



Lock alla taurolidina per gli accessi venosi neonatali: potenzialità future

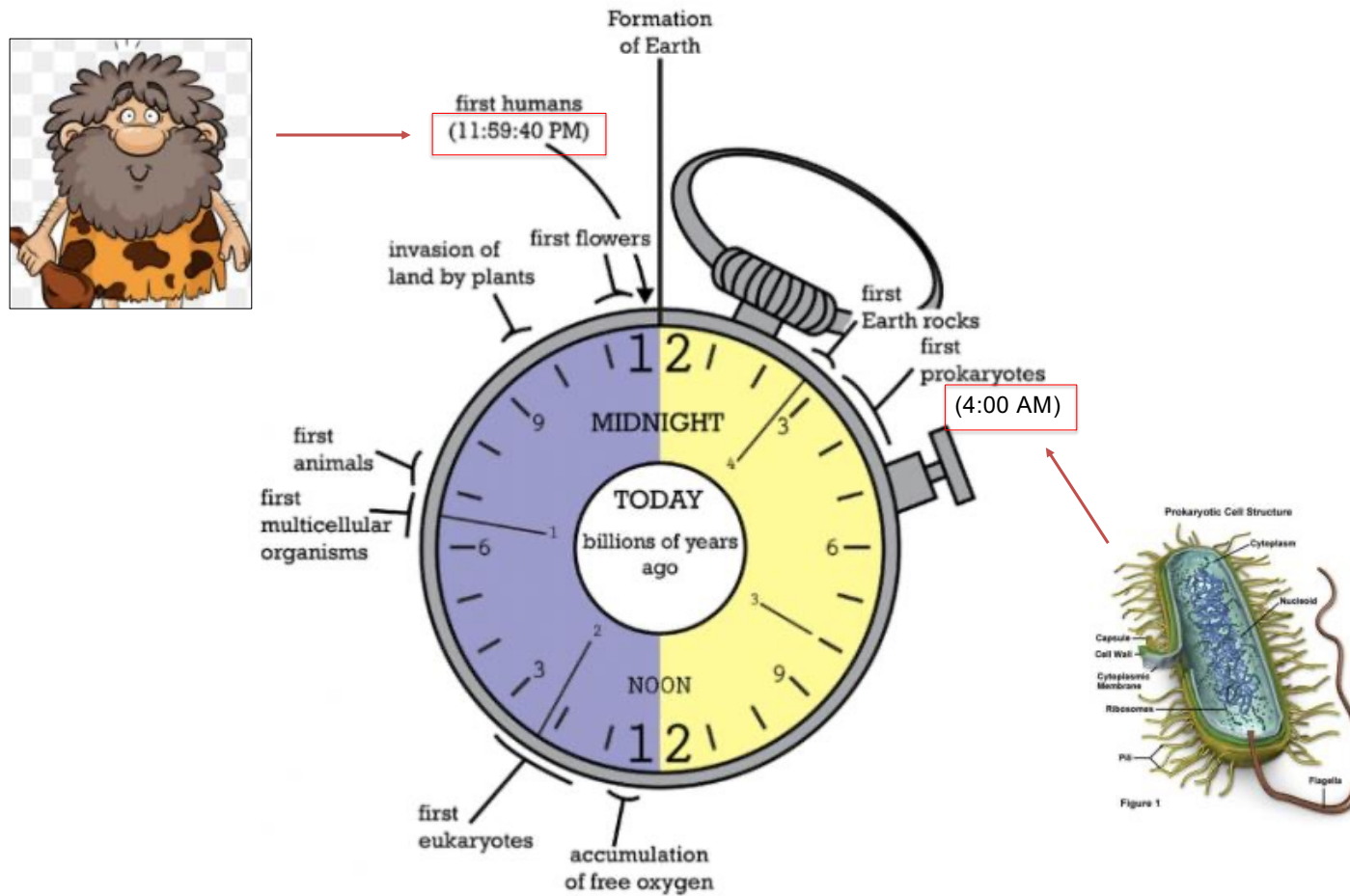
Fiammetta Piersigilli



Neonatal European Vascular Access Team

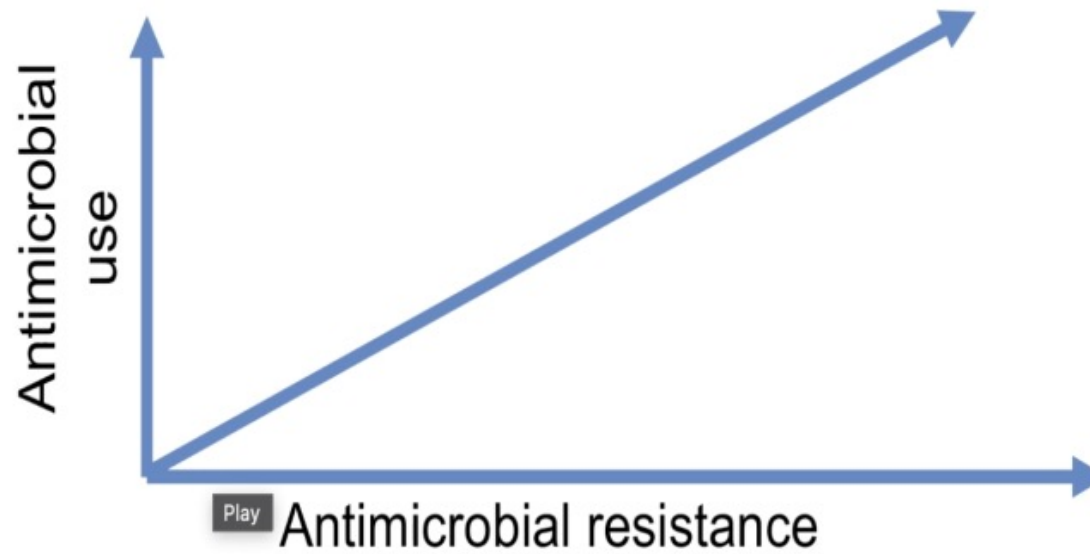


The evolution clock



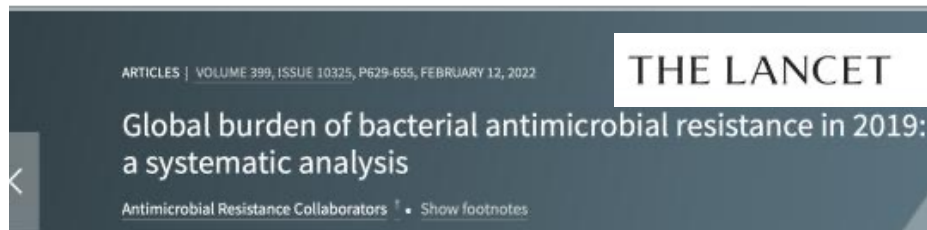
We cannot defeat bacteria!!

Resistance



We cannot defeat bacteria!!

Antimicrobial misuse



1·27 million deaths in 2019
directly attributable to antibiotic resistance

Antibiotic resistance

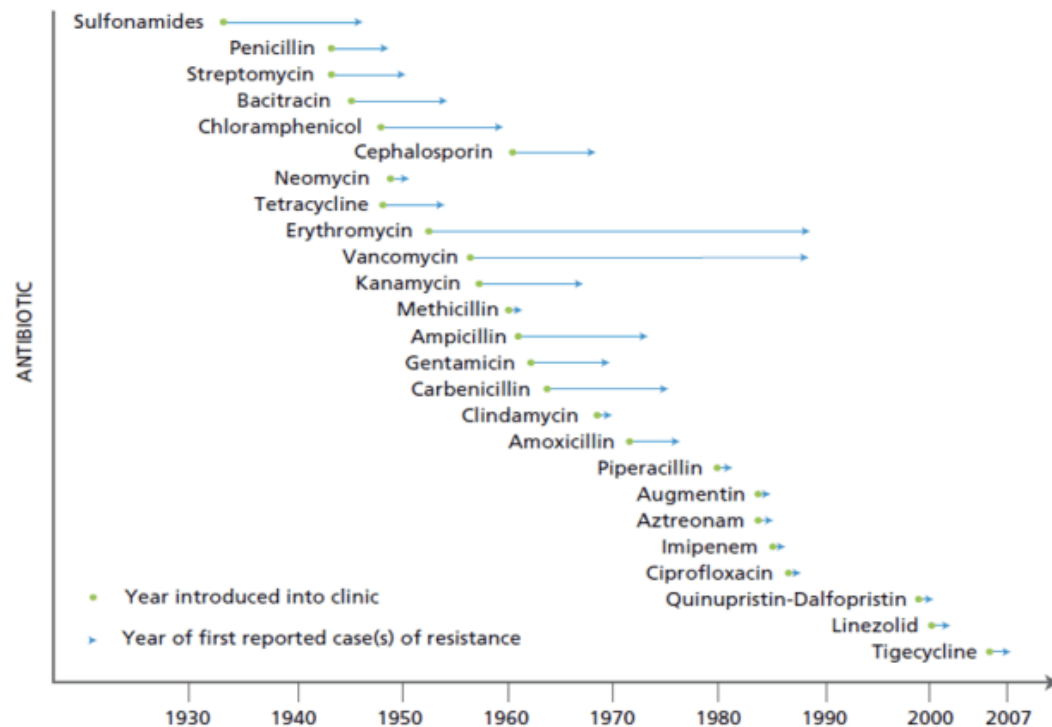


New report calls for urgent action to avert antimicrobial resistance crisis

10.000.000 deaths due to
multidrug resistant
microorganisms in 2050



The perfect storm



Note: Some of the dates are estimates only.

Most new antibiotics are variations of existing antibiotics

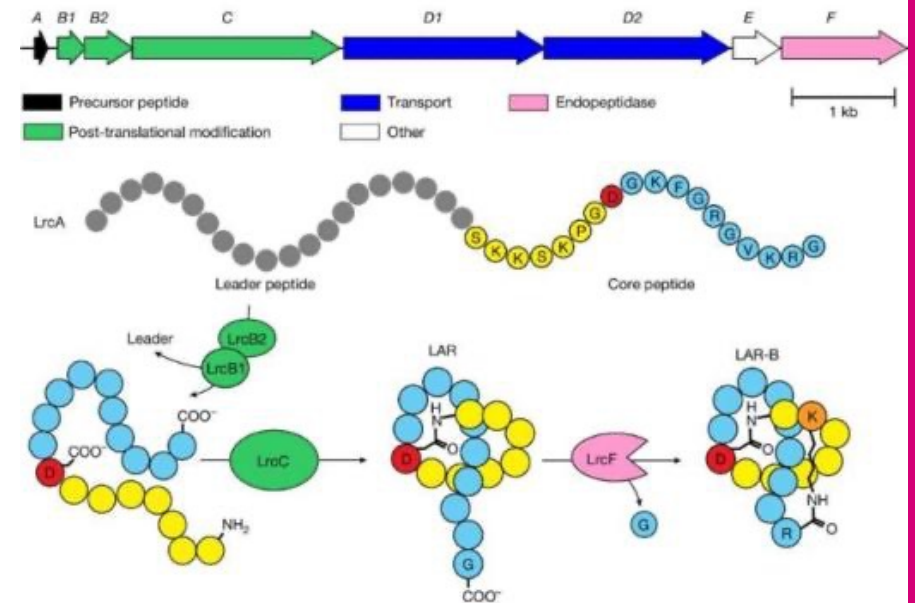
Only 5 new classes of antibiotics in the last 20 years

A broad-spectrum lasso peptide antibiotic targeting the bacterial ribosome

[Manoj Jangra](#), [Dmitrii Y. Travin](#), [Elena V. Aleksandrova](#), [Manpreet Kaur](#), [Lena Darwish](#), [Kalinka Koteva](#), [Dorota Klepacki](#), [Wenliang Wang](#), [Maya Tiffany](#), [Akosiererem Sokaribo](#), [Brian K. Coombes](#), [Nora Vázquez-Laslop](#), [Yury S. Polikanov](#) , [Alexander S. Mankin](#)  & [Gerard D. Wright](#) 

Nature **640**, 1022–1030 (2025) | [Cite this article](#)

32k Accesses | **1104** Altmetric | [Metrics](#)



Lariocidins inhibit bacterial growth by binding to the ribosome and interfering with protein synthesis by inhibiting translocation and inducing miscoding

Preterm infants

High risk of LOS in very preterm infants
High morbidity
High mortality



EDITORIAL

Catheter-associated bloodstream infection rates: how low can you go?

Stijn Blot^{1,2*}, Garyphallia Poulakou³ and Jean-Francois Timsit^{4,5}

What else can we do to achieve zero infections?



Should we use antibiotic prophylaxis ?

Avoid prophylactic antibiotics



Cochrane studies		Year	Recommend.
Profylactic antibiotics umbilical artery catheters		2007	No
Profylactic antibiotics umbilical venous catheters		2005	No
Profylactic antibiotics ventilated newborns		2007	No
Profylactic Vancomycin for preterms		2000	No
Prophylactic antibiotics for intercostal catheters		2012	No

No significant reduction of infections

Increase of resistance

CDC Guidelines

Do not administer systemic *antimicrobial* prophylaxis routinely before insertion or during the use of an intravascular catheter to prevent catheter colonization or CRBSI

Infusion Therapy Standards of Practice

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 CVAD-associated BSI, despite implementation of other methods of infection prevention.^{27,62-79} (II)

Prolonged Initial Empirical Antibiotic Treatment is Associated with Adverse Outcomes in Premature Infants

Venkata S Kuppala, MD¹, Jareen Meinzen-Derr, PhD^{1,2,3}, Ardythe L. Morrow, PhD^{1,2,3}, and Kurt R. Schibler, MD^{1,3}

J Pediatr. 2011 November ; 159(5): 720–725. doi:10.1016/j.jpeds.2011.05.033.



300 neonates < 32 GA
No demonstrated EOS



Prolonged initial empiric antibiotic treatment has been associated with increased risk of death, LOS or NEC

The Association of Third-Generation Cephalosporin Use and Invasive Candidiasis in Extremely Low Birth-Weight Infants

C. Michael Cotten, MD^a, Scott McDonald^b, Barbara Stoll, MD^c, Ronald N. Goldberg, MD^a, Kenneth Poole, PhD^b, Daniel K. Benjamin, Jr, MD, MPH, PhD^{a,d}, on behalf of the National Institute for Child Health and Human Development Neonatal Research

3702 ELBW infants
Neonates who survived > 72h



Broad spectrum antibiotics (third generation cephalosporins) were associated with increased risk of invasive candidiasis

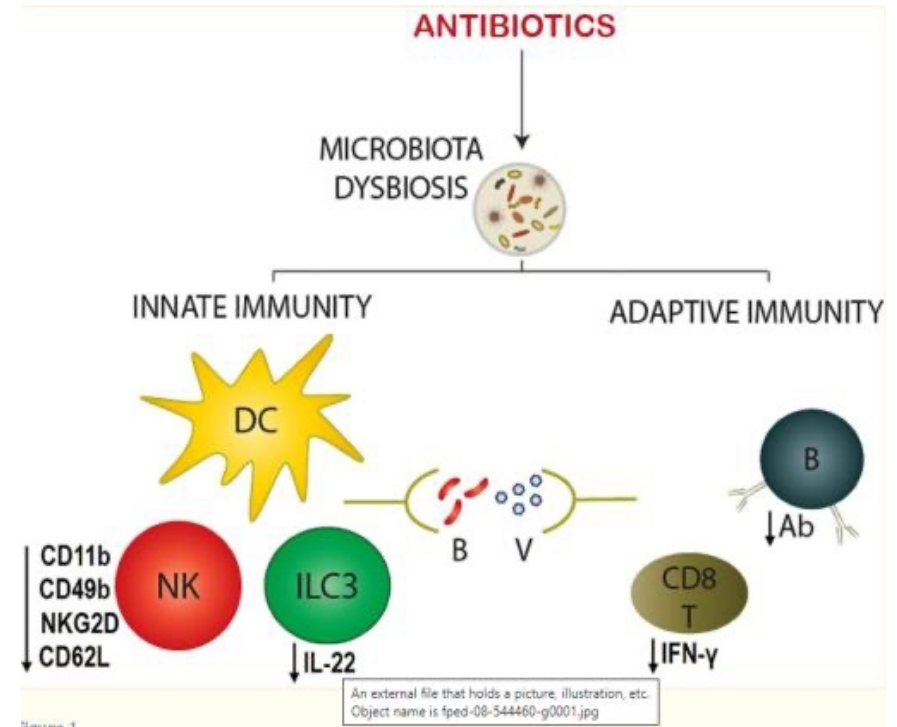
The Dark Side of Antibiotics: Adverse Effects on the Infant Immune Defense Against Infection



Sudhanshu Shekhar* and [Fernanda Cristina Petersen*](#)

Institute of Oral Biology, University of Oslo, Oslo, Norway

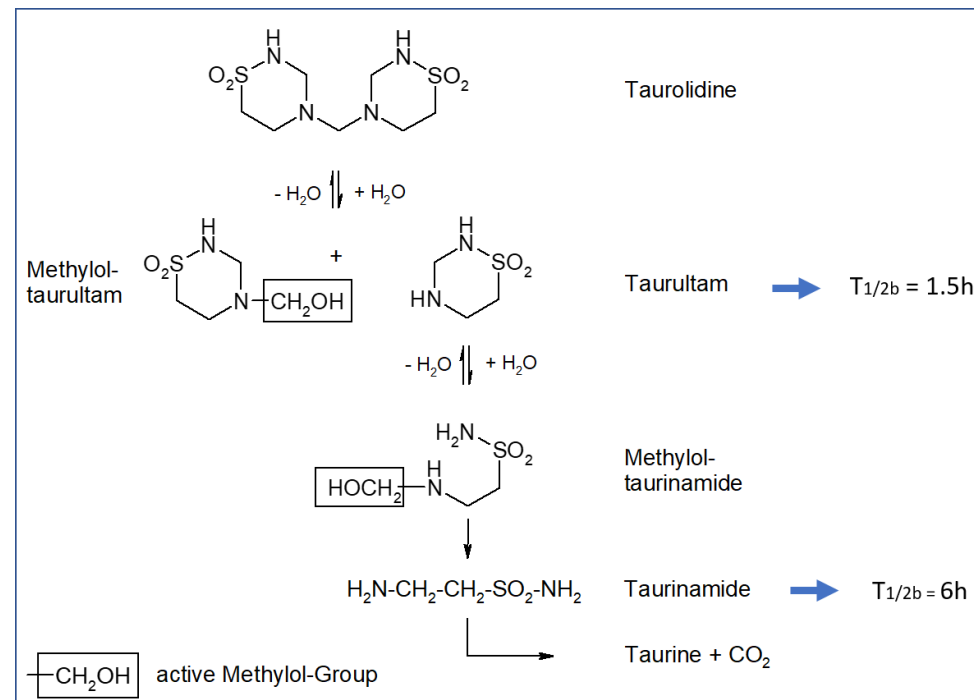
Antibiotic exposure causes microbiota dysbiosis, which in turn alters innate and adaptive immune response to bacterial and viral pathogens



Increased susceptibility to infections in later life

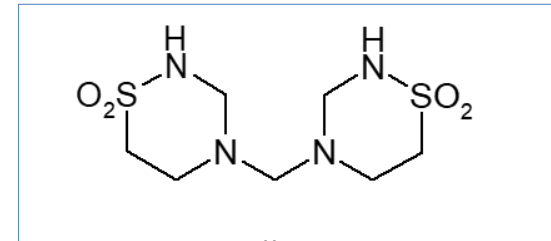
Taurolidine

Derived from the amino acid taurine



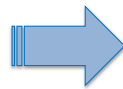
Taurolidine is metabolized rapidly
via other metabolites to taurine

Taurolidine

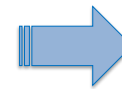
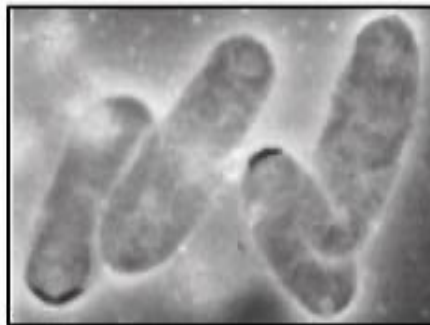


Broad spectrum antimicrobial activity

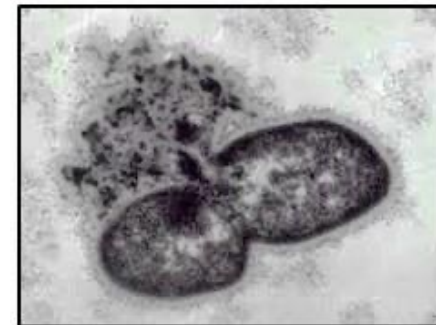
Taurolidine reacts with bacterial fimbriae



Bacteriostatic

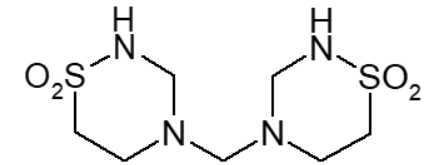


Bactericidal



Destroys bacterial cell wall

Taurolidine



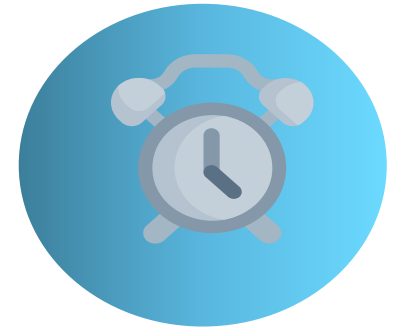
Activity extends across a wide-spectrum of aerobic and anaerobic bacteria and fungi

Antimicrobial spectrum

In vitro activity of taurolidine (MIC₅₀ mg/ml)

<u>Staph aureus</u>	0,25 – 0,5	Acinetobacter spec.	0,5
<u>Staph. epidermidis</u>	0,25 – 0,5	Moraxella catarrhalis	0,5
Enterococcus faecalis	0,25	<u>Pseud. aeruginosa</u>	0,5 – 1,0
Strept. haemolyticus	0,125 – 0,25	Bacteroides fragilis	0,25
Strept. pneumoniae	0,125 – 0,25	Bact. thetaiotaomicron	0,25
Strept. viridans	0,25	Burkholderia cepacia	0,5
Klebs. pneumoniae	0,25 – 0,5	Clostridium difficile	0,125
Klebs. oxytoca	0,125 – 0,5	Clostridium perfringens	0,125
Enterobacter cloacae	0,5	Corynebacterium spec.	0,25
Enterobacter aerogenes	0,5	Peptostreptococcus spec.	0,125 – 0,25
Citrobacter freundii	0,5	Peptococcus spec	0,125
Proteus mirabilis	0,25 – 0,5	Fusobacterium	0,125 – 0,25
Proteus vulgaris	0,25 – 0,5	Salmonella thypimurium	0,8
Morganella morganii	0,25 – 0,5	Shigella flexneri/sonnei	0,8
Serratia marcescens	0,125 – 0,5	<u>Candida albicans</u>	0,5 – 1,0
Listeria monocytogenes	0,5	<u>Rhodotorula spec.</u>	0,125 – 0,5

Lock therapy



Instillation into the catheter lumen of a dose of
antibiotic up to 1000 times the MIC
for a duration that can go from 12 to 48 hours,
for several days,
in combination with systemic antibiotics

Advantages

JVA
ISSN 1129-7298

J Vasc Access 2016; 17 (6): 453-464

DOI: 10.5301/jva.5000576

REVIEW

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



No resistance
Short action

Clinical Nutrition 32 (2013) 538–542



Contents lists available at SciVerse ScienceDirect

Clinical Nutrition

Journal homepage: <http://www.elsevier.com/locate/cinu>

Original article

Absence of microbial adaptation to taurolidine in patients on home parenteral nutrition who develop catheter related bloodstream infections and use taurolidine locks☆☆☆

E.D. Olthof^{a,*}, R.J. Rentenaar^b, A.J.M.M. Rijs^b, G.J.A. Wanten^a

Infection prevention

Publication	Study design	Control group	CRBSI per 1000 cath. days (con/TS)	Catheter Occlusion per 1000 cath. days (con/TS)	Cost per patient (con/TS) EUR	Patient group	Number of Patients (per group; con/TS)	Obser. time (per group)	Catheter type
Jurewitsch et al. 1998 J Parent. and Ent. Nutr.	Case report	Hep 100	8.5/1.5	N.D.	N.D.	High risk	1	1y	N.D.
Jurewitsch et al. 2005, Clinical Nutrition	Prospective	N.D.	10.8/0.8	N.D.	N.D.	High risk	7/7	3m to >10y	Hickman/ PICC
Bisseling et al. 2010, Clinical Nutrition	Prospective randomized	Hep 150	2.0/0.2	0/0	N.D.	High risk	14/16	6m/2y	Hickman/ PAC
Jonkers et al. 2012, Clinical Nutrition Suppl.	Retrospective	Hep 100	1.4/0.3	N.D.	N.D.	All	32 Total	1y	PICC/ PAC
Olthof et al. 2014, Plos ONE	Retrospective	Hep 150	3.0/0.5	0.55/0.27	N.D.	All	167/107	1/2y	Hickman/ PAC
Wouters et al. 2018a, AP&T	Prospective randomized	Saline	1.44/0.33	0.24/0.20	3'786/1'585	Normal risk vs High risk	50/52	1y	Hickman/ Broviac/ PICC/PAC
Arnoriaga et al. 2018, Nutrición Hospitalaria	Retrospective	Saline	3.12/0.76	0.33/0.19	11'635/1'871	High risk	13/13	18/4y	Hickman
Wouters et al. 2018b, Clinical Nutrition	Retrospective	N.A.	0.60	0.12	N.D.	All	270	10y	Hickman/ PAC/non- tunneled/ PICC

Lock profilattico

Clinical Nutrition (2005) 24, 462–465



2005

Clinical
Nutrition

<http://intl.elsevierhealth.com/journals/clnu>

SHORT REPORT

Taurolidine lock: The key to prevention of recurrent catheter-related bloodstream infections

Brian Jurewitsch*, Khursheed N. Jeejeebhoy

Digestive Diseases Program, St. Michael's Hospital, University of Toronto, 30 Bond St., Toronto, Ont., Canada M5B 1W8

Pazienti in NP domiciliare

10.8 ↓ 0.8/1000 gg catetere

Clin Nutr. 2010 Aug;29(4):464–8. doi: 10.1016/j.clnu.2009.12.005. Epub 2010 Jan 12.

Taurolidine lock is highly effective in preventing catheter-related bloodstream infections in patients on home parenteral nutrition: a heparin-controlled prospective trial.

Bisseling TM¹, Willems MC, Versleijen MW, Hendriks JC, Vissers RK, Wanten GJ.

⊕ Author information

Pazienti in NP domiciliare

Trial randomizzato eparina/taurolidina

↓ 10 vs 1 CRBSI

Prophylactic lock

Received: 26 March 2018 | First decision: 27 April 2018 | Accepted: 18 June 2018
DOI: 10.1111/apt.14904



WILEY *AP, T Alimentary Pharmacology & Therapeutics*

Randomised clinical trial: 2% taurolidine versus 0.9% saline locking in patients on home parenteral nutrition

Y. Wouters¹ | M. Theilla² | P. Singer² | S. Tribler³ | P. B. Jeppesen³ | L. Pironi⁴ | L. Vinter-Jensen⁵ | H. H. Rasmussen⁵ | F. Rahman⁶ | G. J. A. Wanten¹

↓ Riduzione X4
rischio di CRBSI

OPEN ACCESS Freely available online

PLOS ONE

Taurolidine Lock Solutions for the Prevention of Catheter-Related Bloodstream Infections: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Yong Liu^{1*}, An-Qiang Zhang², Lin Cao¹, Hong-Tao Xia¹, Jun-Jie Ma¹

6 Trial randomizzati. - 431 pazienti

↓ CRBSI nei pazienti a rischio

Lock del catetere di almeno 30 minuti

Prophylactic lock

HEPATOLOGY AND NUTRITION

Significant Reduction in Central Venous Catheter-related Bloodstream Infections in Children on HPN After Starting Treatment With Taurolidine Line Lock

Chu, Hui-Ping; Brind, Joanne; Tomar, Rajeev; Hill, Susan

Effects of prophylactic use of taurolidine-citrate lock on the number of catheter-related infections in children under 2 years of age undergoing surgery

M. Łyszkowska • G. Kowalewski • M. Szymczak • D. Polnik • A. Mikołajczyk • P. Kaliciński



heparin / taurolidine



8.6 vs 1.1 CRBSI

Standard / taurolidine



16 vs 1 CRBSI

Original article

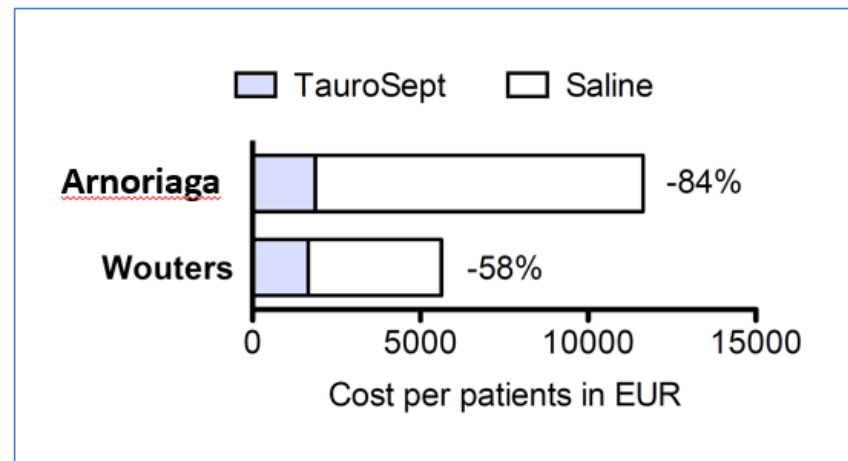
Cost-effectiveness of taurolidine locks to prevent recurrent catheter-related blood stream infections in adult patients receiving home parenteral nutrition: a 2-year mirror-image study

Damien Lannoy ^{a, b}, Alexia Janes ^a, Xavier Lenne ^c, Sébastien Neuville ^a, Julien Bourry ^d, Pascal Odou ^{a, b}, Amélie Bruander ^c, David Seguy ^{c, f, d, *}

Clinical and economic impact of the taurolidine lock on home parenteral nutrition
Impacto clínico y económico de la utilización de taurolidina en pacientes con nutrición parenteral domiciliaria

María Arnoriaga Rodríguez¹, Maite Pérez de Ciriza Cordeu², Miguel Cambior Álvarez¹, Irene Bretón Lasmes¹, Marta Motilla de la Cámara¹, Cristina Velasco Gimeno¹, Loredana Arhip^{1,2}, Pilar García Peris¹ and Cristina Cuerda Compés¹

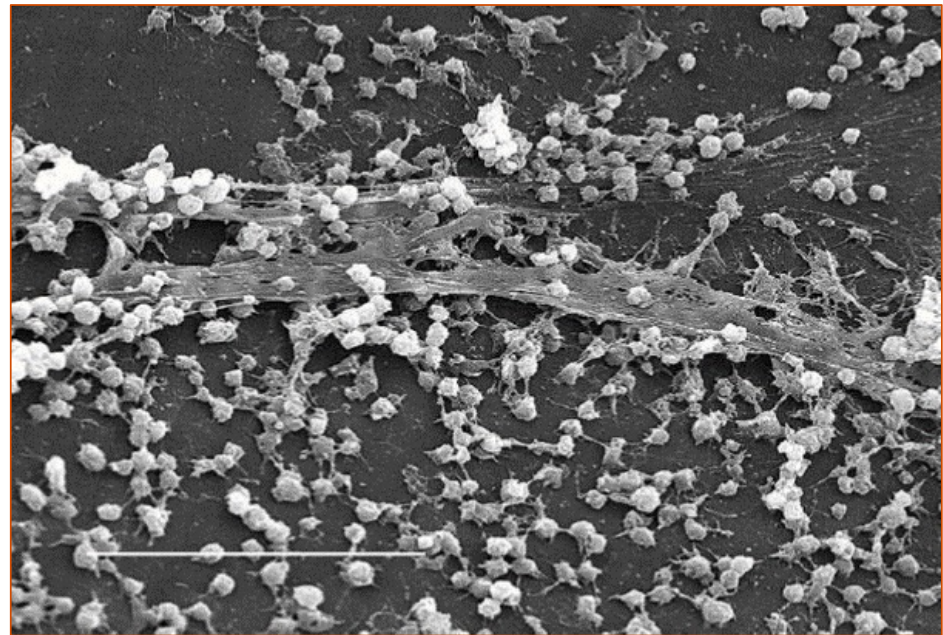
¹Clinical Nutrition and Dietetics Unit, Hospital General Universitario Gregorio Marañón (HUGM), Instituto de Investigación Sanitaria Gregorio Marañón (ISGM), Madrid, Spain; ²Hospital Universitario Donostia, Gipuzkoa, Spain; ³Facultad de Medicina, Universidad Complutense de Madrid, Madrid, Spain



CLABSI

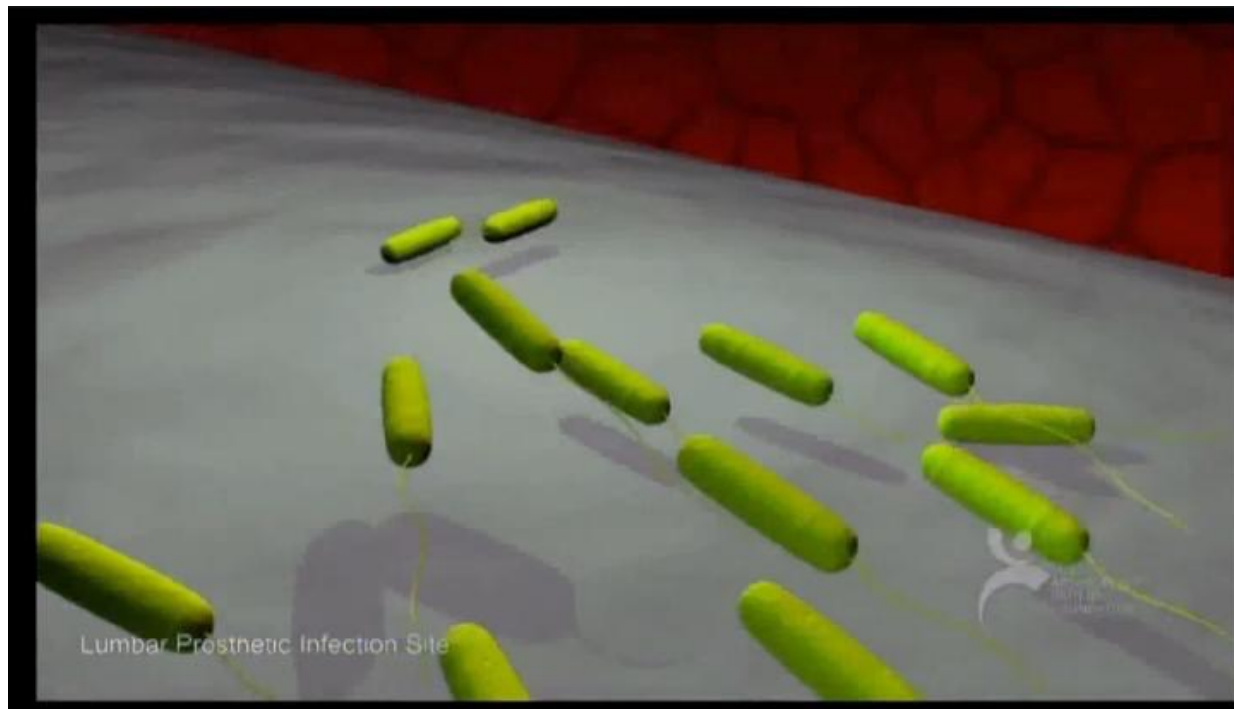
Our enemy ➡ The Biofilm

Extracellular matrix :
Polysaccharides, lipids,
proteins, DNA



Protects bacteria from immune cells
and antibiotics

Reduced metabolism of bacteria leading
to reduced sensitivity to antibiotics



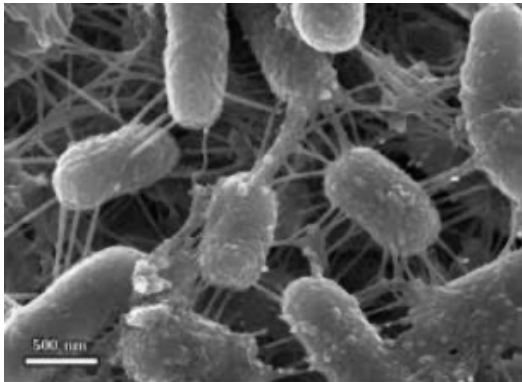
Need for higher doses of antibiotic and
for a longer duration

Formation of new bacterial colonies with
increased resistance to antibiotics

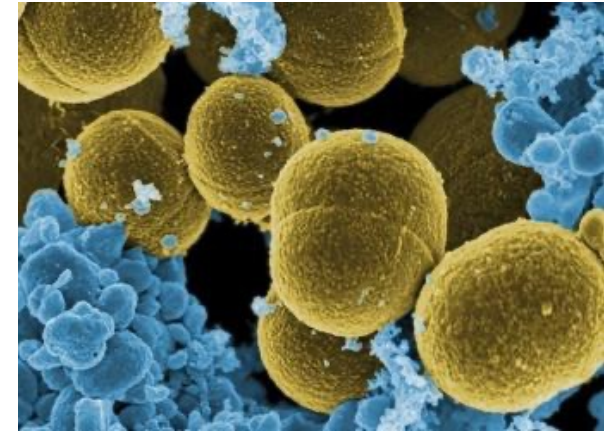
CLABSI

Remove the catheter

Gram -

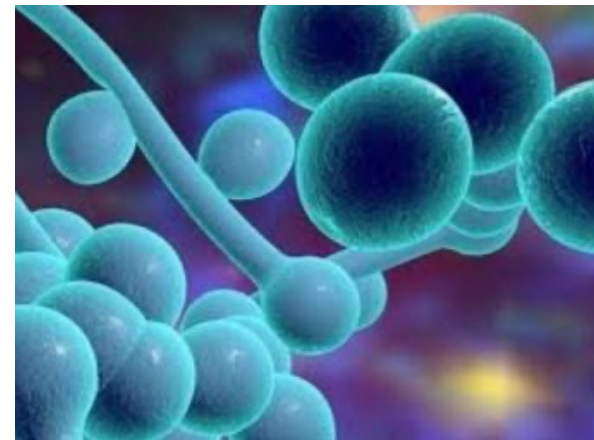


Staphylococcus
aureus



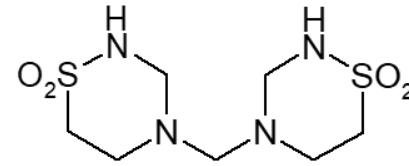
If S. aureus, Pseudomonas, Gram neg infection
AND
patient not improving 72 hours after the start of
antimicrobial therapy

Candida



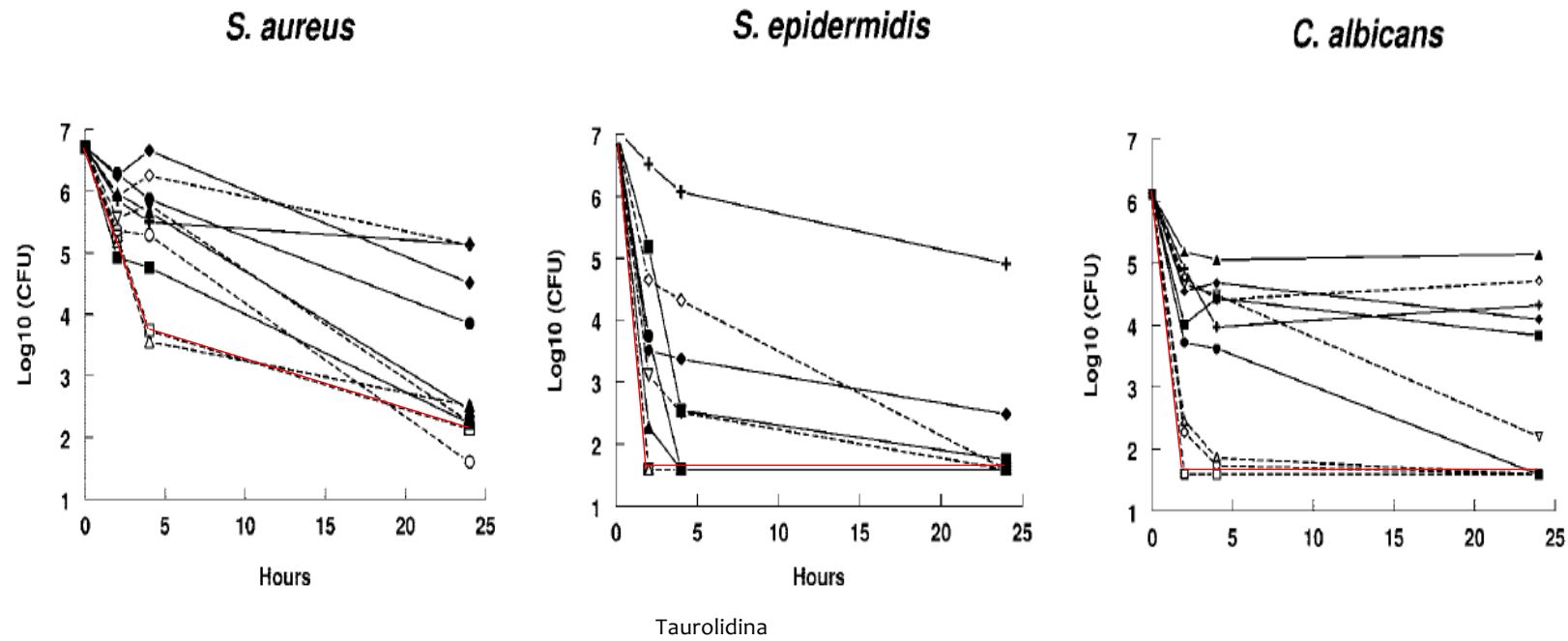
Immediately if fungal infection

Taurolidine



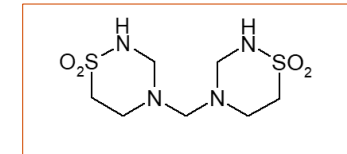
Therapeutic lock

Taurolidine lock vs antibiotic lock



Sherertz et al. Antimicrobial Agents and Chemotherapy. 2006

Therapeutic lock



Original research article

JVA | The Journal of
Vascular Access

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

Fabrizio Brescia¹, Mauro Pittiruti², Giancarlo Scoppettuolo³, Chiara Zanier¹, Elisa Nadalini¹, Paola Bottos¹, Chiara Moreal¹, Valentina Da Ros⁴ and Fabio Fabiani¹



International Journal of Antimicrobial Agents 2

Taurolidine is effective in the treatment of central venous catheter-related bloodstream infections in cancer patients

M. Koldehoff^{a,*}, J.L. Zakrzewski^b

^a Department of Bone Marrow Transplantation, University Hospital Essen, Hufelandstrasse 55, 45122 Essen, Germany

^b Memorial Sloan Kettering Cancer Center, New York City, USA

Received 29 March 2004; accepted 9 June 2004

The Journal of Vascular Access
1–5
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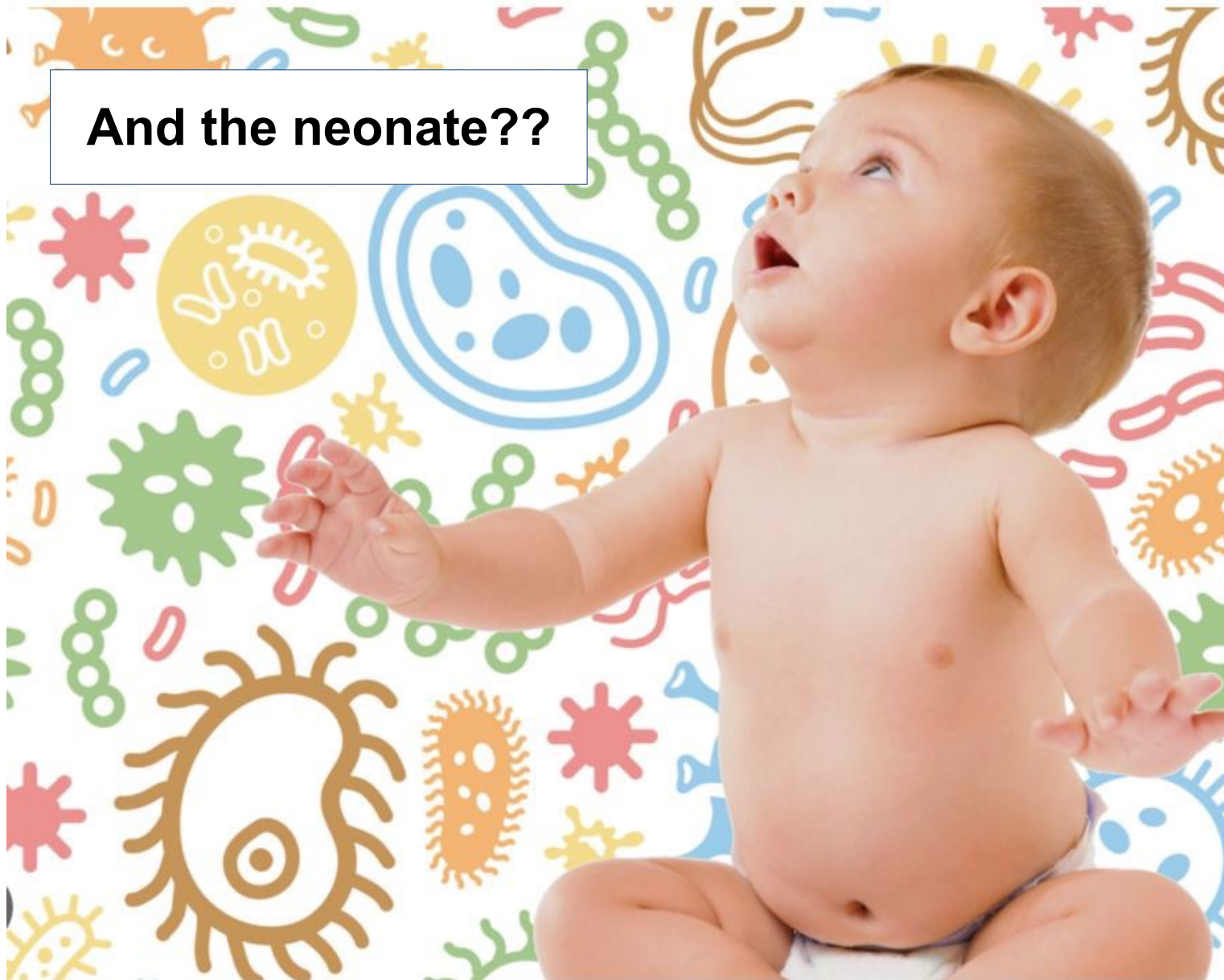
Comparative Study > Zentralbl Chir. 2009 Aug;134(4):350-6. doi: 10.1055/s-0028-1098929.

Epub 2009 Aug 17.

[Spectrum of indications and perioperative management in i. v. port-a-cath explantation – alternative administration of taurolin in case of i. v. port-a-cath infection]

Lock the catheter for 2 hours

And the neonate??



In pediatria

Taurolidina 4% + citrato



Taurolidina 2%
senza citrato

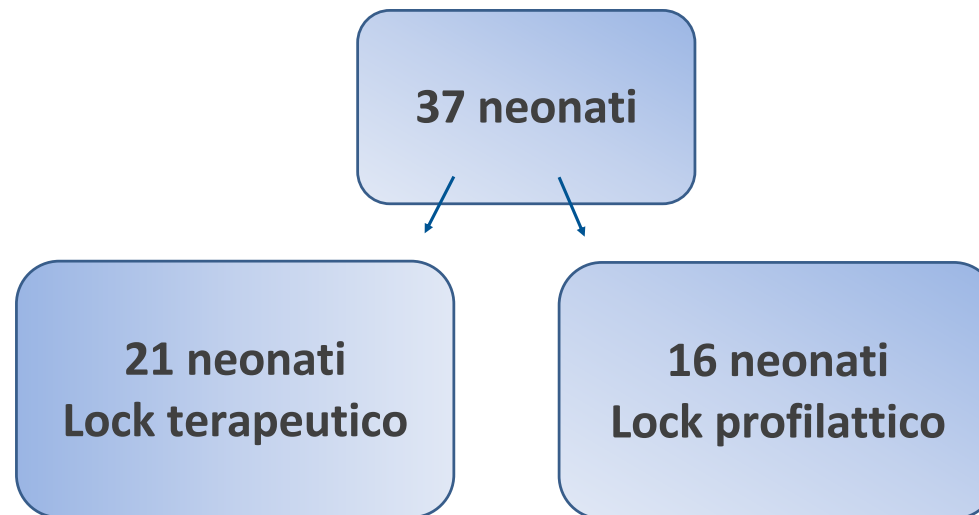


Effetti collaterali pressoché assenti

Senso di nausea, sapore metallico in bocca,
reazioni allergiche?

Use of 2% taurolidine lock solution for treatment and prevention of catheter-related bloodstream infections in neonates: a feasibility study

I. Savarese • S. Yazami • D.U. De Rose • ... C. Auriti • O. Danhaive • F. Piersigilli   • [Show all authors](#)



CICC / FICC / CVC a lungo termine

Lock: 0.3 - 0.5 ml



Alla fine del lock riaspirare il contenuto,
altrimenti sciacquare con fisiologica

Prophylactic lock



16 neonati



Lock di almeno
30 min

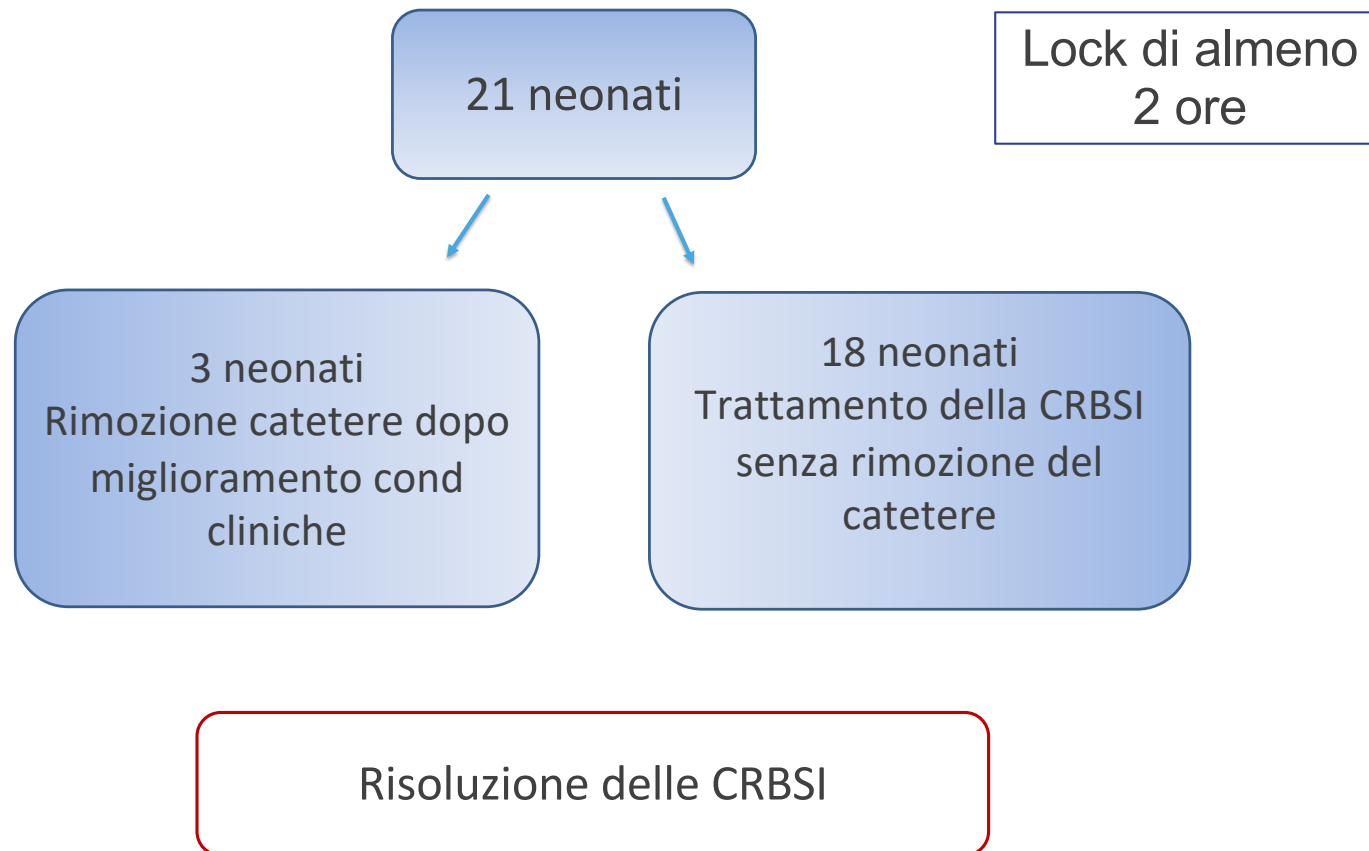
Neonati con fattori di rischio: intestino corto,
prematurità estrema, cardiopatia, chemioterapia

Nessuno sviluppo di CRBSI



1 episodio di conato di vomito dopo il lavaggio del cvc

Therapeutic lock



And the preterm?

Epicutaneo cava catheter



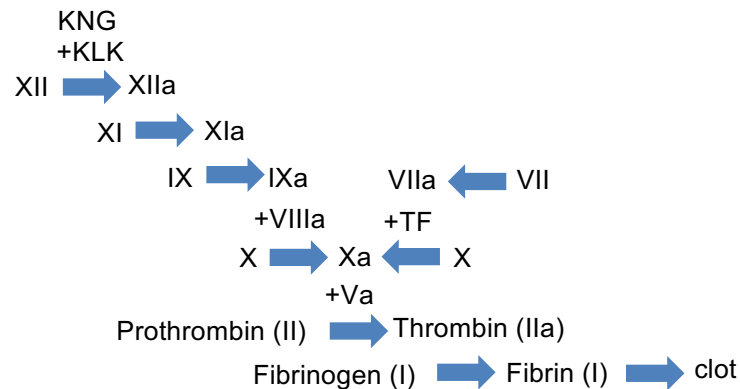
Difficoltà ad eseguire un lock anche solo per 30 min

Infusioni continue (insulina, farmaci vasoattivi)

Ostruzione del catetere (infusione minima 1ml/h)

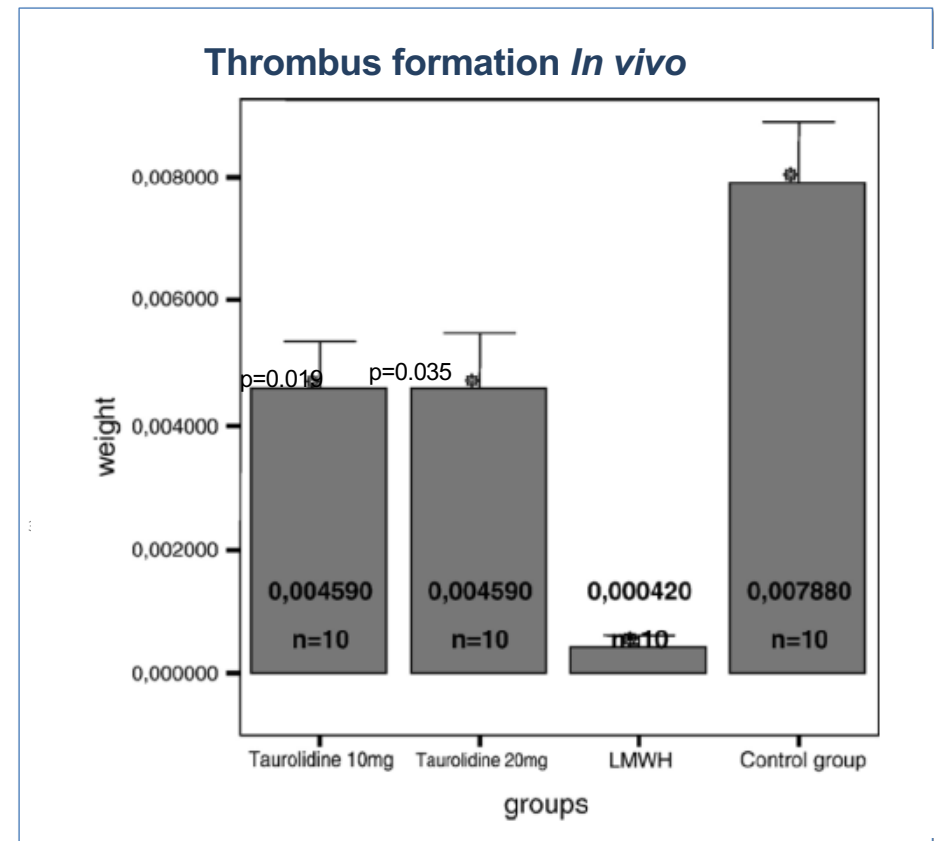
Effetto anticoagulante della taurolidina

Catheter thrombosis: Coagulation factors



Inhibition of coagulation factors

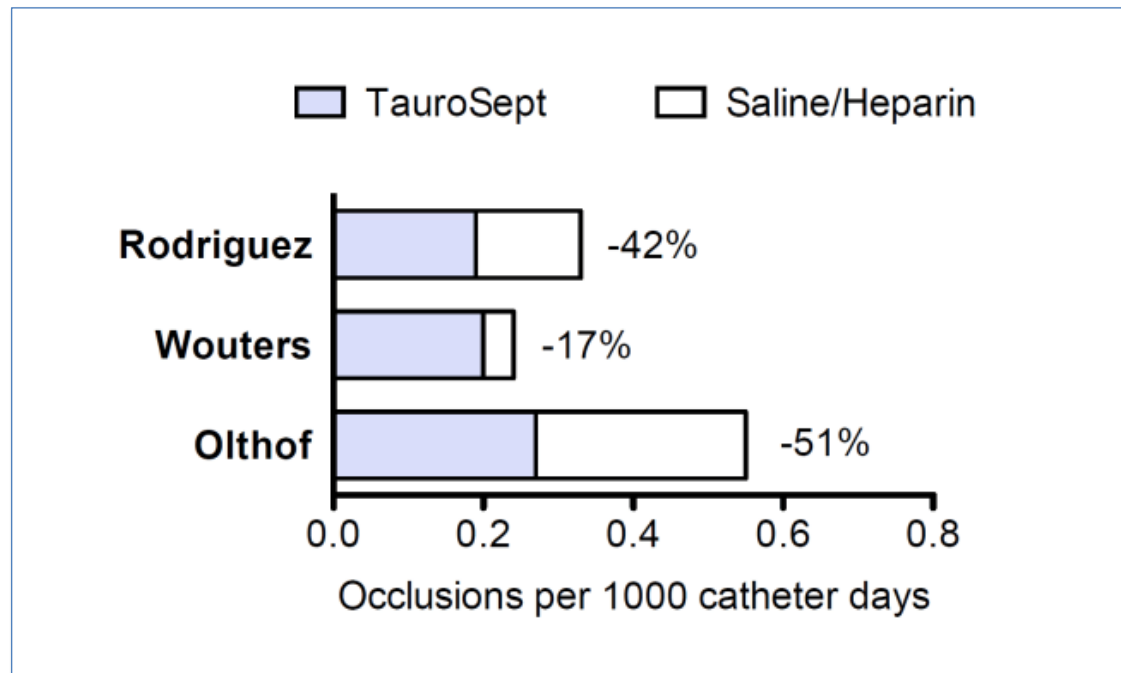
	Control group	Group 1 (taurolidine 10 mg)	Group 2 (taurolidine 20 mg)	P values
Factor II	166.3±6.75	151.4±7.46	145.2±9.36	0.079
Factor V	626.9±52.52	463.4±37.83	437.7±40.75	0.019
Factor VII	640.7±32.71	566.3±29.71	525.5±28.93	0.054 ^a
Factor VIII	237.1±11.53	182.40±7.37	180.91±9.22	0.002
Factor IX	245±16	145.2±9.05	123.2±9.97	0.0001
Factor X	72.9±6.29	64.8±5.96	52.9±6.48	0.086 ^a
Factor XI	229.8±11	188.5±13.89	160.90±10.16	0.002
Factor XII	203.7±6.31	160.7±10	164.8±5.87	0.002



→ Taurolidine mildly inhibits blood coagulation factors

Kaptanoglu et al. 2008

Taurolidine – Inhibition of catheter occlusion



→ Taurolidine inhibits catheter occlusion

Protocol

Epicutaneo cava catheter



Lock for 30 min

0.3 ml taurolidine 2%

Every other day

From the first day, for all the life of the catheter

Take home message



Prevention of CLABSI

Treatment of CRBSI

Decrease of catheter occlusions

Decrease of costs of hospitalization



Neonat.org

Fiammetta.Piersigilli@uclouvain.be