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## Fever in the hospital

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**T**his issue highlights common clinical conundrums facing physicians practicing in the 21st century, namely fever of unknown origin (FUO) and fever in neutropenic patients. Enigmatic causes of fever were classically described by Keefer and Leard in 1955 and by Petersdorf and Beeson in 1961. The medical triumphs of the half century since then have been matched by an increase in immune-compromised hosts and exploitative pathogens, an aging population, implanted biomechanical apparatuses, drug resistance, enhanced diagnostic capabilities, and a plethora of new anti-infective agents. As the article by Kakarala and Chin in this issue reports, the differential diagnosis of fever is as complex as ever.<sup>1</sup> While infections cause about 1/3 of the FUOs in North America, non-infectious etiologies, including malignancies and connective tissue disorders cannot be overlooked. Hosiriluck and Radhi review a management approach for febrile patients with neutropenia, typically a consequence of malignancy and/or chemotherapy.<sup>2</sup>

Further layers of complexity result with the emergence of new pathogens, the re-emergence of old pathogens, and the extension of known infectious agents outside their usual territories. Last year physicians in Texas unfortunately failed to consider the possibility of Ebola virus infection in a patient with a travel history to West Africa where an Ebola epidemic had been brewing for months. As populations increase and global travel becomes the norm, humans provide speedy mechanisms for pathogens to move across continents and catch us by surprise, such as the appearance of Middle East respiratory syndrome coronavirus (MERS-CoV) in the Republic of Korea this summer.<sup>3</sup> Injudicious use of antibiotics has fostered the emergence of bacterial strains, especially among Gram-negative pathogens, resistant to all known antibiotics, which can be spread to our patients via our own hands, especially when they aren't washed. The

anti-vaccine mentality has allowed herd immunity to wane prompting more cases of pertussis in the USA than has been seen in decades and an outbreak of measles earlier this year.<sup>4</sup> Well known pathogens can cause non-specific but severe illness yet occur sporadically enough to allow us to forget them, such as the recent *Listeria monocytogenes* infections transmitted via contaminated ice cream early this spring.<sup>5</sup> Surveillance networks have identified infectious diseases previously unknown in North America, such as Chikungunya virus infection in Florida<sup>6</sup>, enterovirus 68 infections causing severe respiratory disease into January of this year<sup>7</sup>, and cases of *Borrelia miyamotoi* infection in the Midwestern USA.<sup>8</sup> All are reminders for the wise physician when it comes to caring for the patient with a puzzling fever: review what you know (but may have forgotten), look for help when you don't know, and have the humility to admit there's a lot we don't know!

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