Diplôme d'Université d'Antibiothérapie et Chimiothérapie Anti-Infectieuse

Infections Intra-abdominales (IIA) liées aux soins

Pr. Eric Kipnis

Réanimation Chirurgicale | Anesthésie-Réanimation et Médecine Péri-Opératoire | CHU Lille

Opportunistic Infection, Immunity, Environment & Lung Diseases (OpInfIELD) | Univ. Lille - CNRS - Inserm - IPL - CIIL

Opportunistic Infection
Immunity
Environment
& Lung Diseases

Déclaration d’intérêts

- Expertise : MSD, Shionogi, Astra-Zeneca
- Interventions : Pfizer, MSD, Shionogi, LFB, Getinge
- Congrès : LFB, Pfizer, MSD, Shionogi, Octapharma

- https://www.transparence.sante.gouv.fr

Foyers – étiologies

Perforation de viscère creux
(ulcère, cancer, occlusion, traumatisme, infl)

- Estomac
- Voies biliaires
- Côlon
- Grêle
- Diverticule
- Utérus ou trompes
- Vessie

Ischémies/nécroses
(translocation puis perforation)

- Cholécystite alithiasique
- Infarctus intestinal
- Occlusion
- Cancer du pancréas

Extension de foyers infectieux intra-abdominaux
(abcès, perforations)

- Appendicite compliquée
- Cholécystite compliquée
- Diverticulite compliquée
- Abcès hépatique compliqué
- Pancréatites aiguës/coulées/abcès
- Abcès renal/perirenal post PNA
- Fonte splénique purlente
- Salpingite compliquée

Post-opératoires

- Lâchage de (sutures, anastomoses, moignons)
- Contamination per-opératoire
- Translocation bactérienne

Classifications et terminologies…d'utilité variable et limitée

Mécanisme (classification d'Hambourg)

Primitives

- Infection du liquide d'ascite
- Infection de dialyse péritonéale

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Secondaires (à une cause)
- c.f étiologies

Tertiaires
- *secondaire compliquée*

Classifications et terminologies…d'utilité variable et limitée

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  - **post-opératoires**

Tertiaires
- *secondaire compliquée*
  - **post-opératoires**

Classifications et terminologies…d'utilité variable et limitée

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Secondaires (à une cause)
- c.f étiologies
  - **post-opératoires**

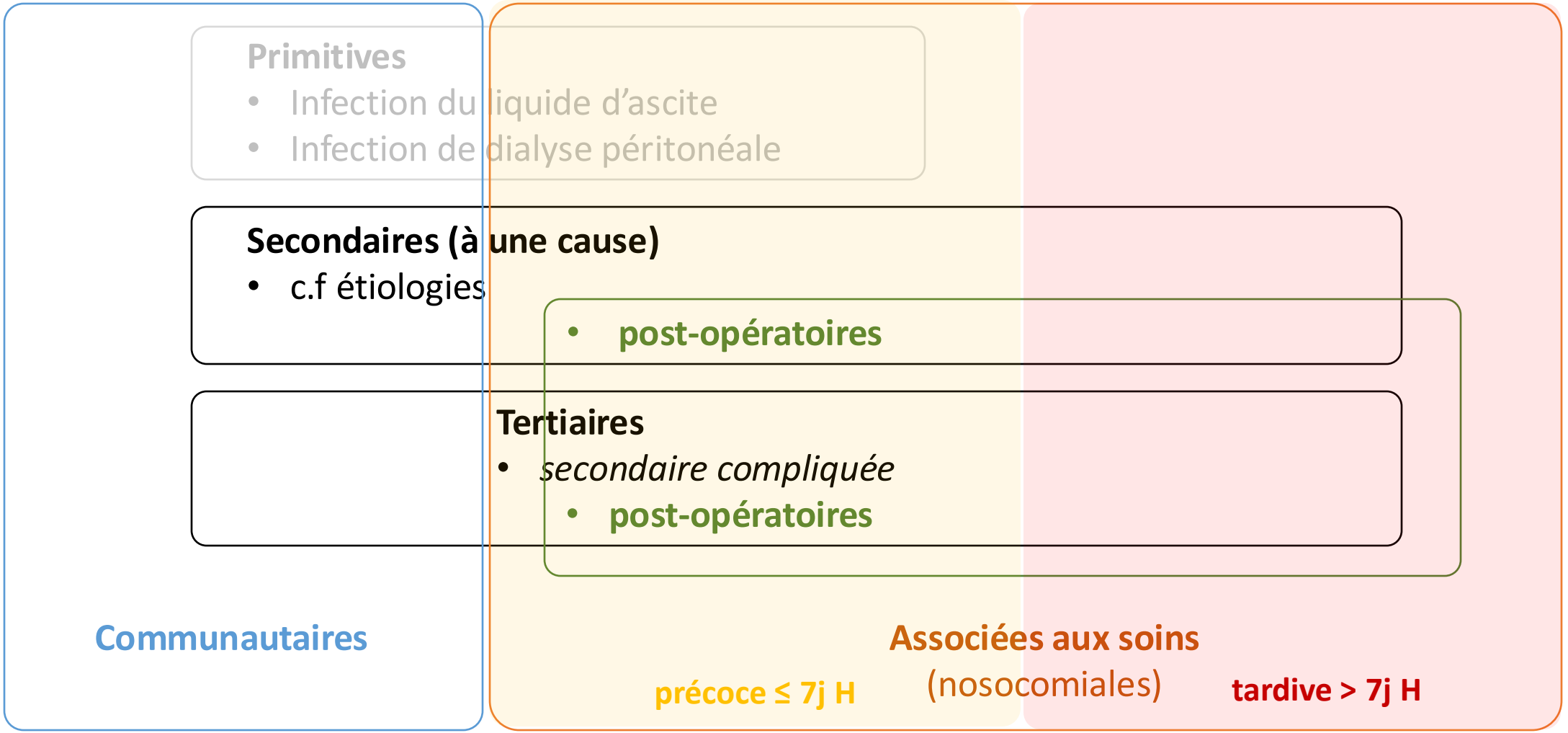
Tertiaires
- *secondaire compliquée*
  - **post-opératoires**

Communautaires

Associées aux soins
(nosocomiales)

Classifications et terminologies…d'utilité variable et limitée

Mécanisme (classification d'Hambourg)



AbSeS study (ESICM)

Intensive Care Med (2019) 45:1703–1717
https://doi.org/10.1007/s00134-019-05819-3

ORIGINAL

Epidemiology of intra-abdominal infection and sepsis in critically ill patients: "AbSeS", a multinational observational cohort study and ESICM Trials Group Project

Stijn Blot[1*], Massimo Antonelli[2,3], Kostoula Arvaniti[4], Koen Blot[1], Ben Creagh-Brown[5,6], Dylan de Lange[7], Jan De Waele[8], Mieke Deschepper[9], Yalim Dikmen[10], George Dimopoulos[11], Christian Eckmann[12], Guy Francois[13], Massimo Girardis[14], Despoina Koulenti[15,16], Sonia Labeau[1,17], Jeffrey Lipman[18,19], Fernando Lipovestky[20], Emilio Maseda[21], Philippe Montravers[22,23], Adam Mikstacki[24,25], José-Artur Paiva[26], Cecilia Pereyra[27], Jordi Rello[28], Jean-Francois Timsit[29,30], Dirk Vogelaers[31] and the Abdominal Sepsis Study (AbSeS) group on behalf of the Trials Group of the European Society of Intensive Care Medicine

AbSeS study (ESICM) et études ancillaires

Drugs (2021) 81:1065–1078
https://doi.org/10.1007/s40265-021-01534-w

REVIEW ARTICLE

Antimicrobial Lessons From a Large Observational Cohort on Intra-abdominal Infections in Intensive Care Units

Dirk Vogelaers[1,2] · Stijn Blot[1] · Andries Van den Berge[1] · Philippe Montravers[3] · for the Abdominal Sepsis Study ('AbSeS') Group on behalf of the Trials Group of the European Society of Intensive Care Medicine

Intensive Care Med (2022) 48:1593–1606
https://doi.org/10.1007/s00134-022-06883-y

ORIGINAL

Poor timing and failure of source control are risk factors for mortality in critically ill patients with secondary peritonitis

Gennaro De Pascale[1,2], Massimo Antonelli[1,2], Mieke Deschepper[3], Kostoula Arvaniti[4], Koen Blot[5,6], Ben Creagh Brown[7,8], Dylan de Lange[9], Jan De Waele[5,10], Yalim Dikmen[11], George Dimopoulos[12], Christian Eckmann[13], Guy Francois[14], Massimo Girardis[15], Despoina Koulenti[16,17], Sonia Labeau[5,18], Jeffrey Lipman[19,20], Fernando Lipovetsky[21], Emilio Maseda[22], Philippe Montravers[23,24], Adam Mikstacki[25,26], José-Artur Paiva[27], Cecilia Pereyra[28], Jordi Rello[20,29], Jean-Francois Timsit[30,31], Dirk Vogelaers[5,32] and Stijn Blot[5,16*] on behalf of the Abdominal Sepsis Study (AbSeS) group and the Trials Group of the European Society of Intensive Care Medicine

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journal homepage: www.elsevier.com/locate/ijantimicag

Epidemiology and age-related mortality in critically ill patients with intra-abdominal infection or sepsis: an international cohort study

Kostoula Arvaniti[a,†], George Dimopoulos[b,†], Massimo Antonelli[c,d], Koen Blot[e], Ben Creagh-Brown[f,g], Mieke Deschepper[h], Dylan de Lange[i], Jan De Waele[j], Yalim Dikmen[k], Christian Eckmann[l], Sharon Einav[m,n], Guy Francois[o], Hans Fjeldsoee-Nielsen[p], Massimo Girardis[q], Bojan Jovanovic[r], Matthias Lindner[s], Despoina Koulenti[t,u], Sonia Labeau[v,w], Jeffrey Lipman[x,y], Fernando Lipovestky[z], Luis Daniel Umezawa Makikado[aa], Emilio Maseda[bb], Adam Mikstacki[cc,dd], Philippe Montravers[ee,ff], José Artur Paiva[gg], Cecilia Pereyra[hh], Jordi Rello[ii], Jean-Francois Timsit[jj,kk], Dana Tomescu[ll,mm], Dirk Vogelaers[nn,oo], Stijn Blot[oo,*], The Abdominal Sepsis Study (AbSeS) Group on behalf of the Trials Group of the European Society of Intensive Care Medicine[‡]

Epidémio - étude AbSeS

Epidémio **prospective mondiale**
Multicentrique **309 réanimations**
2621 patients admis pour ou se compliquant d'IIA

Type of abdominal sepsis	Total *n* (%)*	Community-acquired *n* (%)**	Early onset hospital-acquired *n* (%)**	Late-onset hospital-acquired *n* (%)**
Primary peritonitis	103 (3.9)	33 (32)	28 (27.2)	42 (40.8)
Secondary and tertiary peritonitis	1794 (68.4)	588 (32.8)	431 (24)	775 (43.2)
PD-related peritonitis	9 (0.3)	0	2 (20)	7 (70)
Intra-abdominal abscess	180 (6.9)	36 (20)	49 (27.2)	95 (52.8)
Biliary tract infection	319 (12.2)	117 (36.7)	95 (29.8)	107 (33.5)
Pancreatic infection	165 (6.3)	45 (27.3)	33 (20)	87 (52.7)
Typhlitis	9 (0.3)	0	3 (33.3)	6 (66.6)
Toxic megacolon	42 (1.6)	9 (21.4)	15 (35.7)	18 (42.9)

IIA "secondaires" (puis tertiaires) >> biliaires > abcès ou complications infectieuses de PA

associées aux soins (précoces + tardives) > communautaires

Blot Intens Care Med 2019

Epidémio - étude AbSeS

Epidémio prospective mondiale
Multicentrique 309 réanimations
2621 patients admis pour ou se compliquant d'IIA

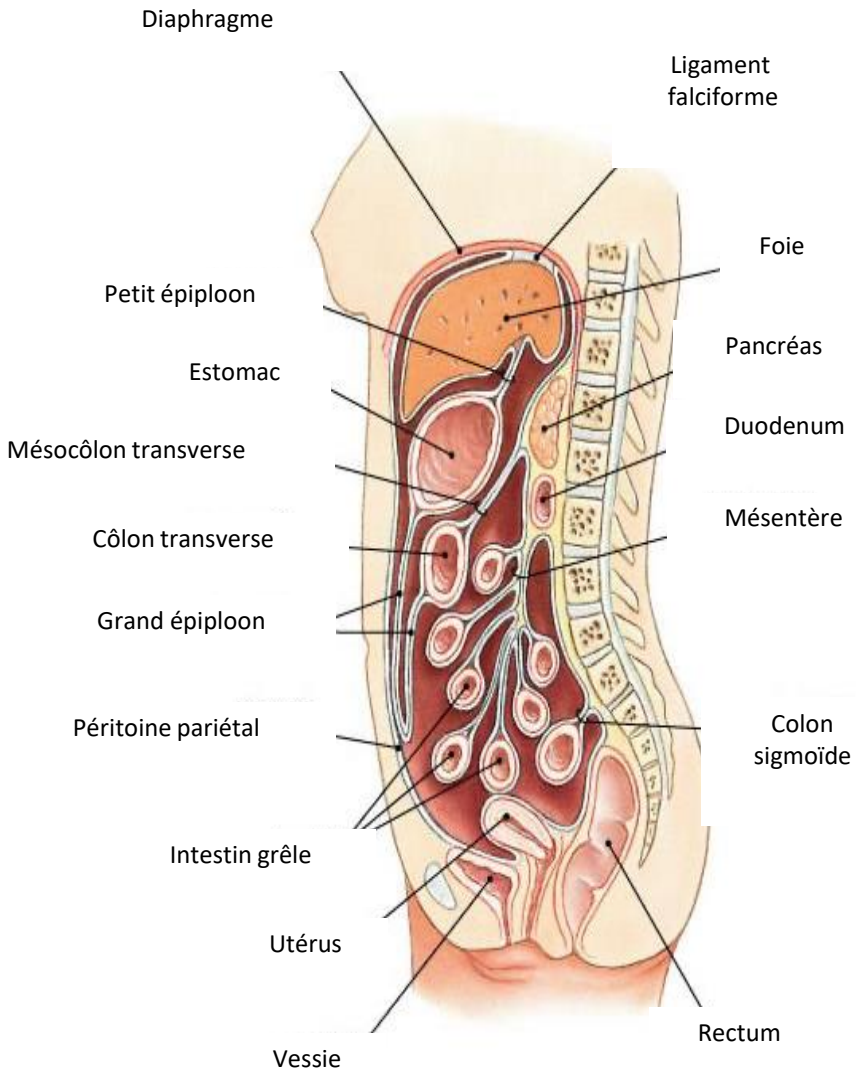
Characteristic	Total cohort ($n = 2621$)	Community-acquired ($n = 828$)	Early onset hospital-acquired ($n = 656$)	Late-onset hospital-acquired ($n = 1137$)	p*
Severity of disease expression					
Infection without sepsis	164 (6.3)	51 (6.2)	42 (6.4)	71 (6.2)	0.981
Sepsis	1590 (60.7)	528 (63.8)	399 (60.8)	663 (58.3)	0.050
Septic shock	867 (33.1)	249 (30.1)	215 (32.8)	403 (35.4)	0.043
Anatomical disruption					
Not present	615 (23.5)	186 (22.5)	166 (25.3)	263 (23.1)	0.413
Yes, with localized peritonitis	981 (37.4)	342 (41.3)	256 (39.0)	383 (33.7)	0.002
Yes, with diffuse peritonitis	1025 (39.1)	300 (36.2)	234 (35.7)	491 (43.2)	0.001

93% graves (sepsis ou choc septique) et <u>associées aux soins (un peu) plus graves</u>

76% avec effraction et pértionite / <u>plus d'effractions et de péritonites diffuses lorsqu'associées aux soins</u>

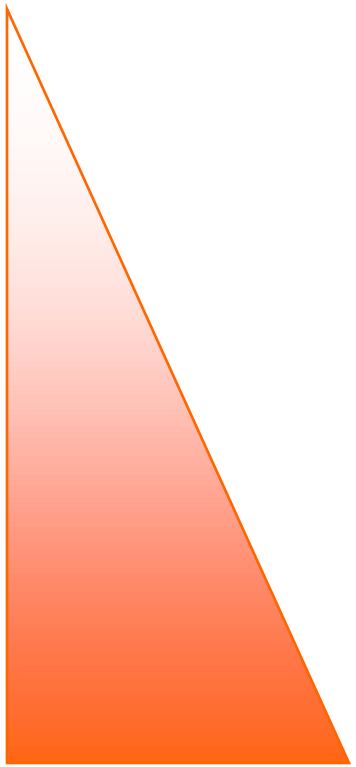
Blot Intens Care Med 2019

Inoculum et écologie selon l'anatomie

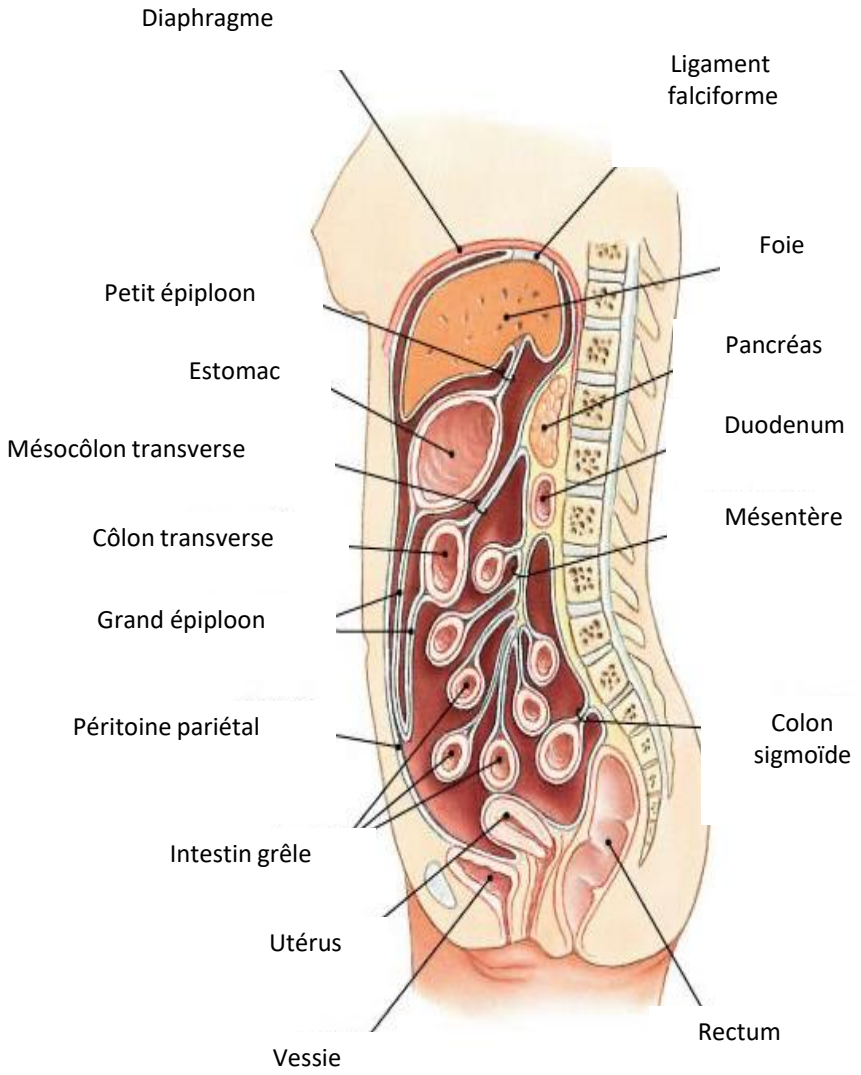


Inoculum et écologie selon l'anatomie

10^2 bactéries/g matières
(anaerobies=10 x aerobies)



10^{14} bactéries/g matières
(**anaerobies**=1000 x aerobies)



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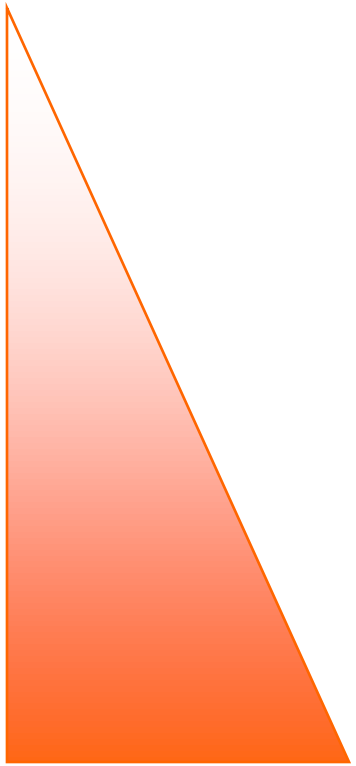

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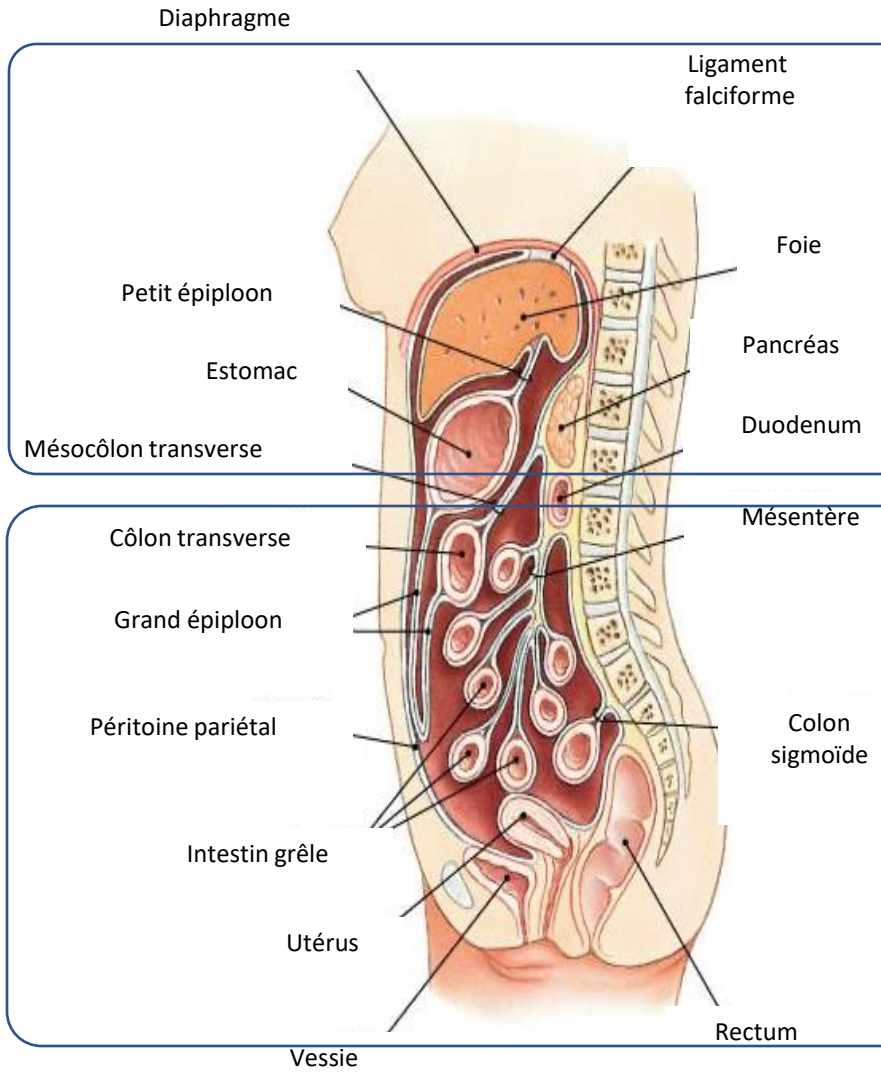

Sus-mésocoliques
- Oesophage
- Gastriques
- Duodénales
- Biliaires

Sous-mésocoliques
- Grêle
- Côlon
- Appendice
- Rectum

Inoculum et écologie selon l'anatomie

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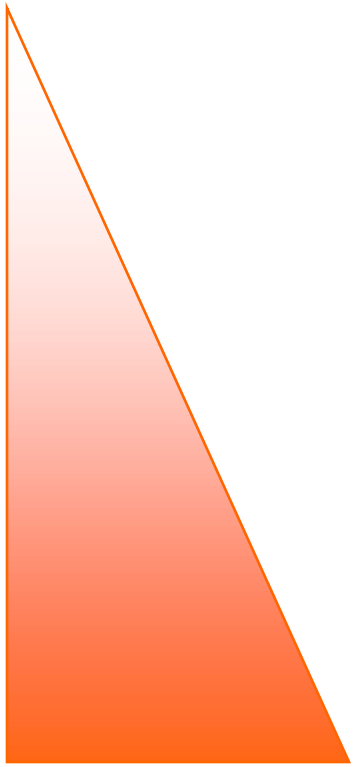

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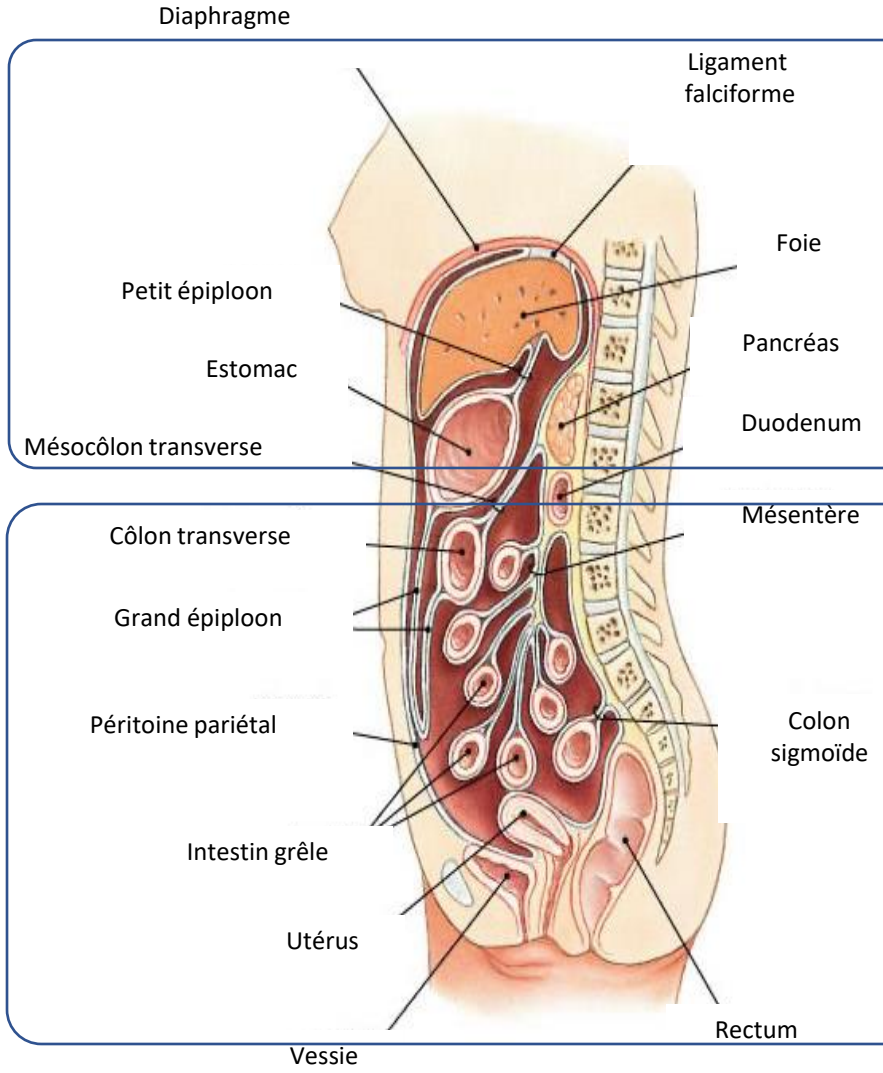

Sus-mésocoliques
- Oesophage
- Gastriques
- Duodénales
- Biliaires

E. Coli
lactobacilles
streptocoques

streptocoques
levures

Sous-mésocoliques
- Grêle
- Côlon
- Appendice
- Rectum

Bactéroïdes
E. Coli
entérobactéries
streptocoques
entérocoques

Inoculum et écologie selon facteurs modificateurs de flore

↗ incoculum
pullulation bactérienne

10^{14} bactéries/g matières
(**anaerobies**=1000 x aerobies)

Modifications

Anti-acides/IPP

Hémorragie digestive

Stase

Iléus

Occlusion

Chirurgie

Flore “colique”

Bactéroïdes
E. Coli

entérobactéries
streptocoques
entérocoques

streptocoques
levures

Messages préalables

1. Anaerobies de culture (très) difficile MAIS TOUJOURS présents

   ⟶ ***<u>anaerobies</u> obligatoirement dans le spectre ATB probabiliste même si plvts négatifs***

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2. Ecologie (hors anaerobie) ± selon site MAIS déviation fréquente vers flore sous-mésocolique

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   ⟶ ***<u>entérobactéries</u> obligatoirement dans le spectre ATB probabiliste***

3. Inoculum énorme ne sera pas “décapité” par 1è dose d’ATB

   ⟶ ***<u>ATB urgente pré-op avant prélèvements</u> intra-abdo***

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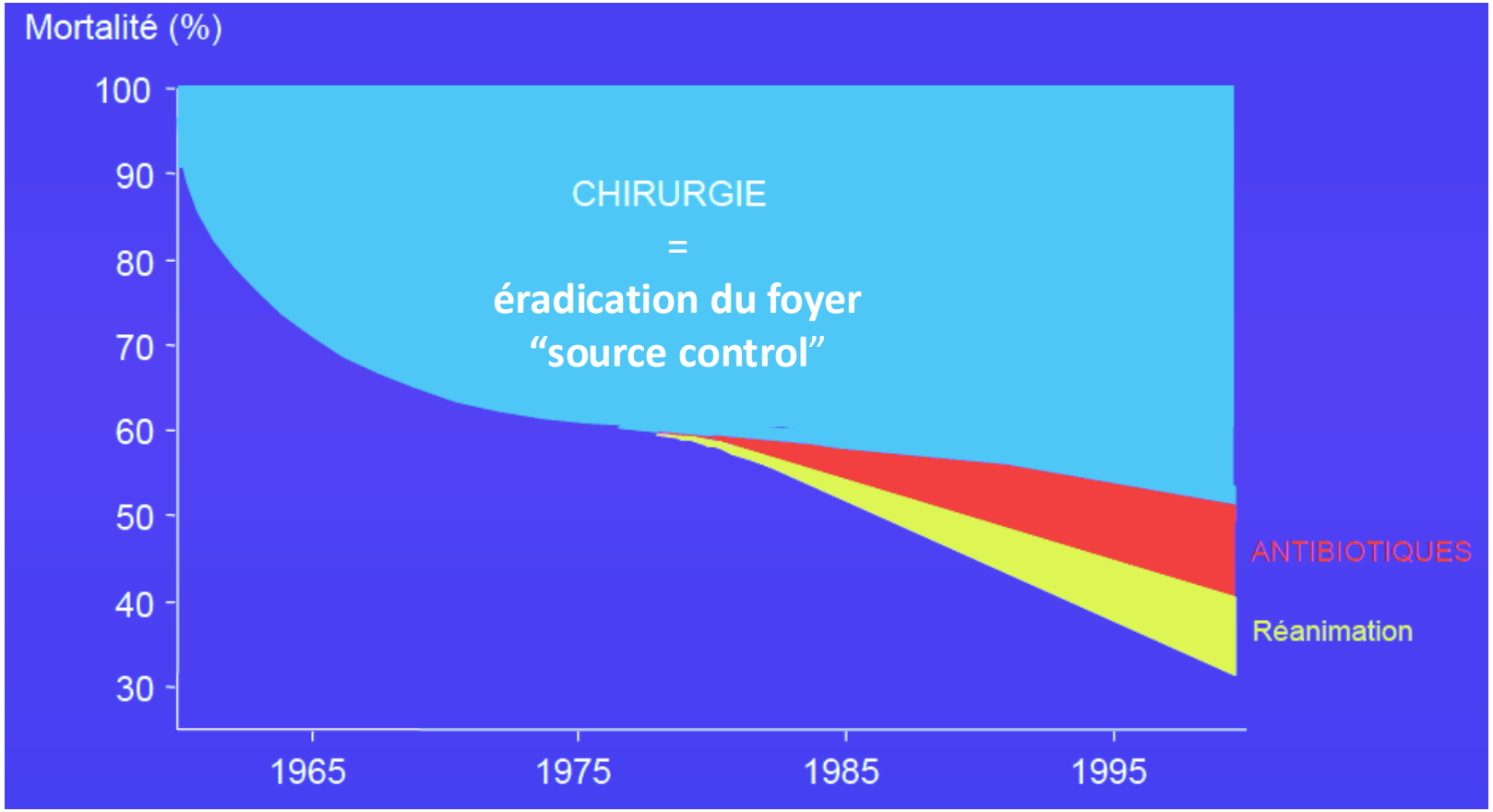
   ⟶ ***<u>ATB urgente pré-op avant prélèvements</u> intra-abdo***

4. Inoculum énorme…donc éradication microbiologique par ATB seuls IMPOSSIBLE

   ⟶ ***<u>éradication du foyer impérative</u>***

Eradication du foyer

Eradication du foyer (“source control”) = chirurgie (ou drainage)



La plus grande part du pronostic = éradication du foyer

Montravers d’après Wittmann 1991 in Intra-abdominal Infections

Eradication

Etapes	But(s)	Moyen(s)
Evaluation pré-op	Gravité	Critères réa
Réanimation pré-op	**Limitation** du sepsis	**ATB probabiliste**
	Stabilisation **pour chirurgie**	Hémodynamique
Eradication du foyer		
1	**Prévention ISO**	Champs, **ATB probabiliste**
	Diagnostic microbiologique	**Plvts péritonéaux per-op**
	Diminution de l'inoculum	**Lavage péritonéal**
	Identification foyer	**Identification cause chirurgicale**
2	**Eradication du foyer**	**Fermeture perforation**
		Résections/anastomose(s)
		Stomie(s)
		Re-lavage péritonéal
3	**Fermeture paroi**	**en 1 temps ou différée**
4	**Inoculum résiduel**	**ATB probabiliste puis adaptée**
Réanimation post-op	amélioration pronostic	pricipes de la SSC

Nombreuses étapes de l'éradication du foyer; toutes critiques

d'après Montravers Intens Care Med 2016

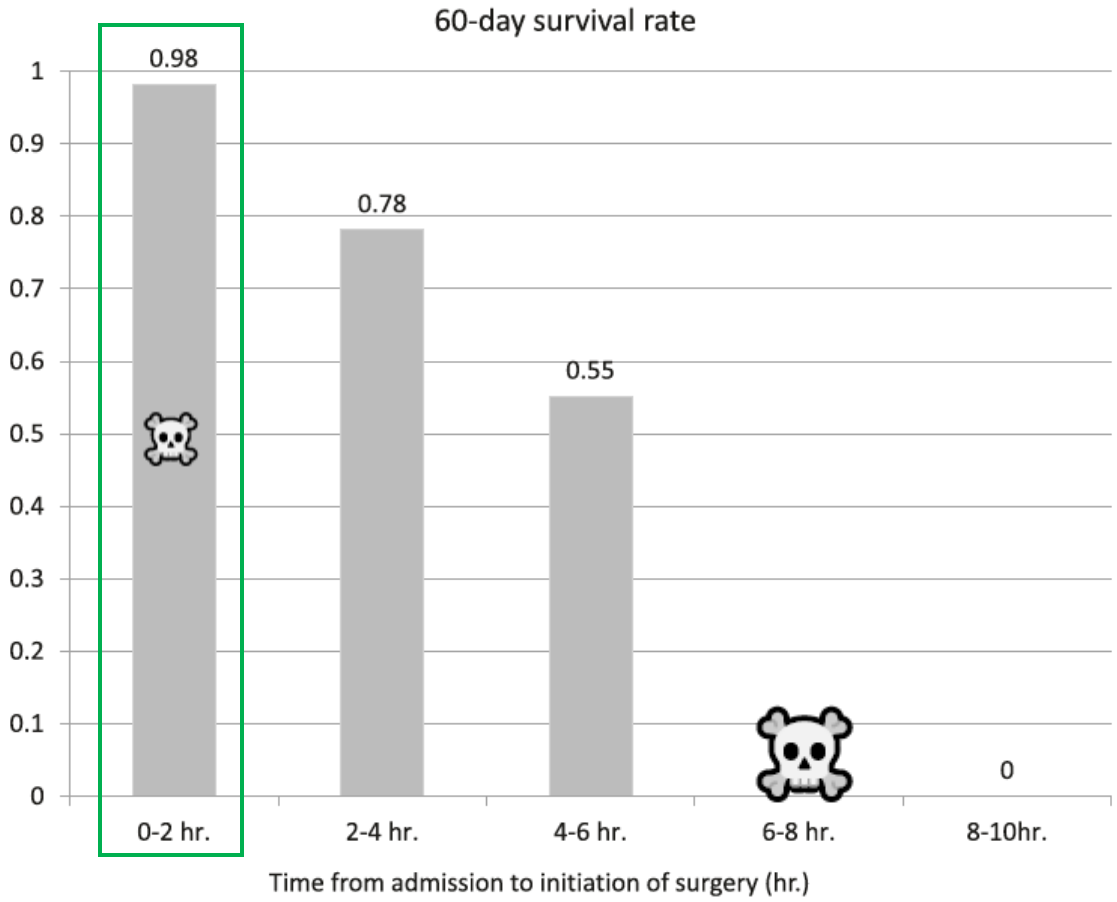
Eradication // antibiothérapie

Foyers	ODDS RATIOS de sur-mortalité		reference
	Eradication foyer (réalisation et/ou délai)	**Antibiothérapie** (adéquation et/ou délai)	
Eradicables (85% IIA)	**2,37**	NS	*Bloos Crit Care 2014*
Angiocholites	**3,4**	1,12	*Karvellas Alim Pharm Ther 2016*
IIA bactériémiques	**7,46**	NS	*Tellor Surg Infect 2015*

La plus grande partdu pronostic, voire LE pronostic = éradication du foyer

Délai d'éradication du foyer

156 **péritonites**
par perforation
en **choc septique**
dans le cadre d'un protocole d'EGDT



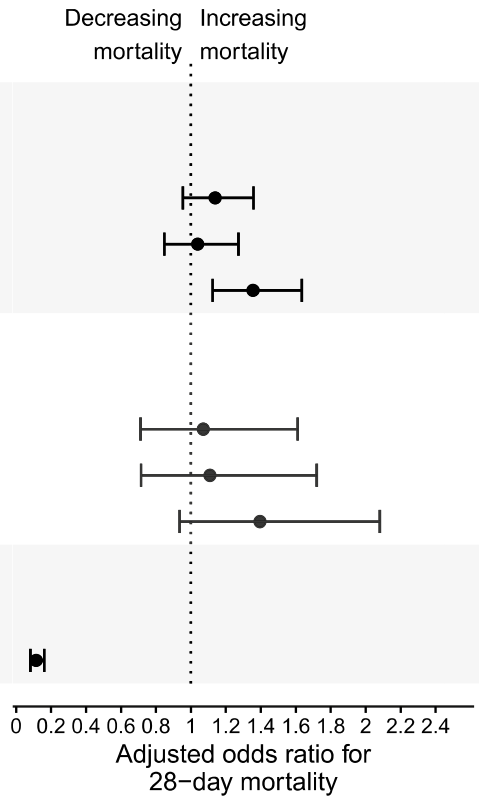
pronostic = délai rapide *(OR = 0.29; 95% CI, 0.16-0.47; P <0.0001)*

Azuhata Crit Care 2014

Succès de l'éradication du foyer

Analyse post-hoc RCT multicentrique sepsis en réa Allemagne
délais ttt :
4792 patients sepsis ATB dont 1595 patients avec eradication foyer chir

Predictor	No. of patients	Observed mortality	Risk−adjusted mortality	OR (95% CI)	P−value
Timing of antimicrobial therapy	4659/4792				0.008*
0−1 hr		364/1270 (28.7)	25.3 (22, 28.9)	1	
1−3 hrs		418/1352 (30.9)	27.8 (24.4, 31.6)	1.14 (0.95, 1.36)	0.149
3−6 hrs		255/836 (30.5)	26 (22.3, 30.2)	1.04 (0.85, 1.27)	0.715
>6 hrs		437/1201 (36.4)	31.5 (27.5, 35.7)	1.36 (1.12, 1.63)	0.001
Timing of surgical source control	1563/1595				0.22*
0−1 hr		92/327 (28.1)	25.1 (19.1, 32.3)	1	
1−3 hrs		85/287 (29.6)	26.4 (20.8, 32.9)	1.07 (0.71, 1.61)	0.743
3−6 hrs		93/293 (31.7)	27.1 (21.3, 33.8)	1.11 (0.71, 1.72)	0.646
>6 hrs		240/656 (36.6)	31.9 (26.7, 37.5)	1.4 (0.94, 2.08)	0.102
Success of source control	1563/1595				
Not successful		179/262 (68.3)	68.7 (60.7, 75.7)	1	
Successful		331/1301 (25.4)	20.2 (16.5, 24.5)	0.12 (0.08, 0.16)	<=0.001



<u>succès de l'éradication</u> …plus que le délai

Rüddel Critical Care 2022

Succès de l'éradication du foyer - étude AbSeS

Echec = inflammation persistante j7 et/ou réintervention dans les 7j
Succès = absence d'échec

	Community-acquired infection		Early-onset hospital-acquired		Late-onset hospital-acquired	
	Localized peritonitis (%)	Diffuse peritonitis (%)	Localized peritonitis (%)	Diffuse peritonitis (%)	Localized peritonitis (%)	Diffuse peritonitis (%)
Septic shock						
Successful source control	5/28 (17.9)	10/26 (38.5)[b]	3/22 (13.6)[b]	7/22 (31.8)[b]	10/28 (35.7)	13/52 (25.0)
Failure of source control[a]	10/18 (55.6)	11/28 (39.3)[b]	4/13 (30.8)[b]	11/18 (61.1)[b]	12/16 (75.0)	32/45 (71.1)
Sepsis						
Successful source control	12/98 (12.2)	9/58 (15.5)[b]	3/57 (5.3)	4/38 (10.5)	10/72 (13.9)	25/94 (26.6)
Failure of source control[a]	16/44 (36.4)	14/45 (31.1)[b]	14/39 (35.9)	17/35 (48.6)	26/51 (51.0)	30/55 (54.5)

gradients de surmortalité signifcatifs <u>surtout si échec d'éradication</u>

selon gravité
selon péritonite diffuse
*selon **nosocomial et tardif***

Vogelaers Drugs 2021

Succès de l'éradication du foyer - étude AbSeS

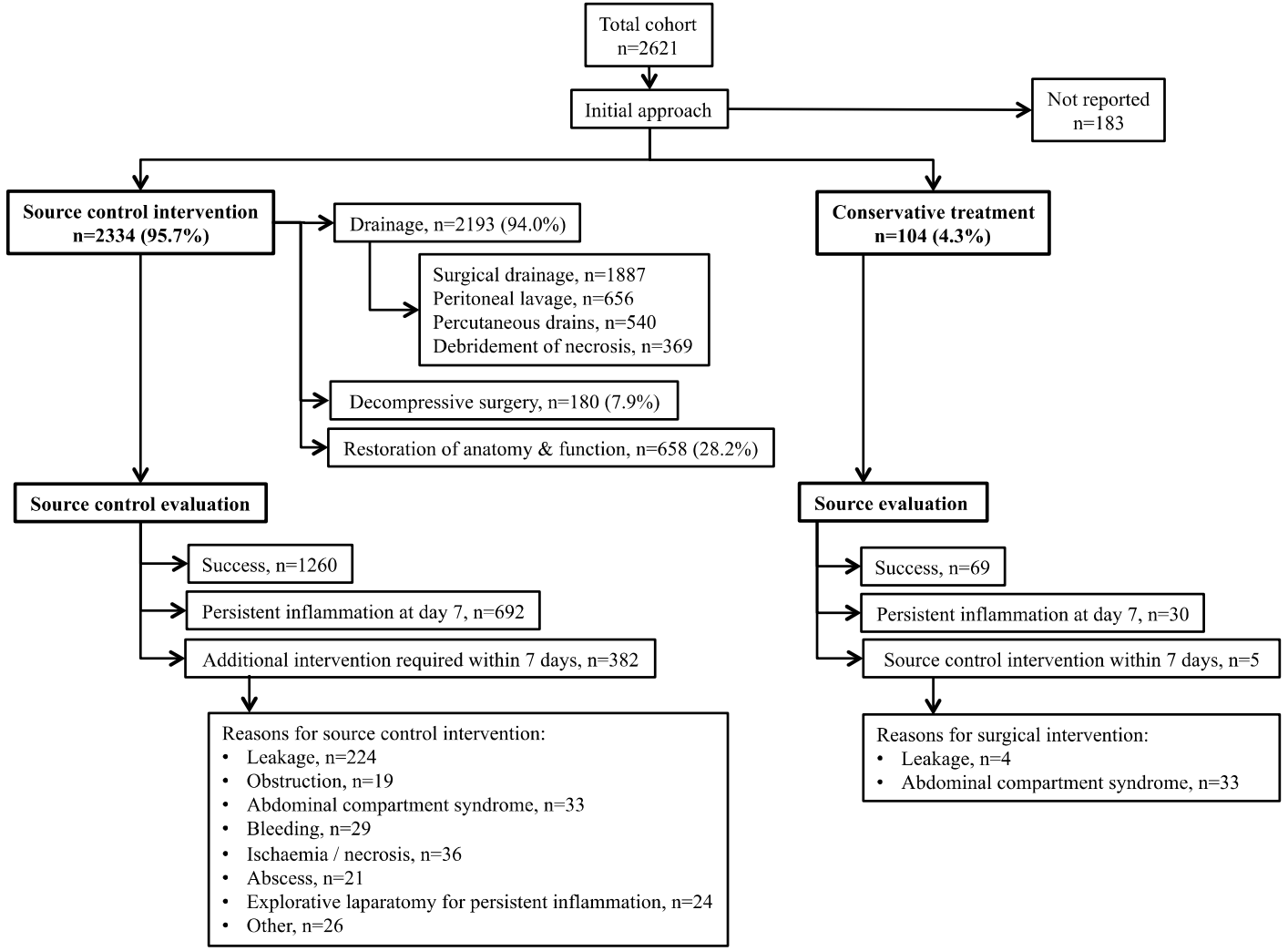
95% d'interventions d'éradication

Succès ***54%***

Echecs

persistance inflammation j7 ***29%***

réintervention dans les 7j ***16%***



Blot Intens Care Med 2019

Succès de l’éradication du foyer - étude AbSeS

Multivariée FdR décès

Source control achievement at day 7	
Success	Reference
Failure, persistent signs of inflammation	4.85 (3.79–6.22)
Failure, additional intervention required following initial approach	1.93 (1.41–2.65)

LE principal déterminant de la mortalité est <u>l’échec d’éradication du foyer (j7)</u>

Blot Intens Care Med 2019

Facteurs de mortalité (*si foyer éradiqué !*) – étude AbSeS

Variable	Model with source control achievement* OR (95% CI)

Donnés chez les patients ayant eu une éradicaiton du foyer avec succès

Blot Intens Care Med 2019

Facteurs de mortalité (*si foyer éradiqué !*) – étude AbSeS

Variable	Model with source control achievement* OR (95% CI)
Setting of infection acquisition	
Community-acquired infection	Reference
Early onset hospital-acquired infection (≤ 7 days)	1.15 (0.84–1.58)
Late-onset hospital-acquired infection (> 7 days)	1.76 (1.34–2.32)
Anatomical disruption	
No anatomical barrier disruption	Reference
Anatomical disruption with localized peritonitis	1.28 (0.95–1.75)
Anatomical disruption with diffuse peritonitis	1.99 (1.49–2.67)
Severity of disease expression	
Infection	Reference
Sepsis	2.44 (1.37–4.66)
Septic shock	5.22 (2.91–10)

nosocomial précoce

nosocomial tardif

effraction péritonite diffuse

gravité

Blot Intens Care Med 2019

Facteurs de mortalité chez patients immunodéprimés (AbSes)

Etude Post-hoc de l'étude AbSes
n = 239 (9.2%)

Variable	Odds ratio (95 % confidence interval)	p-value
Severity of disease expression at time of diagnosis		
Infection	Reference category	–
Sepsis	4.15 (0.80 – 34.67)	0.127
Septic shock	6.64 (1.27 – 55.72)	0.043
Length of ICU stay per 7 days increase		
1–7 days	Reference category	–
8–14 days	0.75 (0.29 – 1.91)	0.548
15–21 days	3.61 (1.16 – 11.53)	0.026
22–28 days	2.17 (0.43 – 10.62)	0.336
>28 days	1.03 (0.35 – 2.95)	0.960
Source control achievement at day 7		
Successful	Reference category	–
Failure, persistent sigs of inflammation	5.48 (2.29 – 12.57)	<0.001
Failure, need for additional intervention	1.66 (0.52 – 4.93)	0.367

Source control interventions in the immunocompromised population.

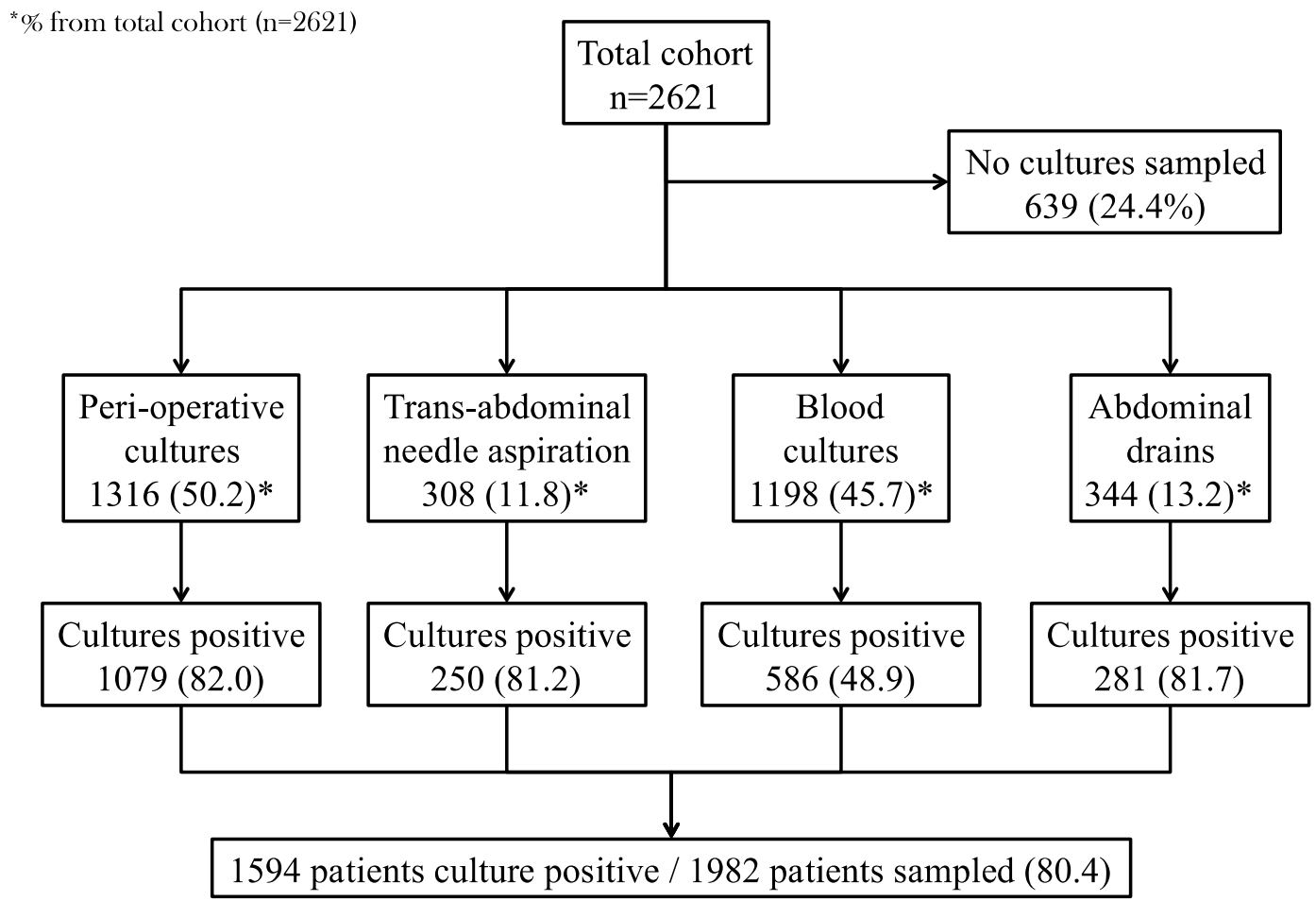
Type of intervention	N (%)
Any type of source control	214*/228** (93.9)
Drainage	201/228 (88.2)
Surgical drainage	175/201 (87.1)
Laparascopic drainage	7/201 (3.5)
Peritoneal lavage	57/201 (28.4)
Percutaneous drains	49/201 (24.4)
Debridement of necrosis	28/201 (13.9)
Decompressive surgery	17/228 (7.5)
Restoration of anatomy	49/228 (21.5)

FdR mortalité : choc septique et l'échec d'éradication du foyer (j7) sur le mode persistance de l'inflammation

Paiva Eur J Int Med 2024

Microbiologie

Rentabilité des prélèvements – étude AbSeS



80 % information microbiologique

Blot Intens Care Med 2019

Ecologie – étude AbSeS

BGN **(60%)**
- ***E. coli*** **(35%)**
- **Klebielles** **(15%)**

Non-fermentants (12%)
- *P. aeruginosa* (6%)
- *A. baumanii* (6%)

Entérococques **(25%)**
- *E. faecalis* (13%)
- *E. faecium* (12%)

Anaerobies **(12%)**
- *Bacteroides* (5%)

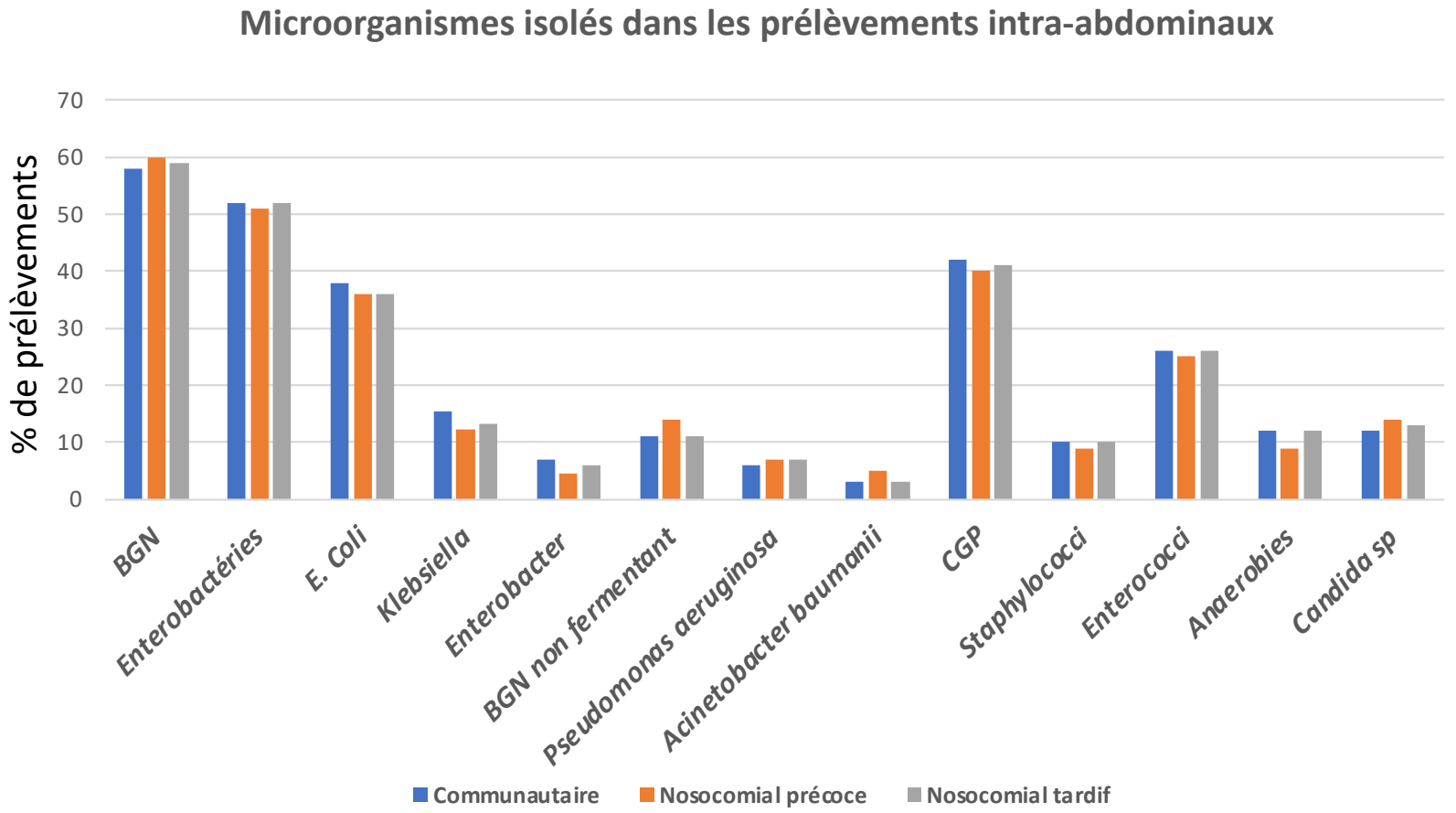
Fongique **(13%)**
- *Candida* (9%)

Micro-organism	Total cohort (*n* = 1982)	Setting of infection acquisition		
		Community-acquired (*n* = 664)	Early onset hospital-acquired (*n* = 482)	Late-onset hospital-acquired (*n* = 836)
Gram-negative bacteria	1161 (58.6)	385 (58)	287 (59.5)	498 (58.5)
Enterobacterales	1024 (51.7)	344 (51.8)	247 (51.2)	433 (51.8)
Escherichia coli	729 (36.8)	252 (38)	172 (35.7)	304 (36.4)
Klebsiella sp.	51 (2.6)	22 (3.3)	12 (2.5)	17 (2)
*Klebsiella oxytoca**	44 (2.2)	23 (3.5)	11 (2.3)	10 (1.2)
Klebsiella pneumoniae	170 (8.6)	57 (8.6)	37 (7.7)	76 (9.1)
Non-fermenting bacteria	233 (11.8)	72 (10.8)	66 (13.7)	95 (11.4)
Pseudomonas aeruginosa	131 (6.6)	41 (6.2)	34 (7.1)	56 (6.7)
Acinetobacter baumannii	61 (6.2)	18 (2.7)	22 (4.6)	21 (2.5)
Enterococci	513 (25.9)	173 (26.1)	121 (25.1)	219 (26.2)
Enterococcus faecalis	257 (13)	83 (12.5)	59 (12.2)	115 (13.8)
Enterococcus faecium	216 (10.9)	70 (10.5)	46 (9.5)	100 (12)
Anaerobe bacteria	231 (11.7)	83 (12.5)	45 (9.3)	103 (12.3)
*Bacteroides sp.**	103 (5.2)	46 (6.9)	17 (3.5)	40 (4.8)
Fungi	258 (13)	80 (12)	71 (14.7)	107 (12.8)
Aspergillus sp.	3 (0.2)	0	2 (0.4)	1 (0.1)
Candida sp.	257 (13)	81 (12.2)	69 (14.3)	107 (12.8)
Candida albicans	173 (8.7)	56 (8.4)	50 (10.4)	67 (8)

Blot Intens Care Med 2019

Ecologie – étude AbSeS

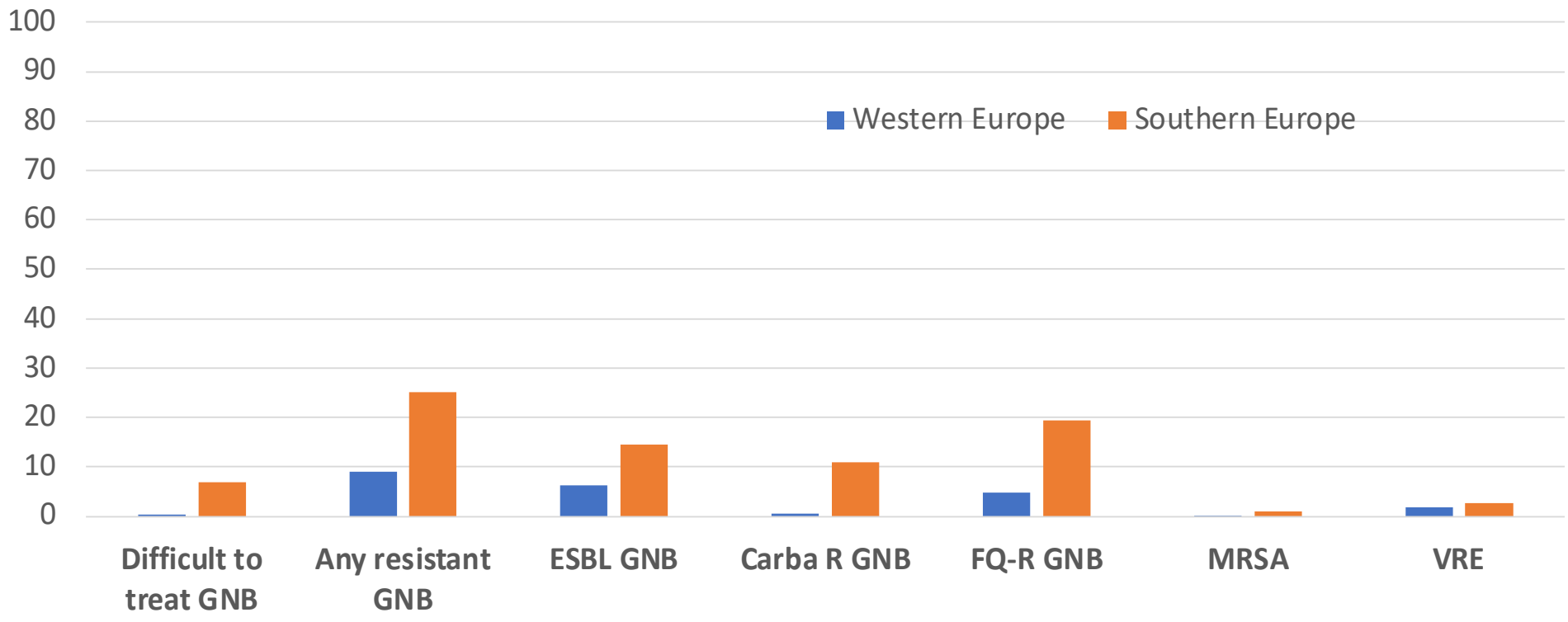
BGN	**(60%)**
E. coli	**(35%)**
Klebielles	**(15%)**
Non-fermentants	(12%)
P. aeruginosa	(6%)
A. baumanii	(6%)
Entérococques	**(25%)**
E. faecalis	(13%)
E. faecium	(12%)
Anaerobies	(12%)
Bacteroides	(5%)
Fongique	(13%)
Candida	(9%)



PAS de différences marquées d'espèces entre communautaire et nosocomial précoce ou tardif !

Blot Intens Care Med 2019

Résistances – étude AbSeS



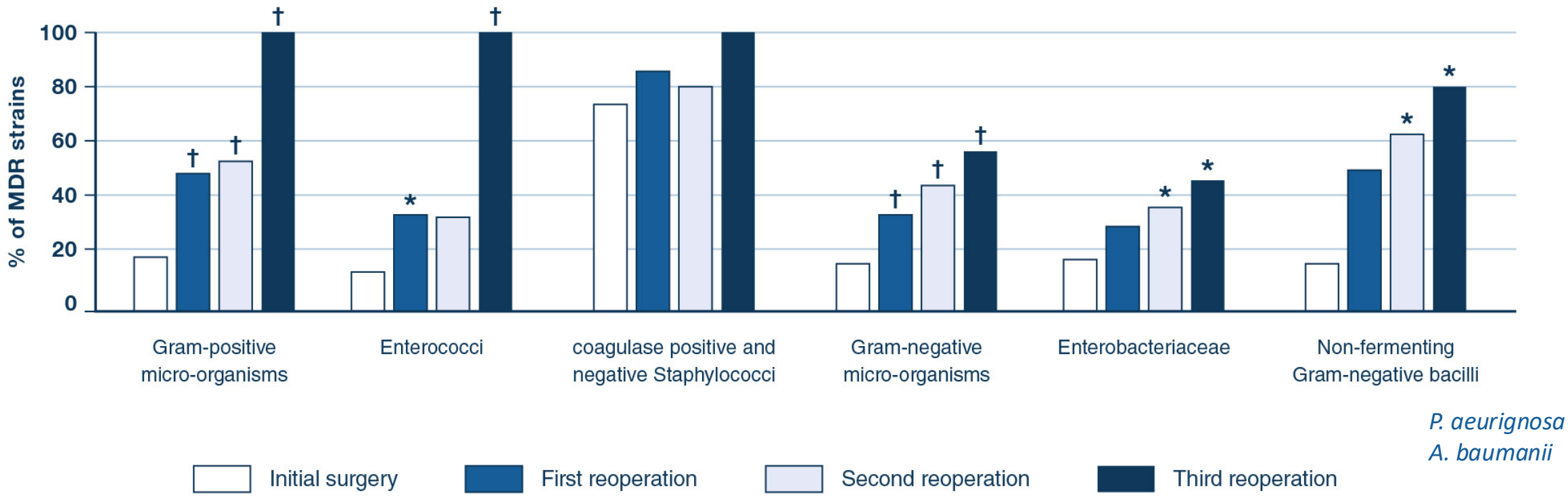
<u>Faibles incidences de résistances problématiques</u> ("difficut to treat", BLSE, EPC…)

Différences surtout géographiques Europe ouest / sud (et est et centrale) – PAS entre communautaire/noso (NS)

Vogelaers Drugs 2021

Remarque sur la multirésistance = IIA *tertiaires*

monocentrique, n = 122



P. aeurignosa
A. baumanii

non-éradication du foyer favorise péritonites tertiaires et sélection de résistances

d'après Montravers Crit Care 2015

Résistances et pronostic – étude AbSeS

Multivarié avec succès d'éradication du foyer

Variable	Model with source control achievement* OR (95% CI)
Empiric antimicrobial coverage	
Anti-MRSA agent	0.77 (0.59–1)
Double anaerobe coverage	–
Antibiotic resistance involvement *	1.49 (1.07 – 2.05)

**BGN BLSE ou BGN productrice de carbapénémase(s) ou ERV ou SARM*

Blot Intens Care Med 2019

Traitement antibiotique approprié – étude AbSeS

	Community-acquired infection		Early-onset hospital-acquired		Late-onset hospital-acquired	
	Localized peritonitis (%)	Diffuse peritonitis (%)	Localized peritonitis (%)	Diffuse peritonitis (%)	Localized peritonitis (%)	Diffuse peritonitis (%)
Septic shock						
Appropriate empiric antimicrobial therapy	8/30 (26.7)	9/31 (29.0)	4/24 (16.7)	12/30 (40.0)	15/31 (48.4)	32/65 (49.2)
Inappropriate empiric antimicrobial therapy	7/16 (43.8)	12/23 (52.2)	3/11 (27.3)	6/10 (60.0)	7/13 (53.8)	13/32 (40.6)
Sepsis						
Appropriate empiric antimicrobial therapy	20/93 (21.5)	12/66 (18.2)	8/55 (14.5)	11/45 (24.4)	22/80 (27.5)	35/99 (35.4)
Inappropriate empiric antimicrobial therapy	8/49 (16.3)	11/37 (29.7)	9/41 (22.0)	10/28 (35.7)	14/43 (32.6)	20/50 (40.0)

globalement 64.8% de traitement approprié

gain global de survie de 6% MAIS NS (manque de puissance)

gain de survie si approprié ***plus marqué si choc septique*** *et* ***s'atténuant pour les nosocomiales tardives***

Vogelaers Drugs 2021

Couvrir les entérococques ? – etude AbSeS

Multivarié avec succès d'éradication du foyer

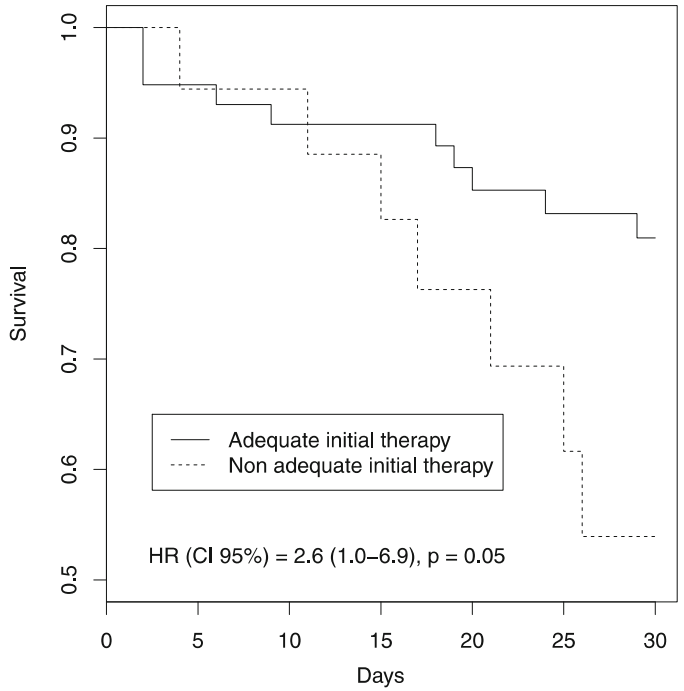
Variable	Model with source control achievement* OR (95% CI)
Empiric antimicrobial coverage	
Anti-MRSA agent	0.77 (0.59–1)
Double anaerobe coverage	–
Antibiotic resistance involvement	1.49 (1.07 – 2.05)

l'isolement d'entérococques ne sortant pas / anti-SARM = vancomycine ou linézolid = anti- E. faecium

Blot Intens Care Med 2019

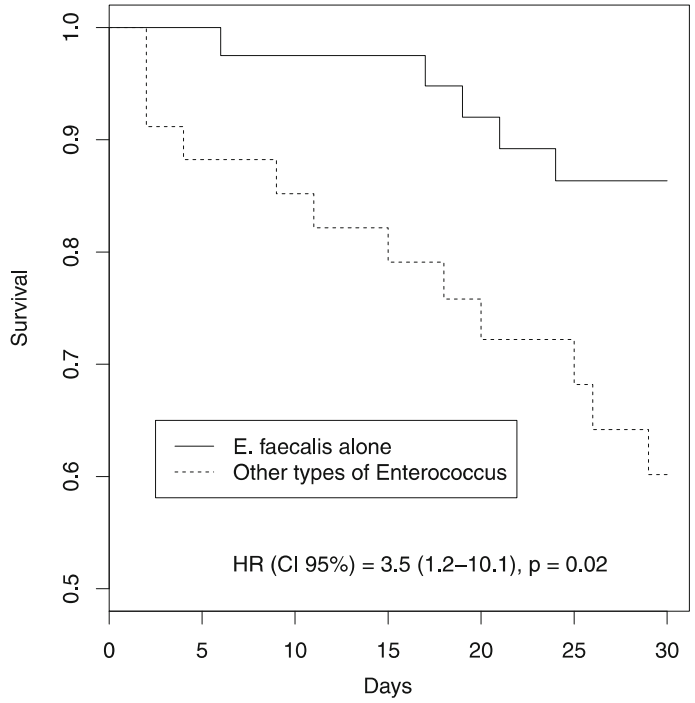
Couvrir les entérococques ?

Rétro OutcomeRea 1997-2016
1017 patients IIA, 76 (8%) à *Enterococcus*



No. of patients at risk

Adequate	58	53	51	50	43	39	37
Non adequate	18	16	16	15	11	9	7



No. of patients at risk

E. faecalis	42	40	39	38	33	30	29
Other	34	29	28	27	21	18	15

adéquation anti-Entérococcus et/ou E. faecalis (sensible)

Morvan Crit Care 2019

Couvrir les entérococques ?

Méta-analyse n = 36 dont 23 essais randomisés contrôlés

Analysis type	*No. of studies*	*Participants*	*RR (95% CI)*	p
Clinical treatment success				
Treatment success based on ITT	1	323	0.93 [0.83, 1.04]	0.22
Treatment success based on mITT	13	5092	0.99 [0.95, 1.03]	0.53
Treatment success based on clinical mITT patients	1	448	0.90 [0.79, 1.03]	0.12
Treatment success based on CE patients	17	5736	0.99 [0.97, 1.00]	0.15
Treatment success based on Ce adult patients	15	5265	0.99 [0.97, 1.01]	0.16
Mortality				
Mortality based on ITT	5	2279	1.16 [0.65, 2.09]	0.61
Mortality based on mITT	9	4359	1.08 [0.74, 1.56]	0.7
Mortality based on CE	1	205	0.71 [0.16, 3.11]	0.65
Adverse effects				
Total adverse effects based on ITT	3	1406	0.96 [0.87, 1.06]	0.37
Total adverse effects based on mITT	13	5717	1.03 [0.98, 1.09]	0.28
Total adverse effects based on CE	2	402	1.15 [0.80, 1.65]	0.44
Clinical Treatment Success based on CE patients stratified according to APACHE II				
APACHE II <10	2	610	0.99 [0.91, 1.08]	0.89
APACHE II ≥10	2	153	0.98 [0.80, 1.20]	0.83

Pas ou peu d'impact d'une ATB probabiliste prenant en compte les entérococques (mais majorité d'infections communautaires)

Zhang Surg Infect 2020

Couvrir les entérococques ?

Méta-analyse n = 36 dont 23 essais randomisés contrôlés

Suspected Factors	*Included studies*	*OR (95% CI)*	*I^2 for heterogeneity*
1 Community Acquired			
1.1 Female	11	0.92 [0.78, 1.09]	0%
1.2 Malignancy	6	1.53 [1.16, 2.03]	49%
1.3 Diabetes Mellitus	6	1.21 [0.96, 1.53]	0%
1.4 Cardiovascular Disease	5	1.27 [0.98, 1.63]	38%
1.5 Liver Disease	4	1.09 [0.49, 2.44]	73%
1.6 Chronic Lung Disease	4	1.24 [0.87, 1.78]	24%
1.7 Renal Diseases	3	1.42 [0.80, 2.52]	0%
1.8 Immunosuppression	3	1.27 [0.83, 1.93]	22%
1.9 Chronic Vascular Disease	2	1.12 [0.79, 1.59]	0%
1.10 GI Hemorrhage	2	3.23 [0.92, 11.37]	65%
1.11 Corticosteroid Use	2	2.46 [1.71, 3.54]	0%
1.12 Myocardial infarction	1	2.033 [0.9548, 4.244]	NA
2 Hospital Acquired			
2.1 Operation	7	2.88 [2.21, 3.75]	0%
2.2 Nosocomial Infection	7	2.81 [2.34, 3.39]	33%
2.3 Any Antibiotic Treatment	5	2.40 [1.74, 3.31]	42%
2.4 Admission to ICU	3	2.54 [1.75, 3.68]	0%
2.5 Indwelling Urinary Catheter	2	1.78 [1.02, 3.11]	0%
2.6 CVC	2	7.80 [0.63, 96.20]	89%
2.7 Inadequate Empirical ATB	1	2.088 [1.006, 4.253]	NA
2.8 Generalized Peritonitis	1	1.449 [0.7129, 2.948]	NA
2.9 Peritonitis Duration more than 24h	1	2.679 [1.157, 6.012]	NA
2.10 MOF	1	2.017 [0.8483, 5.147]	NA

Nosocomial et post-op = FdR significatifs

Zhang Surg Infect 2020

Antifongiques ? – étude AbSeS

Multivarié avec succès d'éradication du foyer

Variable	Model with source control achievement* OR (95% CI)
Empiric antimicrobial coverage	

***ne sort pas : PAS* de différence de mortalité avec ou sans traitement antifongique**

Blot Intens Care Med 2019

Antifongiques ? FdR candidose invasive intra-abdo

2015-2016
cas controle dans 26 réanimations Europe
101 patients réa **candidose invasive intra-abdominale** vs. 101 patients sans

Risk factors[a]	**OR (95% CI)**	***p***
Recurrent gastrointestinal perforation	13.90 (2.65–72.82)	0.002
Anastomotic leakage	6.61 (1.98–21.99)	0.002
Abdominal drain	6.58 (1.73–25.06)	0.006
Receipt of antifungal drugs (7 or more days)	4.26 (1.04–17.46)	0.04
Receipt of antibiotics (7 or more days)	3.78 (1.32–10.52)	0.01

Bassetti Infect Dis Ther 2022

Antifongiques ? - RFE IIA 2015

R16 :

Communautaire **grave**

± si FdR/Scores

échinocandine

R41 :

Dans les **IIA associées aux soins,**

si une levure est observée à l'examen direct

culture du liquide péritonéal est positive à levures

(échinocandine si grave)

Prospective multicenter randomized double-blind study comparing caspofungin to placebo for the treatment of ICU yeast intra-abdominal infection

CASPER study

Sponsor code : PI2018_843_0007

INTERVENTIONAL RESEARCH PROTOCOL

(Research involving the human person)

Version No. *1.4* of *04/12/2018*

EudraCT number: 2018-000407-16

This interventional research study has received funding from *a PHRC-N 2017*

Sponsor:

Amiens-Picardie University Hospital (CHU d'Amiens-Picardie)
Direction de la Recherche Clinique et de l'Innovation,
CHU d'Amiens-Picardie
F-80054 Amiens Cedex 1, France
Phone: +33 322 088 371; Fax: +33 322 089 645

Coordinating investigator:

Professor DUPONT Hervé

RFE 2015 Montravers Anesth Reanim 2015

Antifongiques ? - RFE IIA 2015

R16 :

Communautaire **grave**

± si FdR/Scores

échinocandine

R41 :

Dans les **IIA associées aux soins,**

si une levure est observée à l'examen direct

culture du liquide péritonéal est positive à levures

(échinocandine si grave)

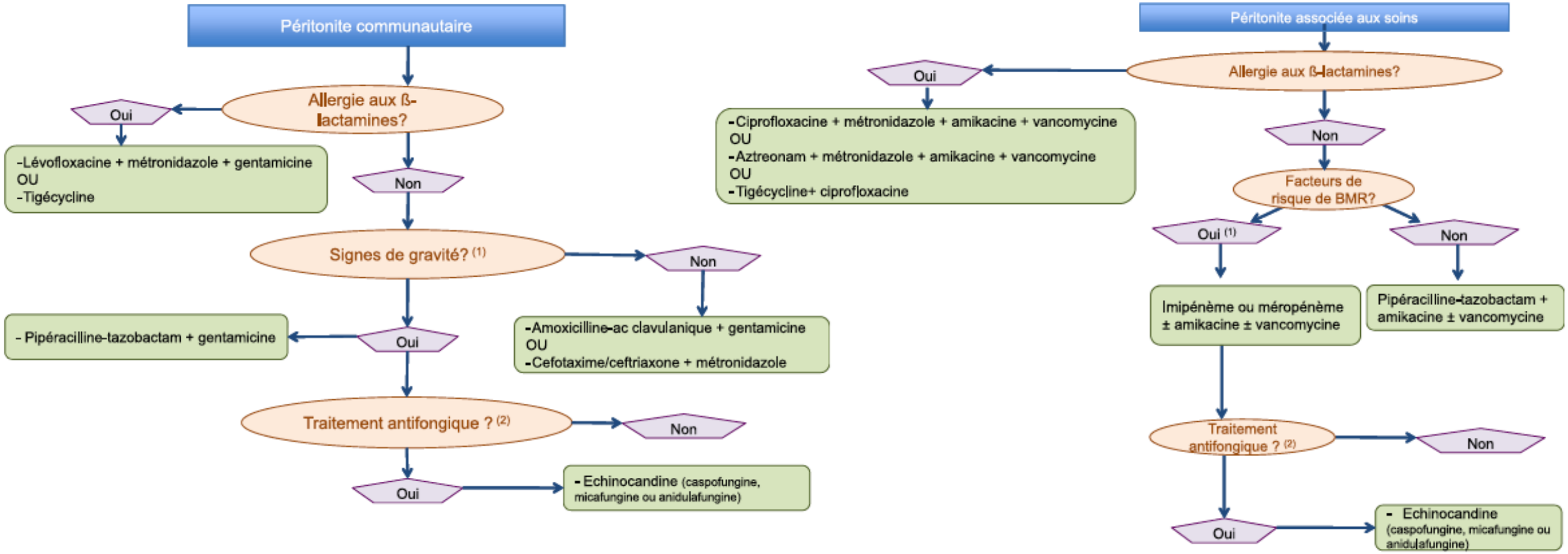
RFE 2015 Montravers Anesth Reanim 2015

Spectres conventionnels d'intérêt

Antibiotic	Anaerobic coverage	*Pseudomonas* coverage	Non-resistant enterococci coverage	Enterobacteriaceae coverage	ESBL coverage
Amikacin	–	+	–	+	+/–
Amoxicillin/ clavulanate	+	–	+	+/–[a]	–
Ceftazidime/ avibactam	–	+[b]	–	+[c]	+
Ceftolozane/ tazobactam	–	+[b]	–	+	+
Cefotaxime	–	–	–	+	–
Ceftazidime	–	+	–	+	–
Ceftriaxone	–	–	–	+	–
Ciprofloxacin	–	+	–	+/–[a]	–
Eravacycline	+	–	+	+[e]	+
Ertapenem	+	–	+/–	+	+
Imipenem-cilastatin	+	+	+[d]	+	+
Meropenem	+	+	+/–	+	+
Metronidazole	+	–	–	–	
Piperacillin/ tazobactam	+	+	+	+	+/–
Tigecycline	+	–	+	+[e]	+

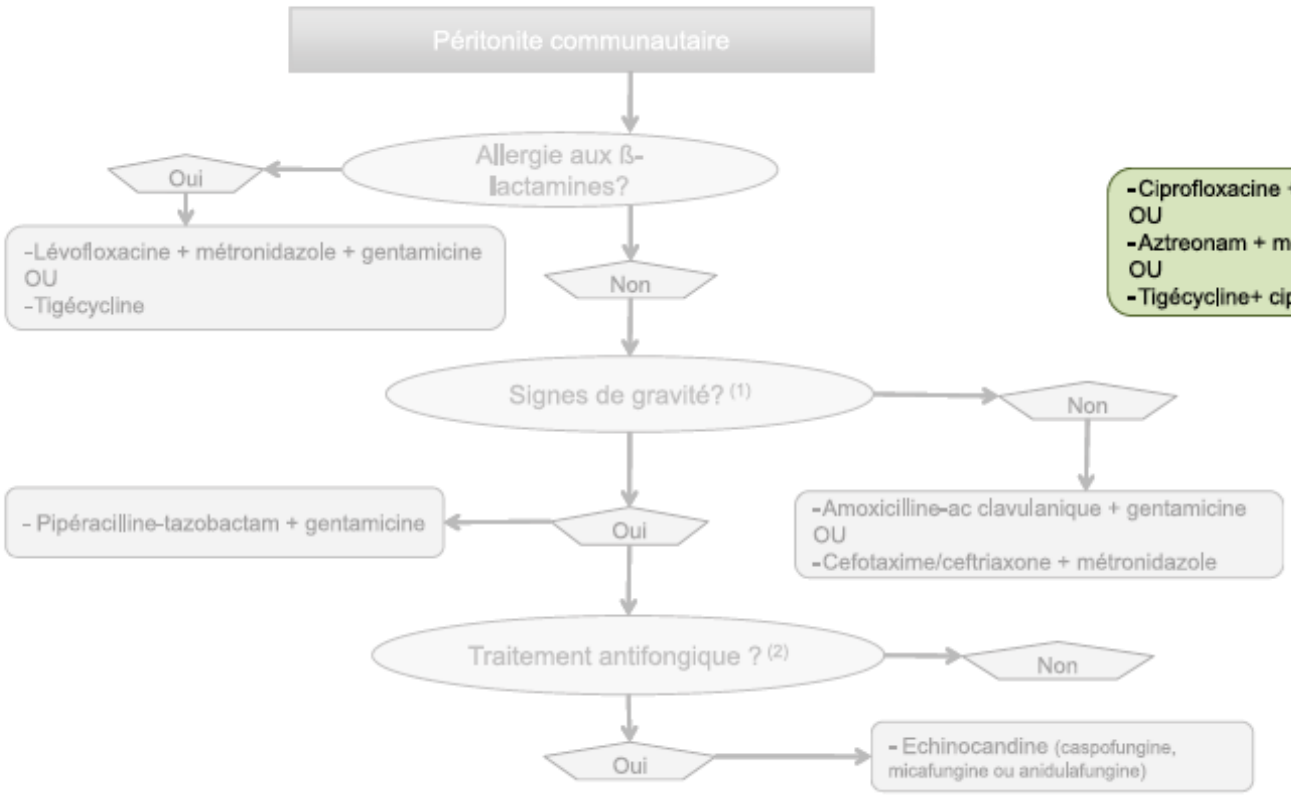
[a]Increasing rates of antimicrobial resistance among Enterobacteriaceae worldwide
[b]Active against MDR *Pseudomonas aeruginosa* except metallo-beta-lactamases (MBL)-producing *Pseudomonas aeruginosa*
[c]Active against carbapenemase-producing *Klebsiella pneumoniae* except MBL-producing Enterobacteriaceae
[d]Imipenem/cilastatin is more active against ampicillin-susceptible enterococci than ertapenem, meropenem, and doripenem
[e]Not active against *Proteus*, *Morganella*, and *Providencia*

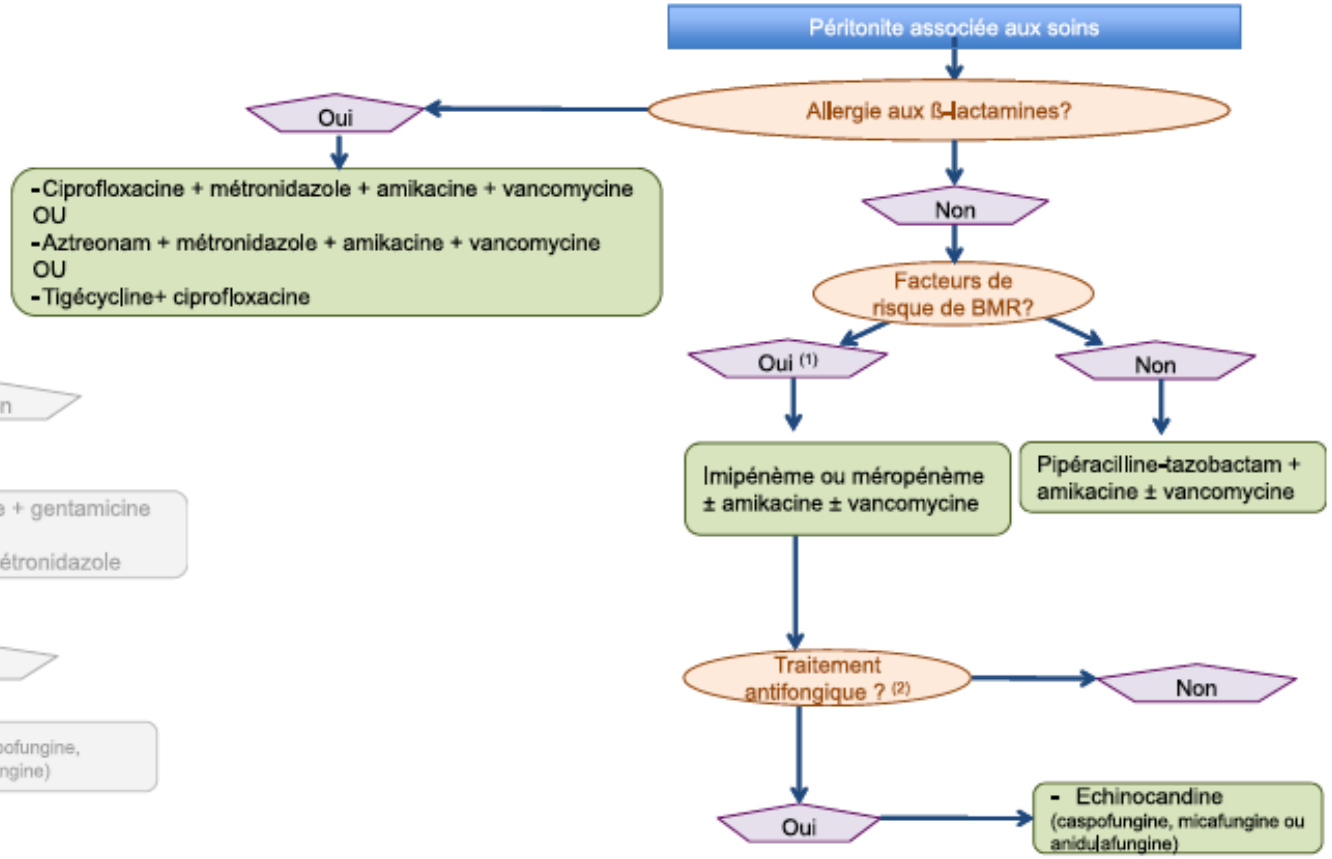
Comment se positionner en antibiothérapie des IIA de réa ?



RFE 2015 Montravers Anesth Reanim 2015

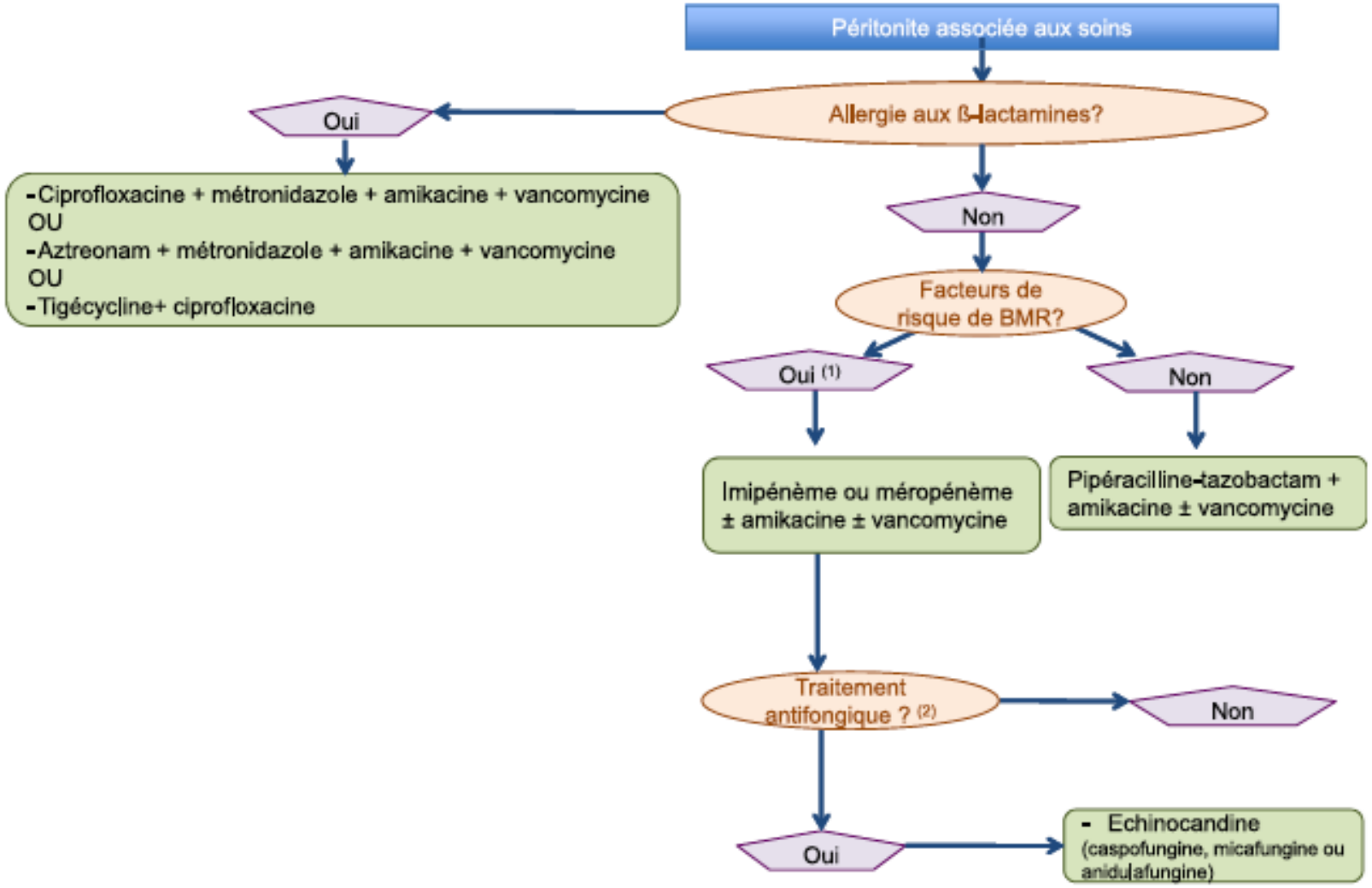
Comment se positionner en antibiothérapie des IIA de réa ?





RFE 2015 Montravers Anesth Reanim 2015

Comment se positionner en antibiothérapie des IIA de réa ?



RFE 2015 Montravers Anesth Reanim 2015

Comment se positionner en antibiothérapie des IIA de réa ?

piéracilline/tazobactam
+
gentamicine

piéracilline/tazobactam
+
amikacine

pénème
+
amikacine

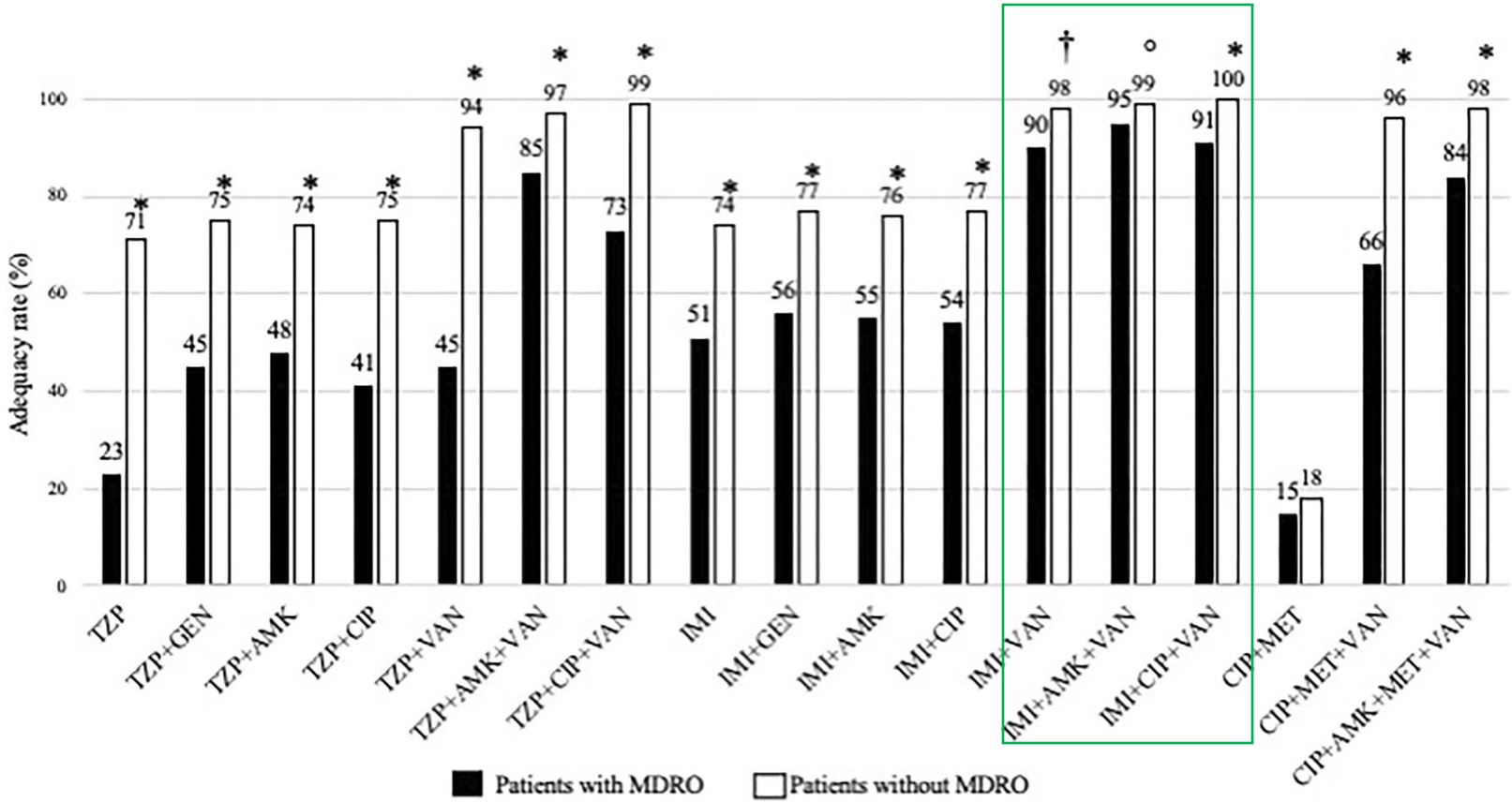
± échinocandine

± vancomycine

RFE 2015 Montravers Anesth Reanim 2015

*Résistance et **IIA post-opératoires***

rétrospective monocentrique n =422 1999-2019

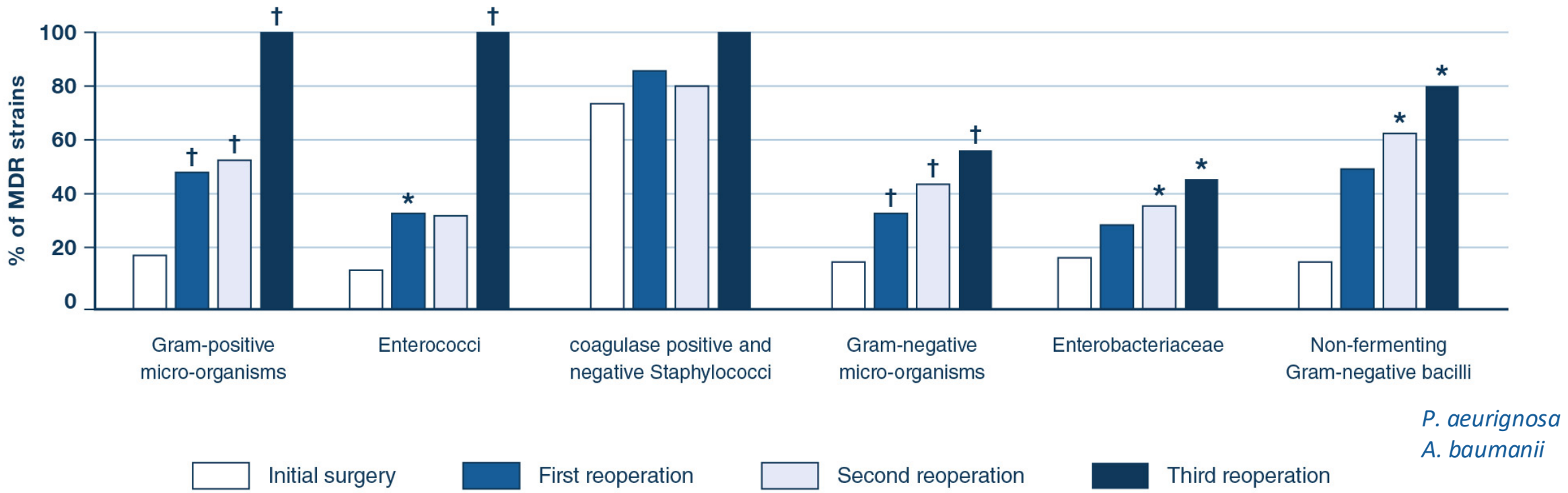


avantage des associations avec pénèmes car augmentation de l'incidence des Enterobactarales BLSE

Montravers World J Emerg Surg 2023

Remarque sur la multirésistance = IIA *tertiaires*

monocentrique, n = 122



P. aeurignosa
A. baumanii

non-éradication du foyer favorise péritonites tertiaires et sélection de multi-résistances

d'après Montravers Crit Care 2015

IIA Liées aux soins = FdR classique de BGN multi-R

Box 18.1 Risk factors and clinical scenarios with increased likelihood of multidrug-resistant (MDR) pathogens in intra-abdominal infections [65–70]

Risk factors for recovery of multidrug-resistant bacteria in patients with intra-abdominal infections
Healthcare-associated infection (outpatient intravenous treatment, wound treatment, antineoplastic therapies, hemodialysis, nursing home residents)
Recent exposure to broad-spectrum antibiotics (<3 months)
Length of hospitalization >5 days
Prior or current admission in intensive care unit
Liver disease
Pulmonary disease
Diabetic foot infection with antibiotic use
Organ transplantation
Corticosteroid use
Patient receiving immunosuppressive agents
Patient with recent exposure in areas with MDR prevalence in the community or in environmental sources
Patient hospitalized in areas with MDR prevalence
Postoperative peritonitis Long time between first and second surgery
Tertiary peritonitis
Recurrent interventions in the biliary tract
Pretreated necrotizing pancreatitis

Péritonite post-opératoire

Péritonite tertiaire

Poulakou in Sartelli Abdominal Sepsis, Hot Topics in Acute Care Surgery and Trauma 2018

Les multirésistances des BGN…et les nouvelles molécules

	Enterobacteriaceae					*Pseudomonas aeruginosa*			*Acinetobacter spp.*	
	ESBL	AmpC	Class-A CBP	mCBP	Class-D CBP	WT	MDR	mCBP	WT	MDR
Ceftolozane-tazobactam	+	IE	-	-	-	+	+	-	-	-
Ceftazidime-avibactam	+	+	+	-	+	+	+	-	-	-
Meropenem-vaborbactam	+	+	+	-	-	+	IE	-	+	-
Imipenem-relebactam	+	+	+	-	IE	+	IE	-	+	-
Plazomycin	+	+	+	+	IE	-	-	-	-	-
Eravacycline	+	+	+	+	+	-	-	-	+	IE
(céfidérocol)	+	+	+	+	+	+	+	+		

Montravers Exp Rev Clin Pharm 2020

Recommandations ESCMID/ESICM antibiothérapie BGN Multi-R

	CRAB	ESBLs	CRPA non-MBL	CRE non-CP	CRE-KPC	CRE-OXA-48	CRE-MBL	Current clinical indications/approval
New antibiotics								
Ceftolozane-tazobactam	No	Yes	Yes	No	No	No	No	FDA and EMA approved for cUTI, cIAI, HAP and VAP
Ceftazidime-avibactam	No	Yes	Yes	+/−	Yes	Yes	No	FDA and EMA approved for cIAI and cUTI, HAP and VAP, and (in EMA only) for the treatment Gram-negative infections in patients with limited treatment options
Meropenem-vaborbactam	No	Yes	No	+/−	Yes	No	No	FDA approved for cUTI, EMA approved for cUTI, HAP and VAP, and for the treatment Gram-negative infections in patients with limited treatment options
Imipenem-cilastatin/ relebactam	No	Yes	Yes	+/−	Yes	No	No	FDA approved for cUTI and cIAI; EMA approved for HAP and VAP and for BSI with a suspected respiratory source, and for the treatment Gram-negative infections in patients with limited treatment options
Plazomicin	No	Yes	+/−	Yes	Yes	Yes	+/−	FDA approval cUTI, EMA application withdrawn
Eravacycline	Yes	Yes	No	Yes	Yes	Yes	Yes	FDA and EMA approved for cIAI
Cefiderocol	Yes	Yes	Yes	Yes	Yes	Yes	Yes	FDA cUTI, HAP and VAP; EMA for the treatment of infections due to aerobic Gram-negative organisms in adults with limited treatment options

Paul Clin Microb Infect 2022

Ceftazidime-avibactam et IIA (AMM poolées)

Etudes poolées d'AMM, toutes randomisées contrôlées notamment RECLAIM/RECLAIM 3 (cIAI) vs. meropenem REPRISE (cIAI/cUTI) vs. BAT

	cIAI	
Patients, *n* (%)	Ceftazidime/ avibactam + metronidazole (*n* = 103)	Comparator (*n* = 128)
Clinical response		
Clinical cure	88 (85.4)	110 (85.9)
95% CI[a]	77.7–91.2	79.1–91.1
Clinical failure	7 (6.8)	3 (2.3)
Indeterminate	8 (7.8)	15 (11.7)
Microbiological response		
Favourable	88 (85.4)	110 (85.9)
95% CI[a]	77.7–91.2	79.1–91.1
Unfavourable	7 (6.8)	3 (2.3)
Indeterminate	8 (7.8)	15 (11.7)

	cIAI	
Patients, *n*/*N* (%)	Ceftazidime/ avibactam + metronidazole (*n* = 103)	Comparator (*n* = 128)
Enterobacterales (all)	86/101 (85.1)	109/127 (85.8)
C. freundii complex	0/1 (0.0)	2/2 (100)
Enterobacter aerogenes	0/0	1/1 (100)
E. cloacae	6/7 (85.7)	6/8 (75.0)
E. coli	62/75 (82.7)	83/96 (86.5)
K. pneumoniae	23/27 (85.2)	16/21 (76.2)
P. mirabilis	3/3 (100)	3/3 (100)
Serratia marcescens	2/2 (100)	1/1 (100)
Other Gram-negative pathogens (all)	7/11 (63.6)	12/12 (100)
P. aeruginosa	3/7 (42.9)	12/12 (100)

Torres J Antimicrob Chemother 2023

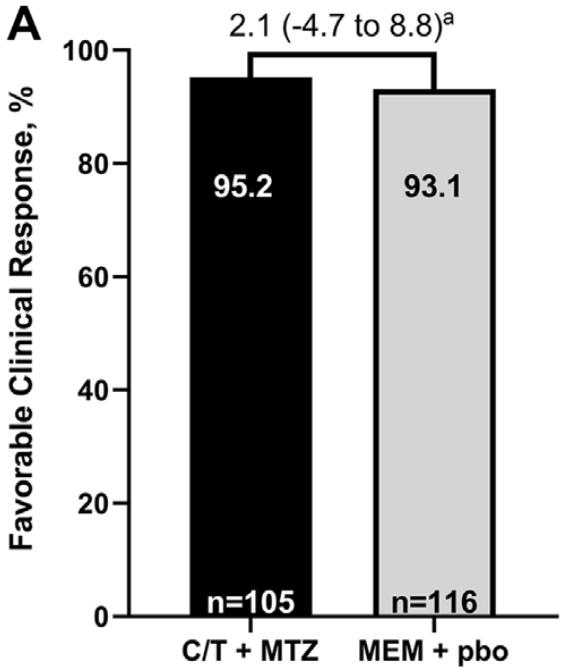
Recommandations ESCMID/ESICM antibiothérapie BGN Multi-R

	CRAB	ESBLs	CRPA non-MBL	CRE non-CP	CRE-KPC	CRE-OXA-48	CRE-MBL	Current clinical indications/approval
New antibiotics								
Ceftolozane-tazobactam	No	Yes	Yes	No	No	No	No	FDA and EMA approved for cUTI, cIAI, HAP and VAP
Ceftazidime-avibactam	No	Yes	Yes	+/−	Yes	Yes	No	FDA and EMA approved for cIAI and cUTI, HAP and VAP, and (in EMA only) for the treatment Gram-negative infections in patients with limited treatment options
Meropenem-vaborbactam	No	Yes	No	+/−	Yes	No	No	FDA approved for cUTI, EMA approved for cUTI, HAP and VAP, and for the treatment Gram-negative infections in patients with limited treatment options
Imipenem-cilastatin/ relebactam	No	Yes	Yes	+/−	Yes	No	No	FDA approved for cUTI and cIAI; EMA approved for HAP and VAP and for BSI with a suspected respiratory source, and for the treatment Gram-negative infections in patients with limited treatment options
Plazomicin	No	Yes	+/−	Yes	Yes	Yes	+/−	FDA approval cUTI, EMA application withdrawn
Eravacycline	Yes	Yes	No	Yes	Yes	Yes	Yes	FDA and EMA approved for cIAI
Cefiderocol	Yes	Yes	Yes	Yes	Yes	Yes	Yes	FDA cUTI, HAP and VAP; EMA for the treatment of infections due to aerobic Gram-negative organisms in adults with limited treatment options

Paul Clin Microb Infect 2022

Ceftolozane-avibactam et IIA (AMM poolées)

Essai randomisé contrôlé
ceftolozane –tazobactam + MTZ vs. meropenem



Characteristics	C/T + metronidazole (N=134)	Meropenem + placebo (N=134)
Male, n (%)	79 (59.0)	85 (63.4)
Age, n (%)		
≤65 y	108 (80.6)	103 (76.9)
66-75 y	26 (19.4)	31 (23.1)
Median (range), y	48.0 (18-75)	55.0 (18-74)
APACHE II score		
Mean (SD)	4.9 (3.1)	5.1 (2.8)
Category, n (%)		
<10	119 (88.8)	126 (94.0)
≥10	15 (11.2)	8 (6.0)

Sun Int J Inf Dis 2022

Recommandations ESCMID/ESICM antibiothérapie BGN Multi-R

	CRAB	ESBLs	CRPA non-MBL	CRE non-CP	CRE-KPC	CRE-OXA-48	CRE-MBL	Current clinical indications/approval
New antibiotics								
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Ceftazidime-avibactam	No	Yes	Yes	+/−	Yes	Yes	No	FDA and EMA approved for cIAI and cUTI, HAP and VAP, and (in EMA only) for the treatment Gram-negative infections in patients with limited treatment options
Meropenem-vaborbactam	No	Yes	No	+/−	Yes	No	No	FDA approved for cUTI, EMA approved for cUTI, HAP and VAP, and for the treatment Gram-negative infections in patients with limited treatment options
Imipenem-cilastatin/ relebactam	No	Yes	Yes	+/−	Yes	No	No	FDA approved for cUTI and cIAI; EMA approved for HAP and VAP and for BSI with a suspected respiratory source, and for the treatment Gram-negative infections in patients with limited treatment options
Plazomicin	No	Yes	+/−	Yes	Yes	Yes	+/−	FDA approval cUTI, EMA application withdrawn
Eravacycline	Yes	Yes	No	Yes	Yes	Yes	Yes	FDA and EMA approved for cIAI
Cefiderocol	Yes	Yes	Yes	Yes	Yes	Yes	Yes	FDA cUTI, HAP and VAP; EMA for the treatment of infections due to aerobic Gram-negative organisms in adults with limited treatment options

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Recommandations ESCMID/ESICM antibiothérapie BGN Multi-R

	CRAB	ESBLs	CRPA non-MBL	CRE non-CP	CRE-KPC	CRE-OXA-48	CRE-MBL	Current clinical indications/approval
New antibiotics								
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Ceftazidime-avibactam	No	Yes	Yes	+/−	Yes	Yes	No	FDA and EMA approved for cIAI and cUTI, HAP and VAP, and (in EMA only) for the treatment Gram-negative infections in patients with limited treatment options
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Eravacycline	Yes	Yes	No	Yes	Yes	Yes	Yes	FDA and EMA approved for cIAI
Cefiderocol	Yes	Yes	Yes	Yes	Yes	Yes	Yes	FDA cUTI, HAP and VAP; EMA for the treatment of infections due to aerobic Gram-negative organisms in adults with limited treatment options

Paul Clin Microb Infect 2022

Recommandations ESCMID/ESICM antibiothérapie BGN Multi-R

	CRAB	ESBLs	CRPA non-MBL	CRE non-CP	CRE-KPC	CRE-OXA-48	CRE-MBL	Current clinical indications/approval
Old antibiotics								
Polymyxins	Yes	Yes	Yes	Yes	Yes	Yes	Yes	FDA: serious infections caused by susceptible strains, when less potentially toxic drugs are ineffective or contraindicated. EMA: treatment of serious infections due to aerobic Gram-negative pathogens in patients with limited treatment options
Aminoglycosides	+/−	+/−	+/−	+/−	+/−	+/−	+/−	EMA and FDA: for the treatment of a variety of bacterial infections
Fosfomycin iv	No	Yes	+/−	+/−	+/−	+/−	+/−	EMA: to treat serious infections when other antibiotic treatments are not suitable. FDA: under review
Aztreonam	No	No	+/−	No	No	No	+/−	EMA and FDA: for the treatment of infections caused by susceptible Gram-negative microorganisms
Tigecycline	Yes	Yes	No	Yes	Yes	Yes	Yes	EMA and FDA: complicated SSTI and IAI (FDA also CAP)
Temocillin	No	Yes	No	No	+/−	No	No	EMA and FDA: orphan drug status for the treatment of infections caused by *Burkholderia cepacia* in patients with cystic fibrosis

Paul Clin Microb Infect 2022

Recommandations ESCMID/ESICM antibiothérapie BGN Multi-R

	CRAB	ESBLs	CRPA non-MBL	CRE non-CP	CRE-KPC	CRE-OXA-48	CRE-MBL	Current clinical indications/approval
New antibiotics								
Ceftolozane-tazobactam	No	Yes	Yes	No	No	No	No	FDA and EMA approved for cUTI, cIAI, HAP and VAP
Ceftazidime-avibactam	No	Yes	Yes	+/−	Yes	Yes	No	FDA and EMA approved for cIAI and cUTI, HAP and VAP, and (in EMA only) for the treatment Gram-negative infections in patients with limited treatment options
Meropenem-vaborbactam	No	Yes	No	+/−	Yes	No	No	FDA approved for cUTI, EMA approved for cUTI, HAP and VAP, and for the treatment Gram-negative infections in patients with limited treatment options
Imipenem-cilastatin/ relebactam	No	Yes	Yes	+/−	Yes	No	No	FDA approved for cUTI and cIAI; EMA approved for HAP and VAP and for BSI with a suspected respiratory source, and for the treatment Gram-negative infections in patients with limited treatment options
Plazomicin	No	Yes	+/−	Yes	Yes	Yes	+/−	FDA approval cUTI, EMA application withdrawn
Eravacycline	Yes	Yes	No	Yes	Yes	Yes	Yes	FDA and EMA approved for cIAI
Cefiderocol	Yes	Yes	Yes	Yes	Yes	Yes	Yes	FDA cUTI, HAP and VAP; EMA for the treatment of infections due to aerobic Gram-negative organisms in adults with limited treatment options

Paul Clin Microb Infect 2022

Recommandations ESCMID/ESICM antibiothérapie BGN Multi-R

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Cefiderocol	Yes	Yes	Yes	Yes	Yes	Yes	Yes	FDA cUTI, HAP and VAP; EMA for the treatment of infections due to aerobic Gram-negative organisms in adults with limited treatment options

Paul Clin Microb Infect 2022

Aztreonam-avibactam (étude d'AMM - REVISIT)

Essai randomisé contrôlé multicentrique n = 422
aztreonam-avibactam vs. meropenem ± colistine
cIAI ou HAP/VAP

	cIAI	
	Aztreonam–avibactam group (n=208)	Meropenem group (n=104)
APACHE II score category*		
≤10	162 (78%)	80 (77%)
>10	46 (22%)	24 (23%)
Primary cIAI diagnosis		
Acute gastric or duodenal perforations	16 (8%)	10 (10%)
Appendiceal perforation or peri-appendiceal abscess	106 (51%)	49 (47%)
Cholecystitis-gangrenous rupture or perforation or progression beyond gallbladder wall	30 (14%)	19 (18%)
Diverticular disease with perforation or abscess	15 (7%)	6 (6%)
Intra-abdominal abscess	26 (13%)	13 (13%)
Other secondary peritonitis	11 (5%)	4 (4%)
Traumatic perforation of the intestines	4 (2%)	3 (3%)

	cIAI		
	Aztreonam–avibactam group	Meropenem group	Difference, % (95% CI)
ITT analysis set	159/208 (76·4%, 70·3 to 81·8)	77/104 (74·0%, 65·0 to 81·7)	2·4% (–7·4 to 13·0)
CE analysis set	143/168 (85·1%, 79·2 to 89·9)	66/83 (79·5%, 69·9 to 87·1)	5·6% (–4·0 to 16·6)

Carmeli Lancet ID 2025

Les limites des études ATB et IIA…et du raisonnement

- Gravité très variable (souvent modérée, péritonites appendiculaires)
- Effet écrasant de l'éradication de la source
- IIA = polymicrobiens (même si non apparent car culture = séléction)

Exemple : eravacycline vs. meropénème (IGNITE 4)

Population	Eravacycline	Meropenem	Difference (95% Confidence Interval)
Modified intent-to-treat	N = 250	N = 249	…
Clinical cure	231 (92.4)	228 (91.6)	0.8 (–4.1, 5.8)
Clinical failure	7 (2.8)	9 (3.6)	…

non-infériorité
92% de succès

Actual primary disease diagnosis		
Complicated appendicitis, n (%)	94 (48.2)	90 (43.9)
Other complicated intra-abdominal infection	101 (51.8)	115 (56.1)
Diagnosed and enrolled preoperatively	7 (3.6)	11 (5.4)
Diagnosed intra-/postoperatively	188 (96.4)	194 (94.6)
Intra-abdominal abscess(es)[a]	119 (63.3)	110 (56.7)
Peritonitis	94 (50.0)	95 (49.0)
Gastric/duodenal perforation	11 (5.9)	12 (6.2)
Complicated cholecystitis	40 (21.3)	45 (23.2)
Perforation of small intestine	7 (3.7)	7 (3.6)
Complicated appendicitis	93 (49.5)	91 (46.9)
Perforation of large intestine	8 (4.3)	12 (6.2)
Diverticulitis with perforation, peritonitis, or abscess	5 (2.7)	7 (3.6)
Other	0	2 (1.0)

50% d'appendicites compliquées

peu graves (SAPS II = 6)

Solomkin Clin Infect Dis 2019

Recommandations ESCMID/ESICM antibiothérapie BGN Multi-R

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Eravacycline	Yes	Yes	No	Yes	Yes	Yes	Yes	FDA and EMA approved for cIAI
Cefiderocol	Yes	Yes	Yes	Yes	Yes	Yes	Yes	FDA cUTI, HAP and VAP; EMA for the treatment of infections due to aerobic Gram-negative organisms in adults with limited treatment options

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Exemple : eravacycline vs. meropénème (IGNITE 4)

Table 6. Clinical Cure at the Test-of-cure Visit by Baseline Pathogen: Microbiological Intent-to-treat Population

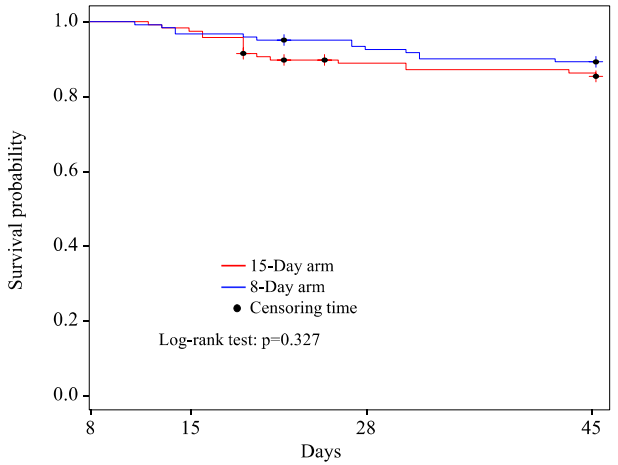
Baseline Pathogen[a]	Eravacycline (N = 195)	Meropenem (N = 205)
Gram-negative aerobes	141/158 (89.2)	153/166 (92.2)
Enterobacteriaceae	129/146 (88.4)	142/154 (92.2)
Escherichia coli	111/126 (88.1)	125/134 (93.3)
Klebsiella pneumoniae	21/21 (100.0)	23/27 (85.2)
Non-enterobacteriaceae	36/38 (94.7)	28/30 (93.3)
Acinetobacter baumannii complex	5/5 (100.0)	2/2 (100.0)
Pseudomonas aeruginosa	18/19 (94.7)	18/20 (90.0)

eravacycline est <u>inactive sur Pa</u>
et néanmoins…94% de guérison clinique !

Solomkin Clin Infect Dis 2019

Durée de l'antibiothérapie des IIA en réa

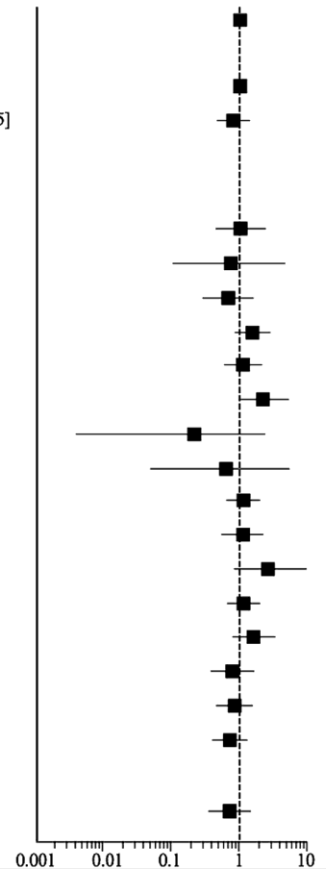
Etude DURAPOP
21 réanimations, France
8j vs. 15j
<u>succès éradication source +</u>



Number at risk (number censored)

8-Day arm	120 (0)	118 (0)	111 (1)	107 (100)
15-Day arm	116 (0)	114 (0)	101 (3)	97 (92)

Primary and secondary outcomes	15-day arm (n=116)	8-day arm (n=120)	Odd-ratios (95%CI)	P value
Primary outcome				
Antibiotic-free days on Day28, median [IQR][a]	12 [6—13]	15 [6—20]	1.08 (1.04—1.125)	1.9×10^{-4}
Secondary outcome				
Length of ICU stay between Day0 and Day45, median [IQR][b]	12 [7—20]	13 [7.75—25]	1.02 (0.99—1.04)	0.14
Length of hospital stay between Day0 and Day45, median [IQR][c]	30 [20—45]	30.5 [18.75—45]	0.80 (0.46—1.38)	0.42
Secondary outcomes				
Organ failure on Day15, n (%)[d]	17/96 (18)	15/90 (17)	1.08 (0.47—2.50)	1.00
Organ failure on Day28, n (%) [e]	4/60 (5)	3/63 (6)	0.78 (0.11—4.82)	1.00
45-day mortality, n (%)	17/116 (15)	13/120 (11)	0.71 (0.30—1.64)	0.43
Additional source control between Day8 and Day45, n (%)	34/116 (28)	48/120 (40)	1.61 (0.90—2.87)	0.101
Reoperations between Day8 and Day45, n (%)	27/166 (23)	31/120 (26)	1.15 (0.61—2.17)	0.65
Percutaneous drainages between Day8 and Day45, n (%)	11/116 (9)	23/120 (19)	2.26 (0.99—5.41)	0.041
Recurrent infection, n (%)[f]	13/14 (93)	14/19 (74)	0.22 (0.004—2.40)	0.21
Superinfection, n (%)[e]	11/32 (34)	14/44 (32)	0.65 (0.05—5.52)	1
New antibiotic therapy, n (%)	45/116 (39)	51/120 (42)	1.17 (0.67—2.03)	0.59
New antibiotic therapy between Day16 and Day28, n (%)	25/102 (25)	29/106 (27)	1.16 (0.56—2.27)	0.75
Bacteraemia between Day8 and Day45, n (%)	5/116 (4)	13/120 (11)	2.69 (0.86—9.96)	0.059
Clinical failure between Day8 and Day45, n (%)	16 (14)	28 (24)	1.18 (0.68—2.05)	0.54
Microbiological failure between Day8 and Day45, n (%)	18 (16)	28 (23)	1.65 (0.82—3.40)	0.13
Emergence of MDR bacteria in surveillance samples, n (%)[g]	23/104 (22)	20/107 (19)	0.81 (0.39—1.67)	0.54
Emergence of MDR bacteria in clinical isolates, n (%)[d]	40/104 (38)	38/108 (35)	0.87 (0.47—1.58)	0.72
Emergence of MDR bacteria in both surveillance samples and clinical isolates confounded, n (%)[g]	52/104 (50)	46/108 (43)	0.74 (0.41—1.32)	0.28
Emergence of fungi, n (%)[g]	27/106 (25)	22/107 (21)	0.75 (0.37—1.51)	0.39



Durée courte 8j

Montravers Intens Cared Med 2018

Conclusions…plus de questions que de réponses

- Les classifications ont peu de sens et les études sont à revoir et homogénéiser en fonction de
  - **éradication** du foyer/succès ou non
  - **gravité** choc septique/sepsis
  - **effraction** digestive/péritonite
  - ± nosocomial tardif/précoce/communautaire
- Impact de l'antibiothérapie très difficile à déterminer,
  - uniquement si éradication avec succès
  - **possible rôle dans les tertiaires/persistantes (et donc R ou multi-R)**

Conclusions…en pratique, IIA en réanimation = grave et/ou noso

- **piperacilline/tazobactam + aminoside (si noso et/ou FdR Pa = amikacine)**

ou

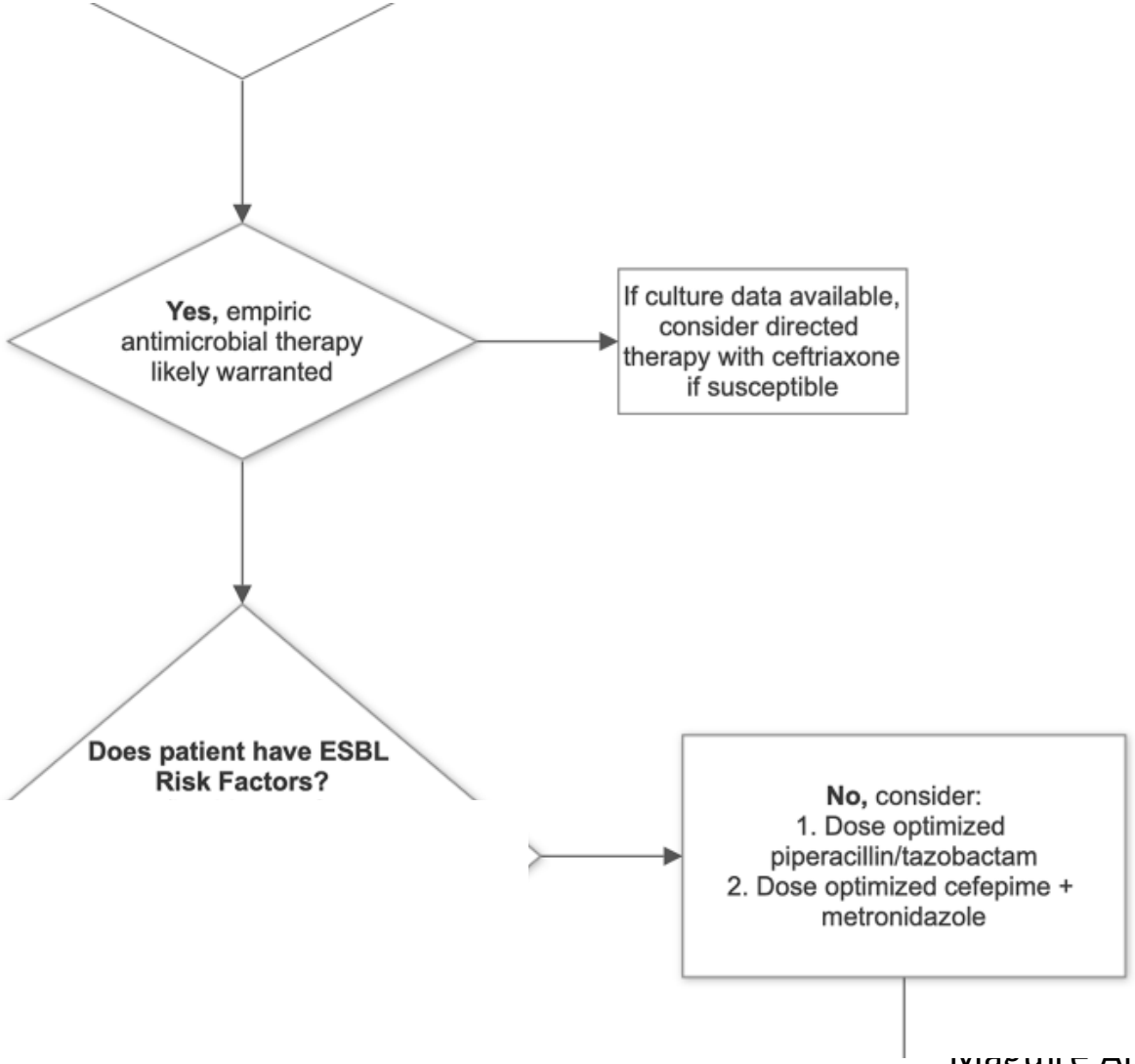
- **pénème + aminoside (surtout si FdR multi-R : post-op, tertiaires…)**
- ± nouvelles molécules
  - si colonisation MDR connue avec ATB gramme
  - si écologie locale particulièrement MDR
- entérococques ?
- **levures (échinocandines…**& wait for CASPER)

Conclusion – Antibiothérapie des IIA liées aux soins

ERADICATION DU FOYER

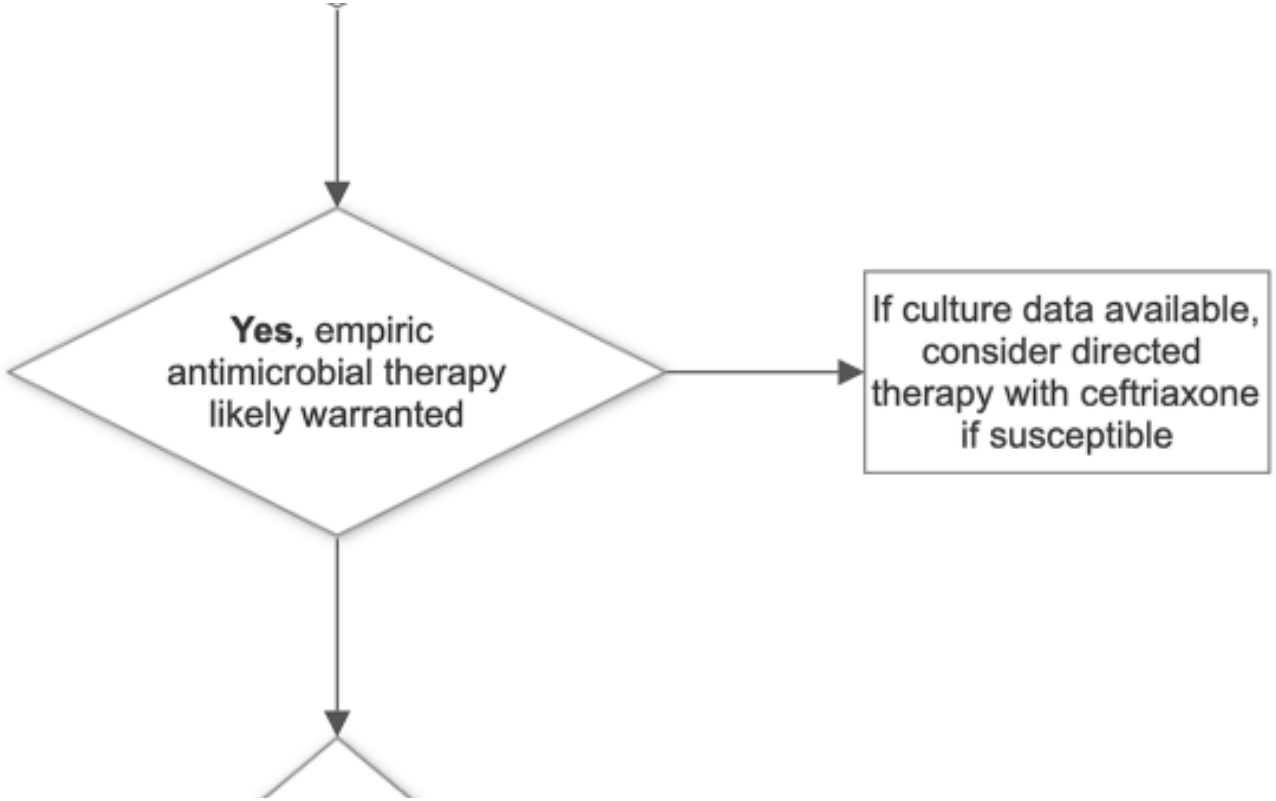
Antibiothérapie

Pancréatites aigus nécrosantes



Maguire Ann Pharmacother 2020

Pancréatites aigus nécrosantes



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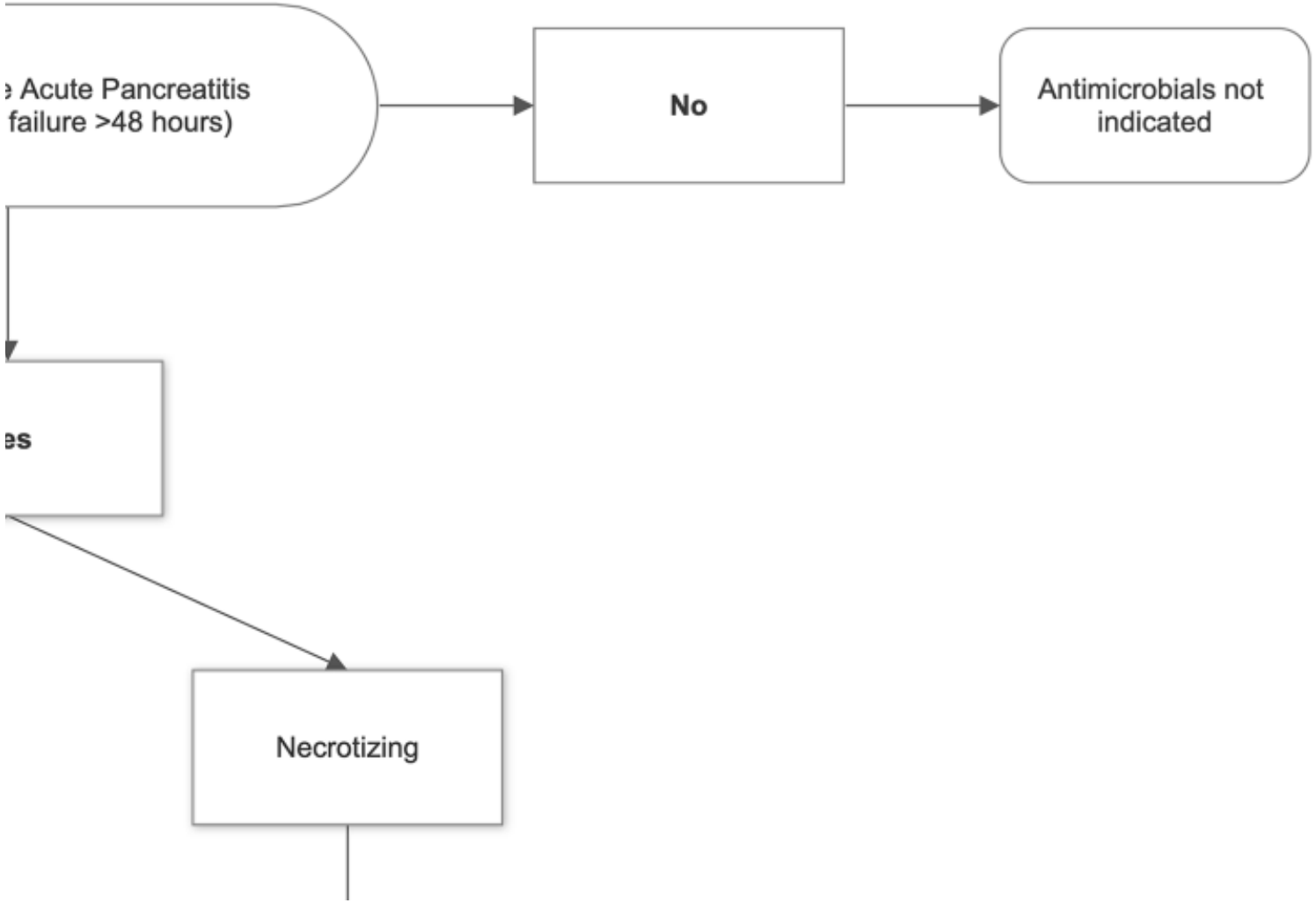
Pancréatites aigus nécrosantes



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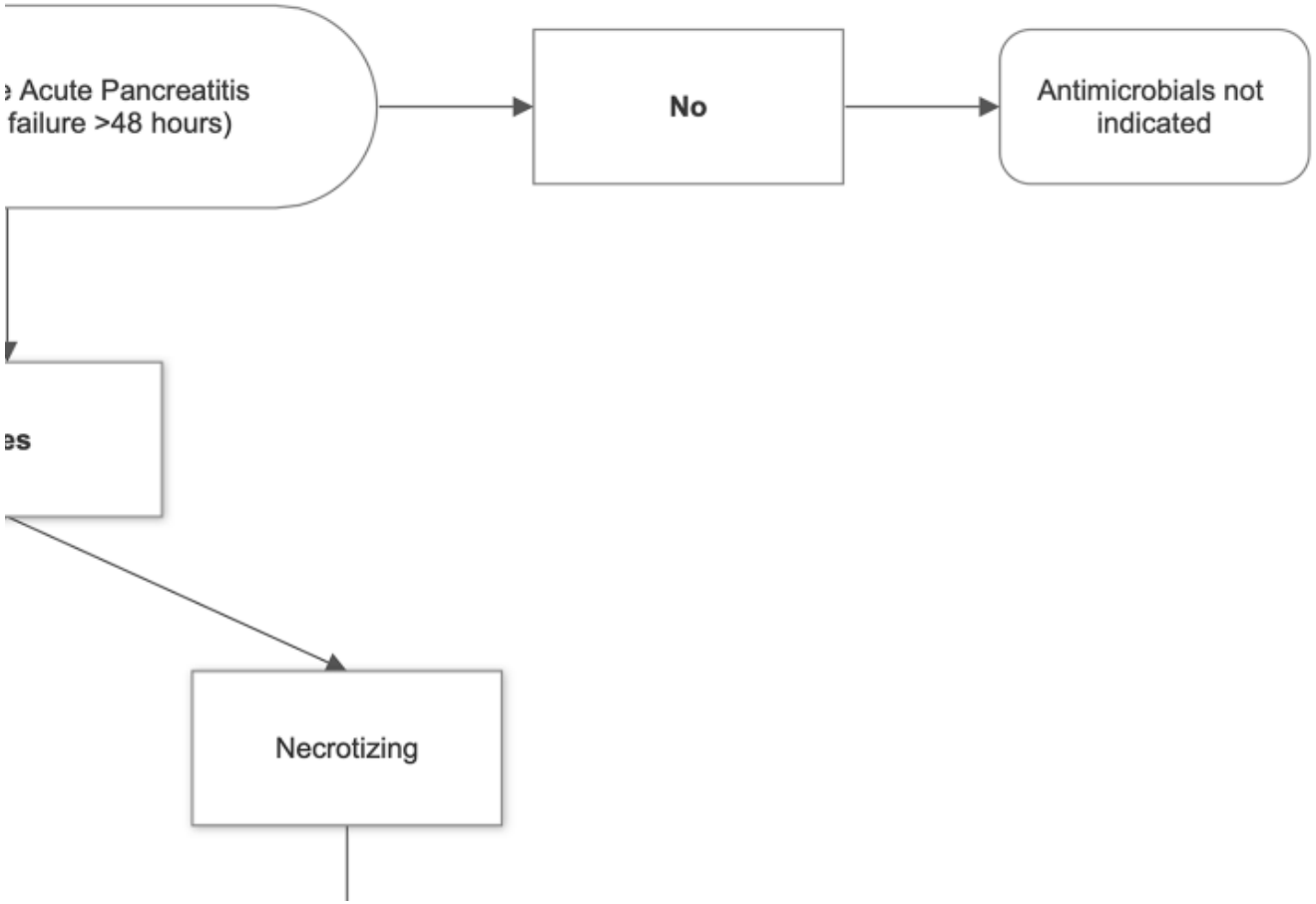
Pancréatites aigus nécrosantes



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Pancréatites aiguës (Etude AbSeS)

Etude post-hoc de l'étude AbSeS
Pancréatites aiguës n = 165 (6,3%)

Independent relationships with mortality in critically ill patients with pancreatic infection.

Risk factor	OR	95%CI	*P*-value
Age (years increase)	1.0	1.0 to 1.1	0.023
Clinical evaluation on day 7 of the pancreatic infection process			
Stable	Reference		
Unstable, persistent signs of inflammation	9.5	3.8 to 23.9	<0.001
Unstable, additional intervention required following the initial approach	4.0	1.3 to 12.2	0.013
Anatomical disruption			
Not present	Reference		
Localized peritonitis	4.4	1.4 to 13.9	0.011
Diffuse peritonitis	1.8	0.7 to 4.6	0.201
Severity of disease expression			
Infection	Reference		
Sepsis	0.5	0.1 to 3.5	0.454
Septic shock	2.4	0.3 to 18.8	0.395

FdR surmortalité =
Age, instabilité associée à inflammation persistante et/ou nécessité de re-intervention (drainage/lavage/nécrosectomie)

DejonckheereJ intensive Med 2023