



Gemelli



Fondazione Policlinico Universitario Agostino Gemelli IRCCS
Università Cattolica del Sacro Cuore



DIAGNOSI CORRETTA DI INFEZIONE CATETERE-CORRELATA (CABSI E CRBSI) NEL NEONATO; OVVERO, QUANDO RIMUOVERE IL DISPOSITIVO?

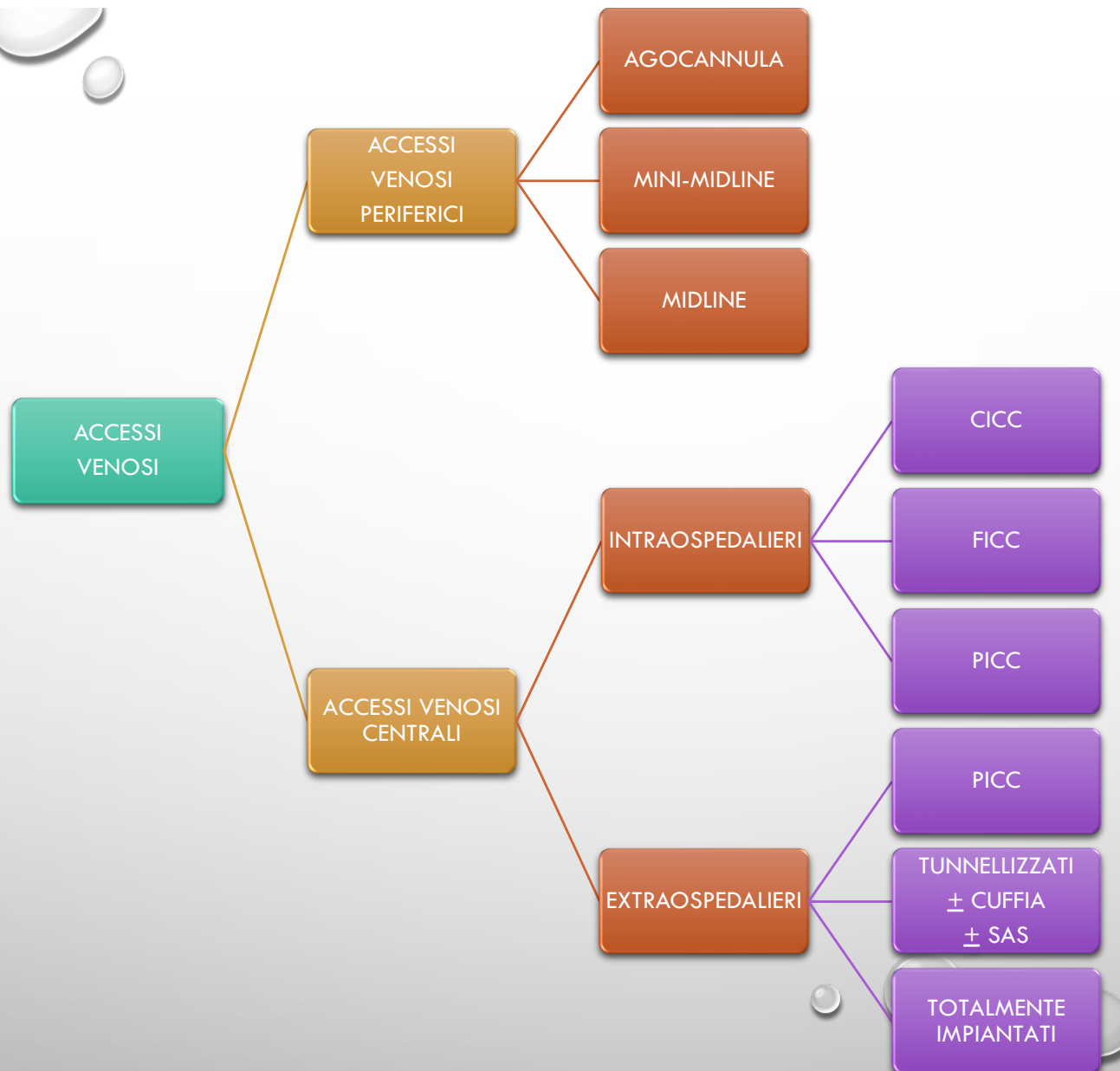
GIANCARLO SCOPPETTUOLO

RESPONSABILE UOS DIAGNOSI E CURA DELLE MALATTIE INFETTIVE DI COMUNITA' E TRASMISSIBILI

CONSULENTE INFETTIVOLOGO CENTRO INTERDIPARTIMENTALE ACCESSI VENOSI CENTRALI

COORDINATORE PERCORSO ENDOCARDITE

FONDAZIONE POLICLINICO UNIVERSITARIO A. GEMELLI – IRCCS ROMA



- **Cateteri ombelicali**
- **Epicutaneo-cavali**

PRIMA TENTAZIONE DEL MEDICO....

- ATTRIBUIRE IMMEDIATAMENTE LA RESPONSABILITA' DELLA FEBBRE AL CATETERE VASCOLARE, ANCORA PRIMA DI AVERE ESEGUITO ALCUNA INDAGINE DIAGNOSTICA
 - IL CATETERE VASCOLARE **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 Intensive and Critical Care Medicine and Coronary Units (SEMICYUC)[☆]



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RESEARCH

Open Access

Should central venous catheter be systematically removed in patients with suspected catheter related infection?

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Abstract

Introduction: Best clinical practice for patients with suspected catheter-related infection (CRI) remains unclear according to the latest Infectious Diseases Society of America (IDSA) guidelines. Thus, the objective of this study was to analyze clinical practice concerning the central venous catheter (CVC) and its impact on prognosis in patients with suspected CRI.

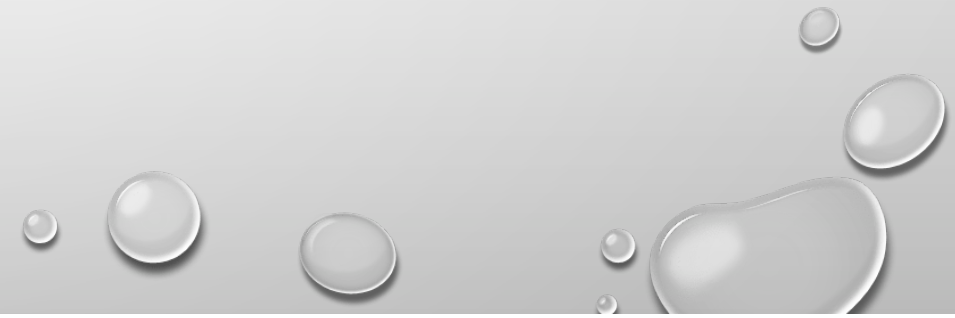
Methods: We performed a prospective, multicenter, observational study in 18 Spanish Intensive Care Units (ICUs). Inclusion criteria were patients with CVC and suspected CRI. The following exclusion criteria were used: age less than 18 years; pregnancy; lactation; human immunodeficiency virus; neutropenia; solid or haematological tumor; immunosuppressive or radiation therapy; transplanted organ; intravascular foreign body; haemodynamic instability; suppuration or frank erythema/induration at the insertion site of the CVC, and patients with bacteremia or fungemia. The end-point of the study was mortality at 30 days of CRI suspicion.

Results: The study included 384 patients. In 214 (55.8%) patients, CVC was removed at the moment of CRI suspicion, in 114 (29.7%) CVC was removed later and in 56 (14.6%) CVC was not removed. We did not find significant differences between survivors ($n = 311$) and non-survivors ($n = 73$) at 30 days according to CVC decision ($P = 0.26$). The rate of confirmed catheter-related bloodstream infection (CRBSI) was higher in survivors than in non-survivors (14.5% versus 4.1%; $P = 0.02$). Mortality rate was lower in patients with CRBSI than in the group of patients whose clinical symptoms were due to other causes (3/48 (6.25%) versus 70/336 (20.8%); $P = 0.02$). We did not find significant differences in mortality in patients with confirmed CRBSI according to CVC removal at the moment of CRI suspicion ($n = 38$) or later ($n = 10$) (7.9% versus 0; $P = 0.99$).

Conclusion: In patients with suspected CRI, immediate CVC removal may be not necessary in all patients. Other aspects should be taken into account in the decision-making, such as vascular accessibility, the risk of mechanical complications during new cannulation that may be life-threatening, and the possibility that the CVC may not be the origin of the suspected CRI.



DIFFICOLTÀ DIAGNOSTICHE

- CRITERI CLINICI (FEBBRE, BRIVIDI...) ASSOLUTAMENTE POCO SPECIFICI
 - CLINICA ESTREMAMENTE POLIMORFA (FEBBRE ISOLATA CON CARATTERISTICHE VARIABILI FINO A SEPSI E SHOCK SETTICO)
 - SEGNI LOCALI DI INFEZIONE MOLTO SPECIFICI MA POCO SENSIBILI
- 

Clinical Presentation

- presentation of neonates with late-onset sepsis differs by gestational age and probable source of infection^{1,4,5}
 - extremely preterm neonates or high-risk neonates can present at any time during neonatal intensive care hospitalization following birth with signs of hospital-acquired infection or late-appearing manifestations of infections acquired at parturition
 - previously healthy and stable late preterm or term neonates typically present from the community following discharge from birth hospitalization
 - some neonates may initially present as well-appearing and febrile but experience clinical deterioration after admission
 - most infections are either hospital- or community-acquired, but some may be late-appearing manifestations of infections acquired at parturition
- clinical signs of late-onset sepsis are non-specific and varied^{1,4,5}
- initial signs of late-onset sepsis may be confined to acute respiratory distress and/or apnea and tachycardia while later signs reflect progressive disease and multiorgan failure, such as respiratory failure, cardiac failure and shock, and kidney failure⁴

- National Institute for Health and Care Excellence (NICE) clinical indicators of possible late-onset neonatal infection
 - ill-looking with mottled skin or ashen appearance
 - feeding difficulties or signs of intolerance, such as abdominal distention
 - hypo- or hyperthermia
 - nonblanching rash
 - cardiorespiratory abnormalities
 - apnea
 - hypoxemia (low oxygen saturation or cyanosis of skin, lips, or tongue)
 - persistent tachycardia or bradycardia
 - signs of respiratory distress, such as tachypnea or grunting
 - neurologic abnormalities
 - seizures
 - concerning behavioral change, such as altered behavior or responsiveness
 - weak high-pitched or continuous cry
 - bulging fontanelle
 - Reference - [NICE 2021 Apr 20:NG195](#)  full-text 

- 
- assess for clinical signs of septic shock including hypothermia or hyperthermia, plus any of
 - hypotension
 - signs of inadequate tissue perfusion such as
 - decreased or altered mental status
 - prolonged capillary refill time
 - diminished pulses
 - mottled cool extremities
 - flash capillary refill, bounding peripheral pulses, wide pulse pressure, or decreased urine output (< 1 mL/kg/hour)
 - Reference - [Crit Care Med 2017 Jun;45\(6\):1061](#)

Skin

- examine skin for^{2,4}
 - jaundice
 - pallor
 - mottling
 - cold clammy skin
 - prolonged capillary refill time
 - edema
 - petechiae, purpura, or bleeding
 - local signs of infection, such as pustules, periumbilical erythema
- vesicular rash on a shallow, erythematous base appearing in isolation or in clusters may be suggestive of herpes simplex virus (HSV) infection; see History and Physical in [Neonatal Herpes](#) for additional information

HEENT

- palpate for bulging fontanelle¹
- assess for purulent eye discharge; see [Neonatal Conjunctivitis](#) for additional information

Chest

- assess for retractions⁴

Abdomen

- assess for
 - abdominal distension¹
 - hepatomegaly⁴
 - splenomegaly⁴

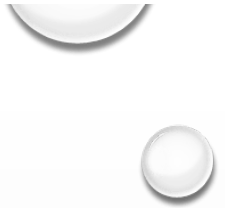
Neuro

- abnormal findings may include^{1,4}
 - hypotonia
 - hyporeflexia
 - abnormal Moro reflex
 - tremors
 - seizure
 - coma
- 

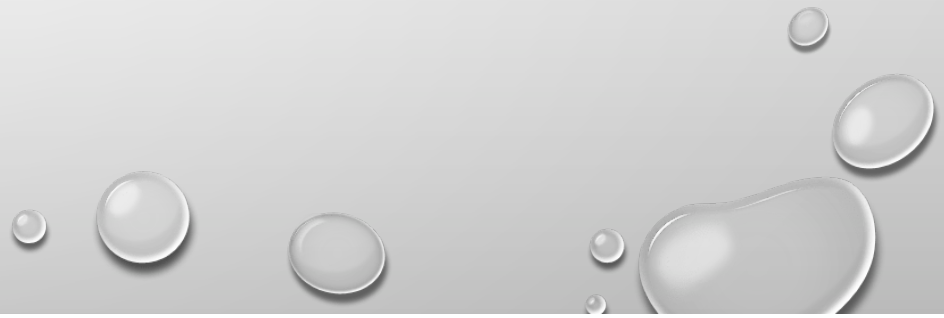
Table 1: Abnormal Vital Signs that Suggest Late-Onset Infection in Neonates ≥ 72 Hours Old

Vital Sign	Indications of Possible Late-onset Infection
Core temperature	≥ 38 degrees C (100.4 degrees F) or < 36 degrees C (96.8 degrees F)
Heart rate	< 100 beats per minute or ≥ 160 beats per minute
Respiratory rate	≥ 60 breaths per minute
Oxygen Saturation	< 90% in room air or increased oxygen saturation over baseline

Reference - NICE 2021 Apr 20:NG195 [PDF](#) full-text [PDF](#) .



DIFFICOLTÀ DIAGNOSTICHE

- DIFFERENTI TESTS DI LABORATORIO, CON DIVERSA SENSIBILITÀ E SPECIFICITÀ
- 

Blood Culture

- blood culture is the diagnostic standard for late-onset sepsis with reported sensitivity for bacteremia > 98%^{1,4,5}
- collection of blood for culture
 - obtain 0.5-1 mL of blood for culture as smaller volumes may miss bacteremia^{1,4}
 - if possible, obtain samples from 2 different sites (2 peripheral sites, or 1 peripheral site and 1 from central venous catheter if present)⁴
 - obtain sample before administering antibiotics if possible, but do not delay antibiotics to obtain specimens in severely ill neonates⁴

Table 2: Reported Diagnostic Performance of CBC Parameters for Identifying Late-Onset Neonatal Sepsis

CBC Parameter	Sensitivity (%)	Specificity (%)
WBC < 5, 000 cells/mm ³	7	96
WBC > 20, 000 cells/mm ³	23	80
ANC < 1,000/mm ³	2	98
Immature/total neutrophil ratio ≥ 0.2	54	62
Platelet count < 50,000 mm ³	8	98

Abbreviations: ANC, absolute neutrophil count; CBC, complete blood cell count WBC, white blood cell count.

Reference - [Neoreviews 2022 Nov 1;23\(11\):738.](#)

C-Reactive Protein (CRP)

- CRP is an inflammatory biomarker produced in the liver in response to infections and other inflammatory conditions⁵
- for neonates with suspected late-onset neonatal sepsis, National Institute for Health and Care Excellence (NICE) recommends measuring baseline CRP when starting empiric antibiotics and again 18-24 hours after starting antibiotics to assess likelihood of infection (NICE Strong recommendation) (NICE 2021 Apr 20:NG195, last updated 2024 Mar 19 [📄](#) PDF [📄](#))
- consensus cut-off value to define elevated CRP is not established⁵
- cutoff values to detect late-onset infection in neonates reported in [systematic review of 20 studies](#) including 1,615 neonates ranged from 2.2 mg/dL to > 5 mg/dL ([Cochrane Database Syst Rev 2019 Jan 14;1\(1\):CD012126](#))
- CRP does not increase until 6-8 hours after onset of infection, and peaks at 36-48 hours^{1,4,5}
- diagnostic accuracy⁵
 - single CRP measurement has limited diagnostic accuracy for late-onset sepsis with reported sensitivity 62% and specificity 74%
 - 3 negative (below cutoff value) CRP measurements measured over first days of late-onset sepsis evaluation and treatment may be used in the decision to discontinue empiric antibiotics with reported sensitivity 98% and negative predictive value 99%

Procalcitonin

- procalcitonin is an inflammatory marker made mainly in the thyroid C cells in response to infection and other tissue injuries; the level increases more rapidly in response to infection than other inflammatory markers
 - it is reported to be more specific than other inflammatory markers for detecting bacterial infection, but it may not be widely available
 - procalcitonin > 0.5 ng/mL is considered elevated in infants aged 8-60 days
 - References - [Pediatrics 2021 Aug;148\(2\)](#), correction can be found in [Pediatrics 2021 Nov;148\(5\)](#)
- a single measurement of procalcitonin lacks diagnostic accuracy for late-onset sepsis with reported sensitivity 92% and specificity 80%; similar to C-reactive protein (CRP), serial measurements of procalcitonin may assist in decision to discontinue empiric antibiotic treatment⁵

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 (>103 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)

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• NHSN CLABSI DEFINITION, JAN 2024

Central line (CL): An intravascular catheter that terminates at or close to the heart, **or** in one of the great vessels **AND** is used for infusion, withdrawal of blood, or hemodynamic monitoring. Consider the following great vessels when making determinations about CLABSI events and counting CL device days:

- Aorta
- Pulmonary artery
- Superior vena cava
- Inferior vena cava
- Brachiocephalic veins
- Internal jugular veins
- Subclavian veins
- External iliac veins
- Common iliac veins
- Femoral veins
- In neonates, the umbilical artery/vein.

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.

Table 1: Laboratory-Confirmed Bloodstream Infection Criteria:

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

Criterion	Comments and reporting instructions that follow the site-specific criteria provide further explanation and are integral to the correct application of the criteria.
LCBI 1 If LCBI 1 criterion is met, consider MBI-LCBI 1	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) 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.
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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.
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Table 1 The main features of currently used surveillance criteria of neonatal CLABSI summarised

From: [Sustainable neonatal CLABSI surveillance: consensus towards new criteria in the Netherlands](#)

	CDC	NEO-KISS	Dutch neonatal CLABSI criteria
Target patient population	≤ 1 year	Very low birthweight infants: birthweight < 1500 g	Neonates: postnatal age ≤ 28 days for term and up to postmenstrual age of 44 weeks for preterm infants
Description of CLABSI criteria	Laboratory-confirmed bloodstream infection (1) with a detected pathogen OR (2) with the same common commensal ^a confirmed by a second blood specimen	Laboratory-confirmed bloodstream infection (1) with a detected pathogen OR (2) with CoNS confirmed by a second blood specimen or one out of 4 laboratory elements Clinical sepsis (3) no detected pathogen	Laboratory-confirmed bloodstream infection (1) with a detected pathogen OR (2) with same common commensal ^a confirmed by a second blood specimen OR (3) with a common commensal and CRP > 10 mg/L
Clinical findings used in criteria	One out of four ^b clinical symptoms for CoNS CLABSI criteria	Two or more out of 16 ^c findings bundled in seven categories for all CLABSI criteria	Clinical symptoms of neonatal sepsis according to the treating physician for "common commensal CLABSI criteria"
Challenges for application in the Dutch setting	Two blood cultures for one event (not common practice, single blood culture policy)	Numerous clinical elements (labour intensive surveillance and possible interference with interrater agreement)	–

CDC, Centers for Disease Control; CLABSI, central line-associated bloodstream infections; CoNS, Coagulase-negative Staphylococci species; CRP, C-reactive protein; NEO-KISS, NEO-Krankenhaus Infektions Surveillance System

^aAccording to the NHSN Master Organism List

^bCDC clinical findings: fever (> 38 °C), hypothermia (< 36.5 °C), apnoea, or bradycardia

^cNEO-KISS clinical findings: (1) fever (> 38 °C) or temperature instability or hypothermia (< 36.5 °C); (2) tachycardia (> 200/min) or new increasing bradycardia (< 80/min); (3) capillary refill time > 2 s; (4) new or increasing apnoea (> 20 s); (5) otherwise unexplained metabolic acidosis (BE < – 10 mval/L); (6) new onset of hyperglycaemia (> 140 mg/dL); (7) other signs of sepsis (skin colour, biochemical signs, increasing oxygen requirement, unstable general status, apathy)

	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

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

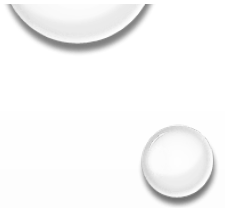
- EMOCOLTURE CONVENZIONALI PRELEVATE CONTEMPORANEAMENTE DAL CATETERE E DAL SANGUE PERIFERICO
- POSITIVITÀ: POSITIVITÀ DELLE COLTURE DA ENTRAMBI I SITI, CON QUELLE CENTRALI POSITIVE 2 E PIÙ ORE PRIMA RISPETTO A QUELLE DAL SANGUE PERIFERICO
- 10 STUDI CONSIDERATI
- SENSIBILITÀ 85%
- SPECIFICITÀ: 81%



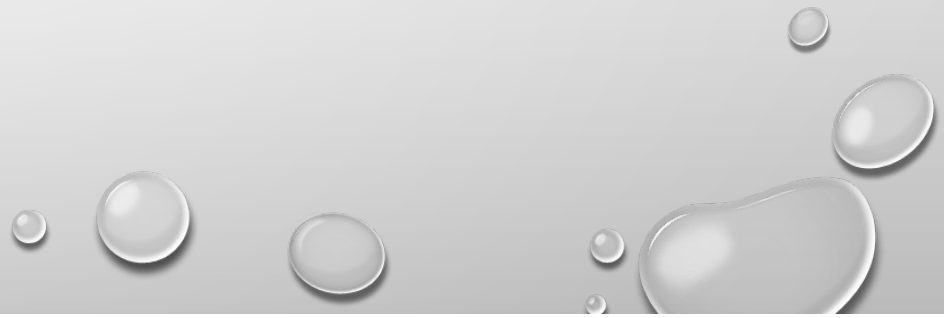
Maki, Ann Inter Med 2005

Table 2 Summary of main diagnostic methods for catheter-related bloodstream infections.

	Criteria for positivity	Interpretation	Comments	Recommendation
<i>Diagnosis without catheter withdrawal</i>				
Paired quantitative blood cultures	Ratio $\geq 3:1$	Both sets are positive for the same microorganism and the set obtained through the catheter has $\geq 3:1$ fold-higher colony count than the peripheral culture	Sensitivity $\approx 79\%$ Specificity $\approx 99\%$ Labor intensive and expensive	A-II
Paired blood cultures for differential time to positivity (DTP)	≥ 120 min	Both sets are positive for the same microorganism and the set obtained through the catheter becomes positive ≥ 120 min earlier	Sensitivity: 72% to 96% Specificity: 90% to 95% Less specificity for long-term catheters The interpretation of DTP should take into account adherence to the technical procedure and the type of microorganism	A-II
Endoluminal brushing	>100 CFU	Indicative of CRBSI	Sensitivity: 95% to 100% Specificity: 84% to 89% It may underestimate CRBSI in short-term catheters Risk of pathogen dissemination and thrombotic complications	C-III



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
- 

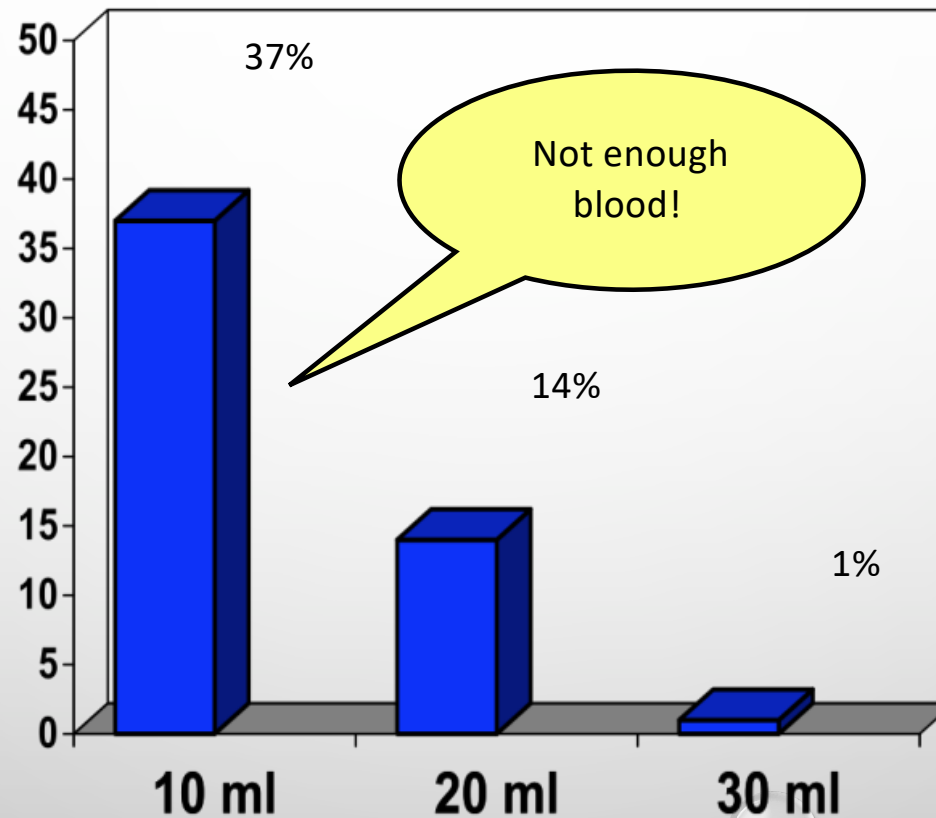
EMOCOLTURE

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



% False Negative vs. volume of Blood

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

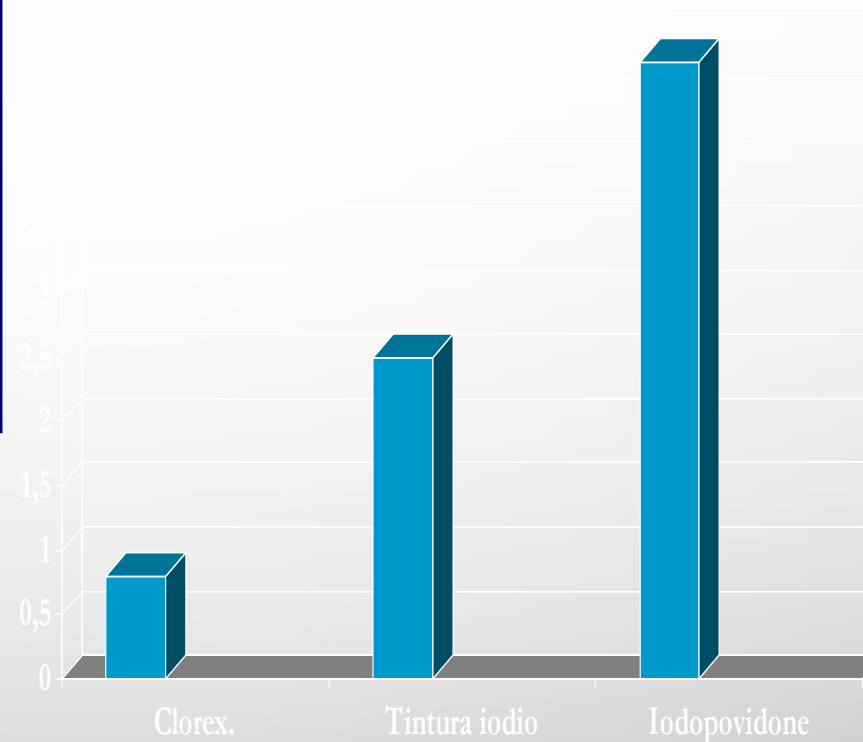
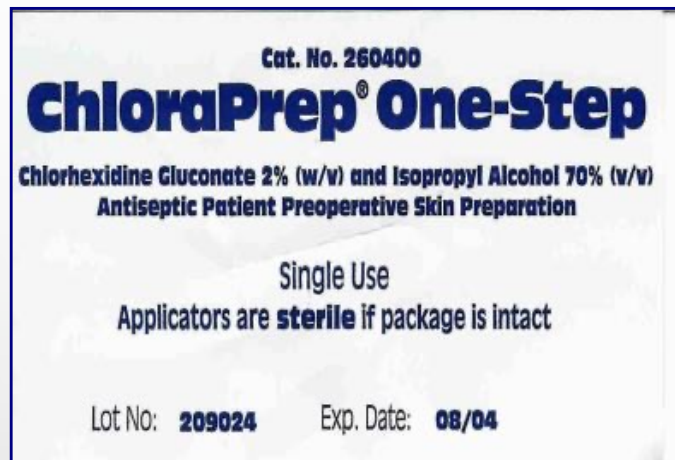


Courtesy of E.J Baron, PhD, Dir of Microbiology Lab, Stanford Hosp

VOLUME DI SANGUE

Peso (Kg)	ml per contenitore	ml per coppia
< 9	1	2
9-14	3	6
15-27	5	10
28-41	10	20
> 42	20	40

CONTAMINAZIONE DELLE EMOCOLTURE RISPETTO ALL'ANTISETTICO IMPIEGATO





medicina *intensiva*

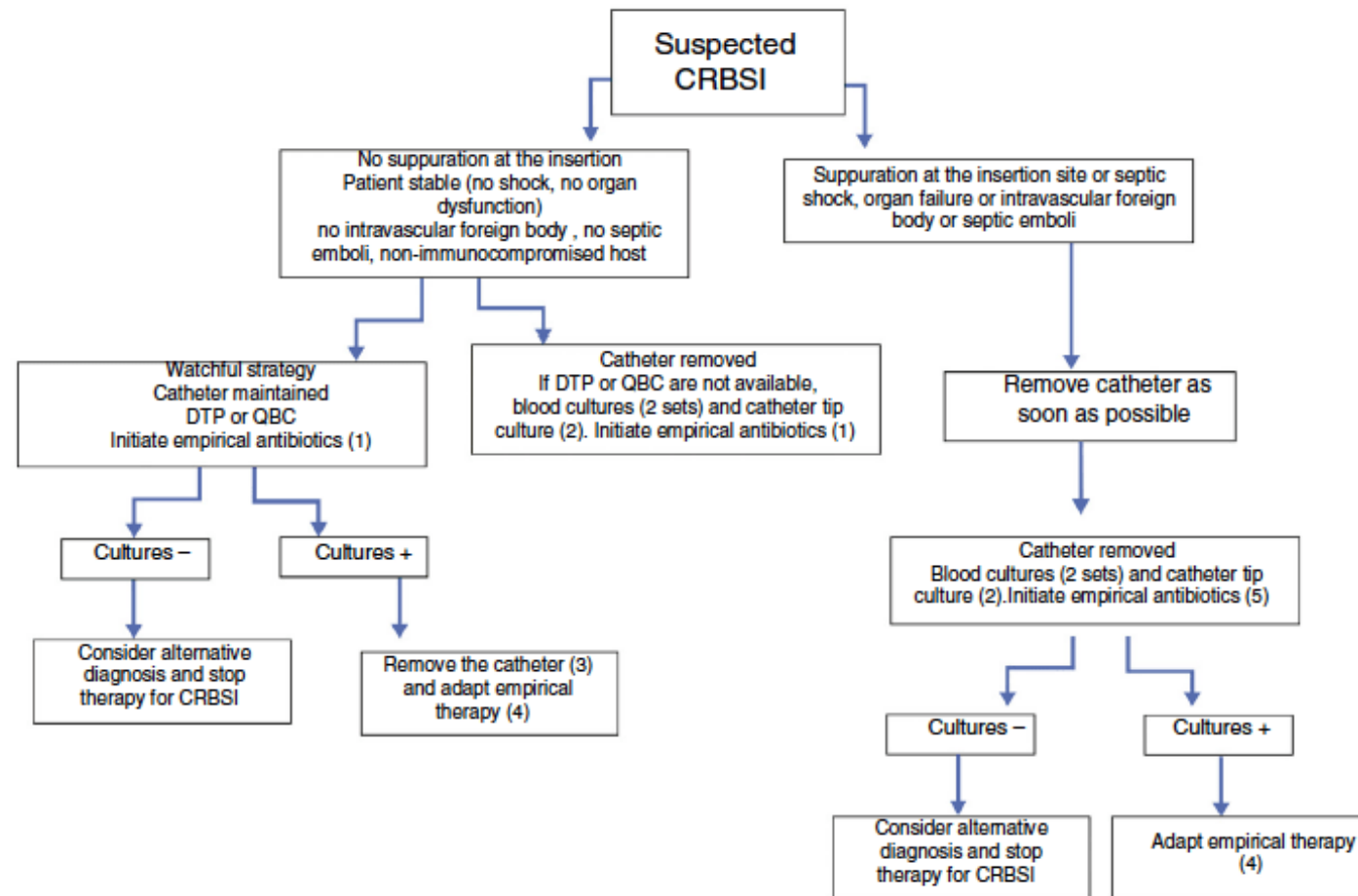
www.elsevier.es/medintensiva



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

Management of IV Access

- Infectious Disease Society of America (IDSA) recommendations on managing pediatric patients, including neonates, with a suspected or proven catheter-related infection
 - indications for catheter removal are similar to adults, however, consider the difficulty in obtaining an alternative venous access site ([IDSA Grade A, Level II](#))
 - closely monitor children treated without catheter removal with regular clinical evaluation and additional blood cultures, and remove the device if there is clinical deterioration or a recurrent catheter-related blood stream infection (CRBSI) ([IDSA Grade B, Level III](#))
 - empiric therapy is similar to adults ([IDSA Grade A, Level II](#))
 - antibiotic lock therapy is recommended when the catheter is salvaged ([IDSA Grade B, Level II](#))
 - in cases when antibiotic lock therapy cannot be used, consider systemic antibiotics through a colonized catheter ([IDSA Grade C, Level III](#))
 - Reference - [Clin Infect Dis 2009 Jul 1;49\(1\):1](#), corrections can be found in [Clin Infect Dis 2010 Feb 1;50\(3\):457](#), [Clin Infect Dis 2010 Apr 1;50\(7\):1079](#)
- no randomized trials found comparing early catheter removal vs. expectant management in neonates with central venous catheters and bloodstream infections ([Cochrane Database Syst Rev 2016 Apr 20;4\(4\):CD008436](#))

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

IDEAL LOCK SOLUTION



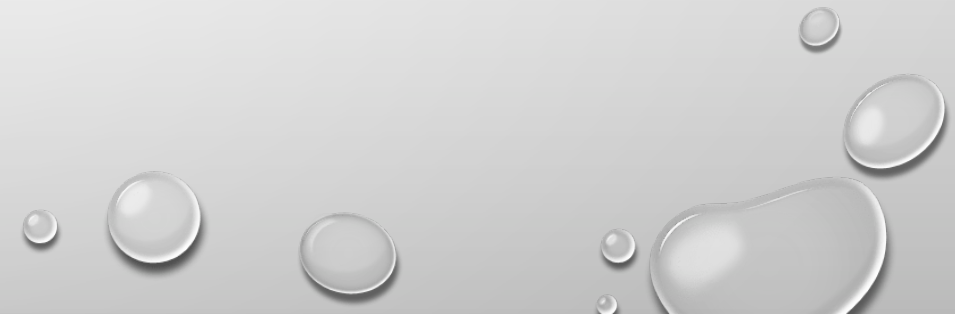
Non è possibile visualizzare l'immagine.

- SPECTRUM OF ACTIVITY SHOULD INCLUDE COMMON OR TARGETED PATHOGENS
- ABILITY TO PENETRATE O DISRUPT A BIOFILM
- COMPATIBILITY WITH ANTICOAGULANTS
- PROLONGED STABILITY
- LOW RISK OF TOXICITY OR ADVERSE EVENTS
- LOW POTENTIAL FOR RESISTANCE
- COST EFFECTIVENESS



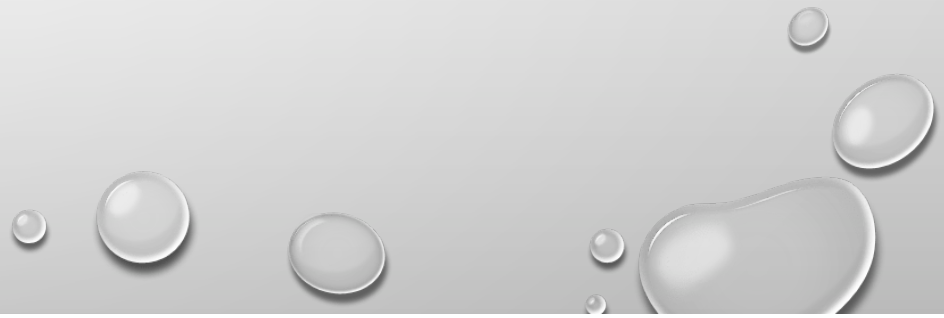
LOCK THERAPY O PROPHYLAXIS

ANTIBIOTICI OPPURE NO?



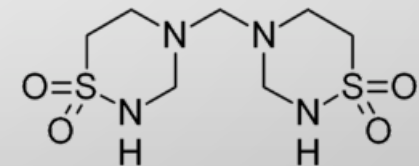


SOSTANZE NON ANTIBIOTICHE UTILIZZATE COME LOCK THERAPY O PROPHYLAXIS

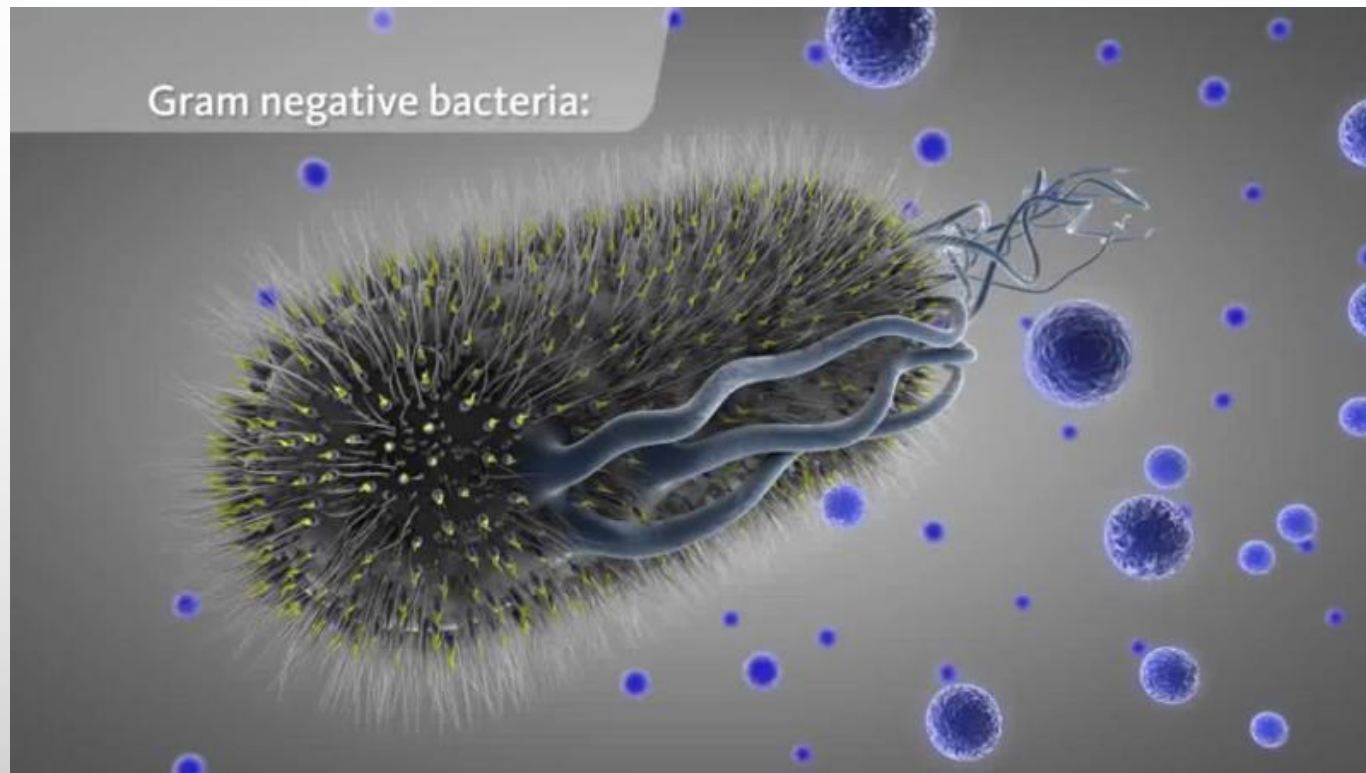
- ETHANOL
 - CITRATE
 - EDTA
 - TAUROLIDINE
- 

TAUROLIDINE

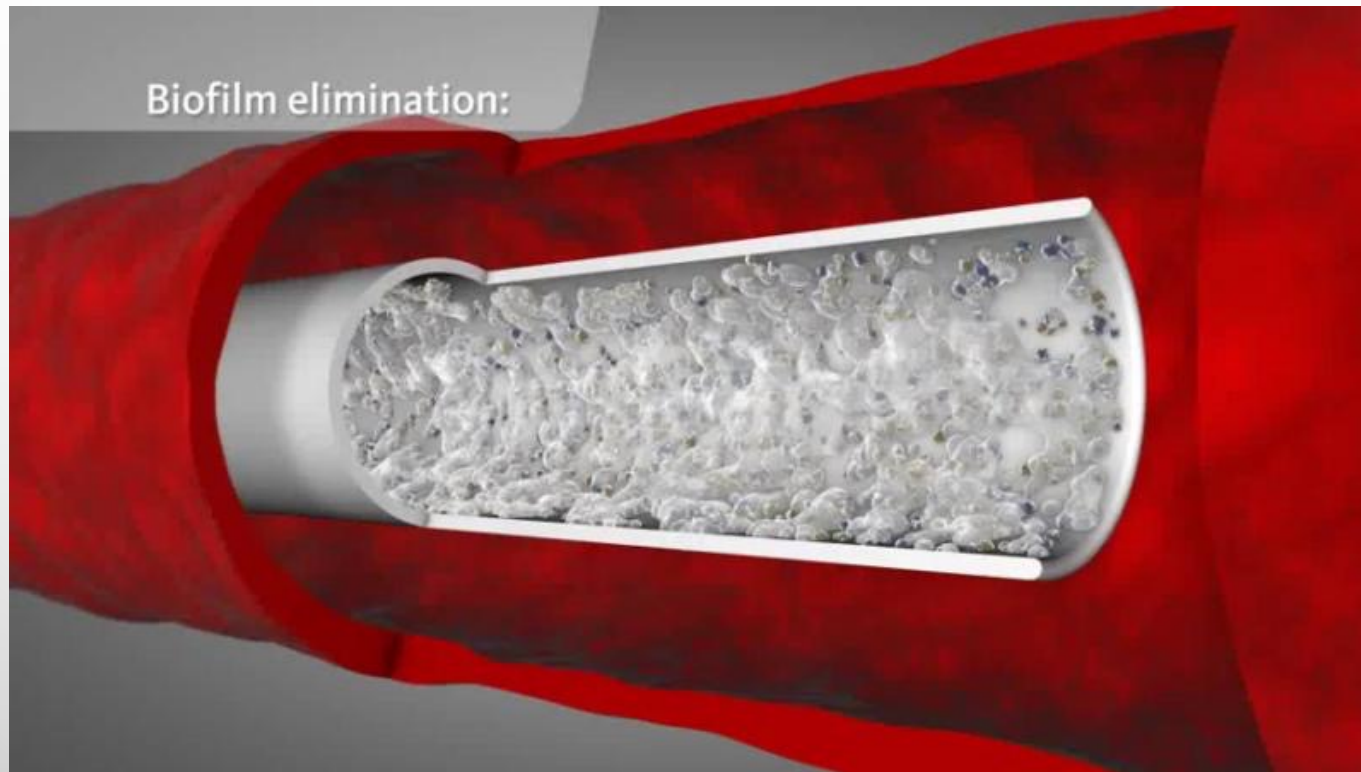
- TAUROLIDINE IS A TAURINE AMINO ACID DERIVATIVE; IT IS AN ANTIMICROBIAL AGENT WITH BROAD SPECTRUM OF ANTIBACTERIAL AND ANTIFUNGAL ACTION
- THE METHYL DERIVATIVES OF TAUROLIDINE INTERACT WITH THE BACTERIAL WALL (PARTICULARLY FLAGELLA AND FIMBRIAE), CAUSING IRREVERSIBLE DAMAGE TO THE BACTERIAL WALL, WHICH 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.



TAUROLIDINA: MECCANISMO DI AZIONE



TAUROLIDINA: ELIMINAZIONE DEL BIOFILM SULLA PARETE INTERNA DI UN CATETERE



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

Aysenur Demirok¹, David H C Illy¹, Sietse Q Nagelkerke², Michiel F Lagerweij³,
Marc A Benninga¹, Merit M Tabbers¹

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.

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.

CONCLUSIONI

- LA DECISIONE DI RIMUOVERE O MENO UN CATETERE VASCOLARE IN CORSO DI EPISODIO FEBBRILE DEVE ESSERE ASSOLUTAMENTE INDIVIDUALIZZATA
- TALE DECISIONE E' STRETTAMENTE DIPENDENTE DALL'ACCURATEZZA DELLA DIAGNOSI DI CRBSI/CABSI
- I CRITERI CHE IMPONGONO LA RIMOZIONE DEL CATETERE NEL NEONATO SONO SIMILI A QUELLI DELL'ADULTO
- IN CASI SELEZIONATI, IN NEONATI CON RICONOSCIUTA DIFFICOLTA' DI RIPOSIZIONAMENTO, E' POSSIBILE TENTARE UN SALVATAGGIO DEL CATETERE, COMBINANDO TERAPIA ANTIBIOTICA SISTEMICA E LOCK THERAPY, PREFERIBILMENTE RAPPRESENTATA DA SOSTANZE NON ANTIBIOTICHE CON EFFETTO ANTIMICROBICO. IN TAL CASO, SARA' CRUCIALE MONITORARE STRETTAMENTE L'ANDAMENTO CLINICO PER COGLIERE PRECOCEMENTE EVENTUALI SEGNI DI DETERIORAMENTO E MONITORARE STRETTAMENTE LA RISPOSTA MICROBIOLOGICA ALLA TERAPIA VERIFICANDO LA NEGATIVIZZAZIONE DELLE EMOCOLTURE

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

«La compagnia» rispose Piccolo Drago.



GRAZIE PER L'ATTENZIONE!

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