

## Generic medicines are not substandard medicines

Sir—Carol Adelman and Jeremiah Norris (Dec 22/29, p 2174),<sup>1</sup> who work for the industry-funded Hudson Institute, advocate the use of patented drugs, pointing to what they say are risks associated with generic drugs. They confuse generic drugs with old, substandard, ineffective, and counterfeit drugs.

Generic does not mean old. The 1996 World Trade Organisation (WTO) Agreements mandate all member countries to provide 20-year patent protection for medicines. Before that date, however, many countries (including Spain, Finland, and India) thought of medicines as too important to subject to market monopolies and exempted them from patentability. All drugs in these countries could, therefore, be generic. This situation is still true for countries that have not implemented the WTO Agreements.

Drug quality is important. Médecins sans Frontières advocates for improved quality surveillance. We support WHO's efforts to assist countries by assessing quality of many technically complicated pharmaceutical products, including the prequalification of generic antiretroviral suppliers.

Generic does not, however, mean unsafe or ineffective, just as patented does not necessarily mean safe and effective. Most medicines on the WHO Model Essential Drugs List are generic. Many vital patented drugs are excluded from the list because they do not meet the affordability criteria. For drug resistance and treatment adherence, generic companies may be in a better position to provide effective treatments by producing certain combinations and formulations that brand companies cannot or will not produce.<sup>2</sup>

Counterfeiting is a separate issue referring to the deliberate and fraudulent mislabelling of medicines for identity or source. Counterfeiting mostly concerns expensive branded drugs.

The only consistent practical difference between generic and patented drugs is their price. Because market monopolies drive prices up, generic agents are less expensive. The price of patented drugs is a barrier to access to medicines for many diseases that are common in less-developed countries. Access to AIDS medicines has increased strikingly in some countries through the use of generic drugs.<sup>3</sup> Affordable, high-quality, generic alternatives exist for many diseases causing substantial mortality and

morbidity in the less-developed world (eg, trachoma, kala-azar, and cryptococcal meningitis<sup>4</sup>), which, if the right prohealth policies are implemented, could be used to increase access in all countries in need.

Introduction of market competition through parallel importation (competition between branded drugs) or compulsory licence (competition with generic drugs) is an important way to lower drug prices in a sustainable way. The Brazilian government, for example, has used extensive generic production and the threat of compulsory licensing to reduce the price of AIDS drugs. The declaration at the WTO meeting in Doha in November, 2001,<sup>5</sup> which states clearly that countries can rightfully overcome patents, should encourage other countries to implement and use a compulsory licensing system for expensive drugs they deem essential in their health-care system.

Drug quality, safety, and effectiveness are matters of great concern. So is lack of access to essential medicines in the developing world. It is essential for millions of people that the latter is not limited by confusing and bias concerns over the former.

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### Authors' reply

Sir—It is discouraging that Nathan Ford and Ellen 't Hoen divert attention from the merits of science to disparage our institutional affiliation. More than 80% of Hudson Institute funding comes from individuals, foundations, and governments. We do not cast aspersions over the funding sources of Médecins Sans Frontières to engage in scientific debate with them.

First, we do not advocate use of only patented drugs. We do advocate standard practice of using both generic and patented drugs, as necessary. This

policy diverges from that of Médecins Sans Frontières, which advocates using only the cheapest generic drugs from developing countries such as India.

Second, we do not confuse generic drugs with “old, substandard, ineffective, and counterfeit drugs”, as Ford and 't Hoen say. Unfortunately, the chances of getting such drugs are much higher when searching for the cheapest drugs in developing countries. The high prevalence of these dangerous drugs in Nigeria and southeast Asia is alarming, as noted by other scientists: “The most probable cause of the poor quality of drugs is absence of adequate quality assurance during manufacture. Substandard drugs sold in the pharmacies of less-developed countries could contribute to global microbial resistance and therapeutic failure of infectious diseases.”<sup>1</sup>

Our main point is the same as that made by Li Wan Po<sup>2</sup> from the Centre for Evidence-Based Pharmacotherapy, that price should not be the only basis by which a supplier is chosen. Countries should buy high-quality generics, high-quality patented drugs, or both. For the safety of their citizens, however, they should not buy only the cheapest drugs from developing countries.

While older generic drugs can certainly be appropriate, WHO has voiced some concerns. They note that the increasing prevalence of strains of common pathogenic bacteria resistant to widely available, relatively cheap antimicrobials in the Essential Drug List is dangerously eroding their effectiveness.<sup>3</sup> Rubin<sup>4</sup> has noted that it is not the striking episode of an epidemic due to antibiotic-resistant organisms that is at issue; rather, it is the growing problem of endemic infection due to organisms resistant to formulary drugs.

Focusing on patents and compulsory licensing, as do Ford and 't Hoen, ignores the many real barriers to treating infectious diseases in poor countries—poverty, corruption, and lack of health-care infrastructure. In a study of 53 African countries, patents and patent law were not seen as a major barrier to treatment access, and the researchers noted that the option to patent antiretroviral drugs in Africa has frequently gone unexercised.<sup>5</sup> If patents and prices were the most important barrier to improved health care in developing countries, why has tuberculosis not been treated and cured with the low-priced, quality generic drugs that have been available for years?

To assert, as Ford and 't Hoen do, that quality, safety, and effectiveness

are not issues in the access to medicines debate is wrong and a disservice to the people whom the Hudson Institute and Médecins Sans Frontières wish to help.

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- 1 Taylor RB, Shakoor O, Behrens RH, et al. Pharmacopoeial quality of drugs supplied by Nigerian pharmacies. *Lancet* 2001; **357**: 1933–36.
- 2 Li Wan Po A. Too much, too little, or none at all: dealing with substandard and fake drugs. *Lancet* 2001; **357**: 1904.
- 3 Implementation of WHO's revised drug strategy: safety and efficacy of pharmaceutical products—forty-fifth World Health Assembly. Geneva: WHO, March 18, 1992.
- 4 Rubin RH. A comparative analysis of some drugs on the EDL. In: A discussion paper on the issues raised by a WHO resolution vis-à-vis US trade interests. Boston, MA: Harvard Medical International, Oct 3, 1996.
- 5 Attaran A, Gillespie-White L. Do patents for antiretroviral drugs constrain access to AIDS treatment in Africa? *JAMA* 2001; **286**: 1886–92.

## Motivation behind infant rape in South Africa

Sir—Rachel Jewkes and colleagues (Feb 23, p 711)<sup>1</sup> write that child rape is not exotic; however, we aimed to highlight infant rape with associated perineal injury. In our practice in Johannesburg, perineal mutilation of infants (hardly an injury that fails to present for medical treatment) has recently emerged as a distinct clinical entity.

Jewkes and colleagues dispute the assertion that the virgin cleansing myth is an important cause of child sexual abuse. The idea that sex with a virgin will cure men of sexually transmitted infection is not new, nor exclusively African. In renaissance Europe, it was widely believed that syphilis could be cured by intercourse with a virgin. In 1925, Samuel Cameron<sup>2</sup> wrote: “The disgusting superstition, surviving amongst ignorant and vicious men, that contact with an immature vulva will cure venereal disease, is still responsible [for transmission of gonorrhoea] in many cases.” In a South African sexual-health workshop, reported by Jewkes herself in 2000, 32.7% of participants believed sex with a virgin could cure HIV infection. After 14 sessions of 2–3 h each, this myth was still believed by 20% of the participants.<sup>3</sup>

Jewkes believes that a 1% seroconversion rate in raped children from Cape Town<sup>4</sup> disproves the cleansing myth because the rate is too low. This reported rate is falsely low, since HIV testing in the early years of

the study was haphazard, and since 1997 all children have received postexposure prophylaxis (Sebastian van As, personal communication).

In consensual sex in developed countries, the average risk of transmission per contact for unprotected receptive anal intercourse with an HIV-positive man is around 5%; for unprotected receptive vaginal intercourse this risk is less than 1%.<sup>5</sup> The risk after rape is much greater and although multiple penetrations by multiple perpetrators, dry sex, the presence of other sexually transmitted infections, and the occurrence of perineal injury increase the risk after rape, a low seroconversion rate is still consistent with a high HIV-positivity rate among perpetrators. The fact that few perpetrators admit that the myth motivated their actions is hardly surprising given that around 63% of traced offenders are not even tried for their crimes in South Africa and only 7% receive a prison sentence.<sup>4</sup>

We agree with Jewkes and colleagues that rape in South Africa occurs in the context of a society inured to very high levels of violence, with fractured families and communities and extreme inequality between the sexes. However, the high level of poverty to which they correctly refer as a contributory factor cannot be divorced from high levels of ignorance and illiteracy, which we believe potentiate dangerous beliefs and traditions. We concur that the virgin cleansing myth is not the only motivation behind the appalling levels of rape in South Africa, but we believe it is important. We add our voices to that of Charlene Smith, the noted South African rape activist, who has questioned why there is a paucity of research on this practice or vociferous advocacy to challenge it.

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- 1 Jewkes R, Martin L, Penn-Kekana L. The virgin cleansing myth: cases of child rape are not exotic. *Lancet* 2002; **359**: 711.
- 2 Davidson R. This pernicious delusion: law, medicine and child sexual abuse in early 20th Century Scotland. *J Hist Sex* 2001; **10**: 62–67.
- 3 Jewkes R, Matubatuba C, Metsing D, et al. Stepping stones: feedback from the field. <http://www.actionaid.org/stratshope/ssjewkes.html> (accessed March 5, 2002).
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- 5 Roland M. Prophylaxis following non-occupational exposure to HIV. <http://hivinsite.ucsf.edu/InSite.jsp?page=kb-07-02-07#S1X> (accessed March 5, 2002).

## Intestinal permeability and coeliac disease

Sir—Ian Perry and colleagues (Nov 17, p 1729–30),<sup>1</sup> comment on our July 28 Commentary.<sup>2</sup> We agree with them in principle that there have been important advances in our knowledge of molecular biology, especially in relation to their interaction with tight junctions in coeliac disease.

However, our remit was to provide a Commentary on the report by Cummins and colleagues.<sup>3</sup> The original report related to the timing of improvements in intestinal permeability and intestinal morphometry in treated coeliac disease. Hence our main thrust related to intestinal morphometry, with some reference to zonulin, and other adhesion molecules. Our Commentary was not designed to be an exhaustive review of the subject.

The use of cytokine-regulated expression of adhesion molecules and its effect on the disruption of intercellular junctions provides a useful insight into the pathophysiology of coeliac disease, but measurement of these molecules is currently of no practical use for diagnosis or follow-up of coeliac disease. By contrast, the intestinal permeability test is a reliable, practical, outpatient-based test and it is useful in screening for coeliac disease.

We therefore maintain that the use of intestinal permeability tests for intestinal morphometric improvements in treated coeliac disease still provide useful insights into the pathophysiological events at the mucosal level.

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- 1 Perry I, Iqbal T, Cooper B. Intestinal permeability in coeliac disease. *Lancet* 2001; **358**: 1729.
- 2 Johnston SD, Smye M, Watson RGP. Intestinal permeability and morphometric recovery in coeliac disease. *Lancet* 2001; **358**: 259.
- 3 Cummins AG, Thompson FM, Butler RN, et al. Improvement in intestinal permeability precedes morphometric recovery of the small intestine in celiac disease. *Clin Sci* 2001; **100**: 379–86.

## DEPARTMENT OF ERROR

*Chronic fatigue syndrome: a step towards agreement*—A typographical error in paragraph 4 of this Commentary by Christopher Clark and colleagues (Jan 12, p 97) may cause some confusion. Only four of the six dissenters were clinicians, as described lower down the paragraph.