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Charlotte Lewden, Thierry May, Eric Rosenthal, Christine Burty, Fabrice Bonnet, et al.. Changes in causes of death among adults infected by HIV between 2000 and 2005: The "Mortalité 2000 and 2005" surveys (ANRS EN19 and Mortavic).. Journal of Acquired Immune Deficiency Syndromes, Lippincott, Williams & Wilkins, 2008, 48 (5), pp.590-8. 10.1097/QAI.0b013e31817efb54 . inserm-00337877

HAL Id: inserm-00337877

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Submitted on 22 May 2014

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Title: Changes in cancer mortality among HIV-infected patients: The ANRS Mortalité 2005 survey.

Running head: Cancer mortality in HIV-infected patients

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Keywords: HIV, cancer, hepatocarcinoma, non-Hodgkin lymphoma, cause of death, epidemiology.

Financial support

Agence Nationale de Recherches sur le Sida et les Hépatites Virales (ANRS) through a grant from the Scientific Sector-based Group number^o5 (CSS5)

Words: 2115 Tables: 2

Abstract

Background: The current study aimed at describing the distribution and characteristics of malignancy-related deaths in human immunodeficiency virus- (HIV) infected patients using data obtained from a national survey conducted in France in 2005 and at comparing them to those obtained from a similar survey in 2000.

Method: The underlying cause of death was documented using a standardized questionnaire fulfilled in French hospital wards and networks involved in the management of HIV infection.

Results: Among the 1,042 deaths recorded in 2005 (*versus* 964 in 2000), 344 were cancer-related (34%) with a significant increase from 2000 (29%) ($p=0.02$); these deaths were distributed as 134 acquired immunodeficiency syndrome- (AIDS) related and 210 non-AIDS-related cancer deaths. Among cancer-related causes of death, proportion of hepatitis-related cancers (6% in 2000 vs 11% in 2005) and non AIDS/non hepatitis-related cancers (38% in 2000 vs 50% in 2005) significantly increased between 2000 and 2005 ($p=0.03$ and $p=0.01$ respectively), as compared to AIDS-related cancer and adjusted on age and gender.

Among AIDS events, the proportion of non-Hodgkin lymphoma- (NHL) associated deaths was not statistically significantly different between 2000 and 2005 (11 and 10%, respectively).

Conclusion: In this study, an increasing proportion of lethal non-AIDS cancers was shown from 2000 to 2005, meanwhile the proportion of lethal AIDS-related cancers remained stable in HIV-infected patients. Thus, cancer prophylaxis, early diagnosis and improved management should be included in routine long-term follow-up of HIV-infected patients.

Introduction

Human immunodeficiency virus- (HIV) infected patients are at increased risk of non-Hodgkin lymphoma (NHL), Kaposi sarcoma and cervical cancer, considered as acquired immunodeficiency syndrome (AIDS) events in the 1993 revised classification system for HIV infection [1]. This increased risk seems to be partly related to oncogenic virus coinfections (Epstein-Barr Virus, Human Herpes Virus 8, Human Papillomavirus, Hepatitis B virus [HBV]) as well as to cellular immunodepression as demonstrated during the use of immunosuppressive drugs, particularly in transplantation field [2, 3]. The widespread use of combination antiretroviral therapies (cART) in industrialized countries since the mid 90s was associated with a dramatic decrease in both mortality and AIDS events incidences. However, the incidences of NHL and cervical cancer decreased in a lower proportion than the other opportunistic infections [4, 5]. Prolonged life expectancy was associated with a diversification of morbidity and causes of death such as cardiovascular events, hepatic complications, bacterial infections and non-AIDS cancers [6-12]. In a previous national survey conducted in France in 2000, we showed that non-AIDS cancers accounted for 12% of deaths and all cancers (ie, AIDS- and non-AIDS-related malignancies) for 29% of the deaths [13]. Monitoring epidemiologic trends would permit to define priorities in terms of prevention, early detection and management of AIDS and non-AIDS malignancies. The objectives of the present study were to describe the distribution and characteristics of malignancy-related deaths in HIV-infected patients in France in 2005 as well as at assessing changes from 2000.

Patients and Methods

Data collection

All hospital wards and networks known to be involved in the management of HIV infection in France were contacted, including wards participating in the "Mortalité 2000" survey. Apart from a greater number of contacted physicians than in 2000, the study design was similar to that of the previous survey [7].

Physicians were asked to prospectively report and document deaths with an abstract of the cause of death for HIV-infected adults (18 years or older), every three months in 2005. Each death case was then documented using a standardized questionnaire, including all contributing causes of death, diseases present at time of death and a global assessment of the underlying cause of death. One physician was especially dedicated to the survey in the coordinating team, and oversaw harmonization of data collection. Double reports were identified by cross-match of the dates of birth and death. Hepatitis C virus (HCV) infection was defined as the presence of serum HCV-antibodies or HCV-ribonucleic acid (RNA), excessive alcohol consumption as a daily alcohol intake higher than 50 grams and/or five glasses, and poor socio economic conditions as no health insurance, no employment, no accommodation, income below 535 € per month and/or immigrant in illegal situation.

Determination of the underlying cause of death

Information contained in the questionnaire was used to determine the underlying cause of death according to the International Classification of Diseases -10th revision (ICD-10) rules: the underlying cause of death was defined as the disease or injury, that initiated the sequence of morbid events leading to death [14]. The algorithm of determination was adapted to specific concerns in HIV infection [7] and allowed categorization of deaths as follow: AIDS-related causes according to the 1993 clinical classification [1], deaths related to infection with HCV and/or hepatitis B virus (HBV) including hepatocarcinoma, cancers and

other causes neither related to AIDS nor to HCV/HBV, and adverse effects of antiretroviral treatment. The latter was considered as the underlying cause of death only when this was the explicit conclusion of the physician. Cancers were classified as AIDS-related when active pathology at time of death included one AIDS-defining cancer according to the classification of the Centers for Disease Control and Prevention (CDC) for HIV infection as revised in 1993 [1]: high grade NHL including Burkitt and immunoblastic lymphoma, primary brain lymphoma, Kaposi sarcoma and cervical cancer. Other cancers were classified as either hepatitis-related hepatocarcinoma or non-AIDS-/non-hepatitis-related cancer.

Statistical analysis

The distribution of malignancy-related causes of death was compared between 2000 and 2005 using the chi-square and Kruskal-Wallis tests. To compare the distribution of causes of cancer-related deaths between 2000 and 2005, we performed a multinomial logistic model adjusted for gender and age. Statistical analyses were performed using Statistical Analysis System software (SAS, version 9.0).

Results

A total of 1,042 deaths were reported in 2005 (*versus* 964 in 2000), among around 78,000 HIV-infected patients followed (at least one contact in 2004) at the 340 wards participating in the survey. Documentation was available for 1,013 decedents (97%): 76% were men, the median age was 46 years (*versus* 41 years in 2000), the known duration of HIV infection was 12 years (*versus* 8 years), 87% had received an antiretroviral treatment (*versus* 86%), 47% had less than 500 copies/mL of plasma HIV-RNA (*versus* 33%), and the median CD4 lymphocytes count was 161/mm³ (*versus* 94/mm³) with 55% of patients (*versus* 68%) having a CD4 cell count below 200/mm³ and 12% (*versus* 9%) above 500/mm³.

Underlying causes of death

In the Mortalité 2005 survey, the most frequent underlying cause of death was an AIDS-defining illness in 375 cases (36% *versus* 47% in 2000) followed by non-AIDS-/non-hepatitis-related cancer (n = 173; 17% *versus* 11%), liver-related cause (n = 154; 15% *versus* 13%) cardiovascular disease (n = 88; 8% *versus* 7%), suicide (n = 50; 5% *versus* 4%), and other infections (n = 46; 4% *versus* 7%).

Overall, 344 malignancy-related causes of death representing 34% of deaths were recorded and distributed as NHL (N=84, 10% of the causes of death), Kaposi sarcoma (N=25, 3%), hepatitis-related hepatocarcinoma (N=37, 4%) and non-AIDS/non-hepatitis cancers (N=173, 17%) (Table 1). This proportion statistically significantly increased since 2000 where malignancies accounted for 29% of the causes of death (p=0.02) (Table 2). Adjusted on age and gender, the proportion of deaths attributed to hepatocarcinoma or to non-AIDS/non-hepatitis cancers statistically significantly increased from 2000 to 2005, with a greater diversification of cancer types. The proportion of AIDS-defining cancers remained stable during the same period.

Patients who died from non-AIDS/non-hepatitis related cancers were older than others (49 years in median), known to be HIV-infected for 11.9 years in median, moderately immunosuppressed (median count: 205 CD4/mm³ in 2005, 218 CD4/mm³ in 2000), and 61% had less than 500 copies/mL of plasma HIV-RNA (table 1).

Respiratory cancers were the most frequent among lethal non-AIDS/non-hepatitis-related cancers (n = 65 including 53 lung cancers and 12 nose and throat cancers). Their proportion was stable between 2000 and 2005 (5 and 6%, respectively). Patients who died from respiratory cancers were older in median in 2005 (50 years) than in 2000 (46 years) and moderately immunosuppressed at time of death (median: 163 CD4/mm³) in 2005 but more than in 2000 (median: 262 CD4/mm³). Ninety-one percent of them had been previously

treated with antiretrovirals and 63% had less than 500 copies/mL of plasma HIV-RNA. Ninety percent of patients were smokers and 34% had excessive alcohol consumption.

A great increase in the proportion of lethal digestive cancers was observed from 2000 to 2005, especially pancreatic cancer responsible for 10 cases of death in 2005 *versus* three cases in 2000, whereas the proportion of anal cancers remained stable. The rate of lethal hemopathies, including Hodgkin's lymphoma, remained similar between 2000 and 2005. Seven patients died from breast cancer in 2005 but none in 2000, and 10 patients died from skin cancer (four melanoma and six non-melanoma) *versus* two patients in 2000.

Hepatocarcinoma was mainly associated with hepatitis C coinfection in 2005 whereas aetiology was better balanced between hepatitis B and hepatitis C in 2000. Patients who died from hepatocarcinoma were 49 years-old in median and known to be HIV-infected for 15 years in median. Ninety-five percent of them had been previously treated with antiretrovirals, 69% had less than 500 copies/mL of HIV-RNA at time of death with a moderate immunosuppression (median of 231 CD4/mm³ in 2005 *versus* 157 CD4/mm³ in 2000). Thirty-eight percent of patients had excessive alcohol consumption.

Among AIDS events, the proportion of NHL-associated deaths (n = 103, including 16 primary brain NHL) was not different between 2000 and 2005 (11 and 10%, respectively) with CD4 cell count in the same magnitude (median: 86/mm³ in 2000 *versus* 76/mm³ in 2005, for systemic NHL). However, 32% of the patients who died from NHL had CD4 cell count above 200/mm³ at time of death. The proportion of lethal Kaposi sarcoma and cervical cancer remained similar during the two periods of survey.

Discussion

In this large national prospective survey specifically designed to assess the primary cause of death in HIV-infected patients, we showed that malignancies accounted for more than one third of the cause of death in this population of patients with a statistically significant progression since 2000.

The proportion of non-AIDS cancers also significantly increased from 2000 to 2005 although these patients had a median CD4 count at a similar level (218/mm³ in 2000 *versus* 205/mm³ in 2005). These results are consistent with those of the D:A:D study which showed that immunosuppression, as reflected by the latest CD4 count, was strongly associated with the risk of death from non-AIDS-defining malignancies, with a median CD4 cell count at 211 /mm³ at time of death [15]. The risk of non-AIDS cancer is higher in HIV-infected patients than in the general population [16, 17]. The increasing proportion of lethal non-AIDS-defining malignancies may be related first to this subpopulation ageing (46 years in 2000 *versus* 49 years in 2005) but also to a bad control of risk factors (ie, tobacco for respiratory cancers, Human papillomavirus infection for anal cancer). The increasing proportion of respiratory malignancies emphasizes the need for a better implementation of active smoking cessation programs. In addition, the increased proportion of lethal digestive cancers (especially pancreatic cancer) observed in this survey as well as that of lethal breast cancers (7 patients in 2005 *versus* none in 2000) are to be underlined.

The role of cART is still a matter of debate. Burgi et al showed that cART appeared to be beneficial in protecting against the development of malignant disease [18], whereas conflicting results have been reported in the D:A:D study especially for Hodgkin's disease [15]. This issue is thus to be specifically addressed in further studies in order to provides evidence-based recommendations for cART treatment in those patients. The beneficial role of

cART might be delayed for non-AIDS-defining causes of death, especially cancers. In this way, mortality rate was shown to reach a similar level to the general population in a subgroup of HIV-infected persons whose CD4 cell count was above $500/\text{mm}^3$, after several years of cART treatment [19]. Over this five-year period, the proportion of hepatitis-related hepatocarcinoma significantly increased confirming data observed in other series [20]. However, the proportion of hepatitis B-related hepatocarcinoma remained stable while a 3-fold increase was observed for hepatitis C-related hepatocarcinoma during the same time. The widespread use of antiretrovirals (eg, emtricitabine, tenofovir) efficient against hepatitis B virus might explain this discordant change over time. On the other side, we noticed an increased proportion of HCV-related hepatocarcinoma in this ageing population despite a better control of HIV disease (median CD4 count at $231/\text{mm}^3$ in 2005 *versus* $157/\text{mm}^3$ in 2000) suggesting that control of HCV is insufficient among HIV-infected patients.

Despite the widespread use of cART and improved management of long-term antiretroviral treatments, the proportion of AIDS-defining cancers and particularly NHLs did not decrease over time. NHL remained the most frequent AIDS-defining event leading to death. The incidence of NHL has decreased dramatically since the introduction of cART but less than the other opportunistic infections and remains stable since 1996 [21]. Moreover, the response rate and the survival rate remain poor (around 75%) particularly in patients with CD4 less than $100/\text{mm}^3$, history of previous opportunistic infections and poor general status [22]. As the risk of NHL occurrence clearly decreases as the CD4 count increases, the best way to prevent NHL could be to reach or maintain a high level of CD4 count [23]. However, other factors independent of immunosuppression like HIV and EBV replication may also have an impact on NHL occurrence risk [21-24].

In conclusion, this study showed a stable proportion of AIDS-cancers leading to death between 2000 and 2005 meanwhile an increasing proportion of patients dying from non-AIDS cancers was noticed in HIV-infected patients. These include lung cancers, nose and throat cancers, digestive and pancreas cancers, skin cancers, breast cancers and anal cancers. Cancer prevention, screening, early diagnosis and improved management should be included in routine long-term follow-up of HIV-infected patients and could have some immediate impact on mortality. Moreover, as the median CD4 level was below 250/mm³ in this population of HIV-infected patients, the therapeutic goal should be to maintain or to reach a CD4 count level as high as possible in addition to other usual prevention policy systematically implemented in this population, in order to prevent cancer-related deaths.

References

1. Centers for Disease Control and Prevention. 1993 revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults. *MMWR* **1992**; 41:1-19.
2. Lowsky R, Lipton J, Fyles G, et al. Secondary malignancies after bone marrow transplantation in adults. *J Clin Oncol* **1994**; 12:2187-92.
3. Curtis RE, Rowlings PA, Deeg HJ, et al. Solid cancers after bone marrow transplantation. *N Engl J Med* **1997**; 336:897-904.
4. Palella FJ Jr, Delaney KM, Moorman AC, et al. Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. HIV Outpatient Study Investigators. *N Engl J Med* **1998**; 338:853-60.
5. CASCADE Collaboration. Survival after introduction of HAART in people with known duration of HIV-1 infection. *Lancet* **2000**; 355:1158-9.
6. Bonnet F, Morlat P, Chêne G, et al. Causes of death among HIV-infected patients in the era of highly active antiretroviral therapy. *HIV Medicine* **2002**; 3:195-9.
7. Lewden C, Salmon D, Morlat P, et al. Causes of death among HIV-infected adults living in industrialized countries. A national study over the year 2000. *Int J Epidemiol* **2005**; 34:121-30.
8. Sackoff JE, Hanna DB, Pfeiffer MR, Torian LV. Causes of death among persons with AIDS in the era of highly active antiretroviral therapy: New York City. *Ann Intern Med* **2006**; 145:397-406.

9. Petoumenos K, Law MG. Risk factors and causes of death in the Australian HIV Observational Database. *Sex Health* **2006**; 3:103-12.
10. Palella FJ Jr, Baker RK, Moorman AC, et al. Mortality in the highly active antiretroviral therapy era: changing causes of death and disease in the HIV Outpatient Study. *J Acquir Immune Defic Syndr* **2006**; 43:27-34.
11. Sabin CA, Smith CJ, Youle M, et al. Deaths in the era of HAART: contribution of late presentation, treatment exposure, resistance and abnormal laboratory markers. *AIDS* **2006**; 20:67-71.
12. The Data Collection on Adverse Events of Anti-HIV Drugs Study Group. Liver-related deaths in persons infected with the human immunodeficiency virus: the D:A:D study. *Arch Intern Med* **2006**; 166:1632-41.
13. Bonnet F, Lewden C, May T, et al. Malignancies-related causes of death at the era of HAART: The French survey "Mortalité 2000". *Cancer* **2004**; 101:317-24.
14. International Classification of Diseases. Tenth Revision ed. Geneva: World Health Organization; 1993.
15. The Data Collection on Adverse Events of Anti-HIV Drugs (D:A:D) Study group. HIV-induced immunodeficiency and mortality from AIDS-defining and non-AIDS-defining malignancies: The D:A:D Study. *AIDS* (In press)
16. Herida M, Mary-Krause M, Kaphan R, et al. Incidence of non-AIDS-defining cancers before and during the highly active antiretroviral therapy era in a cohort of human immunodeficiency virus-infected patients. *J Clin Oncol* **2003**; 21:3447-53.
17. Clifford GM, Polesel J, Rickenbach M, et al. Cancer risk in the Swiss HIV Cohort study: associations with immunodeficiency, smoking, and highly active antiretroviral therapy. *J Nat Cancer Inst* **2005**; 97:425-32.

18. Burgi A, Brodine S, Wegner S, et al. Incidence and risk factors for the occurrence of non-AIDS-defining cancers among human immunodeficiency virus-infected individuals. *Cancer* **2005**; 104:1505-11.
19. Lewden C, Chene G, Morlat P, et al. HIV-infected adults with a CD4 cell count greater than 500 cells/mm³ on long-term combination antiretroviral therapy reach same mortality rates as the general population. *J Acquir Immune Defic Syndr* **2007**; 46:72-7.
20. Rosenthal E, Pialoux G, Bernard N, et al. Liver-related mortality in human-immunodeficiency-virus-infected patients between 1995 and 2003 in the French GERMIVIC Joint Study Group Network (MORTAVIC 2003 Study). *J Viral Hepat* **2007**; 14:183-8.
21. Bonnet F, Balestre E, Thiébaud R, et al. Factors associated with the occurrence of AIDS-related non-Hodgkin lymphoma in the era of highly active antiretroviral therapy: Aquitaine Cohort, France. *Clin Inf Dis* **2006**; 42:411-7
22. Boué F, Gabarre J, Gisselbrecht C, et al. Phase II trial of CHOP plus rituximab in patients with HIV-associated non-Hodgkin's lymphoma. *J Clin Oncol* **2006**; 24:4123-8.
23. CASCADE collaboration. Systemic non-Hodgkin lymphoma in individuals with known date of HIV seroconversion: incidence and predictors. *AIDS* **2004**; 18:673-81.
24. Bonnet F, Jouvencel AC, Parrens M, et al. A longitudinal and prospective study of Epstein-Barr virus load in AIDS-related non-Hodgkin lymphoma. *J Clin Virol* **2006**; 36:258-63.

Table 1: Patients' characteristics according to the underlying cause of death (NHL, hepatitis-related hepatocarcinoma, non-AIDS/non-hepatitis cancers, and non-cancer causes) - The Mortalité 2005 survey.

	NHL (N = 84)	Hepatitis-related hepatocarcinoma (N = 37)	Non-AIDS/non-hepatitis cancers (N = 173)	Non-cancer deaths (N = 676)
Gender male (%)	81	81	80	74
Age (years, median, IQR)	48 [41-55]	49 [45-56]	49 [45-58]	45 [40-53]
Duration of HIV infection (years, median, IQR)	9.6 [0.9-15.0]	15.4 [10.5-17.9]	11.7 [6.6-16.1]	11.9 [5.6-17.0]
AIDS stage (%)	100	43	48	62
CD4 count (/mm ³ , median, IQR)	76 [20-239]	231 [116-367]	205 [75-360]	172 [41-361]
CD4 > 500/mm ³ (%)	7	11	11	14
Previous antiretroviral treatment (%)	88	95	90	86
ARV treatment duration (years, median, IQR)	7.8 [0.8-11.0]	9.7 [6.3-12.1]	8.2 [5.3-10.9]	8.2 [4.2-10.9]
HIV-RNA < 500 copies/mL (%)	48	69	61	43
Intravenous drug user (%)	15	62	23	33
Hepatitis C (%)	15	78	29	42
Hepatitis B (%)	8	23	9	13
Poor socio-economic conditions (%)	25	16	22	34
Alcohol (%)	13	38	26	33
Tobacco (%)	39	56	63	58

IQR: interquartile range; HIV: human immunodeficiency virus; AIDS: acquired immunodeficiency syndrome;

ARV: antiretroviral treatment;

Table 2: Cancer-related causes of death. The Mortalité 2000 and the Mortalité 2005 surveys.

	Mortalité 2000		Mortalité 2005		p-value
Documented deaths (<i>reported</i>)	924 (964)		1013 (1042)		
Cancer-related causes of death	269	(29%)	344	(34%)	0.02
Cancer aetiology					
AIDS	149	(55%)	134	(39%)	-
Hepatitis	17	(6%)	37	(11%)	0.03*
Non-AIDS/non-hepatitis-related	103	(38%)	173	(50%)	0.01*
AIDS	n=149		n=134		
Non Hodgkin lymphoma	105	(11%)	103	(10%)	
Kaposi sarcoma	40	(4%)	25	(3%)	
Cervical cancer	4	(<1%)	6	(<1%)	
Hepatitis-related	n=17		n=37		
Hepatitis C	8	(1%)	28	(3%)	
Hepatitis B	7	(<1%)	6	(<1%)	
Hepatitis B and C	2	(<1%)	3	(<1%)	
Non-AIDS/non-hepatitis-related	n=103		n=173		
Respiratory	50	(5%)	65	(6%)	
Lung	44		53		
Nose and throat	6		12		
Digestive	6	(<1%)	13	(3%)	
Pancreas	3	(<1%)	11	(1%)	
Anal	6	(<1%)	11	(1%)	
Skin	2	(<1%)	10	(1%)	
Hodgkin's lymphoma	12	(1%)	9	(<1%)	
Other hemopathies	5	(<1%)	8	(<1%)	
Breast	3	(<1%)	7	(<1%)	
Central nervous system	4	(<1%)	6	(<1%)	
Others**	12	(1%)	33	(3%)	

*Comparisons are adjusted on age and gender

**See Appendix for details

Appendix

“Other” causes of death observed in the Mortalité 2000 and Mortalité 2005 studies.

Mortalité 2000: unknown origin (N=4), prostate (N=3), uterus (N=1), hepatocarcinoma (N=1), intrahepatic bile duct (N=1), connective and soft tissue (N=1), penis (N=1), bladder (N=1).

Mortalité 2005: Unknown origin (N=15), hepatocarcinoma (N=4), ovary (N=2), prostate (N=2), uterus (N=2), penis (N=2), bladder (N=2), head face and neck (N=1), kidney (N=1), intrahepatic bile duct (N=1), mandible (N=1).

Mortalité 2005 (ANRS EN19) Group, in collaboration with Mortavic Group

Available on <http://etudes.isped.ubordeaux2.fr/M2005/TELECHARGTS/M2005_GroupeEtude.pdf>

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Financial support

ANRS (CSS5) Agence Nationale de Recherches sur le Sida et les Hépatites Virales

Other supports

CMIT Collège des Universitaires de Maladies infectieuses et Tropicales

SFLS Société Française de Lutte contre le Sida

SNFMI Société Nationale Française de Médecine Interne

SPILF Société de Pathologie Infectieuse de Langue Française

ADELFA Association des Epidémiologistes de Langue Française

GERMIVIC Groupe d'Etude et de Recherche en Médecine Interne et Maladies Infectieuses sur le
Virus de l'hépatite

FPRRH Fédération des Pôles de Références et Réseaux Hépatites

AFEF Association Française Etude du Foie

SRLF Société de Réanimation de langue Française

SPLF Société de Pneumologie de Langue Française

Mortalité 2005 (ANRS EN19) in collaboration with Mortavic, List of participants

Available on <http://etudes.isped.u-bordeaux2.fr/M2005/TELECHARGTS/M2005_ListeParticipants.pdf>

Abbeville S Redecker / **Agen** Y Imbert P Rispal / **Aix En Provence** T Allegre J Riou M Marquant / P Undreiner/ **Ajaccio** J Abino / **Albi** P Barel / Greziller/ **Alencon** Gosse/ **Ales** A Lagier D Bastide / **Amiens** J Schmit N Decaux / **Angers** J Chennebault P Fialaire P Abgueguen J Loison / **Annecy** J Gaillat / **Annonay** E Legrand / **Antibes** **Juan Les Pins** J Dor D Quinsat L Lerousseau Chavillon E Toquet-Maillet / **Argenteuil** L Sutton P Genet / **Arlés** J Salord / **Arpajon** G Raison / **Arras** D Dubois / Y Lierman J Bervar / **Auch** B Castan / **Aulnay Sous Bois** D Malbec J Delassus / **Auxerre** R Bakir / **Avignon** G Lepeu G Pichancourt A Theodourou-Touchais / Olivier A De La Blanchardiere / **Bar Le Duc** P Evon / Y Aubry/ **Basse Terre** B Giffo / **Bayonne** F Bonnal S Labarrere / **Bazas** M Amanieu / **Beauvais** D Valet / **Belfort** J Faller P Eglinger F Duchene / **Besancon** P Humbert / J Dupond / J Estavoyer B Hoen C Roche C Chirouze J Faucher / **Beziers** E Oziol A Saad M Cabrol / **Blaye** P Gateau S Seiberras / **Blois** C Vidal / A Mazari / **Bobigny** M Bentata P Honore / O Bouchaud / **Bois Guillaume** C Bessin / **Bondy** V Jeantils S Tassi / O Fain / **Bordeaux** M Dupon / P Morlat J Beylot D Lacoste M Bonarek N Bernard F Bonnet / J Ragnaud / M Longy-Boursier P Mercie / C Series / **Bordeaux Armees** B Portal F Terrier / **Boulogne** E Rouveix C Olivier / J Vaillant / **Boulogne Billancourt** S Moulias / T Hanslik / **Bourg En Bresse** P Granier / T Colucci/ **Bourges** M Mornet / L Aaron Y Guimard J Agbodjan J Julien / **Bourgoin Jallieu** M Fabre / **Brest** M Garre / Gouerou O Savary J Nousbaum / **Brest Armees** H Granier / **Briancon** P Brousse / **Caen** R Verdon P Feret / Guivarch/ **Cahors** S Sire / **Cannes** P Simonet S Tempesta B Vialatte / **Castres** L Prudhomme / **Cayenne** F Djossou S Bichat M Nacher P Couppie / **Chalon Sur Saone** Dellinger / **Chalons En Champagne** J Picard / Sabbagh/ **Chambery** O Rogeaux / **Charleville Mezieres** C Penalba / **Chartres** C Aubert/ **Chaumont** C Alba/ **Clamart** P Galanaud A Delavalle F Boué / G Defuentes / **Clermont De L'oise** J Pik / **Clermont-Ferrand** H Laurichesse J Beytout L Cormerais / **Clichy** B Fantin A Uludag / J Mantz J Cohen / **Colmar** F Kohser / N Plaisance G Blaison M Martinot / **Colombes C Minozzi** C Ferreira F Zeng / **Compiègne** Y Domart D Merrien D Zylberait / **Corbeil-Essonnes** A Devidas I Turpauld P Chevojon / **Coulommiers** M Bardet / **Coutances** P Jacquemard / **Creteil** A Sobel C Jung C Dumont / M Chousterman / B Housset L Bassinet / F Schortgen / **Dax** P Lose / **Desertine** O Antoniotti E Nehme / **Digne Les Bains** P Granet Brunello / **Dijon** H Portier M Grappin M Buisson M Duong C Braconnier A Waldner-Combernoux/ **Dinan** J Laine / **Dole** A Brousse / **Douai** G Cardon / F Visticot / **Draguignan** M Vella/ **Dunkerque** F Bonnevie / Vanrenterghem/ **Eaubonne** T Soupison / N Gruat / J Roche Sicot J Saraux A Lepretre L El Hajj / J Roche Sicot J Saraux A Lepretre L El Hajj / **Ecrouves** Frossard/ **Elbeuf** M Brung Lefebvre / **Epinal** I Beguinot H Schuhmacher / **Etampes** J Hirsch / **Evreux** / G Reumont / Saad/ **Eysses Galan**/ **Foix** Estebe/ **Fort De France** A Cabie S Abel / D Quist / **Frejus** E Counillon R Armero P Del Giudice / **Frelinghien** V Gamblin / **Fresnes I Bouchard** / **Garches** P De Truchis H Berthe / **Grenoble** P Leclercq C Brambilla E Gineste F Sarrot-Reynauld / Jenny/ **Ingwiller** J Class / **Ivry Sur Seine** A Raynaud-Simon / **Kourou** F Alvarez / **La Roche Sur Yon** P Perre O Aubry I Suaud / **La Rochelle** I Courbes B Batejat / **La Teste De Buch** A Dupont / **Lagny Sur Marne** P Lagarde F David-Ouaknine / **Landerneau** E Le Moigne / **Langon** B Caumont / **Laon** M Robin / **Laval** J Hoel / **Le Chesnay** J Doll P Colardelle S Roussin-Bretagne / A Greder Belan / J Bedos F Bruneel / **Le Grand Luce** F Thibous Lemeunier / **Le Kremlin Bicetre** J Delfraissy C Goujard M Rannou / **Le Port** P Wind/ **Le Puy En Velay** B Monange / **Lens** C Lamblin K Cochonot / M Balquet / **Levallois Perret** D Champetier De Ribes G Force / **Libourne** J Ceccaldi / J Marcos / **Lille** Y Hammou / X Codaccioni / **Limoges** P Weinbreck C Genet / M Debette-Gratien / **Lisieux** L Geffray / **Longjumeau** Y Le Mercier / **Longuenesse** Follet/ **Lons Le Saunier** B Duvert / Lacroix/ **Loudun** A Arnaud / **Lure** Y Selles / F Levasseur/ **Lyon** J Touraine F Jeanblanc / C Trepo N Benmakhlouf B Lebouche / D Peyramond A Boibieux C Chidiac C Delorme / E Carbonnel / V Baty / **Macon** J Kisterman X Roubert / **Mantes La Jolie** F Granier F Tremolières C Billy V Perronne / **Marmande** J Testaud / **Marseille** J Gastaut M Drogoul G Fabre / J Moreau E Vanderghenst / M Bourliere / J Ruiz / P Philibert / T Gamby / N Petit / **Marseille Armées** F Simon / **Maubeuge** Fontaneau/ **Mende** P Meissonnier / **Menton** J Bayada / **Metz** B Christian A Armand / **Metz Armees** M Galzin / **Millau** D Dumas / **Mont De Marsan** S De Witte / **Montbeliard** J Jobard / **Montelimar** A Poncet / B Caillet / **Montpellier** J Reynes C Merle De Boever M Siffert A Bourgeois A Villadoro C

Tramoni / V Faucherre / D Larrey / O Jonquet Landreau / **Montreuil** M Andre C Winter / **Morlaix** C
 Roge / **Mulhouse** G Beck-Wirth B Drenou M Benomar / **Nanterre** M Ruel K Chemlal / **Nantes** F
 Raffi P Morineau-Le Houssine C Guerbois Le Bavec / F Lemesre / **Narbonne** B Masson / **Nemours** F
 Loison M Razafimahery / **Nevers** J Lebas De Lacour / **Nice** P Dellamonica V Mondain-Miton E Cua
 N Oran L Valerio / E Rosenthal J Fuzibet / A Tran / P Brocker / P Barrelier / **Nimes** D Vincent J
 Mauboussin C Barbuat I Rouanet / N Jourdan / A Sotto F Del Bucchia J Jourdan / **Niort** M Lapine /
Noumea P Capdevielle / **Noumea Nouvelle Caledonie** F Lacassin-Beller F Droetto / **Noyon** G Diab F
 Grihon / **Orleans** P Arsac / L Hocqueloux / **Orsay** M Levasseur / **Paimpol** M Fourdilis / **Papeete** P
 Jarno / **Paris** J Derouineau / P Morel F Timsit / A Compagnucci / E Oksenhendler L Gerard J Delgado
 / D Sereni C Lascoux-Combe / J Viard B Dupont A Maignan / J Bergmann P Sellier J Magnier / G
 Pialoux V Godard A Goetschel M Lebrette / L Weiss D Tisne-Dessus / C Leport J Ecobichon U
 Colasante / L Guillevin D Salmon-Ceron M Pietri A Brunet B Silbermann P Blanche / H Schoen M
 Valantin P Hausfater V Martinez / S Herson A Simon C Brancon / P Girard A Begle G Raguin C
 Lupin / J Molina D Ponscarne V Garrat P Cabotin M Janier E Spindler / P Yeni J Gerbe / J Cabane /
 J Ziza J Aerts / J Carlet J Gilquin I Auperin B Misset A Crof / J Piette P Cacoub / G Turpin / B Varet /
 N Dupin / C Le Jeunne E Aslangul / S Pol / T Poynard P Lebray / N Carbonell / P Benlian / M Goujon
 / J Dhainaut J Charpentier / J Andrieu / M Brunel / N Landgraf / M Bary / **Pau** Pouyanne/ **Perigueux** J
 Meraud / C Riviere / **Perpignan** H Aumaître M Saada / H Cros / **Pessac** J Pellegrin R Adjeoda /
Pierre Benite I Durieu H Rousset D Vital-Durand / **Pointe A Pitre** I Lamaury M Sow / **Poissy** D
 Hillion H Masson / **Poitiers** B Becq-Giraudon G Le Moal / C Silvain / **Pontoise** O Danne L Blum /
Quimper J Larzul P Perfezou / **Reims** C Rouger / J Novella / **Rennes** C Michelet P Tattevin C
 Arvieux F Souala M Delmont-Hanry D Guyader / V Gandemer / C Camus / Taverson/ **Roanne** M
 Lutz / **Rochefort** M Climas / **Roubaix** J Wemeau / **Rouen** I Gueit P Suel / F Caron / **Saint Denis** D
 Mechali M Khuong-Josses / **Saint Die Des Vosges** Y Etienne / **Saint Etienne** F Lucht A Fresard V
 Ronat / Vergnon / Garcier/ **Saint Girons** J Deluca / **Saint Laurent Du Maroni** A Randrianjohany /
Saint Omer H Monnot / **Saint Pierre De La Réunion** P Poubeau H Andre / **Saint-Brieuc** C Beuscart
 / M Aubry/ **Saint-Denis** E Hurbin/ **Saint-Mande** T Debord C Rapp / **Saint-Martin** F Bissuel V
 Walter / **Saint-Martin-De-Re** J Ferret/ **Saint-Michel** M Bonnefoy A Riche / **Saint-Nazaire** J Marot C
 Michau / **Saintes** E Bonnin / T Padeloup / **Salouel** G Chaby / **Sarrebourg** E Grilliat / **Saverne** E
 Wurtz / F Loth / **Sete** B Kitschke / **Soissons** D Line / **St Denis De La Réunion** C Gaud C Sautron / **St**
Etienne P Cathebras / **St Germain En Laye** Y Welker / **St Nazaire** D Sandron / **Strasbourg** J Lang P
 Fischer / J Pasquali H Lalanne / C Chartier / C Berlin / E Andres / D Christmann Y Hansmann / P
 Fraisse / **Suresnes** O Bletry D Zucman C Majerholc / M Stern L Couderc / **Tarbes** J Petitou /
Thionville F Truchetet J Pouaha / **Thonon Les Bains** P Romand / **Toulon** A Lafeuillade V Lambry /
Toulon Naval P Bernard / **Toulouse** D Adoue M Duffaut / B Marchou D Garipuy L Cuzin / B
 Marchou D Garipuy L Cuzin / M Uzan / J Vinel S Metivier / A Didier R Rouquet / **Tourcoing** Y
 Mouton Y Yazdanpanah F Marysse / B Guery K Faure / **Tours** J Besnier P Le Bret P Nau H
 Sigogneau / **Troyes** J Bressieux E Libbrecht L Rezzouk / **Tulle** A Collignon/ **Valence** B Ponceau /
Valenciennes X Kyndt / A Vermersch-Langlin / **Vandoeuvre Les Nancy** T May C Burty / P Lederlin
 / **Vannes** Y Poinsignon / **Verdun** C Creusat / **Vernon** C Richard / **Vesoul** C Merle/ **Vierzon** A
 Essayan / **Villejuif** D Vittecoq C Bolliot / **Villenauxe-La-Grande** Quignard/ **Villeneuve St Georges**
 O Patey S Dellion / **Villeneuve/Lot** I Chossat.