

Infection issues in neurosurgery: shunting and external drainage

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Generally the infection rate in neurosurgery is low. The two areas where this can be the exception are CSF shunting and external ventricular drainage.

I will deal with these separately

Infections in CSF shunting: causes, diagnosis, treatment and prevention

Incidence of infection in shunts

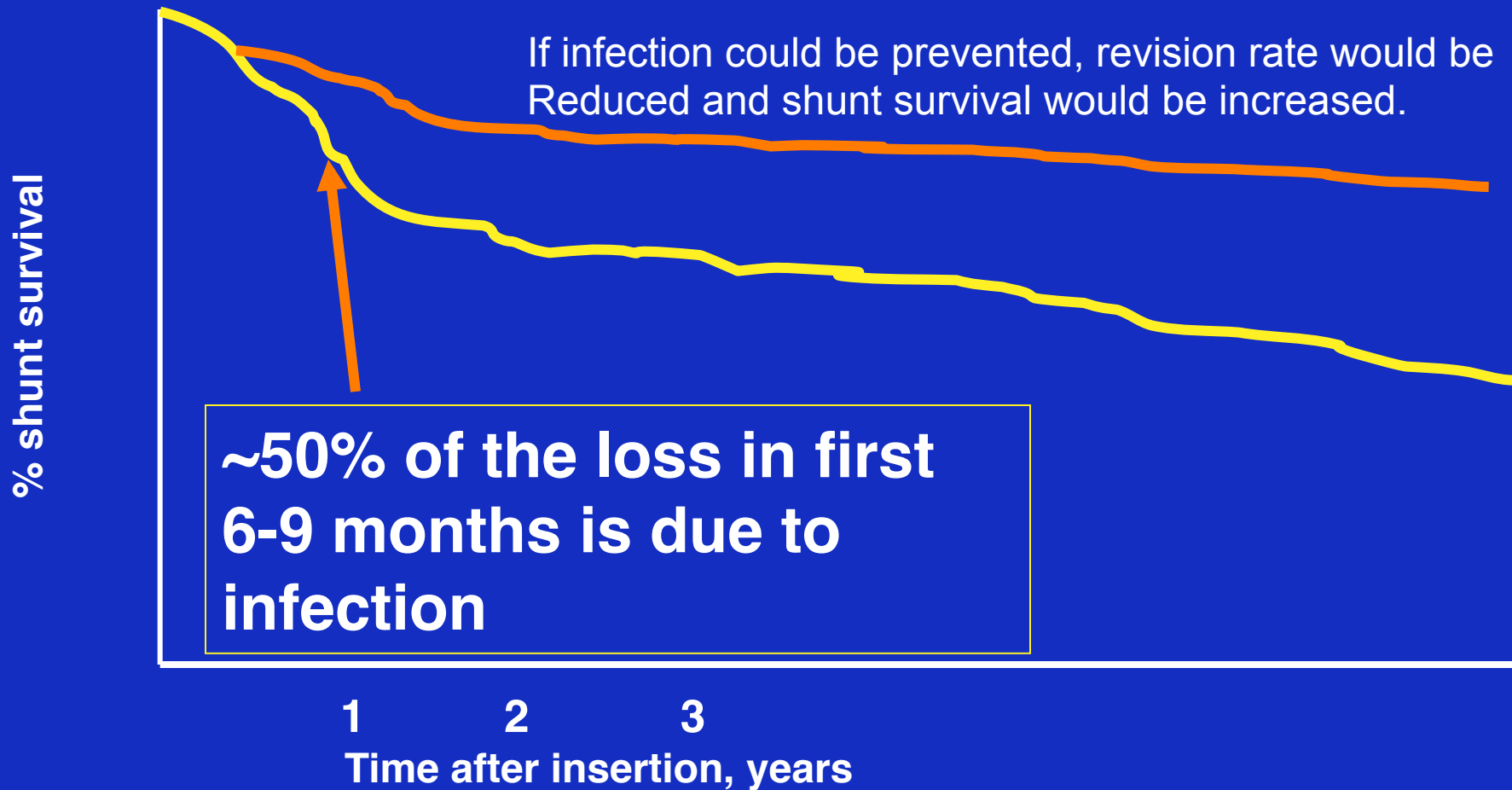
“Around 10%” (eg Duhaime 2006, Hanlo et al 2003) but this figure is an average of data from several sources. Rates in many units are now lower than this.

In infants <6mo when shunted, it is much higher – up to 20% (Renier et al 1984; Pople et al 1992, Key et al 1995)

Kulkarni et al 2001: 4-5 times as likely in this group as in older children

The reason for this is multifactorial, but Pople et al 1992 found a much higher bacterial number on the skin at the surgical site in this age group, with more shunt – pathogenic strains. This is probably related to extended hospital stay preoperatively. Poor skin cover is also an issue.

Shunt survival



Medical consequences of shunt infection

- Ventriculitis
- Secondary infection from EVD
- Frequent relapse and need for re-operation – up to 26%

(Kestle et al J Neurosurg 105, 177-181, 2006)

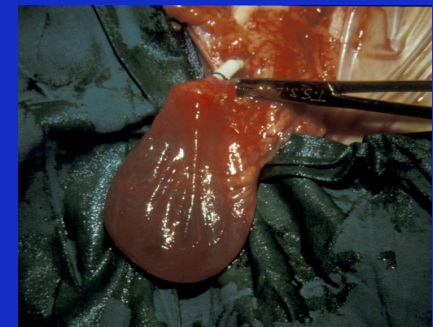
- Loculated ventricles

(Jamjoom et al Acta Neurochir 138, 714-719, 1996)
after S epidermidis)



- Peritonitis
- Peritoneal cysts, abscesses
- Loss of absorptive capacity

Often presents as distal obstruction (Bayston & Spitz, Zeit Kinderchir 22, 419-424, 1977)



Infective peritoneal cystic obstruction

- **Almost all shunt infections begin at operation, even though clinical presentation can be much later.**
- **Others are secondary to, eg, gut perforation, skin erosion**



Poor skin cover, poor valve siting or use of too big a valve in babies causes wound dehiscence.

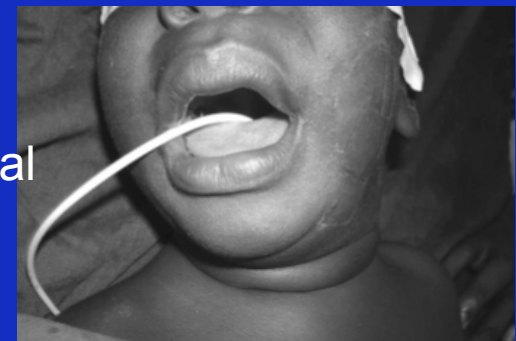
Ghritlaharey et al, Ped Surg Internat 23:575-80, 2007 (10 cases)



We have seen two similar cases in UK, where parents brought the child to A&E with "a worm in his bottom"

Per-oral extrusion! Odebode, B J Neurosurg 21:235-6, 2008

This is very unusual and we have not seen a case



Causative bacteria

- **Mainly staphylococci**
 Mainly CoNS* (S epidermidis)
 Some S aureus
- **Propionibacterium acnes**
- **Occasional gram negatives eg E coli**

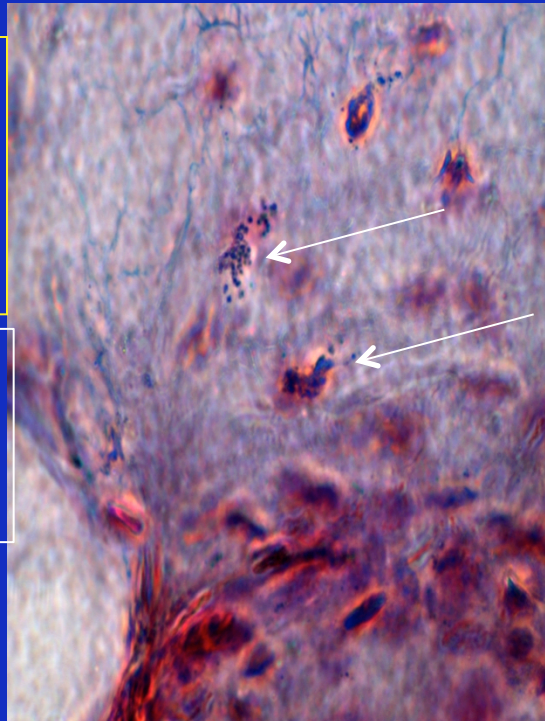
*CoNS = Coagulase negative staphylococci, ie not S aureus

Source of bacteria in shunt infection: mainly the patient's skin

Skin prep “sterilises” only the surface of the skin; most bacteria live in follicles, sweat glands etc

We investigated this using full thickness skin biopsy after skin prep

Double prep,
alcoholic
povidone
iodine



Culture of biopsy: *S epidermidis* X 2 and
P acnes

50% of biopsies culture – positive
100% PCR-Positive

Saba, Scammell & Bayston 2006
Ismail, Glen, Scammell & Bayston 2010

The same result was
obtained with alcoholic
chlorhexidine

Skin bacteria in the incision

After skin preparation, the patient's skin re-colonises within 15-25 min



Microbiological “map” showing bacteria in the incision at the time of shunt placement

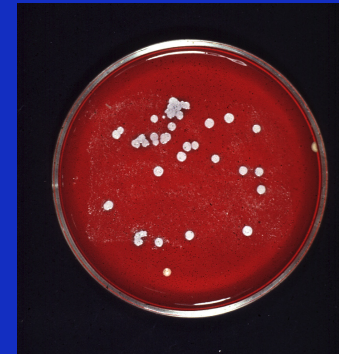
Bacteria from the skin surface (from under drapes) and from cut skin edges then enter the incision

Bayston & Lari 1974;
Raahave 1974

Bacteria in the operation field

(Bayston & Lari Dev Med Child Neurol 16, 16-22, 1974)

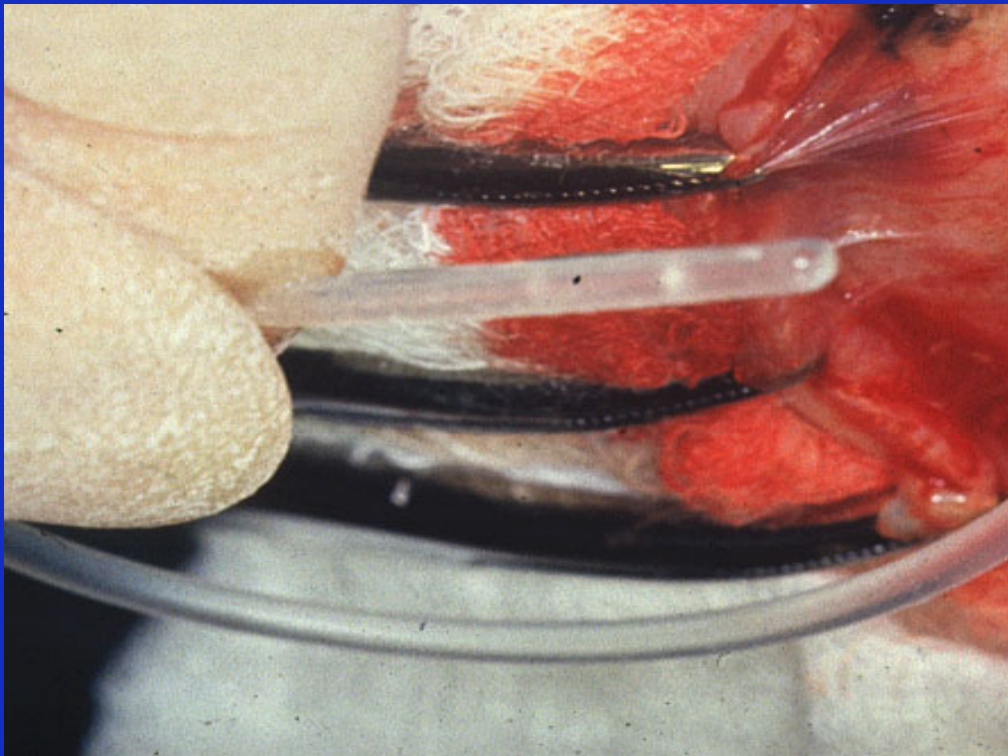
- Consecutive shunt operations 100
- Bacteria in **incision** 58%
- Bacteria from **patient** 32%



- Shunt **infections** 11
- **Due to bacteria from patient** 9

(Two untypable and source undetermined,
but not from air, environment etc)

During insertion, bacteria contaminate the shunt, instruments, gloves etc, and are pushed into the ventricular system and down the catheter track. They also enter the inside of the catheters during connection and through eye-holes.

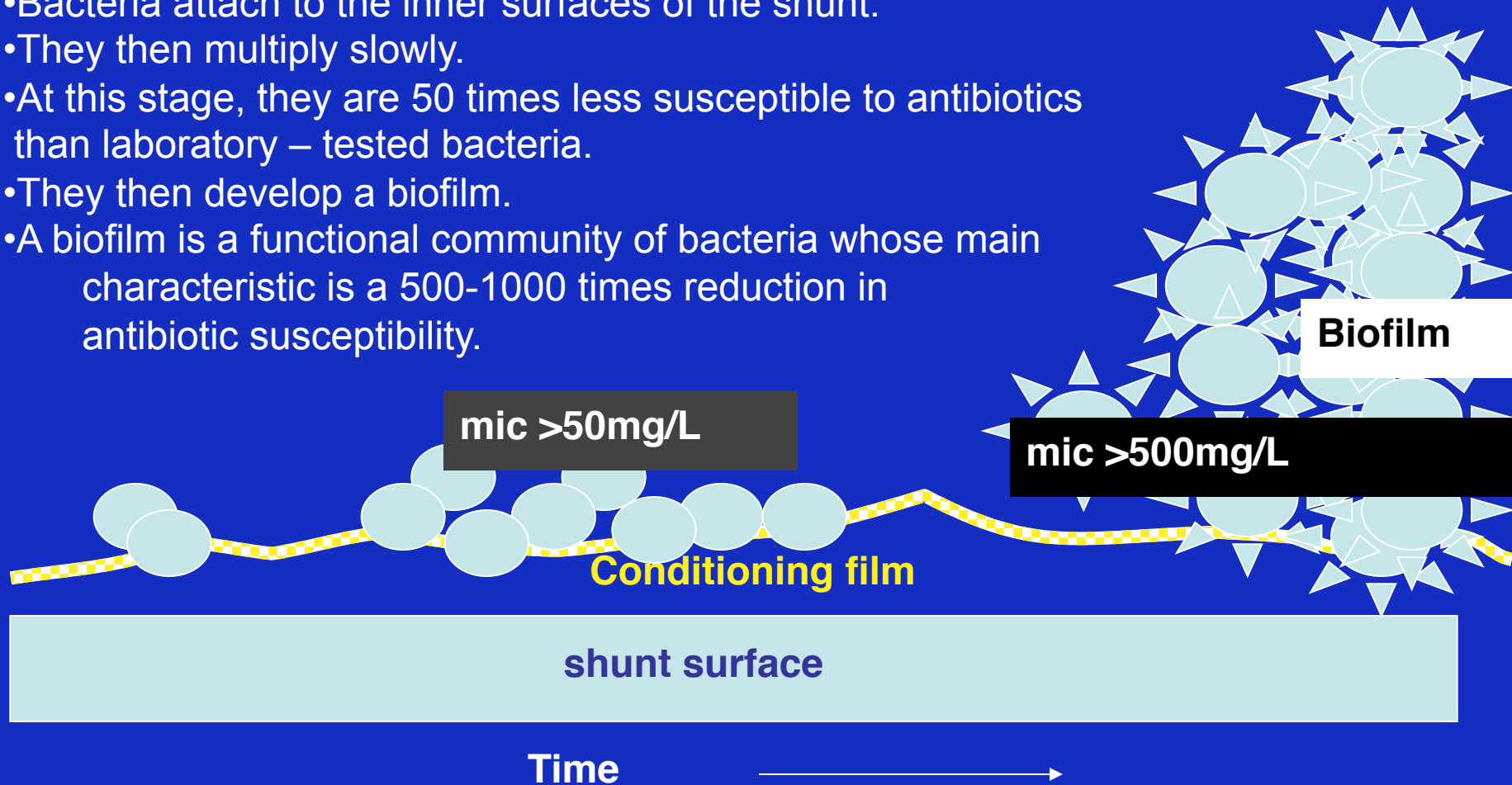


What do the bacteria do when they get inside the shunt?

- **How do they cause shunt infections?**
- **Why are they so difficult to treat?**

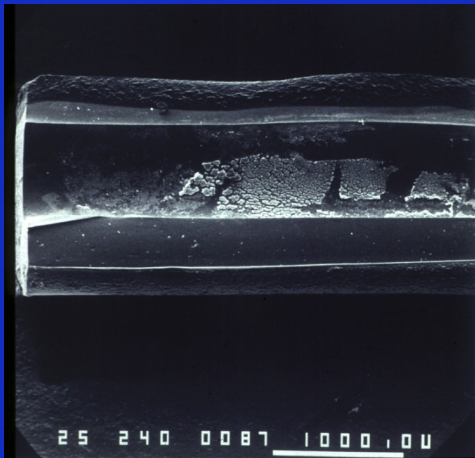
Mechanism of shunt infection

- Bacteria attach to the inner surfaces of the shunt.
- They then multiply slowly.
- At this stage, they are 50 times less susceptible to antibiotics than laboratory – tested bacteria.
- They then develop a biofilm.
- A biofilm is a functional community of bacteria whose main characteristic is a 500-1000 times reduction in antibiotic susceptibility.



Mechanism of shunt infection

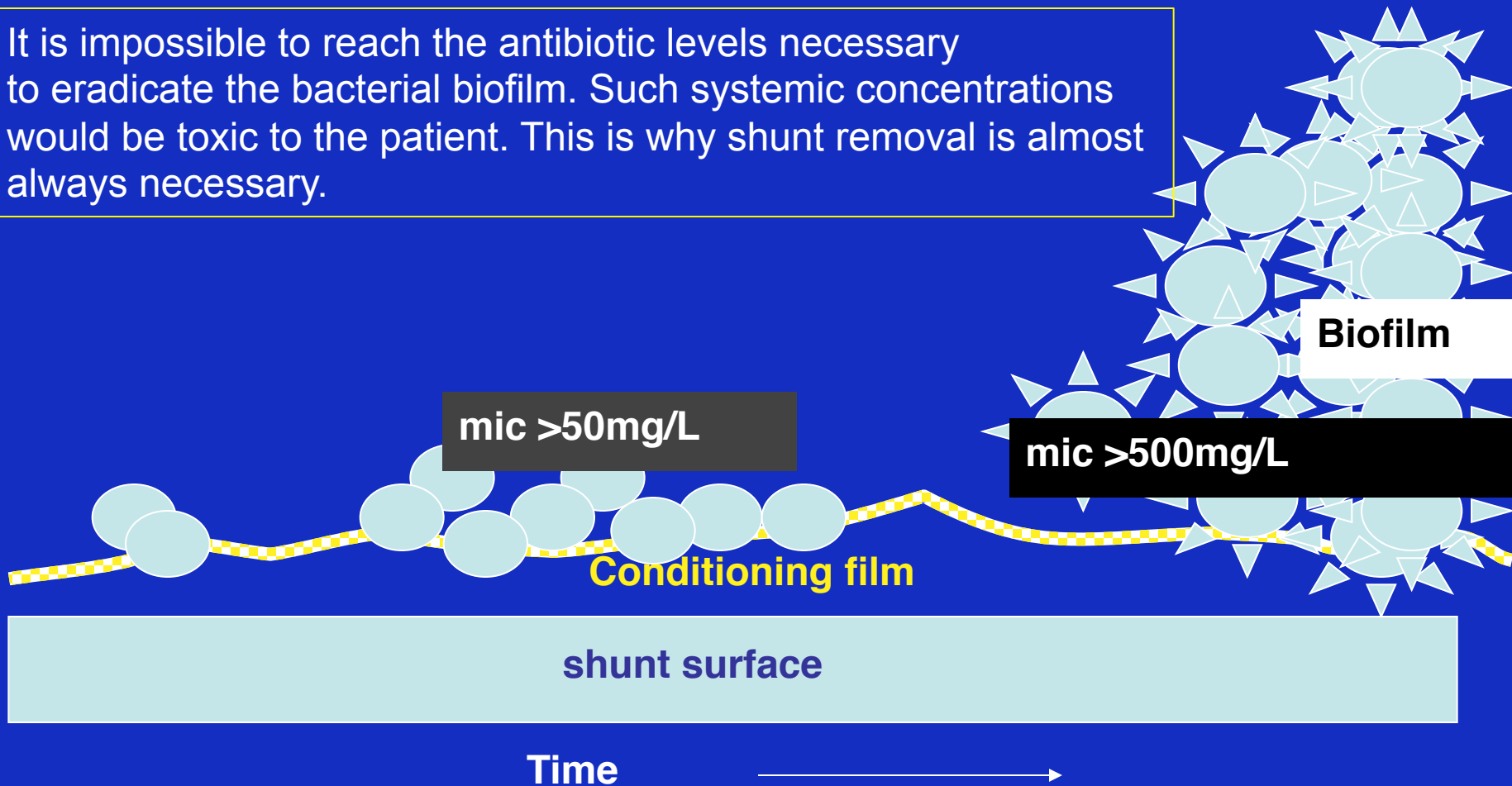
This is an electron microscope image of the inside of a colonised shunt. The plaques are 100% bacteria, growing as a biofilm.



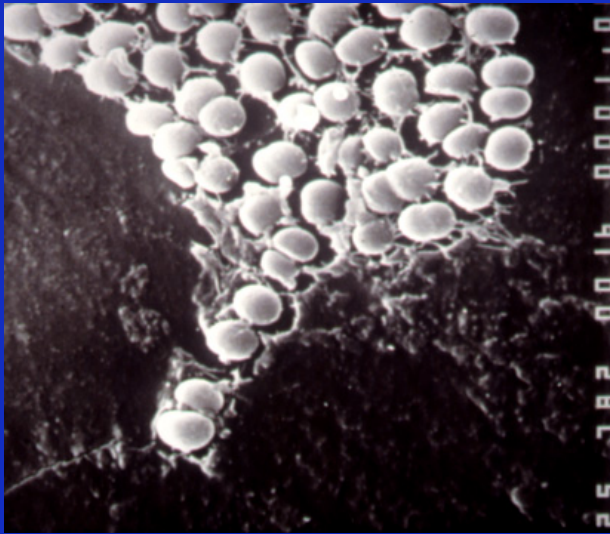
Bacteria grow slowly inside the catheters: CSF is not a good culture medium. It contains only $1/40^{\text{th}}$ as much protein and $2/5^{\text{th}}$ as much glucose as lab culture media, and little or no iron.

Mechanism of shunt infection

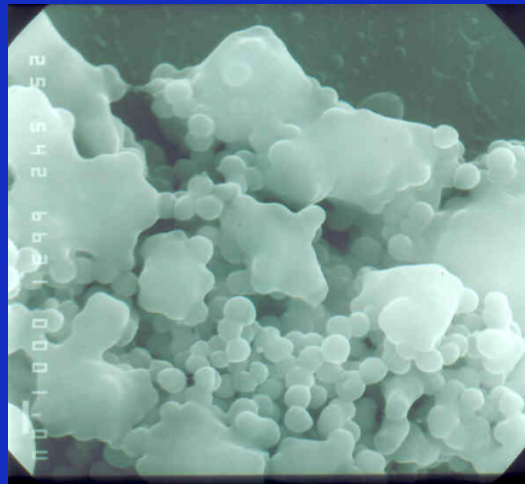
It is impossible to reach the antibiotic levels necessary to eradicate the bacterial biofilm. Such systemic concentrations would be toxic to the patient. This is why shunt removal is almost always necessary.



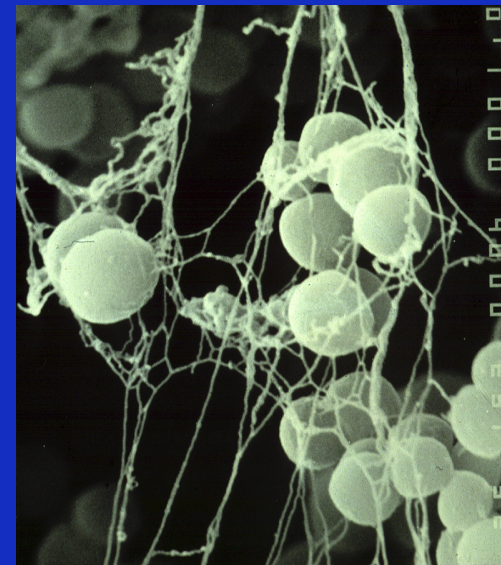
Biofilm formation inside shunts



These electron microscope images show bacterial biofilms inside removed shunts. The biofilms are held together by a “glue” produced by the bacteria.

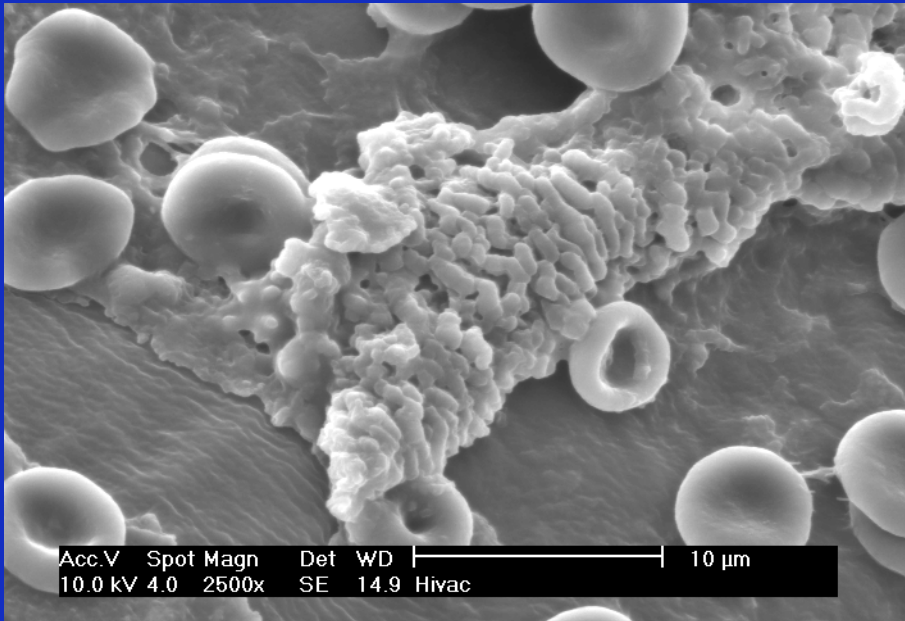


The first “medical” biofilm was described in 1972, from a CSF shunt.



Bayston & Penny,
Devel Med Child
Neurol 14,25-28,
1972; Bayston, Zbl
Bakt 16, 133-141,
1987; Guevara et al
J Neurosurg 67,
438-485, 1987; Fux
et al Clin Microbiol
Infect 12, 331-337,
2006.

Propionibacterium acnes biofilms



Propionibacteria are often missed by laboratories as they grow very slowly (7-14 days) and are anaerobic. They are normal skin commensals, like *S epidermidis*.

Probably all bacteria can produce biofilms, given suitable conditions. This anaerobic shunt pathogen, *P acnes*, is shown in a freshly removed shunt catheter.

Bayston et al J Biomed Mater Res 81A, 705-9, 2007

Diagnosis of shunt infection

Two main routes for shunting: Ventricle to abdomen (VP) and ventricle to cardiac atrium (VA)

At first, most were VA, now most are VP



Ventriculoperitoneal

Ventriculoatrial

Differences between VA and VP shunts

In both cases, almost all infections are caused by skin bacteria at the operation to insert or revise the shunt.

In VP shunts, most infection becomes evident within 6 months of operation, mainly due to distal catheter obstruction.

In VA shunts, infections can appear years after operation, and obstruction due to infection is uncommon. Nevertheless, epidemiological and serological evidence shows that most infections still date from surgery. There is no evidence that they are associated with dental procedures.

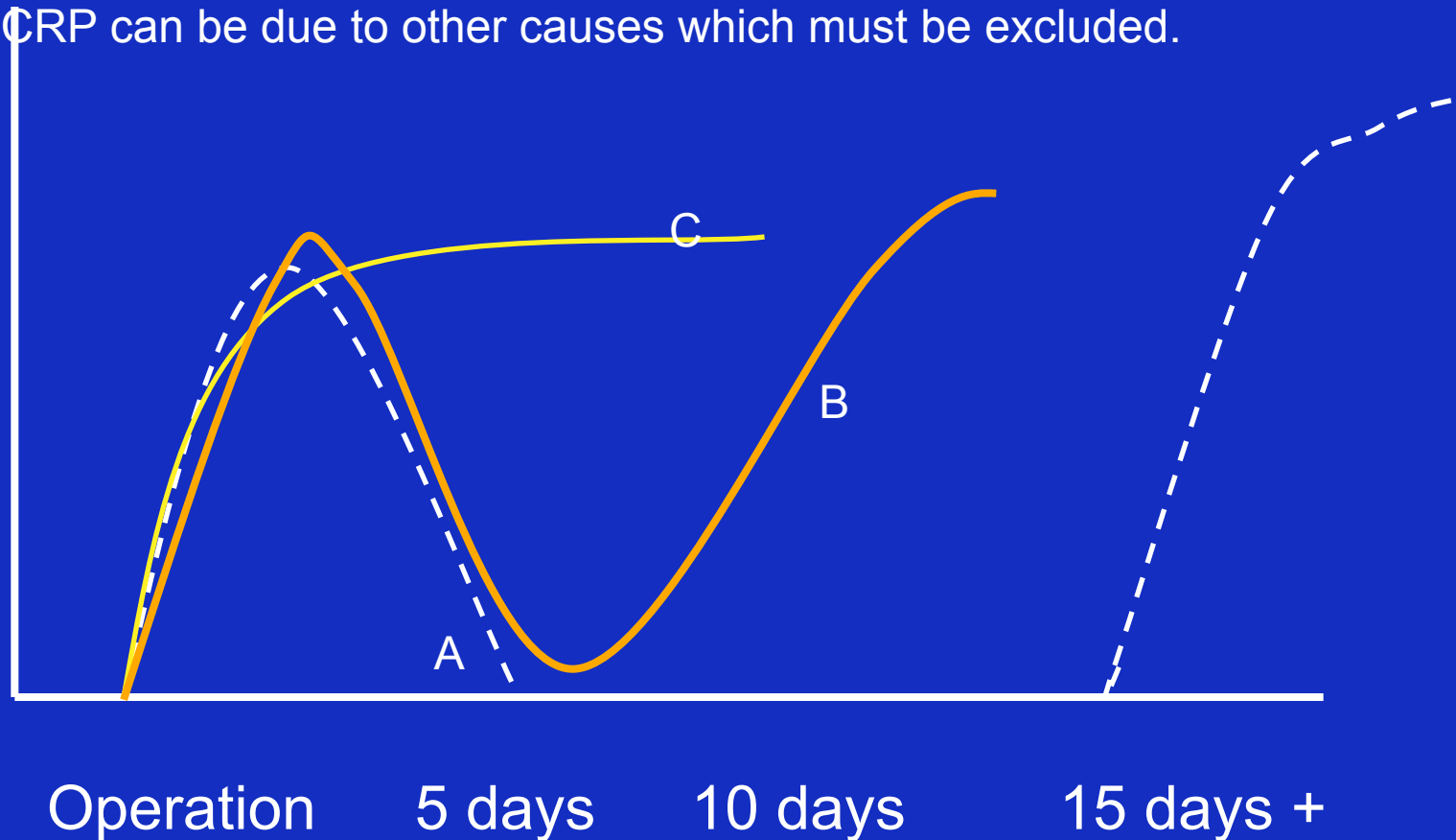
Diagnosis of VP shunt infection

- ≤ 6 months since operation (usually)
- Blood culture usually negative
- Raised serum C-reactive Protein
- Return of hydrocephalus symptoms due to distal obstruction
- Erythema over catheter track (often)
- Pyrexia (not always)
- Positive shunt tap (**Gram stain!** and culture)

Ensure that Gram stain is done on CSF sample. This detects bacteria that might not grow in normal culture, and it helps to distinguish contaminants. Cultures should include anaerobic media and be incubated for 10-14 days.

CRP in VP shunt infection

CRP rises after all surgery, and falls in about 5 days after VP shunt (A).
In infection, it might fall then rise again later (B), or it might not fall post-operatively (C).
Raised CRP can be due to other causes which must be excluded.



Diagnosis of VA shunt infection

- Sometimes years since operation
- Usually no evidence of shunt malfunction
- Positive blood culture in most cases
- Anaemia (iron - resistant) common
- Positive shunt tap (**Gram stain!** and culture)**
- Pyrexia 90% (intermittent)
- Immune complex disease if > 1yr after operation

** See notes on prolonged anaerobic culture on earlier slide.

Delayed infection in VA shunts

- **Still begins at operation** - culture / serological evidence for this
- Bacterial antigen enters bloodstream over a long period
- This leads to a very high antibody titre
- Bacterial antigen combines with antibody to form immune complexes
- Deposition of immune complexes on basement membranes in kidney, skin, joints, lungs etc
- Deposition of complement on immune complexes, then tissue damage from immune response
- Leads to Immune Complex Disease

Immune complex disease (ICD)

- **Nephropathy (shunt nephritis)**
- **Arthropathy**
- **Capillary vasculitis – skin rash, sometimes haemorrhagic**
- **Non - productive cough**

The patient is usually initially referred to a nephrologist, rheumatologist, orthopaedic surgeon, dermatologist, respiratory physician etc etc

Prevention of ICD

- Due to failure to diagnose the infection promptly
- Antibody to S epidermidis produced early after infection- within a few weeks
- Simple antibody test available:
 Anti-staph epidermidis titre (ASET)
- Age-related normal rises are documented.
- Discriminatory titres, eg normal 320, infected 2560

Clayton et al. Occult Ventriculo-atrial shunt infection: a forgotten condition.
Cerebrospinal Fluid Res. 2 Suppl 1, S23, 2005

Reaper et al. Use of ASET in the diagnosis of VA shunt infection.
BMJ Case Reports 2012; doi:10.1136/bcr.2012.006164

Treatment of shunt infections

- Originally (1961) they were treated like any other staphylococcal infection, with antibiotics only.
- Now accepted that it is necessary to remove the shunt in almost every case to ensure first –time success.
- Reasons for antibiotic treatment failure:

Poor antibiotic penetration into CSF

Biofilm formation requiring very high antibiotic levels for long time

Treatment of shunt infection

BSAC Guidelines 1995 (Gram positive bacteria)

- Shunt out, EVD in, manage carefully!
- Intraventricular vancomycin 20mg/day (shown to be safe)
- Intravenous / oral rifampicin, intravenous / oral flucloxacillin
- Continue 7days. Check clinical and lab improvement.
- If clinically improved (temp normal, etc) and CSF cultures negative after 48hr incubation, shunt ASAP after this, **giving last dose of antibiotics at surgery. Do not “stop and wait”**
- Outcome: high 1st time cure rate with no relapse
- Saving on hospital stay and adverse effects of antibiotics
- Problem: getting people to do it!

Treatment of shunt infection

Variations

- For MRSA, vancomycin needs to be given IV as well
(If CSF inflammatory response is good, skip intraventricular vancomycin for *S aureus*)
- Teicoplanin or linezolid can be considered (Linezolid gives good CSF levels on po or iv dosage)
- For MRSE etc, Intravenous trimethoprim if rifampicin - resistant
- Continue until clinical and CSF response.
- Reshunt ASAP after this, giving last dose of antibiotics at surgery.
- Do not “stop and wait” (Grave risk of EVD infection)
- For Gram negatives, treat as meningitis

Treatment of shunt infection

Exception to the “shunt out” rule:

- Community - acquired meningitis in shunted persons (haemophilus, meningococcus, pneumococcus): Treat as meningitis **but do not remove shunt!** (unless obstructed)

(O’Keeffe et al. J Infect 22: 77-9, 1991; Stern et al. Child’s Nerv Syst 4: 164-5, 1988; Rennals et al. J Pediatr 97: 424-6, 1980)

Patients with shunts and community – acquired meningitis are less sick and respond more rapidly.

Strategies for prevention

Changes in surgical practice:

“bundling”

Putting into practice a package of “common sense”

measures, none of which alone necessarily has RCT evidence

It must be consensual, it must be audited, and results should be fed back monthly.

Changes in protocols

eg Choux et al 1992, Choksey & Malik 2004:

- Formulation of rigorous theatre protocol
- Obligatory compliance
- General “smartening - up” of procedures
- Senior / experienced operators
- Usually dramatic reduction, but due to Hawthorne Effect? (improvement due to increased attention, data feedback etc)
- If so, will it “wear off”?

Possible key features of “new” protocols

- Rigorous asepsis
- Often double gloving (remove outer pair to handle shunt at insertion)
- Protect skin edges: use of antimicrobial protectors (eg sterile textile soaked in gentamicin or povidone iodine)

(Bayston 1977, Tabara & Forrest 1982, Fitzgerald et al 1984, Kestle et al 1993, Choksey & Malik 2004)

This measure reduces bacterial contamination of the surgical site from the skin

Shaving?

- **Do not shave the head! This damages the skin and increases infection risk**
- **Clip hair if necessary**
- **Prep hair the same as skin**

Double Gloving

- Tulipan et al 2006

Sequential non –randomised study

863 procedures:	single 521	15.2%
	double 342	6.7% $p=0.0002$

- Double gloves are intended to protect the surgeon
- Top pair should be removed before touching the shunt
- Wash gloves in alcohol before touching the shunt?
- Use “no – touch” technique instead?

Intravenous antibiotics for prophylaxis

- Few reach CSF in antibacterial concentrations
- Vancomycin, gentamicin, cephalosporins, flucoxacillin, nafcillin, etc do not give sufficient levels
- Rifampicin, chloramphenicol, trimethoprim do give reasonable levels, but have problems
(Rifampicin can not be used alone due to resistance mutation, and chloramphenicol is bacteristatic and potentially toxic)

Prophylactic antibiotics for shunting

Brown et al Lancet 344, 1994:

- Previous meta-analyses used very poor inclusion criteria: poorly discriminating, low quality scores, most papers should not have been included.
- No clear evidence of benefit unless the infection rate was $>15\%$

Studies on antibiotic prophylaxis in shunting

- Google: 25,700 papers!
- Some papers claim benefit, some not
- Haines 1994: meta-analysis, 8 trials included.
- “The results suggest that antibiotic prophylaxis does reduce the risk of shunt infection, but that **statistically apparent reduction in risk is limited to situations in which an unusually high baseline rate of infection is experienced.** The only studies reporting a statistically significant protective effect have control infection rates **in excess of 20%**”

**Possibly due to poor
antibiotic penetration into
CSF?**

**Assays show very low CSF levels during
shunt surgery**

Prophylactic antibiotics for shunts

Bayston et al Zeit Kinderchir 45, Suppl 1, 5-7 1990:

Intraventricular vancomycin 10mg pre-op: no reduction
in infection rate

But: Ragel et al J Neurosurg 105:242–247, 2006 :

- Systemic cefazolin plus gentamicin: 5.4%
- Intraventricular gentamicin 4mg: 6.2%
- **Intraventricular gentamicin plus 10mg intraventricular vancomycin: 0.4%**

This is encouraging but it needs systematic confirmation

Antimicrobial shunt catheters

- Bactiseal (Codman)
- Mechanical properties intact (Bayston 1980)
- Antimicrobial activity: must cover most shunt pathogens (Bayston & Milner 1981)
- Definitive description of process etc (Bayston et al 1989)
- Cerebral toxicology: non toxic (Abed et al 1994)
- Duration of activity (Bayston et al 1997)
- Mode of action (Bayston et al 2004)

Conflict of Interest: The author consults for Codman, and receives speaker fees as named inventor of Bactiseal.

Clinical efficacy of antimicrobial shunt catheters

12 clinical trials (varying quality; some too small, others sequential etc)

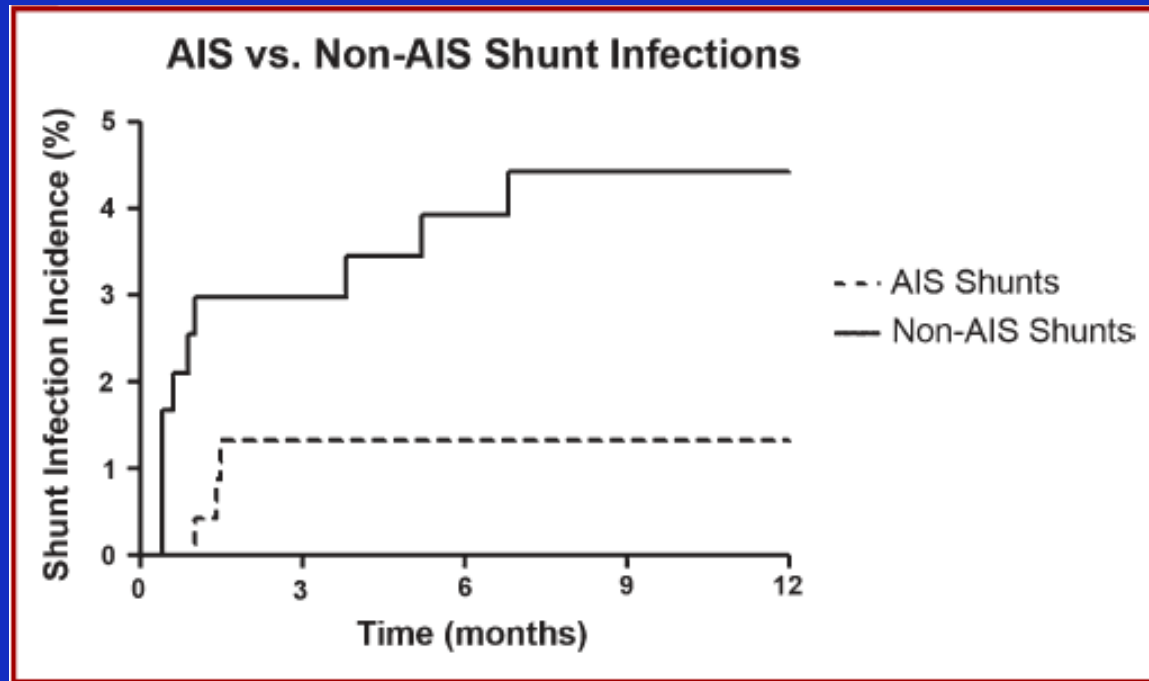
- Mean reduction in infection rates, plain catheters compared to Bactiseal:

11.96% to 3.98%

No resistance resulting from their use

Safe for use in neonates (Sciubba et al Ped Neurosurg 2008; 44: 91-96)

Farber et al Neurosurgery 69:625–629, 2011



AIS = antimicrobial shunt system.
3 vs 10 infections, AIS vs plain

Significant benefit in reduced infection and shunt survival

Cost savings of antimicrobial shunts

- Attenello et al Neurosurgery: 66 (2), 284–289 2010:
- Over 18 months, shunt infection reduced from 12% in plain shunts to 3.2% in Antimicrobial Shunt Systems
- Total cost of each infection \$50k
- Total savings (including catheters) \$1,234,599

Silver –processed shunt catheters

- A silver-processed shunt (Silverline) is now available
- A large multicentre randomized control trial (the BASICS Trial) has begun in UK to compare Silverline, Bactiseal and plain shunts.

Conclusions

- Shunt infections should be treated vigorously with intraventricular antibiotics where possible, to reduce the relapse rate.
- Infection rates can be reduced by “bundling” changes, and by antimicrobial shunts.