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SQUAMOUS CELL CARCINOMA (SCC)

Squamous cell carcinoma (SCC) is an uncontrolled growth of abnormal cells arising in the squamous cells, which compose most of the skin's upper layers (the epidermis). SCCs often look like scaly red patches, open sores, elevated growths with a central depression, or warts; they may crust or bleed. They can become disfiguring and sometimes deadly if allowed to grow. An estimated 700,000 cases of SCC are diagnosed each year in the US, and between 3,900 and 8,800 people died from the disease in the US in 2012. Incidence of the disease has increased up to 200 percent in the past three decades in the US.

SCC is mainly caused by cumulative ultraviolet (UV) exposure over the course of a lifetime; daily year-round exposure to the sun's UV light, intense exposure in the summer months, and the UV produced by tanning beds all add to the damage that can lead to SCC.

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. Often the skin in these areas reveals telltale signs of sun damage, including wrinkles, pigment changes, freckles, "age spots," loss of elasticity, and broken blood vessels.

WHO GETS SCC

People who have fair skin, light hair, and blue, green, or gray eyes are at highest risk of developing the disease. But anyone with a history of substantial sun exposure is at increased risk. Those whose occupations require long hours outdoors or who spend extensive leisure or recreation time in the sun (especially playing golf or other sports) are in particular jeopardy. Anyone who has had basal cell carcinoma is also more likely to develop SCC, as is anyone with an inherited, highly UV-sensitive condition such as xeroderma pigmentosum.

Squamous cell carcinomas are at least twice as frequent in men as in women, partly because of more time spent in the sun. Most SCCs appear in people over 50, but in recent years more and more young people in their 20s and 30'sare being diagnosed with the disease. The number of women under age 40 diagnosed with SCC has especially increased in the last 30 years, and many experts attribute this to their greater use of indoor tanning. More than 419,000 cases of skin cancer in the US each year are linked to indoor tanning, and over 70 percent of tanning salon patrons are females. The majority of skin cancers in African-Americans are squamous cell carcinomas, usually arising on the sites of preexisting inflammatory skin conditions or burn injuries. Though naturally dark-skinned people are less likely than fair-skinned people to get skin cancer, it is still essential for them to practice sun protection. All skin types are at risk of skin cancer. Cumulative exposure to sunlight causes most cases of squamous cell carcinoma. Frequent use of tanning beds also multiplies the risk of squamous cell carcinoma; people who use tanning beds are 2.5 times more likely to develop squamous

cell carcinoma than those who don't. But skin injuries are another important source. The cancer can arise in burns, scars, ulcers, long-standing sores, and sites previously exposed to X-rays or certain chemicals (such as arsenic and petroleum by-products).

Chronic infections and skin inflammation can also give rise to squamous cell carcinoma. Furthermore, HIV and other immune deficiency diseases, chemotherapy, anti-rejection drugs used in organ transplantation, and even excessive sun exposure itself all weaken the immune system, making it harder to fight off disease and thus increasing the risk of developing squamous cell carcinoma and other skin cancers. Studies have shown that organ transplant recipients are up to 250 times more likely than the general population to develop SCC.

Occasionally, squamous cell carcinomas arise spontaneously on what appears to be normal, healthy skin. Some researchers believe the tendency to develop these cancers can be inherited.

Precancerous conditions

Certain potentially precancerous growths, or precancers, most of them resulting from cumulative sun damage, can be associated with the later development of squamous cell carcinoma.

Actinic or Solar Keratosis

These rough, scaly, slightly raised growths, ranging in color from brown to red and from about 1 mm to 1 inch in diameter, are found on sun-exposed areas of the body, most often in older people. They can be the first step on the road to squamous cell carcinoma, and some experts even consider them the earliest form of SCC. From two to ten percent of untreated actinic keratoses (AKs) advance to squamous cell carcinoma, sometimes with two years, according to different studies. Indeed, 40 to 60 percent of squamous cell carcinomas begin as untreated actinic keratoses.The more AKs that go untreated and the older these lesions are, the greater the chance that one or more may develop into invasive SCC.

AKs are often palpable before becoming visible, and can be felt by running your fingers over sun-exposed areas; this can provide an early sign of their development.

Actinic Cheilitis

This form of actinic keratosis occurs most often on the lower lip, causing it to become dry, cracked, scaly and pale or white. Why the lower lip? Because it receives more sun exposure than the upper lip. If not treated promptly, actinic cheilitis can lead to squamous cell carcinoma on the lip. If your lips are frequently chapped or burning, you may have actinic cheilitis.

Leukoplakia

Arising in the mucous membranes, these white patches on the tongue, gums, cheeks, or elsewhere inside the mouth have the potential to develop into squamous cell carcinoma. They may be caused by sources of chronic irritation, such as habitual alcohol

consumption or tobacco use, or rough edges on teeth or dentures. They may even be caused by a long-time habit of biting the inside of the lip; however, leukoplakias on the lips are mainly caused by sun damage.

Bowen's disease

This is now generally considered an early, noninvasive stage of squamous cell carcinoma. It appears as a persistent red-brown, scaly patch that may resemble psoriasis or eczema. If untreated, it may invade deeper structures. Bowen's disease is most often caused by exposure to the sun or to arsenic, but radiation and other chemical carcinogens, genetics and trauma also may play a role. The human Papillomavirus (HPV), highly transmissible through sexual contact, has been documented as a cause of one form of Bowen's disease affecting the genitals. HPV can also arise in the mucous membranes of the nose and mouth as well as on the skin. The FDA approved an HPV vaccine for use by females aged 9–26 in 2006, and one for 9-26-year-old males (as well as another vaccine for females) in 2009. The vaccines areconsidered highly effective in preventing HPV and thereby reducing the risk of both genital warts and cervical cancer as well as Bowen's disease.

TREATMENT

Squamous cell carcinomas detected at an early stage and removed promptly are almost always curable and cause minimal damage. However, left untreated, they eventually penetrate the underlying tissues and can become disfiguring. A small percentage even metastasize to local lymph nodes, distant tissues, and organs and can become fatal. Therefore, any suspicious growth should be seen by a physician without delay. A tissue sample (biopsy) will be examined under a microscope to arrive at a diagnosis. If tumor cells are present, treatment is required.

Fortunately, there are several effective ways to eradicate squamous cell carcinoma. The choice of treatment is based on the tumor's type, size, location, and depth of penetration, as well as the patient's age and general health.

Treatment can almost always be performed on an outpatient basis in the ambulatory care at the TBRHSC. A local anesthetic is used during most surgical procedures. Pain or discomfort is usually minimal, and there is rarely much pain afterwards.

Mohs Surgery

Using a scalpel or curette (a sharp, ring-shaped instrument), a physician trained in Mohs surgery removes the visible tumor with a very thin layer of tissue around it. While the patient waits, this layer is sectioned, frozen, stained and mapped in detail, then checked under a microscope thoroughly. If cancer is still present in the depths or peripheries of this excised surrounding tissue, the procedure is repeated on the corresponding area of the body still containing tumor cells until the last layer viewed under the microscope is cancer-free. Mohs surgery spares the greatest amount of healthy tissue, reduces the rate of local recurrence, and has the highest overall cure rate — about 94-99 percent — of any treatment for SCC. It is often used on tumors that have recurred, are poorly

demarcated, or are in hard-to-treat, critical areas around the eyes, nose, lips, ears, neck, hands and feet. After tumor removal,, the wound may be allowed to heal naturally or may be reconstructed immediately; the cosmetic outcome is usually excellent.

SURGICAL EXCISION

The physician uses a scalpel to remove the entire growth, along with a surrounding border of apparently normal skin as a safety margin. The wound around the surgical site is then closed with sutures (stitches). The excised tissue specimen is then sent to the laboratory for microscopic examination to verify that all cancerous cells have been removed. A repeat excision may be necessary on a subsequent occasion if evidence of skin cancer is found in the specimen. The accepted cure rate for primary tumors with this technique is about 92 percent. This rate drops to 77 percent for recurrent squamous cell carcinoma.

CURRETTAGE

This technique is usually reserved for small lesions. The growth is scraped off with a curette (an instrument with a sharp, ring-shaped tip), and burning heat produced by an electrocautery needle destroys residual tumor and controls bleeding. This procedure is typically repeated a few times, a deeper layer of tissue being scraped and burned each time to help ensure that no tumor cells remain. It can produce cure rates approaching those of surgical excision for superficially invasive squamous cell carcinomas without high-risk characteristics. However, it is not recommended for any invasive or aggressive SCCs, those in high-risk or difficult sites, such as the eyelids, genitalia, lips and ears, or other sites that would be left with cosmetically undesirable results, since the procedure leaves a sizable, hypopigmented scar.

CRYOTHERAPY

The physician destroys the tumor tissue by freezing it with liquid nitrogen, using a cotton-tipped applicator or spray device. There is no cutting or bleeding, and no anesthesia is required. The procedure may be repeated several times at the same session to help ensure destruction of all malignant cells. The growth becomes crusted and scabbed, and usually falls off within weeks. Redness, swelling, blistering and crusting can occur following treatment, and in dark-skinned patients, some pigment may be lost. Inexpensive and easy to administer, cryosurgery may be the treatment of choice for patients with bleeding disorders or intolerance to anesthesia. However, it has a lower overall cure rate than the surgical methods. Depending on the physician's expertise, the 5-year cure rate can be quite high with selected, generally superficial squamous cell carcinoma; but cryosurgery is not often used today for invasive SCC because deeper portions of the tumor may be missed and because scar tissue at the cryotherapy site might obscure a recurrence.

RADIOTHERAPY

X-ray beams are directed at the tumor, with no need for cutting or anesthesia.

Destruction of the tumor usually requires a series of treatments, administered several times a week for one to four weeks, or sometimes daily for one month. Cure rates range widely, from about 85 to 95 percent, since the technique does not provide precise control in identifying and removing residual cancer cells at the margins of the tumor. The technique can involve long-term cosmetic problems and radiation risks, as well as multiple visits. For these reasons, though this therapy limits damage to adjacent tissue, it is mainly used for tumors that are hard to treat surgically, as well as patients for whom surgery is not advised, such as the elderly or those in poor health.

PHOTODYNAMIC THERAPY

PDT can be especially useful for growths on the face and scalp. A chemical agent that reacts to light, such as topical 5-aminolevulinic acid (5-ALA) or methyl aminolevulinate (MAL), is applied to the growths at the physician's office; it is taken up by the abnormal cells. Hours later, those medicated areas are activated by a strong light. The treatment selectively destroys squamous cell carcinomas while causing minimal damage to surrounding normal tissue. However, the treatment is not yet FDA-approved for squamous cell carcinoma, and while it may be effective with early, noninvasive tumors (e.g., Bowen’s disease), overall recurrence rates vary considerably (from 0 to 52 percent), so the technique is not currently recommended for invasive SCC. Redness and swelling are common side effects. After treatment, patients become locally photosensitive for 48 hours where the light-sensitizing agent was applied, and must avoid both outdoor and indoor light and be careful to use sun protection.

LASER THERAPY

This therapy is not yet FDA-approved for SCC, though it can be used for superficial lesions, with recurrence rates similar to those of PDT. The skin's outer layer and variable amounts of deeper skin are removed using a carbon dioxide or erbium YAG laser. This method is bloodless, and gives the physician good control over the depth of tissue removed. It actually seals blood vessels as it cuts, making it useful for patients with bleeding disorders, and it is also sometimes used when other treatments have failed. But the risks of scarring and pigment loss are slightly greater than with other techniques.

TOPICAL CREAMS

5-fluorouracil (5-FU) and imiquimod, both FDA-approved for treatment of actinic keratoses and superficial basal cell carcinomas, are also being tested for the treatment of some superficial squamous cell carcinomas. Successful treatment of Bowen's disease, a noninvasive SCC, has been reported. However, invasive SCC should not be treated with 5-FU. Some trials have shown that imiquimod may be effective with certain invasive SCCs, but it is not yet FDA-approved for this purpose. Imiquimod stimulates the immune system to produce interferon, a chemical that attacks cancerous and precancerous cells, while 5-FU is a topical form of chemotherapy that has a direct toxic effect on cancerous cells.

Because most treatment options involve cutting, some scarring from the tumor removal should be expected. This is most often cosmetically acceptable with small cancers, but

removal of a larger tumor often requires reconstructive surgery, involving a skin graft or flap to cover the defect. Mohs surgeons are trained in reconstructive surgery, so visit to a plastic surgeon is usually unnecessary.

Squamous cell carcinomas usually remain confined to the epidermis (the top skin layer) for some time. However, the larger these tumors grow, the more extensive the treatment needed. They eventually penetrate the underlying tissues, which can lead to major disfigurement, sometimes even the loss of a nose, eye or ear. A small percentage spread (metastasize) to distant tissues and organs. When this happens, squamous cell carcinomas frequently can be life-threatening.

Metastases most often arise on sites of chronic inflammatory skin conditions and on the ear, nose, lip, and mucosal regions, including the mouth, nostrils, genitals, anus, and the lining of the internal organs.

Recurrence, Prevention and Detection

Anyone who has had one squamous cell tumor has an increased chance of developing another, especially in the same skin area or nearby. That is usually because the skin has already suffered irreversible sun damage. Such recurrences typically occur within the first two years after surgery. A squamous cell carcinoma can recur even when it has been carefully removed the first time.

Thus, it is crucial to pay particular attention to any previously treated site, and any changes noted should be shown immediately to a physician. SCCs on the nose, ears, and lips are especially prone to recurrence. Even if no suspicious signs are noticed, regularly scheduled follow-up visits *including total-body skin exams* are an essential part of post-treatment care. Should the cancer return, the physician may recommend a different type of treatment the next time. Certain methods, such as Mohs micrographic surgery, can be highly effective for preventing and treating recurrences.

While squamous cell carcinomas and other skin cancers are almost always curable when detected and treated early, it is best to prevent them in the first place. Make these sun safety habits part of your daily health care routine:

- **Seek the shade**, especially between 10 AM and 4 PM.
- **Do not burn.**
- **Avoid tanning and never use UV tanning beds.**
- **Cover up** with clothing, including a broad-brimmed hat and UV-blocking sunglasses.
- **Use a broad spectrum (UVA/UVB) sunscreen** with an SPF of 15 or higher every day. For extended outdoor activity, use a water-resistant, broad spectrum (UVA/UVB)sunscreen with an SPF of 30 or higher.
- **Apply 1 ounce** (2 tablespoons) of sunscreen to your entire body 30 minutes before going outside. Reapply every two hours or immediately after swimming or excessive sweating.
- **Keep newborns out of the sun.** Sunscreens should be used on babies over the

age of six months.

- **Examine your skin** head-to-toe every month.
- **See your physician every year** for a professional skin exam.