in gut motility. Inflammatory bowel disease (IBD), in contrast, encompasses Crohn disease and ulcerative colitis, and is in fact related to chronic inflammation of the gut that may be autoimmune in nature. This clouds the results of the study, as it is unclear whether patients were assessed for a history of IBS, IBD, or both. In their article "Extracutaneous manifestations and complications of inherited epidermolysis bullosa" published in the September 2009 issue of the *Journal,* Fine et al[2] also use the ambiguous term "irritable bowel disease" in Table IV. It is unclear whether the authors are actually referring IBS versus IBD versus some other entity. There is a need for greater precision in our use of these terms so that we are consistently referring to the same disorders.

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Reply

To the Editor: As aptly reminded by Dr Haemel, irritable bowel syndrome (or, irritable bowel disease [IBD], as it is known in the United Kingdom) and inflammatory bowel disease (IBD) are indeed entirely different entities. We intentionally chose to cite both in Table IV, because the literature supports either occurring in some epidermolysis bullosa (EB) patients, particularly those with severe generalized types of EB. The presence of either in an EB patient does not constitute causality, however, because common conditions may independently arise in rare diseases without any linked pathophysiology. The rare occurrence of IBD in dystrophic EB is intriguing, though, because it is known that some IBD patients have circulating autoantibodies to type VII collagen. Whether absence or diminution of mutationally abnormal type VII collagen in the colon of dystrophic EB patients might lead to clinical findings similar to those of ulcerative colitis is unclear, but the occurrence of IBD in other EB types, most notably EB simplex and junctional EB, suggests the likelihood that the development of IBD in EB is merely coincidental.

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Research letters

Safety of etanercept in patients with psoriasis and hepatitis C virus assessed by liver histopathology: Preliminary data

To the Editor: We report the preliminary results of a prospective clinical study in which two patients with psoriasis, psoriatic arthritis (PsA), and chronic hepatitis C virus (HCV) infection received etanercept. Its effect on liver disease was monitored by the periodic measurement of serum transaminase and viral load. Liver biopsy specimens were obtained at baseline and 12 months into treatment. The literature was reviewed for papers describing tumor necrosis factor—alfa (TNFα) antagonist administration to patients with chronic HCV and autoimmune diseases (Table I; available online at http://www.eblue.org).

Patient 1, a 43-year-old white man with a 25-year history of severe psoriasis vulgaris and a 10-year history of PsA, was diagnosed with chronic HCV (genotype 4)

infection 6 years before coming to observation. In 2002, a liver biopsy was consistent with mild chronic liver disease and initial portal fibrosis. Cyclosporine, administered in 2002 for worsening PsA, was withdrawn after several months because of drug-induced renal dysfunction; his HCV status (viral load and liver function) was apparently unaffected by treatment. In 2005, when he came to observation, his Psoriasis Area and Severity Index (PASI)[1] score was 24.

Patient 2, a 62-year-old white man with a 10-year history of psoriasis, a 4-year history of PsA, and chronic HCV (genotype 1) infection diagnosed in 2002, was admitted to our department in 2005 for worsening of his cutaneous disease (PASI score, 25). Previous psoriasis treatments included topical corticosteroids, topical vitamin D derivatives, cyclosporine (1998-2000), psoralen plus ultraviolet A light phototherapy (2003), and narrowband ultraviolet B light phototherapy (2004).

The severe clinical conditions and the concern about the effects of other systemic drugs prompted the subcutaneous administration of etanercept (25 mg twice weekly) in both patients. Neither received HCV treatment (interferon or pegylated interferon, with or without ribavirin) in the preceding year or did so during the study. Both patients gave their written informed consent to participate.

Liver function was monitored by alanine aminotransferase, aspartate aminotransferase, gamma-galactosyltransferase, bilirubin, alkaline phosphatase levels and HCV-RNA viral load at baseline and at 1, 3, 6, 9, and 12 months. Liver biopsies, performed at baseline and 12 months into treatment, were examined blindly by the same experienced pathologist.

Both the cutaneous and the joint disease improved greatly in both patients. Liver function was not significantly affected. The viral load lightened slightly at 6 and 9 months (Fig 1), possibly because of intrinsic fluctuations.

The PASI scores of patient 1 fell to 14, 6, and 2 on weeks 12, 24, and 52, respectively. The baseline biopsy specimen revealed severe piecemeal necrosis without bridging necrosis, severe portal inflammation, grade 3 fibrosis (a Knodell score of 14/18),[2] and moderate steatosis (Fig 2, *A*). The specimen collected at 12 months exhibited moderate piecemeal necrosis without bridging necrosis, moderate portal inflammation, and grade 3 fibrosis (a Knodell score of 10/18; Fig 2, *B*).

The PASI scores of patient 2 declined to 10, 4, and 3 on weeks 12, 24, and 52, respectively. The first biopsy specimen revealed moderate portal inflammation and minimal fibrosis without periportal necrosis (a Knodell score of 5/18) and severe steatosis (Fig 2, *C*); the second documented an unchanged histologic activity index and mild steatosis (Fig 2, *D*).

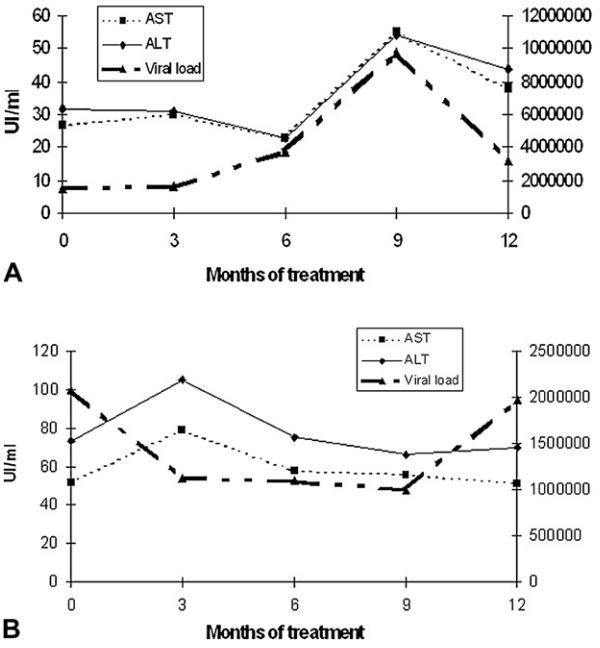

Fig 1. Serum transaminase and viral load during etanercept treatment in patients 1 (**A**) and 2 (**B**).

At the time of writing, both patients are still receiving the same dose of etanercept (25 mg twice weekly).

More than 60 patients with chronic HCV and an immunomediated disease (psoriasis, PsA, rheumatoid arthritis, Crohn disease, or ankylosing spondylitis) treated with an anti-TNFα agent have been described (Table I; available online at http://www.eblue.org). Etanercept or infliximab were given as monotherapy, sometimes combined with drugs such as cyclosporine or interferon alfa 2a and ribavirin. Serum transaminase and viral load were monitored for 3 to 41 months. Serum transaminase remained unchanged or decreased significantly in some patients; viral load did not change significantly in most patients and normalized in some. The main drawback of these studies is the lack of histopathologic evaluation of the effect of treatment on the liver. Nonetheless, they do suggest that anti-TNFα treatment is both safe and effective in patients with an immunologic disease and chronic HCV.[3-5]

This is the first study showing the safety of etanercept in patients with psoriasis and HCV by liver histopathology. Etanercept did not seem to compound the liver damage, as assessed by the Knodell score at 1 year posttreatment. Further observation and the definitive results will show whether TNFα antagonists such as etanercept can be considered as the drugs of choice for patients with HCV and an autoimmune disorder.

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