sibility that EPO use may promote tumor-related adverse events. This information should be considered in the care of individual patients. In the event EPO treatment is undertaken, maintenance of hemoglobin of 90–100 g/L (9–10 g/dL) should be the target. In the setting of adequate iron stores and serum EPO levels <100 ng/mL, EPO, 150 U three times a week, can produce a slow increase in hemoglobin over about 2 months of administration. Depot formulations can be administered less frequently. It is unclear whether higher hemoglobin levels, up to 110–120 g/L (11–12 g/dL), are associated with improved quality of life to a degree that justifies the more intensive EPO use. Efforts to achieve levels at or above 120 g/L (12 g/dL) have been associated with increased thromboses and mortality rates. EPO may rescue hypoxemic cells from death and contribute to tumor radioresistance.

NAUSEA AND VOMITING

The most common side effect of chemotherapy administration is nausea, with or without vomiting. Nausea may be acute (within 24 h of chemotherapy), delayed (>24 h), or anticipatory of the receipt of chemotherapy. Patients may be likewise stratified for their risk of susceptibility to nausea and vomiting, with increased risk in young, female, heavily pretreated patients without a history of alcohol or drug use but with a history of motion or morning sickness. Antineoplastic agents vary in their capacity to cause nausea and vomiting. Highly emetogenic drugs (>90%) include mechlorethamine, streptozotocin, DTIC, cyclophosphamide at >1500 mg/m^2, and cisplatin; moderately emetogenic drugs (30–90% risk) include carboplatin, cytosine arabinoside (>1 mg/m^2), ifosfamide, conventional-dose cyclophosphamide, and anthracyclines; low-risk (10–30%) agents include 5FU, taxanes, etoposide, and bortezomib, with minimal risk (<10%) afforded by treatment with antibodies, bleomycin, busulfan, fludarabine, and vinca alkaloids. *Emesis* is a reflex caused by stimulation of the vomiting center in the medulla. Input to the vomiting center comes from the chemoreceptor trigger zone (CTZ) and afferents from the peripheral gastrointestinal tract, cerebral cortex, and heart. The different emesis "syndromes" require distinct management approaches. In addition, a conditioned reflex may contribute to anticipatory nausea arising after repeated cycles of chemotherapy. Accordingly, antiemetic agents differ in their locus and timing of action. Combining agents from different classes or the sequential use of different classes of agent is the cornerstone of successful management of chemotherapy-induced nausea and vomiting. Of great importance are the prophylactic administration of agents and such psychological techniques as the maintenance of a supportive milieu, counseling, and relaxation to augment the action of antiemetic agents.

Serotonin antagonists (5-HT$_3$) and neurokinin 1 (NK1) receptor antagonists are useful in "high-risk" chemotherapy regimens. The combination acts at both peripheral gastrointestinal and CNS sites that control nausea and vomiting. For example, the 5-HT$_3$ blocker dolasetron, 100 mg intravenously or orally; dexamethasone, 12 mg; and the NK1 antagonist aprepitant, 125 mg orally, are combined on the day of administration of severely emetogenic regimens, with repetition of dexamethasone (8 mg) and aprepitant (80 mg) on days 2 and 3 for delayed nausea. Alternate 5-HT$_3$ antagonists include ondansetron, given as 0.15 mg/kg intravenously for three doses just before and at 4 and 8 h after chemotherapy; palonosetron at 0.25 mg over 30 s, 30 min before chemotherapy; and granisetron, given as a single dose of 0.01 mg/kg just before chemotherapy. Emesis from moderately emetic chemotherapy regimens may be prevented with a 5-HT$_3$ antagonist and dexamethasone alone for patients not receiving doxorubicin and cyclophosphamide combinations; the latter combination requires the 5-HT$_3$/dexamethasone/aprepitant on day 1 but aprepitant alone on days 2 and 3. Emesis from low-emetic-risk regimens may be prevented with 8 mg of dexamethasone alone or with non-5-HT$_3$, non-NK1 antagonist approaches including the following.

Antidopaminergic phenothiazines act directly at the CTZ and include prochlorperazine (Compazine), 10 mg intramuscularly or intravenously, 10–25 mg orally, or 25 mg per rectum every 4–6 h for up to four doses; and thiethylperazine, 10 mg by potentially all of the above routes every 6 h. Haloperidol is a butyrophenone dopamine antagonist given at 1 mg intramuscularly or orally every 8 h. Antihistamines such as diphenhydramine have little intrinsic antiemetic capacity but are frequently given to prevent or treat dystonic reactions that can complicate use of the antidopaminergic agents. Lorazepam is a short-acting benzodiazepine that provides an anxiolytic effect to augment the effectiveness of a variety of agents when used at 1–2 mg intramuscularly, intravenously, or orally every 4–6 h. Metoclopramide acts on peripheral dopamine receptors to augment gastric emptying and is used in high doses for highly emetogenic regimens (1–2 mg/kg intravenously 30 min before chemotherapy and every 2 h for up to three additional doses as needed); intravenous doses of 10–20 mg every 4–6 h as needed or 50 mg orally 4 h before and 8 and 12 h after chemotherapy are used for moderately emetogenic regimens. 5-9-Tetrahydrocannabinol (Marinol) is a rather weak antiemetic compared to other available agents, but it may be useful for persisting nausea and is used orally at 10 mg every 3–4 h as needed.

DIARRHEA

Regimens that include 5FU infusions and/or irinotecan may produce severe diarrhea. Similar to the vomiting syndromes, chemotherapy-induced diarrhea may be immediate or can occur in a delayed fashion up to 48–72 h after the drugs. Careful attention to maintained hydration and electrolyte repletion, intravenously if necessary, along with antimotility treatments such as "high-dose" loperamide, commenced with 4 mg at the first occurrence of diarrhea, with 2 mg repeated every 2 h until 12 h without loose stools, not to exceed a total daily dose of 16 mg. Octreotide (100–150 μg), a somatostatin analogue, or opiate-based preparations may be considered for patients not responding to loperamide.

MUCOSITIS

Irritation and inflammation of the mucous membranes particularly afflicting the oral and anal mucosa, but potentially involving the gastrointestinal tract, may accompany cytotoxic chemotherapy. Mucositis is due to damage to the proliferating cells at the base of the mucosal squamous epithelia or in the intestinal crypts. Topical therapies, including anesthetics and barrier-creating preparations, may provide symptomatic relief in mild cases. Palifermin or keratinocyte growth factor, a member of the fibroblast growth factor family, is effective in preventing severe mucositis in the setting of high-dose chemotherapy with stem cell transplantation for hematologic malignancies. It may also prevent or ameliorate mucositis from radiation.

ALOPECIA

Chemotherapeutic agents vary widely in causing alopecia, with anthracyclines, alkylating agents, and topoisomerase inhibitors reliably causing near-total alopecia when given at therapeutic doses. Antimetabolites are more variably associated with alopecia. Psychological support and the use of cosmetic resources are to be encouraged, and "chemo caps" that reduce scalp temperature to decrease the degree of alopecia should be discouraged, particularly during treatment with curative intent of neoplasms, such as leukemia or lymphoma, or in adjuvant breast cancer therapy. The richly vascularized scalp can certainly harbor micrometastatic or disseminated disease.

GONADAL DYSFUNCTION AND PREGNANCY

Cessation of ovulation and azoospermia reliably result from alkylating agent– and topoisomerase poison–containing regimens. The duration of these effects varies with age and sex. Males treated for Hodgkin's disease with mechlorethamine- and procarbazine-containing regimens are effectively sterile, whereas fertility usually returns after regimens that include cisplatin, vinblastine, or etoposide and after bleomycin for testicular cancer. Sperm banking before treatment may be considered to support patients likely to be sterilized by treatment. Females experience amenorrhea with anovulation after alkylating agent therapy; they are likely to recover normal menses if treatment is completed before age 30 but unlikely to recover menses after age 35. Even those who regain menses usually experience premature