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PRACTICE POINTER

When to suspect a non-melanoma skin cancer

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What you need to know

- Non-melanoma skin cancer (NMSC) is more commonly diagnosed than all other malignancies combined
- Consider risk factors for NMSC in all patients presenting with non-melanocytic skin lesions
- A typical cutaneous squamous cell carcinoma may be a growing, tender, firm, skin-coloured nodule, sometimes with adherent surface scale, crust, or central ulceration

Assessing non-melanocytic skin lesions is a routine part of general practice. The key concern for patient and doctor is often whether the lesion may be a basal cell carcinoma or squamous cell carcinoma, collectively termed non-melanoma skin cancer (NMSC). This article aims to help primary care clinicians, who may not routinely have access to dermoscopy and biopsy, to identify possible NMSC lesions, which require further specialist assessment or monitoring.

How this article was made

We searched for relevant journal articles in the *British Journal of Dermatology*, *BMJ*, and British Association of Dermatology guidelines. A secondary literature search was conducted using Google Scholar with the key words "basal cell carcinoma," "squamous cell carcinoma," "non-melanoma skin cancer" associated with "risk factors," "treatment," "management," "follow-up."

Why is non-melanoma skin cancer on the increase?

Non-melanoma skin cancer is more commonly diagnosed than all other malignancies combined,[1] and the incidence of skin cancer is rising, with rates of NMSC predicted to reach almost 400 000 per year in the UK by 2025.[2] This is thought to be due to a combination of people living longer, increased exposure to ultraviolet (UV) light, and improved data collection and diagnostic tools.[3 4] Risk factors are summarised in table 1, with the key environmental risk being UV exposure from tan-seeking behaviour and outdoor activities without adequate sun protection.[1 2] Both basal cell carcinomas and cutaneous squamous cell carcinomas are more common with increasing age, with incidence of cutaneous squamous cell carcinomas peaking at 66 years of age.

Assessment of a non-melanocytic skin lesion

Box 1 summarises the procedure for assessment of a non-melanocytic skin lesion.

Box 1: Assessing a non-melanocytic skin lesion

- What type of lesion is it?
  - Dome shaped, raised lesion (nodule ≥0.5 cm, papule <0.5 cm)
  - Cyst (under the skin causing a protrusion with overlying skin normal)
  - Plaque (flat topped, raised lesion)?
- Where is it (a high risk site?) and what size is the lesion?
- Is it well defined or poorly defined at the edges?
- What is the appearance of the surface? Such as:
  - Eroded (superficial skin loss)
  - -Ulcerated (full thickness epidermal skin loss)
  - Scaly (white adherent scales)
  - -Crusted (yellow dried exudate)
- What is the colour? Such as:
  - Pigmented (brown to black)
  - Vascular (red, purple, or black)
  - Translucent and/or shiny (suggestive of basal cell carcinoma)
- What does the surface feel like? Smooth, rough, filliform (finger-like projections)
- Palpate area to assess induration (a palpable, raised, hardened area)
- Stretch the skin to help estimate the extent of tissue involvement. You may be able to detect subtle extension (thickening or texture change) into surrounding tissues, particularly with basal cell carcinomas
- Remove crust or scale with an alcohol swab to reveal the underlying lesion. If it bleeds this is more suggestive of cutaneous squamous cell carcinoma, especially if there is underlying ulceration

When should you suspect a cutaneous squamous cell carcinoma?

A typical cutaneous squamous cell carcinoma may be a growing, tender, firm, skin coloured nodule, sometimes with surface adherent scale, crust, or central ulceration. Key characteristics that differentiate cutaneous squamous cell carcinomas from other lesions include ulceration, pain or tenderness, induration (localised hardening and thickening of soft tissue), and presence of a cutaneous horn (fig 1, box 2). A history of growth in size over a period of one to three months is typically described. Cutaneous squamous cell carcinomas tend to have a dull appearance compared with basal cell carcinomas, which have a pearly surface. They can vary in size from a few millimetres to centimetres in diameter.

Box 2: Features suggestive of cutaneous squamous cell carcinoma

- Hyperkeratotic plaque with indurated base
- Painful, tender, eroded or ulcerated lesion
- Rapidly growing lesion over weeks

A cutaneous horn can arise from a cutaneous squamous cell carcinoma or a non-malignant lesion. Clues that the horn is arising from a cutaneous squamous cell carcinoma include pain, induration and erythema at the base, and if the width of the lesion is greater than the height of the horn (fig 1).[1]

A common differential is an actinic keratosis. Actinic keratoses are considered precancerous and present as scaly plaques which can have similarities to cutaneous squamous cell carcinoma clinically, but typically lack the features listed in box 2.[2] A comparison of features is demonstrated in fig 2. If the history and clinical features do not include rapid growth, tenderness, ulceration or induration, these can be managed in primary care. Based on available evidence, progression from actinic keratosis to cutaneous squamous cell carcinoma appears to be low (less than 1 in 1000 per year during 5-year follow up).[13] A Cochrane review did not find any strong evidence that treating actinic keratoses reduced risk of squamous cell carcinoma,[14] and the British Association of Dermatologists (BAD) suggests treatment should be dependent on patient preference.

When should you suspect a basal cell carcinoma?

Basal cell carcinomas typically present as a "non-healing" nodule or sore which grows slowly over months to years, remaining otherwise asymptomatic. They are classified based on their clinical presentation into nodular, superficial, morphoeic, and pigmented basal cell carcinoma.[15]

Nodular basal cell carcinomas are the most common subtype, accounting for around 50-70% of basal cell carcinomas.[16] They typically have a rolled edge, telangiectasia, and a central depression, with or without erosion or ulceration (fig 3).[5]

Superficial basal cell carcinomas account for about 5% of basal cell carcinomas[16] and typically present as a slow growing scaly pink patch (fig 4).

Morphoeic basal cell carcinoma—A slowly enlarging white scar is suggestive of a morphoeic basal cell carcinoma (fig 5). These can have extensive subclinical spread.

Pigmented basal cell carcinomas account for around 6% of basal cell carcinomas.[17] They present as a brown or black pearly nodule or plaque and therefore can be confused with melanoma (fig 6). If there is any uncertainty, they should be referred urgently to rule this out.

When to refer?

Refer patients with suspected cutaneous squamous cell carcinoma urgently to a dermatologist (to be seen within two weeks). Suspected basal cell carcinomas can generally be referred routinely unless there is concern about squamous cell carcinoma or melanoma. If there is uncertainty between basal cell carcinoma and benign differentials, the patient can be referred routinely for a specialist opinion, or a photograph of the lesion can be sent through a teledermatology service if available. Alternatively, an initial biopsy could be considered in primary care if the lesion is low risk and present on the trunk or limbs. If this is undertaken, a photograph should be taken before the procedure to document the site. In some areas, primary care minor surgery services may be able to perform excisions of low risk nodular basal cell carcinomas, ensuring a clinical margin of 4-5 mm.[18] Referral recommendations for suspicious skin lesions are summarised in table 2.

What else might it be?

Common benign lesions

Benign lesions can also be difficult to distinguish from NMSC. In our urgent skin cancer clinics, commonly seen benign differentials include keratoacanthoma, intradermal naevi, sebaceous hyperplasia, and dermatofibroma.

Keratoacanthoma often grow quickly over just a few weeks, have a crateriform appearance, and will typically start to regress after a period of rapid growth (fig 7). Keratoacanthoma are considered benign but can be hard to distinguish from cutaneous squamous cell carcinoma clinically and histologically (particularly on punch biopsy). If there is doubt, refer in the same way as cutaneous squamous cell carcinoma.

Intradermal naevi are skin coloured lesions which may grow slowly in size over years, simulating the change of an early basal cell carcinoma, but they do not have the typical pearly appearance. While telangiectasia may be present on the surface, they appear as comma-like vessels rather than demonstrating an arborising (branching) pattern as seen in basal cell carcinomas (fig 8).

Sebaceous hyperplasia are skin coloured papules which may have a central depression (fig 9). They often have a slightly yellowish appearance. Dermoscopy demonstrates a ring of yellowish nodules representing the hyperplastic sebaceous glands. These may also have telangiectasia on the surface, but these do not cross the midline.[20]

Dermatofibroma typically occur on the limbs and are firm to palpate (fig 10). They might exhibit the dimpling sign, where lateral pressure to the lesion produces dimpling of the lesion.[21]

Malignant differentials to consider

Other malignant diagnoses to consider for a non-pigmented skin nodule include Merkel cell carcinoma, atypical fibroxanthoma, and amelanotic melanoma, all of which should be referred urgently to secondary care for management. A key feature of each of these is rapid growth. Merkel cell carcinoma typically presents as a rapidly growing, often painless, firm, pink or red nodule on sun exposed sites.[22] Atypical fibroxanthoma is a spindle-cell tumour, which presents as a red, juicy, often ulcerated nodule, growing over a few months, on the head and neck of sun damaged individuals.[23] Amelanotic melanoma is a form of melanoma with little or no pigment, presenting as a rapidly growing, red or pink nodule, with or without ulceration. The patient may describe a pigmented lesion previously being present at the site of the lesion.

Scaly plaques

The differential diagnosis for a scaly plaque includes superficial basal cell carcinoma, actinic keratosis, intraepidermal squamous cell carcinoma (also known as Bowen's disease) and common inflammatory causes such as psoriasis, eczema, and tinea infections.

Bowen's disease represents full thickness dysplasia of the skin epidermis (the top of layer of skin), and also presents as a scaly plaque on sun exposed sites (fig 11). They tend to be more erythematous, well defined, and larger than actinic keratoses and have a higher risk of progression to cutaneous squamous cell carcinoma (3-5%).[14] Dermoscopy demonstrates surface scales and glomerular vessels in 90% of cases.[24]

Inflammatory and fungal causes of a scaly plaque tend not to be limited to sun exposed sites of skin, instead presenting with a more typical distribution of the suspected condition (for example, extensor surfaces for psoriasis and flexor surfaces for eczema). They are often itchy. Where there is uncertainty, a trial of topical corticosteroid or topical antifungal can be provided with a follow-up review to check whether the lesion has resolved.

An opportunity for sun safety advice

If no suspicious lesion is identified, the patient can be booked a follow-up appointment to review the lesion again or advised to return if the lesion develops any concerning features such as pain, ulceration, or growth in size. A consultation about a skin lesion is a good opportunity to discuss sun safety advice. A popular way of remembering how to stay safe in the sun is to slip (on a long sleeve top), slop (on sun cream with sun protection factor (SPF) ≥30), slap (on a wide brim hat), seek (shade where possible), and slide (on sunglasses for eye and eyelid protection from ultraviolet light).[25-27] Further advice on sun protection is provided in box 3.

Box 3: Sun safety advice

- Do not to let your skin burn
- Avoid exposure to the sun between 10 am and 3 pm
- Use high factor sun creams (sun protection factor (SPF) ≥30) protecting against UVA and UVB light
- Apply sun cream liberally 15-30 minutes before going outside
- Reapply sun cream every 2 hours and after swimming
- More information for patients is available at:
  - NHS. Sunscreen and sun safety. https://www.nhs.uk/live-well/healthy-body/sunscreen-and-sun-safety/
  - Cancer Research UK. Ways to enjoy the sun safely. https://www.cancerresearchuk.org/about-cancer/causes-of-cancer/sun-uv-and-cancer/ways-to-enjoy-the-sun-safely
  - British Skin Foundation. How to stay safe in the sun. https://www.britishskinfoundation.org.uk/how-to-stay-safe-in-the-sun

Education into practice

- What features of a non-melanocytic skin lesion would alert you to a possible NMSC?
- Do you offer education regarding UV exposure to your patients with a recent diagnosis of NMSC?
- What other factors are important when assessing a patient's risk of developing NMSC?
- What changes do you advise patients to look out for in a skin lesion that appears benign?

How patients were involved in the creation of this article

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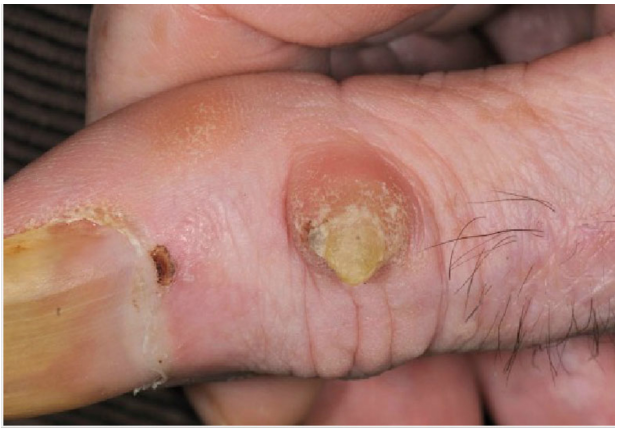

Fig 1 | Typical appearance of cutaneous squamous cell carcinoma: an indurated base with dull appearance, surface scale, ulceration or a keratin horn

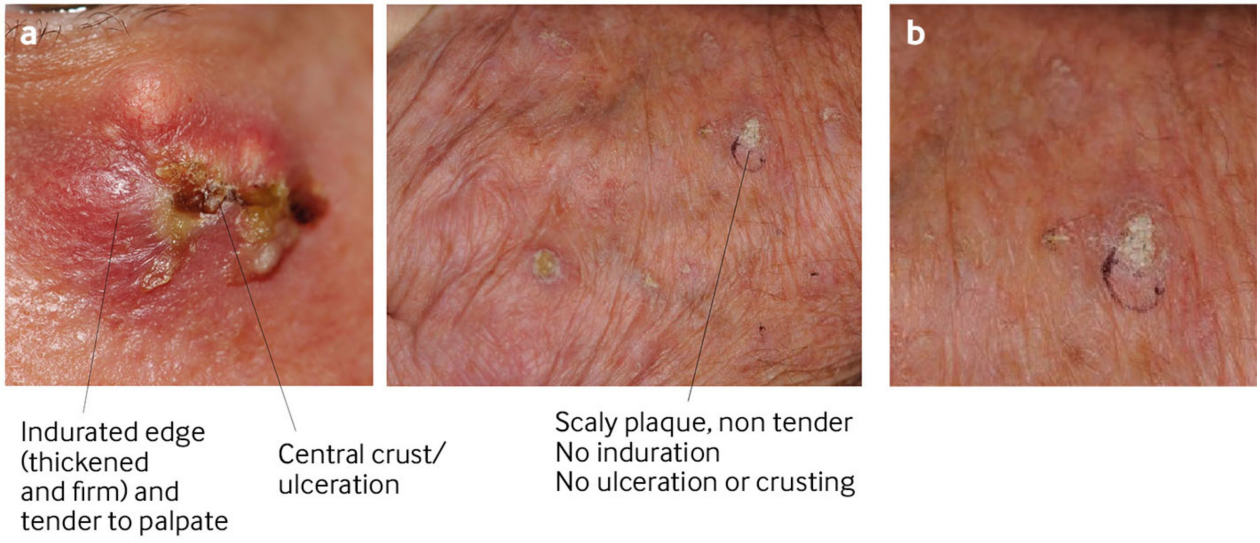

Fig 2 | Differences between a cutaneous squamous cell carcinoma (left) and actinic keratosis (centre, with higher magnification right). The large, rapidly growing carcinoma was under the right eye (a high risk location) of a young man who was a regular sunbed user. Actinic keratosis presents as a small scaly plaque with mild background erythema

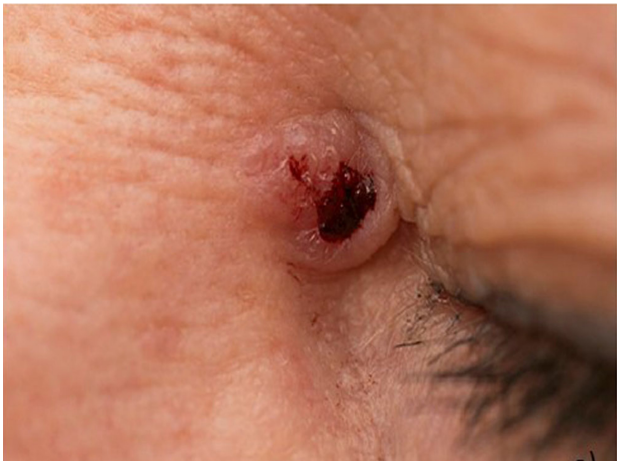

Fig 3 | Nodular basal cell carcinoma on the left medial canthus

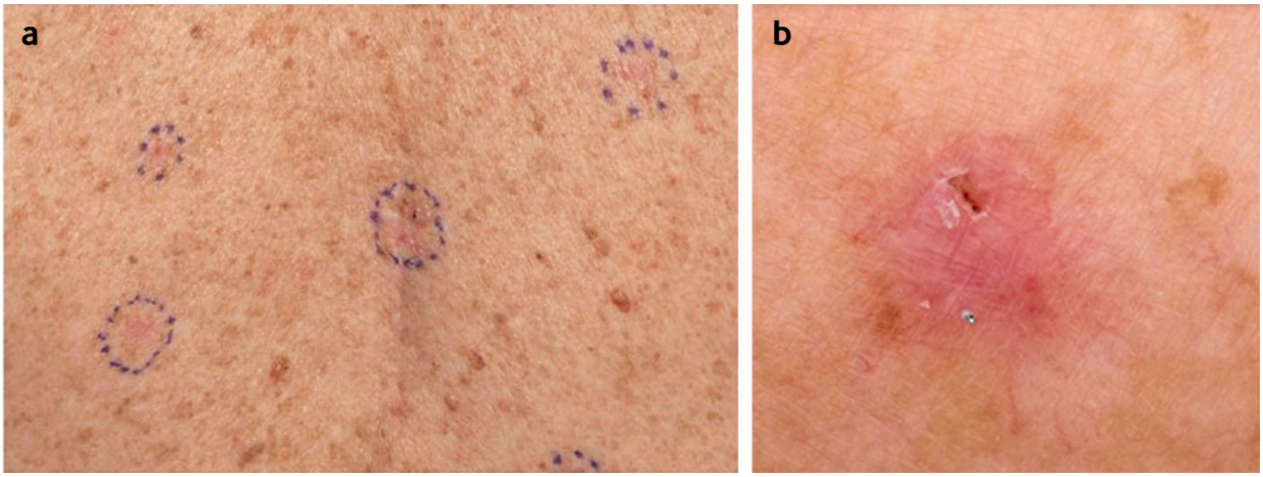

Fig 4 | Superficial basal cell carcinoma on the back (left) with high magnification of a single patch (right)

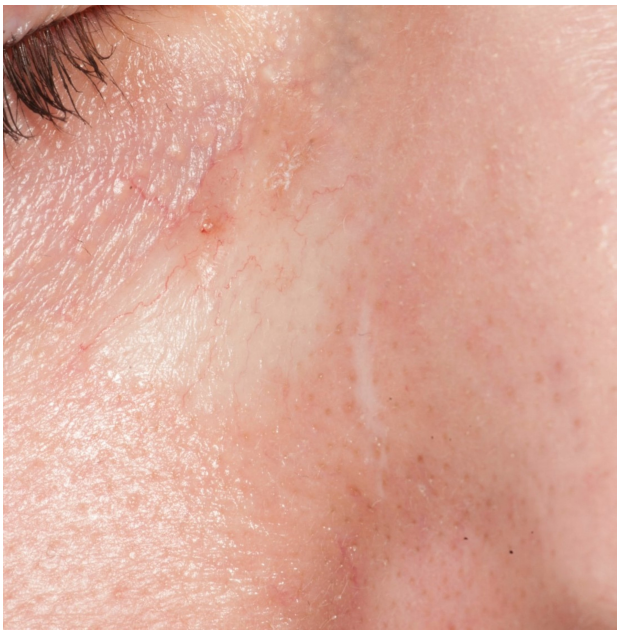

Fig 5 | Morphoeic basal cell carcinoma below the eye

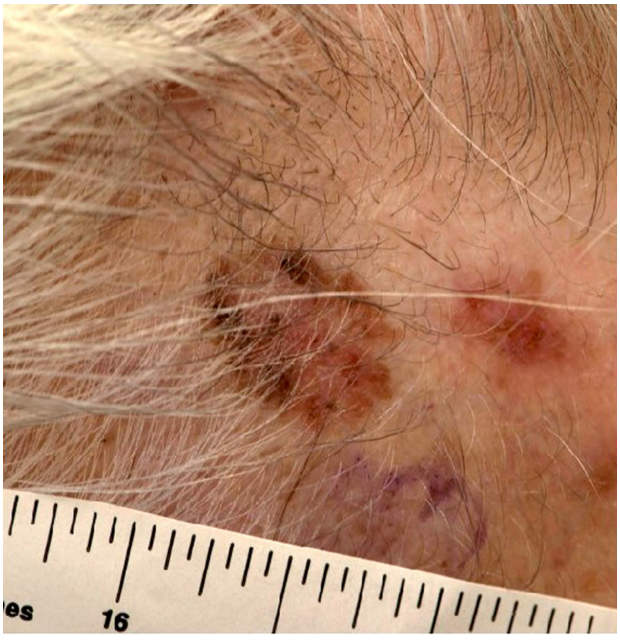

Fig 6 | Pigmented basal cell carcinoma on the right forehead

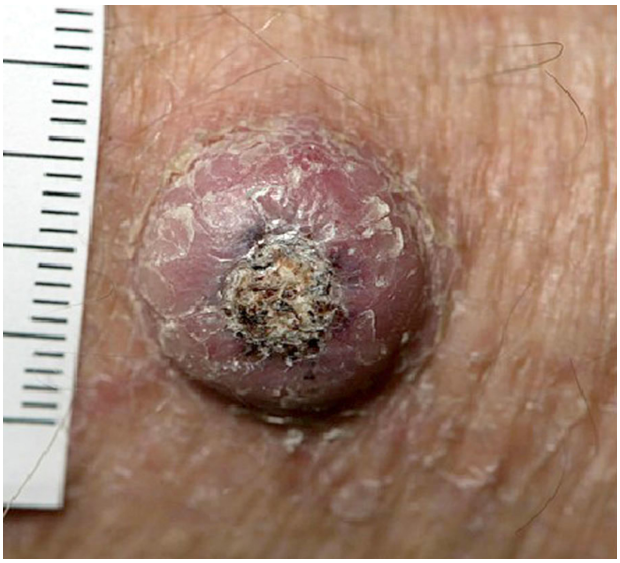

Fig 7 | Keratoacanthoma on the right forearm

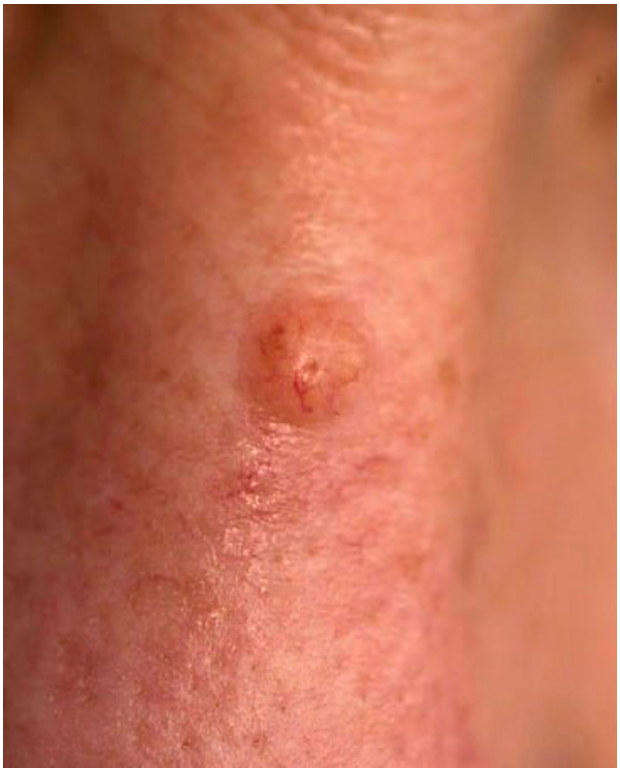

Fig 8 | Intradermal naevus on the nasal bridge

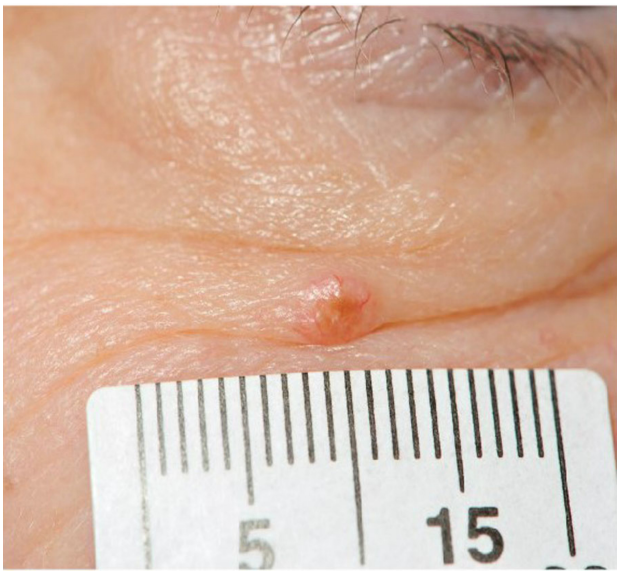

Fig 9 | Sebaceous hyperplasia below the left eye

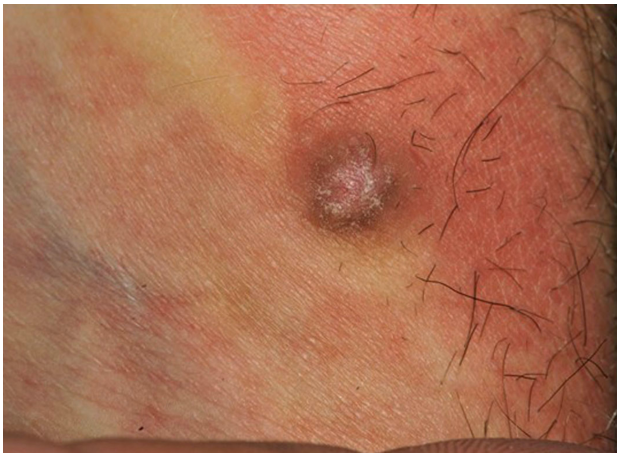

Fig 10 | Dermatofibroma on the right forearm

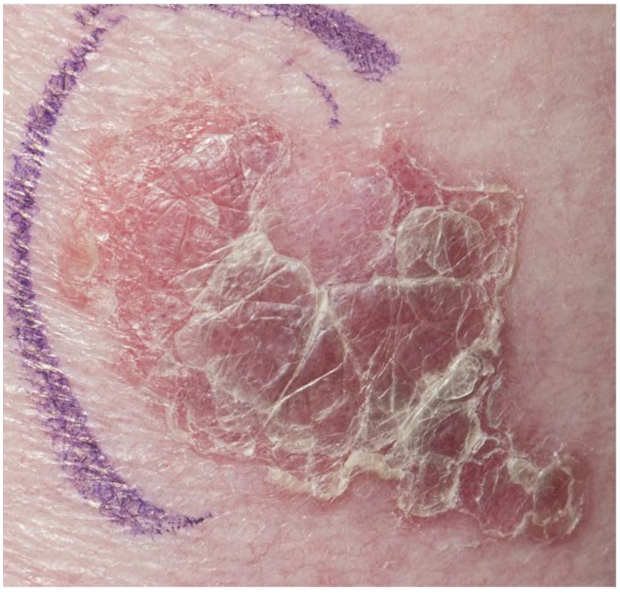

Fig 11 | Bowen's disease (intraepidermal carcinoma) on the lower leg

Table 1 | Risk factors for non-melanoma skin cancer

Risk factor	Questions to ask	Comments
Age		NMSC is more common over the age of 40 years,[5] especially in head and neck region.
UV exposure	Occupation Outdoor hobbies Holidays abroad Living abroad Past sunburn Sunbed use Use of SPF or hat	Using a sunbed for 12 minutes per week over a 15 year period is associated with 90% increased risk of cSCC by the age of 55 years.[6] Age standardised incidence of cSCC for median use of sunbed was 39.7/100 000 per year, versus 26.6/100 000 for non-use.[6]
Other environmental exposures	Exposure to: Tar Arsenic Petrol substances Radiotherapy	Exposure to tar, arsenic, and petrol substances may be associated with cSCC, but the specific level of exposure that confers an increased risk is not clear.[7]
Areas of chronic inflammation	"What was there before the lesion developed?"	cSCC can develop in areas of chronic inflammation such as ulcers, scars, burns, sinus tracts, inflammatory dermatoses, and sites of chronic blistering.[3] BCC can develop at sites of previous trauma and scarring or sebaceous naevi.[5]
Immunosuppression	Previous solid organ transplants Any other causes of immunosuppression including medications	Incidence of cSCC is 65 times higher in recipients of solid organ transplants than non-recipients[8]; incidence of BCC is 10 times higher in recipients. Chronic lymphocytic leukaemia increases the risk of cSCC by 8.6 times compared with general population.[9]
Skin type (Fitzpatrick type I and II)	"Do you burn easily in the sun?"	Rates of BCC 10-20 time higher in skin types that burn easily.[10]
Actinic keratosis or intra-epidermal carcinoma (IEC) History of skin cancer	Previous skin cancer Previous lesions	IECs carry a 3-5% lifetime risk of conversion to invasive cSCC. After diagnosis of SCC there is a 50% risk of developing another NMSC at 5 years and a 30% chance of developing another SCC at 5 years[11]
Genetic risk factors or family history of cSCC	Family history of skin cancer or genetic conditions with an increased risk of skin cancer	Xeroderma pigmentosum is associated with a 10 000-fold increase in incidence of NMSC by age 20.[4] Albinism is associated with NMSC. Gorlin syndrome is an autosomal dominant condition associated with developing large numbers of BCCs, often from a young age. Other features include palmar pits, macrocephaly, and skeletal abnormalities.

UV = ultraviolet light. NMSC = non-melanoma skin cancer. SPF = sun protection factor. cSCC = cutaneous squamous cell carcinoma. BCC = basal cell carcinoma.

Table 2 | Referral guidelines for suspicious skin lesions[19]

Suspected lesion	Action
Cutaneous squamous cell carcinoma	Urgent dermatology review within 2 weeks
Keratoacanthoma	Urgent dermatology review within 2 weeks
Basal cell carcinoma	Routine dermatology referral. Consider review within 2 weeks if there is a particular concern that a delay may have a significant impact on prognosis.[19] If low risk basal cell carcinoma, consider treatment in primary care if accredited primary care physician is available.
Other lesions of diagnostic uncertainty	If the lesion could be cutaneous squamous cell carcinoma, melanoma or other skin cancer with malignant potential, such as Merkel cell carcinoma, refer for urgent review within two weeks. Consider teledermatology opinion for other lesions where there is diagnostic uncertainty.
Actinic keratoses in people who are immunosuppressed, multiple or relapsing lesions, or if red flags develop during observation period	Urgent dermatology review within 2 weeks