

# South Asia today: William Osler's world with antibiotics



In the past 5 years, *The Lancet Global Health* has reported seminal Articles about typhoid, typhus, tuberculosis, and antimicrobial resistance. This Comment will address these common problems in a different perspective over a longer time frame in south Asia. Typhoid and typhus fevers are the first two chapters in William Osler's *The Principles and Practice of Medicine*, published in 1892.<sup>1</sup> It is disheartening that well over a century later, south Asia continues to have a large burden of these diseases, despite antibiotics. Additionally, antimicrobial resistance—including antibiotic-resistant typhoid fever—is on the increase. For example, extensive drug-resistant typhoid fever in Pakistan's Sindh province has been documented since November, 2016.<sup>2</sup> The H58 strain of *Salmonella enterica* serotype Typhi, which is ubiquitous in south Asia, became extensively drug resistant by acquiring a so-called highly promiscuous DNA molecule (ie, a plasmid) from another common bacterium such as *Escherichia coli*. It will be no surprise if the extensively drug-resistant typhoid organism (which currently responds to only azithromycin and not ceftriaxone among the commonly used, effective typhoid drugs) spreads to other parts of Pakistan, or indeed the rest of the subcontinent, making treatment of this common disease daunting.

Regarding typhus, the absence of proper recognition of its varied clinical presentation continues to confuse medical practitioners in south Asia. Recently, typhus (eminently treatable with antibiotics)<sup>3</sup> has been shown to be an important cause of acute encephalitic syndrome, which could potentially be mistaken for other well established causes such as Japanese encephalitis (unresponsive to antibiotics) as reported from Gorakhpur, Uttar Pradesh, India.<sup>4,5</sup>

Antimicrobial resistance is not limited to typhoid in this subcontinent. For example, every day patients in this region walk into the emergency rooms with urinary tract infections due to *E coli* sensitive to only the last-resort antibiotics such as imipenem or colistin. Some years ago the same kind of infections caused by an *E coli* promptly responded to treatment with a fluoroquinolone, but not anymore.<sup>6</sup> Proper antibiotic stewardship as well as, crucially and effectively, dealing with the thousands of unregulated pharmacies with rampant over-the-counter sale of antibiotics has to be a priority of the local

governments. Otherwise, antimicrobial resistance will continue to flourish in this region, and indeed the world.

Vaccine administration is an underrated method of controlling antimicrobial resistance. The good news is that recently Nepal successfully completed vaccinating 20 000 children in a randomised controlled trial planned over 2 years to study the effectiveness of the new, more immunogenic conjugate typhoid vaccine so that the results might inform typhoid policy not only for Nepal but in the neighbourhood as well.<sup>7</sup>

Another devastating disease in south Asia,<sup>8</sup> presented in great detail in Osler's 1892 textbook,<sup>1</sup> is tuberculosis. Except, as in the case of typhoid and typhus, countries now have effective antibiotics against tuberculosis. In the control of tuberculosis, sputum examination for acid-fast bacilli using the Xpert MTB/RIF assay<sup>9</sup> (Cepheid, Sunnyvale, CA, USA) has recently been recommended by WHO as the primary method in making a diagnosis of pulmonary tuberculosis. This recommendation is a welcome change, and if done properly, especially using this assay in active case finding, it might well prove to be a game changer.

But unfortunately—just as its predecessor, the microscope for acid-fast bacilli stains—the Xpert MTB/RIF assay machine needs proper maintenance and repair. Additionally, public engagement is going to be vital for the success in introducing a new diagnostic aid. Unfortunately in many parts of south Asia, for example Nepal, both adequate ongoing maintenance work on these machines and public engagement need strengthening to make a substantial difference in tuberculosis control. Public engagement is often taken for granted in south Asia. Therefore, establishing public engagement networks will be key to tackling tuberculosis.

Is it possible that in the quest (albeit important) for elaborate molecular studies in diseases such as tuberculosis, investigators and scientists are neglecting the basics? Proper contact tracing, for example, which formed the basis in the control of smallpox and recently Ebola virus disease, is not given due importance for tuberculosis control in this region. The focus has been exclusively on the index patient with scant attention paid to household or work contacts. How will tuberculosis ever be controlled in this fashion?<sup>8</sup>

Understandably, Osler's book does not include emerging infectious diseases and the preparedness or

absence thereof. Unlike southeast Asia, fortunately, south Asia has not been the centre of a recent, major emerging infectious disease outbreak. However major outbreaks of Zika virus disease, Ebola virus disease, Middle East respiratory syndrome coronavirus, and avian influenza continue to be potentially devastating threats,<sup>10</sup> which will not require a passport to cross from one densely populated country to another. Obviously in this region, populated by a fourth (about 1.7 billion people) of the human population, surveillance and early detection of outbreak is paramount—but figuring out exactly how it will be achieved is a huge task.

*The Lancet Global Health* can continue to help by reporting worthwhile Articles from this region and raising the awareness of health-care professionals and subsequently policy makers regarding these common and emerging infectious diseases. In this way, the health security of not only south Asia but of the whole world will be enhanced.

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I declare no competing interests.

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