- 37 Viberti G, Mogensen CE, Groop LC, Pauls JF for the European Microalbuminuria Captopril Study Group. Effect of Captopril on progression to clinical proteinuria in patients with insulin dependent diabetes mellitus and microalbuminuria. *JAMA* 1994;271:275-9.
- 38 Lewis EJ, Hunsicker LG, Bain RP, Rohde RD for the Collaborative Study Group. The effect of angiotensin converting enzyme inhibition on diabetic nephropathy. *N Engl J Med* 1993;329:1456-62.
- 39 Hannedouche T, Landais F, Goldfarb B, El Esper N, Fournier A, Godin M, et al. Randomised controlled trial of Enalapril and betablockers in non diabetic chronic renal failure. *BMJ* 1994;309:833-7.
- 40 Maschio G, Alberti D, Janin G, Locatelli F, Johannes FE, Mann MD, et al. Effect of the angiotensin converting enzyme inhibitor Benazepril on the progression of chronic renal insufficiency. *N Engl J Med* 1996;334: 939-45.
- 41 Walma EP, Van Dooren C, Van der Does E, Prins A, Mulder P, Hoes AW. Accuracy of an oscillometric automatic blood pressure device: the OMRON HEM403C. *J Human Hypertens* 1995;9:169-74.
- 42 Harrison DW, Crews WD Jr. The Takeda Model UA-751 blood pressure and pulse rate monitor. *Biomed Inst Tech* 1992;26:325-7.
- 43 Padfield PL, Lindsay BA, McLaren JA, Pirie A, Rademaker M. Changing relation between home and clinic blood pressure measurements: do home measurements predict clinic hypertension? *Lancet* 1987;iii:322-4.
- 44 Aylett M. Use of home blood pressure measurements to diagnose white coat hypertension in general practice. *J Human Hypertens* 1996;10:17-20.
- 45 Jackson R, Barham P, Bills J, Birch T, McLennan L, MacMahon S, et al. Management of raised blood pressure in New Zealand: a discussion document. *BMJ* 1993;307:107-10.
- 46 McGrath BP. Is white coat hypertension innocent? *Lancet* 1996;348:630.

Intravenous antimicrobial therapy in the community: underused, inadequately resourced, or irrelevant to health care in Britain?

Dilip Nathwani, Peter Davey

The NHS Executive is keen to promote "hospital at home" services in Britain, as part of its philosophy of keeping more care in the community and also to relieve the increasing demand for hospital beds. One such service is the provision of intravenous antimicrobial therapy in the community. Yet, compared with the United States, where home or outpatient intravenous antimicrobial therapy programmes are well developed, experience in Britain and Europe is limited, reflecting a difference in cultural attitudes and healthcare structures between the two continents. Only a few units in Britain currently run home intravenous antimicrobial therapy programmes, and several issues need to be addressed if more treatment is to be provided outside hospital. These include an assessment of the need for community intravenous antibiotic treatment and which patient groups many benefit. The main motive for community intravenous treatment should be better patient care and not simply a reduction in healthcare costs. At present the pace of change is being set by a few clinical enthusiasts and by commercial organisations, whereas the NHS deserves a more organised strategy for purchasing treatment with intravenous antibiotics in the community.

Following the development of the Rochester needle by Dr Thomas Massa in 1950 intravenous administration of fluids, drugs, and nutrients became common in hospitals. Over 20 years passed before the first report of community based intravenous treatment—of 13 patients with osteomyelitis.¹ Further experience documented substantial financial savings to the hospital from community intravenous therapy,^{2,4} making it popular with third party payers.⁵ However, patients also benefited through shorter stays in hospital,⁶ a consequent reduction in the incidence of hospital acquired infections,⁷ and improvement in quality of life.⁵ Practical problems can be solved by selecting drugs which need to be administered only once daily,⁸ such as ceftriaxone or teicoplanin, or by using mechanical devices which facilitate administration.⁹ Most publications on community intravenous therapy are from the United States, where this it is now a multimillion dollar business.⁵ Why has Britain been so slow to follow this lead?

Conservatism in Britain

In response to escalating healthcare costs the British government has shown keen interest in managed competition¹⁰ and encouraged a change in the balance from secondary to primary care.¹¹ In 1995 a directive

from the NHS Management Executive instructed all purchasers to provide "high tech healthcare at home" through contracts with providers.¹² In the case of intravenous drugs, the directive aimed to discourage shifting the prescription of the drugs into the community without giving thought to providing the whole service of preparing and administering them. The directive put the onus on purchasers to determine local needs for high technology community services and make provision to meet those needs.

What is the need for community intravenous antibiotic treatment in Britain? In Britain about 60% of all antibiotics in hospital are administered orally, whereas in much of Europe and the United States most antibiotics in hospital are given intravenously. Furthermore, only 30% of patients in Britain are receiving antibiotics when they are discharged from hospital and these are predominantly administered orally.¹³ Therefore, if community intravenous antimicrobial therapy is going to become more common in Britain there has to be considerable change in treatment philosophy with respect to serious infection. For example, if intravenous therapy is indicated or oral therapy contraindicated for whatever reason in hospital, and the patient no longer needs other ancillary services that cannot be provided at home, he or she could be discharged home with intravenous drugs administered in the community rather than kept in hospital purely for observation of receipt of intravenous therapy. However, the patient must be closely monitored throughout the treatment, with sufficient support and follow up.

Examples of barriers to change include the belief that "primary care is listening and talking to patients and has nothing to do with coping with high tech therapies in the community," or, from a patients perspective, "If I am ill enough to require intravenous therapy I should be in hospital."

A survey of hospital doctors in Britain identified several obstacles to community intravenous antibiotic therapy: reluctance to try something new; lack of good clinical data relevant to the British health infrastructure; practical organisational problems including funding the likely increase in drug costs; and concern about reducing the number of available hospital beds.¹⁴ Despite these reservations there is growing experience in Britain of community intravenous therapy for recurrent infections in patients with cystic fibrosis¹⁵ and cancer,¹⁶ for chronic orthopaedic infections such as osteomyelitis and septic arthritis,¹⁷ and for infections complicating AIDS.¹⁸

Experience elsewhere

What issues does community intravenous therapy raise for purchasers? In the Netherlands, a country

Infection and Immunodeficiency Service, King's Cross Hospital, Dundee DD3 8EA

Dilip Nathwani, consultant physician

Medicines Monitoring Unit, Department of Clinical Pharmacology, Ninewells Hospital and Medical School, Dundee DD19SY

Peter Davey, reader in clinical pharmacology and infectious diseases

BMJ 1996;313:1541-3

Fig 1—Osteomyelitis of the femur is one indication for community intravenous antibiotic treatment

whose healthcare system is based on a strong primary care structure similar to ours, provision of community intravenous therapy is already well established.¹⁹ A detailed study concluded that the cost of home therapy of patients with cystic fibrosis was 48%–63% less than the same treatment in hospital in the Netherlands.²⁰

The crucial element in the economic equation is the value which is attached to a day in hospital.²¹ In Britain early discharge of patients does not save the hospital money in the short term; indeed, the likely immediate impact is to increase the cost per patient day.²² Providers and purchasers must develop a business plan for community intravenous therapy which includes realistic estimates of the short term and long term consequences for their budgets. However, we believe that the principal motive for community intravenous treatment should not be reduction in healthcare costs but better care of the patient. Unless we establish agreed standards for quality of care this form of therapy is unlikely to be adopted by patients, providers, or purchasers, and the reputation of community services will suffer.²³

Fig 2—Round trip distances that patients had to travel to receive outpatient intravenous treatment in our centre in Dundee

There is no shortage of information from other countries which could form the basis for British practice. Examples include standards developed by the Dutch council for the home care of cancer patients,²⁴ the home infusion therapy indicators developed by the United States Joint Commission on Accreditation of Health Care Organisations,²⁵ and, also from the United States, the quality indicator groups system for intravenous infusion therapy.²⁶ Quality assurance models must incorporate standards for the structure through which care is given; the process of selecting, assessing, training, and treating patients; and indicators of satisfactory clinical outcome.²⁷

In the United States a new jargon is evolving to describe the potential problems of community intravenous therapy. For example, the adjective “nosohusial” (home acquired) has been suggested as a parallel term to “nosocomial” (hospital acquired) in descriptions of infections.²⁸ Guidelines for control of infection at home need to be incorporated into quality assurance models.²⁹

What happens in Britain now?

How are community intravenous services currently provided in Britain? Experiences from units in Oxford, Dundee, and London illustrate different approaches to fit local needs and resources. In Oxford, for example, the service has evolved around the treatment of predominantly orthopaedic (fig 1) and endovascular infections.¹⁷ In London, at the Hammersmith Hospital, orthopaedic surgeons treated a small number of patients with infected prosthetic orthopaedic implants¹⁴ using once daily intramuscular antibiotics. In both centres the service was based on a community liaison nurse, who supported and educated district nurses as well as patients in administering the antibiotics in the community while liaising regularly with the hospital staff.

In Oxford the service for community intravenous antibiotic administration was based on an existing structure for support of home parenteral nutrition, which included a hospital based nurse trained to insert central intravenous lines. In contrast, for haematology patients at the Royal London Hospital and orthopaedic patients in Dundee home therapy was possible only if the community intravenous therapy was administered by the patient or a carer. For most patients in these centres community intravenous therapy has been primarily based around attendance at a day ward, where appropriate monitoring, support, and treatment is administered.^{14 30} However, in many cases this involves substantial travel for patients (fig 2). This is very much in line with the United States model of office or outpatient intravenous antibiotic therapy.

Funding of community intravenous services in Britain remains predominantly hospital based, and purchasing decisions remain largely unresolved. Hospital doctors and individual general practitioners may well be enthusiastic about community therapy, but there is likely to be more general concern about the clinical, legal, and financial responsibility for such a service as general practitioners become increasingly concerned about being asked to prescribe treatments that are outside their therapeutic experience. Moreover, like so many new initiatives in primary care, community intravenous therapy depends on an adequate mechanism for shifting funds from secondary care.³¹

The NHS should have a strategy

In conclusion, community intravenous therapy of patients with chronic or recurrent infections in Britain presents no major practical problems provided that there is adequate community support and clear definitions of clinical responsibility between hospital

and community services. Once the organisational structure and funding for treating these relatively well defined conditions has been established it may be reasonable to consider the potentially larger issue of intravenous treatment for patients with acute infections in the community. We are concerned that the pace for change is being set by a few clinical enthusiasts and by commercial organisations who have a vested interest in promoting community intravenous care. The NHS deserves a more organised strategy for purchasing treatment with intravenous antibiotics in the community.

- 1 Antoniskis A, Anderson BC, Van Volkinburg EL, Jackson JM, Gilbert DN. Feasibility of outpatient parenteral antibiotics. *West J Med* 1978;128:203-6.
- 2 Balinsky W, Nesbitt S. Cost-effectiveness of outpatient parenteral antibiotics: a review of the literature. *Am J Med* 1989;87:301-5.
- 3 Thickson ND. Economics of home intravenous services. *Pharmacoeconomics* 1993;3:220-7.
- 4 Rubinstein E. Cost implications of home care on serious infections. *Hosp Formul* 1993;28 (suppl1):46-50.
- 5 Milkovich G. Benefits of outpatient parenteral antibiotic therapy: to the individual, the institution, third-party payers and society. *Int J Antimicrob Agents* 1995;5:27-31.
- 6 Malik I, Khan WA, Karim M, Aziz Z, Khan MA. Feasibility of outpatient management of fever in cancer patients with low risk neutropenia: results of a prospective randomised trial. *Am J Med* 1995;98:224-31.
- 7 Parker SE, Davey P. Pharmacoeconomics of intravenous drug administration. *Pharmacoeconomics* 1992;1:103-15.
- 8 Craig WA. Selecting the antibiotic. *Hospital Practice* 1993;28(suppl 1):16-20.
- 9 Kravitz GR. Advances in IV delivery. *Hospital Practice* 1993;28 (suppl 1):21-7.
- 10 Enthoven A, Kronick R. A consumer-choice health plan for the 1990s: universal health insurance in a system designed to promote quality and economy (in two parts). *N Engl J Med* 1989;320:29-37, 94-101.
- 11 Coulter A. Shifting the balance from secondary to primary care. *BMJ* 1995;311:1447-8.
- 12 NHS Management Executive. *Purchasing high-tech health care for patients at home*. Leeds: NHSME, 1995 (EL (95)5).
- 13 Halls GA. The management of infections and antibiotic therapy: a European survey. *J Antimicrob Chemother* 1993;31:985-1000.

- 14 Non-inpatient use of parenteral antibiotics. Discussions of a national working party meeting, February 1995. In: Finch R, Davey P, eds. *Home and outpatient management education*. London: Medicine Group (Educational), 1995.
- 15 Gill S. Home administration of intravenous antibiotics to children with cystic fibrosis. *Br J Nursing* 1993;2:767-70.
- 16 Kohler JA. Recent advances in the management of paediatric cancer. *Postgraduate Update* 1991;42:950-8.
- 17 Kayley J, Berendt AR, Snelling MJM, Moore H, Hamilton HC, Peto TEA, Crook DWM, et al. Safe intravenous antibiotic therapy at home: experience of a UK based programme. *J Antimicrob Chemother* 1996;37:1023-30.
- 18 Welch J, Forsey P, Graham E. Home treatment of cytomegalovirus retinitis with intravenous Ganciclovir. *Genitourin Med* 1990;66:460.
- 19 Postema CA. Home treatment and reimbursement in The Netherlands. *Int J Antimicrob Agents* 1995;5:39-43.
- 20 Bakker W, Vinks AATMM, Mouton JW. Continue intraveneuze thuisbehandeling van luchtweginfecties met ceftazidim via een draagbare pomp bij patienten met cystische fibrose; een multicentrisch onderzoek. *Ned Tijdschr Geneesk* 1993;137:2486-90.
- 21 Davey PG, South R, Malek M. Impact of glycopeptide therapy after hospital discharge on inpatient costs: a comparison of teicoplanin and vancomycin. *J Antimicrob Chemother* 1996;37:623-34.
- 22 Lowson K. Health economics for clinician managers. *Clinician in Management* 1993;2:8-12.
- 23 Nolet B. Patient care issues in outpatient intravenous antibiotic therapy. *Infect Dis Clin Pract* 1993;3:225-6.
- 24 Schrijvers G, van der Linden B. Quality, costs and cultural beliefs in outpatient treatment with parenteral antibiotics: a comment. *Int J Antimicrob Agents* 1995;5:45-6.
- 25 Kunkel MJ. Quality Assurance. *Hospital Practice* 1993;28 (suppl 1):33-8.
- 26 Shaughnessy PW, Crisler KS, Kramer AM. *Quality of care indicators in home care: preliminary indicators and directions for future research*. Denver: University of Colorado Health Sciences Center, 1989.
- 27 Donabedian A. Evaluating the quality of medical care. *Milbank Q* 1966;4:155.
- 28 Graham DR. Nosohusial infections: complication of home intravenous therapy. *Infect Dis Clin Pract* 1993;2:158-61.
- 29 Simmons B, Trusler M, Roccaforte J, Smith P, Scott R. Infection control for home health. *Infect Control Hosp Epidemiol* 1990;11:362-70.
- 30 Nathwani D. New option in the treatment of serious and chronic infections. *Hospital Update* 1995;21:2-3.
- 31 Crump BJ, Pantan R, Drummond MF, Hawkes RA. Transferring the costs of expensive treatments from secondary to primary care. *BMJ* 1995;310:509-12.

(Accepted 26 September 1996)

Grand Rounds—Hammersmith Hospital

Persistent fever in pulmonary tuberculosis

Drug malabsorption should be considered

Malabsorption of rifampicin and other antituberculous drugs is becoming an increasing problem, particularly in HIV positive patients with tuberculosis. Its occurrence presents a formidable challenge to doctors as persistently low drug doses can result in multiple drug resistance. We describe the case of an HIV negative man with pulmonary tuberculosis and a persistent fever, despite two months treatment with rifampicin, isoniazid, and pyrazinamide. We discuss possible causes of this fever, including cytokine release, drug induced fever, drug resistance, and drug malabsorption. The case presented here highlights the difficulties in detecting the malabsorption.

Case history

A 47 year old white, unemployed factory worker presented with a four month history of cough, sputum, weight loss, and anorexia. His bowel habit was normal with no diarrhoea or steatorrhoea. He had a history of chronic schizophrenia, and his only other serious illness was a pneumococcal pneumonia in 1990. He was taking no drug treatment, smoked 20-30 cigarettes a day, and drank 40 units of alcohol a week.

On examination he was unwell and cachectic. He had a fever of 38.3°C and had finger clubbing. He was normotensive (pulse 90 beats/min). Auscultation of the chest revealed crepitations and bronchial breathing at the right base. Chest radiography showed multiple cavitating lung lesions, and sputum was positive for acid fast

bacilli. Pulmonary tuberculosis was diagnosed, and combination therapy (rifampicin, isoniazid, and pyrazinamide) was started with three tablets a day (daily total: rifampicin 360 mg, isoniazid 150 mg, pyrazinamide 900 mg). His HIV status was negative.

After three weeks of supervised hospital treatment, the patient had orange urine, but his swinging fever persisted (up to 39°C). Repeated blood cultures were negative, and an abdominal ultrasound scan was normal. A two week course of prednisolone 50 mg daily made no difference to the fevers, and after an episode of hypotensive collapse the prednisolone was changed to intravenous hydrocortisone 100 mg four times a day. Intramuscular streptomycin 500 mg was added to cover the possibility of a resistant mycobacterial strain. Nasogastric feeding was also started for albumin support.

The fevers settled with the intravenous hydrocortisone, and a week later this was exchanged for oral prednisolone (60 mg daily), at which point the fevers returned. Sensitivities of the original sputum became available: the *Mycobacterium tuberculosis* was sensitive to rifampicin, isoniazid, and pyrazinamide. Drug induced fever was excluded as 48 hours without rifampicin, isoniazid, and pyrazinamide made no difference to the swings in fever. Daily streptomycin was continued during this period.

The patient failed to improve, and repeat sputum analysis two months into treatment showed persistence of acid fast bacilli. Serum rifampicin concentrations

Hammersmith Hospital, London W12 0HS

Case presented by:
Maha T Barakat, senior house officer in respiratory medicine
Chairman: J Scott, director of medicine

Discussion Group:
J M B Hughes, professor of thoracic medicine
M Walport, professor of rheumatology
J Calam, senior lecturer in gastroenterology
J S Friedland, senior lecturer in infectious diseases
P W Ind, senior lecturer in respiratory medicine
C McKenna, senior lecturer in psychiatry

Series edited by: Dr Simon D Taylor-Robinson.

BMJ 1996;313:1543-5