

## Stages of fibrosis and grades of necro-inflammatory activity

Necro-inflammatory activity and fibrosis are two major histological features of chronic hepatitis C that are included in different proposed classifications.<sup>9-12</sup> One of the few validated scoring systems is called the METAVIR scoring system.<sup>11-12</sup> This system assesses histological lesions in chronic hepatitis C using two separate scores, one for necro-inflammatory grade (A for activity) and another for the stage of fibrosis (F). The stages of fibrosis are illustrated in Figure 5.

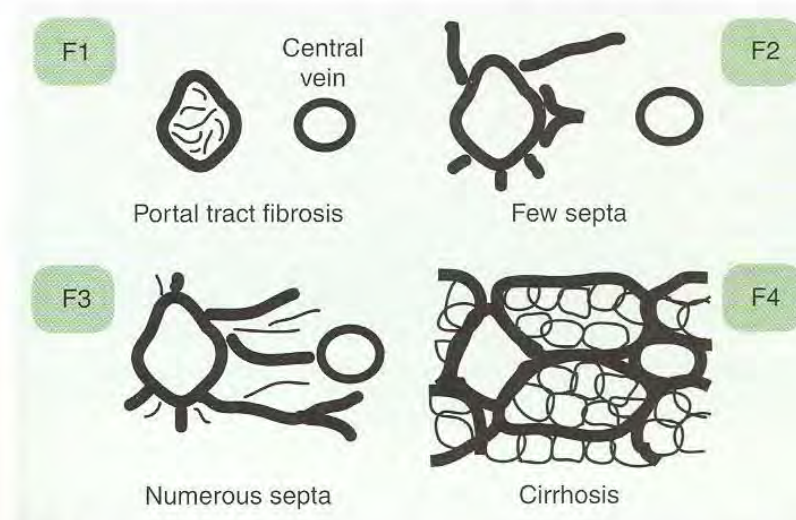
Grades for activity (A) are as follows:

- A0 = no histological activity
- A1 = minimal activity
- A2 = moderate activity
- A3 = severe activity

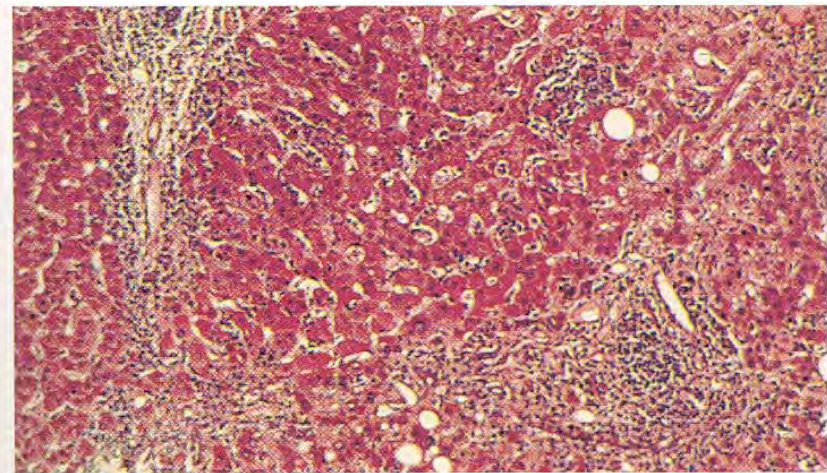
The degree of activity was assessed by integration of the severity of both piecemeal (periportal) necrosis and lobular necrosis, as described in a simple algorithm.<sup>12</sup> The intra- and inter-observer variations of this METAVIR scoring system are lower than those of the widely used Knodell scoring system.<sup>9-10</sup> For METAVIR fibrosis stages, there is an almost perfect concordance ( $\kappa = 0.80$ ) among pathologists. The Knodell scoring system for fibrosis is 0, 1, 3, 4; there is no stage 2 and therefore the scoring is non-linear. The activity grade ranges from 0 to 18 with the sum of periportal necrosis, intralobular and portal inflammation grades. The modified Histological Activity Index is more detailed, with four different features and continuous grades and the modified fibrosis staging includes seven stages (range 0-6).

Activity grade, which represents a measure of necrosis, is not a good predictor of fibrosis progression. In fact fibrosis alone is the best marker of ongoing fibrogenesis.<sup>13</sup> So far, no study has demonstrated clearly that activity grades are predictive of fibrosis progression independently of fibrosis stage.<sup>14</sup> Fibrosis stage and inflammatory grade are

correlated but for one-third of patients there is discordance. Clinicians should not take a 'significant activity' as a surrogate marker of 'severe disease'. The clinical hallmark of major necrosis and inflammation—severe acute hepatitis and fulminant hepatitis—are very rare compared with



**Figure 5a** The METAVIR fibrosis staging system. F0 = normal liver (no fibrosis); F1 = portal fibrosis without septa; F2 = portal fibrosis with few septa; F3 = numerous septa without cirrhosis; F4 = cirrhosis.



**Figure 5b** Biopsy of chronic hepatitis C stage METAVIR F3 (extensive fibrosis) with grade A3 (severe activity). Reproduced courtesy of Prof. Pierre Bedossa.