that exclude Marshallese migrants from Medicaid, have restricted their access to health care.[2] Almost half (46%; 183/394) of the adult Marshallese population that was sampled was uninsured.[2] The large majority (80%; 312/392) did not have a primary care provider, and half (196/389) stated they needed to see the doctor in the past year but did not because of cost.[2] As Shah and colleagues point out, Marshallese children were also excluded from the ARKids First programme until 2017 (during the outbreak period). Despite low rates of insurance, the clear majority (92%; 1536/1676]) of children aged 5 to 17 years affected in the outbreak were vaccinated with two or more doses of measles, mumps, and rubella vaccination.[1]

Qualitative studies have shown that other social determinants of poor health at multiple levels of the community ecology are barriers to health-care access, including low access to transportation, food insecurity, limited English language proficiency, and scarce Marshallese medical translators.[4] Successful health interventions for reaching the Marshallese community in Arkansas have been culturally adapted and have used community health workers and non-traditional models of care, such as home visiting programmes.[5] These findings reinforce the need for culturally sensitive and informed outbreak-response efforts to engage this marginalised community.

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Host genetic factors can impact vaccine immunogenicity and effectiveness

Darren Westphal and Asha Bowen[1] commented on the study of Virgie Fields and colleagues[2] about a mumps outbreak in a highly vaccinated Marshallese community of Arkansas (USA). Their Comment provides an important discussion about the factors that can explain the outbreak in this specific situation. Westphal and Bowen ended their article with the following question: "Is vaccine effectiveness equal among all populations?"

Considering genetic diversity in a broad sense and data about susceptibility and resistance patterns of distinct human populations to different pathogens, we believe that vaccine effectiveness should differ according to the human population targeted. Different patterns of vaccination effectiveness among different populations would result from complex interactions of the host, pathogen, and environmental factors. In this sense, such differential patterns could arise because of (although not exclusively as a result of) distinct or characteristic host genetic factors such as frequencies of specific alleles of, for example, major histocompatibility complex genes in a given human population. As an example, we would like to call attention to an immune system-related genetic variant that is suggested to affect vaccine immunogenicity. Ganczak and collegues[3] have shown the homozygous genotype of CCR5Δ32 to be associated with reduced hepatitis B virus (HBV) vaccine immunogenicity. CCR5Δ32 is a 32-base-pair deletion in the coding region of the *CCR5* gene that affects CCR5 protein expression. CCR5 is a chemokine receptor involved in various immune reactions and pathological processes, including susceptibility to HIV infection and the inflammatory state seen in rheumatoid arthritis, cancer, and other diseases.[4] Since this genetic variant presents a characteristic distribution, being typically more frequent among populations of European origin,[5] the newly described influence of CCR5Δ32 on HBV vaccine immunogenicity demonstrates how the genetic background of different populations might influence the effectiveness of vaccines. This point highlights the importance of not only ethnic origin but also the geographical distribution of the human population under investigation.

We acknowledge that it is unlikely that a given specific genetic variant would substantially affect the effectiveness of most vaccines. Following this same reasoning, we are not affirming that genetic factors would indeed explain the results of Fields and colleagues. However, the scenario mentioned above reminds us that the influence of human genetic factors on vaccine effectiveness is a neglected issue. Studies exploring the genetic variability of distinct human groups can help us to understand differentiated patterns of vaccine response among different human populations.

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Purulent bronchitis in 1917 and pandemic influenza in 1918

A remarkable *Lancet* paper, which is probably the first description of the so-called 1918 Spanish influenza outbreak,[1] is omitted from the journal's Pandemic influenza: 100 years microsite. We wish to draw attention to this work, both to augment the excellent timeline of landmark events in influenza history in the microsite and to describe this early paper's relevance to understanding the origin of the 1918 influenza pandemic.

With great clarity Hammond and colleagues,[1] British army medical officers serving in Étaples, France, described purulent bronchitis that presented with a "symptom complex so distinctive as to constitute a definite clinical entity" in 71 soldiers who died during the winter of 1916–17. They detailed the clinical, bacteriological, and postmortem features of the disease, typically including dyspnoea without orthopnoea, cyanosis, tachycardia, thick, purulent sputum obstructing the upper airways, and right-sided heart failure. Importantly, they noted that the disease carried high risk of death and that it affected young adults—although the age group was not surprising in the context of the military encampment, which was the largest complex of hospitals serving the Western Front. Publication rapidly stimulated another British military medical group to report a similar outbreak in Aldershot, UK, in March to May, 1917.[2]

Although the clinical features described in these and subsequent reports varied—eg, the quantity of pus expectorated by patients, the extent of lung consolidation, and the degree of right-sided heart failure—sufficient consistency of clinical, bacteriological, and postmortem findings existed for some contemporary clinicians and scientists to conclude that purulent bronchitis was an early manifestation of 1918 influenza and its sequelae.[3,4]

Nevertheless, proof would require confirmation that both purulent bronchitis and so-called Spanish influenza were caused by the same virus. Fortunately, one of the authors of the 1917 *Lancet* paper, William Rolland, a histopathologist and general practitioner, kept a box of samples from soldiers who died, fixed in wax and mounted on glass slides, including samples from lung, lymph node, and diaphragm (figure). After his death in 1943, Rolland's wife disposed of many of his belongings, but his son, Charles Rolland, rescued the slides and subsequently passed them on as family heirlooms to his son-in-law, Jim Cox.

Analysis of viral genetic sequences from this human tissue, if technically successful, would confirm or deny whether the outbreak of purulent bronchitis in France in the winter of 1916–17 was indeed influenza caused by the same virus as the 1918 pandemic. Confirmation would mean that current alternative hypotheses, such as that the earliest known cases of the pandemic were detected in China in 1917, or in Kansas, USA, in early 1918,[5] could be definitively discounted.

Hopefully, the results of genetic sequencing of material in the slides will be available later in 2019.

***Figure*: Slide from Dr William Rolland's collection, "Private Cherry, tissue attached diaphragm", Feb 18, 1917**
Specimen is from one of the patients documented in reference 1.

For **Pandemic influenza: 100 years** see https://info.thelancet.com/pandemic-flu-100?utm_campaign=pandemicflu100&utm_source=boombox%C3%82

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