Management of non-melanoma skin cancers: BSC, SCC

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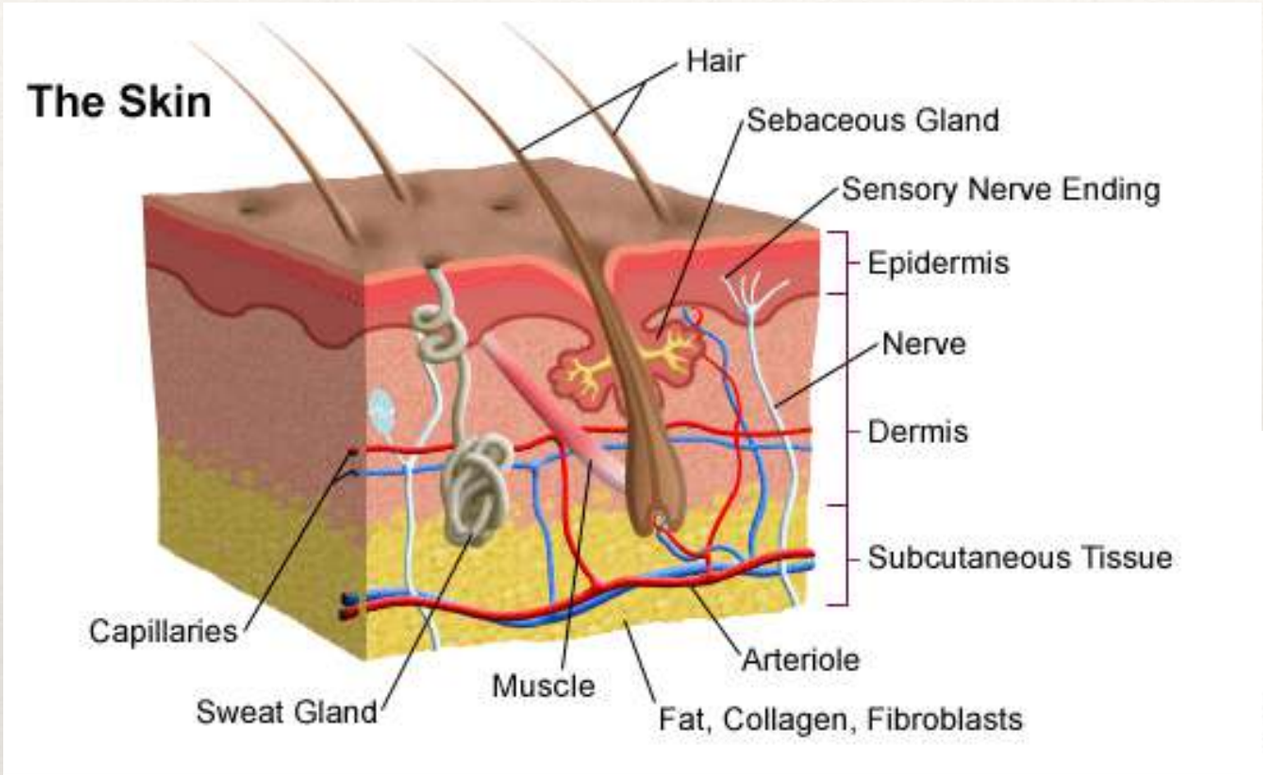
Outline

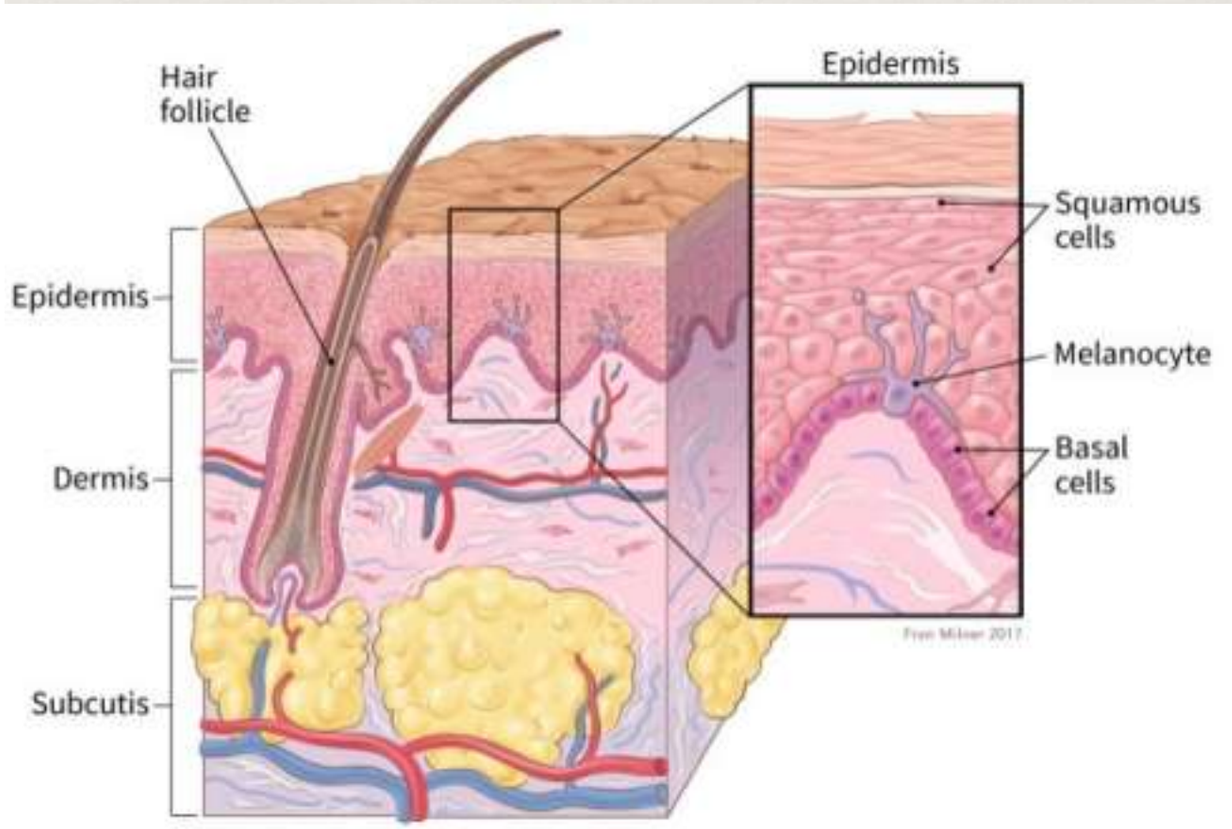
- Introduction
- Anatomy of the skin
- Epidemiology
- Risk factors
- Pathogenesis
- Clinical presentation
- Diagnosis
- Treatment
- Prognosis
- Prevention

Introduction

- Non- melanoma skin cancers (NMSCs) or keratinocyte carcinomas, are BCC and SCC
- More prevalent than all other cancers combined.
- BCC is the most common cancer in humans
- SCC is the second most common skin cancer
- Sunlight exposure plays a major impact in the development of these cancers
- Low mortality rate, but may lead to disabilities and high cost for treatment

Anatomy of the skin





Epidemiology

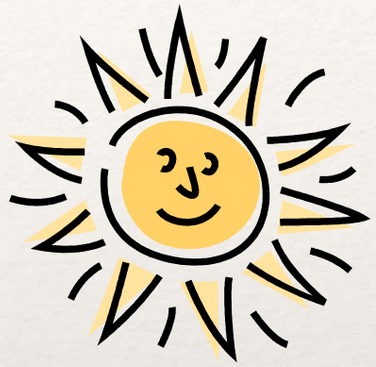
- Incidence of 1,000/100,000 people/year in Australia
- The incidence is less than 1/100,000 people/year in Japan
- Europe (129.3 in men, and 90.8 in women per 100,000 person-years
- In US: 450 per 100.000 person-years
- In Africa: lowest rates in parts of Africa (<1/100000 person−years for BCC)
- The incidence of NMSC is 18-20 times that of melanoma
- Mortality rate is 1-2%
- The ratio of BCC:SCC is generally in the order of 4:1

RISK FACTORS

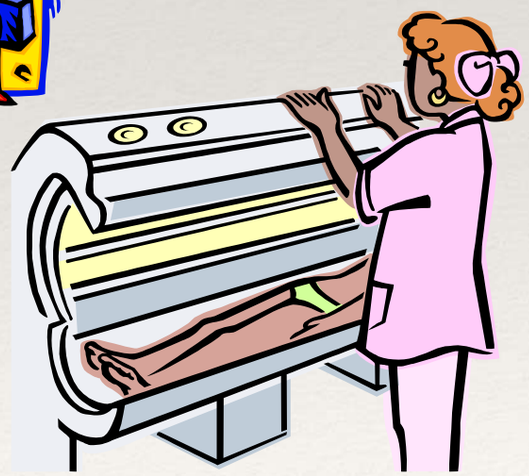
- **INHERITED (uncontrollable):**
  - Genetic: albinism, xeroderma pigmentosum
  - >50 “normal” moles
  - ANY atypical moles
  - Low pigmented skin, light complexion, blond or red hair, blue or green eyes, freckles
  - Family or personal history of skin cancer

RISK FACTORS

- **BEHAVIORAL/ ENVIRONMENTAL**



  - **UVR exposure**
  - Any blistering sunburns under age 20
  - Sporadic exposure of normally covered skin
  - Regular use of tanning beds
  - Frequent sunning
  - Scars from chronic ulcers and burns
  - Chronic ulcers
  - Immunosuppression
  - Exposure to radiotherapy
  - Smoking



Pathogenesis

- UVR exposure leads to cellular damage and DNA alteration
- Indirect DNA damage by production of free radicals and UV-induced immunosuppression
- Keratinocyte apoptosis led by the p53/p21/bax/bcl-2 pathway followed by a hyperproliferative phase, leading to epidermal hyperplasia
- Clones of mutated cells within the epidermis give rise to a focal area of loss of normal architecture and cellular atypia resulting in a focal disorder of keratinisation that is clinically perceived as an ‘actinic keratosis’ later forming SCC.
- The cell of origin from which BCC arises are immature, pluripotent cells associated with the hair follicle. Of note, the gene most often altered in BCCs is the *PTCH1* gene followed by p53

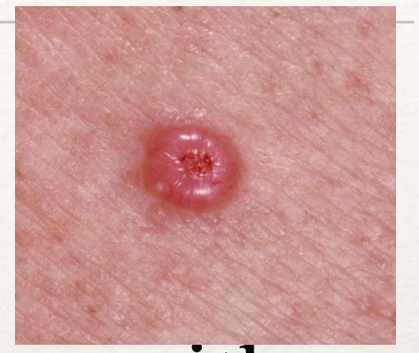
Basal cell carcinoma

- Locally invasive malignancy, arising from epidermal basal cells
- Most common type
- Appears in light skinned adults, above 40 yrs
- male>female
- Incidence proportional to sun exposure and age, and inversely proportional to the amount of melanin
- Slow growing, rarely metastasize

BCC types

- Nodular BCC
- Superfical
- Ulcerative
- Pigmented
- Basisquamous
- Turban- cylinderinoma

Clinical presentation



- Appears as flesh- or pink-coloured, pearly papules with ulceration or telangiectatic vessels.
- Consult for crusting and recurrent bleeding
- Occurs mainly on head and neck in males
- On the upper limbs followed by the head and neck are the more common locations in females

Diagnosis

- **History**
- **Full skin examination**
- **Biopsy**
  - For any suspicious lesion
  - Can be shave, punch or excisional biopsy.
  - 80% accuracy for punch and shave
  - The biopsy should include deep reticular dermis
- **Imaging studies:**
  - Performed for extensive disease, such as bone involvement, perineural invasion, or deep soft tissue involvement, is suspected.
  - MRI vs CT scan

Treatment

- Goals of treatment are:

1. To completely remove the tumor to prevent for recurrence

2. To correct any functional impairment resulting from resection

3. To give best cosmetic results

Local treatment

1. **Curettage and electrodesiccation (C&E)**

- Scraping away tumor tissue with a curette down to a firm layer of normal dermis and denaturing the area by electrodessication
- Overall 5-year cure rates ranging from 91% to 97%
- Higher recurrence rates (19%–27%)
- Operator-dependent and optimal cure rates are achieved by experienced practitioners
- Should not be used to treat areas with terminal hair growth
- If the subcutaneous layer is reached during the course of C&E, then surgical excision should generally be performed instead.
- Can be cosmetically disfiguring as the wound is left to heal by primary intention

BCC Local treatment

2. Excision with Postoperative Margin Assessment

- Achieves 5-year disease-free rates of over 98%
- For well-circumscribed BCC lesions less than 2 cm in diameter, excision with 4-mm clinical margins should result in complete removal in more than 95% of cases

3. Mohs Micrographic Surgery or Excision with Intraoperative Frozen Section Assessment

- Gold standard treatment for BCC
- High cure rate and tissue-sparing benefit
- Allows intraoperative analysis of 100% of the excision margin.
- Two meta-analyses published in 1989 associated MMS with a 5-year recurrence rate of 1.0% for primary BCC, and 5.6% for recurrent BCC.

BCC Local treatment

4. **Excision with complete circumferential peripheral and deep-margin assessment (CCPDMA) using intraoperative frozen section (IOFS) assessment**

- Acceptable as an alternative to MMS provided it includes a complete assessment of all deep and peripheral margins

Radiation Therapy

- **Indications:** adjuvant therapy for positive margins, patient's choice, surgery is contraindicated or impractical
- Two meta-analyses reported 5-year recurrence rates of 8.7% and 10% after RT on primary and recurrent BCC, respectively.
- Efficacy of RT is better for BCCs that are less advanced, primary (vs. recurrent), or with smaller diameter or nodular histologic subtype (vs. any other subtype)
- A prospective study randomized 347 patients to receive either surgery (standard excision with free margins ≥2 mm from visible borders) or RT as primary treatment of BCC.
- RT resulted in higher recurrence rates than surgery (7.5% vs. 0.7%; *P* = .003), poorer cosmetic outcomes, and more postoperative complications.
- **Disadvantages**: cost, high recurrence rate, poor cosmesis, long course of treatment and risk for future skin cancers

Avril MF, Auperin A, Margulis A, et al. Basal cell carcinoma of the face: surgery or radiotherapy? Results of a randomized study.

Br J Cancer 1997;76:100-106.

BCC Superficial therapies

Should be reserved for those patients where surgery or radiation is contraindicated or impractical

1. **Topical Therapies with 5- fluorouracil (5-FU) or imiquimod**

- Good option for patients with multiple superficial BCCs
- A prospective trial reported an 85% 5- year disease-free rate in superficial BCC.
- May cause erythema, pruritus, hypo/hyperpigmentation, crusting, bleeding, erosions
- Disadvantage: No histologic confirmation of tumor clearance

2. Cryosurgery

- Involves application of liquid nitrogen up to -60c
- In prospective trials, cryosurgery has been shown to result in BCC recurrence rates ranging from 5% to 39%.
- Poorer cosmetic outcomes compared with other treatment options, hypertrophic scars and altered pigmentation.

BCC Superficial therapies

3. Photodynamic Therapy

- PDT involves the application of a photosensitizing agent on the skin followed by irradiation with a light source
- Excellent or good cosmetic outcomes higher with PDT versus surgery
- Surgery superior to PDT in terms of efficacy (complete clearance, 1-year and 5-year recurrence rates)

Summary

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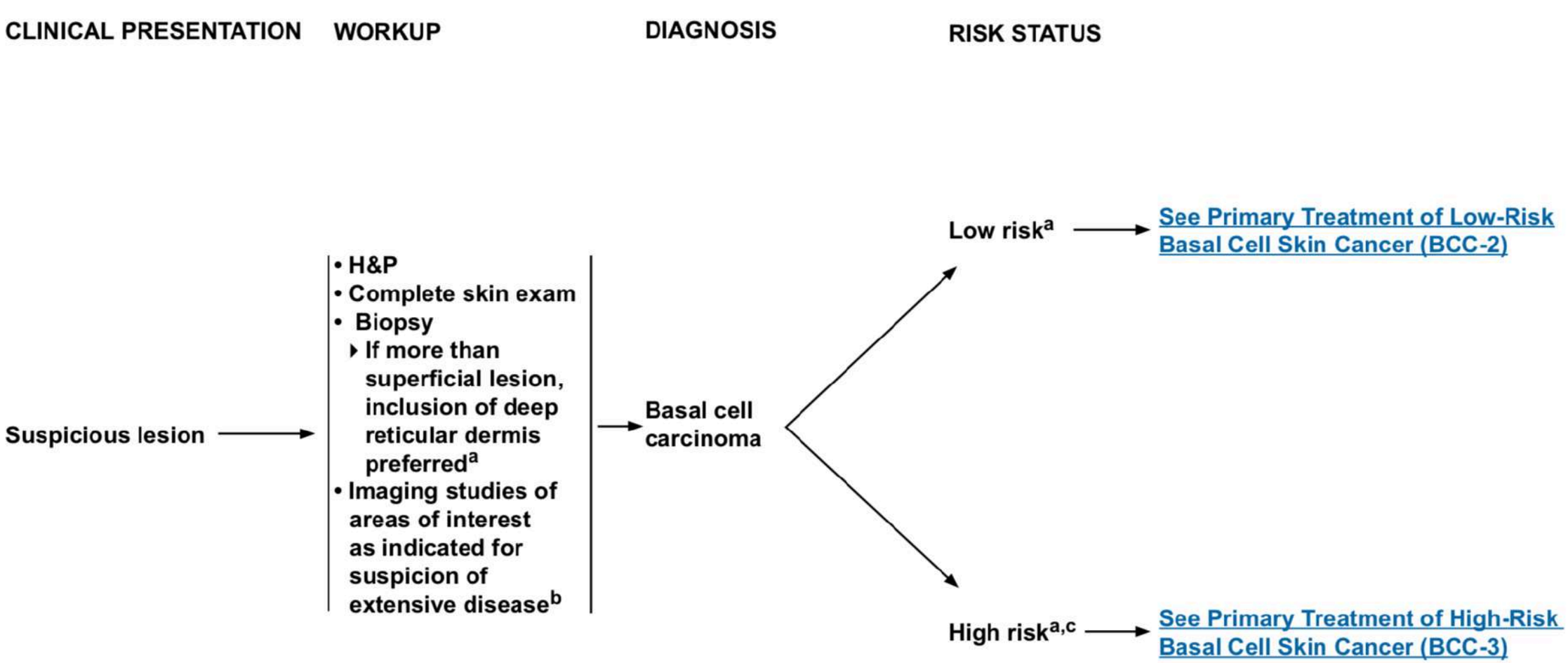

Summary

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RISK FACTORS FOR RECURRENCE

H&P	Low Risk	High Risk
Location/size	Area L <20 mm	Area L ≥20 mm
	Area M <10 mm[1]	Area M ≥10 mm
		Area H[3]
Borders	Well defined	Poorly defined
Primary vs. Recurrent	Primary	Recurrent
Immunosuppression	(-)	(+)
Site of prior RT	(-)	(+)
Pathology		
Subtype	Nodular, superficial[2]	Aggressive growth pattern[4]
Perineural involvement	(-)	(+)

Area H = "mask areas" of face (central face, eyelids, eyebrows, periorbital, nose, lips [cutaneous and vermilion], chin, mandible, preauricular and postauricular skin/sulci, temple, ear), genitalia, hands, and feet.
Area M = cheeks, forehead, scalp, neck, and pretibia.
Area L = trunk and extremities (excluding pretibia, hands, feet, nail units, and ankles).

[1]Location independent of size may constitute high risk.
[2]Low-risk histologic subtypes include nodular, superficial, and other non-agressive growth patterns such as keratotic, infundibulocystic, and fibroepithelioma of Pinkus.
[3]Area H constitutes high risk based on location, independent of size. Narrow excision margins due to anatomic and functional constraints are associated with increased recurrence rates with standard histologic processing. Complete margin assessment such as with Mohs micrographic surgery is recommended for optimal tumor

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PRIMARY TREATMENT[d]

ADJUVANT TREATMENT

Low-risk basal cell skin cancer[a,d]

Curettage and electrodesiccation:
- **Excluding terminal hair-bearing areas, such as the scalp, pubic and axillary regions, and beard area in men**
- **If adipose reached, surgical excision should generally be performed**

or

Standard excision with 4-mm clinical margins and postoperative margin assessment and second intention healing, linear repair, or skin graft[e]

Margins

Positive → **Mohs micrographic surgery or resection with complete circumferential margin assessment[h]**
or
Standard re-excision for area L regions[i]
or
RT[f] for non-surgical candidates[d]

Negative

or

RT[f,g] for non-surgical candidates[d]

See Follow-up (BCC-4)

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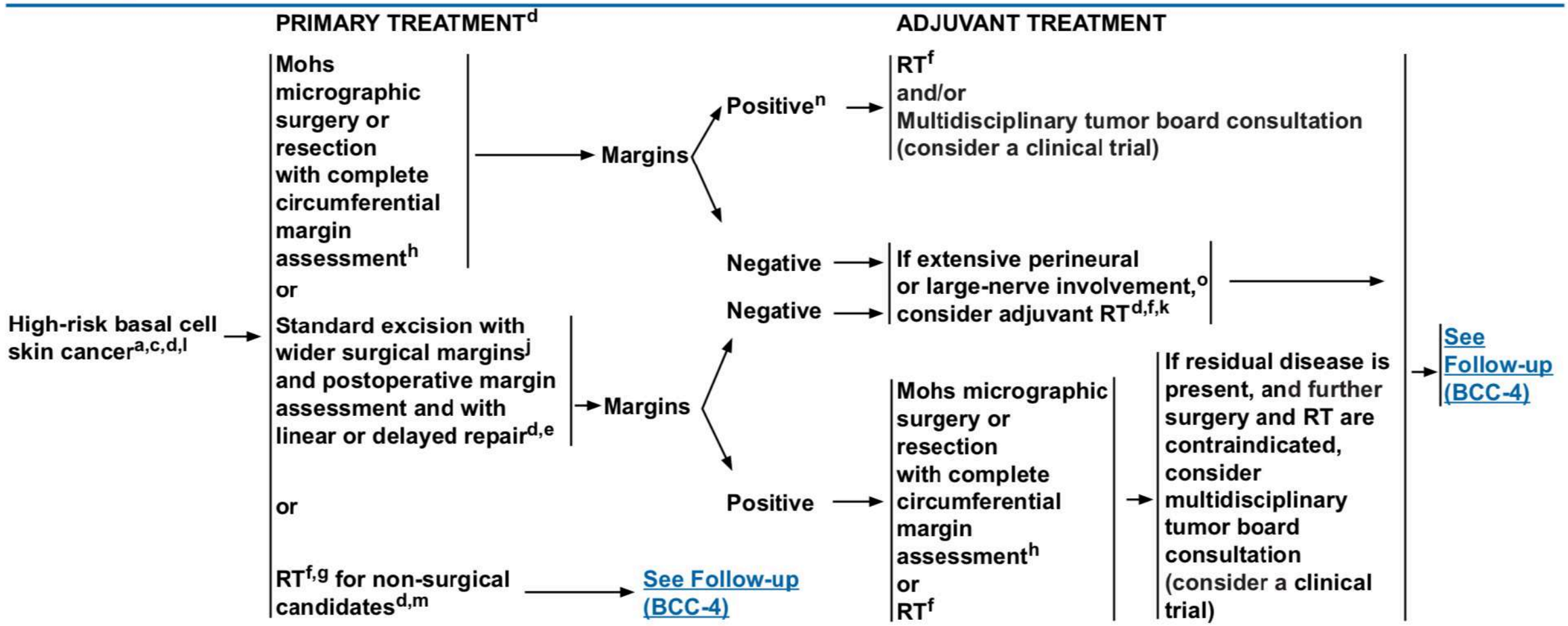


FOLLOW-UP

- H&P
  - Including complete skin exam every 6–12 mo for first 5 years, and then at least annually for life
- Patient education:
  - Sun protection
  - Self-examination

RECURRENCE

- Local → Follow Primary Treatment Pathways (BCC-1)
- Nodal or distant metastases → Surgery and/or RT[m]; Multidisciplinary tumor board consultation (consider a hedgehog pathway inhibitor[p] or clinical trials)

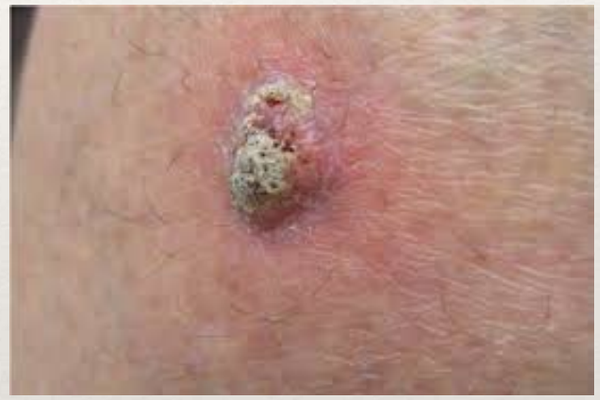
Squamous cell carcinoma

Squamous cell carcinoma

- From keratinizing epidermal cells
- Less common than BCC
- Can be highly aggressive
- Has the potential to metastasise
- Highly associated with scars and chronic wounds

Clinical presentation

- Sites: face particularly the lip, ear, nose, cheek and eye- lid, neck, scalp, forearms, and dorsal hands
- Colour: flesh toned, erythematous
- Mole: crusting, ulceration, hyperkeratosis



- Can be flat with raised border, nodular, or plaque-like with induration
- Occasionally painful and tender: sign of perineural invasion.

Diagnosis

- Full skin examination including regional nodes
- Biopsy for any suspicious lesion
- CT or MRI for extensive disease
- FNA or core biopsy for palpable nodes

Staging

American Joint Committee on Cancer (AJCC)

TNM Staging Classification for Cutaneous Squamous Cell Carcinoma of the Head and Neck (cSCC) (8th ed., 2016)

Primary Tumor (T)

TX	Primary tumor cannot be assessed
Tis	Carcinoma *in situ*
T1	Tumor smaller than 2 cm in greatest dimension
T2	Tumor 2 cm or larger, but smaller than 4 cm in greatest dimension
T3	Tumor 4 cm or larger in maximum dimension or minor bone erosion or perineural invasion or deep invasion*
T4	Tumor with gross cortical bone/marrow, skull base invasion and/or skull base foramen invasion
T4a	Tumor with gross cortical bone/marrow invasion
T4b	Tumor with skull base invasion and/or skull base foramen involvement

*Deep invasion is defined as invasion beyond the subcutaneous fat or >6 mm (as measured from the granular layer of adjacent normal epidermis to the base of the tumor); perineural invasion for T3 classification is defined as tumor cells within the nerve sheath of a nerve lying deeper than the dermis or measuring 0.1 mm or larger in caliber, or presenting with clinical or radiographic involvement of named nerves without skull base invasion or transgression.

Regional Lymph Node (N)

Clinical N (cN)

NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in a single ipsilateral lymph node, 3 cm or smaller in greatest dimension and ENE(−)
N2	Metastasis in a single ipsilateral node larger than 3 cm but not larger than 6 cm in greatest dimension and ENE(−); or metastases in multiple ipsilateral lymph nodes, none larger than 6 cm in greatest dimension and ENE(−); or in metastasis in bilateral or contralateral lymph nodes, none larger than 6 cm in greatest dimension and ENE(−)
N2a	Metastasis in a single ipsilateral node larger than 3 cm but not larger than 6 cm in greatest dimension and ENE(−)
N2b	Metastasis in multiple ipsilateral nodes, none larger than 6 cm in greatest dimension and ENE(−)
N2c	Metastasis in bilateral or contralateral lymph nodes, none larger than 6 cm in greatest dimension and ENE(−)
N3	Metastasis in a lymph node larger than 6 cm in greatest dimension and ENE(−); or metastasis in any node(s) and clinically overt ENE [ENE(+)]
N3a	Metastasis in a lymph node larger than 6 cm in greatest dimension and ENE(−)
N3b	Metastasis in any node(s) and ENE (+)
Note: A designation of “U” or “L” may be used for any N category to indicate metastasis above the lower border of the cricoid (U) or below the lower border of the cricoid (L). Similarly, clinical and pathological extranodal extension (ENE) should be recorded as ENE(−) or ENE(+).	

The 8th Edition Cancer Staging System will be implemented on January 1, 2018.
For the AJCC 7th Edition Staging Manual, visit www.springer.com.

Treatment

- Surgical excision: mainstay of treatment
- Mohs: higher accuracy and lower recurrence rates
- 4mm margin for tumor <2cm, 6mm margin for >2cm
- Sentinel lymhnode biopsy: no proven benefit yet about patient outcome
- Radiotherapy as primary or adjuvant
- Node dissection
- Systemic therapy: responses reported, further studies needed. To consider mucosal SCC guidelines

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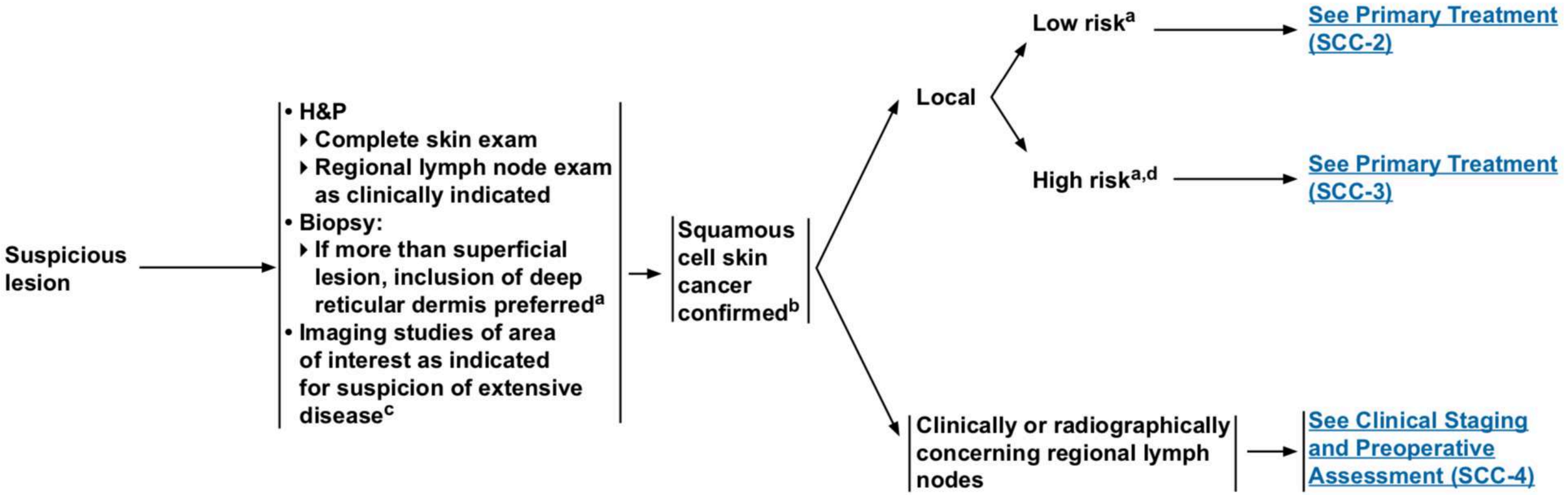

RISK FACTORS FOR LOCAL RECURRENCE OR METASTASES

	Low Risk	High Risk
H&P		
Location/size[1]	Area L <20 mm Area M <10 mm[4]	Area L ≥20 mm Area M ≥10 mm Area H[5]
Borders	Well-defined	Poorly defined
Primary vs. recurrent	Primary	Recurrent
Immunosuppression	(-)	(+)
Site of prior RT or chronic inflammatory process	(-)	(+)
Rapidly growing tumor	(-)	(+)
Neurologic symptoms	(-)	(+)
Pathology		
Degree of differentiation	Well or moderately differentiated	Poorly differentiated
Acantholytic (adenoid), adenosquamous (showing mucin production), desmoplastic, or metaplastic (carcinosarcomatous) subtypes	(-)	(+)
Depth[2,3]: Thickness or Clark level	<2 mm or I, II, III	≥2 mm or IV, V
Perineural, lymphatic, or vascular involvement	(-)	(+)

Area H = "mask areas" of face (central face, eyelids, eyebrows, periorbital, nose, lips [cutaneous and vermilion], chin, mandible, preauricular and postauricular skin/sulci, temple, ear), genitalia, hands, and feet.
Area M = cheeks, forehead, scalp, neck, and pretibia.
Area L = trunk and extremities (excluding pretibia, hands, feet, nail units, and ankles).

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PRIMARY TREATMENT[e]

ADJUVANT TREATMENT

Local, low-risk squamous cell skin cancer[a,e]

Curettage and electrodesiccation:
- **Excluding terminal hair-bearing areas, such as scalp, pubic, axillary regions, and beard area in men**
- **If adipose reached, surgical excision should generally be performed**

or

Standard excision with 4–6 mm clinical margins and postoperative margin assessment and second intention healing, linear repair, or skin graft[f]

Margins

Positive → **Mohs micrographic surgery or resection with complete circumferential margin assessment[i]**
or
Standard re-excision for area L regions[j]
or
RT[g] for non-surgical candidates[e]

Negative

or

RT[g,h] for non-surgical candidates[e]

See Follow-up (SCC-6)

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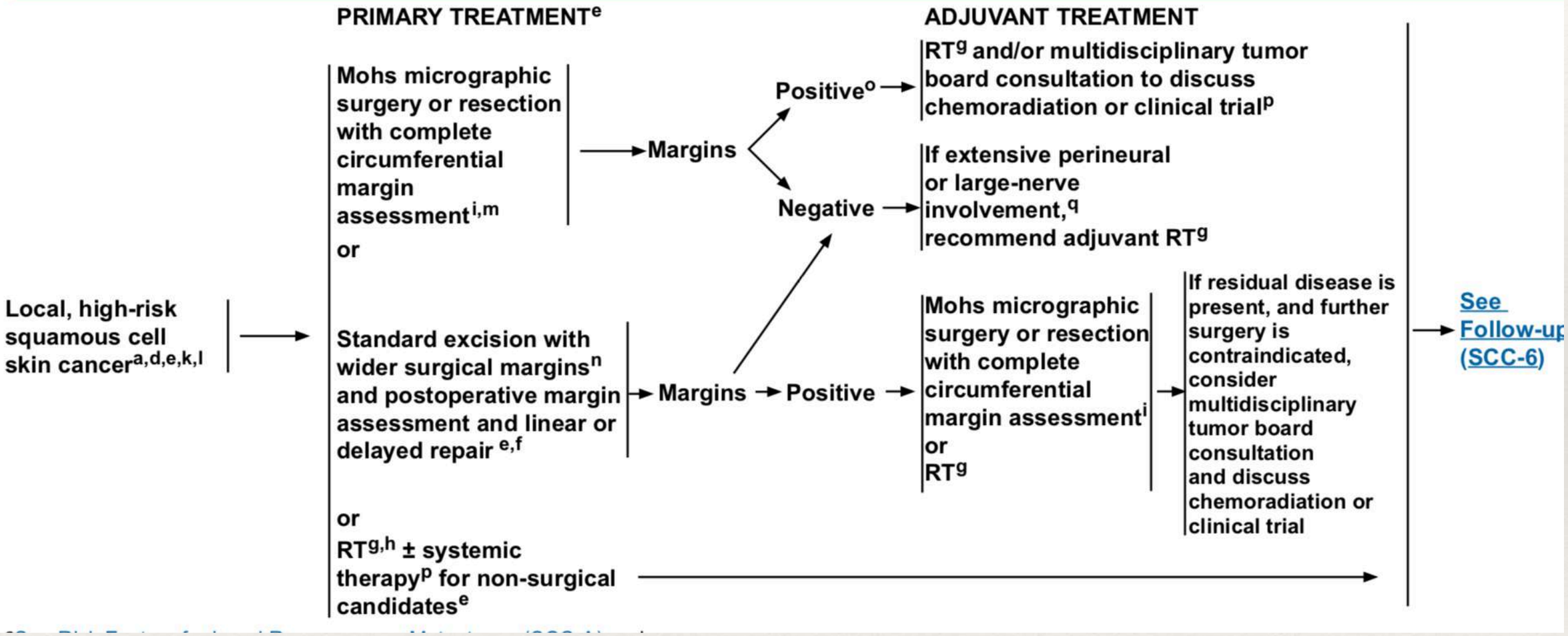

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CLINICAL STAGING AND PREOPERATIVE ASSESSMENT

PRIMARY TREATMENT[e]

ADJUVANT TREATMENT

Palpable regional lymph node(s) or abnormal lymph nodes identified by imaging studies → FNA or core biopsy

Negative → Consider re-evaluation: clinical, CT with contrast of the nodal basin, repeat FNA, core biopsy, or open lymph node biopsy

- Negative → See Follow-up (SCC-6)
- Positive → See Regional Lymph Nodes (SCC-5)

Positive → • CT with contrast of the nodal basin to determine size, number, and location of nodes
• Chest/abdominal/pelvic CT with contrast or PET/CT as clinically indicated to rule out distant disease

→ Surgical evaluation[r]

- Operable disease
  - Head and Neck → See Regional Lymph Nodes (SCC-5)
  - Trunk and extremities → Excision of primary tumor and regional lymph node dissection → Consider RT,[g] especially if multiple involved nodes or extracapsular extension (ECE) is present
- Inoperable disease → RT[g] ± concurrent systemic therapy[s] → Observe[t] → See Follow-up (SCC-6)

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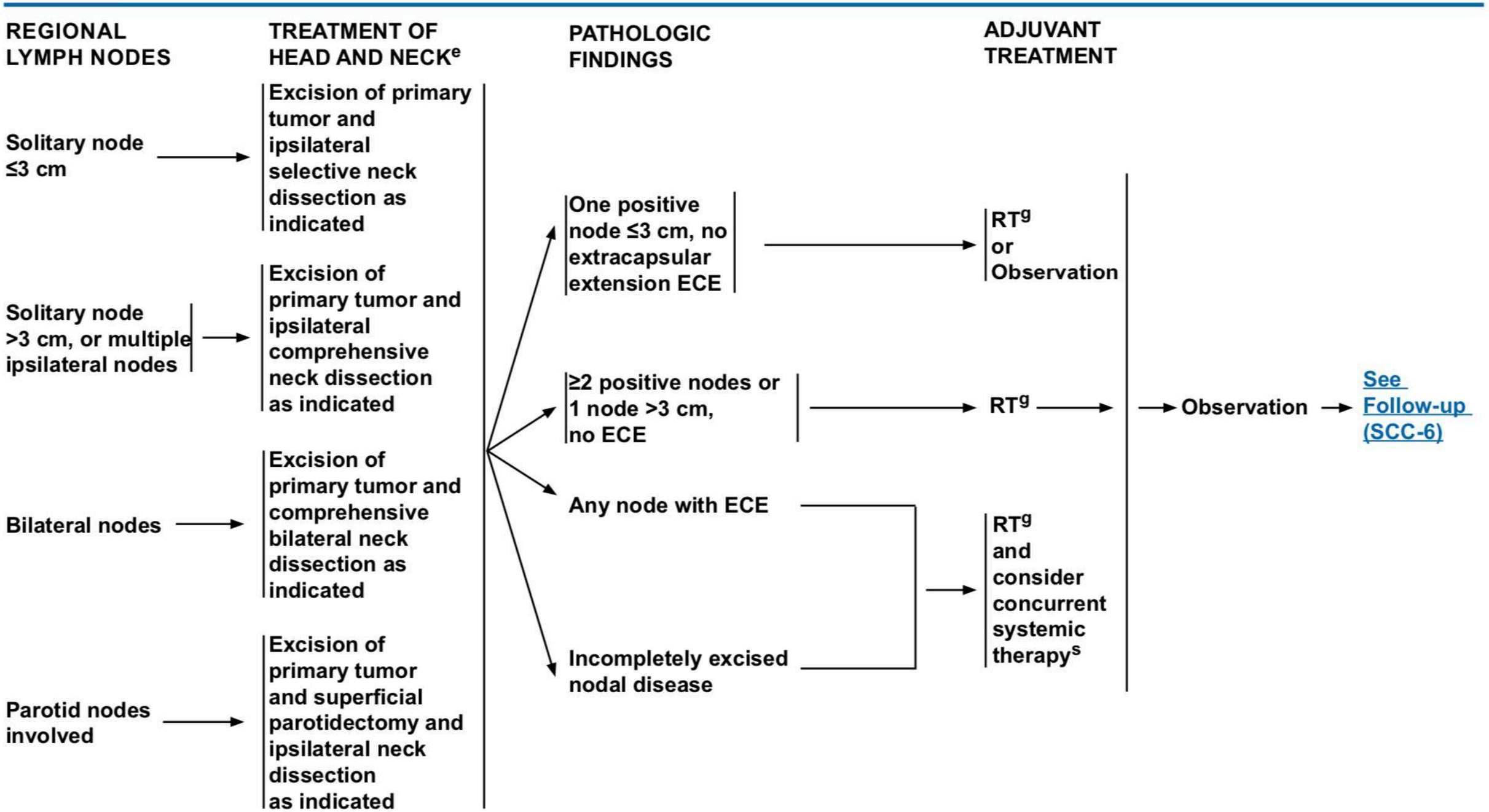

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FOLLOW-UP

Local disease:

- H&P[u,v]
  - Every 3–12 mo for 2 y, then every 6–12 mo for 3 y, then annually for life
- Patient education
  - Sun protection
  - Self examination of skin

Regional disease:

- H&P[u,v,w]
  - Every 1–3 mo for 1 y, then every 2–4 mo for 1 y, then every 4–6 mo for 3 y, then every 6–12 mo for life
- Patient education
  - Sun protection
  - Self examination of skin and lymph nodes

RECURRENCE

- Local → See Primary Treatment for local disease (SCC-1)
- New regional disease → See Primary Treatment for regional disease (SCC-4)
- Regional recurrence or distant metastases → Multidisciplinary tumor board consultation[x]

[u]Including complete skin and regional lymph node exam

Prognosis

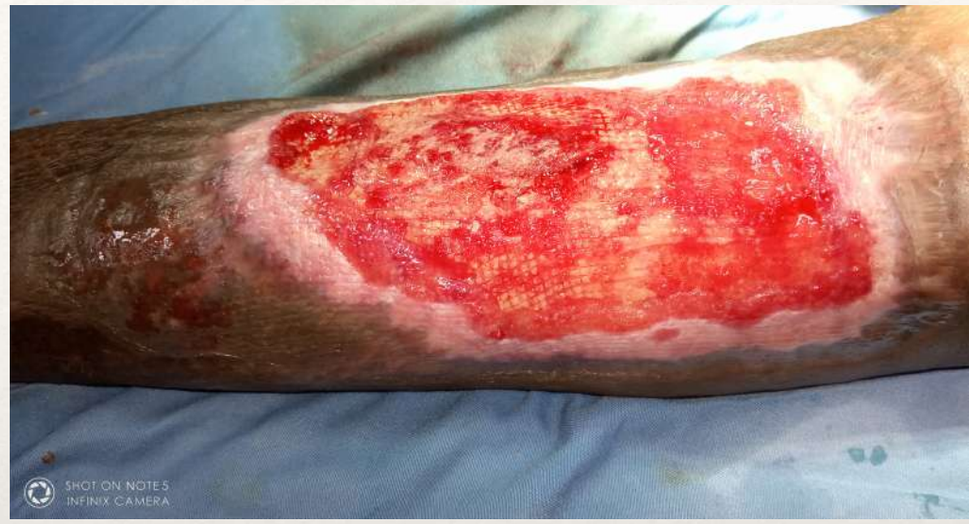
- Low mortality rate: 0.12/100000 cases
- Patient with BCC has 10 times potential risk to develop another BCC compared to the general population
- 95% of recurrences for SCC occur within 5 years, with 70–80% of these recurrences occurring within the first 2 years

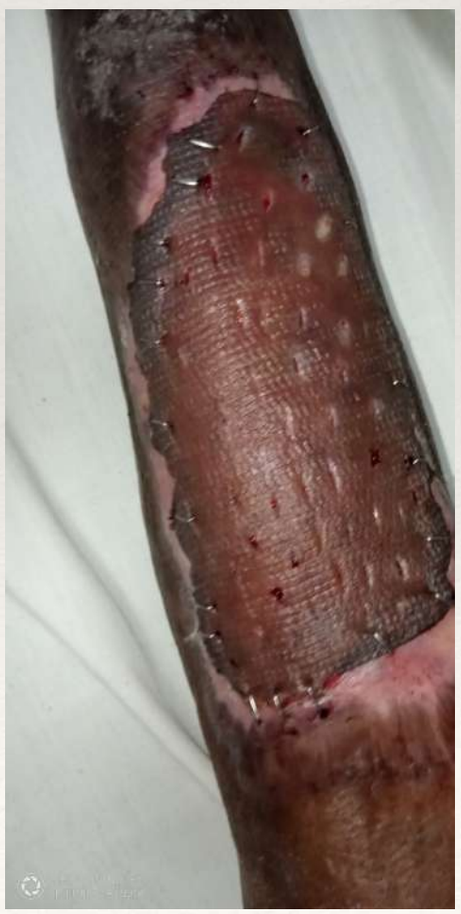
Prevention

- Avoid/limit UVR exposure
- Use of sunscreens
- To use hats, clothing, shade and avoidance of the sun around the middle of the day
- Avoid recreational sunbathing and do not use sun lamps, tanning beds, or tanning salons
- Examine the skin regularly.
- Education programs pointing out the signs of early NMSC in populations with a high incidence rate.

Case

- 74y, F, left leg ulcer for many years
- Excised- SCC, free margins
- Reexcision and Skin graft
- Recurrence, ipsilateral nodes
- Management ??





Take home

- Skin cancer is rare
- Low mortality rate
- Can lead to disability
- Treatment is expensive
- Prevention is possible
- Biopsy for any suspicious lesion
- Awareness ++++

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Thank you