Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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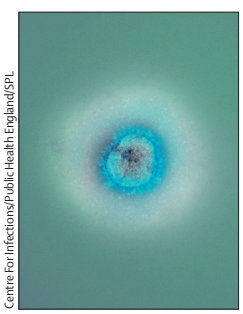
Rapid diagnostics urgently needed for killer infections



Centre For Infections/Public Health England/SPL

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Respiratory tract infections (RTIs) cause millions of deaths worldwide. They are caused by disparate bacteria, viruses, fungi, and parasites that have similar presentations and thus cannot be easily distinguished clinically. There is presently no standardised, rapid, accurate, sensitive, and specific point-of-care diagnostic test available that can identify causative pathogens within a few hours of consultation. Therefore, patients presenting with RTIs at all points of health care are empirically treated with broad-spectrum antibiotics designed to cover many possible pathogens.

The management of patients with RTIs is further complicated by the growing global threat posed by the emergence and spread of antibiotic-resistant bacteria[1] (including multidrug-resistant strains of *Mycobacterium tuberculosis*[2]) and azole-resistant fungi.[3] Clinicians are often unaware of the presence of more than one pathogen, although co-infections of bacteria[4] or other respiratory viruses[5] and influenza are well described, as are bacterial, viral, or parasitic infections with pulmonary tuberculosis.[6] Autopsy studies of patients who die because of RTIs suggest that, in many cases, the empirical antibiotic treatment prescribed was inappropriate for the causative pathogens, and that co-infections were not suspected before death.[7]

New and emerging pathogens with epidemic potential also pose diagnostic challenges. Global scientific and political attention is currently focused on two new viruses associated with severe RTIs and high mortality: the avian influenza A H7N9 virus from China and novel coronavirus from the Arabian Peninsula. Both were rapidly reported by the Program for Monitoring Emerging Diseases (ProMED). On March 31, 2013, the China Health and Planning Commission reported three cases of avian influenza A H7N9—a virus originating from poultry and wild birds.[8] As of May 14, a total of 132 confirmed cases of avian influenza A H7N9 (with 35 deaths; 27% case fatality) had been recorded by ProMED. The first case of novel coronavirus was reported in September, 2012, from Saudi Arabia. As of May 15, 2013, a total of 40 cases (with 20 deaths; 50% case fatality) have been reported to WHO according to ProMED: 30 in Saudi Arabia (15 deaths); two in Jordan (two deaths); four in the UK (two deaths); two in Germany (one death), and two in France (no deaths). Most cases were linked with the Middle East. The source of the novel coronavirus remains unknown. Person-to-person transmission has been recorded, but only in individuals with comorbidities, according to ProMED.

Transmission of RTIs—particularly imported influenza viruses—at mass gatherings is well documented,[9] and poses a threat to global health security. About 10 million pilgrims from 183 countries are expected to visit Mecca and Medina in Saudi Arabia for the Umrah and Hajj pilgrimages in 2013, and will be in close proximity to each other, thus posing a major public health concern. Rapid serological diagnostic tests for the novel coronavirus are in development and will be useful for surveillance and cross-sectional and longitudinal cohort studies.

Advances in molecular diagnostics have been applied to simultaneous detection of pathogens and their antibiotic resistance from one sputum sample. The absence of rapid accurate diagnostic tests for pulmonary tuberculosis was further compounded by the widespread inability to screen for drug-resistant bacteria. The introduction of the GeneXpert MTB/RIF Assay, which detects *Mycobacterium tuberculosis* DNA and rifampicin resistance from sputum samples in 2 h, could revolutionise tuberculosis diagnostics.[10] A lateral flow immunoassay for detection of meticillin-resistant *Staphylococcus aureus* in sputum is also now available.[11] Although several new rapid molecular diagnostic platforms capable of simultaneously identifying both pathogens and the genetic determinants of

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antimicrobial resistance are emerging,[12] they do not seem to be well suited to clinical presentations or downstream management strategies for patients with RTIs. Furthermore, none can identify new emerging organisms for which genetic sequences are unavailable. However, rapid sequencing technologies linked to bioinformatics have provided proof of diagnostic principle in a short time.[13]

Until new diagnostics are developed to serve clinical need, the mainstay of clinical management for any RTI will remain dependent on imperfect diagnostics and linked to empirical broad-spectrum antibiotics. Thus, clinicians have to maintain clinical awareness of other possible causes of RTIs, whether they are opportunistic or not.

An ideal diagnostic test for RTIs should be rapid (a result within 1 h of consultation), cheap, easy to use, sensitive, and specific, and should screen for many microorganisms and their antibiotic resistance. Furthermore, the diagnostics platform should be transportable, robust, and ideally run on solar power for use in the remote health-care settings in developing countries. Whether or not an ideal diagnostic platform for RTIs can be delivered, advances in biotechnology give hope. Such a device would improve the health and lives of patients with RTIs worldwide, and would also contribute to global health surveillance and security. To achieve this ideal, physicians, scientists, biotechnology companies, funding agencies, and governments need to work together to drive the development of improved diagnostic tests for both developed and developing countries.

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We declare that we have no conflicts of interest.

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Corrections

Powell C, Kolamunnage-Dona R, Lowe J, et al, on behalf of the MAGNETIC study group. Magnesium sulphate in acute severe asthma in children (MAGNETIC): a randomised, placebo-controlled trial. Lancet Respir Med *2013; 1: 301–08*—In this Article (published online April 22), the fourth sentence of the Findings section of the Summary should have been "The clinical effect was larger in children with more severe asthma exacerbation (p=0·03) and those with symptoms present for less than 6 h (p=0·049)". In table 1, the age range for both $MgSO_4$ and placebo groups should have been 2—15. And in table 3, the footnote p=0·143 for interaction between attack duration and $MgSO_4$ should have been added to the legend. This correction has been made to the online version as of May 30, 2013, and the printed Article is correct.