authors used data gathered from 33 clinical trials and 19 cohort studies involving more than 20 000 patients and 102 different treatment regimens to show that initially isoniazid-resistant disease was associated with significantly poorer outcomes than was isoniazid-sensitive disease. They used statistical methods to demonstrate that use of standard WHO first-line drug regimens in patients with isoniazid-resistant tuberculosis could lead to 60 000 new multidrug-resistant cases annually. This study should prompt clinicians to establish fully the drug-resistance pattern before prescribing an anti-tuberculosis regimen especially in places where the prevalence or incidence of resistance to isoniazid is high.

An investigation by the European Respiratory Society and European Centre for Disease Prevention and Control of the effect of the European standards for tuberculosis care[7–9] published in 2012 showed that adoption of this important document is still suboptimal and that more advocacy and training are necessary. In other words, publication of evidence-based standards or guidelines[10] is important, but not sufficient to achieve high-quality diagnosis, treatment, and prevention of tuberculosis and latent tuberculosis infection.[11,12] The findings of Gegia and colleagues[2] are really useful to guide the upcoming WHO guidelines on tuberculosis treatment and the joint American Thoracic Society, Euopean Respiratory Society, US Centers for Disease Control and Prevention, and Infectious Diseases Society of America treatment guidelines on drug-resistant tuberculosis.

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When free is not fair: the case of vaccine donations

On Oct 10, 2015, Médecins Sans Frontières (MSF) rejected Pfizer's proposed donation of 1 million doses of its branded pneumococcal conjugate vaccine (PCV).[1] The news caused a stir in the global health community; after all, free essential health goods might be considered something to be celebrated.

This decision represents the latest development in a prolonged advocacy campaign spearheaded by MSF, which aims to reduce the cost of PCV, and presents a timely opportunity to examine the case for vaccine donations. In their rejection of Pfizer's offer, MSF cited several concerns related to the donation of pharmacological agents—namely, conditions attached to donation agreements, the sustainability of programmes dependent on donations, and the deleterious effect of donations on the incentive to reduce prices.

To understand MSF's concerns, the history of drug donation programmes should be explored. Perhaps the

most thoroughly documented case in the drug donation debate is the decision by Pfizer to donate fluconazole (Diflucan) for use in South Africa in 2000. To facilitate the treatment of HIV-related opportunistic infections, activists had lobbied for either a price reduction or the issue of a voluntary license to permit generic production of fluconazole. At the time, manufacturers in Thailand were marketing generic fluconazole for US$0·29 per unit, while Pfizer continued to dictate the cost of the same drug in South Africa, charging as much as $8·25 per unit.[2] Pfizer subsequently delayed the delivery of Diflucan, causing local activists to illegally import 3000 capsules of generic fluconazole from Thailand to demonstrate the ease by which the drug could be provided to patients.[3] In the months following Pfizer's commitment to donate Diflucan, the company imposed the following conditions: clinical use would be limited to patients with cryptococcal meningitis, thereby excluding many patients with oral or oesophageal candidosis; the drug would only be available for patients in South Africa; and the donation agreement would expire after a period of approximately 2 years. Although some of these decisions were later retracted, a year passed before the first batch of donated Diflucan arrived in South Africa. During this period, Pfizer also remained a key litigant in a case against the South African government, which challenged legislation intended to make medicines more affordable.[4]

The Diflucan partnership has since been described as an "institutional compromise midwifed by conflict between public and private interests".[5] However, the motivation to engage in donation programmes, and the terms on which such programmes are negotiated, are clearly primarily determined by strategic financial considerations; Hank McKinnell, the then chief executive officer of Pfizer, revealed that "the marginal cost of our drugs is very low, so if we give away a drug to somebody who wouldn't otherwise buy it, the profit impact of that action on us is just about zero".[6]

The unpredictable nature of such profit-constrained philanthropy was central to MSF's rejection of Pfizer's proposed donation of branded azithromycin for the treatment of trachoma in Mali.[6] Instead, MSF paid to import a generic version of the drug, thereby ensuring market competition and supply continuity. The misalignment of public health and private corporate priorities is arguably the most important criticism of donated pharmaceuticals: as Baker and Ombaka[7] have explained, "market size and expected profits are the main drivers of entry of generic drugs", whereas donations "capture market share, and thus demotivate generic entrants". Such a strategy could have ramifications in the case of PCV, particularly given the anticipated entry of the Serum Institute of India's ten-valent PCV at the affordable price of $2 per dose within the next 2 years.[8]

Further concerns include the ability of donation programmes to distort rational drug use and to disproportionately burden public health structures, particularly when such schemes are run in parallel to national systems for procurement and distribution.[9] Finally, critics have cautioned that donation programmes tend to only meet a fraction of requirements. The decision by Boehringer Ingelheim to donate nevirapine for the prevention of vertical transmission of HIV in the early 2000s is a good example; the donation was limited to a particular subpopulation and distracted from the urgent need to reduce the cost of antiretroviral treatment for all patients who are HIV positive.[10] One notable exception to this trend was Merck's pledge to donate ivermectin "wherever needed for as long as needed" for the treatment of onchocerciasis.[9]

With these criticisms in mind, a donation of 1 million units of PCV is clearly an inadequate solution given the global burden of pneumococcal disease. Although vaccine donations could help a finite number of children, they do little to help the millions of children requiring immunisation against pneumococcal infection every year. Without a sustained commitment to price reductions, and healthy competition between pharmaceutical companies, vaccine donations will remain an ineffective remedy to the global burden of vaccine-preventable diseases.

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How long until routine *Helicobacter pylori* antimicrobial susceptibility testing?

Three excellent consensus reports about the management of *Helicobacter pylori* infection and its treatment in adults have been published.[1–3] Recommendations for eradication therapy are given, supported by many experts in the field. We agree with the reports that the goal of *H pylori* therapy should be eradication in at least 90% of treated patients. The three reports emphasise the increased resistance of *H pylori* to antimicrobials and the implication of resistance in treatment failures. Although culture-guided therapy is associated with higher eradication success rates as referred by two of the reports and corroborated by others,[1,2,4,5] why is the main recommendation of the consensus papers not when possible, in all patients undergoing an endoscopy, a request for *H pylori* culture and its antimicrobial susceptibility or molecular determination of resistance must be performed?

Antimicrobial susceptibility testing has been routinely done on most clinical bacterial isolates for over half a century. Why then did gastroenterologists resign themselves to saying susceptibility testing of *H pylori* is not currently clinically practical? In the 21st century, it is not acceptable to read that *H pylori* culture is troublesome and time-consuming. Most microbiology laboratories are able to culture *H pylori* from gastroduodenal biopsies. Every day these laboratories culture samples that are more troublesome, more time-consuming, and more risky than *H pylori*. Most clinical laboratories can culture campylobacter from faeces, a microorganism that needs the same atmospheric requirements as *H pylori*, and similar staff training and laboratory costs.

In 1999 our working group published a paper entitled "How long for the routine *H pylori* antimicrobial susceptibility testing? The usefulness of the string test to obtain helicobacter for culture",[6] and 17 years later we are asking the same question. Since the commercial production of the string test (Entero-Test; HDC Corporation, Mountain View, CA, USA) ended, the only way to obtain *H pylori* strains is by endoscopy. Until 2013, Entero-test allowed the culture of *H pylori* without endoscopy;[7] because of the interruption in the manufacture of the Entero-test, only a few institutions used it.[6,8–11] Apart from the string test, our laboratory has cultured more than 17 000 samples of gastroduodenal biopsies and susceptibility testing was done in almost all positive cultures (>7800). It is surprising that despite the rampant increase of antimicrobial resistance, the idea is still being promulgated that the study of antimicrobial susceptibility is not useful in *H pylori* infection.

As in all other bacterial infections, we encourage gastroenterologists and primary care physicians who treat patients infected with *H pylori* not to be content with knowing only if their patients are infected with *H pylori*. When doing an endoscopy in those patients, the biopsy should be sent to the microbiology laboratory for culture of *H pylori*, and if positive, susceptibility must be tested at least against the five most commonly used antimicrobials: amoxicillin, clarithromycin, metronidazole, tetracycline, and levofloxacin. It is time to break the myth that *H pylori* culture is troublesome and time-consuming.

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