Club exercise, and retain a copy of the relevant Thistle QA Participation Certificate as proof of registration on a Thistle QA EQA.

**Cycle 24 - Organism 3:**

**Proteus Infections**

*Proteus* species are part of the Enterobacteriaceae family of gram-negative bacilli. *Proteus* species are most commonly found in the human intestinal tract as part of normal human intestinal flora, along with *Escherichia coli* and *Klebsiella* species. *Proteus* is also found in multiple environmental habitats, including long-term care facilities and hospitals. In hospital settings, it is not unusual for gram-negative bacilli to colonize both the skin and oral mucosa of both patients and hospital personnel. Infection primarily occurs from these reservoirs.

*Proteus mirabilis* causes 90% of *Proteus* infections and can be considered a community-acquired infection. *Proteus vulgaris* and *Proteus penneri* are easily isolated from individuals in long-term care facilities and hospitals and from patients with underlying diseases or compromised immune systems.

*Proteus* species possess an extracytoplasmic outer membrane, a feature shared with other gram-negative bacteria. In addition, the outer membrane contains a lipid bilayer, lipoproteins, polysaccharides, and lipopolysaccharides.

Infection depends on the interaction between the infecting organism and the host defence mechanisms. Various components of the membrane interplay with the host to determine virulence. Inoculum size is important and has a positive correlation with the risk of infection.

Certain virulence factors have been identified in bacteria. The first step in the infectious process is adherence of the microbe to host tissue. Fimbriae facilitate adherence and thus enhance the capacity of the organism to produce disease. *E coli*, *P mirabilis*, and other gram-negative bacteria contain fimbriae (i.e. pili), which are tiny projections on the surface of the bacterium. Specific chemicals located on the tips of pili enable organisms to attach to selected host tissue sites (e.g. urinary tract endothelium). The presence of these fimbriae has been demonstrated to be important for the attachment of *P mirabilis* to host tissue.

The attachment of *Proteus* species to uroepithelial cells initiates several events in the mucosal endothelial cells, including secretion of interleukin 6 and interleukin 8. *Proteus* organisms also induce apoptosis and epithelial cell desquamation. Bacterial production of urease has also been shown to increase the risk of pyelonephritis in experimental animals. Urease production, together with the presence of bacterial motility and fimbriae, may favour the production of upper urinary tract infections (UTIs) by organisms such as *Proteus*.

Enterobacteriaceae and *Pseudomonas* species are the microorganisms most commonly responsible for gram-negative bacteraemia. When these organisms invade the bloodstream, endotoxin, a component of gram-negative bacterial cell walls, apparently triggers a cascade of host inflammatory responses and leads to major detrimental effects. Because *Proteus* and *Pseudomonas* organisms are gram-negative bacilli, they can cause gram-negative endotoxin-induced sepsis, resulting in systemic inflammatory response syndrome (SIRS). SIRS has a mortality rate of 20-50%. Although other organisms can trigger a similar response, it is useful to consider gram-negative bacteraemia as a distinct entity because of its characteristic epidemiology, pathogenesis, pathophysiology, and treatment. The presence of the sepsis syndrome associated with a UTI should raise the possibility of urinary tract obstruction. This is especially true of patients who reside in long-term care facilities, who have long-term indwelling urethral catheters, or who have a known history of urethral anatomic abnormalities.

The therapy of *Proteus mirabilis* meningitis with gentamicin alone and in combination with chloramphenicol has been studied in rabbits. Antibiotics were administered for 8 hr. Samples of serum and cerebrospinal fluid (CSF) obtained simultaneously were assayed at 2-hr intervals for antibiotic concentration and counts of bacteria in CSF. The percentage of penetration ([concentration in CSF divided by concentration in serum] x 100%) of gentamicin ranged from 14% to 23%, but very large dosages were required to kill bacteria in the CSF. Although the minimal bactericidal concentration (MBC) of gentamicin was 1 microgram/ml, killing in vivo occurred only when concentrations in CSF were 10--30 times the MBC. The high concentration required for bactericidal activity in vivo may be explained by the reduced pH of infected CSF (mean pH, 6.98; range, 6.69--7.18). The bactericidal action of gentamicin was abolished by the simultaneous administration of chloramphenicol. Titres of bacteria in CSF were reduced 2.60 log<sub>10</sub> (mean) with gentamicin therapy vs. 0.92 log<sub>10</sub> (mean) with combination (P less than 0.01).

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### **CPD Questions:**

1. What percentage of *Proteus* infections are caused by *Proteus mirabilis*?
  2. What role does apoptosis play in *Proteus* infections?
  3. What antibiotic therapy regime is recommended by your laboratory?
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