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DIAGNOSI E TRATTAMENTO CRBSI

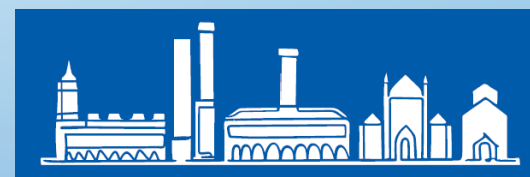
GIANCARLO SCOPPETTUOLO

DIRETTORE UOS DIAGNOSI E CURA DELLE MALATTIE INFETTIVE DI COMUNITÀ E TRASMISSIBILI

CONSULENTE INFETTIVOLOGO CENTRO INTERDIPARTIMENTALE ACCESSI VENOSI CENTRALI

COORDINATORE PERCORSO ENDOCARDITE ED ENDOCARDITIS TEAM

FONDAZIONE POLICLINICO UNIVERSITARIO A. GEMELLI – IRCCS ROMA



**TRANQUILLO,
È SOLO PER SCOPRIRE
CHI FA LA FESTA
NEL TUO SANGUE!**

**MA È PROPRIO
NECESSARIO?**



PRIMA TENTAZIONE DEL MEDICO....

- ATTRIBUIRE IMMEDIATAMENTE LA RESPONSABILITA' DELLA FEBBRE AL CV, ANCORA PRIMA DI AVERE ESEGUITO ALCUNA INDAGINE DIAGNOSTICA
 - SOPRATTUTTO NEL PAZIENTE OSPEDALIZZATO (MA ANCHE NEL PAZIENTE DOMICILIARE) IL CV **È SOLO UNA DELLE POSSIBILI CAUSE DI INFEZIONE**
- RIMUOVERE IL CATETERE VASCOLARE
 - IN LETTERATURA È BEN DESCRITTO CHE CIRCA IL 70% DEI CVC RIMOSI SOLO CON CRITERIO EMPIRICO NON HANNO RAGIONE DI ESSERE RIMOSI
 - CRITERI PER LA RIMOZIONE IMMEDIATA DI UN CATETERE VASCOLARE? SÌ, MA IN CASI SELEZIONATI
- RICHIEDERE SUBITO DOPO LA RIMOZIONE IL POSIZIONAMENTO DI UN NUOVO CATETERE...

Clinical Practice Guidelines for the Diagnosis and Management of Intravascular Catheter-Related Infection: 2009 Update by the Infectious Diseases Society of America

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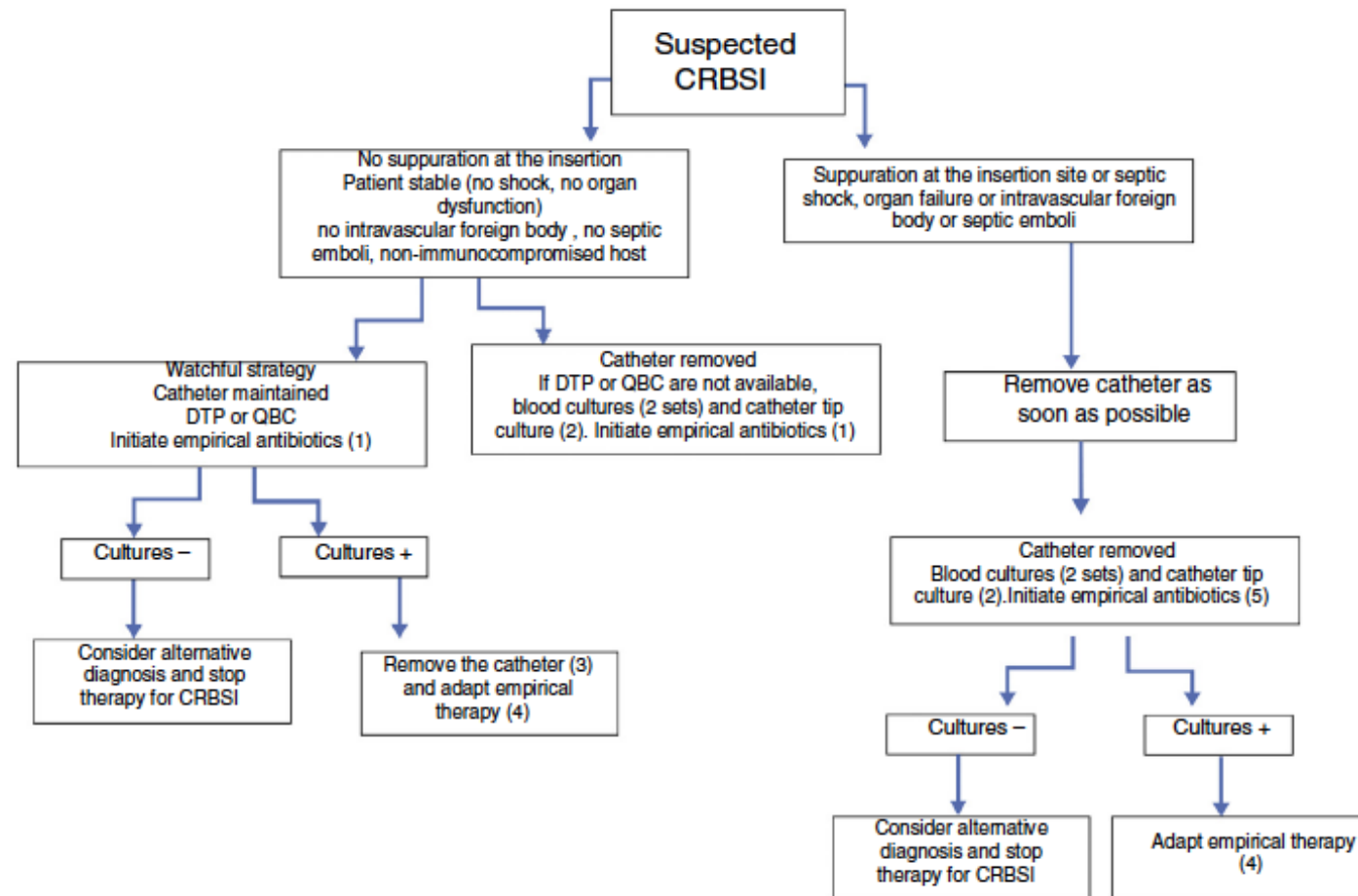


CONSENSUS STATEMENT

Diagnosis and treatment of catheter-related bloodstream infection: Clinical guidelines of the Spanish Society of Infectious Diseases and Clinical Microbiology and (SEIMC) and the Spanish Society of Spanish Society of Intensive and Critical Care Medicine and Coronary Units (SEMICYUC)[☆]



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CLABSI/LCBSI E CRBSI

Table 1.

Two definitions of central venous catheter-related bloodstream infections

Bloodstream infection	Definitions
Catheter-related bloodstream infection	Clinical signs of sepsis and positive peripheral blood culture in the absence of an obvious source other than CVC with one of the following: Positive semiquantitative (>15 CFU) or quantitative ($>10^3$ CFU) culture from a part of the catheter with the same organisms isolated peripherally Simultaneous quantitative blood cultures with a ratio of $\geq 3:1$ (CVC vs. peripheral) Time difference of ≤ 2 hours leading to culture positive between CVC and peripheral cultures
Central line-associated bloodstream infection	Primary bloodstream infection in a patient who had a central line within the 48 hours period before development of infection Infection must not be related to an alternative cause

CVC, central venous catheter; CFU, colony forming unit.

Adapted from Bell T, et al. Infect Dis Clin North Am 2017;31:551-9, with permission of Elsevier. [3]

Bloodstream Infection Event (Central Line-Associated Bloodstream Infection and Non-central Line Associated Bloodstream Infection)

Table of Contents

Introduction.....	2
Settings	2
Key Terms and Abbreviations.....	2
Definitions Specific to Bloodstream Infection (BSI) / Central Line Associated Bloodstream Infection (CLABSI)	
Surveillance	3
Laboratory Confirmed Bloodstream Infection (LCBIs) Hierarchy; Types of LCBIs.....	3
Types of Central Lines for NHSN reporting purposes.....	5
Devices Not Considered Central Lines for NHSN Reporting Purposes.....	6
Table 1: Laboratory-Confirmed Bloodstream Infection Criteria:	6
Table 2: Mucosal Barrier Injury Laboratory-Confirmed Bloodstream Infection (MBI-LCBI)	10
Reporting Instructions: See below for a Summary of CLABSI Exclusions and Reporting Requirements.	12
Reporting Instructions	13
Blood Specimen Collection.....	14
Table 3: Examples of Associating the Use of Central Lines to BSI Events (CLABSI).....	16
Pathogen Exclusions and Reporting Considerations	18
Table 4: Reporting Speciated and Unspeciated Organisms Identified from Blood Specimens.....	19
Table 5: Examples Illustrating the MBI-LCBI Criteria for Neutropenia.....	19
Monthly Summary Data	20
Table 6: Examples of Denominator Day counts for Device Days	21
Table 7: Denominator Data Collection Methods.....	23
Data Analyses	26
Table 8: CLABSI Measures Available in NHSN	29
References.....	30
Appendix: Secondary BSI Guide (not applicable to Ventilator-associated Events [VAE]).....	31

• NHSN CLABSI DEFINITION, JAN 2024

Notes:

1. Neither the type of device nor the insertion site is used to determine if a device is considered a central line for NHSN reporting purposes.
2. At times, a CL may migrate from its original central location after confirmation of proper placement. NHSN does not require ongoing verification of proper line placement. Therefore, once a line has been designated a CL it remains a CL, regardless of migration, until removed from the body or patient discharge, whichever comes first. CL days are included for any CLABSI surveillance conducted in that location.
3. An introducer is an intravascular catheter, and depending on the location of the tip and its use, may be considered a CL.
4. A non-lumened intravascular catheter that terminates at or close to the heart or in a great vessel that is not used for infusion, withdrawal of blood or hemodynamic monitoring is not considered a CL for NHSN reporting purposes (for example, non-lumened pacemaker wires.)
 - There are some pacemaker wires that do have lumens, which may be considered a central line.

Types of Central Lines for NHSN reporting purposes:

1. Permanent central line: Includes:
 - a. Tunneled catheters, including tunneled dialysis catheters
 - b. Implanted catheters (including ports)
2. Temporary central line: A non-tunneled, non-implanted catheter
3. Umbilical catheter: A vascular catheter inserted through the umbilical artery or vein in a neonate. All umbilical catheters are central lines

Eligible Central Line: A CL that has been in place for **more than two consecutive calendar days** (on or after CL day 3), following the *first access* of the central line, in an inpatient location, during the current admission. Such lines are eligible for CLABSI events and remain eligible for CLABSI events until the day after removal from the body or patient discharge, whichever comes first. (See [Table 3](#) for examples).

Eligible BSI Organism: Any organism that is eligible for use to meet LCBI or MBI-LCBI criteria. In other words, an organism that is not an excluded pathogen for use in meeting LCBI or MBI-LCBI criteria. These organisms may or may not be included on the NHSN Organisms List accessed via the [spreadsheet](#) or refer to the new [NHSN Terminology Browser](#). Contact NHSN for guidance regarding organisms that are not included on the NHSN Organisms List.

January 2024

Device-associated Module
BSI



Devices **Not** Considered Central Lines for NHSN Reporting Purposes:

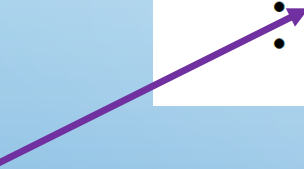
- Arterial catheters unless in the pulmonary artery, aorta, or umbilical artery
 - Arteriovenous fistula
 - Arteriovenous graft
 - Atrial catheters (also known as transthoracic intra-cardiac catheters, those catheters inserted directly into the right or left atrium via the heart wall)
 - Extracorporeal life support (ECMO)
 - Hemodialysis reliable outflow (HERO) dialysis catheter
 - Intra-aortic balloon pump (IABP) devices
 - Peripheral IV or Midlines
 - Ventricular Assist Device (VAD)
- 

Table 1: Laboratory-Confirmed Bloodstream Infection Criteria:

Must meet **one** of the following LCBI criteria:

Criterion	<i>Comments and reporting instructions that follow the site-specific criteria provide further explanation and are integral to the correct application of the criteria.</i>
	Once an LCBI determination is made, proceed to the MBI-LCBI definitions, and determine if the corresponding MBI-LCBI criteria are also met (for example, after meeting LCBI 2, investigate for potential MBI-LCBI 2)
LCBI 1 If LCBI 1 criterion is met, consider MBI-LCBI 1	Patient of any age has a recognized bacterial or fungal pathogen, not included on the NHSN common commensal list: 1. Identified from one or more blood specimens obtained by a culture OR 2. Identified to the genus or species level by non-culture based microbiologic testing (NCT)* methods (for example, T2 Magnetic Resonance [T2MR] or next-generation sequencing (NGS). Note: <i>If blood is collected for culture within 2 days before, or 1 day after the NCT, disregard the result of the NCT and use only the result of the CULTURE to make an LCBI surveillance determination. If no blood is collected for culture within this time period, use the result of the NCT for LCBI surveillance determination.</i> AND Organism(s) identified in blood is not related to an infection at another site (See Appendix: Secondary BSI Guide). *For the purposes of meeting LCBI 1, NCT is defined as a methodology that identifies an organism directly from a blood specimen without inoculation of the blood specimen to any culture media.

LCBI 2 If LCBI 2 criterion is met, consider MBI-LCBI 2	Patient of any age has at least <u>one</u> of the following signs or symptoms: fever (>38.0°C), chills, or hypotension AND Organism(s) identified in blood is not related to an infection at another site (See Appendix: Secondary BSI Guide). AND The same NHSN common commensal is identified by culture from two or more blood specimens collected on separate occasions (see Blood Specimen Collection). For common commensal organisms, see the Common Commensal tab of the NHSN Organism List accessed via the spreadsheet or refer to the new NHSN Terminology Browser. Notes: 1. Criterion elements must occur within the 7-day IWP (as defined in Chapter 2) which includes the collection date of the positive blood specimen, the 3 calendar days before and the 3 calendar days after. 2. The two matching common commensal specimens represent a single element for use in meeting LCBI 2 criterion, and the collection date of the first specimen is used to determine the BSI IWP. 3. At least one element (specifically, a sign or symptom of fever, chills, or hypotension) is required to meet LCBI 2 criterion; the LCBI 2 DOE will always be the date the first element occurs for the first time during the BSI IWP, whether that be a sign or symptom or the positive blood specimen.
---	--

LCBI 3 If LCBI 3 criterion is met, consider MBI-LCBI 3	Patient ≤ 1 year of age has at least one of the following signs or symptoms: fever ($>38.0^{\circ}\text{C}$), hypothermia ($<36.0^{\circ}\text{C}$), apnea, or bradycardia AND Organism(s) identified in blood is not related to an infection at another site (See Appendix: Secondary BSI Guide). AND The same NHSN common commensal is identified by a culture from two or more blood specimens collected on separate occasions (see Blood Specimen Collection). For common commensal organisms, see the Common Commensal tab of the NHSN Organism List accessed via the spreadsheet or refer to the new NHSN Terminology Browser. Notes: 1. Criterion elements must occur within the 7-day IWP (as defined in Chapter 2) which includes the collection date of the positive blood specimen, the 3 calendar days before and the 3 calendar days after. 2. The two matching common commensal specimens represent a single element for use in meeting LCBI 3 criterion, and the date of the first is used to determine the BSI IWP.
---	---

	A	B	C	D
1	Common Commensals (CC)			
2	It is possible that your laboratory may identify an organism that cannot be found when referencing the NHSN Organism List. DO NOT interpret the absence of an organism to mean the event is not reportable. If you have an organism which is not found on the NHSN Organism List, please contact us at nhsn@cdc.gov for guidance on appropriate reporting.			
3	NHSN Code	NHSN Display Name	SNOMED Preferred Term	SNOMED Code
4	ACTSP	Actinomyces	Actinomyces	40560008
5	ACTBO	Actinomyces bovis	Actinomyces bovis	59806008
6	ACTDENT	Actinomyces dentalis	Actinomyces dentalis	426330001
7	ACTFUNK	Actinomyces funkei	Actinomyces funkei	419012004
8	ACTGR	Actinomyces gerencseriae	Actinomyces gerencseriae	113416002
9	ACTGRAE	Actinomyces graevenitzi	Actinomyces graevenitzi	113417006
10	ACTIS	Actinomyces israelii	Actinomyces israelii	46369004
11	ACTNA	Actinomyces naeslundii	Actinomyces naeslundii	8940004
12	ACTORIC	Actinomyces oricola	Actinomyces oricola	425488009
13	ACTORIS	Actinomyces oris	Actinomyces oris	447175005
14	ACTRADI	Actinomyces radidentis	Actinomyces radidentis	427691003
15	ACTUROG	Actinomyces urogenitalis	Actinomyces urogenitalis	409827009
16	ACTVI	Actinomyces viscosus	Actinomyces viscosus	33529006
17	AEGU	Aerococcus	Aerococcus	9008009
18	AECH	Aerococcus christensenii	Aerococcus christensenii	409818008
19	AESGN	Aerococcus sanguinicola	Aerococcus sanguinicola	427222006
20	AEUR	Aerococcus urinae	Aerococcus urinae	243230001
21	AEURQ	Aerococcus urinaeequi	Aerococcus urinaeequi	430979003
22	AEURH	Aerococcus urinaehominis	Aerococcus urinaehominis	409819000
23	AEVI	Aerococcus viridans	Aerococcus viridans	78803006
24	ASNSP	Alpha-hemolytic Streptococcus, not S pneumoniae	Alpha-hemolytic Streptococcus not Streptococcus pneumoniae	713921004
25	ARCSP	Arcanobacterium	Arcanobacterium	51714009
26	ARCHA	Arcanobacterium haemolyticum	Arcanobacterium haemolyticum	44723000
27	ARCPLUR	Arcanobacterium pluranimalium	Arcanobacterium pluranimalium	428939003
28	ARTSP	Arthrobacter	Arthrobacter	56214009
29	ARTAGIL	Arthrobacter agilis	Arthrobacter agilis	113432004
30	ARTASTR	Arthrobacter astrocyaneus	Arthrobacter astrocyaneus	113433009
31	ARTCITR	Arthrobacter citreus	Arthrobacter citreus	44955005
32	ARTCRYS	Arthrobacter crystallopoietes	Arthrobacter crystallopoietes	113435002
33	ARTFLAV	Arthrobacter flavus	Arthrobacter flavus	429762004
34	ARTGAND	Arthrobacter gandavensis	Arthrobacter gandavensis	428332000

CABSI

CATHETER ASSOCIATED BLOODSTREAM INFECTIONS

➤ PERIPHERAL CATHETERS

- ❖ STANDARD PERIPHERAL CATHETERS
- ❖ LONG PERIPHERAL CATHETERS (MINIMIDLINE)

PLABSI

➤ MIDLINE (PERIPHERAL)

MABSI
MRBSI?

➤ CENTRAL CATHETERS

- ❖ CICC, PICC, FICC
- ❖ TOTALLY IMPLANTED
- ❖ TUNNELED
- ❖ DIALYSIS

CLABSI²¹
CRBSI



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M. Sánchez^q, J. Vallés^r

DIAGNOSI MICROBIOLOGICA



**CON
RIMOZIONE
DEL CATETERE**

**SENZA
RIMOZIONE
DEL CATETERE**

EMOCOLTURE QUANTITATIVE APPAIATE

- EMOCOLTURE CONVENZIONALI PRELEVATE CONTEMPORANEAMENTE DAL CATETERE E DAL SANGUE PERIFERICO
- POSITIVITÀ: POSITIVITÀ DELLE COLTURE DA ENTRAMBI I SITI, CON UNA CONCENTRAZIONE DI MICRORGANISMI DAL CATETERE 3-5 VOLTE SUPERIORE A QUELLA DEL SANGUE PERIFERICO
- 10 STUDI CONSIDERATI
- SENSIBILITÀ: 87%
- SPECIFICITÀ: 98%
- **TEST PIU' ACCURATO IN ASSOLUTO!**



DIFFERENTIAL TIME TO POSITIVITY

- EMOCOLTURE CONVENZIONALI PRELEVATE CONTEMPORANEAMENTE DAL CATETERE E DAL SANGUE PERIFERICO
- POSITIVITÀ: POSITIVITÀ DELLE COLTURE DA ENTRAMBI I SITI, CON QUELLE CENTRALI POSITIVE 2 E PIÙ ORE PRIMA RISPETTO A QUELLE DAL SANGUE PERIFERICO
- 10 STUDI CONSIDERATI
- SENSIBILITÀ 85%
- SPECIFICITÀ: 81%



Maki, Ann Inter Med 2005

Utility of Differential Time to Positivity in Diagnosing Central Line–Associated Bloodstream Infections: A Systematic Review and Meta-Analysis

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Background. Differential time to positivity (DTP), defined as pathogen growth at least 2 hours earlier from catheter versus paired peripheral blood cultures, is sometimes used to diagnose central line–associated bloodstream infections (CLABSI). Previous studies assessing DTP, however, have been small, provided conflicting results, and did not assess heterogeneity across important subgroups.

Methods. We systematically reviewed the diagnostic characteristics of DTP for CLABSI using MEDLINE, Embase, WoS, CINAHL, LILACS, AMED, and the Cochrane database. Studies were included if they reported sensitivities, specificities, predictive values, likelihood ratios, or 2 × 2 tables of DTP for diagnosing CLABSI. Extracted data were analyzed by using forest plots, bivariate model meta-analysis, and QUADAS-2 quality assessment.

Results. We identified 274 records, of which 23 met the criteria for meta-analysis. Among 2526 suspected CLABSIs, DTP demonstrated a summary sensitivity of 81.3% (95% confidence interval [CI]: 72.8%–87.7%), specificity of 91.8% (95% CI: 84.5%–95.8%), positive likelihood ratio of 9.89 (95% CI: 5.14–19.00), and negative likelihood ratio of 0.20 (95% CI: .14–.30). Covariate analysis based on catheter duration, study design, and patient immune status demonstrated no significant differences. However, DTP performed worse for *Staphylococcus aureus* (low sensitivity but high specificity) and *Candida* (high sensitivity but low specificity) compared to other organisms.

Conclusions. DTP performs well in ruling CLABSIs in or out. Obtaining paired catheter and peripheral blood cultures for DTP when the infectious source is unclear may prevent unnecessary line removal and diagnostic tests. However, this must be balanced against higher contamination rates from catheter cultures.

Keywords. DTP; CLABSI; sensitivity; specificity; meta-analysis.

Utility of Differential Time to Positivity in Diagnosing Central Line Associated Bloodstream Infections: A Systematic Review and Meta-Analysis

Dhaliwal et al., 2023 | *Clinical Infectious Diseases*



BACKGROUND: Differential time to positivity (DTP) supports the diagnosis of central line associated bloodstream infections (CLABSI) when blood cultures from a catheter become positive at least two hours before peripheral blood cultures. The purpose of this systematic review is to determine the diagnostic characteristics of DTP in diagnosing CLABSI



SEARCH STRATEGY AND STUDIES INCLUDED: A search was performed using MEDLINE, Embase, Web of Science, CINAHL, LILACS, AMED and the Cochrane database. Studies were eligible for inclusion if they reported sensitivities, specificities, predictive values, likelihood ratios, or 2x2 tables of DTP for diagnosing CLABSI.



METHODOLOGY: The identified studies were screened for inclusion by two independent reviewers. The extracted data were analysed by creating forest plots, performing bivariate model meta-analysis, and assessing quality using QUADAS-2.

INCLUDED STUDIES

Qualitative review: 28
Quantitative review: 23
of Suspected CLABSI: 2526



RISK OF BIAS: many of the included studies were at high risk of bias with respect to the reference standard

[95% CI]

Sensitivity 81.3% [72.8 - 87.7]

Specificity 91.8% [84.5-95.8]

Positive Likelihood Ratio 9.89 [5.14 - 19.00]

Negative Likelihood Ratio 0.20 [0.14 - 0.30]

Additional Findings

- Covariate analysis based on catheter duration, study design, and patient immune status demonstrated no statistical significance
- DTP for *Staphylococcus aureus* and *Candida* CLABSIs performed poorly compared to other organisms.

CONCLUSION: DTP performs well in ruling CLABSIs in or out. Obtaining paired catheter and peripheral blood cultures for DTP when the infectious source is unclear may prevent unnecessary line removal and diagnostic tests, although this needs to be balanced against potentially higher contamination rates from catheter cultures.

DIFFICOLTÀ DIAGNOSTICHE

- MANCANZA DI PROTOCOLLI OMOGENEI PER L'ESECUZIONE DELLE EMOCOLTURE (NUMERO DI PRELIEVI DA EFFETTUARE, SITO DEL PRELIEVO, DISINFEZIONE DELLA CUTE, TIMING DI PRELIEVI SERIATI, VOLUME DI SANGUE DA PRELEVARE, CONTAMINAZIONI...)
- DIFFICOLTA' NELLA INTERPRETAZIONE DEI RISULTATI DELLE EMOCOLTURE

EMOCOLTURE

- QUANTE?
- QUANDO?
- QUANTO SANGUE?
- QUALE ANTISETTICO?
- “DISCARD VOLUME”?





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PERCORSO DIAGNOSTICO

INFEZIONI DEL TORRENTE CIRCOLATORIO

Gruppo di Lavoro Organizzativo dei
Percorsi Diagnostici (GLOPD)

Coordinatore: Cristina Giraldi
c.giraldi54@gmail.com
Proprietà intellettuale di AMCLI ETS.



2. EMOCOLTURA PERCHÈ, QUANDO E COME

2.1 Perché

L'emocoltura rappresenta il *gold standard* per la diagnosi delle BSI. È anche la metodica con il miglior rapporto costo/efficacia permettendo di isolare, identificare e testare la sensibilità agli antimicrobici degli isolati batterici e/o fungini. (Singer *et al.*, 2016; Rhodes *et al.*, 2017, De Plato *et al.*, 2020)

2.2 Quando

BOX: L'emocoltura, nel sospetto di BSI, deve essere effettuata quanto prima, non appena viene formulato il sospetto clinico; soprattutto in caso di sepsi e shock settico. Non è raccomandato attendere il picco febbrile o l'insorgenza di brividi.

Una emocoltura va prescritta in risposta al sospetto clinico di batteriemia, associata non solo alla sepsi ma anche a polmonite, meningite, osteomielite e ad altre infezioni. Molti possono essere gli indicatori clinici che inducono alla prescrizione dell'esame, tra cui: la valutazione di segni di infezione localizzata con possibile coinvolgimento sistemico, la febbre o l'ipotermia, la presenza di brividi, la frequenza cardiaca elevata, la riduzione della pressione arteriosa, la variazione della frequenza respiratoria, l'alterato stato di coscienza. A corredo di una clinica suggestiva, il laboratorio fornisce degli importanti elementi che possono essere utili nella valutazione globale, come la conta dei globuli bianchi nell'emocromo, la proteina C reattiva (PCR), la procalcitonina, la proadrenomedullina, i lattati e più recentemente la presepsina (Singer *et al.*, 2016; De Plato *et al.*, 2020; Azim *et al.*, 2021).

Nonostante il timing di esecuzione delle emocolture sia uno dei principali fattori che influenza la sensibilità del metodo, ad oggi non esiste ancora un consenso a riguardo (Lamy *et al.*, 2016; De Plato *et al.*, 2020). Tuttavia, alcuni accorgimenti sono raccomandabili:

- L'esame deve essere prescritto tempestivamente a fronte del sospetto clinico;
- La batteriemia spesso non correla con segni e sintomi specifici, pertanto, non è indicato attendere la comparsa di brivido e/o del picco febbrile per eseguire il prelievo;
- L'esame deve essere eseguito prima o il più lontano possibile dall'inizio della terapia antibiotica empirica, questo tuttavia non deve causare ritardi nell'iter terapeutico (Rhodes *et al.*, 2017).

2.3 Come

BOX: La letteratura più recente indica che la "single sample strategy" presenta alcuni vantaggi rispetto allo standard corrente, basato sulla "multi sample strategy", soprattutto se si dispone di un team di personale dedicato e in generale nei reparti di terapia intensiva. In queste condizioni è consigliabile effettuare l'emocoltura tramite una singola venipuntura, utilizzando un kit con materiale pre-ordinato, secondo la tecnica "single sample strategy", prelevando circa 40 mL totali di sangue.

L'esame deve essere eseguito da personale infermieristico formato (è consigliata la presenza di due infermieri, ove praticabile) o addirittura di un *team* dedicato (es. tipo "PICC team") ed è consigliato organizzare un *kit* di prelievo che consenta di avere a disposizione del team tutti i dispositivi necessari per una corretta esecuzione (compresi i dispositivi per la disinfezione). Le modalità di prelievo, conservazione e invio dei flaconi devono essere codificate in procedure scritte da trasmettere a tutti i reparti e da esplicitare nella carta dei servizi del laboratorio.

Laddove possibile è generalmente raccomandata la "*single sample strategy*" ovvero il singolo prelievo di 30–40 mL di sangue da venipuntura periferica, da ripartire nei diversi flaconi di emocoltura (Jaimes *et al.*, 2004). La "*multi sample strategy*" viene utilizzata in specifiche circostanze, non solo legate alla tipologia di paziente, ma più spesso al sospetto di infezione: per esempio questa strategia è alla base della diagnosi di batteriemia associata ad endocardite infettiva subacuta (3 venipunture ad intervalli regolari in 24h, da ripetere in caso di negatività) (Li

et al., 1994; CLSI, 2022; Riedel *et al.*, 1975; Miller *et al.*, 2018; Dellinger *et al.*, 2013) oppure nel sospetto di infezione correlata a device (almeno 1 set dal device e 1 o più dalla vena periferica, simultaneamente).

Nel paziente con CVC, in cui si sospetti (o non si possa escludere) una sepsi catetere-correlata è indispensabile effettuare il prelievo:

- da vena periferica e dal/i catetere/i, contemporaneamente, dopo aver disinfettato il raccordo con soluzione alcolica, se compatibile con il materiale del CVC, senza scartare la prima quantità di sangue prelevato perché è quella con la più alta concentrazione di microbi. Il prelievo quando possibile dovrebbe essere effettuato scegliendo un accesso venoso posto dal lato opposto rispetto a dove è posizionato il CVC (es: CVC lato destro, accesso venoso a sinistra) (CLSI, 2022)
- Immettere rigorosamente la stessa quantità di sangue in ciascun flacone, ciò consentirà l'interpretazione dei risultati sulla base dei tempi di crescita.
- da vena periferica, (set: aerobi + anaerobi), prelevato come di consueto

Prelievo da vena periferica

Il set di prelievo a doppio ago (DA) (farfalla) per la raccolta del sangue direttamente nei flaconi corredato o meno di ISDD (*initial specimen diversion device*) è generalmente da preferirsi perché riduce i rischi di puntura accidentale per l'operatore, anche se non riduce quello di una possibile contaminazione nel prelievo. Infatti, la percentuale di contaminazione con il dispositivo a DA è del 3.7% contro il 2% dell'ago singolo (Rupp *et al.*, 2017). L'introduzione di *device* corredati da ISDD ha prodotto risultati preliminari molto soddisfacenti, riducendo, in uno studio, il tasso di contaminazione, da 1.78% allo 0.22%. Tuttavia, ulteriori studi più ampi sono necessari per accertare il reale impatto di tali *device*.

A corredo di procedure che ad oggi hanno un elevato grado di standardizzazione e con una rigorosa letteratura si vuole sottolineare che:

- È essenziale strofinare le mani per almeno 30 secondi con gel idroalcolico, prima di procedere al prelievo;
- È essenziale una corretta disinfezione della cute con una soluzione alcolica al 70% e clorexidina al 2% (30 secondi di attesa perché si asciughi);
- È essenziale una corretta disinfezione del tappo dei flaconi di emocoltura con lo stesso presidio antisettico usato per la disinfezione della cute nel rispetto delle indicazioni riportate dal produttore. Questo avviene idealmente poco prima del prelievo;
- È consigliato posizionare l'ago in vena e collegare il set di prelievo prima nel flacone per aerobi, poi nel flacone per anaerobi;
- È essenziale monitorare attentamente durante il prelievo la quantità di sangue prelevato in modo da inoculare ottimamente i flaconi, mantenendo i flaconi verticali e controllando il livello di liquido all'interno.

Non esistono in commercio flaconi sottovuoto capaci di raccogliere una quantità definita di sangue; quindi, il volume di sangue deve essere monitorato durante il prelievo dall'operatore. Se il prelievo venoso è effettuato anche per raccogliere sangue per altre determinazioni, i flaconi per emocoltura devono essere inoculati per primi al fine di evitare contaminazioni.

Il prelievo con siringa non è raccomandato.

Prelievo nel paziente con CVC, in cui si sospetti (o non si possa escludere) una batteriemia catetere-correlata

A corredo di procedure che ad oggi hanno un elevato grado di standardizzazione e con una abbondante letteratura in campo infermieristico si vuole sottolineare che:

- È essenziale che il prelievo dal/dai cateteri venga eseguito contemporaneamente con quello da vena periferica, dopo aver disinfettato il raccordo con un adeguato presidio antisettico;
- È essenziale non scartare la prima quantità di sangue prelevato dal CVC perché è quella con la più alta concentrazione microbica;
- È essenziale rispettare i volumi di inoculo cercando di immettere in ogni flacone la stessa quantità di sangue: ciò consentirà l'interpretazione dei risultati sulla base dei tempi di crescita.

3. MODALITÀ E TEMPI DI INCUBAZIONE DELLE EMOCOLTURE

BOX: I flaconi di emocoltura devono essere incubati il più velocemente possibile, e comunque entro 2 ore dal prelievo, in sistemi di monitoraggio automatizzati che mantengano i flaconi in osservazione continua. Il tempo di incubazione raccomandato è di 5 giorni.

La maggior parte dei laboratori di microbiologia clinica sono dotati di sistemi semiautomatizzati o automatizzati per il monitoraggio continuo delle emocolture che consentono la rilevazione di emocolture positive in un tempo medio compreso fra le poche ore e 3 giorni, garantendo la rilevazione della positività in tempi più contenuti rispetto ai vecchi metodi manuali basati su ispezione visiva del flacone, colorazione di Gram e sub-coltura in cieco di flaconi per emocoltura a intervalli di tempo stabiliti *a priori* (24-48h di incubazione). Nei sistemi a monitoraggio continuo, il periodo di incubazione standard delle emocolture raccomandato è di 5 giorni ad una temperatura di 35 ± 2 °C (CLSI, 2022; Hagiya *et al.*, 2019, Lamy *et al.*, 2016, Lamy *et al.*, 2018, Lamy *et al.*, 2019, Lamy *et al.*, 2020).

Il 92-95% delle emocolture si positivizza entro le prime 24-48 ore di incubazione (Lamy *et al.*, 2019) con tempi in alcuni casi più lunghi per lieviti, batteri anaerobi e batteri particolarmente esigenti (vedi di seguito).



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M47

Principles and Procedures for Blood Cultures

This guideline includes recommendations for collecting, transporting, and processing specimens for blood culture, as

Table 2. Indications for Obtaining Initial Blood Cultures^{31,32,34-44}

Conditions	Notes
Febrile neutropenia	
Fever without a source	
Suspected endovascular infections, including CLABSIs	
Suspected infective endocarditis	
Suspected sepsis	
• Cholangitis • Complicated pneumonia • Complicated SSTIs • Meningitis • Osteomyelitis • Pyelonephritis • Septic arthritis	• These syndromes are frequently associated with bacteremia. • Examples of complicated SSTIs include burn wounds, immersion injuries, puncture wounds from animal bites, infections in patients with neutropenia or other immunocompromising conditions, pyomyositis, gangrene, necrotizing fasciitis, and myonecrosis.
Unexplained leukocytosis	

Abbreviations: CLABSI, central line–associated bloodstream infection; SSTI, skin and soft tissue infection.

3.3.1 Timing of Specimen Collection for Blood Culture

It has been common practice to collect specimens for blood culture at arbitrary 30- to 60-minute intervals. However, studies show no difference in microbial recovery when specimens are collected for blood culture simultaneously, as opposed to at spaced intervals for up to 24 hours.⁴⁶ Collecting specimens when the patient's fever spikes does not significantly affect blood culture positivity rates.^{33,46}

As a practical matter, specimens for blood cultures should be collected simultaneously (or over a short time frame). Drawing blood at intervals is indicated only when it is necessary to document continuous bacteremia in patients with suspected infective endocarditis or other endovascular infections (eg, CRBSIs).

3.3.3 Number of Blood Culture Sets

For adult patients with a suspected BSI, the current recommendation is to obtain two to three blood culture sets per episode within a 24-hour period. Multiple sets should **always** be obtained to ensure adequate blood volume. Additionally, the results of a single blood culture set are more difficult to interpret than the results of multiple sets. Follow-up blood culture sets should not be repeated for two to five days after the initial sets are obtained, because the blood does not immediately become sterile after antimicrobial therapy is initiated.

Several studies have investigated the optimal number of blood culture sets for detecting bacteremia or fungemia.⁶⁸ In a study conducted in 1975, based on 80 patients from whom 20-mL blood specimens were collected,⁶⁹ the cumulative yield of pathogens from three blood culture sets was 80% from the first set, 88% from two sets, and 99% from three sets.⁶⁹ Results from another study in 1983, based on 282 patients from whom 15-mL blood specimens were collected,⁵ are similar to the 1975 study results. The cumulative pathogen yield from these cultures was 91% from the first blood culture set and > 99% (281 / 282) from two sets. In both studies, blood culture sets were analyzed with conventional (ie, manual) blood culture systems.

In a similar study in 2004, based on 163 patients from whom blood culture sets were obtained and analyzed with a CMBCS,^{5,6} the cumulative pathogen yield from three blood culture sets, with a blood volume of 20 mL each (excluding patients with infective endocarditis), was 65% from the first set, 80% from two sets, and 96% from three sets.⁶ For patients with infective endocarditis, the yield was 90% from the first blood culture set.⁶ A subsequent study in 2007 assessed the incremental yield of sequential 20-mL blood culture sets obtained from 687 patients.⁷ In this study, the yield was 73% from the first blood culture set, 90% from two sets, 98% from three sets, and > 99% from four sets. Compared with pathogen yields from cultures analyzed with conventional blood culture systems, the lower cumulative pathogen yield from cultures analyzed with a CMBCS may be due to several variables, including^{5,6,69}:

3.4.1 Blood Culture Bottle Preparation

Immediately before venipuncture is performed, the rubber septum on the blood culture bottle(s) or evacuated tube(s) should be disinfected with 70% isopropyl alcohol by rubbing the rubber septum with friction and then allowing it to dry. For more information on collecting diagnostic specimens by venipuncture, see CLSI document GP41.⁹⁰

Blood should not be drawn directly into blood culture bottles (eg, using a multisample needle and tube holder assembly or drawing from an intravenous [IV] access device with a tube holder assembly). Doing so poses a risk of broth-medium reflux into the patient's vein. Additionally, the volume of blood collected directly into blood culture bottles or tubes cannot be controlled. At least one manufacturer markets blood culture bottles approved for direct filling. The manufacturer's instructions for collecting blood specimens must be followed. Blood culture bottles should be kept upright when these directly filled devices are used. To prevent clotting, blood culture bottles or tubes should be inverted gently several times after blood is drawn.

Some studies show a significant reduction in blood culture specimen contamination when an aliquot of blood is discarded before blood culture bottles or tubes are filled. When tubes are used for the discard, their stoppers should be disinfected with alcohol before collection. Recently, self-contained devices that achieve initial specimen diversion without requiring extra collection tubes have become available. Studies have also demonstrated reduced blood culture contamination rates when these devices are used.⁹¹⁻⁹⁶ More data are needed to support the recommendation that a discard is needed before all blood culture specimen collections. Each institution should consider the costs and benefits of implementing such protocols and/or devices.

For adults with suspected bacteremia, at least two blood culture sets should be obtained, from two separate venipuncture sites. A maximum of four blood culture sets should be obtained. The aerobic blood culture bottle should be inoculated first, because sometimes it is difficult to collect 8 to 10 mL of blood per bottle (15 to 20 mL/set). The aerobic bottle is the more critical one in which to inoculate low-volume specimens. It is important not to under- or overfill the bottles. These actions can cause inaccurate test results.

For pediatric patients with suspected bacteremia (see Subchapter 3.3.2), one aerobic blood culture bottle should be filled, as ordered by the HCP. The weight-based volume recommendations in Subchapter 3.3.4 should be followed. Anaerobic blood culture bottles should be included only when clinically indicated.

3.4.2 Skin Disinfection

To minimize the risk of contaminating blood specimens with skin flora, the venipuncture site requires a minimum 30-second friction scrub with an appropriate disinfectant. When using commercially packaged preparation kits, the HCP must follow the manufacturer's instructions. Many disinfectants have been used clinically over the past 50 years, including rubbing alcohol (70% isopropyl), tincture of iodine, povidone-iodine, iodophors, chlorine-peroxide, and chlorhexidine gluconate.⁹⁷

Iodine-containing preparations require sufficient time to disinfect surfaces (30 seconds for tincture of iodine and 1½ to 2 minutes for iodophors). Iodine should be removed from the skin after the procedure is complete (see CLSI document GP41⁹⁰). Chlorhexidine gluconate requires the same amount of time on the skin as tincture of iodine. However, it is not typically associated with allergic reactions and does not need to be cleaned off the skin after the procedure is complete. Chlorhexidine gluconate may be used for infants over 2 months of age, children, adolescents, and adults. However, because it can cause irritation or chemical burns, it should be used with caution in premature babies and in babies under 2 months of age.⁹⁸

To disinfect an adult patient's skin before collecting a blood culture specimen, the HCP should⁹⁹:

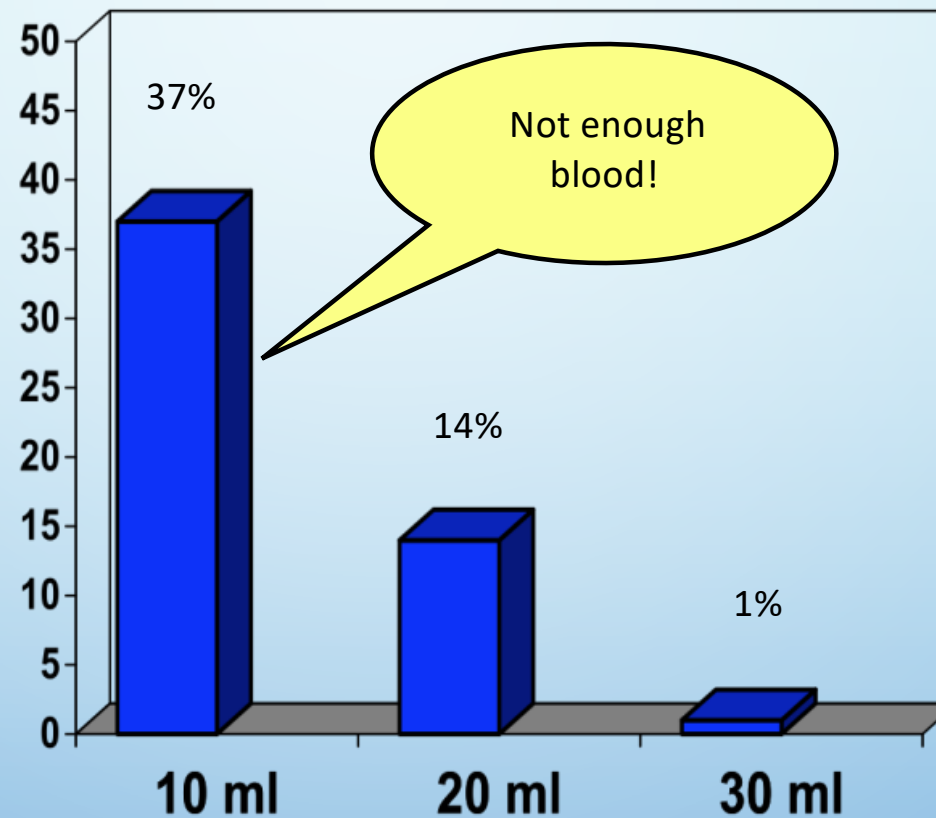
1. Cleanse the venipuncture site with friction for 30 seconds, using a clean or sterile gauze pad with 70% isopropyl alcohol or a commercially prepared alcohol pad.
2. Allow the alcohol to air dry.
3. Apply the second disinfectant.
4. Allow the disinfectant to remain in contact with the patient's skin for the duration recommended by the manufacturer.

After cleansing the site, the HCP should avoid palpating the patient's vein.

Similar methods of skin antisepsis also apply to pediatric patients. However, chlorhexidine gluconate should be used with caution in babies under 2 months of age. Multiple applications of 70% isopropyl alcohol are an acceptable alternative for skin disinfection for these patients. Consistent with recommendations for adults, blood drawn from an IV catheter should be accompanied by a peripheral blood draw.

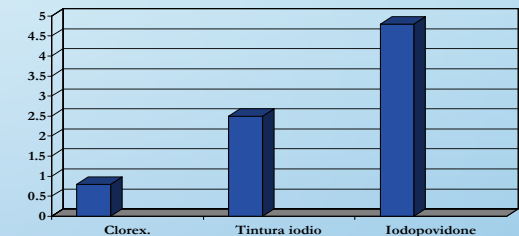
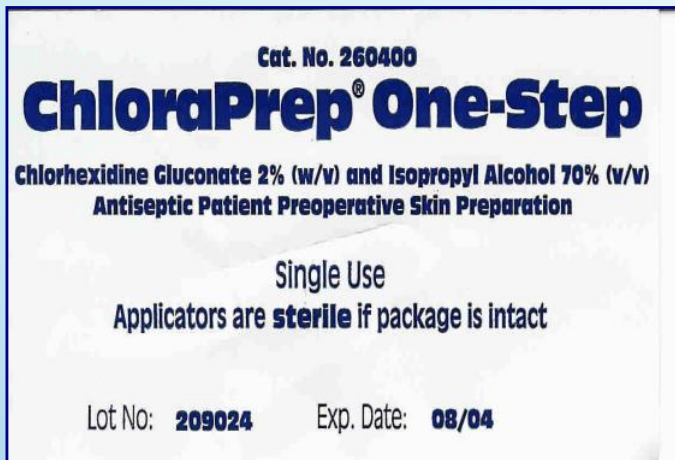
% False Negative vs. Volume of Blood

% False Negative
(blood culture is negative but patient is really septicemic)



Courtesy of E.J Baron, PhD, Dir of Microbiology Lab, Stanford Hosp

CONTAMINAZIONE DELLE EMOCOLTURE RISPETTO ALL'ANTISETTICO IMPIEGATO



Baylor, 2006



medicina *intensiva*

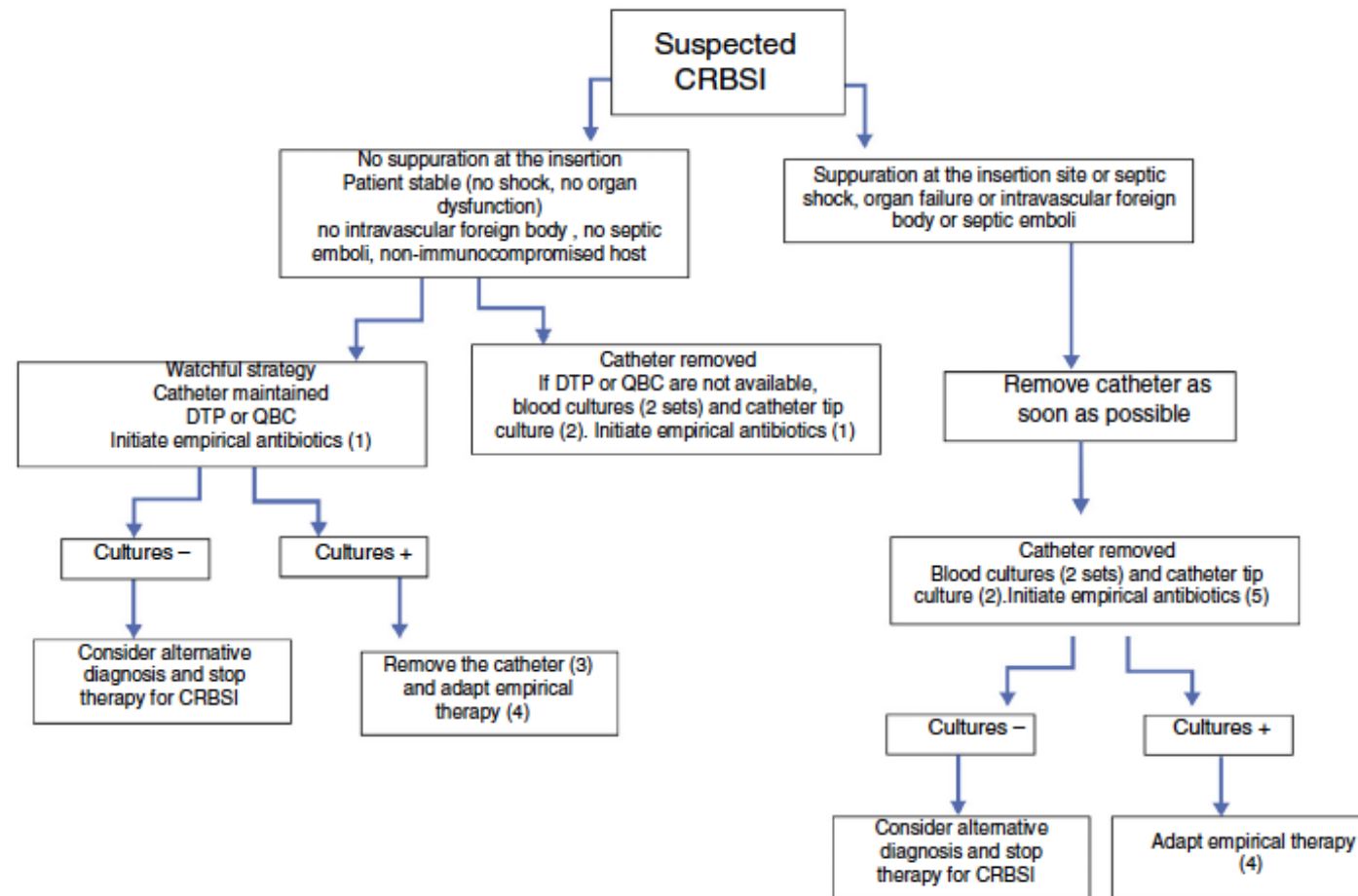
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CONSENSUS STATEMENT

Diagnosis and treatment of catheter-related bloodstream infection: Clinical guidelines of the Spanish Society of Infectious Diseases and Clinical Microbiology and (SEIMC) and the Spanish Society of Intensive and Critical Care Medicine and Coronary Units (SEMICYUC)☆





Confirmed CRBSI

Coagulase-Negative
Staphylococcus

- CoNS (1)
- Consider catheter removal (if not done) (2)
- Antimicrobial therapy for 5 days (3)
- Vancomycin is the first option (4)
- Echocardiography is not mandatory (5)
- Remove catheter if *S. lugdunensis* is isolated
- Catheter retained
 - Antimicrobial therapy for 10-14 days
 - Vancomycin in the first option (4)
 - ALT with vancomycin for 10-14 days
 - Echocardiography is not mandatory (5)

Staphylococcus aureus

- Removal of the catheter is mandatory
- Antimicrobial therapy for 14 days (6)
- Cloxacillin or cefazolin are the alternatives for MSSA
- Vancomycin or daptomycin are the alternatives for MRSA (7) (8)
- Echocardiography is mandatory

Enterococcus spp.

- Removal of the catheter is mandatory
- Antimicrobial therapy for 7-14 days
- Ampicillin is the drug of choice for susceptible strains (9)
- Vancomycin is the alternative for strains resistant to ampicillin (10)
- Echocardiography is mandatory

Gram-negative
bacilli

- Remove the catheter (if not done) (2)
- Antimicrobial therapy for at least 7 days (3)
- Antimicrobial therapy must be chosen based on the susceptibility results
- Echocardiography is not mandatory (5)
- Catheter retained (11)
 - Antimicrobial therapy for 10-14 days
 - Antimicrobial therapy must be chosen based on the susceptibility results
 - ALT for 10-14 days
 - Echocardiography is not mandatory (5)

Candida spp.

- Removal of the catheter is mandatory
- Antifungal therapy for 14 days after the first negative blood culture (12)
- Targeted antifungal therapy must be chosen based on the susceptibility results (13)
- Echocardiography is mandatory

Clinical Practice Guidelines for the Diagnosis and Management of Intravascular Catheter-Related Infection: 2009 Update by the Infectious Diseases Society of America

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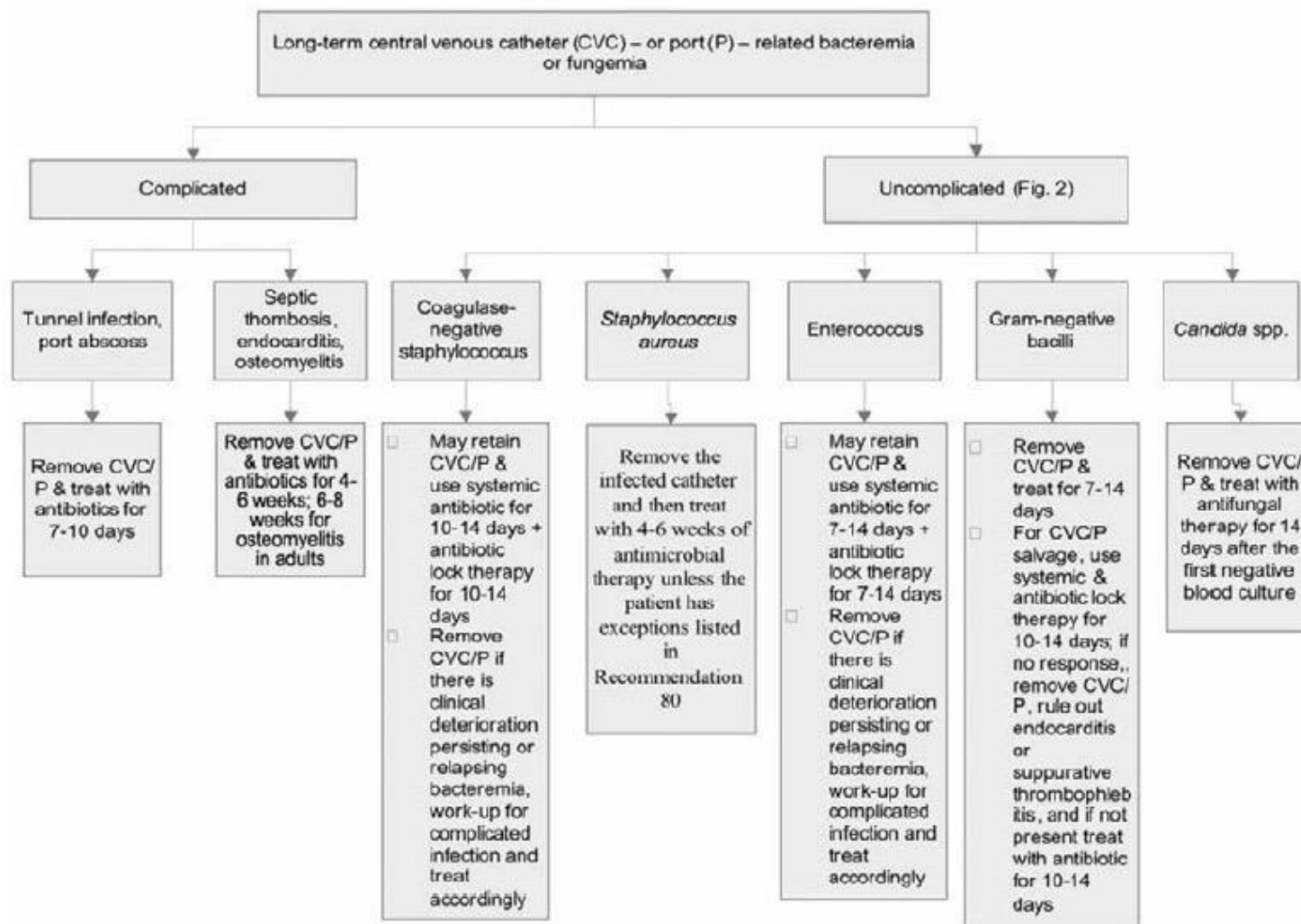


Figure 3. Approach to the treatment of a patient with a long-term central venous catheter (CVC) or a port (P)-related bloodstream infection.

Table 4 Indications for catheter removal in patients with CRBSI.

CRBSI presenting with septic shock

CRBSI caused by certain pathogens: *S. aureus*,
non-fermenting Gram-negative bacilli, *Candida* spp.
or *Mycobacterium*

Metastatic complications (endocarditis, thrombophlebitis
or septic pulmonary embolism)

Bacteremia (or candidemia) persisting after 72 h of
adequate treatment

Pus is observed at the insertion site

Signs of infection at the subcutaneous tunnel

No possibility of antibiotic lock therapy

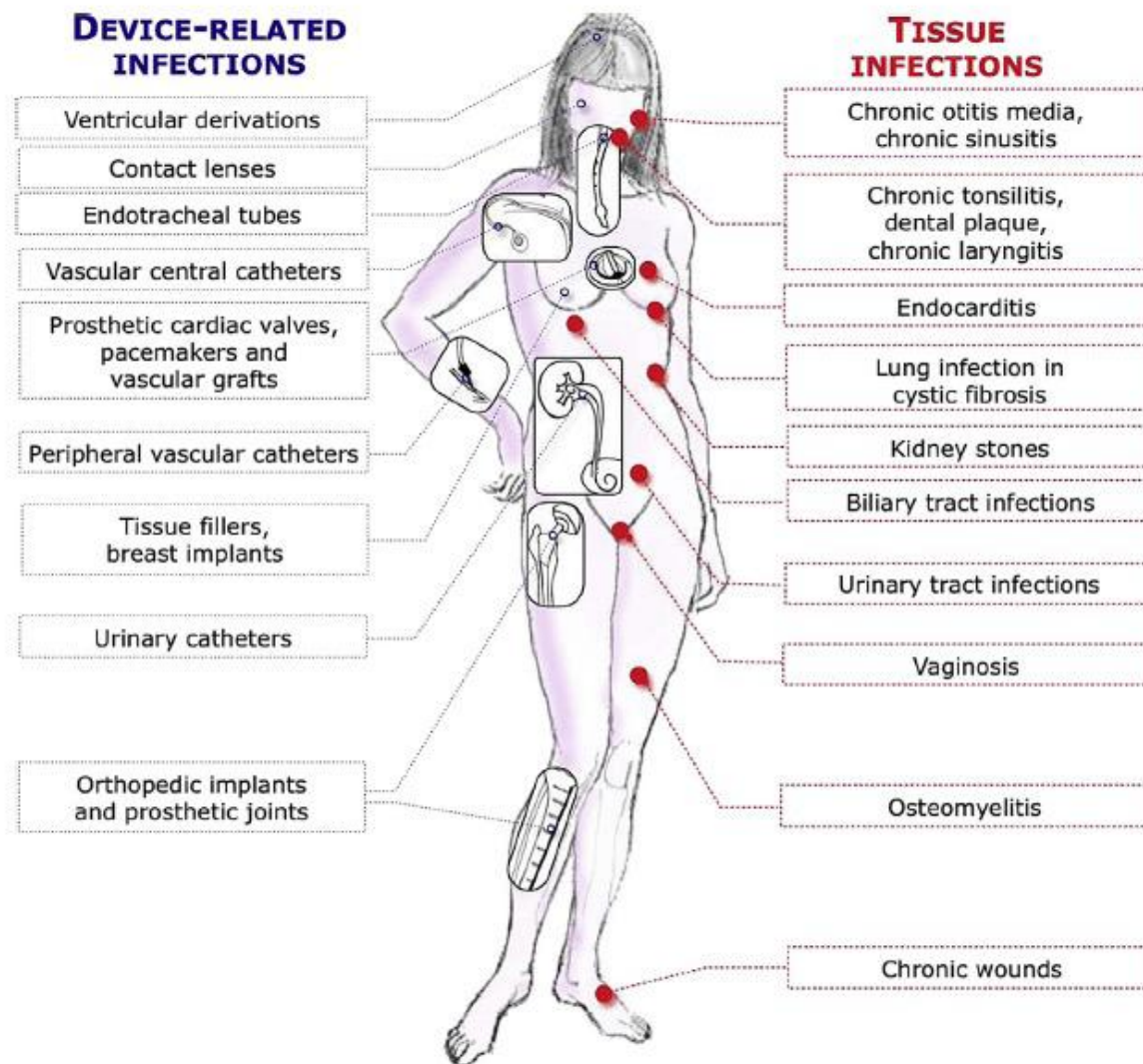
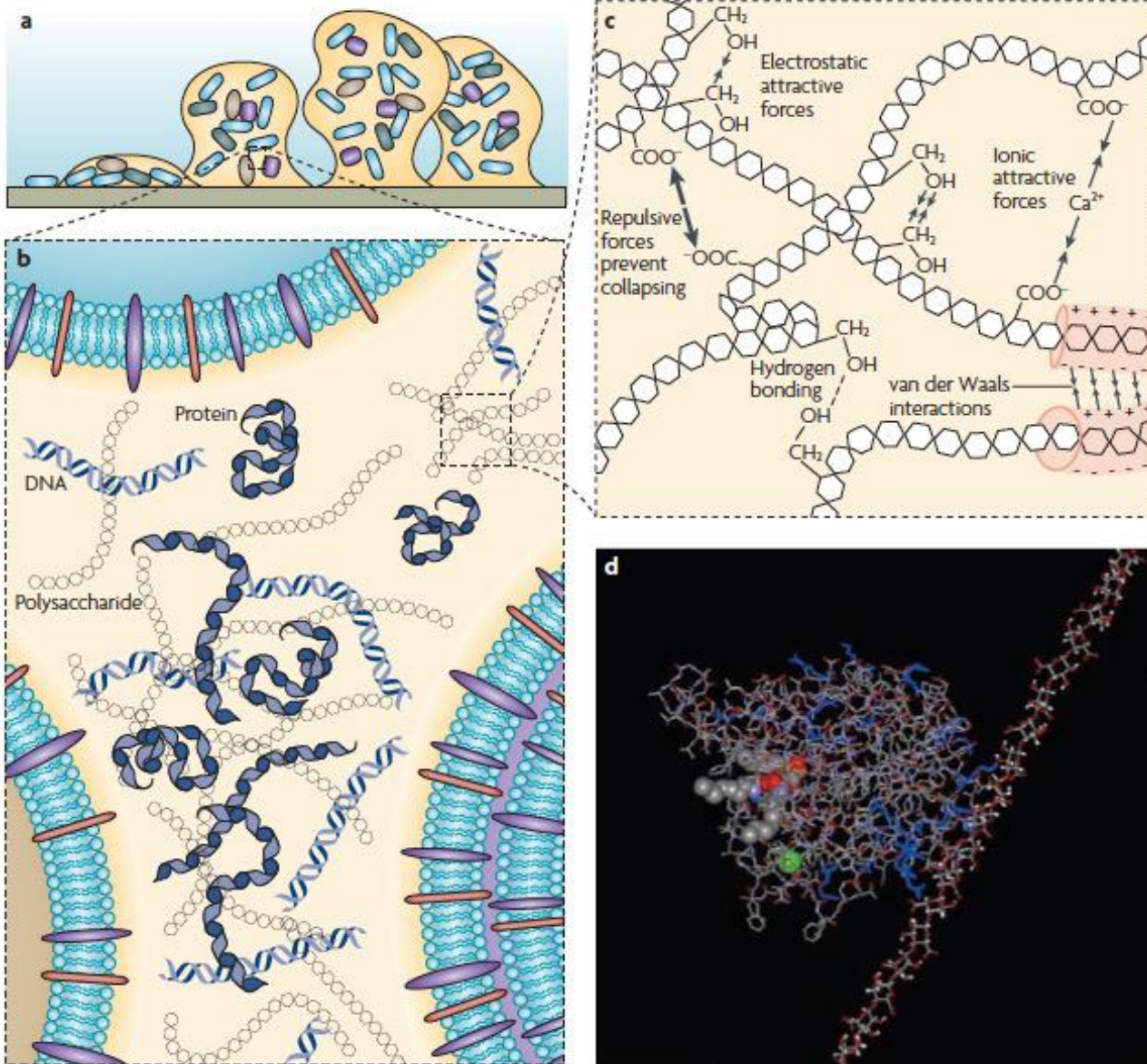


FIG. 1. Typical biofilm infections (3) (reproduced with permission).



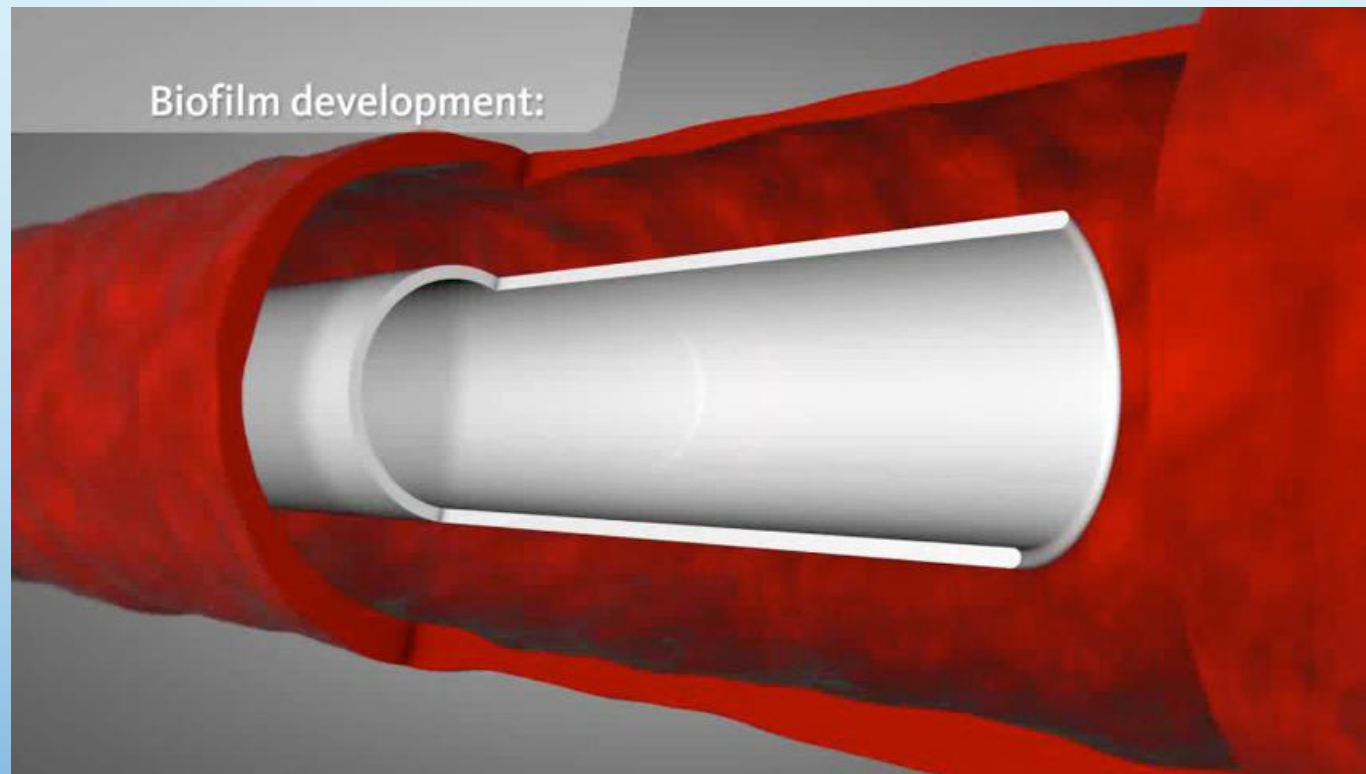
The ECM is composed of water, polysaccharides, proteins, extracellular DNA and lipids (12, 18, 20, 21). ECM provides mechanical stability to biofilms, improve their adhesion onto catheters and form a cohesive, three-dimensional polymer network that interconnects biofilm cells. It also protects microbial cells against external aggressions including host immune defences and antibiotics (20).

BIOFILM

The main characteristics of infections related to the presence of a biofilm are:

- Resistance to antibiotics
- Resistance to immune system cells

BIOFILM DEVELOPMENT ON THE WALL OF A VASCULAR CATHETER



Antibiotic-lock therapy: a clinical viewpoint

Expert Rev. Anti Infect. Ther. 12(1), 117–129 (2014)

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Antibiotic lock therapy (ALT) – instillation of high concentrations of anti-microbial agent with or without anti-coagulant into the lumen of central venous catheters – is considered a valid conservative treatment for catheter-related bloodstream infection (CRBSI) in patients highly dependent on maintaining the catheter. Results from randomized controlled studies have indicated that the effectiveness of ALT is moderate, but recent findings from experimental studies and observational case series point to considerable efficacy and safety of this therapy, which is usually associated with concomitant systemic treatment. In this article, the current knowledge about ALT for patients with CRBSI is reviewed and discussed, with emphasis on existing controversies and the results obtained according to the various uses of the catheters and the etiologies of infection.

KEYWORDS: antibiotic lock therapy • catheter-related sepsis • conservative management • permanent central venous catheter

ANTIMICROBIAL LOCK PROPHYLAXIS

SHEA/IDSA 2022 GUIDELINES, FOR THE POTENTIAL EMERGENCE OF ANTIMICROBIAL RESISTANCE, SUGGEST TO USE ANTIBIOTIC LOCK SOLUTIONS AS A PREVENTIVE STRATEGY ONLY FOR THE FOLLOWING: A) **PATIENTS WITH LONG-TERM HEMODIALYSIS CATHETERS**; B) **PATIENTS WITH LIMITED VENOUS ACCESS AND A HISTORY OF RECURRENT CLABSI**; C) **PATIENTS WHO ARE AT HEIGHTENED RISK OF SEVERE SEQUELAE FROM A CLABSI (EG, PATIENT WITH RECENTLY IMPLANTED INTRAVASCULAR DEVICES, SUCH AS PROSTHETIC HEART VALVE OR AORTIC GRAFT).**

INS 2024: **USE ANTIMICROBIAL LOCKING SOLUTIONS FOR THERAPEUTIC AND PROPHYLACTIC PURPOSES IN PATIENTS WITH LONG-TERM CVADS IN THE FOLLOWING CIRCUMSTANCES: A) PATIENTS WITH A HISTORY OF MULTIPLE CLABSIS; B) HIGH-RISK PATIENT POPULATIONS; C) IN FACILITIES WITH UNACCEPTABLY HIGH RATES OF CLABSI, DESPITE IMPLEMENTATION OF OTHER METHODS OF INFECTION PREVENTION.**



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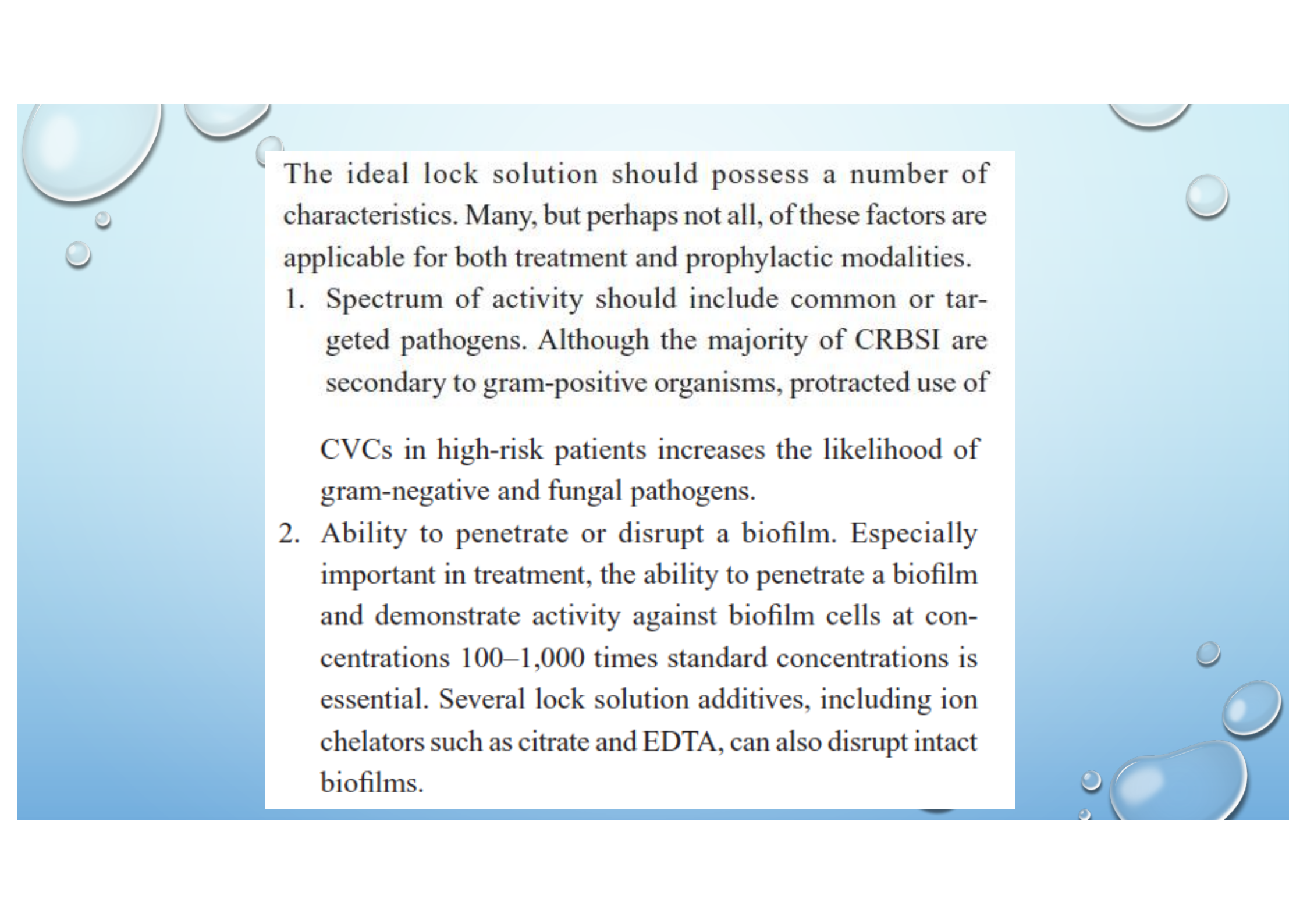


CONSENSUS STATEMENT

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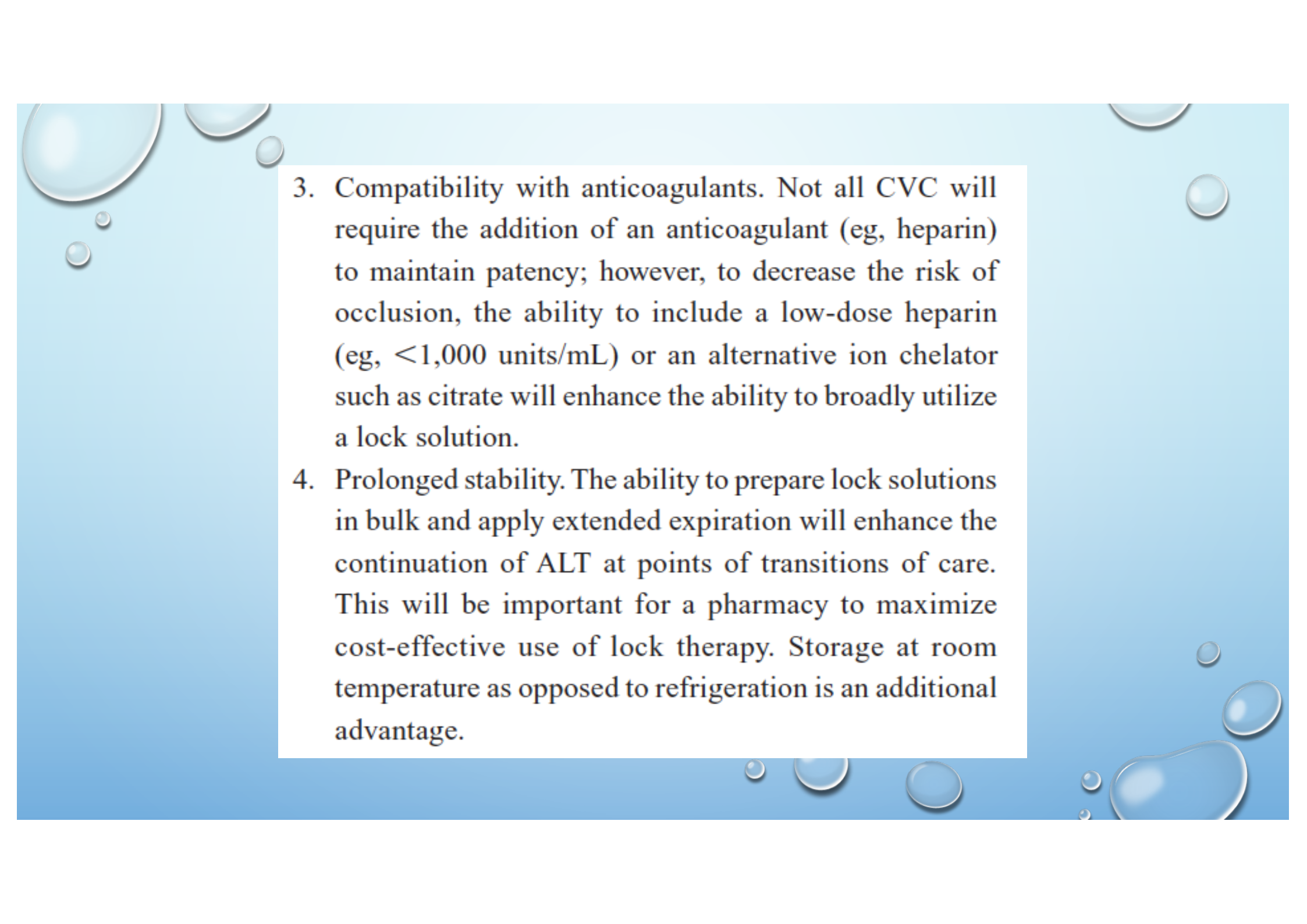


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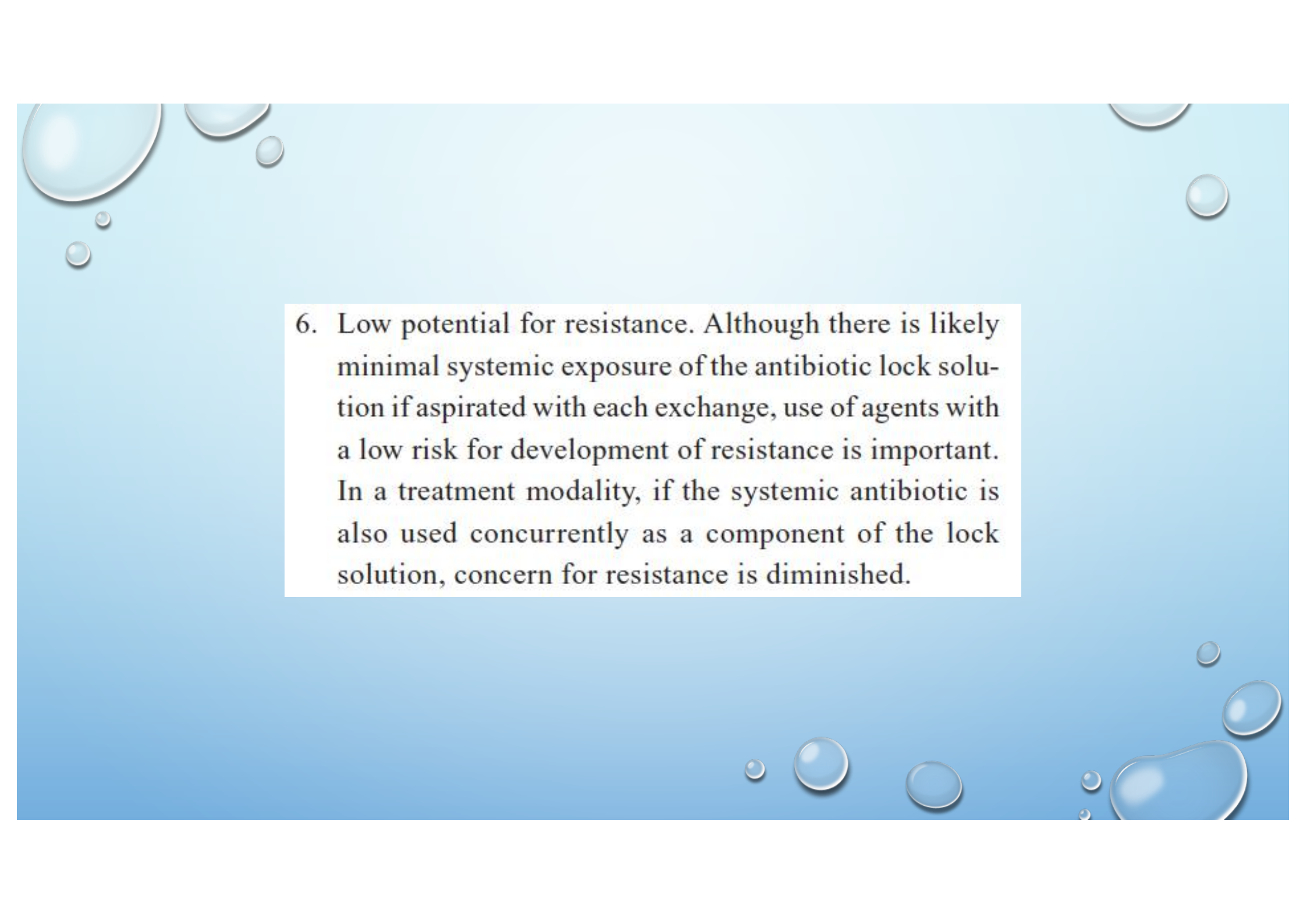


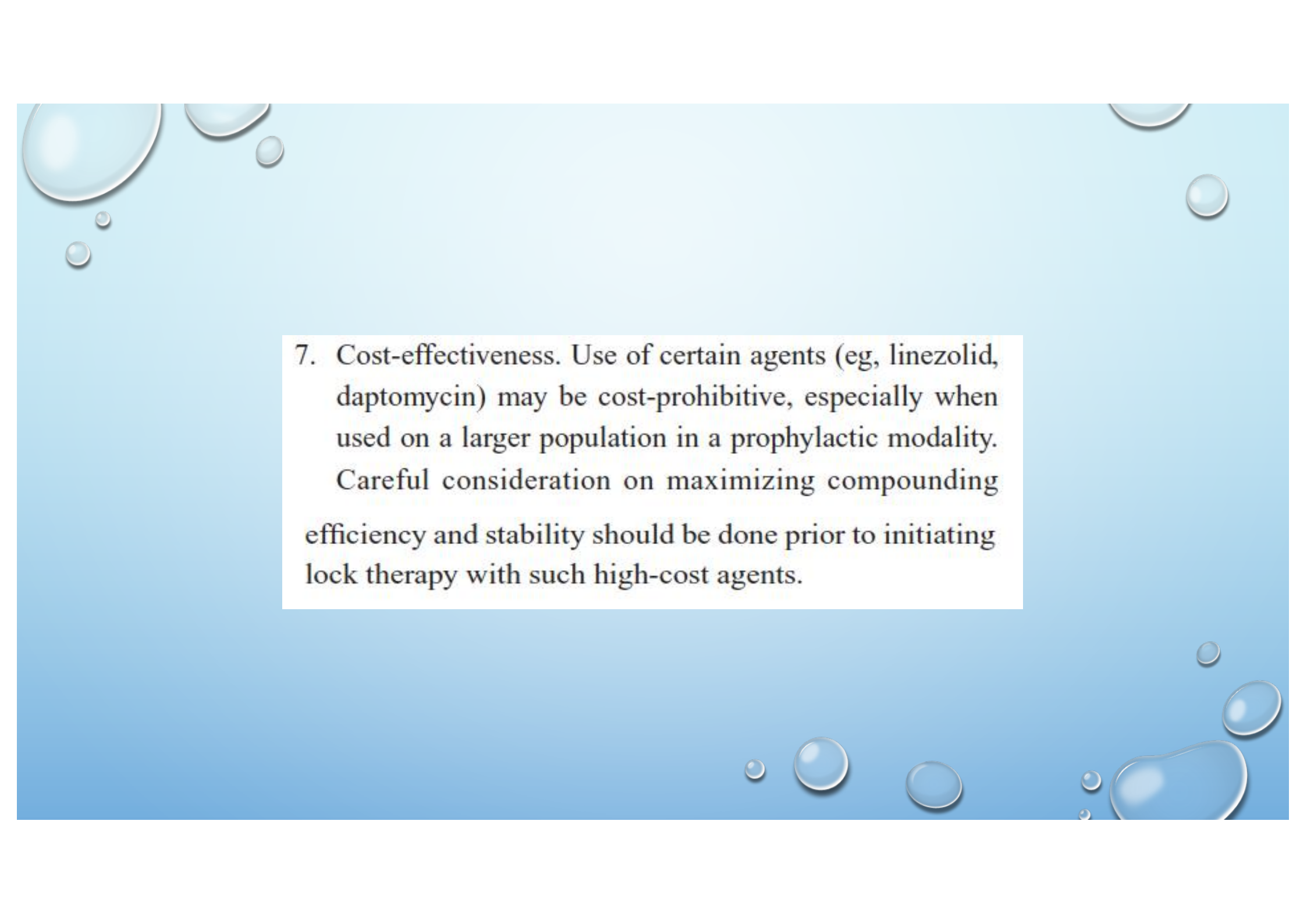
The ideal lock solution should possess a number of characteristics. Many, but perhaps not all, of these factors are applicable for both treatment and prophylactic modalities.

1. Spectrum of activity should include common or targeted pathogens. Although the majority of CRBSI are secondary to gram-positive organisms, protracted use of CVCs in high-risk patients increases the likelihood of gram-negative and fungal pathogens.
2. Ability to penetrate or disrupt a biofilm. Especially important in treatment, the ability to penetrate a biofilm and demonstrate activity against biofilm cells at concentrations 100–1,000 times standard concentrations is essential. Several lock solution additives, including ion chelators such as citrate and EDTA, can also disrupt intact biofilms.

- 
3. Compatibility with anticoagulants. Not all CVC will require the addition of an anticoagulant (eg, heparin) to maintain patency; however, to decrease the risk of occlusion, the ability to include a low-dose heparin (eg, <1,000 units/mL) or an alternative ion chelator such as citrate will enhance the ability to broadly utilize a lock solution.
 4. Prolonged stability. The ability to prepare lock solutions in bulk and apply extended expiration will enhance the continuation of ALT at points of transitions of care. This will be important for a pharmacy to maximize cost-effective use of lock therapy. Storage at room temperature as opposed to refrigeration is an additional advantage.

5. Low risk of toxicity and adverse events. The small volumes used in the intraluminal space do not lend themselves to high risk of toxicity. However, higher concentrations of specific agents (eg, aminoglycosides and citrate) have been associated with significant toxicity and should be avoided when using ALT.^{18,19} There is additional concern if these solutions are flushed as opposed to aspirated, which could expose the patient to higher concentrations of anticoagulants (eg, heparin). Ethanol at higher concentrations may be associated with minor adverse events, especially in low-weight neonates.¹⁴ Catheter occlusion is another possible adverse event with ALT, especially in the absence of a low-dose anticoagulant in solution.

- 
6. Low potential for resistance. Although there is likely minimal systemic exposure of the antibiotic lock solution if aspirated with each exchange, use of agents with a low risk for development of resistance is important. In a treatment modality, if the systemic antibiotic is also used concurrently as a component of the lock solution, concern for resistance is diminished.

The background of the slide is a light blue gradient. It is decorated with several realistic water droplets of various sizes, some with highlights and shadows, giving them a 3D appearance. The droplets are scattered across the top and bottom edges of the slide.

7. Cost-effectiveness. Use of certain agents (eg, linezolid, daptomycin) may be cost-prohibitive, especially when used on a larger population in a prophylactic modality. Careful consideration on maximizing compounding efficiency and stability should be done prior to initiating lock therapy with such high-cost agents.

Table I Summary of biofilm penetration for select antibiotics

Antibiotic class/agent	Microorganism	Extent of penetration	Rate of penetration	Reference
Fluoroquinolones				
Ciprofloxacin	<i>Bacillus cereus</i> , <i>Pseudomonas fluorescens</i>	100%	NR	10
	<i>Pseudomonas aeruginosa</i>	100%	Rapid	74
	<i>P. aeruginosa</i>	25%–50%	Rapid	75
	<i>Klebsiella pneumoniae</i>	80%–100%	Rapid	11
	<i>Staphylococcus aureus</i> , <i>Staphylococcus epidermidis</i>	86%–100%	NR	76
Levofloxacin	<i>P. aeruginosa</i>	100%	Rapid	75
Rifamycins				
Rifampin	<i>S. epidermidis</i>	79% to >90%	Rapid	77,78
Oxazolidinones				
Linezolid	<i>S. epidermidis</i>	~100% ^a	Rapid	79
Lipopeptides				
Daptomycin	<i>S. epidermidis</i>	≥100% ^b	Rapid	80
Tetracyclines				
Tetracycline	<i>B. cereus</i> , <i>P. fluorescens</i>	88%–93%	NR	10
Macrolides				
Erythromycin	<i>B. cereus</i> , <i>P. fluorescens</i>	72%–86%	NR	10
	<i>S. epidermidis</i>	45%–93%	Variable/slow	81

Beta-lactams

Ampicillin	<i>K. pneumoniae</i> (beta-lactamase positive)	0%	NA	11
	<i>K. pneumoniae</i> (beta-lactamase negative)	80%–100%	Rapid	11
Oxacillin	<i>S. aureus</i> , <i>S. epidermidis</i>	<70%	NR	76
Piperacillin	<i>P. aeruginosa</i>	50%–100%	Rapid	75
	<i>P. aeruginosa</i>	0%–15%	NR	82
Cefotaxime	<i>S. aureus</i> , <i>S. epidermidis</i>	68%–70%	NR	76
Imipenem	<i>P. aeruginosa</i>	50%–100%	Rapid	75

Glycopeptides

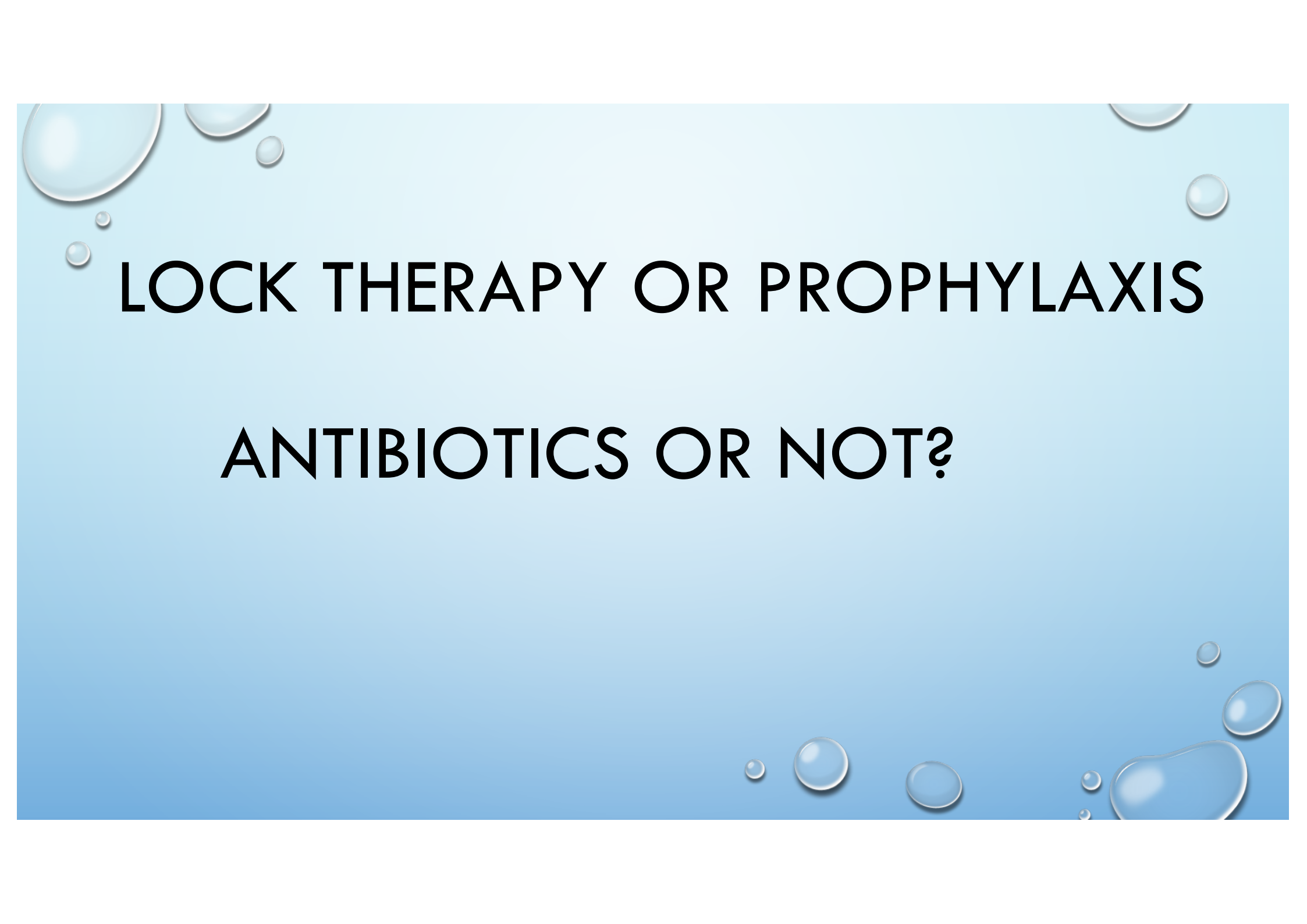
Vancomycin	<i>S. aureus</i> , <i>S. epidermidis</i>	<70%	NR	76
	<i>S. epidermidis</i>	Adequate ^c	Slow	77,83
	<i>S. aureus</i>	Adequate ^{b,d}	Slow	9

Aminoglycosides

Streptomycin	<i>B. cereus</i> , <i>P. fluorescens</i>	0%–60%	NR	10
Tobramycin	<i>P. aeruginosa</i>	40%	Slow	74
Gentamicin	<i>P. aeruginosa</i>	<25%	Slow	75
Amikacin	<i>P. aeruginosa</i>	<25%	Slow	75
	<i>S. aureus</i> , <i>S. epidermidis</i>	79%–98%	NR	76

Notes: ^aComparable penetration compared to isolates of planktonic cells; ^bmeasured as intensity of fluorescence using confocal microscopy or other methods; ^cvancomycin concentrations reportedly exceeded the minimal inhibitory concentrations and minimal bactericidal concentrations for tested isolates; ^drepresents vancomycin concentrations from 15–45 µg/mL.

Abbreviations: NA, not applicable; NR, not reported.

The background is a light blue gradient, darker at the bottom. It is decorated with several realistic water droplets of various sizes, some with highlights and shadows, scattered across the top and bottom edges.

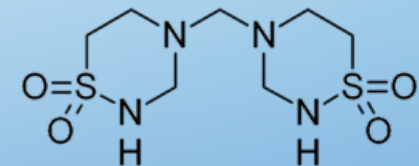
LOCK THERAPY OR PROPHYLAXIS ANTIBIOTICS OR NOT?

NON-ANTIBIOTIC SUBSTANCES USED FOR LOCK THERAPY OR PROPHYLAXIS

- ETHANOL
- CITRATE
- EDTA
- TAUROLIDINE

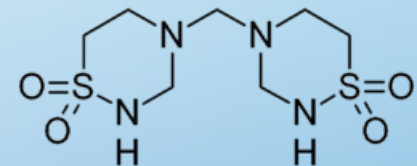
TAUROLIDINE

- TAURINE AMINO ACID DERIVATIVE, AN ANTIMICROBIAL AGENT WITH BROAD SPECTRUM OF ANTIBACTERIAL AND ANTIFUNGAL ACTION
- THE METHYL DERIVATIVES OF TAUROLIDINE INTERACT WITH THE BACTERIAL WALL (PARTICULARLY FLAGELLA AND FIMBRIAE), CAUSING IRREVERSIBLE DAMAGE TO THE BACTERIAL WALL, WHICH CONSISTS OF AN INABILITY TO ADHERE (THUS AN INABILITY TO FORM BIOFILM!)
- UNLIKE ANTIBIOTICS, TAUROLIDINE ACTS BY A CHEMICAL REACTION AT THE LEVEL OF THE BACTERIAL WALL.
- THE OTHER MECHANISM OF ACTION IS THE INACTIVATION OF BACTERIAL EXO- AND ENDOTOXINS. THIS MAKES THE INDUCTION OF BACTERIAL RESISTANCE HIGHLY UNLIKELY.
- TAUROLIDINE HAS A BACTERICIDAL EFFECT ON GRAM-POSITIVE AND GRAM-NEGATIVE BACTERIA, INCLUDING MDR, AND FUNGI.
- THERE ARE CURRENTLY NO REPORTED RESISTANCES TO TAUROLIDINE.

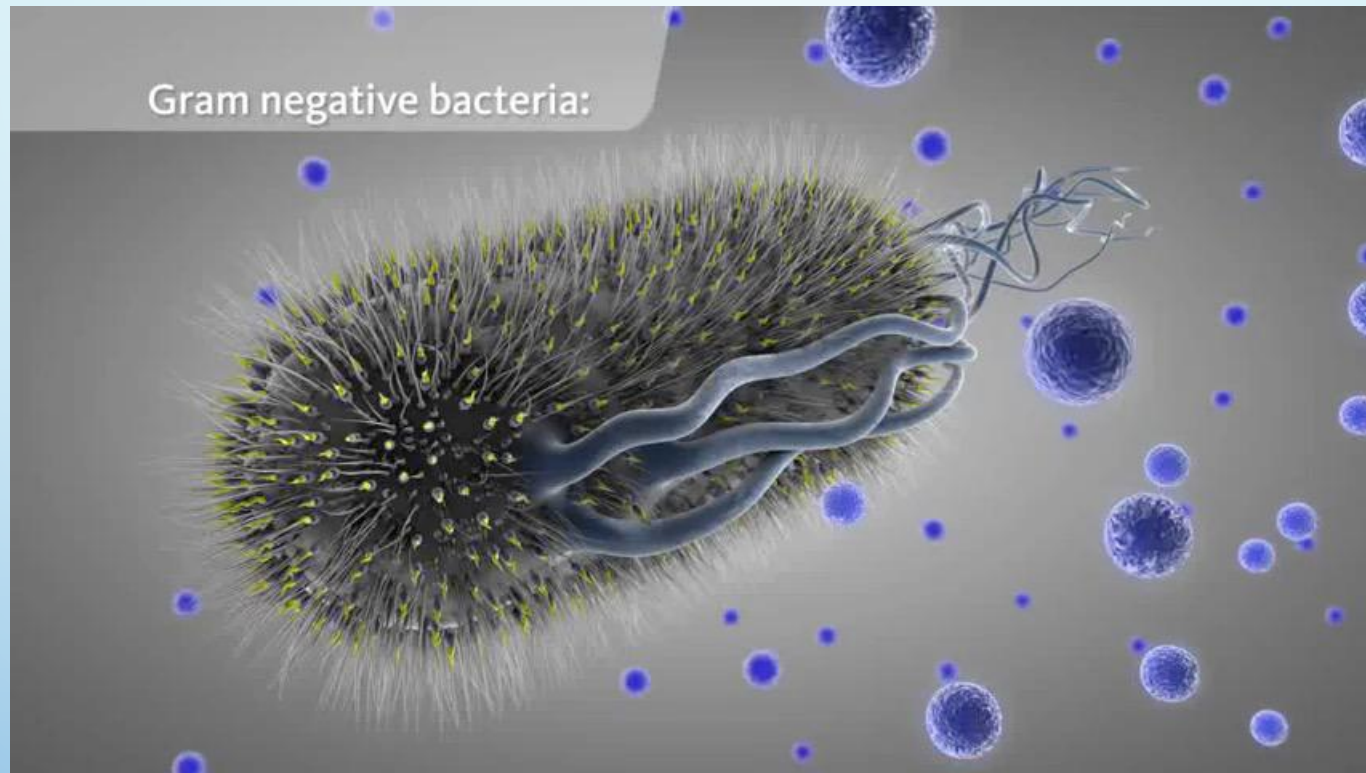


TAUROLIDINE: AVAILABLE FORMULATIONS

- TAUROLIDINE (1.34% OR 2%)
- TAUROLIDINE + CITRATE 4%
- TAUROLIDINE + CITRATE 4% + HEPARIN
- TAUROLIDINA + CITRATE 4% + UROKINASE



TAUROLIDINE: MECHANISM OF ACTION



TAUROLIDINE: ELIMINATION OF BIOFILM ON THE INNER WALL OF A CATHETER



J Leukoc Biol. 1995 Sep;58(3):299-306.

Taurolidine, an antilipopolysaccharide agent, has immunoregulatory properties that are mediated by the amino acid taurine.

Watson RW¹, Redmond HP, Mc Carthy J, Bouchier-Hayes D.

+ Author information

Abstract

Taurolidine has bactericidal and antilipopolysaccharide properties. It is broken down into the amino acid taurine, which has been shown to modulate intracellular calcium activity, a critical component in the priming and activation of macrophages and polymorphonuclear leukocytes. We hypothesized that taurolidine may function to enhance immune activity in these cells. The aim of this study was to investigate the immunological effects of taurolidine and correlate findings with survival after a septic challenge in a murine model. Study 1: CD-1 mice underwent cecal ligation and puncture, were randomized to receive taurolidine (200 mg/kg body weight/i.p.) or saline control, and studied for end point survival. Study 2: CD-1 mice were randomized to receive taurolidine (200 mg/kg body weight/i.p.) or saline control. Peritoneal macrophages (PM luminal diameters) were assessed for O₂⁻, NO, tumor necrosis factor-alpha (TNF-alpha), CD11b, phagocytosis, and PMN influx. O₂⁻, TNF-alpha, CD11b expression, and phagocytosis were significantly increased in the taurolidine group. Study 3: PM luminal diameters were cultured in vitro +/- 0.5 mg/ml taurolidine and PM luminal diameter antimicrobial function assessed (O₂⁻, NO, TNF-alpha, and phagocytosis). O₂⁻, TNF-alpha, and phagocytosis were significantly increased, whereas NO was reduced. Study 4: PM luminal diameters were also cultured with taurine (0.5 mg/ml). Similar increase in O₂⁻, TNF-alpha, and phagocytosis were identified. Intracellular PM luminal diameter [Ca²⁺] was also assessed and increases in free, unbound intracellular [Ca²⁺] occurred after taurine culture. Thus, in addition to its bactericidal and antilipopolysaccharide activity, taurolidine primes PM luminal diameters for enhanced antimicrobial activity and these effects appear mediated by the amino acid taurine.

Original research articles

Taurolidine lock in the treatment of colonization and infection of totally implanted venous access devices in cancer patients

Fabrizio Brescia ¹, Mauro Pittiruti ², Giancarlo Scoppettuolo³, Chiara Zanier¹, Elisa Nadalini¹, Paola Bottos¹, Chiara Moreal¹, Valentina Da Ros⁴, and Fabio Fabiani¹

Background: Taurolidine lock is known to be effective in preventing catheter-related infections in a variety of venous access devices, including long term venous access devices for chemotherapy. Though, literature about the use of taurolidine for treating catheter colonization or catheter-related blood stream infection is scarce.

Method: We have retrospectively reviewed the safety and efficacy of 2% taurolidine lock for treatment of catheter-colonization and of catheter-related bloodstream infection in cancer patients with totally implanted venous access devices. Diagnosis of colonization or catheter-related infection was based on paired peripheral and central blood cultures, according to the method of Delayed Time to Positivity.

Results: We recorded 24 cases of catheter-related infection and two cases of colonization. Taurolidine lock—associated with systemic antibiotic therapy—was successful in treating all cases of catheter-related infection, with disappearance of clinical symptoms, normalization of laboratory values, and eventually negative blood cultures. Taurolidine lock was also safe and effective in treating device colonization. No adverse effect was reported.

Conclusion: In our retrospective analysis, 2% taurolidine lock was completely safe and highly effective in the treatment of both catheter-colonization and catheter-related bloodstream infection in cancer patients with totally implanted venous access devices.

Keywords

Oncology access, techniques and procedures, catheter-related bloodstream infection, catheter-colonization, taurolidine lock

Catheter salvage or removal in catheter-related bloodstream infections with *Staphylococcus aureus* in children with chronic intestinal failure receiving home parenteral nutrition and the use of prophylactic taurolidine catheter lock solution: A descriptive cohort study

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Affiliations + expand

PMID: 38605559 DOI: 10.1002/jpen.2630

Abstract

Background: Children with chronic IF require long-term home parenteral nutrition (HPN), administered through a central venous catheter. Catheter-related bloodstream infection (CRBSI) with *Staphylococcus aureus* is known to be a serious infection with a high mortality rate and risk of complications. A standardized protocol on the management of *S aureus* CRBSIs in children receiving HPN is lacking. The aim of this study is to evaluate the effectiveness and safety of the current management in an HPN expertise center in the Netherlands.

Methods: We performed a retrospective descriptive cohort study between 2013 and 2022 on children 0-18 years of age with chronic IF requiring long-term HPN. Our primary outcomes were the incidence of *S aureus* CRBSI per 1000 catheter days, catheter salvage attempt rate, and successful catheter salvage rate. Our secondary outcomes included complications and mortality.

Results: A total of 74 patients (39 male; 53%) were included, covering 327.8 catheter years. Twenty-eight patients (38%) had a total of 52 *S aureus* CRBSIs, with an incidence rate of 0.4 per 1000 catheter days. The catheter salvage attempt rate was 44% (23/52). The successful catheter salvage rate was 100%. No relapse occurred, and no removal was needed after catheter salvage. All complications that occurred were already present at admission before the decision to remove the catheter or not. No patients died because of an *S aureus* CRBSI.

Conclusion: Catheter salvage in *S aureus* CRBSIs in children receiving HPN can be attempted after careful consideration by a multidisciplinary team in an HPN expertise center.

Keywords: *Staphylococcus aureus*; catheter-related bloodstream infection; intestinal failure; pediatric.



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Original article

Taurolidine-related adverse events in patients on home parenteral nutrition frequently indicate catheter-related problems

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Home parenteral nutrition
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Thrombosis

SUMMARY

Background & aims: A catheter-related bloodstream infection (CRBSI) is a serious complication of home parenteral nutrition (HPN) treatment. Despite taurolidine's frequent use as catheter lock solution (CLS) to prevent CRBSIs and its presumed favourable safety profile, data on taurolidine-related adverse events (AEs) and the clinical implications thereof remain merely anecdotal. Aim of this study was to explore taurolidine-related AEs in our large cohort of HPN patients and to develop an algorithm on how to deal with these AEs in clinical practice.

Methods: This retrospective cohort study comprised all adult HPN patients who used taurolidine as a CLS between 2006 and 2021 at our national HPN referral centre. Primary outcome was to identify taurolidine-related AEs. Secondary outcomes were median time to a taurolidine-related AEs and development of a clinical algorithm. A taurolidine-related AE was defined as an event that occurred directly after instillation of taurolidine in the CVAD or at start of fluid/PN infusion.

Results: In total, 470 patients used taurolidine during 700.232 catheter days. In 89 (19%) patients, 103 mild- to severe AEs related to taurolidine were observed. Six patients developed an allergic reaction. Reported AEs compromised vascular access device-related problems (group A) or taurolidine-related problems (group B) in 53 (51%) and 50 (49%), patients, respectively. In groups A and B, 51 (85%) and 21 (18%) patients presented with taurolidine infusion-related pain. Upon rechallenge, 45 (85%) and 16 (32%) patients, respectively, successfully resumed taurolidine locking without residual symptoms.

Conclusion: In this study, use of taurolidine as CLS was generally safe. Most reported AEs were vascular access device-related, and the majority of symptoms concerned pain. Upon rechallenge, a substantial number of patients, especially those in whom pain was the main symptom, could resume CLS locking after addressing the underlying catheter-related problem. Based on these results, we present a clinical algorithm for patients with possible taurolidine-related symptoms.

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Evidence-based criteria for the choice and the clinical use of the most appropriate lock solutions for central venous catheters (excluding dialysis catheters): a GAVeCeLT consensus

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TABLE I - Panel recommendations

The role of lock in preventing occlusion of NDCVA

The role of anticoagulant lock is only marginally important in the management of NDCVA, in terms of prevention of lumen occlusion. Future assessment of the role of citrate lock in NDCVA is desirable and considered of increasing importance. The benefit of citrate might be more focused on its action against biofilm and against bacteria rather than on its anticoagulant effect.

Heparin lock and citrate lock both guarantee an effective anticoagulant action, which is proven to be useful in DCVA rather than in NDCVA.

Trombolytic/fibrinolytic drugs, as currently available, are neither safe nor cost-effective for prevention of occlusion of NDCVA, while they have a definite role in the treatment of lumen occlusion due to blood clots.

Saline lock is as appropriate as anticoagulant lock in prevention of occlusion of NDCVA.

A pulsatile positive “push and pause” (“start and stop”) technique is the most appropriate methodology of flushing.

The role of lock in preventing infection of NDCVA

While antibacterial lock (specifically with antibiotics) has a clear role in clinical practice as a treatment of some selected catheter-related blood stream infection, the use of antibacterial lock for the purpose of prevention of catheter colonization and/or infection is a new field which demands further research, as it may prove to have an important clinical role in some selected populations of high risk patients where the standard bundles of infection prevention appear to be ineffective or insufficient.

Non-antibiotic antibacterial lock will have a major future role for prevention of catheter colonization and infection. While ethanol lock is highly effective, due to concerns about its safety, the drugs most likely to be used as antibacterial lock are taurolidine and citrate, which have optimal characteristics in terms of safety, efficacy and cost-effectiveness.

The association that is most promising as antibacterial/anticoagulant lock, in NDCVA as in DCVA, is taurolidine/citrate. Further studies should clarify which populations of patients might benefit of this association, and which concentrations of taurolidine and of citrate might be associated with the best outcome in terms of safety and efficacy.



Nutrición Hospitalaria



Revisión

Evidence-based recommendations of the Andalusian Group for Nutrition Reflection and Investigation (GARIN) for the management of adult patients with short bowel syndrome

Recomendaciones basadas en la evidencia del Grupo Andaluz para la Reflexión e Investigación en Nutrición (GARIN) para el manejo del paciente con síndrome de intestino corto

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Abstract

In order to develop evidence-based recommendations and expert consensus for the nutritional management of patients with short bowel syndrome (SBS), we conducted a systematic literature search using the PRISMA methodology plus a critical appraisal following the GRADE scale procedures. Pharmacological treatment with antisecretory drugs, antidiarrheal drugs, and somatostatin contributes to reducing intestinal losses. Nutritional support is based on parenteral nutrition; however, oral intake and/or enteral nutrition should be introduced as soon as possible. In the chronic phase, the diet should have as few restrictions as possible, and be adapted to the SBS type. Home parenteral nutrition (HPN) should be individualized. Single-lumen catheters are recommended and tauridine should be used for locking the catheter. The HPN's lipid content must be greater than 1 g/kg per week but not exceed 1 g/kg per day, and omega-6 fatty acids (ω 6 FAs) should be reduced. Trace element vials with low doses of manganese should be used. Patients with chronic SBS who require long-term HPN/fluid therapy despite optimized treatment should be considered for teduglutide treatment. All patients require a multidisciplinary approach and specialized follow-up. These recommendations and suggestions regarding nutritional management in SBS patients have direct clinical applicability.

Keywords:

Short bowel syndrome. Home parenteral nutrition. Teduglutide.

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Home parenteral nutrition

What is the catheter of choice for HPN in patients with SBS?

As a consensus of experts our proposal is to individualise the choice of access based on the patient's characteristics and the site's experience	95.38 %
We recommend using single-lumen catheters or using a lumen exclusively for PN when using multiple-lumen catheters	100 %

What is the ideal catheter lock?

We recommend locking the catheter with tauridine in all cases	98.46 %
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What method of administration should we use?

We suggest administering the HPN cyclically	98.46 %
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INS 2024

O. Use antimicrobial locking solutions for therapeutic and prophylactic purposes in patients with long-term CVADs in the following circumstances: patients with a history of multiple CABSIs, high-risk patient populations, and in facilities with unacceptably high rates of CLABSI, despite implementation of other methods of infection prevention (see Standard 61, *Parenteral Nutrition*).^{15,39,46-53} (II)

b. Antiseptic locking solutions include solutions used alone or in numerous combinations, including, but not limited to, ethanol, sodium bicarbonate, taurolidine, citrate, concentrated sodium chloride, and ethylenediaminetetraacetic acid (EDTA).^{15,49-51,53-56} (II)

CONCLUSIONS

- CVAD INFECTIONS ARE DIFFICULT TO TREAT WITHOUT CATHETER REMOVAL
- IN SOME PARTICULAR CATEGORIES OF PATIENTS (PATIENTS HIGHLY DEPENDENT ON MAINTAINING CATHETER, MOSTLY WITH TUNNELED OR TOTALLY IMPLANTED CATHETERS) GUIDELINES, IN CASE OF INFECTION, SUGGEST ATTEMPTING RESCUE BY ADMINISTERING LOCK THERAPY IN ADDITION TO SYSTEMIC ANTIBIOTIC THERAPY.
- IN CASES OF UNCOMPLICATED INFECTIONS AND LOW-VIRULENCE MICROORGANISMS, THIS STRATEGY HAS BEEN SHOWN TO BE VERY EFFECTIVE
- THE LOCK SOLUTIONS MOST WIDELY USED TODAY ARE NOT ANTIBIOTICS, BUT OTHER SOLUTIONS WITH ANTIMICROBIAL ACTIVITY.
- AMONG THESE, A VERY EFFECTIVE, SAFE, AND COST-EFFECTIVE SOLUTION IS TAUROLIDINE AS BOTH LOCK THERAPY AND LOCK PROPHYLAXIS (ESPECIALLY IN PATIENTS WITH HEMODIALYSIS CATHETERS AND PATIENTS ON HOME PARENTERAL NUTRITION)
- TAUROLIDINE HAS ALSO BEEN SHOWN TO BE EFFECTIVE TOWARD HIGHLY VIRULENT BACTERIA SUCH AS *S. AUREUS*, CURRENTLY NOT YET CONSIDERED BY GUIDELINES AS CANDIDATES FOR ERADICATION BY LOCK THERAPY

«Cos'è più importante» chiese Grande Panda,
«il viaggio o la meta?»

«La compagnia» rispose Piccolo Drago.



Gemelli



Fondazione Policlinico Universitario Agostino Gemelli IRCCS
Università Cattolica del Sacro Cuore



GRAZIE PER L'ATTENZIONE!

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