Letters to the Editor

Characteristics of chronic hepatitis C and response to interferon therapy in older patients

SIR—Patients with chronic hepatitis C are at high risk of cirrhosis and hepatocellular carcinoma [1], especially after age 50 [2]. We investigated the epidemiological, virological and histological characteristics of a large group of older patients with chronic hepatitis C virus and assessed the safety of interferon therapy and the response rate in this group.

Between 1993 and 2000 we studied 94 patients (41 men and 53 women), aged 65 or older (mean age 67.8, range 65–80) and referred for chronic hepatitis C virus infection. We excluded three patients who were hepatitis B surface antigen positive and 12 who had a history of heavy alcohol abuse (> 50 g/day).

All patients (except three who clinically decompensated cirrhosis) had a liver biopsy. These were graded for the degree of fibrosis and the histological activity index of Knodell et al. [3]. The annual progression of fibrosis was defined according to the formula described by the METAVIR co-operative group [4] and was calculated in 47 patients whose disease duration had been determined.

Twenty-three of these patients were selected for interferon therapy (3 MU of interferon-α2b three times a week) according to the severity of their liver disease. None had cirrhosis or hepatocellular carcinoma. A biochemical response was defined as normalization of alanine amino transferase (ALT) levels and a complete response as normalization of ALT levels and no detectable hepatitis C virus RNA, at the end of therapy and 6 months after the end of treatment. We noted side effects and quantified them during each visit. All results are expressed as mean ± SEM.

The main routes of contamination were blood transfusion (n = 50, 53.2%) or unknown (n = 43, 45.8%). One patient, a nurse, had acquired the virus from her working environment. Genotype 1b was predominant (n = 68, 72.34%). Among subjects contaminated by blood transfusion, 37 (74%) had genotype 1b, three (6%) genotype 1a and two (6%) genotype 2. Among those for whom the route of contamination was unknown, 29 (67%) had genotype 1b, three (7%) genotype 1a and two (4.6%) each genotypes 1 and 2. The global Knodell score was 9.36 ± 0.53. The histological activity index and fibrosis scores were 7.29 ± 0.41 and 2.09 ± 0.15 respectively. Twenty-four patients had cirrhosis (25.5%), 19 were Child’s A, two Child’s B and three Child’s C in the Child–Pugh classification. Six of them developed hepatocellular carcinoma during the follow-up. None had normal livers. The duration of the disease was estimated in 47 patients who had been contaminated by transfusion, giving a mean duration of 19 years (range 7–39). The annual fibrosis progression rate was 0.14 ± 0.023 fibrosis units per year in these patients.

Ten men and 13 women, mean age 66.8 years (range 65–72), were treated with interferon. Nineteen of these had genotype 1b (82.6%), one genotype 1a, one 2a, one 3a and one 5a. The global Knodell score was 11.2 ± 0.68 and the histological activity index and fibrosis scores were 8.9 ± 0.58 and 2.69 ± 0.24 respectively. The duration of disease was known in 13 patients; the mean duration was 18.3 years (range 10–34). A biochemical response was observed in five patients (15%) and a complete response in six (18%). The treatment was discontinued in five patients because ALT levels were still above the upper limit of normal after 3 or 6 months of therapy. Seven patients had to discontinue therapy because of severe side effects: one with severe asthenia, two with non-specific digestive troubles, two with depression, one with severe leucopenia and thrombocytopenia, and one with facial paralysis. We noted leucopenia in 17.3% of the subjects, hypertension in 13%, asthenia and digestive troubles in 8.6% and headache, skin reaction, depression, elevated thyroid-stimulating hormone or hyperglycaemia in 4.3% of patients respectively.

In this study, one of the characteristics of older patients with chronic hepatitis C was severe parenchymal liver disease. This confirms other studies that have already assessed the severity of disease in patients over 65 and shown that age might be one characteristic which determines the degree of liver disease, which is also reflected by the duration of exposure [5].

Our main histological finding is the fibrosis progression rate, one of the most interesting prognostic markers of hepatitis C virus infection that has never been specifically assessed in older patients with chronic hepatitis C. The mean fibrosis progression rate in the present study was 0.14 (SEM 0.023). This is similar to the rate found in a previous study in all patients with chronic hepatitis C regardless of age [4]. Although hepatitis C virus infection in older patients is no more severe than in younger patients, the duration of exposure is longer and histological lesions are more advanced, thus explaining the high percentage of cirrhosis [6].

Few studies have assessed the role of interferon in older individuals. We and others [7–9] have observed a biochemical response rate of around 30%. Thus, our study confirms that the use of interferon in older patients is as effective as in younger subjects. In our study, the types of side effects were similar to those described in younger adults but we had to stop treatments more often because patients could not tolerate them.
Letters to the Editor

Our study demonstrates that age is not a contra-indication to interferon therapy. Because of their severe liver disease, older patients should be given the opportunity to undergo treatment in order to avoid progression to cirrhosis and hepatocellular carcinoma. At present, combination therapy is the recommended treatment for chronic hepatitis C, but a high percentage of older people will not be eligible for this therapy because of the severe anaemia induced by ribavirine and may be candidates for pegylated-interferon. These patients should be treated and closely monitored.

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Creutzfeld–Jakob disease presenting as recurrent falls in an older person

SIR—Rare clinical conditions may present with common clinical presentations, such as falls, poor mobility and failing memory in older people.

We would like to share our experience of the difficulty we faced in arriving at the correct diagnosis in a 72-year-old woman who presented initially with a fractured neck of femur after a fall in the city centre. She was lucid during this admission but was noted to have intermittent jerky movements.

A few weeks after her discharge home, she was readmitted after another fall. Her son expressed worries about his mother’s unsteadiness, frequent falls and forgetfulness, although the physical examination was unremarkable during her time in acute medical care.

After her transfer for rehabilitation, her mental state deteriorated rapidly. She started to lose her comprehension skills and became mute. Initial preliminary blood investigations, computed tomography brain and magnetic resonance imaging scan were all normal. Her son’s persistent wish for a positive diagnosis led to the possibility of Creutzfeldt–Jakob disease or primary vasculitis of the central nervous system being raised by the visiting neurologist. Electroencephalogram and cerebrospinal fluid analysis were unhelpful. Gradually she developed definite myoclonus and rigidity before her death.

Her death was provisionally certified as being caused by Creutzfeldt–Jakob disease. This was confirmed at autopsy. On review of the neuropathological findings at the National Creutzfeldt–Jakob Disease Surveillance Unit in Edinburgh, the brain histology was found to show a widespread spongiform encephalopathy predominantly involving the basal ganglia and thalamus, with minor vacuolation in the cerebral and cerebellar cortex. Immunocytochemistry for prion protein gave a positive reaction in all areas of the grey matter, and Western blot analysis showed a prion protein, isoform type 2A. DNA analysis showed valine homozygosity at codon 129 in the prion protein gene. These histological and biochemical features are typical for sporadic Creutzfeldt–Jakob disease. The absence of genetic abnormalities in the prion protein gene addressed the family’s understandable fears of this being a potentially inheritable disorder.

It has been suggested that Creutzfeldt–Jakob disease is not being missed in elderly people [1] but this case indicates that (at least in some cases) it is diagnosed very late. The importance of suspecting this diagnosis in patients with rapid cognitive deterioration and its neuropathological confirmation at autopsy cannot be overemphasized.

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**An uncommon but important cause of severe chest pain in an older population**

SIR—A 71-year-old man presented with a 3-day history of severe retrosternal chest pain, vomiting and absolute dysphagia. This started while he was eating. He had self-medicated previously for reflux symptoms but had no other medical problems. A barium swallow showed a smooth intraluminal mass extending inferiorly. At endoscopy, a large haematoma was seen arising from the proximal oesophagus. His symptoms resolved with conservative management. A subsequent endoscopy showed only minor residual scarring.

Oesophageal haematomas in the absence of major trauma, initially thought to be rare events, are increasingly being recognized in older patients [1–7]. Usually there is a history of severe retrosternal pain, often triggered by the ingestion of a food bolus or by coughing or retching [2–7]. These factors are thought to damage submucosal blood vessels within the upper oesophagus either via direct trauma or indirectly through a sudden rise in intravascular pressure. Further bleeding leads to progressive submucosal dissection, severe pain and obstructive symptoms. Impaired haemostasis increases the risk of such bleeding and concomitant usage of anticoagulants or antiplatelet agents, thrombocytopenia and various coagulopathies have all been implicated as risk factors [3–7]. Hypertension has also been implicated, but this probably reflects the chance association of a common condition with a rarer one.

The major differential diagnosis is from cardiac pain, and features such as sweating, tachycardia and pallor may lead to confusion—particularly in an older person who may already have an abnormal electrocardiogram. In most cases, the presence of dysphagia and odynophagia points towards the correct diagnosis [6].

Barium swallow usually demonstrates a smooth filling defect lying posteriorly in the lower half of the oesophagus [2–5]. At endoscopy a blue/purplish swelling is often seen, often with mucosal ulceration. This can lead to the erroneous diagnosis of a malignancy [6].

Conservative management is appropriate, although dislodgement of the clot at endoscopy has occurred without reported adverse outcome [2]. Recurrence has been described but there are no data indicating whether anticoagulant or antiplatelet drugs influence this [6].

Oesophageal haematomas remain a rare but important differential cause of chest pain in an older population. With increasing use of warfarin and antiplatelet agents in a population at high risk of vascular diseases, the condition will become more common. Recognition is important, as confusion with cardiac pain could lead to the potentially fatal use of anticoagulation or thrombolysis.

**Letters to the Editor**

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**Short-term admission of acutely ill older people to nursing homes by general practitioners: a national questionnaire survey**

SIR—There are a variety of models of intermediate care designed to prevent older people being admitted to hospital [1–5]. We have become aware of a further model of intermediate care that has evolved over the past few years—so-called ‘general practitioner-led nursing home bed schemes’.

These schemes aim to act as an alternative to acute hospital admission. The general practitioner admits acutely ill older patients from their homes and retains clinical responsibility whilst they are being cared for in a nursing home. The admissions are limited in time, typically for 14 days. The schemes vary in other characteristics: whether a nursing co-ordinator visits the patient before admission, whether they run throughout the year and whether the general practitioners are paid an additional (non-general medical services) fee for the care of patients. We report details of all identifiable general practitioner-led nursing home bed schemes in England and Wales.

In the first phase, we sent 377 questionnaires to the chief executives of all the primary care groups in England and local health groups in Wales, and the ‘winter pressure leads’ of all the health authorities in England and Wales. We designed a short questionnaire to determine whether respondents were aware of any such scheme and, if so, to identify a key contact who would be best able to describe it. We received 227 responses
Letters to the Editor

(179 from primary care or local health groups and 48 from health authorities) after one reminder (response rate 60.2%). Of these, 88 respondents identified potential schemes and 106 gave key contacts.

In the second phase, we sent a detailed questionnaire to the 106 key contacts. This included questions that determined whether the scheme matched our definition and factual questions about the scheme. We received 57 responses after one reminder (response rate 53.7%). Seven schemes were identified twice. Four did not match the definition. Seven respondents reported schemes that had run in the past. Reasons for discontinuation included inadequate funding, lack of general practitioners’ awareness or enthusiasm leading to under-use of the scheme, concerns about availability of nursing home beds and ‘inappropriate admissions’. Three respondents reported that they were planning schemes. Eight respondents reported that they had never had a scheme and were not planning one. We therefore found 28 schemes that matched our definition.

In the third phase, we used structured telephone interviews with individuals representing the identified schemes, to clarify and to enlarge upon the details obtained on the questionnaire.

Details of the schemes are shown in Table 1. The median number of patients admitted to nursing homes per month was 5 (range 1–20), with 12 schemes admitting >10 per month. The median number of nursing homes admitting patients per scheme was 4 (range 1–20). Seventeen of the schemes paid the general practitioners an additional fee per patient. Twenty-two of the schemes run throughout the year, the remaining six during winter months only. A nursing co-ordinator visits patients before admission in 14 of the schemes.

This survey is part of the modelling phase of the evaluation of this complex intervention. It delineates its major components and shows that there are sufficient schemes to support further rigorous evaluation [6]. This model of care has not been described before.

We believe that our comprehensive survey identified most, if not all, such schemes in England and Wales. The schemes we identified varied considerably in size and organization, suggesting that they have been shaped by local needs and partnerships. Nationally, the effect of this model on emergency admission rates is likely to be small, since there are only 28 schemes. Important questions remain about the safety and cost-effectiveness of this model of care, the most effective

| Table 1. General practitioner (GP)-led nursing home schemes in England and Wales |
|---------------------------------|------------------|-------------------|------------------|------------------|
| Health authority               | No. of patients admitted/month | Pre-admission co-ordinator visit | GP fee | No. of nursing homes |
| Avon                           | 5                              | Yes                | Yes              | 1                |
| Bexley                         | 16                             | No                 | Yes              | 15               |
| Bury & Rochdale                | 20                             | Yes                | No               | 20               |
| Calderdale & Kirklees          |                                |                    |                  |                  |
| Dewsbury                       | 10                             | No                 | Yes              | 6                |
| Huddersfield                   | 20                             | Yes                | Yes              | 10               |
| Cambridge                      | 10                             | Yes                | No               | 3                |
| Dorset                         | 1                              | No                 | No               | 1                |
| Dudley                         | 10                             | Yes                | No               | 8                |
| Dyfed Powys                    | 10                             | No                 | Yes              | 1                |
| Ichyd Morganwrga               | 10                             | No                 | Yes              | 12               |
| Leeds                          | 5                              | Yes                | No               | 5                |
| Lincolnshire                   | 3                              | Yes                | Yes              | 1                |
| Liverpool                      | 18                             | Yes                | Yes              | 4                |
| North & East Devon             | 5                              | No                 | Yes              | 1                |
| North Wales                    | 5                              | Yes                | No               | 1                |
| North Norfolk                  | 5                              | Yes                | Yes              | 2                |
| Northumberland                 | 5                              | Yes                | Yes              | 15               |
| Portsmouth & South East Hampshire | 20                           | No                 | Yes              | 1                |
| Sandwell                       | 5                              | Yes                | No               | 4                |
| Shropshire                     | 5                              | No                 | No               | 1                |
| Solihull                       | 8                              | Yes                | Yes              | 1                |
| Somerset                       | 3                              | Yes                | Yes              | 1                |
| South West Devon               | 12                             | No                 | Yes              | 8                |
| Torbay                         | 13                             | No                 | Yes              | 3                |
| West Surrey                    | 2                              | No                 | Yes              | 4                |
| Wiltshire                      |                                |                    |                  |                  |
| North                          | 4                              | Yes                | No               | 2                |
| West                           | 8                              | No                 | No               | 2                |
| Worcestershire                 | 5                              | Yes                | Yes              | 5                |

*Scheme operational in winter only.
ways of delivering it, and whether or not it should be expanded.

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