

Conduite Pratique du Diagnostic en Pathologie Respiratoire Médicamenteuse & Iatrogène

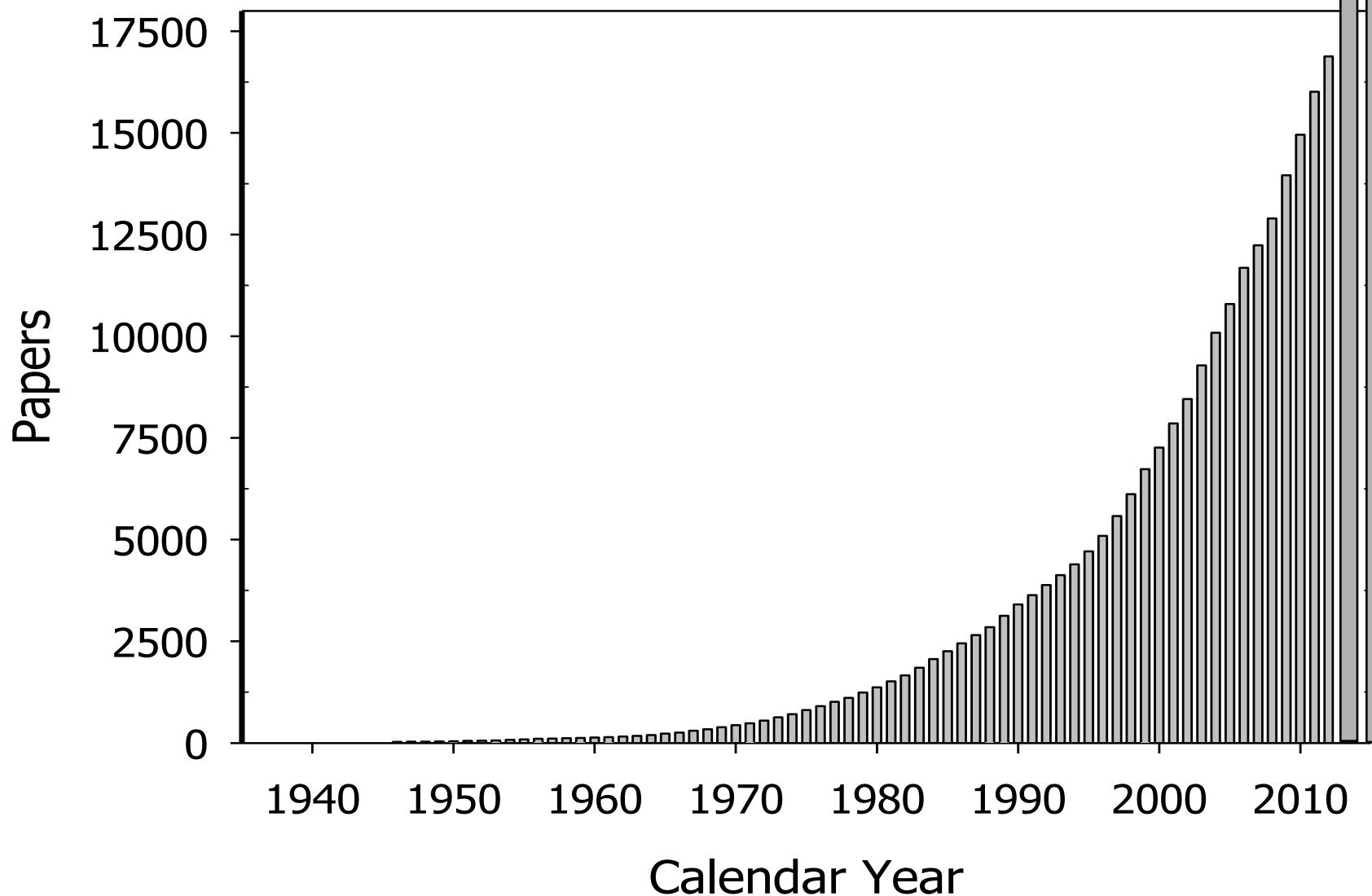
Service Pneumologie et Réanimation Respiratoire
CHU Dijon-Bourgogne

www.pneumotox.com

Zones d'intérêt (DSMB Bayer - Onxeo - Roche)

1197
25200

1197
26130





The Drug-Induced Respiratory Disease Website

Philippe Camus 2012- v2

Pascal Foucher - Philippe Camus 1997- v1

Department of Pulmonary Medicine and Intensive Care University Hospital Dijon France

Contribution: Ph Bonniaud, N Baudouin, A Fanton, C Camus, N Favrolt, M Guerriaud, L Jacquet

BROWSE BY »

DRUGS

PATTERNS

List All

A B C D E F G H I J K L M N O P Q R S T U V W X Y

Z

ACE inhibitors (ACEI)

I.b I.c IV.a IV.d V.a V.b V.d VIII.a VIII.q IX.e X.d
XVIII.k

5

ATRA

I.b I.k II.a II.b II.f II.k III.a V.a V.m VI.a VI.d
XII.c

4

Abacavir

I.a I.f II.a II.b IV.d X.a XV.d

2

Abciximab

III.a X.f

3

Acebutolol

I.b I.d V.a V.d

2

SEARCH

Search by keyword



Advanced search

NOTE LEGEND



LEGEND PATTERNS



LATEST NEWS

Wed, 12 Jun 2013 09:28:47

[Alerts - Warnings](#)

Sun, 26 May 2013 17:55:11

[To our pathology colleagues](#)

Tue, 14 May 2013 10:27:01

[Diagnosing DIRD](#)

Wed, 20 Feb 2013 16:42:42

17:36

Browse

DRUGS PATTERNS

A

Abacavir	1	>
Abciximab	4	>
Acebutolol	2	>
Acetaminophen	0	>
Acetazolamide	4	>
Acetylcysteine	5	>
Acetylsalicylic acid	5	>

DRUGS **PATTERNS**

A

Abacavir 1 >
Abciximab 4 >
Acebutolol 2 >
Acetaminophen 0 >
Acetazolamide 4 >
Acetylcysteine 5 >
Acetylsalicylic acid 5 >

17:36

Browse

DRUGS PATTERNS

I : Interstitial - infiltrative lung disease

- a : Acute cellular interstitial lung disease/pneumonia >
- b : Subacute interstitial pneumonia. Similar to but less severe than 1a >
- c : Pulmonary infiltrates and eosinophilia. Eosinophilic pneumonia (>
- d : Organising pneumonia (BOOP - AFOP) >
- e : Desquamative interstitial pneumonia (DIP pattern) >
- f : Lymphocytic interstitial pneumonia (LIP pattern) >
- g : Pulmonary fibrosis >

DRUGS **PATTERNS**

I : Interstitial - infiltrative lung disease

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Problèmes actuels

- ❑ Diagnostic malgré test de réintroduction négative
- ❑ Journaux ‘Open access’: 1000€...
- ❑ Fake Journals: Reviewing?...
- ❑ Big data
- ❑ 146 papiers douteux
- ❑ Oshima *et al.* 2012
 - [Why is the incidence of post-vaccination interstitial pneumonia high in Japan?] Nihon Naika Gakkai Zasshi 2012; 101: 186-7
- ❑ Pneumotox: Chaque article est réévalué

Leflunomide Use and Risk of Lung Disease in Rheumatoid Arthritis: A Systematic Literature Review and Metaanalysis of Randomized Controlled Trials

Richard Conway, Candice Low, Robert J. Coughlan, Martin J. O'Donnell, and John J. Carey

ABSTRACT. *Objective.* To evaluate the relative risk (RR) of pulmonary disease among patients with rheumatoid arthritis (RA) treated with leflunomide (LEF).

Methods. We searched PubMed, Embase, and the Cochrane Central Register of Controlled Trials to April 15, 2014. We included double-blind randomized controlled trials (RCT) of LEF versus placebo or active comparator agents in adults with RA. Studies with fewer than 50 subjects or shorter than 12 weeks were excluded. Two investigators independently searched both databases. All authors reviewed selected studies. We compared RR differences using the Mantel-Haenszel random-effects method to assess total respiratory adverse events, infectious respiratory adverse events, noninfectious respiratory adverse events, interstitial lung disease, and death.

Results. Our literature search returned 5673 results. A total of 8 studies, 4 with placebo comparators, met our inclusion criteria. There were 708 respiratory adverse events documented in 4579 participants. Six cases of pneumonitis occurred, all in the comparator group. Four pulmonary deaths were reported, none in the LEF group. LEF was not associated with an increased risk of total adverse respiratory events (RR 0.99, 95% CI 0.56–1.78) or infectious respiratory adverse events (RR 1.02, 95% CI 0.58–1.82). LEF was associated with a decreased risk of noninfectious respiratory adverse events (RR 0.64, 95% CI 0.41–0.97).

Conclusion. Our study found no evidence of increased respiratory adverse events in RCT of LEF treatment. (J Rheumatol First Release March 15 2016; doi:10.3899/jrheum.150674)

Concordance imagerie-anapath?

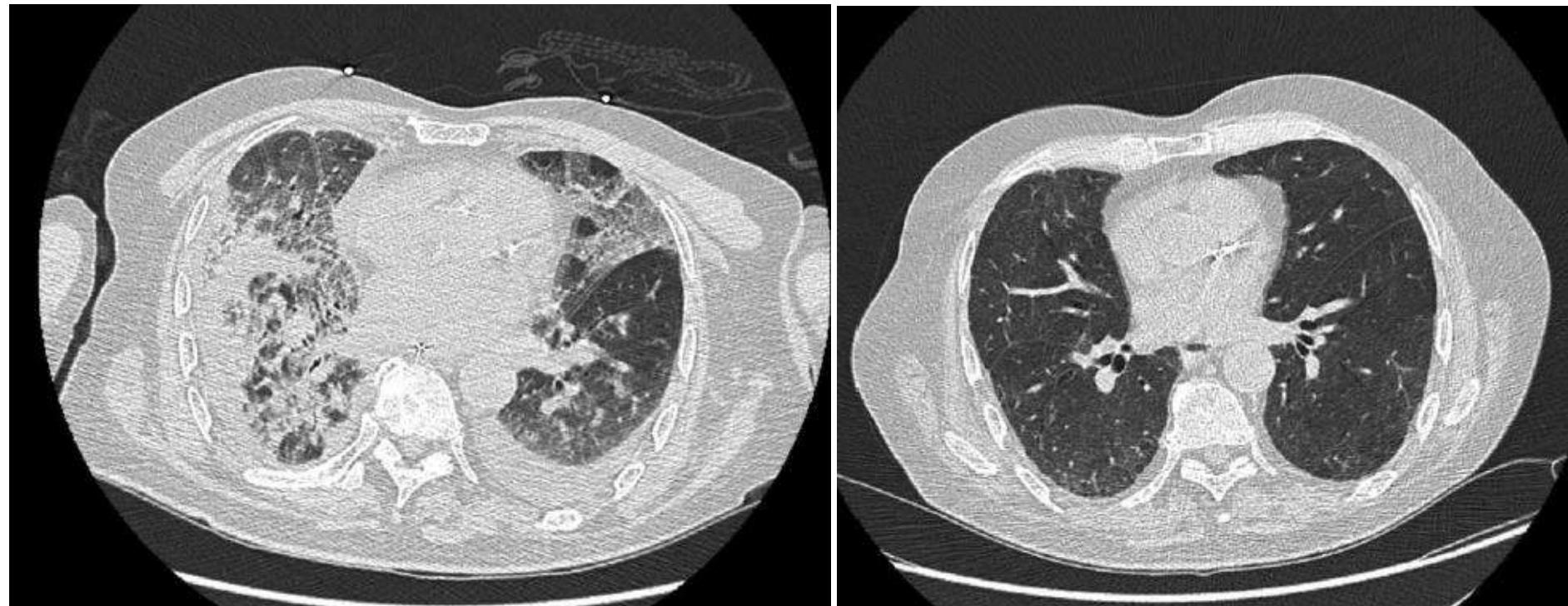
- ❑ Cleverley 2002: 20 Pnl médicamenteuses
 - ❑ Concordance: 45%
 - ❑ Discordance: 55%
- ❑ Blackhall 2013: 103 Pnl
 - ❑ Concordance: 18.4%
 - ❑ Discordance: 51.5%
 - ❑ Pas de diagnostic: 30.1%
- ❑ Kayatta 2013: 194 Pnl
 - ❑ Concordance: 15%
- ❑ BOOP, DAD, PIC, PINS etc... *Sine pathology*
 - ❑ 36 papiers...

2013

CASE REPORT

Mesalazine-induced lung fibrosis

Ebraheem Alskaf, Amer Aljoudeh, Frank Edenborough



Successful Crizotinib Rechallenge After Crizotinib-Induced Interstitial Lung Disease in Patients With Advanced Non-Small-Cell Lung Cancer

Nobuhiro Asai, Etsuro Yamaguchi, Akihito Kubo

Clinical Practice Points

- Although the development of the anaplastic lymphoma kinase tyrosine kinase inhibitor (ALK TKI), as well as epidermal growth factor receptor (EGFR) TKIs, has a great impact and has led to a paradigm shift in the treatment of advanced non–small-cell lung cancer (NSCLC), the occurrence of drug-induced interstitial lung disease (ILD) remains problematic.
- We report a successful rechallenge of crizotinib after crizotinib-induced ILD in a patient with ALK-rearranged NSCLC. To our knowledge, this is the second case successfully treated and the first short review of crizotinib-induced ILD.
- Comparing the 2 successfully treated cases, including ours, with the fatal case previously reported, we found some common characteristics in the successful case and our case, among which was the fact that our patient had no risk of EGFR TKI–induced ILD. The risk factors for EGFR TKI–induced ILD may be related to crizotinib-induced ILD.
- Although crizotinib-induced ILD may be fatal, some patients might benefit from rechallenge of the drug. It is important to elucidate the clinicopathologic characteristics of ALK TKI–induced ILD and to determine its risk factors.

Successful Crizotinib Rechallenge After ILD

Figure 1 (A) Chest Computed Tomography (CT) Showed Crizotinib-Induced Interstitial Lung Disease (ILD) in the Right Upper Lobe of the Lung (Blue Arrow). (B) Two Weeks After Crizotinib was Discontinued, Chest CT Showed That ILD had Improved (Blue Arrow) and That the Tumor Regrew (Red Arrowhead)

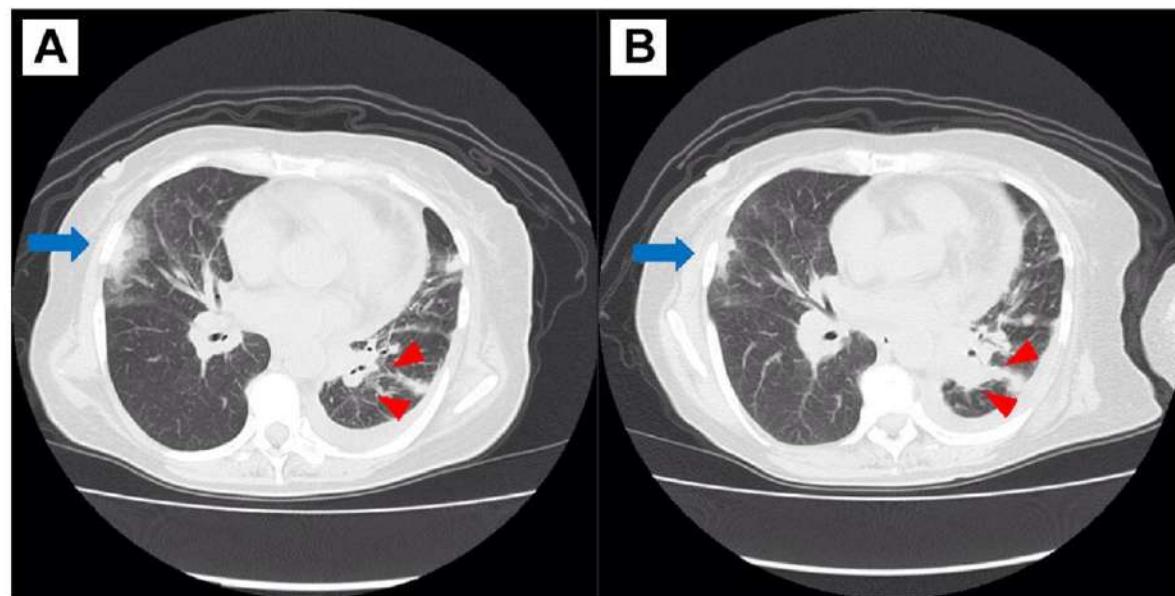
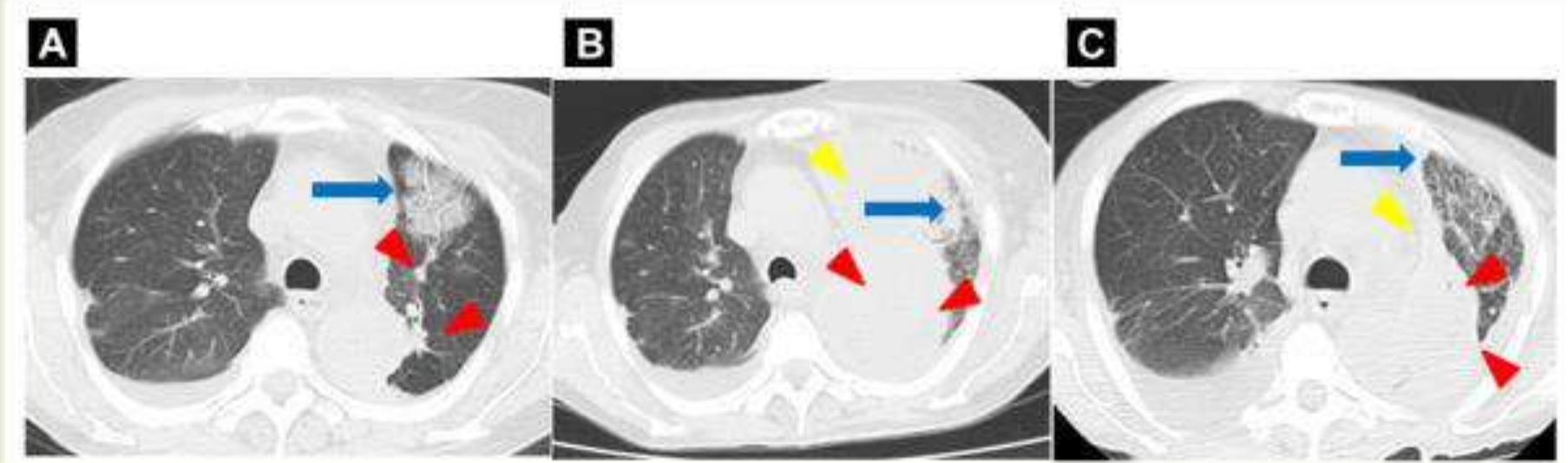


Figure 2 (A) Forty-Five Days After Restarting Crizotinib, Chest Computed Tomography (CT) Showed Crizotinib-Induced Interstitial Lung Disease (ILD) in the Left Upper Lobe of the Lung (Blue Arrow). (B) Four Weeks After Cessation of Crizotinib, Chest CT Showed That the Tumor had Expanded Dramatically, Which Seems to be a Disease Flare, and ILD Remained (Blue Arrow). (C) Chest CT Revealed no Exacerbation of Crizotinib-Induced ILD in the Left Upper Lobe of the Lung (Blue Arrow), Although the Anterior Part of the Tumor Shrank (Yellow Arrowhead) and the Posterior Part of the Tumor did not Regrow (Red Arrowhead), Resulting in Stable Disease According to Response Evaluation Criteria in Solid Tumors





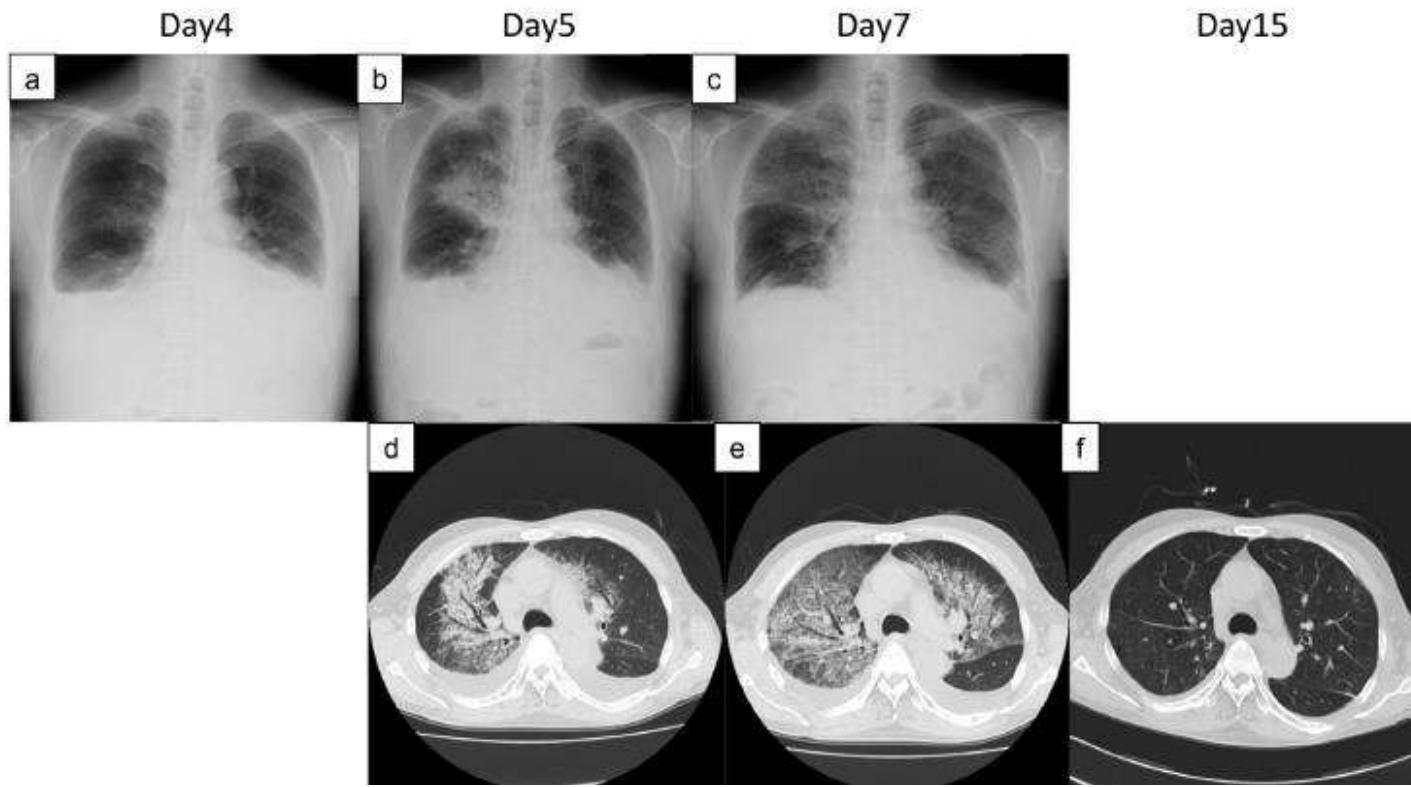
Case report

A case of miriplatin-induced lung injury

Fumio Kumasawa ^{a,*}, Takao Miura ^b, Toshimi Takahashi ^b, Daisuke Endo ^a, Takashi Ohki ^a, Hiroshi Nakagawara ^b, Shuichiro Maruoka ^a, Ichiro Tsujino ^a, Ogawa Masahiro ^b, Yasuhiro Gon ^a, Noriaki Takahashi ^a, Mitsuhiro Moriyama ^b, Shu Hashimoto ^a

^a Division of Respiratory Medicine, Department of Internal Medicine, Nihon University School of Medicine, Tokyo, Japan

^b Division of Gastroenterology and Hepatology, Department of Internal Medicine, Nihon University School of Medicine, Tokyo, Japan



▣ ‘Patients and Methods’

- ❖ Consecutive patients who developed acute respiratory failure while taking apixaban and were subsequently diagnosed as having ILD between February 2013 (sales release of apixaban in Japan) and May 2015. Chest computed tomography results were mandatory to make a positive diagnosis.

INTERSTITIAL LUNG DISEASE DURING APIXABAN THERAPY

3

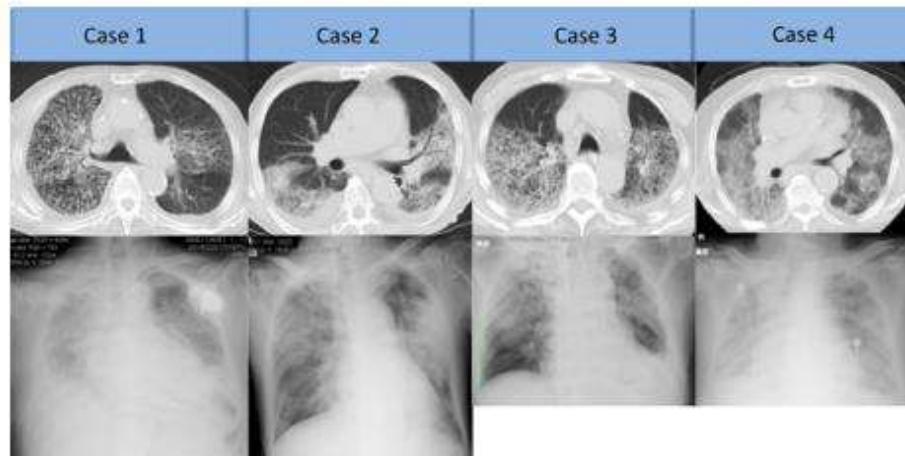


Figure 1. Chest computed tomography and routine radiography early after symptom onset.

Table 3 – Incidence of DLIs in Japan and abroad.

Drug	Japan	Abroad ^a	O.R.
Gefitinib	3.98% (n=1482)	0.3% (United States: n=23,000)	x13.2
Leflunomide	1.81% (n=3867)	0.017% (Abroad: n=861,860)	x106
Bleomycin	0.66% (n=3772)	0.01% (Abroad: n=295,800)	x66
Bortezomib	2.33% (n=3556)	0.16% (Abroad: n=106,832)	x14.6
Erlotinib	4.52% (n=3488)	0.7% (Abroad: n=4900)	x6.5

Modified from References [10–12].

^a Data for some drugs include data from Japan.

LBA

- ❑ Exclusion d'une cause infectieuse (PCR *Pneumocystis*)
- ❑ Utilité
 - ❑ Eosinophilie pulmonaire
 - ❑ PnP du méthotrexate (D'Elia 2014)
 - ❖ 47 cas revus
 - ❖ Ly 21%
 - ❖ Ly + PNN 23%
 - ❖ Ly + Eo 21%
 - ❖ Ly + PNN + Eo 23%
 - ❖ Normal 9%
 - ❑ ?: Amiodarone, nitrofurantoine
 - ❑ Cf Pneumotox

Pathology

- ❑ ‘Regarding drug-related injury, no histopathologic changes are specific for any drug, despite any claims in the literature to the contrary’

Leslie K Arch Pathol Lab Med, 2007; 131: 407

- ❑ TBLB ‘unreliable’
- ❑ OLB: 4.5-6.9%
- ❑ VATS: Mortality up to 2.1%



Impots.gouv.fr - Les dons aux enfant...

Just Before Dying, a Thrill at 41,000...

financement participatif - Recherche...

Pneumotox » Drug » Apixaban



BROWSE

NEWS

ABOUT

CONTACT



The Drug-Induced Respiratory Disease Website

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Department of Pulmonary Medicine and Intensive Care University Hospital Dijon France

Contribution: Ph Bonniaud, N Baudouin, A Fanton, C Camus, N Favrold, M Guerriaud, L Jacquet



BROWSE BY ▾

DRUGS

PATTERNS

Apixaban



No description available.

Last update 06/10/2014



SEARCH

 Search by keyword[Advanced search](#)

Patterns

I.b Subacute pneumonitis



III.a Alveolar hemorrhage, diffuse (DAH)



SEE ALSO

[Anticoagulants, direct oral](#)



[\(anti-thrombin, -IIa, -Xa\)](#)



[▼ NOTE LEGEND](#)

[▼ LEGEND PATTERNS](#)



LATEST NEWS

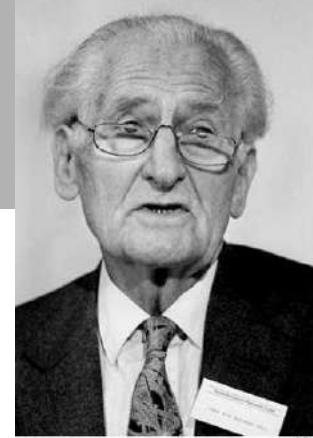
Fri, 22 May 2015 12:24:09

[Alerts. New drug casualties](#)

Sun, 17 May 2015 23:00:06

- ❑ Problèmes actuels
- ❑ Causalité vs. association fortuite: principes généraux
- ❑ Scores - Poids relatif des mots
- ❑ Checklist
- ❑ Management (corticoïdes, réintroductions)
- ❑ Situations particulières

Association or causation? Hill, 1965



Sir Austin Bradford Hill 1891-1991

- ▣ Magnitude of signal (number of cases, O.R.)
- ▣ Consistency (differents places, persons, times)
- ▣ Appropriate timing
- ▣ Dose relatedness
- ▣ Specificity (imaging, lab, BAL, pathology)
- ▣ Unexplained otherwise (u/l disease, infection, LVF, drugs)
- ▣ Coherent: e.g.on-target AEs of biologics
- ▣ Experimental support
- ▣ Analogy with similar drugs/compounds
- ▣ p<0.05

Table I. ADR probability scale

To assess the adverse drug reaction, please answer the following questionnaire and give the pertinent score.

	<i>Yes</i>	<i>No</i>	<i>Do not know</i>	<i>Score</i>
1. Are there previous <i>conclusive</i> reports on this reaction?	+1	0	0	
2. Did the adverse event appear after the suspected drug was administered?	+2	-1	0	
3. Did the adverse reaction improve when the drug was discontinued or a <i>specific</i> antagonist was administered?	+1	0	0	
4. Did the adverse reaction reappear when the drug was readministered?	+2	-1	0	
5. Are there alternative causes (other than the drug) that could on their own have caused the reaction?	-1	+2	0	
6. Did the reaction reappear when a placebo was given?	-1	+1	0	
7. Was the drug detected in the blood (or other fluids) in concentrations known to be toxic?	+1	0	0	
8. Was the reaction more severe when the dose was increased, or less severe when the dose was decreased?	+1	0	0	
9. Did the patient have a similar reaction to the same or similar drugs in <i>any</i> previous exposure?	+1	0	0	
10. Was the adverse event confirmed by any objective evidence?	+1	0	0	
				Total score

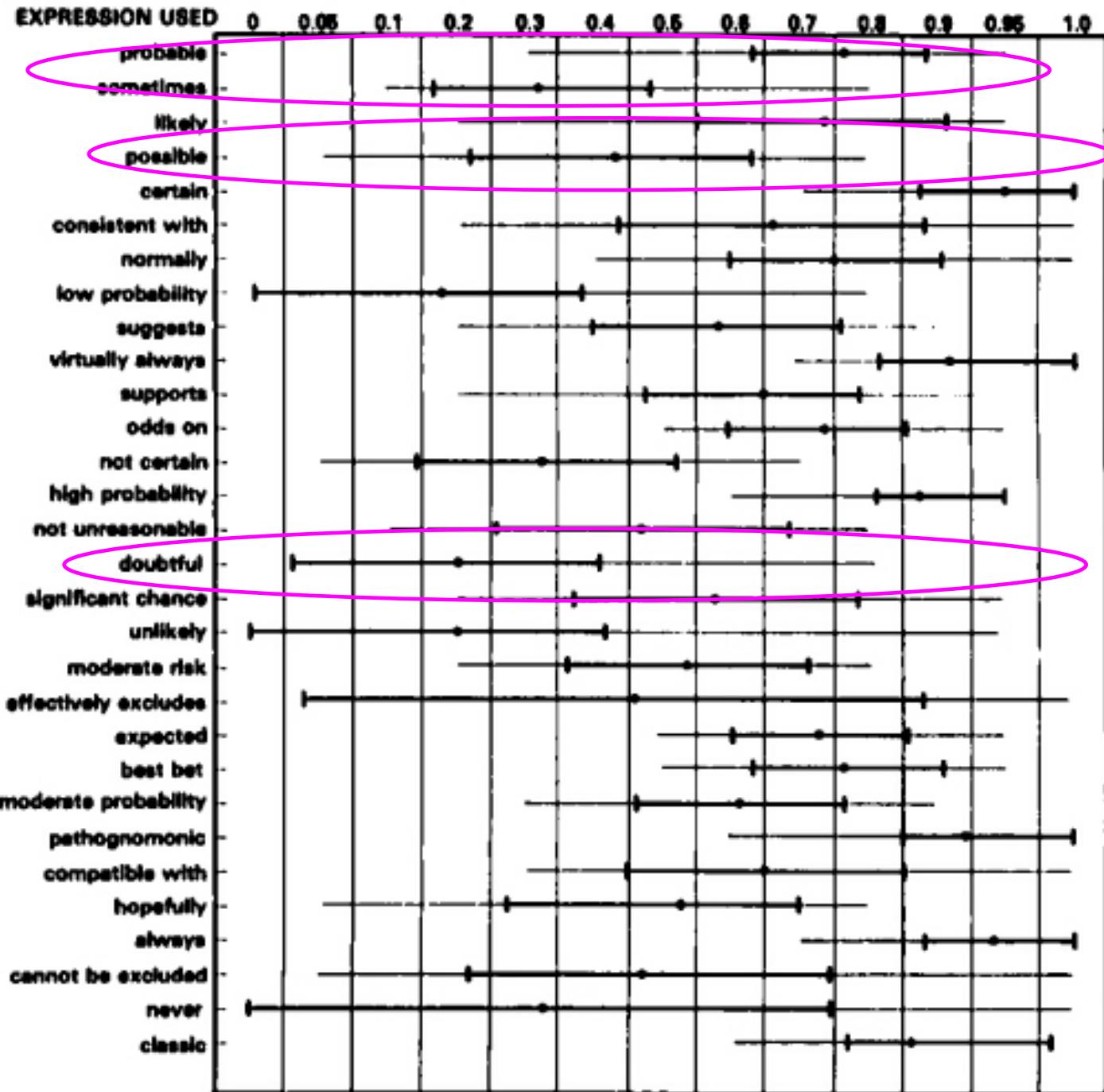
▣ Exclu: 10%

▣ *Possible*

▣ *Probable*

▣ *Plausible*

▣ Certain: <5%



Checklist diagnostique

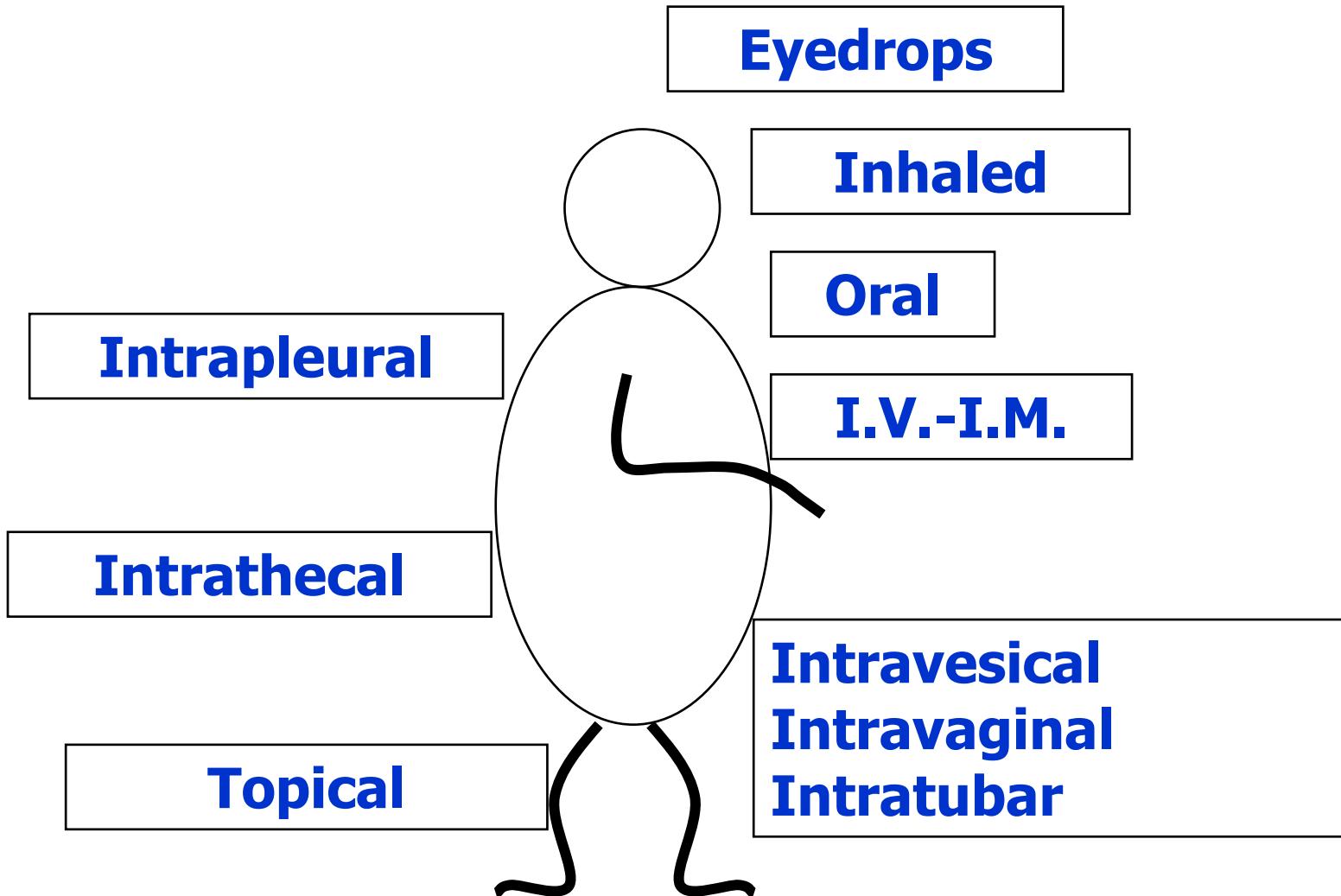
- ❑ Prise du traitement
- ❑ Etat respiratoire préexistant +++
- ❑ Tableau compatible avec le médicament
 - ❑ Clinique
 - ❑ Imagerie
 - ❑ LBA
 - ❑ Histologie
 - ❑ Si besoin contacter Ptox.com

- ❑ Caractère précessif du ttt / aux signes & symptômes
- ❑ Délai d'apparition compatible
 - ❑ Une seconde – 20 ans
- ❑ Signal dans la littérature
 - ❑ ‘-’ à ‘5’
 - ❑ Spécificité (parfois ...)
- ❑ Biomarqueurs: BNP, AAN, ANCA (KL6--)
- ❑ Diagnostic différentiel soigneux
 - ❑ Maladie sous-jacente
 - ❑ Affection ntercurrente

Prise du traitement

- Balayer l'ordonnance
- Tél. pharmacie
- Taux sérique (opiacés, iMTOR, anticoagulants, ? amiodarone)
- Médicaments en vente libre
- Quid si >1 médicament: drug-ranking
- Substances illicites (drug screen)
- Malade inconscient ou ventilé: entourage

Exposure and route of administration



Non médicaments...

- ❑ Sang et dérivés
- ❑ Irradiation
- ❑ Substances addictives (héroïne, cocaïne, Meth-, MDMA), warfarine
- ❑ Excipients: huiles arachide, ricin, triglycérides, talc, crospovidone
- ❑ Adultérants: levamisole
- ❑ Gaz: O₂, NO
- ❑ Phytothérapies
- ❑ Silicone
- ❑ Raticides (brodifacoum, superwarfarines)
- ❑ Barotraumatisme (NPPE, NPPH)
- ❑ Techniques
 - ❑ Vertébroplastie (methacrylate), Onyx, Hydrogel, Liposuction

Case Report

An Overdose Death Involving the Insufflation of Extended-Release Oxymorphone Tablets^{*†}

Shawn P. Vorce, Barry Levine*, Pamela C. McDonough, and
Division of Forensic Toxicology, Armed Forces Medical Examiner System,
1413 Research Blvd., Bldg. 102, Rockville, Maryland 20850

Abstract

Two cases are reported involving the abuse of extended-release oxymorphone hydrochloride tablets (Opana® ER) in combination with alprazolam (Xanax®). Two juvenile females were discovered unresponsive and hypoxic by a male acquaintance. The trio had reportedly crushed and snorted Opana ER tablets and consumed Xanax for recreational purposes. Emergency personnel were able to stabilize one female. The second female was pronounced dead at the scene. Blood and urine samples from the surviving female were collected at the trauma center between 48 and 96 h post incident. Toxicology results showed the presence of oxymorphone, doxylamine, dextromethorphan, alprazolam, α -hydroxyalprazolam, oxazepam, and temazepam in her urine. No drugs were detected in her blood. Toxicology on the deceased female revealed the presence of 0.13 mg/L oxymorphone and 0.04 mg/L alprazolam in her blood. Gastric contents contained 0.25 and 0.93 mg/L of oxymorphone and alprazolam, respectively. Oxymorphone, alprazolam, and α -hydroxyalprazolam were present in her urine. Quantitative results were achieved by gas chromatography-mass spectrometry monitoring selected ions for the oxime-oxymorphone-trimethylsilyl derivative, alprazolam, and the α -hydroxyalprazolam *tert*-butyldimethylsilyl derivative. The established linearity ranges for the opiate and benzodiazepine methods were 0.050–3,000 and 0.025–1,000 mg/L, respectively. The cause of death was reported as multiple drug toxicity, and the manner of death was accidental.

Journal of Analytical Toxicology 2014;38:226–230
doi:10.1093/jat/bku011 Advance Access publication February 11, 2014

Case Report

A Fatality Involving AH-7921

Shawn P. Vorce, Jessica L. Knittel, Justin M. Holler, Joseph Maglilio, Jr, Barry Levine*, Philip Berran and Thomas Z. Bosy

Division of Forensic Toxicology, Armed Forces Medical Examiner System, Dover AFB, Dover, DE 19902, USA

*Author to whom correspondence should be addressed. Email: barry.s.levine3.civ@mail.mil

A case is presented of a 19-year-old white male who was found dead in bed by a friend. While no anatomic cause of death was observed at autopsy, toxicological analysis of his blood identified AH-7921, a synthetic opioid. AH-7921 was isolated by liquid–liquid extraction into *n*-butyl chloride from alkalized samples. Extracts were analyzed and quantified by gas chromatography mass spectrometry in selected ion monitoring mode. The heart blood had an AH-7921 concentration of 3.9 mg/L and the peripheral blood concentration was 9.1 mg/L. In addition to the blood, all submitted postmortem specimens including urine, liver, kidney, spleen, heart, lung, brain, bile and stomach content were quantified. The following concentrations of AH-7921 were reported: 6.0 mg/L in urine, 26 mg/kg in liver, 7.2 mg/kg in kidney, 8.0 mg/kg in spleen, 5.1 mg/kg in heart, 21 mg/kg in lung, 7.7 mg/kg in brain, 17 mg/L in bile and 120 mg/125 mL in the stomach content. The medical examiner reported that the cause of death was opioid intoxication and the manner of death was accident.

unknown drug two nights earlier and reportedly used it the nights of and prior to his death. Medics responding to the scene noted a frothy substance around the victim's mouth, which was confirmed by the doctor who subsequently pronounced the victim deceased.

Upon external examination, the decedent had a 1/4 × 1/4-in. contusion on the forehead and a cast on his left leg due to a broken fifth metatarsal. Remarkable findings upon internal examination included pulmonary congestion and edema with the right lung weighing 1000 g and the left lung weighing 750 g. Hepatomegaly (2030 g) and splenomegaly (370 g) were also observed. All other findings were unremarkable. Appropriate toxicological specimens were analyzed for volatile substances and a postmortem comprehensive drug screen was performed.

The US Army Criminal Investigative Laboratory (USACIL), Forest Park, GA, USA, identified the contents of the vials found at the scene. One vial contained a residue of AH-7921; the

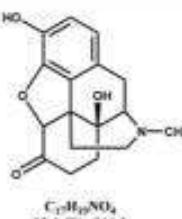


Figure 1. Structure of oxymorphone.

*Only were presented in part at the 2009 SOFT Annual Meeting in Oklahoma City.

†Disclaimer: The opinions or assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the Department of Defense, the Army, Navy, or Air Force.



Poisoning – Home, household

- ❑ Leather conditioner
- ❑ KMnO₄ [Karthik, 2014]
- ❑ Poppy capsules Rachacha
 - ❑ (morphine + codeine)



Kids & adults

- ❑ Household products
- ❑ Disinfectants
- ❑ Pharmaceuticals
- ❑ e-liquid
- ❑ Kerosene (soft drink bottles)
- ❑ Meth lab (poisoning, burns)
- ❑ Brodifacoum rodenticide
- ❑ Paraquat
- ❑ Organophosphates
- ❑ Cinnamon

Table. Selected Nonpharmaceutical Household Products That Are Toxic in Children

Alcohols

Beverage ethanol
Methanol (windshield wiper fluid)
Ethylene glycol (antifreeze)

Caustic agents

Alkalis (drain and oven cleaner, perm relaxers, Clinitest tablets)
Acids (toilet bowl cleaners, antirust compounds)

Food-flavoring additives

Methylsalicylate (oil of wintergreen)

Hydrocarbons

Kerosene
Lamp oil
Mineral seal oil (furniture polish)
Mineral spirits (paint thinner)
Naphtha (lighter fluid)

Industrial chemicals

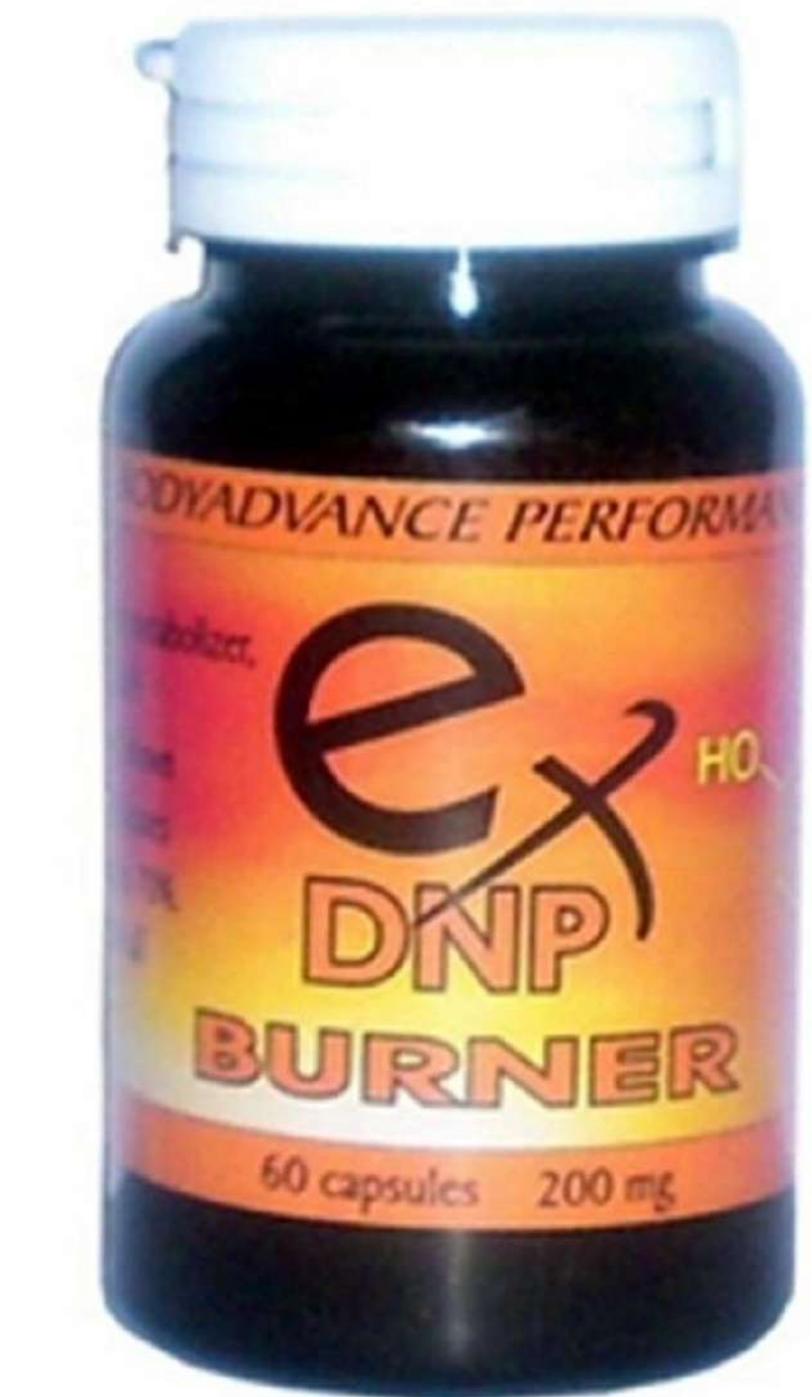
Methylene chloride (paint stripper)
Selenious acid (gun bluing)
Zinc chloride (soldering flux)

Nail products

Acetonitrile (sculptured nail remover)
Methacrylic acid (artificial nail primer)
Nitromethane (artificial nail remover)

Pesticides and/or insecticides

Organophosphates
Lindane
Paraquat



D198501 ALDRICH

2,4-Dinitrophenol

moistened with water, ≥98.0%

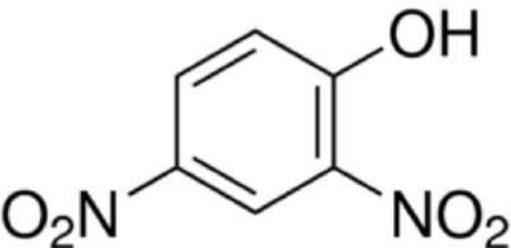
Synonym: α-Dinitrophenol, 2,4-DNP, DNP

◆ FDS

SIMILAR PRODUCTS

CAS Number 51-28-5 | Linear Formula $(O_2N)_2C_6H_3OH$ | Molecular Weight 184.11 | Beilstein Registry Number 1246142

EC Number 200-087-7 | MDL number MFCD00007115 | PubChem Substance ID 24893583

POPULAR DOCUMENTS: [SPECIFICATION SHEET \(PDF\)](#) | [FTNMR \(PDF\)](#)

Commander

Sécurité & Documentation

Protocoles et articles

1

Documentation référencée

38

Propriétés

Related Categories	Building Blocks, C6 to C8, Chemical Synthesis, Organic Building Blocks, Oxygen Compounds, Plus...
vapor density	6.35 (vs air)
assay	≥98.0%
contains	≥15% water

Prix et disponibilité

Conditionnement - SKU	Disponibilité	Prix (EUR)	Quantité
D198501-5G	Disponible pour expédition le 23.09.15 - A PARTIR DE	26.60	0
D198501-100G	Disponible pour expédition le 13.10.15 - A PARTIR DE	31.20	0
D198501-1KG	Espédition estimée le 26.11.15	116.00	0



Bokeh — Wikip...

Ventes aux enc...

96 tears - Rech...

ticagrelor dysp...

Home - PubMe...

Favoris

Pneumotox » D...

BUY DNP ON...

LEGAL NOTICE

POPULAR



100 x Capsules
(200mg) DNP UK BUY
ONLINE

£ 70.00 £ 100.00 **-30%**

Add to cart**More**

30 x Capsules (200mg)
2,4-Dinitrophenol...

£ 28.00 £ 40.00 **-30%**

Add to cart**More**

50 x Capsules (200mg)
2,4-Dinitrophenol...

£ 42.00 £ 60.00 **-30%**

Add to cart**More**

pictures to prove we
make capsules

£ 0.00

Add to cart**More**

2, 4-dinitrophenol

- ❑ Sold from the Internet
- ❑ Oxidative phosphorylation uncoupling in mitochondria
- ❑ Reliance on anaerobic Krebs cycle
- ❑ Energy deficit: adipose tissue (-> weight loss)
- ❑ Energy converted to heat
- ❑ Thermal disruption of enzymes/cells/organism
- ❑ Hyperkalemia, metabolic acidosis, renal damage
- ❑ Management: early charcoal, cooling, ?dantrolene
- ❑ Early hemoperfusion
- ❑ If it does, does improve within 6hrs





Etat respiratoire préexistant +++

- ▣ Tabac (SRIF)
- ▣ Radiographies antérieures
- ▣ Imagerie
- ▣ EFR
- ▣ MG
- ▣ Culture du bilan pneumologique dans:
 - ❖ Maladies de système
 - ❖ Polyarthrite
 - ❖ Amiodarone
 - ❖ Hémato-oncologie

Tableau compatible avec le médicament

Classification

Lung parenchyma ~75%

NSIP (cellular/fibrotic)

DAD

Pulmonary edema

DAH

Opportunistic infection

Vasculopathy

PHT

Thromboembolism

Pleura

Effusion

Thickening

Chest pain

Pneumothorax

Hemoglobin

Methemoglobinemia

Central airway

Angioedema

Hematoma

Other airways

Cough

Acute bronchospasm

Obliterative bronchiolitis

Mediastinum

Lymphadenopathy

Lipomatosis

Heart

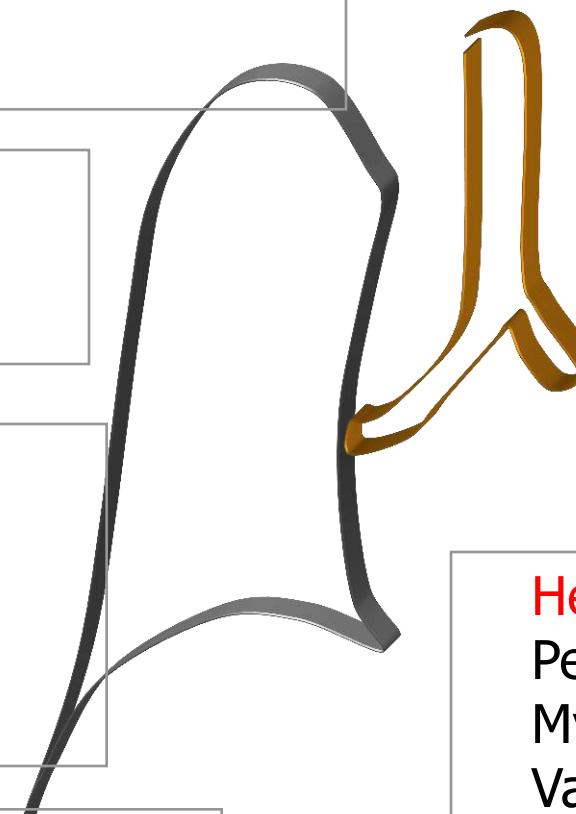
Pericardial effusion

Myocarditis

Valvular heart disease

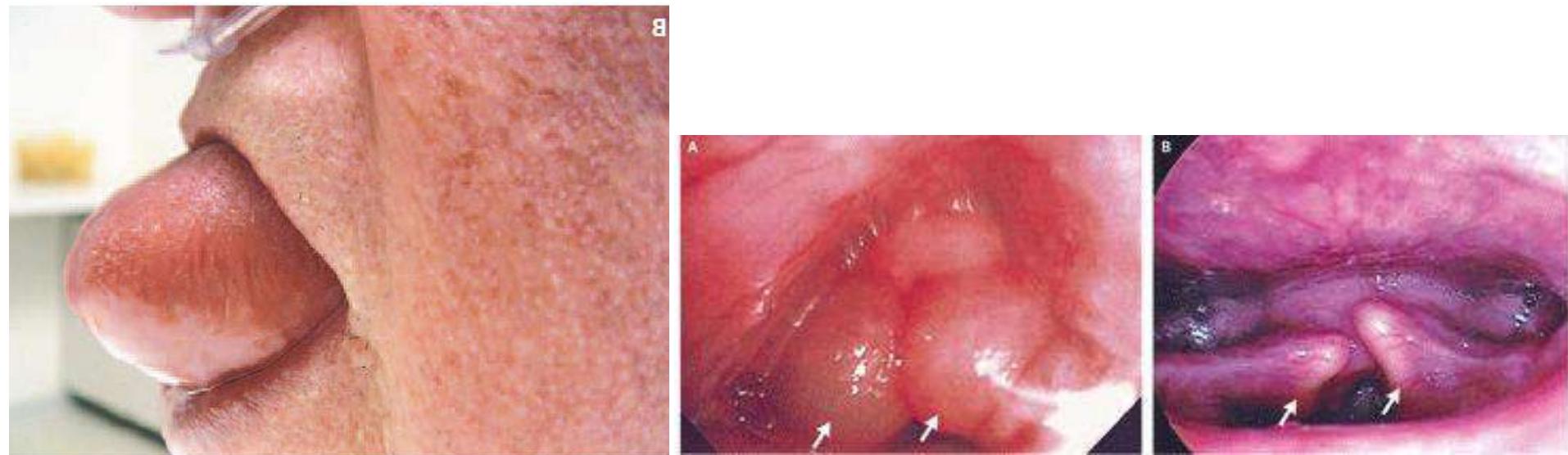
Neuromuscular

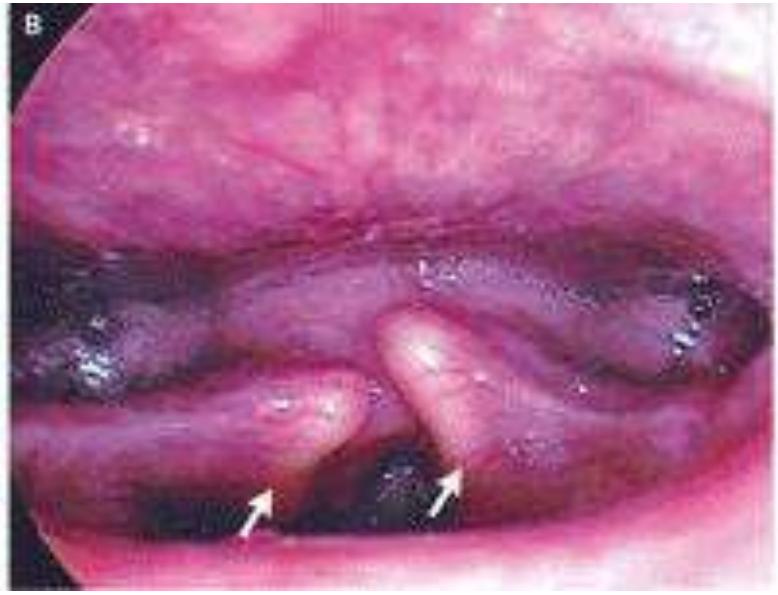
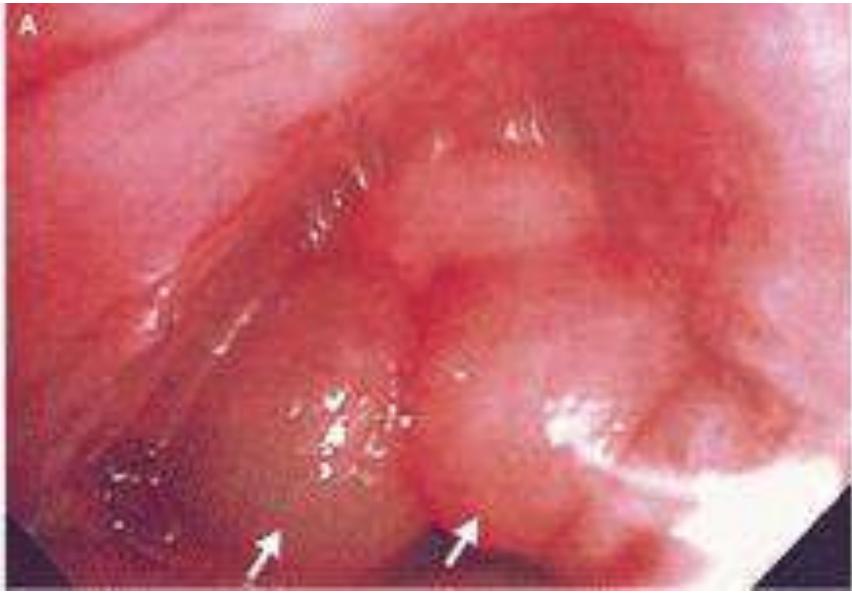
Acute respiratory failure

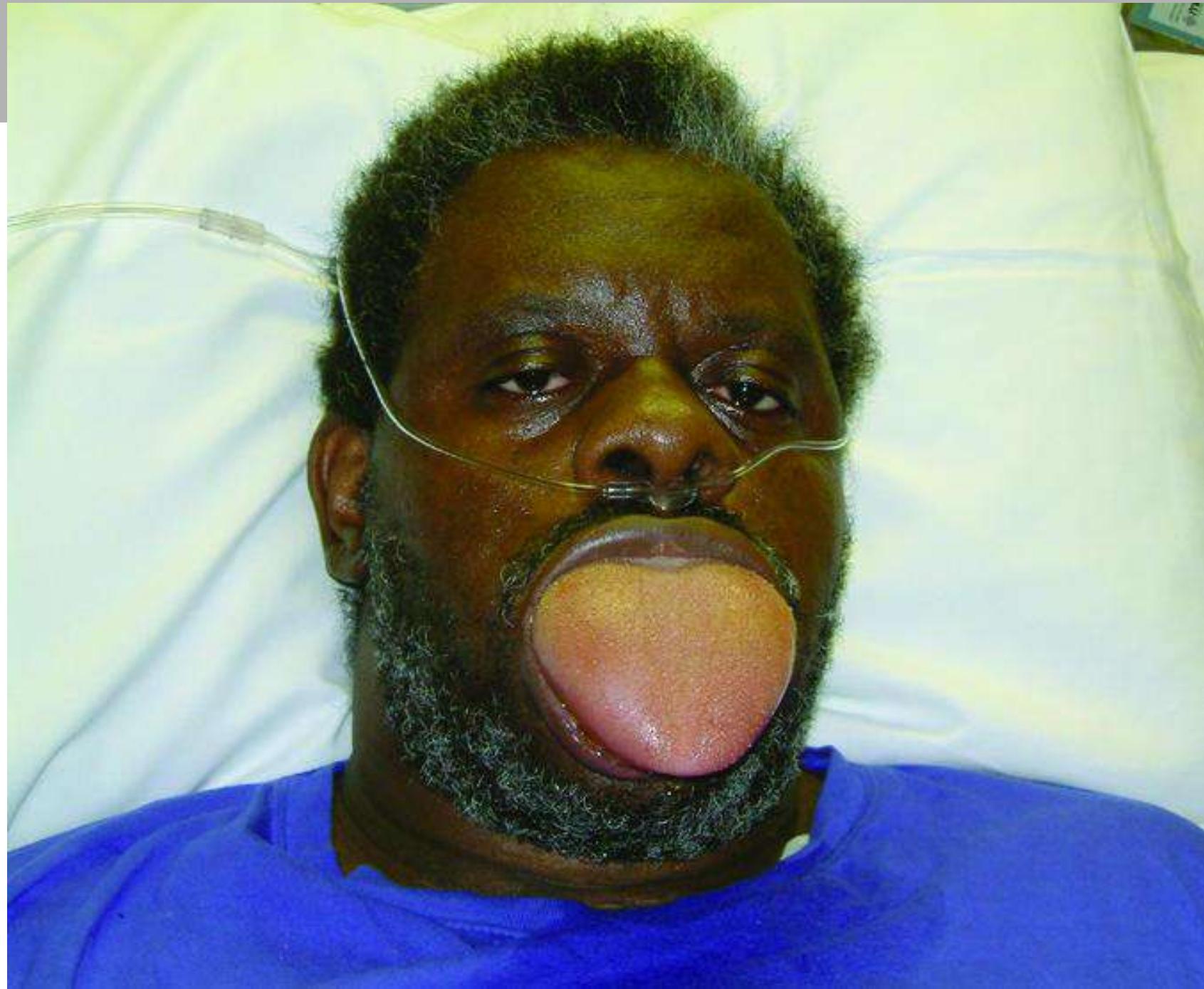


Oedème de Quincke

- ❑ Isolé : IEC
- ❑ Avec anaphylaxie: antibiotiques, AINS, CR, biothérapies
- ❑ +++ Maintien de la VA







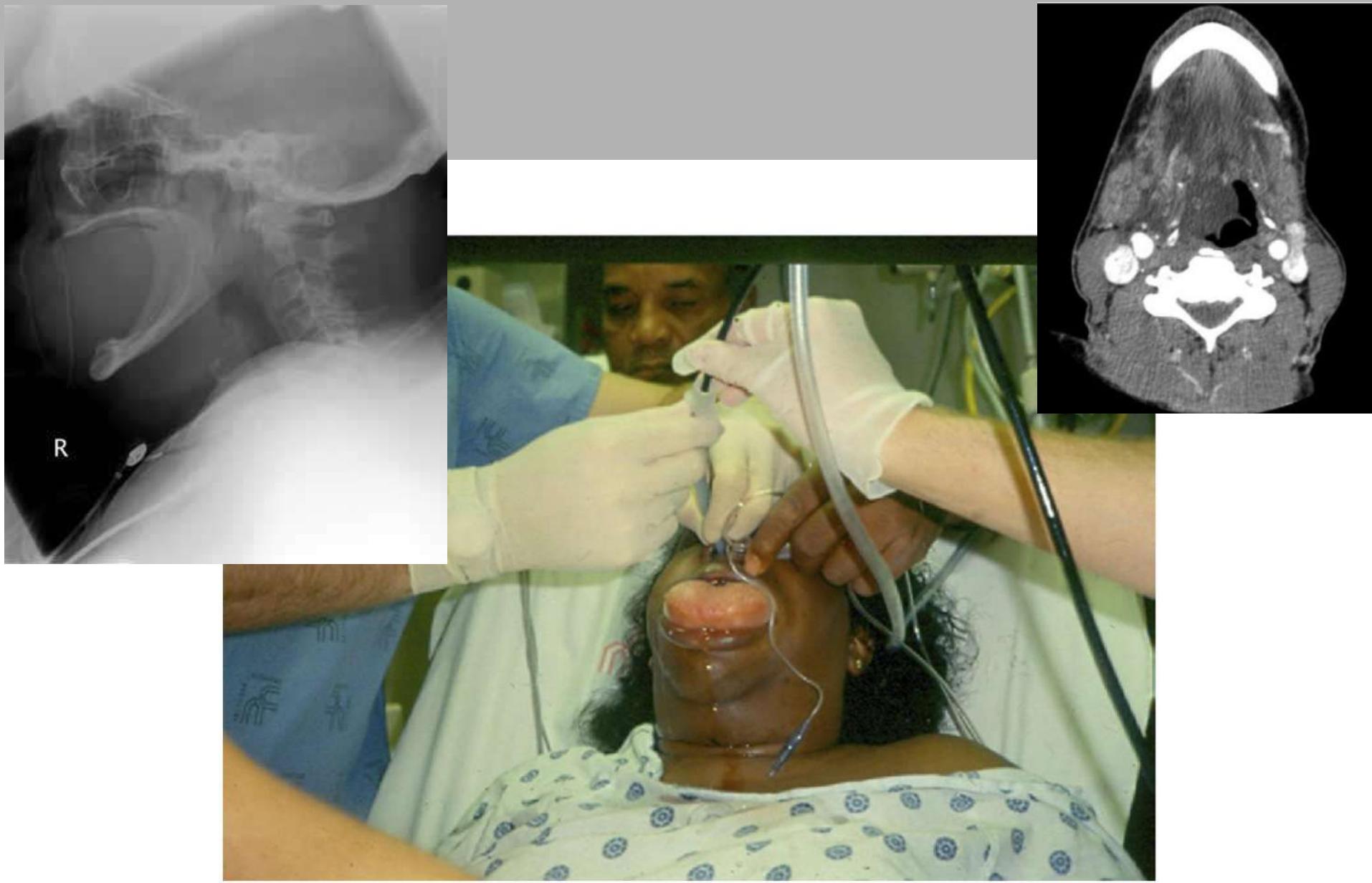
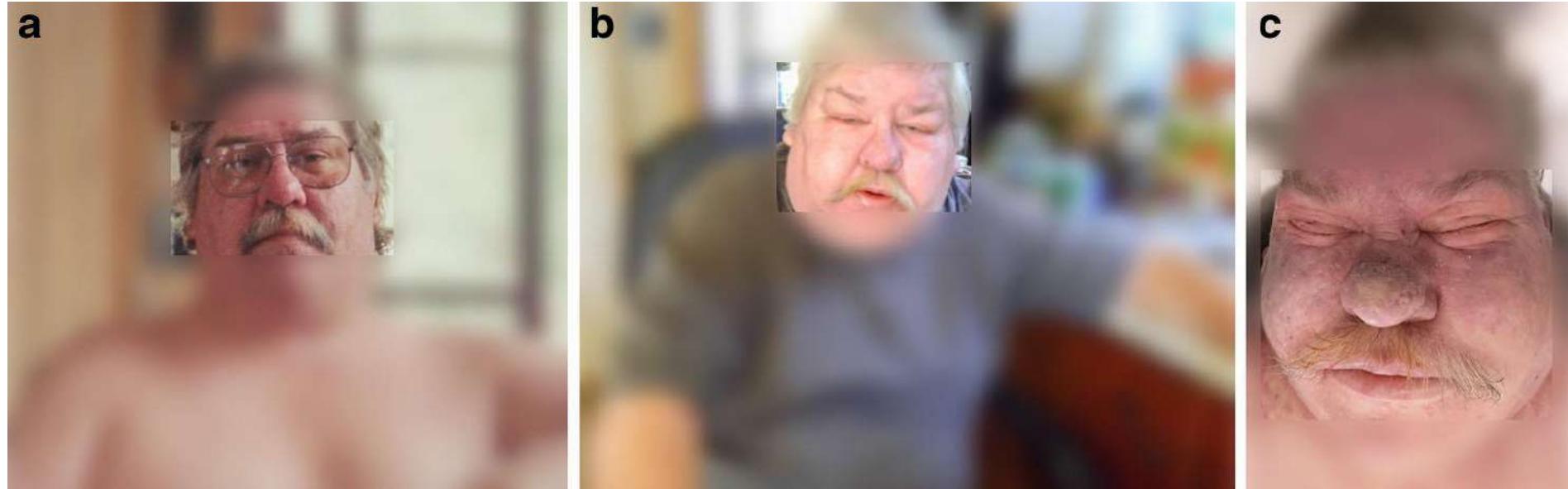


Figure 1. Example of life-threatening ACE inhibitor–induced angioedema with attempted emergency fiber optic nasotracheal intubation. The procedure was unsuccessful, and an emergency cricothyroidotomy was performed with great difficulty.

ACEI-induced UAO



CASE REPORT

Dorothy E. Dean,¹ M.D.; Daniel L. Schultz,² M.D.; and Robert H. Powers,² Ph.D.

Asphyxia Due to Angiotensin Converting Enzyme (ACE) Inhibitor Mediated Angioedema of the Tongue During the Treatment of Hypertensive Heart Disease



Minimal submental edema was also noted [Figure 1].

Treatment included 0.3 mg epinephrine subcutaneously every 20 minutes for three doses, 300 mg cimetidine IV, 250 mg methylprednisolone IV, and 50 mg diphenhydramine IV for two doses. There was no response to this antiallergic treatment, and the soft-tissue swelling of the neck gradually increased. Because of the patient's inability to control

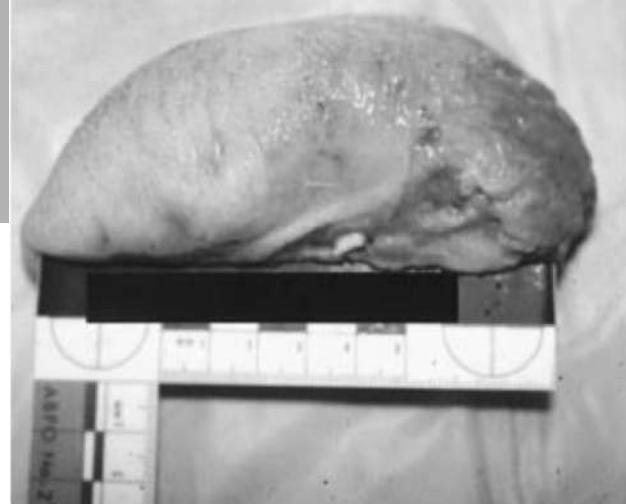


FIG. 2—Angioedema of tongue.





Figure 1.

Coronal computed tomography scan of the abdomen demonstrates segmental edematous small intestine (arrow) in a middle-aged woman.

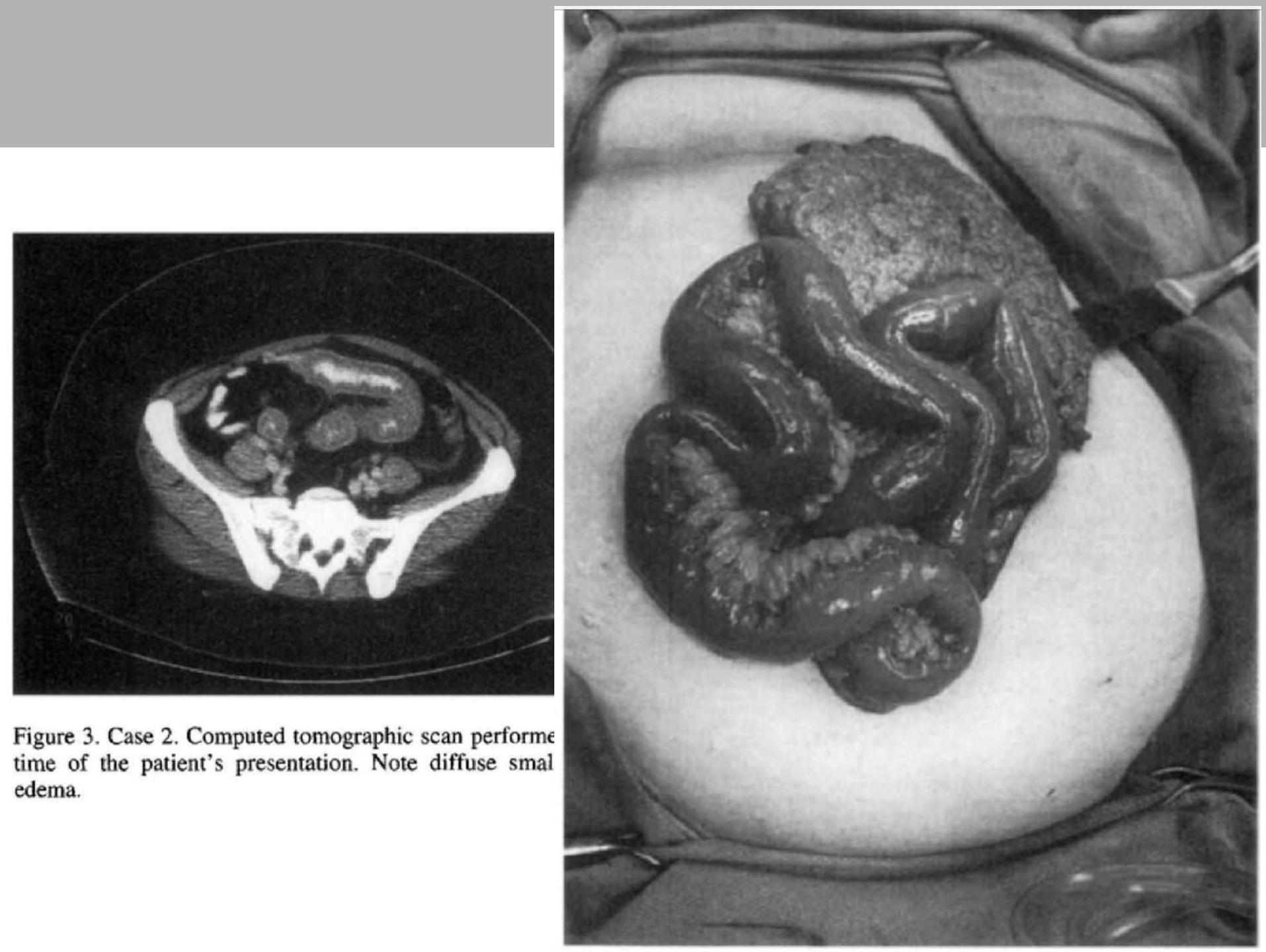


Figure 3. Case 2. Computed tomographic scan performed at time of the patient's presentation. Note diffuse small renal edema.

▣ Asphyxie - atteinte GI

▣ Icatibant (Firazyr®)

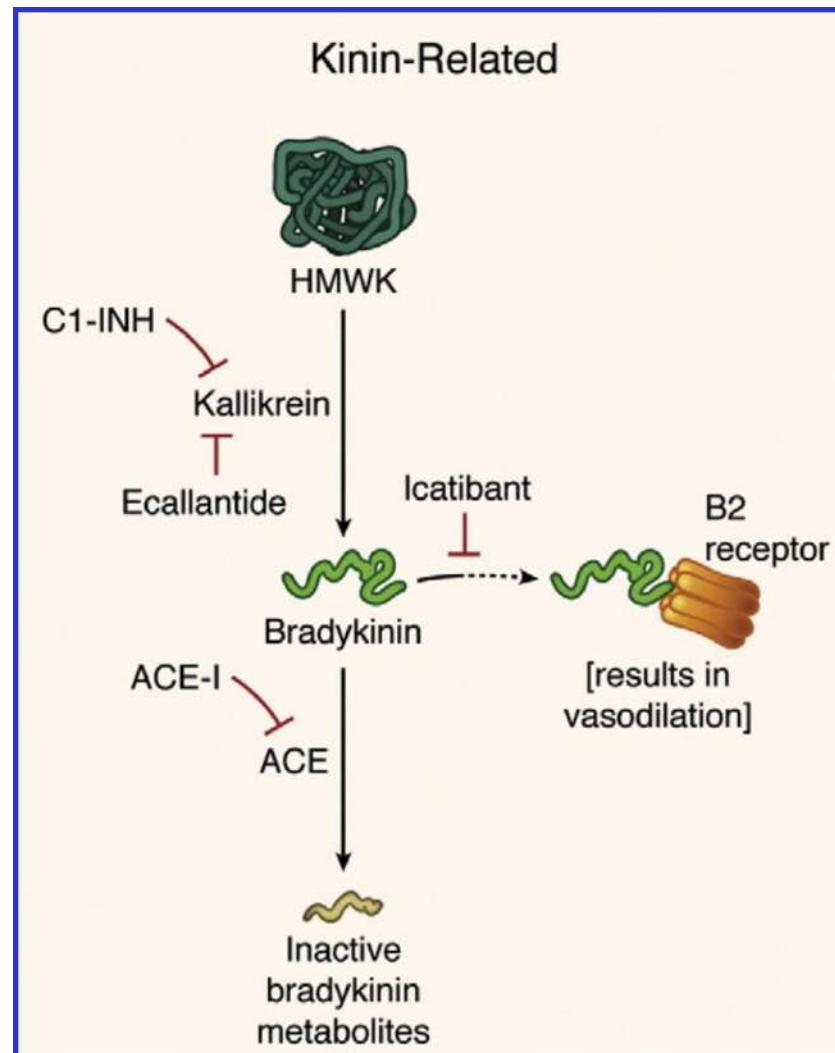
❖ 4.4h vs. 33h

▣ Ecallantide

▣ Concentré C1-i

▣ PFC

▣ Concentré II VII IX X



Classification

Lung parenchyma ~75%

NSIP (cellular/fibrotic)

DAD

Pulmonary edema

DAH

Opportunistic infection

Vasculopathy

PHT

Thromboembolism

Pleura

Effusion

Thickening

Chest pain

Pneumothorax

Hemoglobin

Methemoglobinemia

Central airway

Angioedema

Hematoma

Other airways

Cough

Acute bronchospasm

Obliterative bronchiolitis

Mediastinum

Lymphadenopathy

Lipomatosis

Heart

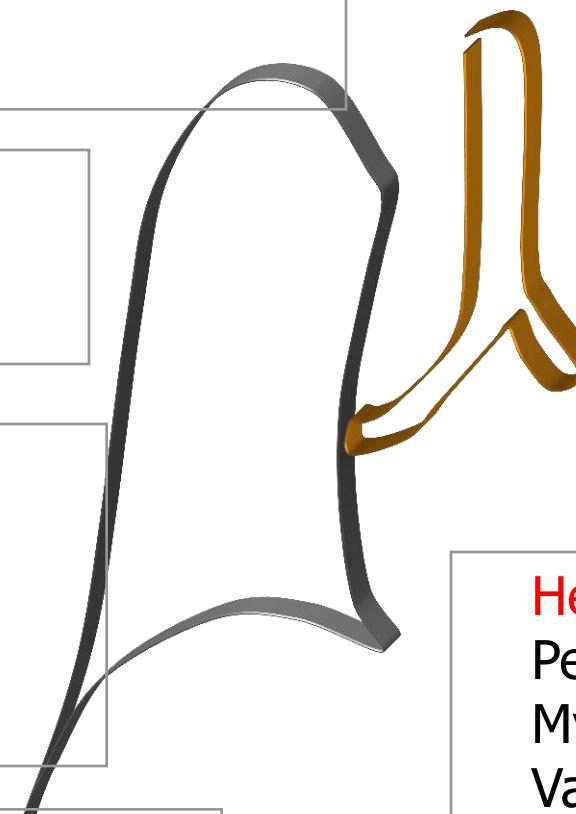
Pericardial effusion

Myocarditis

Valvular heart disease

Neuromuscular

Acute respiratory failure



▣ Toux

- ▣ 35 médicaments, IEC >>
- ▣ 1-2% de toutes les toux
- ▣ Incidence IEC: 5-35%
- ▣ ?Bradykinine-
- ▣ De qq heures à qq années
- ▣ Peut révéler un cancer du poumon
- ▣ Eviction qq soit l'ancienneté !
- ▣ Réintroduction -> récidive
- ▣ ARA2 généralement OK

Bronchospasme catastrophique

- β -bloquants: propranolol (Fallowfield, 1996)

- ❖ 1965-1996: 51 AAG dus au propranolol
 - ❖ 13 décès (5/6 astmatiques connus)

- AINS - Aspirine

- ❖ Plaza 2002: RR ~5

- Substances addictives

- ❖ Heroïne inhalée: RR ~3
 - ❖ Heroïne-cocaine: RR intubation 7-9

- Substances addictives ou alcool: 31% des BS mortels

- Donc: tox-screen







Pill aspiration syndrome



CHEST

Special Features

“Pills” and the Air Passages

*Elif Kiipeli, MD; Danai Khemasuwan, MD, MBA; Pyng Lee, MD, FCCP;
and Atul C. Mehta, MD, FCCP*

Aspiration of a medication in the airways in any form produces a variety of adverse effects, both local and systemic. Furthermore, specific reaction of the airways to each type of pill strongly affects the outcome. It is crucial for pulmonologists and emergency medicine specialists to acknowledge this clinical entity. In addition, airways have been increasingly used to deliver medications such as insulin and prostacycline. These aerosolized medications can also cause local as well as systemic side effects. We review the local and systemic reactions of these “pills” accessing the airways either by incidental aspiration or iatrogenic administration. We address clinical presentation, mechanism of injury, diagnosis, and management of complications of these pills in the air passages.

CHEST 2013; 144(2):651–660

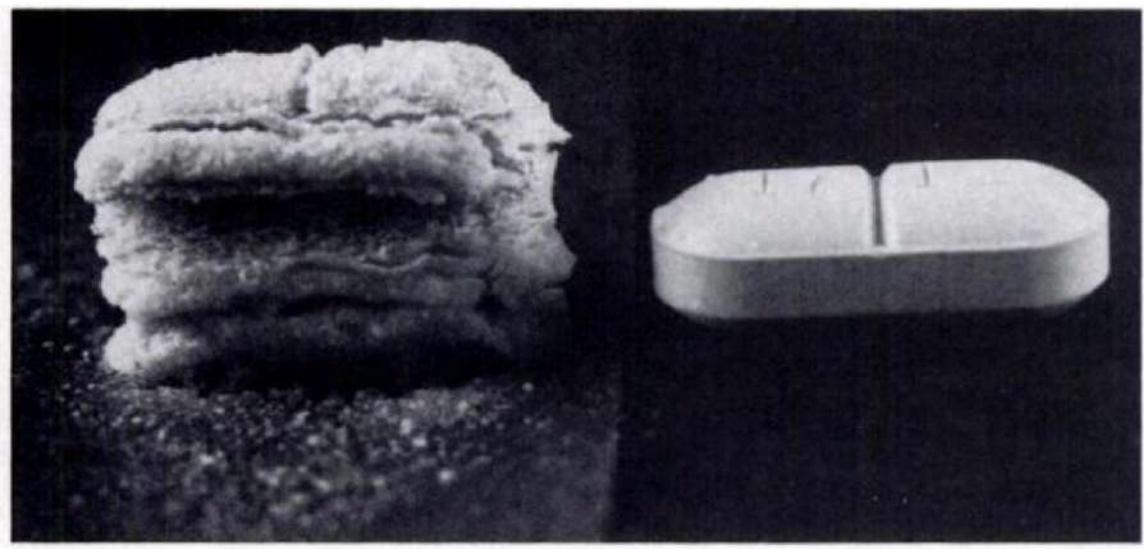


FIGURE 2. Rapid expansion of a sucralfate tablet is seen 30 s after placing it on a wet surface (*left*), compared with a dry tablet (*right*).

The Iron Lady

Horiana B. Grosu¹, Carlos A. Jimenez¹, Georgie A. Eapen¹, David Ost¹, Cesar Moran¹, and Rodolfo C. Morice¹

¹Department of Pulmonary Medicine, The University of Texas MD Anderson Cancer Center, Houston, Texas

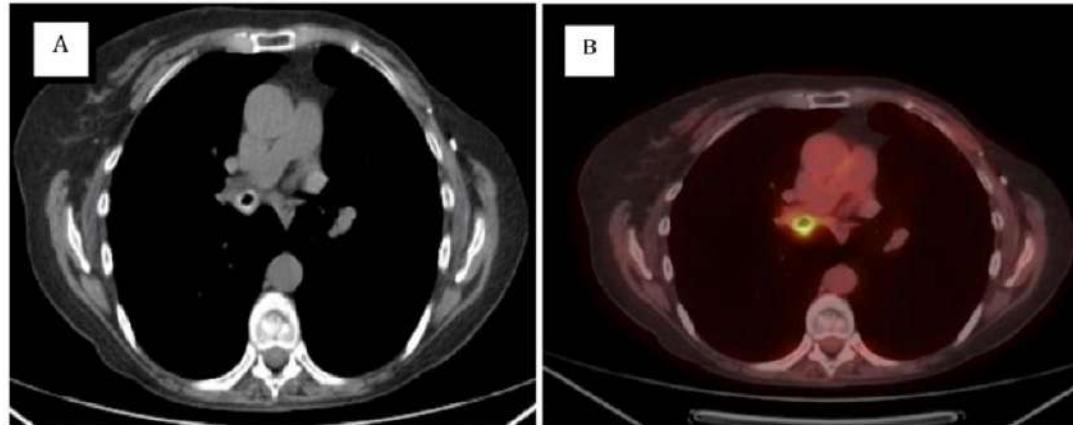


Figure 1. (A) Computed tomography image with circumferential thickening of the bronchus intermedius. (B) Positron emission tomography-computed tomography image with circumferential fluorodeoxyglucose-avid area of the bronchus intermedius.

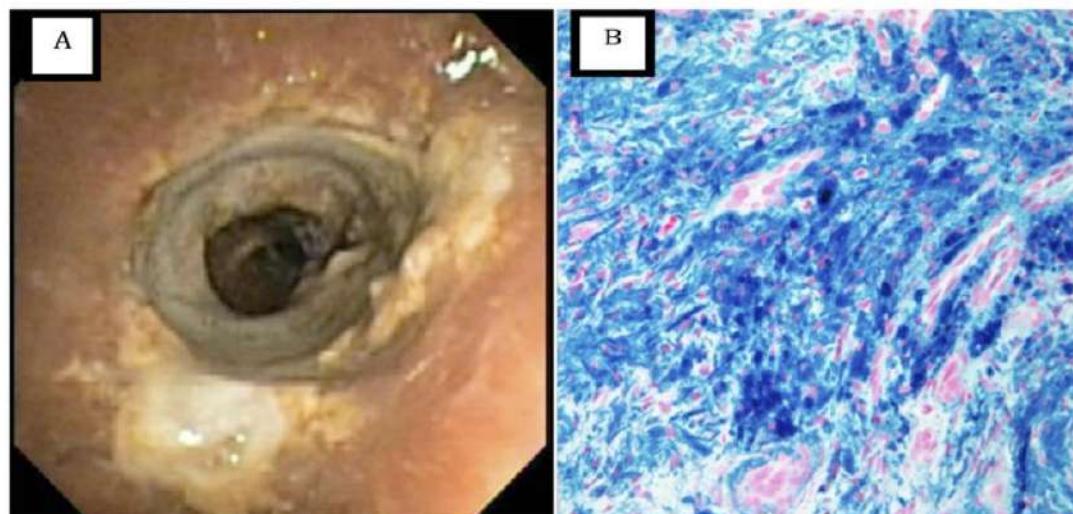


Figure 2. (A) Bronchoscopic view of bronchus intermedius with brown staining and necrosis of the mucosa. (B) Biopsy specimen showing strong positive reaction for iron.

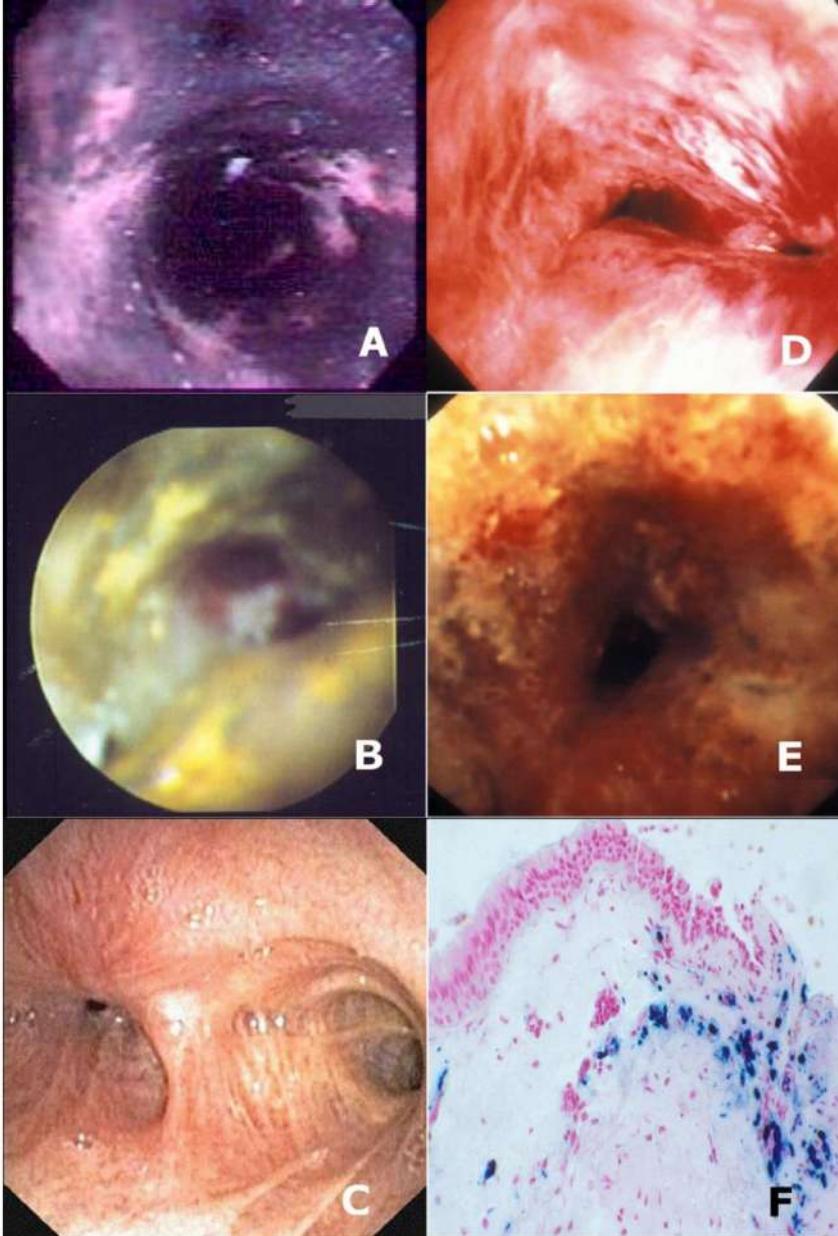


FIGURE 1. A, Charcoal in the tracheobronchial tree. (Reprinted with permission from Rajamani et al.⁴) B, Bronchus intermedius inflammation at day 1 after potassium-pill aspiration. Note, no foreign body was seen in the bronchus intermedius on day 1. C, Bronchus intermedius inflammation at 1 month after potassium-pill aspiration. (Reprinted with permission from Gudavalli et al.¹¹) D, Intense inflammation of the bronchus intermedius following iron-pill aspiration. No foreign body was detected in the bronchus intermedius. E, Intense inflammation of right main stem bronchus following iron-pill aspiration. F, Endobronchial biopsy specimen revealing submucosal deposition of iron particles on Prussian blue stain (original magnification $\times 200$).

Classification

Lung parenchyma ~75%

NSIP (cellular/fibrotic)

DAD

Pulmonary edema

DAH

Opportunistic infection

Vasculopathy

PHT

Thromboembolism

Pleura

Effusion

Thickening

Chest pain

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Central airway

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Acute bronchospasm

Obliterative bronchiolitis

Mediastinum

Lymphadenopathy

Lipomatosis

Heart

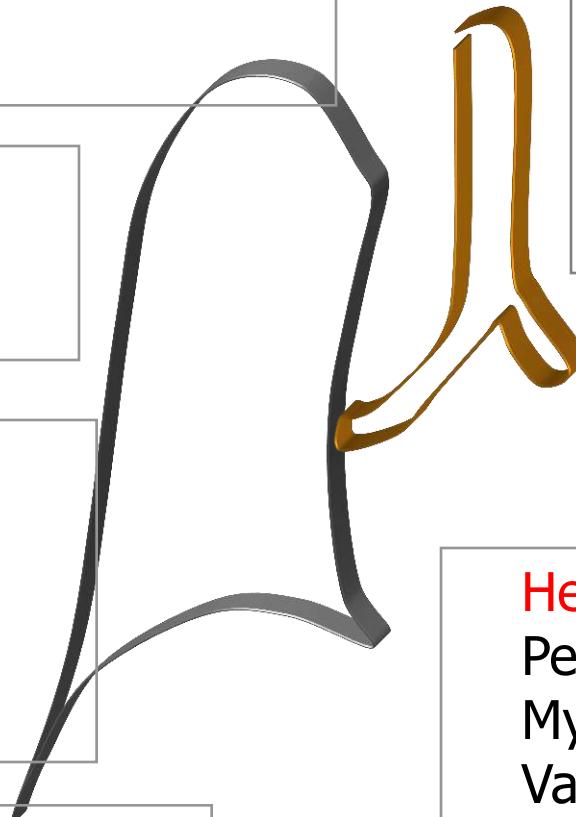
Pericardial effusion

Myocarditis

Valvular heart disease

Neuromuscular

Acute respiratory failure



OV 36.0cm

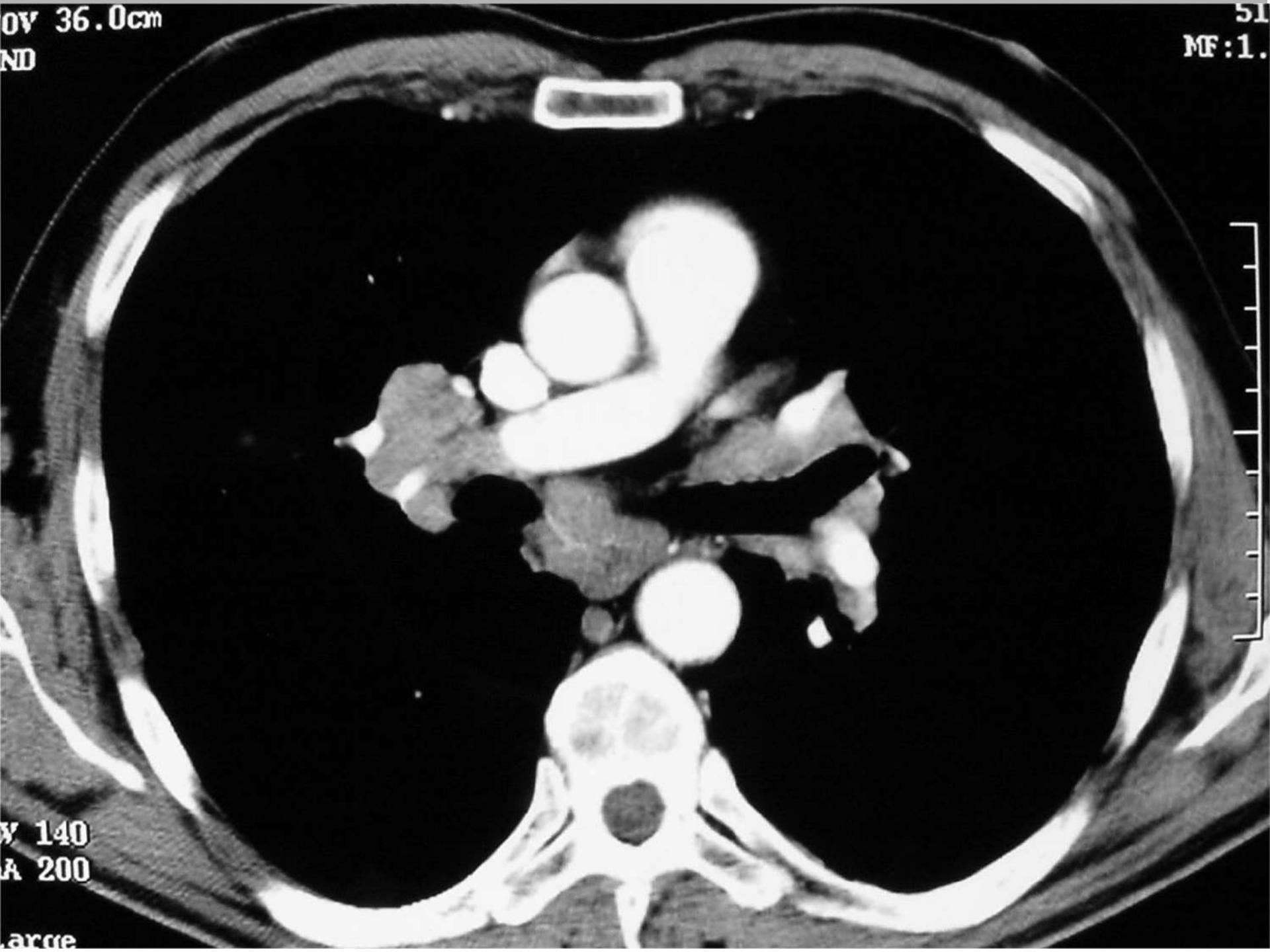
51

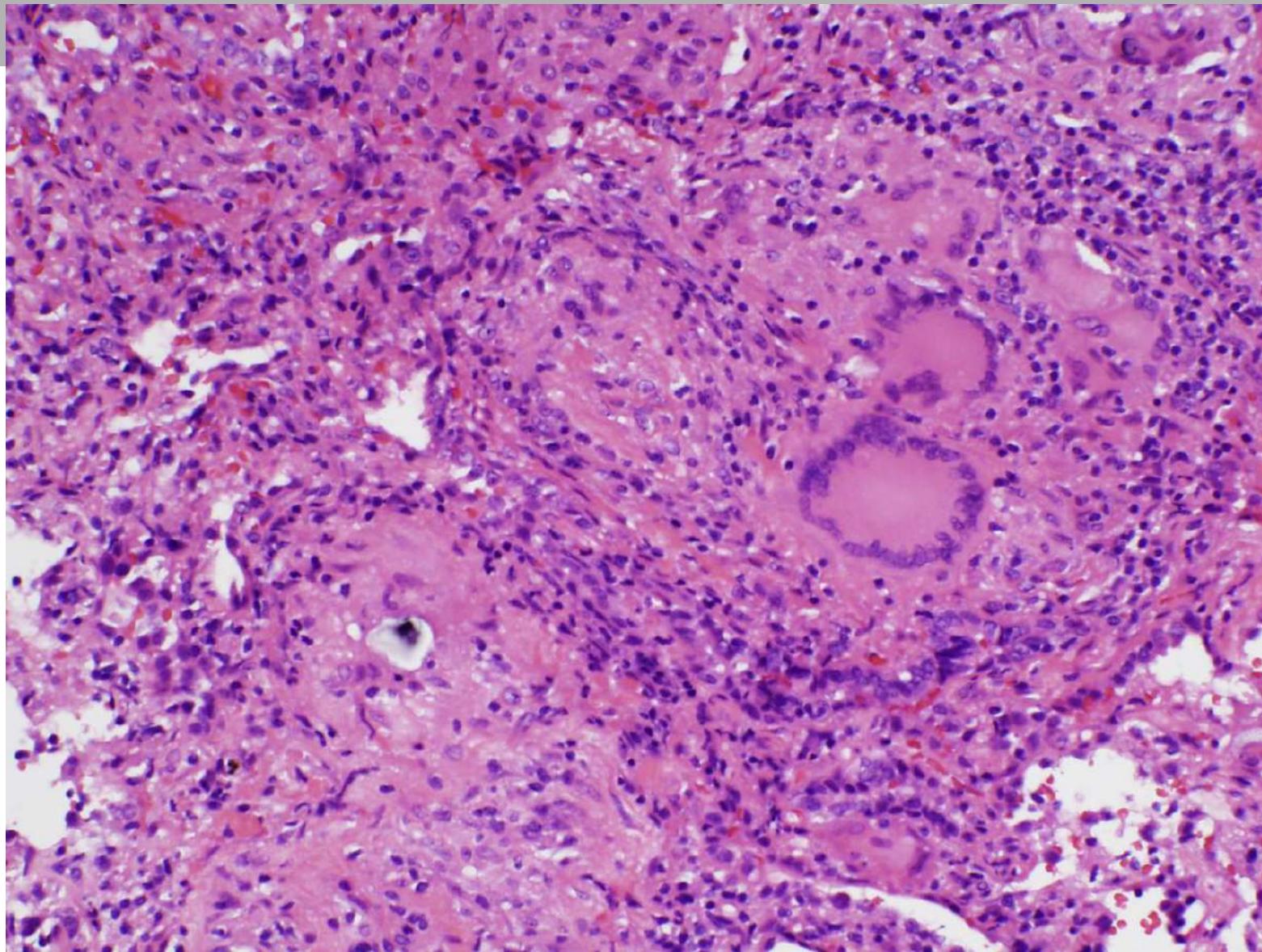
ND

MF:1.

W 140
A 200

large





❖ Courtesy TV Colby

D



D DEBOUT



- Pseudo-sarcoidose

- ❖ Thoracique
- ❖ Peau (tatouages)
- ❖ Autres organes

- Calcémie

- Interferon: alpha, beta
- Anti-TNF: etanercept

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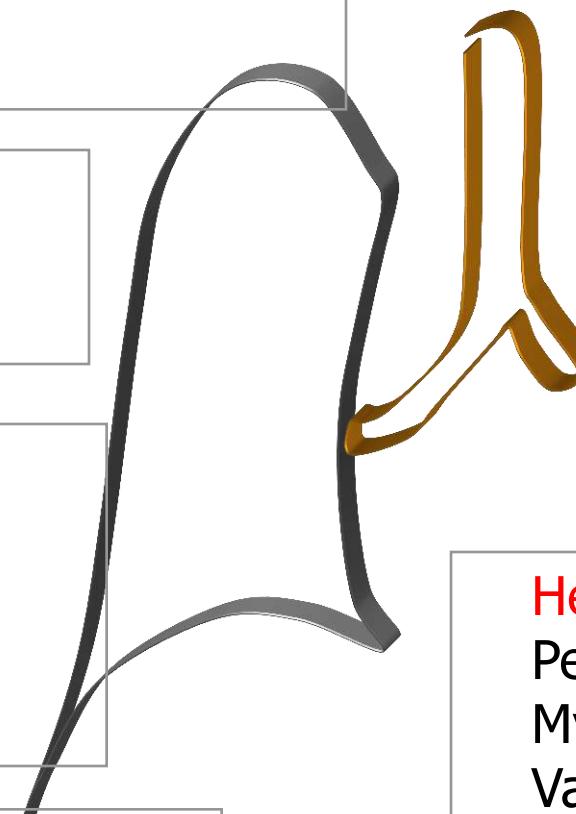
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- 5-FU
- Incidence
 - ❖ 1.3-3%
 - ❖ 5.4% ≥ 800 mg/d
- Angor
- Arythmies
- Cardiomyopathie
- ICG
- IDM
- Mort subite



Figure 1
ECG taken at time of chest pain

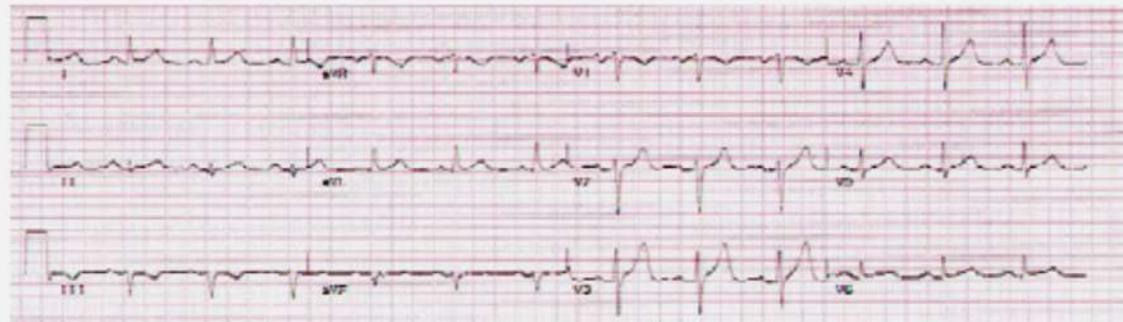
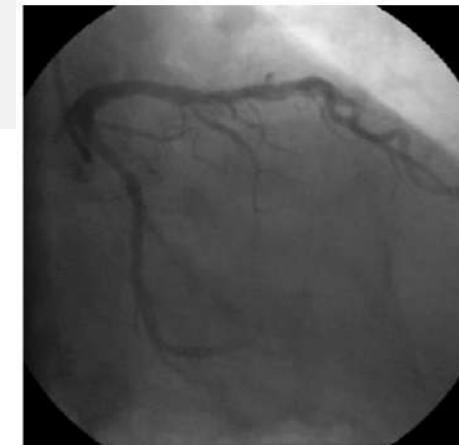


Figure 2
ECG after pain resolved



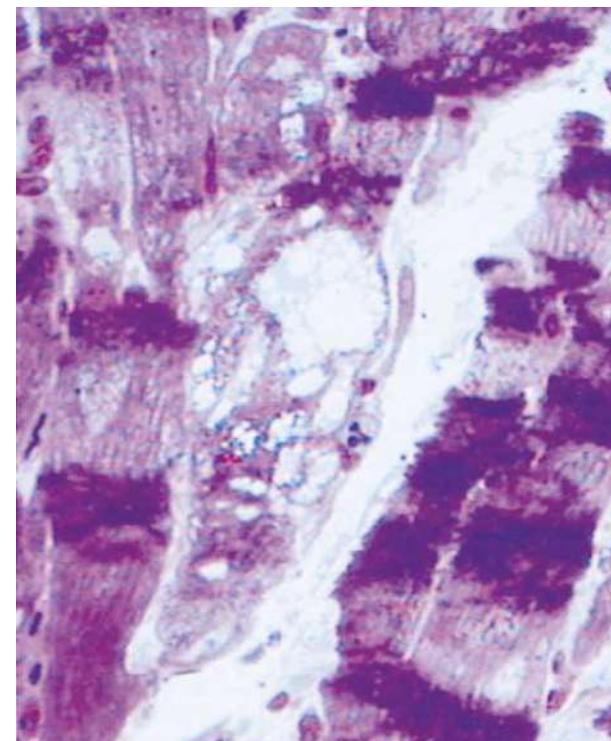
- Arythmies

- ❖ Taxanes, anthracyclines, ifosfamide, FU, gemcitabine, platine
- ❖ Pfs sévères
- ❖ Surveillance K+ Mg++

- Tr de conduction II/III

- Cardiomyopathie (anthracyclines)

- ❖ Echographi



- ❑ [XII \(a\) - Left ventricular dysfunction/failure](#)
- ❑ [XII \(b\) - Valvular heart disease](#)
- ❑ [XII \(c\) - Pericardial effusion - Pericarditis](#)
- ❑ [XII \(d\) - Myocarditis](#)
- ❑ [XII \(e\) - Takotsubo cardiomyopathy](#)
- ❑ [XII \(f\) - Cardiomyopathy](#)
- ❑ [XII \(g\) - Acute coronary event - Myocardial infarction](#)
- ❑ [XII \(h\) - Eosinophilic myocarditis](#)
- ❑ [XII \(i\) - Infective endocarditis](#)
- ❑ [XII \(j\) - Myocardial stunning](#)
- ❑ [XII \(k\) - Pericardial thickening/constriction](#)
- ❑ [XII \(l\) - Arrhythmia, dysrhythmia incl. fibrillation](#)
- ❑ [XII \(m\) - Cardiac-cardiopulmonary arrest](#)
- ❑ [XII \(n\) - Shock, cardiovascular collapse, hypotension](#)
- ❑ [XII \(o\) - Coronary artery disease](#)
- ❑ [XII \(p\) - Long QT syndrome](#)
- ❑ [XII \(q\) - Coarctation of the aorta \(acquired\)](#)

- ❑ [XII \(r\) - Congestive heart failure](#)
- ❑ [XII \(s\) - Heart block \(bundle or AV\)](#)
- ❑ [XII \(t\) - 'Torsades de pointe'](#)
- ❑ [XII \(u\) - Left-sided intracavitory thrombosis](#)
- ❑ [XII \(v\) - Hypertrophic cardiomyopathy](#)
- ❑ [XII \(w\) - Asystole](#)
- ❑ [XII \(x\) - Sinus arrest](#)
- ❑ [XII \(y\) - Pneumopericardium](#)
- ❑ [XII \(z\) - Heart valve thrombosis](#)
- ❑ [XII \(aa\) - Acute aortic vasoconstriction](#)
- ❑ [XII \(ab\) - Pericardial fat necrosis](#)
- ❑ [XII \(ac\) - Right atrial thrombosis](#)
- ❑ [XII \(ad\) - Effusive-constrictive pericarditis](#)
- ❑ [XII \(ae\) - Aortic dissection](#)
- ❑ [XII \(af\) - Coronary arterial spasm](#)
- ❑ [XII \(ag\) - Bradycardia](#)
- ❑ [XII \(ah\) - Endocardial fibroelastosis](#)

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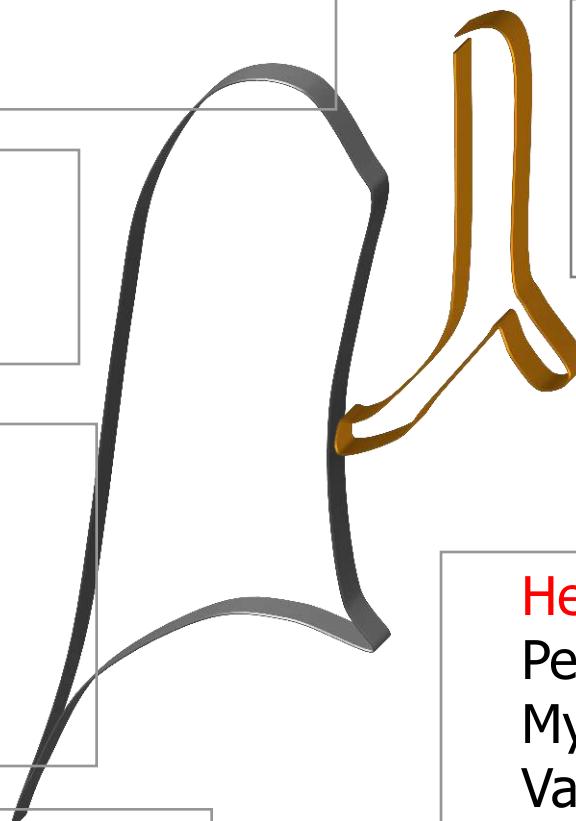
Pericardial effusion

Myocarditis

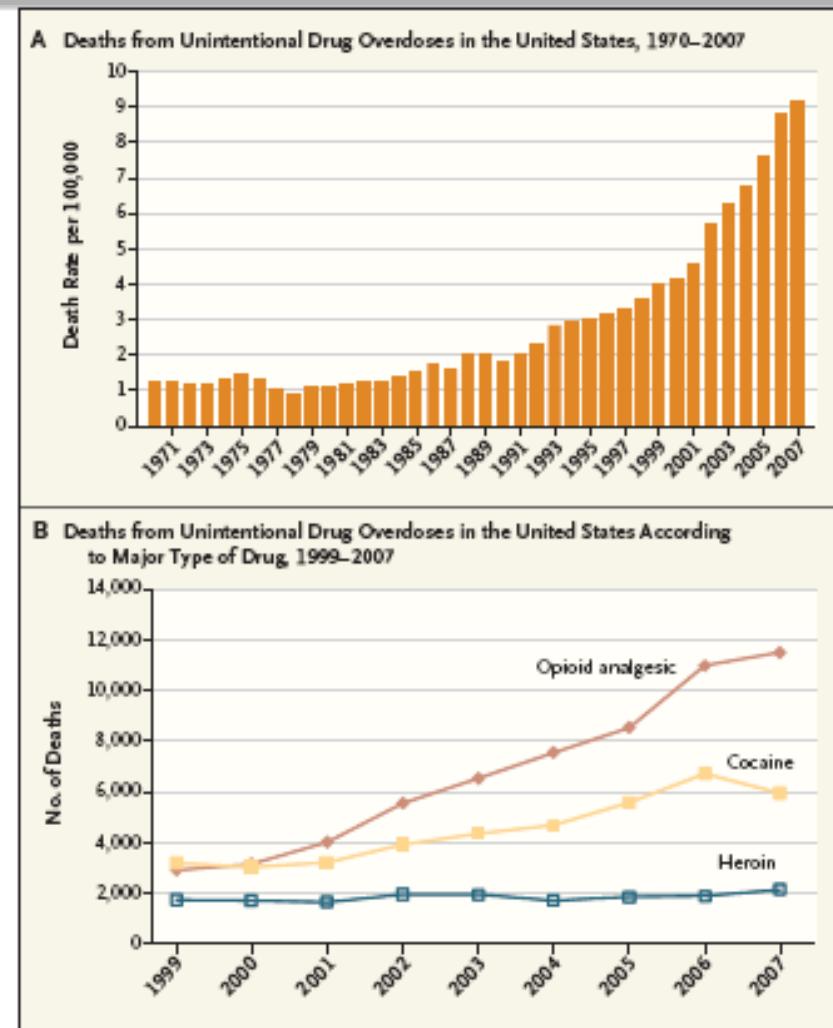
Valvular heart disease

Neuromuscular

Acute respiratory failure



- ❑ Dépression ventilatoire
- ❑ Apnée
- ❑ Arrêt respiratoire
- ❑ ->Naloxone
- ❑ SASC
- ❑ SAOS
- ❑ Paralysie NM



U.S. Rates of Death from Unintentional Drug Overdoses and Numbers of Deaths, According to Major Type of Drug.

Shown are nationwide rates of death from unintentional drug overdoses from 1970 through 2007 (Panel A) and the numbers of such deaths from opioid analgesics, cocaine, and heroin from 1999 through 2007 (Panel B). Data are from the National Vital Statistics System, Centers for Disease Control and Prevention.

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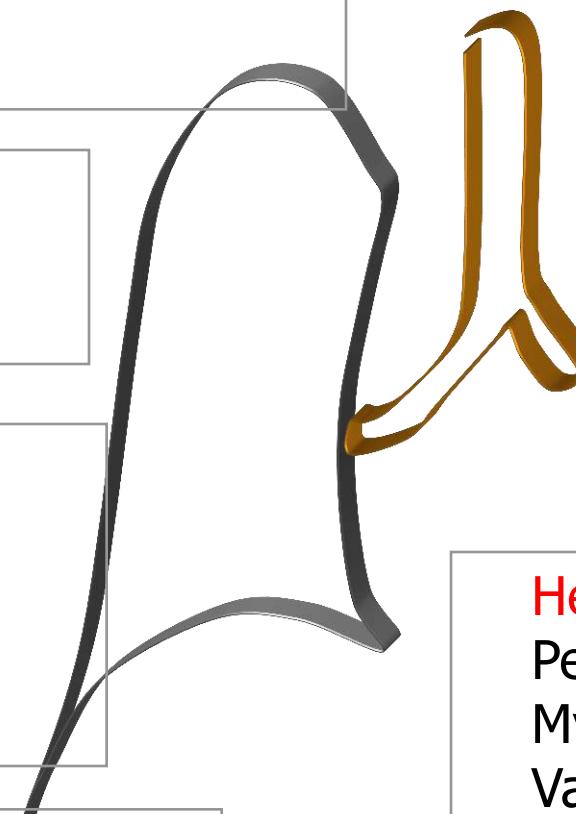
Pericardial effusion

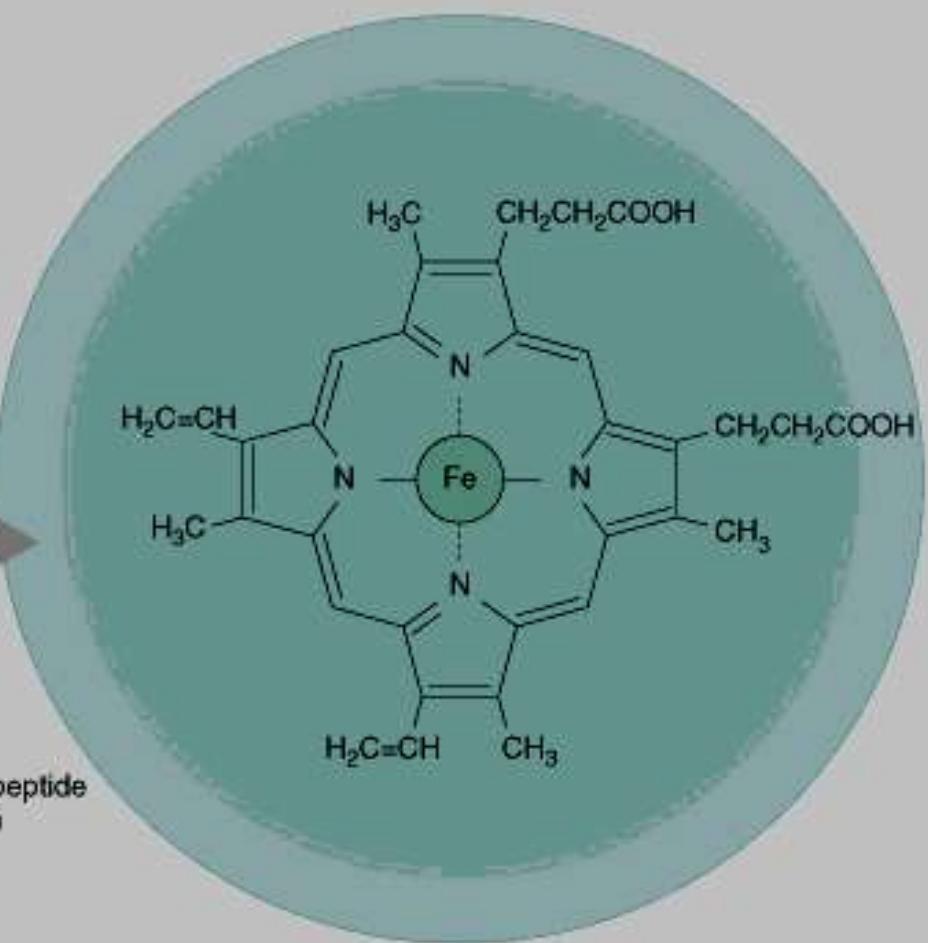
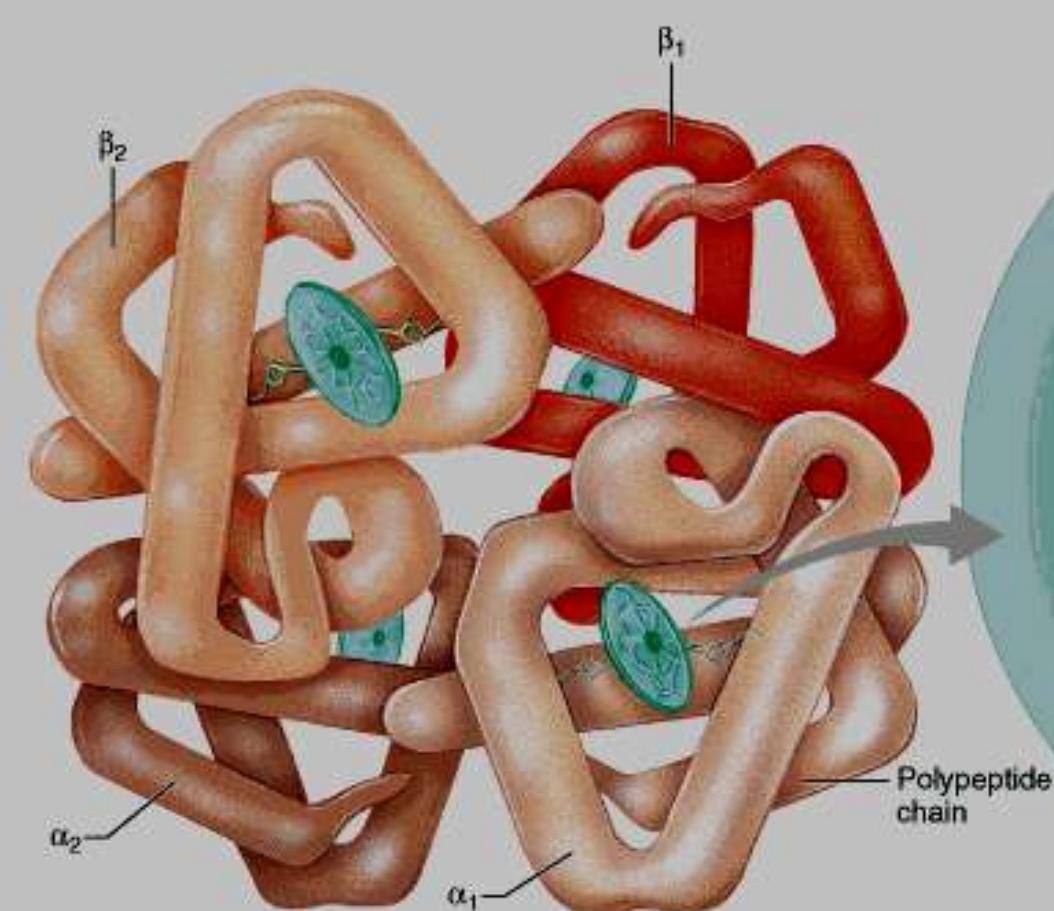
Myocarditis

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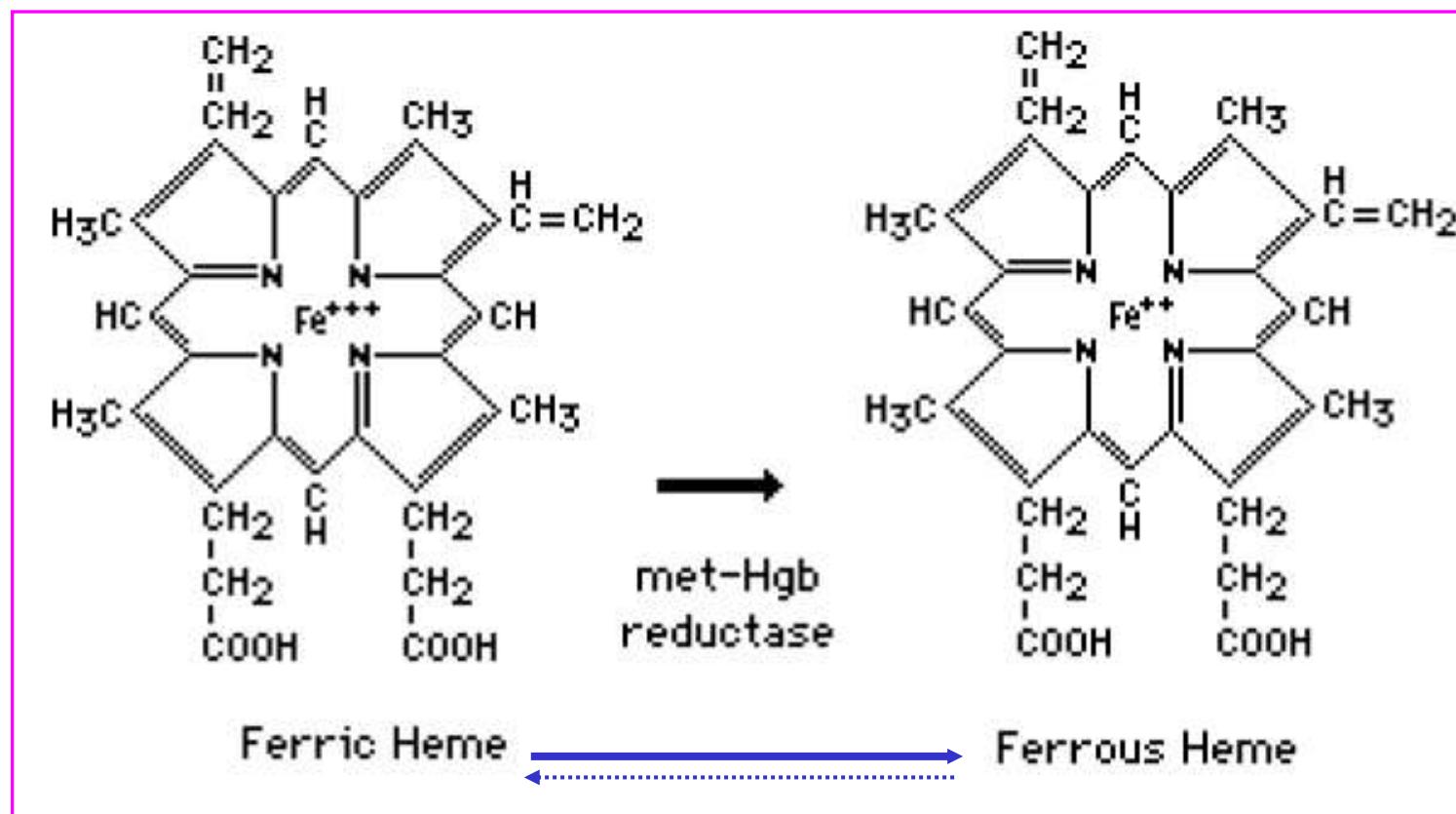
(a) Hemoglobin

(b) Iron-containing heme group

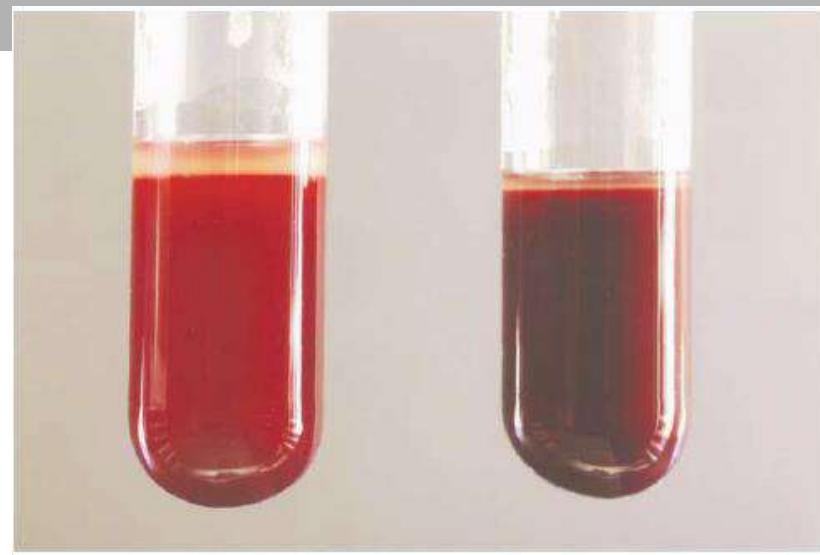
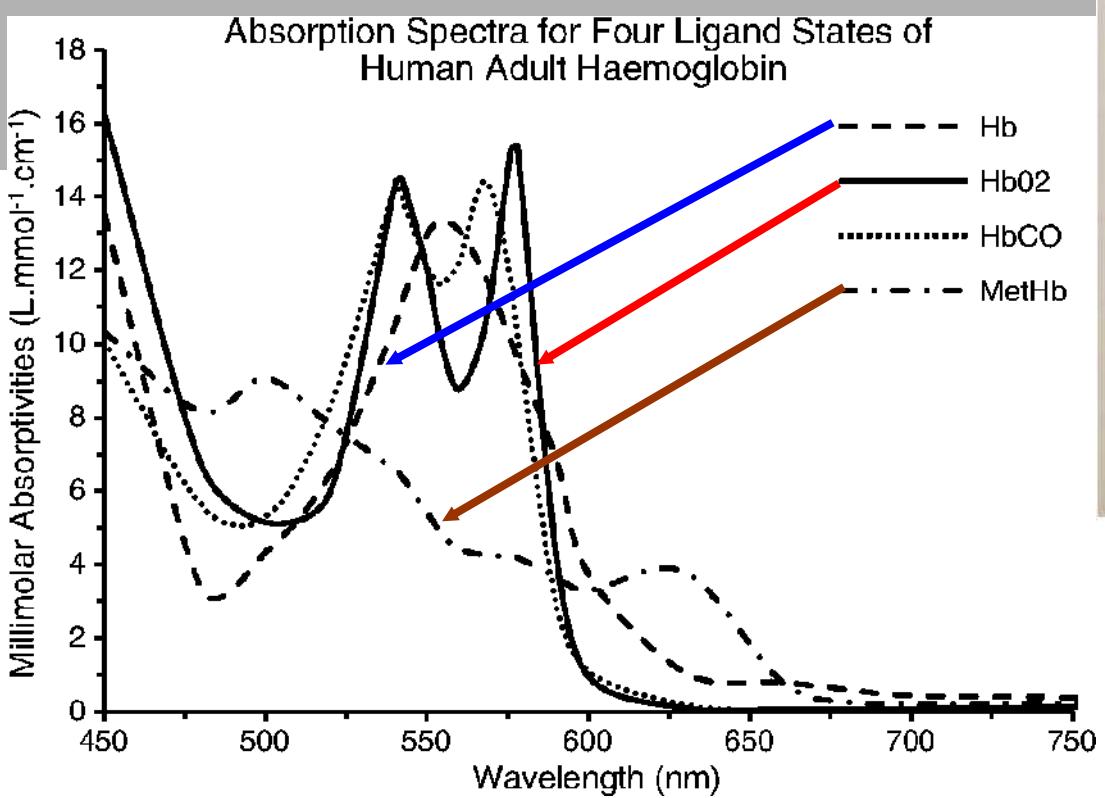
Copyright © 2001 Benjamin Cummings, an imprint of Addison Wesley Longman, Inc.

Méthémoglobine

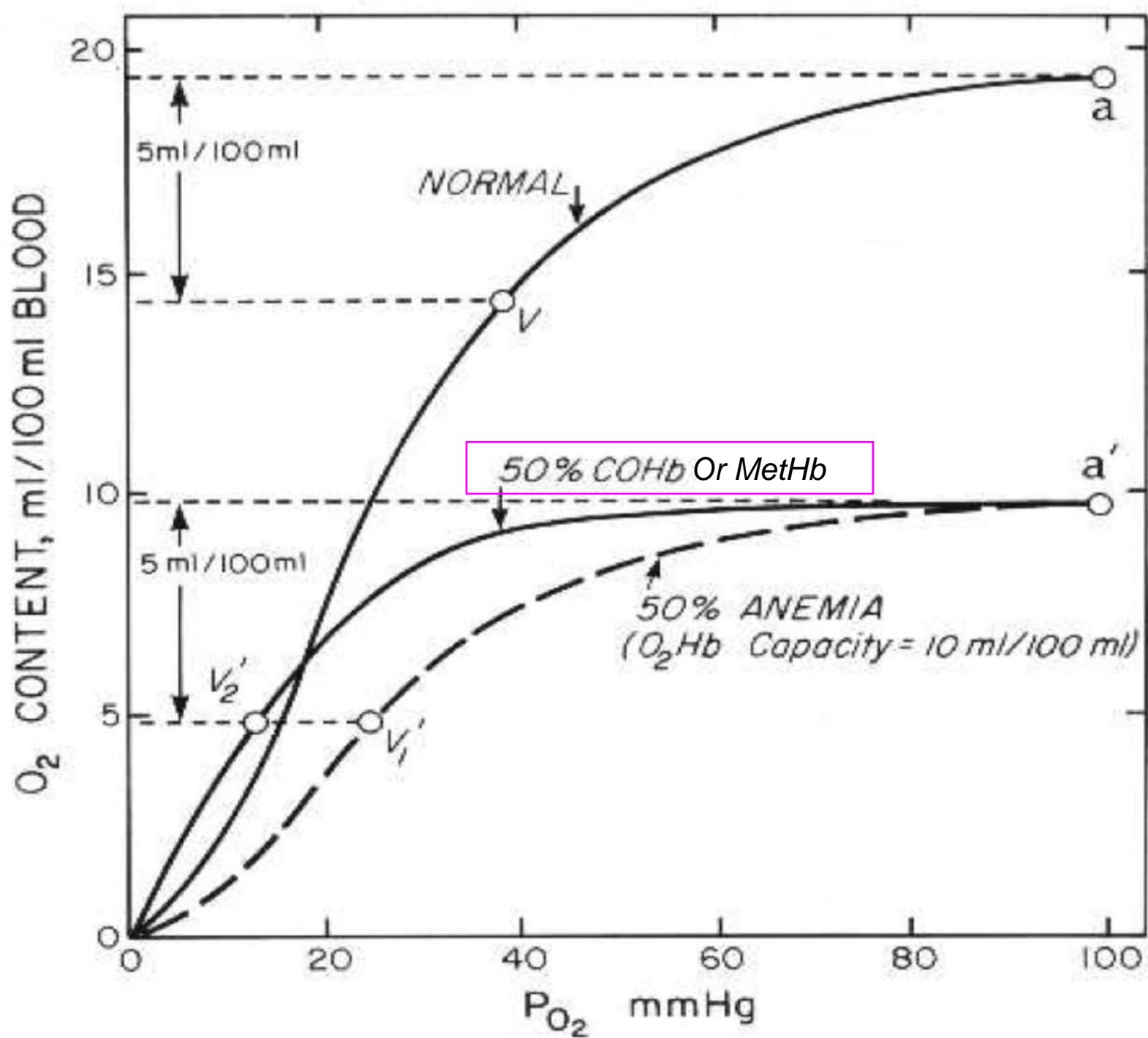
- 1-4 fers ferriques Fe⁺⁺⁺ = **MetHb** incapable de fixer l'O₂
- HbO₂ + Hb-deoxy + HbCO + MetHb = 100%
- 93/4/2/1



- Etat normal <1%
- Attention >2%
- >15-20%: symptômes
- >50-70%: risque de coma / décès

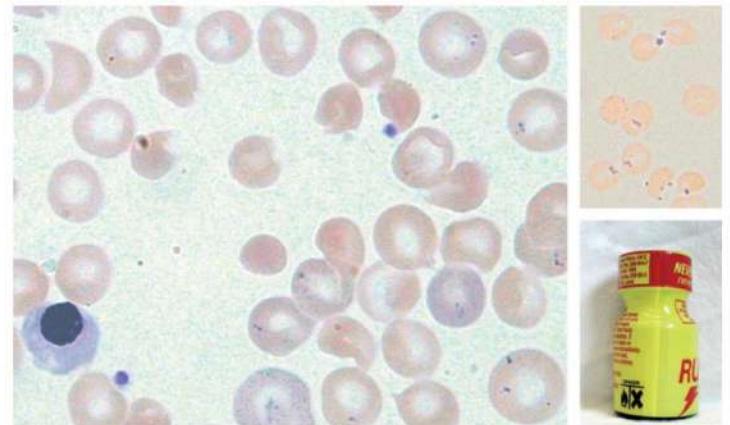
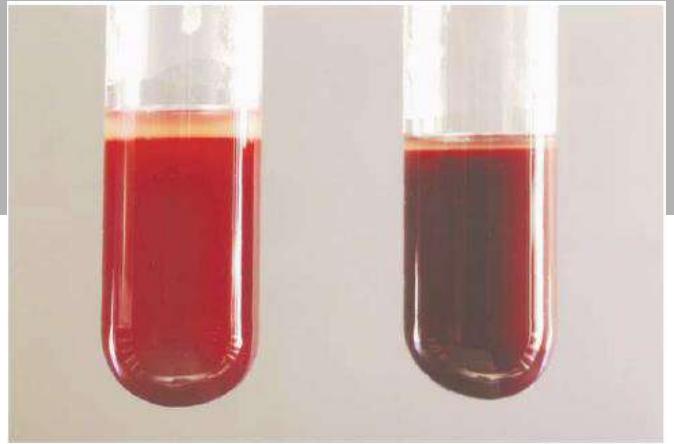






Diagnostic

- Cyanose centrale ardoisée
- Sang brun-chocolat
- Ne rosit pas sur papier filtre ou si bullé avec O₂
- SpO₂ ~70-80%
- PaO₂ (O₂ dissous) N
- SaO₂ calculée d'après PaO₂ faussement N
- SaO₂ - SpO₂ >5%: saturation gap
- Cooxymetrie @ 4-lambda +++
- Cas sévères +A. hémolytique



- P.E.C.
- Arrêt du M
- O₂
- Bleu de méthylène
- Exsanguino-T°
- OHB
- Audit: IDE : 32% Dr: 50%
- Vérifier disponibilité bleu de méthylène...

Table 3. Known Etiologies of Acquired Methemoglobinemia

Medications
Benzocaine: used as topical spray for endotracheal intubation, transesophageal echocardiography, esophagogastroduodenoscopy, bronchoscopy; used as topical cream for hemorrhoids or teething preparation
Chloroquine, quinacrine, primaquine: antimalarials
Dapsone: antibiotic for Hansen disease (leprosy) and other skin infections
Eutectic mixture of local anesthetics (EMLA): topical lidocaine, prilocaine
Flutamide
Lidocaine
Metoclopramide
Nitroprusside
Nitrites
Nitric oxide
Nitroglycerin
Nitrous oxide
Phenazopyridine (Pyridium)
Prilocaine
Riluzole
Silver nitrate
Sodium nitrate
Sulfonamides (sulfasalazine, sulfanilamide, sulfathiazide, sulfapyridine, sulfamethoxazole)
Medical conditions
Pediatric gastrointestinal infection and sepsis
Sepsis
Recreational drug overdose with amyl nitrate, aka "poppers"
Sickle cell crisis
Miscellaneous
Aniline dyes
Fume inhalation (automobile exhaust, burning of wood and plastics)
Herbicides
Industrial chemicals: nitrobenzene, nitroethane (nail polish, resins, rubber adhesives)
Pesticides
Petrol octane booster

From Aah-Bernal et al.¹⁶; adapted with permission.

TABLE 1. Known Etiologies of Acquired Methemoglobinemia**Medications**

Benzocaine^{100,104} used as a spray: endotracheal intubation^{39,72,82,114}, transesophageal echocardiography (TEE)^{76,109}, esophagogastroduodenoscopy (EGD)^{1,17,34,35}, bronchoscopy^{57,62}; used as a topical cream for hemorrhoids or teething preparation^{25,30,113}

Cetacaine^{19,24,97,99,116}

Chloroquine^{13,102}

Dapsone^{70,77,87,95,118,119}

EMLA (Eutectic Mixture of Local Anesthetics) topical anesthetic (lidocaine 2.5% and prilocaine 2.5%)^{21,29,110,111}

Flutamide^{46,56,58,98}

Lidocaine¹¹¹

Metoclopramide^{55,74}

Nitroprusside^{15,51,68,86}

Nitric oxide⁴³

Nitroglycerin^{8,92}

Nitroprusside^{6,9,106}

Nitrous oxide^{66,69}

Phenazopyridine (Pyridium)^{12,31,81}

Prilocaine^{4,20–22,29,110,111,120}

Primaquine^{13,51,53,90,96,102,103}

Riluzole¹¹⁷

Silver nitrate⁴⁵

Sodium nitrate^{26,33}

Sulfonamides (sulfasalazine, sulfanilamide, sulfathiazide, sulfapyridine, sulfamethoxazole)^{64,77,89,115}

Medical conditions

Pediatric gastrointestinal infection, sepsis^{52,67,88,105}

Sepsis^{59,75,84,104,114}

Recreational drug overdose with amyl nitrate (a.k.a. "poppers")^{79,86}

Sickle cell crisis⁴⁰

Miscellaneous
Aniline dyes^{23,38}

Fume inhalation (automobile exhaust, burning of wood and plastics)^{54,60,63}

Herbicides^{10,83,108}

Industrial chemicals: nitrobenzene^{37,61}, nitroethane (found in nail polish, resins, rubber adhesives)^{42,85,101}

Pesticides⁸⁰

Petrol octane booster¹⁶

- Enquête
 - IDE : 32%
 - Docteurs: 50%
- Donc vérifier
 - Connaissance
 - Disponibilité rapide du bleu de méthylène

Classification

Lung parenchyma ~75%

NSIP (cellular/fibrotic)

DAD

Pulmonary edema

DAH

Opportunistic infection

Vasculopathy

PHT

Thromboembolism

Pleura

Effusion

Thickening

Chest pain

Pneumothorax

Hemoglobin

Methemoglobinemia

Central airway

Angioedema

Hematoma

Other airways

Cough

Acute bronchospasm

Obliterative bronchiolitis

Mediastinum

Lymphadenopathy

Lipomatosis

Heart

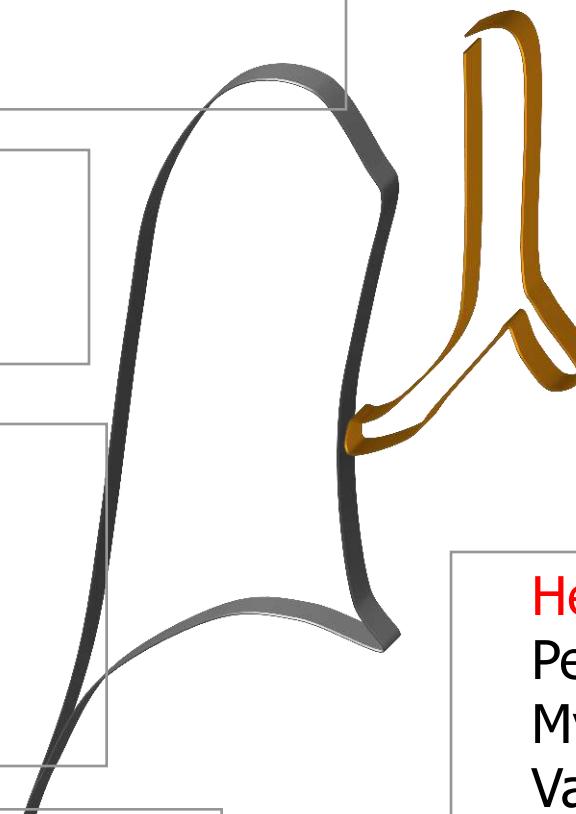
Pericardial effusion

Myocarditis

Valvular heart disease

Neuromuscular

Acute respiratory failure



- Epanchement 82M

- Epaississements – Fibrothorax 27M

- ❖ Ergots+++

- ❖ Benfluorex

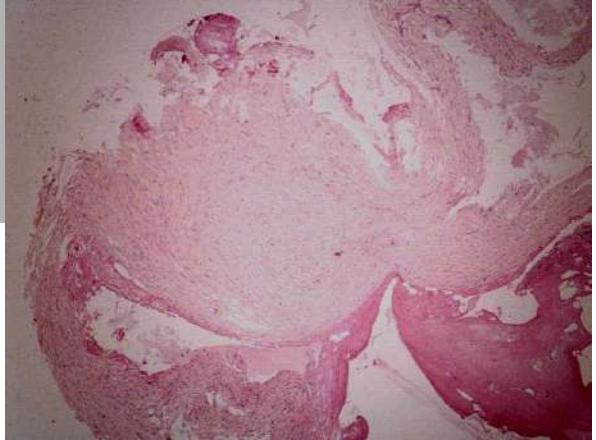
- ❖ Valvulopathies

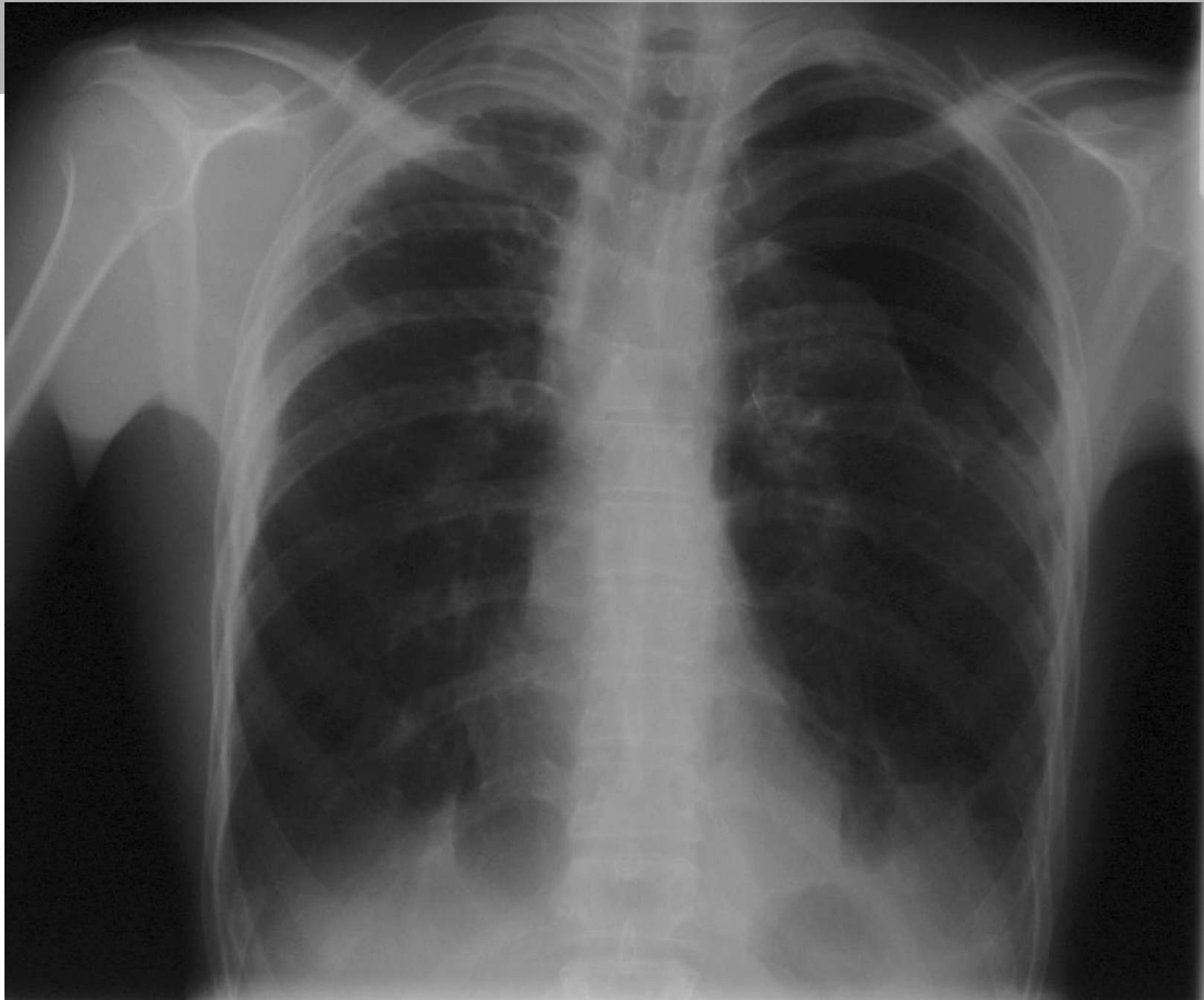
- *Lupus*

- ❖ ANA

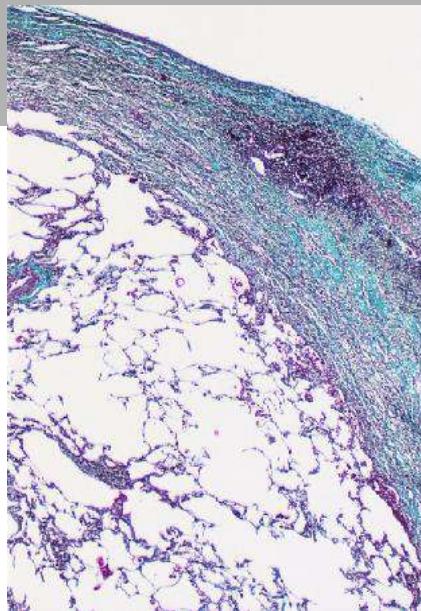
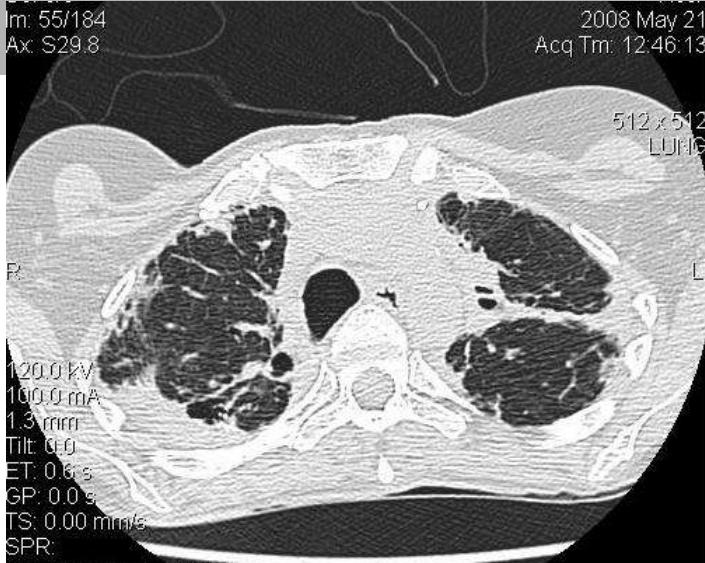
- ❖ Anti-TNF

- PPFE

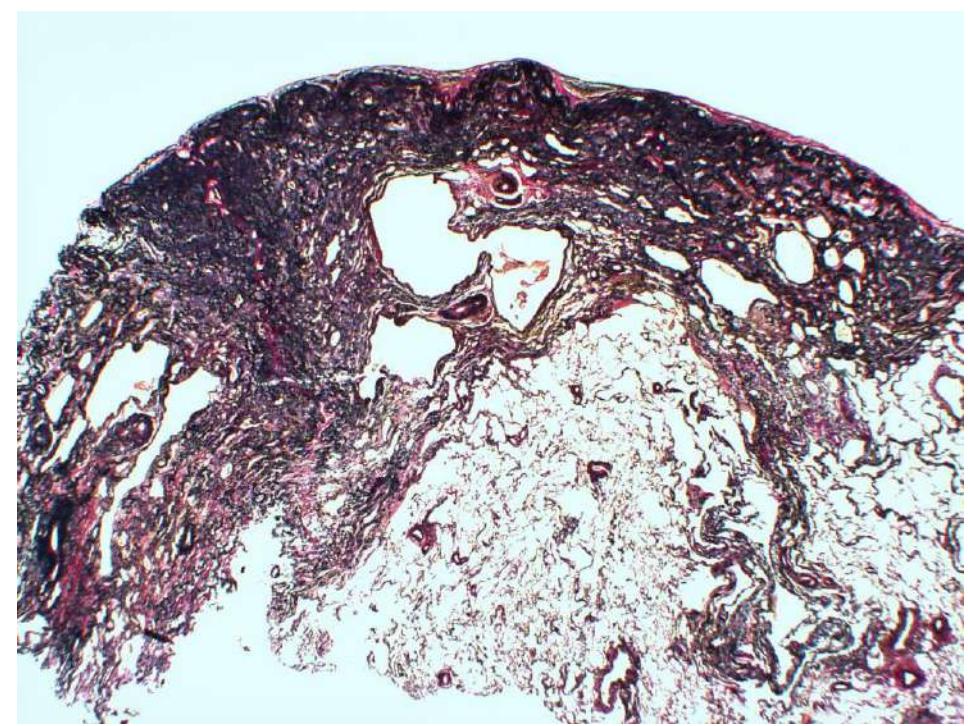
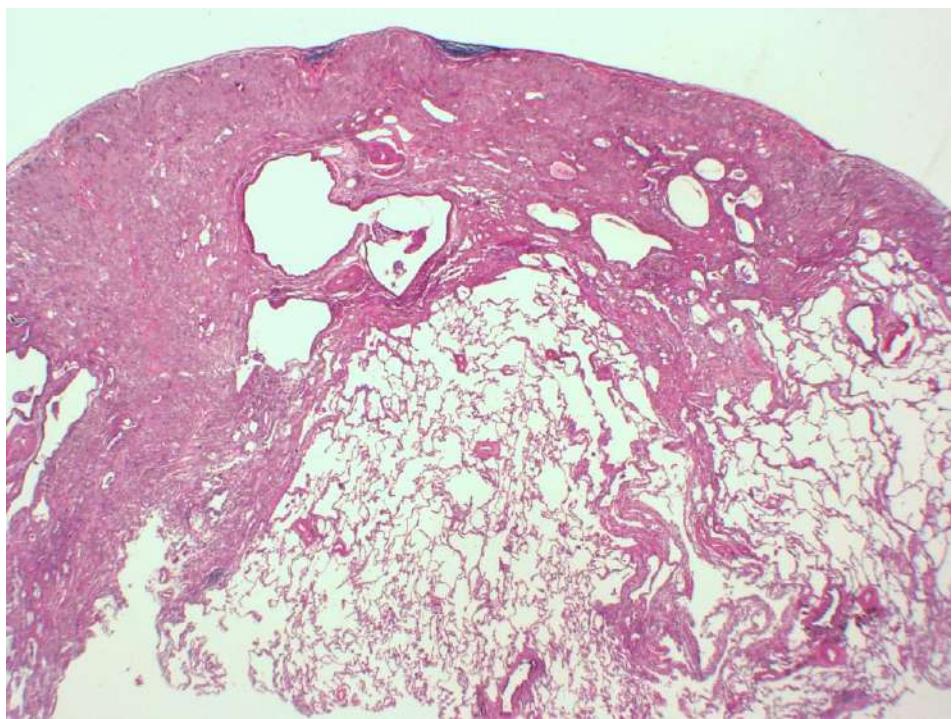




PPFE



- **Dyspnea, chest pain**
- **Platythorax**
- **Restrictive lung function defect, often severe**
- **Distinctive imaging**
- **Significant Hx: Lung Tx 50%. Exposure to cyclophosphamide 10%**



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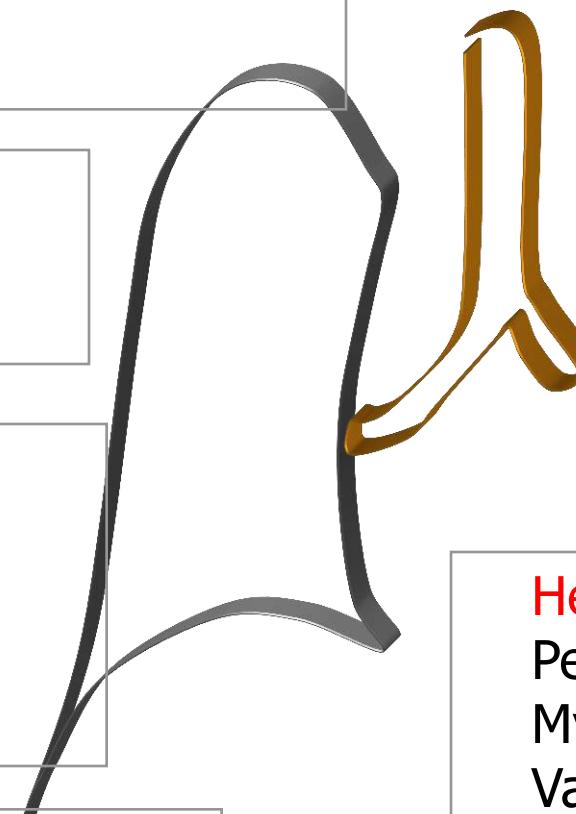
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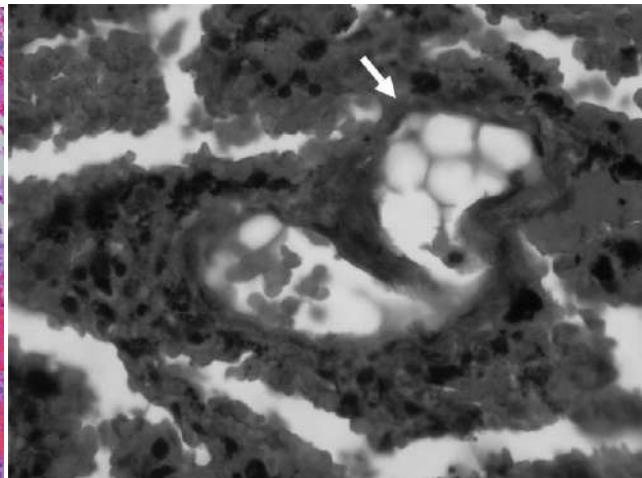
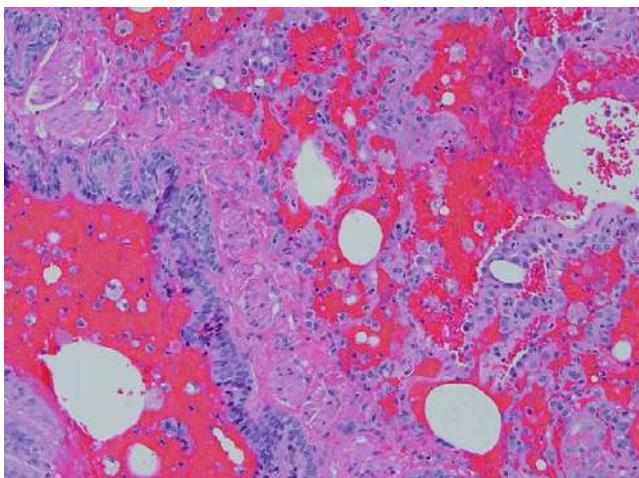
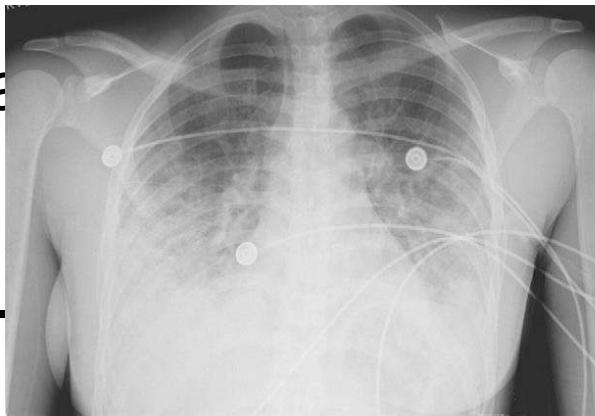


Vasculopathies

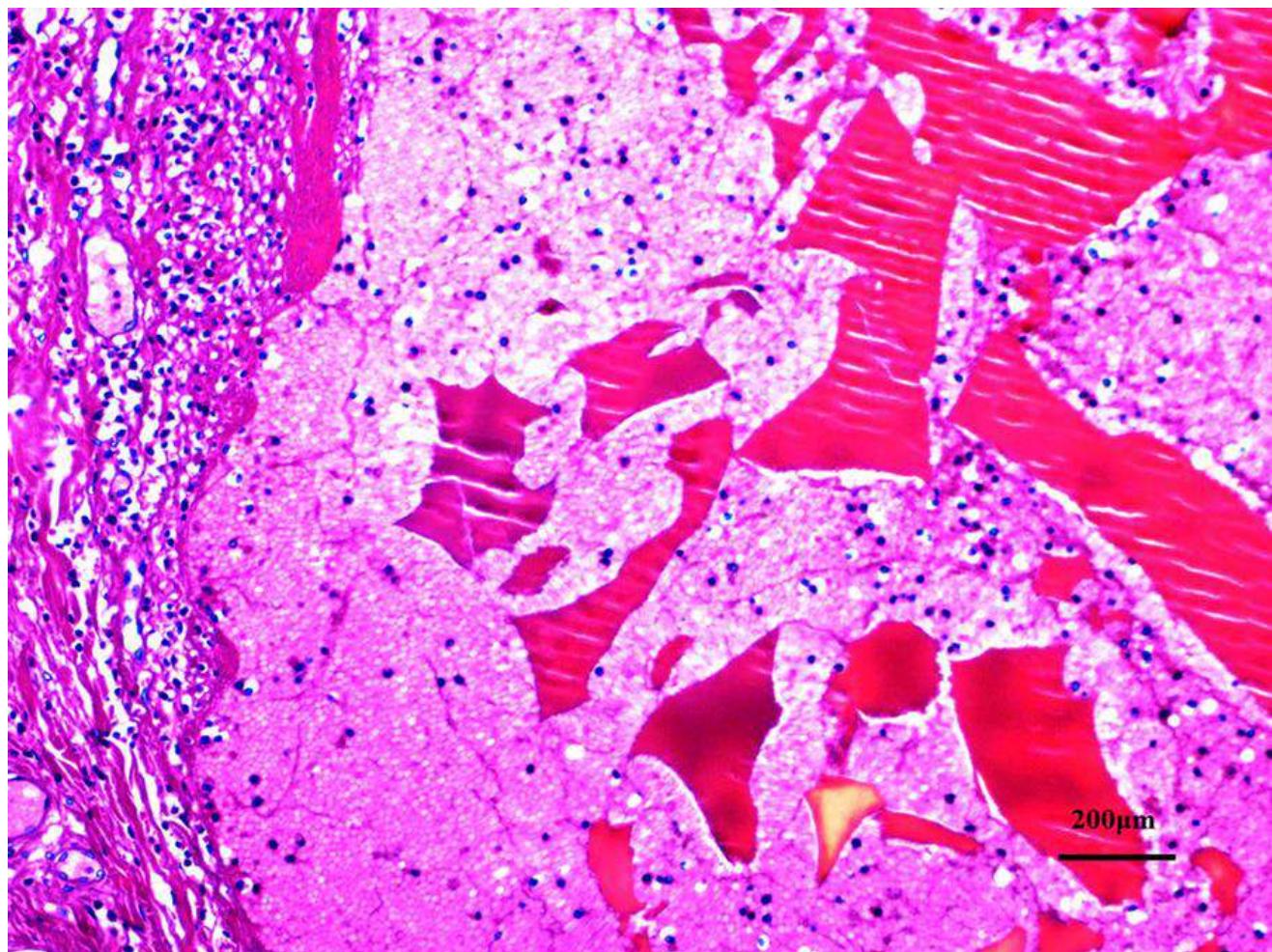
- ❑ HTAP
 - ❑ Anorexigènes
 - ❖ Aminorex, fenfluramine
 - ❖ Benfluorex
 - ❑ Levamisole
 - ❑ Dasatinib - Ponatinib
 - ❑ Interferon
 - ❑ Amphetamines
- ❑ MVO
 - ❑ Mitomycin C
- ❑ MTE

Silicone liquide (Schmid 2005: 33 cases)

- Chirurgie plastique officines non médicales
- Hypoxémie: 92%
- Hémoptysie: 39%
- Hemorragie alvéolaire
- Décès: 24%
- Si s. neuro: 100%...



- Graisse autologue (postliposuction)
- Hydrogel
- Hyaluronate



- ❑ Caractère précessif du ttt / aux signes & symptômes
- ❑ Délai d'apparition compatible
 - ❑ Une seconde – 20 ans
- ❑ Signal dans la littérature
 - ❑ ‘-’ à ‘5’
 - ❑ Spécificité (parfois ...)
- ❑ Biomarqueurs: BNP, AAN, ANCA (KL6--)
- ❑ Diagnostic différentiel soigneux
 - ❑ Maladie sous-jacente
 - ❑ Affection ntercurrente

Précession - Délai d'apparition – Temps -> Acmé

- ❑ Pneumopathie interstitielle
 - 1 semaine – des années / qq jours
- ❑ Eosinophilie pulmonaire
 - Quelques semaines – des années / qq jours
- ❑ Fibrose pulmonaire
 - Quelques semaines – des années / qq mois
- ❑ OAP
 - <1 minute / qq minutes
- ❑ Sténose VAS
 - Quelques heures – quelques années / qq minutes – qq heures
- ❑ Bronchospasme
 - <1 heure / qq minutes
- ❑ Anaphylaxie
 - Quelques secondes / quelques minutes

Précession - Délai d'apparition – Temps -> Acmé

- ❑ Pneumopathie de l'amiodarone
 - ❑ 2 jours– des années / qq jours ou semaines
- ❑ Toux médicamenteuse
 - ❑ Quelques jours – quelques années / graduel



β -bloqueurs; HCT min-hrs



Minocycline semaines



La plupart



Mois-années

Amiodarone, nitrosourées, RTE

retardé



IEC



Signal dans la littérature

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55

The Drug-Induced Respiratory Disease Website

Philippe Camus 2012- v2

Pascal Foucher - Philippe Camus 1997- v1

Department of Pulmonary Medicine and Intensive Care University Hospital Dijon France

Contribution: Ph Bonniaud, N Baudouin, A Fanton, C Camus, N Favrolt, M Guerriaud, L Jacquet

[BROWSE BY »](#)[DRUGS](#)[PATTERNS](#)[List All](#)[A](#) [B](#) [C](#) [D](#) [E](#) [F](#) [G](#) [H](#) [I](#) [J](#) [K](#) [L](#) [M](#) [N](#) [O](#) [P](#) [Q](#) [R](#) [S](#) [T](#) [U](#) [V](#) [W](#) [X](#) [Y](#)

Z

ACE inhibitors (ACEI)

I.b I.c IV.a IV.d V.a V.b V.d VIII.a VIII.q IX.e X.d
XVIII.k

5

ATRA

I.b I.k II.a II.b II.f II.k III.a V.a V.m VI.a VI.d
XII.c

4

Abacavir

I.a I.f II.a II.b IV.d X.a XV.d

2

Abciximab

III.a X.f

3

Acebutolol

I.b I.d V.a V.d

2

SEARCH

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NOTE LEGEND



LEGEND PATTERNS



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Sun, 26 May 2013 17:55:11

[To our pathology colleagues](#)

Tue, 14 May 2013 10:27:01

[Diagnosing DIRD](#)

Wed, 20 Feb 2013 16:42:42

Ergots-Ergolines

I.b I.d IV.a V.a V.c V.m VII.d XI.ac XII.b XII.c XII.g
XVI.ap

4

Erlotinib

I.a I.d I.g I.l I.u I.w II.b V.f XV.c XV.f

3

Erythromycin

VIII.a X.f X.h

II - Pulmonary edema - ARDS
II.b - ARDS

1

Erythropoietin (EPO)

II.b VI.a

2

Estrogens

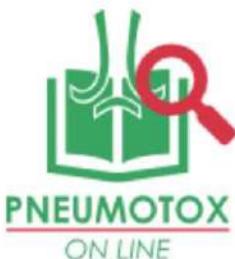
I.aa VI.a XV.au

3

Etanercept

I.b I.d I.g I.m I.q I.w I.y III.a IV.a V.d V.m
VI.a VI.d VII.a IX.e X.e X.f X.k X.m XI.e XI.v XV.a
XV.c XV.e

4



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Erlotinib

3

II.b ARDS

2

Last update 17/05/2012



:

Media

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No drugs

PUBLICATIONS

[Erlotinib-associated acute pneumonitis: report of two cases.](#)

Canadian respiratory journal : journal of the Canadian Thoracic Society
2007;14:167-70 2007

[Erlotinib-associated near-fatal interstitial pneumonitis in a patient with relapsed lung adenocarcinoma.](#)

Chang Gung medical journal 2010 Jan-Feb;33:100-5 2010 Jan-Feb

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Can Respir J. 2007 Apr;14(3):167-70.

Erlotinib-associated acute pneumonitis: report of two cases.

Vahid B, Esmaili A.

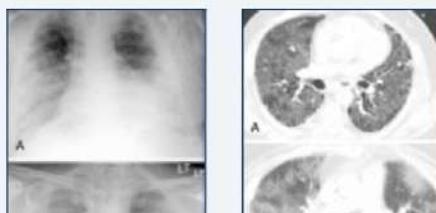
Department of Pulmonary and Critical Care Medicine, Thomas Jefferson University, Philadelphia, Pennsylvania 19107, USA.
Bobbak.vahid@mail.tju.edu

Abstract

Two cases of erlotinib-associated acute pneumonitis are described. The first patient was started on erlotinib treatment for metastatic non-small cell lung cancer. The second patient was treated with erlotinib for metastatic adenocarcinoma of unknown origin. Both patients developed dyspnea and hypoxemia five to six days after initiation of erlotinib treatment. In both cases, computed tomography scan of the chest showed extensive bilateral ground-glass infiltrates consistent with pneumonitis. In both patients, acute pneumonitis resulted in respiratory failure requiring intubation and mechanical ventilation. Diffuse alveolar hemorrhage was excluded by bronchoscopy in both cases. Bronchoalveolar lavage cultures were negative. Erlotinib treatment was stopped and both patients were treated with corticosteroids. The first patient improved gradually and finally was discharged to a rehabilitation centre, but unfortunately the second patient died of Klebsiella sepsis. Naranjo causality scale in both cases suggested a probable association between erlotinib and pneumonitis. Literature on erlotinib-associated pneumonitis is sparse. The clinical presentation and radiographic findings of erlotinib-associated acute pneumonitis are described.

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- Fatal interstitial lung disease after erlotinib for non-small-cell lung cancer [J Thorac Oncol. 2008]
- [Fatal interstitial lung disease associated with oral erlotinib therapy]

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CASE REPORT

Erlotinib-associated acute pneumonitis: Report of two cases

Bobbak Vahid MD¹, Ali Esmaili MD²

B Vahid, A Esmaili. Erlotinib-associated acute pneumonitis: Report of two cases. *Can Respir J* 2007;14(3):167-170.

Two cases of erlotinib-associated acute pneumonitis are described. The first patient was started on erlotinib treatment for metastatic non-small cell lung cancer. The second patient was treated with erlotinib for metastatic adenocarcinoma of unknown origin. Both patients developed dyspnea and hypoxemia five to six days after initiation of erlotinib treatment. In both cases, computed tomography scan of the chest showed extensive bilateral ground-glass infiltrates consistent with pneumonitis. In both patients, acute pneumonitis resulted in respiratory failure requiring intubation and mechanical ventilation. Diffuse alveolar hemorrhage was excluded by bronchoscopy in both cases. Bronchoalveolar lavage cultures were negative. Erlotinib treatment was stopped and both patients were treated with corticosteroids. The first patient improved gradually and finally

Une pneumonite aiguë associée à l'erlotinib : Le rapport de deux cas

On décrit deux cas de pneumonite aiguë associée à l'erlotinib. Le premier patient avait entrepris un traitement à l'erlotinib en raison d'un cancer bronchopulmonaire métastatique non à petites cellules. Le deuxième l'avait commencé en raison d'un adénocarcinome métastatique d'origine inconnue. Les deux patients se sont mis à faire de la dyspnée et de l'hypoxémie de cinq à six jours après le début de ce traitement. Dans les deux cas, la tomodensitométrie du thorax a révélé la présence d'infiltrats bilatéraux étendus « en verre dépoli », compatibles avec une pneumonite, et la pneumonite aiguë a provoqué une insuffisance respiratoire exigeant une intubation et une ventilation mécanique. Chez les deux patients, une bronchoscopie a permis d'écartier la possibilité d'hémorragie alvéolaire diffuse. La culture bronchopulmonaire par lavage était négative. Les deux patients ont abandonné l'erlotinib et entrepris un traitement aux corti-

Canadian
Tuberculosis
Standards,
7th Edition,
available here



17:36

Browse

DRUGS PATTERNS

A

Abacavir	1	>
Abciximab	4	>
Acebutolol	2	>
Acetaminophen	0	>
Acetazolamide	4	>
Acetylcysteine	5	>
Acetylsalicylic acid	5	>

DRUGS **PATTERNS**

A

Abacavir 1 >
Abciximab 4 >
Acebutolol 2 >
Acetaminophen 0 >
Acetazolamide 4 >
Acetylcysteine 5 >
Acetylsalicylic acid 5 >

17:36

Browse

DRUGS PATTERNS

I : Interstitial - infiltrative lung disease

- a : Acute cellular interstitial lung disease/pneumonia >
- b : Subacute interstitial pneumonia. Similar to but less severe than 1a >
- c : Pulmonary infiltrates and eosinophilia. Eosinophilic pneumonia (>
- d : Organising pneumonia (BOOP - AFOP) >
- e : Desquamative interstitial pneumonia (DIP pattern) >
- f : Lymphocytic interstitial pneumonia (LIP pattern) >
- g : Pulmonary fibrosis >

DRUGS **PATTERNS**

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Leflunomide Use and Risk of Lung Disease in Rheumatoid Arthritis: A Systematic Literature Review and Metaanalysis of Randomized Controlled Trials

Richard Conway, Candice Low, Robert J. Coughlan, Martin J. O'Donnell, and John J. Carey

ABSTRACT. *Objective.* To evaluate the relative risk (RR) of pulmonary disease among patients with rheumatoid arthritis (RA) treated with leflunomide (LEF).

Methods. We searched PubMed, Embase, and the Cochrane Central Register of Controlled Trials to April 15, 2014. We included double-blind randomized controlled trials (RCT) of LEF versus placebo or active comparator agents in adults with RA. Studies with fewer than 50 subjects or shorter than 12 weeks were excluded. Two investigators independently searched both databases. All authors reviewed selected studies. We compared RR differences using the Mantel-Haenszel random-effects method to assess total respiratory adverse events, infectious respiratory adverse events, noninfectious respiratory adverse events, interstitial lung disease, and death.

Results. Our literature search returned 5673 results. A total of 8 studies, 4 with placebo comparators, met our inclusion criteria. There were 708 respiratory adverse events documented in 4579 participants. Six cases of pneumonitis occurred, all in the comparator group. Four pulmonary deaths were reported, none in the LEF group. LEF was not associated with an increased risk of total adverse respiratory events (RR 0.99, 95% CI 0.56–1.78) or infectious respiratory adverse events (RR 1.02, 95% CI 0.58–1.82). LEF was associated with a decreased risk of noninfectious respiratory adverse events (RR 0.64, 95% CI 0.41–0.97).

Conclusion. Our study found no evidence of increased respiratory adverse events in RCT of LEF treatment. (J Rheumatol First Release March 15 2016; doi:10.3899/jrheum.150674)

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- ❑ Diagnostic différentiel soigneux
 - ❑ Maladie sous-jacente
 - ❑ Affection ntercurrente

Pathognomonique

- De coup d'œil
 - Bronchogramme de contraste
 - Opacités hypodenses: paraffine
 - Poumon/foie hyperdense: amiodarone
 - Densités vasculaires
 - ❖ Ciment
 - ❖ Lipiodol
 - Talcome pleural



PHOTO QUIZ

An enlarged heart with hyperdense consolidation

B. Hochhegger¹, A. Soares Souza Jr², G. Zanetti¹, E. Marchiori^{1*}

¹Department of Radiology, Federal University of Rio de Janeiro, Rio de Janeiro, Brazil, ²Department of Radiology, Medical School of Rio Preto (FAMERP) and Ultra X, São José do Rio Preto, Brazil,

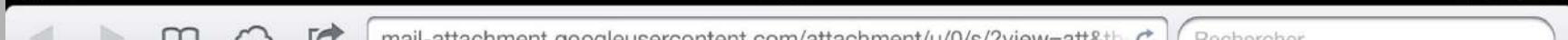
*corresponding author: tel.: +55 (24) 22492777, fax: + 55 (21) 26299017, e-mail: edmarchiori@gmail.com.











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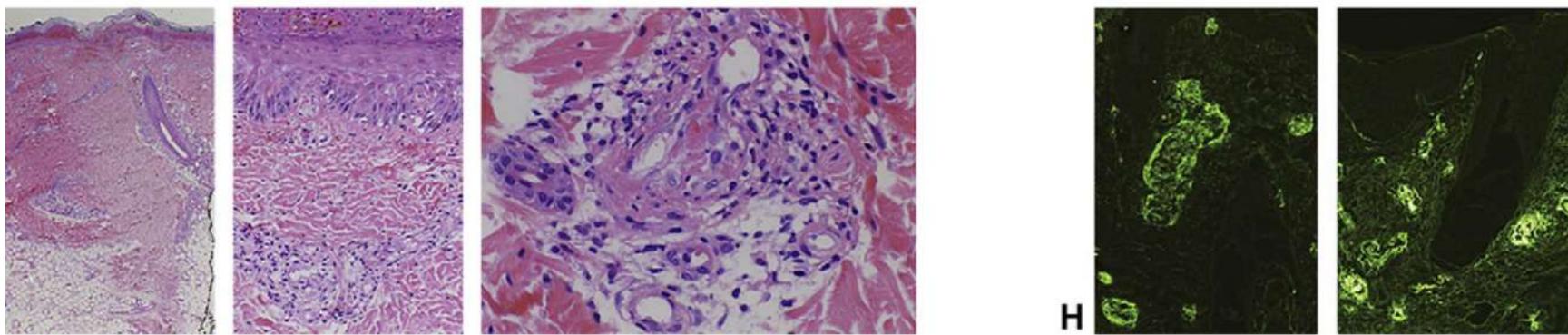
x Characteristic purpura of the ears, vasculitis, and neutropenia-a pot...



D



F



H

■ Réactions cliniques immédiates

■ OAP-flash

- ❖ Produits de contraste
- ❖adrénaline
- ❖ Xylocaïne
- ❖ TACE
- ❖ Héroïne



■ BSAG

- ❖ Bloquants

■ Anaphylaxie

- ❖ Biothérapies

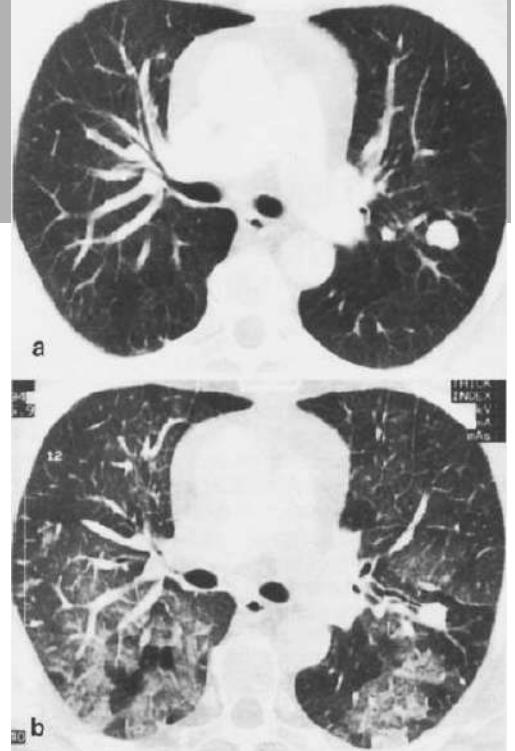
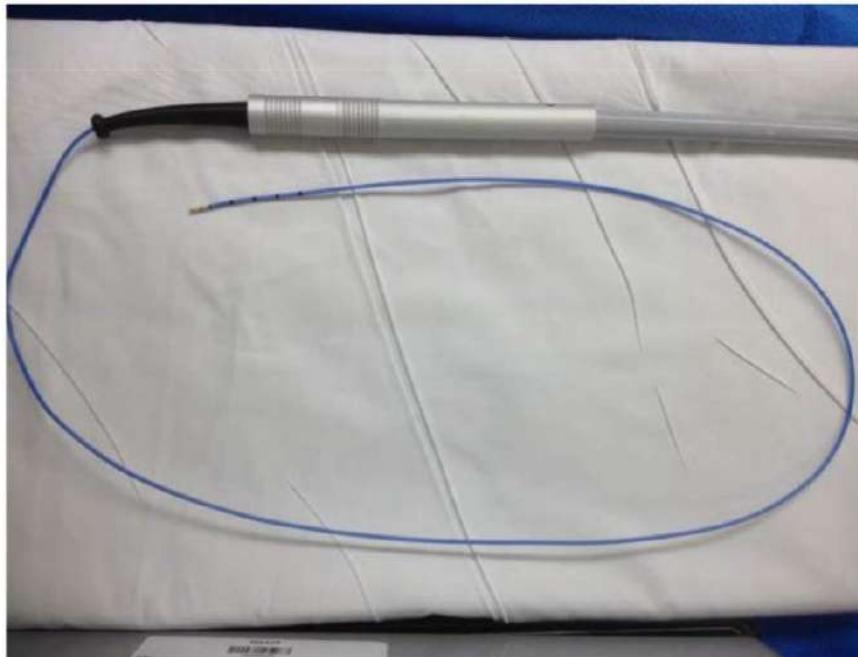
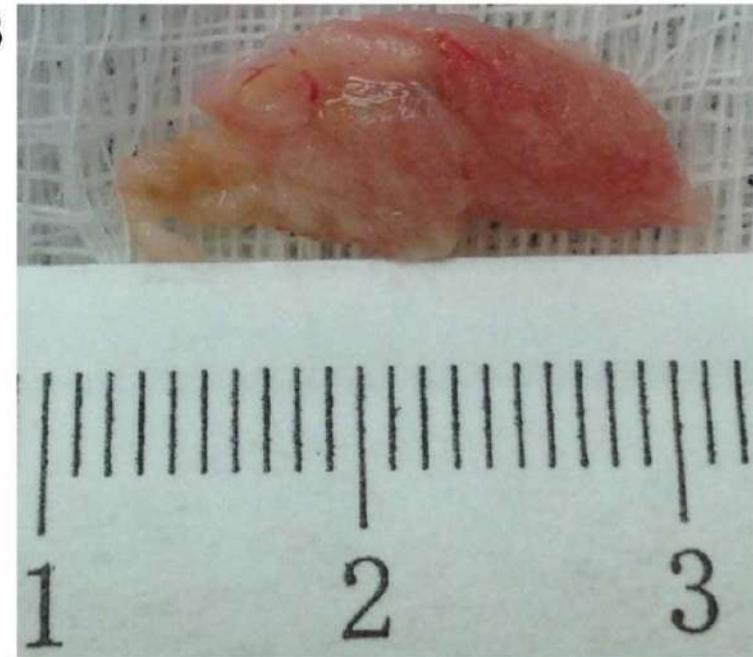
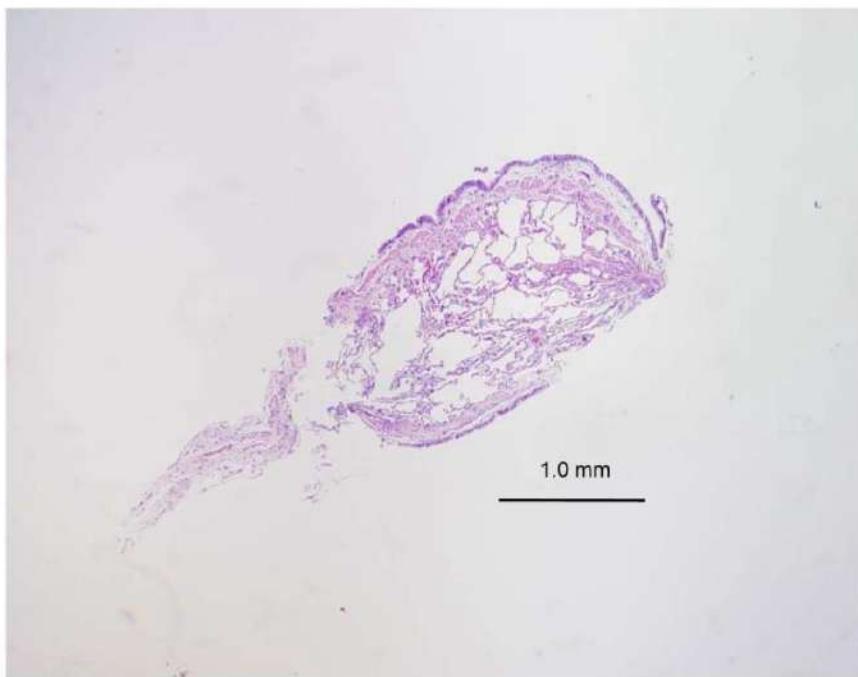
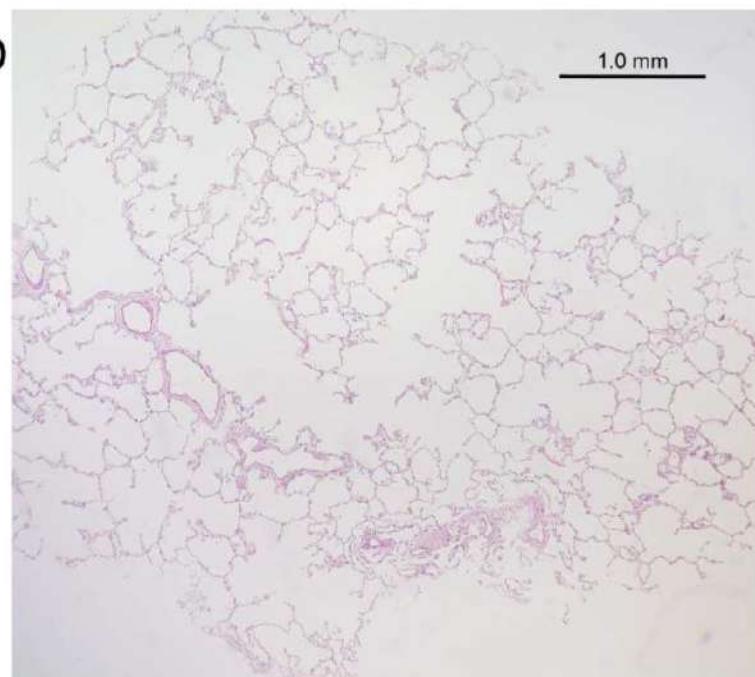


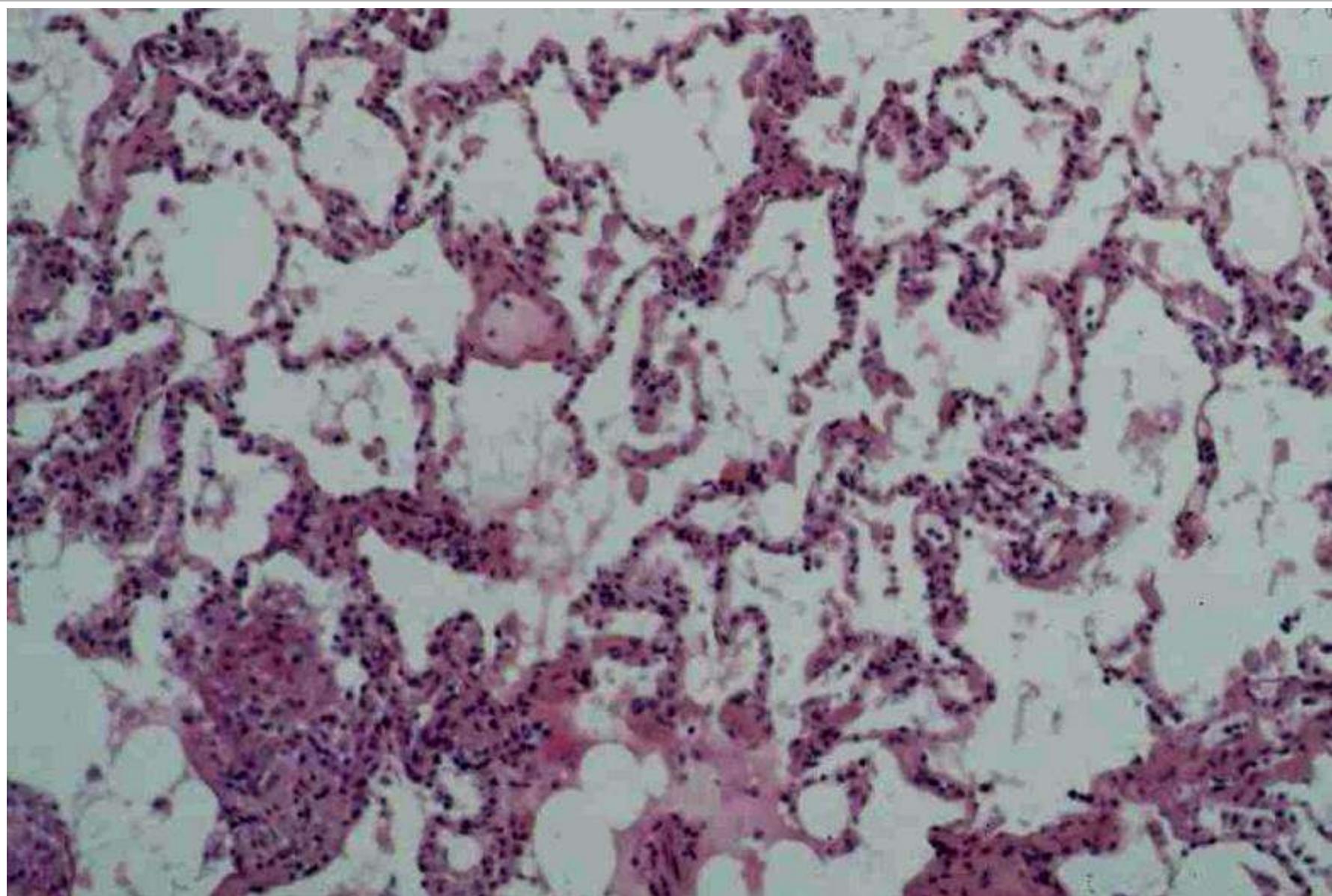
Figure 5. Mushroom plume from pulmonary oedema. This may be seen in opiate deaths.

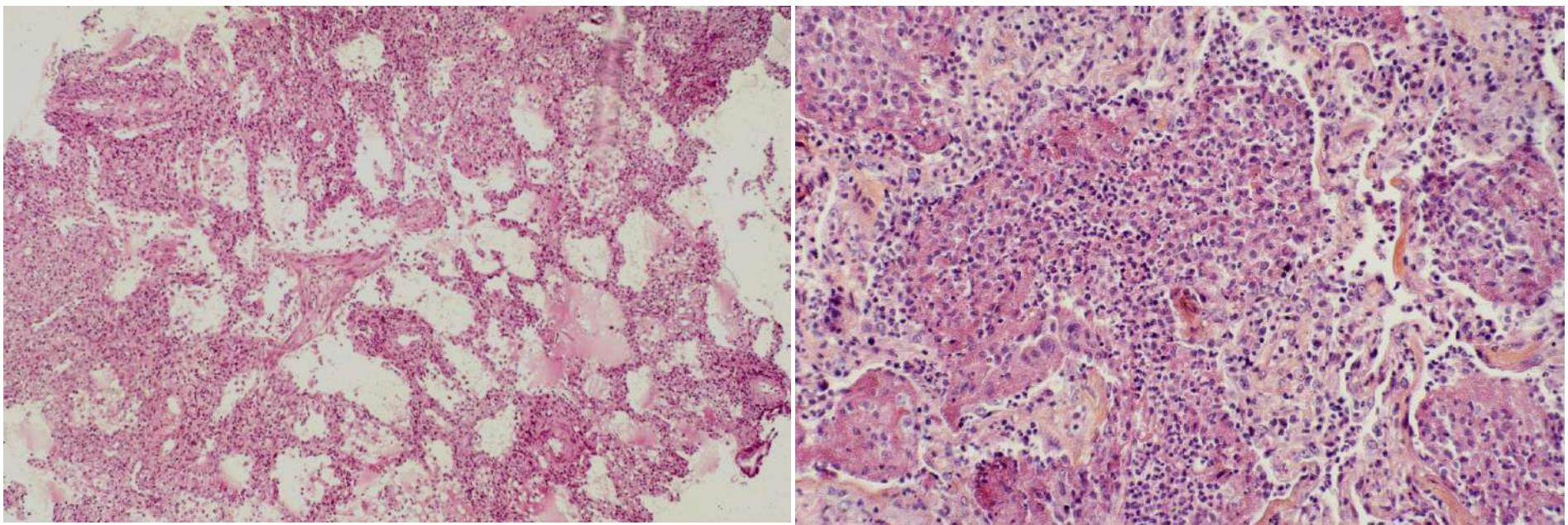
Pathognomonique

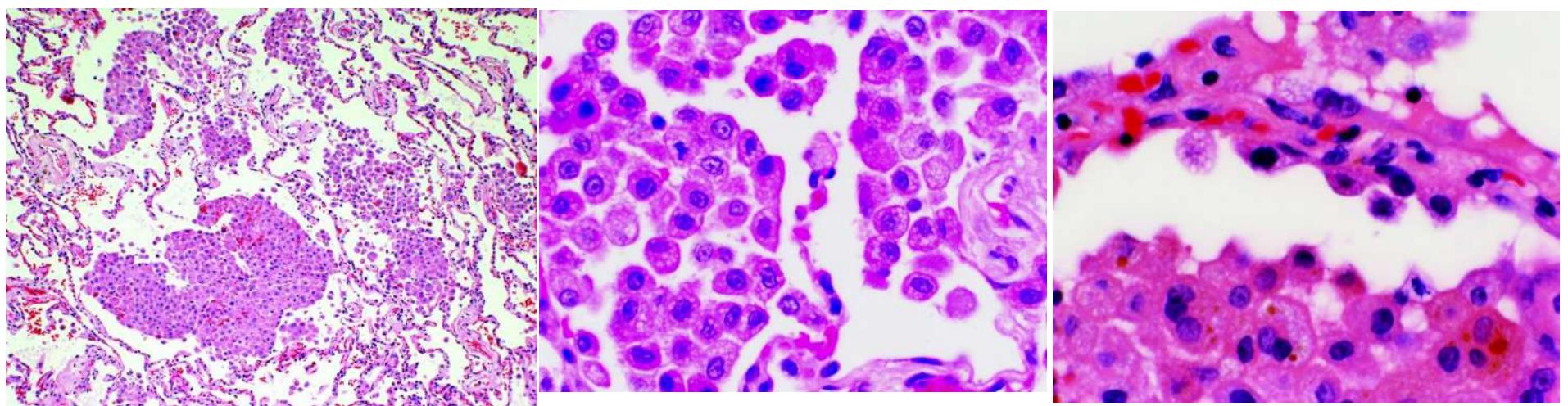
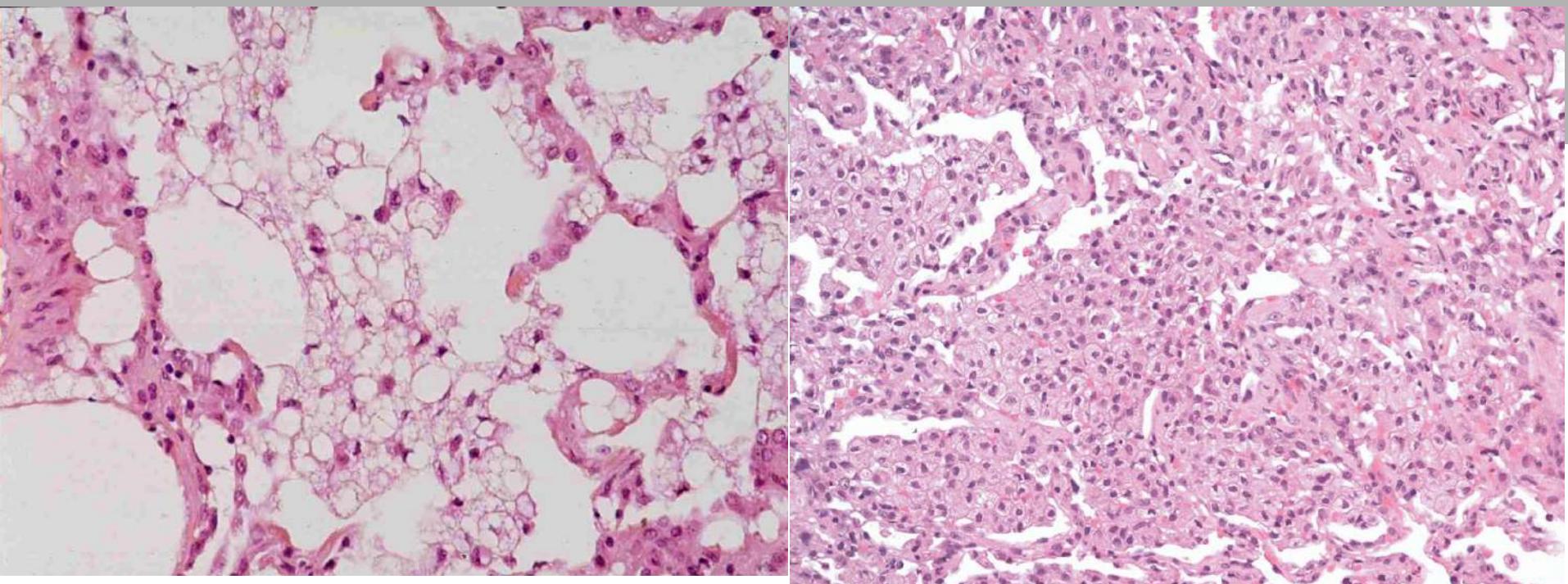
□ Ana-path

A**B****C****D**

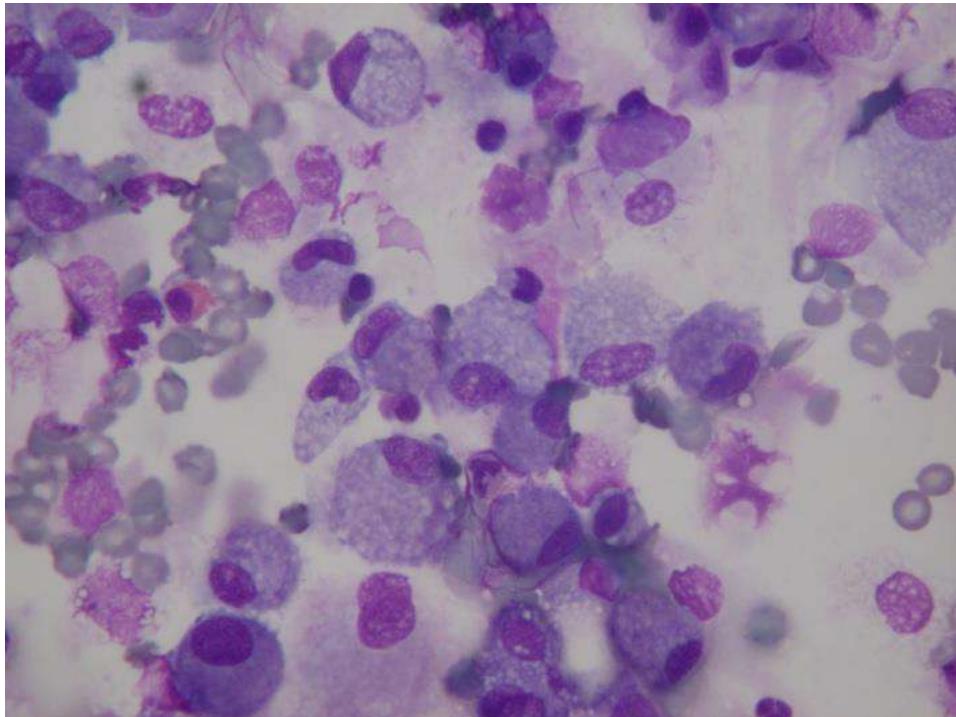
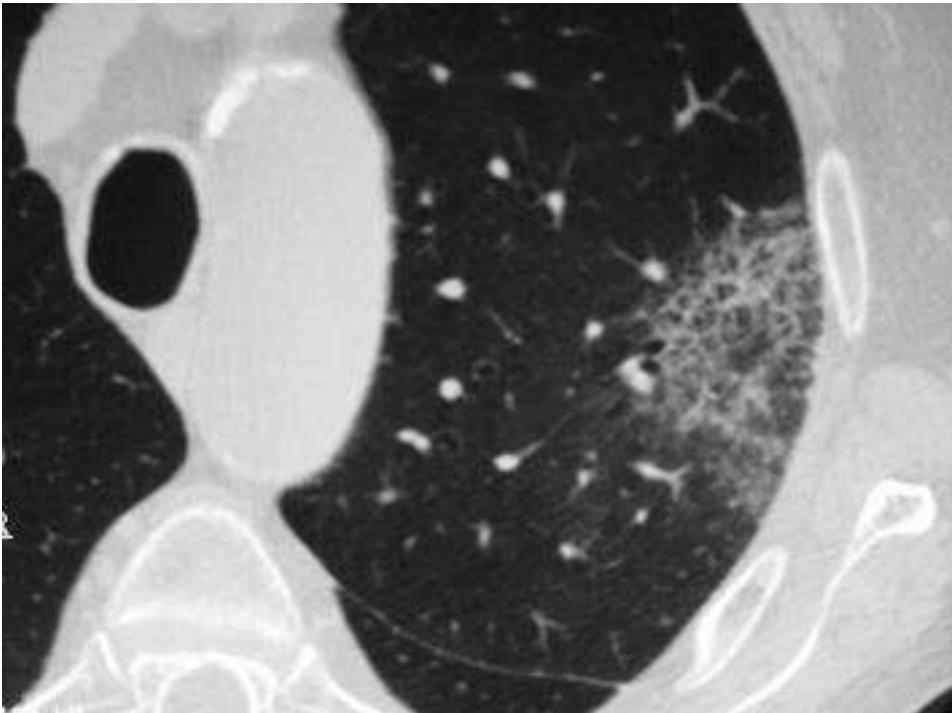
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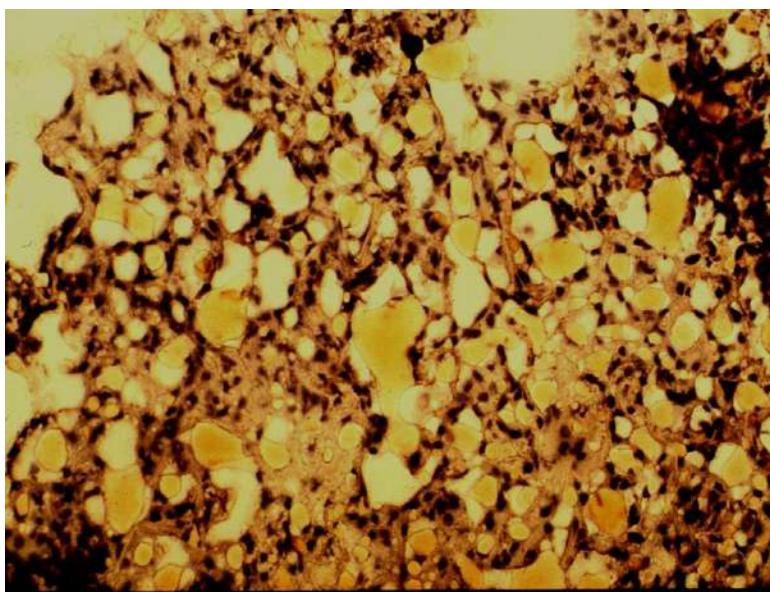
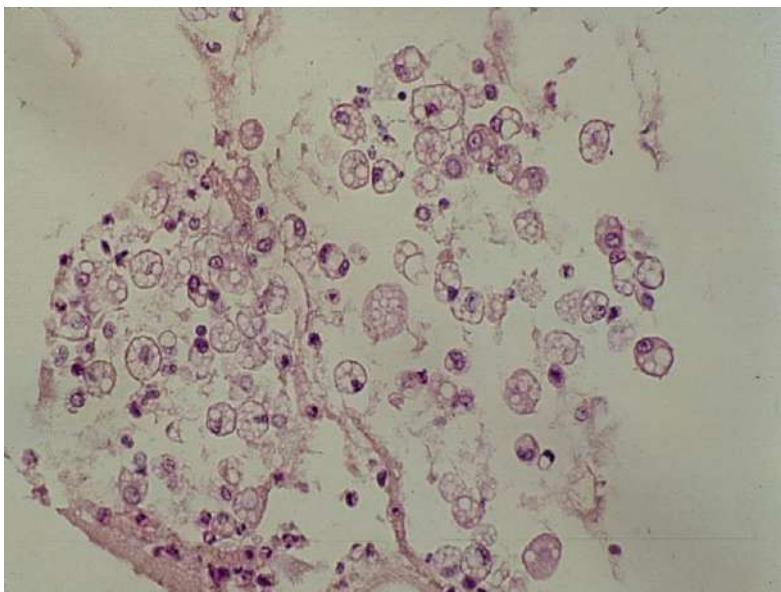
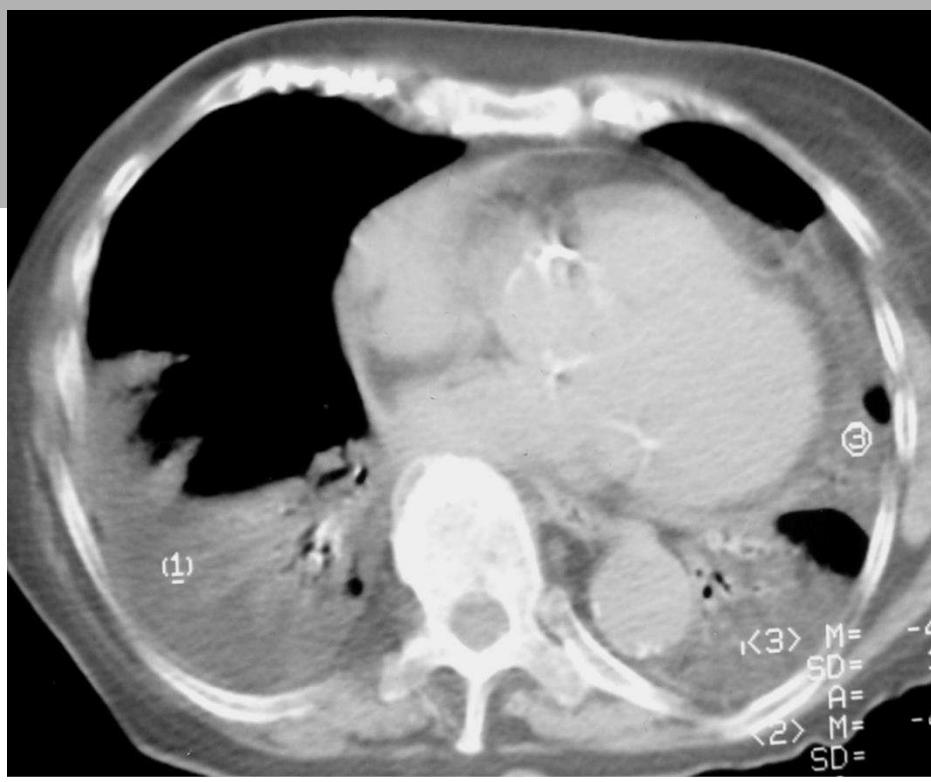






Amiodarone





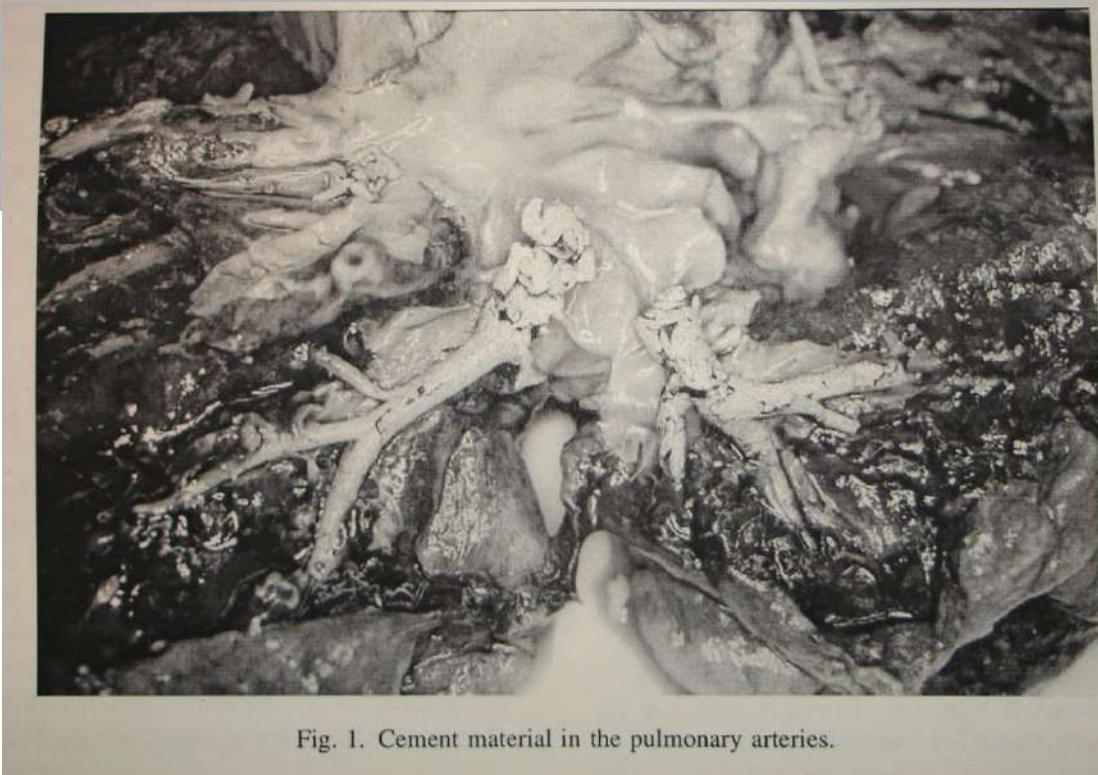
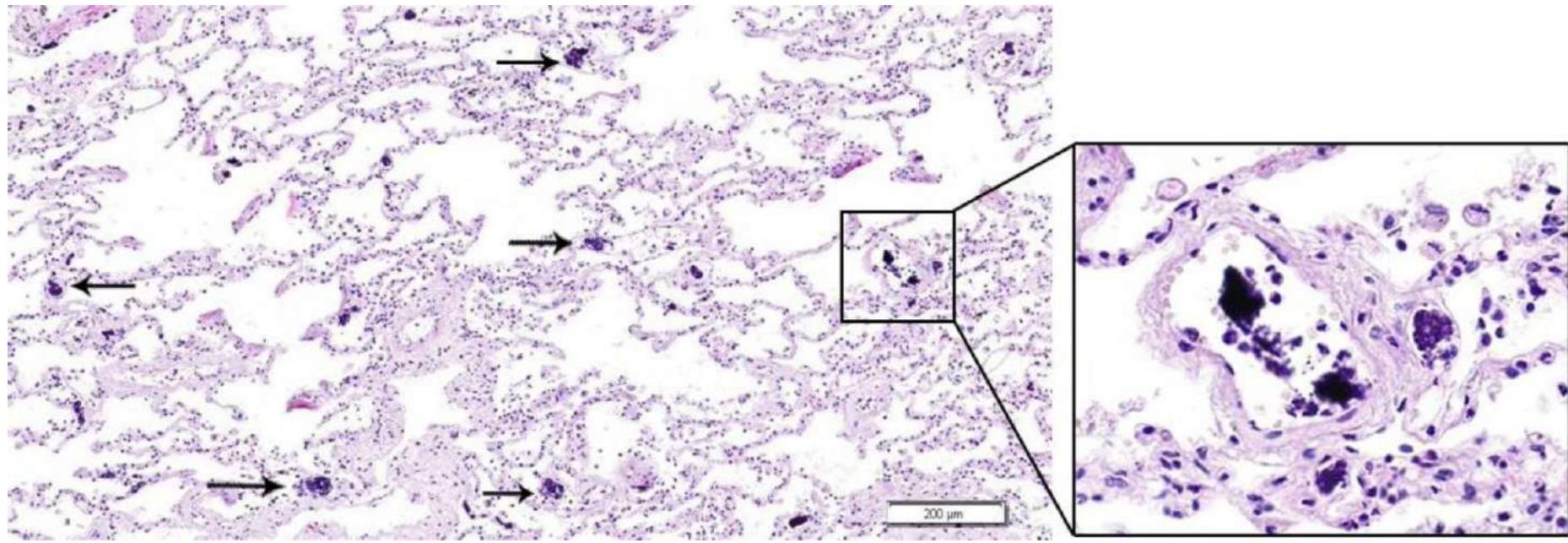
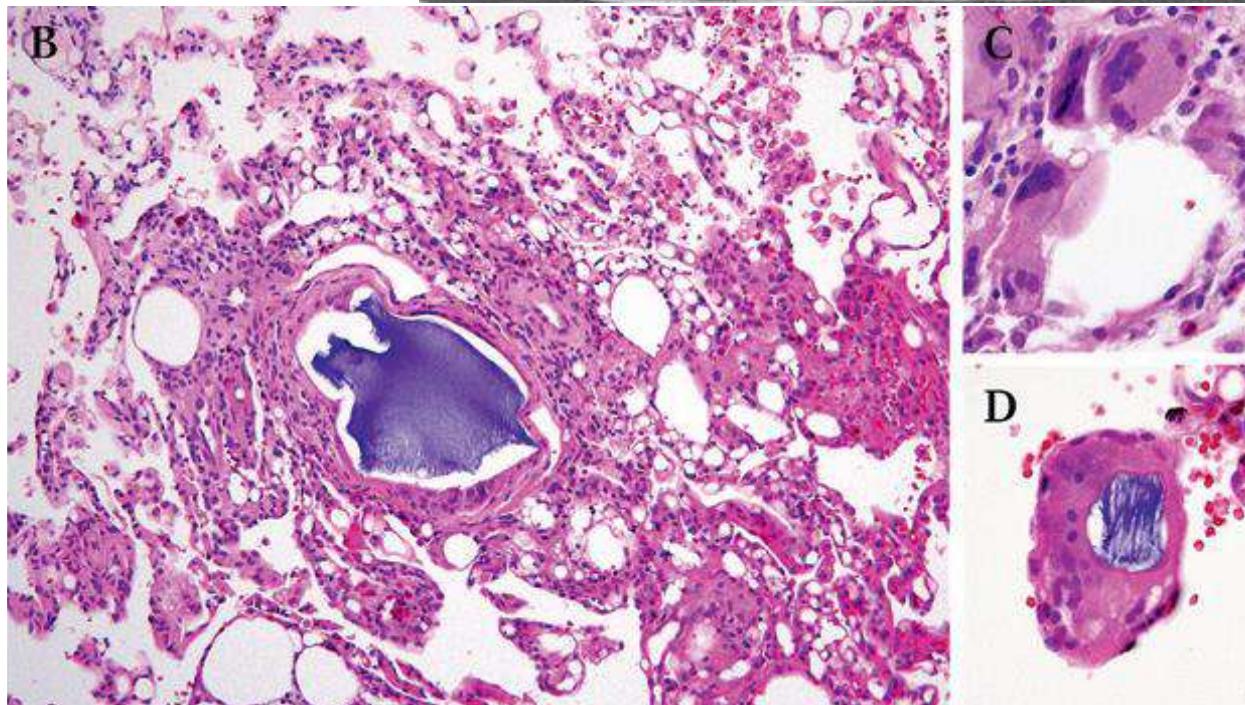
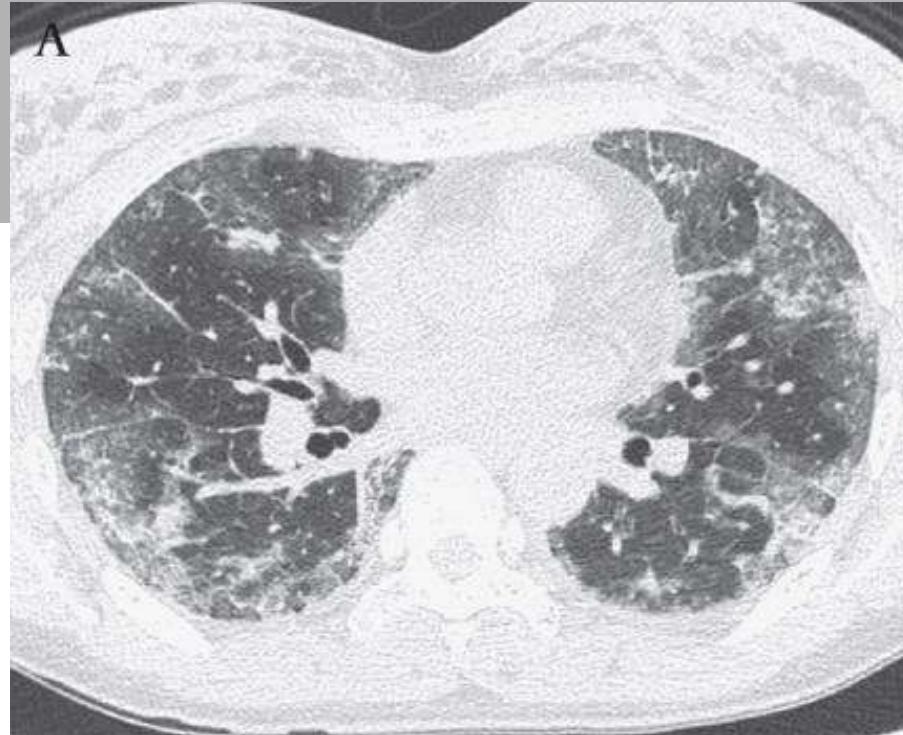


Fig. 1. Cement material in the pulmonary arteries.

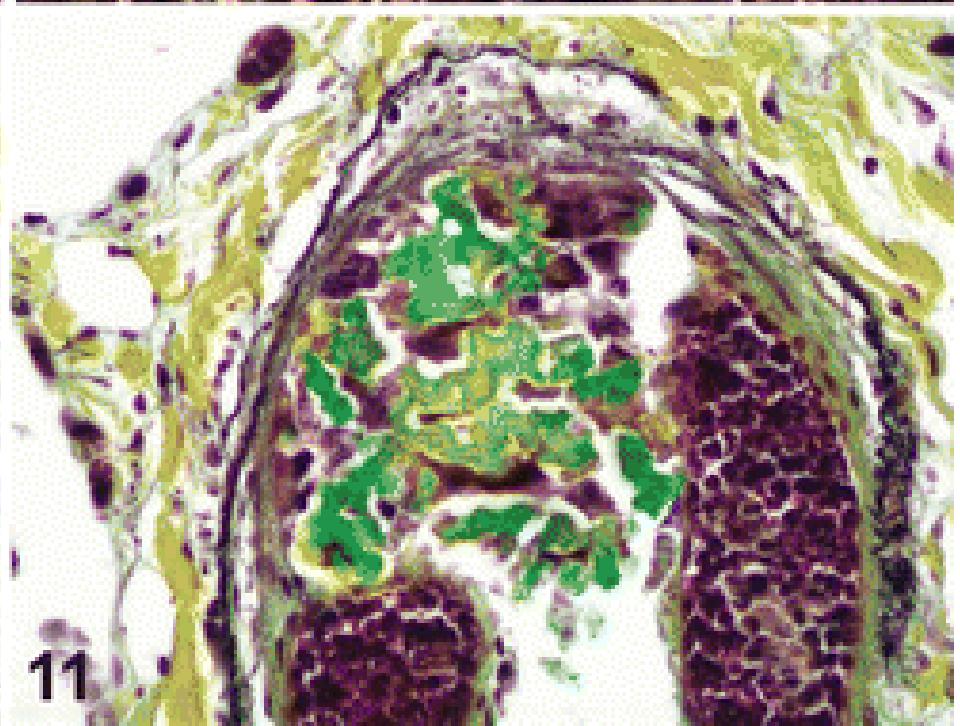
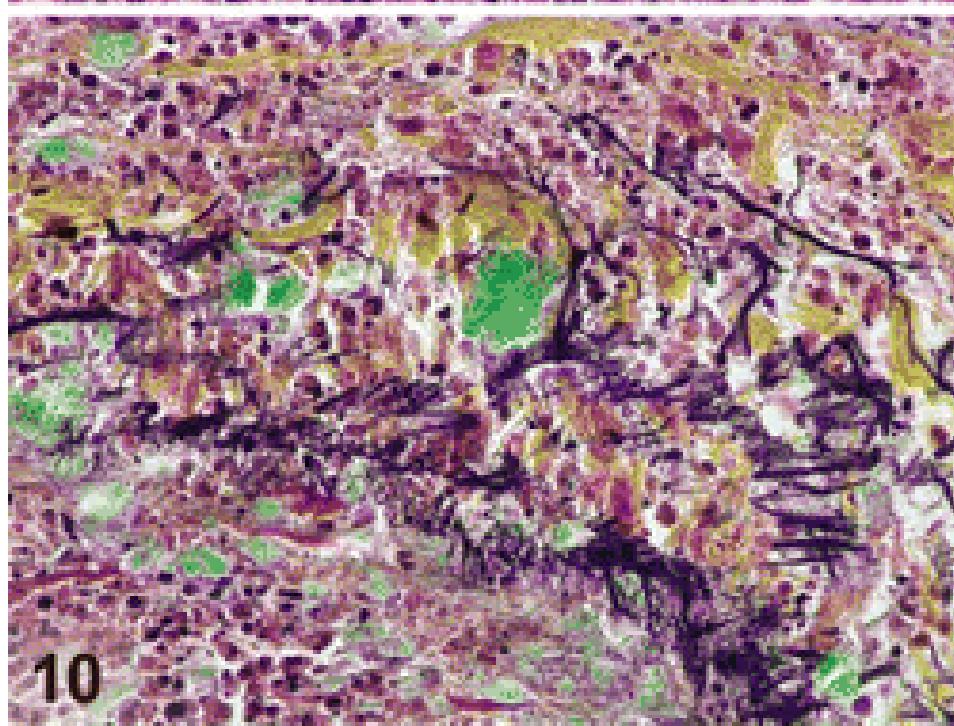
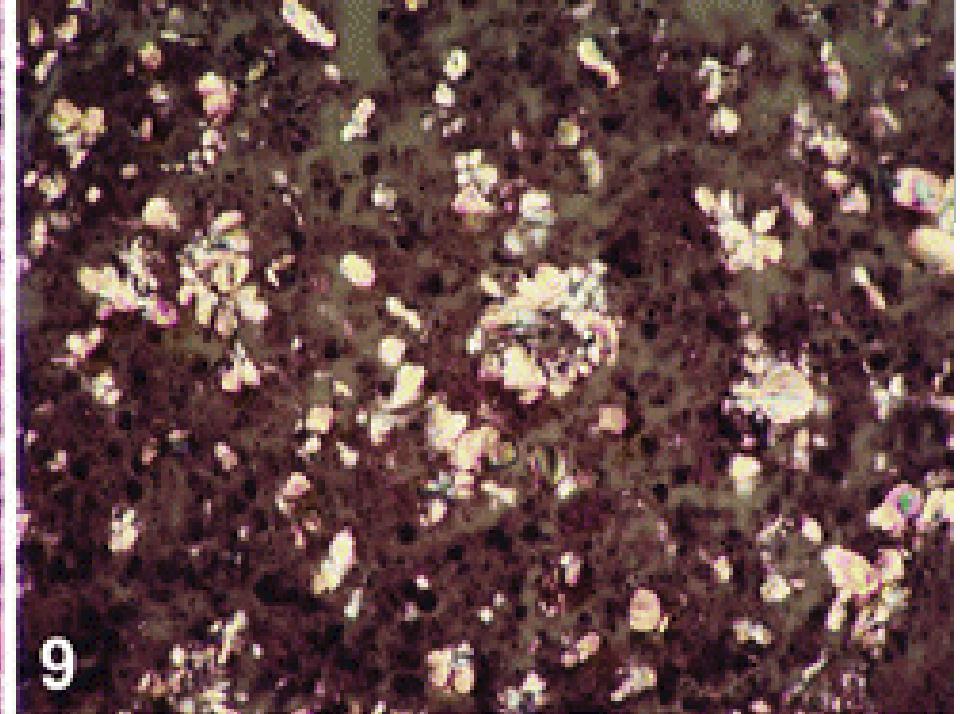
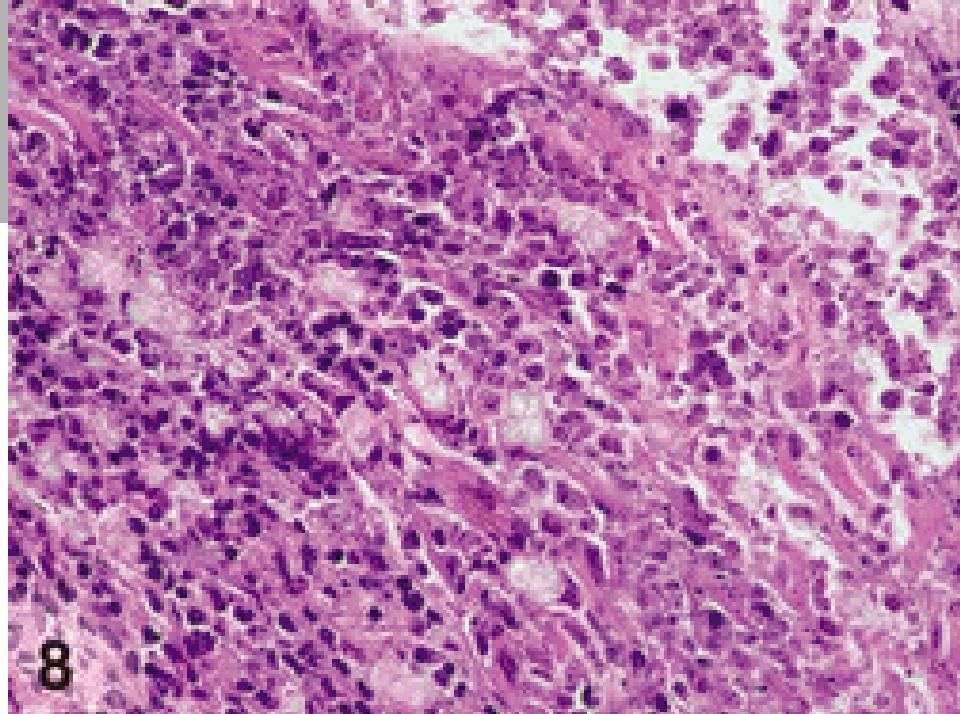


Park, 2010

- Gynéco
- Hyalorunate



- ❑ Oxalate (x3)
- ❑ Crospovidone



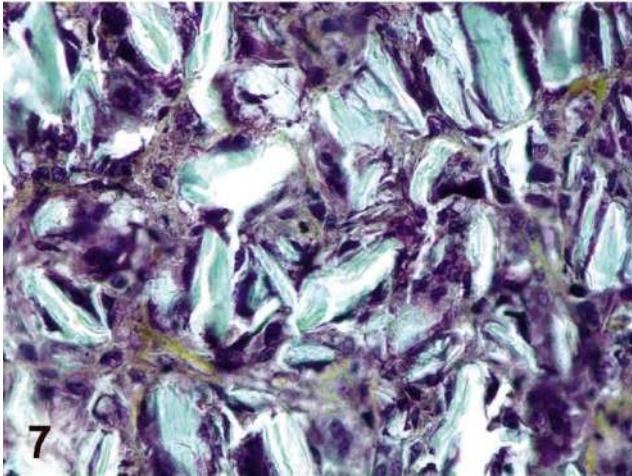
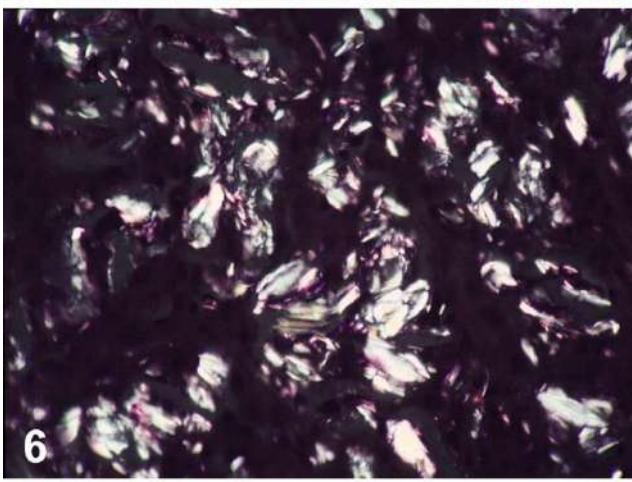
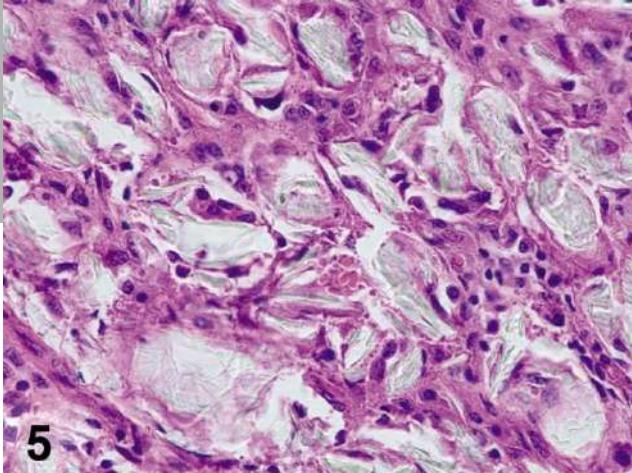
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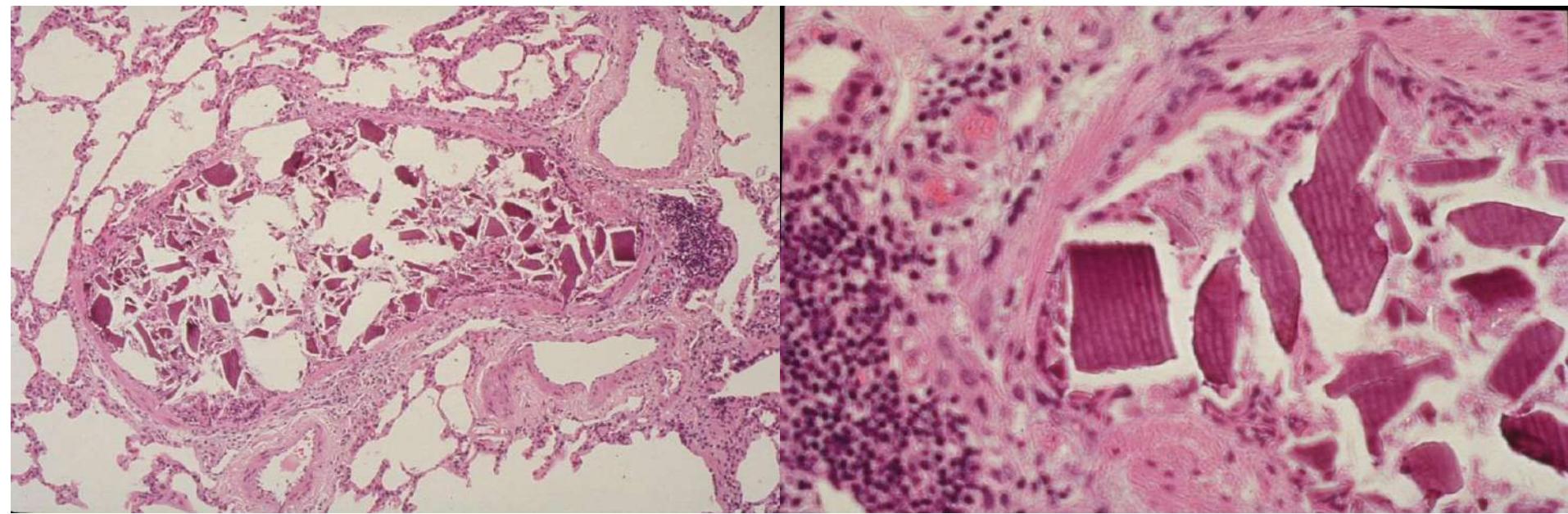
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10

11

■ Talc





Suggestif

- Réactions liées à la pharmacologie du produit
 - Anticoagulants & hémorragie (alvéolaire ou autre)
 - Bloquants ou AINS et bronchospasme
 - Anti-TNF & infection, tuberculose
 - IEC & angioedème asphyxiant
 - Oxydants & MetHb

ORIGINAL ARTICLE

Chronic Nitrofurantoin-Induced Lung Disease

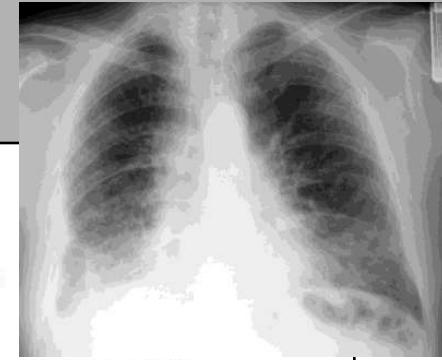
JOSE L. MENDEZ, MD; HASSAN F. NADROUS, MD; THOMAS E. HARTMAN, MD; AND RICHARD J. ST. JOHN, MD

OBJECTIVE: To reassess the clinical and radiological features of chronic nitrofurantoin-induced lung disease and eventual clinical outcome.

PATIENTS AND METHODS: We retrospectively reviewed the medical records of 18 patients with chronic nitrofurantoin-induced lung disease who were seen at the Mayo Clinic in Rochester, Minn, from January 1, 1997, to December 31, 2002.

RESULTS: The median age of the 18 patients was 72 years (range, 47-90 years) at the time of diagnosis; 17 (94%) were women. Onset of symptoms occurred after a median interval of 23 months (range, 10-144 months) following the initiation of nitrofurantoin therapy for the prevention of recurrent urinary tract infections. All patients presented with persistent dyspnea and cough associated with lung infiltrates detected on chest radiography. Ten computed tomograms were available for review and revealed bilateral areas of ground-glass opacities in all cases and showed subpleural irregular linear opacities and patchy consolidation in some cases. Nitrofurantoin therapy was discontinued in all patients, and most improved subsequently; 9 patients received corticosteroid therapy.

CONCLUSIONS: Chronic nitrofurantoin-induced lung disease is seen predominantly in older women who present with respiratory symptoms after a year or more of nitrofurantoin therapy. Associated radiological features are relatively nonspecific but usually include bilateral areas of ground-glass opacities on computed tomography of the chest. Cessation of nitrofurantoin therapy leads to improvement and suffices in the management of some patients, although corticosteroid therapy may be helpful in those more severely affected.





- ❖ 18 patients
- ❖ 17 femmes
- ❖ >23 mois en moyenne
- ❖ Délai diagnostique: 4 mois
- ❖ Eosinophilie périphérique: 17%
- ❖ Biopsies: PINS, BOOP, GIP
- ❖ Eviction: 18/18
- ❖ Corticoïdes: 9/18
 - ▣ Amélioration: 16
 - ▣ Stabililité: 2
 - ▣ Séquelles 12



LETTERS

RECURRENT UTI IN NON-PREGNANT WOMEN

Is “nitrofurantoin lung” on the increase?

Adam D L Marshall *respiratory registrar*, Owen J Dempsey *consultant chest physician*

Chest Clinic C, Aberdeen Royal Infirmary, Aberdeen AB25 2ZN, UK

Gupta and Trautner suggest using nitrofurantoin as prophylaxis for recurrent urinary tract infections (UTIs) in non-pregnant women.¹ They mention the risk of pulmonary toxicity (“nitrofurantoin lung”) associated with prolonged treatment but suggest that this occurs after years of treatment.

In Grampian we have identified 13 patients in the past four years with nitrofurantoin lung, 12 of whom were non-pregnant women receiving prophylactic treatment for recurrent UTI. Ten of them had been treated with nitrofurantoin for 18 months or less before diagnosis (mean treatment duration 14 months). None had been aware of potential lung toxicity, and the prescribing clinicians were surprised by the diagnosis. All patients were advised to stop taking nitrofurantoin, and six also received empirical oral steroids. Serial spirometry (available in nine patients) showed dramatically improved lung function after nitrofurantoin was stopped (mean predicted forced vital capacity 78% at diagnosis, 110% after cessation); serial chest radiographs also showed improvement.

Data from Prescribing Information System for Scotland show that community prescribing of nitrofurantoin more than tripled from 2008 to 2012—from 3.4 to 11 prescribed items per 1000 patients. We believe this change in prescribing, advocated in current guidelines,^{2,3} is reflected in our local experience and elsewhere in the UK.^{4,5} We anticipate a continued increased in

the incidence of nitrofurantoin lung and worry that many clinicians have forgotten the potential for lung toxicity.

Nitrofurantoin lung was initially misdiagnosed as cardiac failure, pneumonia, and, in one case, metastatic cancer. Patients should be advised to report any respiratory symptoms—such as worsening cough or breathlessness—that develop. Current guidelines and primary care prescribing systems should emphasise the potential for toxicity, which is reversible if the association is recognised early.

Competing interests: None declared.

- 1 Gupta K, Trautner BW. Diagnosis and management of recurrent urinary tract infections in non-pregnant women. *BMJ* 2013;346:f3140. (29 May.)
- 2 Gupta K, Hooton TM, Naber KG, Wullt B, Colgan R, Miller LG, et al. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelo-nephritis in women: a 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. *Clin Infect Dis* 2011;52:e103-20.
- 3 Health Protection Agency. Management of infection guidance for primary care for consultation and local adaptation. 2012. www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1279868711402.
- 4 Madani Y, Mann B. Nitrofurantoin-induced lung disease and prophylaxis of urinary tract infections. *Prim Care Respir J* 2012;21:387-41.
- 5 Weir M, Daly GJ. Lung toxicity and nitrofurantoin: the tip of the iceberg? *QJM* 2013;106:271-2.

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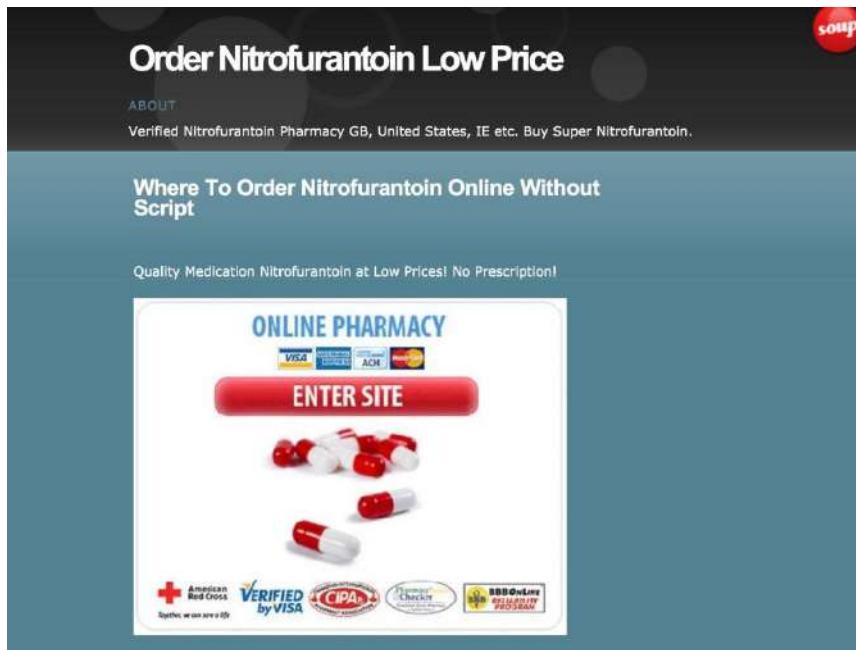
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CASE REPORT

Fatal Nitrofurantoin Lung

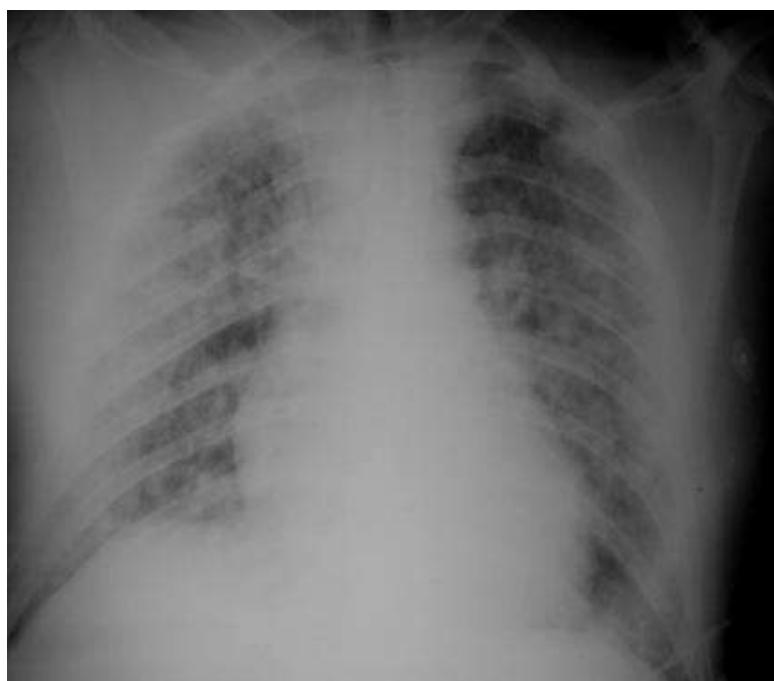
Jai B Mullerpattan*, Rucha S Dagaonkar**, Hardik D Shah**, Zarir F Udwadia***

Abstract

Nitrofurantoin is a drug commonly used for urinary tract infections. It acts by damaging bacterial DNA. It is given in dose of 50-100 mg orally and is generally considered a safe drug but has occasionally been known to cause pulmonary toxicity which is usually reversible and only rarely fatal. We present a case of an elderly lady receiving nitrofurantoin for her urinary tract infection who developed sudden acute lung injury to which she finally succumbed within a few weeks.

Pneumopathies à éosinophiles

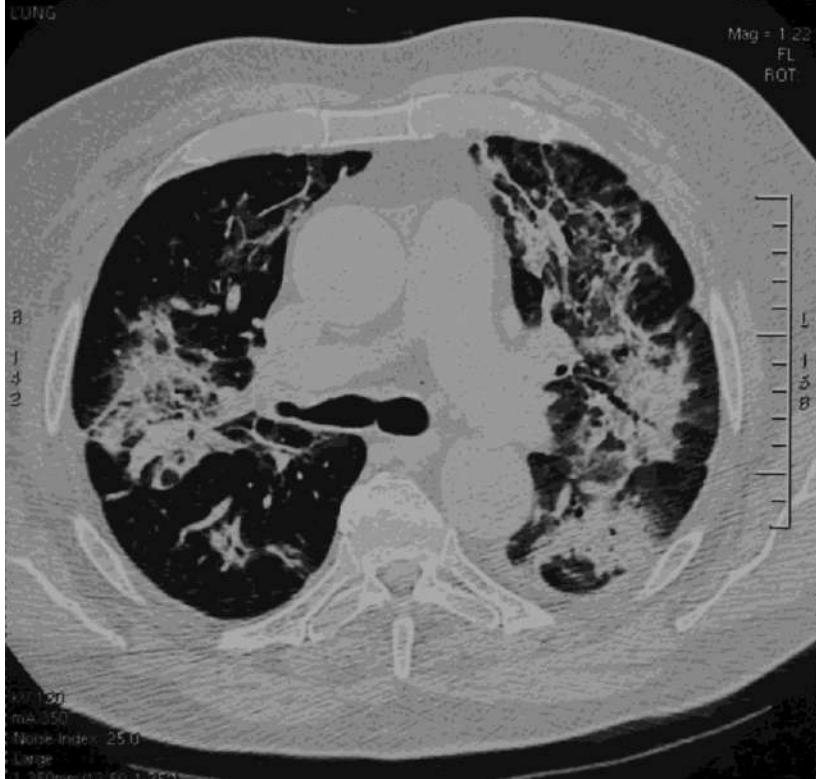
- ▣ 157 M (antibiotiques, AINS)
- ▣ Eosinophilie
 - ❖ Sang >1000
 - ❖ LBA >?
 - ❖ Tissu pulm
- ▣ Récidive > réexposition, monitorage Eo



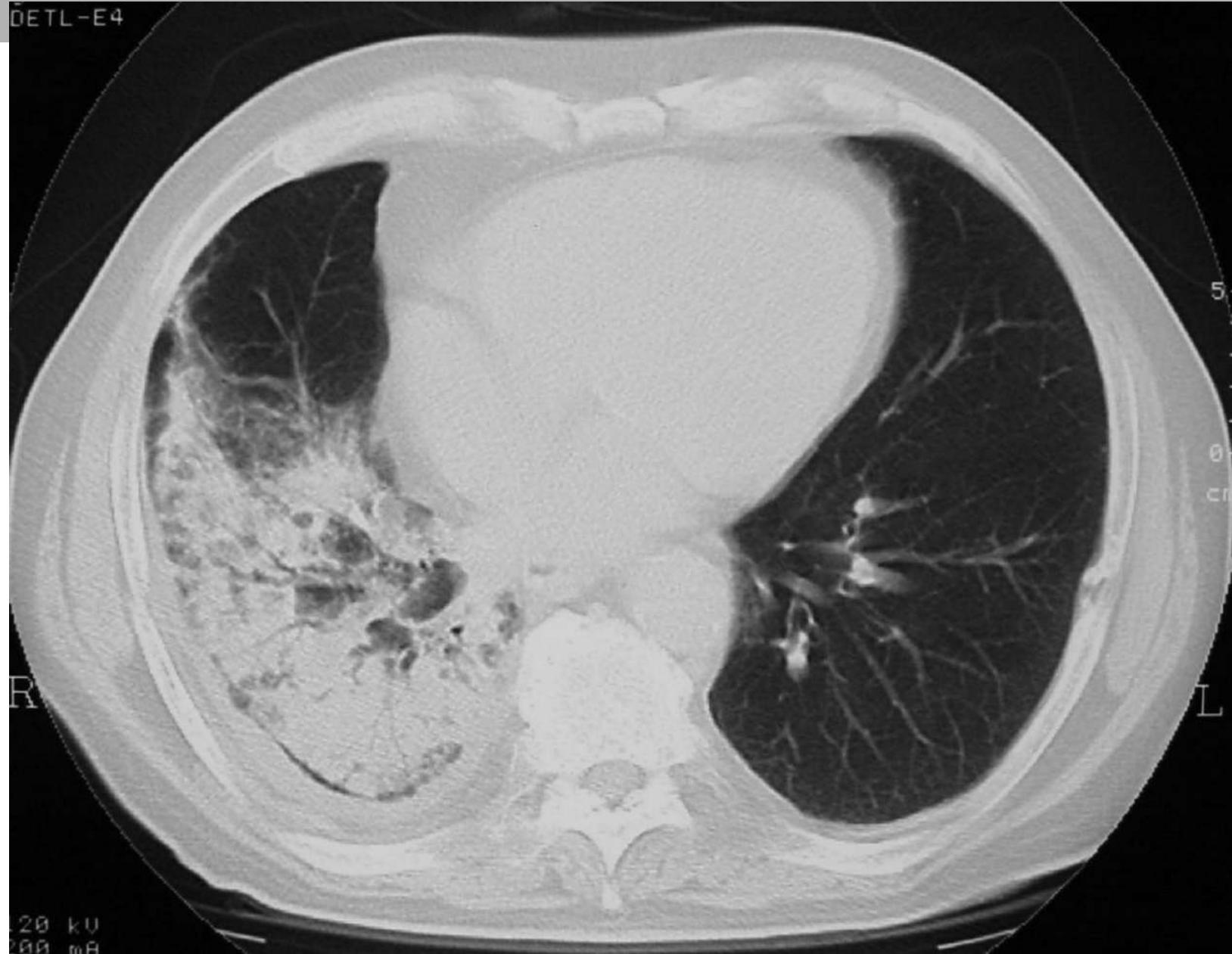
Amiodarone

- ▣ Electivement vers 6-12 mo (150-180 g)
- ▣ Qq jours (post-op), 14 ans...
- ▣ Insidieux (semaines-mois)
- ▣ Dyspnée, toux, fièvre modérée, doul. pleurétiques
- ▣ Présentations très variées

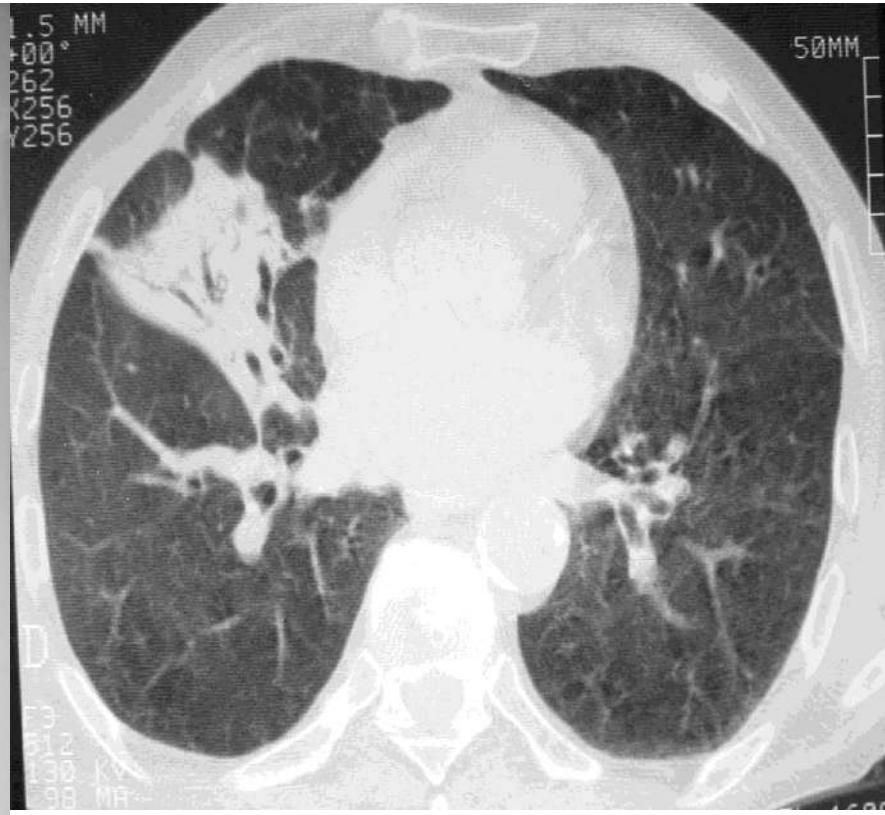




DETL-E4



120 kV
200 mAs



▣ ‘AFOP’

- ❖ Amiodarone
- ❖ Statines
- ❖ FOLFOX

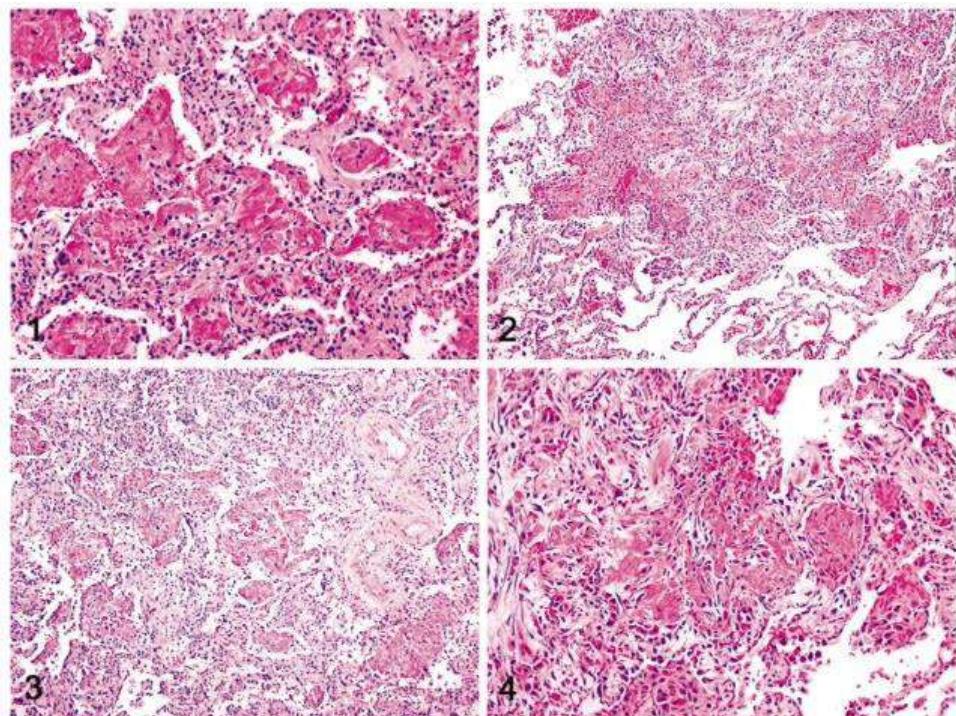
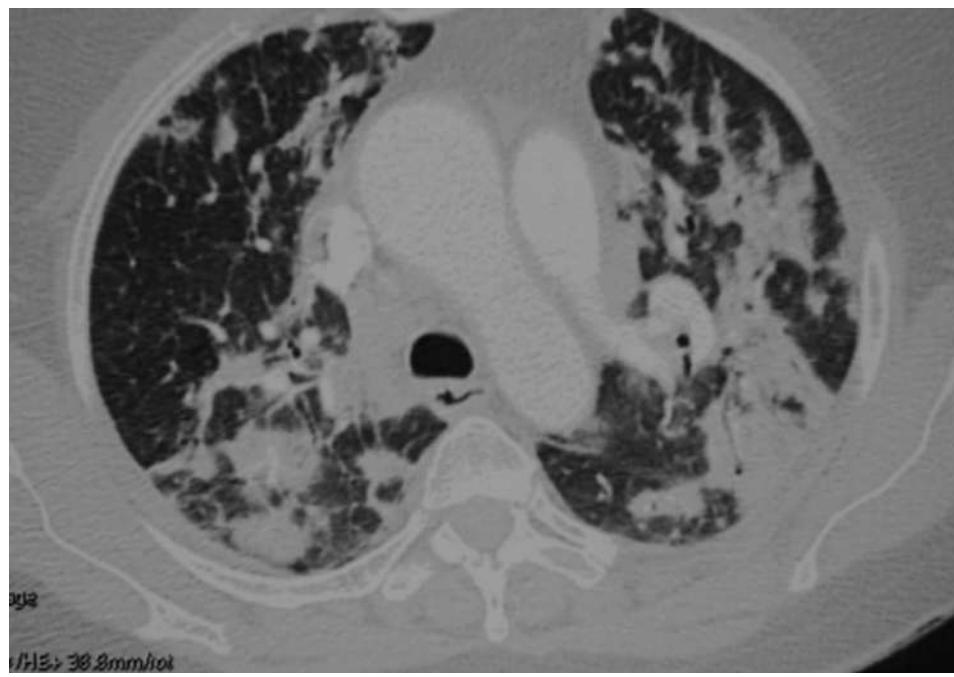
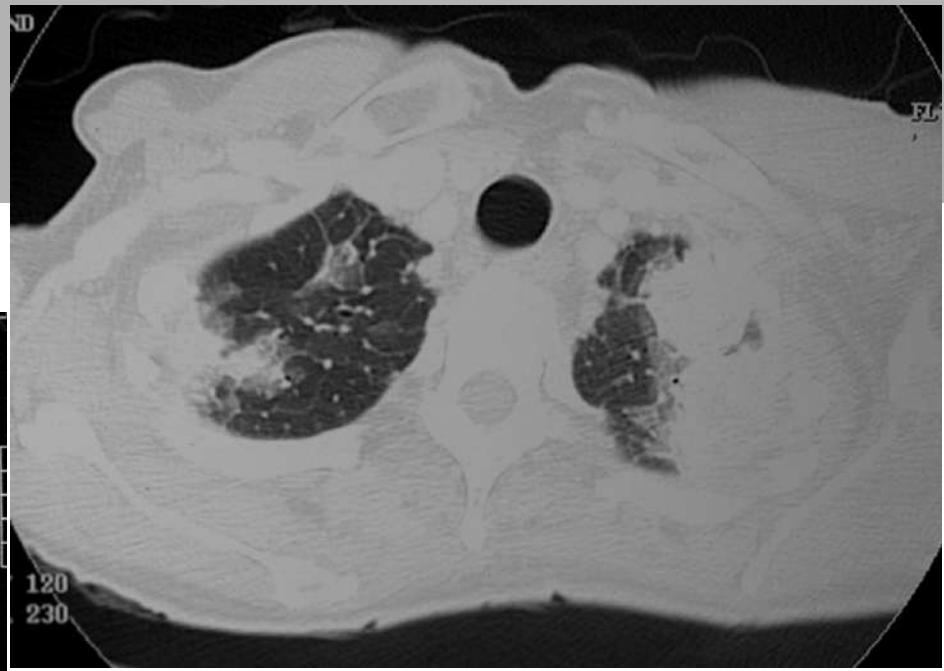


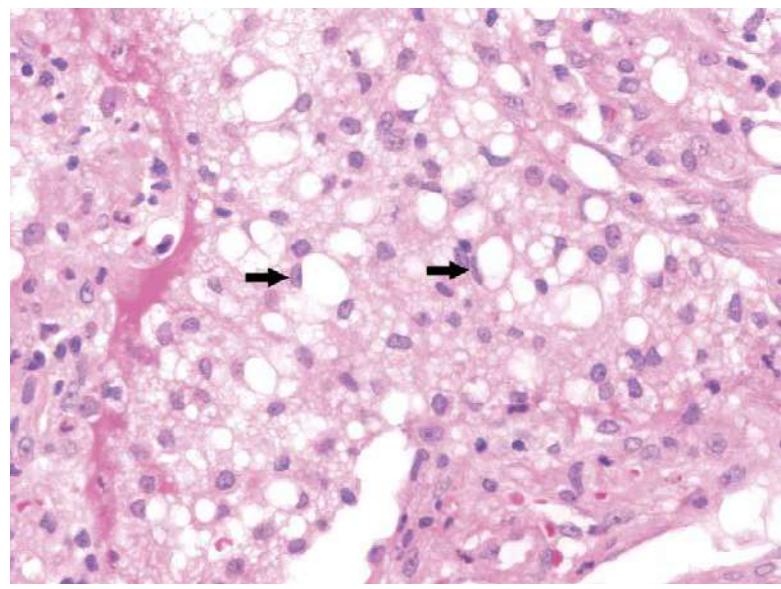
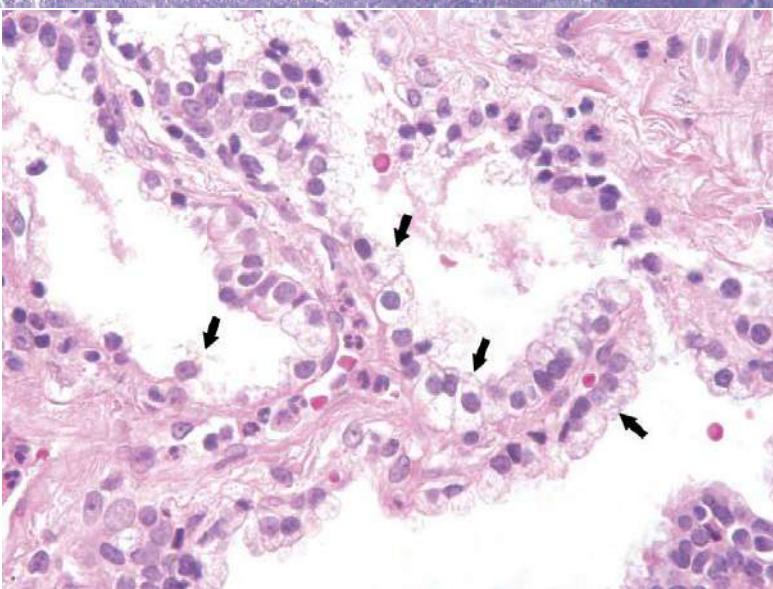
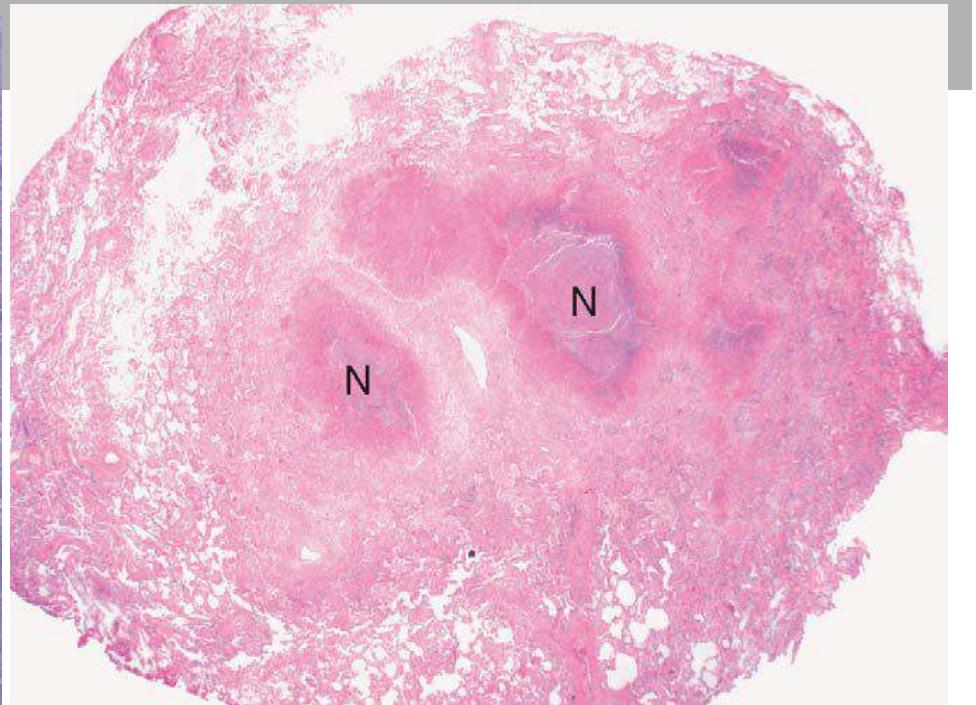
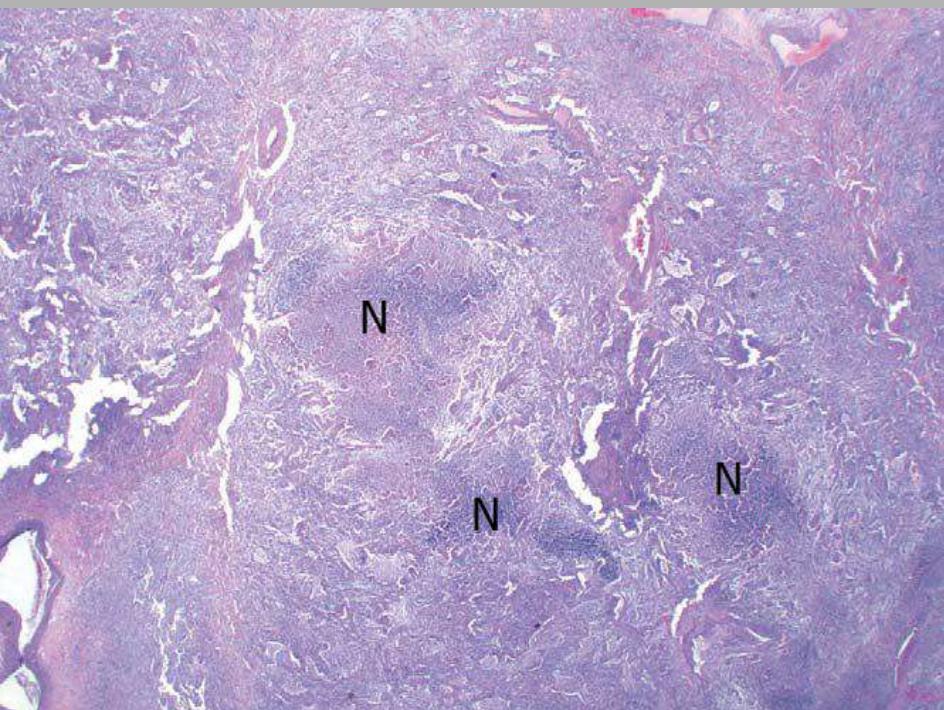
Figure 1. Intra-alveolar fibrin in the form of “fibrin balls” without formation of hyaline membranes (hematoxylin-eosin, original magnification $\times 160$).



38.8

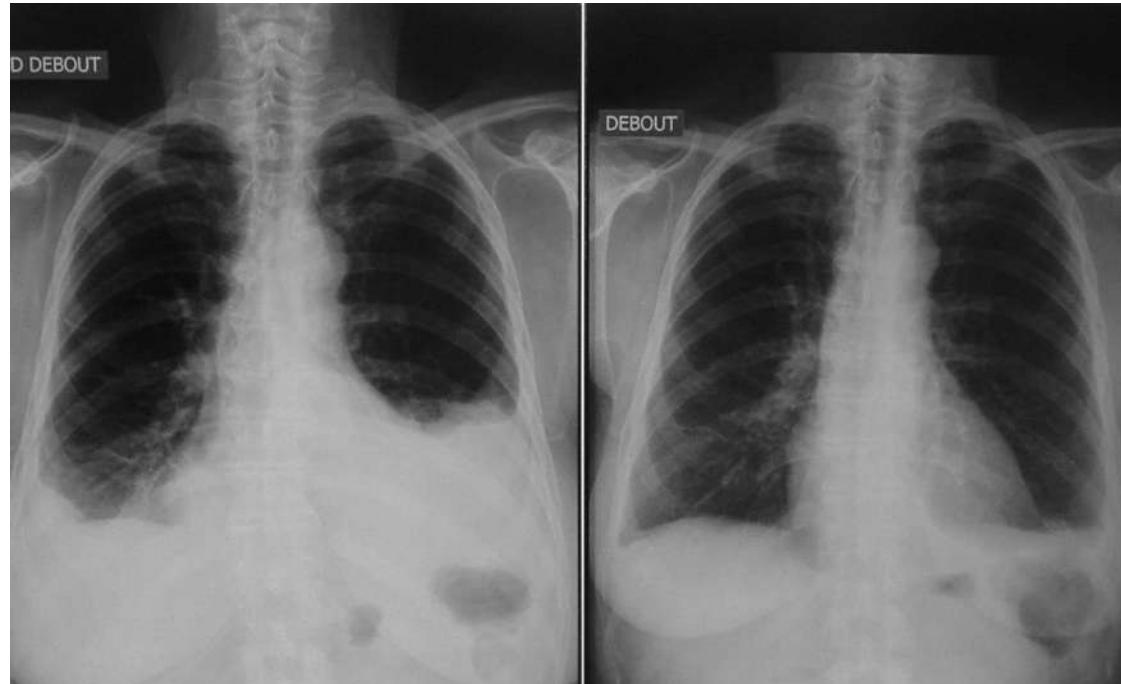
38.8mm/100





'Biomarqueurs'

- Lupus et biothérapies
 - Ramos Casals 2007 92 cas
 - Infliximab 44%, etanercept 40%, adalimumab 16%
 - ANA 79%
 - Anti-dsDNA 72%
 - Polysérite 12%
 - Doser Ac avant ttt



■ Propylthiouracile PTU

- 20~64% des patients développent des ANCA anti-MPO
- La plupart asymptomatiques
- Ac
 - ❖ Titre élevé
 - ❖ Multispecifiques: anti-lactoferrine cathepsin-G, BPIP
- c-ANCA anti-PR3 rares
- 5-10% vascularite
- ¼ Pnl, HAD, capillarite pulmonaire



FIG. 1. Hemorrhagic skin lesions involving the upper arms (right) with rapid onset.



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Systemic Immune Reactions to HMG-CoA Reductase Inhibitors

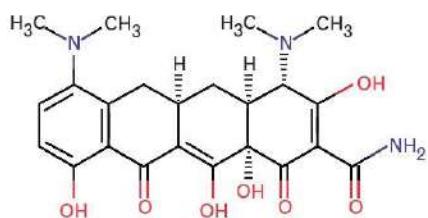
Report of 4 Cases and Review of the Literature

LAWRENCE RUDSKI, MARK A. RABINOVITCH, AND DEBORAH DANOFF

Hydralazine



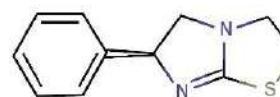
Minocycline



Propylthiouracil



Levamisole



Cocaine

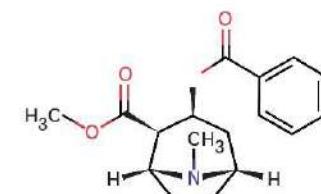


FIGURE 1. Chemical structures of hydralazine, minocycline, propylthiouracil (PTU), levamisole and cocaine. There is a paucity of information regarding structural similarities and differences of these compounds in the literature; therefore, they are represented here for visual review (created using DrugBank).

- Levamisole: 70% des saisies de cocaine coupées
 - 0.1-10% en masse
 - Neutropénie p-ANCA, APL+ – thrombocytopénie
 - Etat actuel: ~200 cas publiés
 - ❖ Age 18-64
 - ❖ Cocaine inhalée ou fumée
 - ❖ Lévamisole confirmé 28%
 - ❖ Neutropénies 69%
 - ❖ Complications cutanées 41%
 - ❖ Récidive à la réexposition: 55%
 - ❖ Mortalité 1.6%

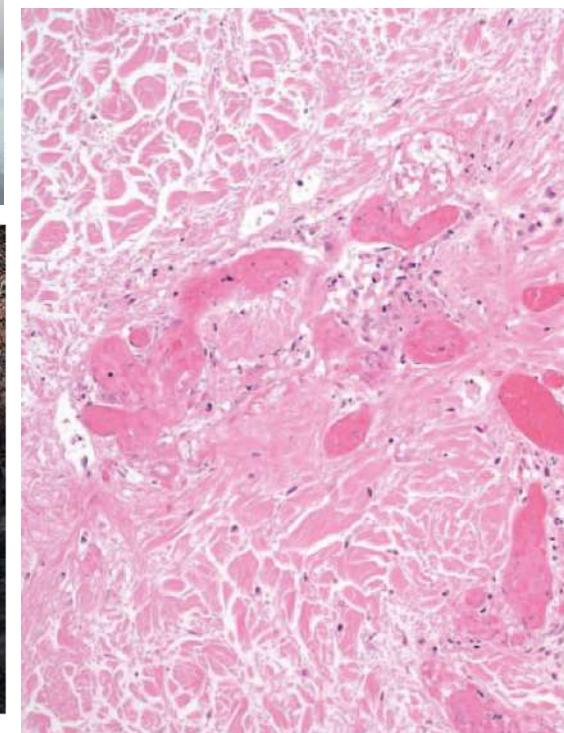




FIGURE 1. Cutaneous defects 4 and 16 days from allegedly smoking free-base cocaine.



FIGURE 2. Cutaneous defects 16 and 28 days from allegedly smoking free-base cocaine.



DD1

- Affection à tropisme pulmonaire
 - PR: Pnl, épanchement, nodules
 - Sclerodermie: fibrose, HTAP
 - MII: Pnl
 - MICI: bronchopathies, DDB, Pnl
 - Vascularite: vascularite pulmonaire, Pnl
 - *Lupus*: Pnl, pleurite, épanchement, MTE
 - Cœur: OAP, HA
 - Transplantation: rejet, infection
 - Pathologie néoplasique...

Autres étiologies des Pnl

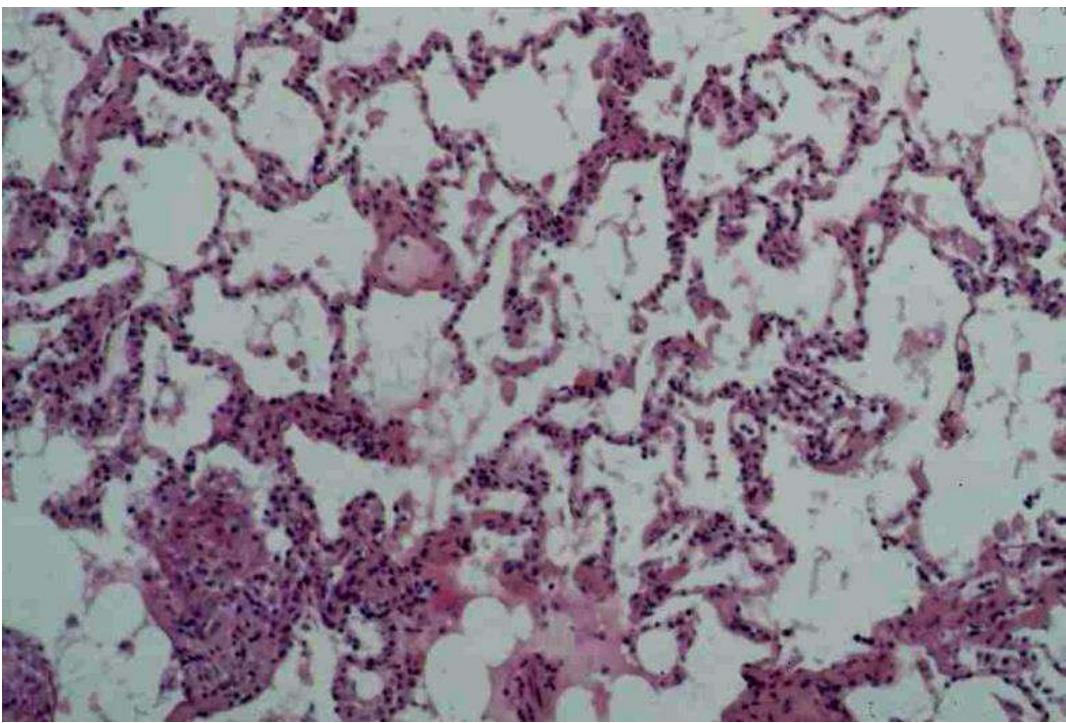
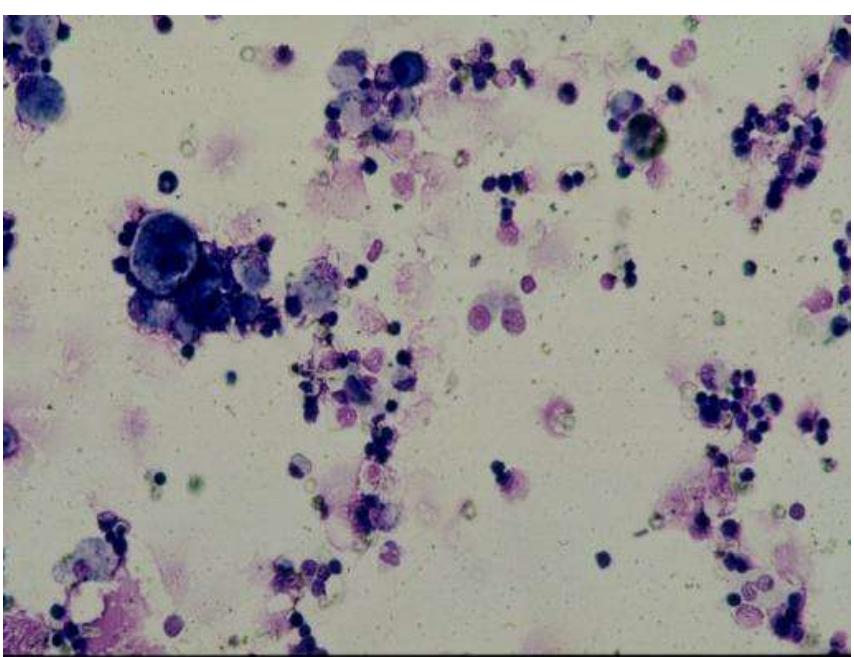
- ❑ Fibrose pulmonaire (tabac, profession, idiopathique)
- ❑ PINS (cellulaire > fibrotique) (MS, antigènes organiques)
- ❑ Pneumopathie à éosinophiles (PAE): idiopathique, parasites
- ❑ BOOP: MS, infection
- ❑ SDRA: infection-sepsis
- ❑ Œdème pulmonaire (cardiogénique, noncardiogénique)
- ❑ Pnl granulomateuse (infection, aspiration)

Situations particulières

- ❑ Devant une PnP aiguë/SDRA
- ❑ RCP: FPI mais le patient reçoit des médicaments...
- ❑ Le pneumologue et la polyarthrite rhumatoïde
- ❑ Le pneumologue en médecine interne
- ❑ Amiodarone
- ❑ Eviction: les risques
- ❑ Réintroduction: risques et possibilités
- ❑ Gestion de la corticothérapie

Pnl aiguë

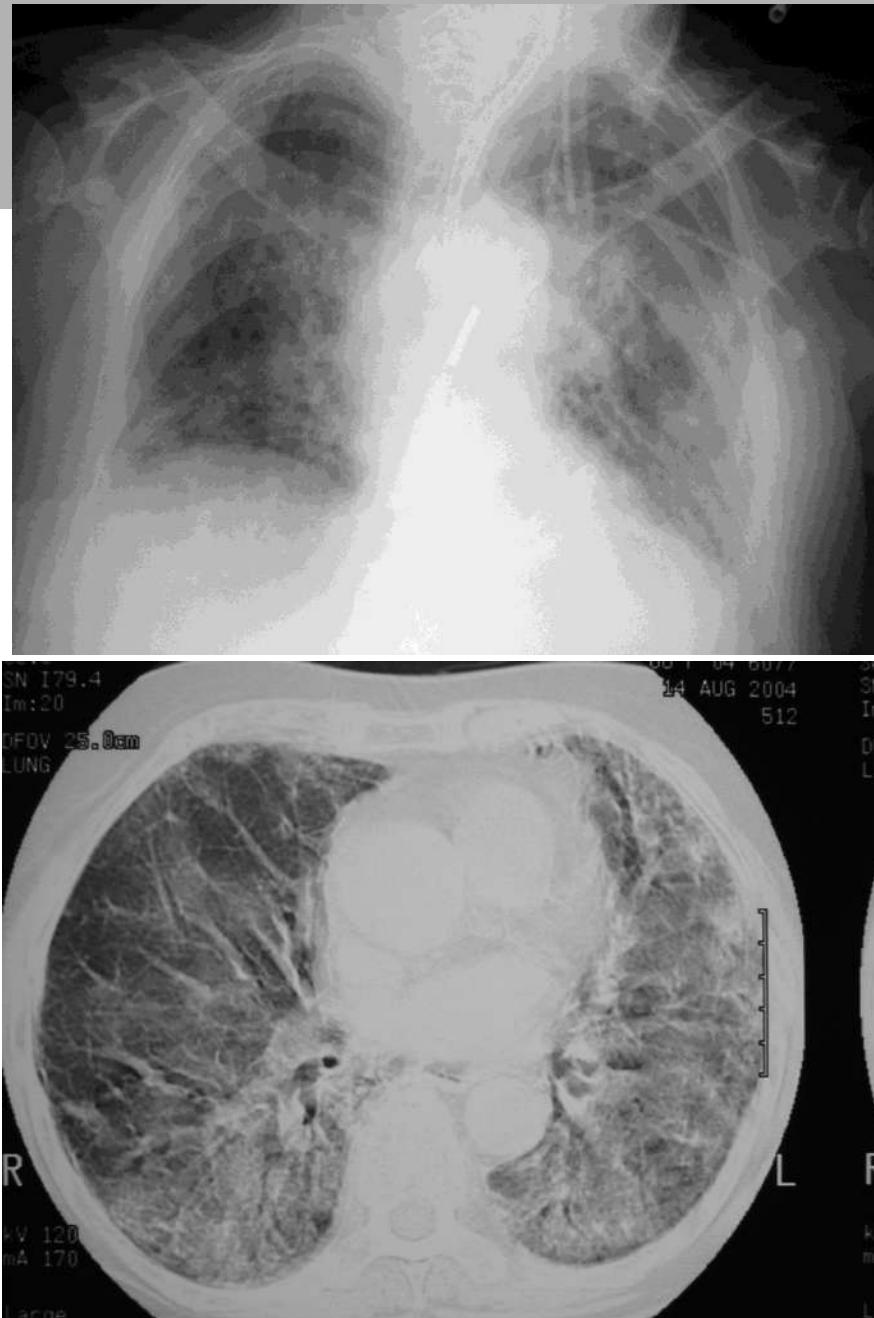
- ❑ ~250 médicaments
- ❑ DD F° immunodépression
 - ❑ Nitrofurantoïne -
 - ❑ Methotrexate +
 - ❑ Idelalisib ++



Nitrofurantoïne

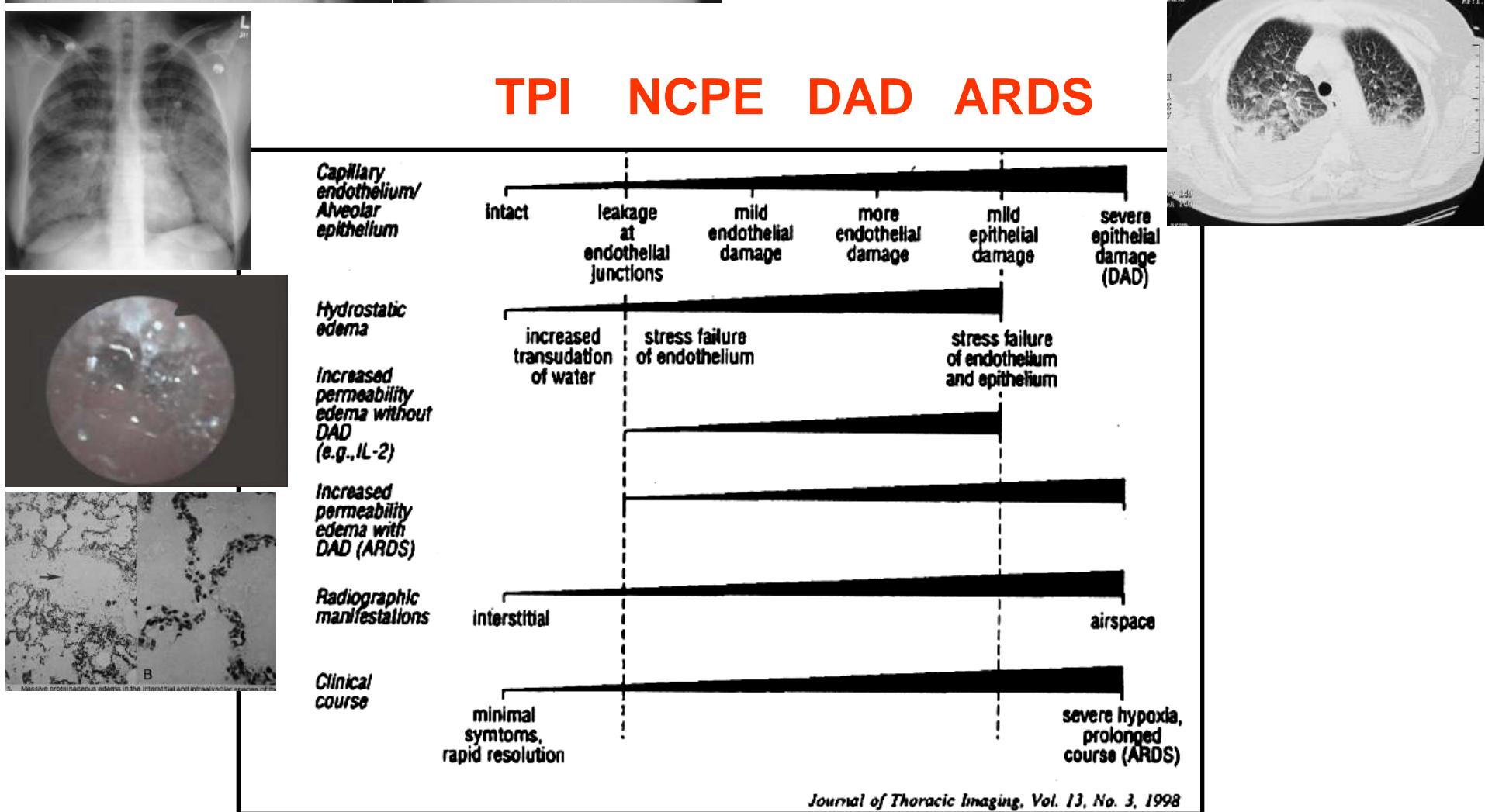
■ PnI aiguë NF

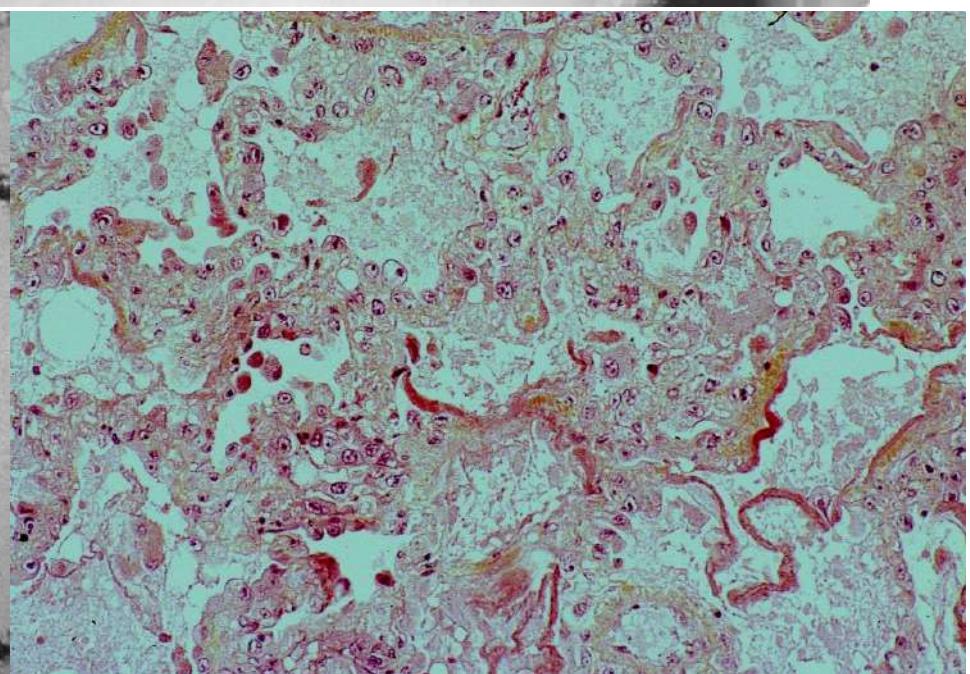
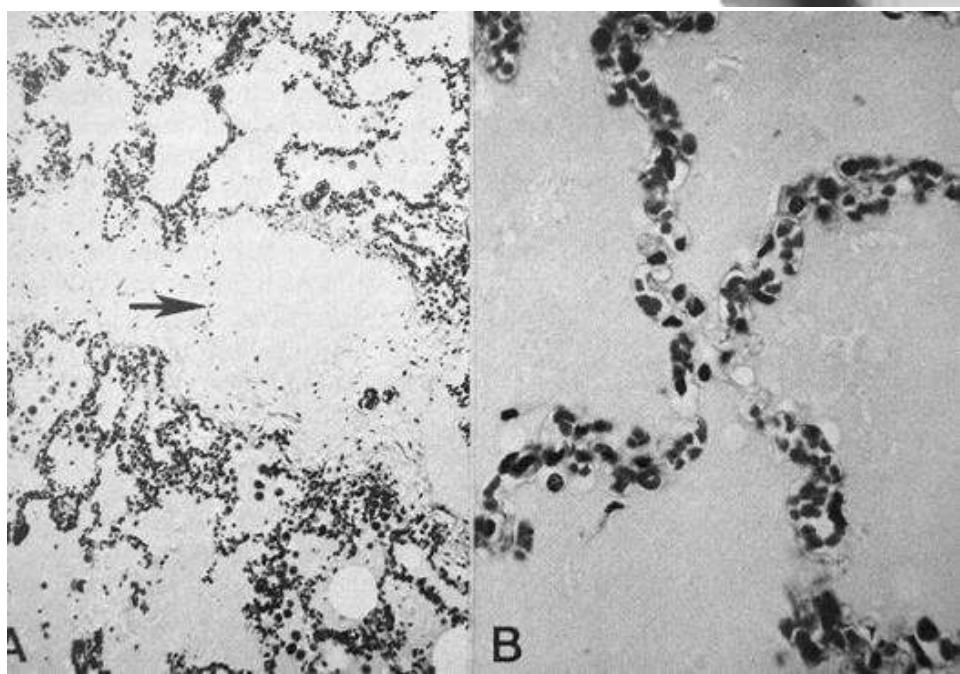
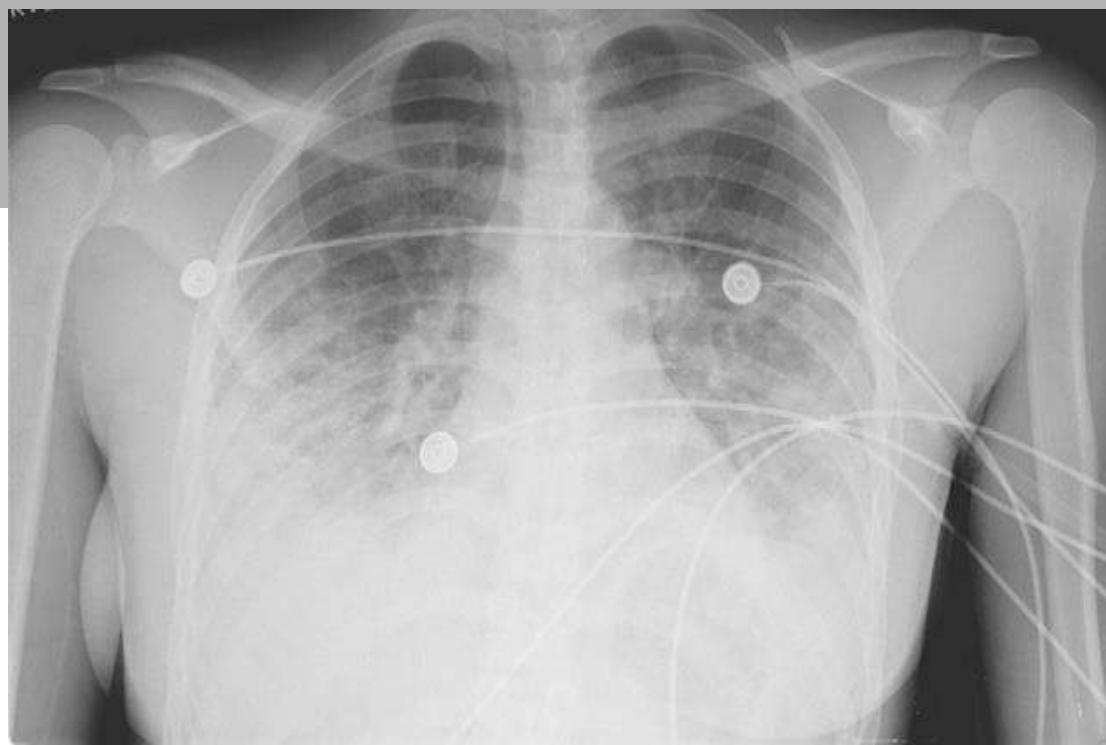
- ❖ <2 semaines
- ❖ Douleurs, fièvre, toux dyspnée
- ❖ Epanchements pleuraux
- ❖ Eosinophilie
- ❖ Eviction+
- ❖ Rechallenge+





TPI NCPE DAD ARDS





- **OAP**

- ❖ Transfusions, docetaxel, gemcitabine, mitomycine, vinblastine

- **DAD**

- ❖ Transfusions, bleo, cyclophosphamide, erlotinib fluorouracil, gefitinib, gemcitabine, mitomycine , nitrosourées, Im-TOR...

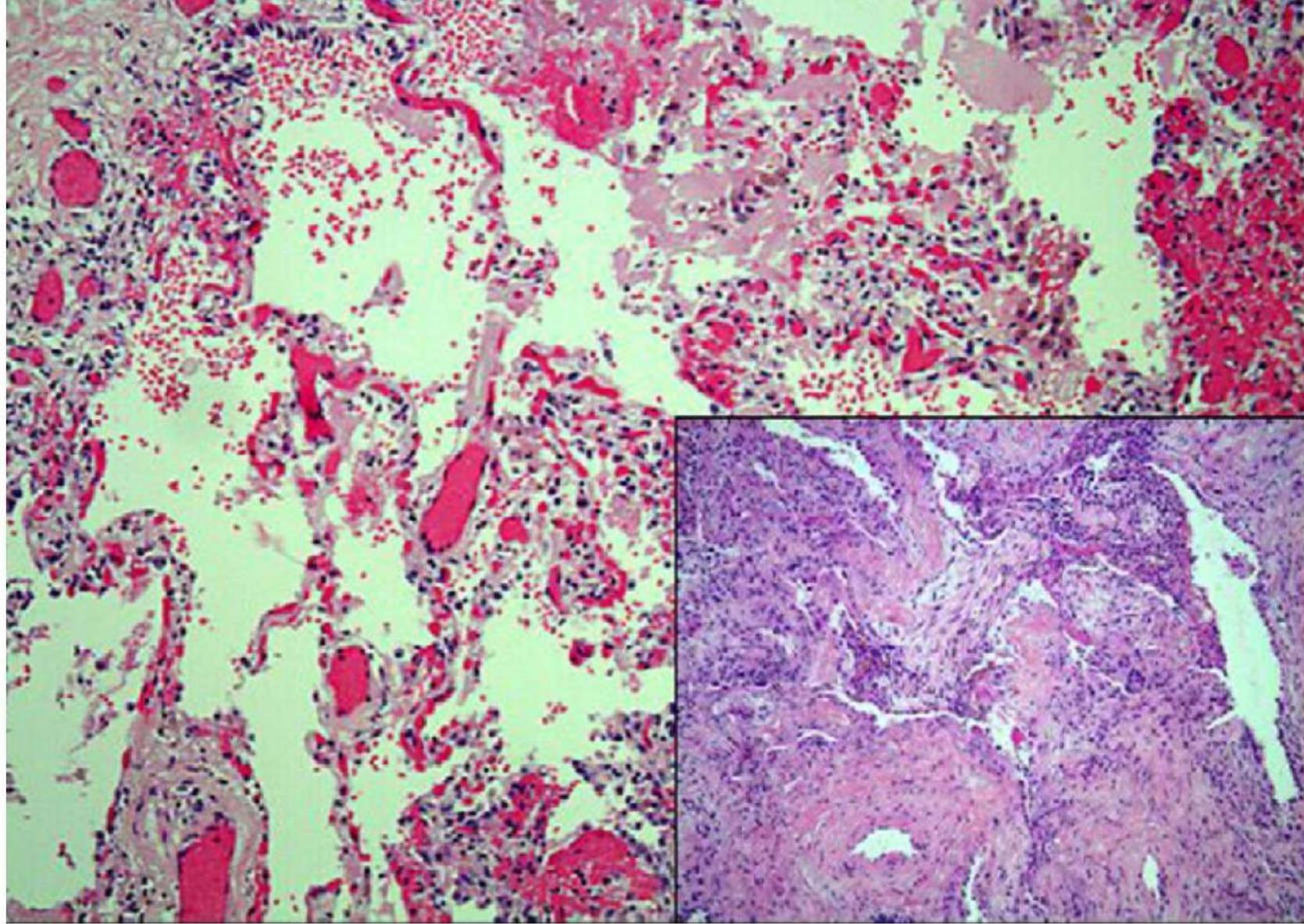


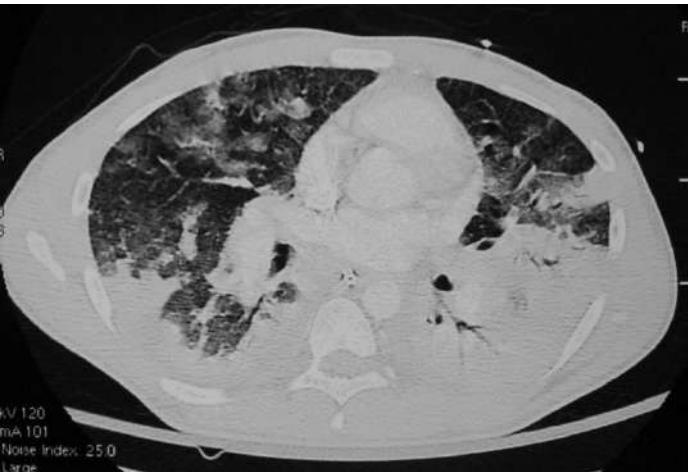
Fig. 2. Diffuse alveolar damage (DAD): interstitial and alveolar oedema and/or fibroblastic proliferation in association with epithelial and endothelial damage and alveolar fibrin laminar accumulation in the form of hyaline membranes.

- Formes graves
 - Adolescent
 - Cannabis + tabac
 - Eosinophilie
 - ❖ Sang 3,100/uL
 - ❖ LBA: 21%
 - Dg: PAE
 - ECMO x48h
 - Extubé à J5
- Minocycline
daptomycine, sulfa, antidepresseurs, AINS



Maladies générales et M

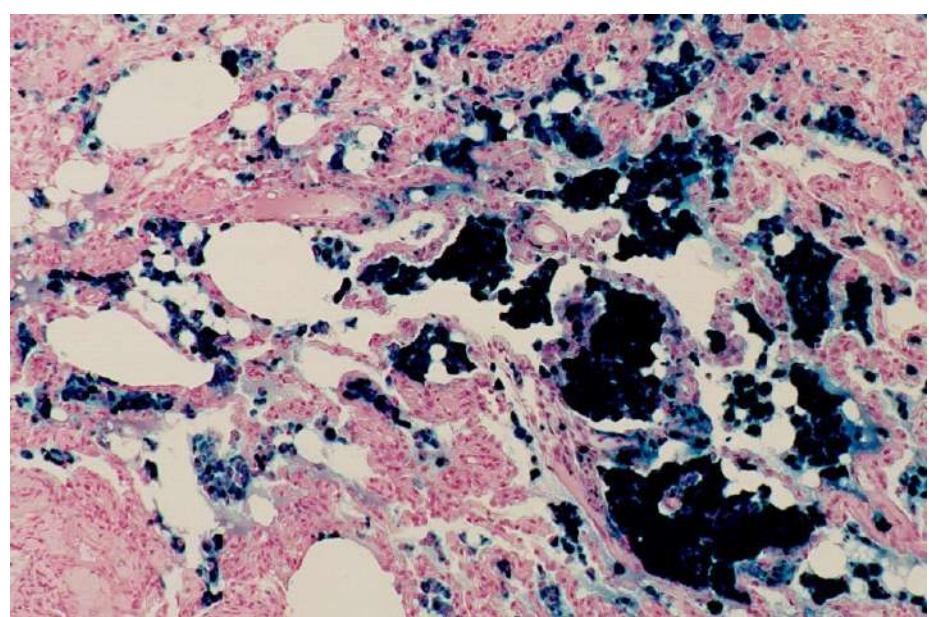
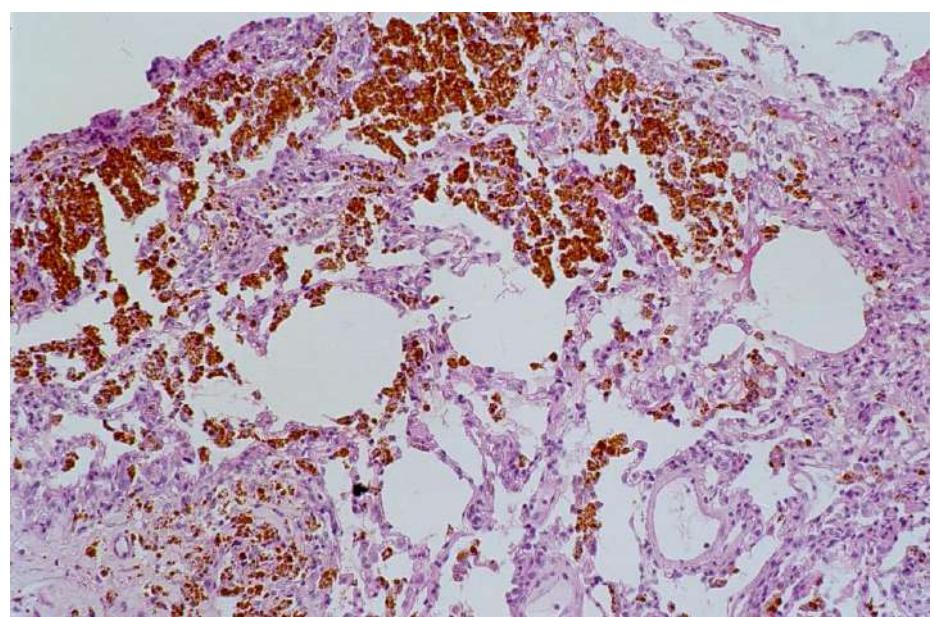
- DRESS: Rash
- Eosinophilie, cytopénie lymphocytes atypiques
- Atteintes viscérales
Rein, foie, SNC, TD, adénopathies
- Myocardite
- EoP ca. 15%



HA

- ❖ AVK
- ❖ NACO
- ❖ Superwarfarins
- ❖ Inh plaquettes
- ❖ Heparine
- ❖ SK, UK
- ❖ Alteplase
- ❖ ImTOR (sirolimus)
- ❖ Propythiouracile
- ❖ Cocaine





Hémorragie alvéolaire

- Héparine: **PROTAMINE**
- Antivitamine-K: **VIT-K PPSB FEIBA CCP**
- Brodifacoum (superWARF) **VIT-K PPSB FEIBA CCP**
- Fibrinolytiques (SK, UK) **AC TRAXENAMIQUE**
- Inhibiteurs GP IIb/IIIa plaquettaires (abciximab, clopidogrel, ticlopidine, tirofiban, eptifibatide)
ABSENCE D'ANTIDOTE
- ACDO (dabigatran, rivaroxaban, apixaban)
ANTIDOTES EN DEVELOPPEMENT
- rTPA

Difficulté: le pneumologue est laissé à lui-même...

- ❑ Le diagnostic de FPI ... nécessite l'exclusion des autres PID ... comprennent principalement les Pnl de cause connue:
 - ❑ Ag organique inhalé responsable de PHS
 - ❑ Médicaments (www.pneumotox.com)
 - ❑ Agent minéral responsable de pneumoconiose (silice, amiante)
- ❑ Ou de contexte déterminé

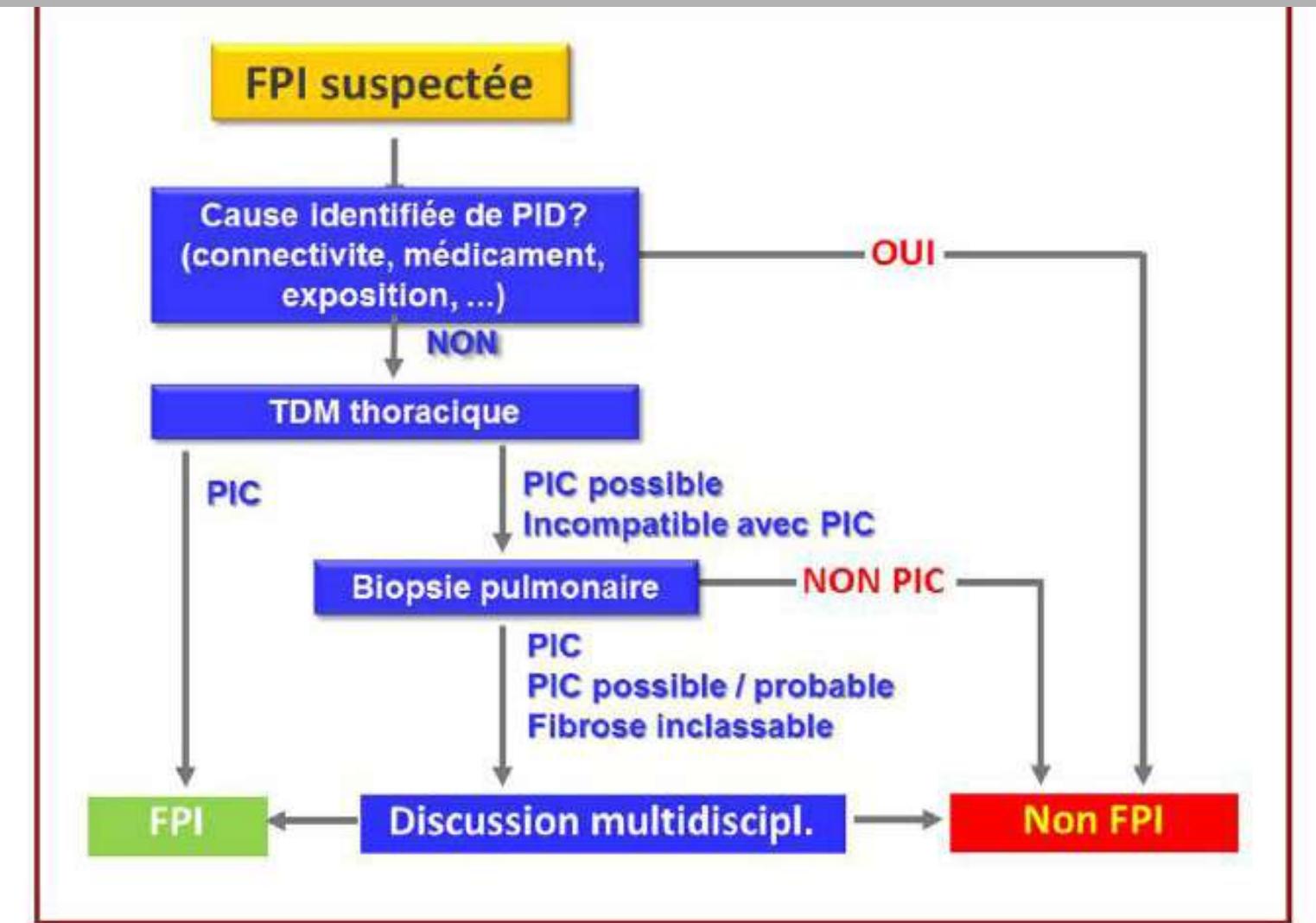
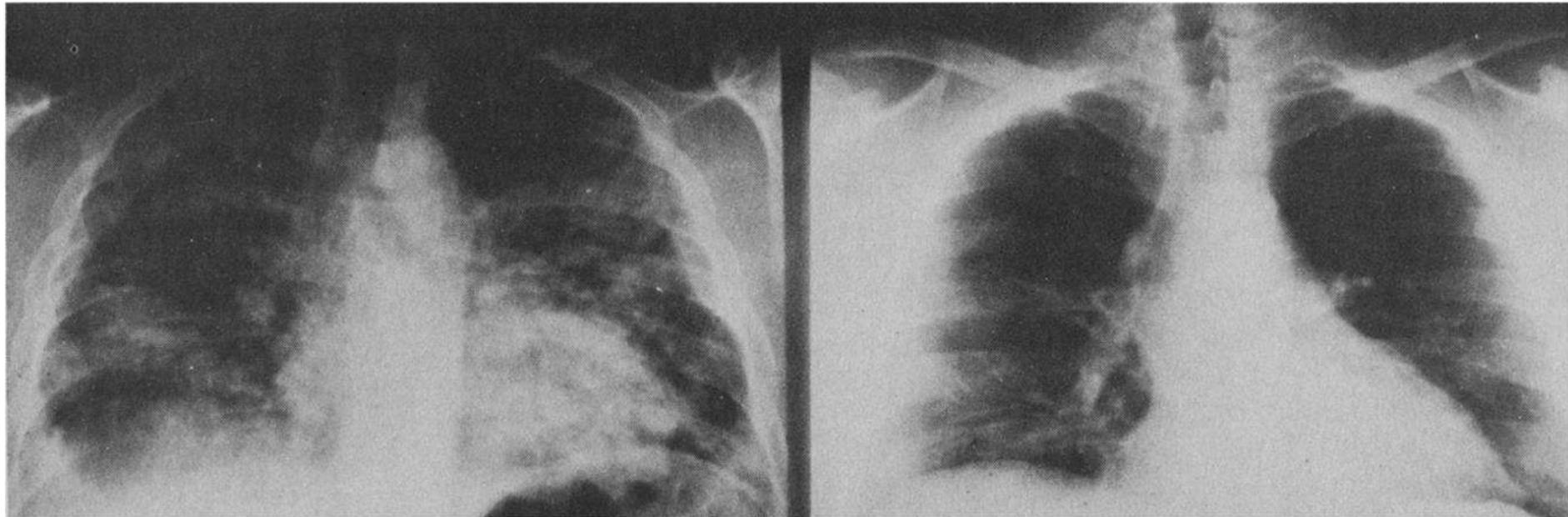
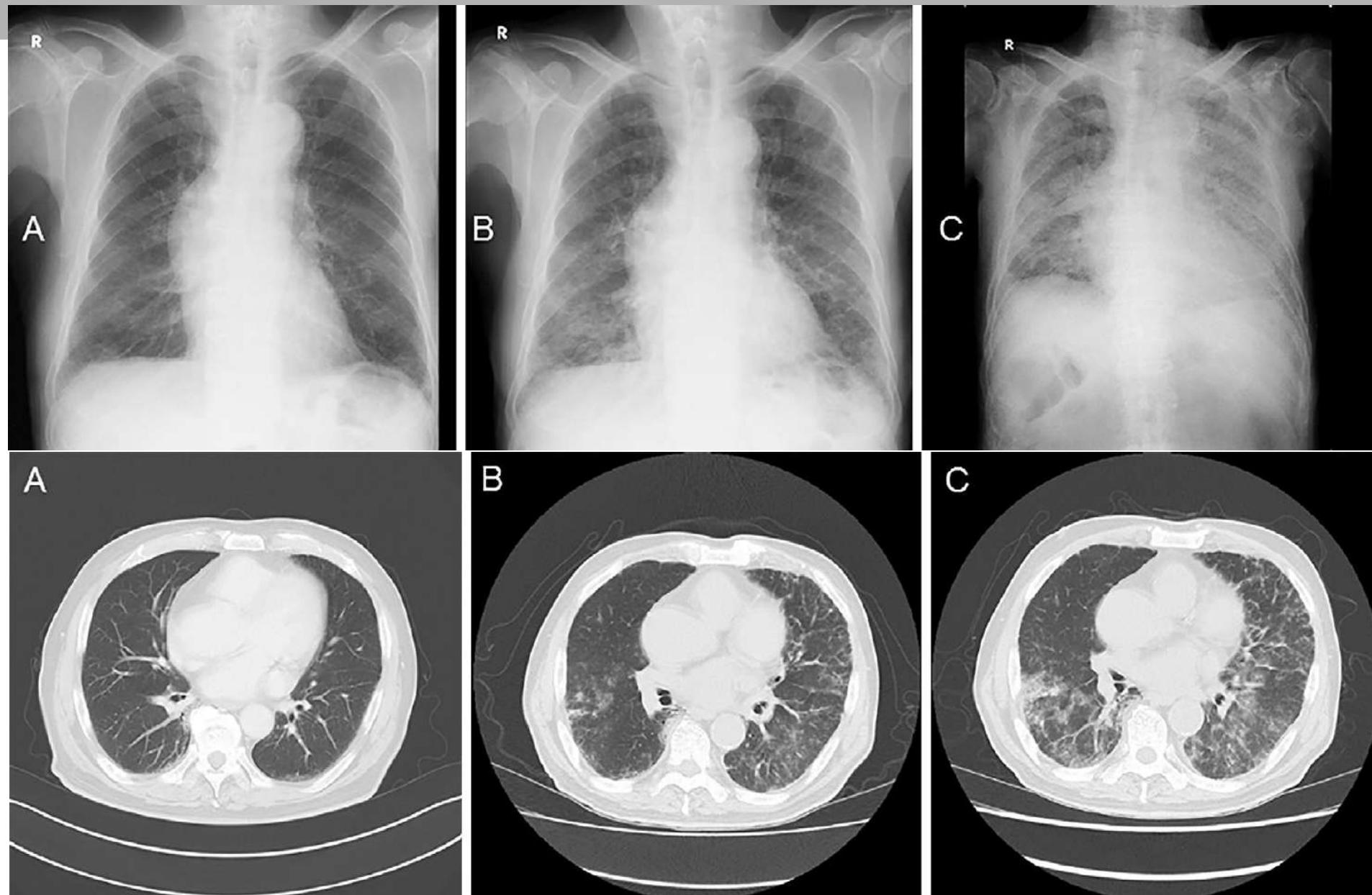


Figure 1. Algorithme diagnostique de la fibrose pulmonaire idiopathique. FPI, fibrose pulmonaire idiopathique ; PIC, pneumopathie interstitielle commune ; PID, pneumopathie interstitielle diffuse, TDM, tomodensitométrie.

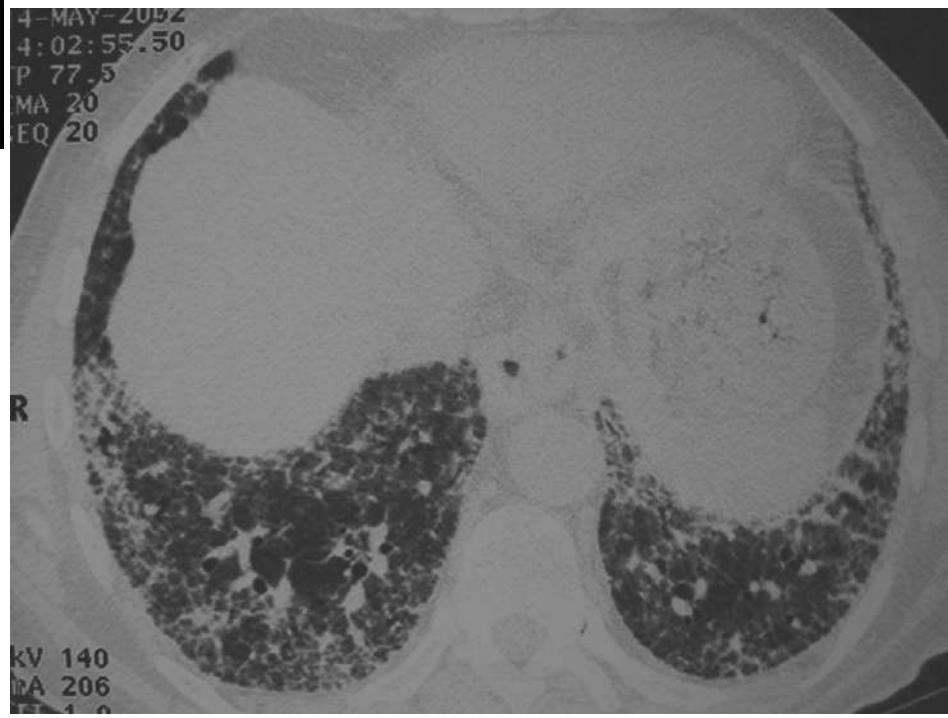
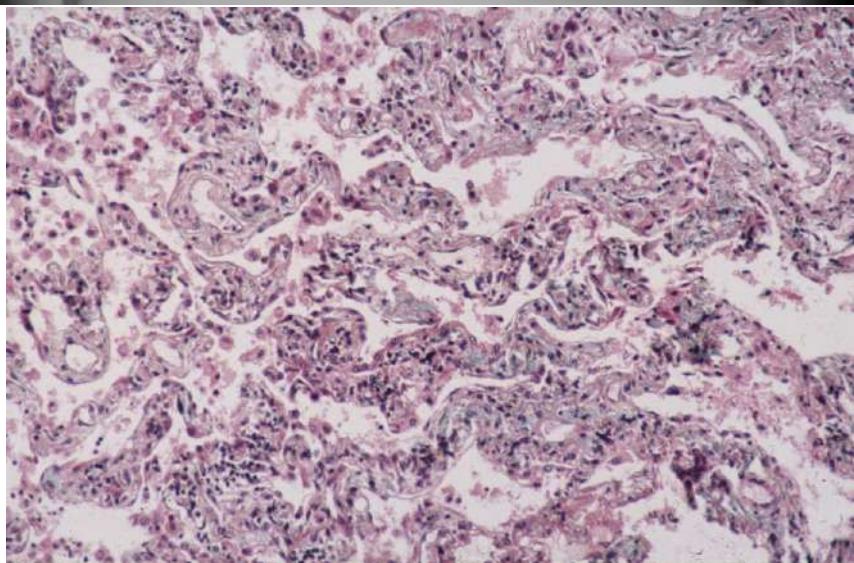
Bleomycine (Bauer, 1983)



Hydroxycarbamide (Imai, 2015)



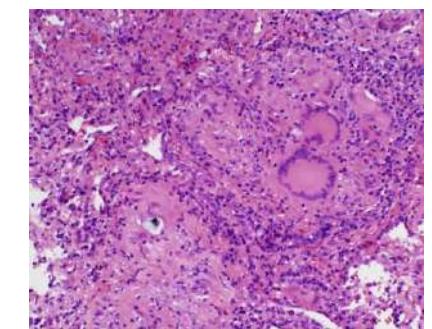
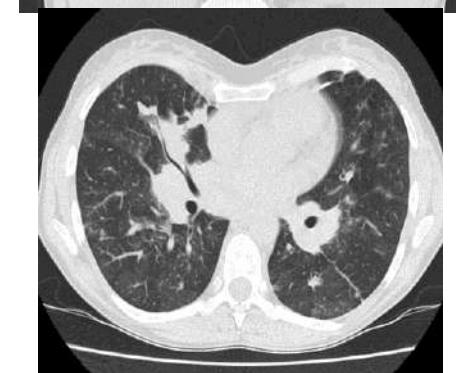
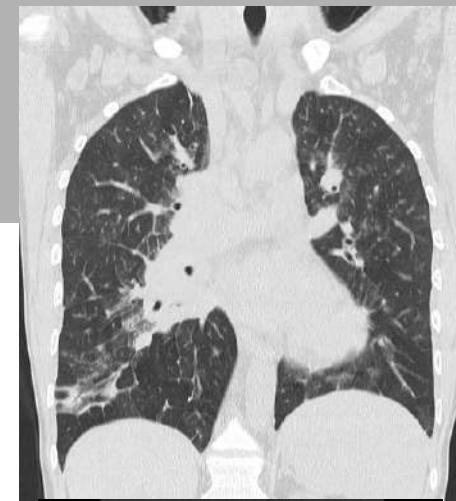
Amiodarone 10-50%



PR

- ❑ Bilan fonctionnel et imagerie précoces
- ❑ Périodicité: 2 ans?
- ❑ Education du patient
- ❑ Vérifier et revérifier TLIG
- ❑ PnI, nodulose, ?BO
- ❑ Vigilance
 - ❑ Methotrexate, ?leflunomide, AINS
 - ❑ Anti-TNF
- ❑ Dixon, 2010
 - ❑ The mortality in patients with RA-ILD is not increased following treatment with anti-TNF compared with traditional DMARDs
 - ❑ Proportion of deaths attributable to RA-ILD is higher in patients treated with anti-TNF therapy, although **reporting bias may exist**

- Granulomatoses & anti-TNF
 - ❖ 40 cas
 - ❖ Dont 24 etanercept
 - ❖ OR x4.0
- Atteinte respiratoire
 - ❖ PnI 68%
 - ❖ ADP 57%
- Atteinte cutanée 33%
- Hypercalcémie
- Résolution complète 67% partielle 22%
- Récidive après réintroduction
- Interferon



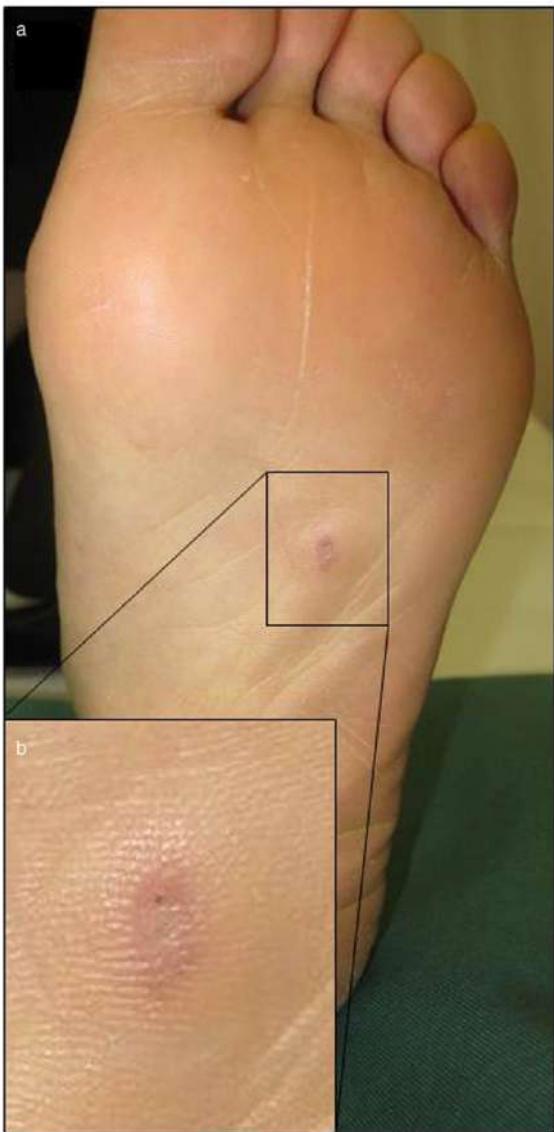
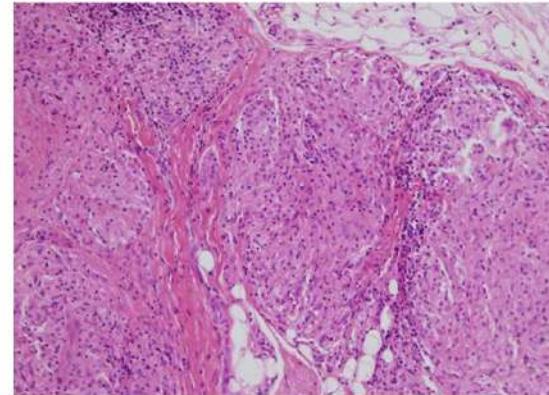


Figure 2 The patient developed a small, painful subcutaneous nodule (black circle) on the sole of her foot that was 10 mm in diameter 10 months after the initiation of therapy. The patient had no complaints about the sole of her foot before treatment.

ated giant cells (Fig. 3). Specific stains showed no evidence of bacterial, fungal or mycobacterial organisms. Biopsy findings were interpreted as consistent with sarcoidosis, although the skin lesion disappeared around the time of biopsy. Further examination was performed to evaluate systemic involvement. Laboratory studies demonstrated moderate leukocytopenia ($2800/\mu\text{L}$), elevated lysozyme ($10.5 \mu\text{g/mL}$; normal, $5.0\text{--}10.2$), and normal angiotensin-converting enzyme (16.9 U/mL ; normal, $8.3\text{--}21.4$) and serum calcium (9.1 mEq/L). Her tuberculin skin test was negative, but ophthalmologic examination revealed uveitis. A chest X-ray (Fig. 1b) and thoracic computed tomography (CT) taken 2 months after combination therapy showed multiple bilateral, paratracheal, subcarinal and hilar adenopathies (Fig. 1d), and a diffuse micronodular interstitial pattern of the lungs (Fig. 1e). Transbronchial lung biopsy revealed the presence of multiple non-caseating granulomas with multinucleated giant cells (Fig. 4). The bronchoalveolar lavage fluid level of lymphocytes was elevated at 38.7% compared with macrophages (56.3%) and neutrophils (5.0%) in a total cell density of $1.67 \times 10^5/\text{mm}^3$. An increased ratio of CD4/CD8 cells of 2.33 was noted. Based on these findings, the patient was diagnosed as having sarcoidosis. She was observed carefully without any additional medication because no significant systemic symptoms were noted. A chest CT taken 20 months after combination therapy showed improvement (Fig. 1f,g). She was also asymptomatic for over 3 years of follow up, and repeated hematological



- ❖ Anticonvulsivants (47.4%)
- ❖ Antibiotiques (18.4%) (minocycline)
- ❖ AINS (13.2%)
- ❖ Allopurinol (5.3%)
- ▣ Latence variable: 3j -105j (25 j)
- ▣ Récupération 95%



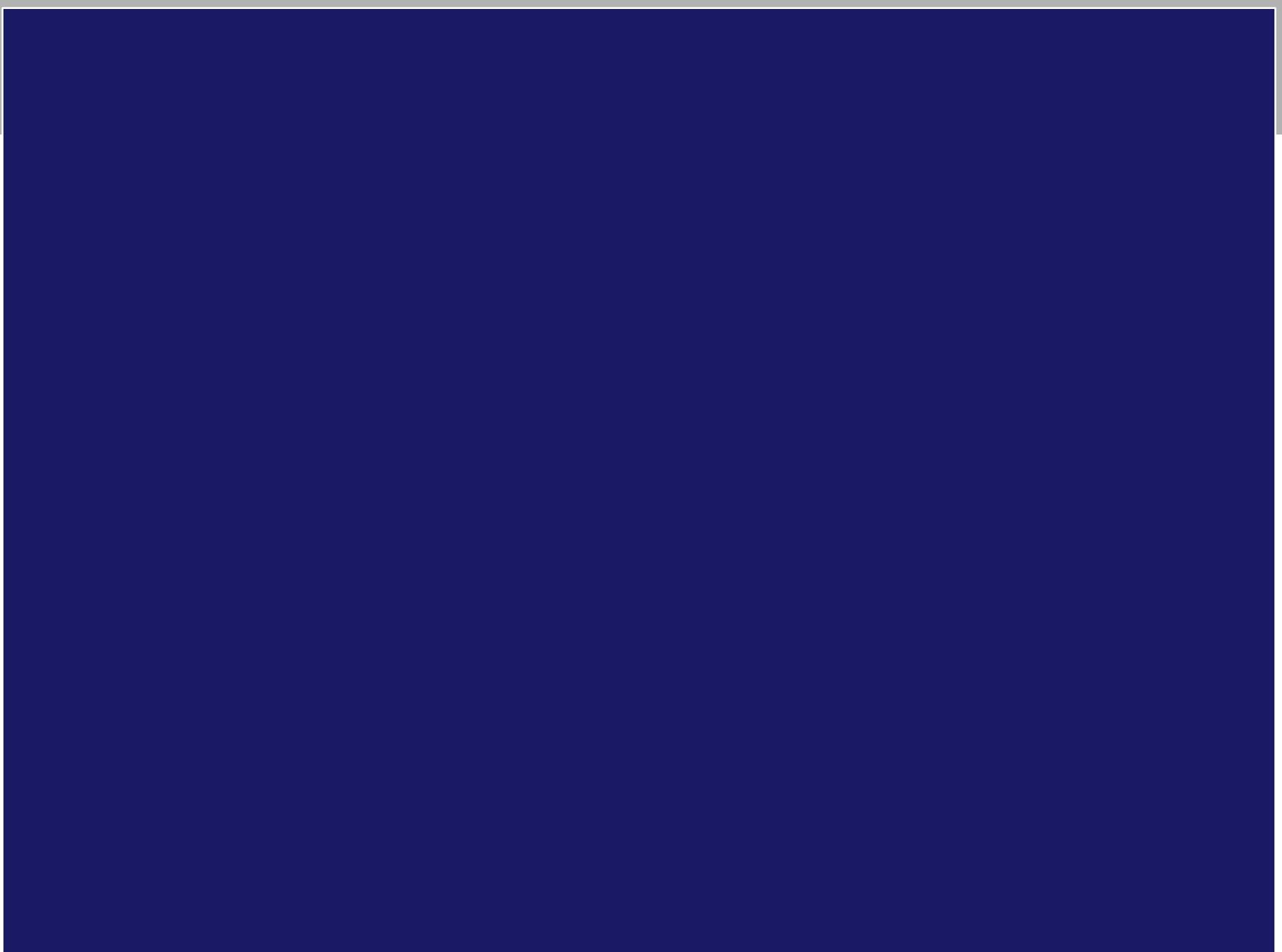


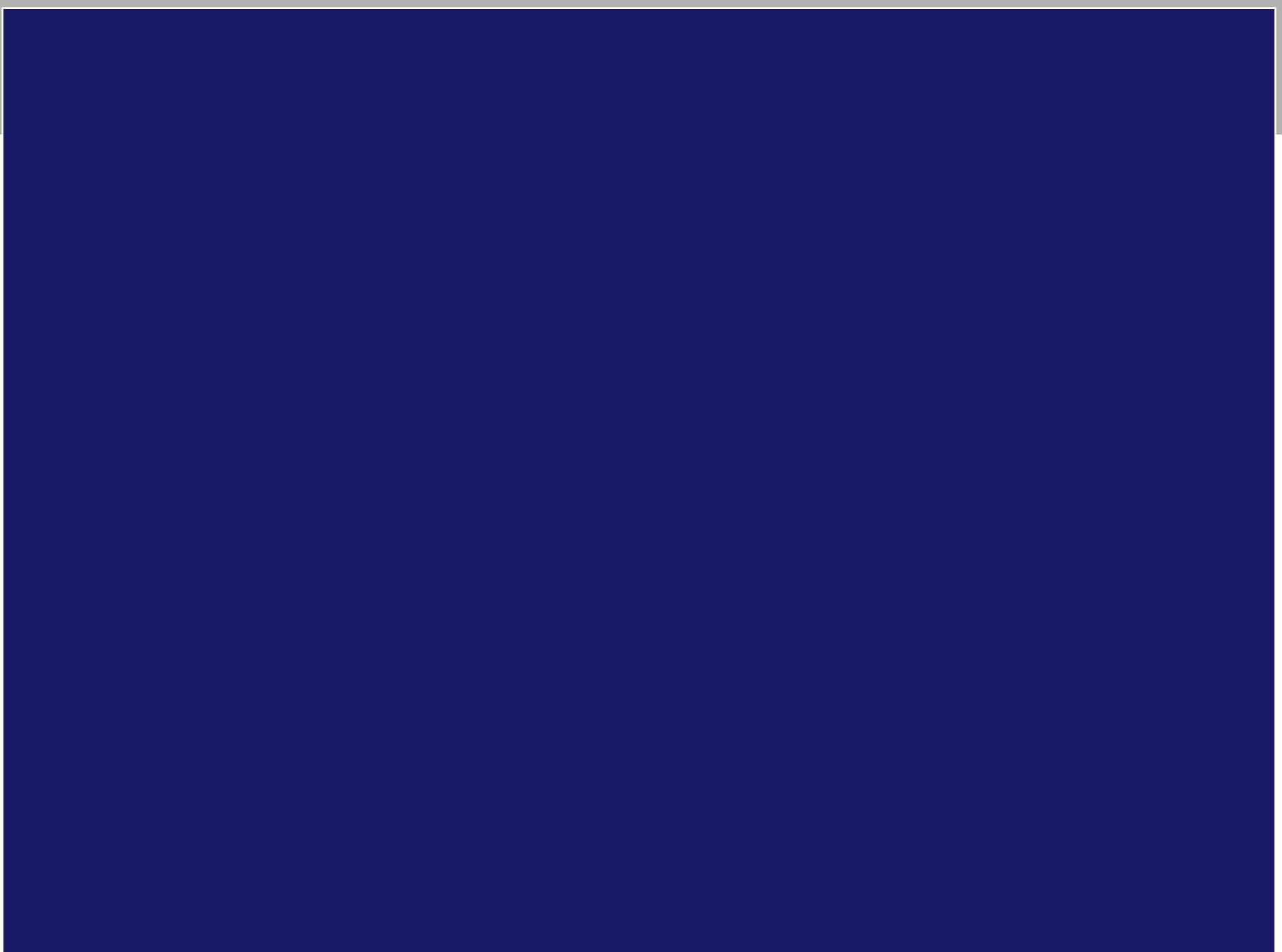
DD2

❑ Affection intercurrente

- ❑ => LBA
 - ❖ Cellularité
 - ❖ *Pneumocystis jiroveci* (IF, PCR)
- ❑ Infection de rencontre
- ❑ Infection opportuniste
- ❑ -> Multiplex assay







Checklist diagnostique

- ❑ Ordonnance, tél. pharmacie, taux sérique
 - ❑ Vente libre?
 - ❑ Quid si >1 médicament
 - ❑ Substances illicites (drug screen)
 - ❑ Si malade inconscient ou ventilé: entourage
- ❑ Etat respiratoire préexistant +++
- ❑ Tableau compatible avec le médicament?
- ❑ Signal dans la littérature
 - ❑ ‘-’ à ‘5’
 - ❑ Spécificité

- ❑ Caractère précessif des symptômes
- ❑ Délai d'apparition: compatible?
- ❑ Biomarqueurs? (BNP, AAN, ANCA)
- ❑ Diagnostic différentiel (M sous-jacente/intercurrente)
- ❑ Situations particulières

- ❑ Problèmes actuels
- ❑ Causalité vs. association fortuite: principes généraux
- ❑ Scores - Poids relatif des mots
- ❑ Checklist
- ❑ Management (corticoïdes, réintroductions)
- ❑ Situations particulières

