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Management of chronic hepatitis C in French departments of internal medicine and infectious diseases

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SUMMARY

This prospective, multicentre study was conducted during 2–30 April 2001 in the internal medicine/infectious diseases services in France and included data from 1858 hepatitis C virus (HCV)-infected patients, half of whom were HIV co-infected. The aims were to outline the type of pre-therapeutic evaluation of HCV infection performed (HCV RNA, genotype, liver biopsy); determine the proportion and characteristics of patients receiving antiviral treatment; and determine if any changes in these parameters had occurred between 1995 and 2001. Patients whom had a complete pre-therapeutic evaluation (39%, 709/1834) and received antiviral treatment (38%, 690/1830) were more likely to have abnormal liver biochemistry, cirrhosis and cryoglobulinaemia ($P<0{\cdot}001$). Injecting drug users and HIV-co-infected patients were less likely to have a complete pre-therapeutic evaluation or receive antiviral treatment ($P<0{\cdot}001$). A complete pre-therapeutic evaluation was more often performed in 2001 than in 1995 (39% *vs.* 6%, $P<0{\cdot}001$), including qualitative HCV RNA testing (91% *vs.* 68%, $P<0{\cdot}001$), genotyping (59% *vs.* 7%, $P<0{\cdot}001$) and a liver biopsy (60% *vs.* 29%, $P<0{\cdot}001$). The frequency of anti-HCV treatment approximately doubled between 1995 and 2001 (20% *vs.* 38%, $P<0{\cdot}001$). Although adherence to consensus recommendations regarding pre-therapeutic evaluation is not ideal, a substantial improvement has occurred since 1995. Nevertheless, means of increasing the availability of antiviral therapies, particularly for patients with HIV co-infection or injecting drug use, require further study.

INTRODUCTION

Chronic infection with the hepatitis C virus (HCV) is a major public health problem. Approximately 1–2% of North Americans and Western Europeans are chronically infected and at risk of complications

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including end-stage liver disease and hepatocellular carcinoma [1]. Since most infected individuals are unaware of their HCV status, widespread serological screening of at-risk groups, including injecting drug users and those exposed to potentially contaminated blood products, has been implemented. In France, where an estimated 600 000 individuals are chronically infected, screening efforts have identified a large population of HCV-infected patients [2, 3]. Although traditionally managed by gastroenterologists and hepatologists, other physicians, such as internists and infectious disease specialists, have assumed a significant proportion of this patient burden. This situation may be considered analogous to the early years following the discovery of the human immunodeficiency virus (HIV), during which physicians in specialized HIV referral centres provided most patient care. As the gravity of this epidemic emerged, the important role of other physicians, including internists, became evident.

In a previous multicentre study by our group, we profiled HCV-infected patients evaluated in the internal medicine and infectious diseases (IM/ID) services in France in 1995 [4, 5]. In this study, the majority of patients were young males infected through injecting drug use; with a high prevalence (56%) of HIV co-infection. Since this study, considerable progress has been made in the management of chronic hepatitis C. In the mid-1990s, interferon monotherapy was the mainstay of treatment, but this therapy led to sustained virological clearance in $<20\%$ of patients [6]. Recent therapeutic advances, including the combination of pegylated interferon alpha and ribavirin, have increased the rate of response to 45–80%, depending on pre-treatment patient characteristics [7–10]. Several consensus conferences have recommended that the decision to initiate such treatment be based on patient parameters including HCV genotype, viral load and liver histological severity [11–13]. However, despite these efforts, the number of infected patients investigated according to these guidelines and subsequently receiving antiviral treatment remains low. Data from two French regional registries revealed that a liver biopsy was performed in $<30\%$ of patients and antiviral treatment was initiated in only 13% [14, 15]. Moreover, data regarding the management practices of physicians other than gastroenterologists and hepatologists is limited.

Therefore, we conducted an updated epidemiological survey of HCV management in the IM/ID services that had participated in our original 1995 study. Our principal objectives were to: (1) determine epidemiological and clinical characteristics of HCV-infected patients evaluated in these departments in 2001; (2) outline the type of pre-therapeutic evaluation performed and predictors of a complete assessment; and (3) determine the proportion and characteristics of patients receiving antiviral treatment. Finally, we aimed to determine if any significant changes in these parameters had occurred between 1995 and 2001, potentially reflecting implementation of recent consensus recommendations and/or improvements in available therapies.

PATIENTS AND METHODS

The IM/ID services of 89 French university and general hospitals participating in the work of the GERMIVIC Study Group were mailed a data collection sheet in January 2001. The questionnaire (available from the authors upon request) was identical to that used during the 1995 study [4, 5] and contained information regarding the date of diagnosis of HCV, patient demographics, presumed mode of transmission, biochemical and clinical characteristics at the time of diagnosis, viral co-infections, virological and histological testing performed, and anti-HCV treatment. Participating centres were asked to provide complete information for each HCV-infected patient [defined by positivity of a third-generation enzyme-linked immunosorbent assay (ELISA)] assessed during the study interval of 2–30 April 2001.

Complete pre-therapeutic evaluation was defined as the combination of HCV RNA by polymerase chain reaction assay (qualitative or quantitative), HCV genotype testing and a liver biopsy. HIV co-infection was defined as positivity of both ELISA and Western blot assays. Hepatitis B virus (HBV) seropositivity was defined as the presence of at least one of the following markers: hepatitis B surface antigen, antibodies to the hepatitis B surface antigen, or antibodies to the hepatitis B core antigen. Abnormal liver biochemistry was defined as at least one abnormal value of alanine aminotransferase, aspartate aminotransferase, gamma-glutamyl-transpeptidase and total bilirubin. All cases of hepatocellular carcinoma required histological confirmation.

Statistical analysis

Categorical variables were compared using Fisher's exact and χ^2 tests and continuous variables using

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Mann–Whitney and Student's t tests, as appropriate. Stepwise multiple logistic regression analysis was used to assess independent associations. Variables included in the multivariate analyses were selected based on the results of univariate analyses ($P<0{\cdot}05$). All tests were two-sided and a P value of $<0{\cdot}05$ was considered statistically significant. All statistical analyses were performed using SAS version 8.1 software (SAS Institute Inc., Cary, NC, USA).

RESULTS

Of the 89 IM/ID services that were contacted, 60 (67%) answered with information regarding 1858 HCV-infected patients; 58% of these patients were evaluated in internal medicine services. Patients were distributed roughly equally throughout France [Ile-de-France region including Paris and surrounding areas, 667 (36%); southern France, 466 (25%); and other regions, 725 (39%)]. The principal characteristics of the 1858 patients are outlined in Table 1. The average ($\pm$S.D.) age was 44 ± 12 years and the majority were male (64%) and of French origin (74%). Clinically evident cirrhosis was present in 11% and hepatocellular carcinoma in 0·8%. In 9%, extra-hepatic manifestations were present including cryoglobulinaemic vasculitis in 62 (3·4%). Other autoimmune manifestations were diagnosed in 40 patients (2·2%) including hyper- or hypo-thyroidism ($n=11$), positive rheumatoid factor ($n=7$), polyneuropathy ($n=6$), Sjögren syndrome ($n=6$), immune thrombocytopenic purpura ($n=3$), haemolytic anaemia ($n=2$) and systemic lupus erythematosus, rheumatoid arthritis, erythema nodosum, autoimmune glomerulonephritis and uveitis ($n=1$ each). Half of the patients were HIV-co-infected and at least one serological marker of HBV infection was present in 14% of patients.

Analysis according to pre-therapeutic evaluation and antiviral treatment

A complete pre-therapeutic evaluation (HCV RNA, HCV genotype and liver biopsy) was performed in 709 patients (39%). Patients with a complete assessment were older and more likely to be male, of French origin and to have abnormal liver biochemistry, cirrhosis and extra-hepatic manifestations including cryoglobulinaemia ($P<0{\cdot}001$, Table 2). By multivariate analysis, characteristics independently associated with a complete assessment included the presence of abnormal liver biochemistry [odds ratio (OR) 2·01, 95% confidence interval (CI) 1·55–2·60, $P<0{\cdot}001$], cirrhosis (OR 2·29, 95% CI 1·59–3·31, $P<0{\cdot}001$) and cryoglobulinaemic manifestations (OR 2·46, 95% CI, 1·26–4·79, $P=0{\cdot}008$). Males (OR 0·77, 95% CI 0·61–0·98, $P=0{\cdot}03$), patients of non-French origin (OR 0·71, 95% CI 0·53–0·92, $P=0{\cdot}01$) and those with HIV co-infection (OR 0·53, 0·42–0·67, $P<0{\cdot}001$) were less likely to be fully assessed. Subsequent antiviral treatment was highly associated with a complete evaluation (OR 4·82, 3·82–6·08, $P<0{\cdot}001$).

Antiviral treatment (interferon alpha with or without ribavirin) was prescribed to 690 patients (38%). Compared with untreated patients ($n=1140$), treated patients were older, more often managed in southern France and more likely to have abnormal liver biochemistry, cirrhosis and cryoglobulinaemic manifestations ($P<0{\cdot}001$, Table 3). A complete pre-therapeutic evaluation was performed in 64% of subsequently treated *vs.* only 22% of untreated patients ($P<0{\cdot}001$). With regards to specific tests, a qualitative HCV RNA (95% *vs.* 89%), a quantitative HCV RNA (74% *vs.* 45%), HCV genotyping (85% *vs.* 44%) and a liver biopsy (93% *vs.* 41%) ($P<0{\cdot}001$ for all) were more common in treated patients. In multivariate analysis (Table 4), patients with abnormal liver biochemistry, cirrhosis, cryoglobulinaemic manifestations and a complete pre-therapeutic evaluation ($P<0{\cdot}01$) were more likely to be treated, whereas injecting drug users, patients with HIV co-infection and those with a new diagnosis of HCV during the study interval were less likely to be treated ($P<0{\cdot}001$ for all variables).

Analysis according to HIV co-infection

Table 5 outlines patient characteristics according to HIV status. By multivariate analysis, HIV co-infection was independently associated with transmission through injecting drug use (OR 6·07, 95% CI 4·73–7·79, $P<0{\cdot}001$), evaluation in the Ile-de-France region (OR 4·67, 95% CI 3·51–6·21, $P<0{\cdot}001$) and non-French origin (OR 2·43, 95% CI 1·84–3·22, $P<0{\cdot}001$) and negatively associated with cryoglobulinaemic manifestations (OR 0·25, 95% CI, 0·11–0·57; $P=0{\cdot}001$). In addition, HIV-positive patients were less likely to have been newly diagnosed with HCV during the study interval (OR 0·20, 95% CI 0·08–0·48, $P<0{\cdot}001$).

In the cohort of HIV/HCV-co-infected patients, multiple logistic regression analysis showed that a

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Table 1. *Principal characteristics of patients with chronic hepatitis C evaluated in the GERMIVIC centres during April 1995 and April 2001*

Characteristic	April 2001 ($n=1858$)	April 1995 ($n=2002$)	P value
Age, years (mean ± S.D.)	44 ± 12	43 ± 10	n.s.
Male sex, %	64	59	0·013
Geographic origin, %			
Metropolitan France	74	86	<0·001
North Africa	9·3	4·4	
Europe	11	4·1	
Black Africa	3·0	1·1	
Antilles	0·8	0·6	
Other	1·6	3·8	
New diagnosis of HCV during study, %	3·5	10·2	<0·001
Mode of transmission, %			
Transfusion	19	20	<0·001
Injecting drug use	57	61	
Needle-stick injury	1·0	0·8	
Unknown	23	18	
Symptoms/signs at diagnosis of HCV, %[a]			
Asymptomatic	34	47	<0·001
Abnormal liver biochemistry[b]	63	52	<0·001
Cirrhosis[c]	11	7·4	0·002
Hepatocellular carcinoma[d]	0·8	0·9	0·91
Cryoglobulinaemic manifestations	3·4	2·7	0·25
Autoimmune manifestations	2·2	3·0	0·12
Other extra-hepatic manifestations	3·4	2·5	0·10
Co-infections, %			
HIV	50	56	<0·001
HBV[e]	14	22	<0·001
Pre-therapeutic evaluation, %			
Qualitative HCV RNA	91	68	<0·001
Quantitative HCV RNA	56	33	<0·001
HCV genotype	59	6·7	<0·001
Liver biopsy	60	29	<0·001
Complete[f]	39	6	<0·001
Anti-HCV treatment, %	38	20	<0·001
In therapeutic protocol	30	35	0·08

HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus.

[a] Some patients have more than one sign/symptom; therefore, the total percentages are greater than 100%.

[b] At least one elevated value of alanine aminotransferase, aspartate aminotransferase, gamma-glutamyl-transpeptidase, or total bilirubin.

[c] Clinically evident cirrhosis (e.g. portal hypertensive bleeding, ascites, hepatic encephalopathy).

[d] Histologically confirmed hepatocellular carcinoma.

[e] At least one of: hepatitis B surface antigen, antibodies to hepatitis B surface antigen, and antibodies to hepatitis B core antigen.

[f] Combination of HCV genotyping, HCV RNA by polymerase chain reaction assay (qualitative or quantitative) and liver biopsy.

complete pre-therapeutic evaluation was independently associated with the presence of abnormal liver biochemistry (OR 2·22, 95% CI 1·47–3·34, $P<0·001$), cirrhosis (OR 2·79, 95% CI 1·50–5·17, $P<0·001$) and subsequent antiviral treatment (OR 7·19, 95% CI 4·92–10·5, $P<0·001$) and negatively associated with evaluation in southern France (OR 0·27, 95% CI 0·15–0·50, $P<0·001$). Anti-HCV treatment was

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Table 2. *Patient characteristics according to performance of complete pre-therapeutic evaluation in 2001*[a]

Characteristic	Complete evaluation ($n=709$)	Incomplete evaluation ($n=1125$)	P value
Age, years (mean ± S.D.)	45 ± 12	43 ± 12	<0·001
Male sex, %	59	67	<0·001
Geographic origin, %			
France	81	70	<0·001
Other	19	30	
Site of evaluation (GERMIVIC centre), %			
Ile-de-France	27	40	<0·001
Southern France	30	23	
Other	43	37	
New diagnosis of HCV during study, %	3	4	0·56
Mode of contamination, %			
Transfusion	23	16	<0·001
Injecting drug use	48	63	
Other	29	21	
Symptoms/signs at diagnosis of HCV, %			
Asymptomatic	24	41	<0·001
Abnormal liver biochemistry	73	57	<0·001
Cirrhosis	16	8	<0·001
Hepatocellular carcinoma	1	0·5	0·05
Cryoglobulinaemic manifestations	6	2	<0·001
Autoimmune manifestations	3	1	0·009
Co-infection, %			
HIV	34	59	<0·001
HBV	12	16	0·023
Anti-HCV treatment, %	63	22	<0·001

HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus.

[a] Combination of HCV genotyping, HCV RNA by polymerase chain reaction assay (qualitative or quantitative) and liver biopsy. Twenty-four patients with missing data are excluded.

associated with abnormal liver biochemistry (OR 2·00, 95% CI 1·31–3·07, $P=0·001$), cirrhosis (OR 4·84, 95% CI 2·57–9·14, $P<0·001$) and evaluation in southern France (OR 2·32, 95% CI 1·42–3·79, $P=0·0008$); it was negatively associated with transmission through injecting drug use (OR 0·49, 95% CI 0·32–0·75, $P<0·001$). Treatment was significantly more likely in the group of patients with a complete pre-therapeutic evaluation (OR 7·57, 95% CI 5·14–11·20, $P<0·001$).

Comparison of 1995 and 2001 surveys

A comparison of the characteristics of the patients evaluated in 1995 ($n=2002$) and 2001 ($n=1858$) revealed several important differences (Table 1). In 2001, the subjects were more often male, with an unknown mode of transmission, abnormal liver biochemistry and cirrhosis ($P<0·001$). On the other hand, patients seen in 2001 were less likely to be of French origin, contaminated through injecting drug use, HBV seropositive and co-infected with HIV ($p<0·001$).

A complete pre-therapeutic evaluation was more often performed in 2001 than in 1995 (39% *vs.* 6%, $P<0·001$). In particular, patients evaluated in 2001 were more likely to have qualitative HCV RNA testing, genotyping and a liver biopsy ($P<0·001$). The frequency of anti-HCV treatment approximately doubled between 1995 and 2001 (20% *vs.* 38%, $P<0·001$).

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Table 3. *Patient characteristics according to receipt of anti-HCV treatment in 2001*[a]

Characteristic	Treated ($n=690$)	Untreated ($n=1140$)	P value
Age, years (mean ± S.D.)	46 ± 12	42 ± 12	<0·001
Male sex, %	61	66	0·08
Geographic origin, %			
France	79	71	<0·001
Other	21	29	
Site of evaluation (GERMIVIC centre, %)			
Ile-de-France	27	41	<0·001
Southern France	33	20	
Other	40	39	
New diagnosis of HCV during study, %	0·1	5	<0·001
Mode of contamination, %			
Transfusion	26	14	<0·001
Injecting drug use	43	65	
Other	31	20	
Symptoms/signs at diagnosis of HCV, %			
Asymptomatic	23	41	<0·001
Abnormal liver biochemistry	74	57	<0·001
Cirrhosis	16	8	<0·001
Hepatocellular carcinoma	0·2	0·4	0·29
Cryoglobulinaemic manifestations	5	2	<0·001
Autoimmune manifestations	3	2	0·19
Co-infection, %			
HIV	34	59	<0·001
HBV	13	14	0·091
Complete pre-therapeutic evaluation, %[b]	64	22	<0·001

HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus.

[a] Interferon alpha (standard or pegylated) with or without ribavirin. Twenty-eight patients with missing data are excluded.

[b] Combination of HCV genotyping, HCV RNA by polymerase chain reaction assay (qualitative or quantitative) and liver biopsy.

DISCUSSION

Whereas previous epidemiological studies of chronic hepatitis C have focused on HCV management by hepatologists and gastroenterologists, this study has enabled us to define the principal patient characteristics and management strategies of French IM/ID departments. Although it is not possible to extrapolate the proportion of all French patients evaluated by these services, this perspective is clearly important considering the large number of patients evaluated during this 1-month study period ($n=1858$). The high response rate (67%) and the approximately even distribution of patients throughout France suggest that a representative sample of patients and physicians was obtained.

The low number of new HCV diagnoses made during the 2001 study period compared with that of 1995 (3·5% *vs.* 10·2%) may reflect the increased screening of at-risk individuals. Recent estimates suggest that the rate of screening of French HCV-infected patients has increased from 5% in 1995 to 60% in 1999 [16–18]. Modes of infection have varied only slightly; a minor decline in infection through injecting drug use has been counterbalanced by an increased rate of sporadic transmission. Interestingly, these findings are discordant with those of a similar study among French hepatologists and gastroenterologists in which the proportion of injecting drug users increased from 25% to 45% between 1991 and 1999 [19].

Table 4. *Principal characteristics associated with anti-HCV treatment in multivariate analysis in 2001*[a]

Variables	OR	95% CI	*P* value
Complete pre-therapeutic evaluation[b]	4·89	3·86–6·19	<0·001
Abnormal liver biochemistry	2·09	1·60–2·72	<0·001
Cirrhosis	2·10	1·43–3·09	<0·001
Cryoglobulinaemic manifestations	2·39	1·19–4·79	0·014
Management in southern France	1·33	1·11–1·75	0·04
New diagnosis of HCV during study	0·12	0·05–0·30	<0·001
HIV co-infection	0·58	0·45–0·76	<0·001
Injecting drug use	0·59	0·46–0·76	<0·001

OR, Odds ratio; CI, confidence interval; HCV, hepatitis C virus; HIV, human immunodeficiency virus.

[a] Interferon alpha (standard or pegylated) with or without ribavirin. Twenty-eight patients with missing data are excluded from this analysis ($n=1830$).

[b] Combination of HCV genotyping, HCV RNA by polymerase chain reaction assay (qualitative or quantitative) and liver biopsy.

Table 5. *Patient characteristics according to HIV status in 2001*

Characteristic	HIV+ ($n=905$)	HIV– ($n=909$)	*P* value
Age, years (mean ± S.D.)	40 ± 7	48 ± 14	<0·001
Male sex, %	69	59	<0·001
Geographic origin, %			
France	64	84	<0·001
Other	36	16	
Site of evaluation (GERMIVIC centre), %			
Ile-de-France	56	16	<0·001
Southern France	15	35	
Other	29	49	
New diagnosis of HCV during study, %	0·8	6	<0·001
Mode of contamination, %			
Transfusion	9	29	<0·001
Injecting drug use	77	37	
Other	14	34	
Symptoms/signs at diagnosis of HCV, %			
Asymptomatic	34	34	1·00
Abnormal liver biochemistry	62	65	0·17
Cirrhosis	9	13	0·006
Hepatocellular carcinoma	1	0·6	0·28
Cryoglobulinaemic manifestations	1	6	<0·001
Autoimmune manifestations	0·7	4	<0·001
HBV co-infection, %	21	8	<0·001
Complete pre-therapeutic evaluation, %[a]	27	50	<0·001
Anti-HCV treatment, %[b]	26	50	<0·001

HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus.

[a] Combination of HCV genotyping, HCV RNA by polymerase chain reaction assay (qualitative or quantitative) and liver biopsy. Forty-four patients with unknown HIV status are excluded.

[b] Interferon alpha (standard or pegylated) with or without ribavirin.

Compared with those evaluated in 1995, patients seen in 2001 appeared to present with more severe HCV-related disease, as demonstrated by a higher frequency of symptoms, abnormal liver biochemistry and cirrhosis at diagnosis. These results also differ from those reported in studies of gastroenterologists and hepatologists in which patients were generally younger, histological lesions milder (more mild hepatitis and less cirrhosis) and the prevalence of extra-hepatic manifestations was lower [14, 18]. Patients seen in IM/ID services are often diagnosed during the investigation with a related and often severe illness (e.g. cryogoglobulinaemic vasculitis) [20–22]. HIV co-infection, which undoubtedly accelerates the progression of HCV-related liver disease, is much more prevalent (50%) in patients evaluated in these departments. Although the number of liver biopsies performed in the GERMIVIC centres increased between 1995 and 2001, the observed biopsy rate (60%) is still lower than that reported among gastroenterologists and hepatologists (87%) [16, 19].

A complete pre-therapeutic evaluation including HCV RNA, HCV genotype and liver biopsy was more frequently performed in 2001 (39%) than in 1995 (6%). The frequency of HCV genotyping increased eightfold and liver biopsies doubled during the study interval. The strongest independent predictor of a complete evaluation was subsequent antiviral treatment (and vice versa). Although a 39% rate for the recommended pre-therapeutic testing seems disappointing from the point of view of a practice audit, the latter finding suggests that the surveyed physicians are practising cost-conscious medicine, that is, only fully investigating those patients who are candidates for antiviral therapy. Patients co-infected with HIV, particularly those contaminated through injecting drug use, were less likely to be fully investigated and subsequently treated. This finding is of concern considering recent studies documenting an increase in liver-related morbidity and mortality among these groups [23–29]. Patients seen during the 2001 study period were twice as likely to be treated as those in 1995 (38% *vs.* 20%). This rate is even higher if one considers only the HIV-negative cohort; half of these patients received interferon-based therapy in the 2001 study. This rate is higher than that recently reported in a US teaching hospital [30] where only 28% of 327 consecutive patients were treated. The predominant reasons for failure to treat in this study were non-adherence to evaluation procedures, medical or psychiatric contra-indications and ongoing substance abuse. These factors probably explain the lower likelihood of treatment observed in HIV-co-infected patients and injecting drug users. Although controversial, withholding treatment from injecting drug users does not appear totally justified and should be reconsidered in the coming years [12, 31, 32]. Some patients were treated outside of current recommendations. For example, in 15% of patients, HCV genotyping was not performed and 7% had no biopsy. Although the latter may reflect scepticism regarding the necessity of routine pre-treatment liver biopsy, extra-hepatic manifestations (independent of underlying liver disease) were the indication for treatment in some of these patients.

In summary, this epidemiological study confirms the importance of the role of the IM/ID services in the management of HCV-infected patients in France; in particular, the HIV-co-infected population. Although adherence to consensus recommendations regarding pre-therapeutic evaluation is not ideal, a substantial improvement has occurred since 1995. Complete assessments are largely limited to patients who are subsequently treated, suggesting the attempted conservation of limited health-care resources. Antiviral treatment is increasingly being offered to HCV-infected patients, particularly those with severe liver disease. Increasing use of antiviral therapies, particularly for patients with HIV co-infection, seems mandatory, particularly after the recent publications of pegylated interferon plus ribavirin treatment in such populations [33–36].

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APPENDIX

The GERMIVIC Study Group (Joint Study Group on Hepatitis C virus of the French National Society of Internal Medicine and the French Society of Infectious Diseases)

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