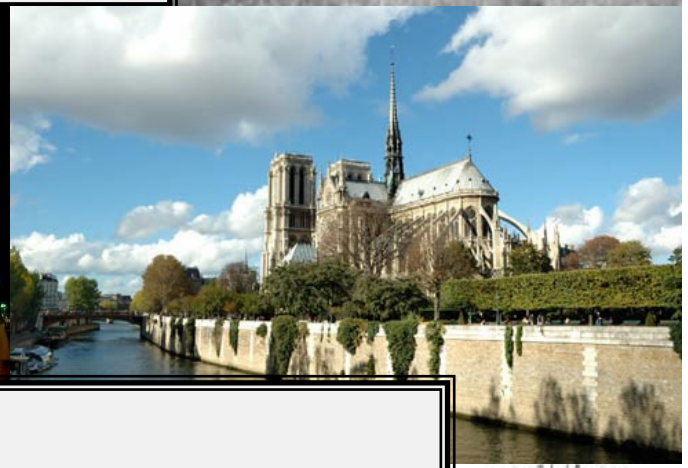
Stratégies Diagnostiques des Infections Pulmonaires du Malade d'Hématologie



É AZOULAY,

Réanimation Médicale Hôpital St-Louis, Univ. Paris 7, France.

Groupe de Recherche Respiratoire en Réanimation des patients Onco-Hématologiques (GRRR-OH).

Groupe de recherche Famiréa®. INSERM U517

ARF in Hematology Patients

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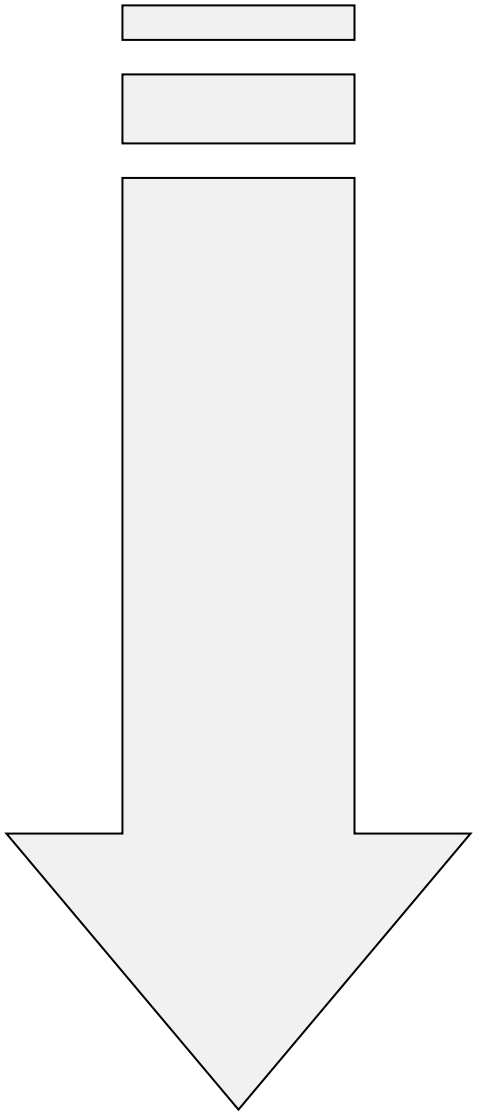
1. A major concern



- ❖ 5% ➢ Oncology patients
- ❖ 10-20% ➢ Hematology patients
- ❖ 40% ➢ Neutropenia
- ❖ 50% ➢ BMT / SCT
- ❖ 50-90% ➢ Mortality (mechanical ventil.)

The Prognosis of Acute Respiratory Failure in Critically Ill Cancer Patients

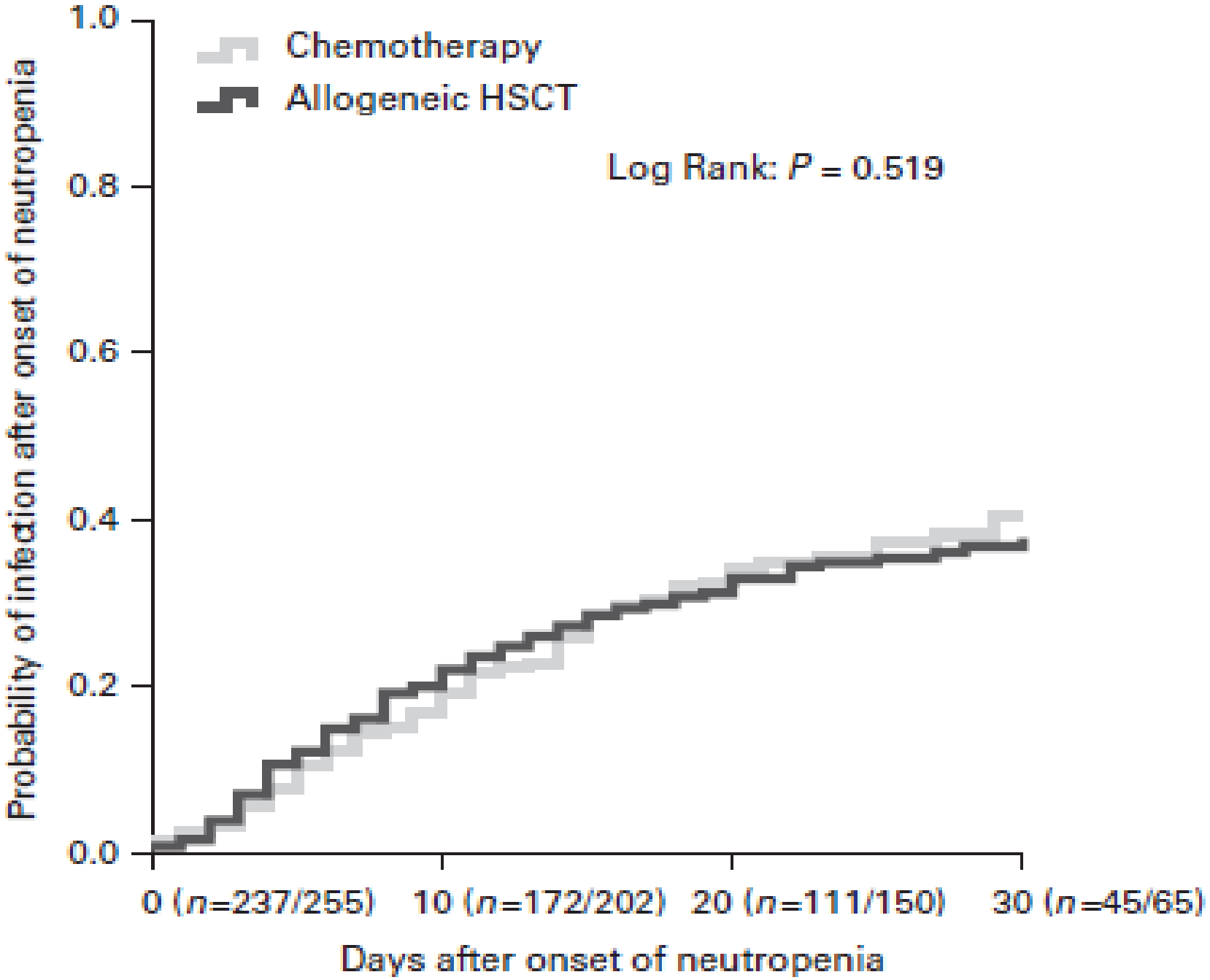
Élie Azoulay, MD, PhD, Guillaume Thiéry, MD, Sylvie Chevret, MD, PhD, Delphine Moreau, MD, Michaël Darmon, MD, Anne Bergeron, MD, PhD, Kun Yang, MD, Véronique Meignin, MD, Magali Ciroldi, MD, Jean-Roger Le Gall, MD, Abdellatif Tazi, MD, PhD, and Benoît Schlemmer, MD

(*Medicine* 2004;83:360–370)

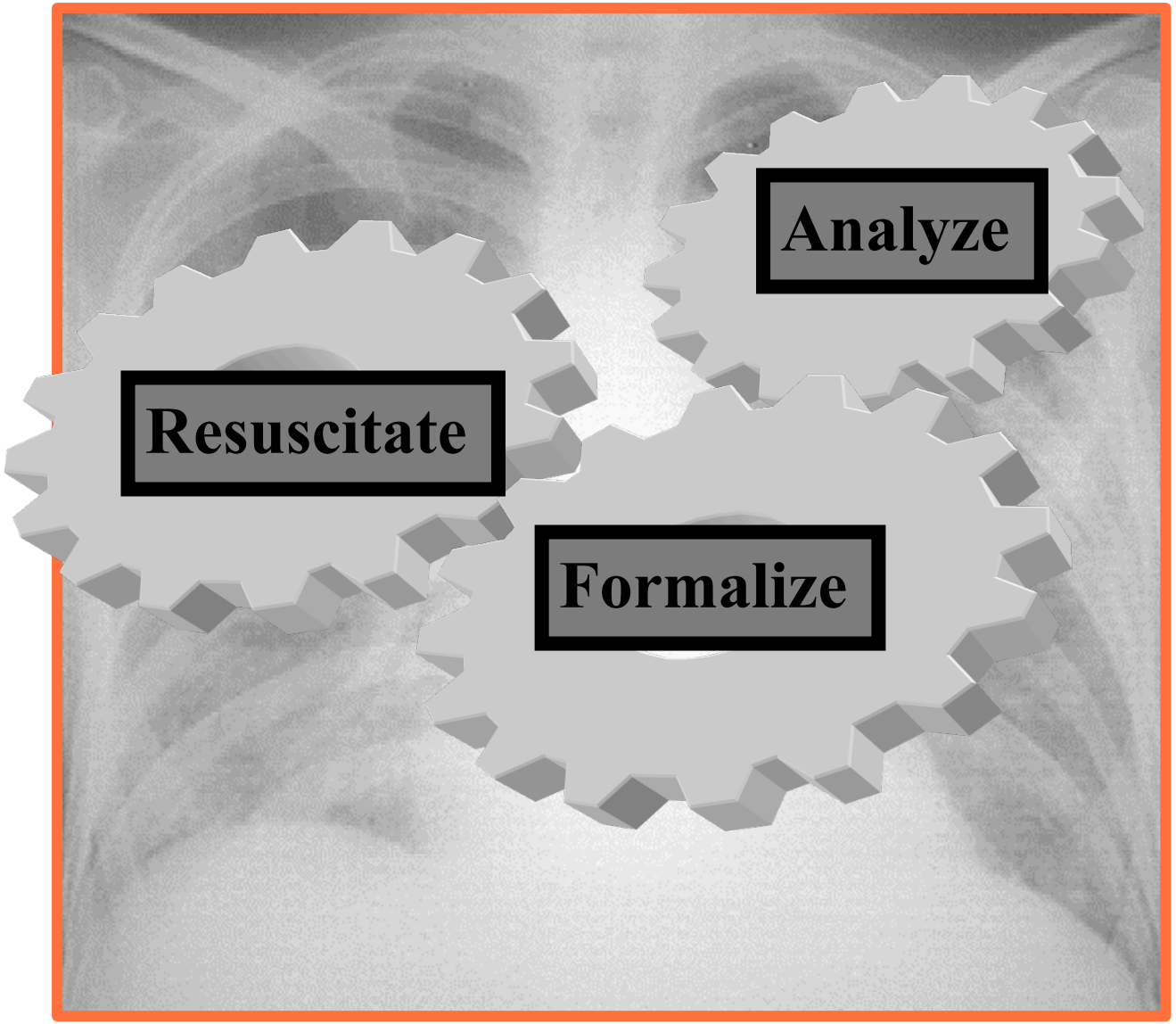
Hôpital	Réanimation	Mortalité H
100 LMC	12 (12)	3 (25)
520 LA	62 (12)	30 (49)
262 Myélome	27 (10.3)	15 (55)
600 Lymphome	48 (8)	21 (44)
150 LLC	11 (7.3)	6 (55)
200 Hodgkin	12 (6)	5 (42)
200 Divers hémato	12 (6)	6 (50)
500 KBP	10 (2)	6 (60)
1250 Sein	9 (0.7)	5 (55)
3782 patients	203 (5.4%)	97 (47.7%)

Respiratory events in patients with hematology malignancies

Auteur	Patients	Incidence	Délai	Analyse	Mortalité
Azoulay 2004 Medicine	Tous	7-12% (203/3782)	~	Diagnostic non identifié	47.7%
Puig. 2007 Leuk Lymphoma	Auto-BMT	15% (49/326)	J11	Myélome Neutropénie	51% vs. 8%
Specchia 2003 Leuk Lymphoma	LA	27.7% (80/288)	/	LAM>LAL No remission	Age Sortie d'aplasie
Chaoui 2004 Leukemia	LA	46% (30/65)	/	Admission en réa	35% vs. 6%


1.0
0.8
0.6
0.4
0.2
0.0
Probability of infection after onset of neutropenia
Chemotherapy
Allogeneic HSCT
Log Rank: P = 0.519
0 (n=237/255)
10 (n=172/202)
20 (n=111/150)
30 (n=45/65)
Days after onset of neutropenia

ARF: Analyze, resuscitate, formalize.



Intensive Care Med
DOI 10.1007/s00134-006-0129-2

REVIEW

Élie Azoulay
Benoît Schlemmer

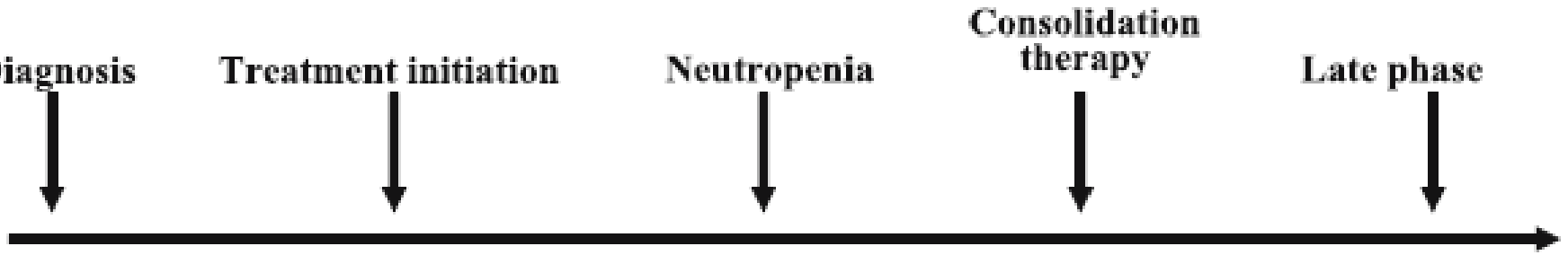
Diagnostic strategy in cancer patients with acute respiratory failure

The DIRECT approach: a guide to select initial antimicrobial treatments and appropriate investigations

Delay since malignancy onset or BMT
Patterns of **I**mmune deficiency
Radiographic appearance
Clinical **E**xperience and knowledge of the literature
Clinical picture
Findings by the high resolution computed **T**omodensitometry (HRCT)

DIRECT D. Delay

AH: alveolar hemorrhage



Diagnosis	Treatment initiation	Neutropenia	Consolidation therapy	Late phase
Infiltration/Lysis	Lysis syndrome Capillary leak syndrome	Severe sepsis	Toxicity	Infiltration Second cancer Toxicity
AH	AH	AH	AH	AH
Overload	Overload	Overload	Overload	Overload
Infections	Infections	Infections	Infections	Infections

Le Poumon leucémique:

François Vincent (Avicenne)

- **Pulmonary leukostasis**
  -
  -

    related to hyperviscosity, leukocytic microthrombi, oxygen steal and hypoxia.

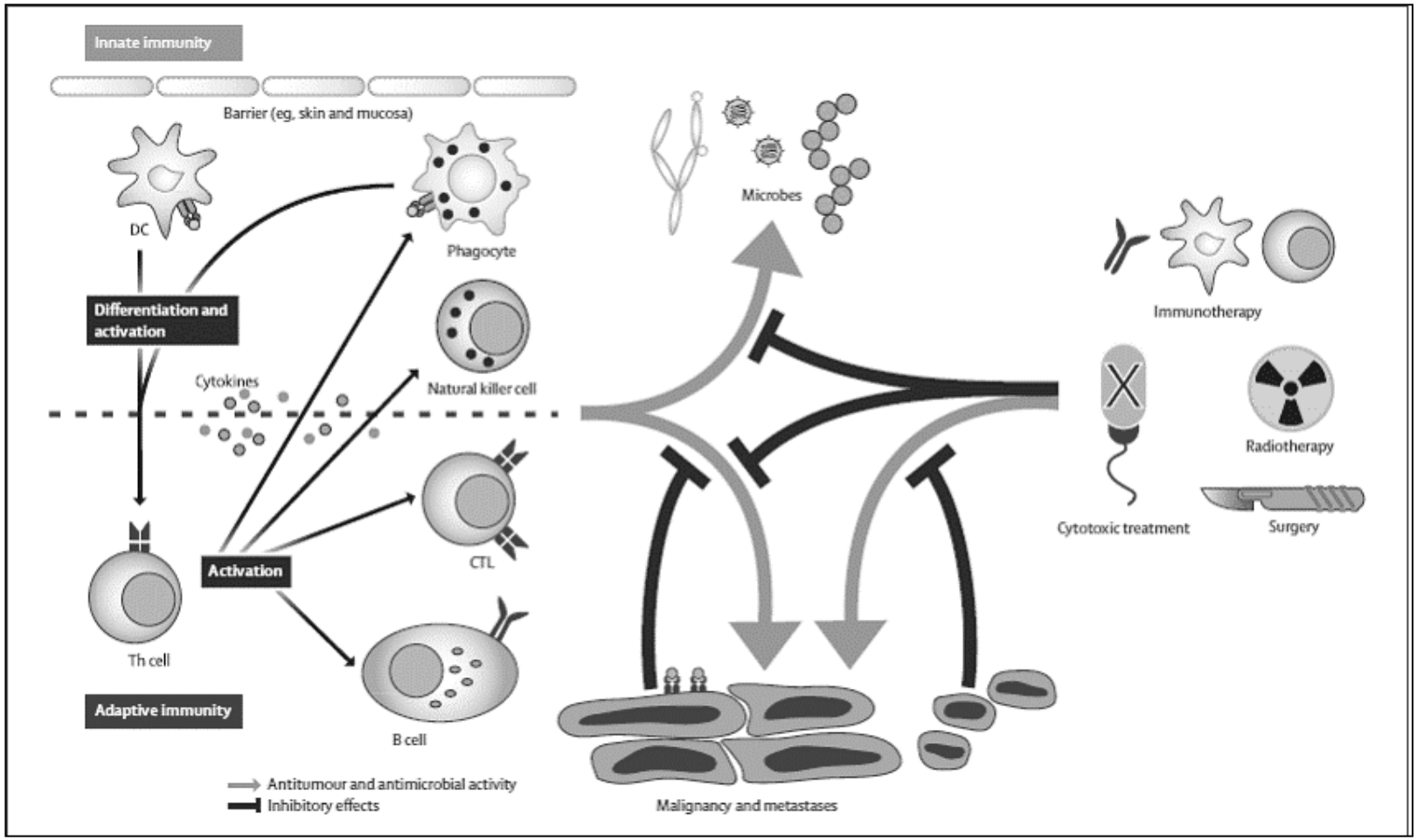
- **Leukemic pulmonary infiltrates**
  - **Blasts are aggregated in vascular lumens**
  - **The infiltrates typically follow the lymphatic routes along the bronchovascular bundles, interlobular septa, and pleural interstitial tissue.**

- **Lysis pneumopathy**
  - **occurs immediately or early after chemotherapy**
  - **Diffuse alveolar damage**

Changes in host defence induced by malignancies and antineoplastic treatment: implication for immuno-therapeutic strategies

Lancet Oncol 2008; 9: 269–78

Thomas Lehrnbecher, Ulrike Koehl, Boris Wittekindt, Konrad Bochennek, Lars Tramsen, Thomas Klingebiel, Stephen J Chanock



Infections in Patients with Multiple Myeloma in the Era of High-Dose Therapy and Novel Agents

Marcio Nucci[1] and Elias Anaissie[2]

[1]University Hospital, Universidade Federal do Rio de Janeiro, Brazil; and [2]University of Arkansas for Medical Sciences, Little Rock, Arkansas

Infectious Complications Associated with Alemtuzumab Use for Lymphoproliferative Disorders

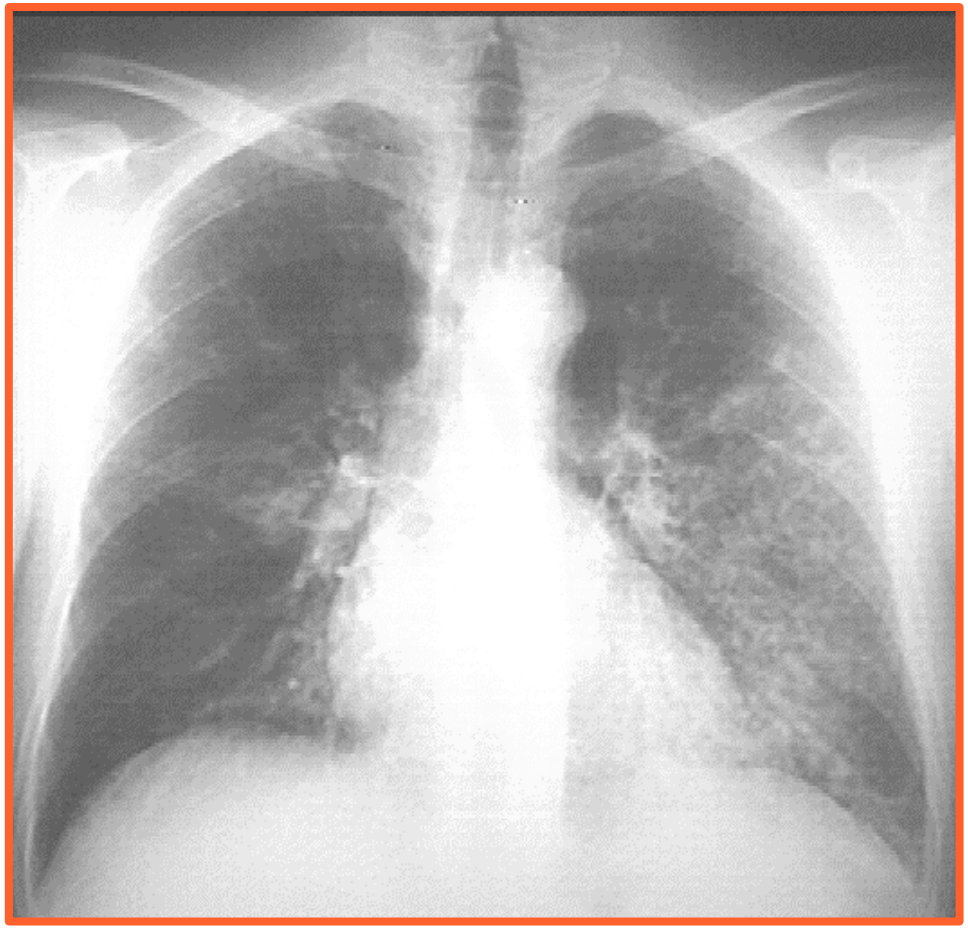
Stanley I. Martin,[1,5,a] Francisco M. Marty,[1,4,5] Karen Fiumara,[2] Steven P. Treon,[3,4,5] John G. Gribben,[6] and Lindsey R. Baden[1,4,5]

Table 2. Opportunistic infectious complications after alemtuzumab treatment.

Infection	No. of patients	No. of HSCTs	Cumulative dose, median mg (range)[a]	Time to clinical infection, median days (range)[b]	No. of deaths[c]
Viral					
Adenovirus pneumonia	1	0	253	274[d]	1
CMV viremia	12	4	253 (3–942)	175 (0–652)	1
CMV pneumonitis and colitis	1	0	103	351	1
HSV infection (localized)	2	1	200 (56–343)	62 (52–72)	0
PML	1	0	379	100	1
VZV infection (localized)	1	0	973	540	0
Bacterial					
Group B *Streptococcus* pyomyositis/bacteremia	1	1	73	8	0
Staphylococcus aureus pyomyositis/bacteremia	1	1	53	570	0
Fungal					
Pulmonary aspergillosis	3	2	56 (53–1129)	120 (79–662)	0
Disseminated cryptococcosis	1	0	379	171	0
Disseminated histoplasmosis	1	1	596	298	0
Parasitic					
Cerebral toxoplasmosis	1	1	553	169	0
Disseminated achanthamebiasis	1	1	942	443	1

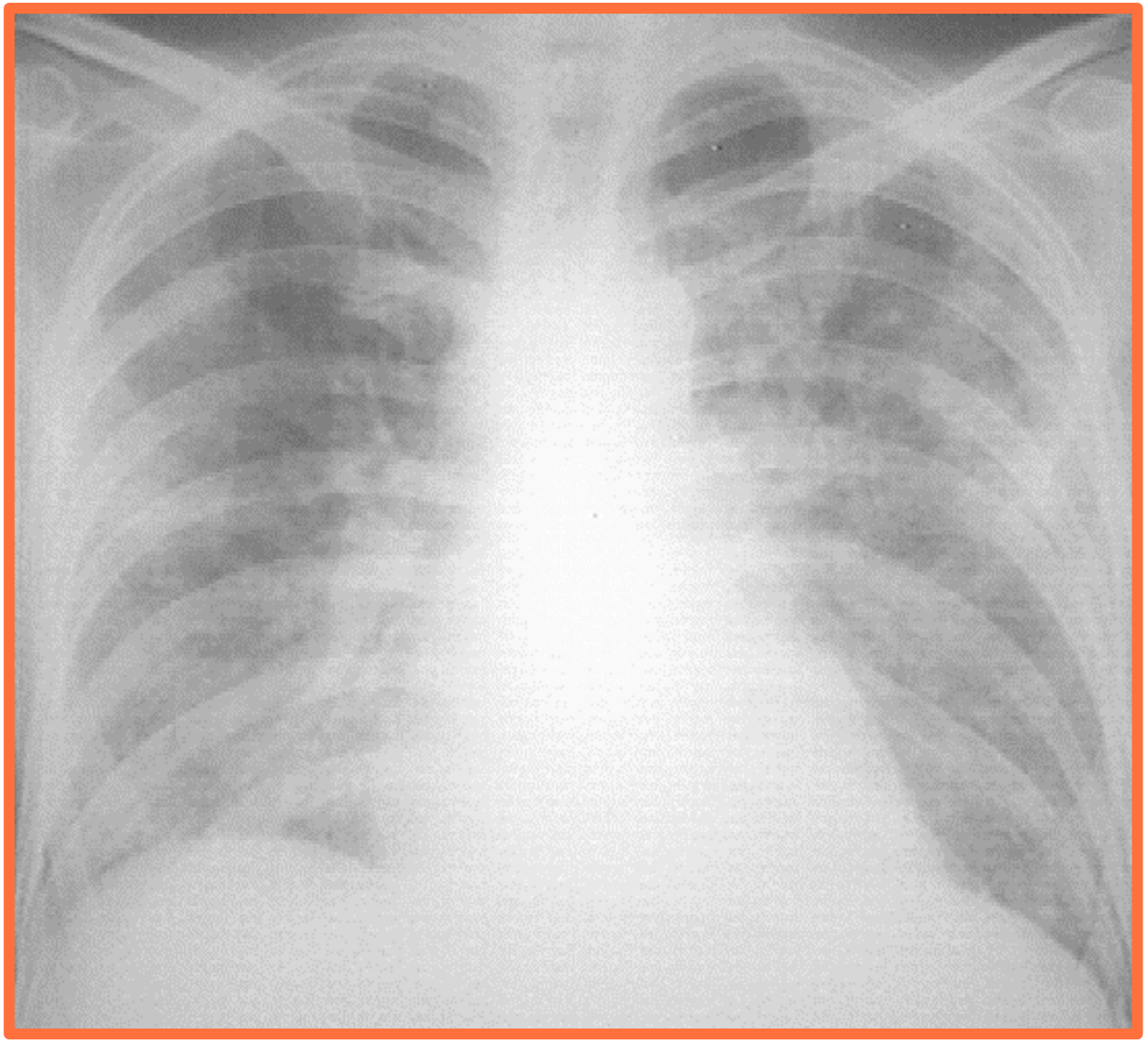
Hairy Cell Leukemia with early ARF

FO-LBA ?



Urine Ag ?

What's your diagnosis ?



DIRECT R. Radiographic appearance not sensitive, nor specific

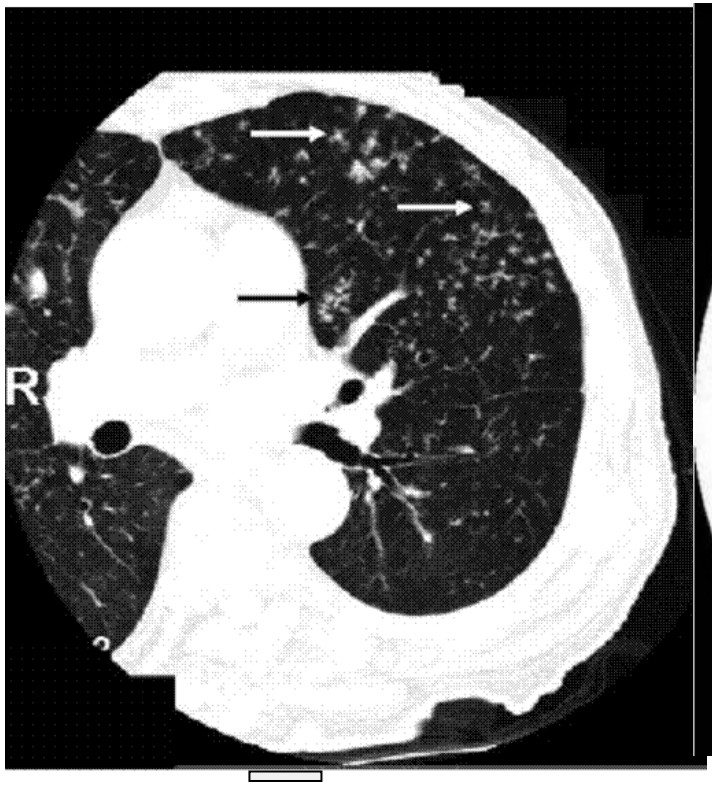
Chest X Ray: so specific ...

Pneumonia in Febrile Neutropenic Patients and in Bone Marrow and Blood Stem-Cell Transplant Recipients: Use of High-Resolution Computed Tomography

J Clin Oncol 17:796-805. © 1999 by American Society of Clinical Oncology.

By Claus Peter Heussel, Hans-Ulrich Kauczor, Gudula E. Heussel, Berthold Fischer, Markus Begrich, Peter Mildenberger, and Manfred Thelen

	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
Ground Glass				
> 0%	74	71	55	85
> 25%	31	82	45	71
> 50%	13	88	35	68
In > 1 lobe	56	79	56	79
Consolidation	33	89	59	73
Ill defined Nodules	57	86	66	81
In > 1 lobe	44	88	64	77
Linear Opacities				
opacities	18	94	58	70
Cavitation	11	98	78	70
Effusion	25	88	50	71



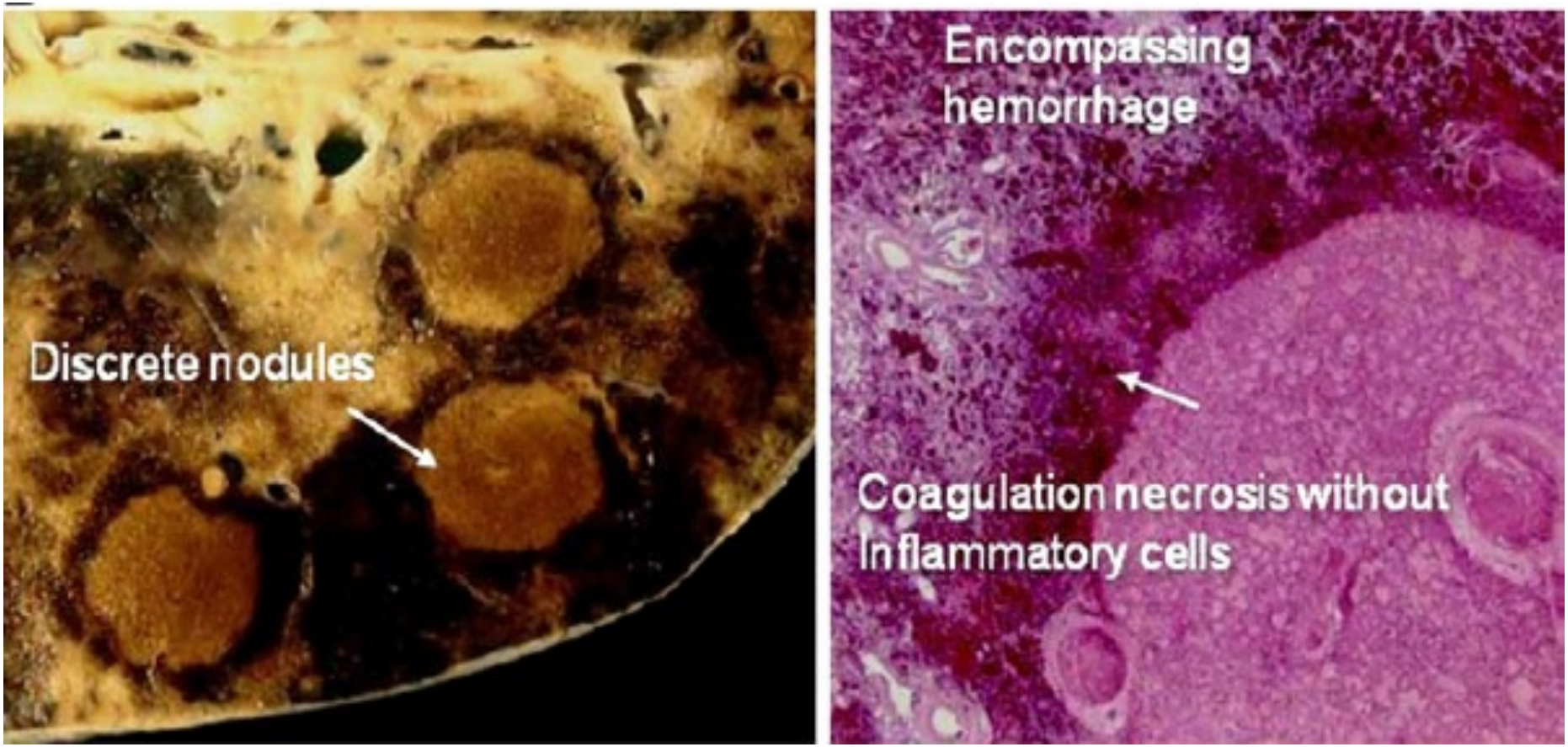
Bronchiolite à Haemophilus

Bronchiolite à PIV 3

Lymphome T agressif

The Diagnostic Value of Halo and Reversed Halo Signs for Invasive Mold Infections in Compromised Hosts

Sarah P. Georgiadou,[1] Nikolaos V. Sipsas,[1] Edith M. Marom,[2] and Dimitrios P. Kontoyiannis[3]



Shibuya K, et al J Infect Chemother 2004; 10: 138–45

- Fungal infections
  - Invasive aspergillosis
  - Mucormycosis
  - Pulmonary candidiasis
  - Cryptococcosis
  - Coccidioidomycosis
  - Phaeohyphomycosis
- Viral infections
  - Herpes simplex virus
  - Varicella-zoster virus
  - Respiratory syncytial virus
  - Cytomegalovirus
  - Myxovirus (including Influenza A)
- Bacterial infections
  - *Coxiella burnetii*
  - *Chlamydia psittaci*
  - *Actinomyces* species
  - Bacterial pneumonia
  - Slow-resolving pneumonia
  - Septic emboli
- Mycobacterial infections
  - *Mycobacterium tuberculosis*
  - *Mycobacterium avium-intracellulare*
- Parasitic infections
  - *Schistosoma (haematobium, mansoni)*
  - *Paragonimus westermani*
  - Hydatid disease
  - *Toxocara canis*
  - *Ascaris suum*
- Systemic diseases
  - Wegener granulomatosis
  - Sarcoidosis
  - Amyloidosis
- Neoplastic diseases
  - Primary
    - Bronchoalveolar carcinoma
    - Squamous cell carcinoma
    - Adenocarcinoma
    - Mucinous cystadenocarcinoma
    - Kaposi sarcoma
    - Angiosarcoma
    - Lymphoma
  - Metastatic lesions
    - Angiosarcoma
    - Choriocarcinoma
    - Osteosarcoma
    - Melanoma
    - Gastrointestinal tract/pancreatic cancer
    - Renal cell carcinoma
    - Lymphoma
  - Various pulmonary diseases
    - Cryptogenic organizing pneumonia
    - Eosinophilic pneumonia
    - Idiopathic hypereosinophilic syndrome
    - Hypersensitivity pneumonia
    - Iatrogenic injuries: pulmonary artery catheterization or transbronchial biopsy (especially in lung transplants)
- Other
  - Endometriosis
  - Drug toxicity (amiodarone)

The Prognosis of Acute Respiratory Failure in Critically Ill Cancer Patients

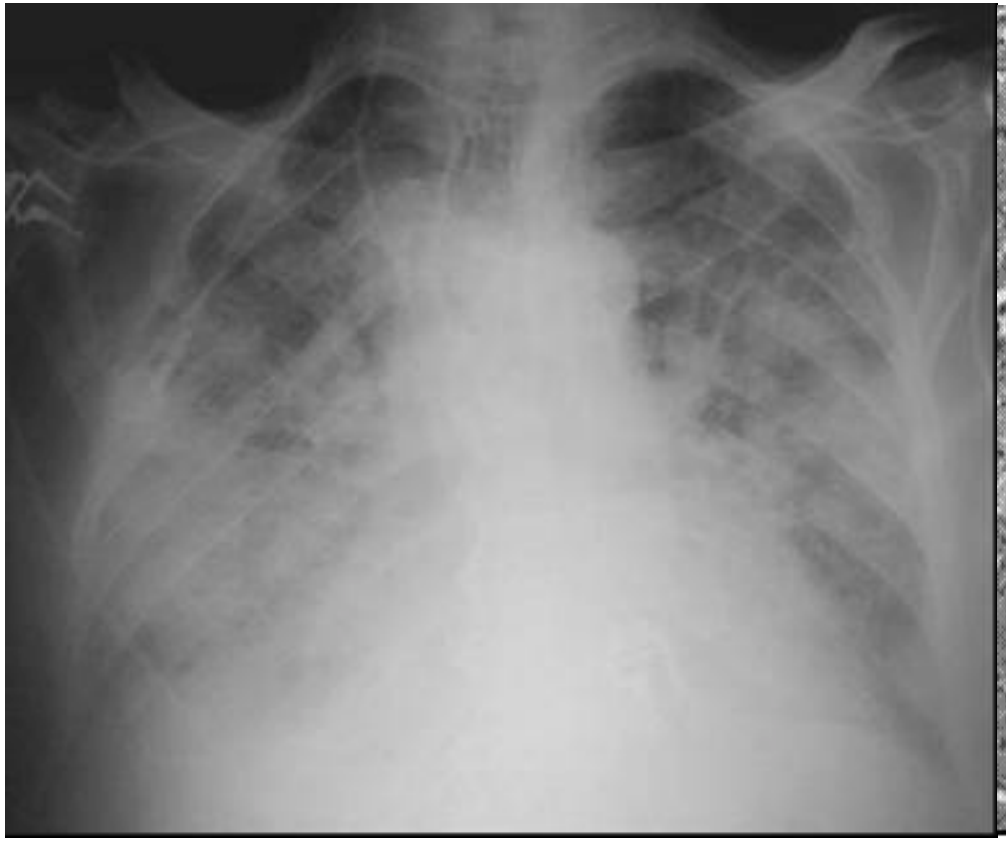
Élie Azoulay, MD, PhD, Guillaume Thiéry, MD, Sylvie Chevret, MD, PhD, Delphine Moreau, MD, Michaël Darmon, MD, Anne Bergeron, MD, PhD, Kun Yang, MD, Véronique Meignin, MD, Magali Ciroldi, MD, Jean-Roger Le Gall, MD Abdellatif Tazi, MD, PhD, and Benoît Schlemmer, MD

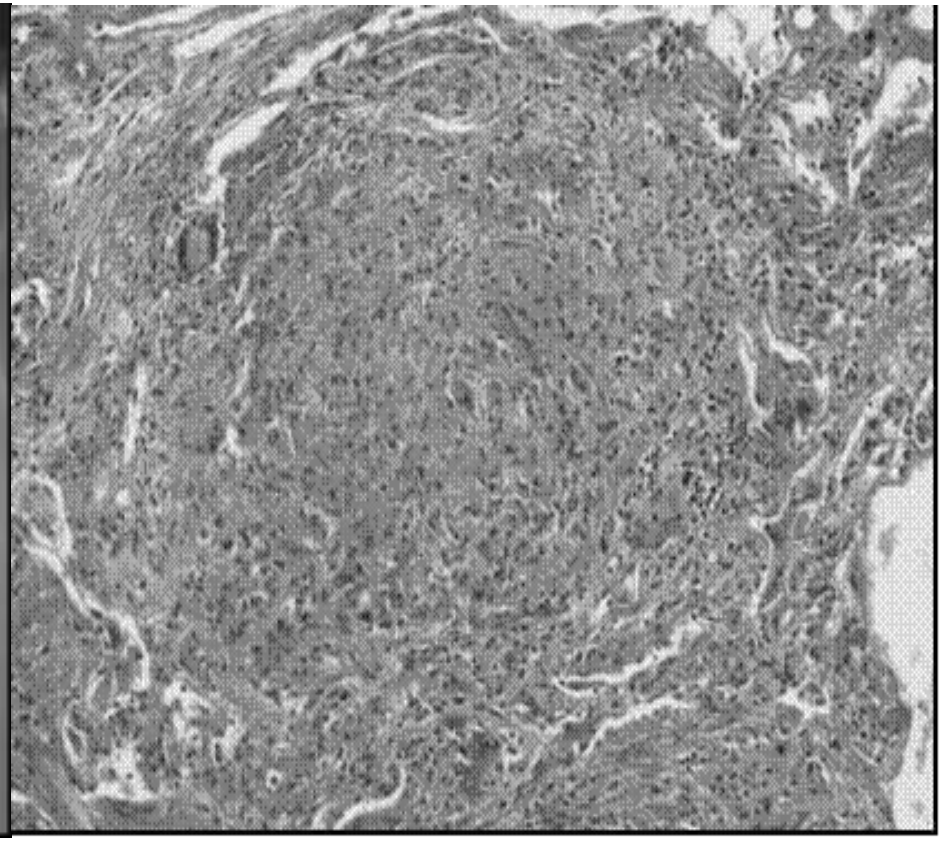
(*Medicine* 2004;83:360–370)

	Odds ratio	95% Confidence Interval	*P* value
Cause of ARF			
Congestive heart failure	0.16	0.03-0.72	0.01
Invasive aspergillosis	3.78	1.05-14.24	0.049
No definite diagnosis	**OR 3.85 (1.26-11.7)**		**P=0.01**
Need for respiratory support			
NIMV only	1.58	0.37-6.70	0.52
NIMV followed by conventional MV	17.46	5.04-60.52	<0.0001
First-line conventional MV	8.75	2.35-32.54	0.001
Late NIMV failure	10.64	1.05-107.83	0.04

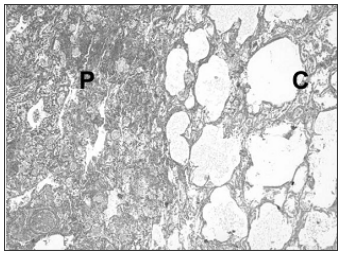
Une Tuberculose Inattendue

Décès après SDRA au cours d'une maladie de Hodgkin





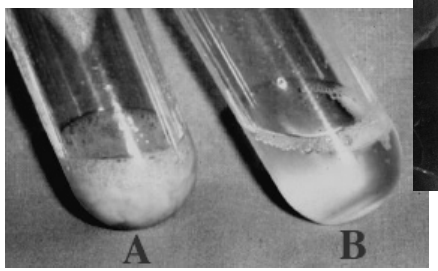
Faire le diagnostic: quelle stratégie?

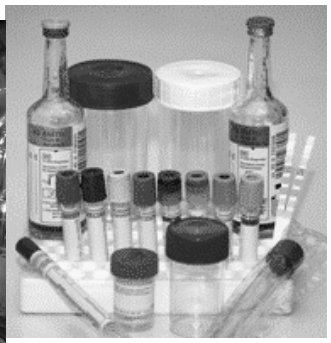


- **Invasive:**
  - **Biopsie pulmonaire**

- **Semi-invasive:**
  - **Fibroscopie-LBA**

- **Non invasive:**
  - **Hémocultures**
  - **Analyse (bactério, myco, BK) des crachats**
  - **Expectoration induite**
  - **Aspiration nasopharyngée**
  - **Antigènes sanguins et urinaires**
  - **Échographie cardiaque**
  - **TDM thoracique HR**





Deux types d'outils diagnostiques

- **<u>Culture-based</u>**
  -
  -
  -

- **<u>Non culture-based</u>**
  -
  -
    galactomannan (GM),
  - **1,3-beta-D-glucan**
  - **Méthodes moléculaires**

- **Pathogènes colonisant**
- **Faux positifs**
- **Faux négatifs**
- **Pas de gold standard**

- **Trop sensibles?**
- **Colonisation ou infection**
- **Pertinence?**

Nosocomial infections in patients with cancer

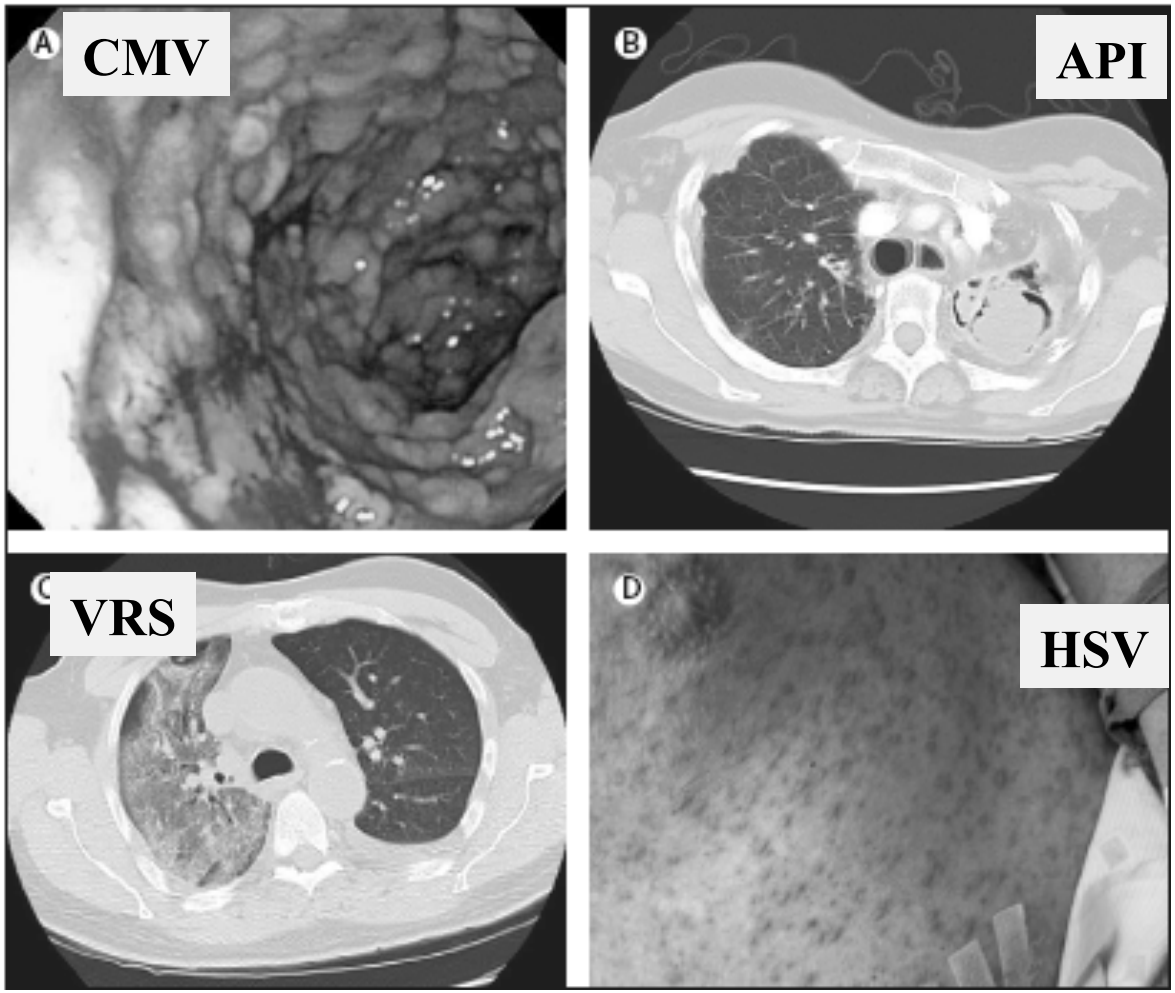
Mini Kamboj, Kent A Sepkowitz

Nosocomial infections are those that become evident 48 h or more after a patient is admitted for treatment in a hospital or in another health-care setting. These infections cause substantial morbidity and mortality in patients who are immunosuppressed. Over the past few decades, understanding of host vulnerability has improved and more rigorous management and infection-control practices have been adopted for treating susceptible populations. Despite efforts, outbreaks continue to occur. In this Review, we outline current knowledge of the incidence and microbiology of various nosocomial infections in patients with cancer—a large, immunosuppressed population.

Lancet Oncol 2009; 10: 589–97

See News page 544

Infectious Diseases Service, Memorial Sloan-Kettering Cancer Center, New York, New York, USA (M Kamboj MD, Prof K A Sepkowitz MD)



Pulmonary Complications in Adult Blood and Marrow Trans

CHEST / 128 / 3 / SEPTEMBER, 2005

Sunita Sharma, MD; Hassan F. Nadrous, MD; Steve G. Peters, MD, FCCP; Ayalew Tefferi, MD; Mark R. Litzow, MD; Marie-Christine Aubry, MD; and Bekele Afessa, MD, FCCP

- **Comparaison des résultats de l'autopsie avec ceux obtenus avant le décès chez 73 pts (39 Allogreffés, 34 Autogreffés)**

- **1. Diagnostics *ante mortem* corrects: 28%**

- **2. Diagnostics *ante mortem* non faits (faux négatifs):**
  - **46% bactéries, 45% aspergillus, 88% HIA**

- **3. Diagnostics *ante mortem* en faux positifs:**
  - **10 aspergilloses, 7 CMV, 22 bactéries, 2 PCP, 12 HIA**

Intensive Care Med
DOI 10.1007/s00134-006-0129-2

REVIEW

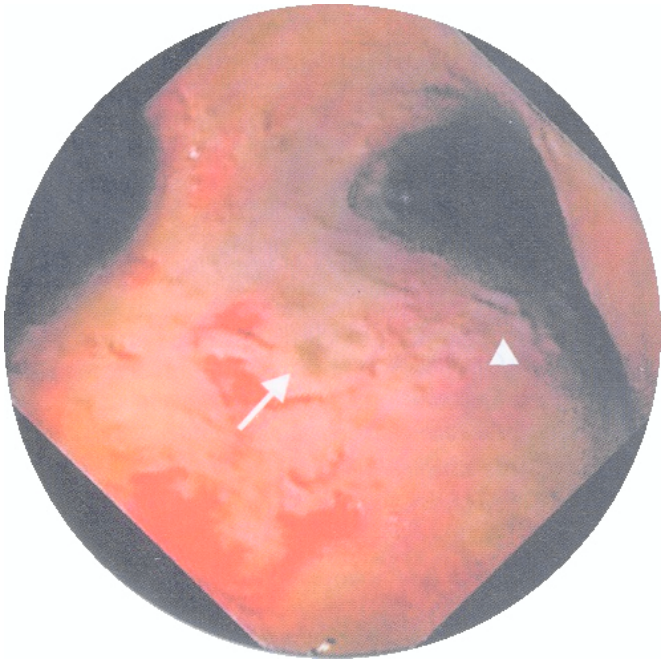
Impact of FOB+BAL

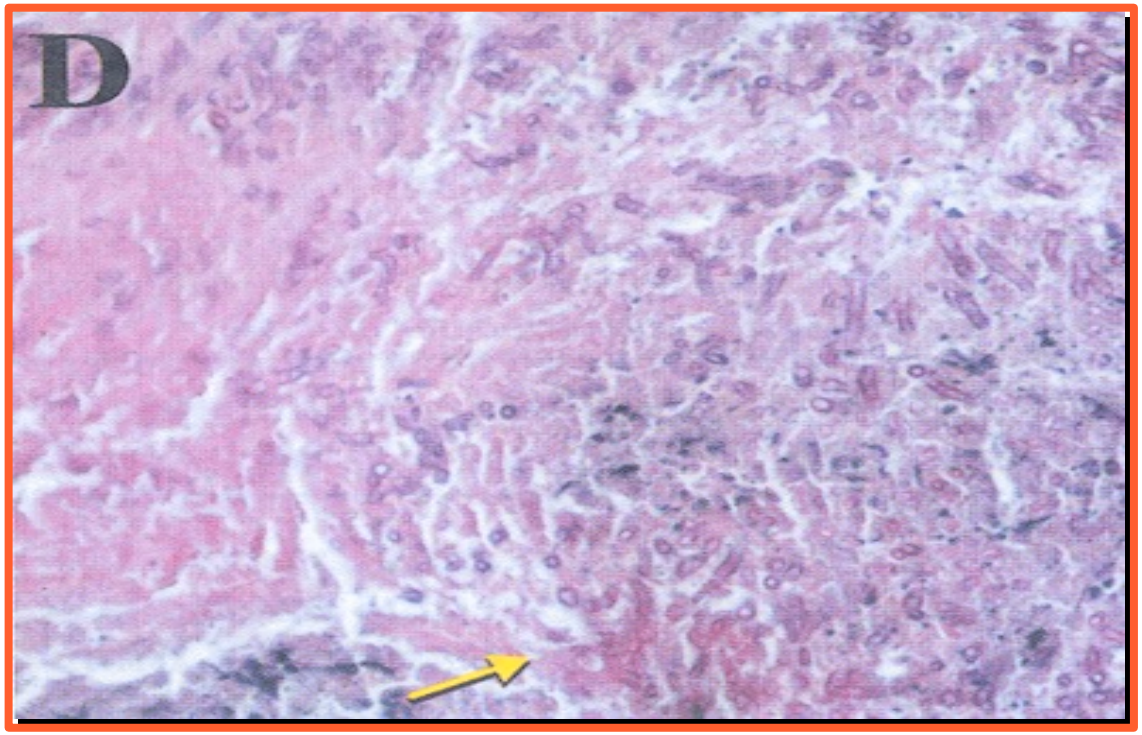
Élie Azoulay
Benoît Schlemmer

Diagnostic strategy in cancer patients with acute respiratory failure

Reference	*n*	Diagnosis	Diagnostic impact	Therapeutic impact
Stover et al. [96]	97	HM	66	–
Martin et al. [142]	100	HM	30	–
Xaubet et al. [143]	96	HM	49	31
Campbell et al. [144]	22	HM	55	–
Pisani et al. [145]	150	HM	39	–
Maschmeyer et al. [146]	46	Neutropenia	30	–
Cordonnier et al. [100]	56	Neutropenia	53	24
Cazzadori et al. [147]	142	HM	36	–
Von Eiff et al. [40]	90	HM	66	65
White et al. [3]	68	HM	31	24
Ewig et al. [28]	49	HM	31	16
Gruson et al. [18]	41	Neutropenia	63	28
Hilbert et al. [22]	24/46	HM	62	71
Murray et al. [2]	27	HM	33	28
Azoulay et al. [4]	203	HM	49.5	45.1
Pagano et al. [148]	127	HM	53	14
Jain et al. [82]	104	HM	56	–
Hohenadel et al. [81]	95	HM	30	–
Total	1537		46.2	34.6

Diagnostic yield of direct visualization





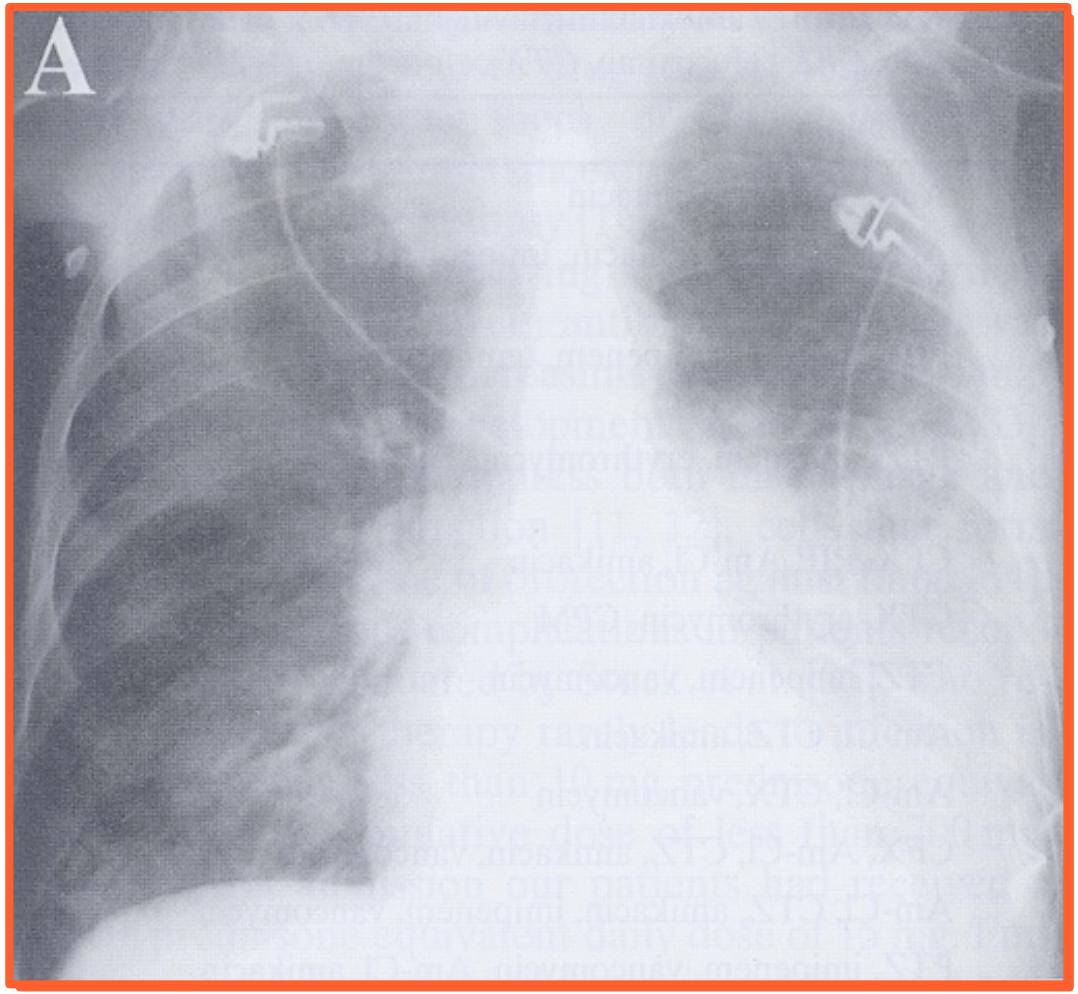
Prognostic Factors of Non-HIV Immunocompromised Patients With Pulmonary Infiltrates*

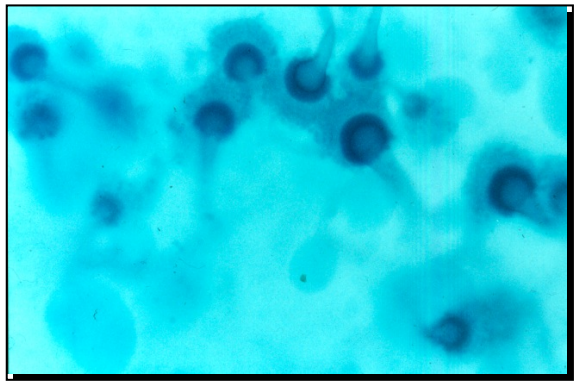
(CHEST 2002; 122:253–261)

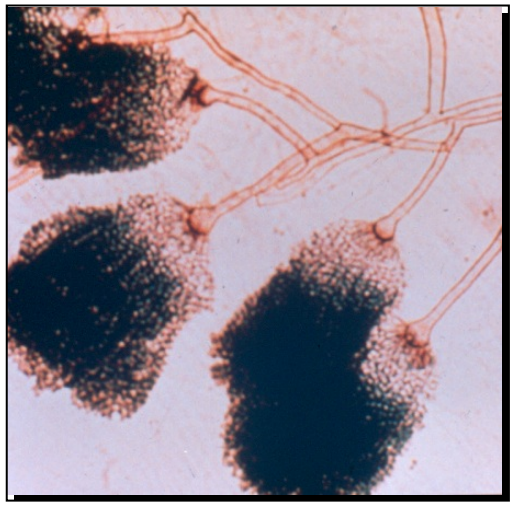
Ana Rañó, MD, PhD; Carlos Agustí, MD, PhD; Natividad Benito, MD; Montserrat Rovira, MD, PhD; Joaquim Angrill, MD; Tomás Pumarola, MD, PhD; and Antoni Torres, MD, PhD

Diagnostic Techniques	Positive/Performed
Blood cultures	32/192 (17)
Aspergillus antigen detection	12/66 (18)
CMV antigen detection	14/98 (14)
Nasopharyngeal wash	13/60 (22)
Sputum	20/78 (26)
Bronchial aspirate	47/89 (53)
Protected specimen brush	31/129 (24)
Bronchoalveolar lavage	70/140 (50)
Transbronchial biopsy†	6/12 (50)
Open lung biopsy‡	2/2 (100)

Pulmonary invasive aspergillosis







Correlation between galactomannan antigen levels in serum and neutrophil counts in haematological patients with invasive aspergillosis

C. Cordonnier[1], F. Botterel[2], R. Ben Amor[1], C. Pautas[1], S. Maury[1], M. Kuentz[1], Y. Hicheri[1], S. Bastuji-Garin[3] and S. Bretagne[2]

A negative result or a low GM index should not eliminate the diagnosis of IA in non-neutropenic patients

	Group 1 (n = 18)	Groups 2 + 3 (n = 81)	
GM index	**<100 PMN**	**≥100 PMN**	**P**
GM index ≥1	8 (44.4)	8 (9.9)	0.001[a]
GM index ≥0.7	8 (44.4)	12 (14.8)	0.009[a]
GM index ≥0.5	11 (61.1)	15 (18.52)	0.001[a]
GM index, median (range)	0.61 (0.08–5.84)	0.19 (0.04–5.31)	0.01[b]
Steroid administration			
Yes	4.63 (4.37–5.84)	0.2 (0.04–1.93)	0.001[b]
No	0.44 (0.08–2.48)	0.18 (0.04–5.31)	0.19[b]
Potentially GM-contaminated antibiotic(s) use			
Yes	4.36 (0.11–5.84)	0.24 (0.04–5.31)	0.76[b]
No	0.57 (0.08–4.96)	0.18 (0.04–2.01)	0.003[b]
Antifungal therapy			
Yes	0.54 (0.08–2.48)	0.17 (0.1–2.29)	0.694[b]
No	1.21 (0.1–5.84)	0.20 (0.04–5.31)	0.006[b]

blood

Prepublished online October 18, 2011;
doi:10.1182/blood-2011-04-351601

The strategy for the diagnosis of invasive pulmonary aspergillosis should depend on both the underlying condition and the leucocyte count of patients with hematological malignancies

Anne Bergeron, Raphaël Porcher, Annie Sulahian, Cédric de Bazelaire, Karine Chagnon, Emmanuel Raffoux, Anne Vekhoff, Muriel Cornet, Françoise Isnard, Benoit Brethon, Claire Lacroix, Jean Louis Poirot, Claire Bouges, Francis Derouin, Abdellatif Tazi and Patricia Ribaud

	Allogeneic BMT	AL
Serum GM>0.5	65%	41%
BAL GM>0.5	64%	56%
Sputa	75%	50%
Bronchial aspirate	71%	18%
BAL	53%	18%

Frequent Detection of Respiratory Viruses in Adult Recipients of Stem Cell Transplants with the Use of Real-Time Polymerase Chain Reaction, Compared with Viral Culture

Marian G. J. van Kraaij,[1] Leontine J. R. van Elden,[2] Anton M. van Loon,[2] Karin A. W. Hendriksen,[2] Laurens Laterveer,[1] Adriaan W. Dekker,[1] and Monique Nijhuis[2]

- – **Cultures + = 21% // RT-PCR + = 63%**

- **que culture (73% vs. 9%)**

- **Colonisation ? 9% des patients sans symptômes ont un virus + en PCR contre 1% des patients avec culture +**

PCR multiplex virales chez 100 patients d'hématologie :

Implications cliniques paradoxales

- **En cas d'atteinte respiratoire infectieuse, une PCR+ est associée á une**
  - **Moindre morbidité,**
  - **Moindre sévérité**
  - **Moindre mortalité**

- **En cas d'atteinte non infectieuse, une PCR+**
  - **Corrige le diagnostic initial**
  - **Etend le faisceau d'arguments**

Schnell et al. Soumis 2011

Active CMV disease does not always correlate with viral load detection

J Ruell[1], C Barnes[1], K Mutton[2], B Foulkes[1], J Chang[1], J Cavet[1], M Guiver[2], L Menasce[3], M Dougal[4] and R Chopra[1]

Bone Marrow Transplantation (2007) 40, 55–61

www.nature.com/bmt

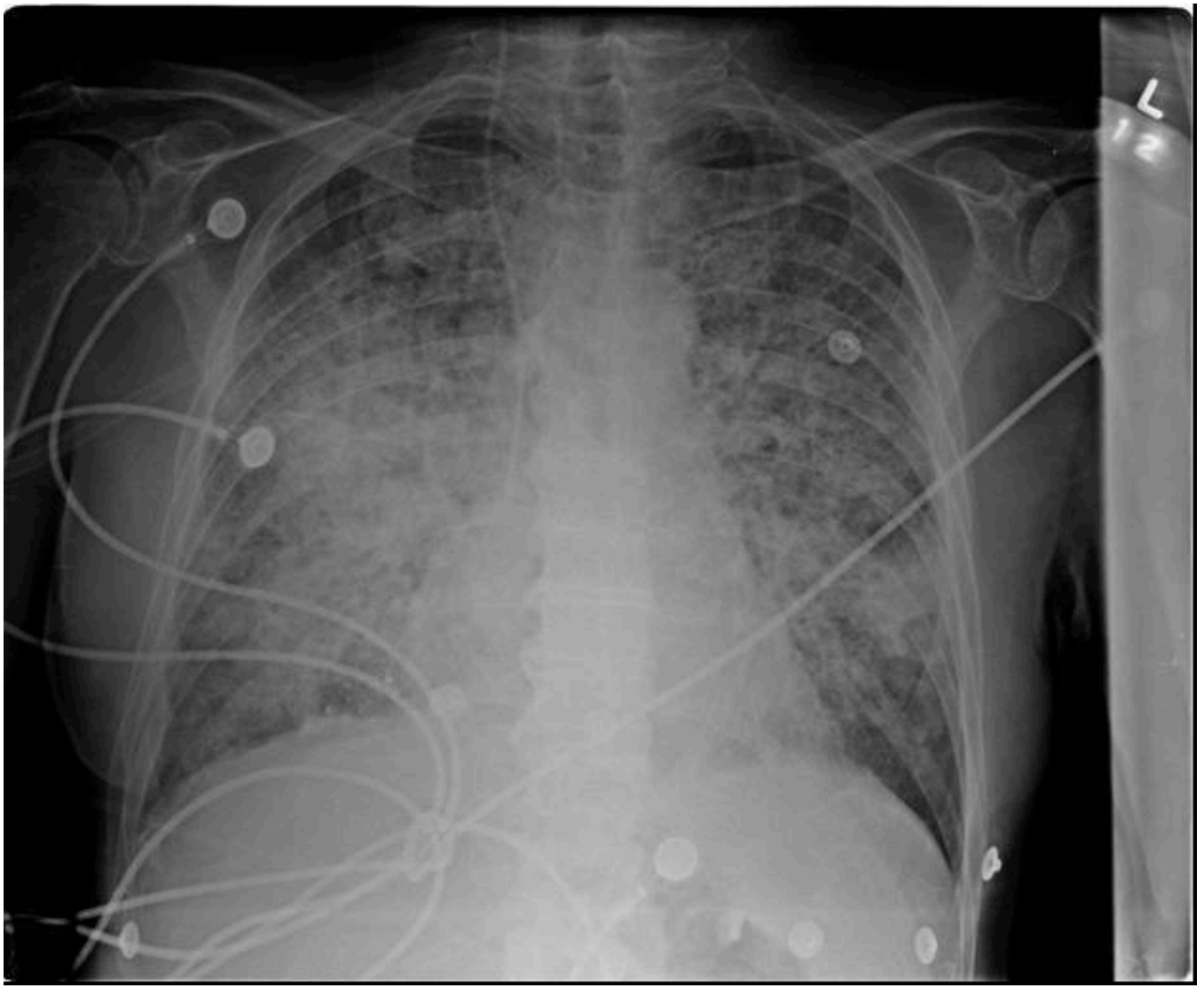
577 BMT (172 Allo), RT PCR CMV + = 30%
Maladie CMV = 8 patients (1%) dont 4 PCR-

Table 5 Patients who developed CMV disease: characteristics

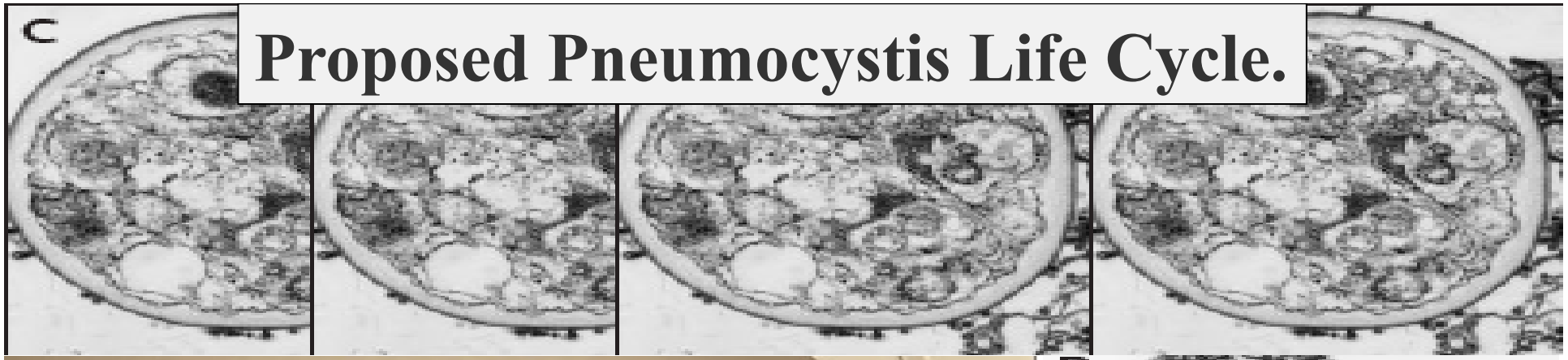
UPN no.	*Disease*	*Risk status*	*Organ affected by CMV*	*Day of PCR detection*[a]	*Day of CMV disease*[a]	*CMV viral copy number*[b]	*Outcome*
1175	Granulocytic sarcoma	R+D+	Retinitis	29	120	(log 3.2) 1772	Alive
1010	NHL	R+D−	Duodenum	35	163	(log 5.3) 202610	Died (CMV pneumonitis)
837	AML	R+D−	Skin	36	266	(log 3.6) 005	Alive
828	MM	R+D+	Sigmoid	19	210	0	Died CMV colitis
930	MM	R+D−	Retinitis	15	300	0	Died (relapsed myeloma)
1099	ALL	R−D+	Retinitis	20	128	0	Died (adenovirus)
939	MM	R+D+	Pneumonia	27	800	0	Alive
1150	AML	R+D−	Sigmoid	25	25	(log 6.1) 1325300	Died (CMV colitis)

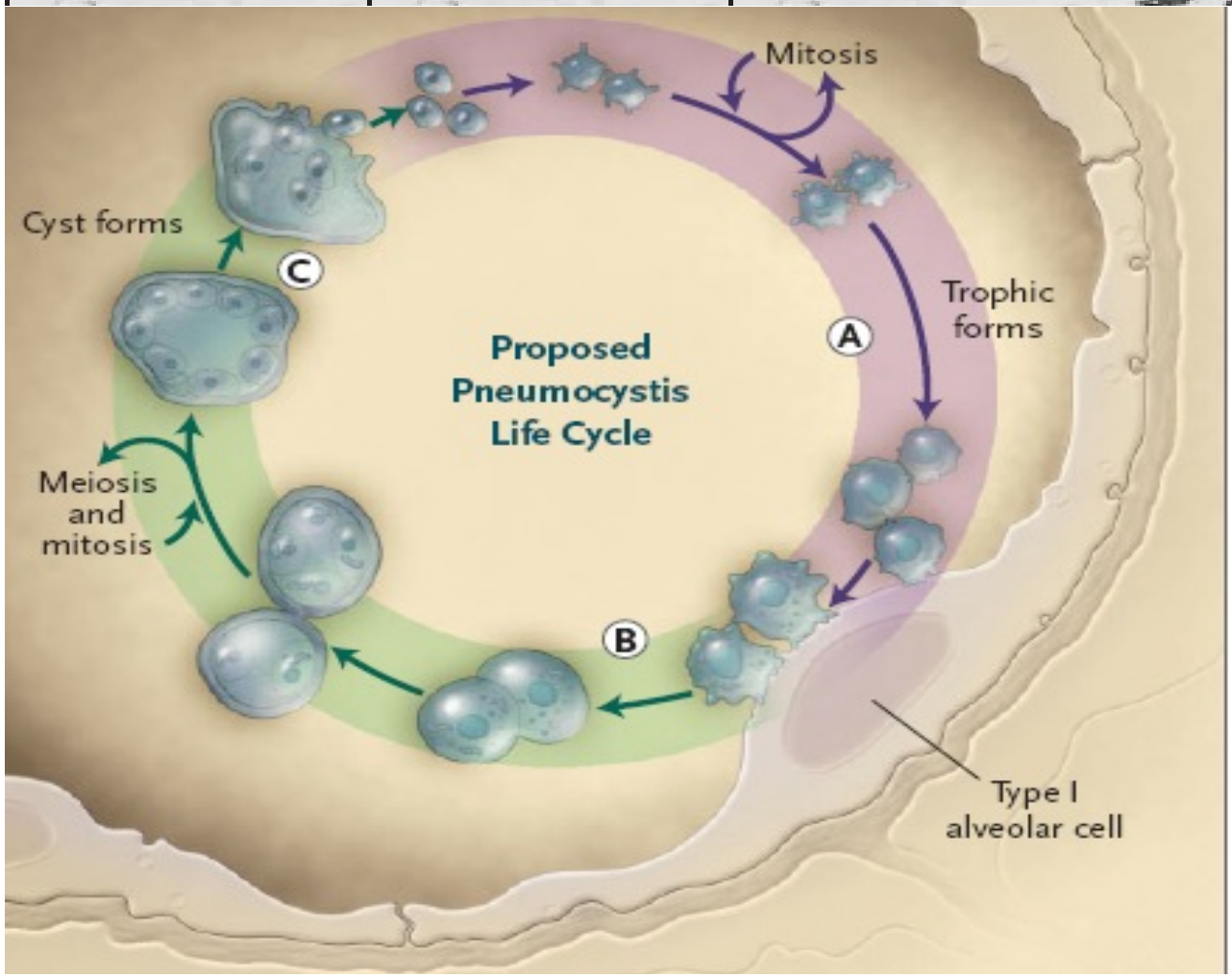
Préférer PCR sur sang total

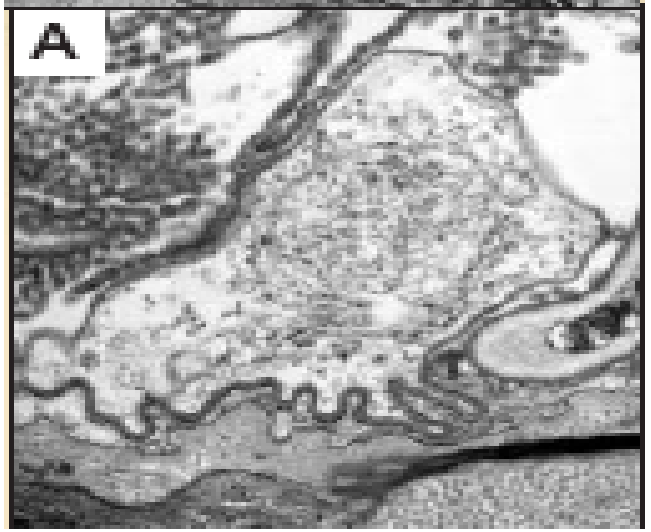
Pneumonie à CMV sans CMV nulle part



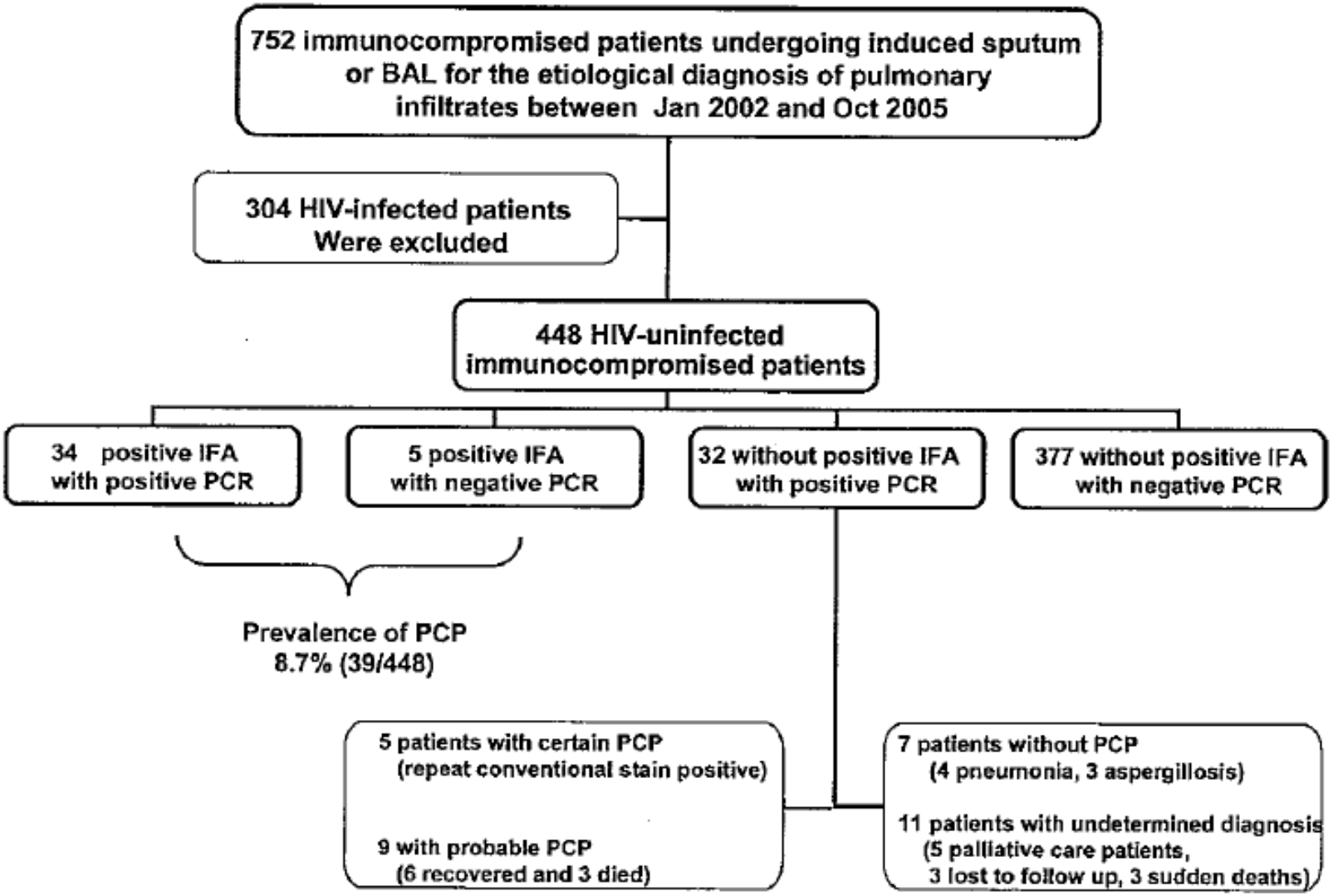
Proposed Pneumocystis Life Cycle.

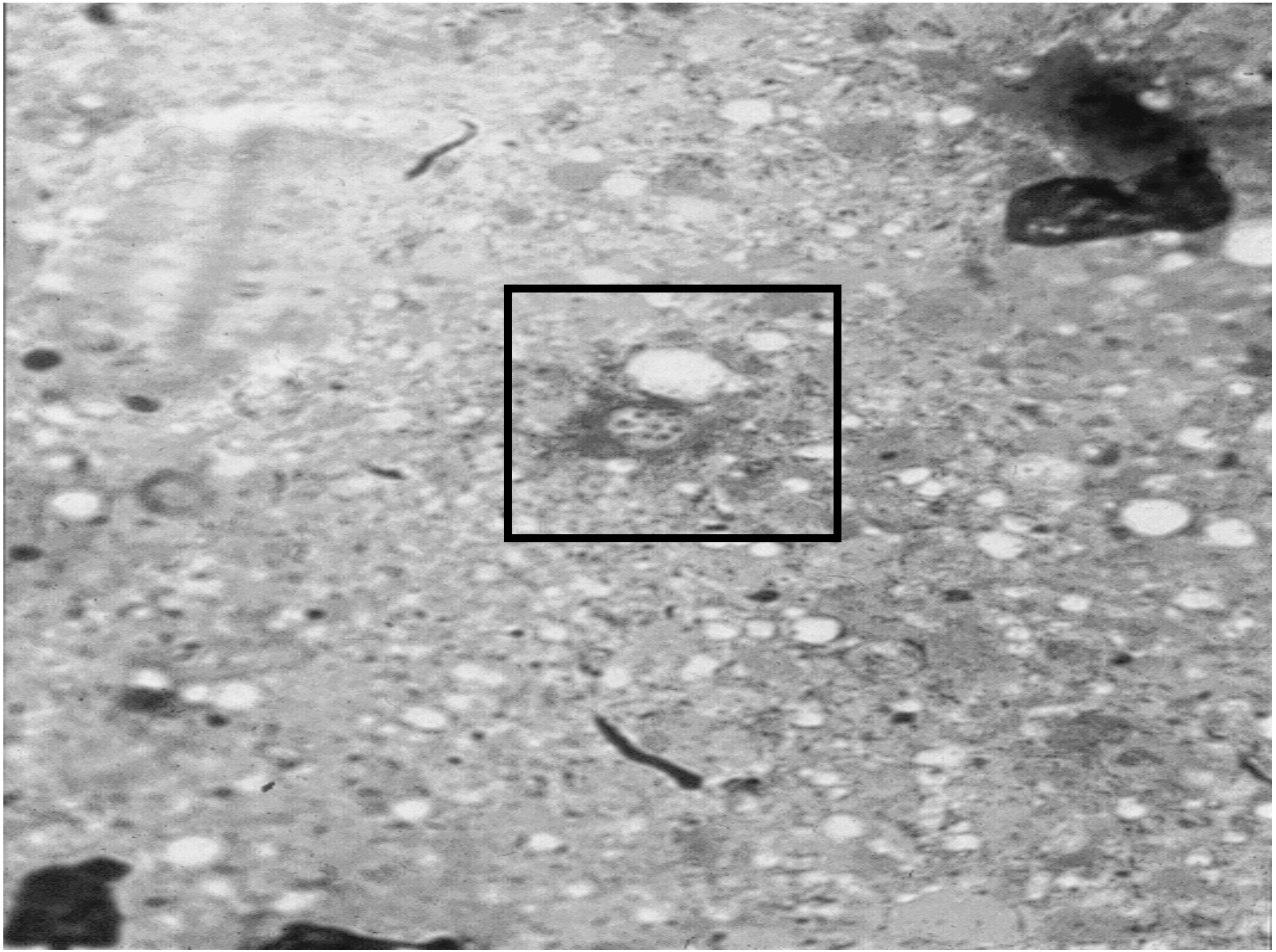






Polymerase Chain Reaction for Diagnosing Pneumocystis Pneumonia in

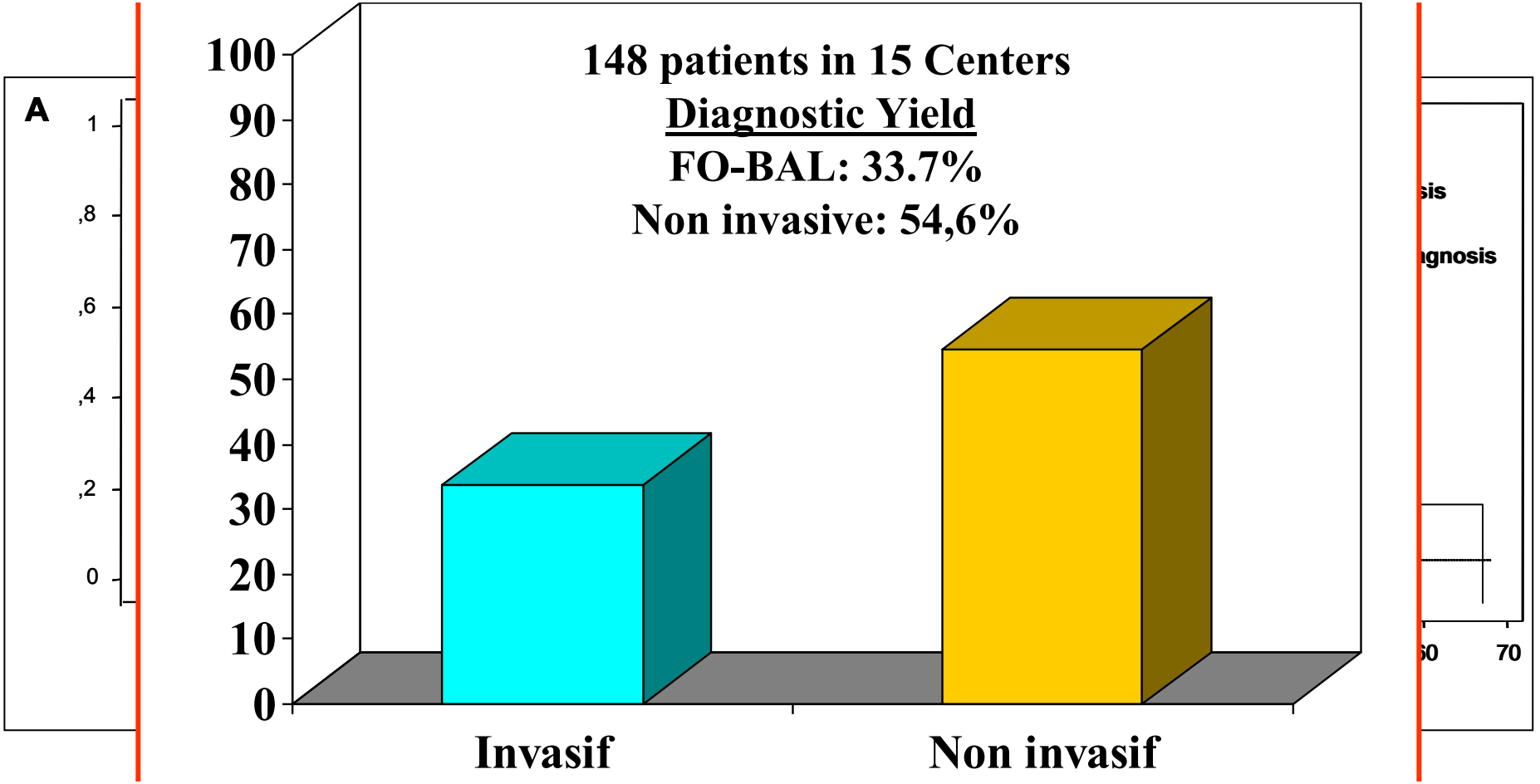


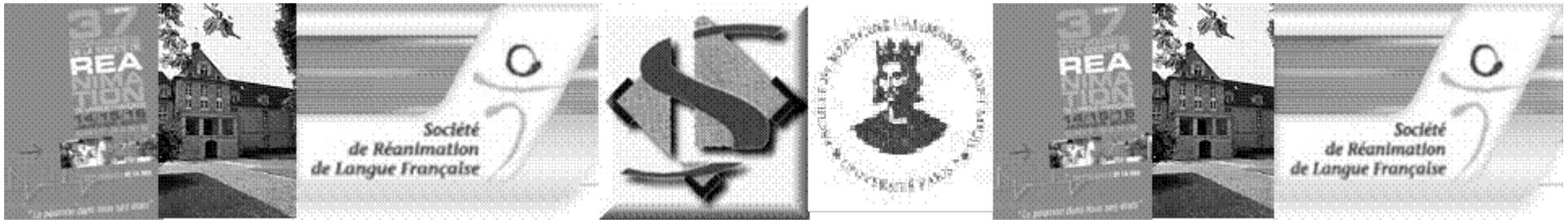


Diagnostic bronchoscopy in hematology and oncology patients with acute respiratory failure: Prospective multicenter data*

Elie Azoulay, MD, PhD; Djamel Mokart, MD; Antoine Rabbat, MD; Frédéric Pene, MD;

Invasive or non invasive diagnostic strategy ?





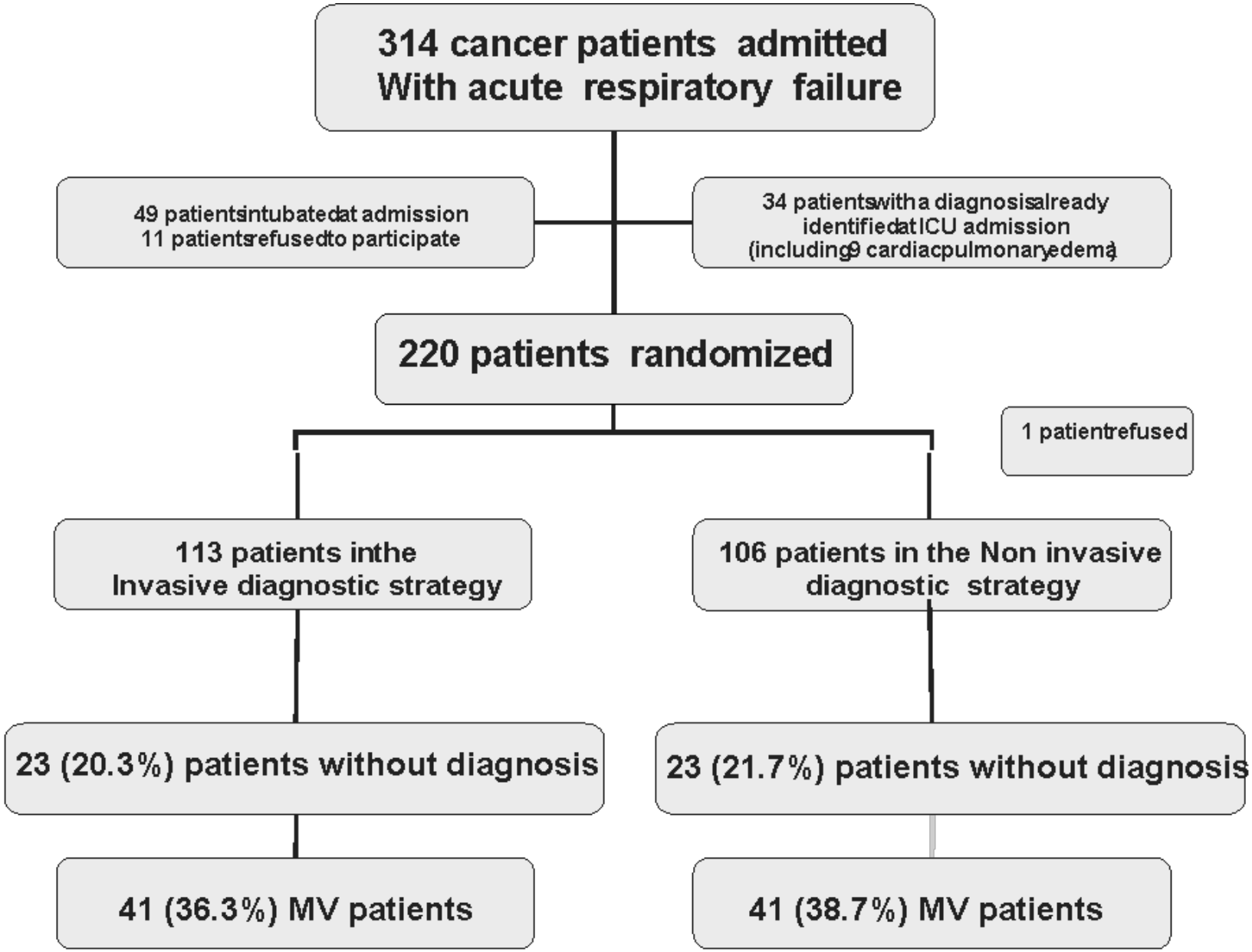
Stratégie Diagnostique Invasive ou Non invasive dans l'IRA du Patient d'Oncohématologie (IRA-OH) :

Essai Randomisé Multicentrique MiniMax®

Diagnostic Strategy for Hematology and Oncology Patients with Acute Respiratory Failure

Randomized Controlled Trial

Élie Azoulay[1], Djamel Mokart[2], Jérôme Lambert[3], Virginie Lemiale[4], Antoine Rabbat[5], Achille Kouatchet[6], François Vincent[7], Didier Gruson[8], Fabrice Bruneel[9], Géraldine Epinette-Branche[1], Ariane Lafabrie[1], Rebecca Hamidfar-Roy[10], Christophe Cracco[11], Benoît Renard[12], Jean-Marie Tonnelier[13], François Blot[14], Sylvie Chevret[3], and Benoît Schlemmer[1]



The MiniMax study, Azoulay et al. 2010

Diagnostic Strategy for Hematology and Oncology Patients with Acute Respiratory Failure

Randomized Controlled Trial

Am J Respir Crit Care Med Vol 182. pp 1038–1046, 2010

Élie Azoulay[1], Djamel Mokart[2], Jérôme Lambert[3], Virginie Lemiale[4], Antoine Rabbat[5], Achille Kouatchet[6], François Vincent[7], Didier Gruson[8], Fabrice Bruneel[9], Géraldine Epinette-Branche[1], Ariane Lafabrie[1], Rebecca Hamidfar-Roy[10], Christophe Cracco[11], Benoît Renard[12], Jean-Marie Tonnelier[13], François Blot[14], Sylvie Chevret[3], and Benoît Schlemmer[1]

Etiologies	MAXI N=113	MINI N=106
Bacteria		
Viruses		
Fongi		
Pneumocystis		
Malignant infiltration		
Cardiac Pulm. Edem		
More than one diagnosis		

Diagnostic Strategy for Hematology and Oncology Patients with Acute Respiratory Failure

Randomized Controlled Trial

Am J Respir Crit Care Med Vol 182. pp 1038–1046, 2010

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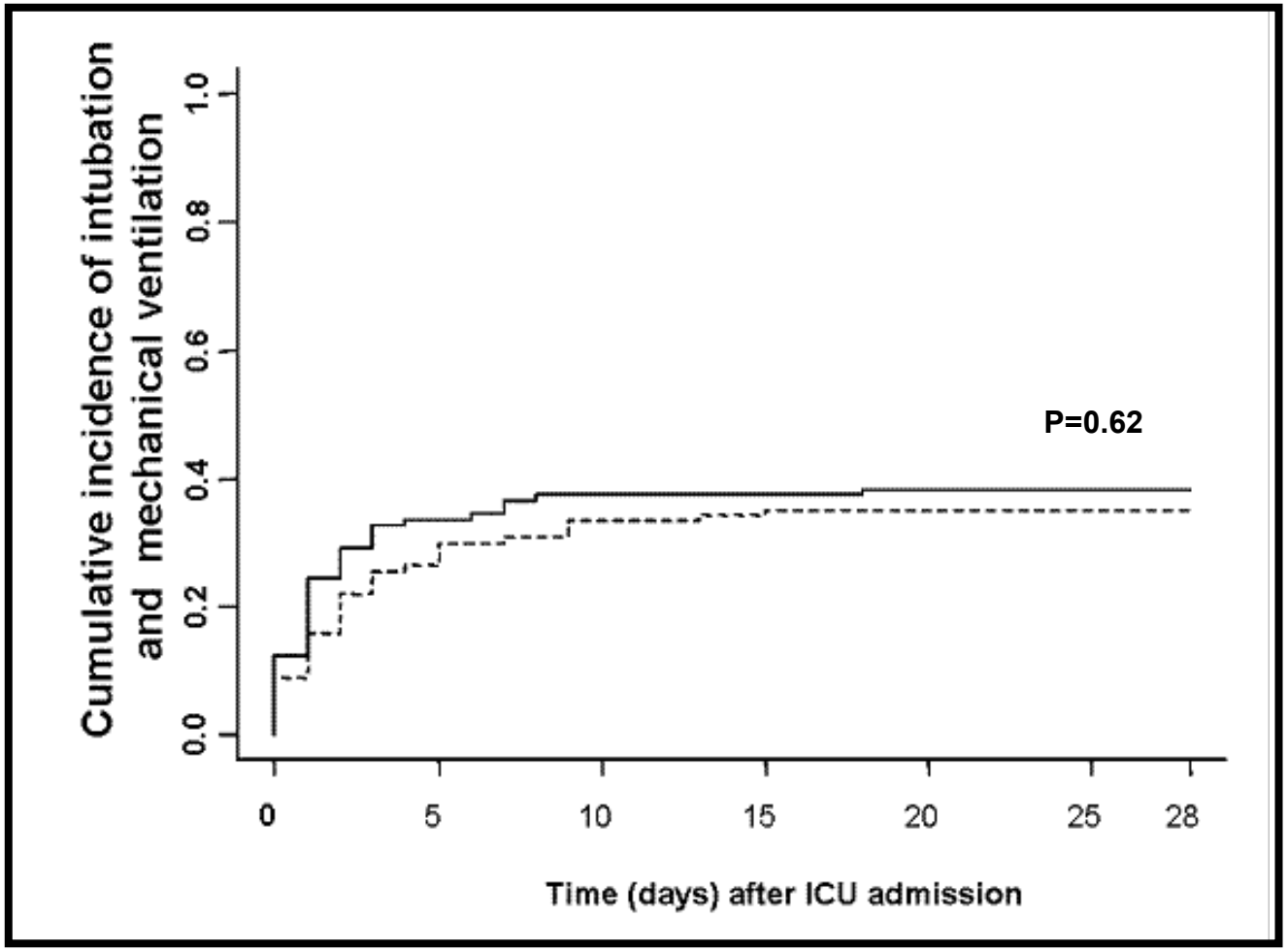
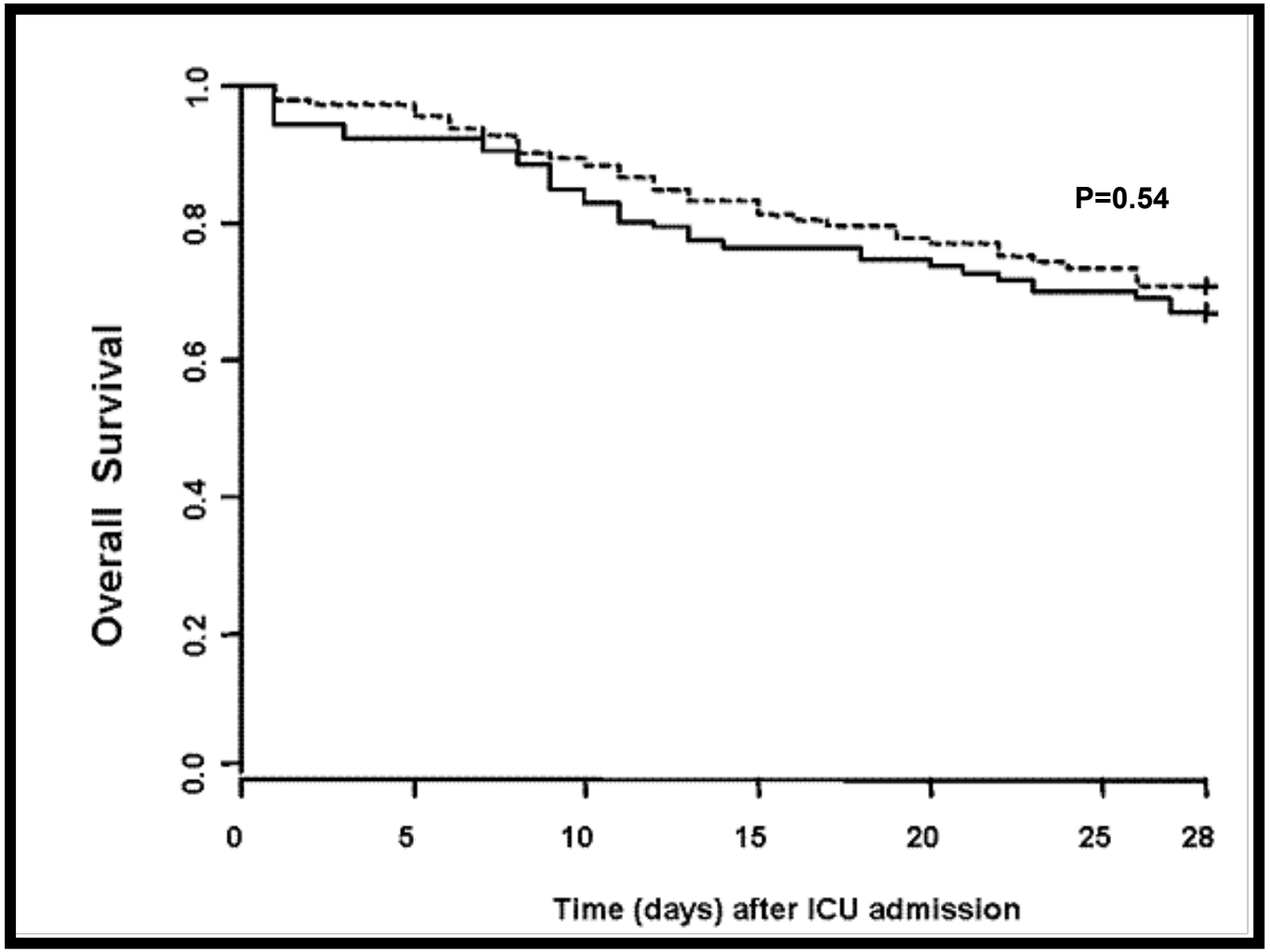
Diagnoses	Diagnosis made by NIT
• CPO: 10	• 10 (100%)
• Fungi: 23	• 22 (95.6%)
• Aspergilus: 18	• 17 (94%)
• Virus: 26	• 24 (92.3%)
• Malignancy: 16	• 13 (81%)
• Pneumocystis: 19	• 15 (79%)
• Bacteria: 86	• 57 (66.3%)

Need for mechanical ventilation



D28 Survival

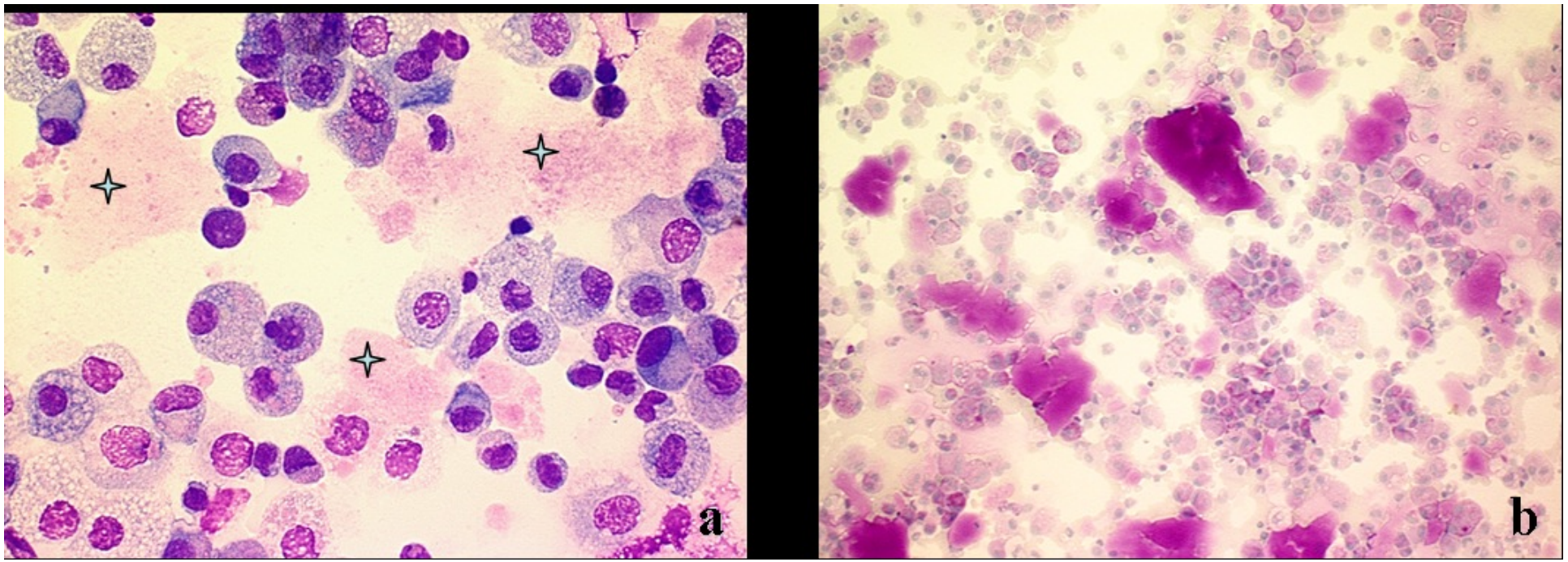


Indications résiduelles du LBA chez les patients OH en IRA

- **En première intention**
  - **Toxicité pulmonaire des médicaments (rare en réa)**
  - **Pneumocystose si diagnostic non invasif inaccessible ou infaisable**
  - **Malade ventilé?**
- **Ensuite…**
  - **Avant une biopsie pulmonaire**
  - **Nouvelle nosologie**
  - **Diagnostic non-infectieux au cours des lympho-prolférations (non neutropénique)**

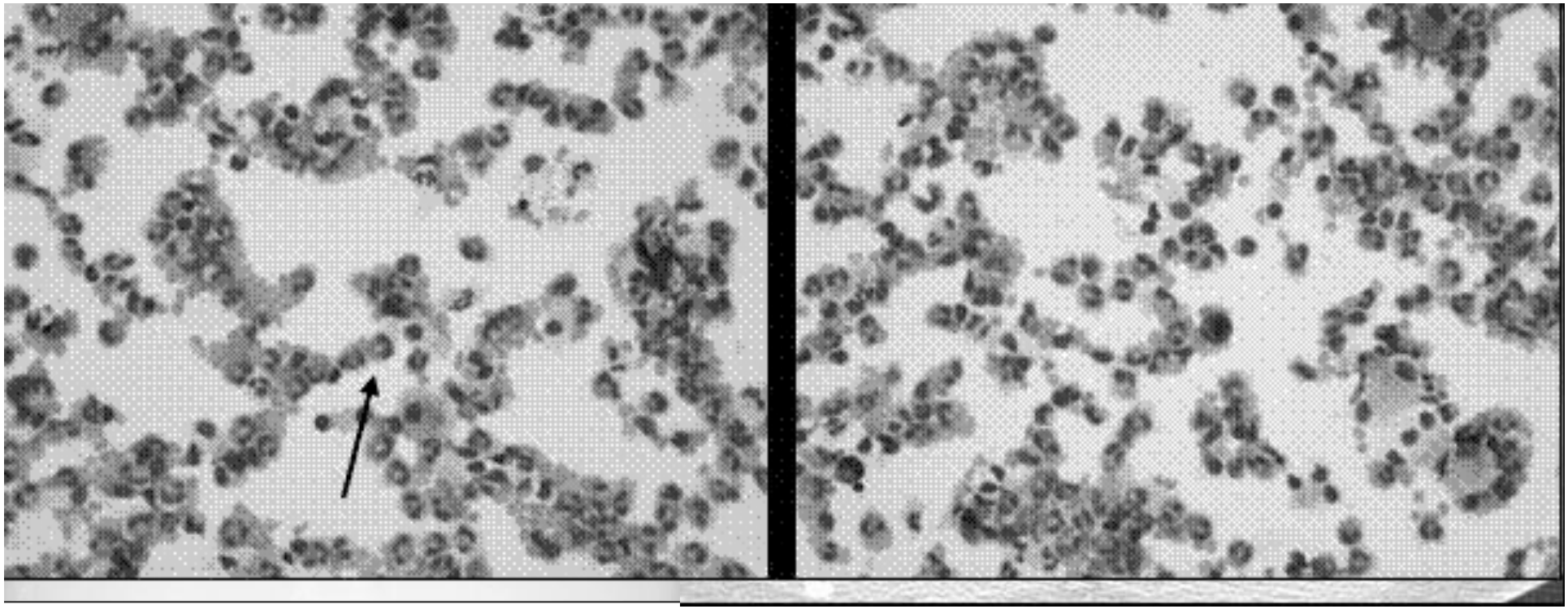
Pulmonary alveolar proteinosis:

Acellular material faintly stained by the MGG (a) pink-red after periodic-acid Schiff (PAS) staining

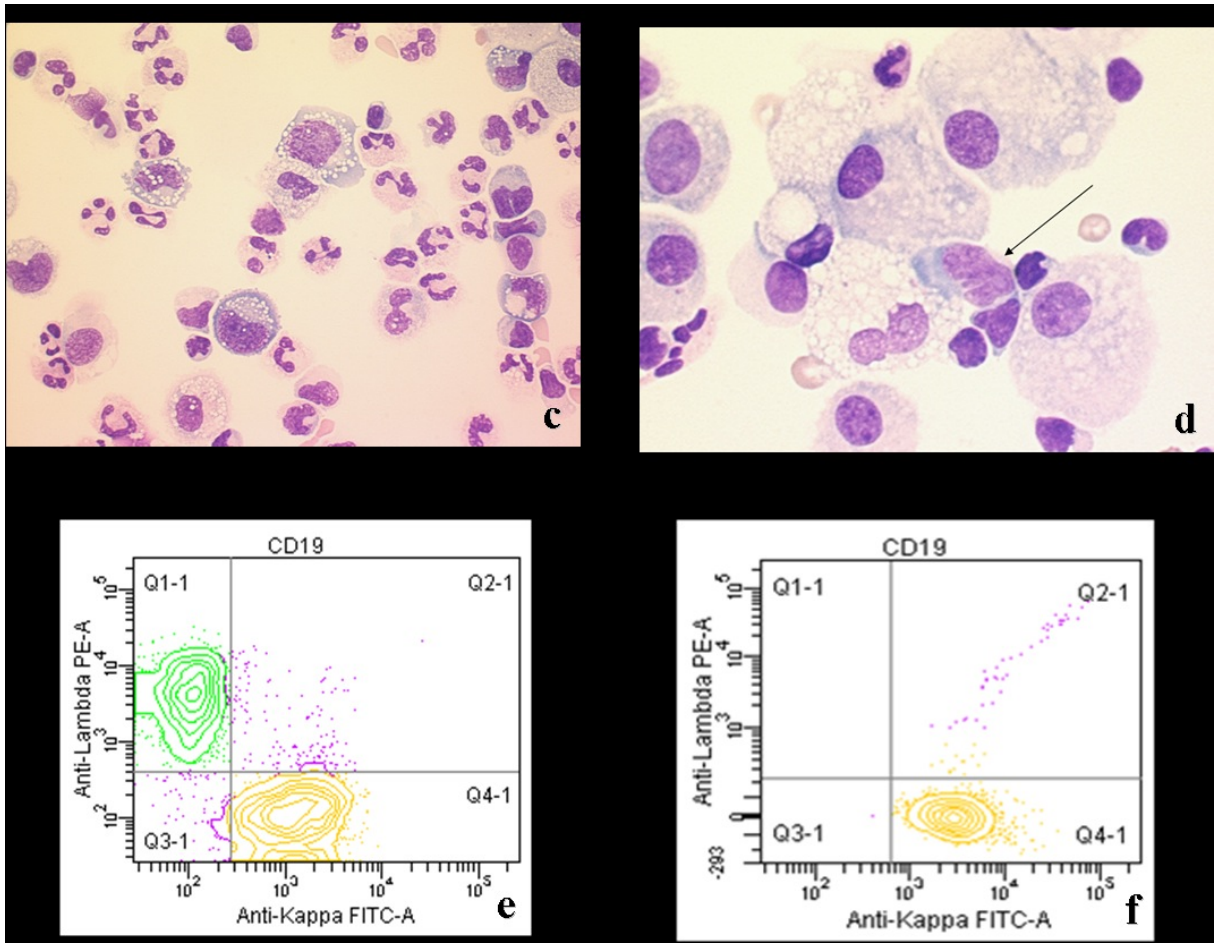


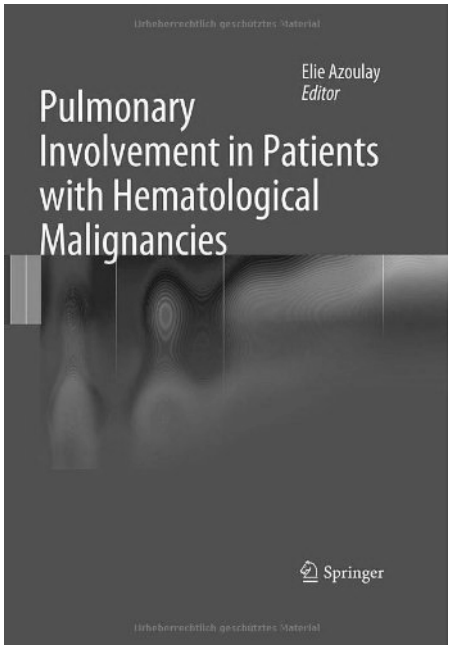
Bernaudin et al. In Pulmonary Involvement in Patients with Hematological malignancies. Springer 2011. Editor, E Azoulay

Leucémie à tricholeucocytes sous 2CDA



Pulmonary non-Hodgkin lymphoma

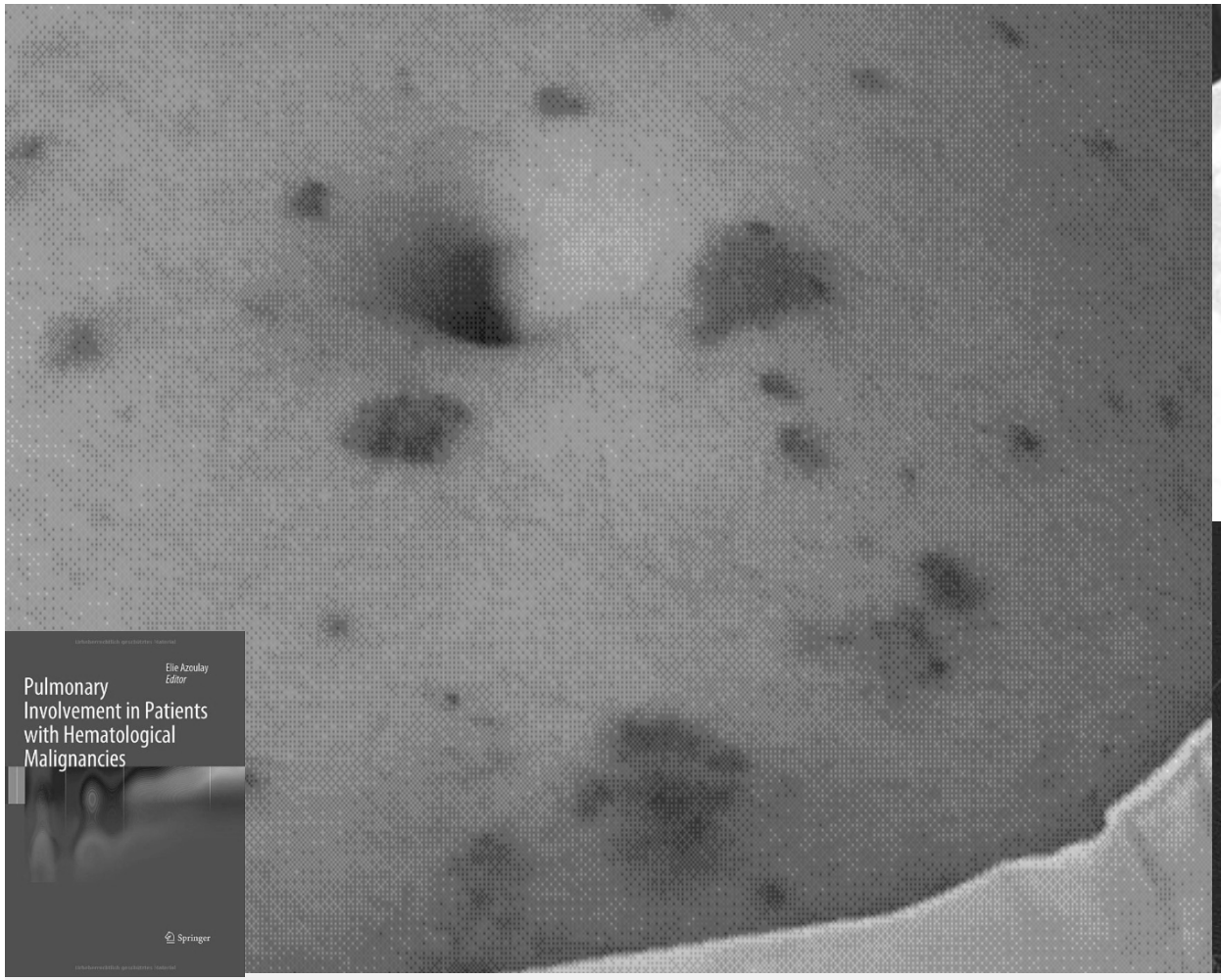


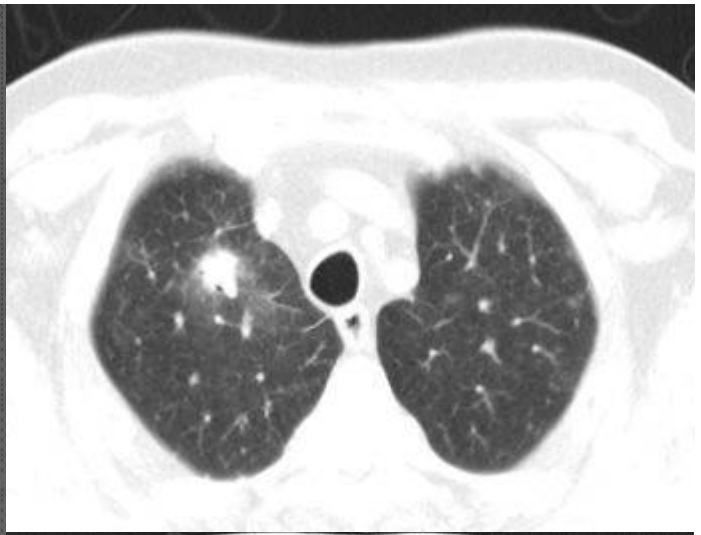


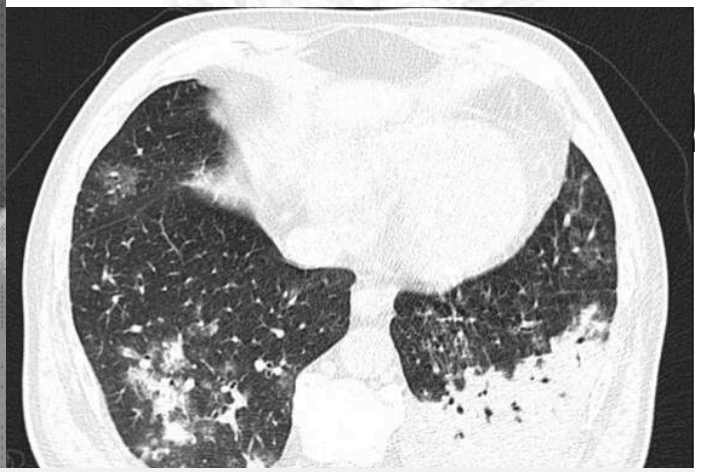
κ light chain restriction demonstrating a B-cell monoclonality

Bernaudin et al. In Pulmonary Involvement in Patients with Hematological malignancies. Springer 2011. Editor, E Azoulay

Fusariose invasive après autogreffe





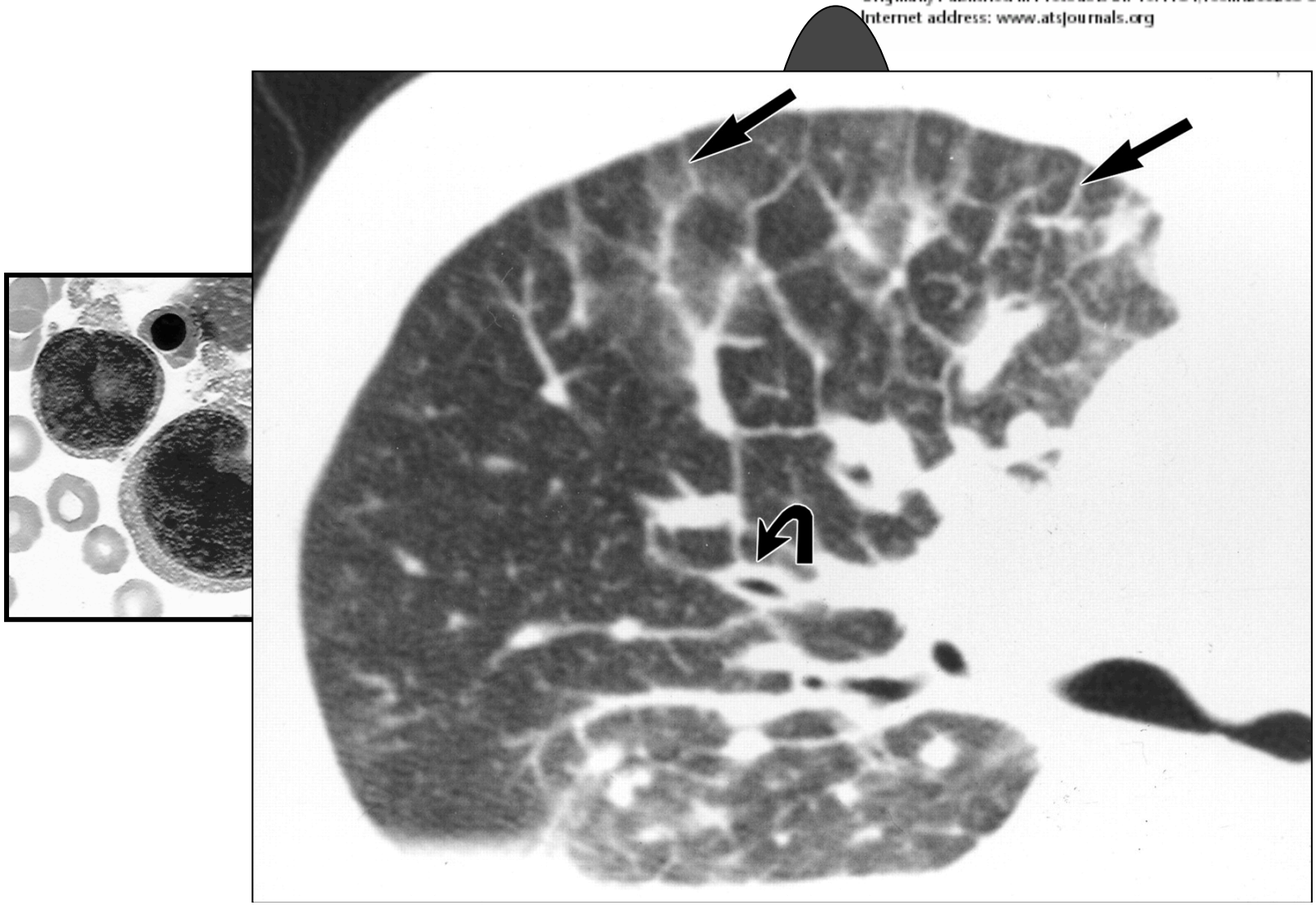


Nucci et al. In Pulmonary Involvement in Patients with Hematological malignancies. Springer 2011. Editor, E Azoulay

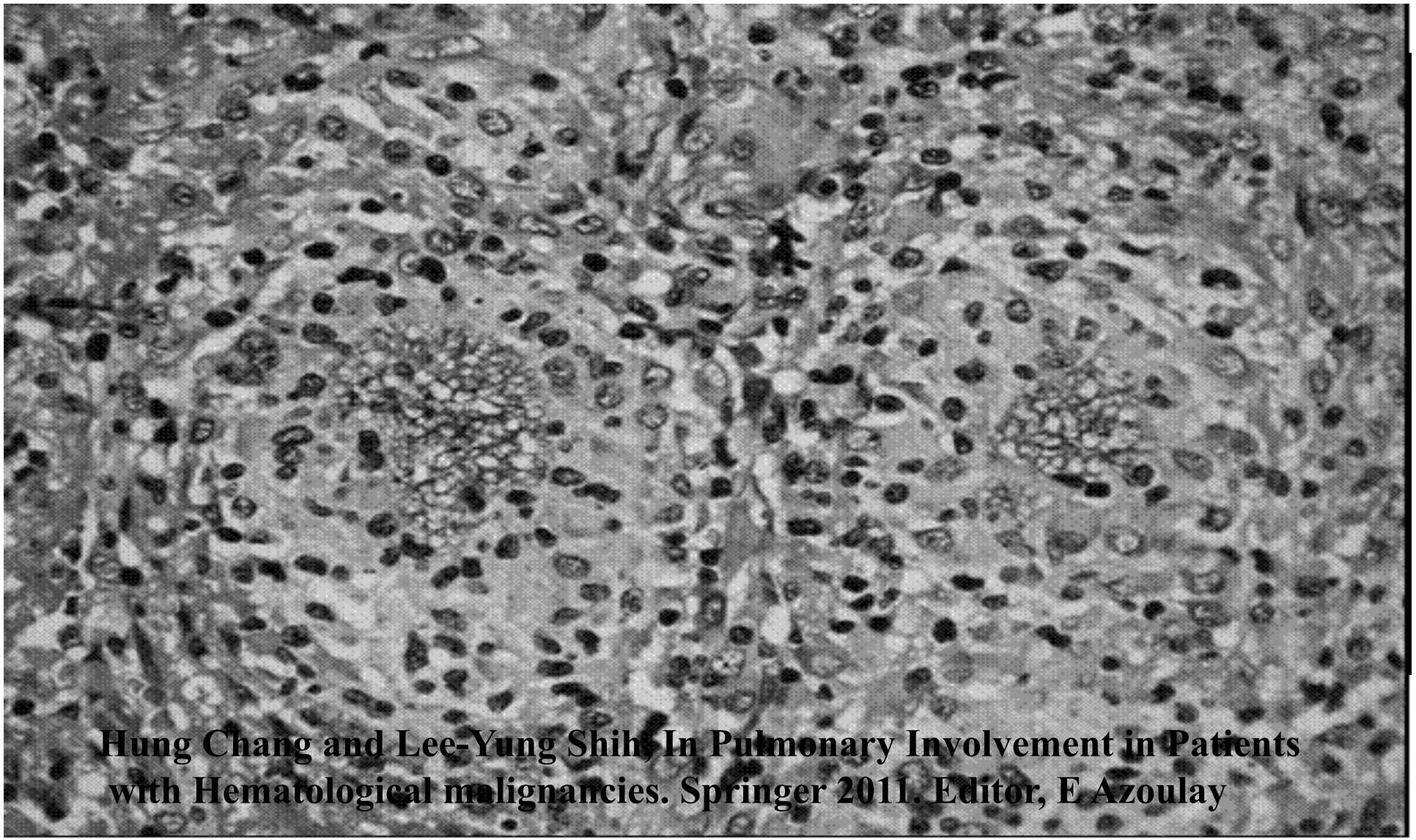
Acute Monocytic Leukemia Presenting as Acute Respiratory Failure

Élie Azoulay, Fabienne Fieux, Delphine Moreau, Guillaume Thiery, Philippe Rousselot, Antoine Parrot, Jean-Roger Le Gall, Hervé Dombret, and Benoît Schlemmer

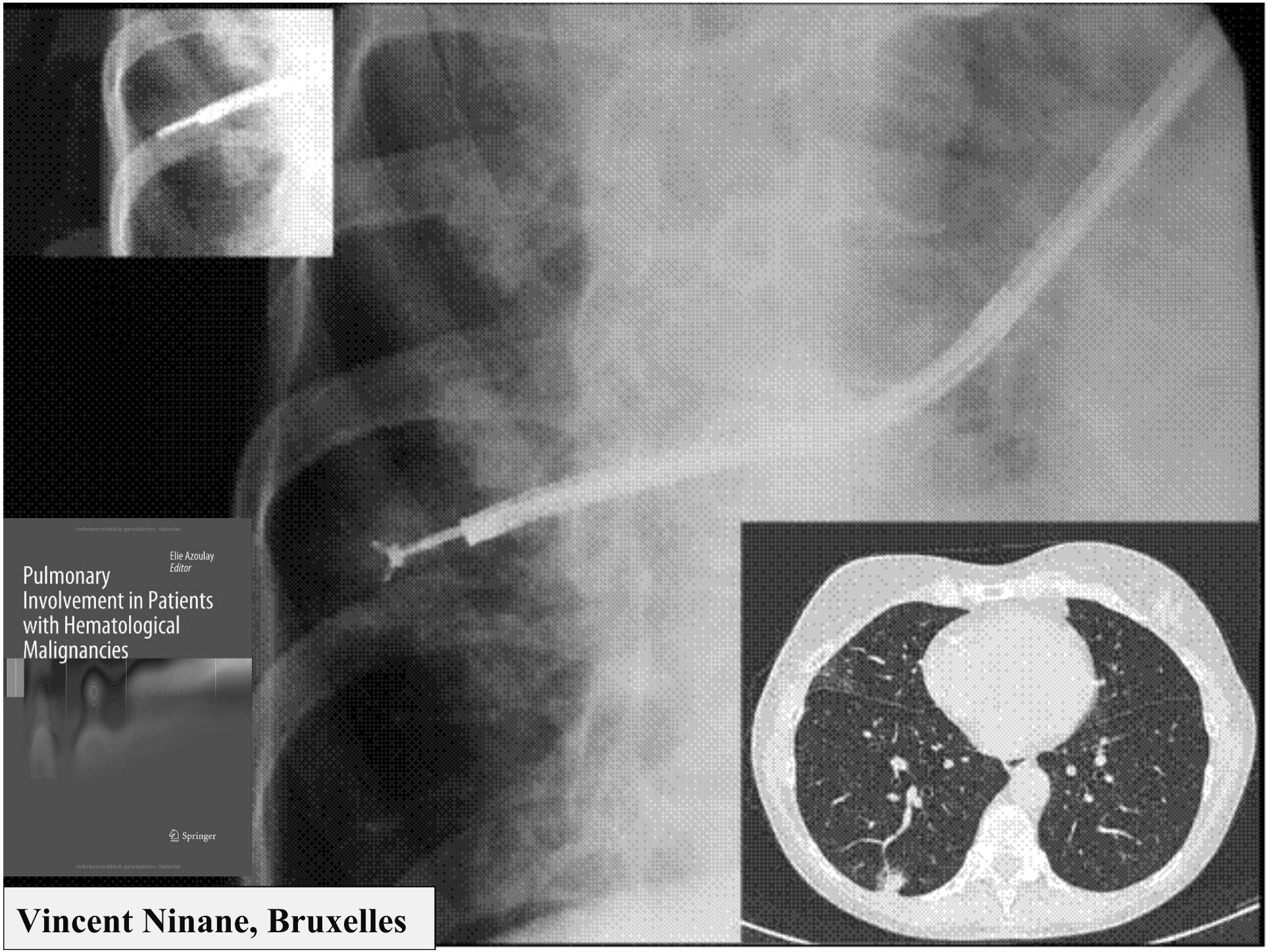
Am J Respir Crit Care Med Vol 167. pp 1329–1333, 2003
Originally Published In Press as DOI: 10.1164/rccm.200206-554OC on February 5, 2003
Internet address: www.atsjournals.org



Vous avez dis Pneumocystose ?

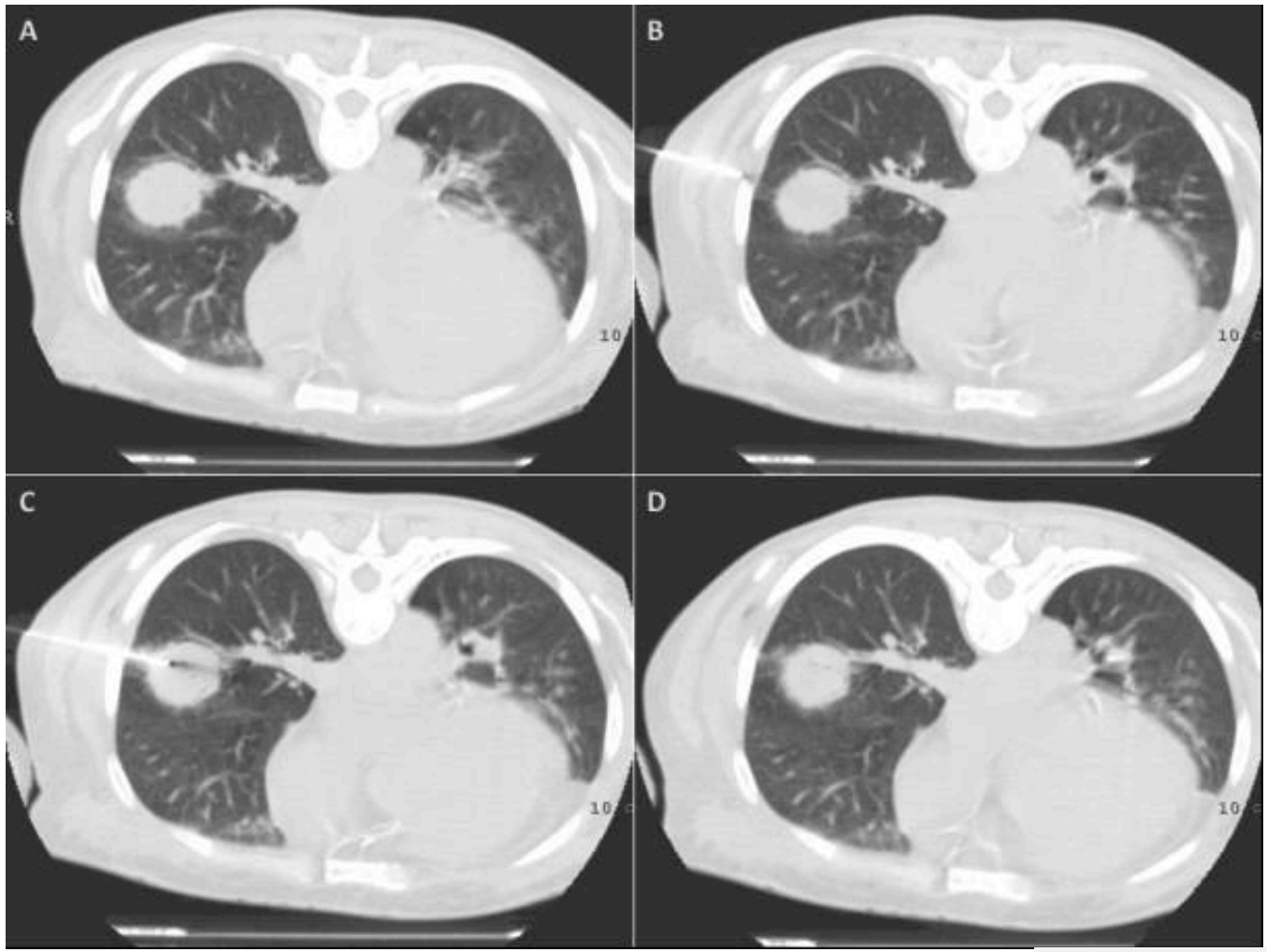


Hung Chang and Lee-Yung Shih, In Pulmonary Involvement in Patients with Hematological malignancies. Springer 2011. Editor, E Azoulay

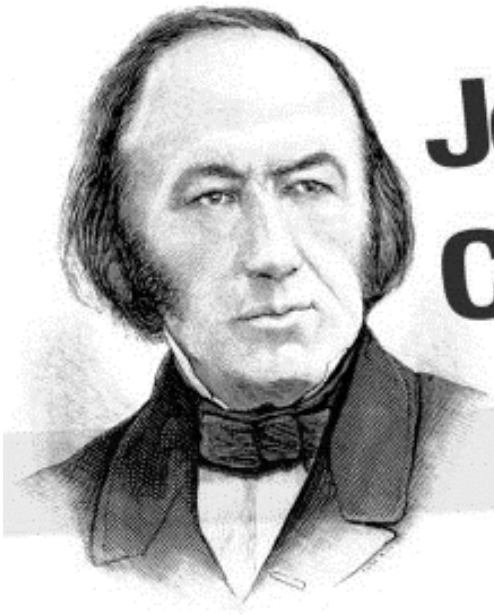


Vincent Ninane, Bruxelles

Un autre cas d'aspergillose pulmonaire invasive



De Bazelaire et al.



Journée de l'Hôpital Claude Bernard

Merci de votre attention !!!

GRRR-OH

Groupe de Recherche Respiratoire en Réanimation Onco-Hématologique

Merci de votre attention !!!

Le signe du halo

92% des patients avec aspergillose invasive (phase précoce)

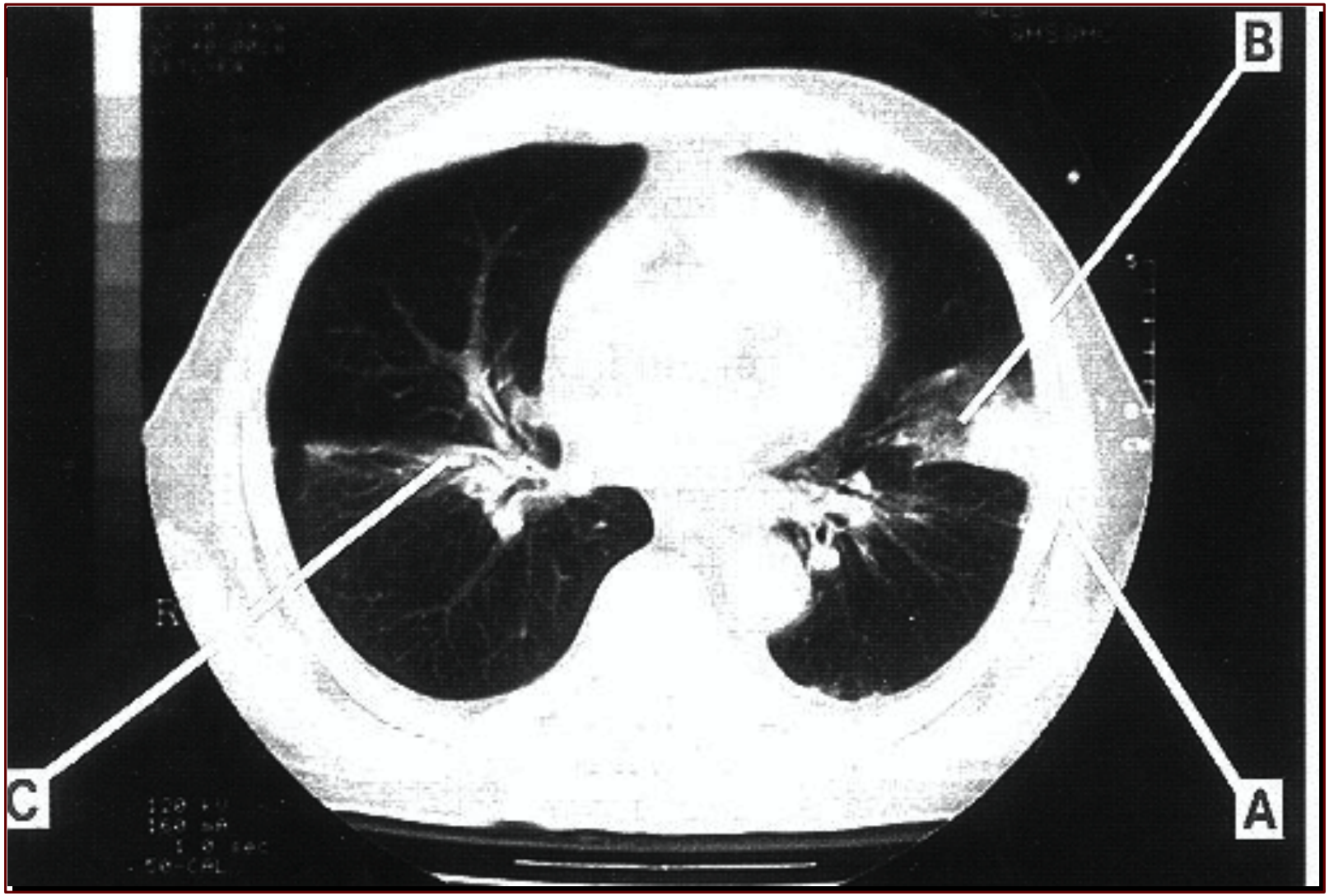


Table 2. Prevalence of the Halo Sign (HS) among Immunocompromised Patients with Invasive Fungal Infection (IIFI)

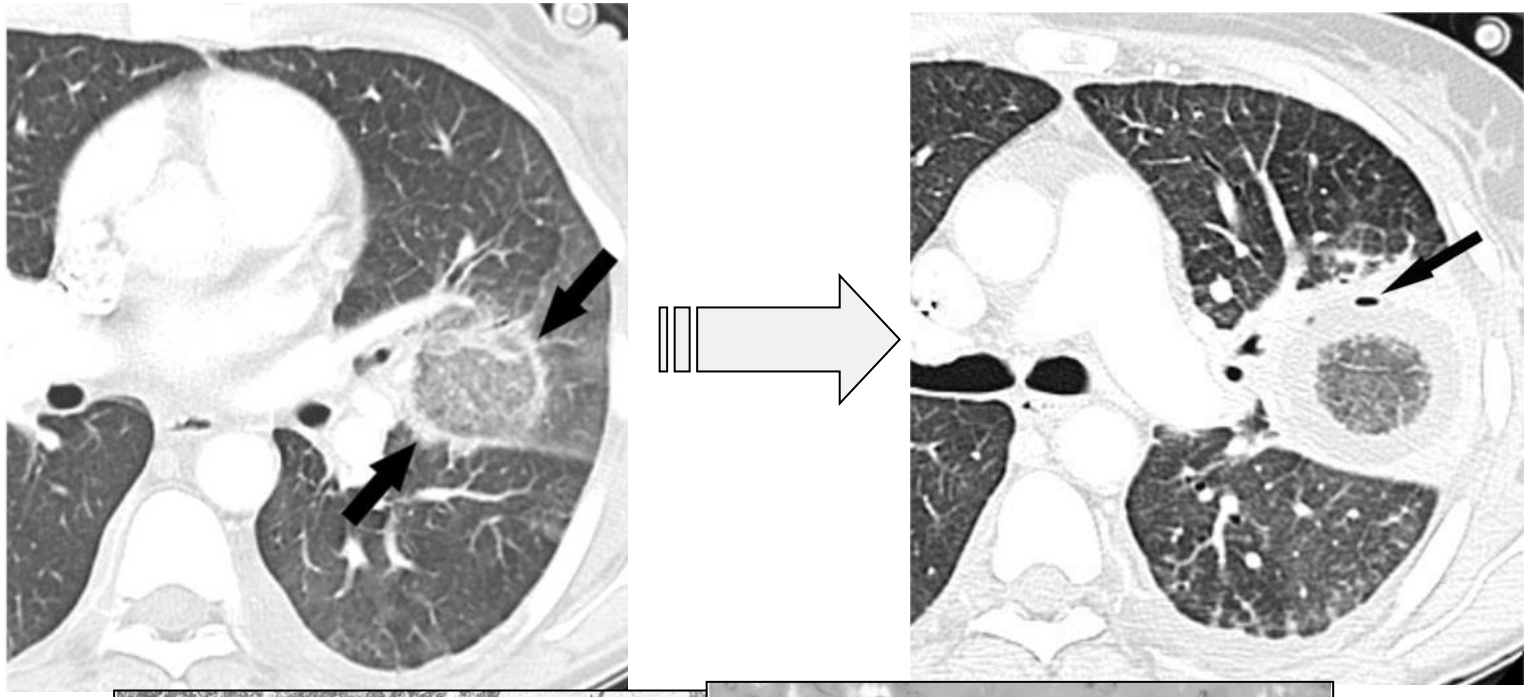
Study	Sample size	Timing of CT scan after the onset of clinical symptoms	Validation of IFI	Presence of the HS
Greene et al [3]	235 patients with IPA (203 with a hematological malignancy, 12 with high-dose corticosteroid use, 11 with AIDS, 8 with solid organ transplantation, and 1 with a solid tumor)	NA	Criteria of the European Organisation for Research and Treatment of Cancer/Mycoses Study Group [42]	143/235 (61%) (135 with a hematological malignancy and 8 with a non hematological malignancy)
Kuhlman et al [5]	9 patients with acute leukemia, neutropenia, and IPA	NA	Sputum culture or histologically via transthoracic needle biopsy aspiration or surgical lobectomy	2/9 (22%)
Blum et al [12]	38 patients with neutropenia (31 with a hematological malignancy, 6 with solid tumors, and 1 with human immunodeficiency virus) and suspected IPA	≤10 days (group A) and >10 days (group B)	Antemortem microscopically, BAL culture, or histologically using surgery/percutaneous needle biopsy/postmortem autopsy	16/22 (72%) with proven IPA in group A and 3/13 (23%) with proven IPA in group B
Bruno et al [13]	68 patients with IPA and 56 patients with bacterial pneumonia and prolonged neutropenia induced by bone marrow transplantation and/or high-dose chemotherapy for hematological malignancies	Within 24 hours	Histologically using lung biopsy or BAL culture	17/68 (25%) in the IPA group and 2/56 (4%) in the bacterial pneumonia group
Escuissato et al [14]	111 patients with proven pulmonary infection after HSCT for hematological conditions	Within 24 hours	Histologically or using culture of BAL, sputum, or blood specimens	10/21 (48%) patients with IFI (17 with IPA, 3 with pulmonary candidiasis, and 1 with both)
Kami et al [15]	48 patients with neutropenia, a hematological malignancy, and suspected IPA who underwent autopsy	NA	Culture or microscopically in lung specimens	13/17 (76%) with proven IPA
Caillot et al [20]	25 patients with a hematological malignancy, neutropenia, and IPA	Days 0, 3, 7, and 14	Histologically using surgical tissue excision	24/25 (96%) on day 0, 8/13 (62%) on day 3, 4/18 (22% on day 7, and 3/16 (19%) on day 14
Brodoefel et al [21]	40 patients with a hematological malignancy and IPA (65% with neutropenia)	Days 1, 4, 8, and 16	Histologically using lung biopsy, positivity for galactomannan antigen, positive BAL culture, or PCR BAL positive	88% on day 1, 63% on day 4 37% on day 8, and 18% o day 16
Hauggaard et al [32]	21 patients with a hematological malignancy, neutropenia, and IPA	Mean, 9 days (range, 1-10 days)	Criteria of the European Organisation for Research and Treatment of Cancer/Mycoses Study Group [42]	20/21 (95%),
Horger et al [33]	45 patients with IPA (42 with a hematological malignancy, 2 with renal transplantation, and 1 with long-term corticosteroid use), 24 of whom had neutropenia	Day 1	Histologically using lung biopsy, positivity for galactomannan antigen, BAL culture, or PCR BAL positivity	38/45 (84%)
Horger et al [34]	43 patients with IPA who were either neutropenic or severely immunocompromised because of hematological disease following high-dose chemotherapy (n = 13) or HSCT (n = 30)	NA	Histologically using lung biopsy, BAL culture, positivity for galactomannan antigen, or a positive PCR in the BAL specimen	31/43 (72%)

Table 3. Prevalence of IFIs in Immunocompromised Hosts with the HS and Specificity of the HS for IFIs

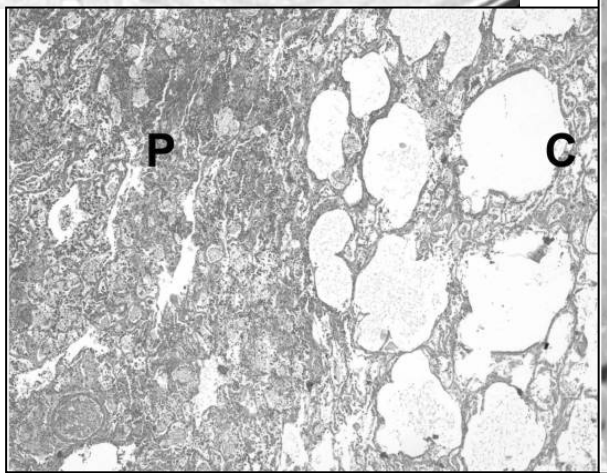
Study	Sample size with the HS	Timing of CT scan after the onset of clinical symptoms	Prevalence of IFIs	Specificity (%)
Blum et al [12]	16 patients with neutropenia and pulmonary infection	≤10 days	16/16 (100%) with IPA and none with bacterial pneumonia	100.0
Bruno et al [13]	19 patients with prolonged neutropenia induced by HSCT and/or high-dose chemotherapy for hematologic malignancies	Within 24 hours	17/19 (89%) with IPA and 2/19 (11%) with bacterial pneumonia	96.4
Escuissato et al [14]	16 patients with a proven pulmonary infection after HSCT for hematological conditions	Within 24 hours	10/16 (63%) with IFIs (mostly IPA), 3/16 with RSV pneumonia, 2/16 with bacterial pneumonia, and 1/16 with CMV pneumonia	92.3
Kami et al [15]	13 patients with neutropenia and a hematological malignancy	NA	13/13 (100%) IPA	100.0
Kami et al [16]	17 patients with a hematological malignancy, HSCT, and a pulmonary infection	NA	15/17 (88%) with IPA and 2/17 (12%) with non-IPA	97.4
Kim et al [35]	23 patients with a hematological malignancy (most with severe neutropenia) and suspected IPA who underwent lung biopsy	Median, 12 days	11/23 (48%) with proven IFIs (mostly IPA) and 12/23 (52.2%) with non-IFIs	20.0
Won et al [37]	5 patients with neutropenia, a hematological malignancy, and suspected IPA who underwent lung biopsy	NA	2/5 (40%) with IPA, 1/5 with PM, and 2/5 with cryptogenic organizing pneumonia	60
Franquet et al [50]	22 immunocompromised patients (HSCT, solid organ transplantation, hematological malignancy, HIV infection, or corticosteroid therapy) with pulmonary infections	NA	4/22 (18%) with IFIs, 7/22 (32%) with viral infections, 6/22 (27%) with mycobacterial infections, and 5/22 (23%) with bacterial infections	67.8

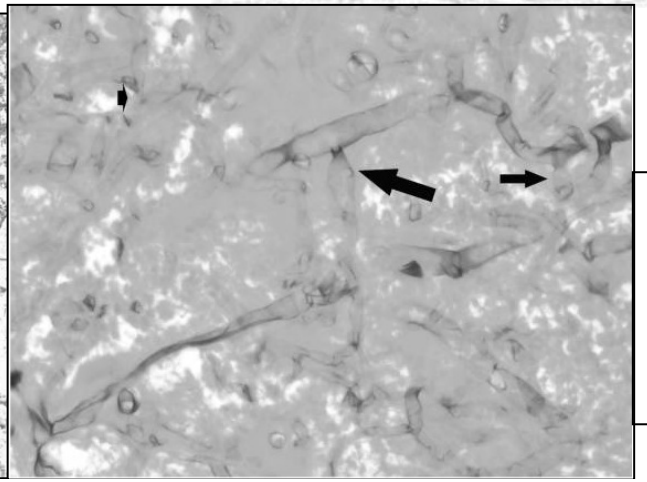
31 ans, Induction LAM, Neutropénie fébrile prolongée

Le signe du halo inversé



Infarctus + hémorragie périphérique





Filaments Non cloisonnées Intra-tissulaires

Diffuse Alveolar Hemorrhage in Allogeneic Bone Marrow Transplantation

A Postmortem Study

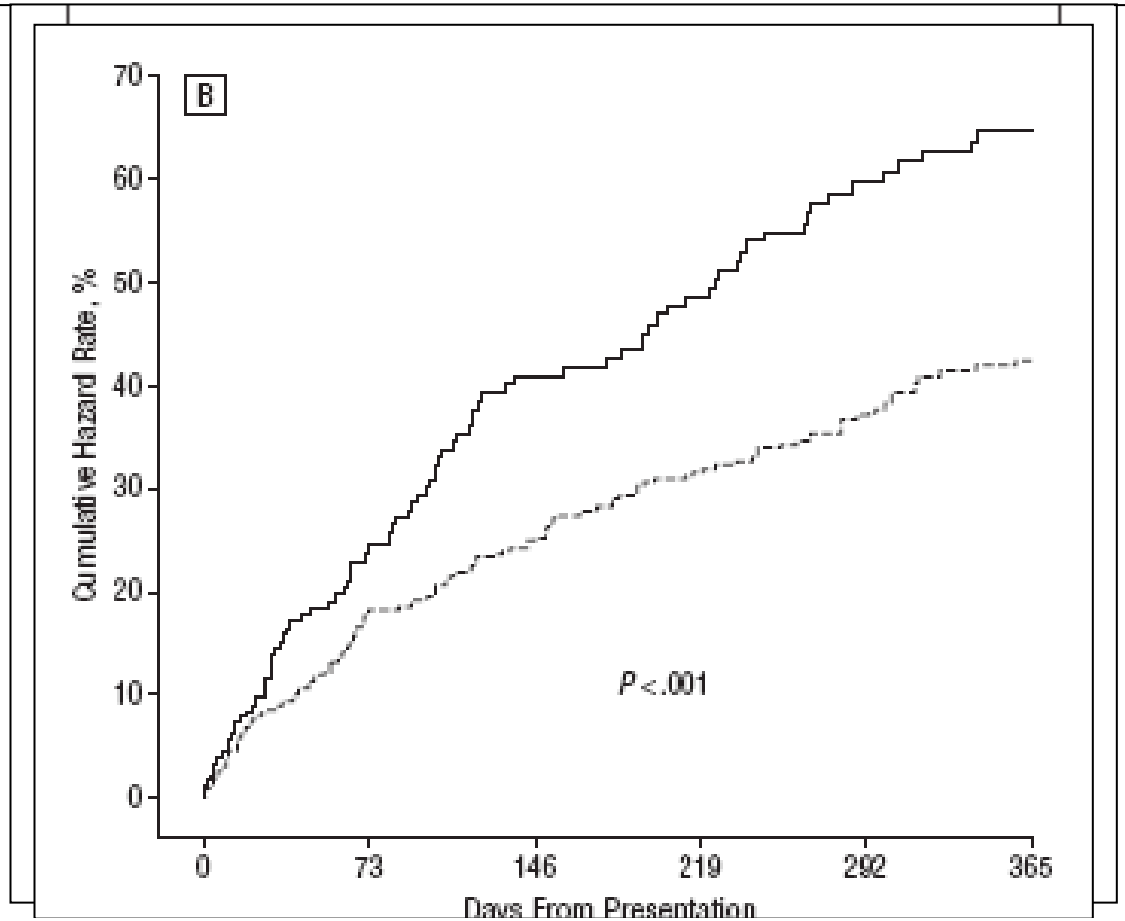
C. AGUSTÍ, J. RAMIREZ, C. PICADO, A. XAUBET, E. CARERAS, E. BALLESTER, A. TORRES, C. BATTOCHIA, and R. RODRIGUEZ-ROISIN

	Group A BMT Patients, n = 47 (%)	Group B Non-BMT Patients, n = 20 (%)	Group C Control Patients, n = 10 (%)
Diffuse alveolar hemorrage	11 (23)†	1 (5)	0
Bacterial pneumonia	11 (23)	9 (45)	3 (30)
Diffuse alveolar damage	13 (28)	2 (10)	3 (30)
CMV pneumonitis	20 (43)	0	2 (20)
Pulmonary aspergillosis	8 (17)	3 (15)	0
Leukemic infiltration	1 (2)	4 (20)	0
Pulmonary edema	0	2 (10)	0
Herpes pneumonia	2 (4)	0	0
Pulmonary infarction	1 (2)	0	0
Postchemotherapy fibrosis	0	1 (5)	0
Pulmonary hypertension	0	1 (5)	1 (10)
Pulmonary tuberculosis	0	1 (5)	0
Bacterial sepsis	0	1 (5)	0
Pulmonary embolism	0	0	2 (20)
Pneumocystis carinii pneumonia	0	0	1 (10)

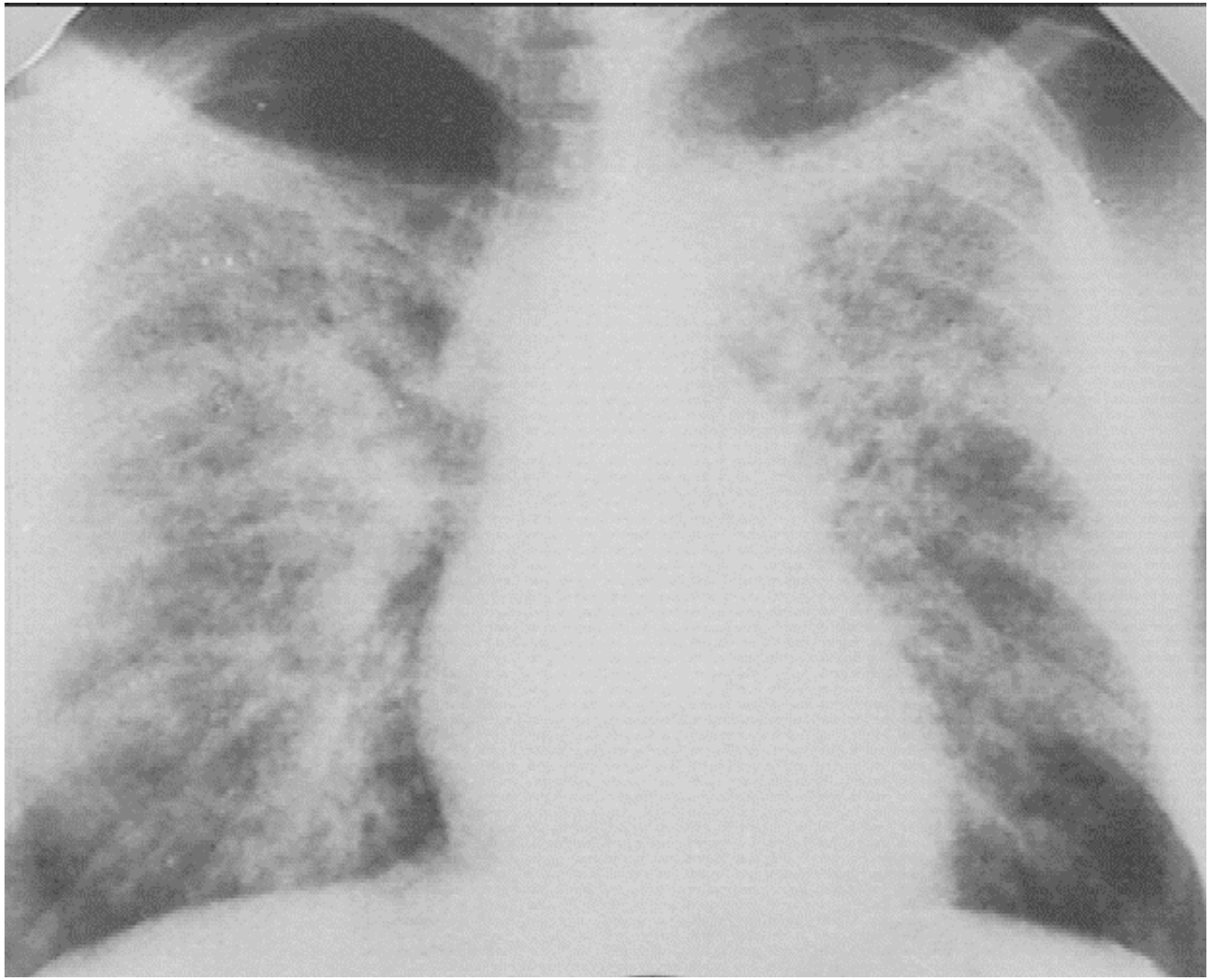
ORIGINAL INVESTIGATION

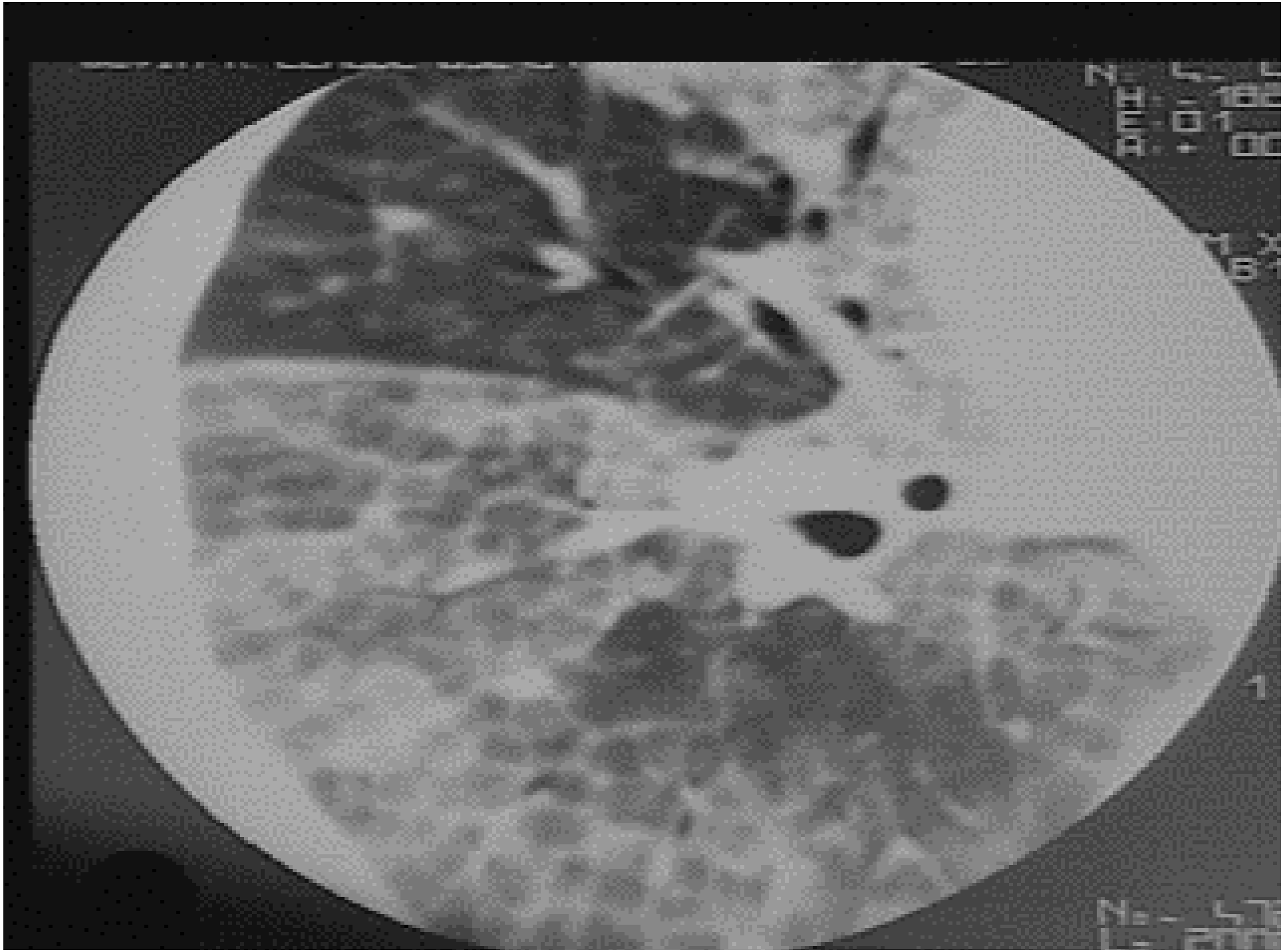
Clinical Uncertainty, Diagnostic Accuracy, and Outcomes in Emergency Department Patients Presenting With Dyspnea

Sandy M. Green, MD; Abelardo Martinez-Rumayor, MD; Shawn A. Gregory, MD; Aaron L. Baggish, MD; Michelle L. O'Donoghue, MD; Jamie A. Green, MD; Kent B. Lewandrowski, MD; James L. Januzzi Jr, MD



Aleveolar proteinosis





Bone Marrow Transplantation, (1997) 20, 681–687

Utility of fiberoptic bronchoscopy in bone marrow transplant patients

P White[1,2,3], JT Bonacum[1,2] and CB Miller[2]

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- ***We don't know whether the risk of FOB justifies the benefit***
- ***Value of FOB in BMT patients should be re-evaluated.***
- ***We suggest a randomized trial assessing the efficacy of empiric treatment without FOB and protocol-directed treatment based on a non-diagnostic FOB***

Bronchoscopic Evaluation of Pulmonary Infiltrates Following Bone Marrow Transplantation*

(CHEST 1997; 111:135-41)

Bowman Gray School of Medicine (Winston, Salem, NC)

Donnie P. Dunagan, MD; Albert M. Baker, MD; David D. Hurd, MD; and

- ***Whether FOB should be performed at all in MV BMT patients should be questioned… because of high associated risk and low probability of benefit***

Use of first line bronchoalveolar lavage in the immunosuppressed oncology patient

Royal Marsden Hospital, Sutton; and [2]Kent Cancer Centre, Maidstone, UK

PV Murray[1], MER O'Brien[1,2], AR Padhani[3], R Powles[4], D Cunningham[5], A Jeanes[3] and S Ashley[1]

Bone Marrow Transplantation (2001) 27, 967–971

- ***FOB+BAL only after a non-diagnostic CT***

Dyspnée et hypoxémie 80jours après une autogreffe de moelle

Prolifération intimale et fibrose des veinules pulmonaires
Obstruction vasculaire progressive
Hypertension pulmonaire après allogreffe, autogreffe, ou
Bléomycine, mitomycine ou carmustine (BCNU)