CLINICAL SIGNIFICANCE OF NON-DIPHTHERIA CORYNEBACTERIUM IN GERIATRIC PATIENTS

Oz: Non-diphtheria corynebacteria are referred as diphtheroid and coryneform, and can be considered as ‘colonizers’ and contaminants. We aim to evaluate the coryneform bacteria isolated in our hospital’s microbiology laboratory together with the patient’s clinical status. Material and Method: Various clinical samples sent to our hospital’s Medical Microbiology Laboratory were Gram stained and cultured in agars. The strains with polymorphonuclear neutrophils and gram-positive bacilli on Gram stain, dominant or absolute growth in culture and growth in the repeated blood cultures were regarded as infectious agents while bacterial growths are not completing those criteria were reported as contamination or colonization. The mean age of the patients was 68.46 (between 47 and 89). C. jeikeium was isolated from blood cultures from 3 patients. C. striatum was isolated from wound cultures of 2 patients, in the bronchial aspirates of 2 patients and in the blood cultures of 1 patient. C. urealyticum was isolated from pre-diagnosed cystitis from 2 patients (105 CFU/ml). C. amycolatum was isolated from wound cultures of 1 patient, and C. minutissium was isolated from 2 patient’s wounds, one patient’s ear and one patient’s catheter and wound. Result: Identification of Corynebacterium species can be difficult because of rapid taxonomic changes. Susceptibility testing of these micro-organisms is not yet standardized. However because of their growing clinical importance, data on these bacteria are accumulating. Non-Diphtheria corynebacteria have emerged as important pathogens causing many serious infections.

Keywords
Corynebacterium; Geriatric Patients
Introduction
Corynebacterium species, or “diphtheroids”, are aerobic, non-spore forming, pleomorphic, Gram-positive bacilli. Non-diphtheria corynebacteria are referred to as diphtheroids and coryneforms and can be considered as ‘colonizers’ and contaminants [1,2]. Nevertheless, the ability of these bacteria to cause life-threatening disease is well established, and over the last decade, there have been increasing reports of their pathogenic potential in numerous clinical scenarios. Including bacteremia and endocarditis [1]. Several species such as C. xerosis, C. amycolatum, C. striatum, C. minutissimum, C. pseudodiphteriticum, C. matruchotii, C. aquaticum, C. genitalium, and C. pseudogenitalium have been related to human infections. Coryneform bacteria exist commensally in the soil, water, human, and animal mucosa and on the skin. Coryneform bacteria other than Corynebacterium diphtheria are often isolated from clinical samples and regarded as contamination. However, after they began to be identified, it has been realized that they are an agent of important infection of geriatric patients and hospital infections. This study aims to emphasize the clinical significance of coryneform bacteria and to draw attention to the problems arising in microbiological diagnosis because coryneform bacteria mostly are not considered as contamination and ruled out. It is quite difficult to determine whether this bacterium is an agent or contaminant; We aim to evaluate the coryneform bacteria isolated in our hospital’s microbiology laboratory together with the patient’s clinical status.

Material and Method
Various clinical samples sent to our hospital’s Medical Microbiology Laboratory were Gram stained, and cultured in agars. The strains with polymorphonuclear neutrophils and Gram-positive bacilli on Gram stain, dominant or absolute growth in culture and growth in the repeated blood cultures were regarded as infectious agents while bacterial growths are not completing those criteria were reported as contamination or colonization. Isolates of Corynebacterium obtained from catheters (≤ 15 CFU by the rollingplate method), urine culture (> 105 CFU/mL) and predominant culture from wound exudates and bronchial aspirates were considered potentially significant. Identification of the agents at stain level was performed with Vitek MS (bioMerieux, France) system.

Results
The mean age of the patients was 68.46 (between 47 and 89). C. jeikeium was isolated from blood cultures from 3 patients. C. striatum was isolated from wound cultures of 2 patients, in the bronchial aspirates of 2 patients and in the blood cultures of 1 patient. C. urealyticum was isolated from pre-diagnosed cystitis from 2 patients. C. amycolatum was isolated wound cultures of 1 patient, and C. minutissimum was isolated from 2 patient’s wounds, 1 patient’s ear and 1 patient’s catheter and wound (Table 1).

Discussion
After much discussion and confusion about their clinical significance, coryneforms have emerged as important pathogens [3]. It is quite difficult to determine whether this bacterium is an agent or contaminant; It must be taken into consideration that coryneform bacteria, which are generally regarded as contamination and as diphtheroids in Gram staining, can be an opportunistic pathogen in patients with risk factors such as a compromised immune system and staying in the intensive care unit in addition to a long-term antibiotic treatment history. That the same coryneform bacterium grew in more than one clinical sample and that dense granular leukocyte or intensive shaped leukocyte and coryneform bacteria were seen in Gram staining is an indication that this situation can be clinically significant. C. striatum survives as a saprophyte on the skin and mucous membranes of asymptomatic individuals. Corynebacterium striatum is an agent of endocarditis and pneumonia and infects surgical wounds. Many hospital-acquired epidemics and osteomyelitis are caused by C. striatum [4]. In addition, meningitis [5], shunt infection [6], endocarditis [7] and peritonitis [8], keratitis [9] cases have been reported [10,11,12]. In a study by Renom et al., C. striatum was isolated from the sputum samples of 21 patients with a chronic obstructive respiratory disease, and it was reported that this isolate can colonize the respiratory tracts of chronic obstructive respiratory disease patients and causes hospital-acquired infections by spreading from person to person [12]. Similarly, Tarr et al. detected C. striatum growth in the bronchoalveolar lavage (BAL) and sputum cultures of a 58-year-old male patient diagnosed with bilateral pneumonia three months after undergoing a heart transplantation; they showed that the pneumonia was reduced after four weeks of vancomycin treatment. While C. striatum growth is mostly regarded as contamination, one study indicated that it can be considered a pathogen in immunocompromised patients with a prolonged hospitalization history undergoing long-term antibiotic treatment [13]. In general, cell renewal decelerates in geriatric patients, and they tend to be open to various infections. Reunès et al. found the Corynebacterium spp. isolation rate to be 0.6% (1/155) in a study conducted on geriatric patients with bloodstream infections [14]. The agent must be identified at type level in case bacterial growth occurs in blood cultures taken in at least two different periods. That these bacteria were isolated from the respiratory tract and blood samples simultaneously and that the same agent was detected in repeated blood samples for analyzing the bacteremia accompanying the pneumonia observed in one patient made us think that C. striatum is highly likely to be the agent. Proven infections have been found most commonly in the setting of immunocompromised patients with respiratory infections, recurrent or continuous instrumentation, chronic ulcers or surgery [11,15]. The nosocomial person-to-person spread has been documented twice [16]. Septic arthritis has been reported in the setting of joint replacement surgery and after accidental scalpel laceration [17]. In the case reported here, several factors enhanced the patient’s risk of infection with C. striatum, including an immune system compromised by age and failing health, prolonged institutionization, the presence of chronic ulcers, the occurrence of pneumonia, a reported blunt trauma to the knee when he fell, and osteoarthritis in the involved knee [2,11,15,18]. In this case, the infecting organism is most likely to have gained access to the patient’s circulation either through the respiratory tract, perhaps during his pneumonia, or through his persistent and
open venostasis ulcers. This case highlights both the growing importance of *C. striatum* as a nosocomial pathogen, and the difficulty microbiology laboratories may encounter when trying to identify this species. It is likely that the number and range of clinically important infections with this organism have been underestimated. The first recognized spontaneous infection of a natural joint with *C. striatum* is reported here, in our study, was isolated from three patients with pulmonary infections, tracheal aspirates were identified as causative pathogen. One patient was isolated from the Diabetic foot wounds. It was isolated from a patient with acute lymphadenitis. Also, a patient who has also caused a surgical site infection (Table 1).

*C. jeikeium* colonizes especially the skin florals of the inguinal, axillary and rectal areas of hospitalized patients. It is evaluated as contamination, but it also plays a role as a slightly pathogenic agent. Various infections caused by *C. jeikeium* are septicemia, meningitis, peritonitis, foreign body infections, osteomyelitis, pneumonitis, and endocarditis. *C. jeikeium* causes hematologic and catheter infections. Infections are mostly observed in patients with nosocomial infections, those with malignity and neutropenia and in patients who are hospitalized for a prolonged duration [19,20,21,22]. Since it has become possible to identify these isolates, there has been an increase in the occurrence rates of these bacteria [2].

In our study, two geriatric and immunosuppressed patients who had a pulmonary infection had growth on their blood culture. In our study, it was isolated as an osteomyelitis-affecting pathogen. One patient was isolated from the wound tissue of a patient with soft tissue infection (Table 1).

*C. minutissimum* can also be an agent of endocarditis, catheter infection, and peritonitis in peritoneal dialysis patients. *C. minutissimum* causes erythrasma infection in healthy people by colonizing the skin. Although this infection is most frequently formed by *C. minutissimum*, it can also be caused by other Corynebacterium species. *C. minutissimum* can also be an agent of endocarditis, catheter infection, and peritonitis in peritoneal dialysis patients. Invasive *C. minutissimum* infection usually occurs in immunocompromised patients and/or patients with skin disruption due to surgery or indwelling devices, such as a central venous catheter or a peritoneal dialysis catheter [23,24]. Although the source of infection was unknown, skin disruption by surgery and a drainage catheter might have contributed to the development of invasive *C. minutissimum* infection in this patient. In conclusion, given an increasing number of cases with the use of indwelling devices causing a breach in the skin barrier [24,25]. Clinicians would be wise to keep this organism in mind as a rare cause of post-surgical abdominal infection. In our study, it was isolated as an osteomyelitis-affecting effect in a diabetic patient. It was also isolated from a diabetic patient.

### Table 1. Clinical distribution of patients

<table>
<thead>
<tr>
<th>Case</th>
<th>Gender</th>
<th>Age</th>
<th>Patient’s diagnosis</th>
<th>Clinic</th>
<th>Culture material</th>
<th>Bacterial growth</th>
<th>The number of sets where growing occurred</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>64</td>
<td>Lower respiratory tract infection</td>
<td>Intensive Care Unit</td>
<td>Tracheal aspirate 100,000 cfu/ml</td>
<td><em>C. striatum</em> (Leukocytes and gram-positive bacilli)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>78</td>
<td>Lower respiratory tract infection</td>
<td>Intensive Care Unit</td>
<td>Tracheal aspirate 100,000 cfu/ml</td>
<td><em>C. striatum</em> (Leukocytes and gram-positive bacilli)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>74</td>
<td>Lower respiratory tract infection</td>
<td>Intensive Care Unit</td>
<td>sputum</td>
<td><em>C. striatum</em> (Leukocytes and gram-positive bacilli)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>82</td>
<td>DM + soft tissue infection</td>
<td>Infectious Diseases</td>
<td>Wound</td>
<td><em>C. striatum</em> (agent) (Abundant leukocytes, gram-positive bacilli)</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>62</td>
<td>Acute lymphadenitis</td>
<td>General Surgery</td>
<td>Wound</td>
<td><em>C. striatum</em> (agent) (Abundant leukocytes, gram-positive bacilli)</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>88</td>
<td>Bowel bypass anastomosis</td>
<td>Surgery site infection</td>
<td>Blood</td>
<td><em>C. striatum</em> (agent)</td>
<td>2</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>47</td>
<td>Lung malignancy</td>
<td>Pulmonology</td>
<td>Blood</td>
<td><em>C. jeikeium</em> (agent?)</td>
<td>1</td>
</tr>
<tr>
<td>8</td>
<td>F</td>
<td>67</td>
<td>DM+ diabetic foot</td>
<td>Internal Diseases</td>
<td>Blood</td>
<td><em>C. jeikeium</em> (agent?)</td>
<td>1</td>
</tr>
<tr>
<td>9</td>
<td>F</td>
<td>89</td>
<td>Pneumonia</td>
<td>Pulmonology</td>
<td>Blood</td>
<td><em>C. jeikeium</em> (agent?)</td>
<td>1</td>
</tr>
<tr>
<td>10</td>
<td>F</td>
<td>66</td>
<td>Cystitis</td>
<td>Urology</td>
<td>Urine</td>
<td><em>C. urealyticum</em> (agent) 10^3 cfu/ml growth</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>M</td>
<td>49</td>
<td>Soft tissue infection</td>
<td>Urology</td>
<td>Wound</td>
<td><em>C. amycolatum</em> (agent) (Abundant leukocytes, gram-positive bacilli)</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>M</td>
<td>68</td>
<td>DM + osteomyelitis</td>
<td>Infectious Diseases</td>
<td>Wound Culture</td>
<td><em>C. minutissimum</em> (agent)</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>F</td>
<td>55</td>
<td>Otitis media</td>
<td>Ear Nose and Throat (ENT)</td>
<td>Ear</td>
<td><em>C. minutissimum</em> (agent) (Rare leukocytes, epithelial cells, gram-positive bacilli)</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>F</td>
<td>63</td>
<td>DM + diabetic foot</td>
<td>Infectious Diseases</td>
<td>Wound</td>
<td><em>C. minutissimum</em> (agent) (Abundant leukocytes, gram-positive bacilli)</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>F</td>
<td>75</td>
<td>Coronary failure, soft tissue infection</td>
<td>Internal Diseases</td>
<td>Catheter + Wound</td>
<td><em>C. minutissimum</em> (agent) (Leukocytes and gram-positive bacilli)</td>
<td></td>
</tr>
</tbody>
</table>

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foot wound. It was isolated in a wound and catheter culture of a patient with coronary artery insufficiency. Otitis media was also seen as effective (Table 1). Identification of *Corynebacterium* species can be difficult because of rapid taxonomic changes. Susceptibility testing of these micro-organisms is not yet standardized. However because of their growing clinical importance, data on these bacteria are accumulating. After decades of confusion on their clinical significance, non-diphtheria corynebacteria have emerged as important pathogens causing many serious infections.

**Conflict of Interest**
No conflict of interest was declared by the authors.

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**Human Rights Statement**
All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

**Animal Rights Statement**
Nonapplicable.

**Scientific Responsibility Statement**
The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

**References**

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