

Isolation of coryneform bacteria from blood cultures of patients at a University Hospital in Saudi Arabia

Hanan A. Babay, MD, KSFP^{Path} (Micro), Abdelmageed M. Kambal, MD, FRCPath.

ABSTRACT

Objective: Coryneform bacteria have been increasingly recognized as opportunistic pathogens in recent years. The aim of this study is to identify and determine the antimicrobial susceptibility of coryneform bacteria isolated from blood cultures of patients seen at King Khalid University Hospital (KKUH), Riyadh, Kingdom of Saudi Arabia and review the literature.

Methods: All coryneform bacteria isolated from blood culture specimens between January 2001 and March 2003 were prospectively identified by API Coryne System (BioMerieux, France). Clinical data were collected from each patient's medical record. Antimicrobial susceptibility to 16 antimicrobial agents were determined by minimum inhibitory concentration (MIC) using E-test (AB Biodisk, Solna, Sweden).

Results: Out of 50 coryneform bacteria isolated, 19 different species were identified. *Corynebacterium propinquum* was the most common species 6/50 (12%) followed by *Corynebacterium auris* 5/50 (10%), *Corynebacterium afermentans*, *Corynebacterium striatum*, *Dermabacter hominis*, *Brevibacterium*, and *Arthrobacter species* 4/50 (8%) each. Underlying chest diseases were common among the patients 11/50 (22%),

followed by different surgeries 10/50 (20%). Of all, 12/50 (24%) patients were from different intensive care units (ICUs), 36/50 (72%) had either vascular, urinary or respiratory intubation. Three patients in ICUs died, one was an elderly patient with gastrointestinal bleeding and 2 teenagers (one had tracheoesophageal fistula and the other was post-arrest road traffic accident patient). Vancomycin was the most active antimicrobial agent against all coryneform species. The majority had MIC <1 µg/ml. For most isolates, the MIC₉₀s of erythromycin, clindamycin, and ciprofloxacin were above the break points. *Corynebacterium striatum* was the only isolate susceptible to ampicillin.

Conclusion: This study revealed that coryneform bacteria are increasingly being recognized as a cause of serious infections in immunocompromised patients. We recommend identification and susceptibility testing of predominant isolates of coryneform bacteria from different clinical sites of seriously ill patients to select the antimicrobial agent necessary for clinical intervention.

Saudi Med J 2004; Vol. 25 (8): 1073-1079

Coryneform bacteria (diphtheroid bacilli) (*Corynebacterium* other than *Corynebacterium diphtheriae*) are members of the normal flora of skin, mucocutaneous membranes and gastrointestinal tract. Some have environmental or animal origin.¹⁻³ They are aerobic or anaerobic gram

positive rods, pleomorphic, non-branching, non-spore forming and non-acid fast.^{1,4} Their pathogenic potential has been questioned.^{1,4} However, during the last few years there have been a number of publications associating coryneform bacteria with human infections, such as bacteremia,

From the Department of Pathology/Microbiology, King Khalid University Hospital, Riyadh, Kingdom of Saudi Arabia.

Received 17th January 2004. Accepted for publication in final form 27th March 2004.

Address correspondence and reprint request to: Dr. Hanan A. Babay, Department of Pathology/Microbiology (32), King Khalid University Hospital, PO Box 2925, Riyadh 11461, Kingdom of Saudi Arabia. Tel. +966 (1) 4672457. Fax. +966 (1) 4672462. E-mail: hahabib@ksu.edu.sa

endocarditis, osteomyelitis, lower respiratory tract, eye and genitourinary infections.⁴⁻⁸ Due to increasing numbers of immunocompromised patients undergoing more invasive diagnostic procedures and intensive treatment as well as improved identification methods for these bacteria in most clinical laboratories.¹ Recently, there have been considerable changes in the taxonomy of many of these organisms based on chemical and molecular methods, with new genera and species being recognized or redefined.^{1,4,9} This paper study the cases of blood stream infections caused by different species of coryneform bacteria isolated at King Khalid University Hospital (KKUH), Riyadh, Kingdom of Saudi Arabia (KSA). The study includes the clinical significance, identification and antimicrobial susceptibility patterns of these organisms and literature review.

Methods. This study was carried out on 50 patients at KKUH between January 2001 to March 2003. This hospital has 850 beds with 5 different intensive care units (ICUs). It provides primary, secondary and tertiary health care. The clinical data collected from each patient's file included: age, gender, ICU admission, clinical diagnosis, antimicrobial treatment, presence of vascular, respiratory and urinary catheters and any other significant findings including outcome.

Laboratory methods. Eight to ten milliliters (mls) of peripheral venous blood was collected from each adult patient (1 ml from children) divided equally and inoculated into aerobic and anaerobic BacT/Alert 3D bottles (Organon Teknika, USA). Bottles showing positive growth index were Gram stained, and those with gram positive club shaped and coryneform bacteria arrangement pattern were subcultured on sheep blood agar (BA), chocolate (CH) and MacConkey agar (MAC) plates. Blood agar and chocolate agar (CHA) were incubated aerobically for 24-48 hours. MacConkey agar plates were incubated aerobically for 24 hours. Identification was made by analytical profile index (API) Coryne System (BioMerieux, France) updated profile with the help of the API LAB soft ware. It was carried out by following the guidelines of the manufacturer.

Antimicrobial susceptibility. Antimicrobial susceptibility was tested by E-test (AB Biodisk, Solna, Sweden) to determine the minimal inhibitory concentration (MICs) of 16 antimicrobial agents on Mueller Hinton agar with 5% sheep blood (Mueller Hinton II, Becton Dickinson, USA). The antimicrobial agents tested were: penicillin, ampicillin, ceftriaxone, cefotaxime, cefuroxime, co-trimoxazole (trimethoprim/sulfamethoxazole) chloramphenicol, imipenem, ciprofloxacin, erythromycin, clindamycin, rifampicin, gentamicin, amikacin, tetracycline and vancomycin.

Results. Of the 50 coryneform bacteria isolated from blood cultures during the study period, 19 different coryneform species were identified. All isolates were catalase positive. Gram stain appearance of the majority of isolates was gram positive, club-shaped arranged as coryneform bacilli. All isolates were aerobes except *Propionibacterium acnes* (*P.acnes*), which grew anaerobically. Colonies of most species were white to yellow in color, non-hemolytic, dry, between 0.5-1.5mm in diameter. However, one isolate of *Corynebacterium propinquum* (*C.propinquum*) was very mucoid. Colonies of the *Brevibacterium species* (*spp*) were cream colored with cheesy odor. None of the isolates grew on MAC plates. The most common species were *C. propinquum* 6/50 (12%), followed by *Corynebacterium auris* (*C. auris*) 5/50 (10%) while *Corynebacterium afermentans* (*C.afermentans*), (Centers for Disease Control [CDC] group ANF-3), *Corynebacterium striatum* (*C.striatum*), *Dermabacter hominis* (*D. hominis*), *Arthrobacter spp*, and *Brevibacterium spp* were 4/50 (8%) each. Fifteen (30%) of the isolates were other coryneform species. Of the 50 patients, there were 30 females (60%) and 20 males. The age range was between 2 days and 83 years. Seventeen of the patients were children, similar number were elderly (>60 years). **Table 1** summarizes the different

Table 1 - Summary of clinical conditions, and risk factors associated with coryneform bacteria blood stream infection.

Clinical conditions	N (%)
Respiratory diseases	11 (22)
Different surgeries	10 (20)
Diabetes mellitus	5 (10)
Cardiac diseases	4 (8)
Septic shock/septicemia	3 (6)
Fever*	5 (10)
Malignancy	2 (4)
Intestinal obstruction	2 (4)
Other conditions†	10 (20)
Risk factors	
Intensive care unit	12 (24)
Vascular, respiratory and urinary catheters	36 (72)
Antimicrobials used	
Ceftazidime	6 (12)
Vancomycin	5 (10)
Other antimicrobials‡	10 (20)
Other bacteria from other sites	18 (36)
Other bacteria from blood culture	4 (8)
Death	3 (6)
*4 children with viral infection and an elderly patient with pyrexia of unknown origin. †Other conditions include: epilepsy, ventriculo-peritoneal shunt, deep venous thrombosis, labor, drowning, hemophilia, Nephrotic syndrome, hypertension, skin disease, pilonidal abscess and nephrotic syndrome. ‡other antimicrobials include gentamicin, ampicillin, clarithromycine, cefuroxime and metronidazole.	

medical conditions, risk factors and outcome of the patients. There were no outbreaks during the study. Twelve of the patients were from ICUs (24%). *Corynebacterium propinquum* and *C. striatum* were the main isolates from these patients (3/12 (25%) each). All together, 11 patients (11/50 (22%) had underlying chest diseases such as pneumonia, bronchial asthma and chronic obstructive pulmonary disease (COPD) and 10/50 (20%) had different surgeries. Other patients had different medical conditions. Five patients were presented with fever only, 4 were children whom they presumed to have viral infections and one elderly patient had pyrexia of unknown origin. All the isolates were obtained as single isolates from blood culture of patients with evidence of infection. No similar isolates were obtained from specimens other than the blood. Three patients (3/50 [6%]) in the intensive care units died, one was an elderly patient with gastrointestinal bleeding and 2 teenagers (one has tracheoesophageal fistula and the other was a post-arrest road traffic accident patient). Thirty-six (72%) of the patients had either vascular, urinary catheters or respiratory intubation. The patient with *Corynebacterium jeikeium* (*C. jeikeium*) was an elderly lady with acute asthma who was eventually cured. The commonly used antibiotics in this series of patients were ceftazidime (12%) and vancomycin (10%). The MIC range and MIC₉₀^s of the 16 antimicrobials are listed in **Table 2**. The MIC of the species isolated once or twice was collectively determined under "other coryneform species". Due to the absence of established standards and a reference sensitive strain for coryneform bacteria, we interpreted the MIC results using the break point values applied by the National Committee for Clinical Laboratory Standards (NCCLS) for organisms other than *Haemophilus influenzae*, *Neisseria gonorrhoeae*, and *Streptococcus pneumoniae*.¹⁰ For penicillin and ampicillin, we used the standard for *Staphylococcus*.^{10,11} Vancomycin was the most active antimicrobial against all coryneform bacteria species with most isolates having an MIC <1 µg/ml. However for *C. jeikeium*, the MIC of vancomycin was 4 µg/ml. Except for *Brevibacterium spp*, the MIC₉₀^s of erythromycin, clindamycin and ciprofloxacin for all isolates were above the break points. *Corynebacterium striatum* was the only isolate susceptible to ampicillin (MIC₉₀ 0.23 µg/ml), its MIC to penicillin was slightly above the break point (MIC₉₀ 0.124 µg/ml). None of the coryneform bacteria studied was multiresistant.

Discussion. Isolation of diphtheroid bacilli from blood culture is usually interpreted as skin contaminants. However, this is not always the case since some coryneform bacteria such as, *C. jeikeium* (CDC group JK) and *C. urealyticum* are well

recognized as important human pathogens.^{1,4} The interest in diphtheroid infections started at approximately 3 decades ago when Johnson and Kaye¹² reported significant isolates from 52 patients: 60% had endocarditis, 10% bacteremia, 10% and 4% had underlying malignancy, and osteomyelitis. Other associated infections reported include keratitis, and peritonitis associated with chronic ambulatory peritoneal dialysis (CAPD).¹³⁻¹⁵ Nowadays, an increasing number of species of coryneform bacteria are being isolated from clinical specimens. However, the evidence for clinical significance of some new species, such as *Corynebacterium argentoratense*, *C. macginleyi*, and *Cellulomonas spp.* is lacking.⁴ Recent reports emphasized the importance of coryneform bacteria in colonization and infection.^{4,16,17} Coryneform bacteria often act as opportunistic pathogens in immunosuppressed hosts with serious underlying illnesses, intravascular catheters and those on broad spectrum antimicrobial agents.^{1,4,5} Our patients also had similar characteristics. Most of the isolates in our study were probably derived from skin following surgery or mucous membranes of the respiratory tract following intubation but in some the origin may have been environmental.

Corynebacterium propinquum (*C. ANF-3*) was the most common isolate in our cases. Since *C. propinquum* is a member of the respiratory tract flora, it was difficult to implicate it in the illnesses of our 6 patients including the patient with pneumonia. However, we would speculate that it might have invaded the blood stream following aspiration. It might be of interest to acknowledge our earlier report of *C. propinquum* from pleural effusion of a patient with squamous cell carcinoma.¹⁸

Corynebacterium auris was reported from ear infections from pediatric patients but none of the isolates in our pediatric patients was from ear infections.¹⁹ *Corynebacterium striatum* is usually an endogenous flora of skin and mucous membranes.²⁰ It is one of the most commonly isolated *Corynebacterium spp.* It has been described as the cause of pulmonary infection, bacteremia, CAPD peritonitis, intrauterine infection, and others.^{15,21,22} It was also implicated in an outbreak in ICU where it was cultured from surfaces and air samples in direct vicinity of infected patients and hands of personnel involved in the management of these patients.²⁰ It was also reported to colonize catheters and ventilation tubes.²⁰ Our isolates were not from any of these sources but rather from blood cultures. Risk factors for acquiring *C. striatum* were reported to be intubation for more than 24 hours, serious illnesses, artificial ventilation and treatment with broad spectrum antimicrobial agents.^{1,20} All our 4 patients had one or other of these risk factors. These isolates may have had an effect on the final outcome

Table 2 - Minimal inhibitory concentration($\mu\text{g/ml}$) of 16 antimicrobials against different coryneform bacteria isolates (N=50).

Antimicrobial agents	<i>C.propinquum</i> MIC range (MIC 90)*	<i>C.auris</i> MIC range (MIC 90)*	<i>C.striatum</i> MIC range (MIC 90)*	<i>C.afermentans</i> MIC range (MIC 90)*	<i>D.hominis</i> MIC range (MIC 90)*	<i>Rodococcus</i> <i>species</i> MIC range (MIC 90)*	<i>Arthrobacter</i> <i>species</i> MIC range (MIC 90)*	<i>Brevibacterium</i> <i>species</i> MIC range (MIC 90)*	<i>Coryneform</i> <i>species</i> † MIC range (MIC 90)*
N (%)	6 (12)	5 (10)	4 (8)	4 (8)	4 (8)	4 (8)	4 (8)	4 (8)	15 (30)
Penicillin	0.006-8 (1.8)	0.38-12 (4.20)	0.047-0.125 (0.12)	0.25-8 (3.64)	0.50-16 (5.4)	0.004->256 (57.9)	0.064-2 (0.74)	0.16-1 (0.39)	0.16-32 (2.5)
Ampicillin	<0.016-2 (0.79)	0.50-4 (2.25)	0.064-0.25 (0.23)	0.25-4 (2.19)	0.50-12 (3.5)	0.032-16 (4.5)	0.094-4 (1.3)	0.32-2 (0.51)	<0.016-4 (1.17)
Ceftriaxone	0.38-6 (2.2)	0.38-12 (4.74)	0.125-2 (0.75)	1-8 (4.27)	0.064-16 (6.9)	0.32-1 (0.43)	0.25-6 (1.86)	<0.16-12 (2.9)	0.032-48 (3.85)
Cefotaxime	0.19-4 (1.4)	0.50-4 (1.98)	0.125-0.75 (0.47)	0.50-6 (3.03)	0.19-8 (2.9)	0.032-2 (0.96)	0.25-3 (1.2)	<0.016-128 (29.1)	0.032-32 (2.9)
Cefuroxime	0.094-4 (1.4)	0.50-16 (4.59)	0.125-0.75 (0.30)	0.38-6 (2.78)	0.25-24 (9.5)	0.016-3 (1.18)	0.047->32 (1.8)	0.032-12 (3.2)	<0.016->32 (4.4)
Imipenem	0.016-0.25 (0.14)	0.125->256 (92.7)	0.023-0.12 (0.058)	0.032->256 (57.6)	0.125-4 (7.86)	0.125-4 (0.13)	0.125-4 (0.98)	0.032-0.5 (0.15)	0.023-0.50 (0.2)
Erythromycin	0.016->256 (79.4)	0.125->256 (144)	0.94->256 (0.4)	0.016->256 (140.4)	6->256 (174.14)	4-32 (8.2)	<0.016-24 (6.3)	0.064-6 (2.2)	0.032->256 (78.1)
Clindamycin	<0.016->256 (77)	0.125->256 (138.3)	0.064->256 (172.2)	1.5->256 (87.18)	0.19->256 (172.8)	0.38-12 (6.04)	0.19-4 (3.5)	0.12-0.38 (0.2)	0.047->256 (51.4)
Rifampin	<0.016->256 (40.8)	<0.016->256 (46.3)	<0.016->256 (57.6)	<0.016-0.016 (0.014)	<0.016 (0.014)	<0.16 (0.014)	<0.06-4 (0.96)	<0.016-12 (4)	<0.016-8 (0.58)
Ciprofloxacin	0.64->256 (43.25)	0.19->32 (23.3)	0.064->32 (8.15)	0.047->32 (14.4)	0.75-8 (2.75)	0.50-12 (1.01)	0.50-32 (8.6)	0.64-2 (0.6)	0.047-32 (4.13)
Chloramphenicol	0.19-24 (4.2)	0.50-48 (18)	0.5-32 (18.4)	1.5-128 (29.9)	0.125->32 (7.9)	1.5-96 (38.1)	0.19-16 (3.0)	0.2-24 (6.7)	0.19-32 (8.05)
Gentamicin	0.016-24 (3.64)	0.047->256 (46.2)	0.38-6 (1.78)	<0.016-0.75 (0.38)	<0.016-32 (13.2)	0.47-1.5 (0.55)	0.50-2 (1.2)	>0.016-3 (0.81)	0.032->256 (16.2)
Amikacin	0.125-6 (3.36)	0.19-4 (0.94)	0.19-3 (1.5)	0.064-0.125 (0.128)	0.047-32 (14.8)	0.32-4 (1.35)	0.16-32 (9.4)	0.064-12 (4.1)	0.125->256 (18.5)
Tetracycline	0.10-2 (0.38)	0.125-24 (4.59)	0.19-32 (0.18)	0.125-0.38 (0.18)	1-8 (2.44)	0.047-0.75 (0.4)	0.064-50 (1.0)	0.19-0.25 (0.19)	0.125-3 (0.90)
Vancomycin	0.19-0.5 (0.3)	0.25-4 (0.31)	0.38-0.50 (0.27)	0.19-0.38 (0.27)	0.50-1 (0.50)	0.19-2 (0.69)	0.38-0.75 (0.46)	0.19-75 (0.38)	0.125-4 (0.63)
Cotrimoxazole	0.25-2 (0.89)	0.50-4 (6.93)	2->32 (9.67)	0.19->32 (14.96)	0.19->32 (6.9)	0.047->256 (65.0)	0.064-24 (7.6)	0.047->32 (14.4)	0.032->32 (4.5)

*MIC₉₀ = MIC for 90% of each *Coryneform species*
†*Coryneform species* = *Turicell oitidis* (2), *C.macginleyi* (2), *C.pseudodiphtheriticum* (2), *Cellulomonas species* (2), *Corynebacterium jeikeiu* (1), *Corynebacterium amycolatum* (1), *Corynebacterium pseudotuberculosis* (1), *Corynebacterium bovis* (1), *Microbacterium species* (1), *Propionibacterium acnes* (1), *C.argentoratense* (1).
C.propinquum - *Corynebacterium propinquum*, *C.auris* - *Corynebacterium auris*, *C.striatum* - *Corynebacterium striatum*,
C.afermentans - *Corynebacterium afermentans*, *D.hominis* - *Dermabacter hominis*, MIC - minimum inhibitory concentration

on these 4 patients. Although reports of infections caused by *C. afermentans* (C.ANF-1) included intravenous catheters related infections and prosthetic valve endocarditis with perivalvular abscess, none of our patients had any of these infections.^{1,8}

Of the 4 *Rhodococcus* (R) spp. in our study, one was with *R. equi* from an elderly women with uncomplicated pneumonia. *Rhodococcus equi* has often been reported from clinical specimens as an important opportunistic pathogen especially in patients with cell-mediated immunity disorders, and also patients with cavitary necrotizing pneumonia, endophthalmitis, psoas and paraspinal abscesses, osteomyelitis, and cervical lymphadenitis.^{1,23,24} Their role in bronchial asthma or other illnesses of our patients is not clear.

All cases of *D. hominis* in our study were elderly women, but no one of the previous reports on coryneform bacteria has a singled out gender as a risk factor. The organism is derived from the skin of healthy individuals and all reports of isolates from blood, abscesses, wound, eye, and skin were lacked of any specific clinical information.^{4,25} Bacteremia seen in the hemophiliac patient in our study could be due to frequent blood transfusions, and also lack of adequate skin hygiene in other elderly patients.

In contrast to *D. hominis*, all our *Arthrobacter* spp. were isolated from males, 2 of them were children with fever. Since this organism is not a member of the skin flora, we would speculate that the source of these isolates could be environmental.¹¹ When Funke et al,²⁶ in 1996 reported isolation of *Arthrobacter* spp. from blood, urine, skin, eye, and vagina they stated that *Arthrobacter* spp. would be more frequently reported if species or genus determination of clinically significant coryneform bacteria were performed more frequently.

Isolates of *Turicella otitidis* (*T. otitidis*) were reported from ear specimens either in pure culture or with gram negative rods as well as from healthy individuals.^{27,28} However, its role in otitis media is not yet confirmed. Our 2 pediatric patients who had ear isolates had no signs or symptoms of ear infection.

Brevibacterium spp. isolated from the 3 of our patients seems to be contaminants since one patient has *Pneumococcal pneumoniae* and the another has *S.milleri* from pilonidal sinus. Some *Brevibacterium* (B) spp. such as *B.epidermidis* and *B.casei* are skin inhabitant while other species have been isolated from raw milk and animal sources.^{1,4} Gruner et al,²⁹ reported *Brevibacterium* spp. from peritoneal fluid in a case of peritonitis related to CAPD. It has also been isolated from cases of osteomyelitis, bacteremia, and CNS shunt infections.^{1,5} Recently, Janda et al,⁵ reported *B. casei* bacteremia associated with Hickmann catheter in a patient with AIDS. It is also reported that it

contributes to body odor especially from moist skin areas.^{4,5} *Brevibacterium mcbrellneri* (along with *Trichosporon beigelli*) has been associated with white piedra.³⁰

Corynebacterium pseudodiphtheriticum (*C.pseudodiphtheriticum*) (also known as *C. hofmannii*) is a rare respiratory pathogen and less commonly causes endocarditis, prosthesis or wound infection or colonization.^{1,4,6} However, there are reports of exudative pharyngitis from a healthy individual, bronchitis, and pneumonia due to this organism with or without other respiratory pathogens from respiratory specimens.³¹ Other reports were from immunocompromised patients with pre-existing pulmonary diseases.⁴ Many patients had endotracheal intubation, which introduced the organism into the lower respiratory tract, or patients with suppressed cough response.³² These reports emphasized the importance of isolating the bacteria in pure culture along with the finding of intracellular diphtheroids on gram stain of properly collected sputum samples or lung tissues and the response to antibiotic treatment.⁶ We feel that *C. pseudodiphtheriticum* in our patient with spinal prostheses could be genuine because it was isolated in pure culture with no other isolates from other sites, and the patient responded to antimicrobial treatment.

Corynebacterium jeikeium (CDC group JK) with multi-resistance to all antimicrobials except vancomycin was first reported in association with endocarditis following cardiac surgery.³³ Lipsky et al,³⁷ reported *C. jeikeium* infections in immunosuppressed hosts with medical devices in place, prolonged hospitalization, and receiving broad spectrum antimicrobials. Other infections of *C. jeikeium* included bacteremia, pulmonary infiltration, meningitis and soft tissue infections.⁹ It was difficult to recognize the role of *C.jeikeium* isolated in one of our patients with bronchial asthma. Most of the reports on *C. macingli* came from eye specimens.³⁴ The role of our isolates from our immunosuppressed patients with solid tumors is not clear.

Other coryneform bacteria associated with eye infection is *Microbacterium* spp.³ Three cases were reported causing endophthalmitis after intraocular foreign body injury and sepsis after hematogenous spread in a patient with hematologic neoplasia.³ It was also reported from mitral valve endocarditis and catheter related septicemia.^{35,36} The isolate in one of our patients may be significant as he was an immunocompromised patient.

Of the coryneform bacteria from animal source among our isolates were *C.pseudotuberculosis* (also known as *Corynebacterium ovis* [*C. ovis*]) and *C. bovis*. The former was rarely reported from human lymphadenitis.² Our patient had eczematous skin disease. *Corynebacterium bovis* is occasionally

described as human pathogen.³⁷ The source of these 2 organisms in our patients is not known nor there was any known history of exposure to sick animals or animal products.

Propionibacterium acnes (*P.acnes*) is found in the skin, large intestine, mouth and conjunctiva.⁴ Reported predisposing conditions for *P.acnes* includes immunosuppression, trauma, diabetes mellitus, obstruction of tissues or ducts, foreign body example, prosthetic valve endocarditis, central nervous shunt infection, shunt associated nephritis and also endophthalmitis following cataract extraction.^{4,38} One isolate from our study was from an immunosuppressed sickle cell patient.

Corynebacterium argentoratense has been reported from human tonsils; however, its role in tonsillitis is not obvious.¹⁷ Its role in our patient with angina would appear to be non-significant. Several studies on susceptibility of clinically important coryneform bacteria have been published.^{11,39} All reported varying activity of different antimicrobials against different coryneform species as were also our findings.^{11,39} Vancomycin appears to be the ultimate therapy for most infections caused by these organisms.^{11,39} Vancomycin resistance has been reported in *C.jejikeium*, *C. urealyticum*, *C. xerosis*, *C. minutissimum* and others.^{1,11,39,40} Previously, we reported *C. propinquum* resistant to vancomycin (MIC 64 µg/ml) from pleural fluid.¹⁸ None of our isolates was multiresistant or vancomycin resistant. Other antimicrobials including cephalosporins, imipenem, aminoglycosides, tetracycline, rifampicin and co-trimoxazole can be used for treatment according to the results of susceptibility testing.

We conclude that coryneform bacteria are increasingly being recognized as causes of serious infections especially in immunosuppressed hosts as seen in this study where almost half of the patients (24 [48%]) had immunosuppressing diseases and risk factors. Among these, 36 (72%) had vascular, respiratory or urinary catheters, 12 (24%) were managed in ICUs for serious medical or surgical conditions and 21 (42%) were treated by different antimicrobial agents (Table 1). We recommend a more detailed and complete identification of coryneform bacteria as the predominant isolate from different clinical sites. Association of coryneform bacteria with disease can be established following the guidelines proposed by Funke et al.⁴ Combined laboratory tests with clinical information about the patients will be important to determine the need for clinical intervention.

References

- Martinez-Martinez L. Clinical significance of newly recognized coryneform bacteria. *Reviews in Medical Microbiology* 1998; 9: 55-68.
- Conor KM, Quirie MM, Baird G, Donachie W. Characterization of United Kingdom isolates of *C.pseudotuberculosis* using pulsed-field gel electrophoresis. *J Clin Microbiol* 2000; 38: 2633-2637.
- Funke G, Haase G, Schnitzler N, Schrage N, Reinert RR. Endophthalmitis due to Microbacterium infections. *Clin Infect Dis* 1997; 24: 713-716.
- Funke G, Graevenitz AV, Clarridge JE, Bernard KA. Clinical microbiology of coryneform bacteria. *Clin Microbiol Rev* 1997; 10: 125-159.
- Janda WM, Tipirneni P, Novak RM. *Brevibacterium casei* bacteremia and line sepsis in a patient with AIDS. *J Infect* 2003; 46: 61-64.
- Manzella JP, Kellogg JA, Parsey KS. *Corynebacterium pseudodiphtheriticum*: a respiratory tract pathogen in adults. *Clin Infect Dis* 1995; 20: 37-40.
- Petit PLC, Bok JW, Thompson J, Buiting AGM, Coyle MB. Native-valve endocarditis due to CDC coryneform group ANF-3: report of a case and review of corynebacterial endocarditis. *Clin Infect Dis* 1994; 19: 897-901.
- Sewell DL, Coyle MB, Funke G. Prosthetic valve endocarditis caused by *C. afermentans* subsp. lipophilum (CDC) coryneform group (ANF-1). *J Clin Microbiol* 1995; 33: 759-761.
- Coyle MB, Lipsky BA. Coryneform bacteria in infectious diseases: clinical and laboratory aspects. *Clin Microbiol Rev* 1990; 3: 277-246.
- National Committee for Clinical Laboratory Standards. Minimum inhibitory concentration (MIC) interpretive standards (µg/ml) for organisms other than *Haemophilus*, *Neisseria gonorrhoeae*, and *Streptococcus pneumoniae*, NCCLS document M7-A3. Villanova (PA): National Committee for Clinical Laboratory Standards; 1993.
- Funke G, Punter V, Graevenitz AV. Antimicrobial susceptibility patterns of some recently established coryneform bacteria. *Antimicrob Agents Chemother* 1996; 40: 2874-2878.
- Johnson WD, Kaye D. Serious infections caused by diphtheroids. *Ann N Y Acad Sci* 1970; 174: 568-576.
- De Wit, Mulla R, Burns A, Phelps RS. Tenckhoff catheter-associated peritonitis caused by coryneform group 1-2. *J Infect* 1993; 26: 341-343.
- Rubinfeld RS, Cohen EJ, Arentsen JJ, Laibson PR. Diphtheroids as ocular pathogens. *Am J Ophthalmol* 1989; 108: 251-254.
- Bhandari S, Meigh JA, Sellars L. CAPD peritonitis due to *Corynebacterium striatum*. *Perit Dial Int* 1995; 15: 88-89.
- Funke G, Ramos CP, Collin M. Identification of some clinical strains of CDC coryneform group A-3 and A-4 bacteria as *Cellulomonas speciosa* and proposal of *Cellulomonas hominis* sp. for some group A-3 strains. *J Clin Microbiol* 1995; 33: 2091-2097.
- Riegel P, Ruimy R, De Briel D, Prevost G, Jehl F, Bimet F et al. *Corynebacterium argentoratense* sp. nov., from the human throat. *Int J Syst Bacteriol* 1995; 45: 533-537.
- Babay HAH. Pleural effusion due to *C. propinquum* in a patient with squamous cell carcinoma. *Annals of Saudi Medicine* 2001; 21: 337-339.
- Funke G, Lawson PA, Collin MD. Heterogeneity within centers for disease control and prevention coryneform group ANF-1-like bacteria and description of *C.auris* sp.nov. *Int J Syst Bacteriol* 1995; 45: 735-739.
- Bradenburg AH, Belkum AV, Pelt CV, Bruining HO, Mouton JW, Verbrugh HA. Patient-to-patient spread of a single strain of *C. striatum* causing infections in a surgical intensive care unit. *J Clin Microbiol* 1996; 34: 2089-2094.

21. Bowstead TT, Santiago SM. Pleuropulmonary infection due to *C. striatum*. **Br J Dis Chest** 1980; 74: 198-200.
22. Peiris V, Fraser S, Knowles C, Norris S, Benet C. Isolation of *C. striatum* from 3 hospital patients. **Eur J Clin Microbiol Infect Dis** 1994; 13: 36-38.
23. Prescott JF. *Rhodococcus equi*: an animal and human pathogen. **Clin Microbiol Rev** 1991; 4: 20-34.
24. Harvey RL, Sustrum JC. *Rhodococcus equi* infection in patients with and without human immunodeficiency virus infections. **Rev Infect Dis** 1991; 13: 139-145.
25. Funke G, Stubbs S, Pfyffer GE, Marchiani M, Collins MD. Characterizations of CDC group 3 and 5 coryneform bacteria isolated from clinical specimens and assignment to genus Dermabacter. **J Clin Microbiol** 1994; 32: 1223-1228.
26. Funke G, Hutson RA, Bernard KA, Pfyffer GE, Wauters G, Collins MD. Isolation of *Arthrobacter cumminsii* sp.nov. and *Arthrobacter woluwensis* sp. nov. **J Clin Microbiol** 1996; 34: 2356-2363.
27. Renaud FN, Gregory A, Barreau C, Aubel D, Frenay J. Identification of *Turicella otitidis* isolated from a patient with otorrhea associated with surgery: differentiation from *C. afermentans* and *C. auris*. **J Clin Microbiol** 1996; 34: 2626-2627.
28. Funke G, Stubbs S, Altwegg M, Carlotti A, Collins MD. *Turicella otitidis* gen.nov., sp.nov., a coryneform bacterium isolated from patients with otitis media. **Int J Syst Bacteriol** 1994; 44: 270-273.
29. Gruner E, Pfyffer GE, Graevenitz AV. Characterization of *Brevibacterium* spp. from clinical specimens. **J Clin Microbiol** 1993; 31: 1408-1412.
30. Mc Bride ME, Ellner KM, Black SH, Clarridge JE, Wolf JE. A new *Brevibacterium* sp. isolated from infected genital hair of patients with white piedra. **J Clin Microbiol** 1993; 39: 255-261.
31. Izurieta HS, Strebel PM, Youngblood T, Hollis DG, Popovic T. Exudative pharyngitis possibly due to *C. pseudodiphtheriticum*, a new challenge in the differential diagnosis of diphtheria. **Emerg Infect Dis** 1997; 3: 65- 67.
32. Freeman JD, Smith HJ, Haines HG, Hellyar AG. Seven patients with respiratory infections due to *C. pseudodiphtheriticum*. **Pathology** 1994; 26: 311-314.
33. Jackman PJH, Pitcher DJ, Pelczynska S, Borman P. Classification of corynebacteria associated with endocarditis (group JK) as *C. jeikeium* sp. nov. **Syst Appl Microbiol** 1987; 9 : 83-90.
34. Riegel P, Ruimy R, De Briel D, Prevost G, Jehl F, Christen R et al. Genomic diversity and phylogenetic relationships among lipid-requiring diphtheroids from humans and characterization of *C. macginley* sp. nov. **Int J Syst Bacteriol** 1995; 45: 128-133.
35. Campbell PB, Palladino S, Flexman JP. Catheter-related septicaemia caused by a vancomycin-resistant coryneform CDC group A-5. **Pathology** 1994; 26: 56-58.
36. Lifshitz A, Arber N, Pras E, Samra Z, Pinkhas J, Sidi Y. Corynebacterium CDC group A-4 native valve endocarditis. **Eur J Clin Microbiol Infect Dis** 1991; 10: 1056-1057.
37. Lipsky BA, Goldberger AC, Tompkins LS, Plorde JJ. Infections caused by nondiphtheria corynebacteria. **Rev Infect Dis** 1982; 4: 1220-1235.
38. Setz U, Frank U, Anding K, Garbe A, Daschner FD. Shunt nephritis associated with *Propionebacterium acnes*. **Infection** 1994; 22: 99-101.
39. Sorriano F, Zapardiel J, Nieto E. Antimicrobial susceptibilities of *Corynebacterium* species and other non-spore-forming Gram-positive bacilli to 18 antimicrobial agents. **Antimicrob Agents Chemother** 1995; 39: 208-214.
40. Nottle FS, Arnold KE, Sweat H, Winton EF, Funke G. Vancomycin-resistant *Aureobacterium* species cellulites and bacteraemia in a patient with acute myelogenous leukaemia. **J Clin Microbiol** 1996; 34: 1992-1994.