

Squamous Cell Carcinoma

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It is estimated that there are between 900,000 and 1,200,000 new skin cancers each year in the United States. 80% of these cases are Basal Cell Carcinomas & 20% are Squamous Cell Carcinomas, which is roughly about 250,000 new cases each year in the US only.

Squamous cell carcinoma is the second most common type of skin cancer. It arises from plate-like cell layer in the epidermis and is due to extensive sun exposure. Squamous cell carcinoma can metastasize if is not treated.

Etiology

Squamous cell carcinoma is typically found on areas often exposed to the sun, such as the scalp, face and neck, however, it can develop on other parts of the body including the mucous membrane and the genitalia.

Although researchers know what causes many cases of squamous cell carcinoma – most notably, excessive exposure to ultraviolet radiation – studies are still underway to determine how this type of cancer develops in parts of the body that are seldom or never exposed to sunlight. Past studies show that nearly 95 percent of all non-melanoma skin cancers are the direct result of DNA changes that occur in the skin after cells are damaged by UVA or UVB rays, and scientists continue to investigate the possible causes of the remaining 5 percent.

Through ongoing studies, researchers are also investigating the exact changes that occur within the body after squamous cells are damaged by UV exposure. Currently, with regard to what causes squamous cell carcinoma, medical professionals know that:

- Healthy skin regenerates itself every few days. As old cells die, they are pushed to the surface of the skin by the new cells developing underneath. The old cells are then sloughed off.
- When squamous cells sustain DNA damage, the cells aren't able to regulate their own growth as they normally should. Abnormal cells can accumulate without dying off and create bumps or sores on the skin.

Risk factors

Many risk factors associated with squamous cell carcinoma have a direct link to UV exposure. For instance:

1. Tobacco

- Patients with smoking habits are at a much higher risk of developing SCCs.

2. UV Exposure

- Extended exposure to UV radiations may introduce mutations in the DNA of the squamous cell layer promoting SCC.
- Males are nearly three times more likely to develop squamous cell carcinoma than females, which may be partially attributed to their comparatively higher tendency to spend time outdoors without adequate sun protection.
- Use of tanning beds. People who use indoor tanning beds have an increased risk of squamous cell carcinoma of the skin.

3. History of precancerous lesions, sunburns or SCC

- A personal history of precancerous skin lesions. Having a precancerous skin lesion, such as **actinic keratosis** or **Bowen's disease**, increases your risk of squamous cell carcinoma of the skin.

- A history of sunburns. Having had one or more blistering sunburns as a child or teenager increases your risk of developing squamous cell carcinoma of the skin as an adult. Sunburns in adulthood also are a risk factor.
- A personal history of skin cancer. If you've had squamous cell carcinoma of the skin once, you're much more likely to develop it again.

4. Racial susceptibility

- Fair skin. Anyone, regardless of skin color, can get squamous cell carcinoma of the skin. However, having less pigment (melanin) in your skin provides less protection from damaging UV radiation.
- If you have blond or red hair and light-colored eyes and you freckle or sunburn easily, you're much more likely to develop skin cancer than is a person with darker skin.

5. Age

- Older adults are more frequently diagnosed with squamous cell carcinoma than younger individuals, presumably due to the cumulative effects of UV exposure over a person's lifetime.
- People with an inherited condition known as xeroderma pigmentosum have an extreme sensitivity to sunlight and are also very susceptible to cellular damage caused by UVA and UVB rays.

6. Genetically Susceptible and Infected individuals

- People with psoriasis and other inflammatory skin diseases often receive ultraviolet light-based treatments, which can increase their risk of developing skin cancer in the future.
- Rare genetic disorder. People with xeroderma pigmentosum, which causes an extreme sensitivity to sunlight, have a greatly increased risk of developing skin cancer.
- Weakened immune system. People with weakened immune systems have an increased risk of skin cancer. This includes people who have leukemia or lymphoma and those who take medications that suppress the immune system, such as those who have undergone organ transplants.

Additional risk factors include exposure to large amounts of arsenic, coal tar or other carcinogenic chemicals; chronic ulcers and a history of radiation therapy for previous cancers. Also, a person who has already been diagnosed with skin cancer has an elevated risk of developing a second skin cancer during his or her lifetime.

Epidemiology

- It commonly affects men > 60 years
- Incidence: More than one million cases each year in the U.S alone.
- About 15,000 people die each year as a result of nonmelanoma skin cancer, mostly metastatic SCC.
- It has been estimated that a Caucasian male born in 1994 has a 9% to 14% chance of developing an SCC within his lifetime. The estimates for white women range from 4% to 9%.
- Fair-skinned phenotype, excessive cumulative overexposure to UV radiation, advancing age, outdoor vocation, or avocation, and sunbelt latitudes.
- The highest risk factors are the presence of Actinic Keratosis or a previous nonmelanoma skin cancer
- Immunosuppressed patients and patients receiving long-term photochemotherapy (PUVA) are especially predisposed to the development of SCCs.
- Countries or Cities near the equator are of higher frequency of developing SCCs.
- High-risk SCCs for metastases and death are those that grow rapidly, become larger than 2 cm, invade deeply and reach a thickness of at least 6 mm, have been treated previously, or are located in high-risk areas such as the vermilion lip, the ear, and the columella of the nose. Patients who are immunocompromised are more predisposed to the development of metastases.

Clinical Presentation

SCCs may occur on all areas of the body, including the mucous membranes and genitals, but are most common in areas frequently exposed to the sun, such as the rim of the ear, lower lip, face, balding scalp, neck, hands, arms and legs. The skin in these areas often reveals telltale signs of sun damage, including wrinkles, pigment changes, freckles, “age spots,” loss of elasticity and broken blood vessels.



Figure 1: Moderately Differentiated SCC

SCCs can often look like scaly patches, open sores, warts or elevated growths with a central depression; they may crust or bleed. They can become disfiguring and sometimes deadly if allowed to grow.

Signs and Symptoms

Skin cancers often do not cause bothersome symptoms until they have grown quite large. Then they may itch, bleed, or even hurt. But typically they can be seen long before they reach this point. Squamous cell carcinoma are usually easy to find early, during a thorough skin examination by a dermatologist. Regular examination of the skin for any new or unusual growths, or changes in the size, shape or color of an existing spot, is key to finding and treating these cancers early.

General warning signs of skin cancer include a new spot or growth that increases in size, or a sore that doesn't heal within two months. In addition, common signs of squamous cell carcinomas include:

- It can be a white-ish or reddish lesion.
- A growing lump with a rough scaly or crusty surface, Slow-growing flat reddish patch.
- Raised growths or lumps, sometimes with a lower area in the center.
- Wart-like growths

Diagnosis

Squamous cell carcinoma can be diagnosed by the following procedures:

1. Skin Examination
 - Examination of abnormal spots or bumps in the skin
2. Biopsy
 - **Shave biopsy:** A sterile razor blade is used to “shave off” the abnormal-looking growth
 - **Punch biopsy:** A special instrument called a punch or a trephine is used to remove a circle of tissue from the abnormal-looking growth
 - **Excisional biopsy:** A scalpel is used to remove the entire growth

Patient is also most probably going to have a history of:

- Smoking habit
- Exposure to UV either by sunlight or artificially
- Precancerous lesion

Types of squamous cell carcinoma:

- Verrucous squamous-cell carcinoma
- Clear Cell SCC
- Spindle cell squamous cell carcinoma
- Adenoid/pseudoglandular squamous cell carcinoma
- Intraepidermal squamous cell carcinoma
- Large cell keratinizing squamous cell carcinoma
- Large cell non-keratinizing squamous cell carcinoma
- Lymphoepithelial carcinoma
- Papillary squamous cell carcinoma
- Papillary thyroid carcinoma
- Small cell keratinizing squamous cell carcinoma
- Spindle cell SCC

Histopathology

- Squamous cell carcinoma is a malignant epithelial tumor which originates in epidermis.
- Tumor cells destroy the basement membrane and form sheets or compact masses which invade the subjacent connective tissue (dermis).
- Tumor cells show signs of epithelial dysplasia.
- Tumor cells may surround and destroy blood vessels, and may invade the lumina of vein or lymphatics.
- In well differentiated carcinomas, tumor cells are pleomorphic/atypical, but resembling normal keratinocytes from prickly layer (large, polygonal, with abundant eosinophilic (pink) cytoplasm and central nucleus). Their disposal tends to be similar to that of normal epidermis: immature/basal cells at the periphery, becoming more mature to the centre of the tumor masses. Tumor cells transform into keratinized squames and form round nodules with concentric, laminated layers, called “cell nests” or “epithelial/keratinous pearls”. The surrounding stroma is reduced and contains inflammatory infiltrate (lymphocytes).
- Poorly differentiated squamous carcinomas contain more pleomorphic cells and no keratinization. (H&E, ob. x10)

Staging and Grading

Complications

Untreated squamous cell carcinoma of the skin can destroy nearby healthy tissue, spread to the lymph nodes or other organs, and may be fatal, although this is uncommon. The risk of aggressive squamous cell carcinoma of the skin may be increased in cases where the cancer:

- Is particularly large or deep
- Involves the mucous membranes, such as the lips
- Occurs in a person with a weakened immune system, such as someone who takes anti-rejection medications after an organ transplant or someone who has chronic leukemia

Treatment of SCCs

References

- DOI: 10.1097/JDN.0b013e3181cb5165
- <https://www.skincancer.org/skin-cancer-information/skin-cancer-facts>