b. Examples of adverse events

The example of interferon-alpha2b (IFN-alpha2b) provides a concrete example of various adverse events. This drug is mainly used for treating melanoma (9) leukemias and lymphomas (10,11,12) and infections by hepatitis B virus and hepatitis C virus (13,14). IFN-alpha2b, as well as all other interferons, are in a class of proteins called cytokines. Hauschild et al. (15) provide a review of the adverse events produced by IFN-alpha2b.

Figure 24.1 (16) identifies the following adverse events:

1. Flu
2. Neutropenia
3. Hepatic damage
4. Anemia
5. Fatigue
6. Depression.

The figure shows the time course of AEs, with continued drug administration, over the course of days, weeks, and months. The listed AEs are those that were specifically caused by the drug.

Neutropenia refers to low neutrophil counts. Neutrophils, which represent the first line of defense against invading bacteria, are part of the innate immunity component of the immune system (neutrophils are not used for acquired immunity). Anemia refers to low red blood cell counts. Liver damage is routinely determined by laboratory tests for the serum levels of the enzyme, alanine aminotransferase (ALT). This enzyme was formerly known as glutamate pyruvate transaminase (SGPT). The presentation of the adverse drug reaction of flu-like symptoms declined with continued administration of the drug. In other words, the patient develops tolerance. This phenomenon of tolerance

[9] Hauschild A, Gogas H, Tarhini A, et al. Practical guidelines for the management of interferon-alpha-2b side effects in patients receiving adjuvant treatment for melanoma: expert opinion. *Cancer*. 2008;112:982–994.

[10] Smith SM, Johnson J, Cheson BD, et al. Recombinant interferon-alpha2b added to oral cyclophosphamide either as induction or maintenance in treatment-naive follicular lymphoma: final analysis of CALGB 8691. *Leuk Lymphoma*. 2009;50:1606–1617.

[11] Baccarani M, Martinelli G, Rosti G, et al. Imatinib and pegylated human recombinant interferon-alpha2b in early chronic-phase chronic myeloid leukemia. *Blood*. 2004;104:4245–4251.

[12] Sirohi B, Powles R, Lawrence D, et al. An open, randomized, controlled, phase II, single centre, two-period cross-over study to compare the quality of life and toxicity experienced on PEG interferon with interferon-alpha2b in patients with multiple myeloma maintained on a steady dose of interferon-alpha2b. *Ann Oncol*. 2007;18:1388–1394.

[13] Lee S, Kim IH, Kim SH, et al. Efficacy and tolerability of pegylated interferon-alpha2a plus ribavirin versus pegylated interferon-alpha2b plus ribavirin in treatment-naive chronic hepatitis C patients. *Intervirology*. 2010;53:146–153.

[14] Shamliyan TA, MacDonald R, Shaukat A, et al. Antiviral therapy for adults with chronic hepatitis B: a systematic review for a National Institutes of Health Consensus Development Conference. *Ann Intern Med*. 2009;150:111–124.

[15] Hauschild A, Gogas H, Tarhini A, et al. Practical guidelines for the management of interferon-alpha-2b side effects in patients receiving adjuvant treatment for melanoma: expert opinion. *Cancer*. 2008;112:982–994.

[16] Hauschild A, Gogas H, Tarhini A, et al. Practical guidelines for the management of interferon-alpha-2b side effects in patients receiving adjuvant treatment for melanoma: expert opinion. *Cancer*. 2008;112:982–994.