



# Chemotherapy and Radiotherapy

## *Effects on the Skin*

PART ONE

Charlene DeHaven, MD

Both chemotherapy and radiation therapy commonly have side effects that involve the skin. Some of these are broad effects from the treatments in general and some are specific to certain chemotherapeutic drugs used. The discussion here will be restricted to those reactions unique to chemotherapy and radiation therapy.

Cancers are composed of abnormal cells that divide rapidly. The faster the tumor's growth rate the more rapidly its cells are multiplying. Although a more rapid rate of cellular division is associated with greater malignant potential, this rapid growth rate also makes the tumor susceptible to chemotherapeutic drugs. Chemotherapy targets cells that are rapidly dividing. The goal of chemotherapy is to kill as many cancer cells as possible so the tumor can either be completely eradicated, i.e. "cured," or placed in remission, a state where there still may be some cancer cells present in the body but the patient is without symptoms and feels well for an extended period of time.

In addition to tumor cells, there are certain normal cells in the body which are also rapidly dividing. Chemotherapeutic drugs target all rapidly-dividing cells and therefore effect not only tumor cells but also any other cells in the body which are undergoing rapid cell division. Other normal rapidly dividing cells include skin and the skin's appendages hair and nails, gastrointestinal cells, bone marrow and its product blood cells, and reproductive cells including sperm and ova. It makes sense that skin effects are commonly seen with chemotherapy since both skin cells and tumor cells are undergoing rapid cell division. Similarly, it makes sense that other common side effects of chemotherapy involve these other organ systems and include ulcers and infections in the mouth, stomach and intestine, anemia, decreases in white blood cells and platelets and temporary loss of reproductive ability. As long as a few of the body's normal cells in skin, GI tract, reproductive tract and bone marrow remain the body can

regenerate and recover these functions once the chemotherapy is stopped.

Extravasation injury is a type of skin injury that occurs when a chemotherapy drug given IV leaks out of the vein and into the skin. Depending on the drug in question, this effect can be mild swelling, local irritation and inflammation or even actual tissue necrosis.

Alopecia is hair loss associated with toxicity to rapidly dividing hair cells. This includes all body hair and is not limited to scalp hair only. Recovery occurs and hair growth resumes after chemotherapy stops although there may be a permanent alteration in hair color, texture or curl.

Certain drugs can cause specific types of allergic or hypersensitivity responses. The platinum derivatives (cisplatin, carboplatin) can cause an IgE-mediated hypersensitivity with itching, redness and swelling occurring within an hour after the infusion is begun. If life-threatening, this reaction is termed "anaphylaxis" and the drug will not be given again in these severe cases. Formation of antigen-antibody complexes occurs with methotrexate which causes a vasculitis (inflammation surrounding blood vessels) or rituximab can cause serum sickness (an illness with flu-like symptoms). A specific type of rash called "erythema multiforme" of which the hallmark is the "target lesion" is caused by antigen-antibody complexes and can occur with a number of medicines including chemotherapeutic agents. Activated T cells cause contact allergy and may be seen with nitrogen mustard (mechlorethamine).

Pigmentary changes can involve the skin, mucous membranes or nails. These may be temporary or permanent. After alopecia, it is not unusual for hair to regrow with a color or texture change. Pigmentary changes are particularly common with the cytotoxic drugs such as alkylating agents or tumor-directed antibiotics. Hyperpigmentation of the gums can be found with cyclophosphamide treatment and is permanent. 5-fluorouracil

(5-FU) treatment is often seen with hyperpigmentation reactions in all areas of skin or in only sun-exposed areas. Pigment changes with 5-FU can also follow the pattern of an underlying vein and appear twisting or serpentine. 5-FU can darken the mucosa of the tongue, conjunctiva of the eyes or nails. Tegafur, a 5-FU analog, can cause circular areas of pigmentation of the palms, soles and nails. Although 5-FU causes discrete areas of hyperpigmentation, other drugs may result in generalized hyperpigmentation. These include busulfan (and has been referred to as the "busulfan tan"), pegylated liposomal doxorubicin, hydroxyurea and methotrexate. Daunorubicin can cause hyperpigmentation in solar-exposed areas. Increased pigmentation in areas of injury or pressure may be seen with cisplatin, hydroxyurea and bleomycin. Some drugs are secreted in sweat and can cause hyperpigmentation under adhesive tape; these include docetaxel, thiotepa and ifosfamide. Circular areas of scalp hyperpigmentation can be associated with daunorubicin.

Part II will include insights into acneiform rashing, the effects of radiation on the skin and more include charting on addressing key side effects with skincare therapies.

*Dr. DeHaven is board certified in Internal Medicine and Emergency Medicine, with specific emphasis in the age management field. Dr. DeHaven acted as Physician in Charge and Director of Practice Management for the Kronos Anti-Aging Clinics. She was the founder and Chief Physician of the Longevity Institute, specializing in Anti-Aging Medicine. She has written extensively on aging related issues. Dr. DeHaven has developed and implemented anti-aging medical protocols for both the Longevity Institute and the Kronos Clinics, pioneering research in hormone replacement therapy, and oxidative stress management. ▲*



# Chemotherapy and Radiotherapy

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PART TWO

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**P**art I discussed general effects of chemotherapy and radiation therapy on skin. Rapidly dividing cell populations include both malignant cells and groups of normal cells. Normal cells undergoing rapid cell division include skin and the skin's appendages, cells of the gastrointestinal tract, bone marrow and its product blood cells and the reproductive cells sperm and ova. Although all these groups of cells are affected by chemotherapy and radiation therapy, the discussion has been confined to skin effects. Included here in Part II will be other dermal effects of chemotherapeutic agents not mentioned in Part I, the effects of radiation therapy on the skin. (Part I was published in the Winter, 2010 issue of "Specialty Skin Care").

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An acneiform rash can be seen with the epidermal growth factor receptor inhibitors such as cetuximab and efitinib. These papules and pustules look like acne although the typical comedone of acne is not found in association with these drugs. Patients receiving the EGF receptor inhibitors commonly have some of these acneiform

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lesions although it is severe in only a small number of patients. Treatment with the tetracycline-type antibiotics may initially be helpful although the lesions tend to recur as chemotherapy continues.

Rashes are also common with the tyrosine kinase signal transduction inhibitors such as imatinib. These may occur in as many as 90% of patients on the higher doses.

Beau's lines are transverse lines seen in nails. Beau's lines can be seen with chemotherapy or other critical illness. The cycles of chemotherapy correspond to the width of the lines in the nail. Many chemotherapy drugs can cause pigmentary changes, bands or lines in the nails.

Oncholysis refers to a lifting up of the nail from the nail bed. It is most commonly seen with paclitaxel and docetaxel but also with cyclophosphamide, doxorubicin, 5-FU, hydroxyurea and the combination of bleomycin plus vinblastine.

Inflammatory changes around the nail even leading to paronychia (an infection adjacent to the nail) can be seen with EGF inhibitors such as gefitinib and cetuximab. The taxanes can also be associated with paronychia.

Acral erythema or hand-foot syndrome is an erythema of palms and/or soles that can be associated with chemotherapy. It can be quite painful and can even result in blistering and sloughing of skin. It may respond to decreasing the dose of the agent.

Photosensitivity can be seen with many chemotherapy drugs. A phototoxic reaction is a type of allergic response seen on sun exposure and consists of edema, redness, pain and tenderness in solar-exposed areas. Phototoxic reactions may ultimately result in permanent hyperpigmentation as they are associated with blistering and severe skin damage. Methotrexate can cause a photoenhancement in which giving the drug several days after sunburn causes the sunburn to reappear.

In patients with autoimmune disorders such as scleroderma or lupus, administration of a chemotherapy agent can result in the appearance of a circular red scaly rash. This is related to the drug but also involves the autoimmune process itself.

Radiation therapy also often results in dramatic changes in the skin. These depend

on the total dose, size of the port (area over which the radiation is administered), depth of penetration (i.e. how close to skin).

Changes of radiation dermatitis may be acute or chronic. Acute changes consist of erythema (redness), irritation, pain or local dermal swelling. Chronic radiation dermatitis can result in scarring, thinning of the skin, telangiectasias, increased sensitivity to other agents or environmental insults. The pathogenesis of radiation dermatitis is free radical damage to cells of the skin. Therapeutic effects of radiation therapy are also on a free radical mechanism. With radiation therapy for carcinoma of the breast, the severity of radiation dermatitis tends to increase with breast size greater than a D cup; this may relate to overall port size required. Considering all patients who receive radiation therapy for carcinoma of the breast, as many as 90% may experience some degree of radiation dermatitis.

Radiation recall dermatitis occurs in a previously irradiated area of skin that develops marked inflammation after chemotherapy is given. Radiation recall dermatitis has been described with dactinomycin. It is more likely with higher doses of chemotherapy and usually occurs with the first dose. IV chemotherapy is more likely to cause this than oral medicines perhaps because IV doses result in more rapid and higher blood levels. However, the radiation recall dermatitis from oral agents tends to last longer than that from IV chemotherapy. It has been described in association with tamoxifen.

Radiation sensitization (also termed radiation enhancement) occurs in the radiation therapy field and within 1-2 weeks after the chemotherapy is given. The skin changes appear the same as that for radiation recall dermatitis and consist of redness, edema, superficial sloughing of skin and superficial ulcerations.

Considerable emphasis should also be given to the pronounced effects caused on the psyche through physical effects in the skin from chemotherapy and radiation therapy. The diagnosis and treatment of cancer often corresponds with one of the most difficult times in the patient's life. Since the patient's external appearance is determined in large part by their skin, any deterioration in their skin as perceived by the patient can worsen depression and self-concept, leading to the exacerbation of emotional difficulties. The impact of these skin changes should not be minimized and every effort should be made to assist the

patient in this regard, both with understanding of the processes involved as well as their treatment.

To view Parts I and II of this article, as well as a tabular summary of all effects discussed, please visit [www.spsscs.org](http://www.spsscs.org).

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