TABLE 61-3 NAUSEA AND VOMITING RISK WITH CANCER THERAPY

EMETIC RISK	PERCENTAGE OF PATIENTS AFFECTED	REPRESENTATIVE AGENTS	RECOMMENDED PREVENTIVE ANTIEMETIC
High	>90	Cisplatin, high-dose cyclophosphamide	NK1 antagonist + dexamethasone + 5HT3 antagonist
Moderate	30-90	Oxaliplatin, doxorubicin, irinotecan	5HT3 antagonist + dexamethasone
Low	10-30	Paclitaxel, etoposide, gemcitabine	Dexamethasone or 5HT3 antagonist or dopamine antagonist
Minimal	<10	Vincristine, bleomycin	Not needed

5HT3, Serotonin receptor; NK1, neurokinin 1.

Pathology

The mechanism is not completely understood but involves an effect of chemotherapy on the gastrointestinal mucosa and central nervous system, such as the chemoreceptor trigger zone (area postrema). The neurotransmitters that are involved include dopamine, serotonin, and substance P.

Treatment

The best approach for treatment is prevention. The prophylactic antiemetic protocol depends on the chemotherapy regimen and emetic risk (see Table 61-3). Randomized clinical trials have established that the combination of a neurokinin 1 (NK1) receptor antagonist (aprepitant or fosaprepitant), a 5HT3 serotonin receptor antagonist, and dexamethasone is the regimen of choice for highly emetogenic chemotherapy. For moderately emetogenic chemotherapy, a 5HT3 antagonist with dexamethasone is usually adequate. All patients should be given a dopamine or 5HT3 receptor antagonist as rescue therapy for intermittent nausea.

Dexamethasone is the preferred treatment for delayed nausea and vomiting in highly and moderately emetogenic chemotherapy. Other agents with proven efficacy include olanzapine for the prevention of both acute and delayed nausea and vomiting. Anticipatory nausea or vomiting is best treated with proper control of symptoms in the initial cycles. When it occurs, it is best treated with a benzodiazepine before chemotherapy.

DERMATOLOGIC TOXICITY

Many chemotherapeutic and targeted agents are associated with dermatologic toxicity, which can lead to patient morbidity, alter quality of life, and affect therapeutic dosing.

Clinical Presentation

Acneiform eruptions are observed with agents targeted against epidermal growth factor receptor (EGFR) in 70% to 80% of patients. The rash is usually erythematous with pustulopapular eruptions over the face, scalp, and upper trunk.

Palmar-plantar erythema, or so-called hand-foot syndrome, is seen with chemotherapeutic agents such as 5-fluorouracil and capecitabine or with tyrosine kinase inhibitors such as sorafenib, sunitinib, and regorafenib. Manifestations can differ slightly between classes of drugs, but they usually involve symmetrical redness of the palms or soles. Tingling and pain may accompany erythema. With progression, painful blistering or skin peeling may occur. Symptoms are frequently observed at pressure areas, such as on the soles of the feet after prolonged standing or running.

Treatment

Treatment of skin rash associated with anti-EGFR therapies is tailored to the severity of the rash and may include topical steroids, oral antibiotics (minocycline or doxycycline), and dose modification or cessation. Sunscreens, reduced sun exposure, and lotions for dry skin should be used for prevention. For hand-foot syndrome, preventive measures such as sunscreens and routine application of lotion to hands and feet are helpful. The most effective treatment is a brief treatment break (typically for several days, until complete resolution occurs), followed by resumption but with a reduced dose of the inciting agent.

TUMOR LYSIS SYNDROME

Definition

Tumor lysis syndrome occurs in malignancies with a high proliferative rate (such as aggressive lymphoma or leukemia), usually after the initiation of cytotoxic chemotherapy. It is an oncologic emergency. Rarely, it can occur spontaneously.

Pathology

Massive tumor cell lysis causes the release of large amounts of potassium, phosphate, and nucleic acids into blood. This leads to rapidly increased production of uric acid, which can precipitate in the renal tubules, causing acute renal insufficiency.

Diagnosis

Tumor lysis syndrome should be suspected in the presence of hyperuricemia, hyperkalemia, hyperphosphatemia, and hypocalcemia. Elevated creatinine can occur with renal damage from uric acid precipitation.

Treatment

In the appropriate clinical setting, tumor lysis syndrome should be anticipated and prevented. An international panel has developed a risk stratification scheme. Aggressive hydration is key to preventing this syndrome and should continue until the tumor burden is largely resolved. Allopurinol at a dose of 150 mg—or, in high-risk cases, rasburicase at a dose of 0.2 mg/kg—can be used for prophylaxis. Rasburicase may also be used to treat severe hyperuricemia and to prevent renal insufficiency.

For a deeper discussion on this topic, please see Chapters 176, "Hypercoagulable States," Chapter 179, "Tumor Lysis," Chapter 245, "Hypercalcemia," and Chapter 400, "Spinal Cord Compression" in Goldman-Cecil Medicine, *25th Edition.*