Chapter-18

BIOLOGICAL EFFECTS OF RADIATION

`[1]Mayuri Ojha

[1]Assistant professor, Department of Radiology, Royal School of Medical & Allied Sciences, The Assam Royal Global University, India

18.1. INTRODUCTION

Radiation, particularly ionizing radiation, has the capacity to alter biological systems by transferring energy to atomic and molecular structures within living organisms. The biological effects of radiation refer to the series of physiological, biochemical, molecular, and cellular changes that occur following exposure to such radiation. These effects form the core foundation of radiobiology, an interdisciplinary science that combines principles of physics, biology, and medicine to understand how radiation interacts with biological matter. This knowledge is critical across diverse fields—ranging from diagnostic radiology and cancer therapy to nuclear safety, environmental protection, and space medicine. Understanding these biological effects not only aids in leveraging the benefits of radiation in clinical practice but also helps mitigate potential hazards in medical, industrial, and natural exposure contexts. Ionizing radiation includes particles or electromagnetic waves such as X-rays, gamma rays, alpha particles, beta particles, and neutrons that possess sufficient energy to ionize atoms by detaching electrons. This ionization process leads to the formation of reactive species such as free radicals, especially when the target is water—a major constituent of cells. The radiolysis of water produces hydroxyl radicals (•OH), hydrogen radicals (•H), and hydrated electrons (e^-aq), which subsequently react with biomolecules like DNA, proteins, and lipids. Among these, DNA is considered the most critical target, as damage to its structure can interfere with vital functions such as cell replication, transcription, and regulation. Single-strand breaks (SSBs), double-strand breaks (DSBs), base alterations, and DNA cross-linking are common forms of DNA damage resulting from radiation exposure. Of these, DSBs are particularly lethal as they can lead to chromosomal aberrations, mutations, or cell death if not accurately repaired [1].

Radiation-induced biological effects are classified into two principal types:

I. Deterministic effects (also called non-stochastic) and
II. Stochastic effects.

Deterministic effects occur above a threshold dose and their severity increases with increasing radiation dose. These effects include skin erythema, epilation, radiation burns, sterility, cataracts, and acute radiation syndrome [2]. In contrast, stochastic effects do not exhibit a threshold; rather, the probability of their occurrence increases with dose, although their severity is dose-independent. These include radiation-induced carcinogenesis and heritable genetic mutations, making them highly relevant in contexts of chronic low-dose exposure, such as in medical imaging or occupational environments. Another crucial concept is radiosensitivity, which varies between different cell types, tissues, and individuals. Cells that are undifferentiated, actively dividing, and have a high mitotic rate—such as those in the bone marrow, gastrointestinal lining, and developing embryo—are more sensitive to radiation. This is described by the Law of Bergonié and Tribondeau, which states that cellular

radiosensitivity is directly proportional to its proliferative capacity and inversely proportional to its level of differentiation. This principle is particularly relevant in radiation therapy, where the goal is to selectively destroy rapidly dividing tumor cells while preserving healthy, non-dividing tissues [3].

18.2. ACUTE RADIATION EFFECTS

Acute radiation effects refer to the immediate or short-term biological responses of tissues and organs to high doses of ionizing radiation delivered over a short period of time, typically minutes to hours. These effects are deterministic in nature, meaning they have a dose threshold below which they do not occur, and their severity increases with the dose once the threshold is surpassed. Acute radiation effects are distinguished from chronic or late effects, which may take months or years to develop. These effects are of critical importance in scenarios involving radiation accidents, radiological terrorism, nuclear warfare, and high-dose radiotherapy, and they are most clearly manifested in tissues with rapidly dividing cells such as the bone marrow, gastrointestinal epithelium, and skin [4].

- **Mechanism of Acute Radiation Injury:** When a large dose of ionizing radiation is absorbed by the body, it causes extensive damage at the cellular level. Ionizing radiation produces free radicals and reactive oxygen species (ROS), primarily through the radiolysis of water. These reactive species induce DNA strand breaks, protein denaturation, and lipid peroxidation, leading to disruption of cellular homeostasis [5]. Rapidly dividing cells are particularly vulnerable because they have less time to repair DNA damage before progressing through the cell cycle. As a result, cell death (apoptosis or necrosis) ensues, especially in tissues with high turnover rates. The cumulative destruction of cells impairs tissue and organ function, manifesting as the clinical symptoms of acute radiation syndromes.
- **Threshold Doses and Severity:** Acute radiation effects become clinically evident only when the radiation dose exceeds certain threshold values. The threshold dose varies depending on the tissue type and the sensitivity of the individual. For example, transient erythema of the skin may appear after 2 Gy, while a dose of >1 Gy to the whole body can initiate systemic symptoms. A whole-body dose of >10 Gy is usually fatal in the absence of prompt medical intervention [6].

18.2.1. Acute Radiation Syndrome (ARS)

Acute radiation syndrome (ARS), also known as radiation sickness, occurs after exposure to high doses (>1 Gy) of penetrating radiation delivered to the whole body or a significant portion of it. ARS is characterized by a predictable pattern of systemic symptoms, progressing through the following phases:

- **Prodromal Phase:** This phase begins within minutes to hours after exposure and may last for several hours to days. Common symptoms include nausea, vomiting, anorexia, fatigue, and diarrhea. The severity of these symptoms correlates with the dose received. Higher doses result in a shorter prodromal phase and quicker progression to more severe symptoms.
- **Latent Phase:** This phase is a deceptive period of clinical improvement that may last from hours to weeks depending on the radiation dose. Although the patient appears to recover, extensive biological damage is progressing at the cellular level, particularly in the hematopoietic and gastrointestinal systems [7].
- **Manifest Illness Phase:** In this phase, the full clinical picture of ARS becomes apparent and is classified into subsyndromes based on the dose:
    - Hematopoietic Syndrome (1–6 Gy): Damage to bone marrow stem cells causes pancytopenia, leading to anemia, increased risk of infection, and hemorrhage. Onset occurs within 1–3 weeks post-exposure. Recovery is possible with medical support, including antibiotics, blood transfusions, or bone marrow transplantation.
    - Gastrointestinal Syndrome (6–10 Gy): This involves the destruction of the intestinal crypt cells, resulting in severe diarrhea, dehydration, electrolyte imbalance, and sepsis. Death usually occurs within 1–2 weeks if supportive care is inadequate.
    - Neurovascular Syndrome (>30 Gy): At extremely high doses, damage to neurons and capillaries in the brain leads to confusion, ataxia, seizures, coma, and ultimately death within 24–48 hours.

This syndrome is invariably fatal.

- **Recovery or Death:** Recovery depends on the radiation dose and the medical interventions available. Mild exposure (<2 Gy) may result in complete recovery over weeks or months. Higher exposures require intensive care and may result in death from infection, bleeding, or multi-organ failure.

18.2.2. Localized Acute Radiation Effects

Localized exposure to ionizing radiation can result in acute tissue reactions, particularly within clinical environments such as radiation therapy. The severity and manifestation of these effects depend on the radiation dose, the duration of exposure, and the radiosensitivity of the tissues involved. The skin is one of the most commonly affected organs in localized exposure, exhibiting a range of reactions that progress with increasing dose. Early effects include erythema (redness of the skin), followed by dry desquamation, where the skin peels due to the loss of superficial cells. With higher doses, moist desquamation may occur, characterized by weeping of the skin and exposure of the underlying dermis. In extreme cases, prolonged or high-dose exposure can lead to ulceration and tissue necrosis [8]. Mucosal surfaces are also highly sensitive to radiation. When areas such as the oral cavity, gastrointestinal tract, or respiratory tract are irradiated, patients may develop mucositis, stomatitis, or esophagitis, depending on the anatomical region treated. These conditions are often painful, can impair nutrition and hydration, and may predispose patients to secondary infections. The eyes can be affected as well, particularly in head and neck radiation. Acute ocular damage includes conjunctivitis and keratitis, which present as redness, tearing, pain, and light sensitivity. Another significant localized effect is on the gonads. Exposure to high doses of radiation can impair gametogenesis, potentially resulting in temporary or permanent sterility, depending on the dose and sex of the patient.

18.2.3. Factors Influencing Acute Radiation Effects

The occurrence and severity of acute radiation effects are influenced by several critical factors. The total radiation dose and the rate at which it is delivered play a foundational role; higher doses and faster dose rates generally lead to more severe biological outcomes. The type of radiation, particularly its Linear Energy Transfer (LET), also affects tissue response. High-LET radiation such as neutrons and alpha particles creates densely ionizing tracks, causing complex DNA and cellular damage that is more difficult to repair than the relatively sparse damage induced by low-LET radiation like X-rays and gamma rays. The volume of tissue irradiated is another key determinant [9]. Whole-body exposure presents a higher risk of systemic effects and multi-organ failure compared to partial-body exposure, where damage is more localized and may be more manageable. Individual susceptibility also plays a role, with factors such as age, underlying health conditions, nutritional status, and genetic predisposition influencing how a person responds to radiation exposure. Additionally, the presence of oxygen within tissues affects radiosensitivity through the oxygen enhancement effect. Oxygen stabilizes the free radicals generated by radiation, amplifying cellular damage. Conversely, hypoxic or poorly oxygenated tissues, as often found in tumors, tend to be more resistant to radiation therapy.

18.2.4. Medical Management of Acute Radiation Effects

Effective management of acute radiation effects, especially in the context of Acute Radiation Syndrome (ARS), requires rapid assessment and comprehensive supportive care. The initial step in medical management involves accurate triage, which includes estimating the radiation dose based on the time of onset of symptoms and monitoring biological markers such as lymphocyte depletion rates. Treatment then proceeds with supportive measures tailored to the severity and type of symptoms experienced. Supportive therapy forms the cornerstone of management and includes intravenous fluids and electrolyte replacement to prevent dehydration and shock, broad-spectrum antibiotics to prevent or treat infections due to immunosuppression, and transfusion of blood components to manage anemia or thrombocytopenia. In cases involving significant bone marrow suppression, hematopoietic stem cell transplantation may be required to restore marrow function and immune competence. Administration of hematopoietic growth factors, such as granulocyte colony-stimulating factor (G-CSF), is also employed to stimulate the recovery of white blood cell counts and enhance immune defense.

In scenarios involving internal contamination with radioactive isotopes, chelating agents may be used to bind and promote the excretion of specific radionuclides. Additionally, radioprotective agents such as amifostine can be administered prior to radiation exposure in controlled settings to reduce tissue injury by scavenging free radicals and supporting cellular antioxidant defenses. The ultimate outcome depends on timely intervention, dose and duration of exposure, and the overall health of the affected individual.

18.3. CHRONIC RADIATION EFFECTS

Chronic radiation effects refer to the long-term biological consequences of prolonged or repeated exposure to low or moderate doses of ionizing radiation. Unlike acute effects, which manifest shortly after exposure and are typically dose-dependent, chronic effects can take months or even years to become clinically apparent. These effects can occur following occupational exposures, environmental contamination, therapeutic radiation, or repeated diagnostic imaging. Chronic radiation damage can involve multiple organ systems and may lead to degenerative, carcinogenic, genetic, or teratogenic outcomes, depending on the dose, dose rate, type of radiation, exposed tissues, and individual susceptibility [10].

18.3.1. Mechanisms Underlying Chronic Radiation Damage

The primary mechanism of chronic radiation injury is the cumulative effect of DNA damage and cellular injury over time. Ionizing radiation causes direct and indirect damage to cellular macromolecules, particularly DNA. While many damaged cells can repair this damage, the repair mechanisms are not always perfect. Misrepair can lead to mutations, chromosomal aberrations, altered gene expression, or loss of cellular function. Over long periods, such sub-lethal damage accumulates, leading to progressive tissue degeneration, fibrosis, vascular damage, or even malignant transformation. Chronic radiation also induces sustained oxidative stress through prolonged generation of reactive oxygen species (ROS) and chronic inflammation, which further contributes to cellular aging (senescence), apoptosis, and necrosis in various tissues. In addition, radiation-induced damage to the microvasculature and endothelial cells leads to ischemia, poor tissue regeneration, and scarring.

18.3.2. Tissue-Specific Chronic Radiation Effects

A. **Skin and Subcutaneous Tissue:** Chronic skin changes due to radiation include hyperpigmentation, telangiectasia (dilated blood vessels), atrophy, alopecia, and ulceration. Repeated or long-term exposure may cause radiation dermatitis, characterized by fibrosis and loss of skin elasticity. In severe cases, non-healing ulcers or radiation-induced skin cancers such as basal cell carcinoma may develop.
B. **Eye:** One of the most well-documented chronic radiation effects in the eye is radiation cataractogenesis**.** The lens of the eye is particularly radiosensitive due to its non-replicating cells. Chronic exposure can lead to opacification of the posterior subcapsular region of the lens, resulting in progressive visual impairment. Cataracts can occur at cumulative doses as low as 0.5 Gy, especially with fractionated or prolonged exposure [11].
C. **Lungs:** Radiation-induced lung injury may manifest as radiation pneumonitis initially and progress to pulmonary fibrosis in chronic phases. The latter is characterized by reduced lung compliance, impaired gas exchange, and decreased pulmonary function. This is particularly relevant in patients receiving thoracic radiotherapy or workers exposed to airborne radioactive dust.
D. **Cardiovascular System:** Chronic radiation exposure can lead to radiation-induced heart disease (RIHD)**.** The damage may include pericarditis, myocardial fibrosis, valvular damage, and accelerated atherosclerosis due to endothelial injury. These effects are especially significant in long-term survivors of cancer therapy involving mediastinal radiation [12].
E. **Gastrointestinal Tract:** Long-term exposure of the gastrointestinal tract to radiation, especially in cancer therapy for abdominal or pelvic tumors, can result in chronic radiation enteritis or colitis**.** Symptoms include persistent diarrhea, malabsorption, abdominal pain, and rectal bleeding due to mucosal damage, vascular sclerosis, and fibrosis of intestinal tissues.
F. **Bone and Marrow:** Bone exposed to chronic radiation may undergo osteoradionecrosis, particularly in

the jaw and pelvic bones. The bone becomes brittle and avascular, leading to fractures and non-healing wounds. In the bone marrow, chronic radiation can result in myelosuppression or aplastic anemia, particularly with cumulative doses above 4 Gy.

18.3.3. Carcinogenic Effects of Chronic Radiation

One of the most critical and concerning long-term biological consequences of chronic radiation exposure is the induction of cancer, a process known as radiation-induced carcinogenesis. Ionizing radiation is a potent carcinogen capable of initiating and promoting oncogenesis through its ability to damage DNA directly or indirectly. The underlying mechanism primarily involves the induction of mutations in nuclear DNA, including point mutations, chromosomal translocations, and deletions, which can disrupt normal cellular regulatory pathways and promote uncontrolled cell proliferation. Prolonged or repeated exposure to low-to-moderate doses of radiation—as might occur in occupational, environmental, or certain medical settings—can cumulatively result in the accumulation of genetic alterations that predispose cells to malignant transformation. Importantly, radiation does not produce a unique type of cancer but rather increases the incidence of cancers commonly seen in the general population. Epidemiological evidence strongly supports the carcinogenic potential of radiation, with studies on atomic bomb survivors, uranium miners, radiologists, and nuclear industry workers consistently showing elevated cancer risks [13]. Leukemia is among the earliest and most well-documented cancers associated with radiation exposure. It typically manifests within 5 to 7 years post-exposure and is linked with relatively lower radiation doses. Apart from leukemia, solid tumors such as thyroid cancer, particularly in children exposed to radioactive iodine isotopes, are significantly associated with radiation. Breast cancer risk is also elevated in women exposed during puberty or early adulthood, a period of high breast tissue sensitivity. Lung cancer has been observed in individuals exposed to airborne radioactive particles, such as radon gas in miners. Furthermore, skin cancers, bone sarcomas, and brain tumors have also been documented following chronic radiation exposure. The latency period for radiation-induced cancers can range from a few years, as in leukemia, to several decades for solid tumors, depending on the type of radiation, the dose received, the age at exposure, and the tissue involved. The risk is particularly pronounced at low to moderate dose ranges (0.1–1 Gy), where stochastic effects—those occurring by chance and without a threshold—are most relevant. Importantly, radiation-induced cancers follow a dose-response relationship, with risk increasing linearly or linearly-quadratically with increasing dose, especially at lower doses where cellular repair mechanisms may be partially effective but not infallible.

Additionally, genetic predisposition plays a crucial role in modulating individual susceptibility to radiation-induced cancer. Mutations in tumor suppressor genes such as TP53 or DNA repair genes like BRCA1/2 can significantly increase sensitivity to radiation and enhance the likelihood of malignant transformation. Moreover, age at exposure is a vital determinant, with younger individuals showing greater susceptibility due to higher mitotic activity and a longer life expectancy during which radiation-induced mutations can manifest clinically. From a clinical and public health perspective, understanding the carcinogenic risks associated with chronic radiation exposure is essential for establishing safety guidelines, implementing dose limits, and designing monitoring programs for at-risk populations. Risk assessments based on large-scale cohorts, such as the Life Span Study of atomic bomb survivors in Hiroshima and Nagasaki, continue to inform international radiological protection standards and medical radiation practices.

18.3.4. Genetic and Reproductive Effects of Chronic Radiation

Chronic exposure to ionizing radiation poses a significant risk not only to the exposed individual but also to future generations through its potential to induce heritable genetic mutations. When radiation affects germ cells—sperm in males and ova in females—there is a possibility that the resulting genetic alterations may be transmitted to offspring. These genetic effects, also termed heritable effects, do not manifest in the exposed individual but may appear in descendants as birth defects, developmental abnormalities, or increased predisposition to disease, including cancer. Although direct evidence of radiation-induced heritable mutations in humans remains limited, primarily due to challenges in long-term multigenerational follow-up and distinguishing radiation-induced mutations from natural background mutation rates, data from animal models have been robust. Studies in mice,

for example, have demonstrated that chronic low-dose radiation exposure increases the frequency of germline mutations, including point mutations, deletions, and chromosomal aberrations, which can lead to observable phenotypic consequences in offspring. These findings have served as a foundational basis for estimating genetic risk in humans and for setting international radiation protection standards, particularly for radiation workers and pregnant women.

In the context of reproductive health, chronic radiation exposure can have deleterious effects on fertility and the functioning of reproductive organs. Male fertility can be compromised due to radiation-induced damage to spermatogenic cells in the testes, leading to oligospermia, azoospermia, or genetic abnormalities in sperm DNA. The extent of damage is dependent on the total dose, dose rate, and duration of exposure. While some effects, such as temporary sterility, may be reversible with low-to-moderate doses, higher cumulative doses can lead to permanent infertility. Similarly, in females, chronic radiation can lead to ovarian dysfunction, reducing the number and quality of oocytes, leading to early menopause, infertility, or genetic abnormalities in ova. A particularly critical concern arises when pregnant women are exposed to chronic radiation. The foetus is highly radiosensitive, especially during the first trimester, when organogenesis and rapid cell differentiation occur. Depending on the dose, radiation quality, and gestational age, radiation exposure may result in teratogenic effects, which include congenital malformations, growth retardation, microcephaly, intellectual disabilities, and neurodevelopmental deficits. The threshold dose for severe foetal effects is generally estimated to be around 100–250 mGy, although lower doses may still pose risks, particularly for cognitive outcomes. Furthermore, prenatal exposure to ionizing radiation has been associated with an increased lifetime risk of cancer, especially leukaemia and central nervous system tumours. Historical data from survivors of the atomic bombings in Hiroshima and Nagasaki, as well as cases of in utero radiation exposure during diagnostic imaging or therapeutic procedures, have reinforced concerns about foetal vulnerability. In recognition of these risks, radiation protection guidelines emphasize strict dose limits for occupational exposure among women of reproductive age and recommend alternative imaging modalities, such as ultrasound or MRI, during pregnancy whenever feasible. Moreover, pre-conception counseling and fertility preservation strategies may be considered for individuals undergoing radiation therapy or those exposed occupationally to ensure reproductive outcomes are safeguarded.

Table: 18.1. Difference between Acute and Chronic Radiation Effect

Feature	**Acute Radiation Effects**	**Chronic Radiation Effects**
Definition	Effects from high-dose radiation over a short period	Effects from low-dose radiation over a long period
Exposure Duration	Minutes to hours	Weeks, months, or years
Onset of Effects	Immediate to short-term (hours to weeks)	Delayed (months to decades)
Dose Level	High-dose exposure (often > 1 Gy)	Low to moderate cumulative doses
Examples	Acute radiation syndrome (ARS), skin burns, nausea	Cancer, genetic mutations, cataracts, cardiovascular disease
Dose Threshold	Yes (deterministic effects)	No threshold (stochastic effects)
Severity Relationship	Severity increases with dose	Probability of effect increases with dose
Biological Mechanism	Massive cell death and tissue damage	DNA mutations, cumulative damage
Common Sources	Nuclear accidents, radiation therapy overdose, radiation warfare	Occupational exposure, environmental contamination, diagnostic imaging
Reversibility	May be partially reversible with prompt treatment	Often irreversible and progress

18.3.5. Determinants of Chronic Radiation Effects

The severity and manifestation of chronic radiation effects are not uniform across individuals or tissues. They are

influenced by a variety of physical, biological, and environmental factors that collectively determine the biological response to long-term radiation exposure. Understanding these determinants is crucial for assessing risk, planning medical radiation use, and implementing protective measures. One of the most significant determinants is the total radiation dose and the rate at which it is delivered. Chronic exposure typically involves low doses administered over extended periods. However, as the cumulative dose increases, so does the risk of stochastic effects such as cancer and genetic mutations. Moreover, the dose rate plays a pivotal role; lower dose rates generally allow more time for cellular repair mechanisms to respond to damage, thereby reducing the severity of biological effects. Conversely, continuous or repeated exposure without sufficient recovery time can lead to the accumulation of unrepaired damage. The quality of the radiation, often expressed in terms of Linear Energy Transfer (LET), also significantly influences chronic radiation effects. High-LET radiation, such as that from neutrons or alpha particles, deposits energy densely along its path, causing more severe and complex damage at the cellular level, including clustered DNA lesions and chromosomal aberrations. In contrast, low-LET radiation (e.g., X-rays and gamma rays) spreads its energy more sparsely, often resulting in damage that is more readily repaired by cellular mechanisms. Nonetheless, low-LET radiation remains a significant concern due to its widespread use in medicine and industry and its deep tissue penetration.

Tissue and organ sensitivity is another important variable. Tissues composed of rapidly dividing cells, such as those in the bone marrow, gastrointestinal tract, skin, and reproductive organs, are inherently more sensitive to radiation because DNA damage in proliferating cells is more likely to be propagated during replication. In contrast, tissues with slower cell turnover, such as the brain or muscle, tend to be more resistant but are not completely immune, especially at higher doses or with long-term exposure. Individual characteristics such as age and overall health status also influence susceptibility to chronic radiation injury. Younger individuals, whose tissues are actively growing and dividing, are generally more radiosensitive and may face higher lifetime risks of radiation-induced effects, including cancer and developmental abnormalities. Additionally, individuals with compromised immune systems, pre-existing health conditions, or genetic disorders affecting DNA repair (e.g., ataxia-telangiectasia, Li-Fraumeni syndrome) are at elevated risk, as their ability to repair or tolerate radiation-induced damage is impaired. Another crucial factor is the pattern of exposure, particularly fractionation and protraction. Fractionation refers to dividing a total radiation dose into smaller doses delivered over time, a practice common in radiotherapy. This allows normal tissues time to repair between exposures and has been shown to reduce the severity of chronic damage. Protraction, the continuous delivery of a low dose over an extended period, similarly provides time for repair and cell recovery, although the biological effectiveness depends on the specific tissue and repair capacity. Tissue oxygenation plays a significant role in modulating radiation effects, particularly through what is known as the oxygen enhancement effect. Well-oxygenated tissues are more radiosensitive because oxygen stabilizes the free radicals generated during radiation exposure, prolonging their lifespan and increasing the probability of DNA and cellular damage. Conversely, hypoxic tissues, such as those found in the cores of solid tumours, are more radioresistant, posing a challenge in therapeutic settings. This phenomenon has important implications in cancer radiotherapy, where strategies such as hyperbaric oxygen therapy or hypoxia-targeted drugs are used to enhance treatment effectiveness.

18.4. STOCHASTIC AND DETERMINISTIC EFFECTS OF RADIATION

The biological impact of ionizing radiation on human tissues can be broadly classified into two fundamental categories: stochastic effects and deterministic effects. These classifications are based on the nature of the biological outcome, its relationship with radiation dose, and the underlying mechanisms. Understanding these two types of radiation effects is essential in radiation protection, medical imaging, radiotherapy, and nuclear safety, as they inform dose limits, risk assessment, and regulatory frameworks.

18.4.1. Stochastic Effects of Radiation

Stochastic effects are radiation-induced health outcomes that occur by chance and whose probability—rather than severity—increases with the dose of radiation received. Unlike deterministic effects, stochastic effects do not have a threshold dose; even a very small amount of radiation exposure has the potential to induce these effects, although

the probability is lower at lower doses. The defining characteristic of stochastic effects is that once an event, such as a mutation in the DNA of a cell, occurs, the biological outcome may manifest much later and may not be directly proportional in severity to the radiation dose received. The most significant stochastic effects associated with ionizing radiation are carcinogenesis (the induction of cancer) and heritable genetic mutations (germline mutations passed to future generations). These outcomes result from radiation-induced alterations in DNA that escape cellular repair mechanisms or are incorrectly repaired. Unlike deterministic effects, where damage occurs due to massive cell loss in tissues, stochastic effects originate from mutations in a single cell that then proliferates abnormally.

Cancer induction is the most well-documented stochastic effect. Extensive epidemiological data from populations exposed to radiation—such as atomic bomb survivors of Hiroshima and Nagasaki, radiotherapy patients, and nuclear industry workers—clearly demonstrate an increased risk of cancers like leukaemia, thyroid cancer, breast cancer, lung cancer, and other solid tumours. These studies have established a linear no-threshold (LNT) model for radiation protection, which assumes that any increment in dose increases cancer risk proportionally, without a safe lower limit. Heritable effects in humans are more difficult to document, as genetic mutations passed to offspring are rare and confounded by various other environmental and biological factors. However, animal studies and molecular biology research support the possibility of transgenerational effects, especially when germ cells are irradiated. Mutations in these cells can lead to congenital anomalies, developmental disorders, or increased disease susceptibility in the offspring. Several factors influence the likelihood of stochastic effects, including:

- **Total dose and dose rate**: Higher cumulative exposures increase the risk.
- **Type of radiation (LET)**: High-LET radiation is more biologically damaging per unit dose.
- **Tissue type**: Some tissues, such as bone marrow, thyroid, and breast, are more prone to radiation-induced malignancy.
- **Age and sex**: Younger individuals and females generally show higher susceptibility due to higher rates of cell division and hormonal influences.
- **Genetic predisposition**: Mutations in DNA repair genes (e.g., BRCA1, TP53) can heighten the risk of stochastic outcomes.

Given the unpredictable nature of stochastic effects and their profound implications for public health, regulatory agencies have adopted radiation protection principles aimed at minimizing unnecessary exposures. These include the ALARA principle (As Low As Reasonably Achievable), dose limits for occupational and public exposure, and strict safety protocols in medical and industrial practices involving radiation.

18.4.2. Deterministic Effects

Deterministic effects—also referred to as tissue reactions or non-stochastic effects—are biological responses that occur when radiation exposure exceeds a specific threshold dose. Below this threshold, such effects are not observed; however, once surpassed, both the likelihood and severity of the biological injury increase with increasing dose. The basis of deterministic effects lies in the direct loss of a significant population of cells within a tissue or organ, compromising its structural integrity or physiological function. This type of effect is dose-dependent, generally reproducible, and often manifests within a relatively short time frame after exposure, although some may be delayed and present over several weeks or months depending on the tissue type and dose. Common examples of deterministic effects include skin erythema, epilation (hair loss), radiation-induced burns, mucositis, gastrointestinal ulceration, cataract formation, temporary or permanent sterility, and in severe cases, acute radiation syndrome (ARS). For instance, erythema may begin to appear at threshold doses of approximately 2–3 Gy, while temporary sterility in males may result from doses in the range of 3.5–6 Gy. At very high whole-body doses—usually above 5 Gy—deterministic effects may lead to systemic failures, such as bone marrow suppression, gastrointestinal breakdown, and multi-organ dysfunction, which
can be fatal if untreated.

Deterministic effects are of critical concern in clinical radiation applications, particularly in therapeutic radiology, where intentional delivery of high-dose radiation is employed to eradicate malignant cells. Despite technological

advances in planning and precision, adjacent normal tissues are often exposed to some degree of radiation, posing a risk of collateral damage. The severity and location of these effects depend on factors such as total dose, fractionation, volume of tissue irradiated, and individual radiosensitivity. Therefore, the prevention and management of deterministic effects are integral aspects of radiation oncology. To protect patients, radiation workers, and the general population, regulatory bodies such as the International Commission on Radiological Protection (ICRP) have established dose limits and safety guidelines. These are designed to keep exposure well below known thresholds for deterministic effects in occupational and diagnostic settings. Emphasis is placed on adherence to the principles of justification, optimization, and dose limitation to ensure that radiation use achieves clinical or societal benefits while minimizing the risk of harmful outcomes.

Mechanistic Basis and Biological Pathways: The underlying mechanisms of deterministic and stochastic effects are rooted in the nature of DNA damage and the cellular response. In deterministic effects, high radiation doses lead to extensive damage in a large population of cells, overwhelming repair mechanisms and resulting in cell death or functional impairment of the tissue. The body's inability to replace lost cells rapidly enough results in the clinical manifestations of deterministic injuries. For stochastic effects, the focus is on the survival of damaged cells that carry mutations. If such cells evade repair or apoptosis and continue to divide, they may initiate cancer. The risk is modulated by genetic factors, immune surveillance, and environmental influences, making the biological outcome highly variable and difficult to predict. Importantly, the presence of oxygen enhances both stochastic and deterministic effects through the oxygen enhancement ratio (OER), which stabilizes free radicals and amplifies DNA damage.

Radiation Dose and Dose-Response Relationships: Deterministic effects follow a sigmoidal dose-response curve characterized by a threshold and a steep increase in effect severity beyond the threshold. For example, skin erythema begins around 2 Gy and becomes more severe at 5–6 Gy. This predictability allows clinicians to manage therapeutic doses to balance tumour control and normal tissue toxicity. Stochastic effects, on the other hand, are described by a linear no-threshold (LNT) model, which posits that even the smallest dose carries a risk of inducing cancer or genetic mutations. While this model is debated, it remains the foundation for radiation protection standards globally. According to the LNT model, doubling the dose roughly doubles the risk, regardless of how low the initial dose is. This model emphasizes the importance of dose minimization and the ALARA (As Low As Reasonably Achievable) principle in all radiation practices. Deterministic effects are commonly encountered in radiotherapy, fluoroscopic procedures, and radiation accidents. For instance, patients receiving high-dose radiotherapy for head and neck cancer may experience mucositis and xerostomia. Interventional radiology procedures can occasionally lead to skin injuries due to prolonged fluoroscopy. These effects are manageable through appropriate dose planning, shielding, and monitoring. Stochastic effects are more relevant in diagnostic radiology and occupational exposure. A patient undergoing multiple CT scans or a radiologist exposed to scatter radiation over many years may face a slightly increased risk of developing cancer. Although the individual risk is small, it becomes significant when extrapolated across populations, underscoring the need for judicious use of imaging and adherence to safety protocols.

Table: 18.2. Difference between Stochastic and deterministic effect

Feature	Stochastic Effects	Non-Stochastic (Deterministic) Effects
Definition	Effects that occur by chance; probability increases with dose	Effects that occur only above a certain dose threshold
Dose Threshold	No threshold; can occur at any dose	Has a threshold; effects appear only above this level
Dose-Response Relationship	Probability increases with dose, not severity	Severity increases with dose
Severity	Independent of dose	Proportional to dose above threshold
Examples	Cancer, genetic mutations	Skin burns, cataracts, sterility, ARS
Latency Period	Typically long (years to decades)	Short to intermediate (hours to weeks)
Cause	DNA mutation in individual cells	Mass cell death or tissue damage

Relevance to Radioprotection	Basis for setting limits for low-level exposure	Basis for setting dose thresholds in therapy/accidents
Affected Systems	Any cell with reproductive potential	Tissues and organs with high cellular turnover
Predictability	Random and probabilistic	Predictable above threshold

18.5. DOSE-RESPONSE RELATIONSHIP IN RADIATION BIOLOGY

The dose-response relationship is a core principle in radiation biology that describes how the magnitude of a biological effect changes in response to varying levels of radiation exposure. It serves as a fundamental basis for assessing risks, establishing safety guidelines, and determining treatment regimens in medical and occupational settings. This relationship illustrates how cells, tissues, and entire organisms react biologically to different doses of ionizing radiation and helps predict the likelihood and severity of radiation-induced damage. One of the most widely discussed models in radiation biology is the linear dose-response model, particularly in the context of stochastic effects such as carcinogenesis and heritable genetic mutations. According to this model, the probability of a biological effect—such as cancer—increases linearly with the radiation dose. Importantly, it assumes there is no threshold dose below which radiation is harmless; even the smallest dose has the potential to cause damage. This assumption forms the basis of the Linear No-Threshold (LNT) hypothesis**,** which is used by organizations like the International Commission on Radiological Protection (ICRP) to derive public radiation safety limits. Epidemiological evidence from atomic bomb survivors and nuclear industry workers supports this model, showing increased cancer risk even at low to moderate doses (typically between 0.1 and 1 Gy).

Another important model is the linear-quadratic dose-response model, which incorporates both a linear component (representing single-event damage) and a quadratic component (representing damage from two independent radiation events). This model is especially relevant in radiation therapy, where it is used to describe the cell survival curve and determine optimal dosing strategies. At lower doses, the linear term dominates, indicating that damage is primarily from single events. At higher doses, the quadratic term becomes more significant, reflecting increased damage due to overlapping ionizations. This understanding is vital for designing fractionated radiation treatments that aim to maximize tumor destruction while sparing healthy tissue. The threshold dose-response model is typically used for deterministic effects—also known as tissue reactions—which do not occur until a certain minimum dose is surpassed. These effects are characterized by a dose threshold, below which no clinical manifestations are observed. Once this threshold is exceeded, the severity of the effect increases with the dose. Deterministic effects include skin erythema, cataract formation, and radiation burns. For example, skin damage may become visible at doses above 2–3 Gy, and temporary male sterility can occur at doses around 3.5–6 Gy. The threshold dose varies depending on the tissue type, individual sensitivity, and exposure conditions.

The sigmoid or S-shaped dose-response model offers a more nuanced view by showing a slow rise in biological effect at low doses, a steep increase at intermediate doses, and a plateau at higher doses where further dose increases yield minimal additional biological effect. This model is frequently used to represent organ-level responses to radiation, where cell death and tissue damage accumulate to a point of functional failure. It is particularly relevant in the context of high-dose radiotherapy and accidental radiation exposures. Several biological and physical factors influence the nature of the dose-response relationship. The type and quality of radiation, measured by Linear Energy Transfer (LET), play a significant role. High-LET radiations, such as alpha particles and neutrons, deposit energy densely along their tracks and tend to cause more severe and complex damage. In contrast, low-LET radiations like X-rays and gamma rays produce more sparsely distributed ionizations, resulting in less severe effects for the same absorbed dose. Similarly, the rate at which radiation is delivered—known as the dose rate—also affects the outcome. Lower dose rates typically allow more time for cellular repair mechanisms to correct the damage, thereby reducing the biological effect. The type of cell or tissue exposed also matters, as different tissues have varying radiosensitivities. Rapidly dividing cells, such as those in the bone marrow, gastrointestinal tract, and reproductive organs, are more sensitive to radiation than non-dividing cells like neurons or muscle cells. This principle is fundamental to both radiation protection and cancer therapy. Oxygenation status further influences the response. Well-oxygenated tissues are more sensitive to radiation due to the oxygen effect, where oxygen stabilizes free radicals produced by ionizing events, thus increasing the

likelihood of permanent DNA damage. The dose-response relationship is not merely academic—it has profound practical implications. In radiological protection, it underpins the justification for exposure limits and guides risk assessment for workers, patients, and the general public. In clinical radiology and oncology, dose-response models are essential for balancing the efficacy of treatment against the risk of side effects, particularly in radiation therapy planning where precision is paramount. These models also inform emergency preparedness strategies for radiological accidents, helping estimate potential health outcomes based on estimated exposure levels.

18.6. SOMATIC AND GENETIC EFFECTS OF RADIATION

Ionizing radiation can affect biological systems in two broad ways, categorized as genetic effects and somatic effects. These classifications are based on the site of radiation-induced damage and the implications for the individual and future generations. Understanding these effects is critical in radiation biology, particularly in fields like radiotherapy, diagnostic imaging, nuclear medicine, and radiological protection.

18.6.1. Somatic Effects of Radiation

Somatic effects are biological consequences of radiation exposure that manifest in the individual who receives the exposure. These effects do not involve the germline and, therefore, are not passed on to subsequent generations. Instead, they directly impact tissues and organs within the exposed person. Somatic radiation effects are categorized based on their onset (acute or chronic) and mechanism (deterministic or stochastic). They can range from relatively mild symptoms such as temporary skin erythema to severe life-threatening conditions including multiple organ failure.

Acute Somatic Effects: Acute somatic effects typically occur following exposure to a high dose of ionizing radiation over a short period, usually in a single event or within a few days. These effects are deterministic in nature, which means they only appear when the radiation dose surpasses a certain threshold. Below this threshold, the effects are absent. However, once the threshold is exceeded, the severity of damage increases proportionally with dose. The most commonly observed acute somatic effects include:

- Radiation dermatitis (ranging from transient erythema to moist desquamation and necrosis),
- Epilation (hair loss) due to damage to hair follicles,
- Hematopoietic syndrome**,** involving suppression of bone marrow leading to infection and hemorrhage,
- Gastrointestinal syndrome, with nausea, vomiting, diarrhea, and malabsorption due to mucosal lining injury,
- Neurovascular syndrome in extremely high-dose exposures, resulting in seizures, unconsciousness, and death within hours to days.

The onset and severity of these symptoms depend on the dose, dose rate, and area of the body exposed. For example, localized doses above 2–3 Gy can result in erythema and hair loss, while whole-body doses of 5–6 Gy are typically lethal without medical intervention.

Chronic Somatic Effects: Chronic somatic effects emerge months or even years following exposure to radiation. These effects are often the result of lower, repeated exposures or insufficient repair of sublethal damage over time. Unlike acute effects, many chronic effects are stochastic, meaning there is no dose threshold, and the probability of occurrence increases with cumulative dose, although the severity is not dose-dependent. Common chronic somatic effects include:

- Radiation-induced fibrosis, leading to loss of organ function,
- Cataract formation from damage to the lens epithelium,
- Delayed organ atrophy, especially in radiosensitive tissues such as the salivary glands, kidneys, and liver,
- Cardiovascular disease, which has been linked to radiation-induced vascular injury,
- Carcinogenesis, particularly in tissues with high mitotic activity (e.g., bone marrow, breast, thyroid).

These effects are of particular concern in occupational settings, space missions, and radiotherapy, where repeated or long-term exposure can occur. Additionally, the latency period for cancers caused by radiation may vary widely, from 5 to 20 years or more.

18.6.2. Genetic Effect of Radiation

Genetic effects of radiation refer to the heritable consequences that arise when ionizing radiation damages the DNA within germ cells—specifically, sperm in males and ova in females. Unlike somatic effects, which impact only the exposed individual, genetic effects carry the potential to affect future generations by altering the genetic material passed on during reproduction. These mutations, once integrated into the germline genome, may lead to various inherited disorders or developmental anomalies in offspring. Although direct evidence of radiation-induced genetic effects in humans is limited due to ethical and observational challenges, extensive research using animal models has convincingly demonstrated the mutagenic potential of ionizing radiation. In laboratory settings, radiation exposure has been shown to increase the incidence of a broad range of genetic anomalies, including point mutations, chromosomal aberrations, deletions, translocations, and even genomic instability that may persist across multiple generations. Importantly, radiation does not generate new types of mutations; instead, it elevates the rate at which spontaneous or naturally occurring genetic changes appear within the population.

The potential outcomes of these heritable genetic changes can vary from minor, subclinical defects to severe congenital malformations and inherited diseases. Some of the most significant concerns include developmental delays, structural abnormalities, reduced fertility, metabolic dysfunctions, and increased susceptibility to cancer. One of the challenging aspects of studying genetic effects is the latency and subtlety with which they may present—often not observable in the exposed individual but potentially emerging in their descendants. The timing of exposure to radiation is also a critical determinant of genetic risk. Pre-conceptional exposure**,** where either parent is irradiated before conception, is particularly significant. In such cases, damaged germ cells may carry mutations into the zygote, thereby affecting the embryo's entire genetic blueprint. This can lead to a variety of outcomes, ranging from failure of implantation or miscarriage to genetic diseases that manifest at birth or later in life. Prenatal exposure, while more commonly associated with somatic effects, also holds relevance for genetic damage if germ cell development occurs during fetal growth. This is particularly crucial during specific stages of gestation, such as organogenesis**,** when the formation of major organs and systems takes place, and neurodevelopment**,** where cognitive and functional brain structures are established. Radiation exposure during these critical windows can result in structural abnormalities, intellectual disabilities, and other developmental disorders. Studies from atomic bomb survivors in Hiroshima and Nagasaki, as well as those from nuclear accidents such as Chernobyl, have underscored the heightened sensitivity of the developing fetus to radiation, particularly between 8 and 15 weeks of gestation—a period during which central nervous system development is most vulnerable. Moreover, genetic effects are influenced by the dose and quality of radiation, as well as the individual's genetic predisposition to DNA repair efficiency or mutagen sensitivity. High doses of high-LET (Linear Energy Transfer) radiation, such as alpha particles or neutrons, are especially potent in causing complex DNA damage that is difficult for cellular repair mechanisms to manage, thereby increasing the risk of mutation propagation. Furthermore, genetic effects tend to show a linear dose-response relationship, with the probability of occurrence increasing proportionally with dose, albeit without a clear threshold—similar to stochastic effects like carcinogenesis.

Table: 18.3. Comparison of Genetic vs. Somatic Radiation Effects

Feature	Somatic Effects	Genetic Effects
Site of Damage	Body tissues (somatic cells)	Germ cells (sperm or ova)
Impact	Individual exposed	Offspring of exposed individual
Heritability	Not heritable	Heritable
Examples	Cancer, skin burns, ARS	Mutations, congenital malformations
Threshold	Often has a threshold (deterministic)	Generally no threshold (stochastic)
Time of Manifestation	Immediate (acute) or delayed (chronic)	May appear in future generations

18.6.3. Radiation Dose and Mutation Frequency

The relationship between radiation dose and the frequency of genetic mutations is a key area of study in radiobiol-

-ogy and radiation protection. Ionizing radiation has the capacity to directly damage the DNA of germ cells, leading to mutations that, if unrepaired or misrepaired, may be inherited by offspring. One of the fundamental principles established through decades of research is that the frequency of these radiation-induced mutations increases in a linear, dose-dependent manner**.** This means that as the radiation dose increases, the number of mutations in the germline cells also rises proportionally. Importantly, the expression of genetic disorders resulting from these mutations follows a stochastic model. In other words, there is no minimum threshold dose below which the risk is zero. Even the smallest doses of radiation may carry some risk of inducing genetic mutations, although the probability of such an event occurring at low doses is relatively small. Unlike deterministic effects—such as skin burns or organ failure—which require a certain threshold of radiation to manifest, stochastic effects like genetic mutations or cancer may occur at any dose level, with the likelihood increasing as the dose increases.

This understanding is supported by comprehensive data obtained from several key populations exposed to radiation. Among these are atomic bomb survivors from Hiroshima and Nagasaki**,** occupationally exposed nuclear workers**,** and individuals affected by nuclear accidents such as Chernobyl and Fukushima. Long-term epidemiological studies on these groups have been instrumental in revealing not just the cancer risks associated with radiation, but also its potential to increase mutation rates. While direct transmission of genetic disorders to subsequent generations in humans has been difficult to confirm with certainty due to genetic variability and environmental confounders, the elevated frequency of chromosomal aberrations and other molecular markers of genetic damage in exposed populations provide compelling indirect evidence. A central concept in evaluating the genetic risks of radiation exposure is the "doubling dose." This term refers to the amount of radiation necessary to double the spontaneous mutation rate in a population. In humans, this dose is estimated to be between 1 and 2 Sieverts (Sv)**.** This estimation provides a benchmark for risk assessment in radiological protection and forms the basis for setting dose limits, particularly for radiation workers and the general public. The doubling dose is derived from extensive comparisons of spontaneous mutation rates in the general population and the increased mutation rates observed in exposed individuals, extrapolated using both animal data and human observational studies. Understanding the dose–mutation relationship is critical in the field of radiation safety and genetics counseling, especially when advising individuals who are planning families and may have had occupational or medical exposure to radiation. It reinforces the importance of ALARA (As Low As Reasonably Achievable) principles in radiation use, aiming to minimize exposure to the lowest levels necessary for diagnostic or therapeutic efficacy while safeguarding future generations from potential genetic harm.

End of Chapter

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