

the differential diagnosis of sepsis or meningitis is broad. Third, although the path to commercialisation is underway, it might be challenging. Inexpensive, straightforward assays are excellent from public health and global health perspectives, but disruptive new technologies are not always adopted.

Irrespective of how successful the commercialisation process is, the authors have developed a novel diagnostic test for *Neisseria meningitidis* that is easy to use and provides results within 90 min. In such a timeframe, results can lead to actionable decision-making, most likely to halt further diagnostic testing. The niche for LAMP in meningococcal disease remains to be established, but the fact that the technique allows diagnostic confirmation at the treating hospital rather than a reference laboratory is a good start.

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## A more detailed picture of the epidemiology of Middle East respiratory syndrome coronavirus



In the *Lancet Infectious Diseases*, Marcel Muller and colleagues<sup>1</sup> present the first, well designed, credible, population-based seroepidemiological study of Middle East respiratory syndrome coronavirus (MERS-CoV) in Saudi Arabia.

Since the initial identification of MERS-CoV in 2012,<sup>2</sup> up to Mar 8, 2015, WHO have reported 1082 cases of infection with this virus, 439 of which ended in death.<sup>3</sup> Most cases were in countries in the Arabian Peninsula, with sporadic travel-related infections occurring elsewhere.

Although clusters of human-to-human transmission of MERS-CoV are well documented, transmission originates from zoonotic events, and therefore identification of the animal sources of MERS-CoV is a priority. Genetically, MERS-CoV is related to bat coronaviruses from China, Saudi Arabia, Europe, and Africa.<sup>2,4–6</sup> On the basis of the evidence so far, none of the bats from these countries are likely to be the reservoir for the virus.

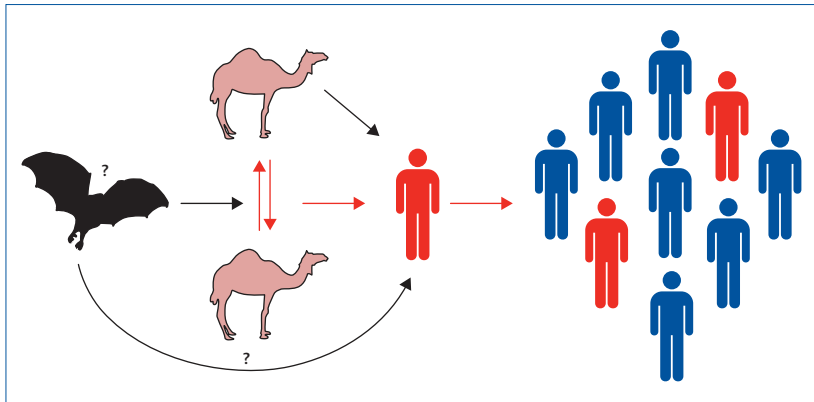
Evidence is accumulating that dromedary camels are a natural host of MERS-CoV. Serological findings suggest

that more than 90% of adult dromedaries in the Middle East and Africa are seropositive for MERS-CoV.<sup>7</sup> The virus isolated from dromedaries has spike proteins with conserved receptor-binding domains for the human dipeptidyl peptidase-4 receptor,<sup>8,9</sup> and MERS-CoV has been detected in camels that were in close contact with people with Middle East respiratory syndrome.<sup>10,11</sup>

The role of camels as a source of human infection with Middle East respiratory syndrome is controversial because many people who have the disease have had no obvious association with camels. Case-control studies that aim to define risk exposures of index patients have not yet been done, and an investigation of MERS-CoV seroprevalence in people in contact with camels yielded negative results (ie, no association was noted).<sup>8,12–14</sup>

The study by Muller and colleagues is the first population-based, seroepidemiological investigation of MERS-CoV infection in an area where zoonotic transmission is sustained. The investigators used a

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**Figure: The epidemiology of Middle East respiratory syndrome coronavirus**  
 Black arrows represent unconfirmed routes of transmission. Red arrows represent plausible routes of transmission. Red human figures represent people infected with Middle East respiratory syndrome.

cross-sectional design that tested serum samples from about 10 000 people in Saudi Arabia whose age and sex distribution was similar to that of the general population. By use of a rigorous serological testing algorithm, the investigators identified MERS-CoV antibodies in 15 (0.15%, 95% CI 0.09–0.24) of 10 009 samples from the general population. Men had a significantly higher proportion of infections (11 [0.25%] of 4341) than did women (two [0.05%] of 4378;  $p=0.025$ ), and more infections were noted in central rural areas than in coastal provinces (14 [0.26%] of 5479 vs one [0.02%] of 4529;  $p=0.003$ ). The investigators also obtained samples from camel shepherds and slaughterhouse workers, and showed that seroprevalence of MERS-CoV was 15–23 times higher in camel-exposed individuals than in the general population. The findings from this study suggest that young men in Saudi Arabia who have contact with camels in cultural or occupational settings are becoming infected with MERS-CoV, often without being diagnosed, and might proceed to introduce the virus to the general population in which more severe illness triggers testing for the virus and disease recognition. This hypothesis could account for cases of Middle East respiratory syndrome without previous animal exposure.

When the data from Muller and colleagues<sup>1</sup> are put into context with those from studies in camels, a clearer picture of the epidemiology of MERS-CoV emerges (figure). Camels seem to be a natural host for MERS-CoV and transmission within camel herds is well established.<sup>15</sup>

However, several questions need to be resolved. The route for camel-to-human transmission is unclear, and could be from one or more of the following: direct contact with infected animals, or consumption of milk, urine, or uncooked meat—all practices that are common in affected countries in the Middle East. An intermediate host could also transmit MERS-CoV between camels and human beings. Finally, whether dromedaries are the natural reservoir or an amplifier host is a hypothesis that is open to further investigation. Muller and colleagues' study is the first step along the way to addressing these questions.

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## Greatest effect of HPV vaccination from school-based programmes



Human papillomavirus (HPV) vaccination programmes have been in use in many countries since 2007 following licensing of the bivalent and quadrivalent HPV vaccines.<sup>1</sup> Clinical trials have shown that HPV vaccines have more than 90% efficacy in preventing high-grade cervical lesions caused by human papillomavirus types 16 and 18,<sup>2,3</sup> which are the two HPV types known to cause 70–80% of cervical cancers and large proportions of other anogenital and oropharyngeal cancers. The quadrivalent vaccine has shown similar efficacy in the prevention of anogenital warts caused by HPV types 6 and 11. Furthermore, both vaccines have shown lower—but still substantial—efficacy against related non-vaccine oncogenic human papillomavirus types.<sup>4,5</sup> Therefore, since rollout of these vaccination programmes began, there has been great anticipation to see whether these promising trial results will translate into substantial reductions in HPV-related disease at the population level.<sup>6</sup> In *The Lancet Infectious Diseases*, Mélanie Drolet and colleagues present the findings of a timely systematic review and meta-analysis assessing the population-level and herd effects of HPV vaccination programmes so far.<sup>7</sup>

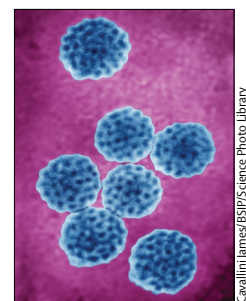
The key findings of the study suggest that in the pre-to-post-vaccination period covered by the 19 included studies, HPV type 16 and 18 infections and anogenital warts have decreased by more than 60% in girls (<20 years of age) when high female vaccination coverage (>50%) was reported. The authors also report significant reductions in HPV types 31, 33, and 45 infections in this same group (relative risk [RR] 0.72 [95% CI 0.54–0.96]) and in anogenital warts in boys younger than 20 years of age (0.66 [0.47–0.91]) and in women 20–39 years of age (0.68 [0.51–0.89]), which provides strong evidence of both cross-protection and herd effects. Smaller, but still significant, reductions in HPV types 16 and 18 infection (RR 0.50 [95% CI 0.34–0.74]) and anogenital warts (0.86 [0.79–0.94]) also occurred in girls and young women in

countries with lower vaccination coverage (<50%), but there was no evidence to suggest either cross-protection or herd immunity in these countries.

Drolet and colleagues aimed to report the population-level effect of vaccination and, although the results are very encouraging, we need to keep in mind that their study included both clinic-based and population-based studies, of which the clinic-based studies might not be representative of the underlying population. Additionally, vaccine coverage for the outcome of HPV prevalence was based on vaccine uptake in the study, which in some cases was substantially larger than that in the underlying population.<sup>8</sup> Although the authors did several subanalyses to investigate heterogeneity, we think it would have been helpful to do an additional subanalysis stratifying the data by clinic-based versus population-based study. Disappointingly, all the included studies were from high-income countries (nine countries in total) and we are therefore none the wiser regarding the effect of vaccination in low-income countries in which the burden of HPV-associated disease is highest.

This report shows that the maximum population-level effect of vaccination is achieved through delivery at a young age with high vaccination uptake rate. A result we found striking is that the greatest effect of vaccination, in both male and female individuals, was recorded for countries such as Australia, New Zealand, and the UK that have school-based vaccination programmes. This finding is corroborated by the results of another recent systematic review that assessed the effect of the quadrivalent vaccine on anogenital warts.<sup>9</sup> In this study, Mariani and colleagues reported that the greatest reductions in anogenital warts were achieved in countries with high vaccination uptake rates, mostly through school-based vaccination programmes, although some non-school-based programmes also achieved high vaccination uptake rates.

One concern with school-based programmes is the



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