

HEMODIALYSIS CATHETER INFECTION

- Introduction
- Diagnosis
- Management
- Prevention
- Conclusion for future direction

SEIED AHMAD TARA M.D.

Shiraz University of Medical Sciences

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The **19th**
International Congress of
**Nephrology, Dialysis
and Transplantation**
(ICNDT)

12-15 December 2023

Homa Hotel, Tehran

Ahmad Tara M.D.

SUMS ,Shiraz,Iran



Why we need local practice guideline for HD CRBSI

- ✓ Different pattern of pathogens
- ✓ Different bacterial resistance
- ✓ Different of catheter usage
- ✓ Different workloads in HD units
- ✓ Different health culture
- ✓ Different locations of HD centers. In hospitals or freestanding.
- ✓ Different economy and access to health care system and insurances
- ✓ Different RRT selection.
- ✓ Different mortality rate in Iranian HD patients
- ✓ Different practice guideline between Europe and US

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IMPORTANCE OF HEMODIALYSIS ACCESS INFECTION

- 8 million CKD patients and **50000** HD patients in Iran
- The 100000 billion rials = **200,000,000** \$ cost to care for ESRD patients in Iran.
- Hospitalization rate is twice per year from cardiovascular and infection problems and adds **0.8 %** expense of care for everyday admission.
- Mortality of HD patients is **17% per year** and infection is the second cause of mortality. Catheter-related bloodstream infections are the most serious of infections
- Risk of infection and related mortality is much higher in TCCs (Tunneled Cuff Catheter) than AVG (Arteriovenous grafts) and arteriovenous fistulae (AVFs).
- **80%** of patient Starting dialysis use TCC as their first access
- **20%** of hemodialysis patients use TCC as maintenance access
- **40 %** of patients dialyzed in Iran use TCC as maintenance access

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Consequences of over usage of TCC in Iran (>40%)

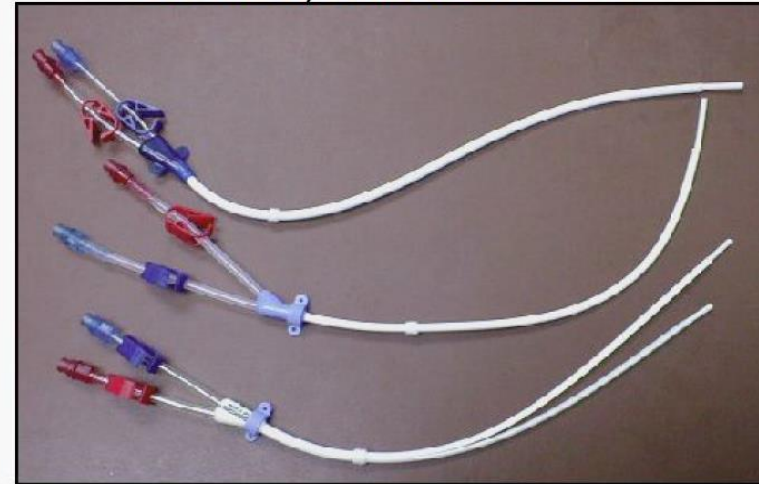
- ✓ Doubling the rate leads to **ten times more infection**.
- ✓ 50000 patients that **20000 on TCC**.
- ✓ At least 2 CRBSI annually leads to **40000 infection events per year**.
- ✓ At least 10 % need hospital admission, with **4000 admissions with serious complications** per year.
- ✓ High rate of morbidity especially metastatic infections and mortality (3 times more mortality than grafts or AVFs).
- ✓ More infections mean more emergence of resistant pathogens.
- ❖ **The most obvious measure that would reduce the frequency of catheter-related bacteremia is to decrease the number of patients using a dialysis catheter.**

Hemodialysis Catheters

Non-tunneled, non-cuffed catheters



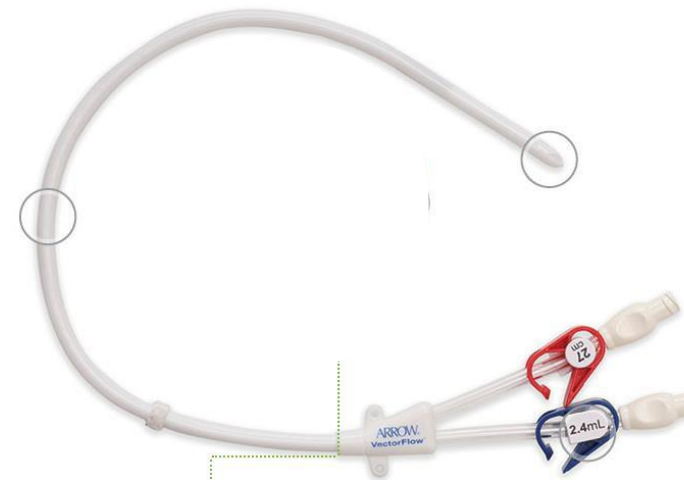
Tunneled, cuffed catheters



CATEGORIES OF INFECTION ASSOCIATED WITH CATHETERS

Infection is the second leading cause of death in dialysis patients, with.

- Infection associated with TDCs be classified into three categories
 - Exit-site infection,
 - Tunnel infection
 - Catheter-related bloodstream infection – CRBSI



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EXIT-SITE INFECTION

- Definition : culture-positive inflammation external to the cuff, localized to the exit site, not extending above the cuff
- It is characterized by localized redness, crusting, and a variable amount of exudate
- If the patient also has systemic symptoms, systemic infection should be suspected and blood cultures should be obtained
- If the blood cultures are positive, the case should be classified as a CRBSI rather than an exit-site infection
- Management:
 - **Local: Mupirocin if failed and increasing drainage systemic AB**
 - **In the case of response failure, exchange with the creation of a new exit site or removal if that is feasible**
- They should be monitored for the development of tunnel infection or systemic symptoms suggesting the appearance of a CRBSI



Exit-Site Infection

TUNNEL INFECTION

- Defined as culture-positive inflammation within the catheter tunnel internal to the **Dacron cuff** with a negative blood culture
- Involvement of the tunnel below the cuff is commonly seen as part of the exit-site infection
- It is a serious problem because the catheter moves **back and forth** within this portion of the tunnel and there is direct communication with the bloodstream(an abscess with a foreign body within it)
- Treatment: **catheter removal** along with parenteral antibiotics chosen according to culture results



Tunnel Infection

MICROBIOLOGY OF ACCESS-RELATED INFECTION

- Gram-positive organisms are responsible for most catheter-related infections
 - Staphylococcal infection, both coagulase-negative and *S. aureus*, accounts for **40–81%** of cases in reported studies (MRSA is common)
- Gram negative (one-third) :Entrobacter & pseudomonas
- Polymicrobial : 15%
- Candida 5%



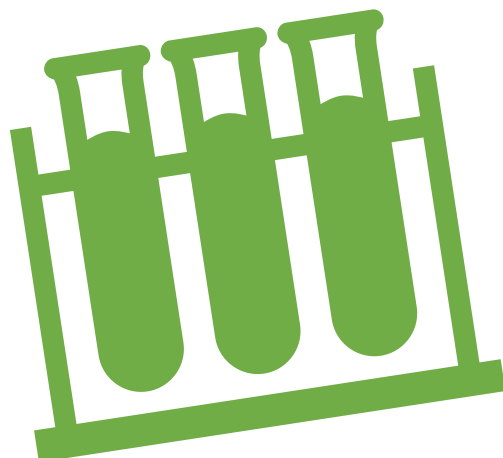
Fifteen-year report of Nosocomial Antibiotic Resistance in Shiraz

2008-2022

گزارش پانزده ساله مقاومت های آنتی بیوتیکی
بیمارستانی در شیراز

۱۴۰۱-۱۳۸۷





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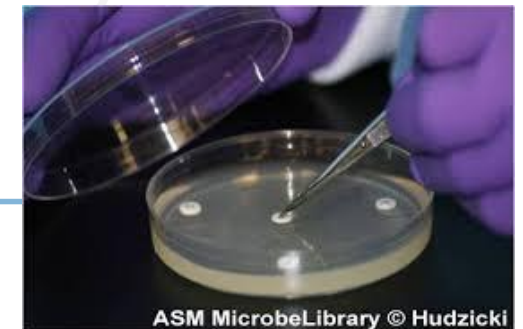
Ahmad Tara M.D.

SUMS, Shiraz, Iran

Isolation & identification

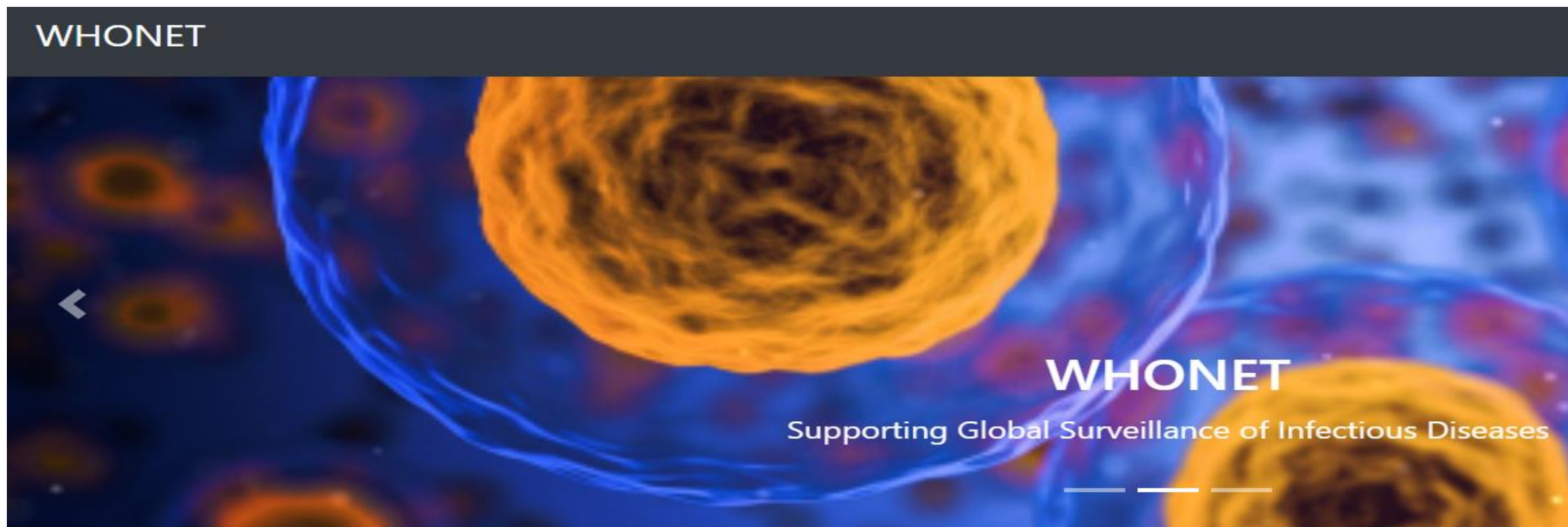
Antimicrobial resistance surveillance

- Isolates were recovered from blood samples incubated in the **BACTEC™**
- ✓ **Identification** of bacteria was done by biochemical differentiation
 - API bioMérieux & Phoenix BD Instrument
- **Susceptibility testing** was performed by disk diffusion according to CLSI (Clinical & Laboratory Standards Institute) criteria & Phoenix BD



Microbiology laboratory information
registration system

Antimicrobial resistance
surveillance

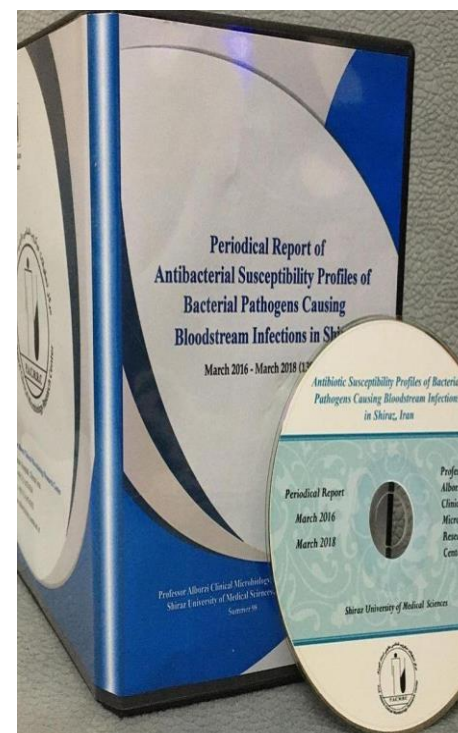
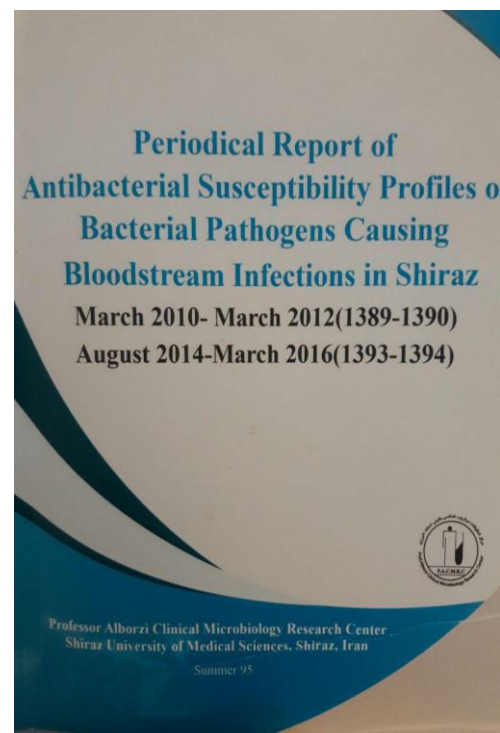
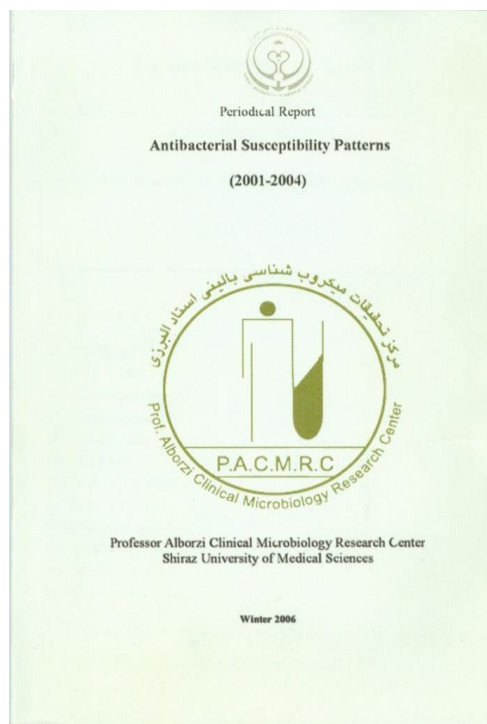


The microbiology laboratory database software.

Publish Surveillance Results

Antimicrobial resistance
surveillance

Periodical Report of Antimicrobial Susceptibility in Shiraz



Periodical Report Antibacterial Susceptibility Patterns

Antibiotic – Susceptibility Profiles of Bacterial
Pathogens Causing Bloodstream Infections in
Shiraz Periodical report
March 2020 – March 2022 (1399-1400)



Prof. Alborzi
Clinical Microbiology Research Center
Center of Excellence for Clinical Microbiology in Iran



The 19th International Congress of Nephrology, Dialysis and Transplantation (ICNDT)

12-15 December 2023 . Homa Hotel, Tehran



Misdiagnosis in lab !



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Nosocomial Infections: Multicenter surveillance of antimicrobial resistance profile of *Staphylococcus aureus* and Gram negative rods isolated from blood and other sterile body fluids in Iran

**Bahman Poorabbas¹, Jalal Mardaneh¹, Zahra Rezaei¹, Mehdi Kalani¹, Gholamreza Pouladfar¹,
Mohammad Hasan Alami², Jafar Soltani³, Ahmad Shamsi-Zadeh⁴, Shahram Abdoli-Oskooi⁵,
Mohammed Jafar Saffar⁶, Abdolvahab Alborzi^{1*}**

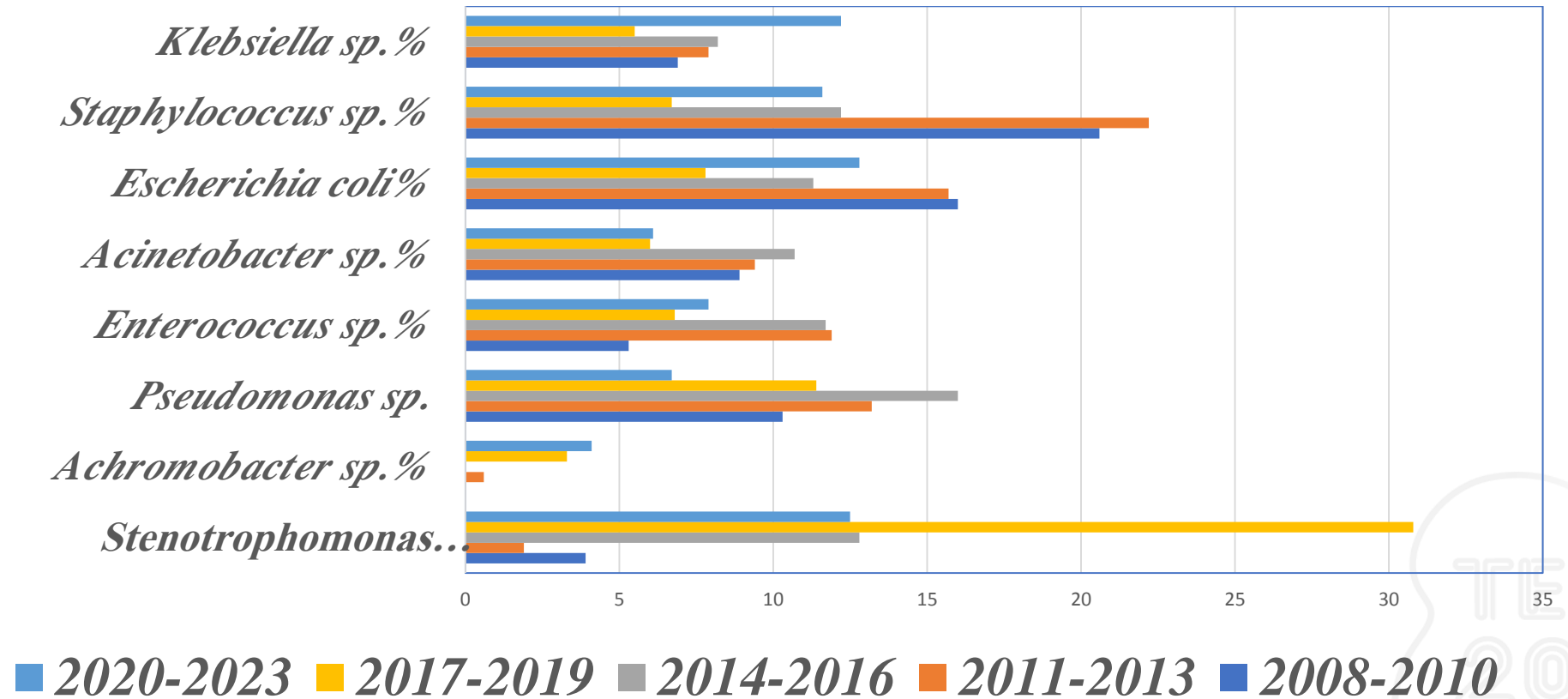
Seven major teaching hospitals located in different geographic areas of Iran (Shiraz, Tabriz, Sari, Mashhad, Sababdah, Ahwaz, Isfahan) in collaboration with the professor Alborzi clinical Microbiology Center (PACMRC), participated in this multicentre collaborative study over the period

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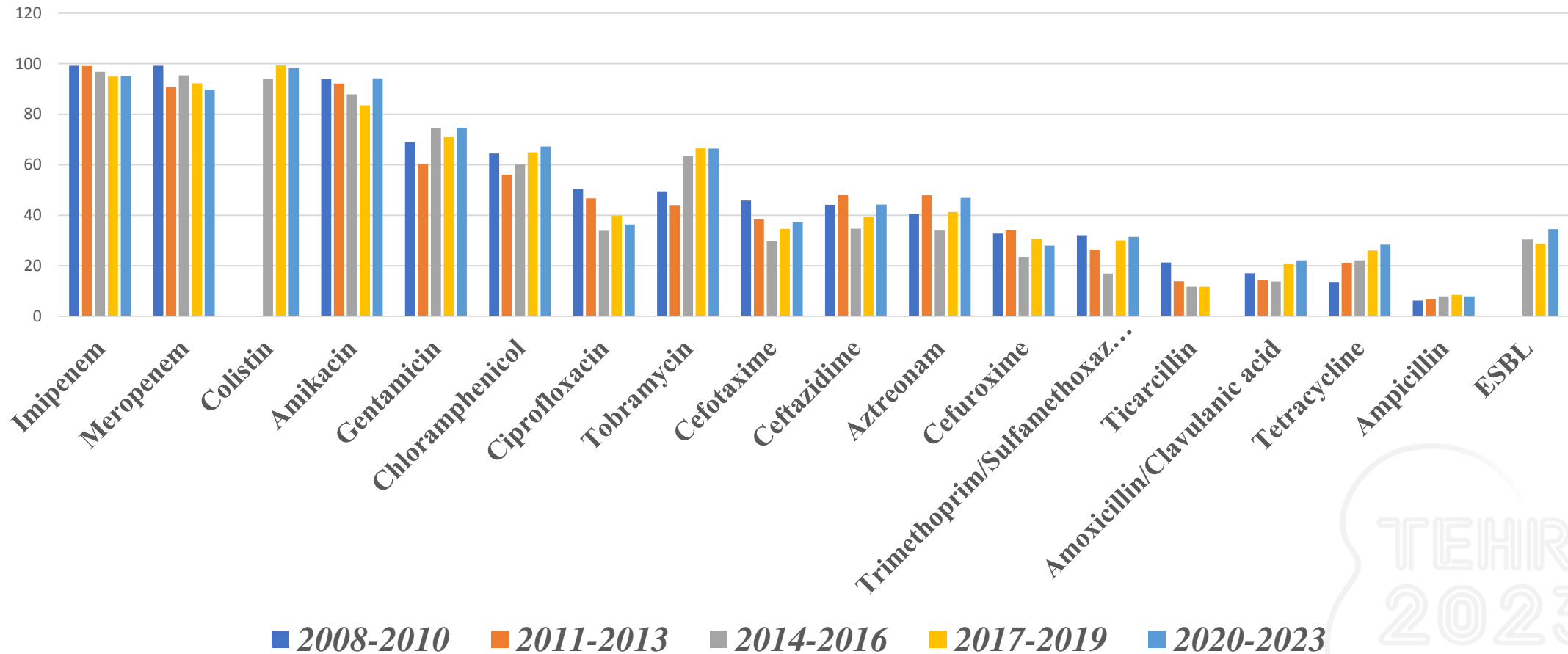
Table 1. Frequencies of isolates obtained from positive sterile body fluid cultures in different cities (N=858).

	City							
	Shiraz	Sari	Tabriz	Mashhad	Sanandaj	Ahwaz	Esfahan	Total
Gram positive cocci (N=224)								
<i>S. aureus</i>	54(24%)	11(5%)	35(15.5%)	1(0.5%)	36(16%)	85(38%)	2(1%)	224
Gram negative bacilli (N=634)								
<i>Klebsiella spp.</i>	22(15%)	47(32%)	12(8%)	31(21%)	16(11%)	8(5%)	12(8%)	148
<i>E. coli</i>	36(24.5%)	39(27%)	13(9%)	25(17%)	21(14.5%)	2(1%)	10(7%)	146
<i>Serratia spp.</i>	11(10.5%)	17(16%)	5(5%)	16(15%)	33(31.5%)	22(21%)	1(1%)	105
<i>Enterobacter spp.</i>	8(21%)	14(37%)	2(5%)	2(5%)	5(13.5%)	4(10.5%)	3(8%)	38
<i>Pseudomonas spp.</i>	19(20%)	45(47.5%)	5(5.3%)	16(16.8%)	4(4.1%)	3(3.2%)	3(3.2%)	95
<i>Acinetobacter spp.</i>	20(30%)	4(6%)	1(1.5%)	24(35.5%)	5(7.5%)	3(4.5%)	10(15%)	67
<i>Stenotrophomonas spp.</i>	5(14%)	10(28.5%)	1(3%)	14(40%)	1(3%)	3(8.5%)	1(3%)	35
Total	175	187	74	129	121	130	42	

The most common pathogenic bacteria Isolated from Bloodstream Infections, in five Episodes, Shiraz, Iran

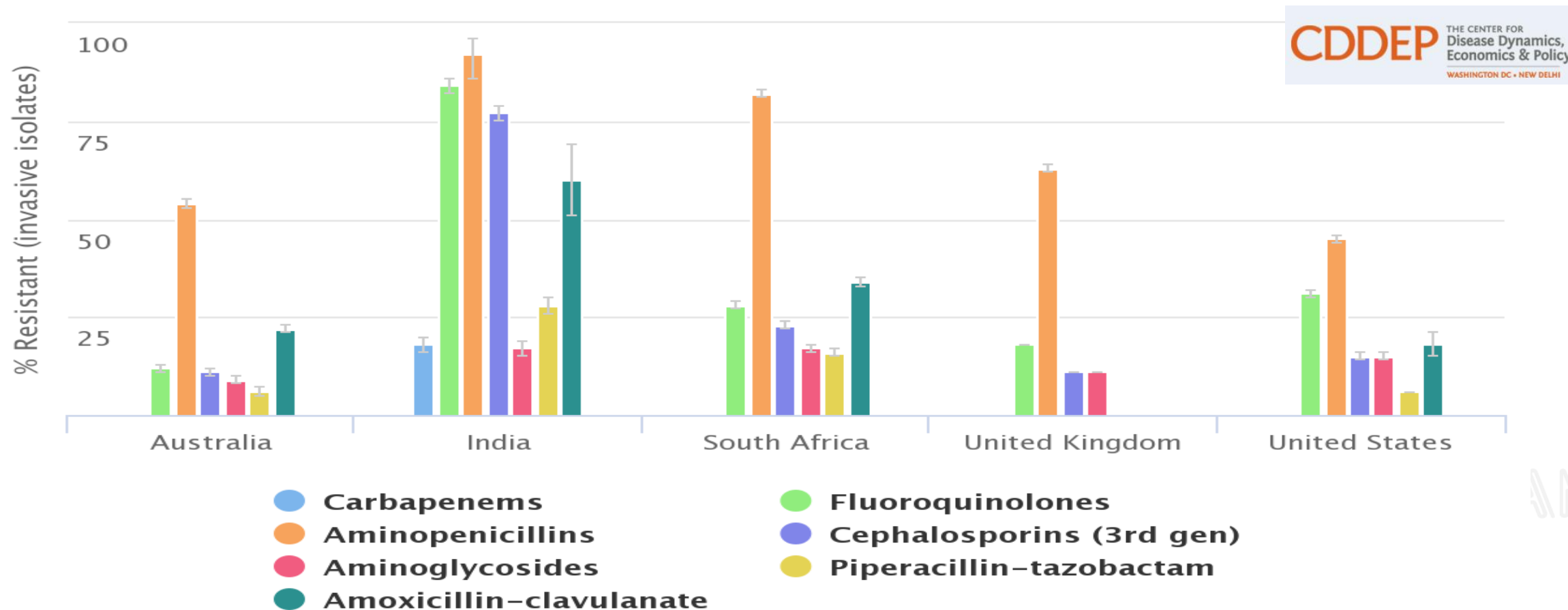


Rates of Sensitivity to Different Antibiotics Tested against 1292 strain of *Escherichia coli* Strains Isolated from Bloodstream Infections, in five Episodes, Shiraz, Iran



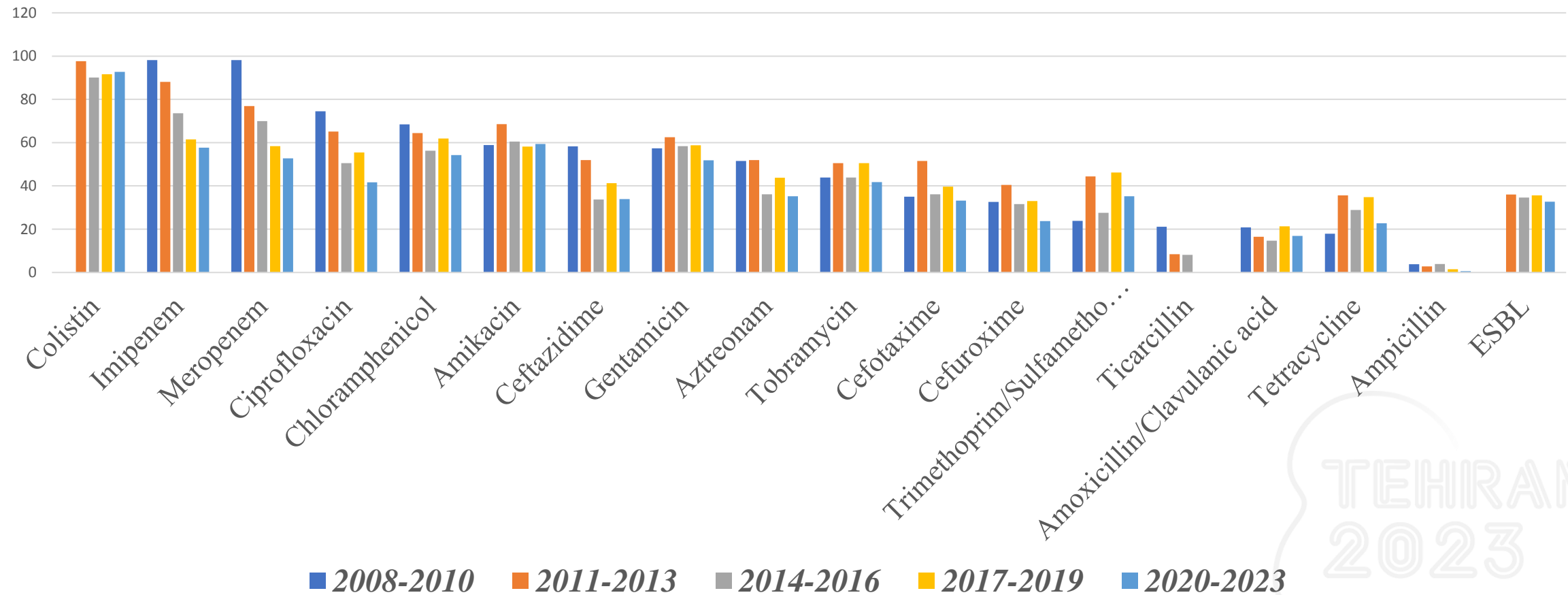
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Antibiotic Resistance of *Escherichia coli*

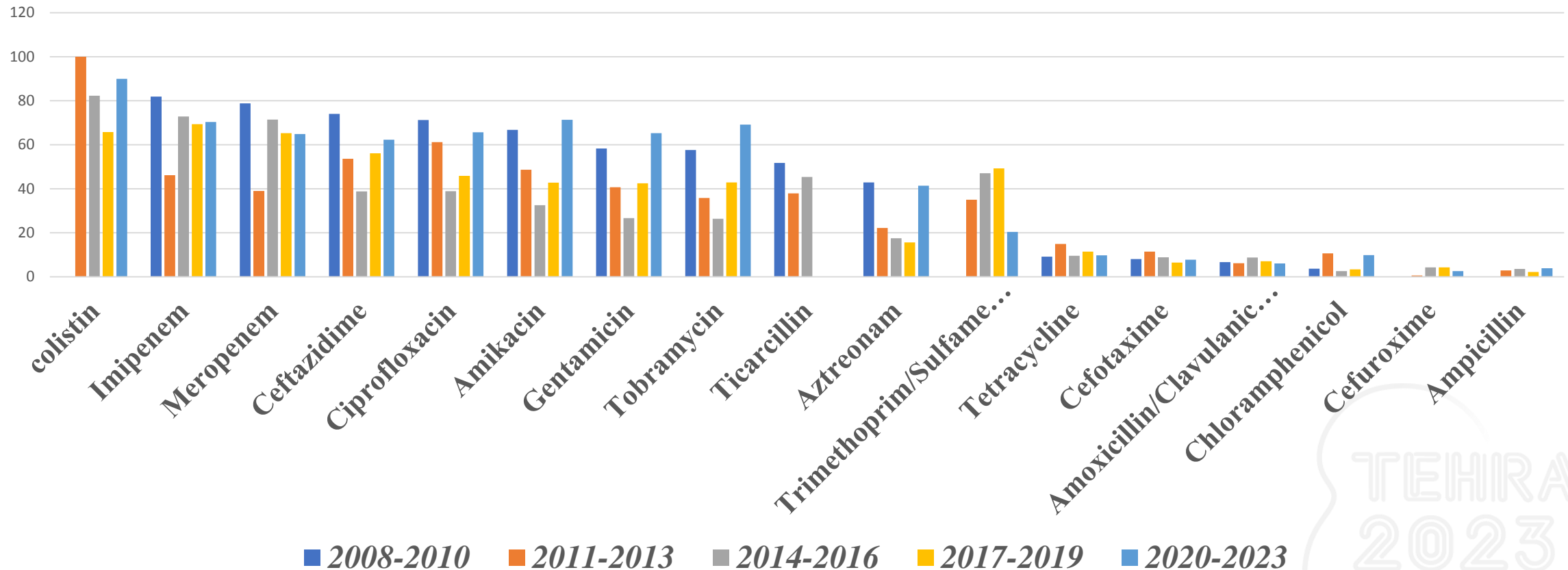


Center for Disease Dynamics, Economics & Policy (cddep.org)

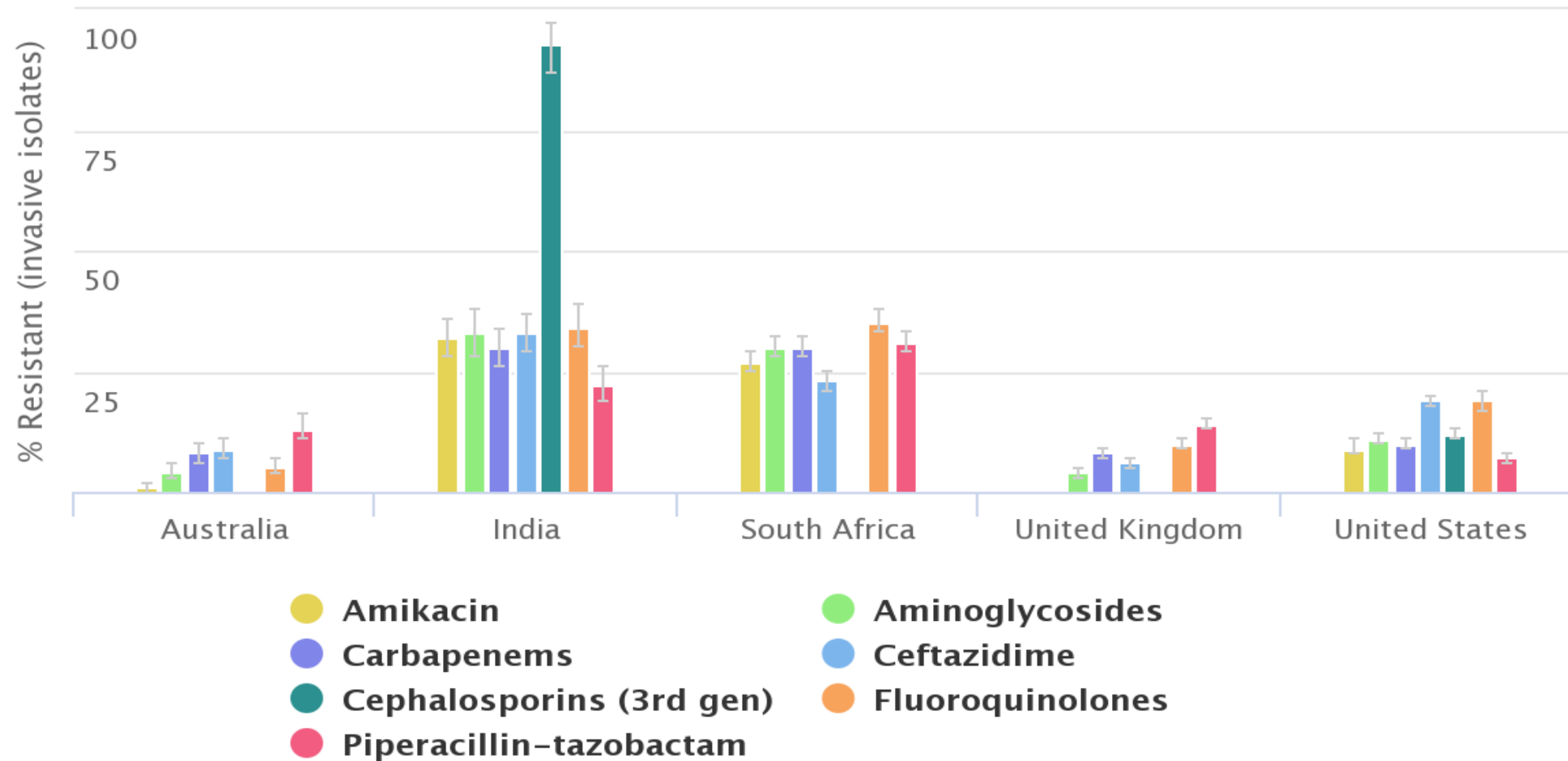
Rates of Sensitivity to Different Antibiotics against 925 strain of *Klebsiella spp.* Strains Isolated from Bloodstream Infections, in five Episodes, Shiraz, Iran



Rates of Sensitivity to Different Antibiotics Tested against 1294 strain of *Pseudomonas Sp.* Isolated from Bloodstream Infections, in five Episodes, Shiraz, Iran



Antibiotic Resistance of *Pseudomonas aeruginosa*

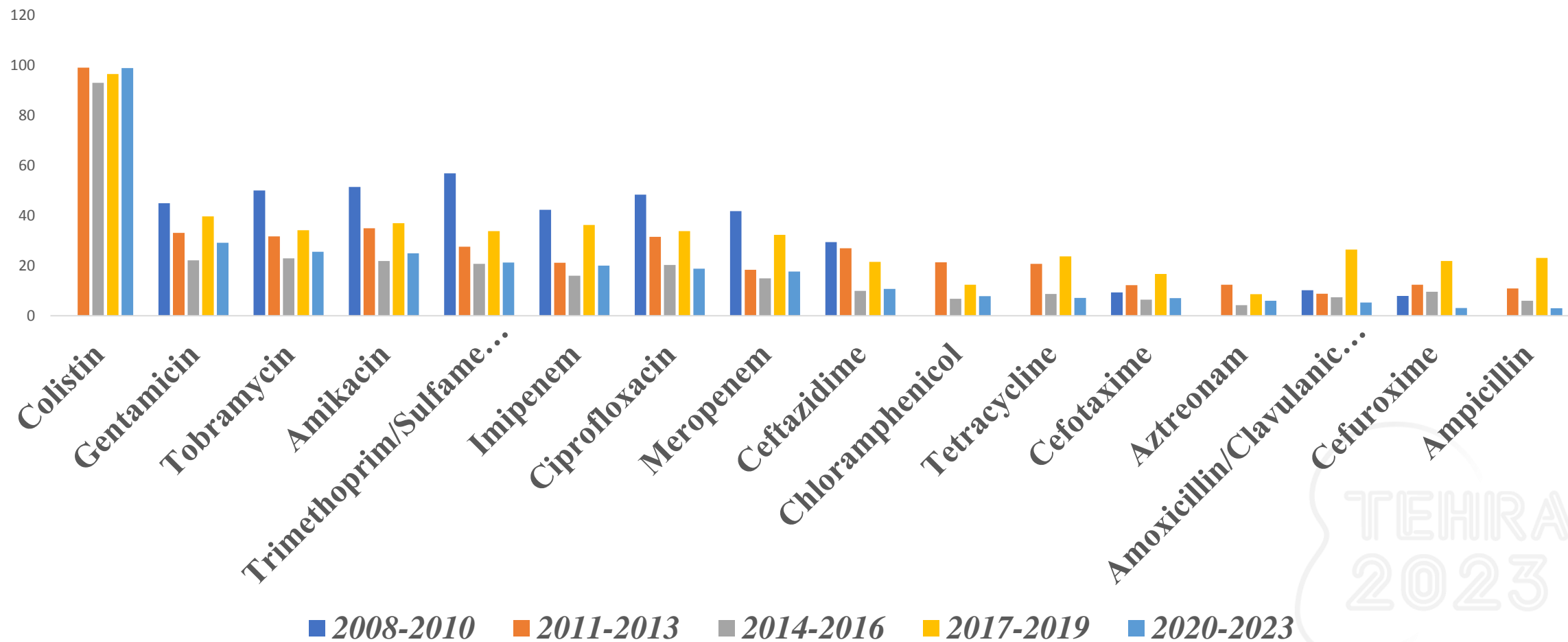


CDDEP THE CENTER FOR
Disease Dynamics,
Economics & Policy
WASHINGTON DC • NEW DELHI

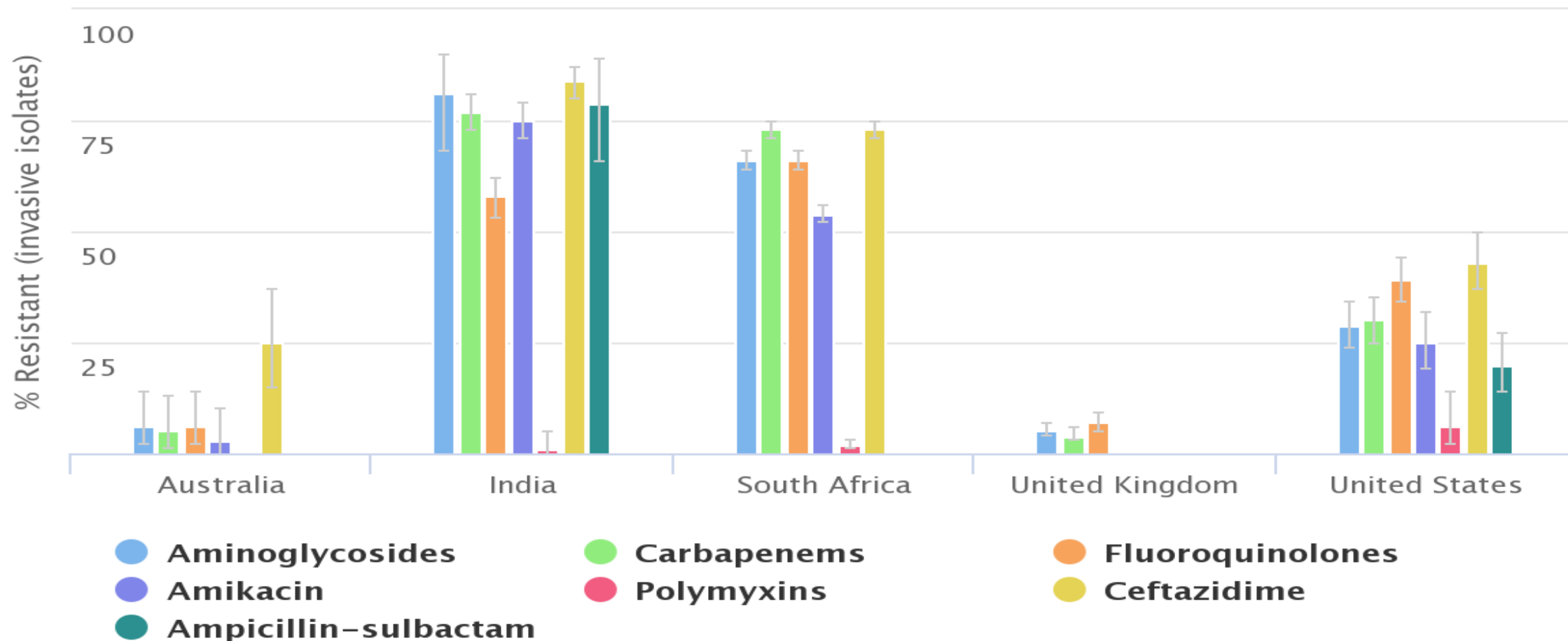
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Center for Disease Dynamics, Economics & Policy (cddep.org)

Rates of Sensitivity to Different Antibiotics Tested against 874 Strains of *Acinetobacter Sp.* Isolated from Bloodstream Infections, in Five Episodes, Shiraz, Iran

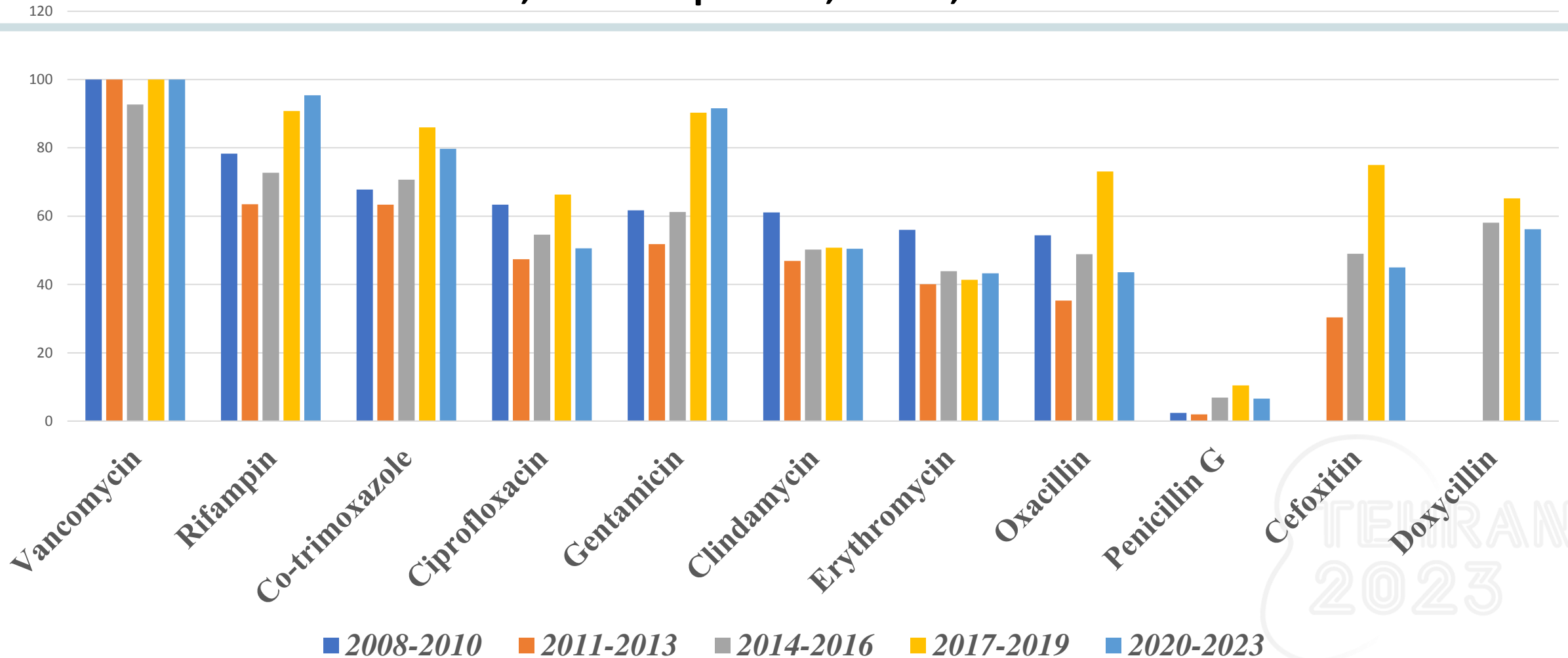


Antibiotic Resistance of *Acinetobacter baumannii*

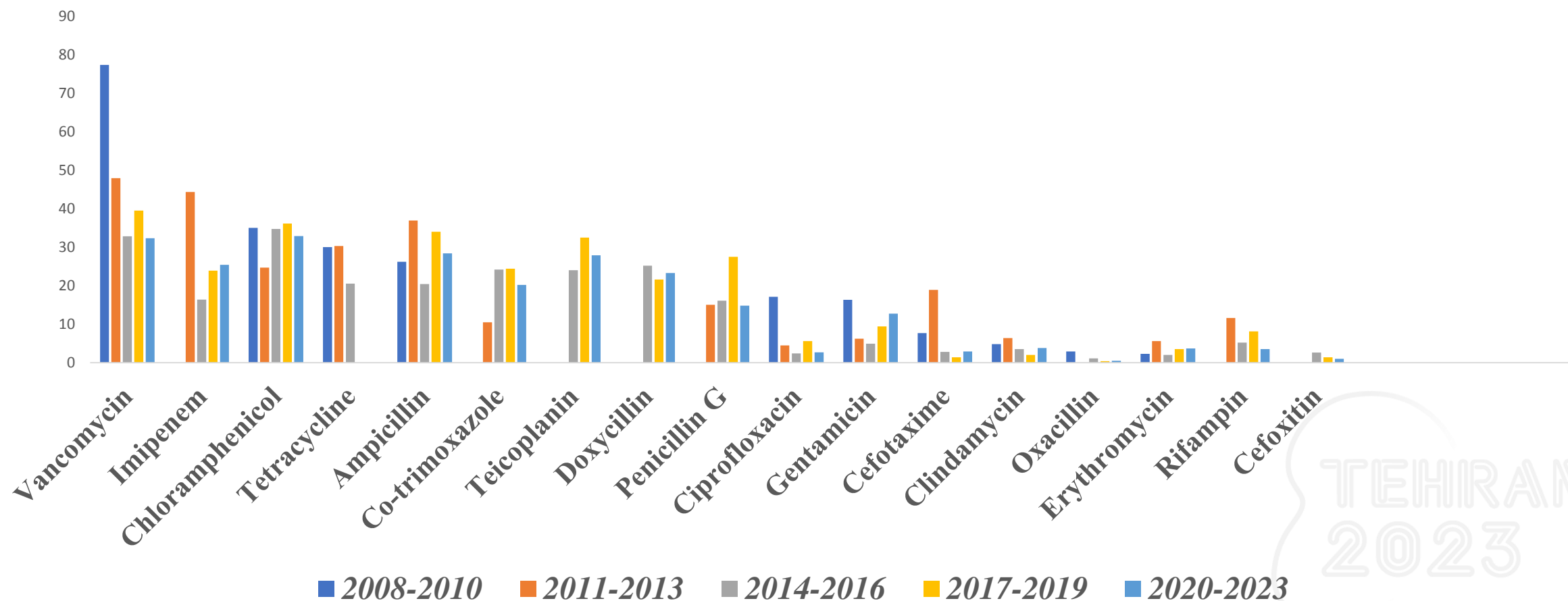


Center for Disease Dynamics, Economics & Policy (cddep.org)

Rates of Sensitivity to Different Antibiotics Tested against 1371 strain of *Staphylococcus sp.* Strains Isolated from Bloodstream Infections, in Five Episodes, Shiraz, Iran



Rates of Sensitivity to Different Antibiotics Tested against 988 strains of *Enterococcus Sp.* Isolated from Bloodstream Infections, in Five Episodes, Shiraz, Iran



Enterococcal Infections Treatment

✓ Ampicillin

- the drug of choice for monotherapy of susceptible *E faecalis* infection.

✓ Vancomycin

- Patients with a penicillin allergy or resistant strains

✓ Nitrofurantoin:

- Enterococcal cystitis

✓ Linezolid

- VRE

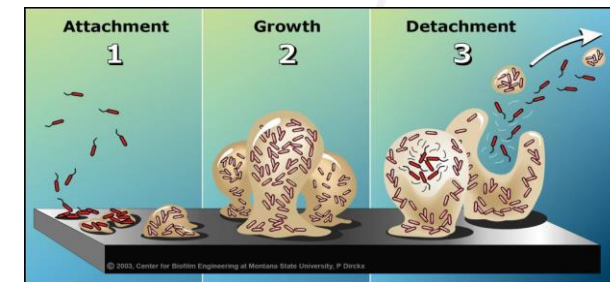
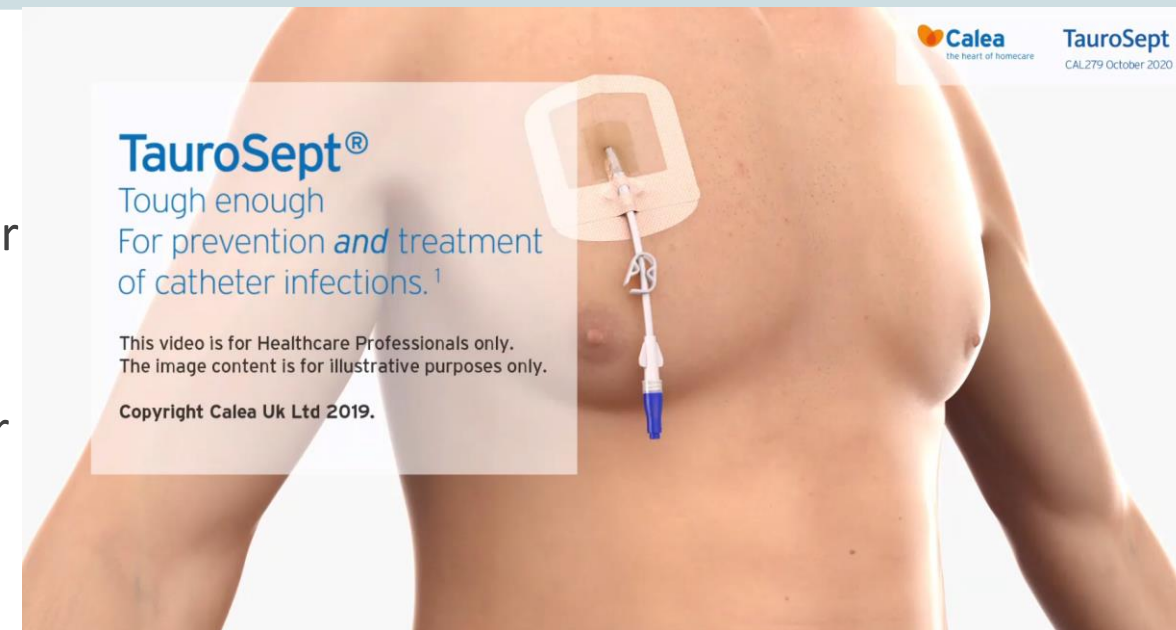
✓ Combination therapy

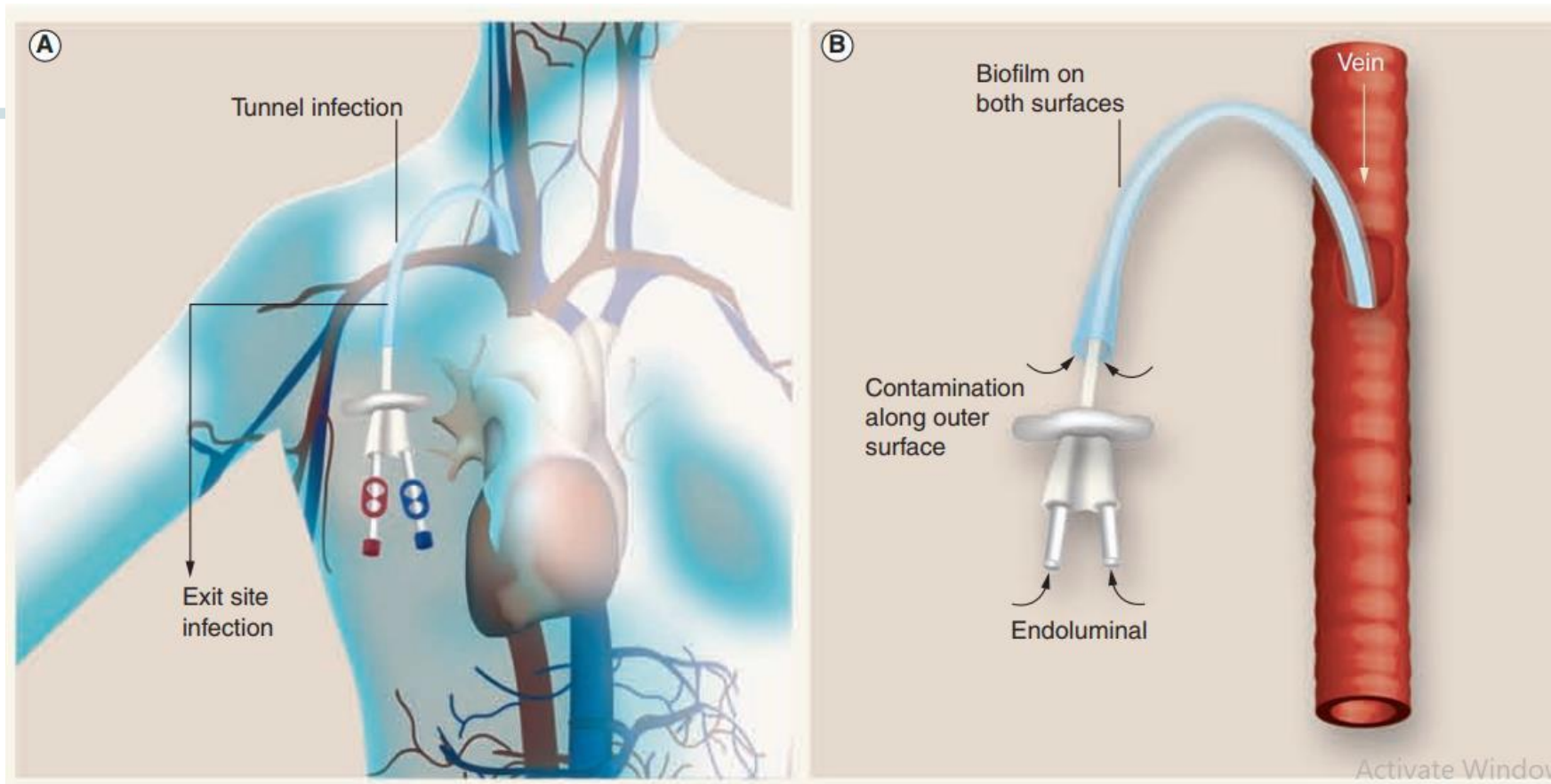
- a cell wall–active agent (eg, **ampicillin**, **vancomycin**) and an aminoglycoside (eg, **gentamicin**, streptomycin)

E. faecalis and E. faecium are naturally (intrinsically) resistant to cephalosporins

PATHOGENESIS: BIOFILM INFECTION

- More than **99.9%** of bacteria grow as aggregated **“sessile”** communities attached to surfaces, rather than as **“planktonic”** or free-floating cells in liquid
- **Within a few seconds**, phenotypic changes in the bacteria remarkably alter protein expression to further produce adhesions that irreversibly anchor the cell to the surface
- The microbial clumps are AB resistant (Biofilm microorganisms are **100–1000 times less susceptible** to antibiotics than their planktonic counterparts.
- **Heparin** is a promoter and **citrate** is an inhibitor of biofilm





The routes of contamination and infection.

(A) The dialysis catheter in the right internal jugular vein. Inflammation at the catheter exit site is defined as exit-site infection and tunnel infection is defined as inflammation of the tunnel superior to the catheter cuff.

(B) The routes of contamination of the dialysis catheter including contamination along the outer surface of the catheter and endoluminal contamination

INCIDENCE OF CRB

- An approximate incidence of one to two episodes of bacteremia per catheter-year
- In one study of 472 patients who had newly placed tunneled hemodialysis catheters, CRBSIs occurred in 35 percent by three months and 54 percent by six months
- Non-tunneled catheters are two- to threefold than tunneled catheters
- 10-fold higher in patients with tunneled catheters than either arteriovenous (AV) fistulas or grafts
- Metastatic infection rate: % specially with *S.aureus*
 - Septic arthritis, osteomyelitis, endocarditis, and epidural abscess

Judging CRB rate

< 1/1000 catheter days—Excellent
1–2/1000 catheter days—Good
3–5/1000 catheter days—Fair
6–7/1000 catheter days—Poor
> 7/1000 catheter days—Really bad



CLINICAL PRESENTATION

- Fever 47%
- Rigors alone 33%
- 20% No fever & rigors
 - Malaise
 - Encephalopathy
 - Hypotension
 - Exit site drainage
 - Catheter dysfunction
- Metastatic infection signs



DIAGNOSIS

- A false-negative diagnosis may increase patient morbidity and a false-positive diagnosis may result in inappropriate prescription of antibiotics and unnecessary procedures. It promotes the emergence of **antibiotic-resistant pathogens** and also generates **excess costs**.
- The diagnosis of CRBSI is confirmed by two blood cultures obtained before administration of antimicrobial therapy. (After AB at one hour the culture becomes negative in 60%)
- CDC definition:
 - **Definite** bloodstream infection: the same organism from a semiquantitative culture of the catheter tip (>15 colony-forming units per catheter segment) and from a peripheral or catheter blood sample in a symptomatic patient with no other apparent source of infection.
 - **Probable** bloodstream infection: defervescence of symptoms after antibiotic therapy with or without removal of catheter, in the setting in which blood cultures confirm infection, but catheter tip does not (or catheter tip does, but blood cultures do not) in a symptomatic patient with no other apparent source of infection.
 - **Possible** bloodstream infection: defervescence of symptoms after antibiotic treatment or after removal of the catheter in the absence of laboratory confirmation of bloodstream infection in a symptomatic patient with no other apparent source of infection.
- Follow-up culture should only be taken after one week of completion of AB therapy. A new tunneled catheter should not be placed until after blood cultures are negative in patients with CRBSI due to Staphylococcus aureus and Candida, and preferably (when feasible) for infections with other organisms



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Treatment of CRBSI in HD patients

KDOQI®

KIDNEY DISEASE OUTCOMES
QUALITY INITIATIVE

National Kidney Foundation

**KDOQI CLINICAL PRACTICE GUIDELINE FOR VASCULAR
ACCESS: 2019 UPDATE**

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TREATMENT

✓ Two strategies:

1. Antimicrobial therapy for systemic infection

- Treatment of catheter-related bacteremia with systemic antibiotics alone (without catheter removal) is relatively ineffective in eradicating the source of infection.
- In several large clinical series, clinical cure in **only 22% to 37%** of patients.

2. Treatment of the catheter-associated biofilm as the source of infection

- Catheter removal:
 - Immediately in Temporary catheters and sometimes in CTC.
- Catheter exchange “save the site rather than the catheter”
- ***Ab lock solution***

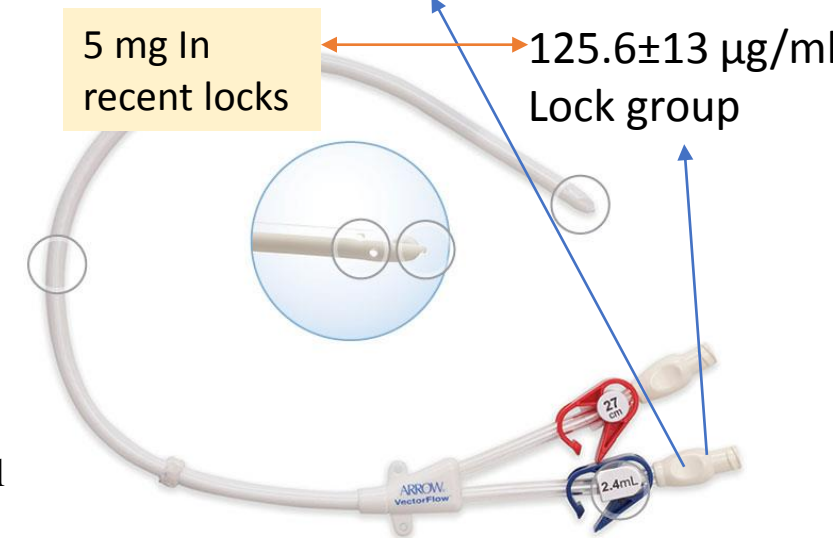


Insufficient penetration of systemic vancomycin into the PermCath lumen -NDT 2000

B Bastani, J Minton, S Islam

- ✓ **Methods.** We compared serum and intraluminal (0.3–0.5 ml aspirate from the venous port of the catheter) vancomycin concentrations in 24 chronic haemodialysis patients, with documented bacteraemia, who had received prior systemic vancomycin therapy with 14 similar patients who had additionally received 'vancomycin-lock technique' (**100 µg/ml of vancomycin in heparin solution**) after each haemodialysis session.
- ✓ **Results.** Despite serum vancomycin concentration of ~17 µg/ml in each group, the vancomycin concentration in the venous hub of the catheter was only 0.2 ± 0.6 µg/ml in the former group, in sharp contrast to 125.6 ± 13 µg/ml in the latter group.
- ✓ In the in-vitro experiments, three PermCaths filled with standard heparin solution were incubated for 48 h in 100 ml of plasma containing **20 µg/ml of vancomycin**.. Vancomycin concentration in each port **was 0.2 ± 0.1 µg/ml in the aspirated samples**.
- ✓ Finally, two PermCaths filled with the standard heparin solution were incubated for 48 h in 100 ml of plasma containing 20 µg/ml of vancomycin, after which the catheters were sectioned at 4-cm intervals. Only the **distal 4 cm** of the catheters had vancomycin concentrations of **2 and 5 µg/ml**, the remaining segments had levels ≤ 0.5 µg/ml intraluminal

vancomycin concentration in the venous hub 0.2 ± 0.6 µg/ml in non lock



serum vancomycin concentration of ~17 µg/ml

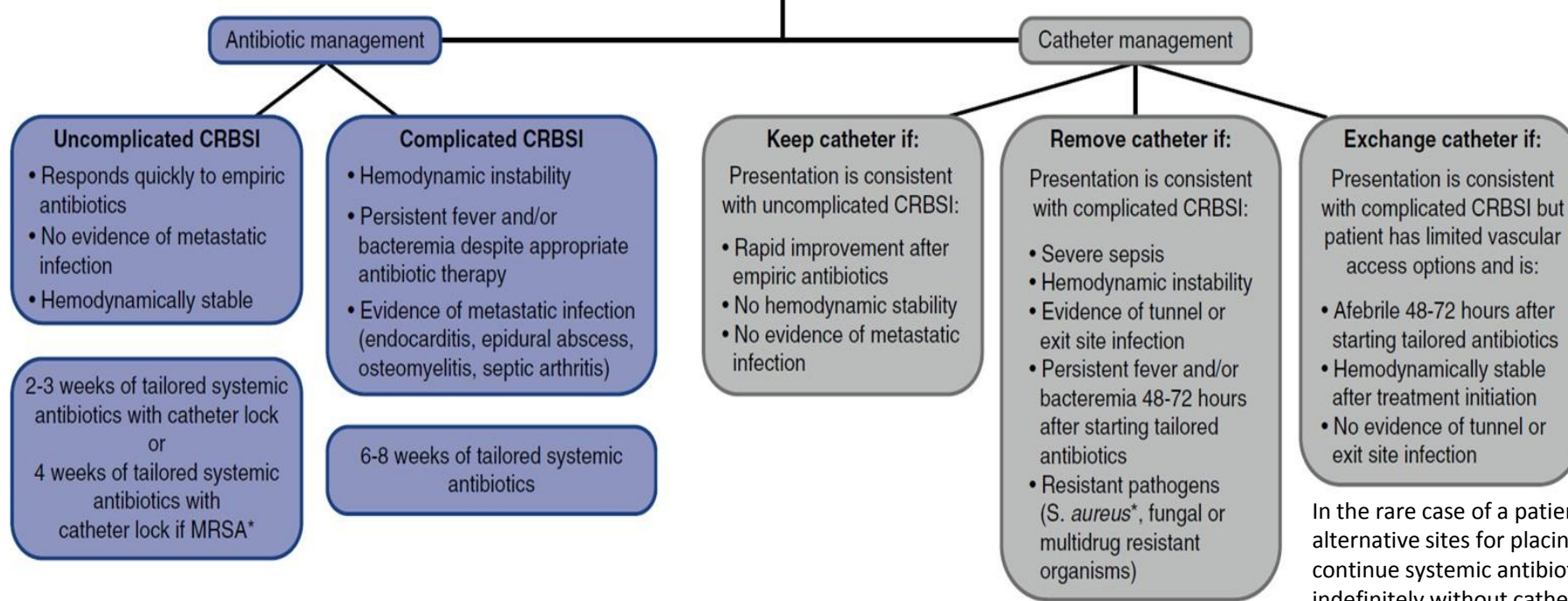
Management of the Hemodialysis Patient with Catheter-Related Bloodstream Infection

Crystal A. Farrington and Michael Allon
Clin J Am Soc Nephrol 14: 611–613, 2019. doi: <https://doi.org/10.2215/CJN.13171118>

Suspected catheter-related bloodstream infection
• Temperature $\geq 37.8^{\circ}\text{C}$ • Rigors • Tunnel or exit site purulence

Obtain blood cultures from the catheter lumen and the dialysis circuit and start empiric antibiotics

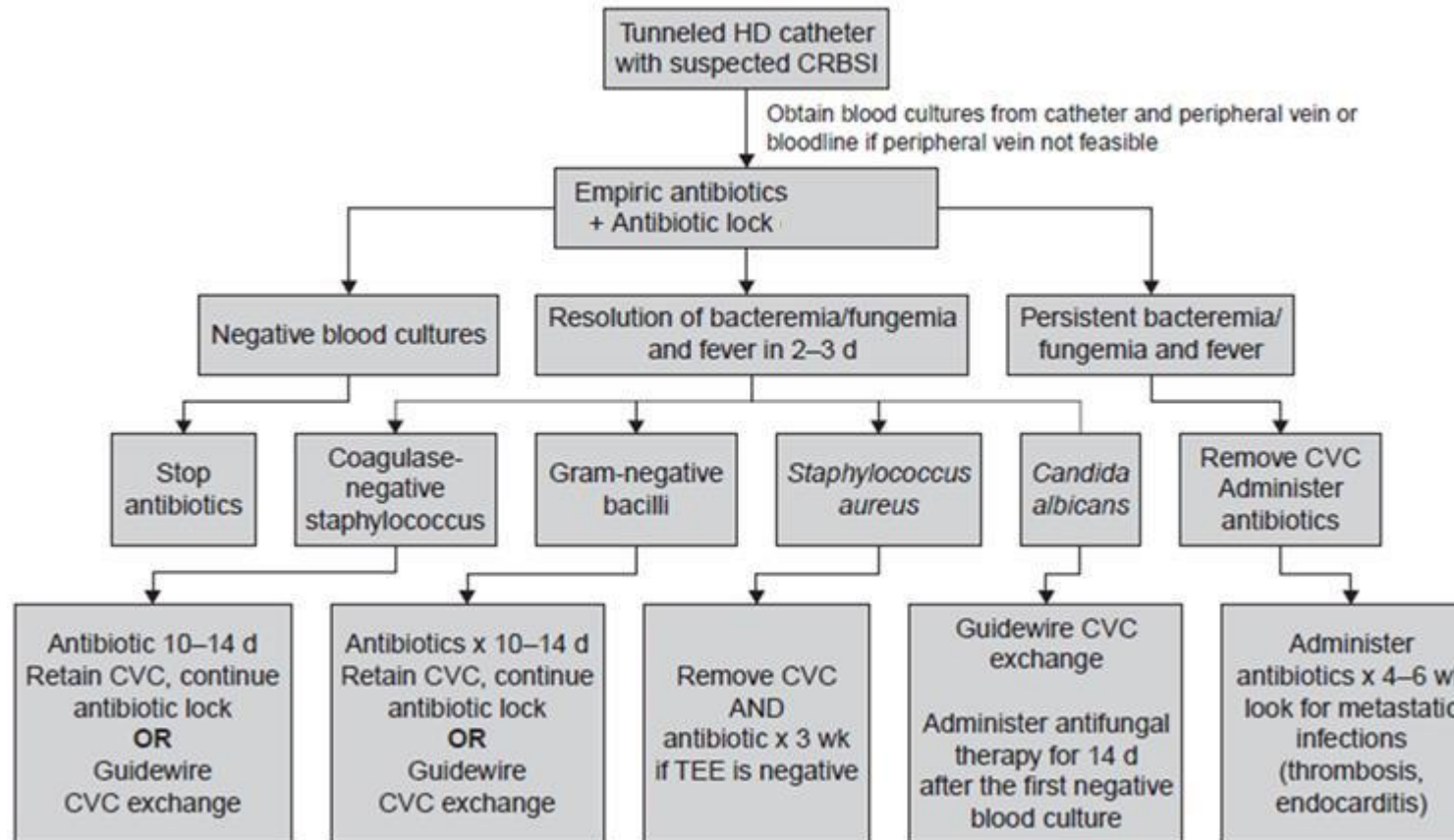
Diagram 1: management of hemodialysis Patient with CRBSI



Systemic antibiotic and catheter lock

	Systemic antibiotic	Catheter lock
Empiric antibiotics	<p>Vancomycin 20 mg/kg loading dose infused over the last one to two hours of hemodialysis (HD) and ceftazidime 1 gm immediately after HD</p> <p>Continue vancomycin 1 gm over the last hour of each subsequent HD session and ceftazidime 1 gm immediately after HD while awaiting blood culture results and antibiotic sensitivities</p> <p>Daptomycin 9 mg/kg given over the last 30 minutes of HD may be used as an alternative to vancomycin in vancomycin-allergic patients or in cases of vancomycin-resistant enterococci (VRE)</p> <p>Gentamicin 1 mg/kg following HD may be used as an alternative to ceftazidime, but carries a substantial risk of ototoxicity</p>	<p>Vancomycin/ceftazidime/heparin: Vancomycin (1 mL of 5 mg/mL in normal saline solution) plus ceftazidime (0.5 mL of 10 mg/mL in normal saline solution) plus heparin (0.5 mL of 1000 units/mL solution)</p>
Gram negative bacteria	Ceftazidime 1 gm immediately after HD	Ceftazidime/heparin: Ceftazidime (1 mL of 10 mg/mL in normal saline solution) plus heparin (1 mL of 1000 units/mL solution)
Methicillin sensitive Staphylococcus aureus	Cefazolin 2 gm immediately after HD	Cefazolin/heparin: Cefazolin (1 mL of 20 mg/mL in normal saline solution) plus heparin (1 mL of 1000 units/mL solution)
Methicillin resistant Staphylococcus aureus	Vancomycin 1 gm infused over the last hour of HD, or daptomycin 9 mg/kg over the last 30 minutes of HD	Vancomycin/heparin: Vancomycin (1 mL of 5 mg/mL in normal saline solution) plus heparin (1 mL of 1000 units/mL solution)

Management of HD catheter with suspected CRBSI according to pathogen



AB LOCK PREPARATION

pharmacy preparation instructions

Storage & Stability:²

Lock Solution	Stability
Vancomycin	72hr at room temp ³
Cefazolin	72hr at room temp ³
Ceftazidime	7 days at room temp ⁴
Ciprofloxacin	7 days at room temp ⁵
Gentamicin	72hr at room temp ³
Ampicillin	24hr at room temp ^{6,7}

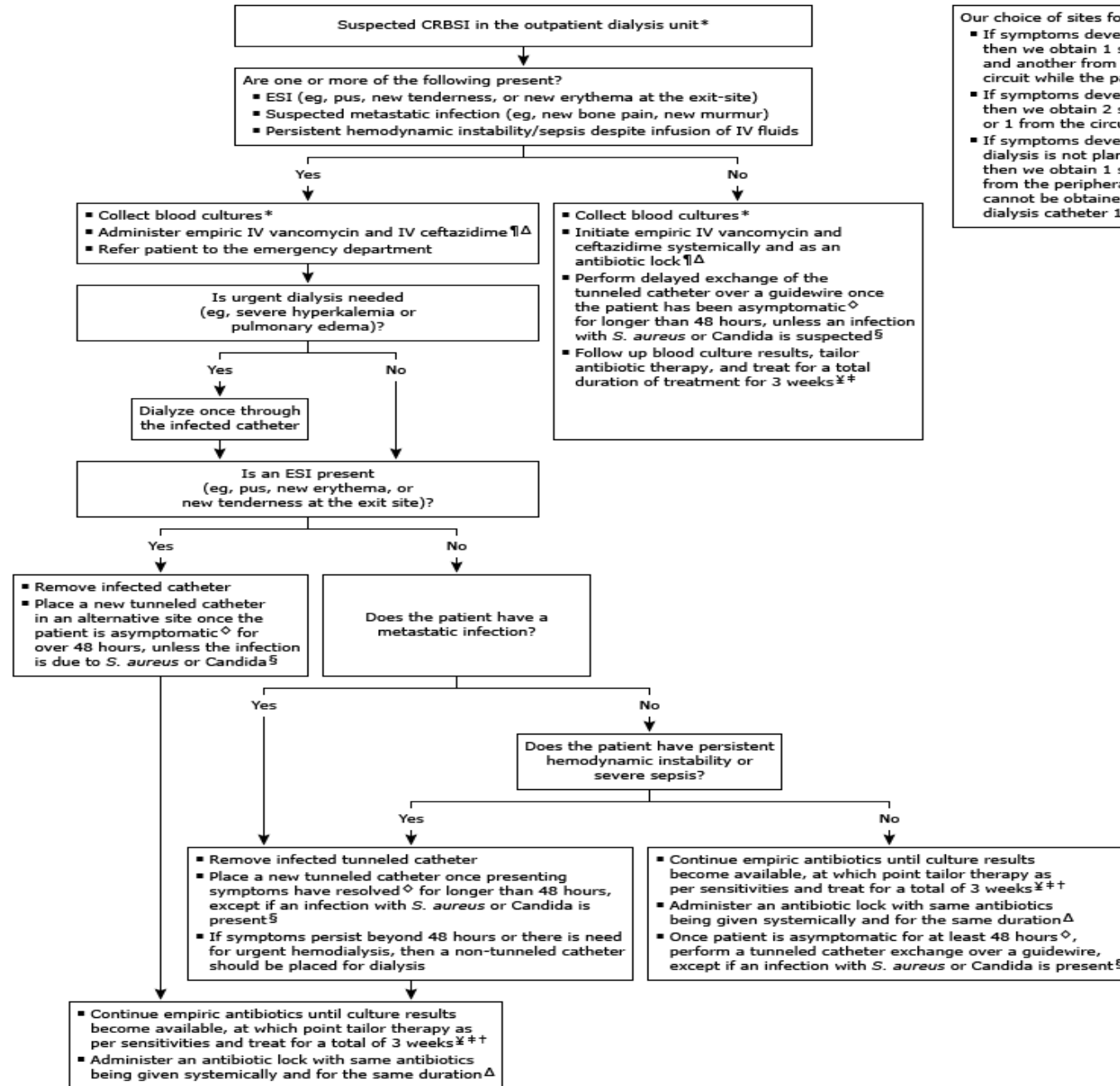
Pharmacy Technician Preparation Instructions

Antibiotic Solution final concentration	Pharmacy preparation instructions
Vancomycin 2.5 mg/mL + heparin 2500 units/mL	<ol style="list-style-type: none"> 1. Dilute 500 mg of vancomycin with 10 mL of NS (50 mg/mL) 2. Remove 1 mL and further dilute with 9 mL of sodium chloride resulting in a vancomycin concentration of 5 mg/mL – Label as "solution A" 3. Draw up 1.5 mL of 5,000 units/mL heparin into a syringe and mix with 1.5 mL of solution A (vancomycin 7.5mg) for 3 mL of final solution *If a precipitate appears when mixing vancomycin with heparin, continue agitating the solution for ~10 seconds until the precipitation resolves
Cefazolin 5 mg/mL + heparin 2500 units/mL	<ol style="list-style-type: none"> 1. Dilute 500 mg cefazolin vial with 10 mL of normal saline (50mg/mL) 2. Remove 1 mL of the cefazolin 50mg/mL solution and further dilute with 4 mL of NS resulting in a cefazolin concentration of 10 mg/mL – Label as "Solution A" 3. Draw up 1.5 mL of heparin 5,000 units/mL into a syringe and mix with 1.5 mL of Solution A (cefazolin 15mg) 4. Dispense 3mL of the final solution
Ceftazidime 0.5 mg/mL + heparin 100 units/mL	<ol style="list-style-type: none"> 1. Dilute 1000 mg ceftazidime product with 10 mL of NS, for a concentration of 100 mg/mL – Label as "solution A" 2. Remove 1 mL of solution A (ceftazidime 100mg) and further dilute with 19 mL of sodium chloride resulting in a ceftazidime concentration of 5 mg/mL – Label as "Solution B" 3. Withdraw 1 mL of solution B (5 mg) and further dilute with 5 mL of NS for a final concentration of 1 mg/mL – Label as "Solution C" 4. Withdraw 1.5 mL of solution C (ceftazidime 1.5mg) and add 0.3 mL of heparin 1,000 units/mL 5. QS to 3 mL with NS
Ciprofloxacin 0.2 mg/ml + heparin 5000 units/mL	<ol style="list-style-type: none"> 1. Starting with a ciprofloxacin 200mg/20mL vial, withdraw 0.06 mL of ciprofloxacin solution (ciprofloxacin 0.6 mg) – label as "solution A" 2. Add 1.5 mL of heparin 10,000 units/mL to solution A (ciprofloxacin 0.6 mg) 3. QS to 3 mL with NS
Gentamicin 1 mg/mL + heparin 2500 units/mL	<ol style="list-style-type: none"> 1. Using 10 mg/mL (2 mL vial) gentamicin, withdraw 1 mL (10mg) and further dilute with 4 mL of NS for a final concentration of 2mg/mL – Label as "solution A" 2. Withdraw 1.5 mL of solution A (gentamicin 3mg) 3. Add 1.5 mL of heparin 5,000 units/mL to the 1.5 mL of solution A, for a total volume of 3 mL
Ampicillin 10 mg/mL + heparin 5,000 units/mL	<ol style="list-style-type: none"> 1. Dilute 1000 mg of ampicillin in 10 mL of NS (100 mg/mL) 2. Withdraw 0.5 mL of the ampicillin 100 mg/mL solution (ampicillin 50mg) 3. Add 1.5 mL of heparin 10,000 units/mL 4. QS to 5 mL with NS 5. Dispense 3mL of final solution

Ab lock therapy in treatment of CRBSI

- ✓ Same as that we choose for treatment
- ✓ If the patient has a history of or active heparin-induced thrombocytopenia, substitute normal saline for heparin.
- ✓ If the volume of the catheter lumen exceeds 2 mL, the difference in volume should be made up with additional heparin or normal saline
- ✓ Some centres may lack Ab locks and continue systemic therapy until the catheter is replaced.
- ✓ The success rates of antibiotic locks in curing CRBSI were highly dependent upon the infecting organism the success rate is :
 - 90 to 100 percent with gram-negative infections
 - 80 percent with *Staphylococcus epidermidis* coagulase-negative staphylococcal infections
 - 60 percent with *Enterococcus* infections,
 - 40 percent with *S. aureus* infections

Suspected CRBSI in the outpatient dialysis unit



Our choice of sites for a blood culture sample are: *

- If symptoms develop between dialysis sessions, then we obtain 1 sample from the dialysis catheter and another from the peripheral vein or hemodialysis circuit while the patient is on dialysis.
- If symptoms develop during a dialysis treatment, then we obtain 2 samples from the hemodialysis circuit or 1 from the circuit and another from a peripheral vein.
- If symptoms develop between dialysis sessions and dialysis is not planned within the following few hours, then we obtain 1 sample from the catheter and another from the peripheral vein. If a peripheral vein sample cannot be obtained, then we obtain 2 samples from the dialysis catheter 10 to 15 minutes apart.

Prevention

Hemodialysis International 2018

REVIEW ARTICLE



Prevention of hemodialysis catheter infections: Ointments, dressings, locks, and catheter hub devices

Ladan GOLESTANEH, Michele H. MOKRZYCKI*

Division of Nephrology, Department of Medicine, Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, New York, USA

Review > Clin J Am Soc Nephrol. 2020 Jan 7;15(1):132-151. doi: 10.2215/CJN.06820619.

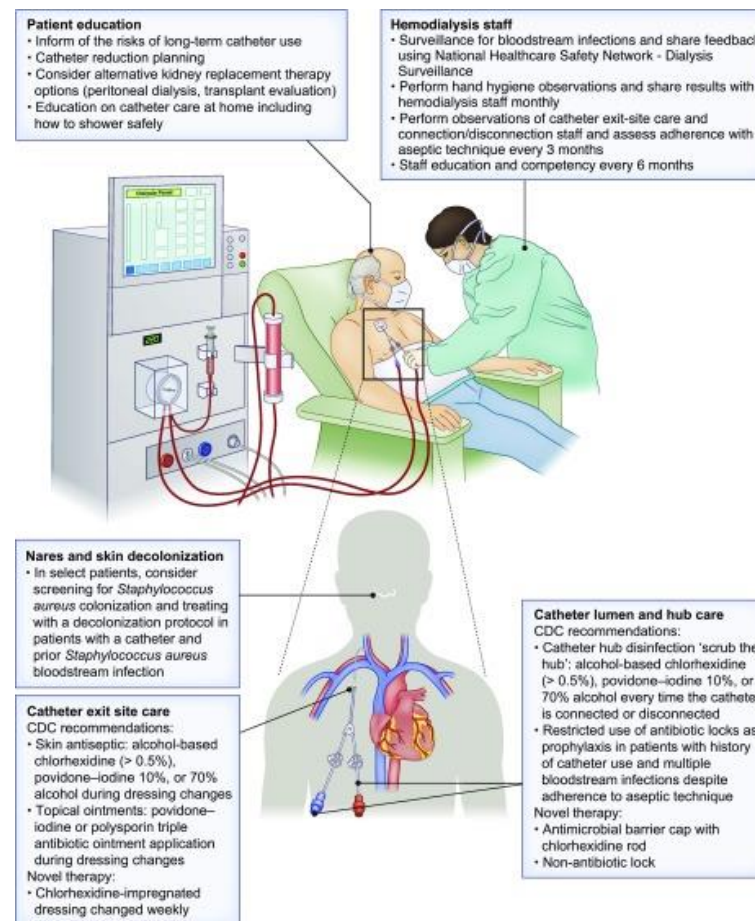
Epub 2019 Dec 5.

Prevention of Bloodstream Infections in Patients Undergoing Hemodialysis

Molly Fisher¹, Ladan Golestaneh¹, Michael Allon², Kenneth Abreo³, Michele H Mokrzycki¹

Affiliations + expand

PMID: 31806658 PMCID: PMC6946076 DOI: 10.2215/CJN.06820619



PROPHYLAXIS

- Systemic Prophylactic Antibiotics

- is a common practice in some institutions , but studies have demonstrated that oral or parenteral antibacterial or antifungal drugs do not reduce the incidence of CRB.

- Exit-Site Infection

- Not for cuffed catheter

- Contamination of the Catheter Hub

- Is the major factor(breathing ,touching ,long exposure to air)
- Elimination of nasal colonization has little effect
- Mask for nurse and patient
- Hub protocol is very effective and important



PROPHYLAXIS

■ Daily Catheter Site Care

- The use of either povidone-iodine ointment or mupirocin at the exit site until it is healed has been advocated (CRB was decreased by 78% by topical mupirocin)
- Prolonging the use of an antibiotic ointment with HD catheters after the site has healed has not been shown to offer any advantage and increases the rate of catheter colonization with Candida

■ Cleansing of the Site

- The site be cleansed with chlorhexidine 2% with 70% alcohol

■ Bandage Covering Site

- Protect from infection and immobilization
- Transparent, semipermeable polyurethane dressings are very popular (no difference in infection rate with gauze)



PROPHYLAXIS

PROTOCOL FOR CATHETER CARE IN THE HEMODIALYSIS FACILITY

- The **patient** and the **nurse** doing the dialysis hook-up should wear a **mask** during the entire time that the catheter is
- The nurse must wear a fresh pair of **disposable gloves** for the hook-up procedure
- Use **two swabs** soaked in chlorhexidine 2% with 70% alcohol
 - Using one hand grasp the connection between the hub and cap with one swab
 - Use the other swab in the opposite hand to cleanse from the catheter connection up the catheter for 10 cm
 - Cleanse the hub connection and the cap vigorously with the first swab
- Remove the cap in preparation for making the connection . Do not allow the hub to touch anything that is not sterile
- The catheter hubs should be **connected immediately** . They should never be allowed to remain exposed to the air
- This procedure should be **repeated at the time the patient is disconnected** at the end of dialysis or for any other reason
- Catheter manipulation should be kept to an absolute **minimum**





Targeting COVID-19 prevention in hemodialysis facilities is associated with a drastic reduction in central venous catheter-related infections

Marco Heidempergher¹ · Gianmarco Sabiu^{1,2} · Maria Antonietta Orani¹ · Giovanni Tripepi³ · Maurizio Gallieni^{1,2,4}

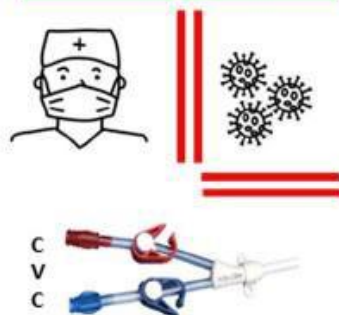
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Study design



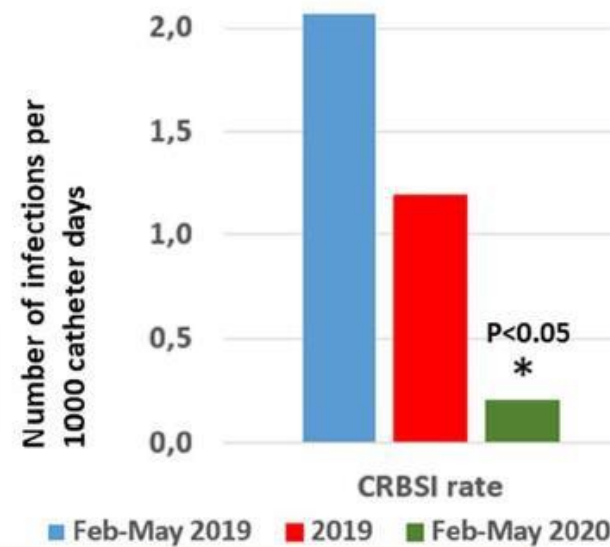
Retrospective cohort study in 71 hemodialysis patients using CVC. Catheter related bloodstream infections (CRBSI) rates during the COVID-19 pandemic were compared to the previous year

Intervention



Stricter infection prevention measures in dialysis units during the COVID-19 outbreak


Outcomes



Just by strengthening the universal precautions because of the COVID-19 pandemic, the rate of CRBSIs fell by 80% compared to the whole 2019 and over 90% compared to the same period of 2019.



Method



The Centers for
Disease Control
Core Interventions for
Dialysis Bloodstream
Infection (BSI)
Prevention

1. Surveillance and feedback using NHSN

Conduct monthly surveillance for BSIs and other dialysis events using CDC's National Healthcare Safety Network (NHSN). Calculate facility rates and compare with rates in other NHSN facilities. Actively share results with front-line clinical staff

2. Hand hygiene observations

Perform observations of hand hygiene opportunities monthly and share results with clinical staff

3. Catheter/vascular access care observations

Perform observations of vascular access care and catheter accessing quarterly. Assess staff adherence to aseptic technique when connecting and disconnecting catheters and during dressing changes. Share results with clinical staff

4. Staff education and competency

Train staff on infection control topics, including access care and aseptic technique. Perform competency evaluation for skills such as catheter care and accessing every 6–12 months and upon hire

5. Patient education/engagement

Provide standardized education to all patients on infection prevention topics including vascular access care, hand hygiene, risks related to catheter use, recognizing signs of infection, and instructions for access management when away from the dialysis unit

6. Catheter reduction

Incorporate efforts (e.g., through patient education, vascular access coordinator) to reduce catheters by identifying and addressing barriers to permanent vascular access placement and catheter removal

7. Chlorhexidine for skin antisepsis

Use an alcohol-based chlorhexidine (>0.5%) solution as the first-line skin antiseptic agent for central line insertion and during dressing changes^a

8. Catheter hub disinfection

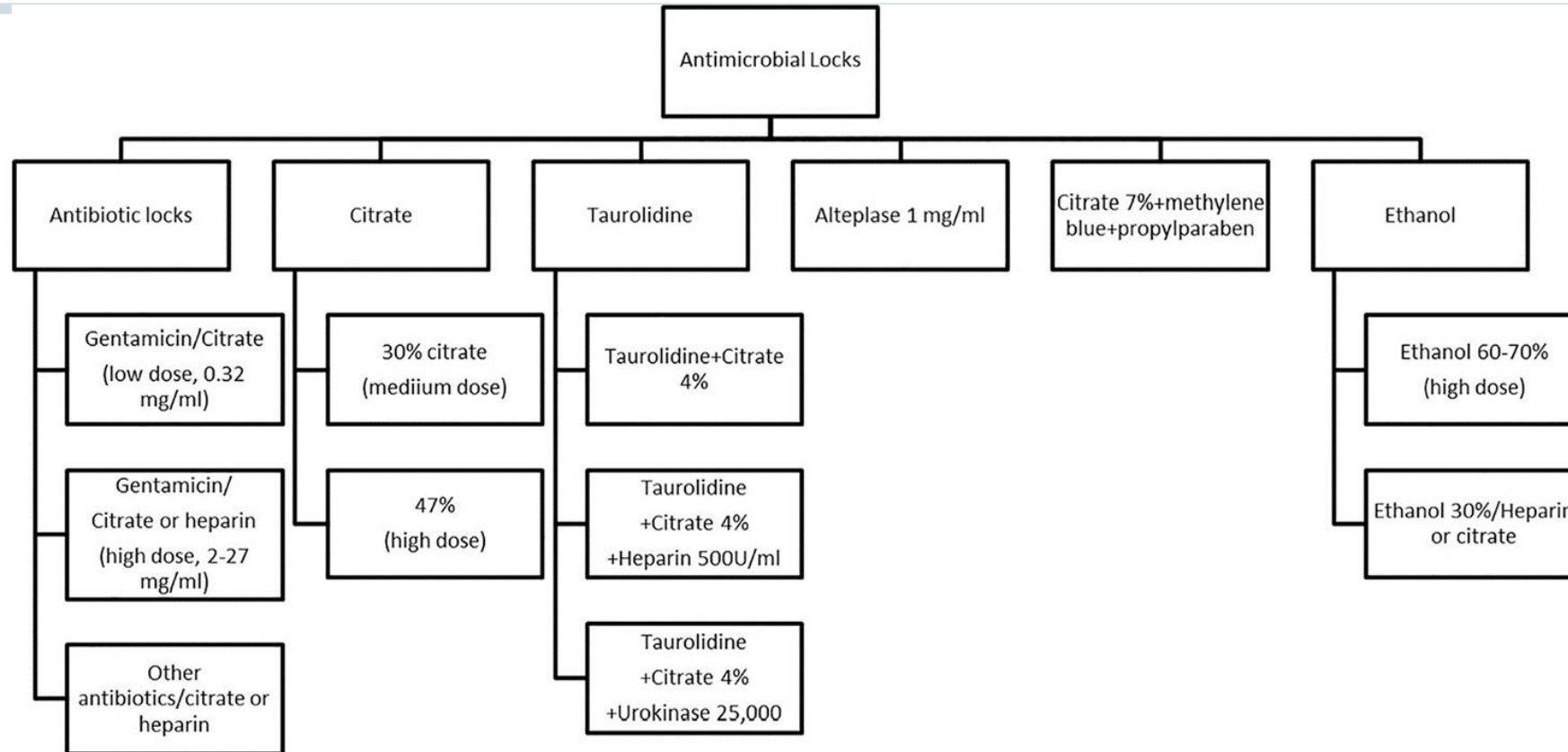
Scrub catheter hubs with an appropriate antiseptic after cap is removed and before accessing. Perform every time catheter is accessed or disconnected^b

9. Antimicrobial ointment

Apply antibiotic ointment or povidone-iodine ointment to catheter exit sites during dressing change^c

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PREVENTION OF HEMODIALYSIS CATHETER INFECTIONS



Seven kinds of antimicrobials (cloxacillin, cefotaxime, linezolid, vancomycin, gentamicin, minocycline, taurolidine) and ethanol can be chosen for preventing CRBSI(K.X. Sheng et al.2020)

The ideal lock solution for prophylaxis

- ✓(1) Cidal activity against a broad spectrum of gram-positive and gram-negative bacteria, as well as fungi
- ✓(2) low likelihood of promoting antibiotic-resistant bacteria
- ✓(3) Compatible with the catheter material and anticoagulant agent
- ✓(4) Safe if inadvertently instilled systemically



Heparin(UFH) catheter lock

PROS	cons
<ul style="list-style-type: none">+ Economic and applicable value.+ No consensus on the optimal concentration.(1000-10000)	<ul style="list-style-type: none">- No antibacterial effect- Promotes the formation of staphylococcal biofilms and makes the patients prone to CRBSI, which increases with increases in heparin concentration and stimulation time- The bacteria associated with heparin-stimulating biofilms have a high level of resistance to vancomycin.- HIT

clinical recommendation:

- 1000 U/mL, Only In patients without a history of HIT and those with a low-risk infection.
- 5000 U/ml, In catheter thrombosis
- Drug compatibility between heparin and other antibiotics, including aminoglycosides, b-lactams, glycopeptides, quinolones, and macrocyclic lipid antibiotics

Low-molecular-weight heparin (LMWH) catheter lock

PROS	cons
<ul style="list-style-type: none">+ HIT RISK lower than 1%+ Limited studies on it.<ul style="list-style-type: none">+ Alteplase use of the tinzaparin group decreased by 47.4% compared to the heparin group.+ Easy to administer+ Predictable clinical effects+ A few side effects	<ul style="list-style-type: none">-Not suitable for lock solution<ul style="list-style-type: none">• Risk of bleeding• Longer half-life• Only partially blocked by Protamine• Cost

Citrate 1

- ✓ A calcium chelator
- ✓ Comparing to Heparin leakage from catheter it doesn't produce systemic anticoagulation
- ✓ In vitro studies have shown it can effectively inhibit biofilm formation and bacterial growth and in higher concentration 30% kill bacteria with completely eradicating preexisting biofilms.
- ✓ 4% citrate is as effective as heparin in preventing thrombosis.
- ✓ Less exchange rate, the use of rt-PA , and incidence of bacteremia.
- ✓ But for large differences in CRBSI it should be combined with an antibiotic.
- ✓ 46.7% :In a prospective randomized controlled study, compared with 5% heparin, 46.7% citric acid showed no significant difference in CRBSI, catheter exit infection, or hospitalization rate, but the number of patients requiring the thrombolytic agent urokinase (u-PA) increased.(protein aggregation)
- ✓ The cumulative survival rate of the catheter decreased by 15% at 6 months; 34% of patients needed to have the dose reduced, and 15% of patients stopped the trial due to abnormal taste and skin sensations.
 - Power A, Duncan N, Singh SK, et al. Sodium citrate versus heparin catheter locks for cuffed Central venous catheters: a single-center randomized controlled trial. Am J Kidney Dis. 2009;53(6):1034–1041.
- ✓ Presently, there seems to be insufficient evidence to confirm that high-concentration citrate is better than heparin in CRBSI.

Citrate 2

- ✓ According to the U.S. Food and Drug Administration, an end-stage renal disease (ESRD) patient died of cardiac arrest shortly after receiving 5 mL of a 47% citrate lock solution after placing central venous tunnel catheters
- ✓ Some believe that it is strictly prohibited to use a high concentration citrate locking solution in patients with internal jugular vein catheters.
- ✓ The KDOQI recommends the use of a low concentration citrate (< 5%) CVC lock solution, if feasible, to prevent CRBSI and CVC dysfunction
- ✓ Citrate can be used as the basic anticoagulant of combined antibacterial locking solution, provided that there is no incompatibility with the antibiotics and antibacterial agents used.

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Plasminogen activators

Pros and cons

- rt-PA can strongly dissolve fibrin by protein hydrolysis and single peptide bond breaking.
- The KDOQI suggests that the success rate of rt-PA in restoring CVC patency is between 50% and 90%
- -No large studies.
- The KDOQI suggests that rt-PA can be used prophylactically as a CVC lock solution once a week to help reduce CVC dysfunction
- However, with regard to CVC without thrombosis, evidence of the effect of the early use of rt-PA as a lock solution on the prevention of thrombosis is limited, which may lead to a waste of medical expenses.

Ab lock as prevention

- No consensus is available on the prevention of catheter dysfunction or catheter-related bloodstream infections in patients undergoing hemodialysis by means of catheter lock solutions.
- Most of the research in prevention and treatment is not long-term.

- Low dose Gentamicin/4% sodium citrate
- Lower CRBSI rate 70% with no adverse effect

TI

A meta-analysis of hemodialysis catheter locking solutions in the prevention of catheter-related infection.

AU

Jaffer Y, Selby NM, Taal MW, Fluck RJ, McIntyre CW

SO

Am J Kidney Dis. 2008;51(2):233.

TI

A randomized trial comparing gentamicin/citrate and heparin locks for central venous catheters in maintenance hemodialysis patients.

AU

Moran J, Sun S, Khababa I, Pedan A, Doss S, Schiller B

SO

Am J Kidney Dis. 2012;59(1):102. Epub 2011 Nov 14.

TI

Comparative effectiveness of two catheter locking solutions to reduce catheter-related bloodstream infection in hemodialysis patients.

AU

Moore CL, Besarab A, Ajluni M, Soi V, Peterson EL, Johnson LE, Zervos MJ, Adams E, Yee J

SO

Clin J Am Soc Nephrol. 2014 Jul;9(7):1232-9. Epub 2014 Jun 26.

دستورالعمل تهیه محلول لاک جنتامایسین ۱ میلی گرم بر میلی لیتر جهت کاتاتر همودیالیز
(Gentamicin lock solution 1 mg/ml for hemodialysis catheter)

۱- در شرایط آسپتیک (استفاده از دستکش، عینک، ماسک و گان محافظ و ضدعفونی کردن سطوح با استفاده از اتانول ۷۰ درصد و ترجیحا زیر هود کلاس ۱۰۰ [ایزو ۵])، ابتدا ۰/۵ میلی لیتر از آمپول جنتامایسین 80 mg/2ml با ۹/۵ میلی لیتر محلول سدیم کلراید تزریقی 0.9% رقیق کرده و در ادامه، ۱۰ آمپول هیپارین 5000 units/1ml به آن اضافه گردد.

۲- در این حالت، غلظت نهایی جنتامایسین، ۱ میلی گرم بر میلی لیتر و هیپارین، ۲۵۰۰ واحد در میلی لیتر است و حجم نهایی، ۲۰ میلی لیتر خواهد شد.

۳- محلول مورد استفاده حتی الامکان باید تازه تهیه شود. "حجم مورد استفاده برای هر لومن کاتاتر همودیالیز" در بزرگسالان و کودکان معمولا به ترتیب ۲ میلی لیتر و ۱ میلی لیتر میباشد. "طول مدت قرارگیری محلول تهیه شده فوق در لومن کاتاتر همودیالیز" به طور معمول حداقل ۶ ساعت و حداکثر ۳ روز توصیه شده است.

• توجه: محلول نهایی بایستی مطابق تصاویر زیر کاملا شفاف و عاری از هر گونه رسوب و ذره ی خارجی باشد. در غیر این صورت، محلول تهیه شده قابل استفاده نبوده و باید دور ریخته شود.



- Gentamicin/Hep
lock solution 1
mg/ml for
hemodialysis
catheter
Namazi hospital Shiraz

Antibiotic lock solutions

Gentamicin +heparin/sodium citrate lock solution

Pros and cons

- gentamycin-citrate (40 mg/mL with 3.13% citrate) performed better than those locked with heparin concerning CRBSI, but the difference in dysfunction was not significant
- gentamicin (8 mg/mL and heparin 1000 U/mL lock solution) was associated with a significant decrease in CRBSI, especially with *Pseudomonas aeruginosa*.

The other two studies confirmed that 5 mg/ mL gentamicin combined with heparin as a lock solution could reduce the incidence and duration of CRBSI but had no significant effect on catheter function, and there was no bacterial drug resistance or clinical ototoxicity.

-Incidence and mortality of gentamicin-resistant CRBSI were significantly higher in hd patients who were given gentamycin 4 mg/ml as a catheter lock within 6 months.

-A low concentration of gentamicin combined with citrate 4% could significantly reduce the rate of CRBSI without microorganisms developing resistance to gentamicin.

-Moran J, Sun S, Khababa I, et al. A randomized trial comparing gentamicin/citrate and heparin locks for Central venous catheters in maintenance hemodialysis patients. *Am J Kidney Dis.* 2012;59(1):102–107.

-Moore CL, Besarab A, Ajluni M, et al. Comparative effectiveness of two catheter locking solutions to reduce catheter-related bloodstream infection in hemodialysis patients. *Clin J Am Soc Nephrol.* 2014; 9(7):1232–1239.

-The incidence of CRBSI in both the low gentamicin concentration (0.32 mg/ml) and high gentamicin concentration (>4 mg/ml) groups was significantly lower than that in the heparin group

Gentamicin +heparin/sodium citrate lock solution

- ✓ Therefore, considering the efficacy and safety, using low concentrations of gentamicin (< 4 mg/mL) and low concentrations of citrate ($< 4\%$) as a lock solution can prevent and treat CRBSI.
- ✓ The low concentration of gentamicin as a blocking solution did not increase the bacterial drug resistance, and the risk of drug toxicity was lower than that of the high concentration gentamicin.



Antibiotic lock solutions

Vancomycin + heparin/gentamicin locking solution.

Pros and cons

- Addition of 2500 U/ml heparin and 5 mg/ml vancomycin was effective in reducing the biofilm formation of *S. epidermidis*, *enterococcus faecalis*, and *S. Aureus*.
- A randomized, double-blind, prospective study, including 131 hemodialysis patients with non-tunnel catheters, showed that compared with heparin (2000 u/ml), vancomycin (5 mg/ml) combined with heparin (2000 u/ ml) reduced the incidence of CRBSI by 82%, but during that period, vancomycin-resistant enterococcus (VRE) was isolated from the vancomycin group, from which these patients had to be hospitalized
- A 12-month study confirmed that the combination of vancomycin (25 mg/mL) and gentamicin (40 mg/mL) could prevent *Staphylococcus* and other gram-negative bacterial infections in tunnelled cuffed catheters (TCCs) and could significantly reduce the incidence of CRBSI and clinical sepsis
- Pooled analysis shows that Vancomycin-containing lock solutions versus heparin lock solutions and found that the incidence of CRBSI was 84% lower in the antibiotic group compared with the heparin group

Antibiotic lock solutions

Cefazolin + gentamicin locking solution

Pros and cons

- The combination of cefazolin and gentamicin is better than vancomycin in stable outpatient HD patients with a low MRSA infection rate.
- The difference in the amount of drug-resistant bacteria was not significant
- However, the reductions in the bacteremia rates remained significant for locks containing vancomycin and gentamicin but not for those containing cefazolin 10 mg/ml and gentamicin 5mg/ml.
- Pooled analysis: CRBSI was 69% lower in the antibiotic group compared with the heparin group.

Antibiotic lock solutions-Clinical recommendation

Yiqin Wang and Xuefeng Sun(2022)

- Gentamicin, vancomycin, and cefazolin are the most commonly used antibiotics for the prevention of CRBSI
- There is insufficient evidence regarding adverse reactions and drug resistance in the use of cefotaxime, minocycline, and cotrimoxazole as locking solutions.
- They are lacking any anticoagulant effect and should be combined with citrate heparin.

The KDOQI guidelines recommend specific prophylactic antibiotic locks for patients in need of a long-term CVC at high risk of CRBSI, instead of using them for routine use.

Antimicrobial agents combined with anticoagulants

Alcohol + heparin/4% sodium citrate combination.

Pros and cons

- HEALTHY-CATH study confirmed that 70% ethanol once a week and 5000 U/mL heparin twice a week could reduce the infection rate compared with 5000 U/mL heparin three times a week;
- Ethanol and anticoagulants can reduce the CRBSI rates by 57% but increase the catheter dysfunction incidence

Antimicrobial agents combined with anticoagulants

Taurolidine

Pros and cons

Taurolidine, a derivative of the amino acid taurine, is one of the latest ALTs and has broad-spectrum antibacterial activity against gram-positive and gram-negative bacteria and fungi (such as Candida) (including MRSA and VRE)

In recent years, in some European countries, a trisodium citrate 30% lock has been gradually replaced by the catheter locking solution containing taurolidine.

At present, there are two commercial lock compound preparations, Taurolock (containing taurolidine and citrate 4%) and Neutrolin (containing taurolidine, heparin, and calcium citrate).

Taurolidin without citrate or Heparin

- ✓ The earliest research report on Taurolock™ that showed its association with increased frequency of catheter thrombosis versus heparin is attributed to Allon. This nonrandomized controlled study showed that although a significantly higher CRB-free survival at 90 days was observed with taurolidine/citrate than with heparin 5,000 U/ml (94 vs. 47%), almost 70% of the patients in the Taurolock™ group required thrombolytics to maintain catheter patency
- ✓ Betjes et al conducted an RCT test involving 58 patients, who mainly had non-tunnel catheters (23.7%), and this study found that the antimicrobial taurolidine may significantly reduce the incidence of catheter-related sepsis but may not increase the risk of side effects.
- ✓ In a randomized controlled trial that included 119 chronic hemodialysis patients, Filiopoulos et al. compared the antibiotic group (Gent 40 mg/ml and heparin 5000 u/ml, group A) and taurolidine/citrate group (group B), and found that the taurolidine/citrate lock was not superior to gentamicin/heparin in the prevention of CRB.
- ✓ Additionally, Solomon et al. found that compared with heparin (5000 u/ml) in a randomized controlled trial, Taurolock did not reduce all-cause bacteremia and was associated with a greater need for thrombolytic therapy.

Taurolidine

- ✓ To increase the antithrombotic effect, Solomon et al added 500 u/ml heparin to 4% taurine citrate, and TauroLockTM-Hep500 (1.35% taurolidine, 4% citrate and 500 u/ml heparin) was compared to TauroLockTM (1.35% taurolidine, 4% citrate) and heparin 5000 u/ml by using retrospective data.
- ✓ Comparing with TauroLockTM, TauroLockTM -Hep500 reduced the need for thrombolysis, which was equivalent to that of heparin 5000 u/ml, and the use of TauroLockTM-Hep500 decreased the bacteremia rates from all causes by a factor of 2
- ✓ An observational study showed that NeutrolinVR was also able to reduce the incidence of CRBSI and catheter thrombosis
- ✓ The pooled analyses of all studies containing the TauroLockTM-Hep500 lock solution showed that the patency of the catheter can be improved by 71% by adding heparin to taurolidine-citrate, but there was no significant difference in the incidence of CRBSI.
- ✓ A prospective randomized controlled study confirmed that the twice-a-week TauroLockTM-Hep500 (taurolidine-citrate-heparin 5000 U/mL) and weekly TauroLock-U25,000 (taurolidine-citrate-urokinase 25000 IU) treatment schemes were very effective in preventing repeated thrombotic dysfunction of tunnel CVC catheters and significantly reduced the catheter replacement rate and the need for rt-PA emergency thrombolysis than TauroLockTM-Hep500 after each HD session, but there was no significant difference in CRBSI

Taurolidine

- ✓ A prospective randomized study from Qatar investigated TaurolockHep500 and TauroLockTM-U25,000 locks at the end of the third hemodialysis of the week in an unselected cohort (prevalent TCC accounted for 65%) and showed that TauroLockTM-U25,000 could improve the catheter survival rate during the last dialysis
- ✓ Similarly, a cohort of TCC-TD high-risk patients or patients with a history of CRBSI in prevalent catheters showed that once a week rt-PA added to the citrate 4% lock solution significantly reduced the comprehensive outcome of catheter loss caused by thrombosis and infection
- ✓ We conducted a pooled analysis of the above studies by including all the studies' patient groups and found that taurolidine combined with citrate-based locking solution can reduce the CRBSI rates by 66% and that the catheter failure incidence decreased by 53% in the hemodialysis patients with CVC after adding urokinase
- ✓ **Therefore, it is confirmed that the taurolidine/citrate combined preparation solution did work, but the effect of taurolidine lock alone is uncertain.**
- ✓ In general, compared with heparin, the taurolidine/citrate locking solution can reduce the incidence of CRBSI, but it was not significant in improving catheter dysfunction.
- ✓ Adding heparin to the taurolidine/citrate locking solution can improve the patency of the catheter, but there was no significant difference in the incidence of CRBSI. However, the addition of urokinase to the taurolidine/ citrate locking solution can reduce both the incidence of CRBSI and the incidence of catheter dysfunction.

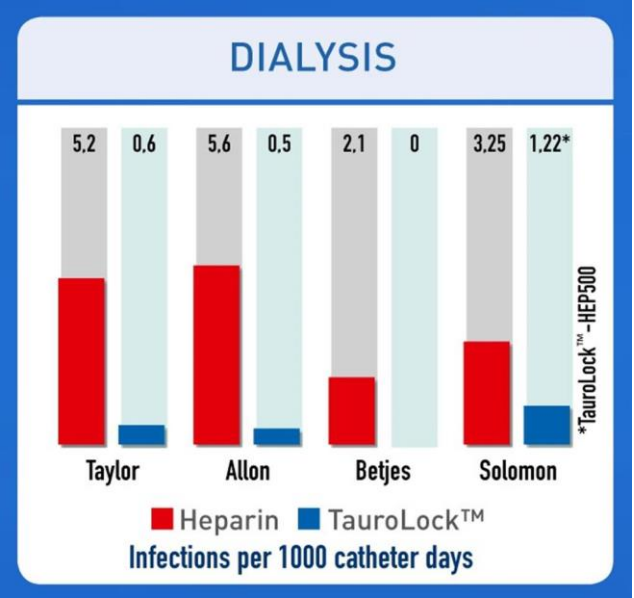
PROPHYLAXIS: LOCKING SOLUTIONS

- Taurolidine, a substance that has been used in Europe since the 1970s
 - Effective against a broad range of gram-negative and gram-positive bacteria as well as many types of fungi
 - CRB rates were reduced to 0.20 episodes/1000 catheter-days



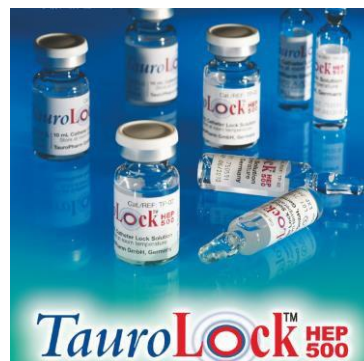
Two Locking Solutions: Taurolidine & Heparine

Prevention



comparison between infections per 1000 catheter days for Heparine & Tauro Lock

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Product selection for application

Product	TauroLock™	TauroLock™ HEP 100	TauroLock™ HEP 500	TauroLock™ UH 25000
Dialysis	•		• • •	• •
Oncology	• • •	• • •		• •
Parenteral Nutrition	• • •	• • •		• •

TauroLock™ catheter lock solutions are available in different containers:

Product	TauroLock™	TauroLock™ HEP 100	TauroLock™ HEP 500	TauroLock™ UH 25000
Ampoule (10 x 3 mL)	•	•		
Ampoule (10 x 5 mL)	•		•	
Vial (100 x 10 mL)	•		•	
Vial (5 x 5 mL)				•

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Taurolock instruction:(Persian)

راهنمای استفاده

محلول آنتی سپتیک و آنتی کواگولانت ترولاک (TauroLock)

محلول آنتی سپتیک و آنتی کواگولانت ترولاک آلمان جهت لاک کردن انواع کاتتر و به جای هپارین لاک مورد استفاده قرار می گیرد. این محلول می تواند از عفونت انواع کاتتر از جمله کاتتر همودیالیز دائم (پرمیکت)، کاتتر همودیالیز موقت (شالدون)، کاتتر ورید مرکزی (CVC)، کاتتر پورت شیمی درمانی و ... جلوگیری کرده و همچنین مانع از ایجاد کلات و مسدود شدن کاتتر شود.

محلول TauroLock Hep500 محتوی ترولیدین (Cyclo-Taurolidine)، سیترات (4% Citrate)، هپارین (Heparin (Mucosa 500 U/ml)) و آب مقطر می باشد.

ترولیدین ماده ایست که از اسید آمینه تورین مشتق شده و خاصیت آنتی باکتریال بر روی انواع باکتری های گرم + و گرم - و قارچ ها دارد. ترولیدین یک Bactericidal است و جداره سلولی باکتری ها را هدف قرار می دهد. همچنین هپارین به همراه سیترات 4% عملکرد ضد انعقادی و آنتی ترومبوتیک داشته و مانع از ایجاد هرگونه کلات در داخل لومن های کاتتر می شوند.

موارد استفاده

- محلول ترولاک برای انواع کاتتر عروقی از جنس سیلیکون (Silicon) یا پلی اورتال (Polyurethane) مورد استفاده قرار می گیرد.
- محلول ترولاک به عنوان محلول مسدود کننده کاتتر (Catheter Lock Solution) شناخته شده و جایگزین مناسبی برای هپارین لاک می باشد.
- محلول ترولاک به جهت پیشگیری از عفونت کاتتر (CRBSI) به عنوان پیشگیرانه (Prophylaxis) و در صورت بروز عفونت در کاتتر به عنوان درمانی (Therapeutic) مورد استفاده قرار می گیرد.

نحوه استفاده

- (۱) ابتدا کاتتر را با 10cc نرمال سالین شستشو دهید. پیشنهاد می گردد از روش Push-Stop انجام گردد.
- (۲) ترولاک را براساس ظرفیت و حجم لومن کاتتر که توسط کمپانی سازنده کاتتر مشخص شده و معمولاً بر روی لومن کاتتر درج شده است از آمپول و یا ویال ترولاک داخل سرنگ بکشید.
- (۳) محلول ترولاک را به آرامی داخل لومن کاتتر تزریق کنید. (سرعت تزریق محلول نباید پیش از 1 ml/sec برای بزرگسالان و بیش از 0.2 ml/sec برای اطفال و نوزادان باشد).
- (۴) در صورت نیاز به استفاده بعدی از کاتتر (جلسه بعدی درمان) می بایست به میزان حجم ترولاک تزریق شده، توسط سرنگ اسپیره شده و محلول ترولاک از لومن کاتتر خارج گردد.
- (۵) قبل از استفاده از کاتتر (شروع درمان) لومن کاتتر را با 10ml نرمال سالین شستشو دهید.

Taurolock instruction:(Persian)

نکات قابل توجه

- محلول ترولاک یکبار مصرف بوده و استفاده مجدد از محلول خطرات جدی برای بیمار خواهد داشت.
- در صورت عدم اطلاع از حجم لومن در کانتنر همودیالیز می توان 2.5cc در هر لومن تزریق نمود.
- باقیمانده محلول در آمپول را می توان داخل سرنگ کشیده و تا ۱۴ روز در دمای اتاق نگهداری نمود. همچنین باقیمانده محلول در ویال را می توان در جلسات بعدی درمان استفاده کرد.
- محلول ترولاک آماده مصرف می باشد و بدلیل کاهش تاثیر عملکرد و تغییر PH، رقیق کردن آن با هپارین و یا نرمال سالین و ... توصیه نمی شود.
- در صورت مشاهده هرگونه رسوب به علت نگهداری نادرست، نباید از محلول استفاده نمود.

شرایط نگهداری

محلول ترولاک در دمای ۳۰-۱۵ درجه سانتی گراد نگهداری گردد. بدین جهت نگهداری آن داخل یخچال و یا یخ زدگی محلول باعث غیر قابل استفاده شدن آن می گردد.

بسته بندی

محلول ترولاک به صورت آماده تزریق در دو نوع آمپول 5cc و ویال 10cc عرضه می گردد.

موارد منع مصرف

- محلول ترولاک مدل (HEP500) برای بیماران یا سابقه حساسیت به ترولیدین و یا مشتقات آن، سینترات یا هپارین ممنوعیت مصرف دارد. همچنین در بیماران دارای ترومبوسیتوپنی و یا بیماران با خطر خونریزی نباید استفاده گردد.
- این محلول نباید به صورت سیستمیک تزریق گردد. محلول تزریق شده در کانتنر در جلسه بعدی درمان اسپیره گردد.

عوارض جانبی

- این محلول هیچ گونه مقاومت آنتی بیوتیکی ایجاد نخواهد کرد.
- تاکنون عارضه ای از این محلول گزارش نشده است. در صورت تزریق سریع محلول و وارد شدن محلول به مسیر خونی به صورت نادر مواردی از هایپوکلسمی خفیف دیده شده است.
- هیچ گونه مطالعاتی در زمینه استفاده از ترولاک در دوران بارداری و شیردهی انجام نشده است. با این حال جهت احتیاط در طی دوران بارداری و شیردهی استفاده نگردد.



Citra-Lock Persian instructions



آمپول سیترا لاک
برای انواع کاتتر



@farrokhimedical



بر خلاف نمونه های موجود در بازار این محصول فاقد هپارین بوده و طبیعتاً بیمار پس از دریافت این محصول دچار بسیاری از مشکلات که در اثر ورود هپارین به داخل خون ایجاد می گردد نمی شود.

شایان ذکر است این محصول مانع از ایجاد لخته در انتهای کاتتر شده و در نتیجه عملکرد کاتتر را نیز بهبود می بخشد.

بدیهی است عملکرد هرچه بهتر و طولانی تر کاتترها باعث بهبود کیفیت زندگی بیماران محترم گردیده و آسایش روانی و جسمی بیشتری را برای آن ها به ارمغان خواهد آورد.

قارچی و باکتریایی حفظ می نماید . این محلول هیچگونه عوارض دارویی نداشته و صرفاً باعث از بین بردن باکتری ها و قارچ ها در ظرف مدت ۲ تا ۴ ساعت می گردد.



بدیهی است با ایجاد فضایی عاری از میکروب های مضر ، مدت زمان عملکرد مفید کاتتر ها طولانی تر شده و بیمار از انواع آسیب های جانبی ناشی از عفونت و تعویض کاتتر مصون می ماند.

این موضوع علاوه بر کاهش ریسک جانی برای بیماران باعث کاهش تحمیل هزینه های بالای تهیه و کارگذاری کاتترها می گردد.

09173156394

Dirinco® شرکت

بر این اساس ، شرکت هلدنکس از بررسی های بسیار بر روی بیماران و همچنین بررسی و ارزیابی نمونه های موجود در بازار و همچنین عوارض آنها بر روی بیماران به فرمولی کاملاً متمایز و انحصاری دست پیدا نموده و هم اکنون در قالب آمپول سیترا لاک در اختیار بیماران و کادر درمان قرار داده است . این محلول حاوی یک ماده آنتی سپتیک با طیف پوششی گسترده بوده و کاتترها را از انواع عفونت های

سیترا لاک
Citra-Lock

کاتتر های عروقی مانند شالدون ، پرمیکت، پورت و کاتتر ورید مرکزی بعنوان یکی از ابزارهای درمانی در مراحل اولیه شروع درمان می باشد.



استفاده و بکارگیری انواع کاتترهای عروقی همواره برای بیماران باعث بروز مشکلاتی از قبیل عفونت های ناشی از وجود باکتری ، قارچ ها و ویروس ها می باشد که از طریق انتهای کاتترها که با پیرون بدن تماس دارند به داخل عروق منتقل می شود.



Catheter Lock Solution

Anti
.Biofilm
.Bacterial
.Coagulant

Citra-Lock™ 30%
Citra-Lock™ 46,7%



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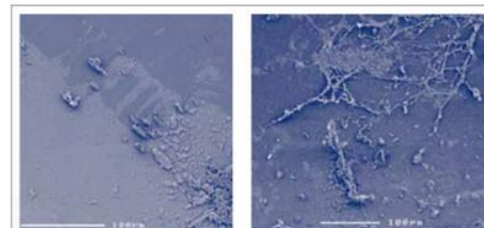
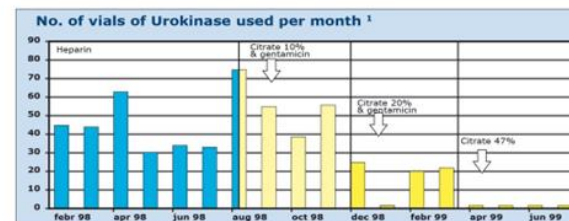
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تهران، یوسف آباد، خیابان
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هفتم، پلاک ۱۲، طبقه ۳

www.manatd.com

Anti Coagulant

Citra-Lock™ reduces the use of thrombolytic agents like Urokinase and tPA, resulting in increased bloodflow and dialysis efficacy.



Bosma W. et al. Nephrol Dial Transplant (2009) doi:10.2093/ndt/gf651

Biofilm Reduction

Citra-Lock™ reduces biofilm formation in central venous catheters

Increased safety & Simplified handling



The new Citra-Lock™ vial features a drip free Luer-Slip/Luer-Lock connector:

- preventing microbial contamination
- protecting against needle stick injuries
- reducing handling steps
- promoting intuitive handling

Art.nr. Citra-Lock™ 46,7%: 24060202

Art.nr. Citra-Lock™ 30% : 24060203

Also Available:

Art.nr. Citra-Lock™ 4% :24060201

Citra-Lock™ is a Dirinco product and registered as a medical device Class.Ib.

CE 1275

The 19th International Congress of Nephrology, Dialysis and Transplantation (ICNDT)

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Citra-Lock Persian instructions

Catheter Lock Solution

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تهران، یوسف آباد، خیابان

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The **Effective** Concentrations

Citra-Lock™

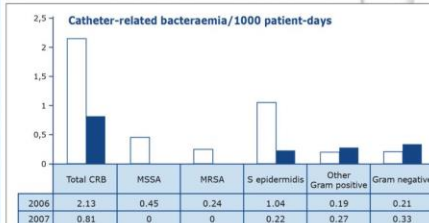
Improve catheter patency

Anti Microbial

Randomised, Clinical Trial Comparison of Trisodium Citrate 30% and Heparin as Catheter-Locking Solution in Haemodialysis Patients 2

	Citrate (30%)	Heparin
Overall catheter removal	28%	43%
Catheter related bacteraemia (per 1000 days)	1.1	4.1
Exit site infections (per 1000 days)	1.3	3.9
Death from catheter related bacteraemia	0	5
Admissions for catheter related infections	6	21
Admissions for catheter related infections (per 1000 days)	0.7	2.7
Bleeding at exit sites (number of patients)	6	19
Thrombocytopenia (number of patients)	2	4
Parathesia or Dysgeusia	9	4

Study Design: Multicentre (10 centres), double blind, randomised controlled, 291 catheters (143 heparin and 148 citrate 30%), 98 tunnelled catheters, 193 non-tunnelled catheters from catheter days 16-547.



Significant declines in catheter-related bacteraemias/1000 patient-days were seen after the introduction of 46.7% TSC amongst methicillin-sensitive *S. aureus* (MSSA), methicillin-resistant *S. aureus* (MRSA) and *S. epidermidis* (*P < 0.001). No significant difference was observed in the incidence of other Gram-positive or Gram-negative bloodstream infection. Open bars, 2006 heparin period; closed bars, 2007 46.7% TSC period.

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Dirinco
Always innovating

Over 10 years



Citra-Lock™

Catheter Lock Solution

Anti
Biofilm
Bacterial
Coagulant

Citra-Lock™ 4%
Citra-Lock™ 30%
Citra-Lock™ 46.7%



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تهران، یوسف آباد، خیابان

فراهانی پور، نیش خیابان

هفتم، پلاک ۱۲، طبقه ۲

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محلول آنتی سپتیک و آنتی کواگولانت سیترا لاک

محلول آنتی سپتیک و آنتی کواگولانت سیترا لاک از موادی همچون تری سدیم سیترات ۴۶.۷٪ و اسید سیتریک تشکیل شده است

که باعث جلوگیری از ایجاد لخته های خونی و تشکیل بایو فیلم و همچنین پیشگیری و درمان عفونت های کاتتری ناشی از تجمع باکتری هایی نظیر از نوک *MSSA*, *MRSA* گرم مثبت ها و گرم منفی ها و فونگی ها می شود. بدین ترتیب با یکبارگیری سیترا لاک عمر کاتتر افزایش یافته و هزینه های درمانی و تعویض کاتتر را به طور قابل توجهی کاهش می دهد و بیمار از نظر روحی و روانی (با از بین بردن عوارض کلات و عفونت مثل: تب و لرز، درد، ...) وضعیت بسیار مطلوبی داشته و دوران درمانی خود را به بهترین شکل سپری خواهد کرد.

طریقه مصرف محلول سیترا لاک:

- دمای نگهداری محلول سیترا لاک ۱۵-۳۰ درجه می باشد.
- برای جلوگیری از سیستیک شدن محلول حتما توجه کنید که هنگام لاک کردن شوت نشود و به صورت **push stop** و به اندازه عدد روی گیره هر لومن و در مدت زمان ۸ ثانیه در هر لاین به آرامی وارد کاتتر شود.
- رعایت پروتکل های بهداشتی اعم از تعویض گان، دستکش، ماسک برای هر بیمار به صورت جداگانه.
- توجه داشته باشید به هیچ عنوان این محلول یخچالی نبوده و نگهداری آن در یخچال باعث از دست دادن خواص این محلول می شود.
- باقی مانده محلول **5CC** سیترا لاک را می شود با رعایت پروتکل های بهداشتی در سرنگ کلامپ شده است باعث ایجاد احساس سوزن سوزن سر انگشتان، طعم آهکن و مزه تلخی در دهان به مدت ۵ ثانیه می شود و سپس در خون حل شده و همه علائم از بین می رود.
- این محلول آماده مصرف می باشد و نیاز به رقیق کردن ندارد.
- نکته: حتما یکبار قبل از دیالیز (بعد از آسپیره کردن) و یکبار قبل از لاک کردن (بعد از دیالیز) با نرماسالین کاتتر شستشو داده شود.
- این محلول آنتی بیوتیک نبوده و مقاومت آنتی بیوتیکی ایجاد نمی کند.

Geistlich Taurosept® = taurolidine 2 %

- ✓ Taurolidine is not an anticoagulant, but it has been shown to have antithrombotic properties.
- ✓ A study published in the BMC Nephrology journal found that taurolidine-based lock solutions were associated with a significantly lower hazard for removal of CVC due to infection or malfunction combined, and for removal of CVC due to infection or malfunction separately
- ✓ Another study published in Europe PMC found that a solution containing 2% taurolidine seems suitable as a hemodialysis catheter lock.
- ✓ In a Swiss cohort, it prevented CRBSI, limited catheter dysfunction, and was cost-efficient.
- ✓ It is unclear how taurolidine prevents coagulation in catheter lock for hemodialysis. However, one possible explanation is that taurolidine may prevent the formation of biofilm on the catheter surface, which can lead to thrombosis and infection.



A 2% taurolidine catheter lock solution prevents catheter-related bloodstream infection (CRBSI) and catheter dysfunction in hemodialysis patients.

Neusser MA, Bobe I, Hammermeister A¹, Wittmann U²

[Author information](#)

British Journal of Nursing (Mark Allen Publishing), 01 Jul 2021, 30(14):S24-S32
<https://doi.org/10.12968/bjon.2021.30.14.s24> PMID: 34288746

Research | [Open access](#) | Published: 13 September 2021

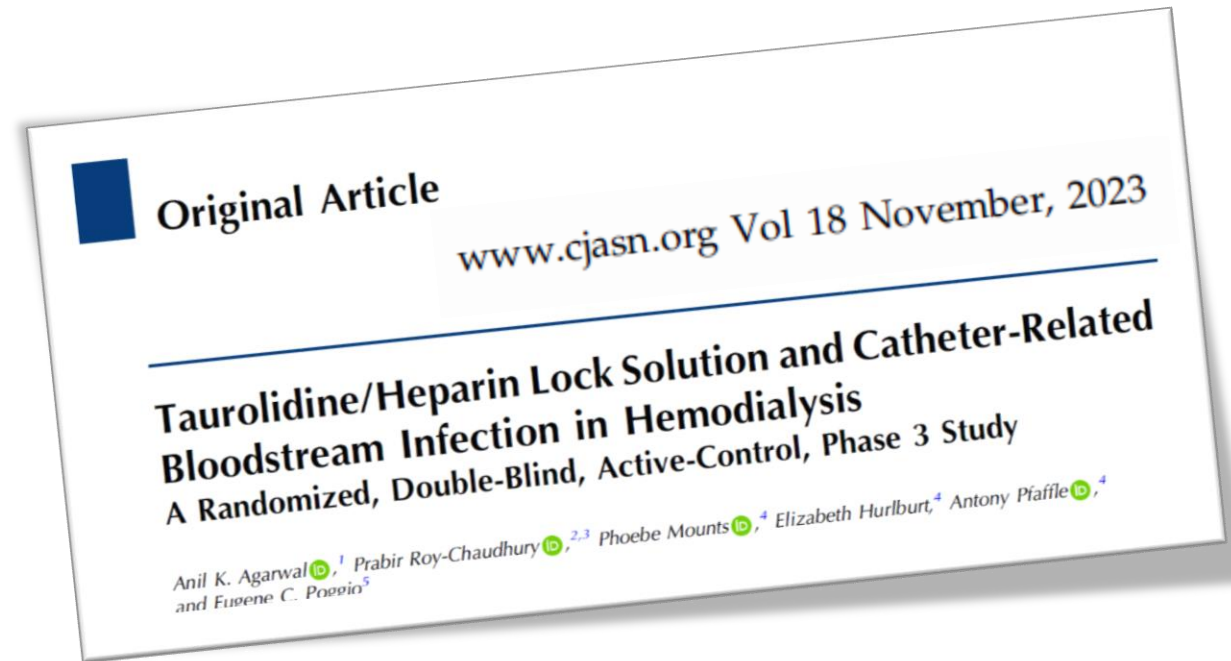
The best solution down the line: an observational study on taurolidine- versus citrate-based lock solutions for central venous catheters in hemodialysis patients

[Sonja van Roeden](#), [Mathijs van Oevelen](#), [Alfero C. Abrahams](#), [Friedo W. Dekker](#), [Joris I. Rotmans](#) & [Sabine C. A. Meijvis](#) on behalf of the DUCATHO study group

[BMC Nephrology](#) 22, Article number: 308 (2021) | [Cite this article](#)

- **LOCK IT- 100 trial**

- compared the efficacy and safety of a taurolidine/heparin catheter lock solution that combines taurolidine 13.5 mg/ml and heparin (1000 units/ml) versus heparin in preventing CRBSIs.
- was a randomized, double-blind, active-control, multicenter, phase 3 study that enrolled adults with kidney failure undergoing maintenance hemodialysis via CVC from 70 US sites. (795 patients)
- nine participants in the taurolidine/heparin arm (n=397; 2%) and 32 participants in the heparin arm (n=398; 8%) had a CRBSI
- 71% reduction risk with taurolidin/heparin.
- Same safety and adverse events compared with heparin.
- based on a prespecified interim analysis, the Data and Safety Monitoring Board recommended terminating the trial early for efficacy with no safety concerns.



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CORMEDIX INC. ANNOUNCES FDA APPROVAL OF DEFENCATH® TO REDUCE THE INCIDENCE OF CATHETER-RELATED BLOODSTREAM INFECTIONS IN ADULT HEMODIALYSIS PATIENTS

November 15, 2023

- *First and only FDA-approved antimicrobial catheter lock solution in the U.S.*
- *Company expects DefenCath to be available in Q1 2024 in the inpatient setting*

Berkeley Heights, NJ – November 15, 2023 – CorMedix Inc. (Nasdaq: CRMD), a biopharmaceutical company focused on developing and commercializing therapeutic products for the prevention and treatment of life-threatening diseases and conditions, today announced that the U.S. Food and Drug Administration (FDA) has approved DefenCath® (taurolidine and heparin) catheter lock solution (CLS) to reduce the incidence of catheter-related bloodstream infections (CRBSIs) for the limited population of adult patients with kidney failure receiving chronic hemodialysis through a central venous catheter (CVC). DefenCath is the first and only FDA-approved antimicrobial CLS in the U.S. and was shown to reduce the risk of CRBSIs by up to 71% in a Phase 3 clinical study.



Take Homework message

Diagnosis, treatment and prevention of hemodialysis catheter infection

Clinical guidelines of the
Iranian society of nephrology
&

Iranian society of infectious diseases and tropical medicine

The **19th**
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