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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 23 Organism 2:

Burkholderia cepacia complex (BCC)

Burkholderia (formerly *Pseudomonas*) *cepacia* is a gram-negative bacterial pathogen of evolving importance in individuals with compromised immunity, particularly patients with cystic fibrosis (CF).

There is growing evidence that *B cepacia* is highly virulent in certain patients with CF and in patients with chronic granulomatous disease (CGD) -- an inborn defect in neutrophil function in which patients are unable to kill ingested bacteria via reactive oxygen radical production. Perhaps the most problematic characteristic of *B cepacia* is its capacity to spread from one patient to another, both within and outside the hospital. In the United States, the median survival for CF patients infected with *B cepacia* is 15.6 years, compared with 27.8 years for those infected with *P aeruginosa* and 39.1 years for those infected with neither.

B cepacia is a highly diverse group of bacteria. Although it has traditionally been classified as a single species (*B cepacia*), it more properly comprises several classes of bacteria, each of which should probably be assigned a different species designation. These unique classes of bacteria are known as genomovars, and the total group of bacteria as the "*Burkholderia cepacia* complex".

The possibility that *B cepacia* can be spread from one CF patient to another has been inferred from the regional differences in prevalence of infection. This contrasts sharply with the relatively consistent frequency of *P aeruginosa* infection in patients in different CF treatment centers.

The clearest initial evidence that *B cepacia* can be spread from one CF patient to another has come from studies at a North American CF summer camp. Although the mode of acquisition was not established, the likelihood of becoming colonized with *B cepacia* was found in other studies to be increased by attendance at a camp with a high prevalence of infected campers and by prolonged attendance at the camp. Subsequent reports from the United Kingdom support the conclusion that *B cepacia* can be spread among CF patients during social contact outside of hospitals and may even be spread from patients with CF to persons without CF.

Determining whether or not a patient with CF is infected with *B. cepacia* is critically important in guiding the care of that patient and in controlling spread to others. Unfortunately, the organism is difficult to culture, and identification in the laboratory is extremely challenging. Since traditional culture methods are relatively insensitive -- there is 1 report of infection being undetected for 2 years -- novel approaches to noncultural identification (for example, a polymerase chain reaction-based technique) are being developed. To enhance the recovery of *B. cepacia* from respiratory secretions, a primary selective agar, such as *B. cepacia* selective agar, should be used. Furthermore, all initial isolates from CF patients should be sent to a reference laboratory for confirmation, since other organisms can be readily misidentified as *B. cepacia*.

Therapy for *B. cepacia* infections presents tremendous challenges because of the organism's high-level intrinsic resistance to a wide range of antimicrobial agents. In fact, *Burkholderia* is among a very select group of microorganisms that are uniformly resistant to cationic peptides, the principal element of non-oxidative phagocytic cell-mediated killing, as well as polymyxin. *B. cepacia* is also predictably resistant to aminoglycosides -- in fact, gentamicin is incorporated into the special selective medium used to isolate the organism from respiratory secretions. In addition to their high-level intrinsic resistance, *B. cepacia* strains develop resistance to multiple antibiotics under the pressure of therapy for acute respiratory exacerbations in CF patients. The high-level intrinsic resistance, the acquired resistance of the organism, and the poor penetration of antibiotics to respiratory secretions (with relative inactivity of the fraction that does penetrate) all conspire to render respiratory tract infections extremely difficult to treat. The most effective agents appear to be carbapenems (meropenem and imipenem); extended-spectrum β -lactams, such as ceftazidime; and trimethoprim-sulfamethoxazole. These antibiotics may be effective as single agents, but there are bacterial isolates for which no single agent is effective in vitro.

The choice of the most appropriate therapy for such infections is extremely difficult and may be guided in part by synergy testing, which is offered at several highly specialized laboratories. Such tests are able to identify the combination of drugs that is most effective in killing a particular bacterial strain in vitro. A recent report indicates that for multiply resistant strains of *B. cepacia*, the most effective combination of antibiotics was meropenem, ceftazidime, and tobramycin. Synergy testing is offered by specialized laboratories at the University of Ottawa, Ontario, and at Columbia University, New York. Unfortunately, there are no clinical reports to provide proof that the combinations predicted to be superior by in vitro synergy testing are, in fact, superior to combinations chosen by other methods. Such clinical correlations will be extremely valuable in guiding the care of patients infected with multi-resistant strains of *B. cepacia*.

CPD Questions:

1. Why are CF patients prone to BCC infections?
2. What is your routine for isolating BCC from CF patients? How many have you isolated in the last six months?
3. Give 3 reasons why BCC infections are hard to treat and cure.

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