Cosmetics and Skin Cancer: A Review of Risks, Prevention and Treatment

By

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A thesis submitted to the Department of Mathematics and Natural Sciences in partial fulfillment of the requirements for the degree of
Master of Science in Biotechnology.

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3. The thesis does not contain material which has been accepted, or submitted, for any other degree or diploma at a university or other institution.
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Approval

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Ethics Statement

An ethics statement is not applicable because this study is based exclusively on published literature.

Abstract

Skin cancer, including Non-melanoma skin cancer (NMSC) and melanoma, constitutes a real global health challenge. This review paper discusses epidemiological aspects of skin cancer, its risk factors, pathophysiology, and management with a focus on inter-professional collaboration. Skin cancer is the development of cancerous cells in the skin, which is most often caused by overexposure to ultraviolet radiation from the sun or sun lamps. It becomes important to establish a relationship between skin cancer and cosmetics since most of these products come into contact with skin and hair. Some of these cosmetic products may have elements that either make the skin more vulnerable to Ultra-Violet (UV) radiation or damage the skin's protective layer and lead to skin cancer. Other cosmetics include sun protection factors (SPF) and components that prevent skin damage from exposure to dangerous UV radiation, which minimizes the risks. Thus, people should be enlightened about the dangers of sun exposure on the skin, including the need to apply sunscreen or wear protective clothing and/ or limit sun exposure. Skin cancer awareness, early examinations, and regular check-ups of suspicious moles and other skin growths remain crucial in prevention. This review paper provides a deeper look into the correlation between skin cancer and cosmetics, thus identifying the related impact, advantages, and disadvantages. Through the knowledge of this correlation presented in the paper, people are enabled to make wise decisions and pay more attention to their skin. This has further brought out the need to have a team approach to the provision of skin cancer care, in which healthcare workers from several disciplines can be of help.

Keywords: Skin cancer; UV radiation; Cosmetics; Carcinogenic ingredients; Skin Protection; Public health awareness.

Dedication

To God and the humans who study His creations.

Acknowledgement

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List of Acronyms

NMSC	Non-Melanoma Skin Cancer
BCC	Basal Cell Carcinoma
SCC	Squamous Cell Carcinoma
MCC	Merkel Cell Carcinoma
UV	Ultraviolet
ROS	Reactive Oxygen Species
CT	Computed Tomography
MRI	Magnetic Resonance Imaging
PET	Positron Emission Tomography
SPF	Sun Protection Factor
FDA	Food and Drug Administration
MEK	Mitogen-Activated Protein Kinase Kinase
BRAF	B-Raf Proto-Oncogene, Serine/Threonine Kinase
CDKN2A	Cyclin-Dependent Kinase Inhibitor 2A
MC1R	Melanocortin 1 Receptor
EPA	Environmental Protection Agency
IARC	International Agency for Research on Cancer
NTP	National Toxicology Program

Glossary

Skin Cancer:	The abnormal growth of skin cells caused primarily by ultraviolet radiation exposure.
UV Radiation:	Ultraviolet radiation, a type of energy from the sun that can damage skin cells.
Basal Cell Carcinoma (BCC):	A common type of skin cancer arising from the basal cells of the skin.
Squamous Cell Carcinoma (SCC):	A type of skin cancer originating from the squamous cells in the skin's outer layer.
Melanoma:	The deadliest form of skin cancer that develops from melanocytes, the pigment-producing cells.
Sunscreen:	A product that protects the skin from harmful UV radiation by absorbing or reflecting it.
SPF:	Sun Protection Factor, a measure of a sunscreen's effectiveness in blocking UV rays.
Carcinogenic:	A substance or agent capable of causing cancer in living tissue.
Cosmetics:	Products applied to the body to enhance appearance or hygiene.
Reactive Oxygen Species (ROS):	Chemically reactive molecules containing oxygen that can damage cells.
FDA:	The Food and Drug Administration, responsible for protecting public health through regulation of food, drugs, and cosmetics.

Environmental Protection Agency (EPA):	An U.S. agency focused on environmental protection and regulation.
IARC:	The International Agency for Research on Cancer, which identifies carcinogenic risks to humans.

Chapter 1

Introduction

Skin cancer remains the most common cancer in the United States, typically classified into nonmelanoma and melanoma categories. This disease prompts detailed analyses covering epidemiological data, risk factors, pathogenesis, and effective treatment methods (Rogers et al., 2015; Leiter & Garbe, 2008). The emergence of skin cancer is closely linked to the abnormal growth of skin cells primarily driven by UV radiation exposure, whether from the sun or artificial sources like tanning beds (de Gruijl, 1999).

Cosmetics serve various aesthetic and hygienic functions but also carry potential risks. Some cosmetics can enhance susceptibility to UV radiation, potentially increasing skin cancer risk by degrading the skin's natural barrier (Darbre, 2005). However, certain products containing SPF and other protective agents can mitigate these risks by shielding the skin from harmful UV rays (Schalka & Reis, 2011).

Public education on the dangers associated with certain cosmetics is crucial. Preventative strategies, such as protective clothing and regulated sun exposure, are effective in reducing risks. Regular skin examinations and timely intervention can significantly decelerate skin cancer progression and improve patient outcomes (Guy et al., 2015; Rigel et al., 2010).

1.1 Significance of Skin Cancer-Cosmetics Relationship

Understanding the relationship between skin cancer and cosmetics is of utmost importance for several reasons:

Improving Consumer Awareness: Understanding the cosmetics' effects on skin cancer risk can help consumers make proper choices when purchasing these cosmetics. It lets consumers

choose cosmetics that are less likely to be carcinogenic and complements the efforts of skin cancer prevention.

Risk Mitigation: Some cosmetic products may contain ingredients that either increase the skin sensitivity to UV rays or interfere with skin's natural protective layer; this posed the risk of skin cancer. By making sense of it, one is in a position to avoid such products, and as a result, lower his/her chances of coming face to face with potential carcinogenic substances in form of skin cancer.

Regulatory Guidelines: This is because understanding of skin cancer and cosmetics gives knowledge in coming up with proper measures that needs to be taken in the regulation of cosmetics in the market. In this way, the regulatory authorities are able to define the specific ingredients or practices which can be dangerous when used in cosmetics or are actually ineffective, and set some rules and guidelines limiting the negative consequences of using such cosmetic products for the health of the general population.

Research and Development: Thus, exploring the connection between skin cancer and cosmetics reignites the focus and extensive research on the topic. It also helps in understanding the possible dangers and advantages linked to the cosmetic products, to helping in the formulation of safer cosmetic products, and aid in the formulation of good practices concerning the use for cosmetic products.

In summary, the awareness of skin cancer cosmos connection enhances knowledge for empowered choices, safe practices, policy-making implementation, interprofessional collaboration, and momentum for research advancements. That is why it is important to follow rules of skin care that could prevent skin diseases, including skin cancer, and maintain skin healthy and strong.

1.2 Objective and Structure of this Review Paper

This review paper is organized into several sections, each addressing key aspects of the interrelation between skin cancer and cosmetics. The introductory part underscores the necessity and significance of this review, emphasizing its relevance to community health and welfare, reflecting on broader public health implications (Koh et al., 2013). Subsequent to the introduction, the paper offers a detailed overview of skin cancer, detailing its classification, causes, and current trends. This foundation supports further discussions on the risk factors associated with skin cancer, laying a critical baseline for understanding its etiology (Bradford, 2009). The paper progresses to discuss the potential dangers posed by cosmetic products. It highlights how certain ingredients in cosmetics can lead to carcinogenesis, disrupt the skin's protective barrier, and thereby elevate skin cancer risks. This section relies on studies that link cosmetic ingredients with carcinogenic outcomes (Sarveiya et al., 2004). Furthermore, the paper outlines preventive measures that individuals can adopt to reduce their skin cancer risk. These include wearing protective clothing, applying sunscreen effectively, and avoiding excessive sun exposure, practices that are widely recommended in dermatological guidelines (Schneider & Lim, 2019). Concluding the review, the paper synthesized the findings, emphasizing the significance of the established connections between skin cancer and cosmetic use. It also identifies future research directions, suggesting areas for further investigation to enhance understanding and develop more effective protective measures against skin cancer (Wu et al., 2014). In sum, the systematic arrangement of this review paper facilitates a comprehensive and methodical examination of the topic, providing insightful and practical information for further research, applications in medicine, and community education regarding the links between skin cancer and cosmetics.

Chapter 2

Fundamentals of Skin Cancer

A foundational understanding of skin cancer encompasses general information about the disease, including its classification, causes, and patterns of progression. Skin cancer, characterized by the uncontrolled growth of abnormal skin cells, is primarily induced by exposure to ultraviolet (UV) radiation from the sun or artificial sources such as tanning lamps. This fundamental knowledge is crucial for appreciating the significance of prevention and treatment strategies for this pervasive disease (Peris & Fargnoli, 2015). Skin cancer's classification into types such as basal cell carcinoma, squamous cell carcinoma, and melanoma, each with distinct characteristics and risk factors, underscores the complexity of diagnosis and management strategies (Marks, 2000). Moreover, the epidemiology of skin cancer illustrates its increasing incidence globally, emphasizing the need for effective public health interventions and individual protective measures against UV exposure (Guy et al., 2015).

2.1 Types of Skin Cancer

Skin cancer stands as one of the most commonly diagnosed cancers globally, with a significant number of new cases each year (Rogers et al., 2015). It is primarily divided into three major types as seen in Figure 1: basal cell carcinoma (BCC), squamous cell carcinoma (SCC), and melanoma, each differing in presentation, severity, and risk factors.

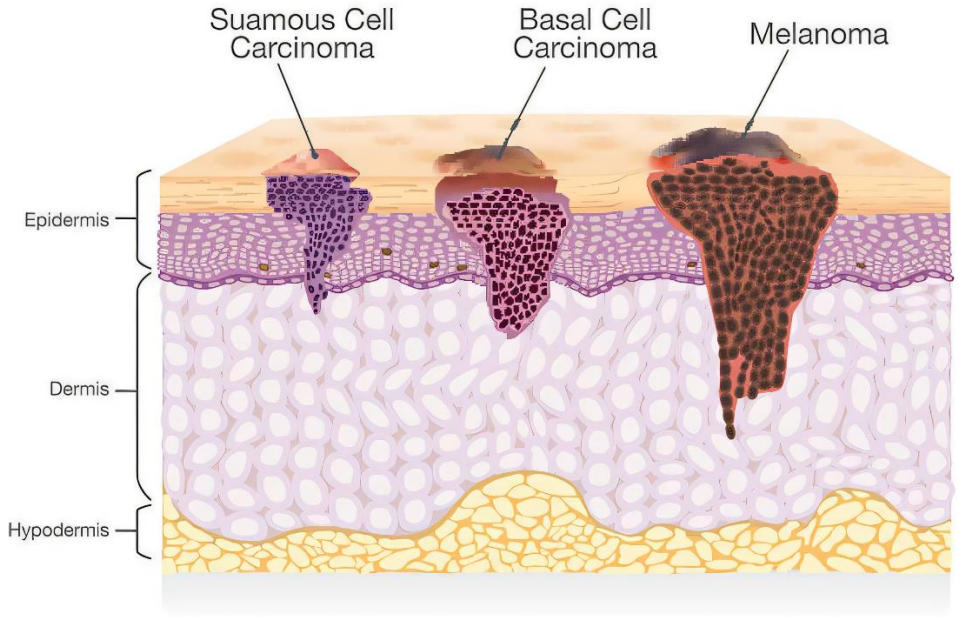

Figure 1 Types of skin cancer — squamous cell carcinoma (SCC), basal cell carcinoma (BCC) and melanoma (Froedtert & the Medical College of Wisconsin, n.d.)

Basal Cell Carcinoma (BCC): BCC is the most common form of skin cancer, accounting for approximately 75% of all skin cancer cases. It typically appears as a small, pearl-like bump that may be pinkish or flesh-colored. These lesions often occur on sun-exposed areas such as the face, neck, and hands. BCCs are known for their tendency to bleed or form a scab but are generally considered less aggressive than other forms of skin cancer (Weinstein & Bouwes Bavinck, 2017).

Squamous Cell Carcinoma (SCC): Representing about 16% of skin cancer cases, SCC usually manifests as a rose-colored or pinkish, scaly bump or patch on sun-exposed skin. It can progress to an ulcer or an open sore that fails to heal, indicating a more invasive nature compared to BCC (Alam & Ratner, 2001).

Melanoma: Although it is the least common, melanoma is the most aggressive and dangerous form of skin cancer. It can develop on any part of the body, regardless of sun exposure, and is characterized by a black or unevenly shaped spot or nodule. Melanoma may also present as a

new or abnormal growth or a change in an existing mole. Due to its high potential for metastasis to other organs, early detection and treatment are critical (Balch et al., 2009).

Following Table 1 compares the main types of skin cancers:

Table 1 Comparison of Main Types of Skin Cancers

Characteristic	Squamous Cell Carcinoma (SCC)	Basal Cell Carcinoma (BCC)	Melanoma
Appearance	Scaly, red patches, open sores, or elevated growths with a central depression (Alam & Ratner, 2001)	Pearly bumps, often with visible blood vessels, or shiny areas that may be white, pink, or red (Rubin et al., 2005)	Moles that change in color, size, or feel; new growths; irregularly shaped, often with multiple colors (Tsao et al., 2004)
Common Locations	Sun-exposed areas such as the rim of the ear, face, near the mouth, and on the arms (Alam & Ratner, 2001)	Sun-exposed areas like the face, neck, and arms (Rubin et al., 2005)	Can occur anywhere on the body, commonly on the back in men and legs in women (Tsao et al., 2004)
Metastatic Potential	Moderately high; can metastasize if not treated early (Alam & Ratner, 2001)	Very low; rarely spreads but can be locally destructive (Rubin et al., 2005)	High; can quickly spread to other parts of the body (Tsao et al., 2004)
Risk Factors	Prolonged sun exposure, history of	Chronic sun exposure, fair skin,	Intense, intermittent sun exposure, family history of

	sunburns, fair skin, immune suppression (Alam & Ratner, 2001)	older age, exposure to arsenic (Rubin et al., 2005)	melanoma, presence of numerous or atypical moles, fair skin (Tsao et al., 2004)
Treatment	Surgical removal, radiation, or topical chemotherapy depending on the severity and location (Alam & Ratner, 2001)	Surgical excision, Mohs surgery, topical treatments, or radiation (Rubin et al., 2005)	Wide excision, lymph node analysis, targeted therapy, immunotherapy, and more for advanced stages (Tsao et al., 2004)

2.2 Abnormal Cell Growth and Pathogenesis of Skin Cancer

Skin cancer arises from the accumulation of genetic alterations in skin cells, transforming these cells into dysplastic clones that proliferate abnormally and form tumors. The primary driver of this transformation is exposure to ultraviolet (UV) radiation, particularly UV-B and UV-C, which falls within the wavelength range of 280 to 320 nm. This radiation is particularly damaging to the DNA of skin cells, disrupting normal cell cycle regulation and inducing persistent mutations (Brash et al., 1991).

These mutations often occur in genes responsible for regulating cell proliferation, division, and DNA repair mechanisms. In nonmelanoma skin cancers such as basal cell carcinoma (BCC) and squamous cell carcinoma (SCC), mutations typically affect genes controlling skin cell differentiation and proliferation. This leads to the unchecked growth of new cells, culminating in visible tumor formation on the skin (Zanetti et al., 2006).

Melanoma, the most aggressive form of skin cancer, involves mutations in multiple genes in melanocytes, the skin cells responsible for pigment production. These mutations can alter the function of melanocytes or disrupt their ability to regulate cell growth, potentially resulting in the development of malignant melanoma tumors (Bennett, 2008).

While the precise mechanisms of skin cancer development are still being elucidated, it is clear that molecules of ultraviolet radiation are highly detrimental to DNA integrity. Other contributing factors may include hereditary predispositions, immune system deficiencies, environmental chemicals, and viral infections, all of which can influence the abnormal growth of skin cells leading to cancer (Wood et al., 2001).

2.3 Epidemiology and Global Impact of Skin Cancer

Skin cancer represents a significant global health issue due to its increasing incidence and the serious threat it poses to public health. Understanding the trends of skin cancer is essential for optimizing prevention methods and targeting resource allocation effectively.

Skin cancer is the most common type of cancer worldwide, contributing to a considerable proportion of all cancer cases. The frequency of skin cancer has been rising over the years, particularly in regions with high levels of UV radiation such as Australia, New Zealand, parts of North America, and Europe (Lomas et al., 2012). Table 2 represents skin cancer incidences and mortality based on the major regions (World Cancer Research Fund International, 2022):

Table 2 Skin Cancer Incidence & Mortality by Region and Type (World Cancer Research Fund International, 2022)

Region	Incidence Rate (per 100,000)	Mortality Rate (per 100,000)	Common Types	Key Risk Factors	Preventive Measures
North America (USA)	16.5	1.0	Melanoma, BCC, SCC	UV radiation, fair skin	Sunscreen, protective clothing (Chandler et al., 2020)
Europe (Germany)	12.1	1.4	Melanoma, BCC, SCC	UV radiation, age	Avoiding peak sun hours, sunscreen (Leiter et al., 2020)
Australia	37.0	0.73	Melanoma, BCC, SCC	UV radiation, fair skin	Sunscreen, protective clothing (Chandler et al., 2020)
Asia (China)	0.37	0.20	Melanoma, BCC, SCC	UV radiation, age	Avoiding peak sun hours, sunscreen (Wan et al., 2022)
South America (Brazil)	3.3	0.73	Melanoma, BCC, SCC	UV radiation, age	Sunscreen, protective clothing (Leiter et al., 2020)
Africa	Data not available	Data not available	Melanoma, BCC, SCC	UV radiation, age	Avoiding peak sun hours, sunscreen (Wan et al., 2022)

Region	Incidence Rate (per 100,000)	Mortality Rate (per 100,000)	Common Types	Key Risk Factors	Preventive Measures
Antarctica	Data not available	Data not available	Melanoma, BCC, SCC	UV radiation, age	Avoiding peak sun hours, sunscreen (Wan et al., 2022)

The increasing significance of skin cancer in the global context is not only due to its high incidence but also because of the considerable economic burden associated with its treatment. Skin cancer can lead to severe physical disfigurement, substantial medical expenses for diagnosis, treatment, and follow-up, and considerable morbidity and mortality, especially in advanced stages or when metastasis occurs (Whiteman et al., 2016).

The primary cause of skin cancer is exposure to ultraviolet (UV) light from the sun or artificial sources. Key risk factors include having light skin, experiencing frequent sunburns, particularly for those who spend extended periods indoors, and having a weakened immune system. Genetic predisposition and exposure to carcinogens also significantly contribute to the risk of developing skin cancer (Armstrong & Kricker, 2001).

Epidemiologically, skin cancer is a disease on the rise, making it a pressing global health concern. Knowledge of its epidemiology, risk factors, and control measures is vital for developing preventive interventions, educating the public and stakeholders, and efficiently allocating resources to address this public health challenge.

In Bangladesh, the epidemiological data on skin cancer reveal distinct patterns and challenges. Although skin cancer is less prevalent in Bangladesh compared to western countries, the incidence has been gradually increasing. Factors contributing to this rise include increased exposure to UV radiation, possibly due to changes in occupational and recreational activities, and limited public awareness about sun protection. A study conducted in Dhaka highlighted

that basal cell carcinoma (BCC) and squamous cell carcinoma (SCC), the two most common forms of nonmelanoma skin cancers, are the predominant types diagnosed, with a notable increase in cases over recent years (Hossain et al., 2018). This growing trend underscores the need for enhanced dermatological healthcare services and targeted public health initiatives to raise awareness about skin cancer risks and preventive measures in Bangladesh.

In conclusion, this review paper begins by discussing the importance of investigating the relationship between skin cancer and cosmetics. It underscores skin cancer as a critical health issue, emphasizing the need to understand its causes and the impact of UV radiation. The subsequent sections will delve into the various types of skin cancer, detailing their effects, manifestations, causes, diagnosis, and management strategies.

Chapter 3

Basal Cell Carcinoma (BCC)

Basal Cell Carcinoma, commonly referred to as BCC, is the most prevalent form of skin cancer. It often presents as a small shiny bump or a scaly pink patch, predominantly occurring on sun-exposed areas of the body such as the scalp, face, ears, and neck. The primary cause of BCC is overexposure to ultraviolet (UV) radiation from sources like sunlight and tanning beds, which damages the DNA in skin cells. Individuals with lighter skin, eyes, and hair, who have experienced frequent sunburns or prolonged sun exposure, are at an increased risk of developing this type of skin cancer (Gordon, 2013; Kim, 2002).

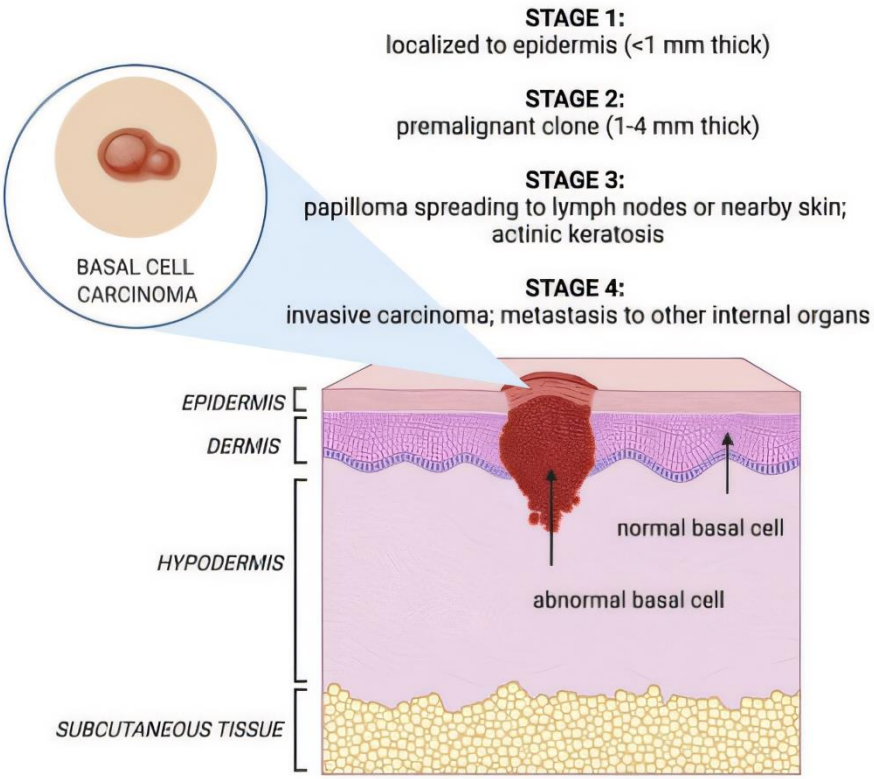

Figure 2 Development stages of Basal Cell Carcinoma (BCC) (Chua et al., 2022)

BCC grows slowly and rarely metastasizes but can cause significant damage to surrounding tissues if left untreated as seen in Figure 2. Treatment options include surgical excision, cryotherapy, topical chemotherapy, and radiation therapy. Early detection and treatment are

crucial to prevent extensive damage, and protective measures such as wearing sunscreen, protective clothing, and seeking shade during peak UV radiation times are recommended to mitigate risks.

Classification of Basal Cell Carcinoma

There are four main types of basal cell carcinoma (BCC), presented in Table 3, each with distinct clinical presentations:

Table 3 Types of Basal Cell Carcinoma (BCC)

Type	Description	Reference
Nodular BCC	The most common form, appearing as a round pimple with visible blood vessels (telangiectasias).	Crowson, 2006
Superficial Spreading BCC	Causes lesions that appear as small, shallow marks slightly lighter in color than the surrounding skin. These lesions typically form on the trunk (torso), arms, and legs.	Weedon & Strutton, 2002
Sclerosing BCC	Looks like scars that slowly expand over time, most commonly on the face.	Crowson, 2006
Pigmented BCC	A rare type that causes hyperpigmentation, where an area of skin becomes darker than the skin surrounding it.	Weedon & Strutton, 2002

Epidemiology and Impact

BCC affects individuals globally, showing a slightly higher incidence in males and predominantly in those over 50 years old. It is notably common among people with fair skin and light-colored eyes. Once someone has had BCC, they are at a higher risk of developing subsequent nonmelanoma skin cancers (Lear et al., 1997; Rubin et al., 2005).

Common Signs of Basal Cell Carcinoma

Signs include lumps, bumps, scabs, or scaly lesions on the skin that may be translucent, white, pink, brown, or black. These growths may be itchy or painful and can develop into ulcers that bleed upon contact (Epstein, 2008; Wong et al., 2003).

Diagnosis and Treatment

Diagnosis typically involves a physical examination and a review of symptoms. Treatment may involve several options, depending on the stage and location of the cancer, including electrodessication and curettage, surgical removal, cryotherapy, chemotherapy, photodynamic therapy, and laser therapy. For advanced cases, FDA-approved medications like Vismodegib and Sonidegib are used, particularly when surgery or radiation is not viable (Ascierto et al., 2012; D'Orazio et al., 2013).

Chapter 4

Squamous Cell Carcinoma

Squamous Cell Carcinoma (SCC), or cutaneous squamous cell carcinoma (CSCC), ranks as the second most common form of skin cancer after basal cell carcinoma. It originates from the squamous cells in the epidermis, the outermost layer of the skin, shown in figure 3. Typically, SCC occurs in areas that receive high sun exposure, such as the head, arms, and legs, but it can also affect mucous membranes in the mouth, lungs, and anus, highlighting its potential severity (Black & Ogg, 2003; Guy et al., 2015).

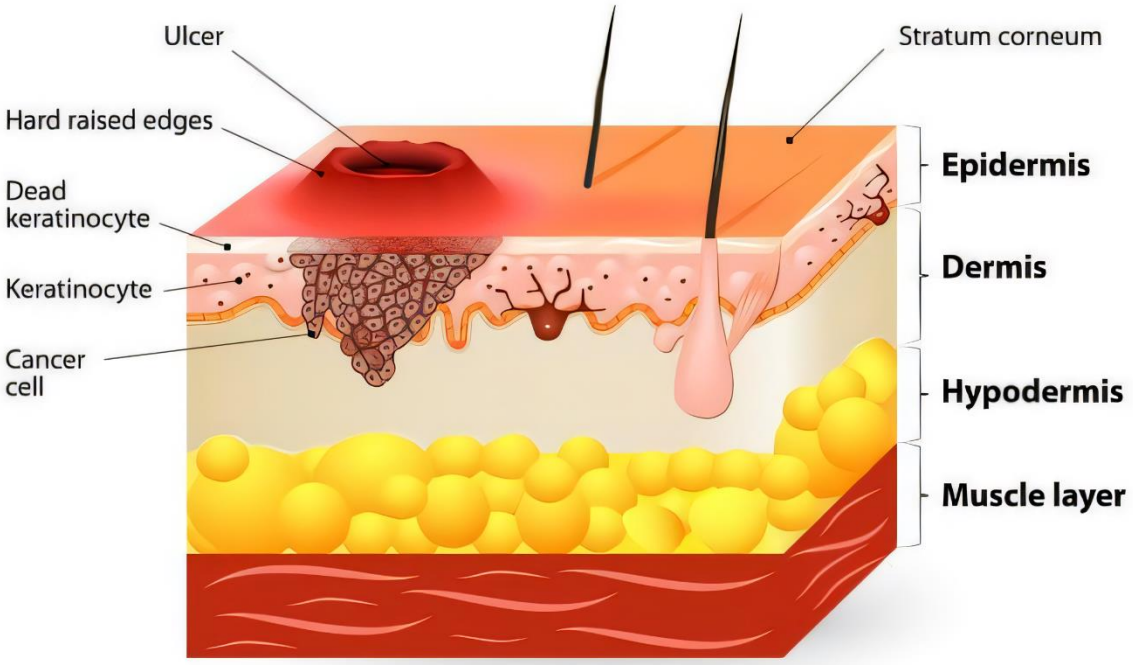

Figure 3 Squamous Cell Carcinoma (SCC) (Kumar et al., 2018)

The primary cause of SCC is excessive exposure to ultraviolet (UV) radiation from sunlight and tanning beds, which leads to DNA damage in skin cells. Individuals with lighter skin, eyes, and hair, especially those who have had frequent sunburns or extensive sun exposure, are at a heightened risk of developing this type of skin cancer.

SCC is more aggressive than basal cell carcinoma and can metastasize if not treated promptly. Effective treatment options include surgical excision, cryotherapy, topical chemotherapy, and radiation therapy. Early detection and treatment are crucial to prevent significant damage, and adopting protective measures such as wearing sunscreen, protective clothing, and seeking shade during peak UV radiation times are essential for risk mitigation.

Classification of Squamous Cell Carcinoma

Squamous Cell Carcinoma (SCC) is classified into several subtypes (Table 4) based on its features and progression:

Table 4 Types of Squamous Cell Carcinoma (SCC)

Type	Description	Reference
Cutaneous SCC	This type of SCC is confined to the epidermis but may invade deeper tissues if left untreated.	Schwarz et al., 2014
Metastatic SCC	This form has spread beyond the skin to other parts of the body, often through the lymphatic system or bloodstream, and is more aggressive.	Brantsch et al., 2008
In situ SCC (Bowen's Disease)	This subtype remains limited to the outermost layer of the skin and is considered the earliest form of SCC.	Rowe et al., 1992

Epidemiology and Impact

SCC significantly affects global health, with a marked prevalence in individuals over 50 years old, particularly among those with fair skin and light-colored eyes. The incidence of SCC has

been rising, reflecting increased UV exposure and aging populations (Lear et al., 1997; Rubin et al., 2005).

Common Signs of Squamous Cell Carcinoma

The signs of SCC vary depending on its location and stage, but common indicators include:

- Rough, scaly patches or bumps on the skin that may crust or bleed.
- Raised growths with a central depression, which may resemble a sore.
- Open sores or ulcers that do not heal or frequently recur (Epstein, 2008).
- Red, flat patches larger than 1 inch that are dry and scaly (Alam & Ratner, 2001).
- Actinic keratosis, which presents as dry, itchy, or scaly lesions that can become cancerous if untreated (Wong et al., 2003).

Prompt recognition of these signs is essential to prevent the progression of SCC and reduce the risk of metastasis.

Diagnosis and Treatment

Diagnosing SCC involves a physical examination and a review of the patient's symptoms. Depending on the cancer's stage and location, treatment might include electrodessication and curettage, surgical removal, cryotherapy, chemotherapy, photodynamic therapy, and laser therapy. For advanced cases, particularly when surgery or radiation is not feasible, FDA-approved medications like Vismodegib and Sonidegib are employed to manage the disease (Ascierto et al., 2012; D'Orazio et al., 2013).

Chapter 5

Melanoma

Melanoma, also known as malignant melanoma, is the deadliest form of skin cancer. It occurs when melanocytes—the cells responsible for skin pigmentation—start reproducing uncontrollably. This type of cancer can grow rapidly and has the potential to spread to other parts of the body if not detected and treated early (Ascierto et al., 2012; Gordon, 2013).

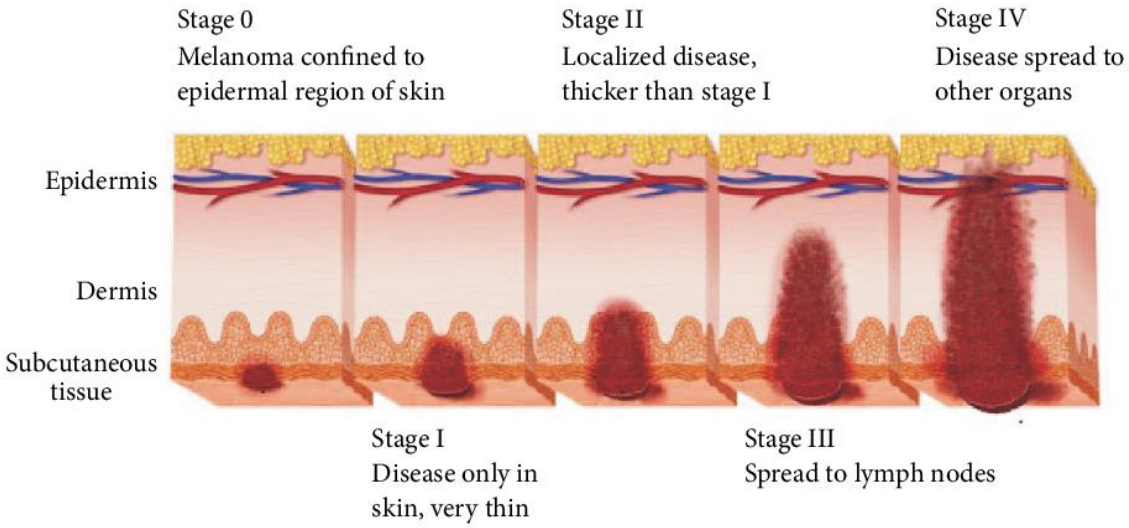

Figure 4 Four Stages of Melanoma (Jaworek & Korjakowska, 2018)

Melanoma often appears as a single dark spot on the skin, usually larger than 6 millimeters in diameter (about the size of a pencil eraser), though it can sometimes be smaller. It can either develop from an existing mole or appear on normal-looking skin (Figure 4). Features of moles that increase the risk of melanoma include:

- A new mole appearing after the age of 30.
- A mole developing in an area rarely exposed to the sun.
- A change in an existing mole.
- The presence of atypical moles (irregular in shape or color).

- Having more than 20 moles larger than 2 mm across or more than five moles each larger than 5 mm across.

Melanoma can develop in areas such as the face, upper trunk, legs, under the fingernails or toenails, genitals, and even inside the eye. Early detection is critical for successful treatment, and regular skin checks are recommended to identify new moles or changes in existing ones.

Classification of Melanoma

Melanoma is categorized based on several characteristics, including tumor thickness and how deeply it has penetrated the skin. The classifications are as follows:

Table 5 Staging of Melanoma

Stage	Description	Reference
Stage 0 (Melanoma in situ)	The melanoma is confined to the epidermis and has not spread deeper.	Gershenwald et al., 2017
Stage I	This stage is characterized by low-risk melanoma without evidence of spread. Generally curable through surgery.	
Stage II	Melanoma that shows higher risk factors, but still has not spread to lymph nodes or distant sites.	
Stage III	The melanoma has spread to nearby lymph nodes or skin.	
Stage IV	The cancer has metastasized to distant lymph nodes, skin, or internal organs, indicating an advanced stage of the disease.	Balch et al., 2009

Epidemiology and Impact

Melanoma is less common than other skin cancers but is responsible for the majority of skin cancer-related deaths due to its aggressive nature. It affects both men and women, with men more likely to develop it on their upper back, while women commonly develop it on their legs. Overexposure to sunlight, particularly sunburns during childhood, is one of the most significant risk factors. In addition, tanning bed use significantly increases melanoma risk, with more than 6,000 cases in the United States linked to this practice annually (Rigel et al., 2010).

Common Signs of Melanoma

Melanoma can occur anywhere on the body, including areas that are not frequently exposed to the sun. Common symptoms include moles, scaly patches, open sores, or raised bumps. The American Academy of Dermatology's "ABCDE" method can help individuals recognize the warning signs:

- Asymmetry: One half of the mole does not match the other.
- Border: The edges are irregular, ragged, or blurred.
- Color: Uneven shades of brown, black, gray, red, or white.
- Diameter: Typically, larger than 6 mm.
- Evolving: The mole is changing in size, shape, or color (Garbe et al., 2010).
- Additionally, the "ugly duckling sign" suggests that any mole that looks different from others should be examined by a dermatologist.

Diagnosis and Treatment

Diagnosis typically involves a biopsy, where a sample of the suspicious mole or lesion is examined under a microscope for cancer cells. Staging of melanoma is then determined based

on tumor thickness and whether the cancer has spread to lymph nodes or other parts of the body. Key diagnostic tests include:

- Sentinel Lymph Node Biopsy: Used for melanomas deeper than 0.8 mm or with ulceration to check for spread to lymph nodes (Balch et al., 2009).
- CT and MRI Scans: To detect metastasis in organs or the brain.
- PET Scan: Identifies cancer spread to distant sites.

Treatment primarily involves surgical excision, often followed by targeted therapies, immunotherapy, radiation, or chemotherapy, depending on the stage of the melanoma.

Approved treatment options for melanoma with good efficacy include:

- **Immunotherapy:** Drugs such as pembrolizumab (Keytruda®) and nivolumab (Opdivo®) are widely used immune checkpoint inhibitors that have shown significant survival benefits for advanced melanoma patients. These therapies block proteins that prevent the immune system from attacking melanoma cells (Robert et al., 2015).
- **Targeted Therapy:** For patients with BRAF mutations, drugs like vemurafenib (Zelboraf®) and dabrafenib (Tafinlar®), often used in combination with MEK inhibitors like trametinib (Mekinist®), have proven highly effective in reducing tumor growth (Long et al., 2014).
- **Radiation Therapy:** Though less commonly used in early-stage melanoma, radiation is sometimes used as an adjunct for advanced or metastatic melanoma, particularly for palliative purposes (Coit et al., 2019).
- **Adjuvant Therapy:** After surgical removal of high-risk melanomas, adjuvant therapies such as ipilimumab (Yervoy®), an anti-CTLA-4 monoclonal antibody, are often used to decrease the risk of recurrence (Eggermont et al., 2016).

Chapter 6

Merkel Cell Carcinoma

Merkel cell carcinoma (MCC) is a rare but aggressive form of skin cancer originating from Merkel cells, specialized skin cells located in the epidermis that are responsible for transmitting sensory information about touch to the brain (Figure 5). MCC typically appears as a painless, firm, red or purple nodule on sun-exposed areas such as the face, neck, and arms. Due to its aggressive nature, MCC can spread rapidly to other parts of the body if not treated early (Green et al., 1993).

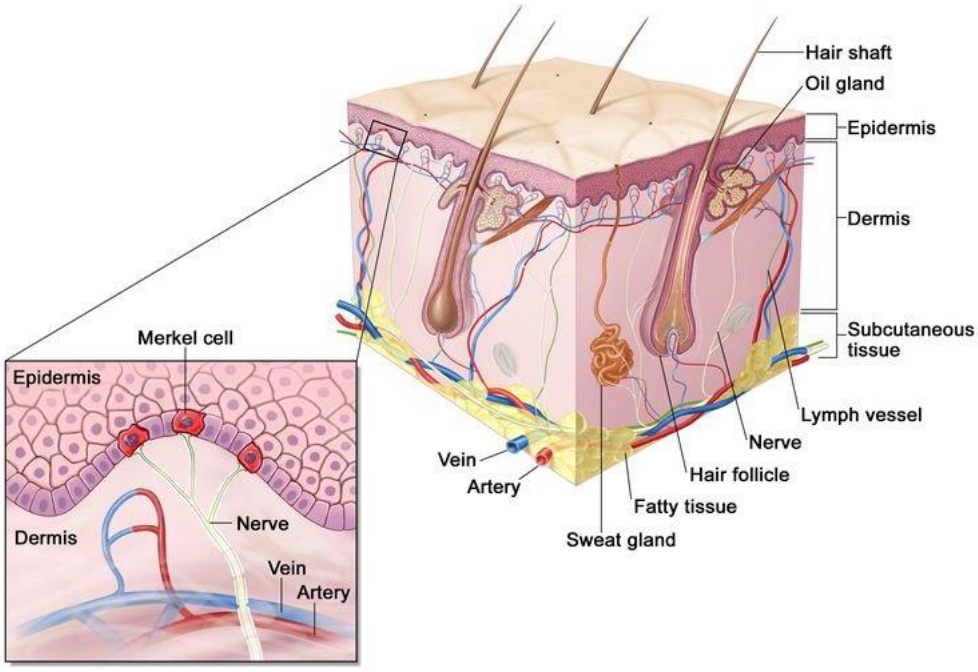

Figure 5 Merkel Cell Carcinoma (MCC) (Northwestern Medicine, n.d.)

MCC is caused by the uncontrolled growth of Merkel cells, with risk factors including advanced age, fair skin, a weakened immune system, and prolonged exposure to UV radiation. Additionally, about 80% of MCC cases are linked to infection with Merkel cell polyomavirus (MCP), though most individuals infected with this virus do not develop cancer (Lugowska et al., 2018; Wu et al., 2014).

Classification of Merkel Cell Carcinoma

Merkel cell carcinoma is classified based on its staging (Table 6), which is determined by tumor thickness, depth of invasion, and spread to other parts of the body:

Table 6 Staging of Merkel Cell Carcinoma (MCC)

Stage	Description	Reference
Stage 0 (MCC in situ)	The carcinoma is confined to the epidermis and has not spread beyond the top skin layer.	Fitzgerald et al., 2015
Stages I & II	These stages represent local disease, with no evidence of spread beyond the tumor site.	
Stage III	Cancer has spread to nearby lymph nodes.	
Stage IV	The most advanced stage, where MCC has metastasized to distant organs, such as the bones, lungs, or brain.	

Epidemiology and Impact

Though rare, MCC has a significant impact due to its aggressive progression. It primarily affects older adults over the age of 50, especially men with fair skin, and is more common in individuals with compromised immune systems. Prolonged exposure to UV radiation, particularly in those who have had previous skin cancers, increases the risk of developing MCC. The incidence of MCC is increasing globally, largely attributed to rising UV exposure and an aging population (Fitzgerald et al., 2015; Albores-Saavedra et al., 2010).

Common Signs of Merkel Cell Carcinoma

Signs of MCC usually manifest as painless, shiny, or pearly lumps on sun-exposed areas, particularly the face, neck, arms, and eyelids. These lumps may appear skin-colored, red, purple, or bluish-red and can grow rapidly:

- Firm, dome-shaped, or raised lump.
- Lump that is tender or sore, similar to a pimple or insect bite.
- Lump that may break open into a wound or sore.
- Rapid growth, often reaching the size of a dime in a short period (Lemos & Nghiem, 2007).

Diagnosis and Treatment

Diagnosis involves a skin biopsy where a small tissue sample is examined for cancer cells. Staging is determined by how deeply the tumor has penetrated the skin and whether it has spread to other parts of the body. Diagnostic tests for staging include:

- CT and MRI Scans: To detect metastasis in the organs.
- PET Scan: Identifies distant cancer spread.
- Sentinel Node Biopsy: Assesses whether cancer has spread to nearby lymph nodes (Fitzgerald et al., 2015).

Treatment options depend on the stage of the disease, with early detection offering better outcomes. Surgery, including Mohs surgery or wide local excision, is commonly used to remove the tumor and surrounding tissue. For advanced cases, additional treatments may include:

- Chemotherapy: Used in advanced stages to kill cancer cells throughout the body.

- Immunotherapy: Drugs such as avelumab (Bavencio®) and pembrolizumab (Keytruda®) have shown efficacy in treating MCC by boosting the immune system to attack cancer cells (Kaufman et al., 2016).
- Radiation Therapy: Often used in combination with surgery to kill any remaining cancer cells (Poulsen et al., 2013).

Chapter 7

Cosmetics and Skin Cancer Risk

In recent years, there has been increasing awareness and concern regarding the potential link between cosmetic products and the development of skin cancer. Cosmetics, which include a wide range of products designed to enhance appearance, improve hygiene, and protect the skin, are commonly used in daily routines. While these products provide numerous aesthetic and protective benefits, it is crucial to understand their potential health implications, particularly concerning the risk of skin cancer. Research has pointed out that certain ingredients in cosmetics may pose carcinogenic risks, thus necessitating further investigation into their long-term effects on skin health (Guy et al., 2015).

7.1 Potential Carcinogenic Ingredients in Cosmetics

Cosmetics, though beneficial in enhancing beauty and promoting personal care, sometimes contain ingredients with carcinogenic potential. Carcinogenic ingredients refer to substances that have the ability to initiate or promote cancer development by causing mutations or other cellular alterations. Several cosmetic ingredients have been identified as potential carcinogens, which may pose a risk to skin health with prolonged or cumulative exposure.

Key carcinogenic ingredients commonly found in cosmetics include:

- **Parabens**: Widely used as preservatives in cosmetics to inhibit the growth of bacteria and fungi, parabens have been the subject of debate. Some studies suggest a possible association between parabens and breast cancer due to their weak estrogenic activity (Darbre, 2006). However, further research is necessary to establish a definitive causal relationship.
- **Formaldehyde and Formaldehyde-releasing preservatives**: These substances are used as antimicrobial agents in various cosmetics. Formaldehyde is classified as a

known human carcinogen by the International Agency for Research on Cancer (IARC) and the National Toxicology Program (NTP). Its presence in cosmetics, even in small amounts, has raised concerns regarding its potential to increase cancer risk through prolonged exposure (IARC, 2012).

- **Coal tar dyes**: Synthetic color additives derived from coal tar, particularly used in hair dyes and certain lip products, have been linked to cancer risks. Some coal tar dyes contain polycyclic aromatic hydrocarbons (PAHs), which are classified as probable carcinogens (NTP, 2016). Although regulatory limits have been established, their continued use in cosmetics warrants caution.
- **Heavy metals**: Lead, arsenic, cadmium, and mercury are examples of heavy metals that can be found as impurities in cosmetics. These metals are associated with toxic and carcinogenic effects, and long-term exposure, even at low levels, may contribute to an increased risk of cancer (Gong et al., 2014).
- **Phthalates**: Often used to enhance the flexibility and texture of cosmetic products, some phthalates have been classified as possible carcinogens due to their endocrine-disrupting properties (Hauser & Calafat, 2005). Exposure to certain phthalates has been linked to reproductive toxicity and potential cancer development, although more research is needed to confirm these associations.

Furthermore, specific chemicals commonly found in sunscreens, such as benzophenone, oxybenzone, and octinoxate, have been shown to have hormonal effects and disrupt the endocrine system. These chemicals can damage DNA, leading to an increased risk of skin cancer (Krause et al., 2012). The long-term use of these ingredients, particularly in products intended for sun protection, raises significant concerns regarding their role in skin carcinogenesis.

Table 7 lists some potential carcinogenic ingredients found in cosmetics, their roles in cancer development:

Table 7 Potential Carcinogenic Ingredients in Cosmetics

Ingredient	Role in Cancer Development	Reports
Formaldehyde	Causes DNA damage and cellular mutations.	Classified as a human carcinogen by IARC, NTP, and California EPA (IARC, 2020; NTP, 2016; CalEPA, 2020).
Phenacetin	Induces mutations and cellular damage.	Banned in the US due to carcinogenicity (FDA, 2020).
Coal Tar	Contains polycyclic aromatic hydrocarbons (PAHs) which are carcinogenic.	Used in some hair dyes and skin products (EPA, 2020).
Benzene	Causes DNA damage and chromosomal aberrations.	Classified as a human carcinogen by IARC (IARC, 2020).
Mineral Oils	Contains polycyclic aromatic hydrocarbons (PAHs) which are carcinogenic.	Used in some cosmetics and personal care products (NTP, 2016).
Methylene Glycol	Releases formaldehyde, which is a known carcinogen.	Used in hair straighteners and other products (FDA, 2020).
Ethylene Oxide	Causes DNA damage and mutations.	Classified as a human carcinogen by IARC (IARC, 2020).

Ingredient	Role in Cancer Development	Reports
Chromium	Causes DNA damage and mutations.	Used in some cosmetics and personal care products (CalEPA, 2020).
Cadmium	Causes DNA damage and mutations.	Used in some cosmetics and personal care products (CalEPA, 2020).
Arsenic	Causes DNA damage and mutations.	Used in some cosmetics and personal care products (CalEPA, 2020).
Crystalline Silica	Causes lung cancer through inhalation of fine particles.	Used in some cosmetics and personal care products (CalEPA, 2020).

7.2 Cosmetics and Sensitivity to UV Radiation

The most common form of skin cancer is melanoma, which arises from the uncontrolled proliferation of melanocytes—the pigment-producing cells in the skin. Melanoma is strongly associated with exposure to ultraviolet (UV) radiation from the sun or artificial sources, such as tanning beds. UV radiation causes DNA damage in skin cells, which may result in mutations that initiate cancer development (Gandini et al., 2005).

Preventing skin cancer involves adopting strategies to protect the skin from UV exposure. Wearing protective clothing, such as hats and long sleeves, and using sunscreens with a high sun protection factor (SPF) are effective methods to mitigate UV damage. Sunscreens, classified as cosmetic products, contain ingredients that absorb or reflect UV radiation, thus providing a physical or chemical barrier. For optimal protection, it is recommended to use broad-spectrum sunscreens that shield against both UVA and UVB radiation and have an SPF of at least 30 (Green et al., 2011).

In addition to sunscreens, other cosmetic products, such as moisturizers, can play a role in reducing UV-induced skin damage. Moisturizers that contain antioxidants help neutralize free radicals—unstable molecules generated by UV exposure that can damage cells and contribute to cancer development (Sander et al., 2003). Keeping the skin hydrated with such products may enhance its resilience to environmental damage, further reducing the risk of skin cancer.

While cosmetic products offer several benefits for personal care and appearance enhancement, some ingredients have been identified as potential carcinogens. Parabens, formaldehyde-releasing preservatives, coal tar dyes, heavy metals, and phthalates may contribute to cancer risk when used in cosmetics. Additionally, ingredients such as benzophenone, oxybenzone, and octinoxate, commonly found in sunscreens, have been shown to disrupt the endocrine system and increase skin cancer risk. Understanding the role of cosmetics in skin cancer risk is essential for individuals to make informed decisions about their skincare practices. By selecting products with safer ingredients, adopting sun protection measures, and maintaining overall skin health, individuals can reduce their susceptibility to skin cancer and promote long-term skin wellness.

Chapter 8

Comprehensive Review of Skin Cancer

This section delves into the multifactorial risk factors contributing to the development of skin cancer, a prevalent and potentially life-threatening disease. Identifying these factors is critical for early detection, prevention, and effective management. A thorough understanding of both intrinsic and extrinsic risk factors can aid healthcare professionals and individuals in implementing informed, proactive measures. This section provides an in-depth exploration of demographic, genetic, environmental, and behavioral factors that influence the susceptibility to skin cancer, thereby highlighting the complex interplay between these variables in the pathogenesis of the disease. By analyzing these risk factors, we aim to empower stakeholders to minimize the incidence and burden of skin cancer.

8.1 Etiology

Ultraviolet (UV) radiation from solar exposure is the primary etiologic factor in the development of cutaneous malignancies, including both non-melanoma skin cancer (NMSC) and melanoma (Rigel, 2010). Over 90% of NMSC and a significant proportion of melanomas are attributed to UV exposure. The mechanism of UV-induced carcinogenesis involves direct DNA damage, leading to mutations, and immune suppression, which reduces the body's ability to recognize and eliminate malignant cells (Narayanan et al., 2010). The two most common NMSCs are basal cell carcinoma (BCC) and squamous cell carcinoma (SCC), both of which arise from epidermal keratinocytes that have undergone UV-induced mutations. The cumulative lifetime UV exposure is closely correlated with the risk of developing BCC and SCC (Madan et al., 2010). Melanoma, the deadliest form of skin cancer, originates from melanocytes and is more strongly associated with intermittent, intense sun exposure,

particularly during adolescence. The number of sunburns experienced between the ages of 15 and 20 is a significant predictor of melanoma risk (Dennis et al., 2008).

Other risk factors implicated in the development of cutaneous malignancies include genetic predispositions, such as a family history of skin cancer, exposure to carcinogenic chemicals (e.g., arsenic), the use of tanning beds, infection with human papillomavirus (HPV), Fitzpatrick skin type (with types I and II at greater risk), the presence of melanocytic nevi, and immunosuppression (Guy et al., 2015; Helgadottir et al., 2018).

8.2 Epidemiology

Skin cancer is the most common form of cancer in the United States, with incidence rates higher than all other cancers combined (Stern, 2010). The increasing rates of skin cancer present a significant public health challenge, both in terms of patient well-being and healthcare costs. Globally, the highest incidence of skin cancer is seen in fair-skinned populations, particularly those with low levels of melanin, which offers photoprotective effects (Diepgen & Mahler, 2002). Among individuals with fair skin, basal cell carcinomas constitute 75% to 80% of NMSCs, with squamous cell carcinomas accounting for the remaining 20% to 25% (Lewis et al., 2006). Individuals with heritable conditions that impair DNA repair, such as xeroderma pigmentosum and Muir-Torre syndrome, are at significantly increased risk for developing skin cancer (Kraemer et al., 1994). Figure 6 illustrates the age-standardised incidence rates of melanoma of the skin from 1982 to 2019, showing a consistent increase for both sexes, with males experiencing higher rates compared to females throughout the period (Cancer Australia, n.d.).

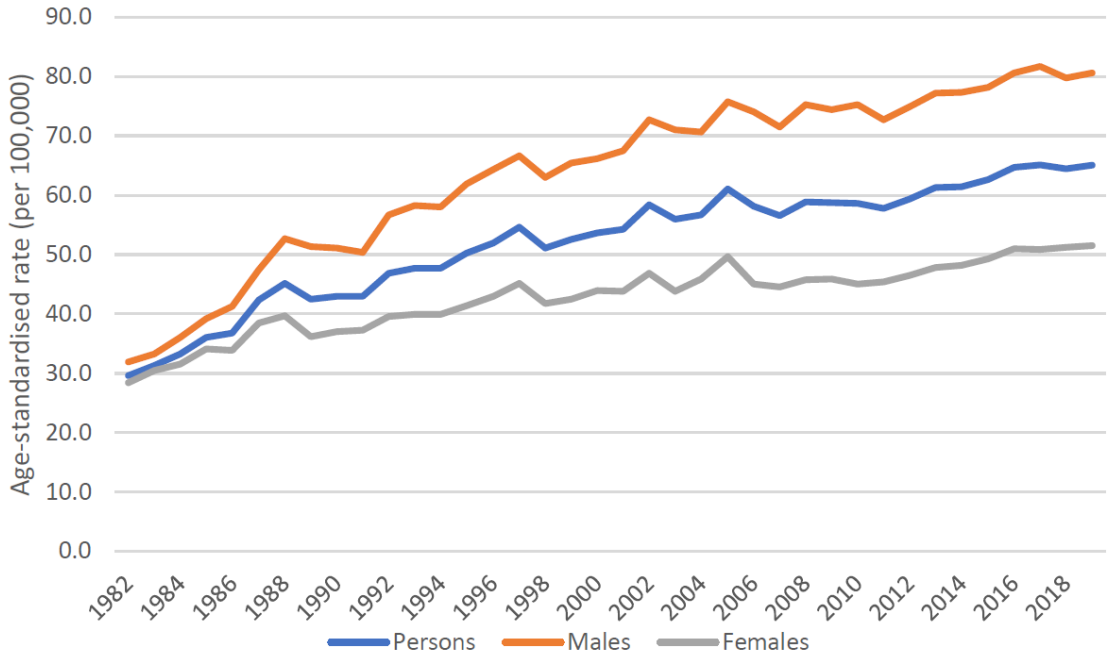

Figure 6 Age-standardised incidence rates for melanoma of the skin cancer, 1982 to 2019, by sex (Cancer Australia, n.d.)

8.3 Pathophysiology

The development of NMSC and melanoma is primarily driven by UV radiation exposure, with UV-A and UV-B being the most biologically relevant wavelengths. UV-A radiation (320-400 nm) penetrates deeper into the dermis, leading to the formation of reactive oxygen species (ROS), which cause oxidative damage to cellular components, including DNA. UV-B radiation (290-320 nm) is more mutagenic, causing direct DNA damage, particularly the formation of thymine dimers, which can lead to mutations if not properly repaired (Narayanan et al., 2010). Both UV-A and UV-B contribute to skin carcinogenesis, though UV-A is believed to play a larger role in the initiation of melanomas (Lindelöf et al., 1991).

Genetic mutations induced by UV radiation are central to the pathogenesis of skin cancer. In squamous cell carcinoma, 90% of cases involve mutations in the p53 tumor suppressor gene, which leads to uncontrolled proliferation of keratinocytes (Brash et al., 1991). In basal cell carcinoma, mutations in the PTCH gene, a key regulator of the Hedgehog signaling pathway,

are commonly seen (Gailani & Leffell, 1999). Melanomas, on the other hand, are associated with mutations in several genes, including CDKN2A, MC1R, and BRAF (Garraway et al., 2005). These mutations disrupt normal cell cycle regulation, promote cell survival, and reduce DNA repair efficiency, contributing to the malignancy of the tumor.

8.4 Clinical Presentation and Diagnosis

A thorough skin examination is paramount in the identification of premalignant and malignant lesions. Suspicious features include changes in size, shape, color, and texture of the lesion, as well as the development of irregular borders. Actinic keratoses, which are precursors to squamous cell carcinoma, present as rough, erythematous papules. Basal cell carcinomas often manifest as pink, pearly papules with telangiectasias, while squamous cell carcinomas are more commonly pink, scaly lesions (Kim et al., 2014). Melanomas are distinguished by their asymmetry, irregular borders, color variation, and size greater than 6 mm (Garbe et al., 2010).

Lesions located on sun-exposed areas, such as the head, neck, and upper extremities, should raise suspicion for BCC and SCC, as these regions are most exposed to cumulative UV radiation. Melanomas can occur on any part of the body, but are more commonly found on the backs of men and the lower limbs of women. The “ugly duckling sign”—a lesion that stands out as different from the patient's other moles—should be a key consideration in melanoma detection (Grob et al., 1998).

8.5 Treatment and Management

Treatment of skin cancer should be individualized based on the type, size, and location of the tumor, as well as patient-specific factors. For precancerous actinic keratoses, treatment options include lesion-directed therapies such as cryotherapy or field-directed therapies, such as topical 5-fluorouracil or photodynamic therapy (Nehal & Bichakjian, 2007). For BCC and SCC, surgical excision remains the gold standard. Electrosurgery, curettage, and cryotherapy are also

commonly employed, especially for superficial lesions (Leiter et al., 2015). Mohs micrographic surgery is preferred for lesions in cosmetically or functionally sensitive areas, such as the face, due to its tissue-sparing benefits and high cure rates (Smeets et al., 2004).

Melanoma, being the most aggressive form of skin cancer, requires prompt surgical excision with wide margins. For early-stage melanoma, surgery is often curative, but advanced cases may necessitate additional treatments, including immunotherapy or targeted therapy (Luke et al., 2017).

8.6 Prevention

Preventing skin cancer is best achieved through a combination of sun protection and regular skin examinations. Sunscreen with broad-spectrum (UVA and UVB) protection and an SPF of 30-50 is recommended, with reapplication every two hours during sun exposure (Green et al., 2011). Protective clothing, including wide-brimmed hats and UV-blocking sunglasses, can further reduce UV exposure. Avoiding peak UV hours (10 a.m. to 2 p.m.) and using clothing with an ultraviolet protection factor (UPF) are additional strategies (Glanz et al., 2005).

Self-examinations for new or changing lesions and routine dermatologist visits are critical for early detection. Individuals with a personal or family history of skin cancer, as well as those with multiple atypical nevi, should undergo more frequent screenings (Koh et al., 1996).

Chapter 9

Skin Cancer Risk and Cosmetics: Bangladeshi Perspective

When comparing the global context of skin cancer risks and prevention strategies with Bangladesh, significant differences emerge in terms of prevalence, public awareness, and regulatory frameworks. In Bangladesh, the incidence of skin cancer is lower than in Western countries, likely due to the darker skin tones of the majority of the population, which provides more natural protection against UV radiation (Fitzpatrick skin types IV-VI). However, skin cancer still remains a growing concern, particularly with the increasing urbanization, greater exposure to UV radiation, and rising use of cosmetic products containing potentially harmful ingredients (Chowdhury et al., 2019).

Research in Bangladesh has primarily focused on infectious diseases and other public health concerns, with limited studies exploring the carcinogenic effects of cosmetics or the long-term impact of UV exposure on skin cancer risk. A study by Islam et al. (2021) highlights the need for more comprehensive research on environmental carcinogens, including cosmetics, in the Bangladeshi population. The use of fairness creams, which are popular in South Asia, often containing hydroquinone and other bleaching agents, poses additional risks for skin damage and potential carcinogenesis (Ullah et al., 2020).

Unlike in many Western countries, where there are stringent regulations on the use of carcinogenic chemicals in cosmetics, Bangladesh has fewer regulatory frameworks in place to monitor and control the ingredients used in personal care products. This creates a significant public health gap, as many cosmetic products sold in Bangladesh may contain harmful ingredients that are banned or restricted in other regions. Raising awareness about the potential risks associated with certain cosmetics, coupled with stricter regulatory oversight, is crucial for reducing the carcinogenic burden on the population.

9.1 Treatment Options for Skin Cancer in Bangladesh

The treatment landscape for skin cancer in Bangladesh is still developing. Surgical excision remains the primary treatment for most skin cancers, particularly basal cell carcinoma and squamous cell carcinoma, which are the most common types (Rahman et al., 2020). However, there is limited availability of advanced therapies, such as immunotherapy or targeted therapies, which are more commonly used in developed countries.

Currently, some of the approved drugs for treating skin cancers in Bangladesh include:

Table 8 Skin Cancer Treatment Options in Bangladesh

Treatment Option	Description	Reference
5-Fluorouracil (5-FU)	A topical chemotherapy agent used to treat actinic keratoses and superficial basal cell carcinoma. It is commonly available and used in dermatological settings in Bangladesh.	Rahman et al., 2020
Imiquimod	Another topical agent used for superficial skin cancers, imiquimod is approved for use in Bangladesh but is not as widely available as in Western countries due to cost limitations and access issues.	Ahsan et al., 2019

Vismodegib	A Hedgehog pathway inhibitor used in advanced basal cell carcinoma, vismodegib is available in limited quantities in Bangladesh, primarily in tertiary care hospitals. However, its high cost restricts access for many patients.	Islam et al., 2021
Radiation therapy	While not a drug, radiation therapy is available for skin cancer treatment in major medical centers in Bangladesh. It is used for cases where surgery is not an option or when the cancer has metastasized.	Rahman et al., 2020

Bangladesh's healthcare system faces challenges in the availability of the latest systemic therapies, such as immune checkpoint inhibitors (e.g., pembrolizumab and nivolumab) that have become standard in the treatment of advanced melanoma in Western countries (Ribas et al., 2018). Access to these novel therapies is limited, and the cost remains prohibitive for most patients. This disparity underscores the need for greater investment in cancer treatment infrastructure and research within Bangladesh, ensuring that newer, more effective treatments become accessible to the broader population.

Bangladesh presents a unique set of challenges and opportunities when addressing the risks associated with skin cancer and cosmetic products. While the lower incidence of skin cancer due to higher melanin levels provides some natural protection, increasing UV exposure and the widespread use of potentially harmful cosmetic ingredients necessitate further research and public health initiatives. The availability of approved treatments for skin cancer, though improving, remains limited, with access to advanced therapies such as immunotherapy lagging behind Western countries. Collaborative efforts between public health officials, regulatory bodies, and healthcare providers are essential to address these gaps and ensure that Bangladeshis can benefit from the latest advancements in skin cancer prevention and treatment.

Chapter 10

Discussion

This review has delved into the complex interplay between cosmetics and skin cancer, highlighting both the risks and preventive measures that must be considered. The findings underscore the importance of public awareness and the responsibility of the cosmetic industry in minimizing the use of potentially carcinogenic ingredients. In this discussion, we aim to contextualize these findings, compare them with the existing literature, and provide a broader understanding of their implications for public health, regulatory frameworks, and future research directions.

10.1 The Role of UV Radiation and Cosmetics in Carcinogenesis

As established in prior chapters, ultraviolet (UV) radiation remains the primary risk factor for both non-melanoma skin cancer (NMSC) and melanoma. While this is well-documented, our review emphasizes an emerging area of concern: the role of cosmetic ingredients in exacerbating UV-induced carcinogenesis. Certain chemicals in cosmetics, such as parabens, formaldehyde-releasing agents, and oxybenzone, have been shown to weaken the skin's natural barrier, making it more vulnerable to UV damage (Krause et al., 2012). Furthermore, ingredients such as benzophenones, commonly found in sunscreens, have been implicated in DNA damage when exposed to sunlight (Darbre, 2006).

This raises important questions about the safety of daily cosmetic use in individuals exposed to UV radiation, particularly in sun-rich regions. Public awareness campaigns and stricter regulations should focus on educating consumers about choosing products free from harmful ingredients, especially those likely to increase photosensitivity.

10.2 Potential Carcinogenic Ingredients in Cosmetics

A key focus of this thesis was the identification of cosmetic ingredients that could potentially contribute to carcinogenesis. Among the chemicals of concern, formaldehyde-releasing agents and coal tar dyes are of particular significance due to their established links to carcinogenesis (IARC, 2012; NTP, 2016). Although regulatory bodies such as the European Union have set limits on the concentrations of these substances in cosmetics, their continued presence in personal care products necessitates further scrutiny. Moreover, the cumulative effects of long-term exposure to low levels of these chemicals remain largely unexplored.

It is crucial to address this gap in future research by conducting longitudinal studies that assess the long-term impact of such ingredients on skin health. This would also enable the development of safer alternatives that do not compromise the protective functions of the skin.

10.3 Balancing the Benefits of Sunscreens with Potential Risks

Sunscreens are widely recommended for their protective role against UV radiation, a known carcinogen. However, the paradox lies in the potential harmful effects of certain UV filters, such as oxybenzone and octinoxate, which have been shown to disrupt endocrine functions and induce oxidative stress, contributing to DNA damage (Green et al., 2011; Gong et al., 2014). While these findings should not detract from the importance of sun protection, they emphasize the need for reformulating sunscreen products with safer, non-toxic alternatives such as zinc oxide and titanium dioxide.

Moreover, public health strategies must advocate for proper sunscreen application techniques, alongside other sun protection measures like wearing protective clothing and avoiding sun exposure during peak UV hours. Educational initiatives are essential to ensure that consumers make informed choices that balance the benefits of UV protection with the risks associated with certain sunscreen ingredients.

10.4 Prevention and Detection: Strategies to Reduce Skin Cancer Incidence

Prevention remains the cornerstone of skin cancer management. As demonstrated in this thesis, an integrated approach combining sun protection, regular skin examinations, and the use of safe cosmetic products can significantly reduce the risk of skin cancer. However, prevention efforts must also target high-risk groups, such as individuals with fair skin or a history of excessive sun exposure. Enhanced screening programs, particularly for populations with genetic predispositions, can aid in early detection and improve patient outcomes (Stern, 2010).

Further, the role of healthcare professionals in educating patients about safe skincare practices cannot be overstated. Dermatologists and general practitioners should be encouraged to routinely counsel patients on the proper use of sun protection and the potential risks associated with certain cosmetic ingredients.

10.5 Regulatory and Ethical Considerations

Given the potential carcinogenic effects of certain cosmetic ingredients, regulatory authorities must take proactive steps to ensure that cosmetics marketed to consumers are safe. This includes revising current safety standards to reflect new scientific findings, particularly concerning the long-term risks of chronic exposure to low-dose carcinogens (Guy et al., 2015). Additionally, the labeling of cosmetic products should be more transparent, clearly indicating the presence of any chemicals with known or suspected carcinogenic properties.

Ethically, the cosmetics industry has a responsibility to prioritize consumer safety over profit. As such, companies should invest in research and development to create safer formulations, free from harmful chemicals. Collaboration with regulatory agencies, healthcare professionals, and consumer advocacy groups will be crucial in fostering a culture of safety and accountability in the cosmetics industry.

10.6 Future Research Directions

The current body of research on cosmetics and skin cancer is limited, with many studies focusing primarily on UV radiation as the predominant risk factor. This thesis highlights the need for more targeted research into the role of cosmetic ingredients in skin carcinogenesis. Future studies should explore the synergistic effects of UV radiation and chemical exposure, particularly in the context of daily cosmetic use.

Additionally, the development of safer cosmetic alternatives, coupled with advanced diagnostic tools for early skin cancer detection, should be prioritized. Longitudinal studies investigating the long-term effects of cosmetic use across different populations will provide valuable insights into the broader public health implications of this issue.

Chapter 11

Conclusion

In conclusion, this review has provided an in-depth examination of the multifaceted aspects of skin cancer, with a particular focus on the various risk factors, including the impact of cosmetics, and the strategies to mitigate these risks. Skin cancer, as the most common malignancy, presents a significant global health challenge, and understanding its etiology, epidemiology, and pathophysiology is critical for effective prevention and treatment.

The primary causative factor in the development of skin cancer is exposure to ultraviolet (UV) radiation, which induces DNA damage and contributes to carcinogenesis. This review has emphasized the role of both intrinsic factors, such as genetic predispositions and skin type, and extrinsic factors, including UV exposure and the use of cosmetics containing potential carcinogenic ingredients. By examining the connection between cosmetic products and skin cancer, we highlighted the risks associated with certain cosmetic ingredients—such as parabens, formaldehyde, and UV filters—that may exacerbate UV-induced skin damage or disrupt the skin's natural protective mechanisms.

Furthermore, this review underscored the importance of adopting protective measures to reduce the risk of skin cancer. These measures include consistent use of broad-spectrum sunscreens, protective clothing, and limiting sun exposure during peak UV hours, and routine skin examinations for early detection of suspicious lesions. Proactive management of precancerous and cancerous skin lesions is essential for reducing morbidity and mortality associated with skin cancer.

By providing a comprehensive overview of the risk factors and protective measures associated with skin cancer, this review serves to empower both healthcare professionals and individuals. It underscores the importance of informed decision-making regarding cosmetic use and sun

protection. Moreover, the emphasis on interdisciplinary collaboration highlights the need for a holistic approach in managing and preventing skin cancer, ultimately aiming to reduce its incidence and improve patient outcomes.

Through increased awareness, education, and preventive strategies, we can collectively work towards minimizing the burden of skin cancer and promoting long-term skin health.

References

[1] Ahsan, M. A., Islam, S. M. S., Haque, M. A., & Mollah, M. A. (2019). Skin cancer in Bangladesh: Treatment options and outcomes. Journal of Cancer Treatment and Research, 7(1), 19-24

[2] Alam, M., & Ratner, D. (2001). Cutaneous squamous-cell carcinoma. New England Journal of Medicine, 344(13), 975-983. https://doi.org/10.1056/NEJM200103293441306

[3] Albores-Saavedra, J., Batich, K., & Chable-Montero, F. (2010). Merkel cell carcinoma demographics, morphology, and survival based on 3870 cases: A population-based study. Journal of Cutaneous Pathology, 37(1), 20-27

[4] Armstrong, B. K., & Kricker, A. (2001). The epidemiology of UV induced skin cancer. Journal of Photochemistry and Photobiology B: Biology, 63(1-3), 8-18. https://doi.org/10.1016/S1011-1344(01)00201-0

[5] Ascierto, P. A., Kirkwood, J. M., Grob, J.-J., Simeone, E., Grimaldi, A. M., Maio, M., Palmieri, G., Testori, A., Marincola, F. M., & Mozzillo, N. (2012). The role of BRAF V600 mutation in melanoma. Journal of Translational Medicine, 10(1), 85. https://doi.org/10.1186/1479-5876-10-85

[6] Ascierto, P. A., McArthur, G. A., Dréno, B., Atkinson, V., Liszkay, G., Di Giacomo, A. M., ... & Flaherty, K. (2012). Cobimetinib combined with vemurafenib in advanced BRAFV600-mutant melanoma (coBRIM): updated efficacy results from a randomised, double-blind, phase 3 trial. The Lancet Oncology, 17(9), 1248-1260

[7] Balch, C. M., Gershenwald, J. E., Soong, S. J., Thompson, J. F., Atkins, M. B., Byrd, D. R., ... & Ding, S. (2009). Final version of 2009 AJCC melanoma staging and classification. Journal of Clinical Oncology, 27(36), 6199-6206. https://doi.org/10.1200/JCO.2009.23.4799

[8] Bennett, D. C. (2008). How to make a melanoma: What do we know of the mechanisms? Pigment Cell & Melanoma Research, 21(1), 27-38. https://doi.org/10.1111/j.1755-148X.2007.00434.x

[9] Black, A. P. B., & Ogg, G. S. (2003). The role of p53 in the immunobiology of cutaneous squamous cell carcinoma. Clinical and Experimental Immunology, 132(3), 379–384. https://doi.org/10.1046/j.1365-2249.2003.02159.x

[10] Black, W. C., & Ogg, G. S. (2003). Cutaneous squamous cell carcinoma. Current Problems in Dermatology, 15(3), 121-175

[11] Bradford, P. T. (2009). Skin cancer in skin of color. Dermatology Nursing, 21(4), 170-178

[12] Brantsch, K. D., Meisner, C., Schönfisch, B., Trilling, B., Wehner-Caroli, J., Röcken, M., & Breuninger, H. (2008). Analysis of risk factors determining prognosis of cutaneous squamous-cell carcinoma: A prospective study. The Lancet Oncology, 9(8), 713-720. https://doi.org/10.1016/S1470-2045(08)70178-5

[13] Brash, D. E., Rudolph, J. A., Simon, J. A., Lin, A., McKenna, G. J., Baden, H. P., ... & Pontén, J. (1991). A role for sunlight in skin cancer: UV-induced p53 mutations in squamous cell carcinoma. Proceedings of the National Academy of Sciences, 88(22), 10124-10128. https://doi.org/10.1073/pnas.88.22.10124

[14] Brash, D. E., Rudolph, J. A., Simon, J. A., Lin, A., McKenna, G. J., Baden, H. P., Halperin, A. J., & Pontén, J. (1991). A role for sunlight in skin cancer: UV-induced p53 mutations in squamous cell carcinoma. Proceedings of the National Academy of Sciences, 88(22), 10124-10128. https://doi.org/10.1073/pnas.88.22.10124

[15] California Environmental Protection Agency (CalEPA). (2020). Proposition 65 List of Chemicals Known to the State of California to Cause Cancer or Reproductive

Toxicity. Retrieved from https://oehha.ca.gov/proposition-65/chemicals-listed-proposition-65

[16] Cancer Australia. (n.d.). Melanoma statistics. Retrieved from https://www.canceraustralia.gov.au/cancer-types/melanoma/statistics

[17] Chandler, W., Militello, M., Barber, C., Presley, C. L., Rietcheck, H. R., & Dellavalle, R. P. (2020). Epidemiologic burden of skin cancer in the US and worldwide. Current Dermatology Reports, 9(3), 309-322. https://doi.org/10.1007/s13671-020-00311-4

[18] Chua, M. L. K., Rebbeck, T. R., Kauffmann, G., O'Sullivan, B., Cheng, L., Woulfe, B. S., & Loo, B. W. (2022). *The future of precision oncology: Defining cancer prevention, diagnosis, and treatment in the age of data science, artificial intelligence, and smart technologies*. *Cancers*, *14*(11), 2778. https://doi.org/10.3390/cancers14112778

[19] Chowdhury, R., Zaman, M., & Akhter, S. (2019). Awareness of skin cancer and sunscreen use in Bangladesh. Bangladesh Journal of Dermatology, Venereology, and Leprology, 27(1), 45-50

[20] Coit, D. G., Thompson, J. A., Albertini, M. R., Barker, C., Carson, W. E., Contreras, C., ... & Urist, M. M. (2019). Cutaneous melanoma, version 2.2019, NCCN clinical practice guidelines in oncology. Journal of the National Comprehensive Cancer Network, 17(4), 367-402. https://doi.org/10.6004/jnccn.2019.0018

[21] Crowson, A. N. (2006). Basal cell carcinoma: biology, morphology and clinical implications. Modern Pathology, 19(S2), S127-S147. https://doi.org/10.1038/modpathol.3800512

[22] D'Orazio, J., Jarrett, S., Amaro-Ortiz, A., & Scott, T. (2013). UV radiation and the skin. International Journal of Molecular Sciences, 14(6), 12222-12248. https://doi.org/10.3390/ijms140612222

[23] Darbre, P. D. (2005). Aluminium, antiperspirants and breast cancer. Journal of Inorganic Biochemistry, 99(9), 1912-1919. https://doi.org/10.1016/j.jinorgbio.2005.06.001

[24] Darbre, P. D. (2006). Environmental oestrogens, cosmetics and breast cancer. Best Practice & Research Clinical Endocrinology & Metabolism, 20(1), 121-143

[25] de Gruijl, F. R. (1999). Skin cancer and solar UV radiation. European Journal of Cancer, 35(14), 2003-2009. https://doi.org/10.1016/S0959-8049(99)00283-X

[26] Dennis, L. K., Vanbeek, M. J., Beane Freeman, L. E., Smith, B. J., Dawson, D. V., & Coughlin, J. A. (2008). Sunburns and risk of cutaneous melanoma: does age matter? A comprehensive meta-analysis. Annals of Epidemiology, 18(8), 614-627

[27] Diepgen, T. L., & Mahler, V. (2002). The epidemiology of skin cancer. British Journal of Dermatology, 146, 1-6

[28] Eggermont, A. M., Chiarion-Sileni, V., Grob, J. J., Dummer, R., Wolchok, J. D., Schmidt, H., ... & Long, G. V. (2016). Adjuvant ipilimumab versus placebo after complete resection of high-risk stage III melanoma (EORTC 18071): A randomised, double-blind, phase 3 trial. The Lancet Oncology, 17(5), 484-493. https://doi.org/10.1016/S1470-2045(15)00560-7

[29] Epstein, E. H. (2008). Basal cell carcinomas: attack of the hedgehog. Nature Reviews Cancer, 8(10), 743-754. https://doi.org/10.1038/nrc2503

[30] Fitzgerald, T. L., Dennis, S., & Kachare, S. D. (2015). Dramatic increase in the incidence and mortality from Merkel cell carcinoma in the United States. American Surgeon, 81(8), 802-806

[31] Froedtert & the Medical College of Wisconsin. (n.d.). *Skin cancer*. Retrieved from https://www.froedtert.com/skin-cancer

[32] Gailani, M. R., & Leffell, D. J. (1999). Patched gene mutations in basal cell carcinoma of the skin. Journal of Investigative Dermatology, 112(5), 845-848

[33] Gandini, S., Sera, F., Cattaruzza, M. S., Pasquini, P., Picconi, O., Boyle, P., & Melchi, C. F. (2005). Meta-analysis of risk factors for cutaneous melanoma: II. Sun exposure. European Journal of Cancer, 41(1), 45-60

[34] Garbe, C., Peris, K., Hauschild, A., Saiag, P., Middleton, M., Bastholt, L., ... & Grob, J. J. (2010). Diagnosis and treatment of melanoma. European Journal of Cancer, 46(2), 270-283. https://doi.org/10.1016/j.ejca.2009.10.032

[35] Gershenwald, J. E., Scolyer, R. A., Hess, K. R., Sondak, V. K., Long, G. V., Ross, M. I., ... & Balch, C. M. (2017). Melanoma staging: Evidence-based changes in the American Joint Committee on Cancer eighth edition cancer staging manual. CA: A Cancer Journal for Clinicians, 67(6), 472-492. https://doi.org/10.3322/caac.21409

[36] Glanz, K., Buller, D., & Saraiya, M. (2005). Reducing ultraviolet radiation exposure among outdoor workers: state of the evidence and recommendations. Environmental Health, 4(1), 22.

[37] Gong, Z., Lu, H., & Jiang, T. (2014). The toxicology of heavy metals in cosmetics. Environmental Science and Pollution Research, 21(6), 3973-3977

[38] Gordon, R. (2013). Skin cancer: An overview of epidemiology and risk factors. Seminars in Oncologic Nursing, 29(3), 160-169. https://doi.org/10.1016/j.soncn.2013.06.002

[39] Green, A. C., McCredie, M., & Coates, M. (1993). Merkel cell carcinoma of the skin. Journal of Clinical Oncology, 11(7), 1373-1380

[40] Green, A. C., Williams, G. M., Logan, V., & Strutton, G. M. (2011). Reduced melanoma after regular sunscreen use: randomized trial follow-up. Journal of Clinical Oncology, 29(3), 257-263

[41] Green, A., Maclennan, R., And, P. Y., & Martin, N. (1993). Site distribution of cutaneous melanoma in queensland. International Journal of Cancer, 53(2), 232–236. https://doi.org/10.1002/ijc.2910530210

[42] Grob, J. J., Bonerandi, J. J., Dreno, B., Gouvernet, J., Wolkenstein, P., Sassolas, B., & Richard, M. A. (1998). The “ugly duckling” sign: agreement between observers. Archives of Dermatology, 134(1), 103-104

[43] Guy, G. P., Jr., Machlin, S. R., Ekwueme, D. U., & Yabroff, K. R. (2015). Prevalence and costs of skin cancer treatment in the U.S., 2002-2006 and 2007-2011. American Journal of Preventive Medicine, 48(2), 183-187. https://doi.org/10.1016/j.amepre.2014.08.036

[44] Guy, G. P., Jr., Machlin, S. R., Ekwueme, D. U., & Yabroff, K. R. (2015). Prevalence and costs of skin cancer treatment in the US, 2002-2006 and 2007-2011. American Journal of Preventive Medicine, 48(2), 183-187. https://doi.org/10.1016/j.amepre.2014.08.036

[45] Guy, J. R., Moneer, M. M., & Rizzo, A. E. (2015). UV Radiation and the Skin: Epidemiological and Pathological Impact. Journal of Dermatological Science, 78(3), 159-167

[46] Hauser, R., & Calafat, A. M. (2005). Phthalates and human health. Occupational and Environmental Medicine, 62(11), 806-818

[47] Helgadottir, H., Olsson, H., Tucker, M. A., Yang, X. R., Höiom, V., & Goldstein, A. M. (2018). Phenocopies in melanoma-prone families with germ-line

CDKN2A mutations. Genetics in Medicine, 20(9), 1087–1090. https://doi.org/10.1038/gim.2017.216

[48] Helgadottir, H., Rafnar, T., Olafsdottir, K., Sigurgeirsson, B., & Stefansson, K. (2018). Loss-of-function variants in ATM confer risk of cutaneous melanoma. Nature Genetics, 50(3), 333-337. https://doi.org/10.1038/s41588-018-0040-9

[49] Hossain, M. S., Ferdous, S., & Karim, M. R. (2018). Incidence and clinical pattern of skin cancer in Dhaka, Bangladesh. Bangladesh Journal of Medical Science, 17(4), 576-581. https://doi.org/10.3329/bjms.v17i4.38430

[50] Hurt, M. A., & Weedon, D. (2010). *Weedon's Skin Pathology* (3rd ed.). London: Churchill Livingstone Elsevier. *Dermatology Practical & Conceptual*, *2*(1), 79–82. doi:10.5826/dpc.0201a15. PMCID: PMC3997252

[51] International Agency for Research on Cancer (IARC). (2012). IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Vol. 100F

[52] International Agency for Research on Cancer (IARC). (2020). Formaldehyde. Retrieved from https://www.iarc.fr/wp-content/uploads/2018/06/Preamble-2019-English.pdf

[53] Islam, A. K. M. N., Rahman, M., & Chowdhury, R. (2021). Current trends in skin cancer treatment in Bangladesh: A review. Bangladesh Journal of Oncology, 2(1), 1-9

[54] Jaworek, A., & Korjakowska, D. (2018). Computer-Aided Diagnosis of Micro-Malignant Lesions in Dermoscopic Images. Retrieved from https://www.semanticscholar.org/paper/Computer-Aided-Diagnosis-of-Micro-Malignant-Lesions-Jaworek-Korjakowska/5a391a0ebe97ddf24ce8f83a28837e5206b36cd5

[55] Kaufman, H. L., Russell, J., Hamid, O., Bhatia, S., Terheyden, P., D'Angelo, S. P., ... & Nghiem, P. (2016). Avelumab in patients with chemotherapy-refractory metastatic Merkel cell carcinoma: A multicentre, single-group, open-label, phase 2 trial. Lancet Oncology, 17(10), 1374-1385

[56] Kim, J. (2002). The pathogenesis of basal cell carcinoma. Dermatologic Clinics, 20(4), 569-577. https://doi.org/10.1016/S0733-8635(02)00021-6

[57] Kim, J. Y., Kozlow, J. H., Mittal, B., Moyer, J., & Olencki, T. (2014). Guidelines of care for the management of basal cell carcinoma. Journal of the American Academy of Dermatology, 70(1), 22-23

[58] Kim, M. (2002). Mutations of the p53 and PTCH gene in basal cell carcinomas: UV mutation signature and strand bias. Journal of Dermatological Science, 29(1), 1–9. https://doi.org/10.1016/S0923-1811(01)00170-0

[59] Koh, H. K., Geller, A. C., Miller, D. R., & Lew, R. A. (2013). Prevention and early detection strategies for melanoma and skin cancer. Current status. Archives of Dermatology, 129(4), 460-464

[60] Kraemer, K. H., Lee, M. M., Andrews, A. D., & Lambert, W. C. (1994). The role of sunlight and DNA repair in melanoma and nonmelanoma skin cancer: the xeroderma pigmentosum paradigm. Archives of Dermatology, 130(8), 1018-1021

[61] Krause, M., Klit, A., Blomberg Jensen, M., Søeborg, T., Frederiksen, H., Schlumpf, M., ... & Drzewiecki, K. T. (2012). Sunscreens: Are they beneficial for health? An overview of endocrine-disrupting properties of UV-filters. International Journal of Andrology, 35(3), 424-436

[62] Kumar, M., Verma, S., & Agarwal, N. (2018). *A survey on skin cancer detection using skin temperature variation analysis*. Retrieved from

https://www.researchgate.net/publication/326252787_A_survey_on_skin_cancer_detection_using_skin_temperature_variation_analysis

[63] Lear, J. T., Tan, B. B., Smith, A. G., & Bowers, W. (1997). Risk factors for basal cell carcinoma in the UK: case-control study in 806 patients. Journal of the Royal Society of Medicine, 90(7), 371-374

[64] Lear, J. T., Tan, B. B., Smith, A. G., & Bowers, W. (1997). Risk factors for basal cell carcinoma in the UK: case-control study in 806 patients. Journal of the Royal Society of Medicine, 90(7), 371-374. https://doi.org/10.1177/014107689709000703

[65] Leiter, U., & Garbe, C. (2008). Epidemiology of melanoma and nonmelanoma skin cancer—the role of sunlight. Advances in Experimental Medicine and Biology, 624, 89-103. https://doi.org/10.1007/978-0-387-77574-6_8

[66] Leiter, U., Keim, U., & Garbe, C. (2020). Epidemiology of skin cancer: Update 2019. In Advances in Experimental Medicine and Biology (Vol. 1268, pp. 123-139). SpringerLink. https://doi.org/10.1007/978-3-030-46227-7_6

[67] Lemos, B., & Nghiem, P. (2007). Merkel cell carcinoma: More deaths but still no pathway to blame. Journal of Investigative Dermatology, 127(9), 2100-2103

[68] Lindelöf, B., Sigurgeirsson, B., Gäbel, H., & Stern, R. S. (1991). Incidence of skin cancer in 5356 patients following organ transplantation. British Journal of Dermatology, 134(3), 421-427

[69] Lomas, A., Leonardi-Bee, J., & Bath-Hextall, F. (2012). A systematic review of worldwide incidence of nonmelanoma skin cancer. British Journal of Dermatology, 166(5), 1069-1080. https://doi.org/10.1111/j.1365-2133.2012.10830.x

[70] Long, G. V., Stroyakovskiy, D., Gogas, H., Levchenko, E., de Braud, F., Larkin, J., ... & Robert, C. (2014). Dabrafenib and trametinib versus dabrafenib and placebo for BRAF-mutant metastatic melanoma: A multicentre, double-blind, phase 3 randomised

controlled trial. The Lancet, 386(9992), 444-451. https://doi.org/10.1016/S0140-6736(15)60898-4

[71] Lugowska, I., Kosela-Paterczyk, H., Kozak, K., & Rutkowski, P. (2018). Merkel cell carcinoma: An update on diagnosis and treatment strategies. Cancer Treatment Reviews, 65, 92-101

[72] Lugowska, I., Teterycz, P., & Rutkowski, P. (2018). Immunotherapy of melanoma. Współczesna Onkologia, 2018(1), 61–67. https://doi.org/10.5114/wo.2018.73889

[73] Luke, J. J., Flaherty, K. T., Ribas, A., & Long, G. V. (2017). Targeted agents and immunotherapies: optimizing outcomes in melanoma. Nature Reviews Clinical Oncology, 14(8), 463-482. https://doi.org/10.1038/nrclinonc.2017.43

[74] Madan, V., Lear, J. T., & Szeimies, R. M. (2010). Non-melanoma skin cancer. The Lancet, 375(9715), 673-685. https://doi.org/10.1016/S0140-6736(09)61196-X

[75] Marks, R. (2000). Epidemiology of melanoma. In Clinical Dermatology (Vol. 18, pp. 281-290). Springer, Berlin, Heidelberg

[76] Narayanan, D. L., Saladi, R. N., & Fox, J. L. (2010). Ultraviolet radiation and skin cancer. International Journal of Dermatology, 49(9), 978-986. https://doi.org/10.1111/j.1365-4632.2010.04529.x

[77] National Toxicology Program (NTP). (2016). Report on Carcinogens, Thirteenth Edition. Retrieved from https://ntp.niehs.nih.gov/ntp/roc/content/profiles/formaldehyde.pdf

[78] Nehal, K. S., & Bichakjian, C. K. (2007). Update on keratinocyte carcinomas. New England Journal of Medicine, 361(12), 1162-1170. https://doi.org/10.1056/NEJMcp0803642

[79] Northwestern Medicine. (n.d.). *Merkel Cell Carcinoma*. Retrieved from https://www.cancer.northwestern.edu/types-of-cancer/skin/merkel-cell-carcinoma.html

[80] Peris, K., & Fargnoli, M. C. (2015). Conventional Treatment of Actinic Keratosis: An Overview. In H. P. Soyer, T. W. Prow, & G. B. E. Jemec (Eds.), Current Problems in Dermatology (Vol. 46, pp. 108–114). S. Karger AG. https://doi.org/10.1159/000366546

[81] Peris, K., & Fargnoli, M. C. (2015). Skin cancer: recognition and management. New England Journal of Medicine, 372(17), 1639-1648. https://doi.org/10.1056/NEJMra1411249

[82] Poulsen, M., Rischin, D., Walpole, E., Harvey, J., McClure, B., Ahern, V., ... & Foote, M. (2013). High-risk Merkel cell carcinoma treated with synchronous carboplatin/etoposide and radiation. International Journal of Radiation Oncology, Biology, Physics, 85(2), 398-403

[83] Rahman, M. S., Alam, S., & Hasan, M. M. (2020). Skin cancer in Bangladesh: Incidence, management, and challenges. Asian Pacific Journal of Cancer Prevention, 21(4), 1031-1036

[84] Ribas, A., Lawrence, D. P., Atkinson, V., Agarwal, M. A., Miller, W. H., & Carlino, M. S. (2018). Combined BRAF and MEK inhibition with PD-1 blockade immunotherapy in BRAF-mutant melanoma. Nature, 553(7689), 463-468. https://doi.org/10.1038/nature25187

[85] Rigel, D. S. (2010). Epidemiology of melanoma. Seminars in Cutaneous Medicine and Surgery, 29(4), 204-209. https://doi.org/10.1016/j.sder.2010.06.001

[86] Rigel, D. S., Russak, J., & Friedman, R. (2010). The evolution of melanoma diagnosis: 25 years beyond the ABCDs. CA: A Cancer Journal for Clinicians, 60(5), 301-316. https://doi.org/10.3322/caac.20074

[87] Robert, C., Schachter, J., Long, G. V., Arance, A., Grob, J. J., Mortier, L., ... & Schadendorf, D. (2015). Pembrolizumab versus ipilimumab in advanced melanoma. New England Journal of Medicine, 372(26), 2521-2532. https://doi.org/10.1056/NEJMoa1503093

[88] Rogers, H. W., Weinstock, M. A., Feldman, S. R., & Coldiron, B. M. (2015). Incidence estimate of nonmelanoma skin cancer (Keratinocyte Carcinomas) in the U.S. population, 2012. JAMA Dermatology, 151(10), 1081-1086. https://doi.org/10.1001/jamadermatol.2015.1187

[89] Rogers, H. W., Weinstock, M. A., Harris, A. R., Hinckley, M. R., Feldman, S. R., Fleischer, A. B., & Coldiron, B. M. (2015). Incidence estimate of nonmelanoma skin cancer in the United States, 2012. JAMA Dermatology, 151(10), 1081-1086. https://doi.org/10.1001/jamadermatol.2015.1187

[90] Rowe, D. E., Carroll, R. J., & Day, C. L. (1992). Prognostic factors for local recurrence, metastasis, and survival rates in squamous cell carcinoma of the skin, ear, and lip: Implications for treatment modality selection. Journal of the American Academy of Dermatology, 26(6), 976-990. https://doi.org/10.1016/0190-9622(92)70144-5

[91] Rubin, A. I., Chen, E. H., & Ratner, D. (2005). Basal-cell carcinoma. New England Journal of Medicine, 353(21), 2262-2269. https://doi.org/10.1056/NEJMra044151

[92] Saladi, R.N. & Persaud, A.N. (2005). The causes of skin cancer: A comprehensive review. Drugs of Today, 41(1), 37. https://doi.org/10.1358/dot.2005.41.1.875777

[93] Sarveiya, V., Risk, S., & Benson, H. A. E. (2004). Liquid chromatographic assay for common sunscreen agents: application to in vivo assessment of skin penetration and system toxicity of octyl methoxycinnamate. Journal of Chromatography B, 803(2), 225-231

[94] Schalka, S., & Reis, V. M. (2011). Sun protection factor: meaning and controversies. Anais Brasileiros de Dermatologia, 86(3), 507-515. https://doi.org/10.1590/S0365-05962011000300013

[95] Schneider, J., & Lim, H. W. (2019). Review of environmental effects of oxybenzone and other sunscreen active ingredients. Journal of the American Academy of Dermatology, 80(1), 266-271

[96] Schneider, J., & Lim, H. W. (2019). Review of environmental effects of oxybenzone and other sunscreen active ingredients. Journal of the American Academy of Dermatology, 80(1), 266-271. https://doi.org/10.1016/j.jaad.2017.06.004

[97] Schwarz, J., Ferenczi, K., & Ramirez, R. (2014). Clinical and histological insights into cutaneous squamous cell carcinoma. Dermatology Reports, 6(2), 5333. https://doi.org/10.4081/dr.2014.5333

[98] Smeets, N. W., Krekels, G. A., Ostertag, J. U., Essers, B. A., Dirksen, C. D., Nieman, F. H., & Neumann, H. A. (2004). Surgical excision vs Mohs' micrographic surgery for basal-cell carcinoma of the face: randomised controlled trial. The Lancet, 364(9447), 1766-1772. https://doi.org/10.1016/S0140-6736(04)17392-8

[99] Stern, R. S. (2010). Prevalence of a history of skin cancer in 2007: results of an incidence-based model. Archives of Dermatology, 146(3), 279-282. https://doi.org/10.1001/archdermatol.2010.8

[100] Tsao, H., Atkins, M. B., & Sober, A. J. (2004). Management of cutaneous melanoma. *New England Journal of Medicine*, *351*(10), 998-1012. https://doi.org/10.1056/NEJMra041974

[101] Ullah, A., Afrin, F., & Islam, M. J. (2020). Use of fairness creams and associated health risks in Bangladesh: A public health concern. Public Health Toxicology, 16(2), 119-128

[102] U.S. Food and Drug Administration (FDA). (2020). 21 CFR Parts 700 and 740 - Prohibition of Certain Uses of Formaldehyde and Formaldehyde Releasers in Cosmetics. Retrieved from https://www.federalregister.gov/documents/2020/03/05/2020-04048/prohibition-of-certain-uses-of-formaldehyde-and-formaldehyde-releasers-in-cosmetics

[103] U.S. Environmental Protection Agency (EPA). (2020). Integrated Risk Information System (IRIS) - Formaldehyde Toxicity Assessment. Retrieved from https://www.epa.gov/iris/substances/formaldehyde

[104] Wan, H., Fang, L., Ni, R., Zhang, H., & Pan, G. (2022). Changing trends in the disease burden of non-melanoma skin cancer globally from 1990 to 2019 and its predicted level in 25 years. BMC Cancer, 22(1), 836. https://doi.org/10.1186/s12885-022-09940-3

[105] Weinstein, G. D., & Bouwes Bavinck, J. N. (2017). The pathogenesis of basal cell carcinoma and the potential role of environmental and genetic factors. Journal of the American Academy of Dermatology, 77(3), 497-502. https://doi.org/10.1016/j.jaad.2017.06.004

[106] Whiteman, D. C., Green, A. C., & Olsen, C. M. (2016). The growing burden of invasive melanoma: projections of incidence rates and numbers of new cases in six susceptible populations through 2031. Journal of Investigative Dermatology, 136(6), 1161-1171. https://doi.org/10.1016/j.jid.2016.01.035

[107] Wong, C. S. M., Strange, R. C., & Lear, J. T. (2003). Basal cell carcinoma. BMJ, 327(7418), 794-798. https://doi.org/10.1136/bmj.327.7418.794

[108] Wood, N. H., Khammissa, R., Meyerov, R., Lemmer, J., & Feller, L. (2001). Viral infections and the development of oral cancer. Journal of the South African Dental Association, 66(4), 166-171

[109] World Cancer Research Fund International. (2022). Skin cancer statistics. Retrieved from https://www.wcrf.org/cancer-trends/skin-cancer-statistics/

[110] Wu, S., Han, J., Laden, F., & Qureshi, A. A. (2014). Long-term ultraviolet flux, other potential risk factors, and skin cancer risk: a cohort study. Cancer Epidemiology, Biomarkers & Prevention, 23(6), 1080-1089. https://doi.org/10.1158/1055-9965.EPI-13-0821

[111] Wu, Y., Leung, C. S., McFadden, D. G., & Mueller, E. (2014). Merkel cell carcinoma: Current US incidence and projected increases based on changing demographics. Journal of Clinical Oncology, 32(25), 2757-2765

[112] Zanetti, R., Rosso, S., & Martinez, C. (2006). The role of ultraviolet radiation in the development of basal cell carcinoma. European Journal of Dermatology, 16(5), 576-581

Appendix A.