Oncology nurses are well versed in the administration of chemotherapy and management of associated side effects. The side effects range from mild and easily managed to severe and potentially dose limiting, such as hypersensitivity reactions (HSRs). Although severe HSRs are not common and can be seen with any agent, some treatments or medications are associated with much higher risks, such as monoclonal antibodies. Anaphylaxis usually is uniphasic in nature; however, 20% of reactions are biphasic, with symptoms resurging after initial resolution of the original reaction. Some reactions can be delayed, occurring after repeated infusions or presenting days to weeks after the original drug administration. For specific patients, a protracted period of anaphylaxis may occur beyond 24 hours. This article describes the proposed pathophysiology for biphasic and delayed HSRs, as well as management strategies for anaphylaxis. Case reports will illustrate patient presentations for biphasic and delayed HSRs. Oncology nurses must be aware of the risk for HSRs and understand the difference in presentation for biphasic and delayed anaphylactic reactions.