

The unsubstantiated preference for outpatient IV antibiotics

There is growing concern that IV antibiotics are overused. Numerous recent randomized controlled trials have demonstrated that oral therapies are just as effective as their IV counterparts for treating many complex infections.

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ABSTRACT

IV antibiotic therapy is a critical component in the management of infectious diseases. However, there is growing concern that IV antibiotics are overused without improving patient outcomes. In recent years, numerous randomized controlled trials have demonstrated that oral therapies are just as effective as their IV counterparts for treating many complex infections, such as infective endocarditis, osteoarticular infections, and bacteremia. A critical review of the appropriateness of outpatient IV antibiotic prescriptions could aid in improving patient outcomes, maximizing cost-effective care, and minimizing the waste of health care resources.

Established in 2005, the outpatient parenteral antibiotic therapy (OPAT) clinic at Royal Columbian Hospital (RCH) is an integral service that provides care for patients who require IV antibiotics for their infections. OPAT clinics are infusion centres that exist in many hospitals, either as an extension of the emergency department or as a self-sufficient unit

that administers IV medications, most commonly antibiotics, to outpatients. Historically, patients who needed IV antimicrobials were admitted to hospital for the entire duration of their treatment course. OPAT clinics are vital in preventing unnecessary hospital admissions and facilitating early discharge.

At RCH, the OPAT clinic is located in the ambulatory care department, separate from the emergency department, and is staffed by a team of skilled nurses and infectious diseases physicians who oversee the care of patients on IV therapy. The most common route of referral is through the emergency department, where patients are assessed by an ER physician who diagnoses them with a bacterial infection that is judged to require IV antibiotics. These patients are subsequently referred to the OPAT clinic and are evaluated by an infectious diseases physician to ensure the infection diagnosis is correct and to devise an appropriate treatment plan. Patients generally come to the clinic once a day to receive their IV treatment.

This model of antimicrobial delivery has been the standard of care for over 2 decades in BC and has generated massive cost savings by avoiding unnecessary hospitalizations and minimizing nosocomial complications.¹ However, with a growing body of literature that has consistently demonstrated the noninferiority of oral antibiotics to their IV counterparts in treating complex bacterial infections, the value of OPAT needs to be re-evaluated.² Moreover,

IV administration can be associated with increased patient harm and unnecessary resource expenditure. OPAT has clearly established itself as an essential resource in mainstream medicine, but perhaps it is being overused or misused in light of modern evidence.³

In this article, we review a simple set of criteria to guide clinicians in their decision making regarding IV prescriptions, present the data from a recent audit conducted at the RCH OPAT clinic, objectively compare the advantages and disadvantages of IV and oral administration, examine the history of the IV superiority myth, and critically assess our cognitive biases when opting for parenteral therapy.

Criteria to determine the appropriateness of IV administration

Criteria for determining whether IV or oral treatment should be prescribed are often lacking and controversial; therefore, the decision to offer parenteral therapy is frequently arbitrary and based on personal practice habits and cultural norms. If we adopt the published criteria proposed for treating osteomyelitis and infective endocarditis, it becomes clear that most outpatients would qualify for oral therapy from the beginning. In my practice, I follow the same set of principles: (1) there is a safe and effective oral option, (2) the patient is able to swallow and absorb oral medication, (3) the patient is clinically stable, (4) there is no source control problem, and

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(5) there is no psychosocial reason to prefer IV therapy.^{4,5} By encouraging clinicians to follow the same criteria, we can establish a proper standard of care and ensure IV treatments are rationalized.

In one study, 41% of adult patients who received IV antibiotics did not require them (30% could have been switched to oral treatment; 11% did not need antibiotics). Even for patients who were prescribed IV therapy by an infectious diseases physician, it was judged that IV treatment was potentially avoidable in 22% of cases, raising concerns that infectious diseases specialists might also be overprescribing IV antimicrobials and underscoring a potential area for quality improvement.³

Audit at the RCH OPAT clinic

As an infectious diseases physician, I performed an audit of 100 randomly selected patients referred by the emergency department to the RCH OPAT clinic (whom I assessed and treated between March and May 2024) to determine the appropriateness of IV antibiotic prescriptions. Eighty-two patients were confirmed to have a bacterial infection. Skin and soft-tissue infections (50%) and urinary tract infections (13%) were the most common diagnoses for these patients. Ceftriaxone (46%) and cefazolin (40%) were the most commonly prescribed IV agents, while 16 patients (16%) also received a companion oral agent, metronidazole, in combination with ceftriaxone. Patients were transitioned from IV to oral antibiotics after a median of 2 days and an average of 3 days following my assessment. Commonly prescribed oral antimicrobials were cephalexin (31%) and amoxicillin/clavulanate (22%). The median and average durations of oral therapy were 4 and 6 days, respectively. Total durations of therapy were 7 days (median) and 9 days (average). Less than half (48%) of patients with a confirmed bacterial infection met the criteria for IV treatment. The other patients could have been started or continued on oral antibiotics from the beginning. The most common reason to prescribe IV treatment was hemodynamic instability

(21%), of which tachycardia accounted for all cases, followed by inability to tolerate oral medications (9%). No patient had sustained hypotension. Overall, IV antibiotics could have been avoided in 59% of cases.

These eye-opening figures should provoke dialogue about how we use IV medications and spark quality improvement measures to curtail unnecessary consumption of health care resources. In the absence of standardized criteria at our institution, the decision to prescribe oral or IV therapy is somewhat subjective and sometimes a matter of patient or clinician preference.

Practicality of outpatient IV antibiotics

For practical reasons, antimicrobial selection is usually limited to medications that are dosed every 24 hours in the OPAT clinic. Such drugs include cefazolin plus probenecid, ceftriaxone, daptomycin, and ertapenem. This makes it difficult to fine-tune the antibiotic prescription to an agent with the narrowest spectrum of activity, in the spirit of antimicrobial stewardship. Additionally, IV administration is more resource intensive than the oral route, because it requires a nurse to establish and maintain vascular access and administer the medication, and pharmacy support is needed to prepare the medication bag. Patients must secure daily transportation to the clinic, find and pay for parking if applicable, and adhere to instructions on caring for their peripheral IV catheter at home (see RCH's OPAT brochure: <https://patienteduc.fraserhealth.ca/file/opat-rch-outpatient-clinic-intravenous-antibiotic-228563.pdf>). Patients with limited mobility often face challenges attending daily visits and sometimes require friends or family members to assist with transportation.

Compared with oral treatment, IV therapy results in overmedicalization of patients and can profoundly reduce their quality of life without improving infection outcomes. In fact, IV administration can be associated with more adverse effects, mostly related to vascular catheter complications (e.g., superficial thrombophlebitis, infection, drug

extravasation, contact dermatitis from adhesives). Having more patients on IV therapy also means increased traffic and congestion in the hospital environment, which increases staff workload. With informed decision making, most patients prefer oral therapy for treatment of many conditions, including infections, malignancies, and autoimmune diseases.^{6,7}

Advantages and disadvantages of IV and oral antibiotics

When comparing oral and IV antibiotics, the advantages of each mode of delivery become apparent [Table]. Oral treatment offers higher convenience and mobility for patients, avoids the need for vascular access and its associated complications, minimizes medical contact, generates a smaller carbon footprint, and offers higher cost-effectiveness compared with its IV counterpart. Although IV administration causes fewer gastrointestinal side effects and leads to almost instantaneous and 100% drug bioavailability, these advantages are insignificant and mostly irrelevant for the vast majority of patients treated in the outpatient setting. It is not necessary to achieve excessively high peak drug levels for most uncomplicated nonsevere infections. Immediate drug delivery to the site of infection is critical for patients with sepsis or septic shock but is unlikely to be important in other scenarios.

TABLE. The advantages of oral versus IV antibiotics.

	Advantage
Oral	Higher convenience
	Higher patient mobility
	Less contact with health services
	No need for access to IV
	Earlier hospital discharge
	Lower carbon footprint
	Higher cost-effectiveness
IV	Instantaneous and higher bioavailability
	Lower gastrointestinal side effects

PREMISE

Uncertainty is normal in infectious diseases practice

In the field of infectious diseases, it is sometimes difficult to differentiate a bacterial infection from a noninfectious condition. In practice, many clinicians might shoot first and ask questions later when working through the diagnostic process. It is common practice to prescribe antibiotics in the face of diagnostic uncertainty before all clinical information becomes available. This leads to overprescribing of antimicrobials, exposes the patient to unnecessary harms, increases resource use, and can affect patient expectations about the role and utility of IV antibiotics. Instead, it may be prudent to withhold antibiotics for stable outpatients until better diagnostic clarity has been achieved.

History of the IV superiority myth

For decades, clinicians have assumed that IV antimicrobials are superior to oral agents for the treatment of infections based on poor evidence, expert opinion, and established cultural standards.⁸ In fact, there are no controlled trials that have shown IV antibiotics are better than oral. On the contrary, there are many studies that have proven the noninferiority of oral to IV antibiotics in the treatment of bacteremia, osteoarticular infections, complicated urinary tract infections, skin and soft-tissue infections, and even infective endocarditis.⁹ The prevailing myth that IV antibiotics are better than oral continues to be perpetuated in medical practice today, underscoring a widespread oversimplified and misconstrued understanding of a complex topic rooted in infectious disease management principles.

The preference for IV therapy may stem from the introduction of commercially available penicillin in the 1940s when stories of miracle cures following parenteral administration of the antibiotic became commonplace. Years later, the release of primitive oral antimicrobials with low bioavailability was seemingly less effective and made less of an impression on the medical community. Influential physicians at that time concluded that IV therapy was

superior to oral agents, inadvertently leading clinicians and patients to believe that aggressive infections require dramatic and intrusive interventions.⁸ This strongly held belief was left unchallenged and dominated the therapeutic paradigms of infection management for many decades, until 20 to 30 years ago, when randomized controlled trials emerged, finally dispelling the myth of IV superiority.⁹

The route of drug delivery is overemphasized

Other more important factors besides the mode of administration affect the overall efficacy of a drug and warrant careful consideration. These include penetration into the site of infection, antimicrobial spectrum of activity, anti-inflammatory properties, drug–drug interactions, side-effect profile, and published clinical experience. By placing too much emphasis on the route of drug delivery, it is easy to overlook other critical elements that might have a greater impact on outcomes in the management of certain infections. It is a dangerous fixation for both patients and clinicians that distracts us from recognizing the bigger picture.

Cognitive biases impact IV prescriptions

The language we use can subconsciously bias our perception of the effectiveness of antimicrobial therapies, either over- or underestimating their benefits. For example, in my experience, a commonly used justification to escalate to IV treatment is the patient having failed oral antibiotics. After dissecting this phrase, we realize that it is factually incorrect and misleading, because it is nearly impossible for a patient to fail oral antibiotics unless every oral agent has been tried. We also need to be careful to not diagnose treatment failure too early in the course of the infection, because symptoms and signs of inflammation might get worse before they get better, and it can take up to 3 days to achieve a good clinical response.¹⁰ Furthermore, blaming the treatment failure on the oral route of delivery is a gross misunderstanding of antimicrobial therapeutics.

If a patient is truly not responding to treatment, then it is important to consider these factors before reflexively switching to IV therapy:

1. Do you have the correct diagnosis? Sometimes, noninfectious conditions can mimic infections (e.g., venous stasis dermatitis).
2. Are you covering the right pathogen(s)? It does not matter whether the patient is receiving IV or oral antibiotics when the culprit pathogen is not being targeted. For example, escalating from oral cephalexin to IV cefazolin, a commonly observed practice in my experience, makes no microbiological sense, as both agents cover similar bacteria.
3. Are you using the right drug? This relates to correct dosing, adequate penetration into the site of infection, and effective activity against the pathogen.
4. Is there a source control problem? For example, perhaps there is an abscess that needs to be drained. Changing from oral to IV administration does not solve this problem.

Barriers to change

Unfortunately, evidence is not always enough to drive a change in practice. Barriers to change are encountered at the patient, clinician, and system levels. In my experience, some patients firmly believe that oral therapy is ineffective based on their past experiences and misunderstandings. Physicians may resort to inappropriate IV prescriptions because of cognitive biases, being out of date with current evidence, and fear of litigation. Systemic obstacles include a remuneration model that encourages physicians to prescribe more IV antimicrobials, a lack of supportive infrastructure and institutional policies to standardize oral antibiotics as first-line treatments, and hospital programs that pay for IV but not oral antibiotics for patients.⁸ For a positive change to be successfully implemented, barriers at all levels must be addressed by involving key parties and firmly establishing institutional evidence-based practice standards.

Conclusions

We need to reassess our proclivity for IV antimicrobials in an era when oral therapy has been proven to be just as effective and carries less burden for patients, health care staff, and the medical system. By encouraging the use of oral treatment and abandoning our biases regarding IV therapy, we can improve the patient experience, minimize resource use, achieve greater cost savings, and maintain sustainable health care for all. In the face of unequivocal evidence, it is time to shift the model of care once again to adopt the position that oral antimicrobial therapy should be the default route of administration unless there is a compelling indication to prescribe IV treatment. We owe it to our patients, ourselves, our colleagues, and our health care system to embrace and promote the best evidence-based practices to optimize patient outcomes at all stages in the delivery of care. ■

Competing interests

None declared.

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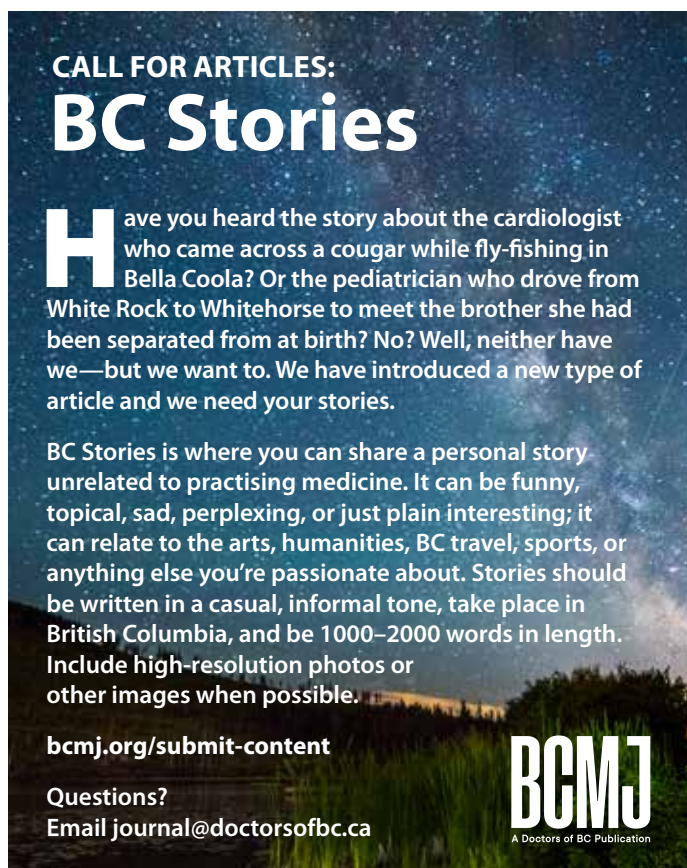
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