

## Rapidly growing mycobacteria of medical importance

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Robert Koch discovered tubercle bacilli and reported it in Berlin, in 1882.<sup>1</sup> In November 1884, Lustgarten<sup>12</sup> reported to the Royal Society of Medicine in Vienna that he had found a bacillus with the staining appearance of tubercle bacilli in syphilitic chancres and gumma. The organism was subsequently named *Mycobacterium smegmatis* and was the first *Mycobacterium*, after the tubercle bacillus, to be identified. After that, others reported the isolation of acid-fast bacilli from the sputum of patients with normal and abnormal chest X-ray. But because these organisms lacked pathogenicity for the quinea pig, there was reluctance to regard them as pathogenic for human beings. In 1959 Tempe and Runyon proposed that mycobacteria other than *M. tuberculosis* did cause disease,<sup>3</sup> and subsequently Runyon developed the first working classification of these organisms in 4 groups, namely photochromogens, scotochromogens, nonchromogens and rapid growers.<sup>4</sup> Moreover, *Mycobacterium* other than tubercle bacilli (MOTT bacilli) were occasionally identified. In 1985 the Center for Disease Control, Atlanta, USA, recognized 23 species of rapidly growing mycobacteria among 54 species of mycobacteria.<sup>5</sup>

Rapidly growing mycobacteria usually appeared as colonies within about 1 week. The initial Gram stains revealed beaded gram positive filamentous organisms that suggested *Nocardia* species. Partial or modified acid fast stains demonstrated bacterial filaments that were actually mycobacteria. They could grow on various microbiological media such as blood agar for isolation of bacteria, sabouraud's agar for isolation of fungi, Lowenstein-Jensen and Middlebrook 7 H10 for isolation of mycobacteria.<sup>6</sup> As with other MOTT bacilli, they could be isolated in nature from sources such as water and soil.<sup>7</sup> They were often considered to be merely saprophytic organisms, but cases of rapidly growing myco-

bacteria as pathogens of cutaneous<sup>8</sup> as well as systemic infection<sup>9</sup> were increasingly reported. At present, the rapidly growing mycobacteria of greatest medical importance are *M. fortuitum*, *M. chelonae* and *M. smegmatis*.

*M. fortuitum* was proposed by da Costa Cruz in 1930<sup>10</sup> for an organism isolated from a subclavicular abscess. Gordon and Smith published a complete description of the species in 1955.<sup>11</sup> *M. chelonae* was applied by Bergey et al. in 1923<sup>12</sup> to a rapidly growing *Mycobacterium* isolated from a turtle in 1903 by Friedemann.<sup>13</sup> These two closely related species were formerly classified as the *M. fortuitum* - *M. chelonae* complex. *M. fortuitum* and *M. chelonae* gave positive results with the arylsulfatase test within 3 days. The nitrate reduction test and iron uptake were positive only for *M. fortuitum*, whereas *M. chelonae* gave negative results in these tests (Table 1).<sup>5</sup>; *M. fortuitum* contains three biovariants, namely *M. fortuitum fortuitum*, *M. fortuitum peregrinum* and the *M. fortuitum* 3rd biovariant complex. *M. chelonae* also contains three biovariants, namely *M. chelonae chelonae*, *M. chelonae abscessus*, and *M. chelonae* (turtle-like).

*M. fortuitum* and *M. chelonae* are capable of producing a variety of clinical infections, and the number of reported cases confirms that this is not a rare occurrence. The most commonly documented illnesses, in order of frequency, are cutaneous disease and deeper infection (usually abscesses) after trauma, infection, surgery, systemic infection (following cardiac surgery), ocular infection,<sup>14</sup> and in the immunosuppressed host disseminated disease may occur. Mostly cases are nosocomial epidemics such as after vaccination,<sup>15</sup> augmentation mammoplasty,<sup>10</sup> and with the case of indwelling catheter<sup>17</sup> among dialysis patients.

The cutaneous lesions are characteristically well localized, nodular, erythematous and often have an area of central necrosis. They have not been found associated with regional lymphadenopathy. Patients do not have fever or an elevated white blood cell count. Pathological findings have revealed

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**Table 1** Identification of rapidly growing mycobacteria of medical importance.

| Descriptive Term    | Species (subspecies)             | Colony morphology | Temperature growth range °C | Arylsulfatase 3 and 14 days | Carbon Sources |          |          |                   |             | Late developing yellow pigment |
|---------------------|----------------------------------|-------------------|-----------------------------|-----------------------------|----------------|----------|----------|-------------------|-------------|--------------------------------|
|                     |                                  |                   |                             |                             | Sodium citrate | Inositol | Mannitol | Nitrate reduction | Iron uptake |                                |
| Rapid growers       | <i>M. fortuitum fortuitum</i>    |                   | 22-40                       | }                           | -              | -        | -        |                   |             |                                |
|                     | <i>M. fortuitum peregrinum</i>   | S                 | 22-37                       |                             | -              | -        | +        | +                 | +           |                                |
|                     | <i>M. fortuitum</i>              |                   | 22-37                       |                             | +              | -        | +        | +                 |             | -                              |
|                     | 3 rd. biovariant complex         |                   |                             |                             |                |          |          |                   |             |                                |
|                     | <i>M. chelonae chelonae</i>      |                   | 22-36                       |                             | +              | -        | -        | -                 | -           | -                              |
|                     | <i>M. chelonae abscessus</i>     | S 60%             | 22-40                       |                             | -              | -        | -        |                   |             |                                |
|                     | <i>M. chelonae</i> (turtle-like) | R 40%             | 22-30                       |                             | +              | -        | -        |                   |             |                                |
| <i>M. smegmatis</i> | S                                | 25-45             | -                           |                             |                |          | +        | -                 | +           |                                |

Note : S = smooth, R = rough

acute and chronic inflammation, and some specimens show microabscesses. Well formed granulomas containing centrally placed Langhans-type giant cells have found.<sup>18</sup>

Systemic infection may occur from 6 to 40 days after operation (median, 40 days).<sup>19</sup> One patient had to be readmitted when pain or drainage from incision occurred. Drainage from the wound is usually watery, serosanguinous or of a greenish turbid nature.

A review of rapidly growing mycobacterial infections complicating 13 cardiac operations revealed 4 *M. fortuitum*, 8 *M. chelonae* and one unidentified species.<sup>19</sup> Among 125 cases of disease due to rapidly growing mycobacteria studied in USA, 83 per cent of isolates of *M. fortuitum* were *M. fortuitum fortuitum*,<sup>9</sup> which can absorb the green color of malachite green after prolonged incubation at 4°C, whereas 80 per cent of isolates of *M. chelonae* were *M. chelonae abscessus*. A survey of MOTT bacilli from 100 samples of water and soil in the Bangkok area in 1987 revealed 57 *M. fortuitum* and 2 *M. chelonae* from soil and 18 *M. fortuitum* and 2 *M. chelonae* from water.<sup>7</sup> This shows that *M. fortuitum* is more prevalent in nature.

The therapeutic management of *M. fortuitum* and *M. chelonae* poses some difficulties. A review of drug susceptibility of *M. fortuitum* and *M. chelonae* disclosed that they are resistant to antituberculous drugs<sup>14</sup> and that only an occasional strain is susceptible to high concentrations of rifampicin and ethambutol. But they are susceptible to aminoglycosides which contain 2-deoxystreptamine rings such as amikacin, gentamicin and kanamycin.<sup>20</sup> As *M. fortuitum* and *M. chelonae* are mycobacteria, to avoid drug resistance more than one drug should be prescribed, and therefore a tetracycline derivative has been recommended.<sup>19,21</sup>

*M. smegmatis*, which closely resembles *M. fortuitum*, is just now playing an important role in medicine.<sup>22</sup> The colony type is smooth for most clinical isolates and rough for labora-

tory strains. It gives a negative 3 day arylsulfatase test, is positive for iron uptake, gives a low semiquantitative catalase test, grows well at 43-45°C, and in 50 per cent of isolates, a late-developing (10-14 days) yellow-to-orange pigment develops. The pigment develops in the dark but is enhanced by light. The pigment is most easily detected on 7H 10 agar plates and is rarely seen on trypticase-soy agar or Mueller-Hinton agar.

Wallace et al.<sup>23</sup> reported 22 clinical isolates of *M. smegmatis*. Seven of the isolates were obtained after cardiac surgery, 12 isolates were from other types of skin and soft-tissue infections and 3 isolates were of respiratory origin. *M. smegmatis* can produce disease in humans, with a pattern of infection very similar to that of *M. fortuitum* and *M. chelonae*. Clinical disease due to *M. smegmatis* has been reported in animals, such as mastitis in bovines and sheep.<sup>24</sup>

*M. smegmatis* is resistant to isoniazid and rifampin, but susceptible to ethambutol, cefoxitin and cefmetazole, and also moderately susceptible to doxycycline, sulfamethoxazole, amikacin and ciprofloxacin.

In the Mycobacteriology laboratory, Department of Microbiology, Siriraj Hospital, Mahidol University, *M. fortuitum* and *M. chelonae* have been increasingly isolated from abscesses of the skin (3-5 cases each year). Judging from these experiences and from literature reports, rapidly growing mycobacteria appear to be far more common than previously described. Because they are common environmental organisms,<sup>26</sup> it is anticipated that their involvement in human disease will be continually seen.

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