SHORT REPORT
Seasonality of clinical isolation of rapidly growing mycobacteria

X. Y. HAN*
Department of Laboratory Medicine, The University of Texas M. D. Anderson Cancer Center, Houston, TX, USA

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SUMMARY
Rapidly growing mycobacteria (RGM) are environmental organisms that have emerged as significant human pathogens. RGM infections show remarkable geographic variations. In this study, based on data from Houston, Texas, RGM were isolated from clinical cultures year-round, although peaks in the summer and autumn correlating with the seasonal variation of temperature and rainfall also were noted. These results may offer some explanation for the summer occurrence of RGM outbreaks at diverse locations.

Seasonal variations for many infectious diseases, such as malaria, vector-borne viral infections, enteric bacterial infections and others are well known because climatic changes affect vectors, abundance of causative organisms and transmission. Rapidly growing mycobacteria (RGM) have emerged as significant human pathogens, causing infections in healthy as well as immunocompromised hosts [1]. RGM are of environmental origin, particularly in water [2, 3], and human infections are usually opportunistic, resulting from contact with contaminated water or soil [4–8]. It has been observed that RGM infections are more common in the South-eastern United States [9], and presumably environmental factors, such as the warm and wet climate in that region, may play a role. In this study, I examined seasonal variation of the isolation of clinical RGM strains in Houston and correlated the pattern with local climatic data. Findings were also used to examine the seasonal pattern of RGM outbreaks reported in the literature.

The RGM strains were consecutive (sporadic) clinical isolates from January 2000 to December 2006 at The University of Texas M. D. Anderson Cancer Center, a 500-bed comprehensive cancer center in Houston, Texas. Most patients with RGM isolates carried primary diagnosis of cancer and some were referred for suspected cancer but found to have a non-cancer diagnosis. About 70% patients were from the greater Houston area and the rest of Texas; out-of-state patients usually required extended stays in Houston to receive anti-neoplastic therapy. Mycobacteria were isolated from culture following standard procedures [10, 11]. The number and results of cultures during the study years was retrieved electronically from the microbiology culture database. The RGM culture-positive rate was calculated as the number of RMG-positive cultures divided by the total number of mycobacterial cultures performed. The RGM organisms were all identified through sequencing analysis of the 16S rRNA gene as described previously [11, 12]. The average climatic data for Houston from 1971 to 2000 were obtained from the
National Climatic Data Center (www5.ncdc.noaa.gov). These long-range data were used as the norm to avoid short-time fluctuations.

During the seven study years, a total of 150 RGM strains (unique isolates from 150 patients) were isolated from 25,332 cultures (from 13,767 patients, mean 1.84 cultures per patient) with a positive rate of 5.9/1000. *Mycobacterium abscessus*, *M. fortuitum* complex, and *M. mucogenicum* were the most common species, together accounting for 136 strains (90.7%). RGM infections included 60 cases of bacteraemias, 34 cases of acute and/or chronic respiratory infections, and 10 cases of other infections involving skin, tissue and wounds. There were 46 strains (30.7%) of which the clinical significance was uncertain. There were 29 cases where one or more concomitant organisms were identified, such as cytomegalovirus, respiratory syncytial virus, various bacteria, and fungi. Comorbidities, such as prior lung injuries, presence of intravascular catheters, and use of glucocorticoid steroids were common. Details of the clinical analysis can be found elsewhere [11].

The cumulative monthly isolation rates are shown in the Figure. These organisms were isolated throughout the year, a finding consistent with the wet and warm climate in this Gulf coastal city. In Houston, the rainfall was abundant all year round with a peak in June (173.7 mm) and a nadir in February (76.5 mm). The monthly mean of daily mean temperatures ranged from 12.4 °C in January to 29.1 °C in July and August (min. 7.2 °C, max. 33.9 °C). As seen in the Figure, a seasonal variation for RGM isolation also is evident. The isolation rates were lowest from January to May (4.2/1000 to 5.1/1000, averaging 4.6/1000, or 48 strains from 10,465 cultures), suggesting a winter effect that followed the lowest temperature (all <15.6 °C) from December to February and less rainfall (all <120 mm) from December to April. As the temperature rose steadily to well above 15 °C from March to May and the rainfall (along with humidity) increased in May (129.8 mm), the RGM isolation rates started to rise in June. They peaked in July and August (7.0/1000), lagging behind the peak rainfall (173.7 mm) in June by 4–8 weeks. Following the drier summer in July and August (<120 mm of rainfall) despite high temperature, the RGM isolation rate dropped to baseline level (4.4/1000) in September. Afterwards, more rainfall in September and October (together 301.7 mm) was followed by the highest peak (9.1/1000) of RGM isolation in October about 2–4 weeks later. The clinical RGM activity remained high in November and December, suggesting a cumulative effect of high temperature and more rainfall throughout the summer and autumn (i.e. probably more environmental RGM activity). The combined RGM isolation rate in October, November, and December was 7.9/1000 (50 strains from 6,337 cultures), significantly higher than the baseline level, i.e. the average of 4.6/1000 from January to May ($\chi^2 = 7.43$, $P = 0.006$). The sharp decline from December to January signified the seasonal shift of RGM activity.

Together, the data analysis showed the following patterns:

1. Year round clinical RGM activity was seen in Houston where monthly temperature is above 12.4 °C and rainfall over 76.5 mm;
(2) both monthly temperature >15 °C and rainfall >120 mm during the preceding month were required for more RGM activity; (3) the summer and fall RGM peaks lagged behind their corresponding peaks of rainfall in the late spring and early autumn by 2–6 weeks; (4) there were also warming and cooling effects of clinical RGM activity following their respective winter months and the long summer and autumn in Houston.

Some RGM infections may be chronic, such as chronic respiratory infection caused by *M. abscessus*, as observed in other clinical settings [13]. Because most of the RGM infections in this study were acute, such chronicity should have negligible effect on the observed seasonality. The effect due to referred patients from other states, particularly drier and colder northern states, should also be minimal due to the required extensive stay in Houston. The low-level fluctuation of the RGM activity from January to May [see Fig. (a)] is consistent with the above assessment.

In extrapolating from climatic changes to environmental RGM growth and risk for clinical RGM infections, the lack of direct environmental RGM data in the present study means that any correlation found must be considered preliminary. However, in the absence of environmental sampling for RGM at multiple sites over different seasons, the use of clinical RGM data may provide a possible proxy for environmental RGM activity. The definitive relationship between RGM environmental growth and risk for clinical infections requires further investigation, although these data suggest that the time from increased temperature and rainfall, to proliferation of environmental RGM, to more human RGM infection, may on average take a few weeks.

The year round clinical RGM activity in Houston may offer some explanation as to why the warm and wet Texas and other Gulf coastal states have seen more RGM infections than other places [9]. The findings of seasonality of clinical RGM and its correlation with climatic changes may be useful for the differential diagnosis of RGM infections and investigation of seasonal outbreaks. In addition to numerous reports of single cases and small series, there have been several previous reports of large single-source outbreaks of RGM infections [4–8]. As summarized in the Table, these outbreaks occurred in diverse geographic locations and included bacteraemias, dermatitis, and surgical wound infections. They all

<table>
<thead>
<tr>
<th>Time</th>
<th>Location and climate</th>
<th>Clinical manifestation</th>
<th>RGM species and source of contamination</th>
<th>Outcome of outbreak and control measure</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>April to November 1982</td>
<td>Louisiana, &gt;21 °C, similar to Houston</td>
<td>Bacteraemia in patients with dialysis</td>
<td><em>Mycobacterium chelonei s.s. abscessus</em>, haemodialyser*</td>
<td>Stopped upon decontamination</td>
<td>[4]</td>
</tr>
<tr>
<td>August to November 1998</td>
<td>Minnesota, 21 °C, short summer</td>
<td>Catheter-related bacteraemia in patients with cancer</td>
<td><em>M. mucogenicum</em>, municipal water with low chlorine level</td>
<td>Stopped after season, more chlorine in water in following years?</td>
<td>[5]</td>
</tr>
<tr>
<td>Started in April, most in July to October 2000</td>
<td>California, 21 °C, temperate</td>
<td>Dermatitis</td>
<td><em>M. fortuitum</em>, nail salon whirlpool tub</td>
<td>Stopped upon closure of salon</td>
<td>[6]</td>
</tr>
<tr>
<td>August to November 2003</td>
<td>Israel, 21–27 °C</td>
<td>Surgical wound infection</td>
<td>‘Mycobacterium jacuzzii’*, outdoor whirlpool tub</td>
<td>Stopped upon decontamination</td>
<td>[8]</td>
</tr>
</tbody>
</table>

* *Mycobacterium chelonei s.s. abscessus = M. abscessus* presently.  † Closely related to *Mycobacterium wolinskyi* and *Mycobacterium smegmatis.*
happened or peaked in the summer/autumn where the local temperatures were around or >21 °C, well above the 15 °C required for elevated RGM activity seen in this study. The outbreaks stopped upon decontamination or removal of the sources. Consistent with our finding of the predominance of M. abscessus, M. fortuitum complex, and M. mucogenicum, these three species (complexes) caused four of the five outbreaks. Of the mycobacterial species isolated from environmental water sources, M. mucogenicum is the most frequent [2]. In our clinical analysis (all sporadic cases) [11], M. mucogenicum caused over half of catheter-related RGM bacteraemias, a finding consistent with water contamination. Conversely, M. abscessus mainly caused respiratory tract infections with a tendency to disseminate through the bloodstream in severely immunocompromised patients while M. fortuitum complex infections are more diverse [11, 13].

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DECLARATION OF INTEREST

None.

REFERENCES