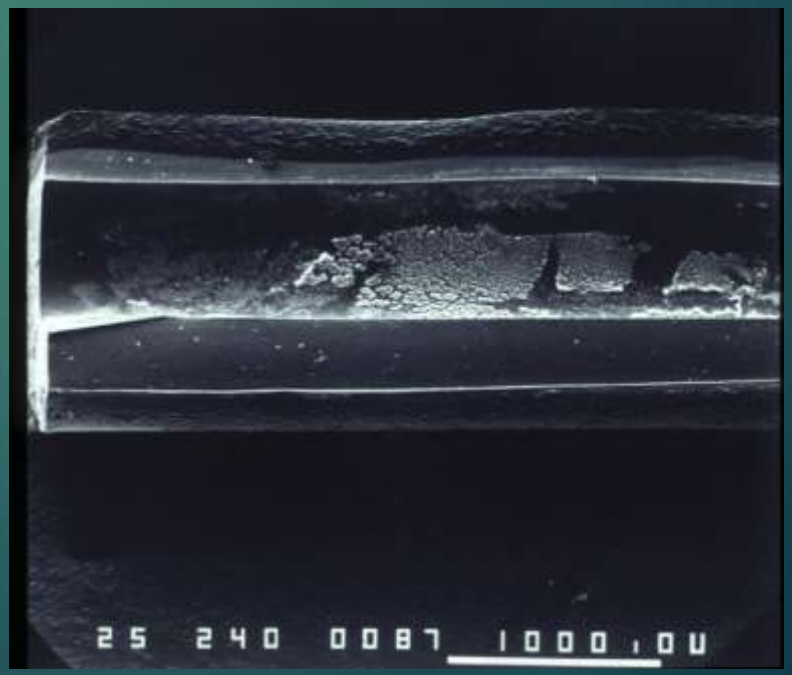
‘Shunt infections can be best managed medically without removal’

CONOR MALLUCCI

ALDER HEY

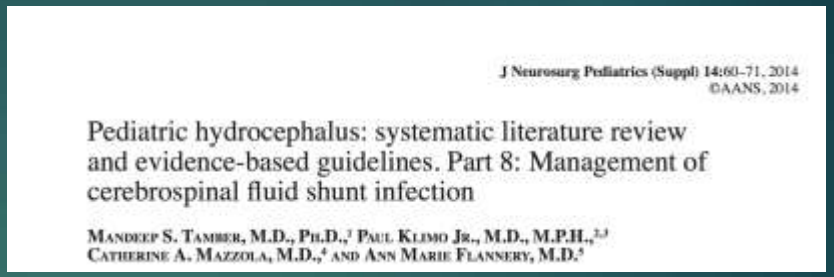
LIVERPOOL



The issues

- Shunt infection management has not changed for >20 years
- Cost to Patient and NHS
- 'Standard therapy' variable -
  - shunt removal essentially 'commits' to 2 weeks of inpatient care and at least 2 more operations
- No 'new' treatments under trial
- Why are we not making any progress?

The literature



J Neurosurg Pediatrics (Suppl) 14:60–71, 2014
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Pediatric hydrocephalus: systematic literature review and evidence-based guidelines. Part 8: Management of cerebrospinal fluid shunt infection

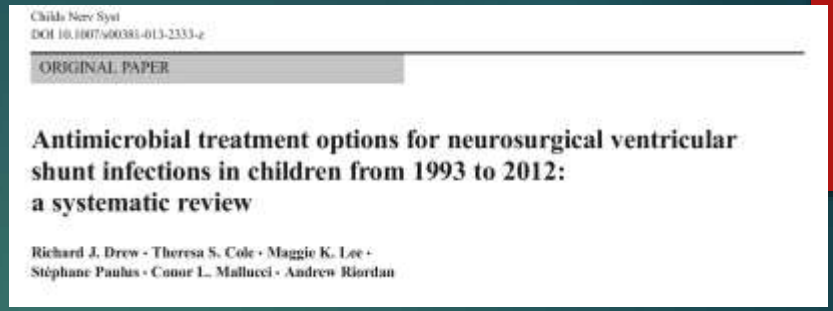
Mandeep S. Tamber, M.D., Ph.D.,[1] Paul Klimo Jr., M.D., M.P.H.,[2,3] Catherine A. Mazzola, M.D.,[4] and Ann Marie Flannery, M.D.[5]

Recommendation: Supplementation of antibiotic treatment with partial (externalization) or with complete shunt hardware removal is an option in the management of CSF shunt infection. Strength of Recommendation: Level II, moderate degree of clinical certainty.

Recommendation: There is insufficient evidence to recommend either shunt externalization or complete shunt removal as a preferred surgical strategy for the management of CSF shunt infection. Therefore, clinical judgment is required. Strength of Recommendation: Level III, unclear degree of clinical certainty.

Recommendation: There is insufficient evidence to recommend the combination of intrathecal and systemic antibiotics for patients with CSF shunt infection in whom the infected shunt hardware cannot be fully removed or must be removed and immediately replaced, or when the CSF shunt infection is caused by specific organisms. The potential neurotoxicity of intrathecal antibiotic therapy may limit its routine use. Strength of Recommendation: Level III, unclear degree of clinical certainty.

The literature


Childs Nerv Syst
DOI 10.1007/s00381-013-2333-z

ORIGINAL PAPER

Antimicrobial treatment options for neurosurgical ventricular shunt infections in children from 1993 to 2012: a systematic review

Richard J. Drew · Theresa S. Cole · Maggie K. Lee · Stéphane Paulus · Conor L. Mallucci · Andrew Riordan

This systematic review has shown that there is very limited data for specific antimicrobial treatment regimes for children presenting with VP shunt infection.

There have not been any randomised controlled trials examining the additional benefit, if any of giving intraventricular therapy in addition or in place of intrave- nous treatment.

Of concern is the very limited information regarding the rate of relapse after treatment in cases which have the shunts re-implanted

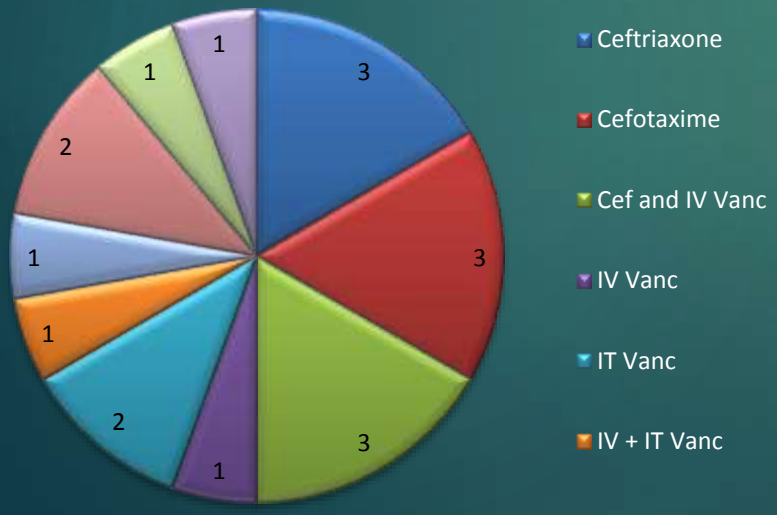
As second-line agents, linezolid and ciprofloxacin also appear to be effective in two separate case series studies on six and seven children, respectively

Mx of Shunt infection questionnaire 17 units replied

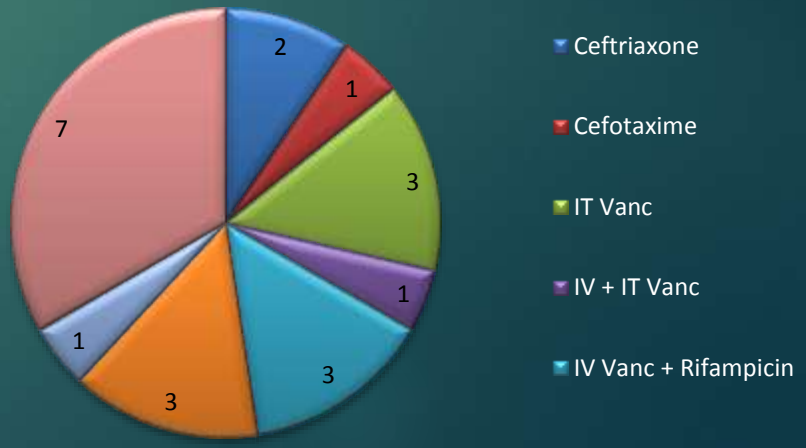
Management after +ve shunt tap

Choice of EVD (all remove shunt and insert EVD)

Empirical Antibiotic Choice

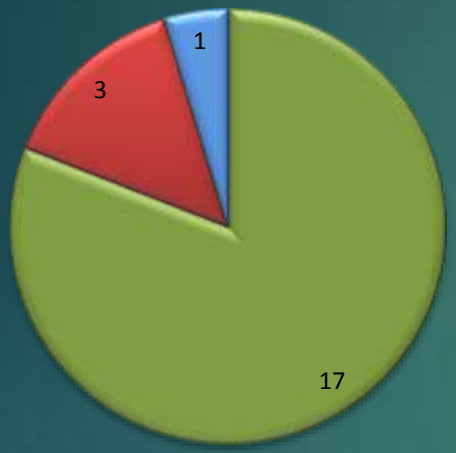


Focused Antibiotic Choice, (after culture)

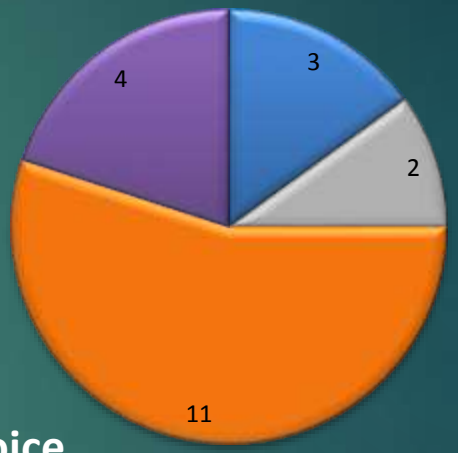


Suspected Shunt Infection

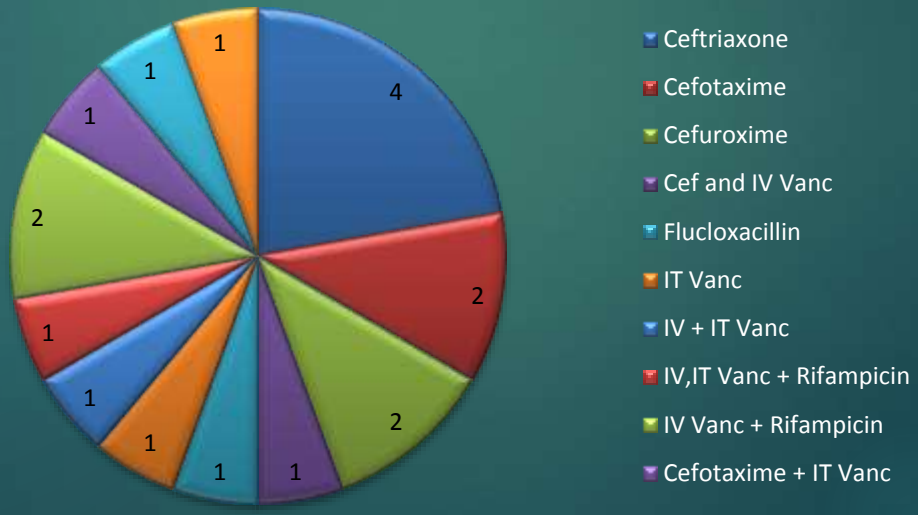
Remove shunt



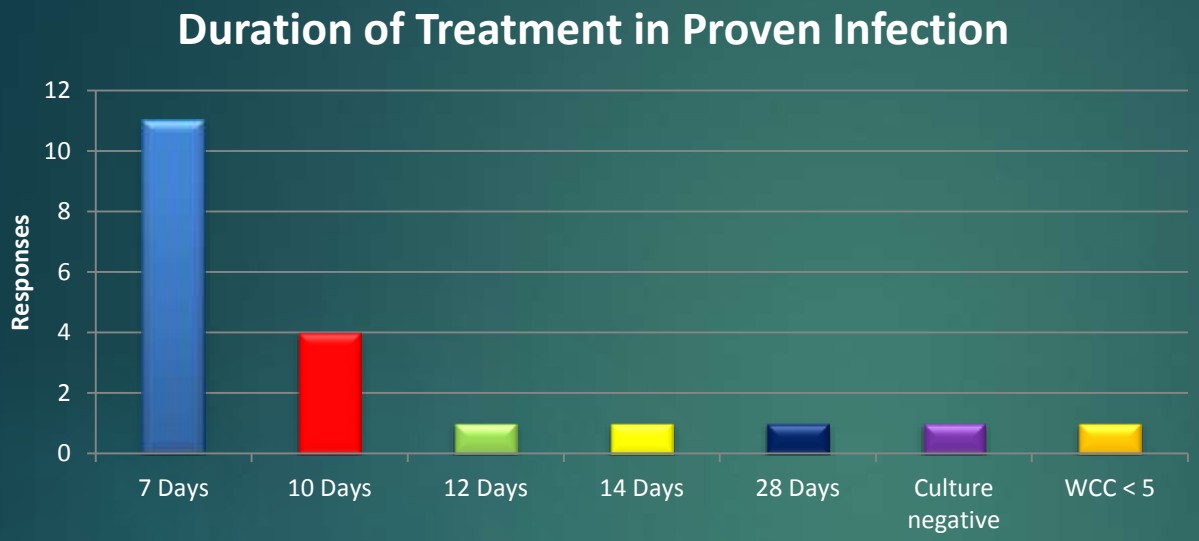
Choice of EVD

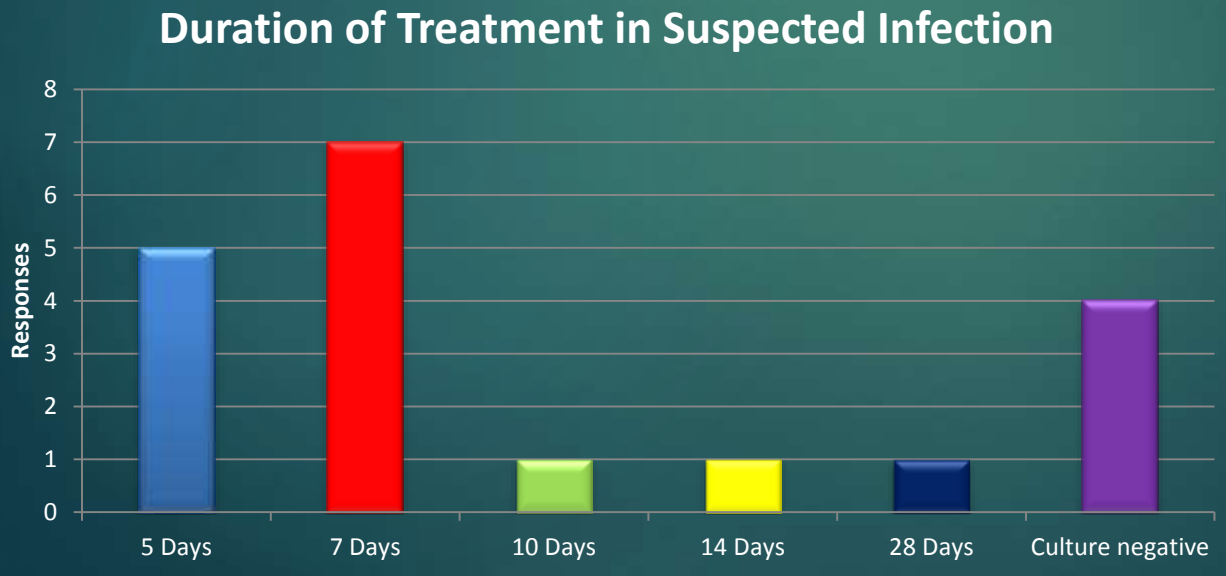


Empirical Antibiotic Choice



Minimum Duration of Antibiotics





STANDARD THERAPY?

- IV VANC +/- IT VANC/RIFAMPICIN +OTHER
- EVD
- CSF EVERY 4 DAYS
- RE-IMPLANT SHUNT AFTER 7 DAYS PLUS NO GROWTH 48 HOURS

- IS THIS NECESSARY FOR ALL SHUNTS????
- CAN WE SAVE SOME???

The Dut[illegible]per

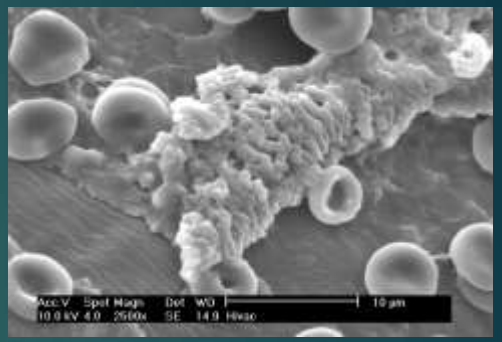

VPD/VAD with known organism
CNS or P. acnes (rifampicine sensitive)
shunt stays in situ
Vanco i.t. (CNS) + rifampicine or penicilline i.v. (P. acnes) + rifampicine, for 10 days from 1e neg culture
CNS or P. acnes (rifampicine resistent)
shunt removal and insertion EVD
Vanco i.t. (CNS) or penicilline i.v. (P. acnes), for 10 days, internalization 7 days after 1st negative culture
S. pneumoniae
H. influenzae
N. menigitidis
shunt stays in situ
Anttbioticics conform non-shunt infecties
S. aureus
shunt removal and insertion EVD
Flucloxacilline i.v., for 14 days, internalization 10 days after 1st negative culture
Entereococcus
shunt removal and insertion EVD
Amoxicilline i.v. or vancomycine i.v., for 14 days, internalization 10 days after 1st negative culture
gram negative rods
shunt removal and insertion EVD
3e generation cefalosporine i.v., for 21 days, internalization 10 days after 1st negative culture
Yeasts
shunt removal and insertion EVD
fluconazol i.v., for 6 weeks, internalization 10 days after 1st negative culture

WHAT CAN WE DO?

Antimicrobial Agents and Chemotherapy

Action of Linezolid or Vancomycin on Biofilms in Ventriculoperitoneal Shunts *In Vitro*

Roger Bayston, Gautham Ullas and Waheed Ashraf
Antimicrob. Agents Chemother. 2012, 56(6):2842. DOI: 10.1128/AAC.06326-11.
Published Ahead of Print 19 March 2012.



. It is hoped that these *in vitro* results will stimulate further clinical trials with linezolid, avoiding surgical shunt removal.

European Journal of Neurology 2005, **12:** 536–542

Clinical experience with linezolid for the treatment of central nervous system infections

T. A. Rupprecht and H.-W. Pfister
Department of Neurology, Ludwig-Maximilian University, Munich, Germany

Linezolid appears to be a safe alternative to vancomycin for therapy-resistant CNS infections because of its good CSF penetration and few sideeffects

J Neurosurg Pediatrics 5:443–448, 2010

Linezolid treatment of shunt-related cerebrospinal fluid infections in children

Clinical article

Adem Yilmaz, M.D.,[1] Nazan Dalgic, M.D.,[2] Murat Müslümanoğlu, M.D.,[1] Mesut Sancar, M.D.,[3] Ibrahim Çolak, M.D.,[1] and Yunus Aydin, M.D.[1]

- 6 patients treated with Linezolid 14-21 days
  - For vancomycin resistant organisms
- 4 had EVD BUT 2 did not
- Mean time to clearance was 4 days

Eur J Clin Microbiol Infect Dis (2005) 24: 603–606
DOI 10.1007/s10096-005-0015-9

CONCISE ARTICLE

P. Castro · A. Soriano · C. Escrich · G. Villalba · M. Sarasa · J. Mensa

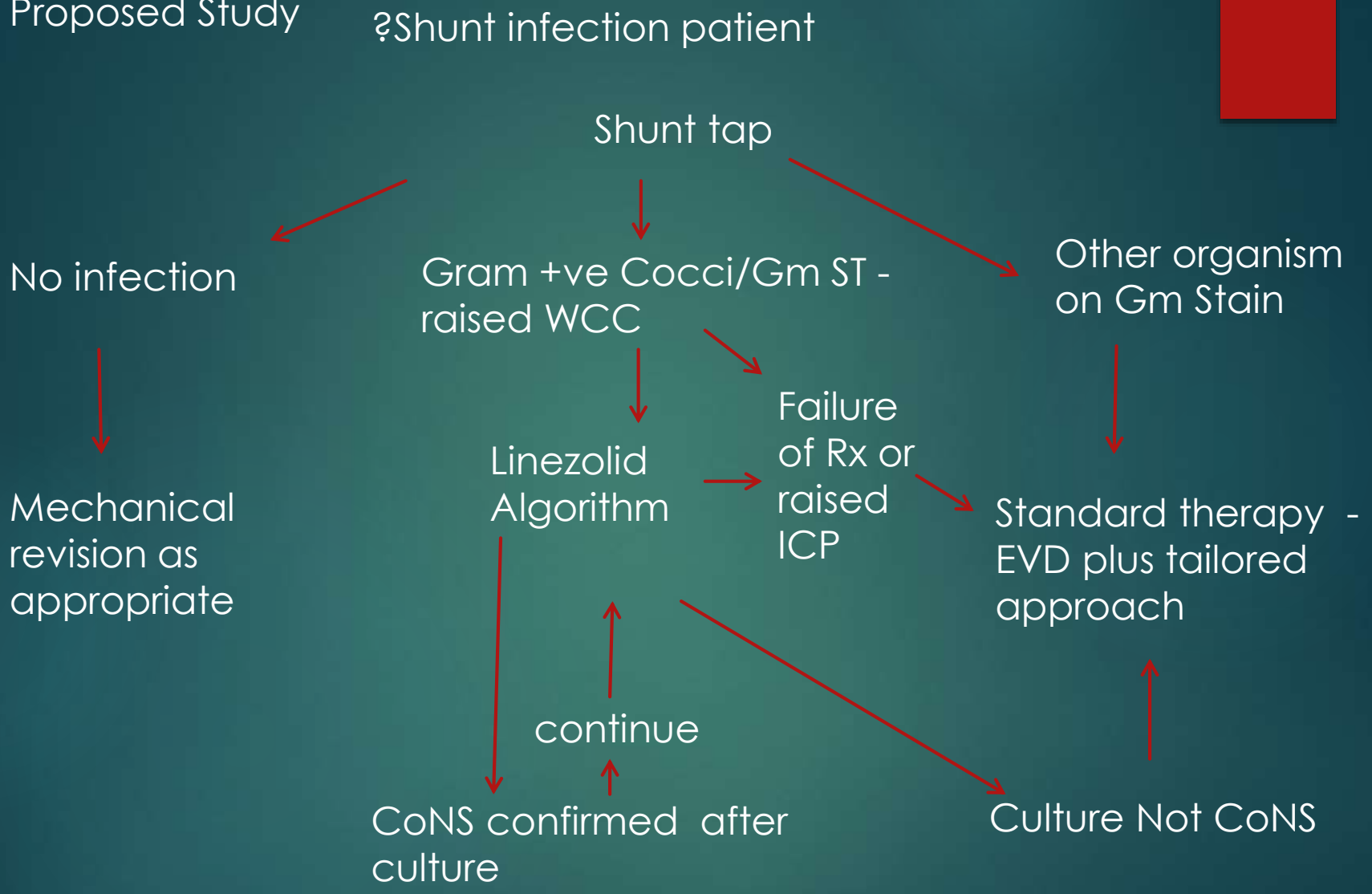
Linezolid treatment of ventriculoperitoneal shunt infection without implant removal

One successful case report after vancomycin failure for staph epidermidis infection

Optimal management of shunt-related infection (BASICS II)

- LINEZOLID STUDY
- Study design?: multi-centre, stepped wedge cluster or randomized trial after a feasibility study
- Primary endpoints
  - ? time to clear CSF
  - ? time to shunt re-insertion
  - SHUNTS SAVED WITH LINEZOLID
- Integrated care pathway of pre-, intra- and post-operative measures for management of shunt-related infections (Delphi consensus process)
- A Quality Improvement package to support effective implementation of the integrated care pathway into clinical practice

Proposed Study



LINEZOLID ALGORITHM

TREATMENT

- IV LINEZOLID START
- CONVERT TO ORAL FOR 28 DAYS
- SHUNT NOT EXPLANTED

MONITORING

- CSF TAP AT 4 DAYS
- CRP/FBC WEEKLY
- CONVERT TO EVD AT ANY POINT IF UNWELL
- FINAL SHUNT TAP 6 WEEKS AFTER END OF TREATMENT

OUTCOMES

- PROPORTION OF SHUNTS SAVED WITH MAIN ALGORITHM
- HEALTH ECONOMICS
- HOSPITAL IN-PATIENT DAYS
- RE-INFECTION RATES OF VP SHUNT

questions

- Is it safe not to explant shunt?
  - Feasibility phase initially trialing EVD and linezolid ? How many patients
  - Is there a question re; ideal therapy – IT vs. IV only
  - Can we still trial Linezolid but with EVD and shunt removal vs. standard therapy?
  - DESIGN OF STUDY??
  - WE NEED RAPID DIAGNOSTICS TO IMPROVE TO FACILITATE TARGETED THERAPY

IMPROVING DIAGNSOSTICS IN SHUNT INFECTION

- NEXT GENERATIONS SEQUENCING
  - COLLABORATION WITH GOSH
- TRANSCRIPTOMICS
- PROTEOMICS

'We hypothesize that detection of bacterial pathogen in CSF from patients with neurosurgical CSF infection will be increased through use of **next generation sequencing**

and that patterns of human host mediators, including transcriptomic, proteomic and cytokine concentration patterns (in blood and/or CSF) can help discriminate between microbiologically confirmed CSF infection and uninfected samples.'

Roseri Group structure

- Steering groups on a per-project basis
- Input from SBNS subspecialty groups
  - Paediatric Neurosurgery (Conor Mallucci)
  - CSF SBNS subgroup
- Input from trainees
  - BNTRC
- Input from methodologists / statisticians
  - Liverpool Clinical Trials Research Centre
  - Cambridge Clinical Trials Unit – Surgery theme
  - MRC Biostatistics Unit
- Input from Microbiology / Infectious Diseases
- Input from SBNS Council (National Neurosurgical Audit Programme)
  - Peter Hutchinson is Council member
- Input from SBNS Academic Committee and RCS Clinical Research Initiative

CONCLUSIONS

- We are not covering ourselves in glory in terms of the Mx of shunt infection
- No progress in decades
- NOT ALL INFECTIONS REQUIRE SHUNT REMOVAL
- A WAY FORWARD THROUGH NATIONAL PROSPECTIVE STUDIES AND NEW AGENTS
- **Shunt infections ~~can~~ SHOULD be best managed medically without removal'**

The average neurosurgeon, despite the sometimes swaggering exterior is very much capable of feelings of love, affection and intimacy.

Unfortunately, these feelings do not involve anybody else.