No Exit: long-term Meropenem usage in OPAT

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Primary infectious issue

- *Pseudomonas aeruginosa* infection of Fenestrated EVAR since 2016 with evolving resistance, not fit for further surgery, currently on OPAT Meropenem lifelong

Past medical history 2016

- 72 year old man
- Abdominal aortic aneurysm
- PCI June 2016 (pre-EVAR, non-obstructive disease)
- Smoker
- Rheumatoid arthritis-not on active treatment
- HTN
- Hypercholesterolaemia
- Right knee replacement 2013
- Left hip replacement 2012

2016

- Fenestrated EVAR September 2016 for AAA
- Admitted November 2016 with a 1 month history of fevers, and night sweats
- Initial blood cultures x1 positive for *Pseudomonas aeruginosa*-Tazocin intermediate. Otherwise sensitive to anti-pseudomonal antibiotics
- No convincing source identified, WCC scan negative circa 1 month after antibiotics started
  - (presumed false negative due to prolonged antibiotic therapy)

2016-2017

- Treated as suspected EVAR infection with 3/12 high dose 750mg BD Ciprofloxacin and Metronidazole
- Metronidazole stopped, ciprofloxacin continued at 750mg BD PO dose until June 2017 (8 months)
- Ciprofloxacin stepped down to 250mg BD PO in June 2017 due to tendonitis
- Elective admission for endovascular left iliac limb extension & embolisation of left internal iliac artery after endoleak of EVAR found on routine scan July 2017

February-June 2019

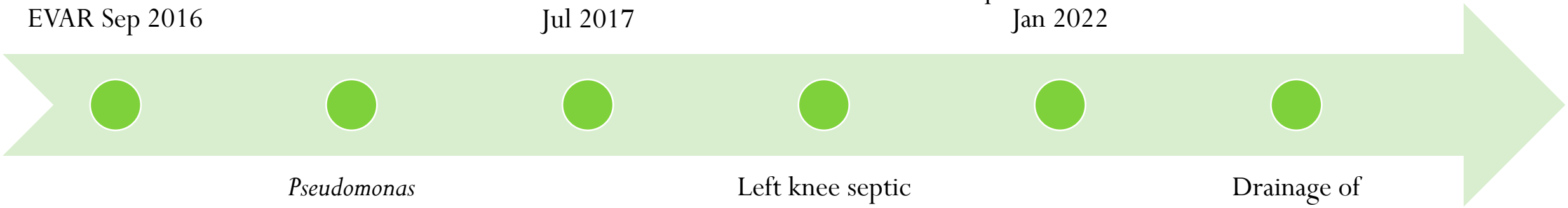
- Left knee septic arthritis February 2019
- Knee aspirate grew 2 distinct *Pseudomonas* subpopulations
  - 1 Ciprofloxacin R, Tazocin R, Aztreonam R, Ceftazadime S, Meropenem S, Gentamicin S
  - 1 pansensitive
- PET scan revealed high uptake along aortic graft March 2019, prosthetic right knee and left hip not infected
- Prolonged admission with Ceftazidime treatment escalated to Meropenem due to static clinical picture and CRP
- Ultimately discharged on Meropenem 2g TDS IV via S-OPAT to complete 12/52
- Stepped down to PO Ciprofloxacin 500mg BD for lifelong suppression
  - aware of the fact that this would be unlikely to work for all isolates

2022

- Surveillance CT angiograms every 3/12 until January 2022
- January 2022 showed
  - *increase in lobular soft tissue surrounding the abdominal aortic graft, now extending into the left psoas and showing progressive extension into the vertebral bodies of L2, L3 and L4. Findings favour low-grade chronic infection*
  - Aspirate of showed 3 *Pseudomonas* subpopulations all Ceftazidime S
- Discharged on IV Ceftazidime via S-OPAT for 8/52 (of planned 12/52)
- CRP was not settling (stuck at 50)
- CT aorta showed thick-walled collection peri-aortic area May 2022
- Readmitted for drainage of periaortic collection off antibiotics revealed 4 different *Pseudomonas* subpopulations of various sensitivities May 2022
  - All retain sensitivity to Meropenem
- Then readmitted and changed to IV Meropenem ongoing since May 2022
  - Initially 1g TDS then 2g BD IV

Currently

- Day 120+ of Meropenem via S-OPAT
- CRP suppressed at 16
- No feasible step-down option
- Despite co-morbidities and age he is still farming



***Pseudomonas* sensitivity pattern**	Tazocin Intermediate	-	1 pansensitive population, 1 R to Ciprofloxacin, Tazocin and Aztreonam	3 subpopulations, all Tazocin and Ceftazidime S, Ciprofloxacin R, 1 Gentamicin R	4 subpopulations, all retain Meropenem sensitivity
IV antibiotics induction	IV Ceftazidime	-	IV Ceftazidime followed by IV Meropenem	IV Ceftazidime x 8/52	IV Meropenem 1g TDS followed by 2g BD
Oral stepdown	Ciprofloxacin 750mg BD	Ciprofloxacin 250mg BD	Ciprofloxacin 500mg BD	-	-
OPAT	C-OPAT	C-OPAT	S-OPAT followed by C-OPAT	S-OPAT	S-OPAT

Discussion

- What is your experience of palliative OPAT?
- What is your experience of MDR-GNB treatment on OPAT?
  - In particular anti-pseudomonal carbapenems?
- What is your experience of AMR emerging on OPAT or C-OPAT?

Updated good practice recommendations for outpatient parenteral antimicrobial therapy (OPAT) in adults and children in the UK

Ann L. N. Chapman[1]*, Sanjay Patel[2], Carolyne Horner[3], Helen Green[2], Achyut Guleri[4], Sara Hedderwick[5], Susan Snape[6], Julie Statham[7], Elizabeth Wilson[8], Mark Gilchrist[9] and R. Andrew Seaton[10]

Table 2. Proposed treatment aims and OPAT service outcomes

	Description
Treatment aim	
cure	To complete an agreed OPAT duration of therapy on either intravenous and/or complicated oral antimicrobials[a] with **no** requirement for long-term antimicrobial therapy.
improvement	To complete an agreed OPAT duration of therapy on either intravenous and/or complicated oral antimicrobials (a) as part of an agreed surgical infection management plan with further surgery planned or (b) where there is a requirement for subsequent long-term or an extended course of oral suppressive antimicrobial therapy, or (c) where potentially infective prosthetic material is still *in situ*.
palliation	To undertake a course of OPAT on either intravenous and/or complicated oral antimicrobials where there are agreed ceilings of care due to comorbidities, with death being the likely outcome.

Palliative outpatient parenteral antibiotic therapy: a review of 5 years of patient data

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Objectives: A review of patients requiring lifelong antibiotics to control, rather than cure, infection was performed ['palliative outpatient parenteral antibiotic therapy (OPAT)']. This was to evaluate emerging themes and complications. The aim was to aid in the management of such patients.

Methods: A retrospective review of the OPAT database over 5 years (2013–17) was performed. Of the 1438 patients, 9 were deemed to have received palliative OPAT.

Results: The palliative cohort represented 0.6% of the total number of patients on OPAT and 8.6% of the bed days saved. Patients fell into two main groups: those with multiple comorbidities that precluded surgical management and those with a terminal condition. Both groups received IV antibiotics with no clear endpoint. The themes to emerge were: patients often had multiple comorbidities with a high operative risk to control the source of infection; a trial of no or oral antibiotics led to resurgence of the infection; vascular patients appeared to tolerate long-term antibiotics well; and conversely, antibiotic side effects were a significant issue in others. Patients with incurable cancer and a coincident infection can be given additional quality of life with the judicious use of appropriate therapy.

Conclusions: There are significant issues surrounding antimicrobial stewardship in the palliative OPAT group that should be considered. Excellent communication is required to deal with these often very complicated patients. There are considerable gains to be made both for patients and the number of bed days saved. The small number of patients accounted for a disproportionate number of bed days saved.

Outpatient parenteral antimicrobial therapy (OPAT) for aortic vascular graft infection; a five-year retrospective evaluation

Niamh Allen [1], Mohamed Adam [2], Grace O'Regan [2], Aoife Seery [2], Cora McNally [2 3], Samuel McConkey [2 3], Aisling Brown [# 4], Eoghan de Barra [# 2 3]

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Abstract

Objectives: An estimated 1% of endovascular aneurysm repair (EVAR) devices become infected, carrying a high mortality rate. Surgical explantation is recommended and prognosis is guarded. This retrospective cohort analysis focuses on the role of outpatient parenteral antimicrobial therapy (OPAT) in the management of aortic vascular graft infections following EVAR.

Methods: Patients who received OPAT for aortic graft infections (AGI) following EVAR from 2014 to 2018 inclusive were identified using the OPAT database. Clinical, microbiological and radiological data were collected. Survivors were followed up for a median of 36 months (range 25-60) after first presentation with infection. Outcomes were assessed.

Results: Eleven cases with 20 OPAT episodes were identified: 10/11 male, median age 76 (IQR 71-81). Median time to presentation was 7 months (range 0-81 months) after EVAR. OPAT lead to a 55% reduction in length of hospital stay. One patient had graft explantation; four others had temporising measures. Eight of 11 were alive a median of 36 months after presentation with infection, having had a median of 2 re-treatments on OPAT (range 1-3). Seven of the eight survivors were on continuous suppressive oral antimicrobials; three were also intermittently on intravenous antibiotics for flares of infection. Patient/ infection outcomes were cure (1/11), improved (7/11), failure (3/11).

Conclusion: AGI following EVAR usually presents in the first year after graft deployment. OPAT has an important peri-operative role in patients suitable for curative surgery. OPAT followed by oral suppressive antimicrobial therapy can be a feasible long-term treatment for non-curative management of AGI. Survival in our cohort was longer than expected, and OPAT was feasible despite the complexity of these infections. OPAT can avoid multiple and lengthy hospital admissions and maximise time at home and quality of life in this cohort with life-limiting infection.

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Case Reports and Series

Evolving antimicrobial resistance in a patient receiving palliative OPAT for a vascular graft infection: A case report

James W.D. Irvine [a], Ann L.N. Chapman [b], Carlos Varon Lopez [b], Kerry Reid [b], Michelle Spittal [b], Steven McCormick [b], Stephanie Dundas [b]

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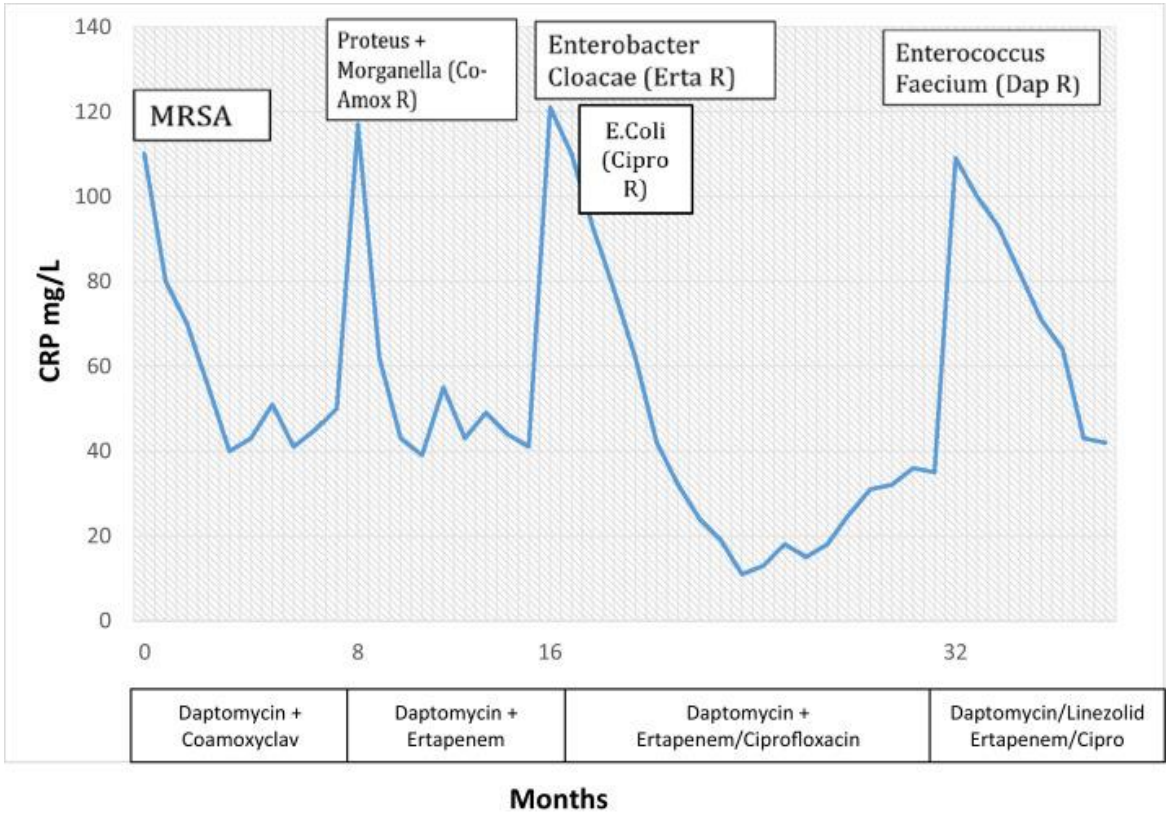
https://doi.org/10.1016/j.clinpr.2019.100002



JOURNAL ARTICLE

Outpatient parenteral antimicrobial therapy (OPAT) in the UK: findings from the BSAC National Outcomes Registry (2015–19) FREE

Mark Gilchrist ✉, David Barr, Felicity Drummond, Alison Muir, John Williams, James Scriven, Susan Snape, Carolyn Hemsley, Chris O Durojaiye, Sanjay Patel ... Show more

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IV antimicrobials used, adults, all OPAT services and years combined

Class/antimicrobial	Total patient episodes	Total OPAT treatment (days)	Mean OPAT duration (days)
Antibacterial			
Ceftriaxone	12 424	157 873	12.7
Teicoplanin	4510	101 194	22.4
Ertapenem	3008	57 917	19.3
Piperacillin/tazobactam	1618	22 461	13.9
Ceftazidime	1308	20 978	16
Daptomycin	1125	27 366	24.3
Meropenem	1016	21 112	20.8
Flucloxacillin	651	13 449	20.7
Linezolid	250	5436	21.7
Tobramycin	231	2671	11.6
Amikacin	173	4449	25.7
Dalbavancin	173	2667	15.4
Gentamicin	168	1323	7.9
Tigecycline	145	5279	36.4
Colistin	98	1438	14.7
Vancomycin	62	1515	24.4
Aztreonam	57	807	14.2
Benzylpenicillin	46	966	21
Temocillin	44	426	9.7
Cefepime	35	777	22.2
Ceftolozane/tazobactam	19	499	26.3

Where do we go from here?

- Discussed with vascular here and in UK centres
  - Surgery would have high immediate post-operative mortality

- Antibiotic programme
  - Continuous Meropenem via S-OPAT?-the patient tolerates it very well and has an excellent quality of life
  - Pulse antibiotics 6 weeks on, 6 weeks off with enhanced imaging?-similar or greater line maintenance, unclear if more or less likely to cause resistance

- Phage therapy
  - One previous case of cure of *Pseudomonas* graft infection with adjunctive phage therapy (Chan et al 2018, *Evolution, Medicine and Public Health*)

Thank you

"Don't forget to take a handful of our complimentary antibiotics on your way out."