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General Administration for Drug Utilization and Pharmacy Practice Administration**

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Role of Oncology Pharmacist in Radiotherapy

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List of Abbreviations

ADL	Activities of Daily Living
bid	Twice daily
CNS	Central Nervous System
GI	Gastrointestinal
GnRHa	Gonadotropin-Releasing Hormone Agonist
Gy	Gray, Unit of radiation dose
HDR	High-Dose-Rate
IGRT	Image-Guided Radiation Therapy
IMPORT	Intensity-Modulated Radiation Therapy
LDR	Low-Dose Rate
NSAIDs	Nonsteroidal Anti-Inflammatory Drugs
prn	As needed
qd	Once daily
RRR	Radiation Recall Reaction
RT	Radiation Therapy
SABR	Stereotactic Ablative Radiotherapy
SRS	Stereotactic Radiosurgery
TESE	Testicular Sperm Extraction
tid	Three times daily

Glossary

Adjuvant Radiotherapy	Radiation that is given in addition to the primary or initial therapy to maximize its effectiveness.
Brachytherapy	Treatment of cancer by the insertion of radioactive implants directly into the tissue.
Curative Radiotherapy	Radiation used to cure cancer.
Embryo Freezing	A procedure in which eggs are removed from the ovary. They are then fertilized with sperm in the lab to form embryos and frozen for future use.
Gonadotropin-Releasing Hormone Agonist	A substance that causes the ovaries to stop making estrogen and progesterone.
Impotence	The inability to have or keep an erection (i.e. erectile dysfunction)
Intraoperative Radiation	Radiation therapy is given during surgery.
Lymphedema	A problem in which the lymph fluid does not drain, it builds up in the tissues and causes swelling.
Neo-Adjuvant Radiotherapy	Radiation used before surgery
Oocyte Cryopreservation	A procedure in which eggs are removed from the ovary and frozen.
Oophoropexy	A surgical procedure in which one ovary or both are suspended. A procedure in which the ovary is elevated and fixed to the abdominal wall.
Ovarian Shielding	A procedure in which a protective cover is placed on the outside of the body, over the ovaries and other parts of the reproductive system, to shield them from scatter radiation.
Ovarian Tissue Freezing	Surgically removing part or all of an ovary and then freezing the ovarian tissue, which contains eggs.
Palliative Radiotherapy	Radiation used to shrink a cancer, slow down its growth, or control symptoms caused by the cancer.
Radical Trachelectomy	An operation to remove most of the cervix and the upper part of the vagina.

Radiotherapy	A cancer treatment modality that involves subjecting the tumor tissue to high doses of radiation to eliminate the cancer cells and reduce tumor size. Low doses of radiation are used for diagnostic imaging to visualize the internal structures of the body. This technique is useful in detecting and identifying tumors and other abnormalities in the body. It is a safe procedure that is widely used in the medical industry.
Sialagogues	Drugs stimulate any functioning salivary gland tissue to produce more saliva.
Sperm Banking	Samples of semen are collected, and the sperm are then frozen and stored (banked) for future use.
Testicular Shielding	Procedure in which a protective cover is placed on the outside of the body to shield the testicles from being scattered to the pelvis when other parts of the body are being treated with radiation.
Testicular Sperm Extraction	A procedure where a sperm is collected through a medical procedure and frozen for future use.
Testicular Tissue Freezing	A procedure for boys who have not gone through puberty and are at high risk of infertility.
Trismus	Muscle spasms in the temporomandibular joint.

Aim and Scope

This chapter offers a detailed guide for clinical pharmacists working in oncology facilities that provide radiotherapy services. Its primary focus is to emphasize the crucial role of clinical pharmacists in caring for patients undergoing radiation treatments.

The chapter starts with an introduction that briefly explains the background of radiotherapy, the use of radiation therapy in combination with other cancer treatments, and the different types of radiotherapy administered by radiology technicians under the supervision of radiology specialist physicians.

Furthermore, the guide contains a list of radiation-induced side effects, their corresponding injury locations, and management strategies. It also outlines the pharmacist's role in educating patients and preventing, detecting, and monitoring toxicities.

Introduction

1. History of Radiation

Since its discovery in the 19th century, radiation has been applied to medical procedures. Radiation therapy has been used to diagnose and treat cancer more often since the beginning of the 20th century.¹

X-rays were first discovered in Germany by Wilhelm Conrad Röntgen in 1895. Soon after, it was found that X-rays had clinical benefits in treating cancer. Marie Curie's exceptional contributions to the field of radiation therapy have established her as a pioneering researcher in the scientific community. One hundred years ago, she was awarded her second Nobel Prize for her groundbreaking work on radium, which revolutionized the field.

In recognition of the progress made in this field over the past century, the United Kingdom designated 2011 as the “Year of Radiation Therapy”. This celebration aimed to highlight the advancements and innovations in radiation therapy, which have contributed to improving the quality of life for patients worldwide.²

Since then, radiation treatment has evolved into a specialized medical field known as radiation oncology, which brings together a wide range of medical and scientific experts from other fields. Radiation therapy, also known as radiotherapy, is a crucial component of cancer treatment alongside surgery and systemic therapy. It is also one of the most cost-effective single-modality therapies, making up only 5% of the whole cost of cancer care.²

Imaging techniques, computerized treatment planning systems, radiation treatment equipment (with improved X-ray production and treatment administration), as well as greater knowledge of the radiobiology of radiation therapy, all continue to advance this field at a rapid rate.³

Technology improvements have made radiation therapy precise and accurate, giving people with cancer an actual possibility for a cure even though it was once believed to damage good tissue in its attempt to eliminate cancer cells.¹

2. Radiation Therapy

Radiation therapy, or radiotherapy, is a medical procedure used to treat cancer by administering high doses of radiation to eradicate cancerous cells and reduce tumor growth. At lower doses, radiation is also utilized as an imaging technique to visualize internal structures, such as those of broken bones or teeth. The use of radiation therapy is a complex process that requires a highly trained medical professional, namely a radiation oncologist, to ensure that the correct dosage and application are employed to achieve the best possible clinical outcome. Despite the potential for side effects, radiation therapy is an effective treatment option for many types of cancer.⁴

3. Radiation Therapy's Objectives

The main goal of radiation therapy is to deprive cancer cells of their cell division and proliferation capacity.⁵

- **Curative Radiotherapy (Treat Cancer):** Radiation can be used to cure cancer, prevent it from returning, or stop or slow its growth.⁵
- **Neo-adjuvant radiotherapy:** Makes other treatments more effective – for example, it can be combined with chemotherapy or used before surgery.⁶
- **Adjuvant radiotherapy:** Reduces the risk of cancer returning after surgery.⁵
- **Palliative radiotherapy:** Reduce symptoms in situations where a cure for cancer is not feasible, radiation therapy can serve as a viable treatment method to alleviate pain and other associated symptoms resulting from the cancerous tumor. Furthermore, the therapy can be employed as

a preventive measure to hinder the development of potential issues that may arise from a growing tumor, such as blindness or loss of bowel and bladder control.⁷

4. Radiation Therapy Against Cancer

At high doses, radiation therapy kills cancer cells or slows their growth by damaging their DNA. Cancer cells whose DNA is damaged beyond repair stop dividing or die. When damaged cells die, the body breaks them down and eliminates them.⁴

Radiation therapy is a treatment modality that does not exhibit immediate eradication of cancer cells. Instead, it requires a prolonged treatment regimen spanning days or even weeks to inflict the requisite damage to DNA, which ultimately leads to apoptosis of the cancer cells. Afterward, cancer cells keep dying for weeks or months after radiation therapy ends.⁴

5. Effect of Radiation Therapy on Healthy Cells

Efficacy of radiation therapy in reducing or arresting the growth of cancer cells is well established. However, it can also affect healthy cells located near the cancerous tissue. While healthy cells generally recover following treatment, some individuals may experience severe and persistent adverse side effects. Furthermore, late side effects may manifest months or years after completing radiation therapy, necessitating additional medical intervention. It is therefore imperative that healthcare providers and patients alike are aware of these potential complications associated with radiation therapy.⁸

Protecting Healthy Cells During Treatment

Using as minimal radiation as possible. The radiation dose is calculated to be high enough to kill cancer cells while being low enough to cause minimal damage to healthy cells.⁹

Extending the course of treatment. For several weeks, radiation therapy might be received once a day or twice a day in lesser doses. By distributing the radiation dose, normal cells can regenerate while cancer cells are eradicated.⁹

Radiation directed at a specific area of the body. Aiming high doses of radiation at cancer while limiting exposure to nearby healthy tissue is possible with several forms of radiation therapy. The application of computer technology in the administration of radiation therapy for cancer treatment has led to the development of techniques that enable precise targeting of specific areas within a tumor or the tumor itself. These techniques utilize computer-aided dosimetry to achieve optimal therapeutic outcomes. By providing a more accurate and efficient means of delivering radiation doses to cancerous tissues, these techniques offer significant advantages over traditional methods. In addition, they enhance the ability of clinicians to monitor and adjust treatment plans in real time, thereby improving overall patient outcomes.⁹

6. Usage of Radiation Therapy in Combination with Other Methods of Cancer Treatment¹⁰

Radiation therapy is often used with other cancer treatments modalities.

Radiation therapy and surgery. Radiation therapy may be administered before, during, or after surgical intervention as part of a comprehensive treatment plan. It may be employed to reduce the dimensions of the malignancy before surgery or to eradicate any residual cancerous cells postoperatively. In selected cases, radiation therapy may be delivered intraoperatively, targeting the affected area directly. Termed intraoperative radiation therapy, this approach offers a highly targeted alternative to traditional radiation therapy.¹⁰

Radiation therapy, chemotherapy, and immunotherapy. Radiation may be given before, during, or after chemotherapy and immunotherapy. Before or during these other treatments,

radiation therapy can shrink the cancer so that the treatments work better. After treatment, radiation can be used to kill any cancer cells that remain.¹⁰

7. Factors affecting the choice of radiation therapy used⁴

The type of radiation therapy depends on many factors, including:

- Type of cancer
- Size of the tumor and its location in the body
- How close the tumor is to normal tissues that are sensitive to radiation.
- General health and medical history
- Presence of other types of cancer treatment
- Other factors, such as age and other medical conditions

8. Radiation Lifetime Dose Limits

It is crucial to bear in mind that there exists a threshold to the permissible amount of radiation that any given area of the body can be safely exposed to throughout its treatment. If an area has already undergone a certain amount of radiation, it may not be feasible for a patient to receive radiation therapy in that same area again. Nevertheless, if one area of the body has attained the maximum allowable lifetime dose of radiation, it may still be possible to treat another area provided that the distance between the two areas is suitably taken into account.⁴

9. Radiation Therapy Administration

Radiation therapy is administered in two main forms, namely **external beam** and **internal radiation therapy**. These therapeutic procedures are carried out by a team of specialized nurses and technicians under the guidance of a radiotherapist.¹¹

External beam radiation therapy involves the use of an external machine that directs radiation at cancer cells. Conversely, **internal radiation therapy** involves the placement of radioactive

material inside the body, either in or near the affected area. In some cases, patients may receive a combination of both forms of radiation therapy, depending on their medical condition. It is essential to note that these treatment options require careful consideration of the patient's unique circumstances, and the choice of modality is made on a case-by-case basis.⁴

10. External beam radiation therapy



Figure 1: External Beam Radiation Therapy or Teletherapy¹²

External beam radiation therapy targets a particular area of the body. External beam radiation therapy is a treatment modality aimed at eradicating tumors. This technique employs a large machine that emits radiation and can produce noise. It should be noted, however, that the machine does not come into direct contact with the patient. Instead, it revolves around the patient, delivering radiation from various angles to target the tumor.¹²

The machine's physical characteristics and the radiation it emits make it a powerful cancer-fighting tool. Its size and complexity can pose challenges, but its ability to be maneuvered around the patient to deliver radiation across various planes (from different axes) makes it an invaluable asset to medical professionals.¹²

10.1. Types of External Beam Radiation Therapy^{13,14}

There are many different types of external radiotherapy. The type depends on the type of cancer and its position in the body:

- 3-D Conformal Radiation Therapy
- Intensity-Modulated Radiation Therapy (IMRT)
- Image-Guided Radiation Therapy (IGRT)
- Stereotactic Radiotherapy (SABR) and Stereotactic Radiosurgery (SRS)
- Tomotherapy
- Adaptive Radiotherapy

10.2. Types of Beams Used in Radiation Therapy¹⁵

Radiation beams used in external radiation therapy come from three types of particles, which are:

- Photons
- Protons
- Electrons

During external beam radiation therapy, a common query that arises amongst patients associated with the possible risk of radiation-induced radioactivity. It is pertinent to note that external beam radiation therapy does not render the patient radioactive, thereby obviating any potential threat to other individuals, including neonates, infants, young children, and pregnant women, with whom the patient may come into contact.¹²

11. Internal Radiation Therapy

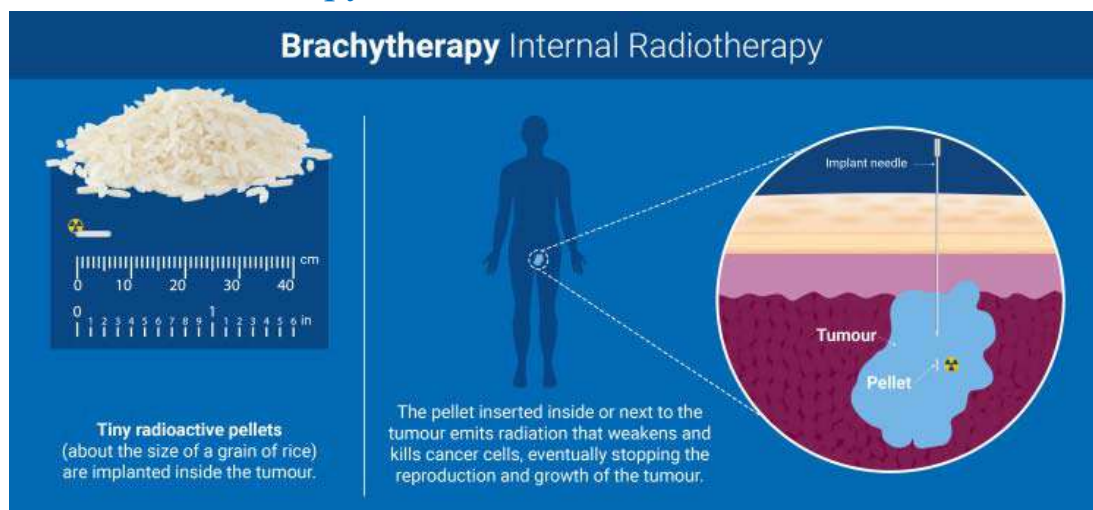


Figure 2: Brachytherapy (Internal Radiotherapy)¹⁶

Internal radiation therapy is a treatment in which a source of radiation is put inside the body. The radiation source can be solid or liquid.¹⁶

In comparison to external radiotherapy, internal radiotherapy is a treatment modality that confers higher radiation doses with fewer associated adverse effects. This is primarily because internal radiotherapy administers radiation from inside the body, near the target tumors, limiting the extent of healthy cell exposure. However, it is important to note that internal radiotherapy is only effective for smaller tumors.¹⁶

11.1. Main Types of Internal Radiotherapy

11.1.1. Radioactive Liquid Treatment (Radioisotope or Radionuclide Therapy)

Discussed in detail in the “Nuclear and Radiological Safety Principles and Practice of Nuclear Pharmacy” guide, you can reach it via the following link:

<https://www.edaegypt.gov.eg/media/ptknvcgg/guide-line-nuclear-and-radiological-safety-principles-and-practice.pdf>

Examples of radioactive liquids include¹⁸:

- Iodine-131 – for thyroid cancer and non-cancerous (benign) thyroid conditions
- Phosphorus (P-32) – for some blood disorders
- Radium-223 – for cancer that has spread to the bones (secondary bone cancer)
- Strontium-89 – for secondary bone cancers

11.1.2. Brachytherapy (Radioactive Implant Treatment)

Brachytherapy, a form of internal radiation therapy, involves the insertion of seeds, ribbons, or capsules containing a radiation source in proximity to the tumor. This specialized treatment is a localized approach that selectively targets the affected area of the body. The radiation source emits radiation for a specified period, analogous to external beam radiation therapy. As such, brachytherapy provides an effective alternative to traditional radiation therapy, particularly in cases in which the tumor is challenging to access or requires high doses of radiation.¹⁷

11.1.2.1. Different Types of Brachytherapy¹⁵

Low-Dose Rate (LDR) implants: The radiation source in this kind of brachytherapy is left in place for one to seven days.¹⁷

High-Dose-Rate (HDR) implants: The radiation source only remained in situ for 10 to 20 minutes at a time during this kind of brachytherapy before being removed.¹⁷

Permanent implants: Upon the placement of the radiation source, the implants are intended to remain within the body for the duration of the patient's life. However, it is important to note that the intensity of radiation emitted by the source will gradually diminish with each passing day. It is imperative to consider this fact when assessing the potential long-term effects of the implant on the patient's health.¹⁷

MammoSite: Targeted radiation therapy is an essential treatment modality in the management of breast cancer following lumpectomy. This therapeutic intervention utilizes a small, flexible balloon that is inserted into the lumpectomy cavity through a minimally invasive incision in the breast. The balloon serves as a focal point for the precise delivery of radiation to the affected breast tissue. This approach offers several benefits, including a reduction in radiation exposure to surrounding healthy tissues, a shorter treatment duration, and fewer side effects. Ultimately, the use of targeted radiation therapy after lumpectomy represents a valuable treatment option for breast cancer patients, as it offers an effective means of achieving tumor control while minimizing the impact on the overall quality of life.¹⁹

Pathophysiology

12. Pathophysiology of Radiation Injury

Ionizing radiation, either directly or indirectly (through reactive oxygen species), destroys DNA, triggering a chain reaction that can lead to cell death. Cell death and resistance vary depending on factors such as degree of differentiation and mitotic rate, as well as cumulative and fractional radiation dose. The immediate effects of organ damage are predominantly characterized by inflammation or epithelial depopulation/repopulation, while the late effects are attributed to fibrosis, vascular injury, or gradual parenchymal injury. The latter can progressively impair the overall functionality of the affected organ.²⁰

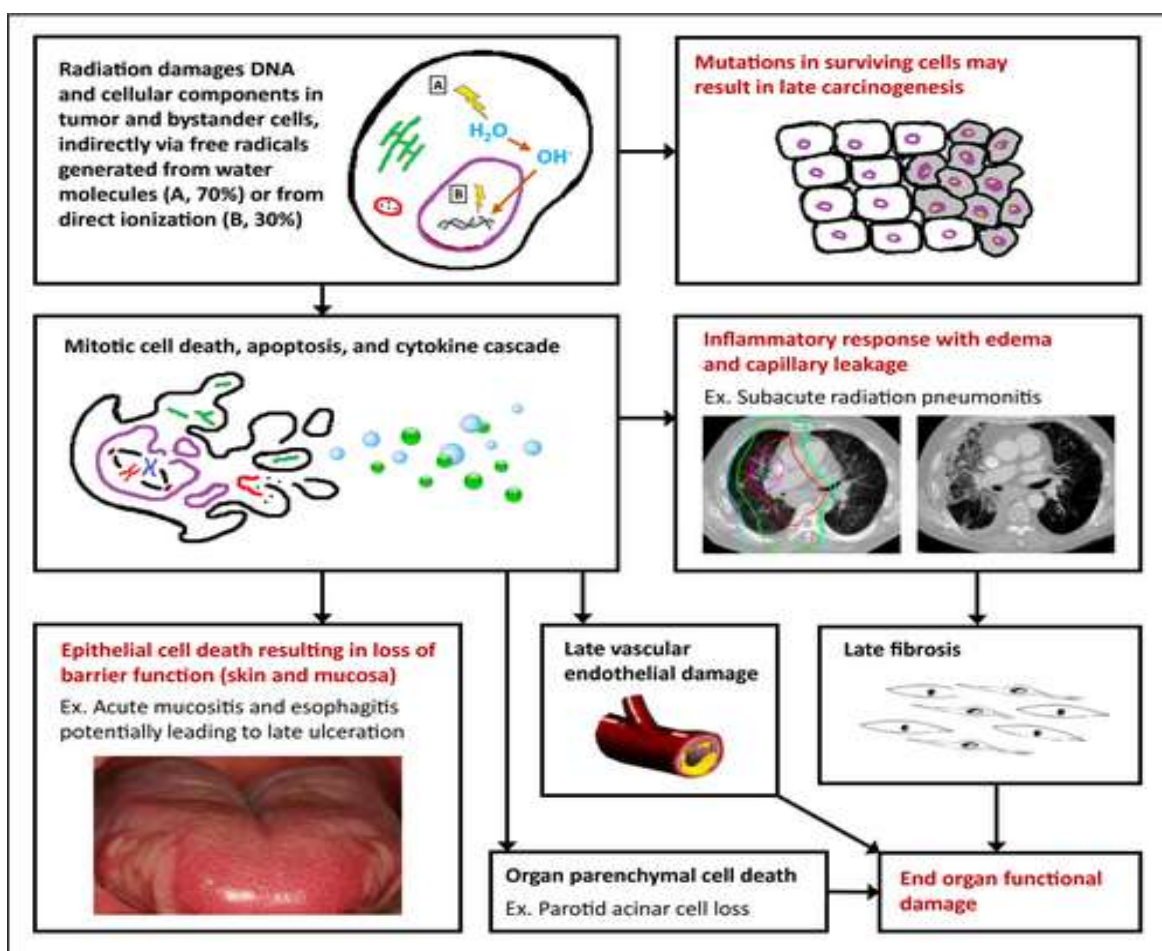


Figure 3: Pathophysiology of radiation effects on normal tissue. Ionizing radiation begins its effects by altering DNA, triggering a chain of events that could lead to toxicity (clinical signs of toxicity are highlighted in red text)²⁰

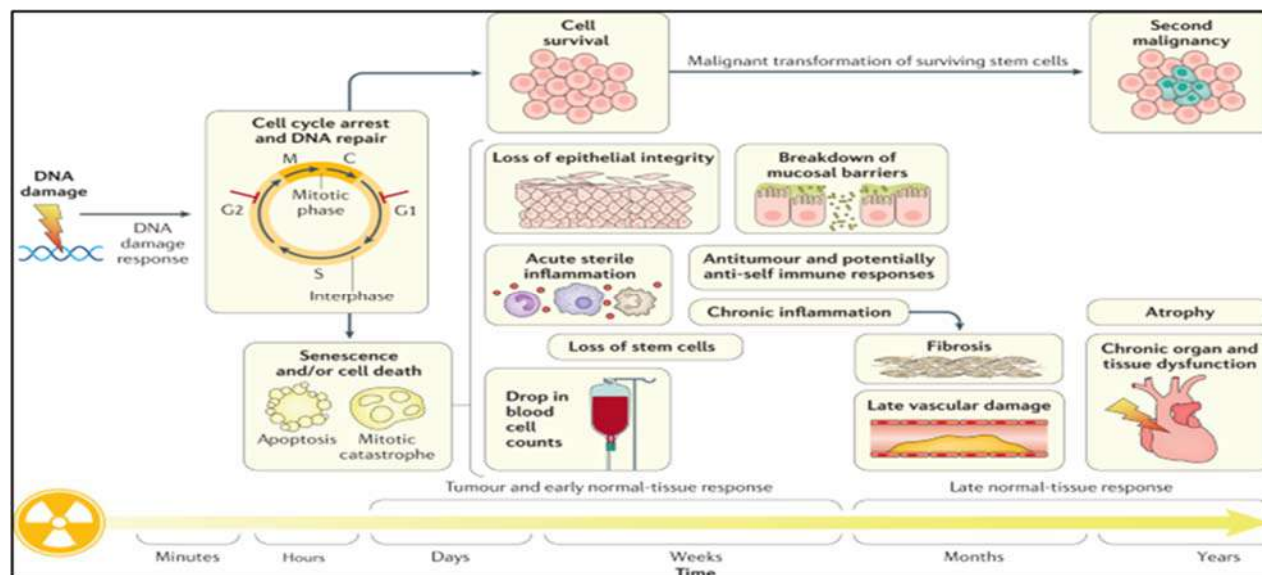


Figure 4: General cellular and tissue responses over time following treatment with radiotherapy²¹

13. Radiotherapy-associated Toxicities

Radiation therapy is used to treat nearly two-thirds of cancer patients, and it frequently causes acute skin and mucosal toxicities. Numerous treatment- and patient-related factors (e.g., total radiation dose and dose fractionation schedule, volume of organ or tissue irradiated, use of concurrent versus sequential chemotherapy, comorbid conditions, functional performance status) affect how severe radiotherapy-associated toxicities are.²²

13.1. Three Major Radiation Toxicities Encountered in Clinical Practice²²

- Radiation dermatitis**, is frequently treated with several topical medications, including water-based moisturizing creams or lotions, topical steroids, anti-inflammatory emulsions, and wound dressings.
- Radiation-induced oral mucositis** can be managed through proper basic oral care practices, appropriate pain management, and medicated mouthwashes and oral rinses and gels.

- c. **Radiation-induced xerostomia** can be treated with sialagogues²³ (drugs stimulate any functioning salivary gland tissue to produce more saliva), saliva substitutes, and moistening medications.

14. Side Effects of Radiotherapy

Radiotherapy treatment can give rise to a series of side effects, which can be treated or prevented. Most of the adverse effects are transient and tend to resolve once the treatment is discontinued. It is essential to note that these side effects can range from mild to severe, and their occurrence and severity depend on various factors such as treatment duration, radiation dose, and the patient's overall health condition. Proper management of these side effects is crucial to ensure successful treatment outcomes and to improve patient's quality of life.²⁴

Radiotherapy side effects are categorized as acute or late effects:

Acute effects appear within 1 to 2 weeks of starting RT and are frequently inflammatory or reflect the depopulation of rapidly proliferating epithelial cells. The timing of symptoms is related to the turnover and transit time for normal tissue stem cells to repopulate damaged tissue; patients who finished RT are advised that acute adverse effects may develop before recovery.²⁴

Late effects frequently appear as fibrosis, vascular injury, infertility, joint problems, lymphedema, mouth problems, rarely, second primary cancers, or other progressive changes in slowly dividing tissues, with end-organ damage manifesting years after treatment. Residual DNA damage may cause delayed carcinogenesis in rare cases.²⁴

Most of these side effects go away a few months after finishing radiation therapy. Late side effects may occur six or more months after radiation therapy is over.

Depending on the part of the body being treated some side effects may happen, such as²⁴:

- Sore skin that might change color to red, lighter, or darker than the usual skin tone.
- Feeling tired
- Hair loss in the area being treated.
- Feeling sick
- Losing of appetite
- Diarrhea
- Mouth problems
- Nausea and vomiting
- Sexual changes
- Swelling
- Urinary and bladder changes

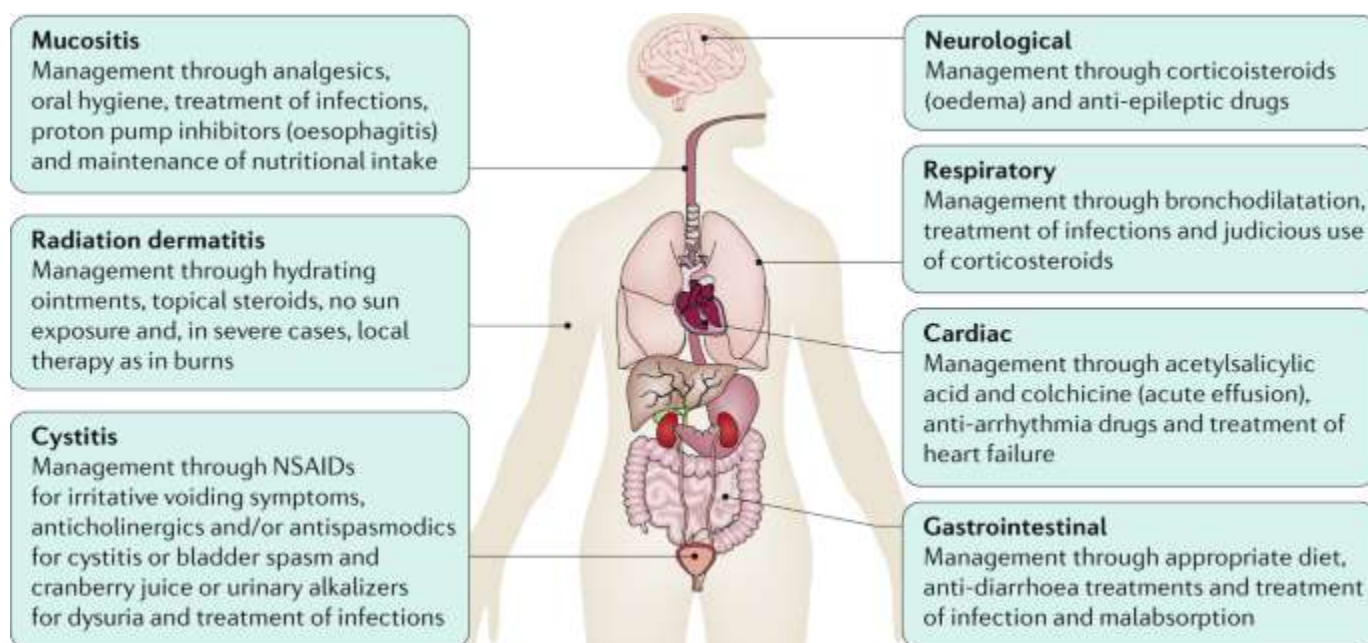


Figure 5: Most common toxicities²⁵

15. Management of Radiotherapy Side Effects

Table 1: Common management considerations ²⁶

Site	Toxicity	Timing	Management
Skin, connective tissues, and breast	Dermatitis	Acute	Maintain skin dryness and prevent irritation, use steroid creams, such as mometasone 0.1% applied twice daily from the start of radiotherapy for high-risk individuals. Aloe, corn starch, and nystatin powder can be used. For severe moist desquamation, adhesive silicone, silver sulfadiazine, and opiates are the recommended treatment options.
	Fibrosis	Late	Pentoxifylline (400 mg bid or tid) and vitamin E (400 IU qd) for 6 months starting 2-4 weeks after RT (e.g., for RT after postmastectomy reconstruction).
	Lymphedema	Late	Physical therapy (manual lymphatic drainage), compression devices/garments, and complete decongestive therapy.
	Bone pain flare	Acute	Dexamethasone 2-8 mg qd for 3-5 days at/before RT or prn for painful bone metastases, depending on expected/observed severity.
CNS	CNS edema/radiation necrosis	Both	Dexamethasone 2-16 mg qd for 1-4 weeks based on severity, with GI prophylaxis and steroid taper for longer courses; bevacizumab/surgery for refractory necrosis.
	Cognitive	Late	Before RT: Memantine 5-10 mg qd, increasing to 20 mg by 4 weeks, total 24 weeks; after RT: donepezil 5 mg qd for 6 weeks, 10 mg qd for 18 weeks.
	Mucositis	Acute	Salt and baking soda/hydrogen peroxide rinse or other mouthwash containing lidocaine, diphenhydramine, antacid, and/or nystatin; opiates if severe and affecting

Head and neck			nutrition, with long-acting (transdermal preferred) and breakthrough.
	Xerostomia	Both	Xylitol-containing candies/gums, saliva substitutes, Amifostine, and mouthwashes.
	Dentition/osteoradionecrosis	Late	Fluoride trays for routine care; pentoxifylline and vitamin E +/- clodronate, antibiotics, and prednisone for conservative management of osteoradionecrosis.
	Fibrosis (dysphagia, jaw, neck)	Late	Speech/language pathologist for dysphagia, jaw physical therapy for trismus ¹⁹ (muscle spasms in the temporomandibular joint), massage therapy for neck stiffness/lymphedema, acupuncture for pain.
Lung	Pneumonitis	Late	Prednisone 40-60 mg qd for 2-4 weeks, tapering over 4-8 weeks total, depending on severity and comorbidities, with GI prophylaxis.
Heart	Pericarditis	Acute	NSAIDs, e.g., ibuprofen 200-800 mg tid prn for 1-2 weeks.
Gastrointestinal	Esophagitis	Acute	Soft/liquid diet; antacids, viscous lidocaine (before swallowing), and/or opiates (before meals); fluconazole for empiric treatment of candida esophagitis.
	Nausea	Acute	Antacids, prn ondansetron, or prochlorperazine (both tid and alternating if severe).
	Gastritis/ulceration	Both	Avoid gastric irritants; antacids and prolonged course of proton pump inhibitors; formalin for refractory bleeding, coagulation if severe.
	Enteritis	Both	Low fiber/residue/fat diet; loperamide (qd or bid) and/or diphenoxylate/atropine; subcutaneous octreotide (100 µg tid for 3-5 days) if refractory with dehydration.
Gastrointestinal	Proctitis	Both	Steroid creams; for late hematochezia, sucralfate enema, formalin, and coagulation.

Genitourinary	Obstructive urinary symptoms	Both	Avoid fluids before sleep, minimize caffeine and alcohol; α -blockers (e.g., initiate/increase tamsulosin dose for 3-6 months after RT); steroids if severe.
	Cystitis	Both	Rule out urinary tract infection; phenazopyridine for dysuria; antimuscarinics (e.g., oxybutynin, solifenacin) for severe frequency, urge incontinence, and/or bladder spasms.
Sexual	Female	Late	Topical estrogens, regular vaginal dilator usage, pelvic floor physical therapy.
	Male	Late	Phosphodiesterase inhibitors (e.g., sildenafil), vacuum devices, and urologic interventions.

16. Treated Areas and Possible Side Effects

Table 2: Possible side effects at the treated areas²⁷

Part of the body being treated	Possible side effects
Brain	Fatigue, hair loss memory or concentration problems nausea and vomiting skin changes, headache blurry vision
Breast	Fatigue, hair loss, tenderness skin changes, swelling (edema)
Chest	Fatigue, hair loss, skin changes throat problems (trouble swallowing) cough, shortness of breath
Head and Neck	Fatigue, hair loss mouth problems skin changes, taste changes throat problems (trouble swallowing) the less active thyroid gland
Pelvis	Diarrhea, fatigue hair loss, skin changes nausea and vomiting sexual problems (men) fertility problems (men) sexual problems (women) fertility problems (women) urinary and bladder problems
Rectum	Diarrhea, fatigue hair loss, skin changes sexual problems (men) fertility problems (men) sexual problems (women) fertility problems (women) urinary and bladder problems
Stomach and Abdomen	Diarrhea, fatigue hair loss, skin changes nausea and vomiting

17. Radiation Recall

Radiation recall occurs when administering certain types of chemotherapy during or shortly after external beam radiation therapy causes a rash that closely resembles a severe sunburn.²⁸

The rash appears on the part of the body that received radiation therapy. Symptoms may include redness, tenderness, swelling, wet sores, peeling skin, and discoloration after the skin has healed.²⁸

Typically, these effects start within days or weeks of starting radiation therapy. But they can also appear months or years later. Radiation recall is treated with corticosteroid medications. Rarely, it may be necessary to wait until the skin heals to continue with chemotherapy.²⁸

Several hypotheses have been presented as to the mechanism of **Radiation Recall Reaction (RRR)**, including a non-immune fixed drug reaction-like condition, dysregulated release of reactive oxygen species, tissue vascular abnormalities, and inadequate DNA repair. All these factors could result in a typical inflammatory microenvironment, leading to tissue stem cell malfunction, keratinocyte necrosis, and skin abnormalities. Alternatively, or in addition, medication exposure may increase low levels of inflammatory tissue cytokines generated by earlier irradiation.²⁹

17.1. Risk Factors of Radiation Recall³⁰

Drugs that are associated with radiation recall and have been reported to cause radiation recall in more than 10 % of patients include:

- Capecitabine
- Cyclophosphamide
- Fluorouracil
- Idarubicin
- Oxaliplatin
- Paclitaxel

- Doxorubicin (free and liposomal)
- Dactinomycin
- Etoposide
- Gemcitabine
- Nab-paclitaxel
- Pemetrexed
- Procarbazine
- Tamoxifen

17.2. Investigations and Diagnosis of Radiation Recall³¹

The physician routinely does the following:

- Takes the patient's previous history of radiation therapy.
- Performs skin assessment.
- Monitors skin for signs of radiation recall.

17.3. Patient Education Tips About Radiation Recall³²

Pharmacists should educate patients about the following items:

- To report any changes in their skin.
- To apply sunscreen before going outdoors and repeat during prolonged exposure.
- To wear loose protective clothing such as long sleeve shirt, and hat when outside.
- To avoid extremes of temperatures.

17.4. Common Toxicity Criteria for Grading Radiation Recall Dermatitis

Vascular damage, epithelial stem cell inadequacy or sensitivity, and idiosyncratic drug hypersensitivity are the probable pathogenic factors. The time interval between radiotherapy and radiation recall dermatitis may happen up to 15 years.³¹

Table 3: Common toxicity criteria for grading radiation recall dermatitis³³

Grade	Radiation Recall Reaction (Dermatologic)
0	No event
1	Faint erythema or dry desquamation
2	Moderate to brisk erythema; patchy moist desquamation, mostly confined to skin folds and creases; moderate edema
3	Moist desquamation in areas other than skin folds and creases; bleeding induced by minor trauma or abrasion
4	Life-threatening consequences; skin necrosis or ulceration of full-thickness dermis; spontaneous bleeding from the involved site; skin graft indicated
5	Death

Patient Education to Control Side Effects of Radiotherapy

18. Ways to Control Side Effects and the Role of the Pharmacists in Patient Education

18.1. Diarrhea^{34,35}

Diarrhea is the passage of 3 or more loose or liquid stools per day (or more frequent passage than is normal for the individual). Diarrhea can occur at any time during radiation therapy to the pelvis, stomach, and abdomen. This is because radiation damages the healthy cells that line the inside of the intestines.

When diarrhea is severe or lasts for an extended period, the body does not absorb enough water and nutrients. This can lead to dehydration or malnutrition.

Patient education tips to prevent complications from diarrhea

Pharmacists should educate patients about the following items:

- Drinking plenty of fluid 8 to 12 cups each day
- Eating small meals that are easy on the stomach
- Eating low-fiber foods
- Eating food that is high in salts such as sodium and potassium
- Keeping the anal area clean and dry
- Avoiding food or drink that can make diarrhea worse

Examples of food and drink that worsen diarrhea include

- Food high in fiber, such as whole wheat bread and pasta.
- A drink that has a lot of sugar, such as regular soda and fruit punch
- Very hot or very cold drinks, juices high in sorbitol (e.g. apple juice), and milk products unless they are low-lactose or lactose-free
- Greasy, fatty, or fried food, such as French fries and hamburgers

- Food and drinks that can cause gas, such as cooked dried beans and raw fruits and vegetables.
- Spicy food, such as pepper, hot sauce, salsa, and chilies.
- Food or drink with caffeine, such as regular coffee, tea, some sodas, and chocolate.
- Sugar-free products sweetened with xylitol or sorbitol, which are found mostly in sugar-free gums and candy.

18.2. Fatigue³⁶

Fatigue is an extreme sense of tiredness and lack of energy that can interfere with a person's usual daily activities. It is a frequent accompanying effect of several cancer treatments, including chemotherapy, immunotherapy, radiation therapy, bone marrow transplant, and surgery. Furthermore, fatigue may be induced by various factors, such as anemia, alterations in appetite, breathing or sleeping difficulties, some medications, depression, infection, pain, and a sedentary lifestyle.

The management of cancer-related fatigue poses a significant challenge for many patients, as it is often resistant to palliative measures such as rest. Cancer-related fatigue may persist for as long as six weeks to a year after the final radiation therapy session.

In conclusion, fatigue is a common sensation that can occur due to a variety of factors, including cancer treatments and other health problems. The management of cancer-related fatigue is often complex and may require tailored interventions to alleviate symptoms and improve quality of life.

Patients' education tips to take some steps to feel better

Pharmacists should educate patients about the following items:

- Sleeping at least eight hours each night.
- Planning time to rest and not to do too much work.

- Exercising, relaxing, eating, and drinking well.
- Ask for help when needed.

18.3. Hair Loss (Alopecia)³⁷

Radiation therapy can lead to hair loss in the body receiving the radiation. This is due to the destruction of rapidly dividing cells, including the hair roots. Hair loss typically commences within two to three weeks following the initial treatment and may persist throughout the treatment regimen. However, the good news is that hair growth is likely to resume within three to six months after the completion of treatment.

Patient Education Tips to Manage Before and After Hair Loss

Pharmacists should educate patients about the following items:

- Washing their hair gently, preferably using a baby shampoo.
- For optimal hair care, it is recommended to use a hairbrush with soft bristles or a wide-tooth comb. This will aid in minimizing hair breakage and damage. If the patient plans to buy a wig, he is advised to do so while he still has hair.
- The patient may feel more in control of hair loss when he plans and decides whether to cut his hair or shave his head.
- Protecting and caring for the scalp by using sunscreen or wearing a hat when going outside.
- It is recommended that the patient be advised against utilizing hair styling tools such as straightening or curling irons, brush rollers or curlers, and electric hair dryers, as well as the use of hair dyes and hairsprays. These items are known to have detrimental effects on the scalp and hair, which can lead to hair damage and in some cases, hair loss. Therefore, it is crucial to exercise caution when selecting hair care products and tools to avoid such occurrences.

18.4. Mouth and Throat Problems³⁸

Irradiation of the head and neck region may result in impairment of the salivary glands and oral tissues, leading to discomfort during mastication and swallowing. The impact of oral complications also referred to as mouth problems, can be magnified when they interfere with eating and drinking, thereby causing dehydration and malnutrition. Following the cessation of treatment, some complications, such as ulceration of the oral mucosa, may diminish, while others, such as gustatory alterations, may extend over weeks, months, or even years. Certain issues, such as xerostomia, may exhibit improvement over time but may never attain full resolution.

Mouth and throat complications may include the following

- Dysgeusia such as a metallic taste
- Xerostomia
- Infections of gums, teeth, or tongue and mouth sores.
- Oral mucositis
- Sensitivity to hot or cold food
- Dysphagia
- Tooth decay (cavities)
- Mouth sores are like little cuts or ulcers in the mouth
- Jaw stiffness and bone changes
- Thick, rope-like saliva

Patient education tips to prevent mouth and throat complications

Pharmacists should educate patients about the following items

- It is important to see a dentist several weeks before beginning treatment.
- Daily mouth examination.
- The tongue, gums, and teeth should all be clean and moist.
- Choosing foods that are easy to chew and swallow.

- Avoid anything that could irritate, burn, or scrape the mouth, such as sharp, crunchy foods, hot foods, spicy foods, fruits, and juices that are high in acid, and all tobacco products.
- Exercising jaw muscles.

18.5. Nausea and vomiting³⁹

Radiation therapy has been known to elicit feelings of nausea, vomiting, or both, which can lead to serious medical issues such as dehydration and malnutrition. Nausea is characterized by an uncomfortable sensation in the stomach, accompanied by a lack of appetite and an urge to vomit. Vomiting refers to the act of expelling the contents of the stomach through the mouth. It is important to note that most cancer treatments, including surgery, some types of chemotherapy, immunotherapy, targeted therapy, and radiation therapy to specific regions of the body, can cause these adverse effects.

There are three types of nausea and vomiting caused by cancer treatment: acute, delayed, and anticipatory. It is crucial to address these side effects as they can severely impact the quality of life of patients undergoing cancer treatment. Clinicians must remain vigilant in identifying and managing these symptoms to ensure that patients receive optimal care.

Patient education tips on ways to manage the following

Pharmacists should educate patients about the following items

- Taking the prescribed anti-nausea medicine appropriately.
- Preventing nausea by eating and drinking bland (foods that are soft and low in fiber), easy-to-digest food and drinks that do not upset the stomach.
- Scheduling meals and drinks (before or after the radiotherapy).
- Eating small meals and snacks.
- Having food and drink that are at room temperature (not too hot and not too cold).
- Drinking plenty of water and fluids.

18.6. Sexual and Fertility Changes⁴⁰

Radiation therapy may result in sexual changes, characterized by hormonal imbalances, and diminished sexual desire or performance. Additionally, there is a possibility for impaired fertility during and after the treatment. Both men and women may experience diverse sexual and reproductive alterations because of radiation therapy. It is crucial to note that these changes can significantly impact patient's quality of life and must be addressed by healthcare professionals proactively.

Exposure to radiation therapy in the regions of the abdomen, pelvis, or spine can potentially cause detrimental effects on the nearby reproductive organs of male patients. This may, in turn, lead to a decline in testosterone levels and sperm counts, consequently resulting in infertility. It is crucial for healthcare professionals to be aware of the potential risks associated with radiation therapy in these areas and to educate patients accordingly, to ensure that they can make informed decisions regarding their treatment.

Women who are not yet in menopause may experience symptoms such as hot flashes, vaginal dryness, and absence of menstruation. This may lead to loss of fertility, which means they may never be able to get pregnant. It is important to educate patients on ways to manage these symptoms.

Complications for women include⁴¹

- Pain or discomfort when having sex.
- Vaginal itching, burning, dryness, or atrophy (when the muscles in the vagina become weak and the walls of the vagina become thin).
- Vaginal stenosis happens when the vagina becomes less elastic, narrows, and gets shorter.
- Symptoms of menopause for women not yet in menopause, such as hot flashes, vaginal dryness, and not having a period.

- Possibility of losing the ability to conceive, which means never being able to get pregnant.

Patient education tips on ways to manage⁴¹

Pharmacists should educate patients about the following items

- Consulting specialized centers for fertility management.
- Ovarian shielding (gonadal shielding) is a procedure in which a protective cover is placed on the outside of the body, over the ovaries and other parts of the reproductive system, to shield them from scattering.
- The physician may prescribe treatment with gonadotropin-releasing hormone agonist, a substance that causes the ovaries to stop making estrogen and progesterone.
- Ask her physician about egg freezing (egg or oocyte cryopreservation), which is a procedure in which eggs are removed from the ovary and frozen.
- Ask her physician about embryo freezing (embryo banking or embryo cryopreservation), which is a procedure in which eggs are removed from the ovary. They are then fertilized with sperm in the lab to form embryos and frozen for future use.
- Ask her physician about ovarian tissue freezing (ovarian tissue cryopreservation), which is considered an experimental procedure, for young girls who haven't gone through puberty and don't have mature eggs. It involves surgically removing part or all of an ovary and then freezing the ovarian tissue, which contains eggs.
- Ask her physician about ovarian transposition (oophoropexy), which is a surgical procedure in which one ovary or both ovaries are either suspended i.e., disconnected from the uterus, or undergo fixation, a procedure in which the ovary is elevated and fixed to the abdominal wall.
- Ask her physician about radical trachelectomy (radical cervicectomy), The cervix, surrounding lymph nodes, and the top portion of the vagina are removed during this procedure. A unique band that holds the uterus closed during pregnancy is then used to join the uterus to the remaining portion of the vagina.

Complications for men include⁴²

- Impotence (erectile dysfunction) means not being able to have or keep an erection.
- Possibility of losing the ability to conceive, which means never being able to have a child, due to having fewer or less effective sperm.

Patient education tips on ways to manage⁴³

Pharmacists should educate patients about the following items

- Consulting specialized centers for fertility management.
- Testicular shielding (gonadal shielding) is a procedure in which a protective cover is placed on the outside of the body to shield the testicles from being scattered to the pelvis when other parts of the body are being treated with radiation.
- Ask his physician about testicular sperm extraction (TESE), which is a procedure for males who are not able to produce a semen sample. Sperm is collected through a medical procedure and frozen for future use.
- Ask his physician about testicular tissue freezing (testicular tissue cryopreservation), which is considered as an experimental procedure at most hospitals. It is done for boys who have not gone through puberty and are at high risk of infertility.
- Ask his physician about sperm banking (semen cryopreservation). Samples of semen are collected and checked under a microscope in the laboratory. The sperm are then frozen and stored (banked) for the future. Sperm can be frozen for an indefinite amount of time.

18.7. Skin Changes⁴⁴

Radiation therapy frequently results in cutaneous reactions, including pruritus, dryness, desquamation, and erythema in the irradiated area. The skin may appear bloated, puffy, or burnt, while patients may develop painful, moist, and infected sores, which are termed wet reactions. These reactions can significantly affect the patient's quality of life and require management. It is

critical to recognize the signs of cutaneous reactions early and manage them proactively to prevent complications.

Skin changes might occur a few weeks after starting radiation therapy. Many of these effects fade within a few weeks of treatment. However, some skin abnormalities may persist long after radiation therapy is completed. Skin in the treatment area may always appear darker and blotchy. It may feel extremely dry or thicker than usual.

Some common skin changes include⁴⁵

- Some common skin changes include⁴⁵ Acne (acneiform eruptions)
- Bed sores (pressure ulcers)
- Blisters
- Burning or skin pain
- Dry skin
- Hand-foot syndrome (palmar-plantar erythrodysesthesia)
- Hyperpigmentation (darker areas of skin, tongue, and joints)
- Hypopigmentation (patches of skin that are lighter)
- Itchy skin (pruritus)
- Keratoacanthoma (dome-shaped skin growth)
- Peeling, flakey, or crusty skin
- Photosensitivity (sunburn easily)
- Rash
- Red or darkened skin
- Painful sores
- Swollen skin

Patient education tips to prevent or manage mild skin and nail changes during cancer treatment:

Pharmacists should educate patients about the following items:

- Do not use talcum powder because this can contain tiny metal particles that can make the soreness worse after radiotherapy.
- Do not rub the treated area too hard because this makes it sore.
- Not to use perfume on the area as this can irritate the skin.
- Washing the skin gently with soap and water and gently pat dry.
- Avoid shaving and do not use heat and cooling pads/ice, or wax and creams for hair removal in the treatment area.
- Protecting the hands and nails by wearing gloves when washing the dishes, or cleaning the house, for example.
- Using sunscreen and sun-protective lip balm.
- Trying to keep the area (areas where the skin folds) clean and dry so it does not become infected.

18.8. Urinary and Bladder Changes⁴⁶

Radiation therapy for the prostate or bladder may result in the occurrence of urinary and bladder problems. These issues are commonly observed between three to five weeks after the initiation of radiation therapy, and they typically subside within two to eight weeks after completion of treatment. It is important to note that the severity of these problems may vary from patient to patient. However, timely medical intervention and care can help alleviate these symptoms.

Radiation therapy can cause urinary and bladder complications, which may include

- Burning or pain when the patient begins to urinate or after he urinates (empty the bladder).
- Trouble starting to urinate.

- Trouble emptying the bladder.
- Frequent, urgent need to urinate.
- Cystitis which is a swelling (inflammation) in the urinary tract.
- Incontinence which is when the patient cannot control the flow of urine from his bladder, especially when coughing or sneezing.
- Waking frequently to urinate.
- Blood in the patient's urine.
- Bladder spasms, which are like painful muscle cramps.

Patient education tips on ways to prevent or manage the following

Pharmacists should educate patients about the following items

- Drinking plenty of liquids at least 8 cups of fluid each day, so that urine is light yellow or clear.
- Avoid coffee, black tea, alcohol, spices, and all tobacco products.
- Ask his physician on ways to prevent urinary tract infections.

18.9. Late effects^{47,48}

The late effects of radiation exposure are highly variable and may become apparent after a considerable period, ranging from several months to years after the initial exposure. Such effects may manifest in any normal tissue that has been exposed to radiation.

The degree of risk associated with long-term side effects is dependent on the specific region treated and the radiation dose administered. Early medical intervention and meticulous treatment planning are essential in mitigating the potential for undesirable long-term effects.

18.9.1. Bone loss⁴⁹

Radiation therapy may cause thinning of the bones only in the part of the body that was treated.

The patient can help lower his risk of bone loss by the following

- Stop smoking and other tobacco products.
- Eating food that is rich in calcium and vitamin D.
- Walking, jogging, or other weight-bearing exercises.

18.9.2. Brain changes⁵⁰

Radiation therapy to the brain can cause complications with thinking and behavior months or years after treatment.

Late effects that may occur depending on the part of the brain that was treated may include:

- | | |
|--------------------------|----------------------------------|
| • Memory loss | • Slow processing of information |
| • Problems doing math | • Personality changes |
| • Problems concentrating | • Movement problem |

18.9.3. Endocrine system changes⁵¹

The endocrine system is a collection of organs and glands that control body functions such as growth, sexual development, reproduction, sleep, hunger, and the way the body uses food. Parts of the endocrine system that may be damaged by cancer treatment include the thyroid, ovaries, and testes. Complications caused by these changes can develop many years after treatment and may include early menopause, infertility, underactive thyroid, overactive thyroid, and weight gain.

18.9.4. Hearing complications⁵²

Treatment with high doses of radiation to the brain can cause ringing in the ears (called tinnitus) or hearing loss that begins months or years after treatment. Patients should have at least one visit with an audiologist after finishing the treatment. Protect hearing by avoiding loud noises and wearing earplugs when using loud equipment.

18.9.5. Heart complications⁵³

Radiation therapy to the chest may cause heart problems that don't show up until years after treatment.

Heart complications caused by cancer treatment may include the following

- A weakening of the heart muscle is known as congestive heart failure.
- Coronary artery disease occurs when the small blood vessels that supply blood and oxygen to the heart narrow.

Patient education tips on ways to manage the following

Pharmacists should educate patients about the following items

- Eating a heart-healthy diet that includes a variety of fruits, vegetables, and whole grains. It also includes lean meats, poultry, fish, beans, and fat-free or low-fat milk or milk products.
- Losing weight and exercising
- Quitting smoking
- Getting enough rest

18.9.6. Joint changes⁴⁷

Radiation therapy can cause scar tissue to form in the joints. These problems can lead to loss of motion in joints, such as the jaw, shoulders, hips, or knees. These problems will occur only in the part of the body that was treated.

18.9.7. Lung complications⁵⁴

Radiation therapy to the chest may damage the lungs. Lung damage can cause shortness of breath, wheezing, fever, dry cough, congestion, and feeling tired.

Patient education tips on ways to manage the following

Pharmacists should educate patients about the following items

- Asking the physician about oxygen therapy
- Losing weight and exercising
- Quitting smoking

18.9.8. Mouth changes⁵⁵

Radiation therapy to the head or neck can cause late side effects in the mouth. Problems may include dry mouth, cavities, or bone loss in the jaw.

Patient education tips on ways to manage

Pharmacists should educate patients about the following items

- Patients may need to have their teeth checked every 1 to 2 months for at least 6 months after radiation treatment.
- Exercising the jaw by opening and closing the mouth 20 times without causing pain, three times a day, even if the jaw is not stiff.
- Stimulating saliva by drinking 8 to 10 cups of liquid per day.
- Using a mouthwash with fluoride every day and avoiding mouthwash that contains alcohol.

18.9.9. Post-traumatic stress⁵⁶

Symptoms of post-traumatic stress can occur at any time, even years after the first cancer treatment.

Symptoms of post-traumatic stress may include

- Frightening thoughts
 - Trouble sleeping
 - Being distracted
 - Feeling alone
 - Feeling hyper
 - Losing interest in daily activities
- Feelings of shock, fear, helplessness, or horror

18.9.10. Lymphedema

Lymphedema is a condition where lymph fluid accumulates in tissues, causing swelling due to inefficient drainage.⁵⁷ Patients may be at risk for lymphedema if part of the lymph system is damaged during surgery to remove lymph nodes or by radiation therapy to areas with large numbers of lymph nodes. Lymphedema can develop many years after treatment.

Patient education tips on ways to manage the following

Pharmacists should educate patients about the following items

- Protecting their skin
- Exercising
- Manual lymph drainage (a light, skin-stretching massage that helps promote the movement of lymphatic fluid out of the swollen limb).
- Wearing compression garments or bandages.

18.9.11. Second primary cancers⁵⁸

It is well established that individuals who have undergone cancer treatment may be at an increased risk of developing a new cancer even after many years of completing treatment. Thus, patients need to undergo regular check-ups throughout their lifetime to detect cancer at an early stage. The importance of these follow-up appointments cannot be overstated, as prompt detection of a new cancer can often lead to successful treatment outcomes. Therefore, it is recommended that patients who have undergone cancer treatment should adhere to a regular follow-up schedule as advised by their healthcare provider.

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Annexes

Grading and Management of Radiotherapy Common Toxicities

Adopted from Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0
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U.S. National Cancer Institute - National Institutes of Health

ANNEX I: Grading and Management of Radiotherapy Common Toxicities

Dermatitis Associated with Radiation-Based Therapy⁵⁹

CTCAE	Grade 1	Grade 2	Grade 3	Grade 4
	Faint erythema or dry desquamation.	Moderate to brisk erythema and/or dry desquamation; patchy moist desquamation, or non-hemorrhagic crusts mostly confined to skin folds and creases.	Moist desquamation or hemorrhagic crusts, non-hemorrhagic crusts other than in skin folds and mostly confined to skin folds and creases; bleeding induced by minor trauma or abrasion.	Life-threatening consequences - Extensive confluent hemorrhagic crusts or ulceration (>50% of the involved field) - Extensive spontaneous bleeding from the involved site (>40% of the involved site); skin necrosis or ulceration of full-thickness dermis or any size ulcer with extensive destruction, tissue necrosis, or damage to muscle, bone, or supporting structures with or without full-thickness skin loss.
Management	Weekly follow-up is adequate unless rapid progression is noted.	- Considering twice weekly assessments to monitor for rapid change. A. Dry desquamation without crusts: - Considering glucocorticosteroid cream or ointment for a limited period (1–2 weeks). - Topical antiseptics and antibiotics at any sign of superinfection. - Considering the use of topical	- Evaluating the need for daily assessment. - Closely monitoring for signs of local or systemic infection. - For grade 3 reactions occurring at <50 Gy, considering brief interruption in treatment. A. Confluent moist desquamation without crusts: - Topical antiseptic - Considering adding daily topical glucocorticosteroid lotion to reduce	- Considering interrupting Treatment until the skin reaction has resolved to at least grade 2. - Skin graft is indicated. - In the case of severe superinfection, considering the use of IV antibiotics if unresponsive to oral antibiotics. - Hospitalizing the patient.

		antiseptics and antibiotics for the prevention of more severe reactions. B. Moist desquamation in skin folds: • Topical antiseptic • Considering adding daily topical glucocorticosteroid lotion to reduce inflammation for a limited period (1–2 weeks). • Topical antibiotics are active against <i>Staphylococcus aureus</i> at any sign of superinfection. Considering systemic antibiotics if superinfection becomes more severe. • Topical eosin or soft zinc preparations in the skin folds. A thin layer of soft zinc preparation may be used in skin folds but should be removed before treatment with radiotherapy to avoid radiation dosimetric problems. Topical eosin in skin folds or on erosive lesions may also be a useful treatment approach. C. Dry desquamation with isolated non-hemorrhagic crusts:	inflammation for a limited period (1–2 weeks). • Topical antibiotics active against <i>S. aureus</i> at any sign of superinfection. • If superinfection becomes more severe, consider the use of IV antibiotics if unresponsive to oral antibiotics. • Topical eosin or soft zinc preparations in the skin folds. A thin layer of a soft zinc preparation may be used in skin folds, but should be removed before treatment with radiotherapy to avoid radiation dosimetric problems. Topical eosin in skin folds or on erosive lesions may also be a useful treatment approach. B. Confluent moist desquamation with crusts: • Topical antiseptic • If superinfection becomes more severe, consider the use of IV antibiotics if unresponsive to oral antibiotics. • Considering debridement using hydrogels. Skin trauma should be	
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		• Topical antiseptic • Considering adding daily topical glucocorticosteroid lotion to reduce inflammation for a limited period (1–2 weeks). • Topical antibiotics active against <i>S. aureus</i> at any sign of superinfection. Considering systemic antibiotics if superinfection becomes more severe. • Topical eosin or soft zinc preparations in the skin folds. A thin layer of a soft zinc preparation may be used in skin folds but should be removed before treatment with radiotherapy to avoid radiation dosimetric problems. • Hydrogels can be used to keep crusts flexible. • Considering debridement using hydrogels. Skin trauma should be avoided to prevent superinfection.	avoided to prevent superinfection. • If hydrocolloid dressings are used, the thickness of the dressing should be considered for the radiotherapy dosimetry. Hydrofiber dressings can be used after the completion of radiotherapy.	
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Mucositis Associated with Radiation-Based Therapy⁶⁰

CTCAE	Grade 1	Grade 2	Grade 3	Grade 4
	Asymptomatic or mild symptoms; intervention not indicated.	Moderate pain or ulcer that does not interfere with oral intake; modified diet indicated.	Severe pain; interfering with oral intake.	Life-threatening consequences: urgent intervention indicated.
Prevention	- It is important for the patient to see a dentist several weeks before beginning treatment. - Daily mouth examination. - The tongue, gums, and teeth should all be clean and moist. - Choosing foods that are easy to chew and swallow. - Avoid anything that could irritate, burn, or scrape the mouth, such as sharp, crunchy foods, hot foods, spicy foods, fruits and juices that are high in acid, and all tobacco products. - Exercising jaw muscles.			
Management	- Bland rinses and topical anesthetics, such as 2% viscous lidocaine swish and spit. - Modifying the diet to limit incidental trauma by avoiding rough and sharp foods.	Normal saline or sodium bicarbonate solutions can provide relief of mild to moderate mucositis pain.	Treating pain with limited risk for systemic absorption using 2% morphine mouthwash which should be a small amount and spit not swallowed. This is for patients with head and neck cancer receiving chemoradiotherapy.	- Considering admission to the hospital for systemic analgesics and ongoing monitoring and evaluation for secondary infections. - Using patient-controlled analgesia with morphine. - Using transdermal formulations of morphine or fentanyl to provide long-lasting background pain control and patient-controlled analgesia to allow for the

				management of breakthrough pain.
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Diarrhea Associated with Radiation-Based Therapy⁶¹

CTCAE	Grade 1	Grade 2	Grade 3	Grade 4
	Increase of <4 stools per day over baseline; mild increase in ostomy output compared to baseline.	Increase of 4 - 6 stools per day over baseline; moderate increase in ostomy output compared to baseline; limiting instrumental ADL.	Increase of ≥ 7 stools per day over baseline; hospitalization indicated; severe increase in ostomy output compared to baseline; limiting self-care ADL.	Life-threatening consequences: urgent intervention indicated.
Prevention	• Drinking plenty of fluid 8 to 12 cups each day. • Eating small meals that are easy on the stomach. • Eating low-fiber foods. • Eating foods that are high in salt such as sodium and potassium. • Keeping the anal area clean and dry. • Avoid foods or drinks that can make diarrhea worse.			
Management	• Providing dietary and fluid modification/advice. • Administering loperamide. • Reassessing after 12–24 hours. • Diarrhea unresolved (persistent grade 1-2) - Continuing loperamide with a higher dose. - Increasing oral fluids and replacing electrolytes. - Considering oral antibiotics. • Diarrhea unresolved after 12–24 hours, treating as per grade 3–4 diarrhea.			

Alopecia Associated with Radiation-Based Therapy⁶²

CTCAE	Grade 1	Grade 2
	Hair loss of <50% of normal for that individual is not obvious from a distance but only on close inspection.	Hair loss of ≥50% is normal for that individual that is readily apparent to others.
Prevention	- Scalp cooling is a method of minimizing radiotherapy-induced alopecia and has been shown to effectively reduce the incidence of hair loss in certain circumstances. - Protect and care for his scalp by using sunscreen or wearing a hat when going outside. - It is recommended that the patient be advised against utilizing hair styling tools such as straightening or curling irons, brush rollers or curlers, and electric hair dryers, as well as the use of hair dyes and hairsprays.	
Management	A different hairstyle may be required to cover the hair loss, but it does not require a wig or hair piece to camouflage.	A wig or hairpiece is necessary if the patient desires to completely camouflage the hair loss; associated with psychosocial impact.