VIH & TABAC le point de vue du pneumologue

Nicolas Van Grunderbeeck

Maladies Infectieuses / Réanimation Polyvalente

CH Lens





« moi j'dis ça, mais je ne suis pas pneumologue »

Dr Hugues Georges, Congrès de Pneumologie de Langue Française Lille, 30 Janvier 2008



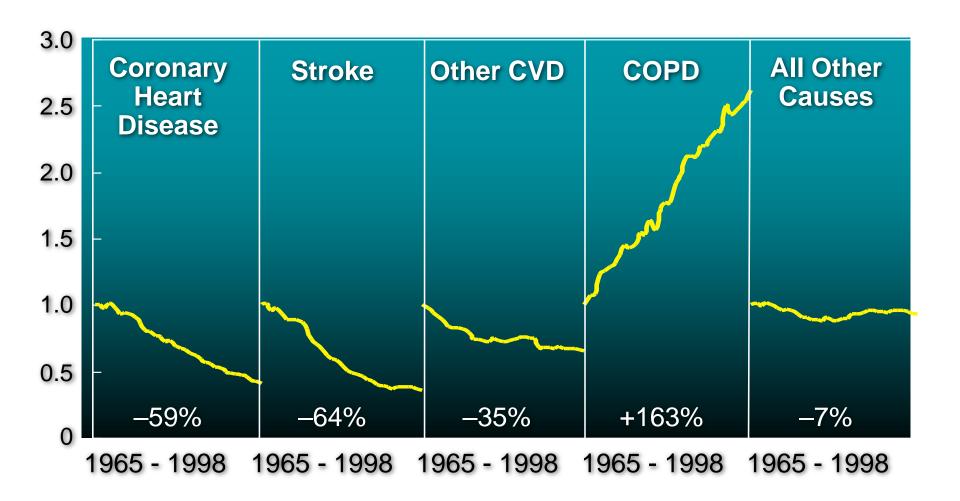
Conflits d'intérêt 2015-2017

- AIR LIQUIDE: invitation congrès ISICEM 2016-2017 Bruxelles, ESICM 2017 Vienne
- BASILEA: intervention
- **EUMEDICA**: invitation congrès International Sepsis Forum Paris 2016
- **JANSSEN**: invitation congrès JNI 2016 Lille
- MSD: investigateur associé AMARCAND2, invitations congrès SRLF 2015-2016
- PFIZER: invitations congrès JNI 2015 Nancy, groupe de travail

VIH et tabac

- Pourquoi (que) la BPCO?
- Épidémiologie
- Physiopathologie
- Particularités de la BPCO dans le cadre du VIH
- Traitements & conséquences

Pourquoi la BPCO?



BPCO/COPD

« BronchoPneumopathie Chronique Obstructive »

La bronchopathie chronique obstructive se caractérise par une baisse insidieuse mais persistante de l'écoulement des gaz inspirés. Les symptômes s'aggravent progressivement, avec un essoufflement à l'effort puis aussi au repos.

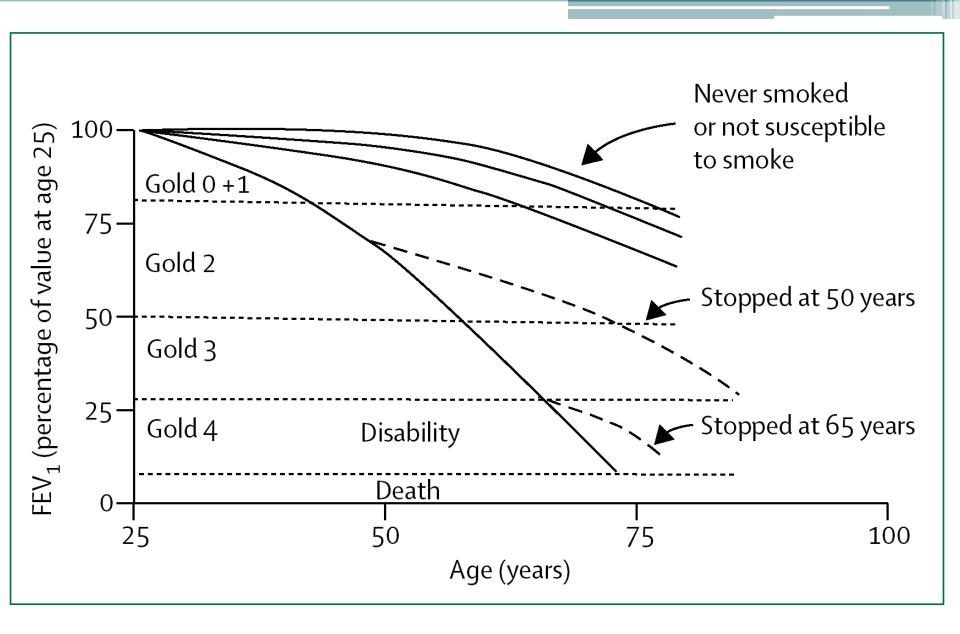
(VEMS/CV < 70% <u>après bronchodilatateurs</u>)

• 3^{ème} cause mondiale de mortalité en 2020? Global, regional, and national age-sex specific mortality for

264 causes of death, 1980–2016: a systematic analysis for the Global Burden of Disease Study 2016

GBD 2016 Causes of Death Collaborators*

- Surreprésentée dans la région
- Sous-diagnostiquée, notamment chez PVVIH
 - Tabagisme 2 à 3 fois plus fréquent chez patients VIH
 - · Corrélation fréquente / niveau socio-économique



Fletcher C. *Br Med J* 1977; 1: 1645-8.

Clinical Infectious Diseases 2013;56(5):727-34

Mortality Attributable to Smoking Among HIV-1-Infected Individuals: A Nationwide, Population-Based Cohort Study

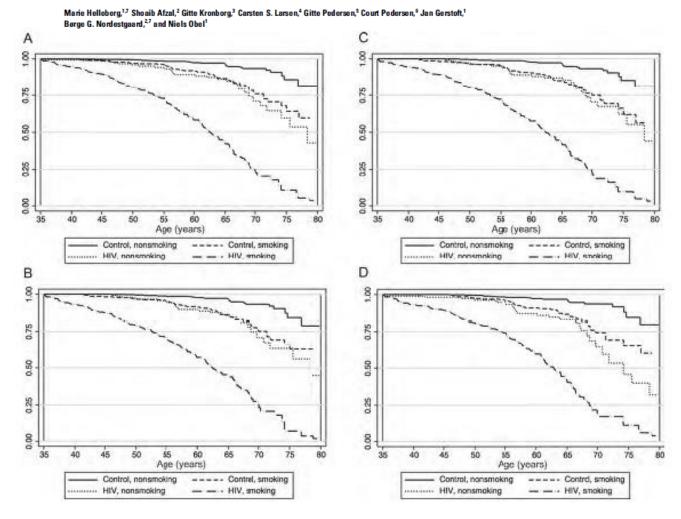
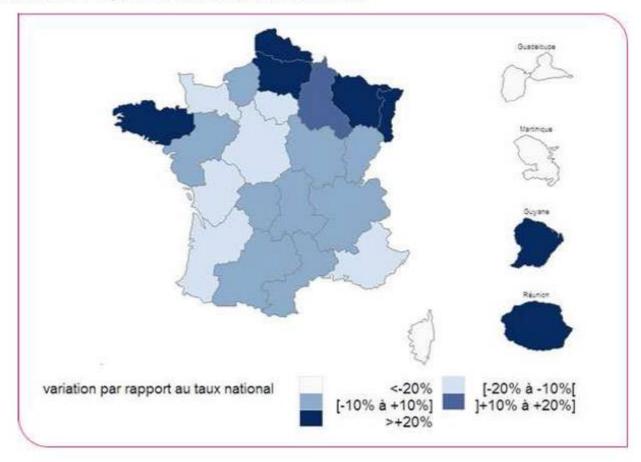


Figure 1. Kaplan-Meier curve showing survival by age, stratified by human immunodeficiency virus and smoking status for all study subjects (A), only males (B), only study subjects of Danish origin (C), and only study subjects from Copenhagen (D). Abbreviation: HIV, human immunodeficiency virus.

O de France...

Variations régionales des taux de mortalité par BPCO, cause initiale de décès, 2005-2007



Ces chiffres sont comparables au nombre de décès constaté au titre du tabagisme qui est supérieur de 40% à la moyenne nationale chez les hommes et de 22% chez les femmes.

Interactions between HIV infection and chronic obstructive pulmonary disease: Clinical and epidemiological aspects

Christine Raynaud144, Nicolas Roche24 and Christos Chouaid34

Respiratory Resarch 2011

Table 2 Main published studies on COPD-HIV interaction in the HAART era

Year of publication	First Author reference	Study period	Type of study	Focus	Number of patients	Main findings
2005	Crothers K [32]	1999- 2000	Observational study prospective cohort	Respiratory symptoms	867	Smoking associated with increase in respiratory symptoms; cough and dyspnea found in 44% of smokers and 25% of non smokers
2006	Crothers K [31]	2001- 2002	Observational study Prospective Case-control Cohort	COPD (self-assessment and coding data)	1014 (713 controb)	Self-assessment prevalence of COPD significantly higher in HIV-infected patients (15% vs 12%, p = 0.04); HIV infection = independent risk factor for COPD
2009	George MP [33]	2003- 2004	Observational study Prospective	Respiratory symptoms, airway obstruction	234	Prevalence of airway obstruction: 6.8%. Age, pack-years, history of bacterial pneumonia and HAVRT = independent risk factors for airway obstruction
2009	Morris A [43]	NR	Observational study Prospective	Pneumocystis colonization and alrway obstruction	42	Colonization by Pneumocystis Jirovecii (26% of cases) associated with increase in airway obstruction and sputum metalloprotease (MMP 12) levels
2010	Drummond MB [36]	1988?	Observational study Prospective Cohort Case-control	Respiratory symptoms. Airway obstruction	288 (686 controls)	Prevalence of alrway obstruction: 15,5%. No influence of HIV status
2010	Cui Q [35]	NR	Observational study Prospective	Respiratory symptoms. Airway obstruction	119	No acceleration of FEV ₁ decline relative to published data for general population
2010	Gingo RM [34]	2007- 2009	Gross- sectional analysis	Airway obstruction	167	64% of patients had impaired diffusion. 21% of patients had irreversible airway obstruction. Incurrible airway obstruction was independently associated with HAART, packyears smoked and intravesous drug use.
2011	Crothers K [37]	1999- 2007	Observational study prospective Cohort Case-control	Coding data	3707 (9980 controls)	HW-infected patients more likely to have diagnoses of COPD (20.3 per 1000 person-years versus 17.5 per 1000 person-years – p < 0.001).

PROTOCOL Open Access



Epidemiology of chronic obstructive pulmonary disease in the global HIV-infected population: a systematic review and meta-analysis protocol

Jean Joel R. Bigna^{1,2*}, Angeladine Malaha Kenne¹ and Serra Lem Asangbeh³

RESEARCH ARTICLE

COPD in HIV-Infected Patients: CD4 Cell Count Highly Correlated

Karine Risso^{1,2}*, Francine Guillouet-de-Salvador¹, Laure Valerio³, Pascal Puglièse¹, Alissa Naqvi¹, Jacques Durant¹, Elisa Demonchy^{1,2}, Isabelle Perbost¹, Eric Cua¹, Charles-Hugo Marquette^{2,4}, Pierre-Marie Roger^{1,2}

1 Service d'Infectiologie, Centre Hospitalier Universitaire de Nice, Nice, France, 2 Université de Nice-Sophia-Antipolis, Nice, France, 3 Département d'Informations Médicales, Centre Hospitalier de la Dracénie, Draguignan, France, 4 Service de Pneumologie, Centre Hospitalier Universitaire de Nice, Nice, France

OPEN ACCESS

Citation: Risso K, Guillouet-de-Salvador F, Valerio L, Puglièse P, Naqvi A, Durant J, et al. (2017) COPD in HIV-Infected Patients: CD4 Cell Count Highly Correlated. PLoS ONE 12(1): e0169359. doi:10.1371/journal.pone.0169359

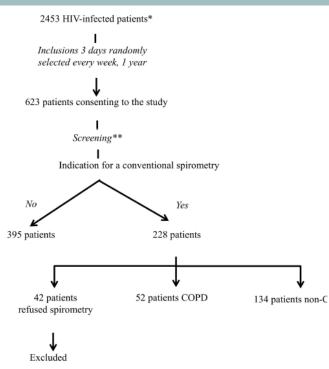


Fig 1. Study's flowchart. * Cohort of HIV-infected patients consulting in infectious departmen'
** Dedicated questionnaire + Hand-Held spirometer.

Table 2. Comparison COPD-patients and non-COPD patients.

Parameters		Univariate analysis	Multivariate analysis		
	Non-COPD COPD		P Value	OR ^d (95% CI)	P Value
	(529)	(52)			
Demographic characteristics					
Age (years) #	47.9 ± 9.8	52.5 ± 9.7	0.001	1.61° (1.14-2.28)	0.007
Male Gender	389 (73.5%)	40 (76.9%)	0.596		
BMI (Kg/m²) #	23.7 ±3.6	21.5 ± 3.4	<0.001	0.78 (0.70-0.89)	<0.001
Toxic exposure					
Current smoker	261 (49.3%)	34 (65.4%)	0.027		
Current or past Smoker	370 (69.9%)	47 (90.4%)	0.002		
Pack-year history#	15.4 ± 17.5	23.6 ± 19.4	0.001	1.28 ^b (1.09-1.50)	0.003
Current/past Cannabis use#	199 (38.9%)	27 (55.1%)	0.028		
IDU#	85 (16.6%)	18 (35.3%)	0.001		
Professional resp. exposure	128 (24.7%)	13 (25.0%)	0.957		
Clinical characteristics					
Respiratory symptoms	107 (20.3%)	29 (55.8%)	<0.001		
Chronic bronchitis symptoms	31 (6%)	14 (27%)	<0.001		
Recurrent acute bronchitis	37 (7%)	12 (23.1%)	<0.001		
Dyspnea	78 (14.7%)	23 (44.2%)	<0.001		
Hosp. for respiratory condition	19 (3.6%)	13 (25.0%)	<0.001		
Previous LRTI	172 (32.5%)	33 (63.5%)	<0.001		
Previous CABP	45 (8.5%)	12 (23.1%)	0.001		
HBV and/or HCV infection#	167 (31.6%)	26 (50.0%)	0.007		
Depression	103 (19.5%)	19 (36.5%)	0.004		
HIV story					
HIV infection duration (years) #	15.2 ± 8.5	18.7 ± 8.5	0.005		
CDC stage			0.376		
A	320 (60.5%)	30 (57.7%)			
В	87 (16.4%)	6 (11.5%)			
C	122 (23.1%)	16 (30.8%)			
CD4 cell count (cells/mm3) #	634 ± 294	497 ± 232	0.001	0.77° (0.68-0.88)	<0.001
<200 cells/mm ³	28 (5.3%)	4 (7.7%)	0.008		
CD4/CD8 cell ratio	0.79 ± 0.51	0.71 ± 0.44	0.271		
CD8 cell count (cells/mm³)	939 ± 467	830 ± 548	0.10		
HIV RNA (log ₁₀ cp/ml) #	1.87 ± 0.79	1.71 ± 0.54	0.054	0.59 (0.32-1.08)	0.088
Undetectable HIV RNA	446 (84.5%)	48 (92.3%)	0.129		
Nadir CD4 cell count (cells/mm3) #	262 ± 191	188 ± 155	0.007		
HAART exposure					
HAART naïve	24 (4.5%)	0 (0.0%)	0.154		
NRTI (months) #	116.3 ± 81.5	128.5±77.9	0.465		
NNRTI (months) #	35.7 ± 48.1	50.7 ± 60.8	0.114		
PI (months)#	63.2 ± 63.8	66.9 ± 65.1	0.863		

Prévalence de 9% parmi les inclus (infections respiratoires récentes exclues)...

Diagnostic nouveau chez 90%... Recommandations inadaptées/FR?

Physiopathologie BPCO/VIH

- Facteurs de risque + fréquents
- Obstruction & distension
- Impact:
 - inflammation chronique(CD4/CD8)
 - nadir CD4
- Pneumocystis & autres infections
- ARV ?!

Morris, George, Crothers, et al.: HIV and COPD

Progression of COPD

Reaction to microbial products (e.g. Pneumocystis)

Restoration of T and B lymphocytes

Autoimmunity

Reaction to microbial products (e.g. Pneumocystis)

Inflammation Lung epithelial injury

Autoimmunity

HIV and COPD: a conspiracy of risks

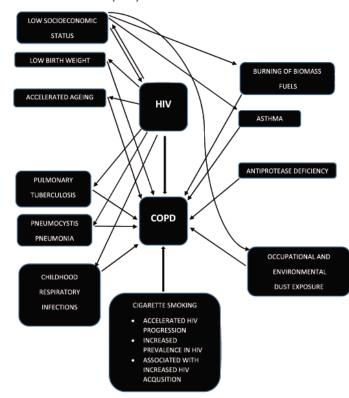


Figure 2. Potential mechanisms of antiretroviral-mediated lung damage in HIV.

HIV and Chronic Obstructive Pulmonary Disease Is It Worse and Why?

Alison Morris¹, M. Patricia George¹, Kristina Crothers², Laurence Huang³, Lorrie Lucht¹, Cathy Kessinger¹, and Eric C. Kleerup⁴ on behalf of the Lung HIV Study

¹Departments of Medicine and Immunology, University of Pittsburgh, Pittsburgh, Pennsylvania; ²Department of Medicine, University of Washington, Seattle, Washington; ³Department of Medicine, University of California, San Francisco, California; and ⁴Department of Medicine, David Geffen School of Medicine, University of California, San Angeles, California

Proc Am Thorac Soc Vol 8. pp 320–325, 2011 DOI: 10.1513/pats.201006-045WR Internet address: www.atsjournals.org

Chronic Lung Disease in Adolescents With Delayed Diagnosis of Vertically Acquired HIV Infection

Treatment for asthma

Dilated cardiomyopathy

Symptoms (current/recent)

Exertional chest tightness

Wheeze on auscultation

Tachycardia (HR >100), at rest

Resting O2 sat <92% at rest

Respiratory rate >25/min at rest

Pulmonary arterial pressure (n = 110)e

Drop of $\geq 5\%$ O₂ sat on exercise testing (n = 72)^d

Hospitalized for LRTI in the past year

Recurrent^b cough ± purulent sputum

>2 courses of antibiotics for LRTI in the past year

Treatment for PCP

NYHA class

2

3

Cough

Sputum

Clubbing

Clinical assessment

Bibasal crackles

<20 mm Hg

>25 mm Hg

50-79

50-79

< 50

20-25 mm Hg

FEV₁, % predicted 80-100

PEFR, % predicted 80-100

Rashida A. Ferrand, 12.3 Sujal R. Desai, 4 Charlotte Hopkins, 3 Caroline M. Elston, 5 Susan J. Copley, 6 Kusum Nathoo, 7 Chiratidzo E. Ndhlovu, 8 Shungu Munyati, 2 Richard D. Barker, 5 Robert F. Miller, 1,9 Tsitsi Bandason, 2 Athol U. Wells, 10

and Elizabeth L. Corbett^{1,2,11} ¹Clinical Research Department, Lo Harare, Zimbabwe; 3Mortimer Mar Medicine, King's College Hospital ⁷Department of Paediatrics and ⁸De University College London, and 101 Liverpool Research Program, Univer

Table 2. Respiratory Symptoms and Signs in Study Participants ment of Respiratory ited Kingdom; Characteristic Patients, No. (% opulation Health, Clinical history om; and 11Malawi-Previously treated for tuberculosis^a 42 (36) History of other cardiorespiratory conditions

11 (9)

7 (6)

1 (1)

19 (16)

48 (41)

77 (66)

72 (62)

20 (17)

22 (19)

2(2)

84 (72)

54 (47)

49 (42)

12 (10)

37 (32)

2(2)

35 (30)

33 (28)

15 (13)

21 (29)

94 (86)

8 (7)

8 (7)

64 (55)

40 (35) 12 (10)

83 (72)

28 (24)

5 (4)

Clinical Infectious Diseases 2012;55(1):145-52

Chronic Respiratory Disease in HIV-Infected Adolescents

Diane Gray

Division of Paediatric Pulmonology, Red Cross War Memorial Children's Hospital, Department of Child and Adolescent Health, University of Cape Town, South Africa (See the HIV/AIDS Major Article by Ferrand et al, on pages 145-52.)

116 patients 14±2,6 ans 69% sous ARV Toux chronique 66% Dyspnée d'effort 21% 40% hypoxémie 45% VEMS diminué 47% Anomalies Rx (bronchiolite / DDB)

infection [1]. In this clinic-based cohort of adolescents with presumed vertically acquired HIV infection, 86% had clinical evidence of chronic respiratory disease. Nearly half of the participants were hypoxic at rest or minimal exertion, a marker of severe lung disease in the absence of primary cardiac pathology. In addition, this damage occurred in many of the adolescents without severe immunosuppression. More than 40% of adolescents with a CD4 count ≥350 cells/µL had clinical and radiologic evidence of chronic respiratory disease. This high-

BPCO

- Évolution naturelle...
 - Exacerbations/ Décompensations
 - Insuffisance respiratoire chronique
 - Insuffisance cardiaque droite
 - · Décès...
- Retentissement systémique
 - Gravité si cachexie (BODE index >VEMS)
 - Impact de la dénutrition
- Pas de traitement curatif
 - Sevrage tabagique, bronchodilatateurs, corticoïdes inhalés, réhabilitation, O2, VNI, VM/trachéotomie, épuration CO2, transplantation?
- Impact majeur sur la qualité de vie

Life's hard...

Dyspnée



Anxiété



Sédentarisation



Déconditionnement

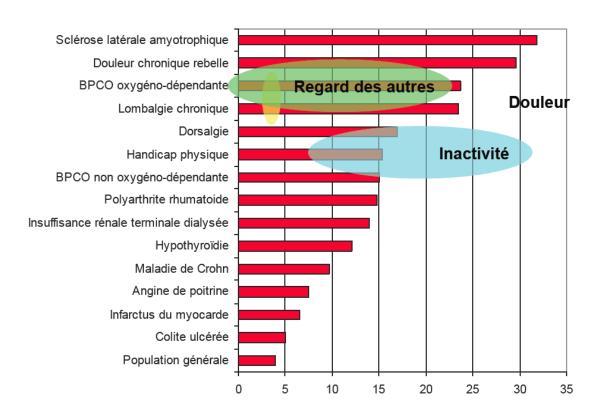


Aggravation de la dyspnée



Dépression

Qualité de vie?





Niveaux de qualité de vie et maladies chroniques

Pr. Grégory Ninot

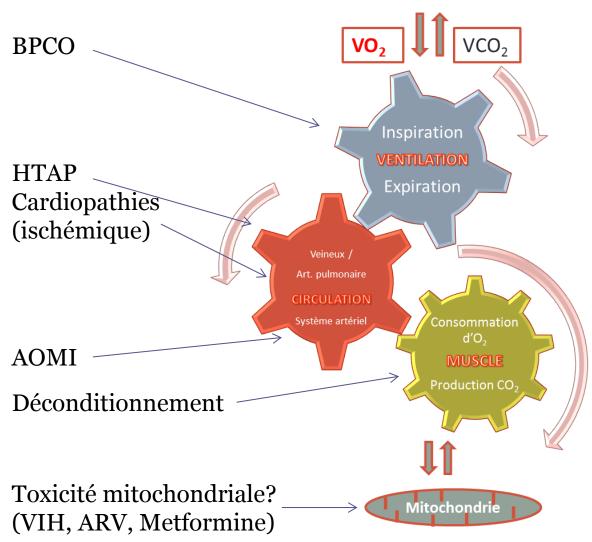
(Bergner et al., 1976, MC)

Images in Pulmonary, Critical Care, Sleep Medicine and the Sciences

Thinker's Sign

Am J Respir Crit Care Med Vol 183. p 413, 2011 DOI: 10.1164/rccm.201010-1754IM Internet address: www.atsjournals.org

La dyspnée d'effort... s'explore à l'effort



Particularités thérapeutiques

- Aucune / bronchodilatateurs
 - · Bénéfice-risque des corticoïdes inhalés??
 - Interactions/boosts
 - Remis en cause /majoration exacerbations (étude FLAME)
 - Et des corticoides systémiques?
- Faisabilité médicaments du sevrage /ARV
 - Remboursement varenicline

Possibilité transplantation?

Conclusions

- Pathologie sous-diagnostiquée
- Nécessité de prévention et dépistage
- Prévalence élevée chez patients pourtant jeunes
- Impact / vieillissement PVVIH
- Mortalité et qualité de vie

Il est des morts plus difficiles à vivre que d'autres. L'asphyxie est de celles-là.

Claude Chopin, L'Hôpital: allô quoi? 2017

Fumer tue

Fumer peut entraîner une mort lente et douloureuse