number and antigen-specificity of the T cells in the blood sample. Responses by helper T cells ($CD4^+$ T cells) are essential for an effective response by the cytotoxic T cells. $CD4^+$ T cells contribute to the immune response to HCV in two ways, namely, by expressing cytokines and by directly contacting $CD8^+$ T cells (53). This direct contact involves CD40 ligand of the helper T cell to CD40 receptor of the cytotoxic T cell. The result is the CD40L/CD40R complex.

VI. KINETICS OF HCV INFECTIONS

The following narrative describes the studies in the bulletpoint list. These are all time-course studies:

- untreated acute HCV infections;
- untreated fluctuating or intermittent acute HCV infections;
- untreated chronic HCV infections;
- biphasic response to IFN-alpha;
- sustained responders versus nonsustained responders, with IFN-alpha treatment.

HCV infections follow one of two different natural courses. These are:

1. acute infections that spontaneously resolve and
2. chronic infections that do not resolve spontaneously (54).

After exposure to HCV, there is a lag time of 1–3 weeks before serum HCV-RNA can be detected. The appearance of anti-HCV antibodies, which is called seroconversion, occurs at 4–10 weeks after exposure to HCV (55).

Acute HCV infections, which occur in about 20% of HCV infections, mean HCV infections where the patient spontaneously recovers within about 6 months. During the acute phase, serum HCV-RNA levels can fluctuate widely and may even be transiently undetectable. Levels of HCV in the bloodstream are usually determined by measuring the viral genome, which consists of RNA, and where measurement is by the polymerase chain reaction (56).

Loomba et al. (57) provides serum HCV-RNA data from three patients who showed the fluctuating pattern (Fig. 21.1). Meyer et al. (58) also shows data on the fluctuating nature of HCV-RNA that sometimes occurs with acute HCV. Where spontaneous clearance does

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