Infections liées aux cathéters Moyens diagnostiques et nouvelles possibilités thérapeutiques ?

Eric Lerebours

Rouen

Les données du problème

Organism	Frequency	Attempt line sterilization +	Success rate of line sterilization
Staph.coag.neg	30-40%	Yes	>85%
Staph.coag.pos	15-20%	Rarely	50% but risks acute endocarditis
Gram neg bact.	30-40%	Yes	50%
Fungi	6-9%	No	Risks metastatic spread. Rarely cleared
Polymicrobial	12%	No	Rarely cleared

Howard L and Ashley C. Gastroenterology 2003

Infections liées aux cathéters « de longue durée »

- Moyens diagnostiques
- Possibilités thérapeutiques
  - Prévention
  - Traitement curatif
  - Prévention de la récidive

IDSA Guidelines. Clinical infectious diseases 2009
ESPEN Guidelines. Clinical Nutrition 2009
I. Raad, H. Hanna, D. Maki. Lancet Infect Dis 2007

Infections liées aux cathéters « de longue durée »

- Moyens diagnostiques
- Nouvelles possibilités thérapeutiques
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  - Prévention de la récidive

Clinical Nutrition 28 (2009) 365–377

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ESPEN Guidelines on Parenteral Nutrition: Central Venous Catheters (access, care, diagnosis and therapy of complications)

Mauro Pittiruti [a], Helen Hamilton [b], Roberto Biffi [c], John MacFie [d], Marek Pertkiewicz [e]

7. Which is the best method for diagnosis of CRBSI?

Diagnosis of CRBSI is best achieved (a) by quantitative or semi-quantitative culture of the catheter (when the CVC is removed or exchanged over a guide wire), or (b) by paired quantitative blood cultures or paired qualitative blood cultures from a peripheral vein and from the catheter, with continuously monitoring of the differential time to positivity (if the catheter is left in place) (Grade A).

Diagnostic microbiologique : quelle méthode ?

- Ablation du cathéter
  - Même germe sur hémoculture et extrémité du cathéter
- Cathéter en place
  - Paire d'hémocultures : V.V.C et périphérie
    - Hémocultures quantitatives
      - Ratio V.V.C / périphérie ≥ 3
    - Différentiel de temps de pousse
      - Différentiel V.V.C / Périphérie ≥ 2h
  - Hémoculture quantitative sur la V.V.C ?
    - Seuil > 100 CFU/ml.
    - I.L.V.C.C ou bactériémie massive ?

IDSA Guidelines. Clinical infectious diseases 2009
ESPEN Guidelines. Clinical Nutrition 2009

Diagnostic microbiologique : quelle méthode ? V.V.C. en place

	Diagnostic criteria	Accuracy		Disadvantages
		Sensitivity	Specificity	
Techniques without CVC removal				
Simultaneous quantitative blood cultures	Quantitative blood culture drawn through CVC yields CFU count five-fold higher or more than CFU count from simultaneously drawn blood from peripheral vein	93%[22]	97–100%[22]	Labour intensive, costly
Differential time to positivity	Blood culture drawn from CVC becomes positive ≥2 h before simultaneously drawn blood culture from peripheral vein	89–90%[22]	72–87%[22]	Hard to interpret when patient is taking antibiotics through the CVC
CVC-drawn quantitative blood culture	Quantitative blood culture from CVC is ≥100 CFU/mL	81–86%[22]	85–96%[22]	Cannot differentiate between CRBSI and high-grade bacteraemia

I. Raad et al. Lancet Infect Dis 2007

Paires d'hémocultures
Les limites et les difficultés

- Impossibilité d'accès à la V.V.C ou à une veine périphérique
  - Pas de retour veineux
  - Réticences pour prélever en périphérie

- Limites techniques
  - Hémocultures quantitatives difficiles à réaliser en pratique
  - Calcul du différentiel de temps de pousse pas toujours disponible
    - Contraintes pour le délai de réalisation et d'envoi. Marquage des flacons…
  - Définition des seuils +++
    - Hémocultures quantitatives : ratios variant de 3 à 10 selon les équipes
  - Prélèvements avant toute antibiothérapie +++

- Résultats plus difficiles à interpréter
  - V.V.C + et périphérie – ⇒ I.L.V.C.C probable ??? Contamination ?
  - V.V.C + seule disponible ⇒ Idem
  - V.V.C – et périphérie + ⇒ I.L.V.C.C peu probable

Traitement des infections liées à la voie veineuse centrale

- Prévention primaire
- Traitement de l'infection
- Prévention de la récidive

Traitement des infections liées à la voie veineuse centrale

- Prévention primaire
- Traitement de l’infection
- Prévention de la récidive

Traitement de l'infection liée à la V.V.C.
La 1ère question à se poser

- *Remove or not remove, that is the question* !*

** Enlever ou ne pas enlever la voie veineuse centrale, là est la question !*

William Shakespeare. Hamlet 1603

Ablation de la voie veineuse

Ablation première

- suppuration tunnel ou abcès sur CIP
-sepsis sévère
- thrombophlébite suppurée
- endocardite
- *candida*
- *staphyloccoccus aureus ?*
- bacille gram négatif ?

Ablation secondaire

- absence d'amélioration à J3
-survenue d'une complication

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9. Which is the best method for the management of CRBSI in long-term central venous access devices?

Removal of the long-term venous access device is required in case of (a) tunnel infection or port abscess, (b) clinical signs of septic shock, (c) paired blood cultures positive for fungi or highly virulent bacteria, and/or (d) complicated infection (e.g., evidence of endocarditis, septic thrombosis, or other metastatic infections). In other cases, an attempt to save the device may be tried, using the antibiotic lock technique (Grade B).

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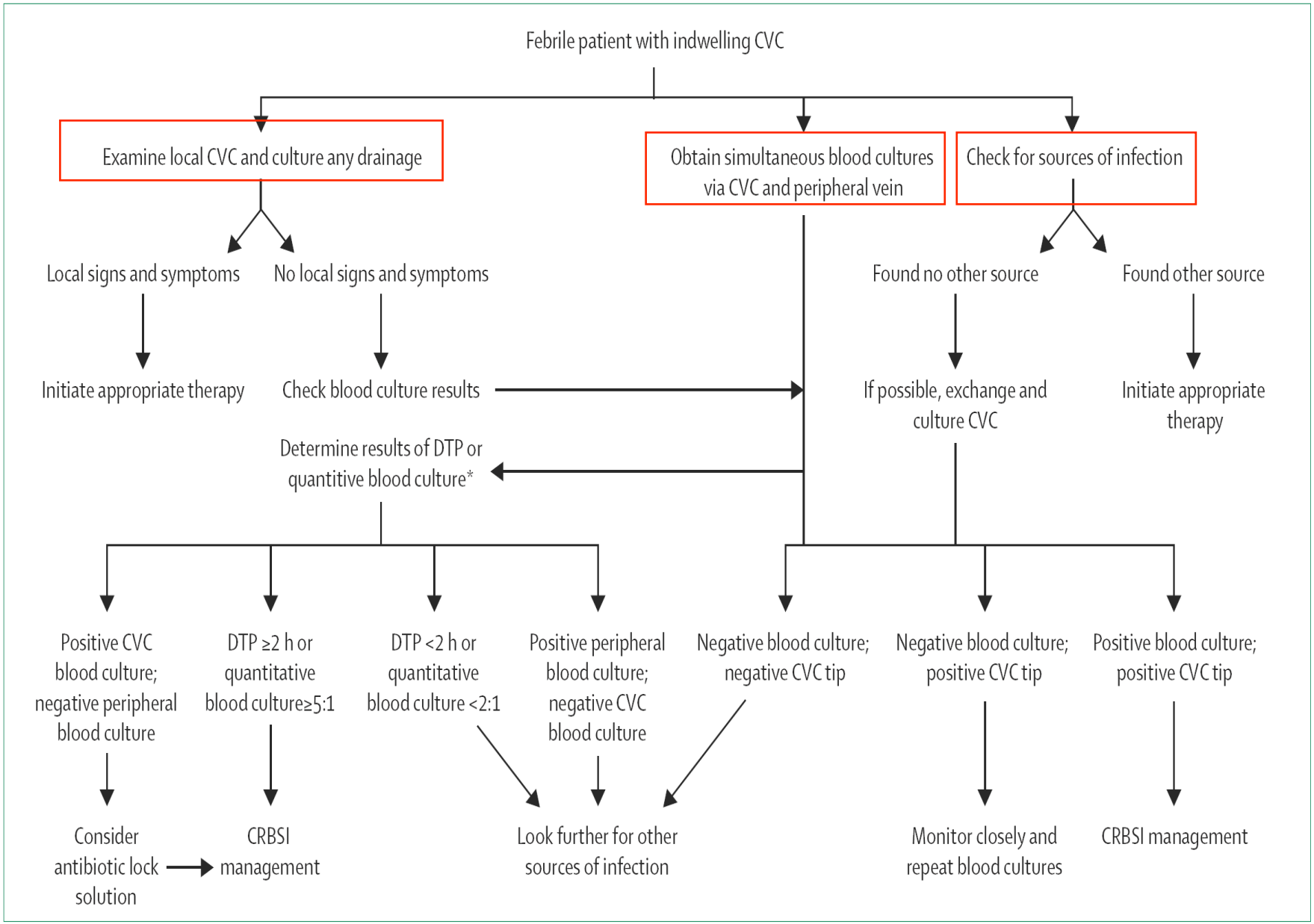
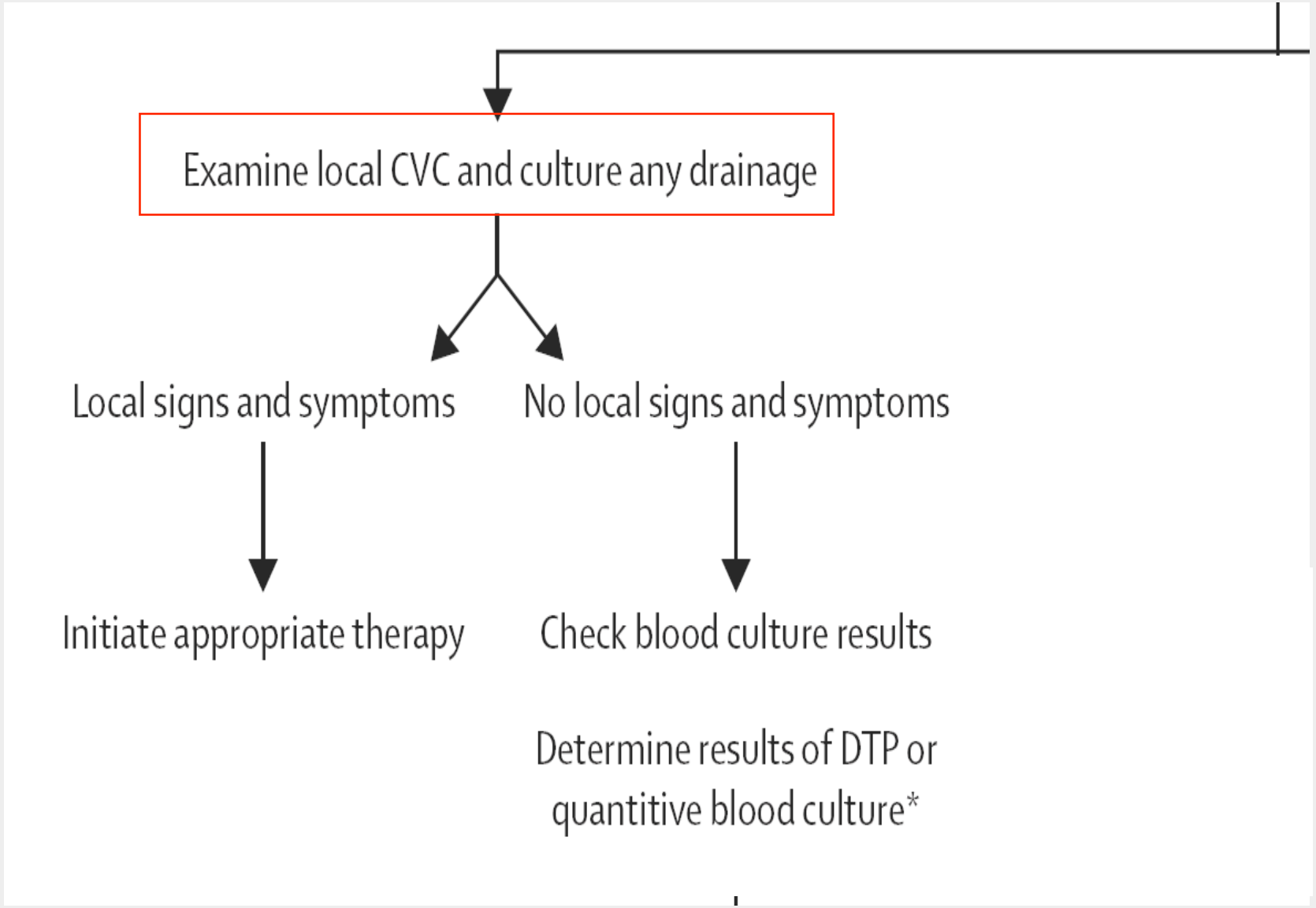
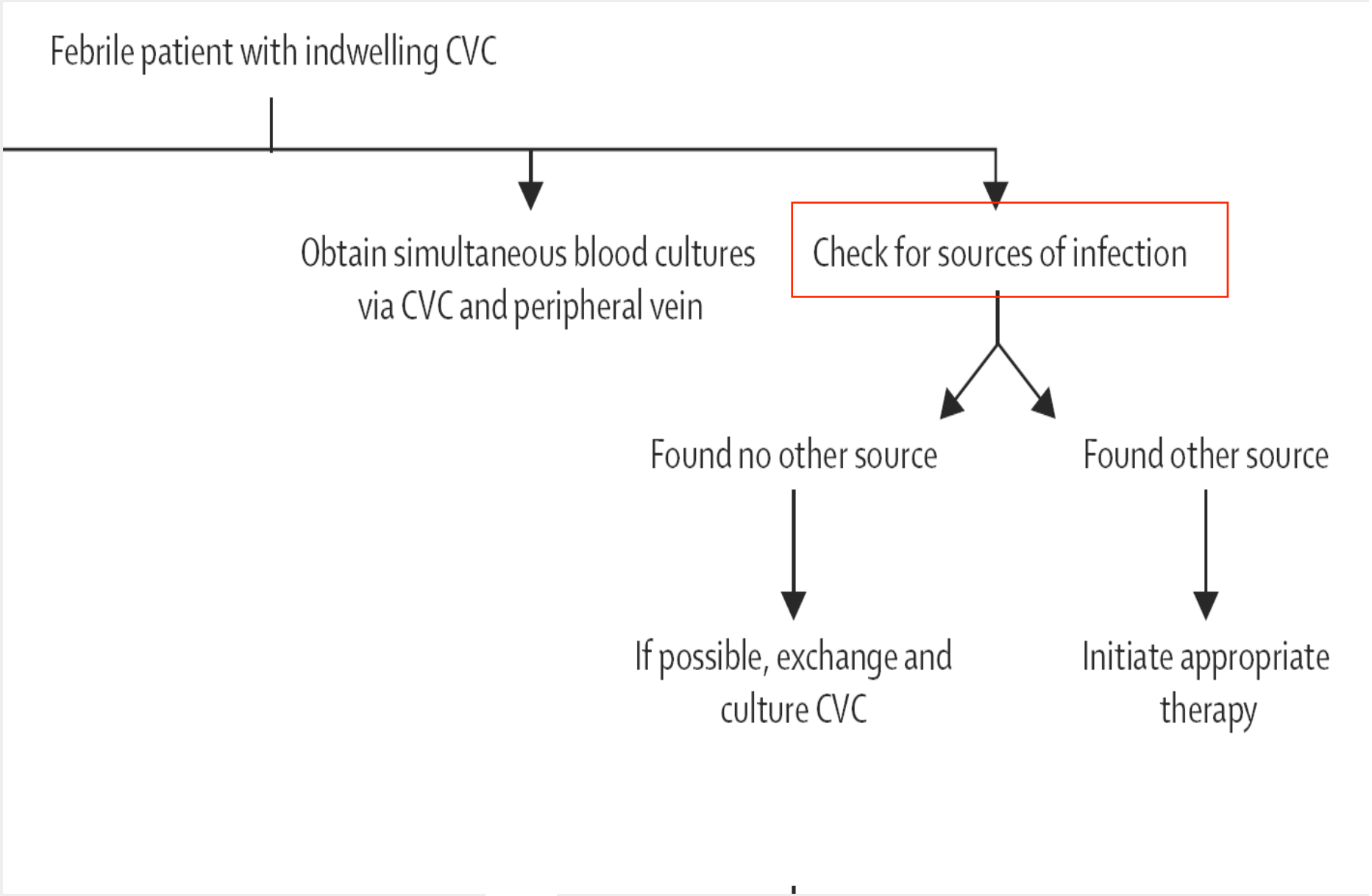
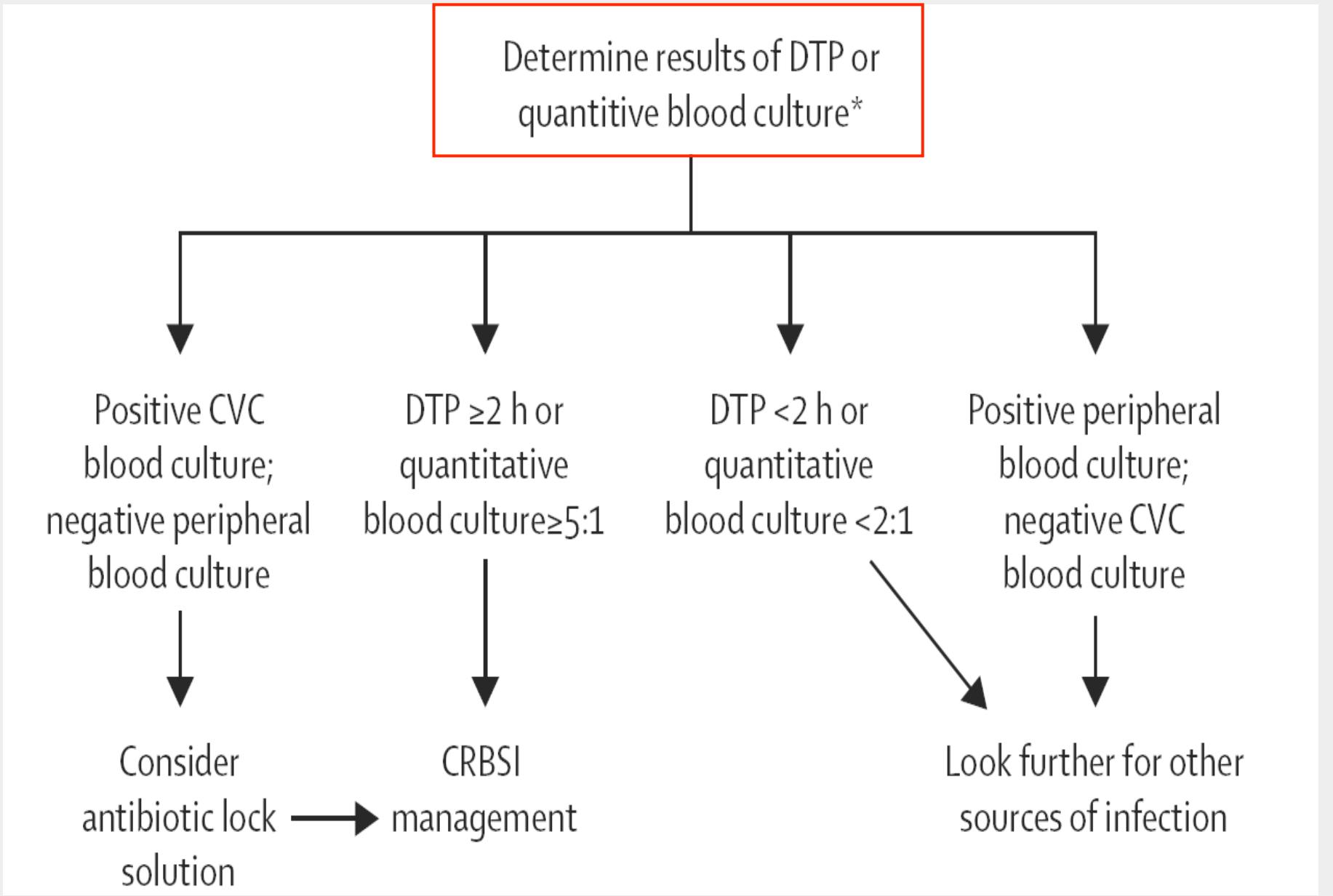


***Figure 2*: Diagnosis of acute febrile episode in a patient with central venous catheter**

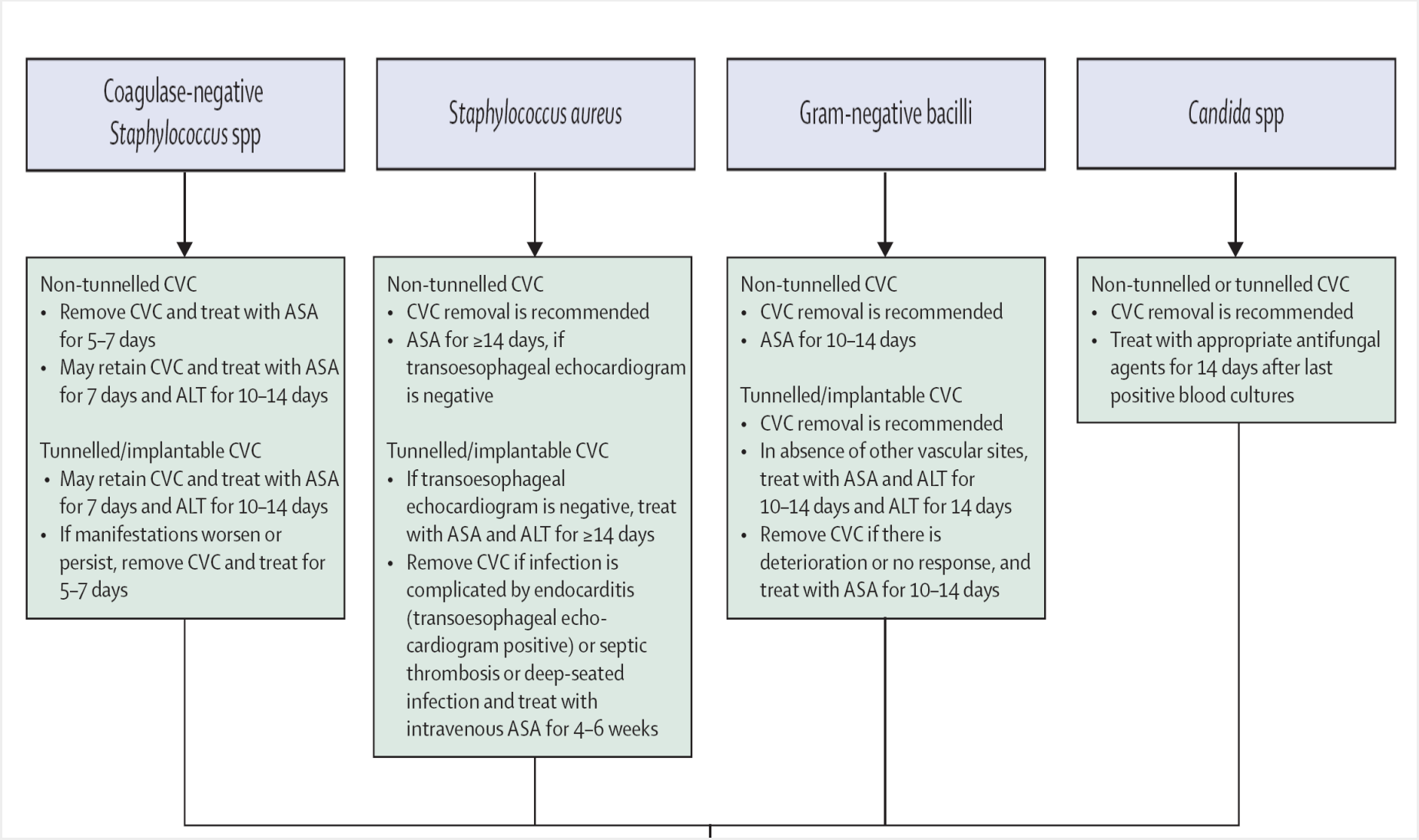
CVC=central venous catheter. DTP=differential time to positivity. *A blood culture is considered positive if the ratio of colony forming units growing from simultaneously drawn central and peripheral blood is ≥5:1 or the DTP is ≥2 h (central blood culture turns positive before simultaneously drawn peripheral blood culture).


Examine local CVC and culture any drainage
Local signs and symptoms
No local signs and symptoms
Initiate appropriate therapy
Check blood culture results
Determine results of DTP or quantitive blood culture*

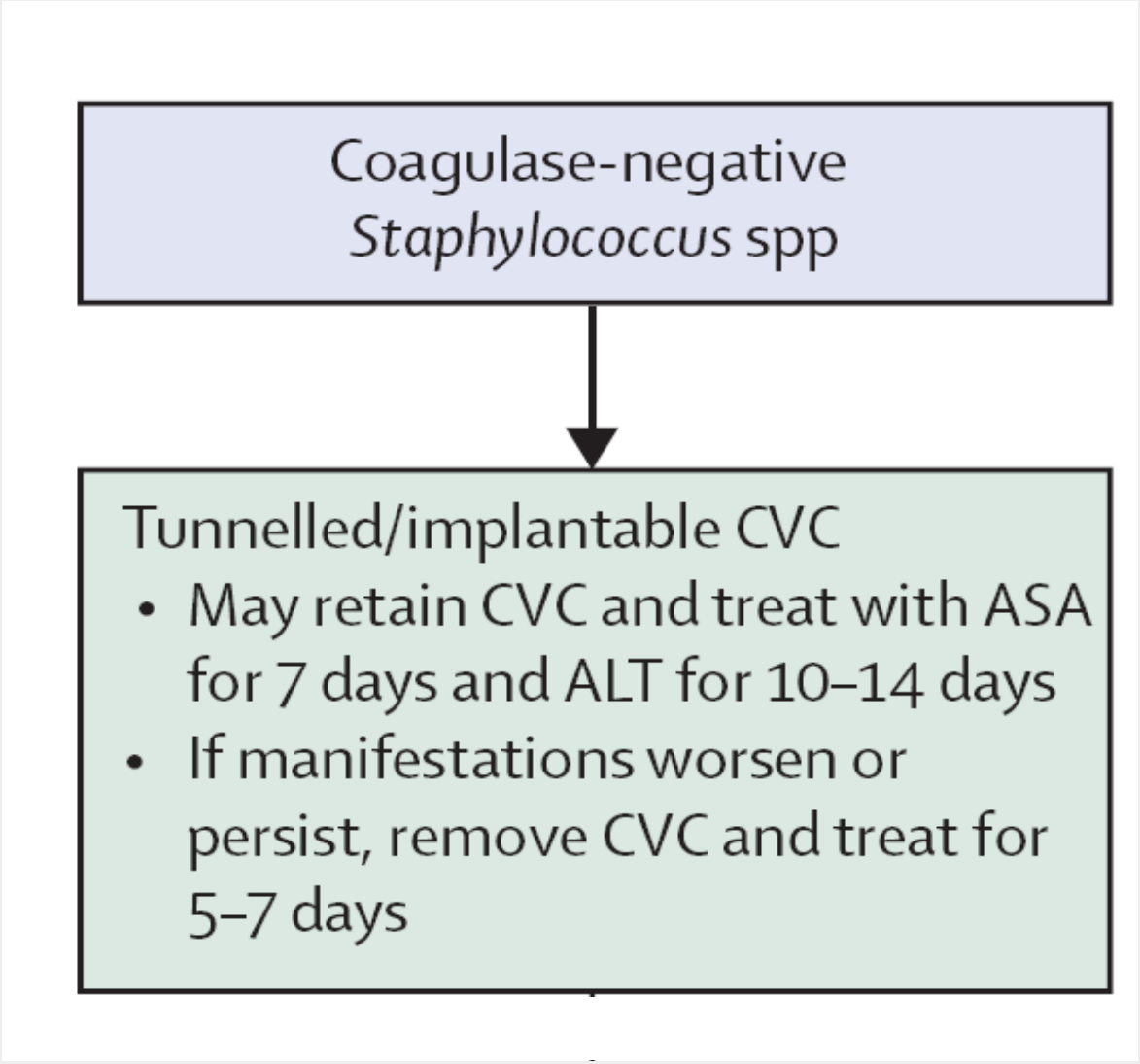

Febrile patient with indwelling CVC
Obtain simultaneous blood cultures via CVC and peripheral vein
Check for sources of infection
Found no other source
Found other source
If possible, exchange and culture CVC
Initiate appropriate therapy


Determine results of DTP or quantitive blood culture*
Positive CVC blood culture; negative peripheral blood culture
DTP ≥2 h or quantitative blood culture≥5:1
DTP <2 h or quantitative blood culture <2:1
Positive peripheral blood culture; negative CVC blood culture
Consider antibiotic lock solution
CRBSI management
Look further for other sources of infection

Traitement de l'infection liée à la V.V.C

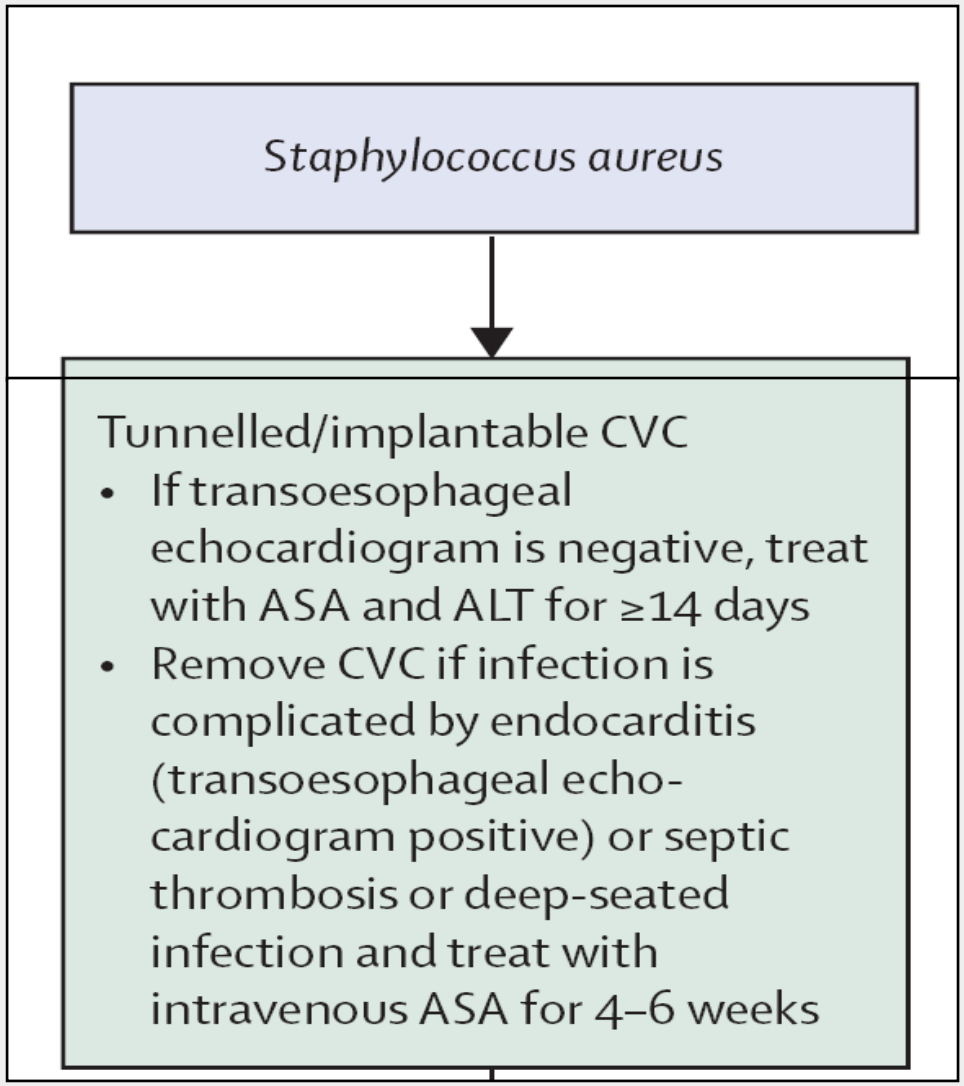


I. Raad et al. Lancet Infect Dis 2007



Question : si la V.V.C est enlevée, le traitement A.B est-il indispensable ?

. CVC=central venous catheter. ASA=appropriate systemic antibiotic. ALT=antibiotic lock therapy.



Ablation de la V.V.C.

Traitement 4 à 6 sem

Traitement plus court > 2sem
-malade non diabétique
-V.V.C enlevée
-Absence de matériel
-Pas de thrombophlébite
-Echo cardiaque normale
-Pas de métastase septique
-Pas de fièvre et Hémocultures
-Négatives à J3

Questions : - une échocardiographie doit-elle être réalisée systématiquement ?
- ablation systématique de la V.V.C ?
- durée du traitement AB

. CVC=central venous catheter. ASA=appropriate systemic antibiotic. ALT=antibiotic lock therapy.

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

Leonard A. Mermel,[1] Michael Allon,[2] Emilio Bouza,[9] Donald E. Craven,[3] Patricia Flynn,[4] Naomi P. O'Grady,[5] Issam I. Raad,[6] Bart J. A. Rijnders,[10] Robert J. Sherertz,[7] and David K. Warren[8]

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71. Catheter removal is recommended for CRBSI due to *S. aureus* and *Candida* species, instead of treatment with antibiotic lock and catheter retention, unless there are unusual extenuating circumstances (e.g., no alternative catheter insertion site) (A-II).

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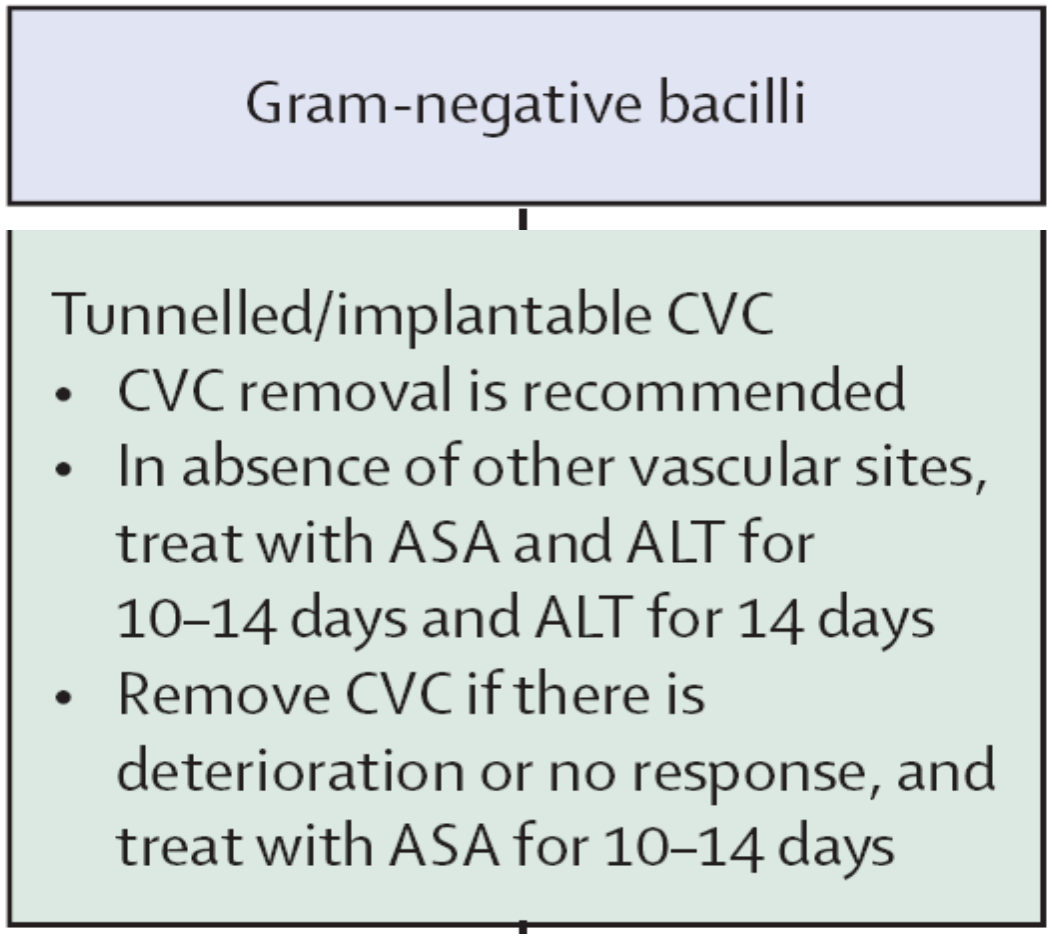
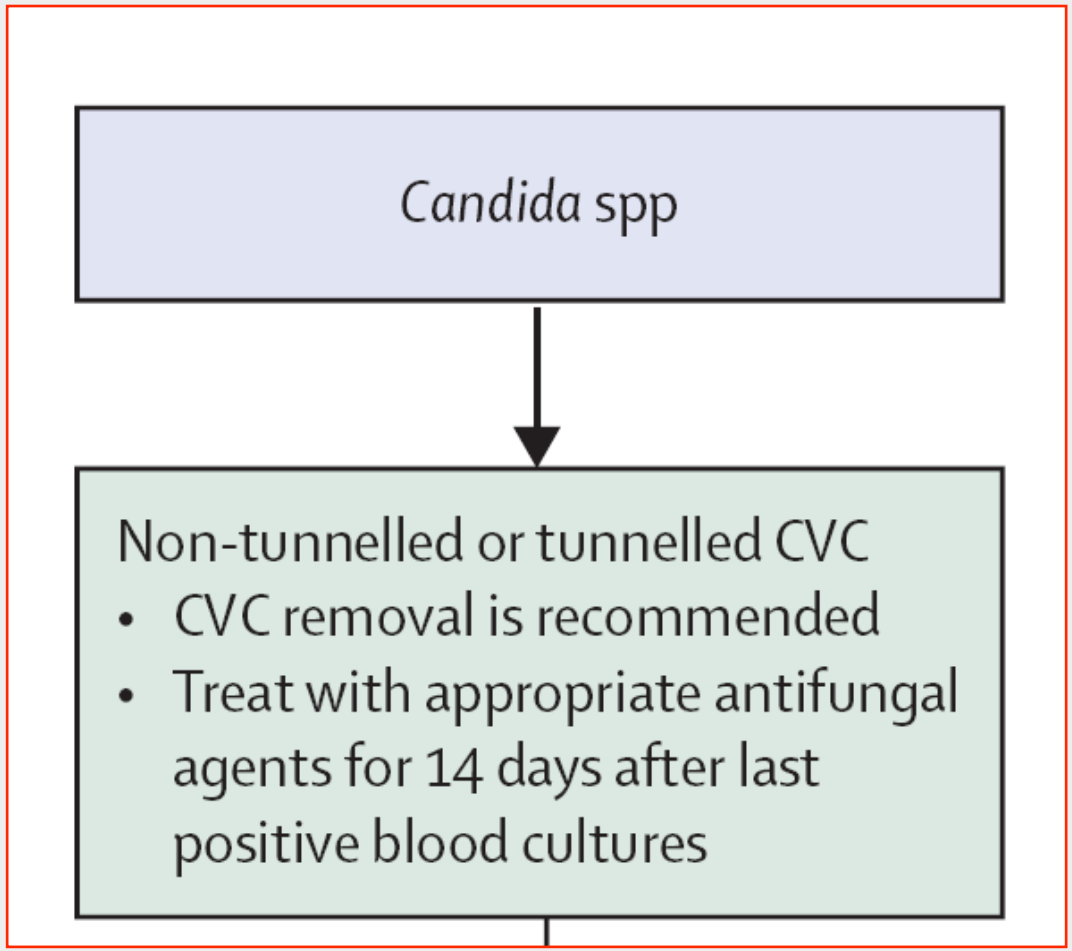


Question : ablation systématique de la V.V.C ?

. CVC=central venous catheter. ASA=appropriate systemic antibiotic. ALT=antibiotic lock therapy.



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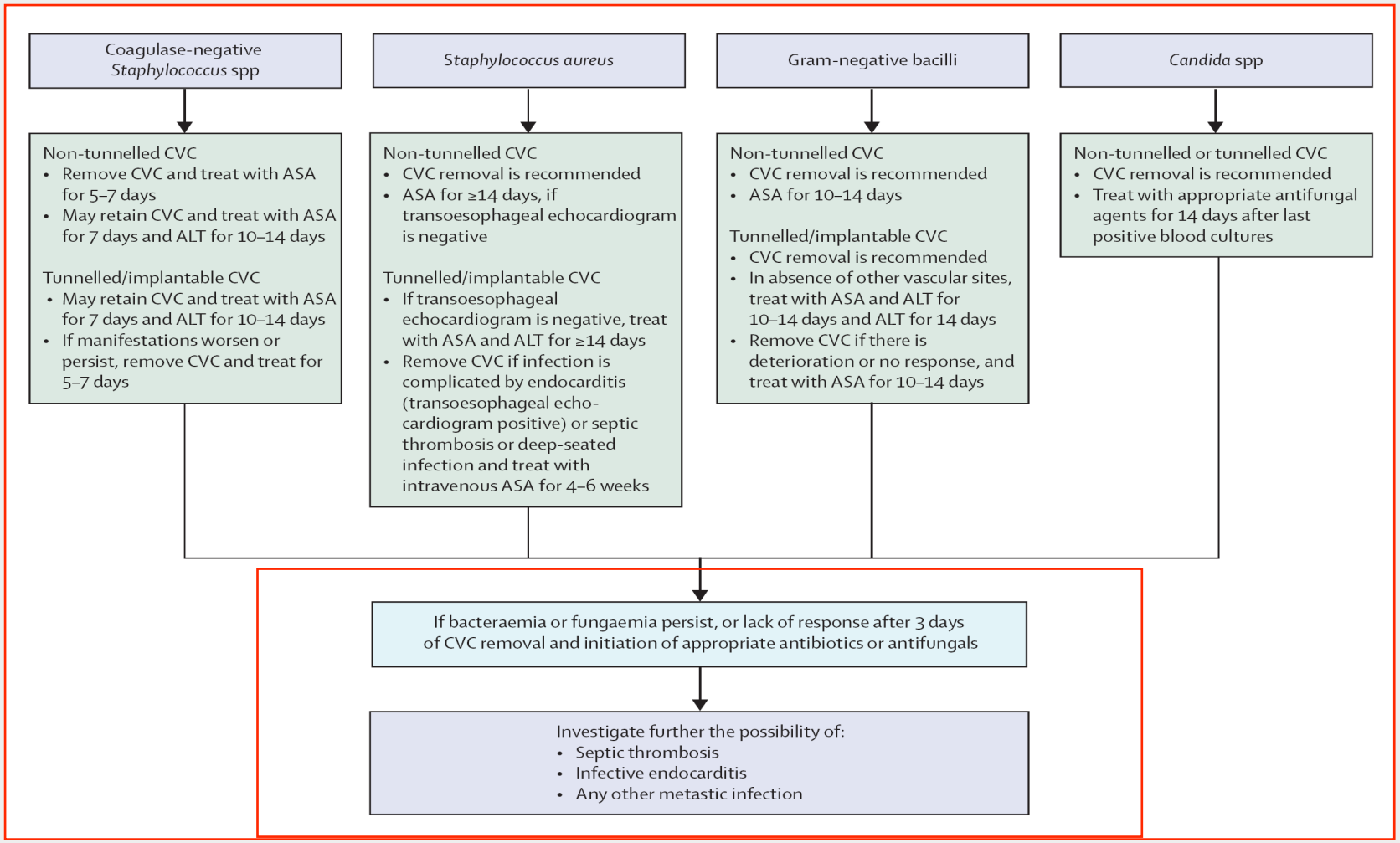
Traitement de l'infection liée à la V.V.C

Fonction du germe responsable



I. Raad et al. Lancet Infect Dis 2007

Antibiothérapie probabiliste

- Vancomycine en 1ère intention
- Couverture des bacilles Gram –
  - Ecologie microbienne locale
  - Sévérité de l'infection
- Couverture de BGN multi-résistants
  - Patient neutropénique
  - Colonisation connue par B.M.R, *P. aeruginosa*
  - Sepsis sévère
- Couverture des infections fongiques
  - Facteurs de risque : ABthérapie prolongée, transplantation, colonisation multiple par *Candida*

Le verrou antibiotique *

Table 9. Final concentrations of antibiotic lock solutions used for the treatment of catheter-related bloodstream infection.

Antibiotic and dosage	Heparin or saline, IU/mL	Reference(s)
Vancomycin, 2.5 mg/mL	2500 or 5000	[100, 275]
Vancomycin, 2.0 mg/mL	10	[275]
Vancomycin, 5.0 mg/mL[a]	0 or 5000	[276, 277]
Ceftazidime, 0.5 mg/mL	100	[123]
Cefazolin, 5.0 mg/mL	2500 or 5000	[100, 277]
Ciprofloxacin, 0.2 mg/mL[b]	5000	[130]
Gentamicin, 1.0 mg/mL	2500	[100]
Ampicillin, 10.0 mg/mL	10 or 5000	[275]
Ethanol, 70%[c] Non recommandé	0	[131]

* Jamais seul, durée ≈14j, changé tous les 24h

IDSA Guidelines. Clinical infectious diseases 2009

IDSA GUIDELINES

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74. At this time, there are insufficient data to recommend an ethanol lock for the treatment of CRBSI (C-III).

Traitements de l'infections liées à la voie veineuse centrale

- Prévention primaire
- Traitement de l'infection
- Prévention de la récidive

Prévention de la récidive de l'infection liée aux DIVLD

- les mesures générales d'hygiène et d'aseptie
- le verrou antibiotique prophylactique : sélection...
- le verrou éthanol
- le verrou taurolidine

Taurolidine : le rationnel

- action antimicrobienne sans résistance bactérienne ou fongique connue, et sans risque de sélection

- action connue de dissolution des thrombi en cas de DIVLD occlus

- action démontrée de dissolution du biofilm de polysaccharides des staphylocoques qui reste inaccessible aux antibiotiques

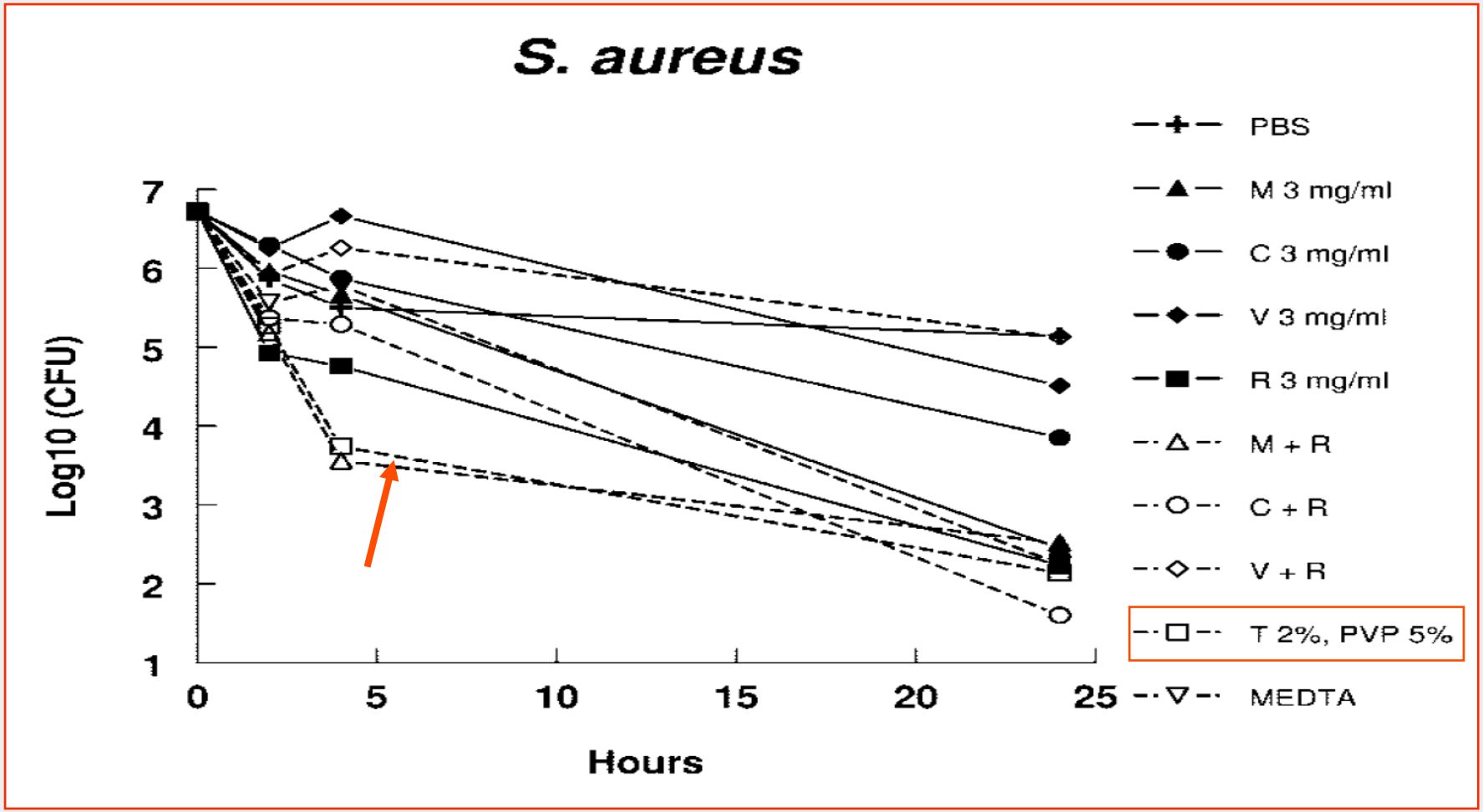
JH Bradshaw et JWL Puntis. J Ped Gastroenterol Nutr 2008

Taurolidine : les données disponibles

- Données expérimentales
  - Activité antimicrobienne de la taurolidine sur la majorité des bactéries Gram + et – et des levures
    - Efficacité pour des concentrations de 250 à 2000 µg/mL
- Données cliniques
  - Hémodialyse
  - Nutrition parentérale de longue durée
  - Oncologie et cancérologie

JH Bradshaw et JWL Puntis. J Ped Gastroenterol Nutr 2008

Efficacité in vitro des différents verrous



RJ Sherertz et al. Antimicrob Agents Chemother 2006

Taurolidine : les données disponibles

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  - Activité antimicrobienne de la taurolidine sur la majorité des bactéries Gram + et – et des levures
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  - Hémodialyse
  - Oncologie et cancérologie
  - Nutrition parentérale de longue durée

JH Bradshaw et JWL Puntis. J Ped Gastroenterol Nutr 2008

Verrou taurolidine

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Original Article

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

Tanya M. Bisseling[a], Martine C. Willems[b], Michelle W. Versleijen[a], Jan C. Hendriks[c], Renate K. Vissers[a], Geert J. Wanten[a,*]

[a] Department of Gastroenterology and Hepatology, Radboud University Nijmegen Medical Centre, PO BOX 9101, 6500 HB Nijmegen, The Netherlands
[b] Department of Vascular Surgery, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands
[c] Department of Epidemiology and Biostatistics, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands

Verrou taurolidine

		Heparin ($n = 14$)	Taurolidine ($n = 16$)	P
Female (n)		10 (71%)	12 (75%)	0.92
Age (yrs (SD)		48·6 (15.9)	55·3 (13·2)	0.75
Cause of intestinal failure (n)	Motility disorder	5 (36%)	5 (31%)	0.84
	High output stoma	1 (7%)	1 (6%)	0.93
	Short bowel syndrome	5 (36%)	6 (38%)	0.94
	Other	3 (21%)	4(25%)	0.86
Type of access	Hickman	8 (57%)	11 (69%)	0.70
	Port-a-cath	6 (43%)	5 (31%)	0.62
New device at start of study		6 (43%)	6 (38%)	0.82
Microorganism causing CRBSI at time of inclusion	Staphylococcus sp.	7 (50%)	9 (56%)	0.83
	epidermidis	5 (36%)	7 (44%)	0.74
	lugdunensis	1 (7%)	1 (6%)	0.93
	aureus	1 (7%)	1 (6%)	0.93
	Other Gram-positives	4 (29%)	2 (13%)	0.36
	Gram-negatives	3 (21%)	4 (25%)	0.86
	Other	0	1 (6%)	0.53

Patient characteristics in number (percentage), except for age; mean (SEM),.
CRBSI = catheter-related bloodstream infection.

Verrou taurolidine

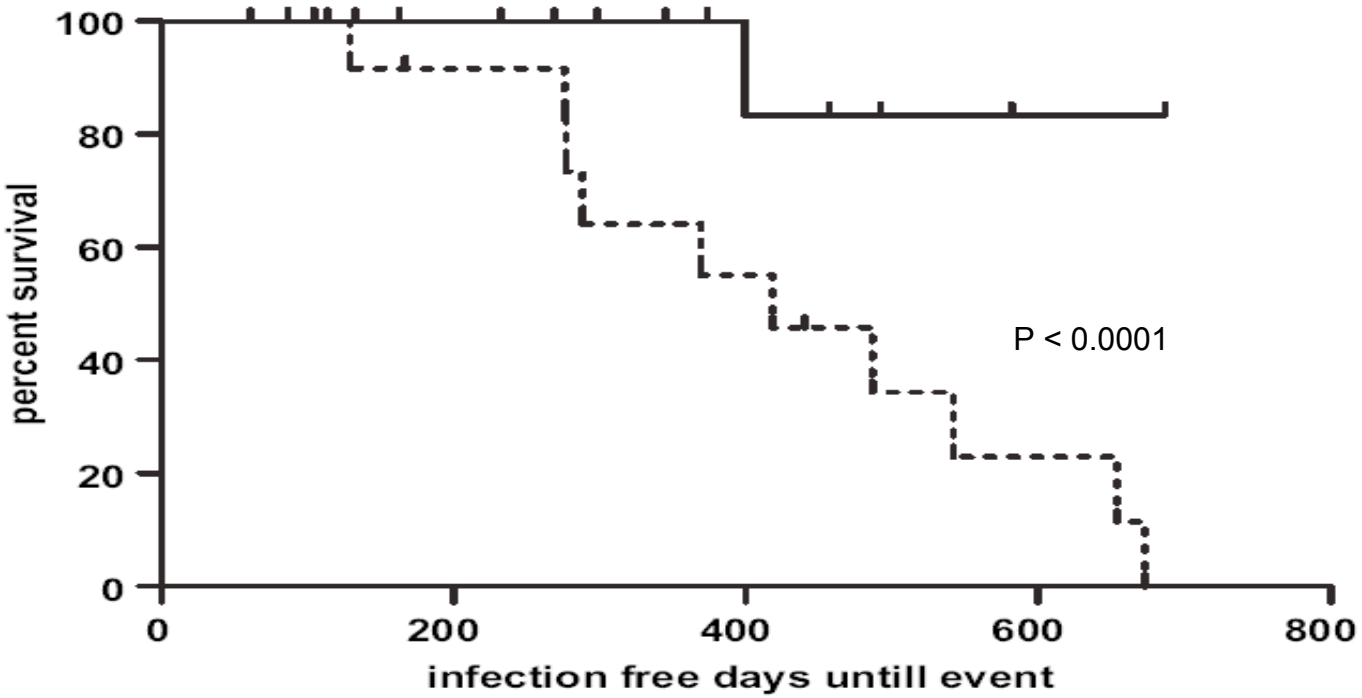

Fig. 2. Kaplan Meier survival curve presenting number of infection-free days until event with taurolidin catheter lock (continuous line) versus heparin catheter lock (interrupted line).

Etude randomisée en double aveugle en cours. PHRC National

Infections liées à la V.V.C
Les questions en suspens

- Staph doré ⇒ intérêt de l'écho cardiaque systématique ?
- Staph coag négatif ⇒ peut-on ne pas traiter si réponse immédiate à l'ablation de la V.V.C. chez un sujet sans facteurs de risque ?
- Verrou AB : intérêt réel et durée optimale en association avec l'antibiothérapie systémique ?
- Quelle est la meilleure stratégie chez les malades avec Hémoc centrale positive et Hémoc périphérique négative ?
- Durée optimale du traitement AB si la V.V.C est retirée ?
- Intérêt des hémocultures de contrôle systématiques à la fin du ttt AB systémique ?

IDSA Guidelines. Clinical infectious diseases 2009