5: Hospital-in-the-home treatment of infectious diseases

Benjamin P Howden and M Lindsay Grayson

Not all patients receiving intravenous antibiotics need to be in hospital

Abstract

- A growing range of infections can be safely and effectively treated with parenteral antimicrobial therapy at home, including cellulitis, pyelonephritis, pneumonia, endocarditis, osteomyelitis, septic arthritis and deep abscesses.
- Patients may be admitted to HITH directly from the emergency department or after a period of in-hospital care; they must be thoroughly assessed for suitability, including clinical stability and social circumstances, and both patient and carer consent must be obtained.
- Patients should be medically reviewed weekly at the hospital to monitor progress of therapy and check for possible complications, including adverse drug reactions.
- Antibiotic selection should be based on appropriate prescribing principles rather than purely dosing convenience.
- Innovative dosing regimens, including once-daily aminoglycosides, continuous-infusion β-lactams (eg, flucloxacillin), once- or twice-daily cephalosporins (eg, cephazolin) and oral fluoroquinolones (eg, ciprofloxacin) provide effective therapy for a wide range of infections that would have previously required in-hospital care.
- Appropriate use of HITH leads to improved patient and carer satisfaction, efficient in-hospital bed use and possibly some financial efficiencies.

MJA 2002; 176: 440–445

WHILE HOME-BASED MEDICAL TREATMENT is age-old, its use for serious medical conditions is relatively new to Australia. Usually termed hospital in the home (HITH) in this country, it is defined as care that would otherwise have to be delivered in hospital because of the nature of the patient's medical or social condition.[1,2] A key use in Australia is for intravenous antibiotic therapy.[1-5] This is equivalent to "outpatient antibiotic therapy" in the United States and will be the focus of our discussion.

HITH has grown in Australia mainly since the mid-1990s, driven by observed improvements in efficiency of hospital bed use and patient satisfaction.[1,2] It has been most used in Victoria, Queensland and Tasmania. In Victoria in 1997–1998, HITH care accounted for 11 159 admissions and 62 301 days of care — about equivalent to a fully occupied 170-bed hospital. For 54% of these admissions, all post-assessment healthcare was entirely at home with no in-hospital admission.[6] Other States have now developed active HITH programs.

Despite the growth in HITH, few randomised trials have assessed its efficacy and cost. Nevertheless, a recent large study of clinical outcomes of HITH intravenous antibiotic programs in four large Victorian urban and regional units found that 94% of treatment courses achieved their expected outcomes.[5] Potential strengths and weaknesses of HITH are summarised in Box 1, and a management algorithm for HITH treatment of infectious diseases in Box 2.

Factors for a successful HITH antibiotic program

Careful patient selection

In Australia, assessment and selection of patients for HITH rests entirely with clinical staff. Careful patient selection is vital to the success of HITH programs and should consider:[7]

- Medical need for parenteral antimicrobial therapy.
- Stability of clinical status.
- Patient and carer ability to manage at home. The most common error made by inexperienced medical staff is to underestimate the difficulties that patients, especially elderly patients, encounter in managing at home when they are ill. This underestimation invariably results in early HITH failure and hospital readmission. Patients who live alone or without a capable carer may therefore be inappropriate, as may patients who live in isolated areas or without a telephone or other means of rapid communication.
- Active substance misuse. This is usually a contraindication.
- Safety of visiting HITH nurses. This is critical — patients who are aggressive or have aggressive relatives or pets are generally not suitable.
- A language barrier between patient and staff that cannot be overcome by interpreters or family members.

Monitoring of complications

Patients and their carers need education to recognise complications of HITH therapy. Most common are problems with intravenous access (eg, line blockages or airlocks,

Series Editors: M Lindsay Grayson, Steven L Wesselingh

Austin and Repatriation Medical Centre, Melbourne, VIC.
Benjamin P Howden, FRACP, Registrar, Microbiology Department;
M Lindsay Grayson, MD, FRACP, FAFPHM, Director, Infectious Diseases Department; Professor of Medicine, University of Melbourne, and Professor of Epidemiology and Preventive Medicine, Monash University, Melbourne, VIC.
Reprints will not be available from the authors. Correspondence: Professor M Lindsay Grayson, Infectious Diseases Department, Austin and Repatriation Medical Centre, Studley Road, Heidelberg, VIC 3084.
Lindsay.Grayson@armc.org.au

1: Potential strengths and weaknesses of hospital in the home*

Strengths

Patient at home with family, able to continue work, school
Sense of empowerment
Fewer nosocomial and cannula-associated infections
Improved utilisation of hospital beds

Weaknesses

Disruption to family routine, increased stress
Sense of abandonment
Inappropriate antibiotic selection
Decreased supervision
Non-compliance with therapy, bed rest, leg elevation
Misuse of intravenous access
Potential for increased duration of intravenous therapy as less medical incentive to stop

* Adapted from Williams et al.[7]

phlebitis and infection) and drug side effects (eg, nausea, vomiting, diarrhoea and allergic reactions).[5,7-11] Many of these complications also occur among in-hospital patients, but the more limited contact between staff and HITH patients necessitates special vigilance.

Patient and carer consent

Patients and their carers must be willing to receive HITH care. Consent acknowledges some responsibility for the patient's health.

Multidisciplinary team

Selecting patients and implementing an HITH program requires a multidisciplinary approach, with contributions from clinicians and nurses, as well as pharmacists, who assist with appropriate antimicrobial choice and preparation. However, the ultimate legal responsibility for the quality of care and outcome of HITH rests with the clinician.[2,12] HITH clinicians need to be experienced in treating infectious diseases and to have a clear understanding of antimicrobial pharmacokinetics. As HITH is becoming increasingly specialised, they also need a special interest in HITH and understanding of the management of complex conditions at home.

Generally, HITH management has been undertaken by interested physicians, or, in some cases, general practitioners, who have the potential to provide better continuity of care. However, as HITH patients are classified as inpatients in most Australian States, GPs cannot charge Medicare for HITH-related services, but must be paid by the relevant hospital. For many GPs, this is a practical disincentive to becoming involved in HITH.

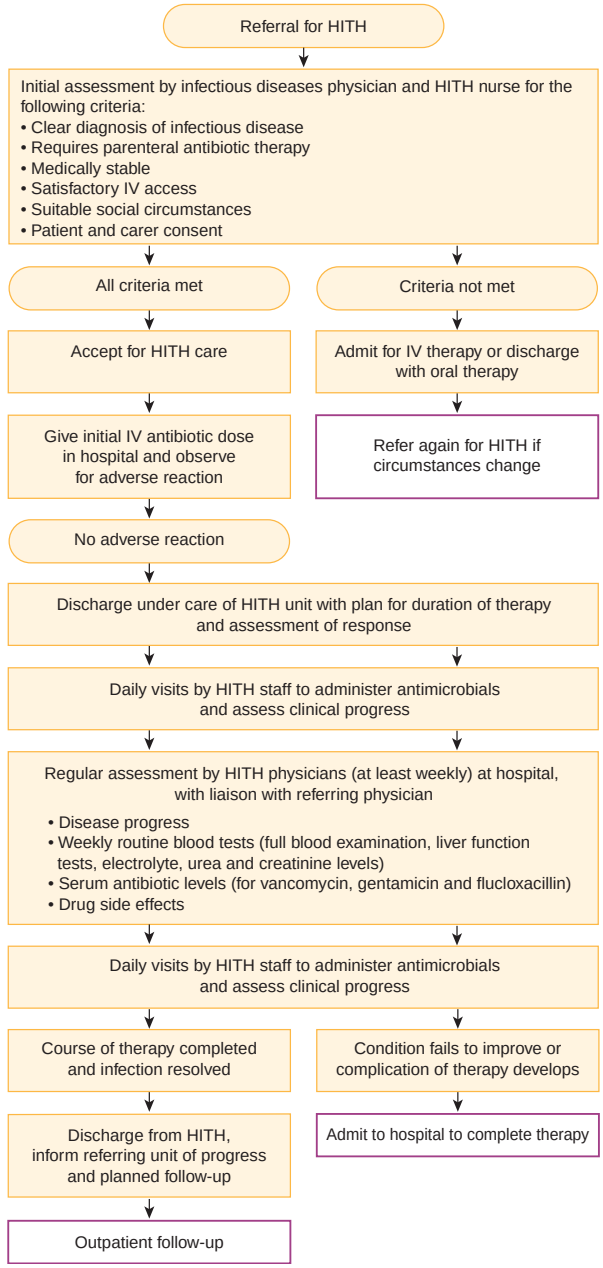
Practical issues in HITH

Venous access

Peripherally inserted central catheters: These have greatly simplified HITH intravenous therapy. Made of flexible silicone, they can generally be inserted and removed on an outpatient basis. They are introduced into the cubital vein under local anaesthesia, advanced into the superior vena cava and held in position with an adhesive dressing rather than suturing. Their longevity and relatively low infection rate allow them to be used for many weeks before replacement.

As peripherally inserted central catheters deliver drugs into high-flow vessels, such as the innominate vein or superior vena cava, they are suitable for administering concentrated antibiotic solutions by both continuous infusion and intermittent dosing. Patency is maintained by a single flush of saline or low-dose heparin after each antibiotic dose.[13]

2: Management algorithm for hospital-in-the-home treatment of infectious diseases



3: Portable infusion devices commonly used for hospital in the home

(Clockwise from top left) *Spring-loaded infusion device* may be used for hands-free delivery of a bolus antibiotic dose over 10 minutes (useful for antibiotic regimens such as once- or twice-daily cephazolin).

Elastomeric infusion device delivers prolonged infusions, including continuous infusion. The expandable bladder is filled with antibiotic, and resulting tension in the bladder drives the infusion. These pumps are single use and relatively expensive, but useful for regimens such as 24-h continuous-infusion flucloxacillin.

Spring-loaded continuous-infusion pump is a reusable alternative to the elastomeric device, but requires a special disposable minibag.

Computerised pumps can be programmed to deliver antibiotics by either continuous infusion or intermittent boluses. These pumps are more expensive and can also have high disposable costs, but have the advantage of sending an alarm if the infusion is interrupted or an airlock occurs.

Routine peripheral intravenous cannulas: These are generally used for short-duration therapy (less than seven days), but must be changed every two to three days to minimise risk of phlebitis.

Antibiotic dosing and delivery

The criteria for selecting antibiotics for HITH are similar to those applied for hospital care — one seeks the agent with the narrowest appropriate antibacterial spectrum, most practical dosing regimen, and lowest purchase and delivery cost. However, HITH has further requirements: the most suitable antibiotics are those that either require infrequent dosing (once or twice daily) or can be given by continuous infusion.

A particular dilemma is posed by agents that can be given once daily but have a broader than necessary antibacterial spectrum (eg, some third-generation cephalosporins) or are not the usual optimal agent (eg, some glycopeptides). These agents should generally be avoided; HITH therapy should use antibiotics that would be considered optimal for in-hospital use. This may necessitate innovative delivery methods, such as continuous-infusion and computerised devices (Box 3).

Aminoglycosides: Clinical data suggest that a once-daily dose of an aminoglycoside (eg, 4–5 mg/kg gentamicin) has similar efficacy to two or three divided doses and probably lower toxicity.[14] Thus, once-daily administration is now the preferred in-hospital and HITH dosing regimen for gentamicin when treating many gram-negative infections, including pyelonephritis, cholangitis, and moderate to severe pneumonia. However, data are lacking on once-daily dosing in treating burns, cystic fibrosis and, especially, endocarditis, and for pregnant women and neonates.[15]

β-Lactams: Studies suggest that the clinical efficacy of β-lactams depends on the proportion of the dosing interval that serum drug concentrations exceed the minimum inhibitory concentration for the pathogen.[16] Thus, β-lactams with a long half-life (eg, ceftriaxone) can be given daily, while those with a short half-life (eg, penicillin, ampicillin, flucloxacillin and dicloxacillin) should be given either frequently (4–6-hourly) or by continuous infusion. As dosing more often than twice daily is generally impractical for HITH care, flucloxacillin, penicillin and some cephalosporins (eg, ceftazidime) are increasingly administered by continuous infusion to treat conditions including endocarditis, osteomyelitis, meningitis, brain abscesses and some severe pneumonias.[7,10,11,17,18] Flucloxacillin appears stable for at least 12 hours after compounding, and even 24-hourly drug preparation and administration by continuous infusion appears to produce satisfactory serum drug concentrations and clinical efficacy for most patients at daily doses of 8–12 g[17,18] (case report, Box 4). Factors limiting use of continuous infusion are availability and cost of accurate drug-delivery devices.

Glycopeptides: Vancomycin and teicoplanin are effective against many gram-positive pathogens, but are generally reserved for infections with β-lactam-resistant bacteria, such as methicillin-resistant *Staphylococcus aureus*, and patients with β-lactam anaphylaxis. Vancomycin generally needs to be administered over at least one to two hours twice daily. Teicoplanin can be given more rapidly once daily, but requires two initial loading doses, is relatively expensive, and its efficacy has been questioned.[15,19] Nevertheless, both agents are generally suitable for most HITH programs.

Antiviral agents: Ganciclovir is effective for both short-term treatment and long-term suppression of serious cytomegalovirus disease when administered in a dose of 5 mg/kg twice or once daily, respectively.[19] These regimens are generally suitable for HITH administration, although the recent availability of oral ganciclovir has reduced the need for long-term intravenous suppressive therapy in some patients.

Oral antibiotics: Some antibiotics have sufficient bioavailability that oral doses achieve serum drug levels comparable to those after intravenous administration. For example, ciprofloxacin and trimethoprim–sulfamethoxazole (larger doses) achieve excellent serum levels in patients with normal intestinal absorption who are not taking antacids.[19] Serum

4: Case history: long-term hospital-in-the-home (HITH) care for osteomyelitis

History: A 60-year-old man who was previously well was admitted to hospital with a fracture of the right tibia caused by a car accident. The fracture was treated with open reduction and internal fixation with prosthetic material. Ten days later, the patient developed chills and inflammation of the surgical wound.

Examination: The patient's temperature was 38.2°C, and the wound was red, tender and discharging.

Investigations: He had a white cell count of 13.2 x 10^9/L (reference range [RR], 4.0–11.0 x 10^9/L), with neutrophils predominating, and raised C-reactive protein level of 250 mg/L (RR, < 5 mg/L). Blood cultures and wound swabs grew *Staphylococcus aureus* that was sensitive to flucloxacillin.

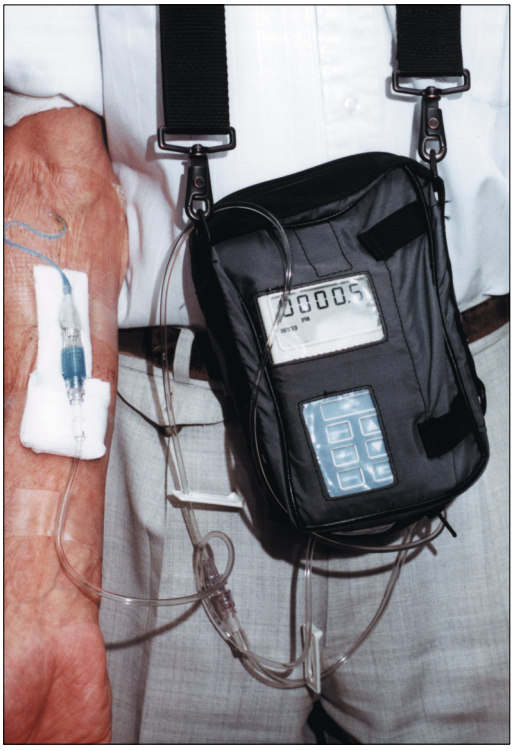
Management and course: Therapy with intravenous flucloxacillin (2 g 4-hourly) was begun. The wound was debrided and revealed infection extending to the bone. The prosthetic material was removed, and an external fixation device applied. A central catheter was inserted peripherally.

Eight days later, after recovering from surgery, the patient was transferred to the hospital-in-the-home program, receiving flucloxacillin (12 g daily) by continuous infusion.

On review in the outpatient department a week later, he complained of nausea. Serum flucloxacillin level was measured and found to be high (65 mg/L) (there is no standard reference range, but nausea appears common when serum levels exceed 40–50 mg/L). The dose of flucloxacillin was reduced over 24 hours to 8 g daily. The nausea resolved, and a repeat flucloxacillin level a week later was 40 mg/L. Intravenous flucloxacillin was continued for a total of six weeks.

At six-month follow-up, the patient was able to walk unaided, with minimal residual pain.

- *The patient was suitable for HITH care after recovering from surgery, as his condition was medically stable but required a prolonged course of intravenous antibiotics.*
- *A peripherally inserted central catheter is optimal for patients requiring intravenous therapy for longer than seven to 10 days, as it avoids the need for regular line changes and has low complication rates.*
- *A computerised pump provides accurate, continuous antibiotic infusion, as well as the safety of monitoring for line blockages and air bubbles.*



Patient receiving a continuous infusion of flucloxacillin via a computerised infusion pump and peripherally inserted central catheter.

levels of ciprofloxacin after twice-daily oral doses of 750 mg are similar to those after eight-hourly intravenous doses of 400 mg. This antibiotic appears very effective therapy for infections including gram-negative osteomyelitis and pyelonephritis.[19-21]

New oral agents that, at once-daily doses, achieve similar serum levels to intravenous therapy are also now available. For example, the new fluoroquinolones gatifloxacin and moxifloxacin provide excellent activity against a wide range of pathogens and are currently being intensively marketed for treating community-acquired pneumonia. However, arguments against their widespread use in Australia for this indication are the current low rates of high-level penicillin resistance in pneumococcal disease, broad spectrum of activity of these agents, and reports of major adverse reactions to other new drugs in this class. Nevertheless, their excellent clinical efficacy at once-daily doses suggests they may eventually be useful in patients with serious infections requiring long-term antibiotic therapy.

Similarly, linezolid (a new oxazolidinone) is available in both oral and intravenous preparations. The oral preparation appears to be effective therapy for serious infections with methicillin-resistant *S. aureus* and vancomycin-resistant enterococci.

Antibiotic treatment regimens

Recommended antibiotic regimens for HITH are summarised in Box 5.

Conditions requiring short-term therapy

Many relatively common infections require only short-term intravenous antibiotics, including cellulitis, the most common indication for HITH antibiotic therapy in Australia, accounting for about 46% of treatment episodes.[5] Others in this category include pyelonephritis, pneumonia, bacterial meningitis and infective exacerbations of chronic lung disease and cystic fibrosis. Because of the usual short duration of therapy, these infections are ideally treated with agents that can be given intermittently once or twice daily. This avoids the need for expensive continuous-infusion drug-delivery devices, while minimising daily nursing visits (see case report, Box 6).

For mild to moderate community-acquired pneumonia, the popularity of HITH varies widely, as do outcomes.[5] As patients sick enough to need intravenous antibiotics usually also need supplemental oxygen, some clinicians consider that HITH management is rarely appropriate. Others have reported clinical success with various HITH regimens, particularly ceftriaxone (1–2 g once daily).[7,10]

For some of these infections, new oral agents with high bioavailability may reduce the need for intravenous therapy. For example, recent studies suggest that oral fluoroquinolones (eg, ciprofloxacin, 500–750 mg twice daily) are highly effective therapy for pyelonephritis, and may be suitable alternatives to parenteral therapy for patients with satisfactory gastrointestinal absorption[20] (see Box 5).

5: Antibiotic treatment regimens for hospital in the home

Condition	Regimen	Comments
Common conditions requiring short-term therapy		
Cellulitis	*Preferred* Cephazolin (2 g IV twice daily)[15,22] *or* cephazolin (2 g IV once daily) *plus* probenecid (1 g orally daily)[23,24]	Cephazolin, a first-generation cephalosporin, has comparable clinical efficacy at these doses to once-daily ceftriaxone,[22,23] and a narrower antibacterial spectrum, which may be more desirable.
	Alternative Ceftriaxone (1 g IV daily)[25] *or* flucloxacillin (8 g IV daily by continuous infusion)[18]	Flucloxacillin is generally avoided, as it must be delivered by continuous infusion, which requires expensive equipment.
Pyelonephritis	*Preferred*[15] Gentamicin (4–6 mg/kg/d IV) *or* ceftriaxone (1 g IV daily)	Intravenous gentamicin and ceftriaxone should be followed by oral therapy to complete a total of 14 days' treatment.
	Alternative Ciprofloxacin (500–750 mg orally twice daily)[20]	Ciprofloxacin is not the usual first choice for in-hospital treatment of pyelonephritis, but oral administration is a significant practical advantage. However, it is listed by the Pharmaceutical Benefits Scheme only for antibiotic-resistant pathogens.
Pneumonia (community-acquired, moderate severity)	*Preferred* Ceftriaxone (1 g IV daily)[7,10]	Careful patient selection is essential. Ceftriaxone is not the usual first choice for in-hospital care, and few patients require its broad-spectrum activity.
Cystic fibrosis (infective exacerbations)	*Preferred* Cefepime (2 g IV twice daily) *plus* tobramycin (4–6 mg/kg IV daily)[26]	Few data are available; choice of regimen should be based on susceptibilities of isolated pathogens. Ceftazidime (2 g twice daily) has been used successfully instead of cefepime,[26] but for inpatients is usually given three times daily.
Meningitis	*Preferred* Ceftriaxone (2 g IV daily)[11]	Australian guidelines recommend 2 g twice daily,[15] but once-daily dosing appears effective for patients well enough to be managed by HITH.[11]
Less common serious conditions requiring prolonged therapy		
Osteomyelitis and septic arthritis (MSSA)	*Preferred* Flucloxacillin (8–12 g IV daily by continuous infusion for 4–6 weeks)[17,18]	Continuous-infusion flucloxacillin has been used only after the patient's condition was stabilised by intermittent therapy as inpatient.
	Alternative Vancomycin (1 g IV twice daily for 4–6 weeks)	Vancomycin is used if severe penicillin allergy, or causative organism is methicillin-resistant *Staphylococcus aureus*.
Endocarditis (uncomplicated, caused by viridans streptococci)*	*Preferred* Ceftriaxone (2 g IV daily for 4 weeks)[27]	Ceftriaxone therapy commonly follows inpatient therapy with intermittent penicillin.
	Alternative[28] Ceftriaxone (2 g IV daily) *plus* gentamicin (3 mg/kg/d IV) (both for 2 weeks) *or* penicillin (8.4 g/d IV by continuous infusion for 4 weeks)	Most authorities recommend two to three doses of gentamicin per day for endocarditis. Penicillin use is supported by case reports only, not controlled trials, but is recommended by some.[15]
Endocarditis (MSSA)	*Preferred* Flucloxacillin (8–12 g IV daily by continuous infusion for 6 weeks)[17,18]	Used after stabilisation of patient's condition by inpatient therapy with intermittent flucloxacillin; experience is limited.
Cytomegalovirus disease	*Preferred* Ganciclovir (5 mg/kg IV twice daily for 2–3 weeks)[15,19]	May be followed by long-term suppressive therapy (eg, 5 mg/kg/d IV or 3 g/d orally).

IV = intravenously. MSSA = methicillin-susceptible *Staphylococcus aureus*.
* Endocarditis of a native valve with no complications; causative organism has a penicillin minimum inhibitory concentration < 0.1 μg/mL.

Conditions requiring prolonged therapy

Serious, less common diseases that are often suitable for HITH care include endocarditis, osteomyelitis and septic arthritis, deep abscesses (eg, brain, psoas and liver) and cytomegalovirus disease in transplant recipients and people with HIV infection. As therapy is generally prolonged, long-term intravenous access is often needed (eg, peripherally placed central catheters). Conditions such as endocarditis and osteomyelitis may be suitable for innovative treatment regimens, such as continuous-infusion β-lactam therapy using computerised or elastomeric delivery devices (case report, Box 4).

Conclusions

Treatment of certain infections through a suitable managed HITH program provides a safe, effective and efficient alternative to in-hospital care and generally improves patient satisfaction. Careful patient selection is critical. The need

6: Case history — short-term hospital-in-the-home (HITH) care for cellulitis

History: A 35-year-old woman presented to the emergency department with painful cellulitis of the left leg and fever of two days' duration. She was previously well and had no known drug allergies.

Examination: She had a fever (temperature, 38.3°C), and cellulitis and swelling of the left lower leg, with tender left inguinal lymphadenopathy and tinea pedis. She was haemodynamically stable.

Investigations: Her white cell count was 14.2 x 10^9/L with neutrophils predominating (reference range [RR], 4.0–11.0 x 10^9/L). Blood cultures were sterile.

Management and course: A peripheral intravenous cannula was inserted, and cephazolin (2 g) was administered intravenously. This produced no adverse effects, and the patient was admitted to HITH from the emergency department to continue cephazolin (2 g intravenously twice daily).

On review four days later in the outpatient department, the leg erythema was resolving, and therapy was changed to oral cephalexin (500 mg four times daily) for a further five days.

On follow-up at the end of antibiotic therapy, the patient's general practitioner successfully treated the tinea pedis, which was the likely portal of entry for the infection, with topical clotrimazole.

- *Although flucloxacillin is active against both the common pathogens in cellulitis (streptococci and* Staphylococcus aureus*), its 4–6-hourly dosing schedule is impractical for HITH, while continuous infusion is probably not warranted given the usual short duration of therapy (less than seven days).*
- *Once-daily ceftriaxone (1–2 g) has efficacy in cellulitis, but its broad antibacterial spectrum may make it less suitable for this indication than cephazolin, a first-generation cephalosporin.*[25]
- *Most cellulitis episodes require less than seven days' intravenous therapy; switching to oral agents, such as flucloxacillin, dicloxacillin, cephalexin or clindamycin, after initial improvement generally results in cure.*[5,23]

for HITH care is likely to grow as more patients request optimal medical care with minimum lifestyle disruption, and as governments increasingly emphasise efficient hospital bed use. Ongoing research into HITH care is needed to ensure that it remains evidence-based and safe.

Evidence-based recommendations*

- Clinically stable patients with uncomplicated viridans streptococcal endocarditis can be safely treated at home with four weeks of intravenous ceftriaxone (2 g daily) after initial inpatient treatment[27] (E4).
- Daily intravenous cephazolin (2 g) plus oral probenecid (1 g) is as effective as daily intravenous ceftriaxone (1 g) for home treatment of moderate to severe cellulitis in adults[23,24] (E2).
- Continuous infusion of flucloxacillin appears safe and effective for home treatment of serious staphylococcal infections (eg, osteomyelitis, deep abscesses and some cases of endocarditis) after initial inpatient treatment[17,18] (E4).
- In some circumstances, pyelonephritis can be successfully treated with oral fluoroquinolones instead of intravenous antibiotics[20] (E2).

* Evidence-based recommendations are currently difficult to formulate for hospital-in-the-home antibiotic treatment, as published data are limited.

References

1. Grayson ML. Hospital in the home — is it worth the hassle? [editorial]. *Med J Aust* 1998; 168: 262–263.
2. Montalto M. Hospital in the home: take the evidence and run [editorial]. *Med J Aust* 1999; 170: 148-149.
3. Shepperd S, Iliffe S. Hospital at home versus in-patient hospital care [Cochrane Review]. Cochrane Library 1. Oxford: Update Software, 2002.
4. Caplan GA, Ward JA, Brennan NJ, et al. Hospital in the home: a randomised controlled trial. *Med J Aust* 1999; 170: 156-160.
5. Grayson ML, Stanley K, Montalto M, et al. The Victorian Hospital-in-the-Home Outcomes Study. Abstracts from the Australian Home and Outpatient Intravenous Therapy Association Annual Scientific Meeting 2000. Melbourne; 13 Oct 2000.
6. Department of Human Services, Victoria. 1997/98 Hospital in the Home Program: final results. Department of Human Services, Victoria, Nov 1998.
7. Williams DN, Rehm SJ, Tice AD, et al. Practice guidelines for community-based parenteral anti-infective therapy. *Clin Infect Dis* 1997; 25: 787-801.
8. Grayson ML, Silvers J, Turnidge J. Home intravenous antibiotic therapy: a safe and effective alternative to inpatient care. *Med J Aust* 1995; 162: 249–252.
9. Hoffman-Terry ML, Fraimow HS, Fox TR, et al. Adverse effects of outpatient parenteral antibiotic therapy. *Am J Med* 1999; 106: 44-49.
10. Gilbert DN, Dworkin RJ, Raber SR, Legget JE. Drug therapy. Outpatient parenteral antimicrobial drug therapy. *N Engl J Med* 1997; 337: 829-838.
11. Tice AD, Strait K, Ramey R, Hoaglund PA. Outpatient parenteral antimicrobial therapy for central nervous system infections. *Clin Infect Dis* 1999; 29: 1394-1399.
12. Poretz DM. Evolution of outpatient parenteral antibiotic therapy. *Infect Dis Clin North Am* 1998; 12: 827-834.
13. Ng PK, Ault MJ, Ellrodt AG, Maldonado L. Peripherally inserted central catheters in general medicine. *Mayo Clin Proc* 1997; 72: 225-233.
14. Munckhof WJ, Grayson ML, Turnidge JD. A meta-analysis on the safety and efficacy of aminoglycosides given either once daily or as divided doses. *J Antimicrob Chemother* 1996; 37: 645-663.
15. Therapeutic Guidelines Limited. Therapeutic guidelines: antibiotic. Version 11, 2000. Melbourne: Therapeutic Guidelines Limited, 2000.
16. Turnidge JD. The pharmacodynamics of beta-lactams. *Clin Infect Dis* 1998; 27: 10-22.
17. Leder K, Turnidge JD, Korman TM, et al. The clinical efficacy of continuous-infusion flucloxacillin in serious staphylococcal sepsis. *J Antimicrob Chemother* 1999; 43: 113-118.
18. Howden BP, Richards MJ. The efficacy of continuous infusion flucloxacillin in home based therapy for serious staphylococcal infections and cellulitis. *J Antimicrob Chemother* 2001; 48: 311-344.
19. Kucers A, Crowe S, Grayson ML, Hoy J, editors. The use of antibiotics. 5th ed. Oxford: Butterworth Heinemann, 1997.
20. Mombelli G, Pezzoli R, Pinoja-Lutz G, et al. Oral vs intravenous ciprofloxacin in the initial empirical management of severe pyelonephritis or complicated urinary tract infections: a prospective randomized clinical trial. *Arch Intern Med* 1999; 159: 53-58.
21. Lew DP, Waldvogel FA. Osteomyelitis. *N Engl J Med* 1997; 336: 999-1007.
22. Leder K, Turnidge JD, Grayson ML. Home-based treatment of cellulitis with twice-daily cephazolin. *Med J Aust* 1998; 169: 519-522.
23. Grayson ML, McDonald M, Gibson K, et al. Once-daily IV cephazolin 2 g and oral probenecid 1 g is equivalent to once-daily IV ceftriaxone and oral placebo for the treatment of moderate–severe cellulitis in adults. *Clin Infect Dis* 2002. In press.
24. Brown G, Chamberlain R, Goulding J, et al. Ceftriaxone versus cefazolin with probenecid for severe skin and soft tissue infections. *J Emerg Med* 1996; 14: 547-551.
25. Deery HG. Outpatient parenteral anti-infective therapy for skin and soft tissue infections. *Infect Dis Clin North Am* 1998; 12: 935-949.
26. Wolter JM, Bowler SD, Nolan PJ, McCormack JG. Home intravenous therapy in cystic fibrosis: a prospective randomised trial examining clinical, quality of life and cost aspects. *Eur Respir J* 1997; 10: 896-900.
27. Francioli PB. Ceftriaxone and outpatient treatment of infective endocarditis. *Infect Dis Clin North Am* 1993; 7: 97-116.
28. Rehm SJ. Outpatient intravenous antibiotic therapy for endocarditis. *Infect Dis Clin North Am* 1998; 12: 879-901. ❑