Panorama in medicine

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Outpatient parenteral antimicrobial therapy

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Outpatient parenteral antimicrobial therapy (OPAT) is the administration of intravenous antimicrobial therapy to patients in an outpatient setting or in their own home. First developed in the 1970s in the US for the treatment of children with cystic fibrosis, OPAT has expanded and is now standard practice in many countries. In the UK, is now being increasingly used for patients with severe or deep seated infections who require parenteral treatment but are otherwise stable and well enough not to be in hospital; these patients may be discharged early to an OPAT service or may avoid hospital admission altogether.
What type of infections can be treated?

Cellulitis
Data from several large retrospective case series show that outpatient treatment with once daily ceftriaxone is also safe and effective. If there is concern about possible meticillin resistant Staphylococcus aureus (MRSA) infection, teicoplanin or daptomycin are alternatives.

Bone and joint infections

Infective endocarditis
US, European, and UK guidelines now recommend OPAT as part of routine clinical care with the appropriate safeguards to minimise risk, include daily nurse review, once or twice weekly physician review.
Other uses
Resistant urinary tract infections, central nervous system infections, and low risk neutropenic sepsis.

Which patients are suitable?
Patients need to be clinically stable. Patients with substance misuse or serious mental health problems may not be suitable. In addition, there must be no other barrier to discharge from hospital. For example, although diabetic foot infections may be suitable for OPAT, but require other care that has to be provided in hospital, diabetic control, vascular assessment, and surgical intervention.
How is OPAT delivered?

Three service models can be used to deliver OPAT, all of which have been shown to be effective:

1. an ambulatory care centre,
2. a nurse attending the patient’s home, or
3. self administration.
The model of OPAT used largely determines the type of intravenous access. Options include “butterfly” needles for each dose, short term **peripheral cannulas**, or, for longer antibiotic courses, peripherally inserted **central cannulas** or tunnelled central lines. **Novel delivery devices** allow patients greater freedom to continue normal daily activities. For example, **portable elastomeric** infusion devices can be carried in the patient’s pocket or a carrying pouch and deliver continuous infusions over 24 hours.
What are the benefits?
OPAT has been shown to be cost effective in many healthcare contexts. Reducing direct costs, bed capacity, low rate of healthcare associated infection.

What are the risks?
Because of the reduced level of supervision, at least 25% of patients experience an adverse reaction of some type, ranging from mild antibiotic associated diarrhoea to severe line infections. Line related bacteraemia, air embolism, drug hypersensitivity, and drug induced blood dyscrasia. About 10% of patients will require readmission.
One further potential risk is overuse of intravenous antimicrobial therapy as an alternative to oral agents purely because an OPAT service exists. Similarly, there is also a risk that a broad spectrum once daily parenteral antimicrobial agent could be chosen in preference to a potentially more efficacious agent requiring multiple daily doses for reasons of convenience alone.
How can the risks be reduced?
It is clear that OPAT delivered through a formal service structure, the core team should comprise, as a minimum, an OPAT specialist nurse, doctor, infection specialist and a pharmacist. Patients on prolonged courses of antimicrobials can be reviewed weekly, or less frequently if stable, those receiving treatment for cellulitis should be reviewed daily to allow switching from intravenous to oral therapy as soon as clinically appropriate.
What is the future of OPAT in the UK?

a. improve patient choice while maintaining service quality
b. reduce healthcare costs and
c. improve service efficiency.

Use of OPAT is likely to continue to expand in the UK.
Summary points

Outpatient parenteral antimicrobial therapy (OPAT) allows patients requiring intravenous antibiotics to be treated outside hospital, is suitable for many infections, especially cellulitis, bone and joint infections, and infective endocarditis.

Antibiotics can be administered in an outpatient unit, at home by a nurse, or by the patient or a carer. Patients should be assessed by a doctor and specialist nurse to determine medical and social suitability. Evidence suggests that OPAT is safe as long as it is administered through a formal service structure.
Adult whooping cough
A 64-year-old man was admitted to the medical service with a presumed asthma exacerbation. His symptoms had worsened during the preceding 3 weeks despite treatment with oral glucocorticoids, leading him to present to the emergency department multiple times with a progressive cough. He also reporting having associated chest tightness and difficulty eating and sleeping, without any post-tussive emesis. Shortly after his admission, the medical team heard a characteristic “whooping” cough.
He was given azithromycin, and samples were obtained for serologic testing and for nasopharyngeal culture of *Bordetella pertussis*. The patient’s cough abated and his respiratory status improved during the next 5 days. Further questioning revealed that the patient had never been vaccinated against pertussis. He received a diptheria–tetanus–acellular pertussis (DTaP) vaccine approximately 1 month after discharge.
What is the most accurate way of measuring the core temperature?

In an intubated patient, insertion of a thermistor probe in the lower third of the esophagus is the preferred method.

A thermistor probe in contact with the tympanic membrane accurately reflects brain temperature, provided that the ear canal is free of snow and cerumen and is well insulated against the environment.
Ultrasound imaging for lumbar punctures and epidural catheterisations: systematic review and meta-analysis

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14 studies with a total of 1334 patients were included (674 patients assigned to the ultrasound group, 660 to the control group). Five studies evaluated lumbar punctures and nine evaluated epidural catheterisations. Six of 624 procedures conducted in the ultrasound group failed; 44 of 610 procedures in the control group failed. Ultrasound imaging reduced the risk of failed procedures (risk ratio 0.21 (95% confidence interval 0.10 to 0.43), P<0.001). Risk reduction was similar when subgroup analysis was performed for lumbar punctures (risk ratio 0.19 (0.07 to 0.56), P=0.002) or epidural catheterisations (0.23 (0.09 to 0.60), P=0.003). Ultrasound imaging also significantly reduced the risk of traumatic procedures (risk ratio 0.27 (0.11 to 0.67), P=0.005), the number of insertion attempts (mean difference −0.44 (−0.64 to −0.24), P<0.001), and the number of needle redirections (mean difference −1.00 (−1.24 to −0.75), P<0.001).

**Conclusions** Ultrasound imaging can reduce the risk of failed or traumatic lumbar punctures and epidural catheterisations, as well as the number of needle insertions and redirections.
How should resuscitation fluids be administered to a hypothermic patient?

Intravenous fluids should be warmed (38 to 42°C) to prevent further heat loss. A considerable volume of fluid is often required because of the volume loss with cold diuresis (polyuria due to hypothermia-induced vasoconstriction and diminished release of antidiuretic hormone) and vasodilatation during rewarming.
What treatment options are available for patients with IBS?

About 25% of patients with constipation-predominant IBS have slow colonic transit. Treatment with intestinal secretagogues (e.g., lubiprostone and linaclotide) or prokinetic agents (e.g., tegaserod) is effective in relieving constipation and associated IBS symptoms such as pain and bloating.
Randomized, controlled trials of the nonabsorbed antibiotic rifaximin have shown a benefit in the treatment of IBS (without constipation) and a meta-analysis has demonstrated the efficacy of probiotics, particularly for abdominal pain and bloating. Dietary measures may also be helpful. The fat content of a meal, rather than the carbohydrate content, appears to have a key role in sensations of discomfort and pain.
Q. **What is the most useful laboratory test for the diagnosis of celiac disease?**

A. Measurement of serum **IgA anti–tissue transglutaminase** antibodies is recommended for initial testing in persons who do not have concomitant IgA deficiency because of its high sensitivity (**94%**), high specificity (**97%**), **IgG** anti–tissue transglutaminase antibodies can be measured in persons with IgA deficiency. Measurement of **IgA anti-endomysial** antibodies is nearly **100% specific** for active celiac disease, but it should be used only as a **confirmatory test** in the case of **borderline** positive or possibly **false positive** results, as occurs in other autoimmune diseases, including type 1 diabetes.
Measurement of **deamidated gliadin peptide antibodies** of the **IgG class**, which has recently been introduced as an alternative test, is reported to have better sensitivity and specificity than measurement of IgG anti–tissue transglutaminase antibodies as a screening test for celiac disease in IgA-deficient patients. The sensitivity of serologic testing is markedly reduced in patients with a gluten-restricted diet; patients should therefore not restrict their diet before testing.
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<tr>
<th>Test</th>
<th>Sensitivity (Range)</th>
<th>Specificity (Range)</th>
<th>Comments</th>
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<tr>
<td>IgA anti-tTG antibodies</td>
<td>&gt;95.0 (73.9–100)</td>
<td>&gt;95.0 (77.8–100)</td>
<td>Recommended as first-level screening test</td>
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<tr>
<td>IgG anti-tTG antibodies</td>
<td>Widely variable (12.6–99.3)</td>
<td>Widely variable (86.3–100)</td>
<td>Useful in patients with IgA deficiency</td>
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<td>IgA antiendomysial antibodies</td>
<td>&gt;90.0 (82.6–100)</td>
<td>98.2 (94.7–100)</td>
<td>Useful in patients with an uncertain diagnosis</td>
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<td>IgG DGP</td>
<td>&gt;90.0 (80.1–98.6)</td>
<td>&gt;90.0 (86.0–96.9)</td>
<td>Useful in patients with IgA deficiency and young children</td>
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<tr>
<td>HLA-DQ2 or HLA-DQ8</td>
<td>91.0 (82.6–97.0)</td>
<td>54.0 (12.0–68.0)</td>
<td>High negative predictive value</td>
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* Data are from Husby et al. and Giersiepen et al. DGP denotes deamidated gliadin peptides, and tTG tissue transglutaminase.
Weight reduction

This is a general guide to the amount of calories you need to be in deficit to lose a specific amount of weight:

If you are in a deficit of 500 calories per day you will lose approximately 1 pound per week.

To lose 20 pounds in a year you will need to eat 200 calories less per day than you were eating when your weight was stable.

To lose 20 pounds in 1 month you would need to eat 2400 calories less per day (this is why very overweight people who have been eating around 4000 calories per day can lose weight quicker than lighter people, as they can reduce their intake by 2400 calories per day and still eat enough to sustain themselves).
Transfusion for GI Bleeding

NEJM January 3, 2013
Acute upper gastrointestinal bleeding is a common emergency condition associated with high morbidity and mortality. Transfusion may be lifesaving in patients with massive exsanguinating bleeding. However, in most cases hemorrhage is not so severe, and in such circumstances the safest and most effective transfusion strategy is controversial.
What were the hemoglobin thresholds for transfusion in the restrictive- versus liberal-strategy group in this study?

In the restrictive-strategy group, the hemoglobin threshold for transfusion was 7 g per deciliter, with a target range of 7 to 9 g per deciliter. In the liberal-strategy group, the hemoglobin threshold for transfusion was 9 g per deciliter, with a target range of 9 to 11 g per deciliter.
Q. What were the findings concerning the rate of further bleeding in patients in the restrictive- versus liberal-transfusion strategies in this study?

A. The rate of further bleeding was significantly lower in the restrictive-strategy group than in the liberal-strategy group: 10% (45 patients), as compared with 16% (71 patients) (P=0.01). In the subgroup of patients with cirrhosis, the risk of further bleeding was lower with the restrictive transfusion strategy than with the liberal transfusion strategy among patients with Child–Pugh class A or B and was similar in the two groups among patients with Child–Pugh class C.
Q. What do the authors postulate as a potential reason for a harmful effect of transfusion?

A. According to the authors, the harmful effect of transfusion may be related to an impairment of hemostasis. Transfusion may counteract the splanchnic vasoconstrictive response caused by hypovolemia, inducing an increase in splanchnic blood flow and pressure that may impair the formation of clots.
Peginesatide in Patients Undergoing Hemodialysis

NEJM January 24, 2013
Partial correction of anemia with erythropoiesis-stimulating agents (ESAs) is a cornerstone of therapy for patients undergoing hemodialysis, because these agents increase hemoglobin levels, which results in a reduction in blood-transfusion rates. Partial correction of anemia has also been reported to enhance quality of life.
Peginesatide is a synthetic, pegylated, peptide-based ESA that was approved by the Food and Drug Administration in March 2012 for the treatment of anemia due to chronic kidney disease in adults undergoing hemodialysis. It stimulates the erythropoietin receptor in vivo. Peginesatide is administered monthly. Peginesatide administered once a month was as effective as epoetin administered one to three times a week in maintaining hemoglobin levels.
Aspirin
Aspirin is conventionally regarded as an agent that prevents arterial thrombosis, an effect mediated through inhibition of platelet cyclooxygenase-1, resulting in decreased synthesis of thromboxane A2.

In high-risk patients, aspirin reduces by one quarter the frequency of arterial thrombosis.
In 1977, aspirin (at a dose of 600 mg twice daily) was shown to reduce the risk of venous thrombosis when it was given to patients after they had undergone hip arthroplasty. Thirty-five years later, guidelines include aspirin as one option for preventing venous thromboembolism after orthopedic surgery. However, many experts regard aspirin as inferior therapy for this indication, preferring treatment with conventional anticoagulants (heparin, fondaparinux, or warfarin) or the new oral agents (dabigatran or rivaroxaban).
In part, this approach reflects scientific considerations: anticoagulants are especially active in the low-flow, low-shear venous vasculature where fibrin-rich clots form — in contrast to the high-flow, high-shear arterial circulation where platelet adhesion and aggregation are more important.
Two recent clinical trials, the Warfarin and Aspirin (WARFASA) study and the Aspirin to Prevent Recurrent Venous Thromboembolism (ASPIRE) study, evaluated aspirin as compared with placebo in patients with unprovoked venous thromboembolism who had completed initial treatment with heparin followed by warfarin for a minimum of 6 weeks. The WARFASA study, in which 402 patients were included in the analyses, showed a 42% reduction in the rate of recurrence of venous thromboembolism with aspirin as compared with placebo (rate of recurrence, 6.6% vs. 11.2% per year; hazard ratio with aspirin, 0.58; 95% confidence interval [CI], 0.36 to 0.93; P = 0.02);
How should these studies influence practice?

Acute unprovoked VTE treated with anticoagulation for at least 3 months.

For patients who then wish to stop anticoagulation, a switch to aspirin at a dose of 100 mg daily will reduce by one third the risk of recurrent venous thromboembolism, as well as of arterial cardiovascular events, and may also attenuate the early burst of thrombosis recurrence after cessation of oral anticoagulation.
Could aspirin represent a reasonable intermediate option between the extremes of indefinite anticoagulation and no ongoing anticoagulation?

Indeed, a dual benefit of aspirin in both arterial and venous circulations might be expected: Atherosclerosis is a risk factor for unprovoked venous thromboembolism, and patients with idiopathic venous thromboembolism are at increased risk for subsequent arterial cardiovascular events.
Aspirin is **inexpensive**, does **not** require **monitoring** (in contrast to warfarin), and **does not accumulate in patients with renal** insufficiency (in contrast to dabigatran and rivaroxaban); in addition, if major bleeding occurs or the patient requires urgent surgery, the antiplatelet effects of aspirin can be reversed with transfusion of platelets.

**Among patients with unprovoked venous thromboembolism who have completed initial anticoagulation**, aspirin would seem to be a reasonable option for long-term **dual prevention** of recurrent venous thromboembolism and arterial cardiovascular events.
β blockers for heart failure: which works best?
Chatterjee and colleagues’ systematic review and network meta-analysis considered the comparative efficacy of β blockers in patients with heart failure with reduced ejection fraction. The analysis included 21 randomised trials (total of 23 122 patients) that compared β blockers with other β blockers or other treatments. Seven β blockers were investigated: carvedilol, metoprolol (tartrate and succinate), bisoprolol, bucindolol, nebivolol, and atenolol. The long term use of certain β blockers in patients with heart failure reduces hospital admissions and improves symptoms, quality of life, and survival. The authors concluded that β blockers in patients with heart failure seemed to exhibit a class effect rather than an individual drug effect.
ASthma

Editorial

NEJM September 3, 2012
Tiotropium for Asthma — Promise and Caution

In patients with poorly controlled asthma despite treatment with inhaled glucocorticoids and LABAs, adding tiotropium significantly reduced the risk of episodes of the worsening of asthma and asthma exacerbations requiring treatment with systemic glucocorticoids and provided sustained bronchodilation.