Antibiotics lock/coated/impregnated catheter and heparin lock catheter

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Antibiotics lock catheter

Antibiotic lock versus systemic antibiotics for catheter related infections in immunocompromised pediatric patients.

Objectives

- Describe indications for systemic antibiotics versus antibiotic lock therapy
- Evaluate type of antibiotic and treatment duration for antibiotic lock
- Timing of the antibiotic lock: early/late
- Antibiotic lock as prevention of catheter associated bacteremia

Background: Catheter related infections

- Leading cause of morbidity and mortality in critically ill hospitalized patients
- Organisms:
  - Coagulase – negative staphylococci
  - Staphylococcus aureus
  - Gram-negative bacteria
  - Candida ssp.

Sources of infection

- Colonization from the skin
- Intraluminal / hub contamination
- Hematologic seeding

Clinical evaluation -CRI

- Local inflammation
- Sepsis
- Blood culture
- Catheter dysfunction
- Rapid improvement following catheter removal

Treatment

- Type of device
- Infecting pathogens
- Presence of alternative venous access sites
- Duration of anticipated need for access

Treatment

- Catheter removal
- Systemic antibiotics
- Antibiotic lock therapy (ALT)- little evidence to support recommendation

Antibiotic lock

- First publication 1988-Messing et al
- Higher concentration, longer duration of activity at the infected site without potential side-effects of systemic exposure
- Concentration and intra-luminal dwell time: lack of evidence based recommendations

Lack of firm recommendations for individual patients

- Immunocompromised population
- Pathogenesis of CRI complicated
- Virulence of the pathogens variable
- Host factors not well defined
- Lack of diversity between studied populations
- Absence of compelling clinical data to form recommendations

Data

- Uncomplicated catheter-related bacteremias: Infectious Disease Society of America – systemic antibiotics (7days) +ALT (14 days)
- Local, systemic, extra-luminal CRI –ALT should be combined with systemic treatment for at least 72 hours

Data

- Search strategy:
  Pub Med (1990-2008)
- Selected studies:
  Pediatric patients only
  Prophylaxis with ALT,
  Treatment with combined therapy (SA+ALT)
- 9 studies met above criteria!

Antibiotic-heparin lock solutions: adults and children

Antimicrobial lock solutions

Active ingredient	Concentration (mg⁄L)
Vancomycin a	0.025–10
Teicoplanin a	0.025–2.5
Linezolid a	0.2–2
Amikacina,b	1–10
Gentamicin	1–10
Ciprofloxacin	0.125–2
Ceftazidime	0.5–2
Amphotericin B desoxycholate	2 (in glucose 5% w⁄v)

- A: Stable for ‡ 24 h without loss of efficacy when combined with heparin 100 U⁄mL.
- B: Vancomyin 25 mg⁄L + amikacin 25 mg⁄L + heparin 100 000 U⁄L in NaCl 0.9%
- Note: Standard antibiotic lock technique ampoules prepared by the hospital
- pharmacy must be protected carefully against contamination with bacteria and
- fungi, and should be filter-sterilized and stored in a refrigerator.

Data: Prevention

- 3 studies:
  - –prospective double blind study, prospective cohort study, literature review (both children and adults)
  - –Vancomycin/heparin/ciprofloxacin, vancomycin/heparin, minocycline/ethylenediaminetetraacetate, vancomycin/teicoplanin
- Results:
  - –Time to develop CRI longer with ALT
  - –rate of total line infections decreased
  - –no port infections or thrombotic events were observed compared to ports flushed with heparin only

Data: Treatment

- 6 studies:
  - –2 case reports, 4 open pilot studies
  - –Vancomycin/heparin, ciprofloxacin/heparin, amikacin/heparin, urokinase /vancomycin, ampicilin alone+ systemic antibiotics
- 168 episodes of CRI:
  - –143 (85%) episodes cured (negative bld cx –mean: 4days-1month),10 catheter removals, median catheter follow up -96 days,168 days (1 study),25 (15%) episodes of therapeutic failure (recurrence of febrile bacteremia),1 death.

ALT Evidence based guidelines - Significance

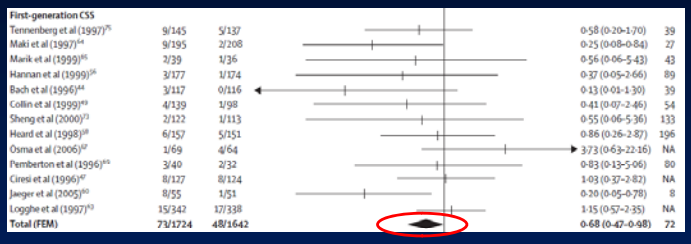
- Decrease in mortality and morbidity related to catheter related infections
- Limit use of systemic antibiotic
- Prevent resistance
- Improve quality of life
- Lack of serious complications
- Cost effective?

Coated Catheters

- Theory: decrease extraluminal catheter colonization and intraluminal colonization if interior surface of catheter also coated
- Types
  - –Heparin + benzalkonium bonded (activity on inner and outer surface)
  - –Silver + platinum coating on inner & outer surface
  - –Chlorhexidine and silver sulphadiazine
    Outer ± inner coating
  - –Antibiotic coating on outer & inner surface: minocycline and rifampin

Casey AL et al. Lancet Infect Dis. 2008;8:763-76
Gilbert RE and Harden M. Curr Opin Infect Dis. 2008;21:235

1st Generation Chlorhexidine and Silver Sulphadiazine vs. Standard



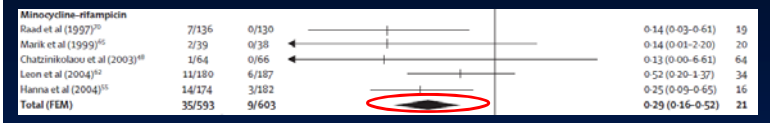
RR 0.68 (0.47-0.98)

2nd Generation Chlorhexidine and Silver Sulphadiazine vs. Standard

OR 0.47 (0.20-1.10)

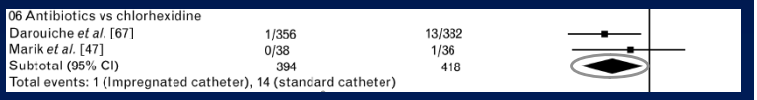
- No additional benefit of outer and inner coating

Minocycline/Rifampin vs. Standard



RR 0.29 (0.16-0.52)

Minocycline/Rifampin vs. Chlorhexidine



RR 0.12 (0.02-0.67)

Coated Catheters: Considerations

- Heparin and Minocycline/Rifampin coatings appear to be more effective than other coatings
- Limited data regarding:
  - Risk of development of minocycline or rifampin resistance
  - Risk of selection of fungal organisms
- In a different pooled analysis:
  - Treatment effect seen with catheters in place for 5-12 days but not 13-20 days
  - Treatment effect seen for femoral and internal jugular insertion sites but not in studies using exclusively subclavian insertion sites

Hockenhull JC et al. Health Technol Assess. 2008;12(12).

Coated Catheters: Considerations

- Decision to use coated catheters depends on local factors
  - Extent of adoption of best practice
  - Duration of catheterization
    - May need to make protocol based on expectations of duration of catheterization at individual patient level rather than unit level
  - Usual sites of catheters
  - Concerns about rifampin resistance
    - May choose not to use catheters with rifampin coating in patients with endovascular hardware

Other Technologies

- Antiseptic hubs
  - No published clinical data supporting efficacy
- Dressings containing chlorhexidine (e.g. Tegaderm™ CHG dressing)
  - No published clinical data supporting efficacy
- Antimicrobial lock solutions
  - Not recommended for routine use
  - Could be considered in individual patients with limited venous access & history of recurrent CLABSI or in patients at risk for severe sequelae of CLABSI (e.g. new prosthetic heart valve)

Use prophylactic antimicrobial lock solution in patients with long term catheters who have a history of multiple CRBSI despite optimal maximal adherence to aseptic technique.

Catheter Locks

- Technique by which an antimicrobial solution is used to fill a catheter lumen and then allowed to dwell for a period of time while the catheter is idle.
- Antibiotics of various concentrations that have been used either alone (when directed at a specific organism) or in combination (to achieve broad empiric coverage)
- Formulations made in-house
- Studies are limited; populations are hemodialysis, neonates, patients with neutropenia

Antibiotic/Antiseptic Catheters

Antibiotic/Antiseptic Catheters

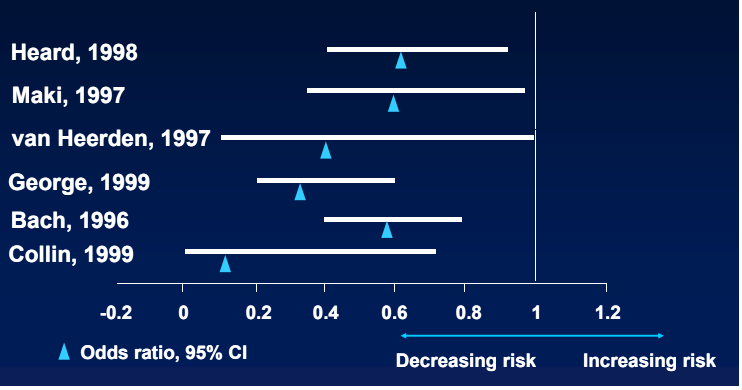
Use an antimicrobial or antiseptic-impregnated CVC in adults whose catheter is expected to remain in place >5 days if, after implementing a comprehensive strategy to reduce rates of CR-BSI, the rate has not sufficiently decreased. The comprehensive strategy should include the following 3 components: educating persons who insert and maintain catheters, use of maximal barrier precautions, and a 0.5% chlorhexidine preparation for skin antisepsis during central venous catheter insertion.

Efficacy of Chlorhexidine-Silver Sulfadiazine Catheters for Prevention of CR-BSI

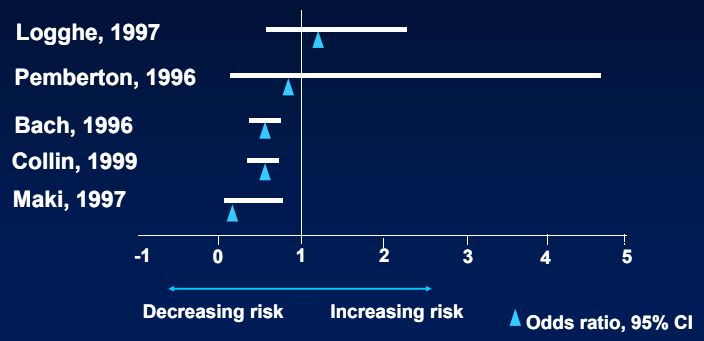
Reference	Colonization RR	Blood Stream Infection RR
Maki, 1997	0.56 (0.36-0.89)*	0.2 (0.03-0.95)*
van Heerden, 1997	0.4 (0.1-1.0)*	--
Heard, 1998	0.59 (0.34-0.97)*	--
Bach,1996	0.6 (0.4-0.9)*	0.5 (0.4-0.7)*
Collin, 1999	0.1 (0.0-0.7)*	0.5 (0.4-0.7)*
George, 1999	0.3 (0.2-0.6)*	--
Pemberton, 1996	--	0.8 (0.2-4.7)
Logghe, 1997	--	1.2 (0.6-2.3)

Mermel, Ann Intern Med 2000; 132:391-402
Eggimann and Pittet, Advances in Sepsis, 2000

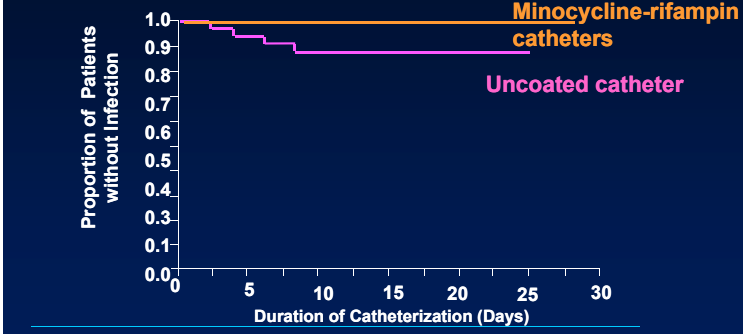
Efficacy of Chlorhexidine-Silver Sulfadiazine Catheters for Prevention of Catheter Colonization



Efficacy of Chlorhexidine-Silver Sulfadiazine Catheters for Prevention of CR-BSI



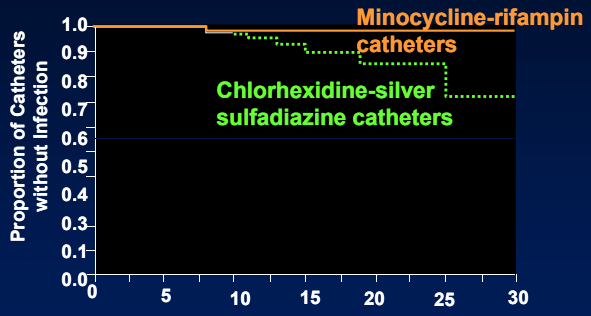
Time to Occurrence of CR-BSI with Minocyline-Rifampin Catheter



Catheters (n)	266	170	50	11	6	1	0

Raad, Annals Intern Med 1997

Risk of Bloodstream Infections Using Two Types of Impregnated Catheters



Catheter	No. at Risk						
M/R	365	214	93	48	20	9	4
C/SS	382	246	96	39	18	5	2

Darouiche NEJM 1999

Eliminating Catheter Related Infections

Annals of Internal Medicine | ARTICLE

Effect of a Second-Generation Venous Catheter Impregnated with Chlorhexidine and Silver Sulfadiazine on Central Catheter–Related Infections

A Randomized, Controlled Trial

Mark E. Rupp, MD; Steven J. Lisco, MD; Pamela A. Lipsett, MD; Trish M. Perl, MD, MSc; Kevin Keating, MD; Joseph M. Civetta, MD; Leonard A. Mermel, DO, ScM; David Lee, MD; E. Patchen Dellinger, MD; Michael Donahoe, MD; David Giles, MD; Michael A. Pfaller, MD; Dennis G. Maki, MD; and Robert Sherertz, MD

Background: Central venous catheter-related infections are a significant medical problem. Improved preventive measures are needed.

colonized at the time of removal compared with control catheters (13.3 vs. 24.1 colonized catheters per 1000 catheter-days, $P < 0.01$). The center-stratified Cox regression hazard ratio for coloni-

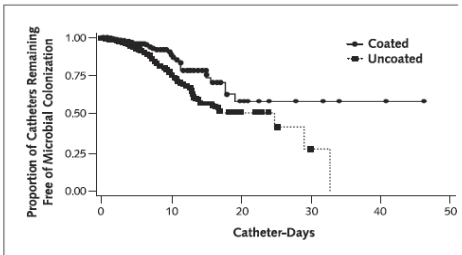
Annals of Internal Med 2005

Eliminating Catheter Related Infections

- 777 Catheters
- 393 Control catheters and 384 antiseptic catheters
- Funding source: Arrow
- Sponsor collected and analyzed the data
- Difference in BSI not significant (0.42/1000 catheter days vs 1.24/1000 catheter days)

Eliminating Catheter Related Infections

Figure 2. Kaplan–Meier curve demonstrating initial study catheters free of microbial colonization versus time.



Catheters remaining, *n*	Day 0	Day 10	Day 20	Day 30
Antiseptic CVC	345	68	13	3
Control CVC	362	68	16	1

Heparin lock catheter

Flushing is Important

- Flushing removes blood, glucose or other contaminants that may support microbial growth.
- Use of pre-filled syringes for flushing reduces the risk of extrinsic contamination.
- Use of pre-filled syringes avoids outbreaks associated with vial contamination/re-use.

導管維護與沖管

- 放置導管是為了因應臨床治療之需求,但導管維護不良將影響治療成效，進而可能造成 ：
  - ✓治療週期延長,如： 因導管相關併發症產生的醫療需求
  - ✓住院天數增加
  - ✓增加病患因更換導管的疼痛不適及風險
  - ✓放置新導管的成本

導管沖洗
是評估並保持導管暢通的重要管路維護技術之一

沖洗導管的目的

沖管是透過針筒約0.9%生理鹽水注入導管內， 以達到：

- 確認導管在首次插入時的正確位置
- 確保導管在輸藥前的正確位置
- 確保藥物已無殘留在導管內,完全投與病人
- 確保將兩種不相容的藥物分隔開， 避免不良反應
- 在中央靜脈導管抽血前後或輸血後保持導管通暢
- 在輸送營養液後沖管確保導管無乳脂殘留
- 保持間歇輸藥的導管孔道通暢
- 減少管路流量異常

導管相關合併症

- 因導管堵塞， 可能導致後續嚴重的併發症 ：
  - ✓ 滲漏（內滲),無腐蝕性溶液流到皮下組織中
  - ✓ 外滲,具腐蝕性溶液流到皮下組織中,腐蝕性溶液會造成組織的壞死

以上皆可能因無充分沖管引發!?

沖管三步曲 A-C-L of Flushing

- A- Assess 導管功能評估
  透過回血判斷導管通暢是必須的!
  - ✓ 在導管初次置入時
  - ✓ 導管留置期間
- C- Clear 沖管
  沖洗導管內腔血液及藥液
- L – Lock 封管
  - ✓ 在執行導管治療間隔中,每次結束需以適當溶液(正壓)封管

Catheter Locking

- Heparin lock solution 10 units per mL
- Creates a column of fluid inside the catheter lumen to enhance patency
- Required for central venous catheters used intermittently

沖封管的方法

在中央靜脈導管

- **SASH**
  - ✓S =鹽水Saline
  - ✓A=給藥Administer medication
  - ✓S=鹽水Saline
  - ✓H=肝素鹽水 Heparin

在外周短靜脈導管

- **SAS**
  - ✓S =鹽水Saline
  - ✓A=給藥 Administer medication
  - ✓S=鹽水 Saline

Peripheral Catheters

- 2 to 3 mLs Normal saline
  - Flushing & locking
- Heparin is not used
- No difference in patency of peripheral catheters with saline vs heparin

沖管溶液的種類

- 多劑量的沖管液
  - –大瓶裝，如: 30ml 0.9% 生理鹽水
  - –大輸液袋，如: 250ml、500ml或者 1000ml 的 0.9% 生理鹽水

多次抽取使用-----高風險！

Multiple Dose Vials (MDV)

- **RISK far outweighs their benefits**
- **Bacterial contamination rates from 0% to 27%**
- **Contains benzyl alcohol as preservative**
  - –Limit volume of bacteriostatic normal saline to no more than 30 mL in 24 hours in adults
  - –Contraindicated in neonates
- **Bacteriostatic, not bacteriocidal**

多劑量輸液袋/ 瓶

- 由護理人員手工準備的沖洗注射器易產生污染
  - –根據英國醫院腫瘤、重症監護室和透析室研究發現，以無菌空針從單劑量瓶溶液由護士手工配置的沖洗液中，污染機率高達 8%


8 hepatitis cases linked to clinic

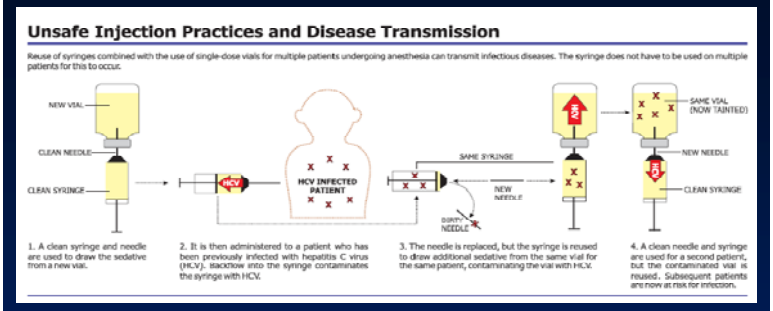
Brooklyn Bug

Hepatitis C outbreak among clinic patients

Clinic linked to 8 cases of hepatitis C; 2,200 at risk

Hepatitis C outbreak

Strikes 8 endoscopy patients of B'klyn clinic



Source: www.**southernnevadahealthdistrict**.org

傳統配製與預充式的對比研究

- 回顧從25個中度急症的護理單位收集的研究資料 (Rosenthal, 1999)
  - –到院患者均使用中心靜脈導管
  - –62位患者使用 2 個月以上的預充式針筒沖洗靜脈管路
    - 發現3 例併發症: 1例導管相關性感染，1例靜脈炎，1例導管堵塞
  - –64位患者使用 2 個月以上護士手工配置的沖洗液進行沖洗靜脈管路
    - 發現15例併發症: 10 例感染，5 例堵塞，3 例靜脈炎

Worthington Study (2001)

- 研究使用無菌空針由單次使用的安瓶抽取生理鹽水作為靜脈導管沖洗
- 研究單位包括: 加護病房, 腫瘤科, 洗腎中心及外科病房等
- 研究發現:
  - –8%污染來自針筒尖端及生理鹽水, 且延伸污染到中央靜脈導管及導管接頭
  - –護士沒有在打開前先消毒生理鹽水安瓶外周表面
- 後繼研究用預充式生理鹽水, 發現可節省 68% 工時
- 建議: 應盡早採納最新沖管基準

Worthington et al, " Are contaminated flush solutions an overlooked source for catheter related sepsis?" in The Hospital Infection Society. 2001, p. 81-83

Calop Study (2000)

- 手工配置預充式生理鹽水來進行外周靜脈導管及中央導管沖管
  - –8% 手工預充的生理鹽水受污染
  - –對照研究：Trautmann 等人也觀察到有7.8%生理鹽水受污染

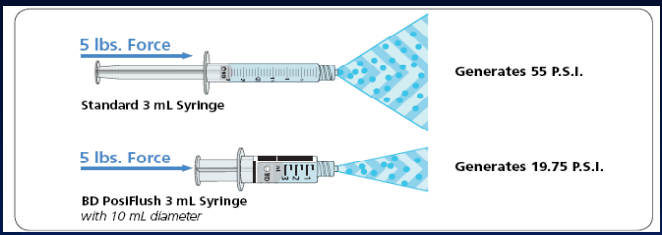
Calop J, "Maintenance of peripheral and central intravenous infusion devices by 0.9% sodium chloride with or without heparin as a potential source of catheter microbial contamination" in Journal of Hospital Infection. 46:161-162則

預充式生理食鹽水特點

Syringes特殊的管徑設計

- 特殊的注射器的設計
  - ✓注射器不論 3、5、 10mL 直徑統一規格，沖洗時產生較小的壓力(PSI)
  - ✓改變針筒活塞內芯設計，材質較硬不易回彈，減少血液回流至導管內腔

針筒直徑與施予導管壁的壓力



在靜脈及導管內承受的壓力 = 施加在針筒推柄的力 (磅) ÷ 針筒內周面積 (半徑^2 X π)

psi = pound per square inch ** 大於25 psi, 血管會受傷害

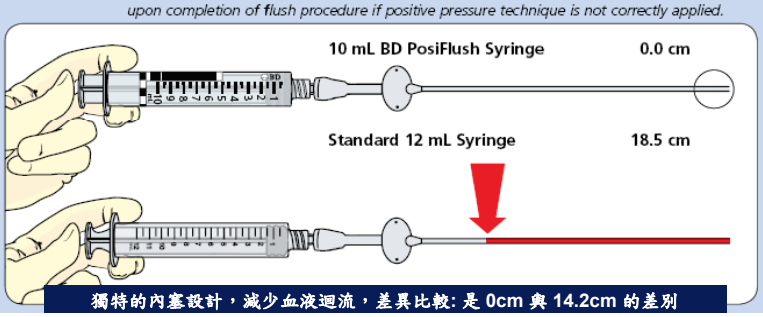
Force applied to syringe plunger rod	1mL standard syringe	3 mL standard syringe	5 mL standard syringe	10mL standard syringe
5 pound	94.2 psi	55.1 psi	28.6 psi	19.8 psi

BD PosiFlush™ Saline Syringes are designed to eliminate syringe-induced blood reflux.*

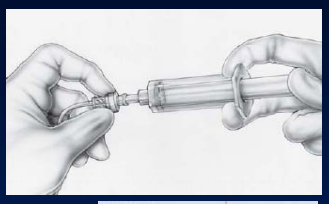
BD PosiFlush Saline Syringes are designed to eliminate syringe-induced blood reflux*, enhancing catheter maintenance protocols.

BD PosiFlush™ 沖管過程零回血(針對PICC的實驗)

Graphic depicts the average amount of blood aspirated into the catheter upon completion of flush procedure if positive pressure technique is not correctly applied.



獨特的內塞設計，減少血液迴流，差異比較: 是 0cm 與 14.2cm 的差別



當推至賸餘 0.5ml 生理鹽水時, 姆指持續緊按針對內塞頂部

Pre-filling syringe

一邊推液，一邊關閉夾子，移開針筒，最後才放開姆指

多謝聆聽