Conférence n° 6 Pneumocystose quelles particularités chez l'immunodéprimé non-VIH?

DES de Maladies Infectieuses et Tropicales Octobre 2025

Pr Benjamin GABORIT

Service de Maladies Infectieuses et Tropicales

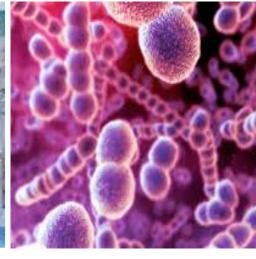
CHU Nantes

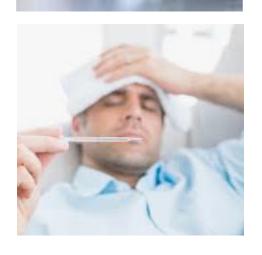
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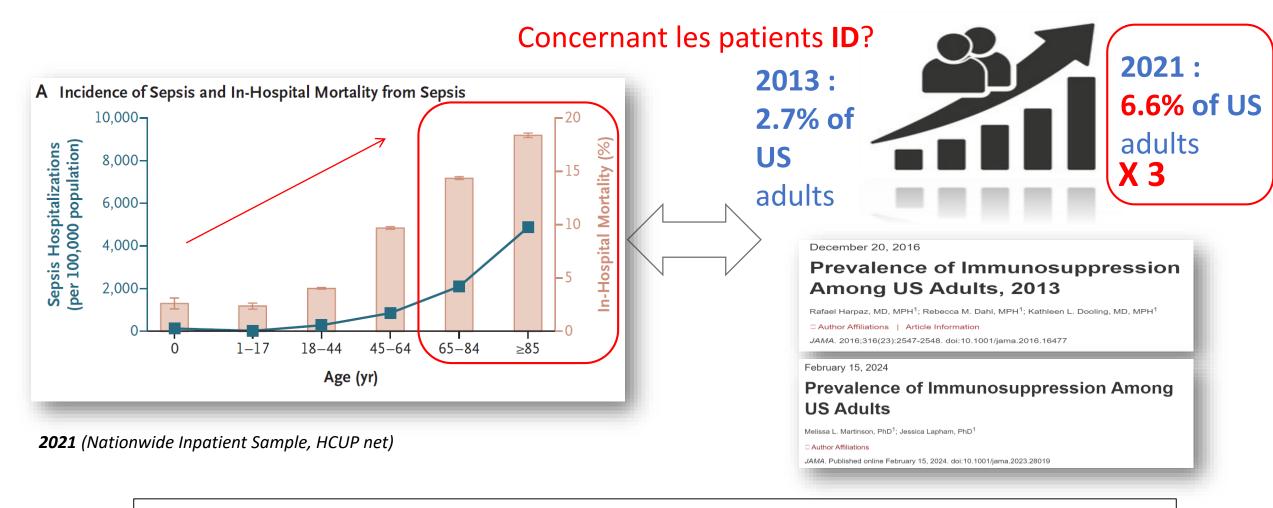
PLAN

POURQUOI ENCORE S'INTÉRESSER À LA DE PNEUMOCYSTOSE?

LES SPÉCIFICITÉS DE LA PNEUMOCYSTOSE (HORS VIH) ?

ACTUALITÉS SUR LES MODALITÉS DIAGNOSTIQUES ET THÉRAPEUTIQUES

LA PRÉVENTION



Vieillissement de la population et augmentation du nombre global de patients immunodéprimés !





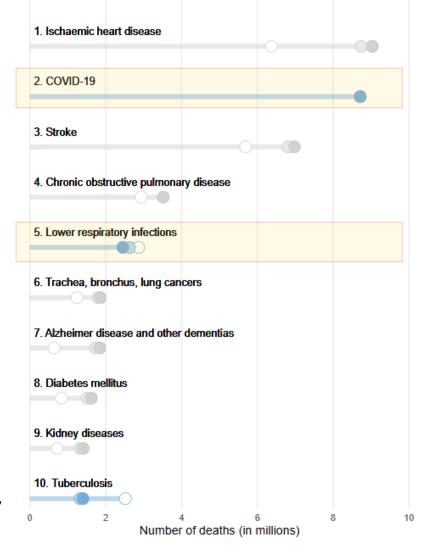
Impact de l'ID au cours des pneumonies





Leading causes of death in 2021 globally

- 5ème cause de mortalité dans le monde en 2021
- Mortalité très variable en fonction du contexte



- > ambulatoire
 - < 1-5% de décès
- à l'hopital
 - 8-10% de décès
- > en USI
 - 27% de décès à 30j
- ≽en USI en cas d'ID
 - 40-48% à 90 jours

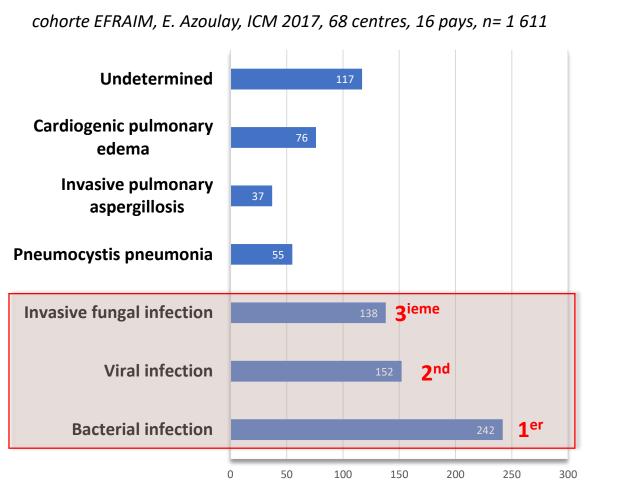
Comment optimiser leur prise en charge?

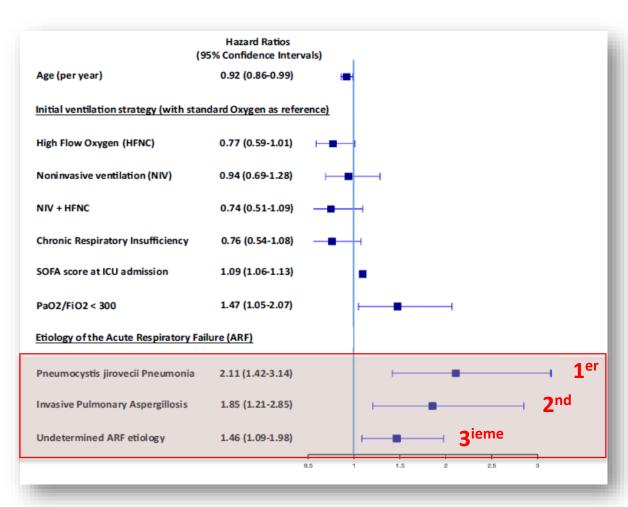
Fine MJ, et al. N Engl J Med. 1997 Cavallazzi R, et al.Chest. 2020 Kalil AC et al. CID 2016

Epidémiologie des SDRA chez l'ID?

Etiologie des DRA de l'immunodéprimé en ICU (n=1 611)

Facteurs de risque de ventilation mécanique?





L'importance de la performance diagnostique chez l'ID

Quelle place de la PCP parmi les IFI en France ?



Les IFI en France ?



2012-2018 N = 10 154 29 centres (RESSIF)

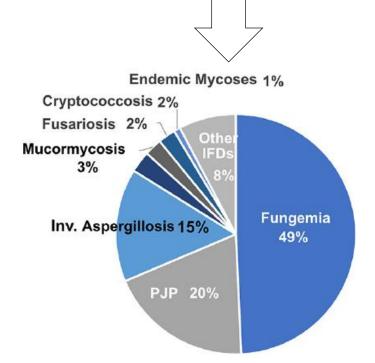




TABLE 1 Characteristics of the 10,886 episodes in 10,154 pat

Results ^b by IFDs				
	Results by IFDs			
Parameter	Fungemia ^c (n = 5,363)	Pneumocystosis (n = 2,106)		
Characteristics of the patients Male sex Median age (years [IQR ^e]) Main underlying risk factor Malignancy Malignancy, including	3,106/5,056 (61.4) 63.4 (22.8) 1,908/5,056 (37.7) 782/1,908 (41.0)	1,322/2,038 (64.9) 61.95 (20.9) 971/2,038 (47.6) 574/971 (59.1)		
hematological malignancy SOT Recent surgery HIV infection Other risk factor No known underlying condition	162/5,056 (3.2) 1,610/5,056 (31.8) 11/5,056 (0.2) 1,351/5,056 (26.7) 14/5,056 (0.3)	310/2,038 (15.2) 5/2,038 (0.2) 334/2,038 (16.4) 405/2,038 (19.9) 13/2,038 (0.6)		
Characteristics of the isolates Intensive care unit Type of IFD	1,924/5,363 (35.9)	564/2,106 (26.8)		
Proven Probable PCR only	5,363/5,363 (100.0)	1,172/2,106 (55.7) 645/2,106 (30.6) 289/2,106 (13.7)		
Means of diagnosis Positive culture Fungal elements in fluids/ tissues	5,363/5,363 (100.0) 1,715/5,363 (32.0)	947/2,106 (45.0)		
Positive antigen detection Positive PCR test Initial antifungal treatment	253/5,363 (4.7) 9/5,363 (0.2)	189/2,106 (9.0) 1,786/2,106 (84.8)		
Caspofungin Fluconazole Voriconazole Liposomal amphotericin B Cotrimoxazole	2,366/4,592 (51.5) 1,424/4,592 (31.0) 100/4,592 (2.2) 150/4,592 (3.3)	3/1,976 (0.2) 5/1,976 (0.3) 7/1,976 (0.4) 4/1,976 (0.2) 1,813/1,976 (91.8)	va rk	
Other drugs or combinations Global mortality at 3 mo	552/4,592 (12.0) 2,003/4,204 (47.6)	144/1,976 (7.3) 461/1,777 (25.9)	Va Es Bo be	

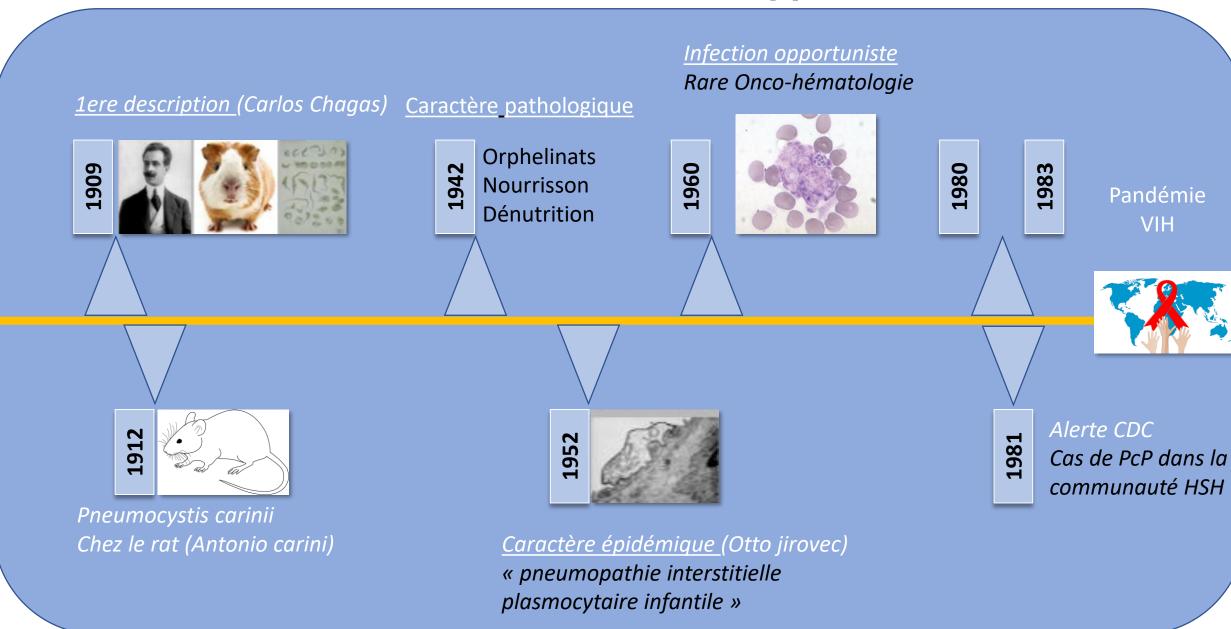
RESEARCH ARTICLE



vareness on Invasive rk (2012 to 2018)

Valérie Letscher-Bru, ^c Sophie Cassaing, ^d , ⁱ Estelle Cateau, ^j Eric Bailly, ^k Maxime Moniot, ^l Bouteille, ^q Marc Pihet, ^r Frédéric Dalle, st bert, ^y Olivier Lortholary, ^{az}

Evolution d'une maladie opportuniste



Epidémiologie actuelle de la PcP

Pandémie VIH

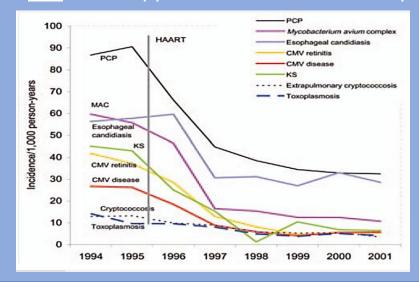




De <u>nouveaux patients à risque</u>

- 7 Onco-hématologie
- 7 Greffés d'organes solides
- → Maladies de système

- VIH: Développement des ARV et de la prophylaxie



Bascule épidémiologique:

- PcP hors VIH (80%)
- Sévérité: décès (26% à 3 mois)

PLAN

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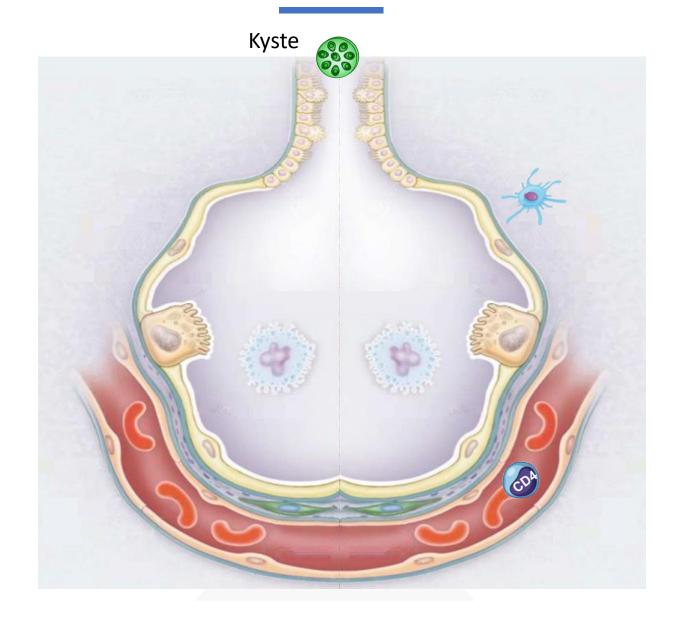
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LA PRÉVENTION

<u>Immunocompétent</u>

- Forme infectante
- Transmission interhumaine



<u>Immunocompétent</u>

- Forme infectante
- Transmission interhumaine

Macrophages Alvéolaires

- Réponse **T CD4 /T CD8**
- Réponse **Humorale**

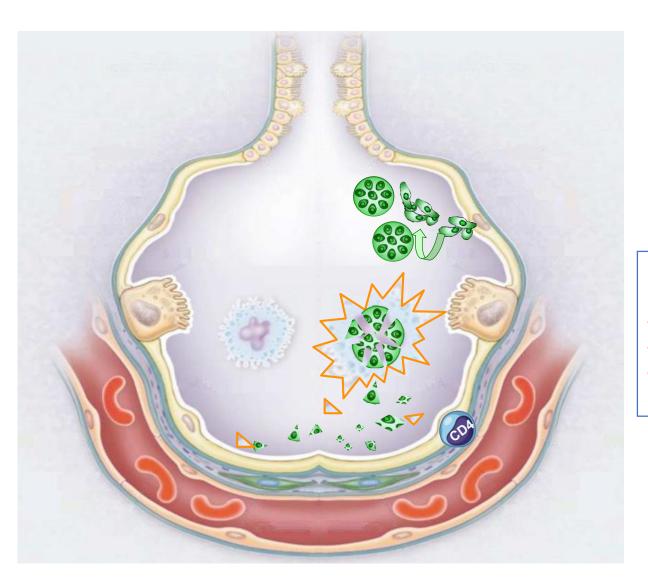


<u>Immunocompétent</u>

- Forme infectante
- Transmission interhumaine

Macrophages Alvéolaires

- Réponse **T CD4 /T CD8**
- Réponse **Humorale**



Echappement avec colonisation de l'hôte

- 10-20 % de colonisation
- 10 jours à 10 mois

=> ED - PCR + BDG-

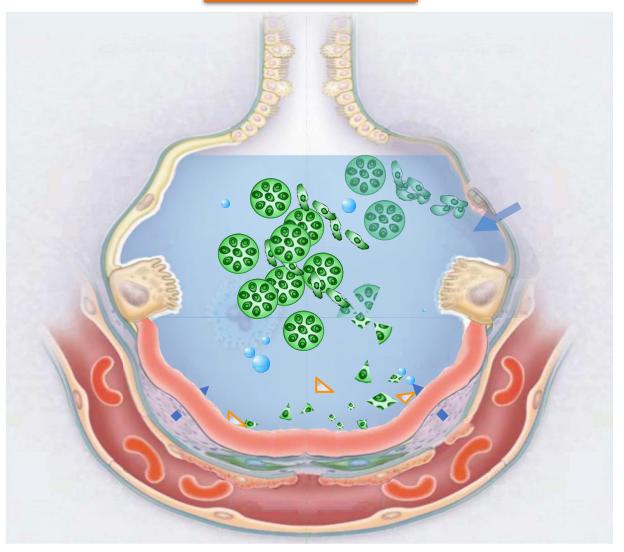
Facteur de risque:

- **Enfants**
- BPCO
- VIH/Corticothérapie

Par le VIH

- < 200 T CD4 (Th1)</p>





Par le VIH

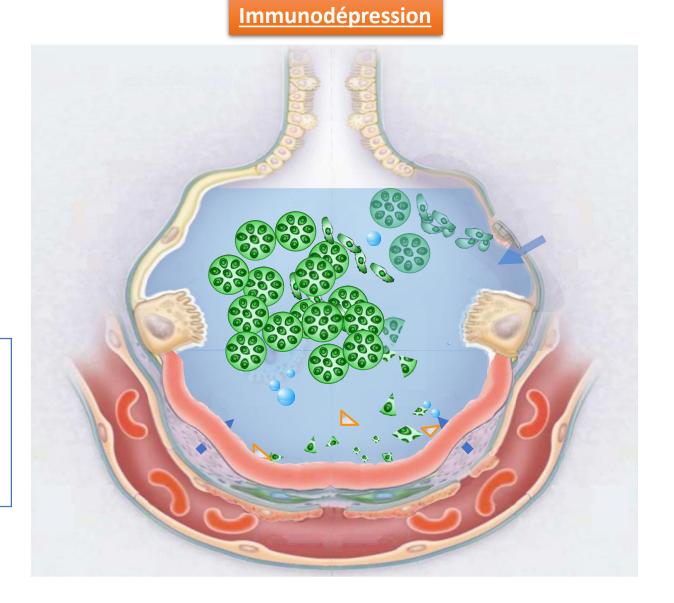
- < 200 T CD4 (Th1)</p>
- ☑ macrophagiques

=> ED + PCR + BDG+



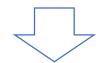
Prolifération PJ

- 🔰 PNN
- *⊃* charge fungique
- = **Bonne tolérance initiale**



Par le VIH

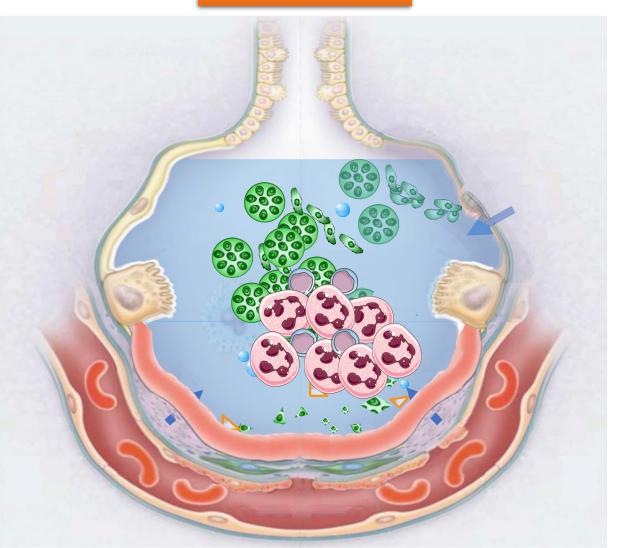
- < 200 T CD4 (TH1)</p>
- <u></u> macrophagiques



Prolifération PJ

- Y PNN
- *⊃* charge fungique
 - = Bonne tolérance initiale

<u>Immunodépression</u>



ID Hors VIH

- IS multifactorielle
- o Polarisation M1
- => ED PCR + BGD+



Faible charge fongique

- **∠** PNN
- 7 Réponse inflammatoire
 - = <u>Lésions plus sévères</u>

Présentations cliniques des PcP

2 tableaux selon le terrain du patient

VIH (20%)

Apparition progressive ~ 1 mois

 $CD4 = 30/mm^3$

Nombreux kystes à l'ED

Meilleur pronostic Mortalité 15%

Presentations Clinique des PcP

2 tableaux selon le terrain du patient

VIH (20%)	Hors VIH (80%)
Apparition progressive ~ 1 mois	Apparition brutale ~ 5 jours
CD4 = 30/mm ³	CD4 = <u>150/mm³</u>
Nombreux kystes à l'ED	ED souvent négatif (PCR++)
Meilleur pronostic Mortalité 15 %	Soins intensifs 50 % Mortalité 30% (50% si VM)

Comment faire le diagnostic?

PLAN

POURQUOI ENCORE S'INTÉRESSER À LA DE PNEUMOCYSTOSE?

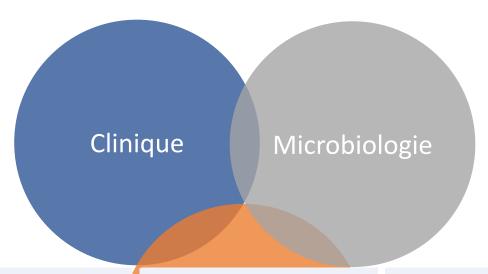
LES SPÉCIFICITÉS DE LA PNEUMOCYSTOSES (HORS VIH) ?

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LA PRÉVENTION

Diagnostic

"Dyspnée fébrile de l'immunodéprimé"





micronodules





Fibrose
Distorsions,
bronchectasies



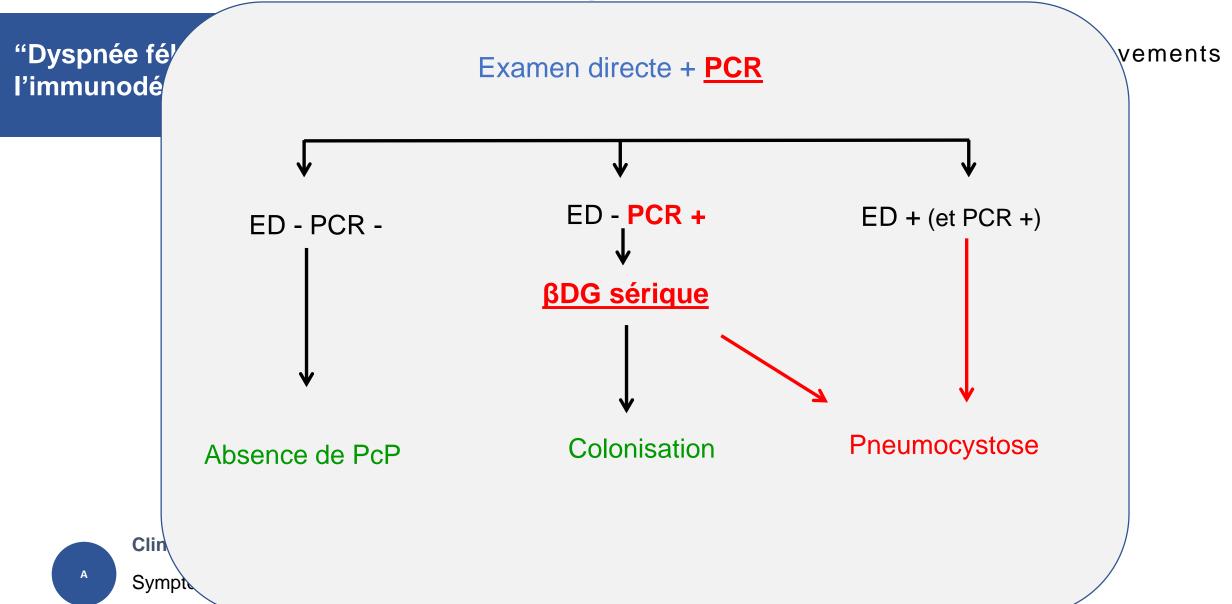
Topographie Périphérique

A

Symptômes peu

Clinique

Diagnostic



Critères diagnostiques hors VIH?

Clinical Infectious Diseases

SUPPLEMENT ARTICLE







Pneumocystis jirovecii Disease: Basis for the Revised EORTC/MSGERC Invasive Fungal Disease Definitions in Individuals Without Human Immunodeficiency Virus

Katrien Lagrou, 1.2.a Sharon Chen, 3.a Henry Masur, 4 Claudio Viscoli, 5.b Catherine F. Decker, 6 Livio Pagano, 7 and Andreas H. Groll⁸

Table 2. Diagnostic Criteria for Definition of Proven and Probable Pneumocystis jirovecii Pneumonia

Description

Proven

Clinical and radiologic criteria, plus:

PCP

- Demonstration of *P. iirovecii* by microscopy using conventional or immunofluorescence staining in tissue or
- Demonstration of *P. jirovecii* by microscopy using conventional or immunofluorescence staining in respiratory speci-

PCP

- Probable Appropriate host factors and clinical and radiologic criteria, plus: - Amplification of *P. jirovecii* DNA by quantitative real-time PCR in respiratory specimen or
 - Detection of β-D-glucan in serum alternative method; another IFD and a false-positive result should be ruled out)

Abbreviations: IFD, invasive fungal diseases; PCP, Pneumocystis jirovecii pneumonia; PCR, polymerase chain reaction.

Table 1. Host Factors, Clinical Criteria, and Microbiologic Criteria Used for the Definition of Pneumocystis jirovecii Pneumonia

Description

Host factors

- Use of therapeutic doses of ≥0.3 mg/kg prednisone equivalent for ≥2 weeks in the past 60 days
- Low CD4+ lymphocyte counts (observed or expected; <200 cells/mm³) induced by a medical condition, anticancer, anti-inflammatory, and immunosuppressive treatment, including but not limited to:
- Primary immunodeficiencies with numeric/functional T-cell deficiency
- Acute leukemia, non-Hodgkin's lymphoma, solid tumors, allogeneic HSCT
- Solid-organ transplantation
- Autoimmune- and hyperinflammatory disorders, including treatment with agents that lead to functional T-cell deficiencies

Clinical criteria

- Fever
- Respiratory symptoms including cough, dyspnea, or hypoxemia
- · Bilateral or diffuse GGO on X-ray with interstitial infiltrates as the predominant feature; alveolar, alveolar-interstitial, and unilateral infiltrates are less frequent
- Extensive, mostly diffuse GGO on CT scans, which typically has an upper lobe and perihilar predominance, sometimes with peripheral sparing or a mosaic pattern; consolidations, small nodules, and unilateral infiltrates are less frequent

/licrobiologic

- Visualization of P. jirovecii by microscopy using conventional staining methods (Gomori methenamine silver, Toluidine Blue O, Giemsa, Calcofluor White) or immunofluorescence staining in tissue, BAL fluid, induced sputum, expectorated sputum, or oral wash
- Amplification of P. jirovecii DNA by quantitative real-time PCR in BAL fluid, induced sputum, or oral wash
- Detection of β-p-glucan in serum if another invasive fungal infection and a false-positive result can be ruled out

Abbreviations: BAL, bronchoalveolar lavage; CT, computed tomography; GGO, ground-glass opacity; HSCT, hematopoietic stem cell transplantation; PCR, polymerase chain reaction.

Performances BDG?

Les performances de PCR et du BDG serum en "vraie vie" ?



Étude retrospective 600 patients ID en USI avec recherche PcP

- 115 PcP prouvés/probables
- éléments associées à la PcP:

Terrain: VIH, Lymphome non hodgkinien, Vascularites, Cancer méta

Imagerie: Verres dépolis

Table 5 Performance of serum BDG for the diagnosis of PJP*

Population	PJP (TP/total)	No PJP (TN/ total)	Sensitivity % (95% CI)	Specificity % (95% CI)	PPV % (95% CI)	NPV % (95% CI)	LR+(95% CI)	LR- (95% CI)
All patients	sumptive/proven F 49/57	TJP 192/270	86 (74–94)	71 (65–76)	39 (30–48)	96 (92–98)	3.0 (2.4–3.7)	0.2 (0.1–0.4)
with serum BDG testing**								

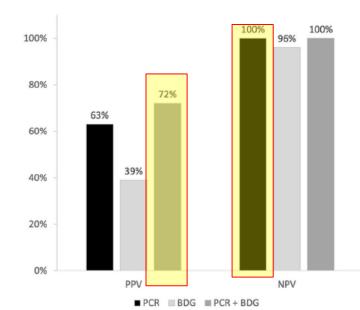


Fig. 2 PPV and NPV for presumptive/proven PJP of serum BDG and respiratory *Pneumocystis* PCR both separately and in combination. BDG, (1,3)-β-D-glucan; NPV, negative predictive value; PCR, polymerase chain reaction; PJP, *Pneumocystis jirovecii* pneumonia; PPV, positive predictive value. Criteria for positivity used

= Utilisation combinée 7 VPP



Performances BDG?

Systematic review

Diagnostic test accuracy of the Fungitell serum $(1 \rightarrow 3)$ - β -D-glucan assay for the diagnosis of *Pneumocystis jirovecii* pneumonia: a systematic review and meta-analysis

Connor Prosty ^{1, *}, Owen Dan Luo ¹, Roy Khalaf ¹, Olivier Del Corpo ¹, Emily G. McDonald ^{2, 3, 4}, Todd C. Lee ^{3, 4, 5}



Results: A total of 26 articles were included comprising 5111 patients and 1150 PCP cases. At the conventional cut-off of 80 pg/mL, the overall pooled sensitivity and specificity were 83.5% (95% 95% CI, 72.8 –90.6) and 75.5% (95% CI, 66.0–83.0), respectively. At a pretest probability of <20% and a BDG <80 pg/mL, the post-test probability would be <5% (negative predictive value > 95%). At 400 pg/mL, sensitivity was reduced to 63.5% (95% CI, 45.8–78.1) with specificity increased to 93.6% (95% CI, 88.6–96.5). At a pretest probability of 47.5%, a BDG >400 pg/mL would have a post-test probability of >90%. Discussion: A categorical approach using <80 pg/mL to rule-out and >400 pg/mL to rule-in PCP may allow for a more nuanced interpretation based on pretest probability. More accurate estimates of pretest probability and further external validation are required. **Connor Prosty, Clin Microbiol Infect 2025;31:542**

Intérêt d'interpréter les résultats en fonction du seuil des BDglucan

- Faible suspicion (<20%): BDG< 80pg/mL permet d'exclure le diagnostic
- Forte suspicion (>50%) : BDG>400pg/mL probabilité >90%
- (80-400) zone d'incertitude ...

Diagnostic: Alternatives?

Clinical Infectious Diseases

MAJOR ARTICLE







Polymerase Chain Reaction on Respiratory Tract Specimens of Immunocompromised Patients to Diagnose *Pneumocystis* Pneumonia: A Systematic Review and Meta-analysis

Lottie Brown, ^{1,®} Riina Rautemaa-Richardson, ^{2,®} Carlo Mengoli, ^{3,®} Alexandre Alanio, ^{4,®} Rosemary A. Barnes, ^{5,®} Stéphane Bretagne, ^{6,®} Sharon C.-A. Chen, ^{7,®} Catherine Cordonnier, ⁸ J. Peter Donnelly, ^{9,®} Werner J. Heinz, ^{10,®} Brian Jones, ^{11,®} Lena Klingspor, ^{12,®} Juergen Loeffler, ¹³ Thomas R. Rogers, ^{14,®} Eleanor Rowbotham. ¹⁵ P. Lewis White, ^{16,®} and Mario Cruciani ^{9,®}

Méta-analyse

- 55 articles, 11 000 PCR, 7800 patients
- o **LBA**: forte Se (98,7%) et Sp 89%
- Crachat induit : haute Se (99%) Sp (81%)
- Aspi NP: Se + faible (89%) et haute Sp 90
- Pas de differences entre VIH + et VIH-

Sample	Sensitivity	Specificity	DOR	LR+	LR ⁻
	(95% CI)	(95% CI)	(95% CI)	(95% CI)	(95% CI)
BALF samples					
qPCR (n = 2673)	0.987	0.893	635	9.194	0.014
	(.968–.995)	(.844–.927)	(269–1498)	(5.727–12.661)	(.001–.027)
cPCR (n = 2254)	0.972	0.954	710	21.178	0.30
	(.932–.988)	(.930–.970)	(305–1652)	(12.438–29.918)	(.004–.056)
IS samples					
qPCR (n = 491)	0.980	0.815	217	5.303	0.024
	(.944–.993)	(.721–.883)	(78–601)	(3.024–7.583)	(.000–.049)
cPCR $(n = 590)$	0.956	0.917	243	11.511	0.047
	(.887–.984)	(.866–.950)	(90–656)	(5.985–17.036)	(.001–.094)
URT samples					
qPCR (n = 352)	0.892	0.905	78	9.340	0.120
	(.710–.965)	(.809–.955)	(26–238)	(2.997–15.682)	(NE245)
cPCR (n = 512)	0.787	0.960	87	19.424	0.222
	(.502–.931)	(.911–.982)	(27–284)	(5.358–33.490)	(NE446)

- -> PCR negative sur prélèvement respiratoire profond permet d'exclure le diagnostic
- -> PCR + à interpreter en fonction du terrain et du type de prélèvement

CID 2024:79 (15 July)

Diagnostic: Alternatives?

Open Forum Infectious Diseases

Comparing Polymerase Chain Reaction Testing of Nasopharyngeal Swab and Lower Respiratory Tract Specimens for the Diagnosis of Pneumocystis jirovecii Pneumonia

Rusheng Chew, 1,2,3,0 Sarah Tozer, 4 Kimberly Ulett, 5 David L. Paterson, 4,6,7 David Whiley. Theo Sloots. David Fielding, 3,8 Christopher Zappala, 3,8 Farzad Bashirzadeh, ⁸ Justin Hundloe, ⁸ Cheryl Bletchley, ⁴ and Marion L. Woods^{3,7}



Clinical Infectious Diseases

MAJOR ARTICLE









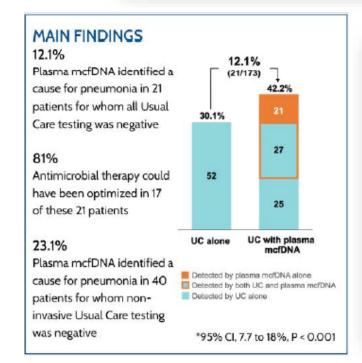
Plasma Microbial Cell-Free DNA Sequencing in Immunocompromised Patients With Pneumonia: A Prospective Observational Study

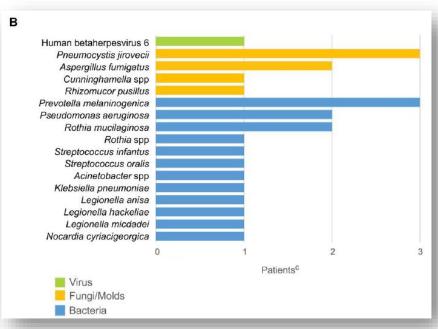
Stephen P. Bergin, ^{1,2} Roy F. Chemaly, ³ Sanjeet S. Dadwal, ⁴ Joshua A. Hill, ^{5,6} Yeon Joo Lee, ^{7,8} Ghady Haidar, ⁹ Alfred Luk, ¹⁰ Alexander Drelick, ^{8,11} Peter V. Chin-Hong, 12 Esther Benamu, 13 Fareed Khawaja, 3 Deepa Nanayakkara, 4 Genovefa A. Papanicolaou, 18 Catherine Butkus Small 811 Monica Fund. 12 Michelle A. Barron, 13 Thomas Davis, 14 Micah T. McClain, 2.15 Eileen K. Maziarz, 15 Deng B. Madut, 15 Armando D. Bedoya, 1 Daniel L. Gilstrap, 1 Jamie L. Todd, 1.2 Christina E. Barkauskas, Robert Bigelow, Jeffrey D. Leimberger, Ephraim L. Tsalik, 15.16.17 Olivia Wolf, Mona Mughar, 18 Desiree Hollemon, Radha Duttagupta, 18 Daniel S. Lupu, 18 Sivan Bercovici, 18 Bradley A. Perkins, 18 Timothy A. Blauwkamp, 18 Vance G. Fowler Jr. 2.15 and Thomas L. Holland 2.15.0



Table 1. Participant Characteristics

Chamatariatia	Patients, No. (%) ^a			
Characteristic	With PJP (n = 71)	Without PJP (n = 40)		
Age, median (IQR), y	66 (55–72)	62 (46–73)		
Sex				
Male	32 (45.1)	19 (47.5)		
Female	39 (54.9)	21 (52.5)		
Immunosuppression type				
Hematological cancer or transplant	13 (18.3)	14 (35.0)		
Solid organ cancer	28 (39.4)	7 (17.5)		
Solid organ transplant	3 (4.2)	7 (17.5)		
HIV positive status	11 (15.5)	1 (2.5)		
Other iatrogenic immunosuppression	14 (19.7)	4 (10.0)		
Other noniatrogenic immunosuppression	2 (2.8)	7 (17.5)		
NP swab <i>Pneumocystis jirovecii</i> PCR result				
Negative	24 (33.8)	40 (100.0)		
Positive	47 (66.2)	0 (0.0)		





Bonne spécificité, mauvaise sensitibilité (0.66) QUID de la colonisation?

Semble Se et Sp mais faible niveau de preuve .. Défis technique ++

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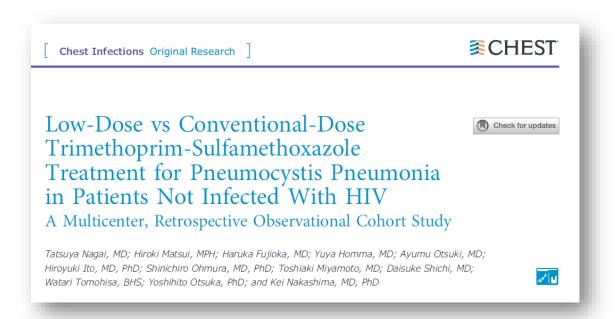
LA PRÉVENTION

LES TRAITEMENTS (VIH)

Pneumocystose : traite	ement curatif			
Traitement de 21 j Diagnostic certain : sig	nes fonctionnels respiratoires et dia	ngnostic fongique/histologique sur crachat	(Se ≥ 80 %), LBA (Se ≥ 90 %)	
	CD4<200/mm ³ et détresse respirato onse au traitement anti-PCP	ire aiguë et radiographie compatible ; pas	de mise en évidence d'autre documer	ntation
Première intention	TMP-SMZ	15/75 mg/kg/j en 3 prises IV (sans dépasser 12 ampoules/j)	Forme orale possible dans les formes modérées sans dépasser 6 cp à 160/800 mg/j	Morlat (AI) EACS IDSA (AI)
	Prednisone	60 à 80 mg/j en 2 prises de j1 à j5, puis 40 mg/j de j6 à j10 et 20 mg/j de j11 à j21	À initier précocement dans les 72 premières heures si PaO ₂ < 70 mmHg ou gradient PaO ₂ /PaO ₂ > 35 mmHg	Morlat (AI) EACS IDSA (AI)
Alternative : formes modérées à sévères	Primaquine+clindamycine	30 mg/j + 3 × 600–900 mg/j (IV ou per os)	En absence de déficit en G6PD	EACS IDSA (AI)
	Pentamidine IV	4 mg/kg/j IV ou IVSE	À privilégier dans les formes sévères	Morlat (AI) EACS IDSA (AI)
Formes réfractaires	Association caspofungine		À discuter en cas de non-réponse au traitement	EACS
Alternatives : formes peu sévères	Primaquine + clindamycine	30 mg/j + 3 × 600–900 mg/j (IV ou per os)	En absence de déficit en G6PD	EACS IDSA (BI)
ped services	Atovaquone	750 mg x 2/j per os	À privilégier dans les formes non sévères en cas de contre-indication au Bactrim®	Morlat (AI) EACS IDSA (BI)
	Dapsone + triméthoprime	100 mg/j + 15 mg/kg/j	En absence de déficit en G6PD	EACS IDSA (BI)



Les (fortes) doses et durée de Bactrim?





Études retrospectives chez non HIV

- 7.5–15 mg TMP/kg/day (reduced dose) Versus 15–20 mg TMP/kg/day (standard dose)
- Critères cliniques et mortalité **équivalentes**
- Moins de toxicité (nausées et hypona)
- ⇒ Études prospectives nécéssaires pour conclure chez qui cela serait pertinent ++
- ⇒ Aucune étude sur la durée : 21 jours VIH, 14 jours hors VIH (ECIL6) ?

La place de la corticothérapie ?

Adjunctive corticosteroids in non-AIDS patients with severe Pneumocystis jirovecii pneumonia (PIC): a multicentre, double-blind, randomised controlled trial



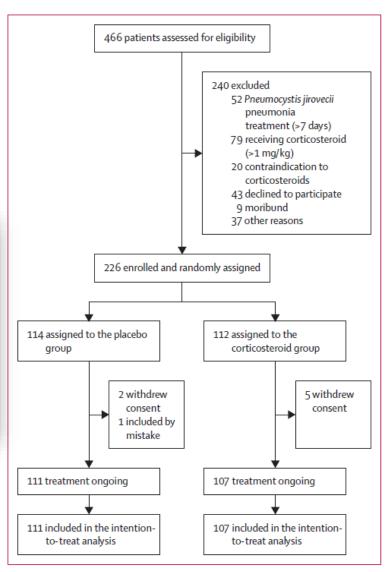
Virginie Lemiale, Matthieu Resche-Rigon, Yoann Zerbib, Djamel Mokart, Nicolas De Prost, Florent Wallet, Pierre Perez, Achille Kouatchet, Laurent Argaud, Maxens Decavèle, édéric Pène, Amelie Seguin, Bruno Megarbane, Laure Calvet, Muriel Picard, Guillaume Rigault, Eric Mariotte, Lila Bouadma, Igor Theodose, Fabienne Tamion, Kada Klouche, Gwenhael Colin, Martine Nyunga, Anne-Sophie Moreau, Elie Azoulay

	Placebo group (n=111)	Corticosteroid group (n=107)	Mean difference (95% CI)	p value
Primary endpoint				
All-cause 28-day mortality	36 (32·4%; 23·9 to 42·0)	23 (21·5%; 14·1 to 30·5)	10·9% (-0·9 to 22·5)	0.069
Secondary endpoints				
Mortality in the ICU*†‡	39 (30·8%; 22·1 to 39·6)	25 (22·8%; 14·6 to 31·0)	8·1% (-3·9 to 20)	0.079
Mortality in hospital‡	43 (31·5%; 22·9 to 40·2)	26 (21·5%; 13·7 to 29·3)	10.0% (-1.6 to 21.7)	0.028
All-cause 90-day mortality*	48 (43·2%; 33·2 to 51·8)	30 (28·0%; 19·0 to 36·1)	15·2% (2·7 to 27·8)	0.022
Invasive ventilation*‡§	18 (26·1%; 15·6 to 36·5)	6 (10·1%; 2·3 to 17·7)	16.5% (3.5 to 29.5)	0.020

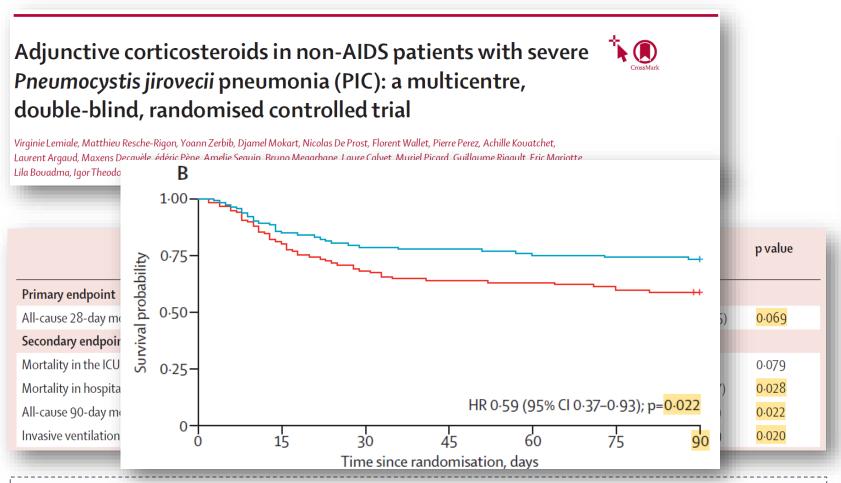
Mortalité

- O D28: **NON significativement** différente (21.5% vs 32.4%, p= 0.069)
- o D90 et la durée de ventilation, en faveur de la corticothérapie
- o Pas plus d'infection ni d'insuline
- Analyse post-hoc, plus de bénéfice chez les patients hors onco-hémato

Lancet Respir Med 2025



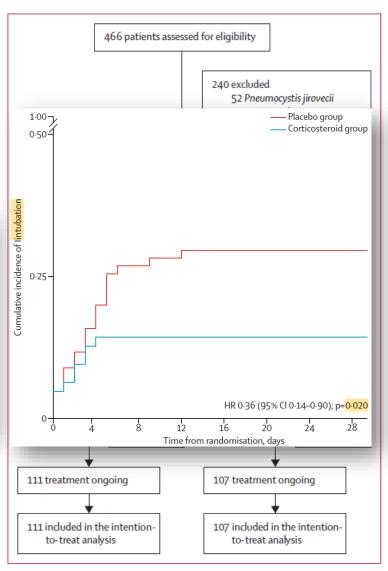
La place de la corticothérapie ?



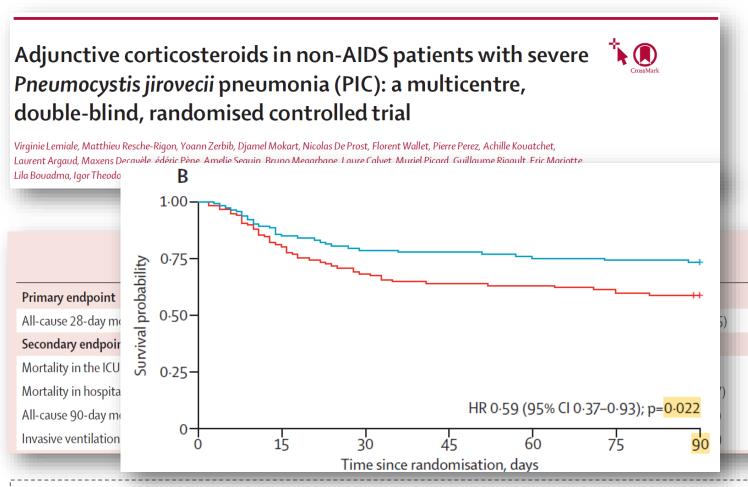
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Lancet Respir Med 2025



La place de la corticothérapie ?

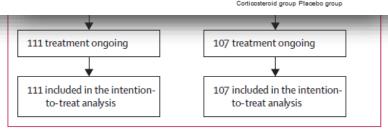


Lancet Respir Med 2025



Mortalité

- O D28: **NON significativement** différente (21.5% vs 32.4%, p= 0.069)
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Projet PNEUMOCYSTIS: création de cohorte multicentrique de PcP

Cohorte multicentrique retrospective dans 3 hopitaux en France

Tous les patients admis avec un **PcP prouvée ou probable diagnosis** (critères EORTC)







- Présence de Kystes à l'examen direct => "PcP prouvé"
- qPCR PJ + => "PcP probable"

= 481 patients inclus

De Janvier 2011 à December 2021



Dr Nahéma Issa, Fabrice Camou, Pr Florent Morio, Dr Benoit Tessoulin Dr Romain Lécuyer, Dr Florian Reizine

Objectifs : Evaluation épidémiologique et des facteurs pronostiques

Analyse « macro » non supervisée des données

Should We Reconsider *Pneumocystis* Pneumonia Presentation and Treatment According to Its Underlying Disease?

An Unsupervised Cluster Analysis of a Retrospective Multicenter Study

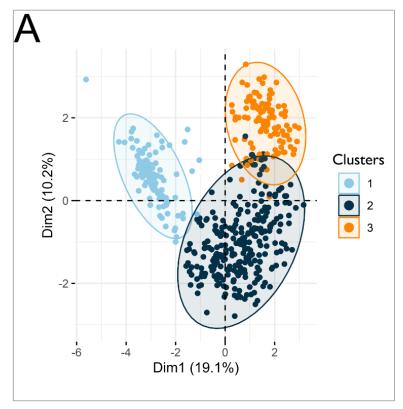
 $\underline{\text{Benjamin Gaborit, MD, PhD}} \overset{\text{q,b}}{\sim} \underline{\boldsymbol{\boxtimes}} \cdot \underline{\boldsymbol{\boxtimes}} \cdot \underline{\boldsymbol{\boxtimes}} \cdot \underline{\boldsymbol{\wedge}} \underline$

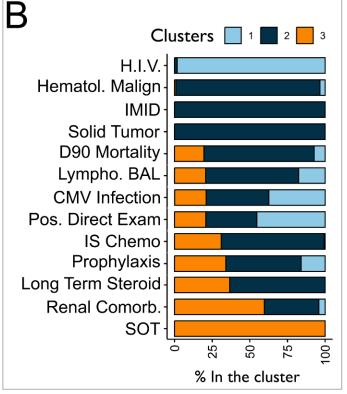
Rose-anne Lavergne, PharmD, PhD c,d · Frederic Gabriel, MD, PhD g · Florent Morio, PharmD, PhD c,d ·

Emmanuel Canet, MD, PhD $^{\rm h}$ · François Raffi, MD, PhD $^{\rm a}$ · David Boutoille, MD, PhD $^{\rm a,b}$ · Anne Cady, PharmD $^{\rm i}$ ·

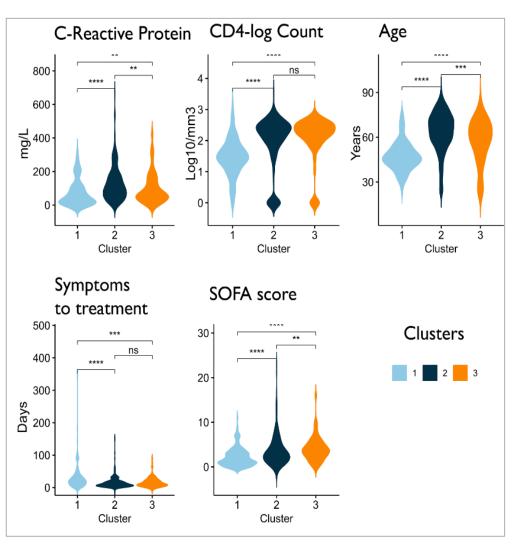
Marie Gousseff, MD $^{\rm i}$ · Yoann Crabol, MD $^{\rm i}$ · Antoine Néel, MD, PhD $^{\rm j,k}$ · Benoît Tessoulin, MD, PhD $^{\rm l}$ ·

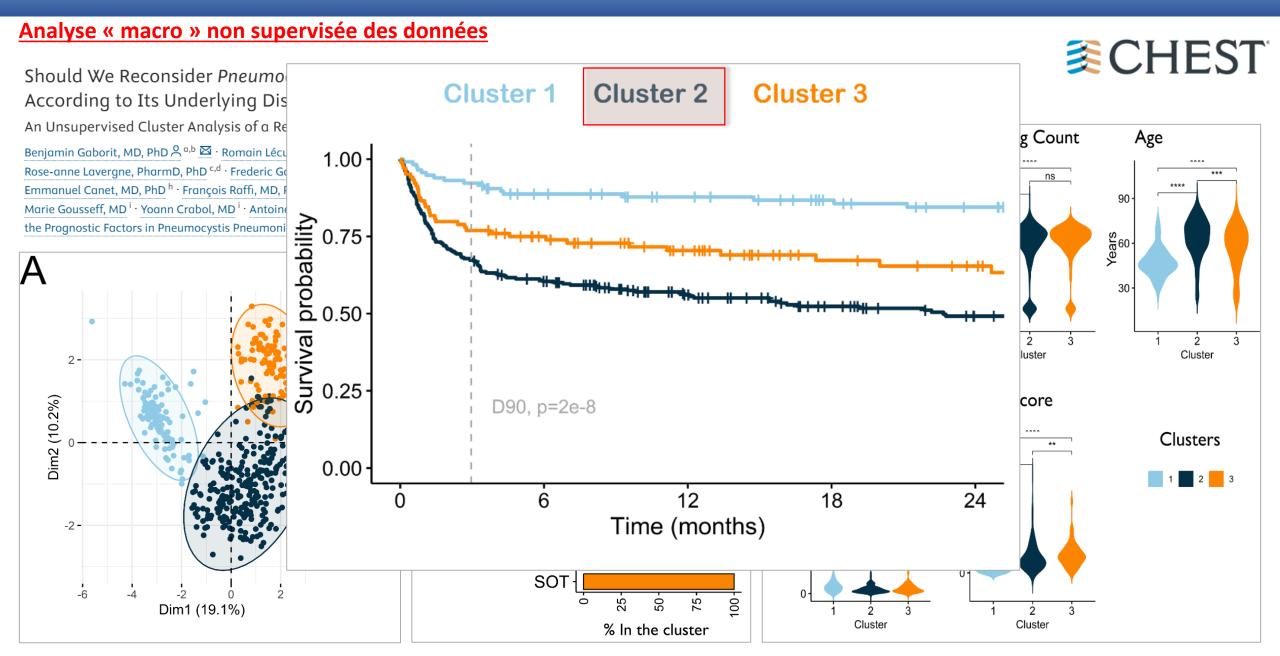
the Prognostic Factors in Pneumocystis Pneumoniae (PRONOCYSTIS) Study Group * Show less











Résultats : Analyse Détailée de la cohotre

ORIGINAL RESEARCH | ARTICLES IN PRESS Characteristics and prognosis factors of *Pneumocystis jirovecii* pneumonia according to underlying disease: a retrospective multicentre study Romain Lécuyer, MD PharmD ↑ • Nahéma Issa, MD ↑ • Fabrice Camou, MD • ... Benoît Tessoulin, MD PhD • 8,508 respiratory samples (induced sputum, bronchial aspiration or BAL) screened for P jirovecii between January 2011 and December 2021 1,238 patients tested positive for *P jirovecii* (qPCR or direct examination) 730 patients with *P jirovecii* airway colonisation 508 patients with *P jirovecii* pneumonia (PcP, proven/probable) 9 patients < 18 years 18 patients with missing data 481 patients with proven or probable PcP 114 HIV-positive patients 367 HIV-negative patients

Over the 10-year **481 patients** with PcP:

- 180 (37.4%) **proven** PcP
- 301 (62.6%) **probable** PcP

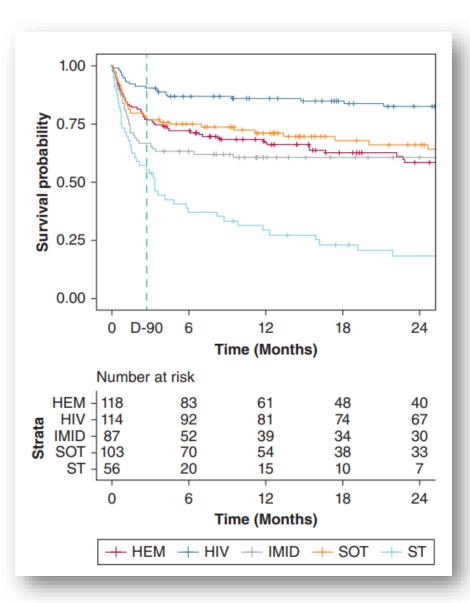
Table 1. Characteristics of Patients (N = 481)

TABLE 1] Characteristics of Patients at the Time of Diagnosis of PcP and Follow-up ($N = 481$)			
Characteristic	Value		
Age, y	58.2 ± 14.7		
Male	306 (63.6)		
BMI, kg/m ²	22.94 ± 9.7		
Albumin, g/L	27.7 ± 13.9		
Chronic underlying disease			
Chronic kidney disease	166 (34.5)		
Chronic pulmonary disease	101 (21.0)		
Underlying cause of immunodeficiency			
Hemotologic malignancy	118 (24.5)		
Acute leukemia	34 (7.1)		
Lymphoma	32 (6.7)		
Chronic lymphoid leukemia	25 (5.2)		
Multiple myeloma	15 (3.1)		
Myelodysplastic syndrome	10 (2.1)		
Chronic myelomonocytic leukemia	2 (0.4)		
Allogeneic HSCT	32 (6.7)		
Autologous HSCT	9 (1.9)		
HIV infection	114 (23.7)		
Therapeutic rupture	68 (14.1)		
Discovery of HIV-positive status	46 (9.6)		
Solid organ transplantation	103 (21.4)		
Immune-mediated inflammatory	87 (18.1)		
disease			
Solid tumor	56 (11.6)		

Positive sputum/BAL direct examination (cysts in smears)	180 (37.4)
Prophylaxis prescribed	50 (10.4)
Aerosolized pentamidine	15 (3.1)
TMP-SMX	25 (5.2)
Atovaquone	9 (1.9)
Prophylaxis observance during the last 2 mo	26 (5.4)
Aerosolized pentamidine	11 (2.3)
TMP-SMX	8 (1.7)
Atovaquone	6 (1.2)
Time from symptom onset to, d	
Hospitalization	14.3 ± 27.6
Anti-Pneumocystis treatment	
TMP-SMX	443 (92.1)
Atovaquone	95 (19.8)
IV pentamidine	12 (2.5)
Respiratory support	396 (82.3)
Mechanical ventilation	109 (22.7)
Exclusive noninvasive ventilation	15 (3.1)
Exclusive high-flow nasal oxygen therapy	44 (9.2)
Exclusive simple nasal oxygen therapy	190 (39.5)
Adjunctive corticotherapy	226 (47.0)
In-hospital mortality	102 (21.2)
90-d mortality	123 (25.6)



Quid des traitements IS et de l'impact des pathologies sous-jacentes ?



->Corticoides (n = 232) chez 63.2% des patients, en moyenne 29.2 mg/J prednisone equivalent

Facteurs pronostiques (90-Day Mortality)?

TABLE 2 Underlying Conditions Associated With 90-Day Mortality in the Overall Population (N = 481)

Univariate Analysis			
Parameter	OR	95% CI	P Value
Characteristic			
Age	1.04	1.02-1.05	< .001
Male	0.90	0.52-1.54	.625
Albuminemia ≤ 30 g/L ^a	3.40	1.89-6.10	< .001
Immunodeficiency			
HIV infection	0.24	0.13-0.47	< .001
Hematologic malignancy	0.88	0.54-1.43	.597
Solid tumor	3.19	1.80-5.65	< .001
Solid organ transplantation	0.86	0.51-1.43	.551
Immune-mediated inflammatory disease	1.94	1.18-3.18	.008
Immunosuppressive drug exposure			
Long-term corticosteroid therapy	2.58	1.68-3.96	< .001

^aItem with > 30% missing values.



Facteurs de mortalité D90 ?

TABLE 3 Factors Associated With 90-Day Mortality in the HIV-Negative Population

	Univariate Analysis (n = 367)		Multivariate Analysis (n = 315)			
Parameter	OR	95% CI	P Value	OR	95% CI	P Value
Characteristic						
Age	1.02	1.00-1.04	.023	1.01	0.99-1.03	.401
Male	0.90	0.52-1.54	.874			
Albuminemia < 30 g/L ^a	4.36	2.33-8.18	< .001			
Chronic kidney disease	0.88	0.56-1.39	.594			
Chronic pulmonary disease	1.10	0.66-1.82	.713			
Immunodeficiency						
Hematologic malignancy	0.61	0.37-1.00	.052			
Solid tumor	2.48	1.39-4.42	.002	5.47	2.16-14.1	< .001
Solid organ transplantation	0.61	0.36-1.03	.061			
Immune-mediated inflammatory disease	1.46	0.88-2.42	.146	2.19	1.05-4.60	.037
Connective tissue diseases	1.57	0.68-3.61	.286			
Immunosuppressive drug exposure	1.59	0.70-3.60	0.265			
Long-term corticosteroid	1.67	1.03-2.71	.035	2.07	1.03-4.31	.045
Steroid daily dose ≥ 10 mg	1.80	1.14-2.85	.010			
Sputum/BAL examination ^b						
Positive direct examinations (cysts in smears) ^c	1.99	1.22-3.24	.005	1.92	1.02-3.62	.043
Neutrophilic BAL profile ^a	3.23	1.65-6.34	.001			
Macrophagic BAL profile ^a	1.19	0.63-2.22	.598			
Lymphocytic BAL profile ^a	0.25	0.11-0.52	< .001			
CMV respiratory coinfection a, d	5.23	2.63-10.4	< .001			
Laboratory findings						
Neutrophils ≥ 7,500/mm ³	1.52	0.93-24.48	.092			
$CD4 \ge 200/mm^{3a}$	1.04	0.46-2.33	.930			
CRP ≥ 100 mg/L ^e	1.79	1.11-2.90	.017			
LDH ≥ 400 ^a	2.76	1.13-6.76	.024			
Severity						
SOFA	1.50	1.35-1.70	< .001	1.58	1.39-1.82	< .001
ICU admission	3.42	2.17-5.51	< .001			

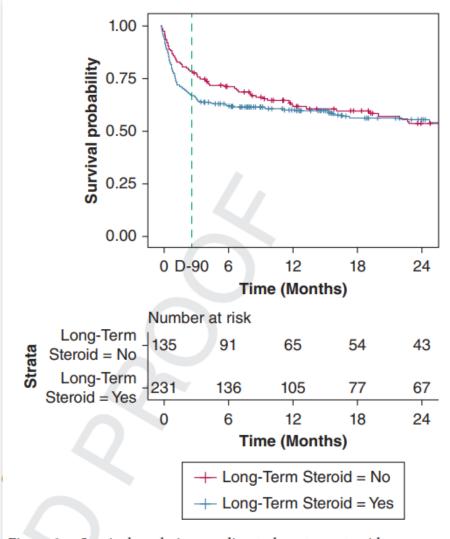
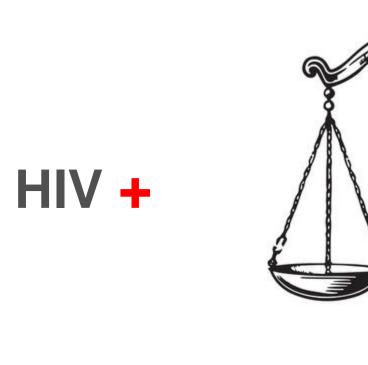


Figure 3 – Survival analysis according to long-term steroid exposure prior to Pneumocystis jirovecii pneumonia diagnosis in patients who are HIV-negative. $D90 = day\ 90$.





Examen directe positif (sputum/BAL) 69.3%

Sans association avec la mortalité 90-day(P.394)

Ni avec le profil neutrophilique au LBA (P = .317)

= Forte proliferation sans inflammation

Examen direct **positif 27.5%**Associé à la mortalité 90-day (*P*.016)
Associé à un profil **neutrophilique au LBA** (*P*.059)

= Forte proliferation <u>et inflammation délétère</u>



Messages (1):



<u>La prophylaxis PcP</u> est TROP rare pour les 2 populations les + graves :

- IMIDs 5.7% (PR, Sarcoïdose, dermato-myosite, ANCA)
- Tumeurs solide 1.8%



les patients IMIDs les plus graves ++

Admission à hospital précocement (2.8 vs 15.8 days, P = .037) Grave (SOFA score 6.9 vs 2.8, P < .001), Mais avec le délais au TTT de la PcP + long (7.6 vs 3.9 days, P = .027),

- -> Elargir les indications de prophylaxis pour les IMIDs +++
- -> Débuter précocément le traitment anti-PcP en cas de pneumonie sévère évocatrice
- -> Impact du terrain => maladies différentes, un traitement personnalisé?



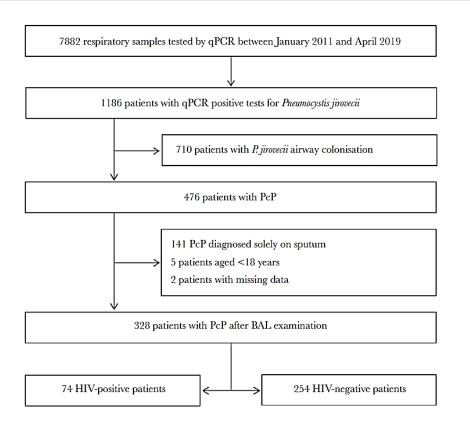
The Journal of Infectious Diseases

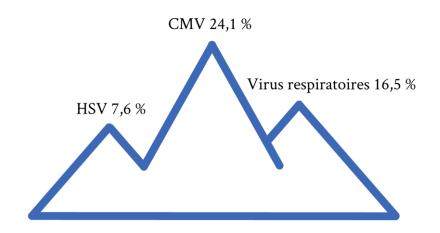
MAJOR ARTICLE



Epidemiology and Clinical Impact of Respiratory Coinfections at Diagnosis of *Pneumocystis jirovecii* Pneumonia

Romain Lécuyer,^{1,2,a} Nahema Issa,^{3,a} Benoit Tessoulin,⁴ Rose-Anne Lavergne,^{2,5} Florent Morio,^{2,5,0} Frederic Gabriel,⁶ Emmanuel Canet,⁷ Céline Bressollette-Bodin,⁸ Aurélie Guillouzouic,³ David Boutoille,^{1,10} François Raffi, ¹ Raphael Lecomte, ¹ Paul Le Turnier, ¹ Colin Deschanvres, ^{1,0} Fabrice Camou, ³ and Benjamin Jean Gaborit, ^{1,10}; PRONOCYSTIS Study Group





- 328 patients avec LBA
- 54% de co-infections
 - 38% **virales** (29% CMV)
 - 23% bactériennes (S.aureus, Pyo)
 - 11% fongiques

The Journal of Infectious Diseases

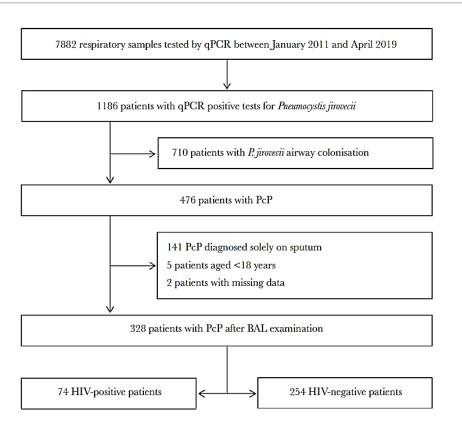
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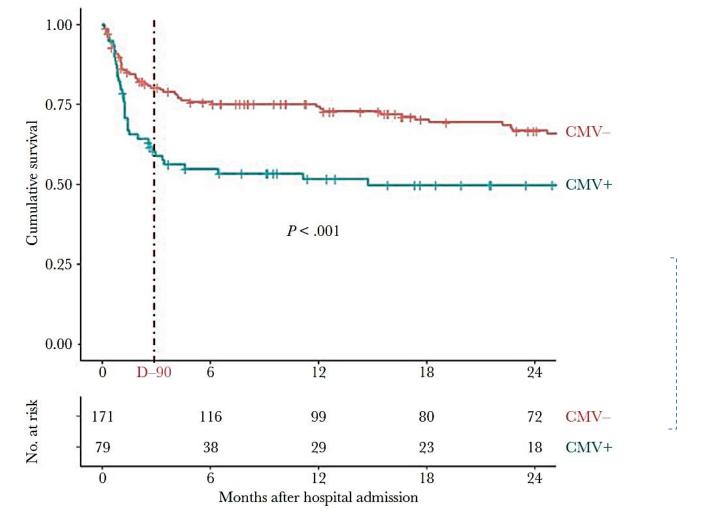
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Impact des co-infections?

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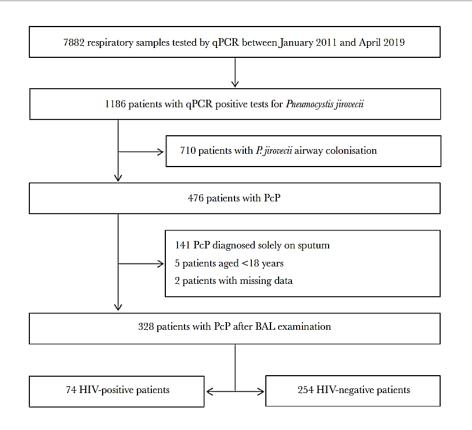
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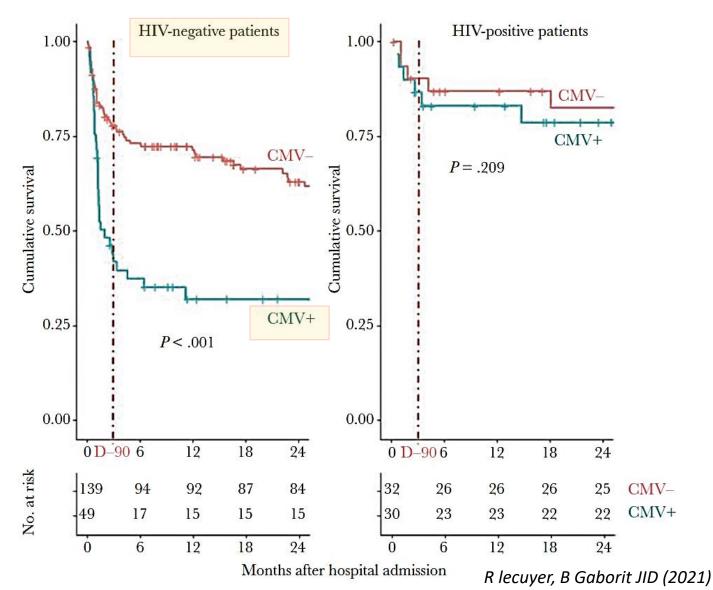
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Months after hospital admission



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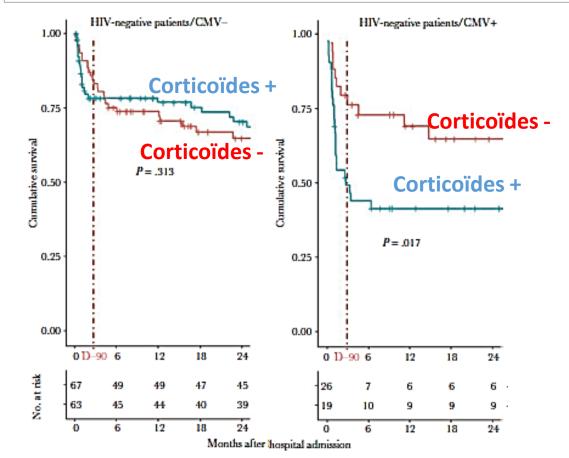
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MAJOR ARTICLE



Epidemiology and Clinical Impact of Respiratory Coinfections at Diagnosis of *Pneumocystis jirovecii* Pneumonia

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Corticothérapie associée à la mortalité des patients avec CMV+ (non VIH)

= Marqueur probable d'ID?

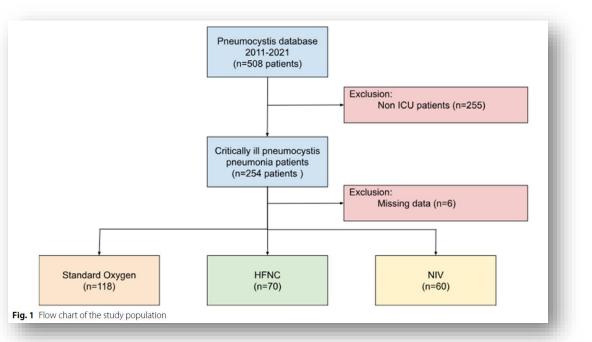
	Univariate Analysis (n = 254)				
Parameter	OR (95% CI)	P			
Characteristics					
Age ≥ 55 y	1.28 (.62-2.66)	.502			
Male	1.31 (.68-2.53)	.414			
BMI < 18.5	0.99 (.30-3.27)	.988			
Chronic kidney disease	1.46 (.76-2.82)	.255			
Chronic pulmonary disease	1.47 (.74-2.94)	.268			
Immunodeficiency					
Hematologic malignancy	0.46 (.2395)	.033			
Solid tumor	0.27 (.06-1.20)	.067			
Solid organ transplant	1.60 (.80-3.20)	.181			
Connective tissue disease	2.48 (1.15-5.33)	.018			
Immunosuppressant	2.28 (.64-8.11)	.192			

+ de CMV si corticothérapie préalable = marqueur d'IS?

RESEARCH Open Access

Respiratory management of critically ill pneumocystis pneumonia patients: a multicenter retrospective study

Florian Reizine^{1*}, Vicky Stiegler², Romain Lécuyer^{3,4}, Benoit Tessoulin⁵, Marie Gallais¹, Fabrice Camou⁶, Florent Morio⁷, Anne Cady⁸, Frederic Gabriel⁹, Emmanuel Canet¹⁰, François Raffi², David Boutoille^{2,11}, Nahéma Issa⁶, Benjamin Gaborit^{2,11,12*} and the PRONOCYSTIS Study Group



Annals of Intensive Care

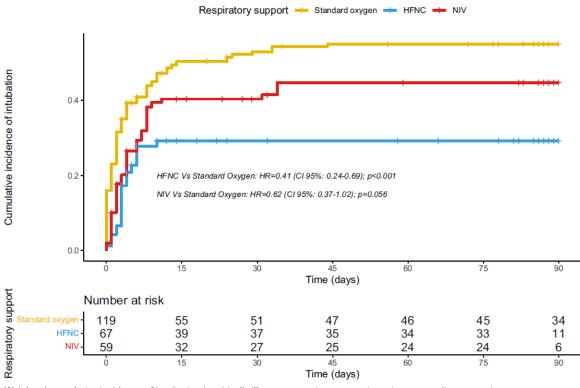


Fig. 2 Weighted cumulative incidence of intubation in critically ill pneumocystis pneumonia patients according to respiratory management

Conclusion Through this multicenter observational study of severe PjP patients, although oxygenation strategy was not associated with D90 survival, HFNC support appeared to be associated with a lower intubation rate. Further prospective studies are warranted to refine respiratory management in critically ill PjP patients.

PLAN

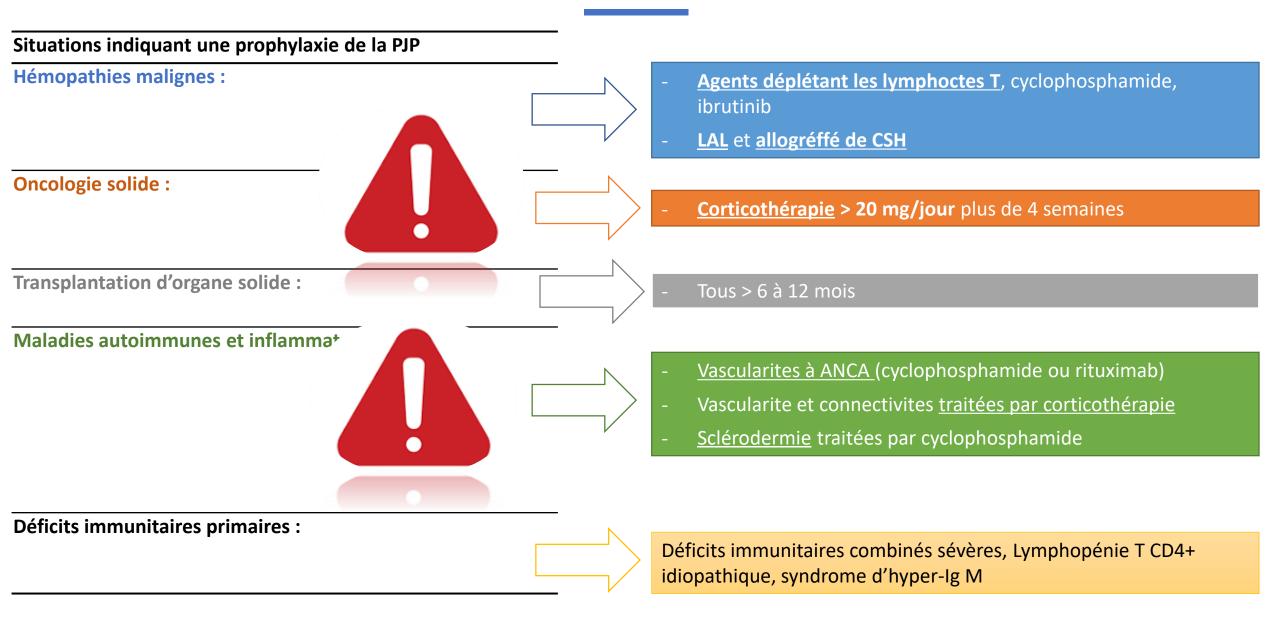
POURQUOI S'INTÉRESSER À LA DE PNEUMOCYSTOSE EN 2024 ?

LES SPÉCIFICITÉS DE LA PNEUMOCYSTOSES (HORS VIH) ?

LES MODALITÉS DIAGNOSTIC ET DU TRAITEMENT EN 2024

LA PRÉVENTION

PROPHYLAXIE: quels patients à risque?



Take Home Message

- Pneumocystose à rechercher (et à traiter) au cours des détresses respiratoires <u>sévères de l'ID</u>
- Les formes de PcP non liées au VIH = Diagnostic difficile et pronostic plus péjoratif
 - TDM thoracique et LBA : pour le diagnostic
 - PCR couplée au BDG: pour identifier les colonisations
 - Maladies auto-immune: pronostic plus sombre, plus de Ctc et de co-infection CMV
- Indications de la Corticothérapie hors VIH => Oui précocement sur les formes sévères
 - Rechercher les co-infections (50% des patients) et les traiter ++
- Développement d'outils diagnostiques : NGS, écouvillons NP
- Prophylaxie à discuter si majoration de l'ID d'un patient (bolus de corticoïde), oncologie, IMIDs (PR, Sarcoïdose, dermato-myosite)..

Merci pour votre attention







Merci de votre attention

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