

- 8 Boccalon H, Boneu B, Emmerich J, et al. Long-haul flights do not activate hemostasis in young healthy men. *J Thromb Haemost* 2005; **3**: 1539–41.
- 9 Dahlback B. Blood coagulation. *Lancet* 2000; **355**: 1627–32.
- 10 Koster T, Rosendaal FR, de Ronde H, et al. Venous thrombosis due to poor anticoagulant response to activated protein C: Leiden Thrombophilia Study. *Lancet* 1993; **342**: 1503–06.
- 11 Hoibraaten E, Mowinckel MC, de Ronde H, et al. Hormone replacement therapy and acquired resistance to activated protein C: results of a randomized, double-blind, placebo-controlled trial. *Br J Haematol* 2001; **115**: 415–20.
- 12 Rosendaal FR, Vessey M, Rumley A, et al. Hormonal replacement therapy, prothrombotic mutations and the risk of venous thrombosis. *Br J Haematol* 2002; **116**: 851–54.
- 13 Scurr JH, Machin SJ, Bailey-King S, et al. Frequency and prevention of symptomless deep-vein thrombosis in long-haul flights: a randomised trial. *Lancet* 2001; **357**: 1485–89.
- 14 Cesarone MR, Belcaro G, Nicolaidis AN, et al. Venous thrombosis from air travel: the LONFLIT3 study—prevention with aspirin vs low-molecular-weight heparin (LMWH) in high-risk subjects: a randomized trial. *Angiology* 2002; **53**: 1–6.
- 15 Dalen JE. Economy class syndrome: too much flying or too much sitting? *Arch Intern Med* 2003; **163**: 2674–76.
- 16 Kelman CW, Kortt MA, Becker NG, et al. Deep vein thrombosis and air travel: record linking study. *BMJ* 2003; **327**: 1072–76.

Registration problems for antiretrovirals in Africa

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Last December, Médecins Sans Frontières (MSF) faced critical shortages of tenofovir in programmes it supports in South Africa and Zimbabwe. The drug is not registered in these countries, but can be used via special authorisation from the drug-regulatory authorities. Procurement of the drug, however, requires an extraordinary supply line between the USA and Africa, which is costly, complex, and all too fragile, leading to a heightened risk of treatment interruption.

Tenofovir disoproxil fumarate has been registered since October, 2001, in the USA and since February, 2002, in Europe and is commonly prescribed as part of a first-line antiretroviral therapy in developed countries. The drug will also be included in the latest WHO guidelines for first-line and second-line antiretroviral therapy in resource-limited settings.¹

In South Africa, MSF uses tenofovir to replace stavudine in first-line therapy for patients who develop symptomatic hyperlactataemia, the main cause of toxicity-driven first-

line regimen change in the country.² The incidence of stavudine-related side-effects will increase as the cohort of patients receiving first-line antiretroviral therapy expands and matures. Recognising this, physicians have requested that the department of health include tenofovir in the first-line treatment regimen in South Africa. The need for tenofovir will certainly increase over time, and possibly dramatically so. Some clinicians have also expressed a strong desire to use tenofovir as a first-line drug. The present reality, however, is that few, if any, clinicians in the public sector have the ability to ship drugs from California; for them, tenofovir is a non-existent drug.

In December, 2002, Gilead announced a programme offering a preferential price for tenofovir in 68 developing countries.³ This list was expanded to 97 countries by March last year.⁴ However, as of October, 2005, almost 3 years after the first preferential prices were announced, tenofovir was registered in only 10 of 97 eligible countries.

Lack of registration is a major barrier to accessing tenofovir in the developing world. In South Africa, the registration filing for tenofovir was not completed until last December. In most other African countries, the dossier has not even been submitted: as of last month, registration of tenofovir had only been applied for in 11 of 53 African countries.

Delays in registration can be caused by national drug-regulatory authorities, which have the power to expedite the registration of essential medicines that can often take years. But the regulatory authorities cannot be blamed if a company has not even submitted the file. The registration of other antiretrovirals launched around the same time as tenofovir have been much quicker: efavirenz is registered in 49 developing countries, the old formulation of lopinavir and ritonavir (Kaletra) in 54 developing countries.

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This problem is by no means limited to tenofovir. In China, many antiretroviral dosages and formulations were, as of late last year, not registered (eg, stavudine and efavirenz syrups) or marketed (such as Kaletra, nevirapine suspension, and nelfinavir). Registration of the new formulation of Kaletra—which does not require refrigeration and is therefore a critical medicine for resource-poor settings—will not be attempted in Africa before it has been granted in Europe.

Companies gain good publicity for announcing discounts for the developing world, but their intentions have to be backed up by a proper commitment to actually make the drugs available. Without this commitment, attempts to reach global treatment targets for HIV/AIDS in the developing world will be seriously hampered. For now, doctors in south Africa faced with patients at risk of developing life-threatening lactic acidosis will have to

inform them that, because the drug they need isn't registered, there is nothing they can offer them.

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- 1 Guidelines development Group. Antiretroviral drugs for the treatment of HIV infection in resource-limited settings: recommendations for a public health approach. June 22–23, 2005: <http://www.who.int/3by5/mediacentre/news51/en> (accessed on March 2, 2006).
- 2 Boulle A, Van Custem G, Goetzec D. Antiretroviral drugs for the treatment of HIV infection in resource-limited settings: recommendations for a public health approach. June 22–23, 2005: <http://www.who.int/3by5/mediacentre/news51/en> (accessed March 2, 2006).
- 3 Gilead. Gilead Sciences to provide access to anti-HIV therapy Viread® in 68 developing world countries at no profit. Dec 17, 2002. http://www.gilead.com/wt/sec/pr_1040081128 (accessed on March 2, 2006).
- 4 Gilead. Gilead expands global access program for HIV therapies to include additional countries in the Caribbean and Latin America; Bahamas manufacturing plant established. March 16, 2005: http://www.gilead.com/wt/sec/pr_686106 (accessed on March 2, 2006).

Drive to eliminate the burden of type 1 diabetes

The individual with type 1 diabetes, whether child or adult, faces a lifetime of inconvenience and restraint, which results from the perpetual need to juggle insulin dose, diet, and exercise. The task of managing the disease—ie, striving to maintain a near-normal blood-sugar concentration to reduce the threat of long-term complications while avoiding the short-term disaster of disabling hypoglycaemia—is hard enough, but it is one that must be tackled while the patient is also trying to live a more or less normal life.

The incidence of type 1 diabetes is rising by 3% per year, and at present more than 90 000 children are affected in Europe alone.^{1,2} No cure is available, and although one day we might be able to prevent diabetes, the main focus of much academic, clinical, and commercial effort currently centres on protecting, or improving, secretion of endogenous insulin in people who have, or who are in the process of developing the disease. Such effort involves work on many different fronts: identification of individuals at risk, protection of the failing β cell, and islet-cell replacement. To be most effective, this work must be coordinated.

The need for such coordination and collaboration was the subject of a day symposium at the European Parliament building in Brussels on Dec 2, 2005. This meeting was convened by a new pragmatic partnership

between the Directorate of Research and Technology Development of the European Union (EU) and the US-based charity, the Juvenile Diabetes Research Foundation (JDRF). JDRF is a highly successful fundraising and lobbying group, founded in 1970 by parents of affected children, that—like the US National Institutes of Health—awards grants to academic institutions worldwide.³ The EU committed more than €44 million to diabetes research in its Research Framework Programmes 5 (1998–2002) and 6 (2002–06); allocations to be made in Programme 7 are currently being debated. The symposium brought together a small group of experts from around Europe to discuss emerging themes in the area of islet-cell protection and replacement, and to talk about the need to establish collaborative networks to undertake the clinical trials necessary to establish the potential effectiveness of any new treatment if adopted in routine practice.

To prevent diabetes it is necessary to identify people who are susceptible to the disease, and this process will depend on knowledge from gene banks, such as the European Type 1 Diabetes Genetics Network,⁴ and development of effective means of protecting β cells, which are known to be threatened by autoimmune destruction. To that end, encouraging results have been achieved using the technique of immunomodulation,

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