

Anaerobe 2010

The 10th Biennial Congress of the
Anaerobe Society of the Americas

Philadelphia, PA USA • July 7-10, 2010

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CLINICAL ASPECTS OF ANAEROBIC INFECTIONS

ANTIBIOTIC DEVELOPMENT: ANYTHING NEW FOR ANAEROBES?

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For the past 10 years attention has focused on the problem of MRSA, ESBLs and KPCs and except for *C. difficile* Infection, very few manufacturers have focused on new agents for anaerobes. Studies of anti-anaerobic activity have mostly been for “added” information.

Ceftaroline, a cephalosporin with MRSA activity has MIC₉₀s of ≥ 64 ug/ml for *B. fragilis*, *B. thetaiotaomicron* and other *Bacteroides* spp. is ≥ 64 ug/ml but good activity (MIC₉₀ ≤ 0.5 ug/ml) vs. *P. asaccharolytica*, *F. nucleatum*, *F. necrophorum*, *F. varium*, and *Veillonella* sp. but not *P. melaninogenica*, *P. buccae*, or *F. mortiferum*. It was active against most gram positive species (MIC₉₀ ≤ 1 ug/ml) including *Actinomyces* sp., gram-positive cocci (except *P. anaerobius-stomatis*) *Propionibacterium* sp., *C. perfringens* and *C. ramosum* but not *C. clostridioforme* and *C. innocuum* (MIC₉₀s 2 ug/ml). **Ceftobiprole**, a similar pyrrolidone cephalosporin with MRSA activity also had similar anti-anaerobic activity as ceftaroline with poor activity against *B. fragilis* and other *Bacteroides* spp. (MIC₉₀ 32- ≥ 128 ug/ml) but was active against most gram-positive cocci, as well as both β -lactamase-positive and β -lactamase-negative strains of *F. nucleatum*. **RWJ 54428** a cephalosporin derivative had modest activity vs. *B. fragilis* (MIC₉₀ 32 ug/ml) and *B. fragilis* group species (MIC₉₀ ≥ 64 ug/ml). The activity of **CXA-101** an antipseudomonal cephalosporin, BMS-247243, and S-3578, vs. anaerobes has not yet been reported. **Tomopenem** (CS-023) has been shown to have similar anti-anaerobic activity to meropenem and doripenem with MIC₉₀ of ≤ 4 ug/ml to *B. fragilis* and *B. thetaiotaomicron*. Against 293 clinical isolates the MIC₉₀s were 0.06- 4 ug/ml. **Razupenem** (SMP-601, PTZ601), another carbapenem with MRSA and ESBL activity is affected by AmpC and carbapenemase enzymes. **LK-157** is a tricyclic carbapenem which is “a potent beta-lactamase inhibitor, combining activity against class A and class C beta-lactamases” but its activity against anaerobes has not yet been reported. **NXL 104** is a beta-lactamase inhibitor with potent activity against class A, including ESBLs and carbapenemases, and class C enzymes. Tested in combination with ceftazidime it had a MIC₉₀ of 16 ug/ml vs *B. fragilis* and *B. ovatus* but MIC₉₀ of ≥ 128 ug/ml vs *B. thetaiotaomicron* and *B. vulgatus*. Against beta-lactamase producing strains of *Prevotella* spp. and *Porphyromonas* spp. its MIC₉₀ was 4 ug/ml.

While no new classes of agents have been developed against anaerobes, there are a variety of agents with variable degrees of anaerobic activity that may have specific clinical utility in the future.

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FUSOBACTERIUM NECROPHORUM IN PHARYNGITIS

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Traditional teaching for pharyngitis focuses on group A beta hemolytic streptococcal pharyngitis. Recent observations suggest that *Fusobacterium necrophorum* causes as much pharyngitis as group A strep in adolescents. Since the main rationale for pharyngitis antibiotic treatment stems from a goal of preventing complications, the observation that an organism that can cause a devastating suppurative complication (the Lemierre syndrome) causes endemic adolescent pharyngitis should change our diagnostic and treatment strategies for these patients.

While we have limited data on the epidemiology of this infection, we can use simulation to compare the risks of *Fusobacterium pharyngitis* with strep pharyngitis. In our initial analyses, we find that *Fusobacterium pharyngitis* may put adolescents at a greater risk for adverse outcomes than does group A strep pharyngitis.

We need more data on this infection. Future studies must confirm incidence estimates and examine the clinical presentation of this newly recognized cause of bacterial pharyngitis. The difficulty of growing this organism from throat swabs provides a short-term research challenge and a long-term diagnostic challenge.

In this talk, I will provide the evidence that we should invest resources to better describe this infection and develop methods for making this diagnosis.

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MULTI-DRUG-RESISTANT *BACTEROIDES FRAGILIS* RECOVERED FROM BLOOD AND SEVERE LEG WOUNDS CAUSED BY AN IED IN AFGHANISTAN

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Case: We present the case of a 23 year-old otherwise healthy male that was injured in an improvised explosive device (IED) blast in OEF. He sustained multiple injuries to include bilateral open tibia and fibula fractures. In addition, the vehicle he was riding in rolled into a local stream thought to be polluted with sewage. By the time he received tertiary care his wounds were noted to be foul smelling. Meropenem was initiated and the patient underwent a right below-the-knee amputation and a left-sided external fixation. Despite ongoing carbapenem therapy, the patient's wounds were repeatedly noted to be purulent during serial debridement and cultures were notable for recurrent *Bacteroides fragilis* growth. Surprisingly, clinical failure persisted despite the addition of metronidazole to his regimen and despite eventual transition to tigecycline therapy.

Susceptibility testing of his *Bacteroides fragilis* isolate was arranged and resistance to penicillin, clindamycin, metronidazole, cefoxitin, meropenem, imipenem, piperacillin with tazobactam, and tigecycline was confirmed. The presence of carbapenemase gene expression and efflux pumps was also confirmed after additional genetic testing. The only antibiotics that displayed *in vitro* susceptibility were moxifloxacin and linezolid. These antibiotics were initiated in combination with aggressive irrigation and serial debridement. With these interventions, left-sided internal fixation was eventually completed and his limb was salvaged without residual evidence of infection. The patient completed an eight week course of combination moxifloxacin and linezolid therapy without adverse event.

Conclusion: This patient's *Bacteroides fragilis* isolate displayed simultaneous resistance to multiple antibiotics routinely utilized in anaerobic infections. This was evidenced by clinical failure, *in vitro* susceptibility testing, and demonstration of genes associated with resistance mechanisms. This case warrants reporting not only due to the rarity of this event, but also the potential implications regarding anaerobic infections in soldiers returning from theater as well as the success of a novel treatment regimen utilizing combination therapy with moxifloxacin and linezolid.

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THE DUTCH APPROACH TO ANTIMICROBIAL RESISTANCE CONTAINMENT

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The Dutch Working group on Antibiotic Policy, known as SWAB (Stichting Werkgroep Antibiotica Beleid) is in the Netherlands the equivalent of the Intersectoral Coordinating Mechanisms (ICM's), recommended by the European Union (2001), to control emerging antimicrobial resistance and promote rational antibiotic use. SWAB's mission is: "To manage, limit and prevent the emergence of resistance to antimicrobial agents among medically important species of micro-organisms in the Netherlands, thereby contributing to the quality of care".

Major initiatives of SWAB are training programmes for rational antibiotic prescribing, development of evidence based prescription guidelines, implementation of tailor made hospital guides for antibiotic treatment and prophylaxis and a surveillance system for antibiotic use and antimicrobial resistance. SWAB's work is made possible by structural funding by the Dutch Centre for Infectious Diseases Control (Centrum voor Infectieziektenbestrijding, CIb) in The National Institute of Public Health and the Environment (RIVM).

The results of continuous surveillance and of prevalence studies on resistance and antimicrobial drug use are published annually by SWAB in NethMap(www.swab.nl). NethMap parallels the system of monitoring antibiotic resistance and usage in animals in the Netherlands, called MARAN, by the Veterinary Antibiotic Usage and Resistance Surveillance Working group (VANTURES, see (www.cidc-lelystad.nl)). NethMap and MARAN provide a comprehensive overview of antibiotic use in the Netherlands in man and in animal husbandry and therefore offer insight in the ecological pressure associated with emerging resistance.

Both SWAB and its veterinary counterpart are represented in an interdepartmental working group of the ministries of health (VWS) and agriculture (LNV), in which the evolution of antibiotic use and resistance in the Netherlands is discussed. NethMap is thus providing insight in the Dutch state of medically important antimicrobial resistance, and compares well with the data of the European Antimicrobial Resistance Surveillance System (EARSS, (www.earss.rivm.nl)). EARSS collects resistance data of invasive bacterial species for the majority of European countries (including the Netherlands), Israël and Turkey.

During the 10th Biennial Congress of the Anaerobe Society of the Americas the most recent data from the surveillance studies by SWAB, MARAN and EARSS will be discussed in their interrelationship.

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CLOSTRIDIUM SPP. IN STOOL SAMPLES OF AUTISTIC CHILDREN

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Autistic behavior is often accompanied by numerous symptoms on the part of gastrointestinal system connected with deregulation of physiological flora. The aim of this study was to characterize strains of *Clostridium* spp. isolated from the stools of autistic children compared with healthy children. Fifty one stool samples were evaluated for this study, obtained from 41 autistic children (32 boys and 9 girls) aged 3 to 18 years and 10 healthy same aged children. After mixing, each stool sample was divided into two parts. Tests for the presence *Clostridium difficile* toxins A & B, *C. perfringens* enterotoxin, IBD Scan (TechLab, Blacksburg, VA, USA) and for *Helicobacter pylori* antigen (HpS, MERIDAN BIOSCIENCE, USA) were performed directly on one half. Each other part after heat shock was cultured onto CBA and Reinforced Clostridial agar (RC), and incubated in anaerobic conditions. All Gram-positive anaerobic bacilli were isolated and identified with use of ANC cards in VITEK 2 compact (bioMérieux, France).

Neither A and B toxins of *C. difficile* nor *H. pylori* antigen were found in evaluated material. Massive growth of anaerobic bacilli was observed in cultures from the stool of autistic children compared with cultures of healthy children. *C. perfringens* strains were cultured from the stool of 30 autistic children (73.2%), while in the control group only in stools from two children (20%). The difference was statistically significant ($p=0.0032$).

We concluded, that *Clostridium* spp. bacilli can be isolated with similar frequency from the stools of autistic and healthy children (85.4% and 90% respectively). The quantitative and qualitative differences include growth character and presence of different species. *C. perfringens* strains were observed significantly more often in the stools of autistic children, when compared to the group of healthy children. Among autistic children *C. perfringens* is more often identified in boys than in girls (90.6% and 66.7%). Differences in the biochemical profile of *C. perfringens* strains isolated from the stools of autistic children, compared to the strains isolated from the stools of healthy children as well as the reference strain, pertained mainly cleavage of arginine and d-xylose.

This study was supported by Polish Ministry of Research and Information Technology Grant Nr 40404132/0949.

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ANTIBACTERIAL ACTIVITY OF TIGECYCLINE IN SERUM AGAINST ANAEROBES ASSOCIATED WITH DIABETIC FOOT INFECTIONS

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Tigecycline (Tig) is a broad-spectrum glycylcycline antibiotic that includes activity against gram-positive and gram-negative anaerobic bacteria (Goldstein, et al. *Antimicrob Agents Chemother* 2006; 50: 3507). To gain data concerning the anti-anaerobic activity of Tig in serum, multiple blood samples were obtained from 6 patients with a complicated skin/soft tissue infection (cSSTI) being treated with Tig 50 mg q12h. Blood samples were obtained at 1, 6, and 12h after the initiation of a 1h infusion. Sera were assayed for Tig concentrations by a validated HPLC assay and tested against 4 anaerobes associated with diabetic foot infection. CLSI methodology was followed to determine MICs, serum inhibitory (SIC) and bactericidal (SBC) concentrations for these strains. SIC and SBCs were performed by diluting test sera two-fold in pooled normal human serum in microtiter plates and then adding test strains suspended in supplemented Brucella broth for a final concentration of $\sim 10^6$ cfu/mL. After anaerobic incubation at 36 °C for 48h, wells were quantitatively subcultured to supplemented Brucella agar and incubated for 48h. The SIC and SBC titers were the inverse of the dilution that showed growth inhibition and a 99.9% reduction of the inoculum concentration, respectively. The Tig serum C_{max} was 0.58 ± 0.32 mg/L and the C_{trough} was 0.24 ± 0.14 mg/L in these patients. Tig exhibited early (1h) and prolonged inhibitory (12h) and bactericidal (12h) activity against isolates of *Bacteroides fragilis* (Tig MIC = 0.5 mg/L), *Prevotella bivia* (Tig MIC = 0.5 mg/L), and *Peptoniphilus asaccharolyticus* (Tig MIC = 0.25 mg/L). Tig also provided prolonged (12h) inhibitory but not bactericidal activity against *Finnegoldia magna* (Tig MIC = 0.5 mg/L). In this study, we found that Tig exhibits antibacterial activity in serum to a greater degree than predicted from its serum concentrations against these anaerobic bacteria.

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***CLOSTRIDIUM SEPTICUM* BACTEREMIA FOLLOWING HEMOLYTIC UREMIC SYNDROME: A CASE REPORT AND REVIEW OF THE LITERATURE**

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Background. *Clostridium septicum* infection following hemolytic uremic syndrome is a rare phenomenon that carries a poor prognosis. The purpose of this report is to describe the clinical and autopsy findings of a case involving a previously healthy 2-year-old male with the clinical diagnosis of hemolytic uremic syndrome; the patient's course was complicated by the development of *C. septicum* sepsis with dissemination of the bacteria to multiple distant organs.

Case Presentation. The child presented to the local children's hospital with one-to-two days of anuria and bloody diarrhea. A clinical diagnosis of hemolytic uremic syndrome was made, presumably secondary to a gastrointestinal illness caused by *Escherichia coli* O157, but never confirmed. His laboratory studies showed leukocytosis, hemolysis, renal failure and thrombocytopenia. Eleven hours after admission, he required intubation and was noted to have fixed and dilated pupils. Head CT revealed pneumocephalus, left-to-right midline shift and uncal herniation. Neurosurgical consultation advised that no intervention was possible. The patient expired 14 hours after admission. Ante-mortem blood cultures grew *Clostridium septicum*. Autopsy examination revealed pneumatosis of the abdominal viscera, as well as necrotizing colitis involving the distal sigmoid colon with patchy involvement of the proximal right colon. Microscopic examination revealed hemorrhage and extensive necrosis of the bowel wall, as well as invasion of the devitalized tissue by bacilliform organisms with minimal inflammatory response. Bacteria were also seen in the brain, lungs, liver and kidneys, also with little or no associated inflammation. In addition, the kidneys showed extensive occlusion of the glomerular capillaries by fibrin and red blood cell thrombi, consistent with hemolytic uremic syndrome.

Discussion. There have been only six previously reported cases of *C. septicum* infection following hemolytic uremic syndrome: four with brain involvement, one with myonecrosis, and one with sepsis and abdominal fasciitis. Injured ischemic colonic epithelium is the likely portal of entry of *C. septicum* in these children, and the mechanism of spread to distant sites appears to be hematogenous. The mortality rate is high at 67 percent, with only two known survivors.

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INCREASE IN DIAGNOSIS OF LEMIERRE SYNDROME AT A LARGE PEDIATRIC REFERRAL CENTER

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Lemierre Syndrome (LS) is a disease characterized by bacteremia due to *Fusobacterium*, thrombosis of a large venous vessel in the neck, with septic embolization. We have noticed a sharp increase in LS at our hospital, beginning in November of 2006.

Purpose: (1) Confirm the sharp rise of LS cases noted at a large pediatric referral center, (2) Identify additional clinical features to aid in the diagnosis of LS.

Summary of methods and results: In order to explore this phenomenon, a chart review was conducted on all patients with a diagnosis of LS or *Fusobacterium* bacteremia since 1986.

Sixteen cases of LS were identified between 1986 and 2009. Only one case was diagnosed between 1986 and 2005, while 15 cases were identified between 2006 and 2009. 14/16 of the cases had a neck thrombosis identified. 12/16 cases had evidence of pulmonary thrombosis. 10/16 cases had thrombocytopenia. 12/16 cases were treated with anticoagulation therapy. 10/16 cases had bacteremia, including 7 with *Fusobacterium*. None of the bacteremic patients were treated with antibiotics ≥ 12 hours before blood culture; however, of the six non-bacteremic LS patients, five had received antibiotics \geq two days.

Conclusion: We have noted a sharp rise in LS since 2006. While this may in part be due to increased recognition, the documented rise in *Fusobacterium* bacteremia suggests a true increase. In several patients where LS was not initially suspected, *Fusobacterium* bacteremia prompted further studies that established the diagnosis. Prior antibiotic therapy, may mask bacteremia making LS more difficult to diagnose. The presence of thrombocytopenia, which was observed in 10/16 cases suggests this finding may be useful in identifying patients with LS.

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PREDISPOSING AND BACTERIOLOGICAL FEATURES OF OTITIS MEDIA

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Otitis media is an infectious condition and is more frequent in children. Its management is complex as the etiologies vary as the disease progresses. A delineation of the clinical conditions with associated microbial involvement became imperative in determining the appropriate therapeutic options. Three hundred and seventy eight patients diagnosed; comprising acute otitis media (AOM) 111, otitis media with effusion (OME) 122, and chronic otitis media (COM) 145 ear samples were screened by culture for bacterial etiology. Pre-school age children (< 5yr) accounted for 46% of cases of otitis media of all three clinical conditions and incidence was more in the wet months (May-October). Unilateral infection which was more common (82%) was predominantly in the left ear (66.8%). Major predisposing factors to infection were age (19.8%), upper respiratory infection (14.8%), poor hygiene and unorthodox practices (14.8%), adenoid inflammation and trauma (8.5% and 6.1% respectively). *Streptococcus pneumoniae* (38.1%), *Peptostreptococcus magnus* (9.5%) *Fusobacterium necrophorum* and *Clostridium perfringens* (< 3.0% each) characterized AOM. A paradigm shift was observed in OME, with *Staphylococcus aureus* (19.1%) and *Bacteroides ureolyticus* (14.9%) dominating the flora. Other *Bacteroides* spp and *Prevotella* accounted for between 7% and 12% of cases. The etiologies in COM were more complex with mixed aerobic-anaerobic component of 68.3%; predominant flora being *Pseudomonas aeruginosa* (14.1%) and *P. magnus* (13.4%). The paradigm-shift is instructive in deciding the line of antibiotic therapy to be instituted.

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ABNORMAL FECAL FLORA IN AUTISTIC CHILDREN WITH GASTROINTESTINAL SYMPTOMS

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In our initial publication on autism with Sandler RH as the first author (J Child Neurol 2000;15:429-435), we noted that 8 of 10 autistic children treated with oral vancomycin and evaluated by a clinical psychologist's blinded review of coded, paired videotapes showed improvement in communication, behavior, cognition and gastrointestinal symptoms. In a subsequent study (Clin Infect Dis 2002;35 (Suppl 1):S6-16) we studied the fecal flora of 13 autistic children and 8 control children by cultural techniques. We noted increased numbers of clostridial species in the autistic group. 7 autistic children were endoscoped and it was notable that 5 of these had no or virtually no nonsporeforming anaerobes or microaerophilic organisms present in the stomach or duodenum. The other two had abnormally high gastric pH (of unknown origin; they were not on any drugs to account for this) and these subjects had many nonsporing anaerobes and microaerophiles in relatively high counts. These two children plus two others also had clostridia of several species. Four control children had no nonsporing anaerobes or microaerophilic bacteria present in the stomach or duodenum; all had normal pH.

Subsequently, we (Song Y et al., Appl Environ Microbiol 2004; 70:6459-6465) studied stool specimens from 15 autistic children and 8 control children by real-time PCR quantitation. *Clostridium bolteae* and clostridia of clusters I and XI, but not XIVab, showed significantly higher counts in autistic children than in controls. Parracho et al. (J Med Microbiol 2005; 54:987-991) studied the fecal flora of autistic children and controls using fluorescent in situ hybridization and found a higher incidence of *Clostridium* clusters I and II in autistic children than in normal controls, and an intermediate level in siblings of autistic children.

In collaboration with Drs. Scot Dowd, John Green, Doreen Granpeesheh and others, we have studied the fecal flora of 33 children with autism and gastrointestinal symptoms, 7 sibling controls without symptoms of autism, and 8 non-sibling controls, using pyrosequencing with titanium enhancement. This powerful molecular tool showed significant differences in the microflora of these groups. The principal difference was in the two most prevalent phyla of intestinal bacteria, *Bacteroidetes* and *Firmicutes*. *Bacteroidetes* was found at high levels in the autistic group whereas *Firmicutes* was high in the control group.

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GENOTYPING OF *PROPIONIBACTERIUM ACNES* STRAINS ISOLATED FROM PATIENTS WITH ACNE VULGARIS AND INVESTIGATION OF RELATIONSHIP BETWEEN GENOTYPE AND ACNE SEVERITY

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Propionibacterium acnes, a member of skin flora, is the most commonly encountered microorganism in acne vulgaris, and can be found in various systemic or disseminated opportunistic infections. Although three genotypes of *Propionibacterium acnes* (types I [Type IA and Type IB], II and III) have been described, there are few epidemiological investigations of their roles in different infections and have not been widely reported. Current study focuses on the relationship between the genotype of *Propionibacterium acnes* and the severity of acne vulgaris. Fifty-eight patients (36 females and 22 males) who attempt to Marmara University Hospital, Department of Dermatology and 62 healthy people (43 females and 19 males) as controls were enrolled in the study. The number of lesions of facial acne, defined as comedones, papules, pustules, nodules and erythema, was recorded and was given a score according to Global Acne Grading System (GAGs). The samples obtained from the acne lesions and from facial skin of control group were cultured in aerobic and anaerobic conditions. *Propionibacterium acnes* was isolated from all patients and control group and identified by conventional methods, and genotypic analysis was made by PCR using specific primers to genotypes. A total of 89 isolates (n:47 patient, n:42 control) showed genotype IA PCR bands, followed by type IB (n:5 patient, n:8 control) and type II (n:4 patient, n:7 control). No type III *P. acnes* has been detected. No significant correlation existed between the genotype of *P. acnes* and severity score of acne lesions. Although the findings did not link *P. acnes* genotype to severity of acnes, the present study did form a database about genotypes of *P. acnes* in Turkey, where molecular investigation of *P. acnes* genotypes has not been performed so far. Our data will be useful for the next study to examine phenotypic properties of these different genotypic *P. acnes* and investigate relationship between acne severities.

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BACTERIAL AETIOLOGY OF DIABETIC FOOT INFECTIONS IN HUNGARY

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Objectives: Diabetic foot ulcer is one of the major complications of diabetes mellitus. Major increase in mortality among diabetic patients observed over the past years is considered to be due to the development of vascular complications, including failure of the wound healing process. Foot infections are frequent complications of these patients, accounting for up to 20% of diabetes-related hospital admissions. Infectious agents are associated with the worst outcomes, which may ultimately lead to amputation of the infected foot, unless prompt treatment strategies are ensued. The present study sought to reveal bacterial etiology of diabetic foot ulcers in diabetic patients of our region.

Methods: A retrospective review of clinical and microbiological data of 139 diabetic patients suffered from moderate-to-severe diabetic foot infections (DFIs), including out- and inpatients in the special wards of our University was carried out over a 5-year period. After debridement, investigators collected wound specimens, mostly by curettage or biopsy, and sent them to the Hungarian Anaerobic Reference Laboratory for aerobic and anaerobic culture.

Results: All of the samples were culture positive, only anaerobic bacteria were present in 34 samples (24.5%). Among the cultures, 97 % were polymicrobial, 2 grew only one microorganism: *C. perfringens* and *C. septicum* in pure culture, 43.7% had both aerobes and anaerobes. A total of 832 bacterial strains were isolated, resulting in an average of 5.98 organisms (range 1 to 21) per lesion: 619 anaerobic-, and 209 aerobic- or facultative bacteria and 4 yeasts were isolated. The predominant aerobic organisms were oxacillin-susceptible *S. aureus* (31.7%), beta-haemolytic (mostly group B) *Streptococcus* species (12.2%), *Enterococcus* species (16.7%), members of the family *Enterobacteriaceae*: *E. coli*, *Proteus*, *Klebsiella*, *Enterobacter*, *Serratia*, *Citrobacter* (52.3%), and *P. aeruginosa* (15.8%). The predominant anaerobes were Gram-positive cocci: 103 isolates, *Prevotella* species: 198 isolates, *Clostridium* species: 50 isolates, and the members of the *Bacteroides fragilis* group: 41 isolates.

Conclusion: Clinical grading and bacteriological study of 139 patients with diabetic foot lesions revealed polymicrobial aetiology. Our findings showed that the density of growth of anaerobes and the number of the isolated anaerobic species were significantly higher than that in previous studies, due to good anaerobe laboratory practice and the adequate sampling.

Anaerobe 2010

The 10th Biennial Congress of the
Anaerobe Society of the Americas

Philadelphia, PA USA • July 7-10, 2010

CLINICAL ASPECTS OF ANAEROBIC INFECTIONS

BACTEREMIA CAUSED BY *CLOSTRIDIUM SORDELLII*: A CASE REPORT AND A REVIEW OF THE LITERATURE

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Purpose: Bacteremia caused by *C. sordellii* has been very rare. Since we had encountered a case of bacteremia in patient with ovarian cancer, we report our case and add the bibliographical consideration based on 16 reported documents for *C. sordellii* bacteremia.

Case: An 84-year-old woman with ovarian cancer and multiple metastasis to liver, spleen, lung, and intrapelvic cavity admitted to our hospital because of severe abdominal pain. Since serum C-reactive protein (CRP) was significantly increased at the level of 41.11 mg/dL, the patient was initially treated with injectable cephalosporin, cefotiam. On the 2nd day after admission, blood culture examination showed positive for Gram-positive bacilli with spores accompanied with gas production, which suspected *Clostridium* species. The microorganism was finally identified as *Clostridium sordellii* using biochemical and molecular-based identification. We changed antimicrobial chemotherapeutic regimen from cefotiam to the combination therapy by tazobactam/piperacillin (2.5g x4/day), meropenem (0.5g x4/day) and clindamycin (600mg x4/day). After induction of new regimen based on bacterial examination, infectious signs and laboratory findings had gradually improved. At the 4th day after admission, blood culture examination showed negative. Since renal dysfunction appeared because of progressive ovarian cancer, we de-escalated the antimicrobial chemotherapy regimen from 3 antimicrobial agents to 2 antimicrobial agents, tazobactam/piperacillin (2.5g x4/day) and clindamycin (600mg x2/day). However, she died on the 19th day after admission because of multiple organ failure for ovarian cancer, although infection control for *C. sordellii* bacteremia had been well.

Conclusion: *C. sordellii* produce several exotoxins (lethal toxin, haemorrhagic toxin, etc.), which lead to progressive edema and shock in humans. *C. sordellii* bacteremia had led to high mortality, and the mortality rate was 62.5% among 16 reported documents for *C. sordellii* bacteremia. Although *C. sordellii* infection have not showed specific signs and symptoms, early diagnosis would be difficult in clinical practice. However, early, adequate, and aggressive antimicrobial therapy including combination therapy would lead to decrease the high mortality when suspected *C. sordellii* infection in clinical practice.