



## SKIN CANCER SCOPING REVIEW

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### SUMMARY

**Introduction:** skin cancer is a pathology with an important frequency in the world, it is generally divided as non-melanoma skin cancer (NMSC) or melanoma. The exact incidence of skin cancer is complex to establish due to lack of diagnostic criteria and sometimes underreporting.

**Objective:** to detail current information related to skin cancer, etiology, epidemiology, pathophysiology, assessment, treatment, differential diagnosis and skin cancer in children.

**Methodology:** a total of 32 articles were analyzed in this review, including review and original articles, as well as clinical cases, of which 23 bibliographies were used because the other articles were not relevant to this study. The sources of information were PubMed, Google Scholar and Cochrane; the terms used to search for information in Spanish, Portuguese and English were: skin cancer, melanoma, actinic keratosis, basal cell carcinoma, squamous cell carcinoma.

**Results:** Skin cancer is found in all races worldwide. However, the risk is substantially higher in those with fair skin because of the photoprotective effects of epidermal melanin. In fair-skinned individuals, about 75% to 80% of nonmelanoma skin cancers are basal cell carcinomas and about 25% are squamous cell carcinomas. Immunosuppression significantly increases the risk of forming cutaneous squamous cell carcinoma throughout life. The incidence of melanoma in pediatric individuals has decreased in recent years. Childhood and adolescent melanoma is not common and accounts for only 1.3% of all cancer cases in individuals under 20 years of age. However, between 15 and 19 years of age, melanoma represents approximately 7% of all cancers.

**Conclusions:** There is a high prevalence of skin cancers worldwide, sometimes going unnoticed and causing important consequences. The diagnosis and treatment of these neoplasms is a significant health problem, which can sometimes be prevented.



*The places most affected are those with the greatest exposure to the sun, so adequate sun protection is crucial to prevent skin cancer. In addition to knowing the pathology, its types and characteristics, it is important to perform a proper skin examination for the correct diagnosis, control and management. Currently there are multiple treatment alternatives such as surgical excision, cryotherapy, chemotherapy, immunotherapy and radiation, which show positive aspects against this pathology.*

**KEY WORDS:** cancer, melanoma, carcinoma, basal cell carcinoma, skin.

## INTRODUCTION

Skin cancer is a pathology with an important frequency in the world, it is generally divided as non-melanoma skin cancer (NMSC) or melanoma. The exact incidence of skin cancer is complex to establish because of the absence of diagnostic criteria and sometimes underreporting. However, multiple epidemiological studies have shown an increasing incidence of both NMSC and melanoma in recent years. The diagnosis and treatment of this type of neoplasm is a very important health problem, especially when it comes to the wellbeing of the affected individual and the costs of health care. Skin cancers are usually located in the parts of the head and neck exposed to the sun, resulting in a remarkable morbidity during diagnosis and treatment. There are multiple types of treatment alternatives such as cryotherapy, chemotherapy, immunotherapy, surgical excision and radiation. Adequate sun protection is essential in the prevention of skin cancer(1-3).

The following is a review of skin cancer, etiology, epidemiology, pathophysiology, assessment, treatment, differential diagnosis and skin cancer in children.

## METHODOLOGY

A total of 32 articles were analyzed in this review, including review and original articles, as well as cases and clinical trials, of which 23 bibliographies were used because the information collected was not important enough to be included in this study. The sources of information were Cochrane, PubMed and Google Scholar; the terms used to search for information in Spanish, Portuguese and English were: skin cancer, melanoma, actinic keratosis, basal cell carcinoma, squamous cell carcinoma.

The choice of bibliography exposes elements related to skin cancer; etiology, epidemiology, pathophysiology, assessment, treatment, differential diagnosis and skin cancer in children.

## DEVELOPMENT

### Etiology

Solar ultraviolet (UV) radiation is the most important etiologic factor in the development of cutaneous malignancies. Most cases of NMSC and melanoma are associated with exposure to UV radiation. Exposure to UV radiation leads to carcinogenesis by a dual mechanism: it causes DNA damage that subsequently results in the formation of mutations and impairs the ability of the host immune system to recognize and eliminate malignant cells. Basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) are the most common presentations of NMSC, and both are derived from mutated epidermal keratinocytes. Cumulative lifetime exposure to UV radiation is closely associated with the risk of developing BCC and SCC. Melanoma is the most lethal of the skin cancers and arises from mutated melanocytes. The risk of showing melanoma is directly associated with sun

exposure in adolescence, intrinsically with the number of sunburns between the ages of 15 and 20. Some other risk factors related to the formation of cutaneous neoplasms are the presence of melanocytic nevi, family history, use of sunbeds, human papillomavirus (HPV), exposure to chemicals, Fitzpatrick skin type, and immunosuppressed state(3-5).

### Epidemiology

There is a high worldwide prevalence of skin cancers, in some countries even more common than all other cancers combined. These cancers are increasing and are a notable health problem from the point of view of the well-being of the affected individual, as well as when comparing health costs. Skin cancer is found in all races of the world. However, the risk is substantially higher in those with fair skin because of the photoprotective effects of epidermal melanin. In fair-skinned individuals, about 75% to 80% of nonmelanoma skin cancers are basal cell carcinomas and about 25% are squamous cell carcinomas. Inherited defects in DNA repair mechanisms, such as those evidenced in xeroderma pigmentosum and Muir-Torre syndrome, also place compromised individuals at increased risk for cutaneous carcinomas(6,7).

### Pathophysiology

Sun exposure is the most notable modifiable risk factor associated with NMSC and melanoma formation. UV radiation can be classified into UV-A, UV-B and UV-C radiation. Sunlight is composed primarily of the elements UV-A at approximately 90% and UV-B at approximately 10%, whereas UV-C rays are usually absorbed by the atmosphere. UV-A rays have a longer wavelength (320-400 nm) and penetrate the dermis, generating free radicals. UV-B rays have a shorter wavelength (290-320 nm), penetrate down to the stratum basale of the epidermis and stimulate the creation of thymine dimers. UV-A and UV-B rays enable the formation of carcinogenesis. Therefore, UV radiation generates cell damage and apoptosis, as well as modifying DNA repair processes, causing DNA mutations(4,7).

The creation of subsequent cutaneous malignant neoplasms from DNA damage by solar radiation is multifactorial, encompassing genetic factors, Fitzpatrick skin type and immunosuppressed status. Approximately 90% of cutaneous squamous cell carcinomas have UV-induced P53 gene mutations leading to uninhibited keratinocyte proliferation. DNA mutations implicated in melanoma are mutations in melanocortin receptor 1 (MCR1), cyclin-dependent kinase inhibitor 2A (CDKN2A), B-Raf and DNA repair enzymes. DNA mutations implicated in basal cell carcinoma are mutations in the p53 gene and the PTCH gene(3,8,9).



### Assessment

A meticulous examination of the skin determines premalignant and malignant skin lesions. It is imperative in ectoscopy to ascertain the location, texture, size, color, shape, borders, as well as any recent alterations of suspicious lesions. Premalignant actinic keratoses usually appear as rough, gritty skin papules on an erythematous base. Basal cell carcinomas usually show as pearly pink papules with telangiectasias. Squamous cell carcinomas are usually pink papules, patches and rough plaques. Melanomas are lesions that usually appear brown to black with asymmetry, irregular borders, diameters greater than 6 mm and color variegation. Any new or changing lesion or lesion that appears different from other nevi on the body is considered highly suspicious, sometimes referred to as the ugly duckling sign.

Basal cell and squamous cell carcinomas are usually seen in areas with the greatest amount of accumulated ultraviolet radiation, such as the nose, ears and upper lip. Melanomas can show up in any region of the body and are usually found on the back and shoulders in men and on the lower limbs in women. Assessment of individuals at risk for cutaneous carcinoma involves a full body skin examination. Suspicious lesions on physical examination will undergo a skin biopsy, under local anesthesia, then the sample is sent for interpretation, if the diagnosis of cutaneous malignancy is confirmed, further intervention is warranted according to the clinical and pathological diagnosis(10,11).

### Treatment

Treatment of precancerous lesions and cutaneous carcinoma should be tailored to the particular individual in order to achieve the best results. In addition to isolated lesions, precancerous actinic keratoses can be managed with lesion-targeted therapies such as cryotherapy. When multiple lesions and diffuse actinic damage are present, topical agents such as 5-fluorouracil, ingenol mebutate and imiquimod can be used, as well as photodynamic therapy following skin sensitization with a topical agent. Initial preventive efforts should be made to reduce the individual's risk of developing cutaneous carcinoma, such as optimizing the immunosuppressive regimen in individuals with solid organ transplantation, as well as proper surveillance programs(3,12).

Basal cell carcinomas and squamous cell carcinomas, if superficial, can be treated with topical therapies. However, standard practice is to treat surgically. Individuals with aggressive and recurrent forms of basal cell carcinoma who are not candidates for surgery are treated with radiation therapy or systemic medications(13,14).

Squamous cell carcinoma of the skin, also called cutaneous squamous cell carcinoma, has a precursor lesion, actinic keratosis, which shows tumor progression. Squamous cell carcinoma of the skin has the potential to metastasize, unusually. The most important risk factor for the development of actinic keratoses and squamous cell carcinoma of the skin is solar ultraviolet radiation. Surgical excision is the primary treatment for cutaneous squamous cell carcinoma; Mohs micrographic surgery is the most commonly used therapeutic

technique for lesions of the head, neck and those with high-risk features. Radiotherapy is used in cutaneous squamous cell carcinoma in individuals of considerable age, unfit for surgery or when clean surgical margins cannot be obtained. Immunosuppression significantly increases the risk of forming cutaneous squamous cell carcinoma throughout life; the risk of metastasis increases in immunosuppressed individuals. Those with cutaneous squamous cell carcinoma should be examined regularly and use UV protective measures(15-17).

Melanoma is the most aggressive and lethal form of cancer, and the management of choice is surgical excision; when detected early, it can be curative. Tumors in more advanced stages have an unfavorable prognosis and usually require adjuvant chemotherapy or immunotherapy(18).

Melanoma is a skin cancer of the melanocytes that arise following a DNA mutation, usually secondary to excessive sun exposure. Individuals with fair skin and hair who live in environments with greater sun exposure are at higher risk. Characteristically, melanoma shows irregularities in shape, irregular color and asymmetry. Occasionally, melanoma shows ulceration and bleeding, which is often linked to a worse prognosis. A needle biopsy usually reveals atypical nests of melanocytes that conglomerate and blend at the dermal-epidermal junction. The depth of the melanoma is essential for prognosis. There are 2 types of staging to assess depth: the Breslow and Clark levels. In the past, the Clark level was used. However, the Breslow level is currently more commonly used because of its greater specificity. According to the depth of the lesion, the 10-year survival rate is modified, also, the depth of a melanoma lesion decreases the margins to resect the lesion(19-21).

### Differential Diagnosis

- Metastatic skin tumors.
- Epithelioid tumor.
- Psoriasis.
- Cherry angioma.
- Benign melanocytic lesions.
- Dysplastic nevus.
- Seborrheic keratoses.
- Sebaceous hyperplasia.
- Nevus.

### Skin Cancer in Children

The incidence of melanoma in pediatric individuals has decreased in recent years. Childhood and adolescent melanoma is not common and accounts for only 1.3% of all cancer cases in individuals under 20 years of age. However, between 15 and 19 years of age, melanoma accounts for approximately 7% of all cancers. Evidence shows that predisposing "pediatric" conditions, such as giant congenital melanocytic nevi or xeroderma pigmentosum, are infrequently reported. Germline inactivating mutations of the CDKN2A gene have been reported in only about 1.5% of cases of early onset melanoma. There is literature suggesting that interactions between sun exposure, nevus development, pigmentary features, and family history of melanoma are the primary determinants of melanoma development in the early 20s. When attempting to make a



diagnosis in pediatrics, specific criteria should be used in order to analyze the peculiarities and different presentations observed in pediatric disease compared to adults, such as a higher prevalence of amelanotic melanoma or a common similarity of benign pediatric lesions. Pediatric melanoma usually shows higher histopathologic stage and higher Breslow depth versus adult melanoma. Pediatric non-melanoma skin cancer, such as basal cell carcinoma and squamous cell carcinoma, is related to genetic conditions and immunosuppression, both iatrogenic and hereditary(22,23).

## CONCLUSIONS

There is a high prevalence of skin cancers throughout the world, sometimes going unnoticed and causing important consequences. The diagnosis and treatment of these neoplasms is a significant health problem, which can sometimes be prevented. The places most affected are those with the greatest exposure to the sun, so adequate sun protection is crucial to prevent skin cancer. In addition to knowing the pathology, its types and characteristics, it is important to perform a proper skin examination for the correct diagnosis, control and management. Currently there are multiple treatment alternatives such as surgical excision, cryotherapy, chemotherapy, immunotherapy and radiation, which show positive aspects against this pathology.

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