Cutaneous squamous cell carcinoma


What is cutaneous squamous cell carcinoma?

Cutaneous squamous cell carcinoma (SCC) is a common type of keratinocytic or non-melanoma skin cancer. It is derived from cells within the epidermis that make keratin — the horny protein that makes up skin, hair and nails.

Cutaneous SCC is an invasive disease, referring to cancer cells that have grown beyond the epidermis. SCC can sometimes metastasise (spread to distant tissues) and may prove fatal.

Intraepidermal carcinoma (cutaneous SCC in situ) and mucosal SCC are considered elsewhere.

Who gets cutaneous squamous cell carcinoma?

Risk factors for cutaneous SCC include:

- Age and gender: SCCs are particularly prevalent in elderly males. However, they also affect females and younger adults.
- Previous SCC or other form of skin cancer (basal cell carcinoma, melanoma) are a strong predictor for further skin cancers.
- Actinic keratoses
- Outdoor occupation or recreation
- Smoking
- Fair skin, blue eyes and blond or red hair
- Previous cutaneous injury, thermal burn, disease (eg cutaneous lupus, epidermolysis bullosa, leg ulcer)
- Inherited syndromes: SCC is a particular problem for families with xeroderma pigmentosum and albinism
- Other risk factors include ionising radiation, exposure to arsenic, and immune suppression due to disease (eg chronic lymphocytic leukaemia) or medicines. Organ transplant recipients have a massively increased risk of developing SCC.

What causes cutaneous squamous cell carcinoma?

More than 90% of cases of SCC are associated with numerous DNA mutations in multiple somatic genes. Mutations in the p53 tumour suppression gene are caused by exposure to ultraviolet radiation (UV), especially UVB (known as signature 7). Other signature mutations relate to cigarette smoking, ageing and immune suppression (eg, to drugs such as azathioprine). Mutations in signalling pathways affect epidermal growth factor receptor, RAS, Fyn, and p16INK4a signaling.

Beta-genus human papillomaviruses (wart virus) are thought to play a role in SCC arising in immune suppressed populations. β-HPV and HPV subtypes 5, 8, 17, 20, 24, and 38 have also been associated with an increased risk of cutaneous SCC in immunocompetent individuals.

What are the clinical features of cutaneous squamous cell carcinoma?

Cutaneous SCCs present as enlarging scaly or crusted lumps. They usually arise within pre-existing actinic keratosis or intraepidermal carcinoma.

- They grow over weeks to months
- They may ulcerate
- They are often tender or painful
• Located on sun-exposed sites, particularly the face, lips, ears, hands, forearms and lower legs
• Size varies from a few millimetres to several centimetres in diameter.

**Squamous cell carcinoma**

More images of squamous cell carcinoma ...

• SCC on the face
• SCC on the lip
• SCC on the ear
• SCC on the limbs

**Types of cutaneous squamous cell carcinoma**

Distinct clinical types of invasive cutaneous SCC include:

• Cutaneous horn – the horn is due to excessive production of keratin
• Keratoacanthoma (KA) – a rapidly growing keratinising nodule that may resolve without treatment
• Carcinoma cuniculatum (‘verrucous carcinoma’), a slow-growing, warty tumour on the sole of the foot.
• Multiple eruptive SCC/KA-like lesions arising in syndromes, such as multiple self-healing squamous epitheliomas of Ferguson-Smith and Grzybowski syndrome

The pathologist may classify the tumour as well differentiated, moderately well differentiated, poorly differentiated or anaplastic cutaneous SCC. There are other variants.

**Subtypes of cutaneous squamous cell carcinoma**
Classification of squamous cell carcinoma by risk

Cutaneous SCC is classified as low-risk or high-risk, depending on the chance of tumour recurrence and metastasis. Characteristics of high-risk SCC include:

High-risk cutaneous squamous cell carcinoma has the following characteristics:

- Diameter greater than or equal to 2 cm
- Location on the ear, vermilion of lip, central face, hands, feet, genitalia
- Arising in elderly or immune suppressed patient
- Histological thickness greater than 2 mm, poorly differentiated histology, or with invasion of the subcutaneous tissue, nerves and blood vessels

Metastatic SCC is found in regional lymph nodes (80%), lungs, liver, brain, bones and skin.

High-risk cutaneous squamous cell carcinoma
**Staging SCC**

In 2011, the American Joint Committee on Cancer (AJCC) published a new staging systemic for cutaneous SCC for the 7th Edition of the AJCC manual. This evaluates the dimensions of the original primary tumour (T) and its metastases to lymph nodes (N).

<table>
<thead>
<tr>
<th>Tumour staging for cutaneous SCC</th>
<th></th>
</tr>
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<tbody>
<tr>
<td>TX</td>
<td>Primary tumour cannot be assessed</td>
</tr>
<tr>
<td>T0</td>
<td>No evidence of primary tumour</td>
</tr>
<tr>
<td>Tis</td>
<td>Carcinoma in situ</td>
</tr>
<tr>
<td>T1</td>
<td>Tumour ≤2cm without high-risk features</td>
</tr>
</tbody>
</table>
| T2 | Tumour ≥2cm  
   Tumour ≤2 cm with high-risk features |
| T3 | Tumour with invasion of maxilla, mandible, orbit or temporal bone |
| T4 | Tumour with invasion of axial or appendicular skeleton or perineural invasion of skull base |

<table>
<thead>
<tr>
<th>Nodal staging for cutaneous SCC</th>
<th></th>
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<tbody>
<tr>
<td>NX</td>
<td>Regional lymph nodes cannot be assessed</td>
</tr>
<tr>
<td>N0</td>
<td>No regional lymph node metastasis</td>
</tr>
<tr>
<td>N1</td>
<td>Metastasis in one local lymph node ≤3cm</td>
</tr>
</tbody>
</table>
| N2 | Metastasis in one local lymph node ≥3cm  
   Metastasis in >1 local lymph node ≤6cm |
| N3 | Metastasis in lymph node ≥6cm |

**How is squamous cell carcinoma diagnosed?**

Diagnosis of cutaneous SCC is based on clinical features. The diagnosis and histological subtype is confirmed pathologically by diagnostic biopsy or following excision.

Patients with high-risk SCC may also undergo staging investigations to determine whether it has spread to lymph nodes or elsewhere. These may include:

- Imaging using ultrasound scan, X-rays, CT scans, MRI scans
Lymph node or other tissue biopsy

**What is the treatment for cutaneous squamous cell carcinoma?**
Cutaneous SCC is nearly always treated surgically. Most cases are excised with a 3–10 mm margin of normal tissue around the visible tumour. A flap or skin graft may be needed to repair the defect.

Other methods of removal include:

- Shave, curettage, and electrocautery for low-risk tumours on trunk and limbs
- Aggressive cryotherapy for very small, thin, low-risk tumours
- Mohs micrographic surgery for large facial lesions with indistinct margins or recurrent tumours
- Radiotherapy for inoperable tumour, patients unsuitable for surgery, or as adjuvant

**What is the treatment for advanced or metastatic squamous cell carcinoma?**
Locally advanced primary, recurrent or metastatic SCC requires multidisciplinary consultation. Often a combination of treatments is used.

- Surgery
- Radiotherapy
- Experimental targeted therapy using epidermal growth factor receptor inhibitors

Many thousands of New Zealanders are treated for cutaneous SCC each year, and more than 100 die from their disease.

**How can cutaneous squamous cell carcinoma be prevented?**
There is a great deal of evidence to show that very careful sun protection at any time of life reduces the number of SCCs. This is particularly important in ageing, sun-damaged, fair skin; in patients that are immunosuppressed; and in those who already have actinic keratoses or previous SCC.

- Stay indoors or under the shade in the middle of the day
- Wear covering clothing
- Apply high protection factor SPF50+ broad-spectrum sunscreens generously to exposed skin if outdoors
- Avoid indoor tanning (sun beds, solaria)

Oral nicotinamide (vitamin B3) in a dose of 500 mg twice daily may reduce the number and severity of SCCs in people at high risk.

Patients with multiple squamous cell carcinomas may be prescribed an oral retinoid (acitretin or isotretinoin). These reduce the number of tumours but have some nuisance side effects.

**What is the outlook for cutaneous squamous cell carcinoma?**
Most SCCs are cured by treatment. Cure is most likely if treatment is undertaken when the lesion is small. The risk of recurrence or disease-associated death is greater for tumours that are > 20 mm in diameter and/or > 2 mm in thickness at the time of surgical excision.

About 50% of people at high risk of SCC develop a second one within 5 years of the first. They are also at increased risk of other skin cancers, especially melanoma. Regular self-skin examinations and long-term annual skin checks by an experienced health professional are recommended.

**We recommend**

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**From around the web**

Enteral nutrition in dementia: a systematic review.
References

- Multi-professional guidelines for the management of the patient with primary cutaneous squamous cell carcinoma 2009 update of original guideline

On DermNet NZ

- Squamous cell carcinoma – pathology
- Intraepidermal SCC (Bowen disease)
- Vulval intraepithelial neoplasia
- Penile intraepithelial neoplasia
- Bowenoid papulosis
- Vulval cancer
- Oral cancer
- Squamous cell carcinoma – common skin lesions course
- Melanoma in skin of colour

Other websites

- Head and Neck Squamous Cell Carcinoma – Medscape Reference
- Squamous Cell Carcinoma – British Association of Dermatologists
- Optimal care pathway for people with basal cell carcinoma or squamous cell carcinoma – Cancer Council of Australia, June
2016
  ● Squamous cell carcinoma - American Academy of Dermatology

Books about skin diseases
See the DermNet NZ bookstore.

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