increased 21-fold after HIV infection.[5] All patients who are infected with HIV from clotting factor concentrate must, therefore, also be infected with hepatitis C. In our centre 10 out of 11 patients who died of liver failure were infected with HIV. This can cause formidable management problems. The failing liver can cause other clotting factor deficiences that are superimposed on the existing deficiency of factor VIII or IX. A severe haemorrhagic state may develop in the final stages of the illness.

Patients with liver cirrhosis are at an increased risk of developing hepatocellular carcinoma, and the same could be true of patients with haemophilia. A worldwide questionaire sent to 11 801 patients with haemophilia identified 10 cases of hepatocellular carcinoma—a risk 30 times higher than normal.[8]

The sexual transmission of hepatitic C virus is an important issue for patients with haemophilia, their families, and those involved in their health care. Studies indicate that transmission is rare.[9] HIV infection has been reported as a cofactor and could reflect the higher viral load of hepatitis C virus in coinfected people.[10] The use of barrier contraception (condoms) is likely to increase safety.

What about treatment? Interferon alfa remains the most promising treatment for hepatitis C. For the patients without haemophilia, liver biopsy is essential in deciding who will benefit from treatment, but this is a hazardous procedure for a patient with haemophilia. Knowledge of other variables, such as hepatitis C virus genotype and viral load, may be helpful as patients with virus types 2 and 3 and with lower viral loads have the greatest chances of responding.[11]

Patients treated with multiple batches of concentrate will have been exposed to a large amount of virus as well as to many viral genotypes.[4 12] Since patients are infected with multiple species, a change in genotype is likely to be due to a change in dominance. The clinical importance of the change in dominance brought about by treatment with interferon is unclear.[12] The ultimate treatment for liver failure is liver transplantation, and this has successfully been performed in patients with haemophilia, curing not only the liver failure but also the haemophilia. The liver, however, may be reinfected with hepatitis C virus, and transplantation is difficult for patients infected with HIV.

The progression of hepatitis C and coinfection with HIV in haemophilic patients will demand tremendous resources over the next decade. It is important to appreciate the achievements that have been made in treating haemophilia despite their devastating side effects. In 1937 Birch wrote a descriptive monograph on haemophilia; she reported that 82 out of 113 patients died before their 15th year and only 6 out of 113 lived beyond the age of 40.[13] We now have recombinant factor VIII (and soon factor IX), which cannot transmit bloodborne viruses. We need the resources to provide these factors for the children with haemophilia who were born after 1985. They are free of the scourges of hepatitis C virus and HIV, and prophylaxis with a safe clotting factor concentrate could offer them a full life without disability.

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1 Kasper CK, Kipnis SA. Hepatitis and clotting-factor concentrates. *JAMA* 1972;221:510.
2 Fletcher ML, Trowell JM, Craske J, Pavier K, Rizza CR. Non-A non-B hepatitis after transfusion of factor VIII in infrequently treated patients. *BMJ* 1983;287:1754-7.
3 Kernoff PBA, Lee CA, Karayiannis P, Thomas HC. High risk of non-A non-B hepatitis after a first exposure to volunteer or commercial clotting factor concentrates: effects of prophylactic immune serum globulin. *Br J Haematol* 1985;60:469-79.
4 Preston FE, Jarvis LM, Makris M, Philp L, Underwood JCE, Ludlam CA, *et al.* Heterogeneity of hepatitis C virus genotypes in hemophilia: relationship with chronic liver disease. *Blood* 1995;85:1259-62.
5 Telfer P, Sabin C, Devereux H, Scott F, Dusheiko G, Lee C. The progression of HCV-associated liver disease in a cohort of haemophilic patients. *Br J Haematol* 1994;87:555-61.
6 Eyster ME, Diamondstone LS, Lien J-M, Ehmann C, Quan S, Goedert JJ. Natural history of hepatitis C virus infection in multitransfused hemophiliacs: effect of coinfection with human immunodeficiency virus. *J Acquir Immun Defic Syndr* 1993;6:602-10.
7 Eyster ME, Fried MW, Di Bisceglie AM, Goedert JJ. Increasing hepatitis C virus RNA levels in hemophiliacs: relationship to human immunodeficiency virus infection and liver disease *Blood* 1994;84:1020-3.
8 Colombo M, Mannucci PM, Brettler DB. Hepatocellular carcinoma in hemophilia. *Am J Hematol* 1991;37:243-6.
9 Brettler DB, Mannucci PN, Gringeri A. The low risk of hepatitis C virus transmission among sexual partners of hepatitis C-infected hemophilic males: an international, multicenter study. *Blood* 1992;80:540-3.
10 Eyster ME, Alter HJ, Aledort LM, Quan S, Hatzakis A, Goedert JJ. Heterosexual co-transmission of hepatitis C virus (HCV) and human immunodeficiency virus (HIV). *Ann Intern Med* 1991;115:764-8.
11 Telfer P, Devereux H, Colvin B, Hayden S, Dusheiko G, Lee C. Alpha interferon for hepatitis C virus infection in haemophilic patients. *Haemophilia* 1995;1:54-8.
12 Devereux H, Telfer P, Dusheiko G, Lee C. Hepatitis C genotypes in haemophilic patients treated with alpa-interferon. *J Med Virol* 1995;45:284-7.
13 Birch CL. *Hemophilia, clinical and genetic aspects.* Urbana: University of Illinois, 1937.

Integrating pharmacy fully into the primary care team

Much to recommend it

Since teamwork, especially in small, cohesive task specific groups,[1] is the central plank on which primary care is now being built, greater interaction between pharmacists and general practitioners could be fruitful. Nevertheless, personal communications from ministers and civil servants reiterate the traditional view that "the separation of prescribing and dispensing ensures that the skills of doctors and pharmacists are used to best effect and that the public has access to both professions." It is time that these attitudes received the same scrutiny that the rest of primary care has received, especially as the cost of distributing medicines through pharmacies accounts for 30-40% of the total medicines bill.[2]

Changes in dispensing are under way in other countries,[3] involving, for example, mail order. But these fail to build on potential professional collaboration, the desirability of which was implied in a Nuffield report of 1986: "closer relations between GPs and community pharmacists would be in the interests of patients and . . . more efficient use of resources within the NHS."[4] An opportunity exists for Britain to pioneer the integration of pharmacy into primary care.

If community dispensing were to become a central function of the primary health care team, with both geographic and functional integration of pharmacy, wide ranging and large scale benefits to patients, health care professionals, and the exchequer could accrue. Linked consultations between patient, doctor, pharmacist and other team members could be a radical new force in primary care.

Exhortations to closer cooperation between community pharmacy and general practice are no substitute for genuine integration, with the professions on the same team sharing work space, hours, databases, and budgets. Furthermore, commercial pressures would be likely to limit the scope of such closer cooperation, given current arrangements. Professional advice is difficult to submit to quality assurance but integration, with constructive mutual scrutiny and criticism by team members sharing the same values and

aims and shielded from the vicissitudes of a competitive commercial environment, would be a substantial and practicable alternative.

Service benefits of integration include one stop care for patients and continuous professional collaboration in establishing and maintaining practice formularies, using drugs and auditing their costs, purchasing, managing budgets, overseeing complex and costly therapeutic regimens, conducting postmarketing surveillance, and reporting adverse reactions. In a recent book, Marinker and Reilly argued that "Primary care pharmacists, based in practices, could become responsible for the pharmaceutical care of the practice population. They would also effect liaison with community and hospital pharmacists, would undertake domiciliary visits where necessary and would certainly emerge as key players in the primary health care team of the future."[5]

As about two thirds of the total drug bill arises from repeat prescriptions, urgent professional collaboration is needed to address this issue. Integration of the professions is the perfect vehicle to deliver rapid and sustained improvements in all aspects of repeat prescribing. Currently, people who ask a pharmacist for advice are often referred for extra consultations with their general practitioner, with consequent delays. This potentially useful source of health care could be made much more effective with a unified team working on a single site.

Integration could yield annual savings of £1bn.[6] Following the introduction of the option for NHS patients (those not exempt from prescription charges) of receiving a private prescription when it would be to their financial advantage, further savings would arise. The number of prescriptions whose value is less than the prescription charge would increase as salaried primary care pharmacists would not need to add a dispensing fee. Ending price maintenance on pharmaceuticals, certainly those whose patent has expired, would yield yet more savings.

Currently, pharmacists and dispensing doctors are the sole beneficiaries of their purchasing acumen. Direct billing of family health services authorities by suppliers could lead to additional savings for the NHS. Concentrating dispensing transactions in fewer locations (only in general practices) and making those pharmacists who supervise NHS dispensing salaried employees would facilitate financial control and would minimise the incentive to fraudulent practice, identified in a recent report by the Audit Commission.[7]

Such arrangements could undergo the necessary piloting almost immediately in existing dispensing practices and others with adequate accommodation. Parliament would have to change the law relating to general practice and pharmacy for the benefits to be realised by the entire population.

With only dispensing based in NHS primary care financed from taxation, where would this leave retail pharmacy? The prosperity, ubiquity, and quality of retail pharmacy could be assured by several changes. Firstly, a monopoly on the sale of all over the counter pharmaceuticals could replace the existing monopoly on "pharmacy only" items, ensuring a measure of professional supervision of sales and facilitating a concentration on the commercial aspects of promoting health and hygiene and managing minor illness. More products could be transferred from prescription only to pharmacy only status. Secondly, as a guard against commercial considerations overriding therapeutic validity, records that could be audited should be considered for some of the more active products sold direct to the public. Thirdly, the removal of price maintenance would promote competitive pricing. Finally, as retail pharmacy would become free of any constraint on the location of new premises, areas previously unable to sustain a pharmacy could then benefit.

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1 Pearson P, Jones K. The primary health care non-team? *BMJ* 1994;309:1387-8.
2 Brown P. Are pharmacists necessary? *Scrip Magazine* 1994 May:3-4.
3 Brown P. Pharmacy's rocky road. *Pharmaceutical Journal* 1994;252:802-3.
4 Clucas K. *Pharmacy. A report to the Nuffield Foundation.* London: Nuffield Foundation, 1986.
5 Marinker M, Reilly P. Judging rational prescribing. In: Marinker M, ed. *Controversies in health care policies, challenges to practice.* London: BMJ Publishing Group, 1994:89-110.
6 Ford S. Community pharmacy. *Br J Gen Pract* 1994;388:534-5.
7 Audit Commission. *Protecting the public purse 2—ensuring probity in the NHS.* London: HMSO, 1994:63.

Chemoprophylaxis in tuberculosis and HIV infection

Is it feasible in developing countries?

Should chemoprophylaxis with a course of antituberculous drugs be given to people infected with *Mycobacterium tuberculosis* and HIV to prevent the reactivation of latent tuberculosis? The decision depends on three factors: the efficacy of the treatment, its cost effectiveness, and whether it is financially and organisationally feasible.

The World Health Organisation estimates that 1700 million people are infected with *M tuberculosis*—one third of the world's population. Symptomatic tuberculosis is becoming an increasing problem owing to population growth, poverty, multidrug resistance, and HIV infection. The risk of active tuberculosis in dually infected people is 3-8% a year, with a lifetime risk of about 50% or more.[1] The WHO has calculated that the global incidence in 1990 of about 7·5 million cases of tuberculosis will increase to about 12 million by 2005 (M C Raviglione, personal communication). Already, worldwide, tuberculosis is the most common cause of death due to a single infectious agent.

Chemoprophylaxis with isoniazid has an efficacy of 25-92% in various risk groups not infected with HIV.[2] Some data are available in people infected with HIV. In a controlled trial in Zambia patients with HIV infection and with Walter Reed stages III and IV disease who were given a B vitamin placebo had an incidence of tuberculosis of 11·2 per 100 person years, which was four times the rate in those receiving daily isoniazid (D Wahhawan *et al*, eighth international conference on AIDS and third world congress on sexually transmitted diseases, Amsterdam, 1992).

In Haiti a 12 month course of prophylaxis with isoniazid reduced the incidence of tuberculosis from 10·0 to 1·7 per 100 person years and also delayed the progression of symptomless HIV infection to active disease and death by an average of 9·7 and 5·3 months respectively.[3] In addition to preventing reactivation of the tuberculosis chemoprophylaxis may also prevent the activation of HIV infected CD4 lymphocytes by *M tuberculosis* and thus the progression from HIV infection to