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FIVE-YEAR RETROSPECTIVE EPIDEMIOLOGICAL SURVEY OF ANAEROBIC BACTERAEMIA IN A UNIVERSITY HOSPITAL AND REVIEW OF THE LITERATURE

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In spite of the developments in microbiological methods, blood cultures remain the cornerstone for the diagnosis of bacteraemia. Classically, minimum of two bottles are collected on a routine basis: an aerobic bottle, allowing preferential growth of aerobic and facultative anaerobic microorganisms, and an anaerobic bottle, providing suitable environment for strict anaerobic bacteria. Recent reports have documented a decrease in anaerobic bacteraemias and have questioned the need for routine anaerobic blood cultures. Bacteraemia due to anaerobic organisms occurs in 0.5–12% of blood cultures worldwide; however, recent studies from Europe and the USA presented inconsistent data regarding the prevalence of anaerobic bacteraemias between 1993 and 2006.

The aims of this retrospective survey were to determine the prevalence of bacteraemias due to anaerobic bacteria and evaluate the importance of anaerobic blood cultures in a university hospital in Szeged, Hungary. We examined the occurrence of bacteraemias due to anaerobic bacteria during a 5-year period, from January 2005 to 2009, in order to identify current trends of anaerobic bacteraemias in our university.

Keywords: blood culture, anaerobes, anaerobic bacteraemia and prevalence, antibiotic resistance

Introduction

Blood culture is a frequently used laboratory test to check for bacteria or other microorganisms in a blood sample; thus, blood cultures are often included in the assessment of a febrile, hospitalized patient. It is common practice in some institutions to inoculate both aerobic and anaerobic media when blood is obtained from the patient for culture. Because of the increasing frequency of aerobic bloodborne infections since the early 1980s, and the declining incidence of anaerobic bloodstream infections, some investigators have advocated selective rather than routine use of anaerobic blood cultures. Thirty years ago, anaerobes accounted for 20–30% of isolations from blood cultures [1, 2]. However, in the 1990th the incidence was lowered to approximately 4% (0.5–12%) of all cases of bacteraemias (or approximately one case per 1000 admissions), with variation by geographic location, hospital patient demographics, and especially, patient age [3–7]. Hence, blood culture sets have consisted almost universally of both aerobic and anaerobic culture media. Today, however, largely owing to surgical prophylaxis and improvements in blood culture technology, anaerobes account for only a small percentage of significant isolates [8–13]. The question is whether the custom and practice of 30 years ago are appropriate today. Because selective use of anaerobic blood cultures would represent a more cost-effective approach to the laboratory evaluation of a potentially infected individual, we decided to evaluate the utility of routine anaerobic blood culture in an adult inpatient population cared for in a big university hospital in Hungary.

Materials and methods

University of Szeged is a 1200-bed, university-affiliated, primary and tertiary care teaching hospital, serving an urban and rural population about of 440,000 people. The university has four intensive care units with different profiles: cardiology–haematology, surgery, and traumatology. Clinical data of patients included in this survey were retrieved from medical records. In the case of febrile patients, two bottles were routinely collected for blood culture: an aerobic bottle, enabling preferential growth of aerobic and facultative anaerobic microorganisms, and an anaerobic bottle, providing preferential growth of strict anaerobic bacteria. All blood culture bottles were placed in a BD Bactec Instrumented blood culture system (Becton Dickinson, US) at 37°C, incubated for 5 days and for 21 days for suspected cases of endocarditis and monitored in accordance with the manufacturer's instructions. Positive bottles were detected by the continuous monitoring

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system and were examined using standard laboratory methods. The significance of isolates was determined through liaison between a medical microbiologist and the clinical team involved in the management of the patient at the time of the first detection of positivity. Positive anaerobic bottle samples were plated on Columbia agar base (Oxoid, Basingstoke, United Kingdom) supplemented with 5% (*v/v*) cattle blood, haemin, and vitamin K_1. For the isolation of anaerobic organisms, cultures were set up and incubated in an atmosphere of 90% N_2, 5% H_2, and 5% CO_2 in an anaerobic chamber (Bactron Sheldon Man, Cornelius, Oregon, USA) for at least 2 days at 37°C, and bacterial identification was performed according to the Wadsworth-KTL Anaerobic Bacteriology Manual and the API 32A kit (bioMérieux, Lyon, France).

A comparison of characteristics was made only between patients with clinically significant bacteraemia (excluding *Propionibacterium acnes*). The chi-square test was used for categorical variables; $P < 0.05$ was regarded as statistically significant.

Results

A total of 43,992 blood cultures were submitted to the laboratory in this studied 5-year period. From those, only 305 (0.69%) strict anaerobic isolates were detected. The number of positive anaerobic blood culture result per 1000 blood cultures performed decreased from 8.74% to 5.36% between 2005 and 2009. *Table 1* shows the prevalence of anaerobic isolates of Gram-negative bacilli, Gram-positive bacilli, and Gram-positive cocci. *P. acnes* accounted for 57.7% of isolates (reported mainly as contaminants because of the long detection time), followed by *Clostridium* spp. (12.8%), *B. fragilis* group spp. (8.9%), anaerobic Gram-positive cocci (5.9%), and *Fusobacterium* spp. (3%). Only in the case of eight patients, multiple bacteraemia caused by mixed anaerobic organisms could be observed. During this period, the proportion of isolated anaerobic species compared to the number of all organisms isolated from blood cultures declined from 6.3% to 4.0%. Similar to the decrease in the number of anaerobic isolates, the number of patients with anaerobic bacteraemia decreased from 69 patients to 44 patients. The most common risk factors for bacteraemia were gastrointestinal surgery and active haematological malignancies with chemotherapy *(Table 2)*. The lower gastrointestinal tract and the oropharynx were the two most frequent presumed or proven sources for relevant bacteraemia. Factors that were considered related to bad prognosis are the following: statistical admission to medical areas, rapid and finally fatal underlying disease, presence of septic shock, renal failure, inappropriate antimicrobial treatment, and the absence of drainage for the septic foci. Fatal outcome correlated with the severity of underlying diseases and the immunosuppressed status of the patients rather than with the causative pathogen or the effectiveness of antimicrobial therapy. The mean age of our patients was 60 years (range: 31–84 years), and 58% were male. The mortality rate for these patients was 22.3%. Twenty-two percent of these patients with anaerobic bloodstream infections came from haematological–oncological departments, 19.2% had cardiovascular disease, and 8.5% had diabetes, suggesting that patients who were infected with anaerobic bacteria tended to have multiple comorbidities. In addition, 13.9% of patients had a past or current history of pneumonia, 25% had gastrointestinal disorders, and 7.4% were undergoing hemodialysis. Underlying gastrointestinal tract disease, pneumonia, malignancy, and multiple disorders were associated with clinically significant bacteraemia ($P = 0.003$, $P = 0.001$, $P = 0.002$, and $P \leq 0.001$, respectively) were associated with bacteraemia. Only 9% of patients had none of the before mentioned risk factors.

Discussion and review of literature

The aims of this study were to determine the prevalence of bacteraemias due to anaerobic bacteria and evaluate the importance of anaerobic blood cultures in a university hospital in Szeged, Hungary. A retrospective survey focused on anaerobic blood culture bottles was performed on blood cultures received in our laboratory from January 2005 to December 2009. Although anaerobic bacteria remain an important cause of bloodstream infections, the prevalence in this period was much lower than the data reported in the literature previously.

The majority of anaerobic bacteraemias are due to Gram-positive bacilli, mostly *Clostridium* spp. Other species causing AB (anaerobic bacteraemia) include *Bacteroides fragilis* group, Gram-positive anaerobic cocci (GPAC), and *Fusobacterium* spp. In this report, we retrospectively analyzed the low proportion of anaerobes out of total blood cultures, and the distribution of different anaerobic bacteria isolated from positive anaerobic blood cultures in order to characterize their involvement in anaerobic blood cultures during a five-year period in a big Hungarian University Hospital. The frequency of anaerobic bacteraemias in our hospitals is much lower than that was suggested in several large studies during the 1990s, probably reflecting a real decline in the incidence. The clinical features of our cases are similar to those of previous studies, and the mortality is still high, despite the use of antibiotics effective against anaerobes. Since most patients were thought to have anaerobic infections at the time that cultures were obtained, they were usually treated empirically. Subsequent blood cultures positive for anaerobes infrequently influenced the clinical management; however, early recognition and appropriate treatment of these infections are of great clinical importance. Our patients with anaerobic bacteraemia had multiple underlying medical problems, which have not changed over the past years. At our University hospital in the South-East Hungary, the incidence of anaerobic bacteraemia is low, although we experience an increase in the number of infections with anaerobic bacteria.

There are probably multiple reasons behind the changes in anaerobic bacteraemias, possibly explaining the different observations in other studies [14, 15]. The re-emergence of anaerobic bacteraemias may depend on geographical region, antibiotic policies of the institution, and the case mix of the study population, including the frequencies of patient co-morbidities and immunosuppression. For now, routine anaerobic blood cultures should not be abandoned.

Number of different studies reported the recovery of anaerobes in patients with bacteraemia during the last decades; at the same time, conflicting data have accumulated regarding the incidence of anaerobic bacteraemias. Anaerobic organisms account for about 4% of bacteraemias (range, 0.5–9%) depending on geographic location, hospital patient demographics, and patient age. According to Dorsher et al., the incidence of anaerobic bacter-

Table 1. Number of anaerobic isolates from blood cultures between 2005 and 2009

Organism(s)	Species of anaerobes isolated from blood cultures between 2005 and 2009				
	2005	2006	2007	2008	2009
No. of anaerobic isolates	78	73	37	65	52
Gram-positive anaerobes					
Actinomyces meyeri	4				
Clostridium butyricum/tyrobutyricum		2		1	1
Clostridium septicum	1			2	
Clostridium innocuum	1				
Clostridium perfringens	1	6	1	7	6
Clostridium spp.	4		5	1	2
Eggerthella lenta		1		1	1
Lactobacillus sp.	1	6	1	2	2
Parviromonas micra	1	1		1	7
Peptoniphylus asacharolyticus	2	4			
Finegoldia magna				1	
Peptostreptococcus anaerobius				2	1
Anaerococcus prevotii				3	1
Propionibacterium propionicus/ granulosum	1		1		
Gram-negative anaerobes					
Bacteroides fragilis	2			8	4
Bacteroides thetaiotaomicron		1	2	2	1
Bacteroides caccae				2	
Bacteroides merdae					1
Fusobacterium necrophorum		1			
Fusobacterium nucleatum	2	2	3	1	
Prevotella denticola	1	1			
Prevotella melanonigenica					1
Prevotella oralis	1				
Prevotella buccae					3
Veillonella parvula	2	1	1		1
Propionibacterium acnes	53 (67.2%)	36 (49.3%)	23 (62.1%)	31 (47.7%)	28 (53.8%)

Table 2. Underlying diseases among patients with clinically relevant anaerobic bacteraemia (excluding *P. acnes*)

Characteristics	No. of patients					*P* value
	2005	2006	2007	2008	2009	
Total patients	19	18	10	28	19	
Male/Female	10/9	13/5	4/6	14/14	13/6	
Age (mean±SD)	57.58±26.4	60.3±18.2	49.2±11.3	66.6±8.3	66.6±9.7	
Anti-anaerobe treatment	8	5	3	12	7	NS
Mortality	3	5	1	8	4	0.003
Cardiovascular disease	5	6	1	4	1	NS
Diabetes (complicated)	3	1	2	1	1	NS
Renal failure	1	1	1	2	2	NS
Gastrointestinal disorders	1	4	2	6	6	0.003
Pneumonia	3	0	0	6	4	0.001
Malignancy	7	3	3	4	4	0.002
Neurological disease	2	2	0	2	0	NS
Sepsis	1	3	2	6	3	0.003
Multiple disorders	9	6	3	10	7	≤0.001

NS: not significant.

aemia from 1974 to 1988 at the Mayo Clinic (Rochester, MN) decreased by 45% [12]. In addition, the percentage of blood cultures positive for anaerobes decreased significantly even though the total number of blood cultures performed increased. The number of anaerobic bacteraemias per 100,000 patient-days also declined over this 15-year period. Organisms of the *Bacteroides fragilis* group ranked third in frequency with respect to other organisms that caused aerobic and anaerobic bacteraemia in 1974 but ranked only seventh in 1988 and caused slightly less than one-half of the anaerobic bacteraemias. The mechanisms responsible for these changes are unclear but might relate to earlier recognition and treatment of localized anaerobic infection, widespread preoperative use of agents prior to bowel surgery and use of broad-spectrum antimicrobial regimens that include agents with activity against anaerobes. Recently, a study from the same institution indicated the re-emergence of anaerobic bacteraemia from 1993 to 2004 [14]. Records from the Mayo Clinic Division of Clinical Microbiology were used to tabulate the number of cases of anaerobic bacteraemia in patients at the clinic for the 12-year period from 1993 through 2004. Medical records for patients with anaerobic bacteraemia were reviewed from these study periods: 1993–1994 and 2004, to identify differences between these two patient populations with different rates of bacteraemia. They found that the mean incidence of anaerobic bacteraemias increased from 53 cases per year during 1993–1996 to 75 cases per year during 1997–2000 to 91 cases per year during 2001–2004 (an overall increase of 74%). The total number of cases of anaerobic bacteraemia per 100,000 patient-days increased by 74%. The number of anaerobic blood cultures per 1000 cultures performed increased by 30%. Organisms from the *Bacteroides fragilis* group, other species of *Bacteroides*, and *Clostridium* species were most commonly isolated. *B. fragilis* group was recovered from 26% to 43%, other anaerobic Gram-negative bacteria and other *Bacteroides* spp. from 8% to 25%, GPAC from 35 to 20%, *Clostridium* spp. from 16% to 46%, non-spore forming Gram-positive bacteria from 4% to 18%, and *Prevotella* and *Porphyromonas* spp. from 2% to 10%.

In contrast, a report from another U.S. community hospital provided no evidence for an increase [15]. They reviewed their experience with anaerobic bacteraemia during 2000–2006 at St. Barnabas Hospital, a 450-bed community hospital in the Bronx, New York, US. This hospital serves a predominantly black and Hispanic community. It has medical, surgical, substance abuse, psychiatric, obstetrics, gynaecology, and neonatal units. There is an oncology service that accounts for <1% of admissions. There was no increase in the incidence of anaerobic bacteraemia from 2000 to 2006. The total number of positive blood culture results ranged from 1036 to 1454. Anaerobic organisms accounted for <2% of positive blood culture results (range: 0.7–1.3%). The number of positive anaerobic culture results per 1000 blood cultures performed was 0.73, which is much lower than the rate of 1.68 positive results per 1000 blood cultures that was reported by Lassmann et al. [14] for the period 1993–1996. *Bacteroides fragilis* accounted for 33% of anaerobes, followed

by *Peptostreptococcus* species (19%). The aetiology of infections was unknown in 42% of the cases. Thirty-two percent of cases had an abdominal or pelvic source, and 23.5% of cases involved soft-tissue infection.

Anaerobic bacteraemia was studied in 32 medical patients (mean age 72 years) in a four-year retrospective analysis by Kornowski et al. in 1993 [16]. Malignancy was the most common underlying disease and probable portal of entry. The gastrointestinal tract was affected most often, followed by the respiratory and urinary tracts. Bacteraemia occurred either following invasive (non-surgical) procedures or spontaneously. The clinical course ranged from asymptomatic bacteraemia, to mild febrile illness, to sepsis, and septic shock (2, 12, 16, and 2 patients, respectively). The case fatality rate was 25%. The causative organisms were *Clostridium* and *Bacteroides* species. All organisms isolated were susceptible to chloramphenicol. Their conclusion was that early diagnosis of AB and prompt treatment may reduce mortality in cases of anaerobic sepsis. The occurrence of anaerobic and aerobic bacteraemias at the University Hospital Basel (UHBS), Switzerland, was estimated, and the proportions of six important groups of anaerobes in relation to 1000 blood cultures as well as in relation to positive aerobic blood culture results over a 10-year period were analyzed [17]. The number of positive anaerobic blood culture results per 1000 blood cultures performed decreased from 12.6 in the period from 1997 to 2001 to 7.0 in the period from 2002 to 2006 ($P < 0.001$), as the proportion of isolated anaerobic organisms did, compared to the number of all organisms isolated from blood cultures (7.6–4.3%), while positive aerobic cultures remained stable. In contrast, the proportion of *Bacteroides fragilis* group members and Gram-positive anaerobic cocci (GPAC) within the anaerobic group increased (26.8–36.7% and 5.4–12%, respectively). The number of patients with anaerobic bacteraemia decreased from 122 patients in 1997 to 69 in 2006. Goldstein and Citron [18] determined the relative annual isolation rate of anaerobic bacteria and the susceptibility of *B. fragilis* group species isolated during 1987 at two community hospitals in Los Angeles, California, US. The relative frequencies of isolation of 261 strains were as follows: *B. fragilis*, 61%; *B. thetaiotaomicron*, 17%; *B. distasonis*, 7%; *B. vulgatus*, 6%; *B. ovatus*, 5%; and *B. uniformis*, 4%. They recovered eight (18%) *Clostridium* spp. and two (4%) *Fusobacterium* spp. One year later, Brook [19] published clinical and microbiologic data about 296 patients with anaerobic bacteraemia seen over 12 years in two military hospitals in Greater Washington DC area. A total of 212 *Bacteroides* spp. were isolated, *B. fragilis* accounted for 78% and *B. thetaiotaomicron* for 14% of the cases among other species; there were 20 (6%) *Fusobacterium* isolates, 63 (18%) *Clostridium* isolates, and 53 (15%) GPAC. The primary source of anaerobic bloodstream infections was the gastrointestinal tract (42%), decubiti and gangrene (10%), the female genital tract (8%), and the oropharynx (7%). The gastrointestinal tract, decubiti, and gangrene were the predominant sources for *B. fragilis* and *Clostridium* species, the female genital tract and oropharynx for anaerobic cocci and *Fusobacterium* spp., and the oropharynx for pigmented *Prevotella* and *Porphyromonas* spp. Predisposing factors to AB were the following: abscesses in the cases of 53; malignancy in 51; surgery in 30; and intestinal obstruction and/or perforation in 27.

Gransden et al. [20] recovered 250 anaerobic isolates between 1969 and 1990 in United Kingdom. There were 138 (55%) *B. fragilis* group isolates, 18 (12%) *Clostridium* spp., 20 (8%) *Peptostreptococcus* spp., and 18 (7%) *Fusobacterium* spp. Peraino et al. [21] reviewed data on episodes of anaerobic bacteraemia that have occurred in a 350-bed community hospital in Santa Monica, California, US. In 1991, 771 of 7397 blood cultures yielded bacteria or fungi; 569 (7.7%) were true positive cultures, and 35 (6.2%) of which yielded 48 anaerobic isolates from 20 patients. The data of these patients were reviewed, and it was determined that 16 of the patients had significant anaerobic bacteraemia. The outcome was fatal for seven (44%) of these 16 patients, including two who died before results were reported. The source of infection was obvious for 11 of the 16 patients, and 50% of patients were receiving antimicrobial agents active against anaerobes before culture results were obtained. Although anaerobic bacteraemia is uncommon in this hospital, their final conclusion was that positive culture results often resulted in a change in the antimicrobial therapy. Sixty-six patients at the University of Michigan Hospitals (UMH) and nine patients at the Ann Arbor Veteran's Administration Medical Center (US) were investigated by Lombardi and Engleberg [22]. These patients had one or more blood cultures positive for an obligate anaerobe between July 1, 1987 and December 31, 1988. The proportion of positive blood cultures yielding obligate anaerobes was 3.2% at the UMH and 1.8% at the other institution. The incidences of clinically significant anaerobic bacteraemia at the two hospitals were 0.68 and 0.54 cases per 1000 patient admissions. Among the 40 patients from whom significant isolates were obtained, 15 (38%) had a fatal outcome. *Bacteroides* and *Clostridium* species accounted for 90% of the isolates and all of the fatal cases. The source for anaerobic bacteraemia was usually obvious; 30 of the 40 patients were given empiric antibiotic therapy for anaerobes. The gastrointestinal tract was the source in two thirds of the cases and was clearly implicated as the source of 80% of the fatal bacteraemia. Noriega et al. [23] published in 1993 seventy-five episodes of clinically relevant anaerobic bacteraemias observed in cancer patients in a cancer center Santiago, Chile. Gastrointestinal (22.7%), haematological (22.7%), and female genital tract (18.6%) cancers were the most common underlying malignant diseases. Among 84 strains of strict anaerobic bacteria recovered in the 75 patients, Gram-negative rods were isolated in 49 patients (58.3%), Gram-positive rods in 29 patients (34.5%), and GPAC in six patients (8%). *Bacteroides* spp. and *Clostridium* spp. were the most frequent pathogens (85.7%). Twenty-one episodes of bacteraemia were polymicrobial, aerobic Gram-positive cocci being the most frequently associated pathogens. When identified, the

primary sites were the gastrointestinal tract (40%), the female genital tract (17.3%), skin and soft tissue (14.6%), the oropharynx (12%), and the lower respiratory tract (6.7%). The source remained unknown in seven cases (9.3%). The overall survival (evaluated 10 days after the occurrence of bacteraemia) was 82.5%. Pulmonary complications were more frequent in patients with fatal outcome in comparison to patients who survived. The mortality rate of the patients adequately treated was 10.3% compared to 41% for the patients not treated or treated inadequately. There was no difference in mortality between patients with monomicrobial and polymicrobial bacteraemia.

Ramos et al. [24] reviewed a total of 231 patients observed over a period of six and a half years in the Fundacion Jimenez Diaz, Madrid, Spain. A total of 131 episodes of AB were retrospectively analyzed with special attention being given to microbiologic, epidemiologic, and clinical factors. The relative frequency of anaerobic bacteraemia was 7.5%. Clinical significance was found in 86 out of the 131 episodes (66%). The isolation of *Bacteroides* spp. was clinically significant in 89% while *Clostridium* spp. was so only in 33%. Mortality related with AB was 32%. The following factors were considered related to bad prognosis: admission to medical areas, rapid and finally fatal underlying disease, presence of septic shock, renal failure, inappropriate antimicrobial treatment, and the absence of drainage for the septic foci. Two thirds of the episodes of anaerobic bacteraemias are deemed to be clinically significant. Correct antimicrobial treatment and surgical drainage of any septic foci significantly improve prognosis. Arzese et al. [25] found 225 anaerobic isolates in a nationwide survey of anaerobic bacteraemia in Italy, between 1991 and 1992. There were 63 (34%) *B. fragilis* group isolates (54 were *B. fragilis* and 13 were *B. thetaiotaomicron*), 28 (11%) *Clostridium* spp., 20 (8%) *Peptostreptococcu*s spp., and 15 (6%) *Fusobacterium* spp. In the other survey, Salonen et al. [26] retrospectively studied the incidence of anaerobic bacteraemia during 6 years (1991–1996) at Turku University Central Hospital in Turku, Finland. The clinical significance of a positive anaerobic blood culture, the effect of a positive culture on the choice of antimicrobial therapy, and the outcome for patients were evaluated. Cultures of blood from 81 patients yielded anaerobic bacteria (4% of all bacteraemias). Anaerobic bacteraemia was clinically significant in 57 patients (0.18 cases per 1000 admissions). Empirical therapy may provide coverage for anaerobes in only half of the patients with AB, and failure to pay attention to the results of anaerobic blood cultures was associated with serious consequences for patients.

Anuradha et al. [27] reviewed cases of anaerobic bacteraemia over 2 years in Mumbai, India. Of 93 blood cultures received with a suspicion of anaerobic bacteraemia, only 17 (18.3%) showed anaerobic growth. A total of 20 anaerobes grew alone while five had a polymicrobial flora. Seven of these patients (4.3%) had pre-existing heart disease while others had history of prior surgery, diabetes mellitus, or urinary tract infection. Oropharynx was the commonest portal of entry, followed by gastrointestinal tract. The anaerobes isolated were GPAC, *Bacteroides fragilis* group, and *Bilophila* and *Eubacterium* species. Fifteen patients developed major complications, such as congestive cardiac failure, systemic embolization, and perforative peritonitis. The mortality rate among the cases with anaerobic bacteraemia was 23.5%, in this study.

The incidence of anaerobic bacteraemia was studied retrospectively, over 62 months at Mont-Godinne University Hospital, Yvoir, Belgium by Blairon et al. [28]. The distribution of organisms, clinical presentations, choice of antimicrobial therapy, and clinical outcome were analyzed. The proportion of positive blood cultures yielding obligate anaerobes was 3.3%. The overall incidence of clinically significant anaerobic bacteraemia was 0.51 cases per 1000 patient admissions (0.61 cases per 10,000 hospital-days) but was significantly higher in patients with active haematological malignancies than in other groups (5.97 per 10,000 vs. 0.33 per 10,000 hospital-days). The *Bacteroides fragilis* group accounted for 61% of isolates, followed by *Clostridium* spp. (12.2%), GPAC and *Leptotrichia* spp. (7.3% each), and *Fusobacterium* spp. (4.8%). The most common risk-factors were gastrointestinal surgery (49%) and haematological malignancies with chemotherapy and/or bone marrow graft (47%). One or more co-morbidities were present in 30 (77.5%) of 39 patients. The lower gastrointestinal tract (41%) and the oropharynx (23%) were the two most frequent presumed or proven sources for bacteraemia, with the origin remaining unknown in eight (20.5%) cases. The overall mortality rate (evaluated 7 days after the occurrence of bacteraemia) was 13%. Fatal outcome correlated with the severity of underlying diseases and the immunosuppressed status of the patients rather than with the causative pathogen or the effectiveness of antimicrobial therapy. Likewise, there was no difference in the mortality rate between patients with monomicrobial and polymicrobial bacteraemia. Overall, their data re-emphasise the importance of anaerobic bacteraemia, especially in patients with haematological malignancies.

Over a two-year period at Auckland City Hospital, Auckland, New Zealand was investigated by Muttaiyah et al. [29]. Anaerobes were isolated from 140 blood culture sets taken from 114 patients. For 59 patients, the isolates were considered to be contaminants. Of note, all *Propionibacterium* spp. were considered contaminants. For the patients with true bacteraemias, the most likely source of infection was intra-abdominal, 26 (50%), mucositis associated with neutropaenia contributed to by cytotoxic therapy, 11 (19%), skin and soft tissue, 4 (8%), pelvic, 5 (9%), and oropharyngeal, 4 (8%). Thirty-five patients were on appropriate therapy prior to the availability of culture results. Five patients died, but only one death was directly attributable to anaerobic bacteraemia. At this institution, anaerobes accounted for 2.3% of all positive blood cultures. Empiric antimicrobial therapy provided appropriate cover for two thirds of the patients. One death was directly attributable to anaerobic bacteraemia. The anaerobic blood culture bottle is routinely used in Japan with little discussion as to its justification or validity. Saito et al. [30]

retrospectively studied the anaerobe bottle yield of obligate anaerobes and the characteristics of, and potential risk factors in, patients with anaerobic bacteraemia during a two-year period (1999–2000) at four university hospitals and one community hospital in Japan. Thirty-four of 18,310 aerobic and anaerobic blood culture sets from 6215 patients taken at the university hospitals, and 35 of 2464 samples taken from 838 patients at the community hospital yielded obligate anaerobes. *Bacteroides* species and *Clostridium* species accounted for 60% of the isolates. Fifty-seven patients from 69 blood culture sets containing anaerobes had clinically significant anaerobic bacteraemia. Among these 57 patients, 24 (49%) were oncology patients, 40 (70%) had an obvious source of anaerobic infection, and 15 (26%) had recent surgery and/or were in an immunosuppressed state. They concluded that the recovery rate of obligate anaerobes isolated from anaerobic bottles was low, and the patients with anaerobic bacteraemia had limited number of underlying diseases or potential risk factors for anaerobic infections.

Another Japanese study made by Iwata and Takahashi [31] performed a retrospective chart review at a private hospital for patients admitted between July 1, 2004 and June 30, 2005 to determine patient characteristics resulting in anaerobic blood culture. During the study period, 17,775 blood culture bottles were sent for analysis, and 2132 bottles (12.0%) were positive for microbial growth. Bacteria were grown from 958 anaerobic bottles (44.7%), and 719 (33.7%) of those were judged to represent real infections, which accounted for 410 cases of bacteraemia. Only 47 cases (11.5%) were detected by anaerobic cultures alone. Among those 47, obligate anaerobes represented 12 cases. Clinical evaluation could have predicted 7 of 12 cases of obligate anaerobic bacteraemia. In the remaining five cases, the source of bacteraemia was unclear. There were 2.7 cases of anaerobic bacteraemia per 1000 blood cultures. The mortality attributable to anaerobic bacteraemia was 50%. Among bacteraemic cases not caused by obligate anaerobes yet diagnosed solely by anaerobic bottles, either the standard two sets of blood were not taken or their clinical outcomes were favorable.

Anaerobic blood culture can be avoided in most cases. Anaerobic blood culture may be most helpful when (1) bacteraemia because of obligate anaerobes is clinically suspected, (2) patients are severely immunocompromised, and (3) source of bacteraemia is not identified correctly by clinical evaluation. Therefore, anaerobic blood cultures may be selectively used according to the potential risk for anaerobic infections. Surveys of anaerobic susceptibility have shown marked regional variations [32–36]; this finding, coupled with the development of resistance in anaerobes to all known agents, makes difficulty the reliable empirical therapy. Many anaerobic species besides the *B. fragilis*/*Parabacteroides* group have developed beta-lactamase activity. In rare instances, resistance to imipenem and to metronidazole has been reported [36–41]. With multiple changes in the resistance patterns of anaerobes, one can expect that therapeutic problems in the future will be compounded by abandonment of the 'complete bacteriology' of blood cultures. The prevalence of anaerobic bacteraemia in relation to patient demographics should be determined on an institution to instution basis to guide blood-culture practices. This approach will ensure that patients and their care will not suffer unnecessarily.

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