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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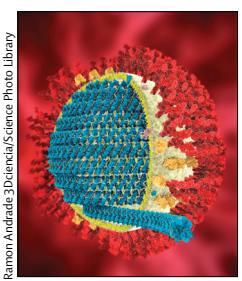
Treating MERS-CoV during an outbreak



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For more on **the number of MERS-CoV cases according to the US Centers for Disease Control and Prevention** see www.cdc.gov

When a new virus emerges, health-care systems face major challenges, not least of which is deciding which treatments to use. The drug development process, from novel compound screening to final approval, can take more than 10 years to complete and cost hundreds of millions of dollars. By contrast, viruses can emerge rapidly, spread widely, and pose a substantial, immediate threat to public health. For example, Middle East respiratory syndrome coronavirus (MERS-CoV) was first reported in November, 2012, and, as of September, 2014, cases have been reported in 21 countries, with 837 confirmed cases and 319 deaths.

Approved drugs can be repurposed for use against various viral infections to shorten the time taken from virus emergence to treatment availability. We, and others, have screened libraries of drugs for anti-MERS-CoV activity in vitro;[1,2] however, the absence of pathological small animal models makes the screening of many drugs in vivo challenging.

The major benefit to the screening of preapproved drugs is that these drugs are not required to undergo extensive safety testing to be used in human beings, since they are already deemed safe for human use. In *The Lancet Infectious Diseases*, Ali Omrani and colleagues[3] report the results of their retrospective cohort study on the use of the preapproved drugs ribavirin and interferon alfa-2a for the treatment of MERS-CoV.

Ribavirin is a synthetic analogue of the ribonucleoside guanosine. Ribavirin contains a carboxamide group on the guanine nucleotide, allowing ribavirin to be incorporated into RNA in place of either adenosine or guanosine and pair equally well with uracil or cytosine. Therefore, ribavirin is thought to introduce hypermutation into RNA replication products by random incorporation of uracil and cytosine. Ribavirin has been shown to have some efficacy for treatment of respiratory syncytial virus[4] and haemorrhagic fever viruses—eg, hantavirus[5] and Lassa fever virus.[6]

Interferon alfa-2a is a type I interferon, an innate immune cytokine involved in the antiviral innate immune response. Type I interferons have been identified as potential treatments for a range of viruses, and pegylated interferon alfa-2a is used in combination with ribavirin to treat hepatitis C virus infection.[7]

Omrani and colleagues present data from the first clinical use of ribavirin and pegylated interferon alfa-2a in patients with MERS-CoV. They show that treatment with ribavirin and pegylated interferon alfa-2a significantly improves survival 14 days after diagnosis of MERS-CoV infection (p=0·004). They note enhanced survival 28 days after diagnosis in patients who received ribavirin and pegylated interferon alfa-2a, but this enhanced survival was not statistically significant (p=0·054). The investigators acknowledge that the sample size in the study was small (44 patients; 20 who received treatment and 24 control patients) and a small sample might affect the statistics in a complex population. Therefore, the data for 28 days after diagnosis have value as a guideline and might be statistically significant in a larger sample of patients.

Despite the small number of patients, this study is the largest clinical test of ribavirin and interferon alfa-2a combination therapy, with previous studies presenting only five[8] and two[9] patients. This study takes advantage of the relatively large number of patients with MERS-CoV being treated at the Prince Sultan Military Medical City, Saudi Arabia, to make some important initial observations on the use of ribavirin and pegylated interferon alfa-2a combination therapy. In any outbreak situation, time to treatment is crucial, and the number of patients needed to undertake large-scale clinical trials might be too small while the pathogen is still rare. By contrast, the initial stages of an outbreak are often the most important for stopping the spread of the pathogen, therefore smaller studies such as this have a very important role as a guide for future clinical trials.

Overall, this study provides important guidance on the use of combination therapy and approved drugs in the treatment of the continuing MERS-CoV outbreak.

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We declare no competing interests.

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Sustaining rotavirus vaccination in Africa: measuring vaccine effectiveness

Diarrhoea is one of the leading killers of children in developing countries worldwide. Rotavirus has been identified as the most common cause of severe diarrhoea in children younger than 5 years, and is responsible for more than 2 000 000 hospital admissions and 450 000 deaths every year.[1] 95% of rotavirus deaths occur in low-income countries in Asia and Africa, with India, Nigeria, Pakistan, Democratic Republic of the Congo, and Ethiopia accounting for 50% of all global deaths. Most countries with a mortality rate exceeding 300 per 100 000 children are in Africa.

Although improvements in hygiene and sanitation coupled with the provision of safe drinking water have helped to reduce diarrhoeal disease, these approaches have been inadequate in preventing the spread of rotaviruses. The efficacies of the two available rotavirus vaccines—Rotarix (GlaxoSmithKline Biologicals, Rixensart, Belgium) and RotaTeq (Merck Vaccines, Whitehouse Station, NJ, USA)—were lower in pre-licensure trials in Africa and Asia (51–64%) than has been reported in high-income countries in Europe and Asia (98%).[2–5] However, because of the large disease burden and the anticipated bigger effect on public health, in 2009 WHO recommended the inclusion of these vaccines in national immunisation programmes, especially in those countries with high child mortality caused by diarrhoea.[6–8] So far, 69 countries worldwide have incorporated rotavirus vaccines into their immunisation programmes.[9] 21 countries in Africa have introduced these vaccines into their Expanded Programme on Immunization (EPI), supported by the GAVI Alliance Accelerated Vaccine Initiative.

However, after the GAVI funding period is complete, these countries will have to pay for the full cost of the vaccine. Sustaining rotavirus vaccination might cease to be a priority and will face competition from other needs for resource allocation from national budgets. Therefore, it is crucial to understand the population effect of routine rotavirus vaccination in countries in Africa, including the potential indirect benefits of vaccination, especially on severe outcomes and deaths from rotavirus and all-cause diarrhoea, and to document savings in health-care costs from vaccination.

Michelle Groome and colleagues' study of the effectiveness of monovalent human rotavirus vaccine against admission to hospital for acute rotavirus diarrhoea in South African children in *The Lancet Infectious Diseases*[10] provides the first evidence-based data from Africa (a region with a very high rotavirus disease burden) for the assessment of the effectiveness


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