'…activism for greater access to HIV medicines has had little effect on the drug research and development agenda'

Treating HIV in the developing world: getting ahead of the drug development curve

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At the 2006 International AIDS Conference (http://www.aids2006.org/), an impressive range of new therapeutic developments for HIV/AIDS were described. Several new drugs, and new drug classes (entry and fusion inhibitors, integrase inhibitors, and maturation antagonists) are offering great hope for more effective treatment [1]. At the same time, however, the conference also saw unrest among treatment activists, who were vocally campaigning for increased access to lopinavir/r, a five-year-old drug recently reformulated but priced out of reach of most developing countries [2].

Ensuring access to affordable antiretrovirals has been on the agenda of the International AIDS Conference for almost 20 years. At the 1988 conference in Stockholm, there was debate about how to ensure people in the developing world could access the treatment of that time, zidovidine monotherapy, which cost ~ US$8000 a year [3]. Today, zidovudine, which is only used as part of a three-drug combination therapy, costs ~US$103 a year [4].

Public pressure and market competition force drug prices down

It was only in 2001 that serious political concern was given to the issue of drug pricing following a court case in which a consortium of multinational pharmaceutical companies tried to prevent the South African Government from passing a law that would facilitate the import of more affordable medicines. The court case received international media attention as an example of how Western commercial interests are harmful to the poorest sufferers, and the pharmaceutical companies were accused of 'medical apartheid' [5]. Bowing to public pressure, the companies dropped the case. Around the same time, Cipla (http://www.cipla.com), an Indian generics firm, offered HIV triple therapy for a dollar a day, [6] setting off a price war between brand and generics producers that, by the end of 2006, has pushed the price of treatment down to ~US$140 per patient per year. Pharmaceutical companies have responded by offering considerable discounts for several antiretroviral drugs and combinations. This price drop has enabled the scaling up of treatment across the developing world, where 1.3 million people are currently receiving antiretroviral therapy. This is still far below the current need, estimated at over 6 million people. [7]

Access to newer medicines must be assured

HIV/AIDS is a chronic disease requiring treatment for life. Access to newer medicines needs to be ensured as drug toxicity and resistance are increasingly confronted. A crucial question, when assessing the pipeline of new antiretrovirals, is whether the newer drugs and classes (the fusion inhibitors, integrase inhibitors, and maturation antagonists) will be affordable and appropriate for all 40 million people currently living with HIV/AIDS, most of whom live in the less-developed world, and not just for the lucky few in the USA and Europe. The history of securing access to two recently developed drugs (tenofovir and lopinavir/r) does not provide grounds for optimism.

Tenofovir was launched by Gilead (http://www.gilead.com) in the USA in 2001 and is now commonly prescribed as a first-line drug in western countries. In the developing world, it is increasingly required both as a first line drug (to replace stavudine in case of toxicity) and a second-line drug (to overcome drug resistance). Tenofovir has been registered for use in the US since 2001 and in Europe since 2002. In December 2002, Gilead announced a programme offering a preferential price for tenofovir in 68 developing countries. This list expanded to 97 countries by March 2005. However, as of October 2005, almost three years after the first preferential prices were announced, tenofovir was registered in only 10 of 97 eligible countries [8]. Given that North America, Europe and Japan represent almost 90% of global pharmaceutical market (estimated at US$602 billion in 2005) [9], it is not surprising that drug registration in the developing world is not treated as a priority concern. In China for example, many antiretroviral dosages and formulations were, as of late 2005, not registered (e.g. stavudine and efavirenz syrups) or marketed (e.g. lopinavir/r, nevirapine suspension and nelfinavir).

Registration of the new tablet formulation of lopinavir/r, which does not require refrigeration and is therefore a crucial medicine for use in tropical countries, is also under prioritized and progressing far too slowly.

Lopinavir/r provides a striking example of how little progress has been made on securing fair prices. Despite concerted pressure from medical and patient groups during 2005, Abbott Laboratories (http://www.abbott.com), which holds the patent, has been reluctant to offer the latest version of this drug at a reasonable price. It finally announced a price reduction at the 2006 International AIDS conference. However, middle-income countries, such as Thailand and Guatemala, still have to pay over US$2200 per patient per year. This is hardly affordable in countries such as Thailand, where the average wage is less than US$1500 a year [10].

Drug development driven by profit, not need

As well as ensuring access to new drugs, there is a need to ensure that drugs in the pipeline are adapted to, and tested in, conditions of the developing world, where people need simple single fixed-dose regimens that do not need to be refrigerated, and can be used in combination with other medications, such as those for TB (the leading cause of death among people with HIV/AIDS), and are suitable for paediatric use. Paediatric formulations that are safe and easy to administer are particularly urgently needed: over 90% of the 2.3 million children living with HIV/AIDS live in the developing world, effectively making paediatric HIV/AIDS a 'rare disease' and the Western market is too small to attract systematic research and development efforts (e.g. tenofovir has yet to be tested on children); those drugs that are developed are marketed at a price that is much higher than equivalent adult doses. [11] Concern regarding the relevance of pipeline products for most HIV patients also extends to vaccines: one of the lead candidate vaccines currently in testing, the Ad5 vaccine from Merck (http://www.merck.com), uses adenovirus 5 as a vector. Given that up to 80% of patients in some African countries are Ad5 immune, it is predictable that there will be a lower response rate in these populations compared to the USA or Europe. As long as drug development continues to follow profit prospects, rather than global public health needs, there will be a continued bias towards 'Western diseases' (and the corresponding markets) [12].

So far, efforts to ensure access to antiretroviral medications for the developing world have been largely driven by people with HIV/AIDS, who fight by necessity for access to medicines one drug at a time. This pressure has brought down the price of some of the older medicines, but the difficulties currently faced in accessing newer medicines demonstrates how limited this approach is. In many respects, the situation is worse than five years ago. Patent protection has come into full force in major generics-producing countries, including India, which currently supplies affordable generics medicines to around half of all people receiving antiretrovirals in the developing world. Such patent protection restricts the ability of companies to make generic versions of newer medicines. Big pharma, meanwhile, has shrugged off the criticism generated from the South Africa court case, and continues to push vigorously for patent protection through legal action. In October 2006, Novartis, the Swiss pharmaceutical giant (http://www.novartis.com), filed a lawsuit against the Indian Government, questioning India's patent law after a patent application for an anti-leukaemia drug was rejected [13].

Ensuring access to medicines is a political responsibility

In addition, activism for greater access to medicines has had little effect on the drug research and development agenda. During the 1980s, US AIDS activists were successful in accelerating clinical trials and registration of antiretroviral drugs, but activism has not been able to influence the drug research and development agenda to ensure that it is tailored to meet the specific needs of the developing world. HIV/AIDS in the developing world should be viewed as a neglected disease, with specific policies implemented to stimulate the development of affordable and appropriate medicines that are tested on patient groups in the developing world from an early stage [14].

Fighting for drugs, one at a time, after they are marketed in the West, is not an appropriate strategy to meet the chronic medical needs of 40 million people. Public pressure must be replaced by a systematic, policy-driven approach. This means governments and industry taking proactive responsibility for ensuring access to medicines for the developing world, rather than reacting too little and too late to the demands of patients.

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