Extended-Spectrum Beta-Lactamase (ESBL):

Beta-lactamase enzymes are produced by a variety of bacteria and are capable of destroying the beta-lactam antibiotics and rendering them ineffective. The genes responsible for beta-lactamase mediated resistance in *Escherichia coli* and *Klebsiella spp.* can acquire point mutations that result in the production of novel beta-lactamas that become capable of hydrolyzing extended-spectrum cephalosporins (e.g., ceftazidime, cefotaxime, and ceftriaxone) and monobactams (e.g., aztreonam) but do not affect cephamycins (e.g., cefotixin and cefotetan) or carbapenems (e.g., meropenem or imipenem). These novel mutant varieties of beta-lactamases with extended spectrum of activity are called as extended-spectrum beta-lactamas (ESB’s). They were first reported in 1983 in Europe and subsequently spread to United States and other parts of the world. Epidemiological studies on ESBL production in large collections of enterobacterial isolates have demonstrated that ESBL’s are currently less of a problem in the United States occurring at less than 5% when compared with Europe (30%) and Latin America (45%). Although these enzymes are commonly described in *E. coli* and *Klebsiella* species they may also occur in other gram-negative bacteria including *Enterobacter, Salmonella, Proteus, Citrobacter, Morganella morganii, Serratia marcescens, Shigella dysentriae, Pseudomonas aeruginosa,* and *Burkholderia cepacia*. ESBL’s can be difficult to detect because they have different levels of activity against various cephalosporins. Clinical laboratories detect ESBL producing organisms by following guidelines from Clinical and Laboratory Standards Institute. It is a two step method, the first of which involves screening for reduced susceptibility to any of the recommended screening agents (ceftaxime, ceftriaxone, ceftazidime, cefpodoxime, or aztreonam). *E. coli* and *K. pneumoniae* or *K. oxytoca* that are able to grow at MIC of 1 mcg/ml for all the drugs indicated above except cefpodoxime (MIC >4mcg/ml) are considered suspicious of ESBL activity: such isolates identified to be positive in the screening test are tested by a confirmatory test by using the screening drug in combination with the beta-lactamase inhibitor such as clavulanate. The inhibition of ESBL by clavulanate and therefore the reduction in the resistance level to the cephalosporin is a positive confirmatory test. If an isolate is determined to be a confirmed ESBL producer the laboratory report indicates that all penicillins, cephalosporins, and aztreonam are resistant, even if the *in-vitro* test results indicate susceptibility to these agents. This is because the presence of an ESBL-producing organism in a clinical infection can result in treatment failure if one of the above classes of drugs is used. The beta-lactamase stable carbapenems (ertapenem, imipenem and meropenem) appear to be clinically effective against ESBL producers. The ESBL producing organisms are often linked to other resistance genes and are multiply resistant to other antibiotics. ESBL-positive isolates have been associated with nosocomial outbreaks and have also been isolated with increasing frequency from patients in extended care facilities. Some of the effective measures that have limited the spread of these resistant bacteria in a hospital setting include implementation of proper infection control practices, restriction of use of oxyziminocephalosporins, and antibiotic cycling. Since April, 2004 our laboratory has identified six ESBL-positive isolates from our patients; five of which were *E. coli* and one was *K. pneumoniae*. One *E. coli* and one *K. pneumoniae* were isolated from blood sample while the other four *E. coli* isolates were obtained from urine samples.
**Blood Culture:**

Blood cultures are obtained to diagnose blood stream infections due to microorganisms. The volume of blood that is obtained for each blood culture is the single most important variable in recovering microorganisms from patients with blood stream infections. The optimal volume of blood that should be obtained from infants and children is not well defined; however the available data suggest that a direct relationship exists between the volume of blood cultured and blood culture recovery rates. Studies have indicated that in children with symptoms of sepsis, low-level bacteremia (10 CFU/ml) occurred in 68% of infants up to 2 months of age and in 60% of children from birth to 15 years of age indicating the need for increasing the volume of blood inoculated into the bottle. Clinical studies have also shown that two to four blood cultures within a 24 hour time period are necessary not only to optimize detection of bacteremia and fungemia but also help to decide the significance of an isolate. Certain species of bacteria such as coagulase negative *Staphylococcus* spp, *Bacillus* (not *B. anthracis*) spp, *Corynebacterium*, Propionibacterium, viridans group *Streptococci*, *Aerococcus*, *Micrococcus* spp., and many others are usually considered a contaminant when isolated from only one blood culture.

Our laboratory employs an automated blood culture incubation system to diagnose blood stream infections. The blood culture bottles are incubated for a total of five days before they are resulted as negative. The figure below shows the different types of pathogens that were isolated in our hospital in the year 2004. The most common microorganisms encountered in the descending order is gram positive bacteria, gram negative bacteria, yeast, anaerobes and mycobacterium. *Staphylococcus* spp is the predominant gram positive organism isolated from blood culture and accounts for nearly 2/3 of the significant gram positive infections, followed by *Enterococcus* spp. Among gram negatives *E. coli*, *Klebsiella* and *Enterobacter* spp are almost equally distributed and together constitute half of all the significant clinical isolates.

![Blood culture 2004](image)

**CME Series**

**Sponsored by Department of Pathology & Laboratory Medicine**

**Date:** Tuesday, January 17, 2006

**Time:** Noon – 13:00

**Location:** Lab Conference Room 2206.10 WT

**Speaker:** Charles Roberts, MD

**Topic:** “The Medical Therapy of IBD”