Non-melanoma skin cancer

National GP conference Rotorua 2009
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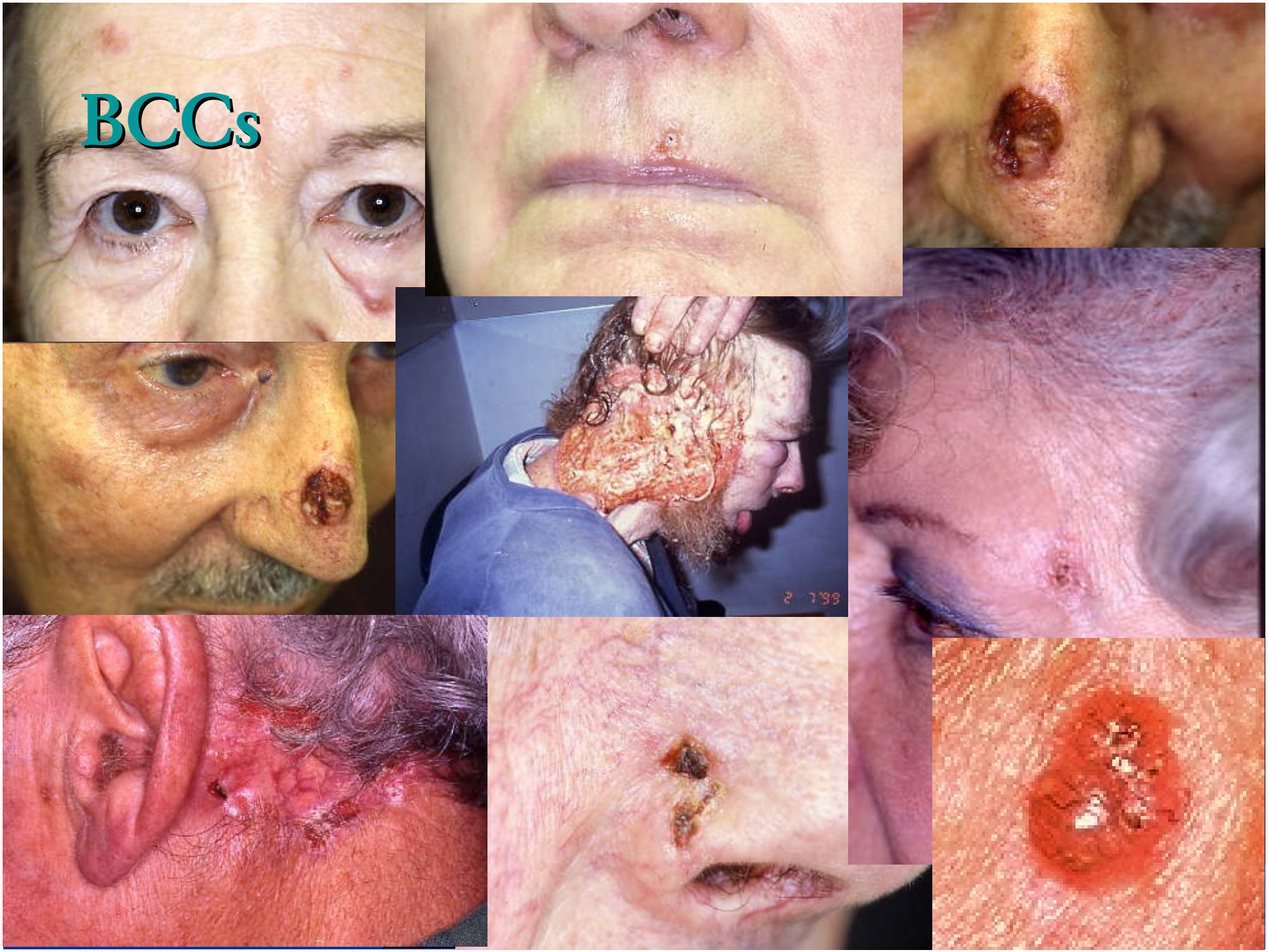
Non-melanoma skin cancer

- Refers to basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) Thus exclude lymphomas, appendageal carcinomas, clear cell acanthoma, etc
- Most common human cancer
- Derived from epidermal keratinocytes
- Rarely metastasize
- Underreported in health statistics / funding support

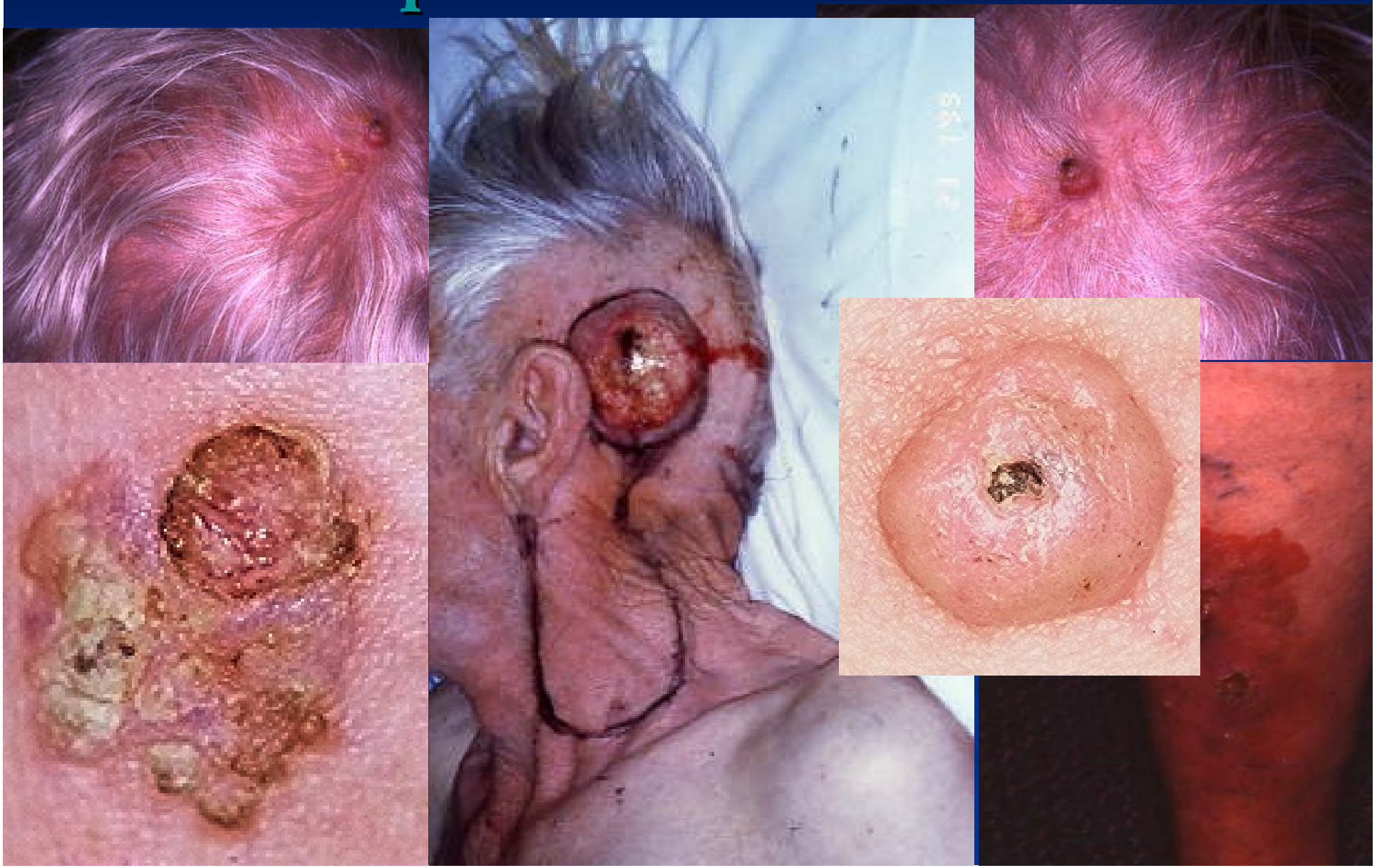
~ 50,000 new cases per year

> 300 New Zealanders die / year

cost NZ ~ $33.4 NZ million /year


BCCs

SCC Squamous cell carcinoma



Non-melanoma skin cancer

- BCC more common e.g. 4:1 BCC:SCC
- ratio changes toward 1:1 BCC:SCC with
  - higher ambient sun exposure
  - Immunosuppression
- Associated risk lesions
  - actinic keratoses
  - Bowen's disease

Non-melanoma skin cancer risk factors

Ultraviolet radiation (UVR)

Sun-sensitive skin

Age

Childhood sun-exposure <10yrs age

Immunosuppression

Further skin cancer risk factors

Chemical carcinogens e.g. Chimney sweeps, arsenic, cutting oils, aromatic hydrocarbons

X-rays, thermal radiation, scars, chronic injury

HPV human papilloma virus

Genetics

Nutrition / diet ?

How nasty is the sun?
Skin mutagenic effects of UVR

- Depend on
  - Amount and wavelength of UVR
  - Cellular antioxidant defences
  - Effectiveness of DNA repair mechanisms
  - Characteristics of target keratinocyte e.g. degree of melanin

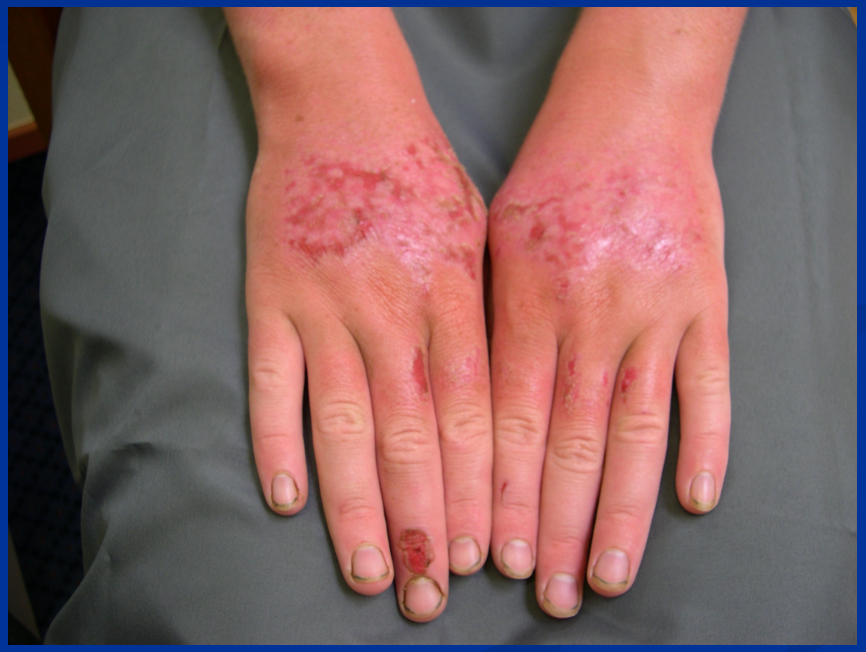
Effects of UVR

- Immunosuppression
  - Non-melanoma skin cancer is proportional to the level and duration of immunosuppression AJD 2007
- Oxidative mitochondrial DNA damage
- DNA photoproducts e.g. cyclobutane pyrimidine dimer formation → skin cancer & photoageing
- Increased skin pigmentation →↓Vit D production
- Thickening of epidermal layer →↓Vit D production

Other UVR effects on skin

- DNA signature mutation, (cytosine changed to thymine) in *p53* tumour suppression gene

→defective DNA repair & ↓ apoptosis of damaged cells thus propagation of mutated keratinocytes →→ skin cancers



Blistering sunburn dorsal hands

Other UVR effects on skin

- DNA signature mutation, (cytosine changed to thymine) in *p53* tumour suppression gene

→defective DNA repair & ↓ apoptosis of damaged cells thus propagation of mutated keratinocytes →→ skin cancers

AJD 2007;48:67-76.

Skin cancer development

UVL UVL UVL UVL UVL

initiation→ → promotion → → cancer

UVB

- 280-315nm
- <10% of sunlight spectral energy
- But main waveband for sunburn / skin cancer induction (?)
- Corresponds to action spectra of DNA
- Direct DNA damage

UVA

- 315-400nm
- DNA damage consequence of indirect effects of reactive oxygen species
- Immunosuppression
- Photo ageing
- More important for melanoma?

BCC

- Intermittent sun-exposed areas
- Holiday or recreational sun-exposure

SCC

- Increasing sun exposure proportional to increase risk
- Occupational sun-exposure
- UVA / PUVA
- Scars, chronic inflammation e.g. lupus, burns, skin fistulae, lichen sclerosis
- HPV human papilloma virus
- Cigarettes

Management of patients with non-melanoma skin cancer

- Detection
- Diagnosis
- Appropriate therapeutic modality
- Secondary prevention

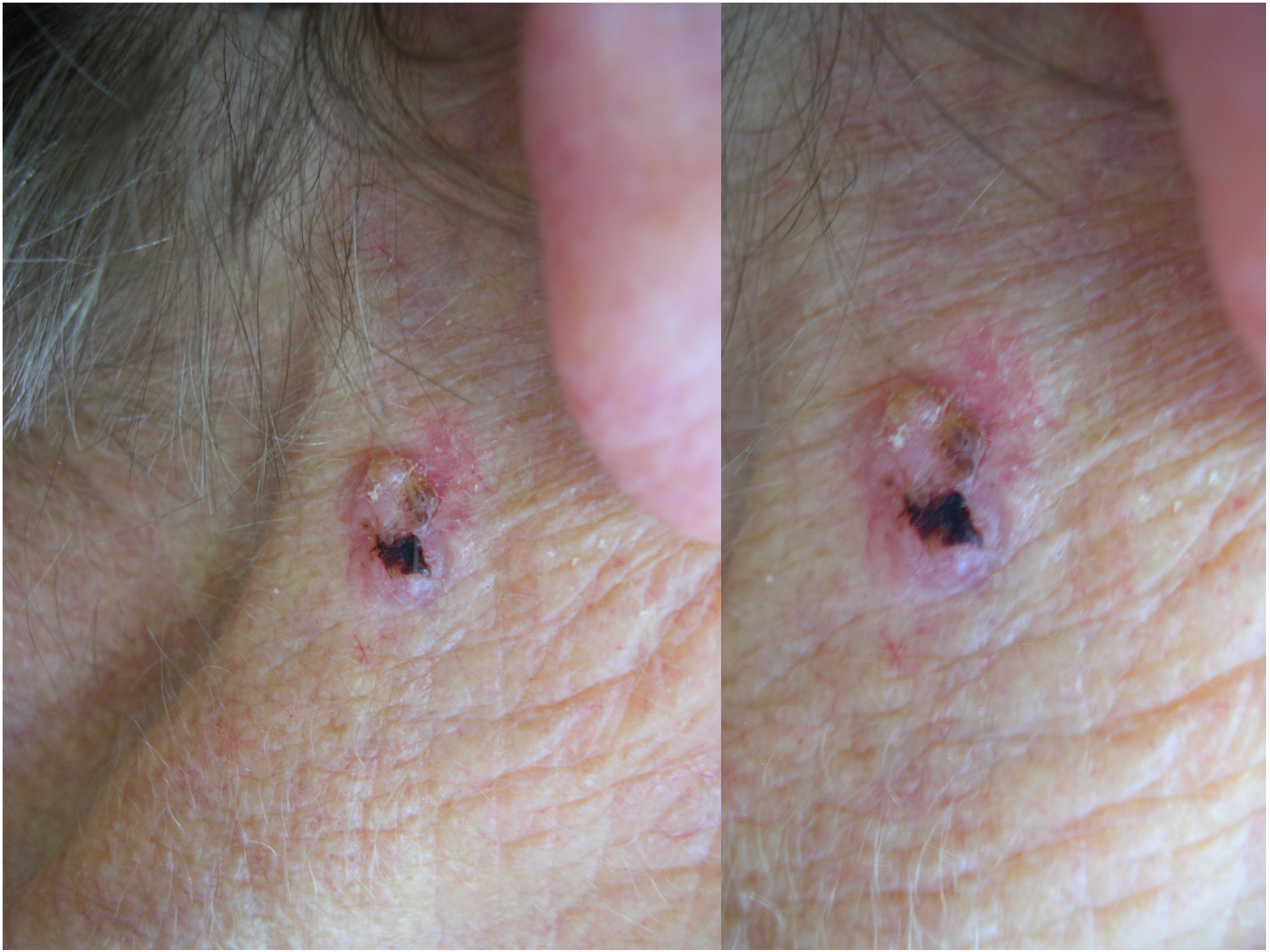
Detection – full skin examination

Non-melanoma skin cancer detection

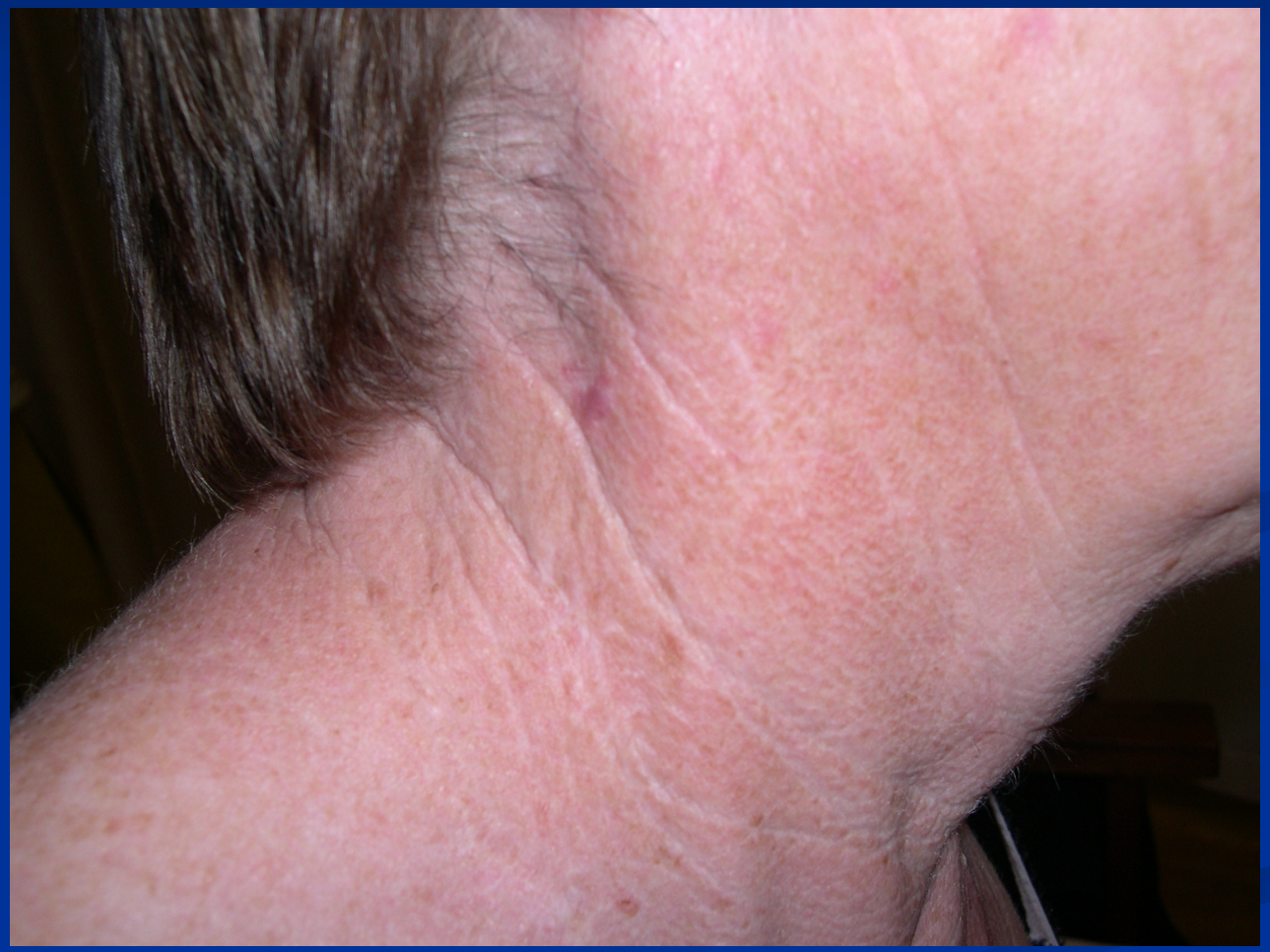
- Awareness of risk factors e.g. sun exposure, fair skin, immunosuppression
- Anatomical site bias
  - Bowen's disease leg
  - Superficial BCC back / torso
  - BCC head and neck, inner canthi, eyelids, retroauricular
  - SCC hands, forearms, upper face, lower lip
- Clinical features

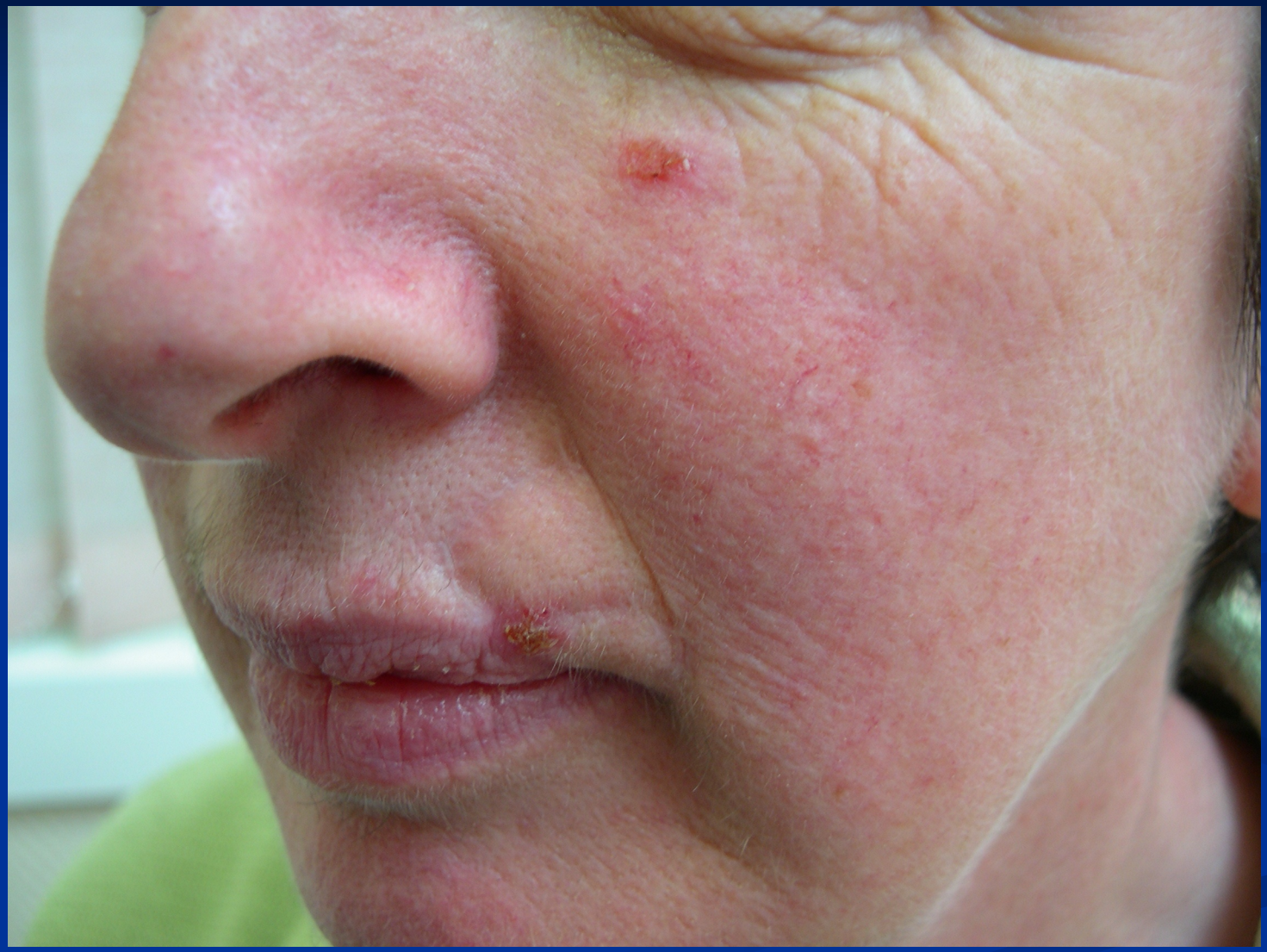
BCC Clinical features vary

- Site – less direct sun sites, very rare on palms, soles
- **Translucent, pearly**, raised, few dilated superficial blood vessels
- +/- pigment flecks
- Erythematous **lichenoid** papule / plaque
- Small, superficial ulcer like excoriation
- Pedunculated, **telangiectatic** like pyogenic granuloma
- **Well-marginated** expanding nodule / thickened plaque
- Morpheic – ill-defined margin, firm palpation, smooth surface, yellowish ivory colour, flat
- **Slow evolution**

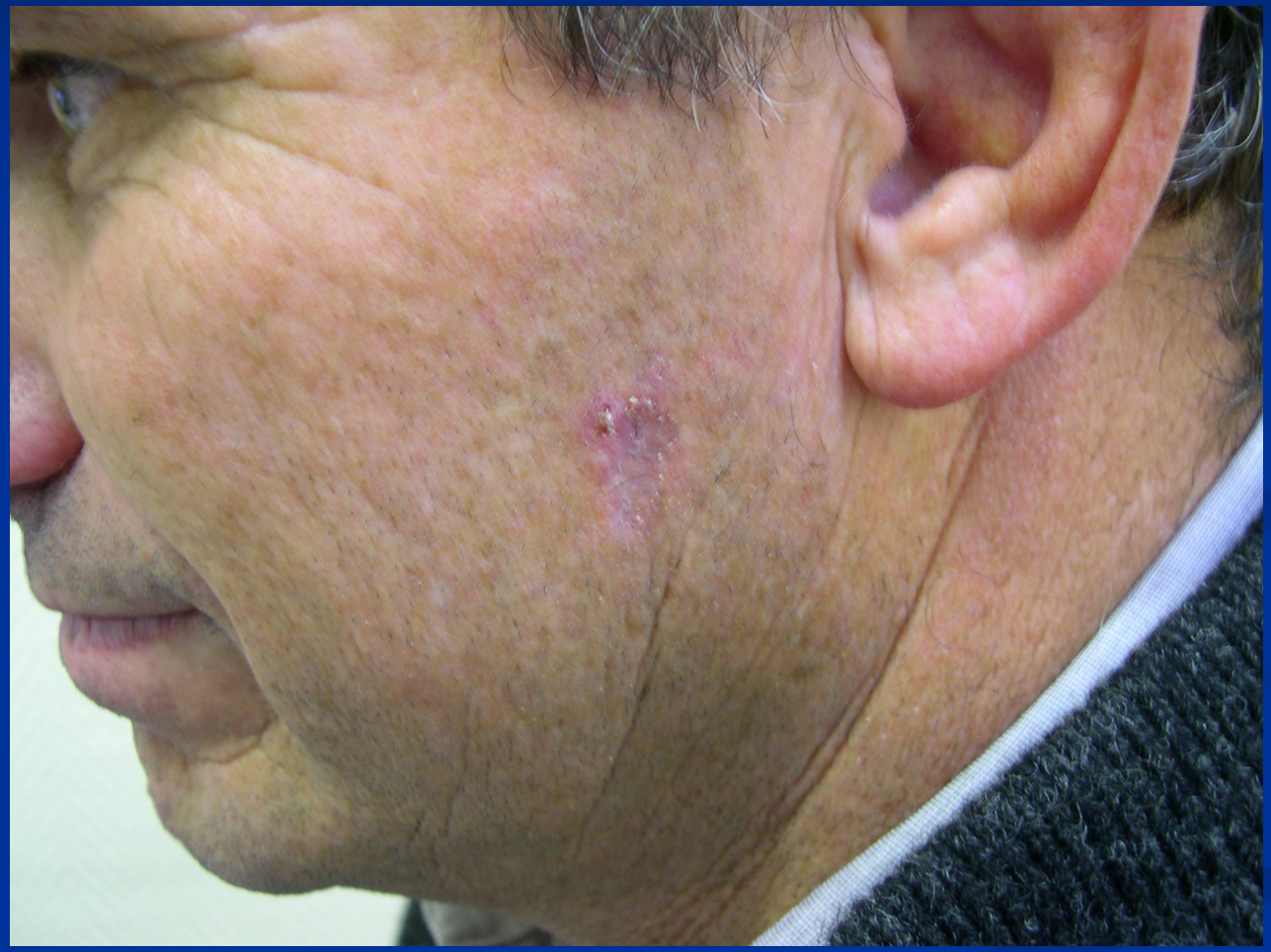


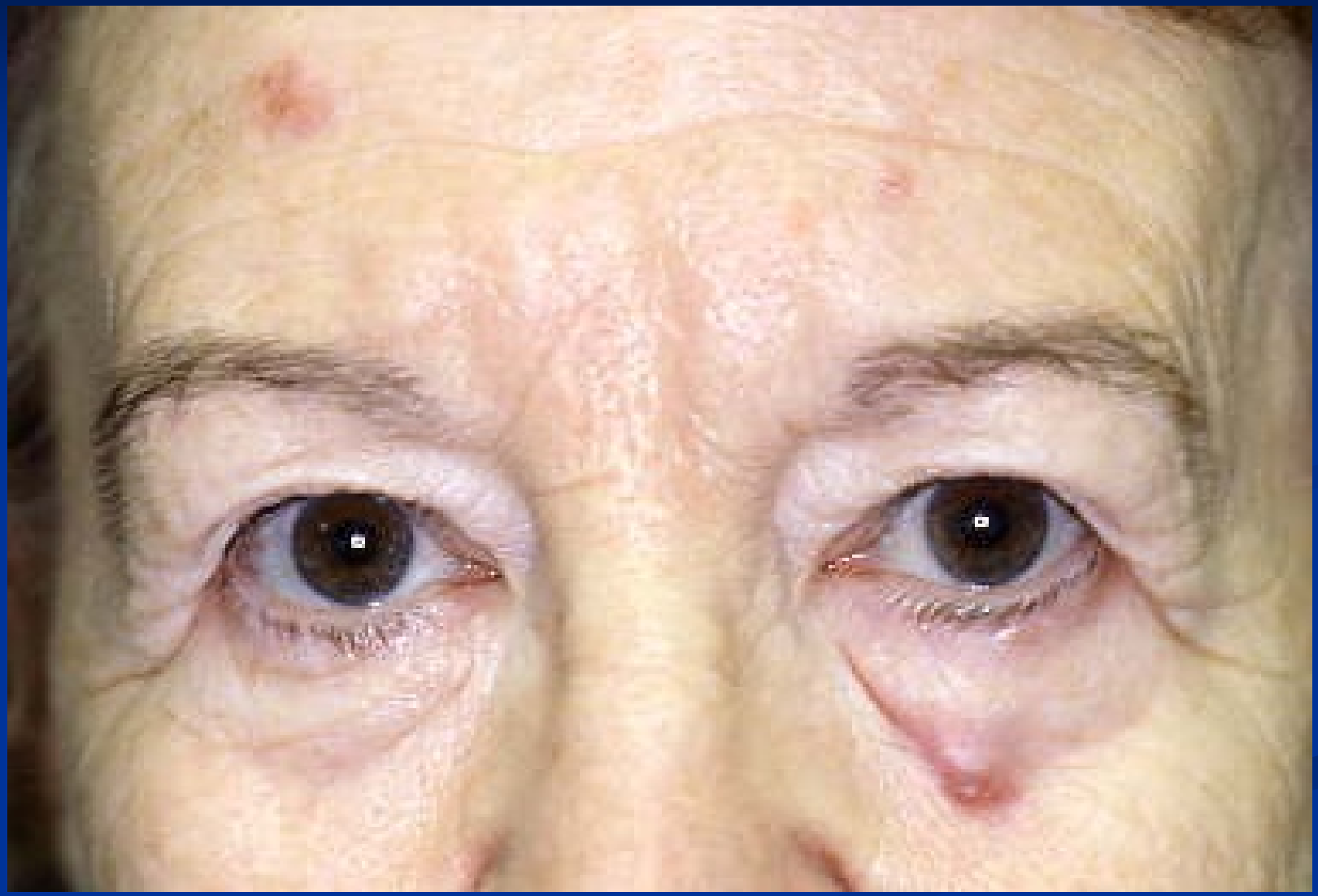
Neck BCC
actinic damaged skin

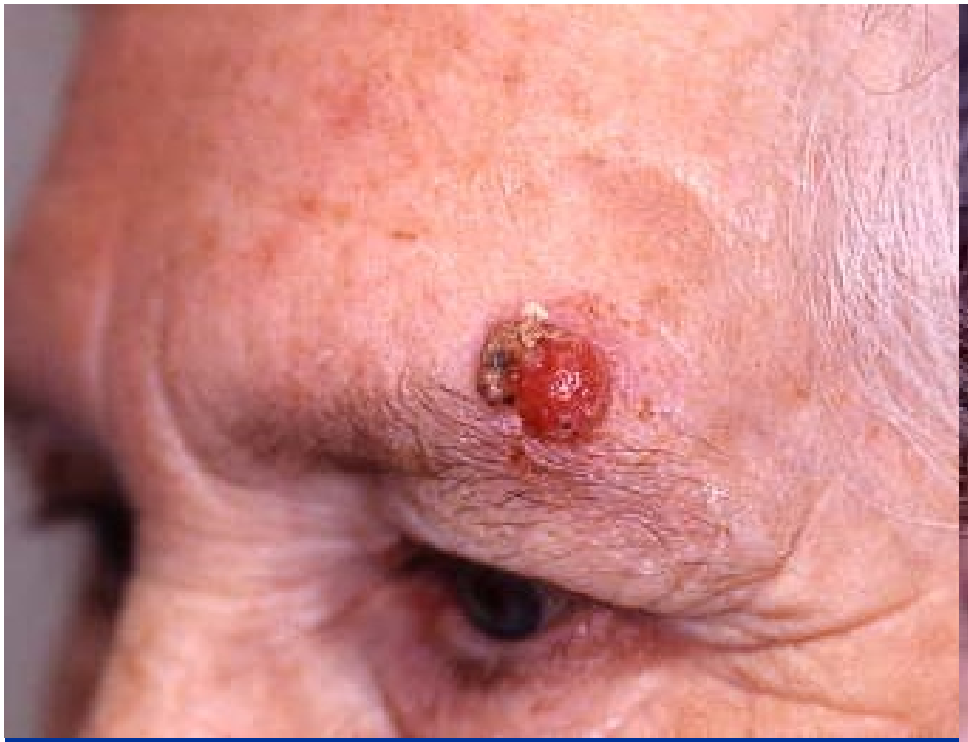


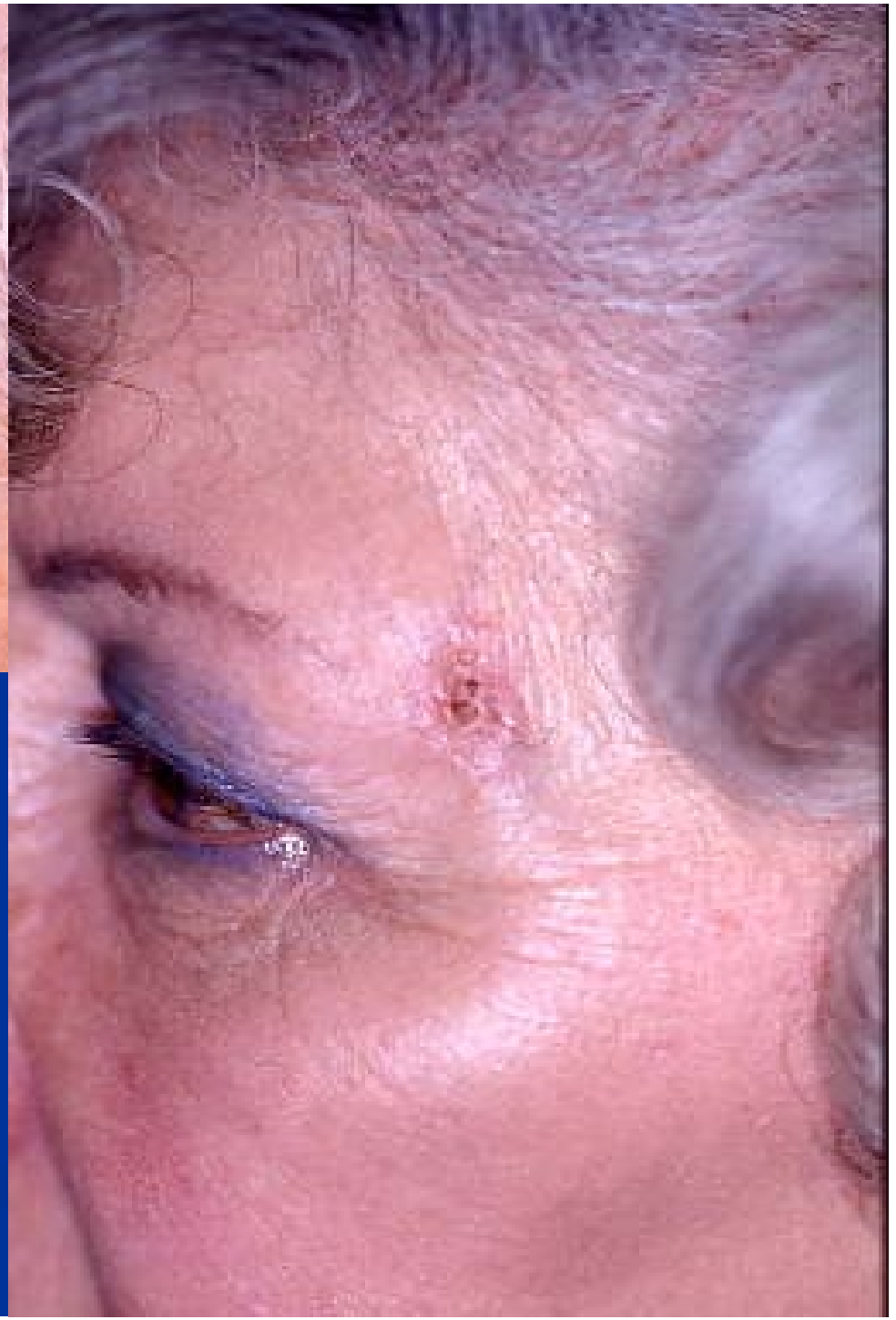


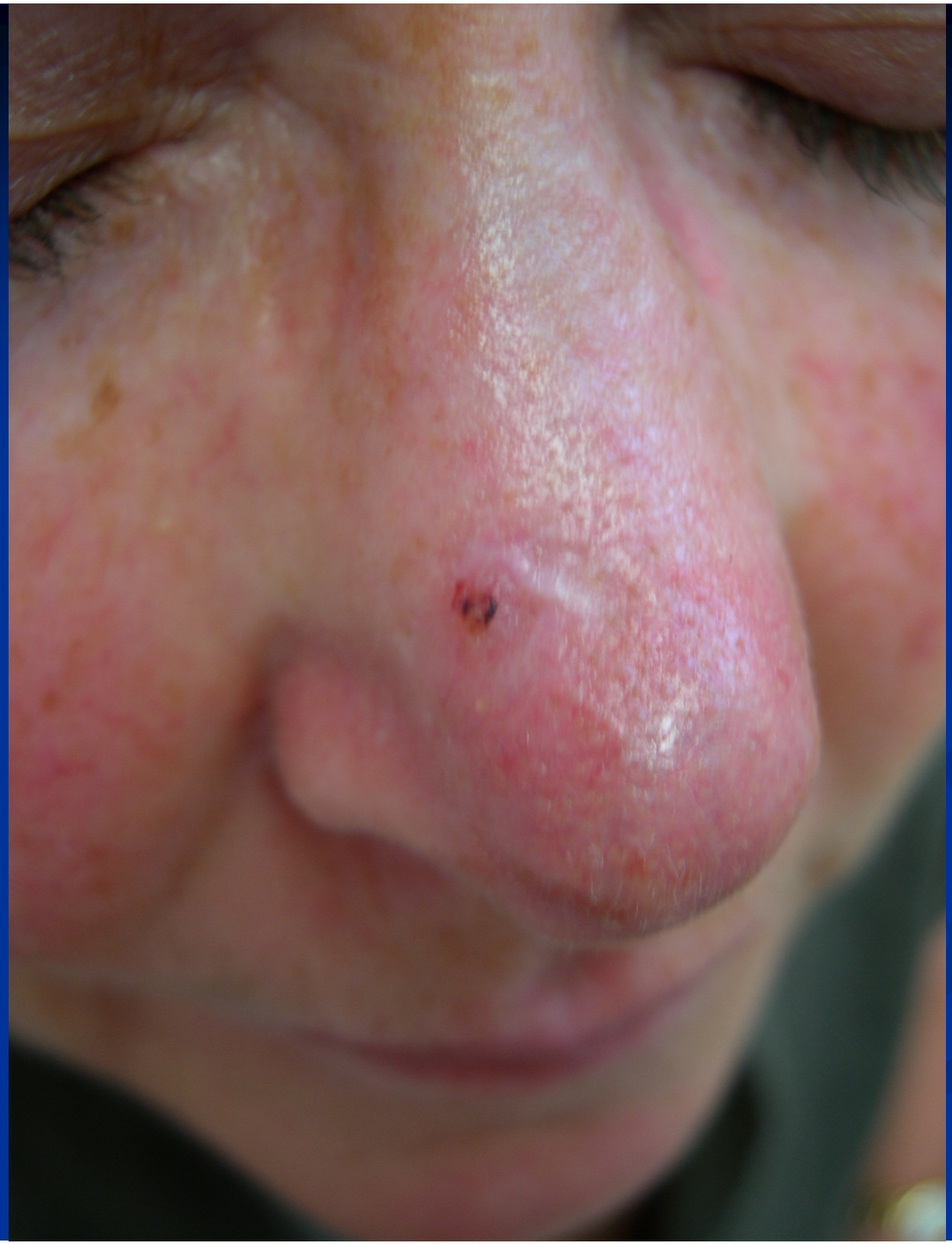
Morpheic BCC

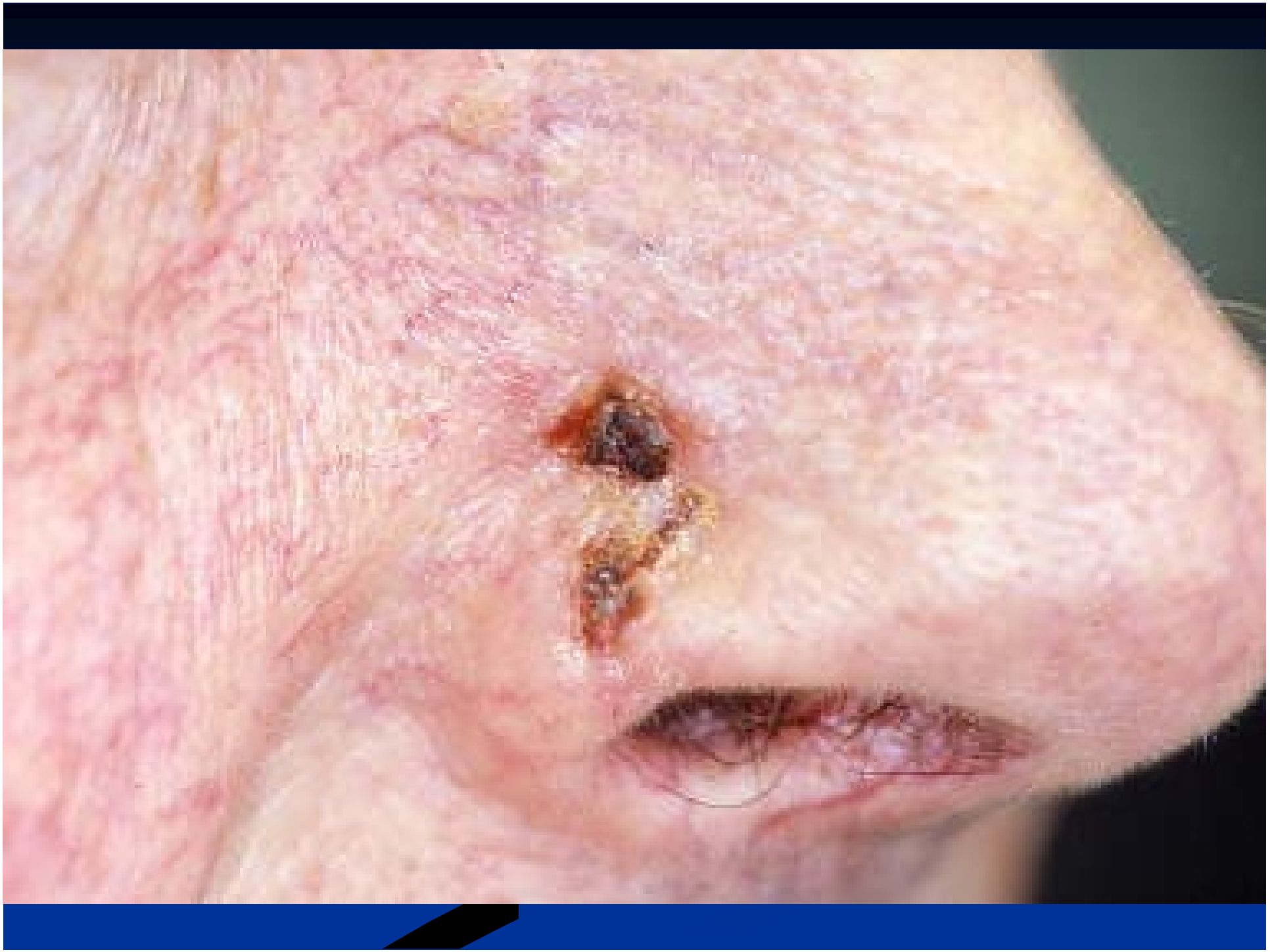




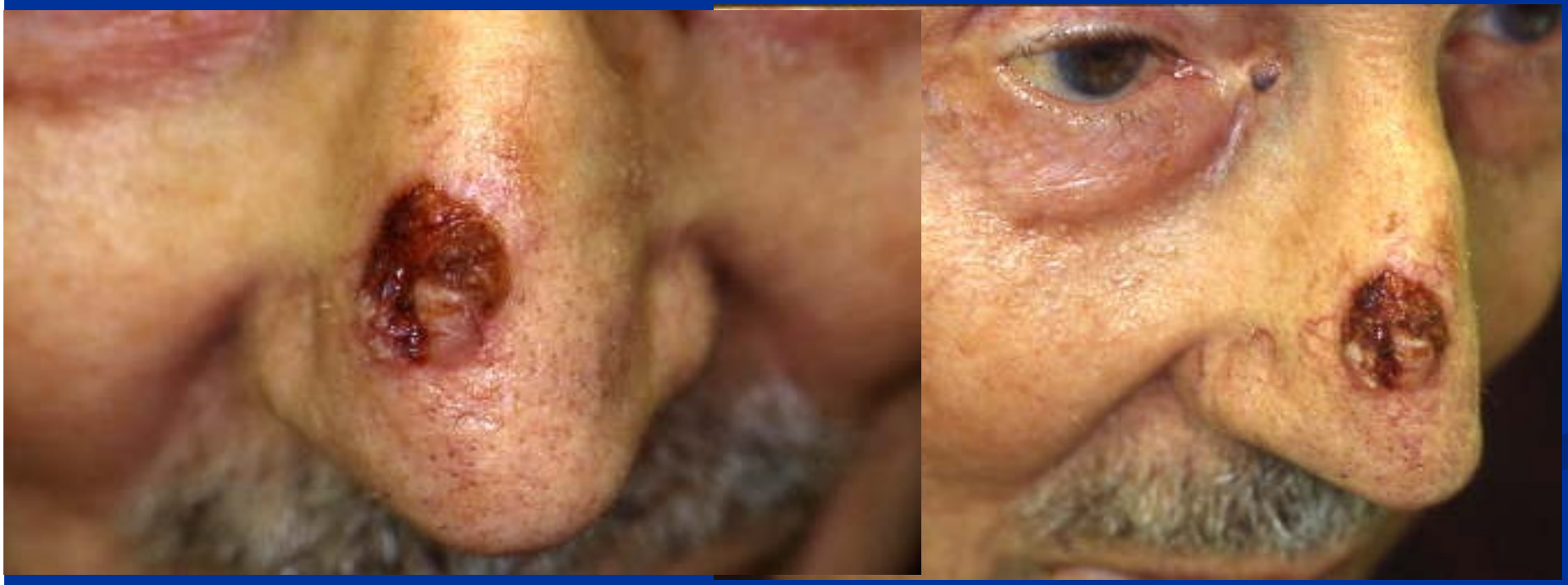




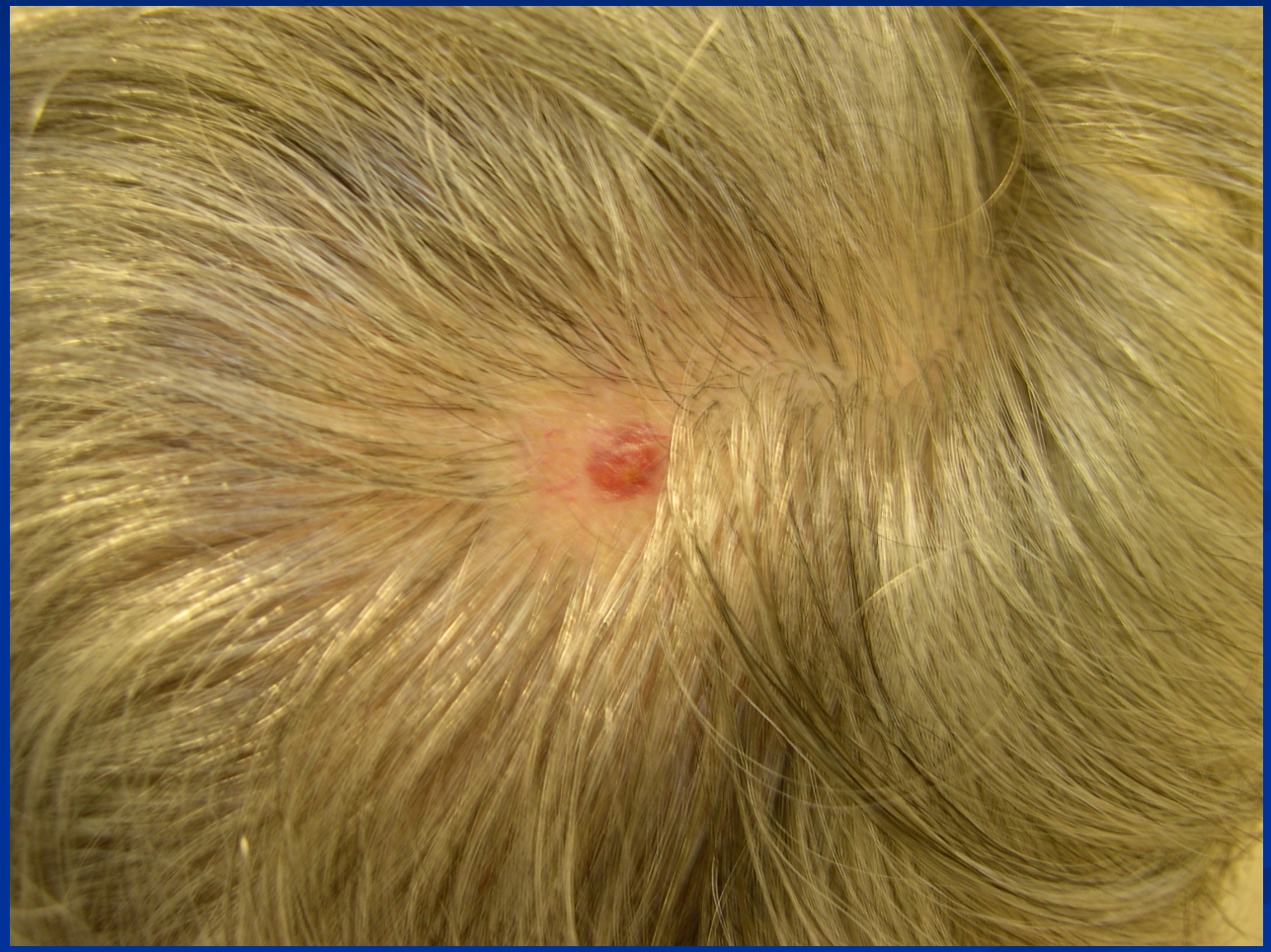




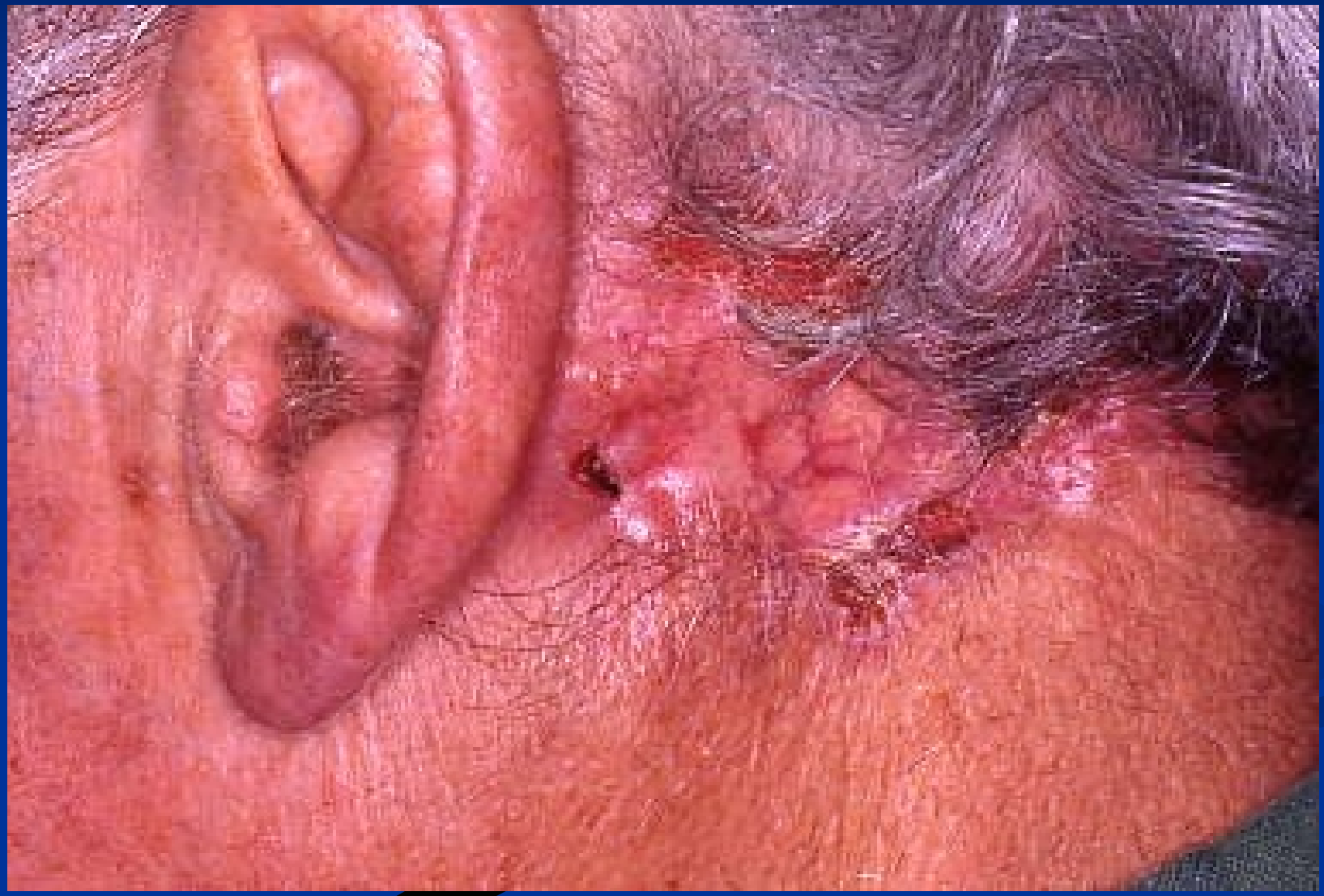
Ulcerated BCC



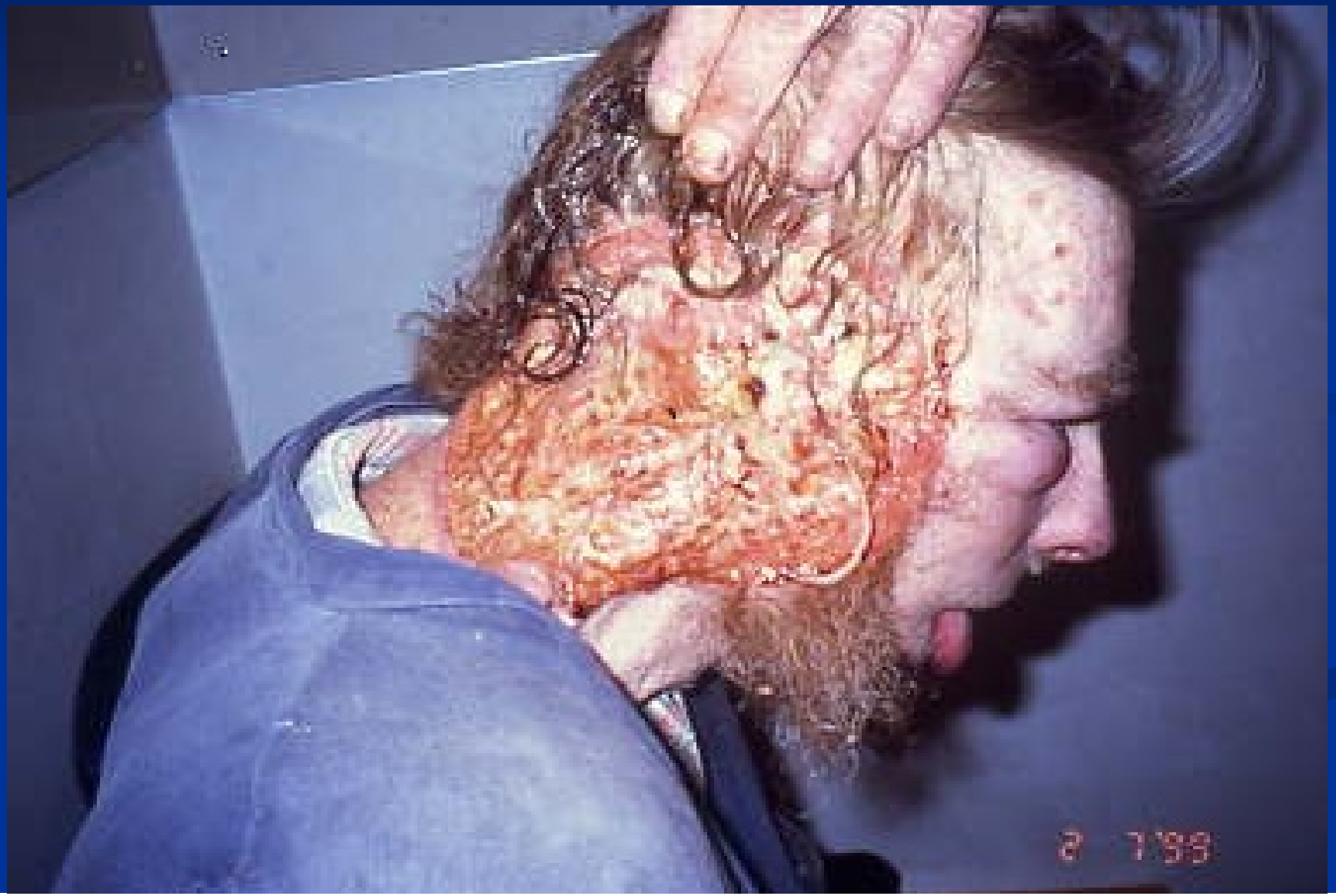
Scalp BCC



Retroauricular invasive BCC

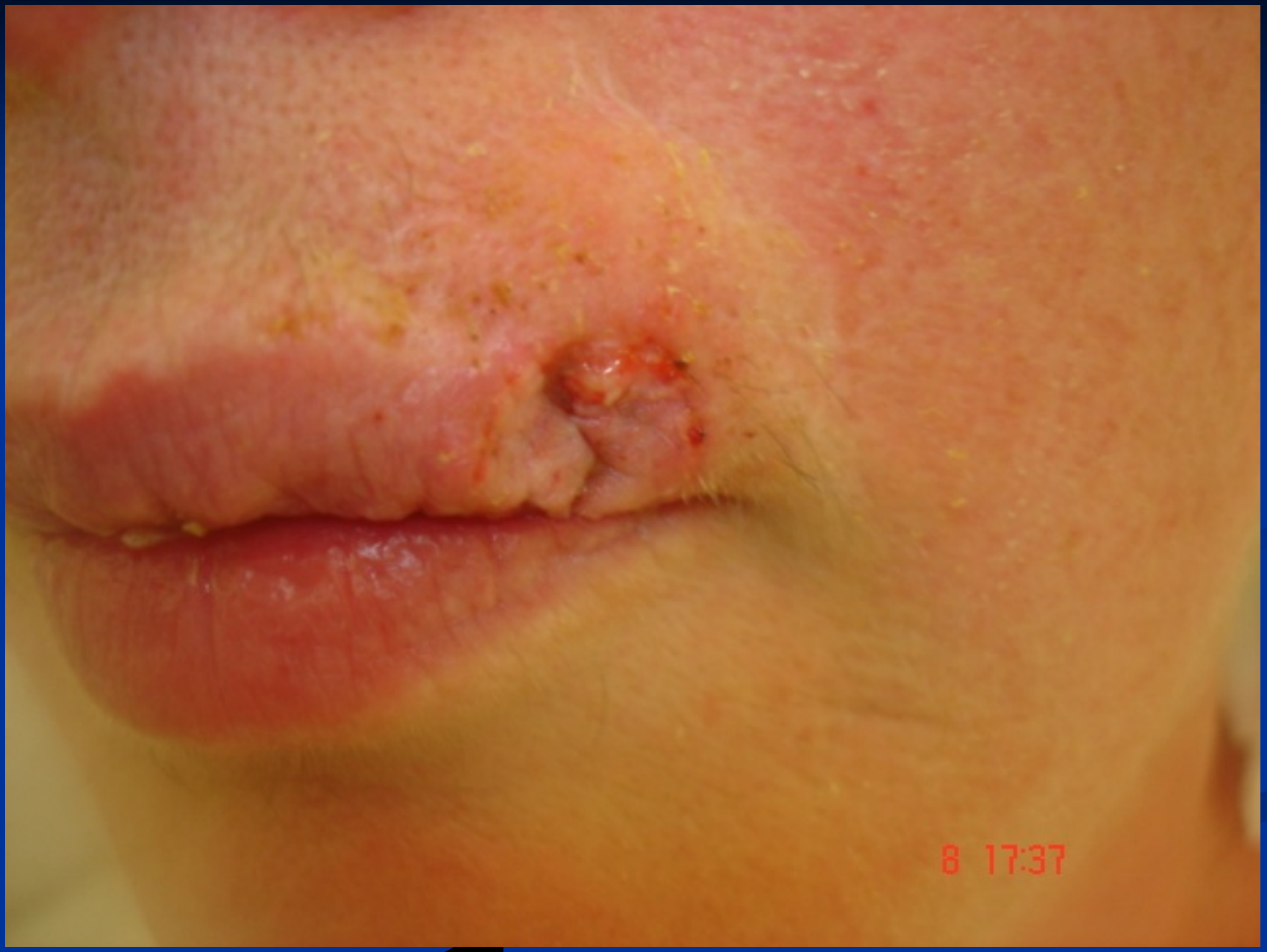


Neglected BCC



SCC clinical features

- Site – most exposed to direct sun
- Typically **arise in sun-damaged skin**
- **Induration**
- Plaque-like, verrucous, tumid or ulcerated
- **Indistinct** peripheral **margin**
- **Surrounding tissue inflamed**, edge opaque yellowish-red
- +/- keratotic crust, erosion, ulcer
- Lip / genitalia – fissure or small erosion failing to heal / recurrent bleeding often presenting sign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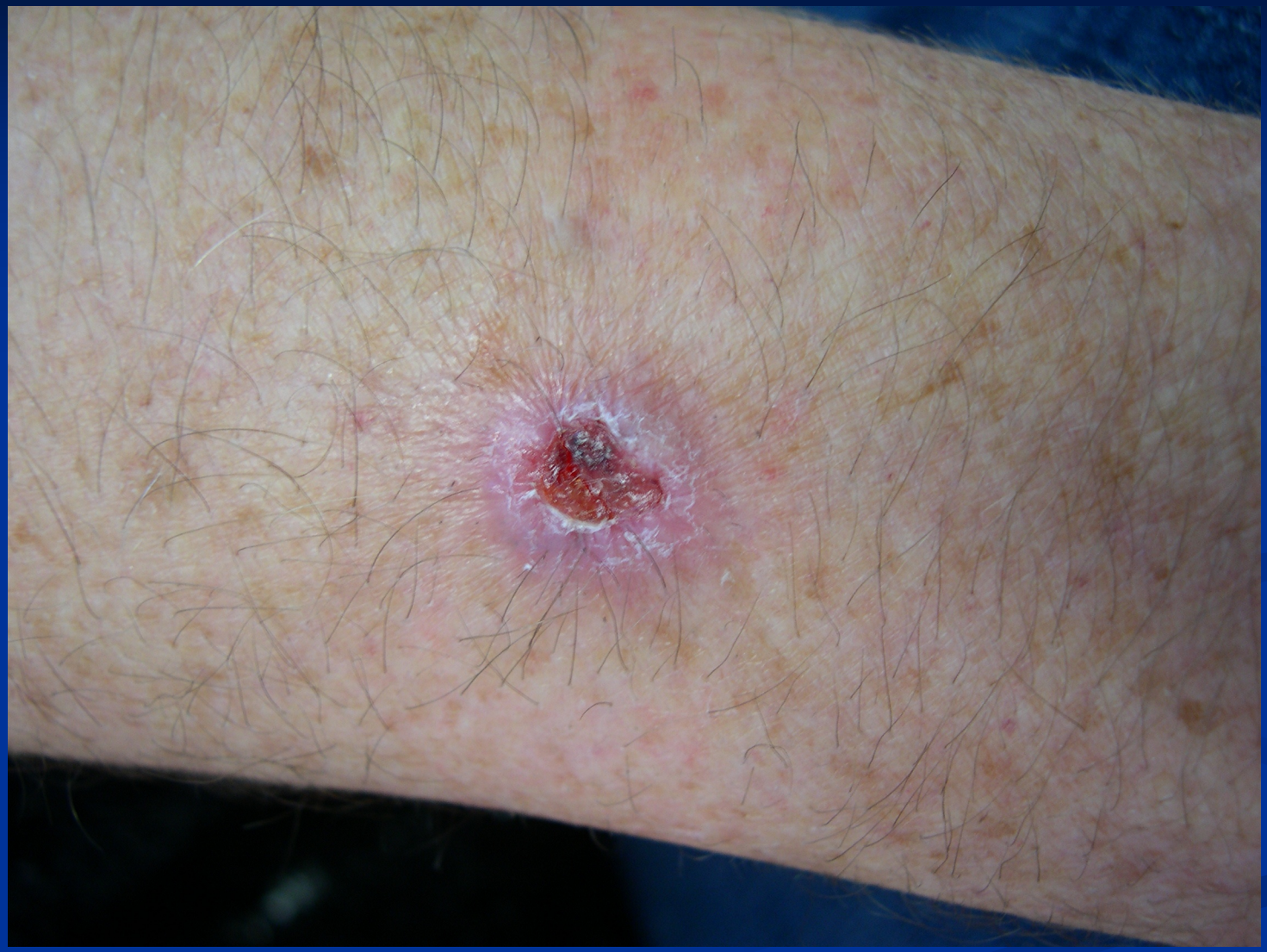
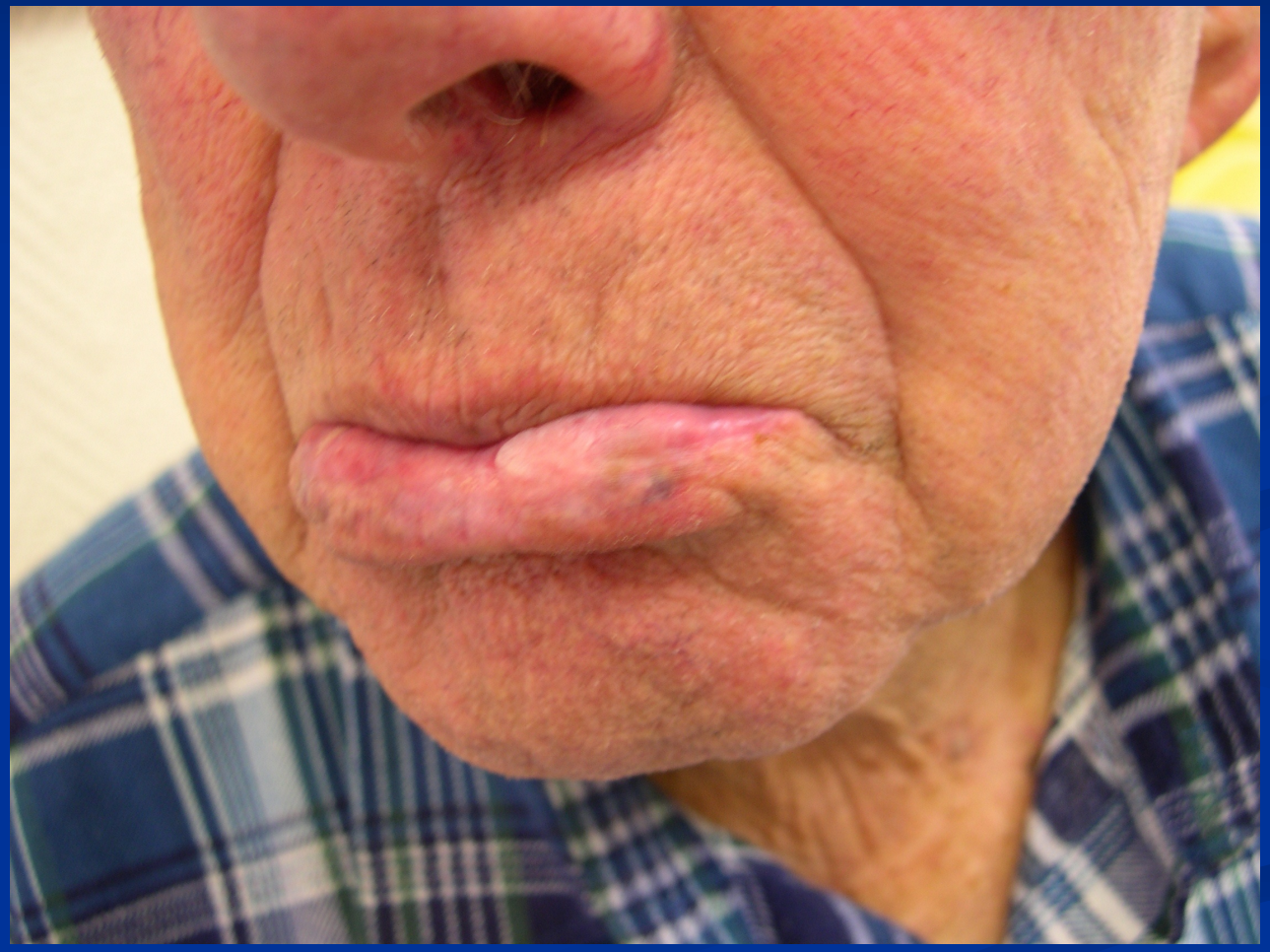
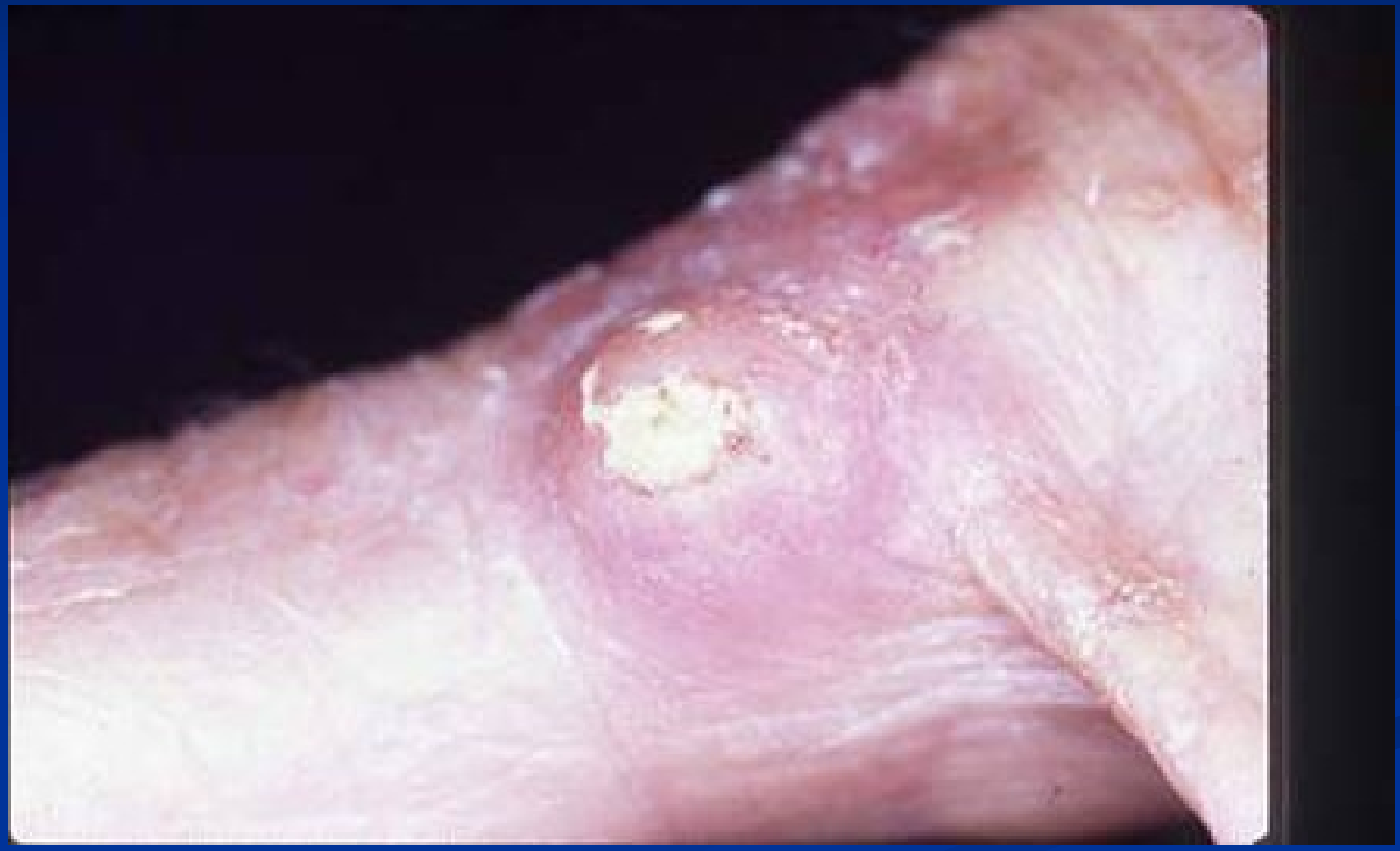


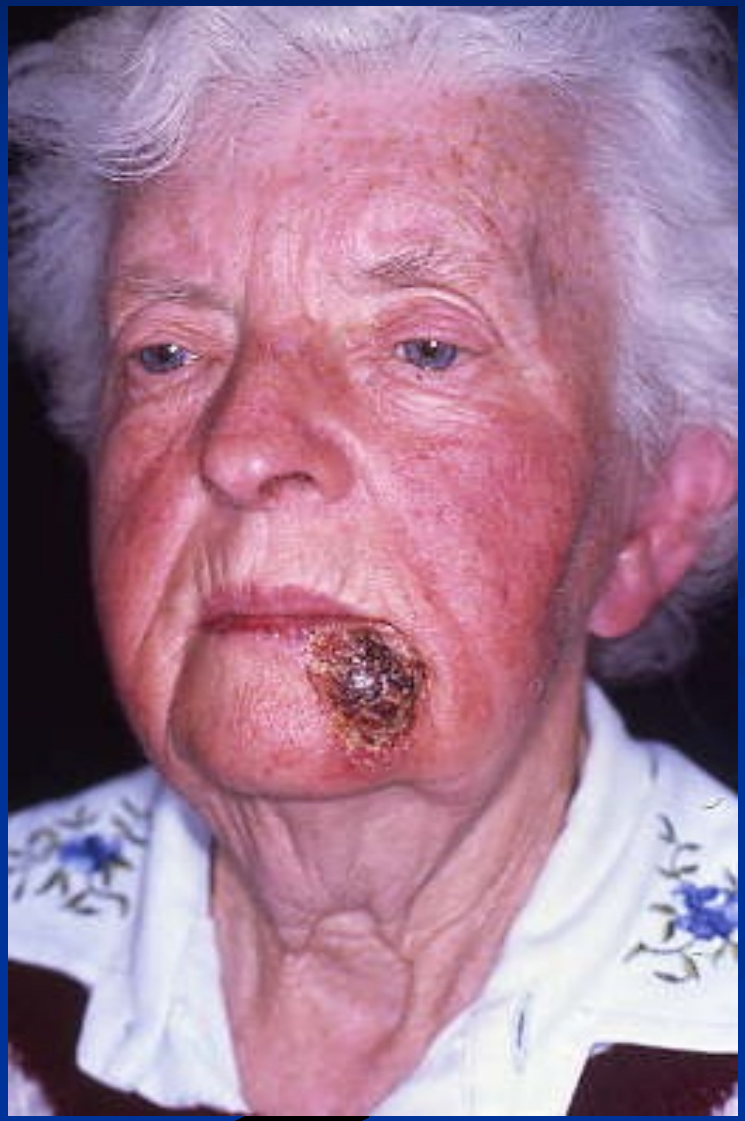
SCC lower lip, thick “leukoplakia”



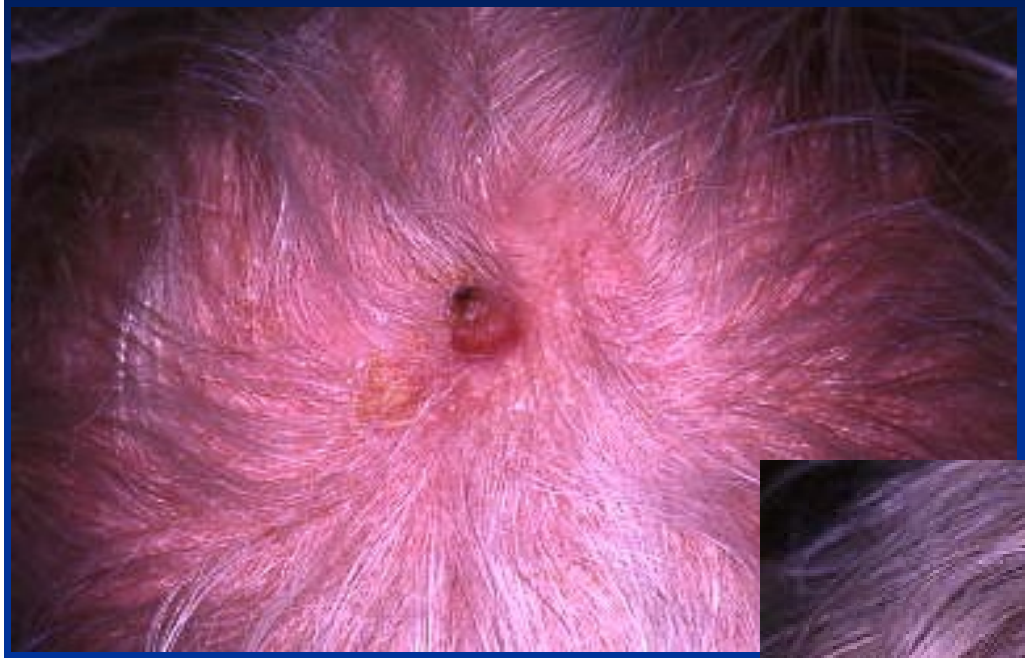
Keratoacanthoma well differentiated SCC

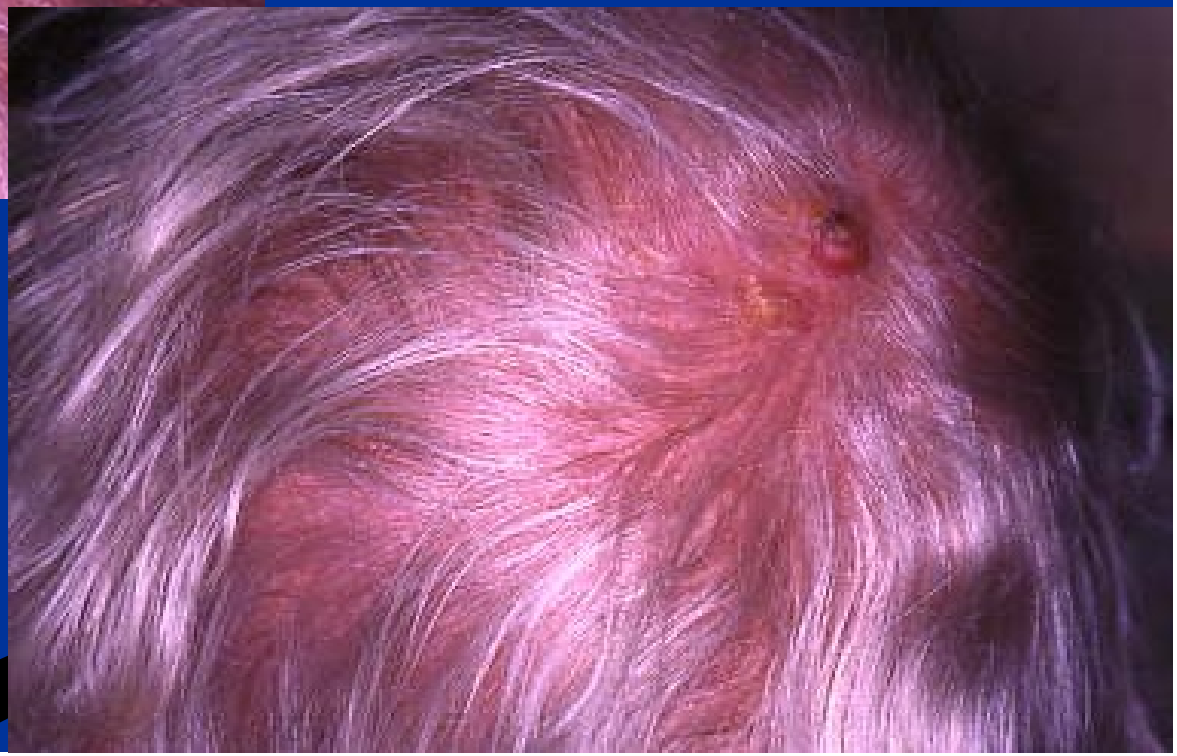


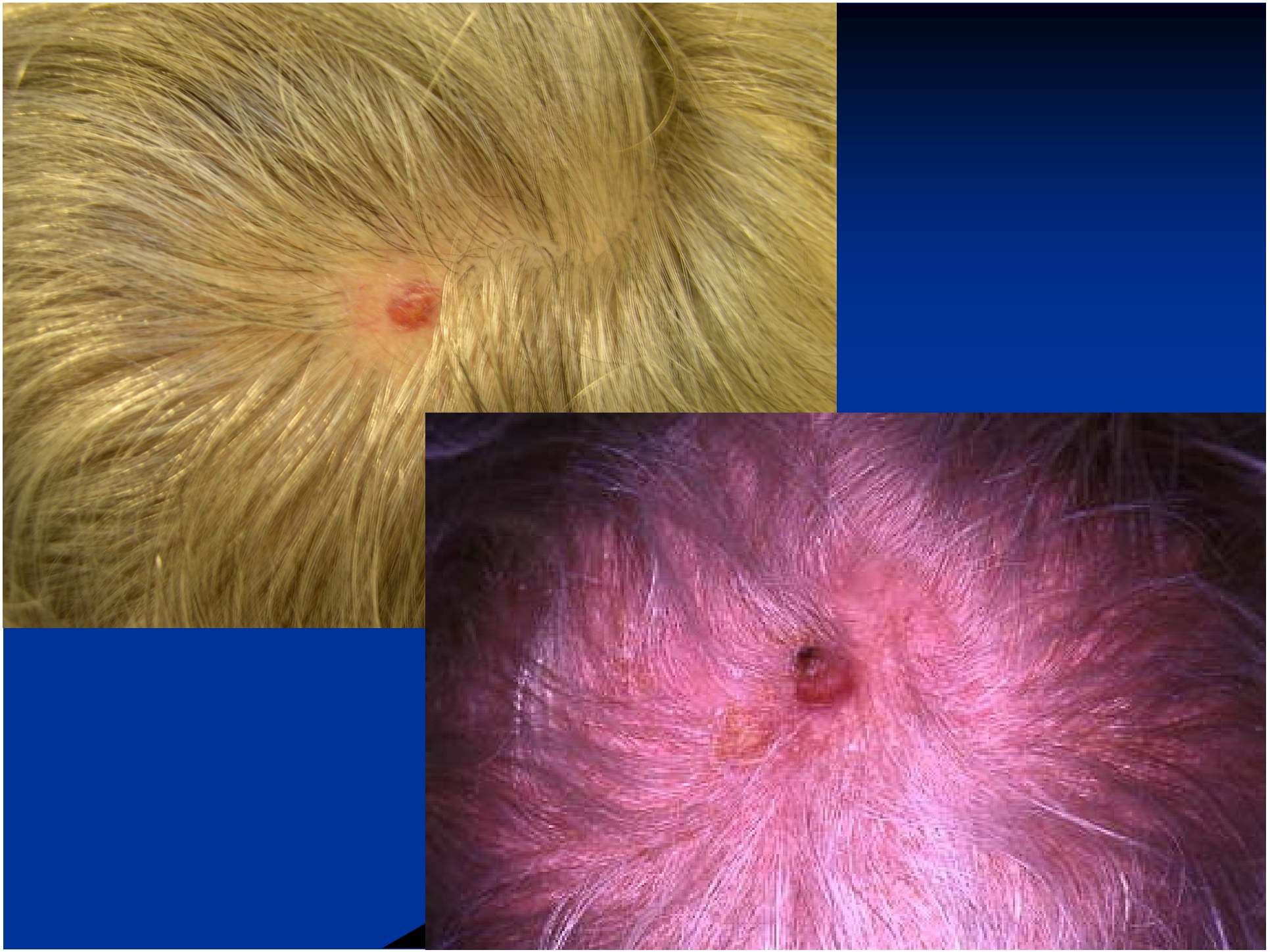
Well differentiated SCC / keratoacanthoma



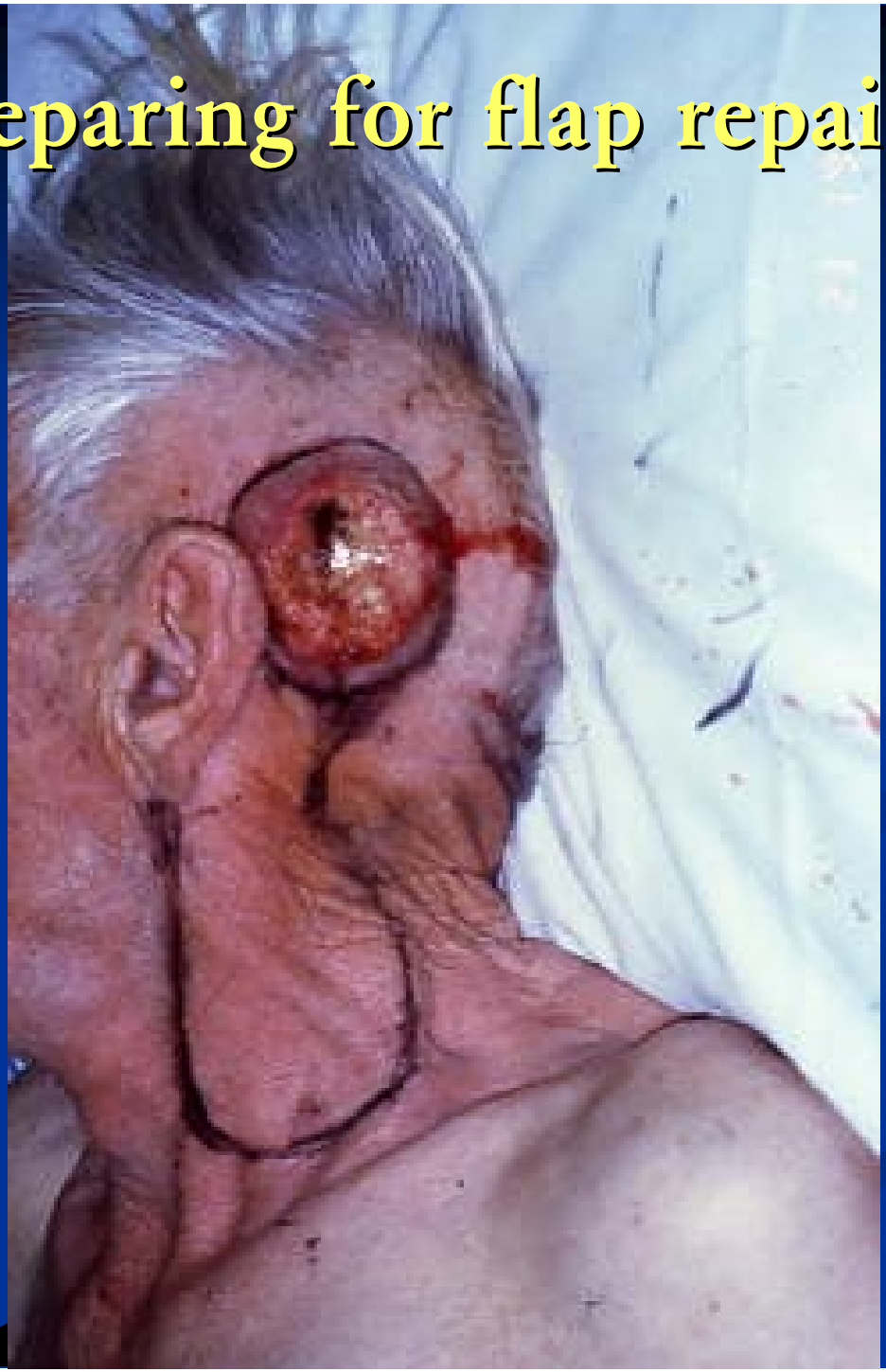
SCC Scalp





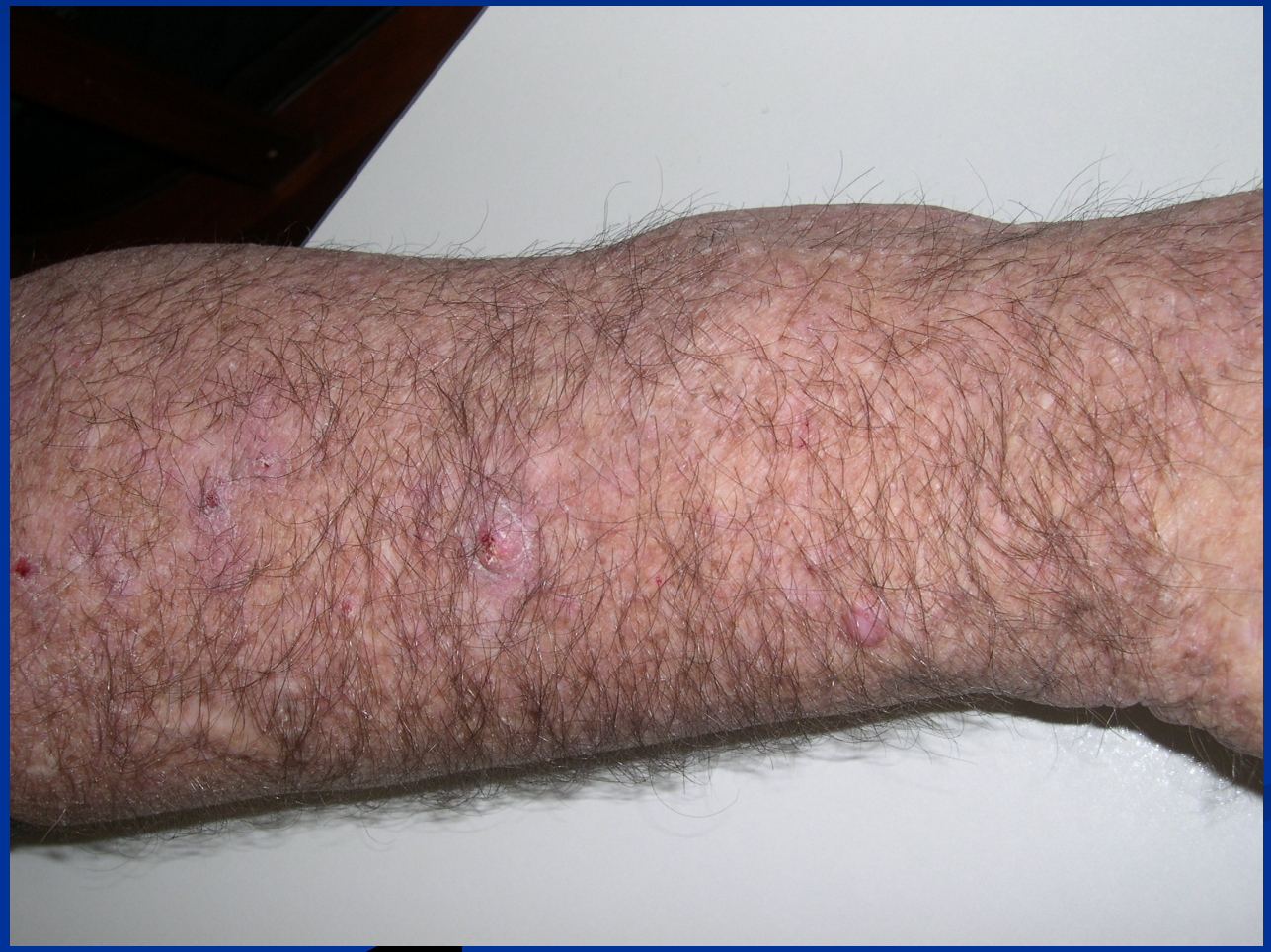


SCC preparing for flap repair



Renal transplant patient forearm

SCC, KA, actinic keratoses



Treatment

- Remove or destroy primary tumour
- Prevent metastasis from SCC
- Secondary prevention

BCC skin cancer surgery

- BCC < 2cm well defined edge
  - 3mm surgical margin 85% tumour clearance
  - 4-5mm surgical margin 95% tumour clearance
- Larger tumours require wider margins
- Consider Moh's surgery referral for:
  - High risk sites e.g. nose, periocular, nasolabial fold
  - Tumours > 2cm
  - Morpheic, infiltrative, micronodular, recurrent

Small, low risk BCCs

- May not require re-excision for incomplete excision on lateral margin if at non-critical site and non-aggressive histology
- Other therapies:
  - Aggressive LN
  - Curettage and cautery
  - Topical therapies e.g. imiquimod e.g. superficial BCC
  - Photodynamic therapy (PDT)

SCC

- Surgery for
  - High risk SCC <1cm, 4mm surgical margin
  - all SCC > 2cm
- Radiotherapy
  - Large, rapidly growing
  - Surgery would be poorly tolerated
  - Adjuvant
- Consider Moh's surgery
  - All high risk SCCs

low risk SCC

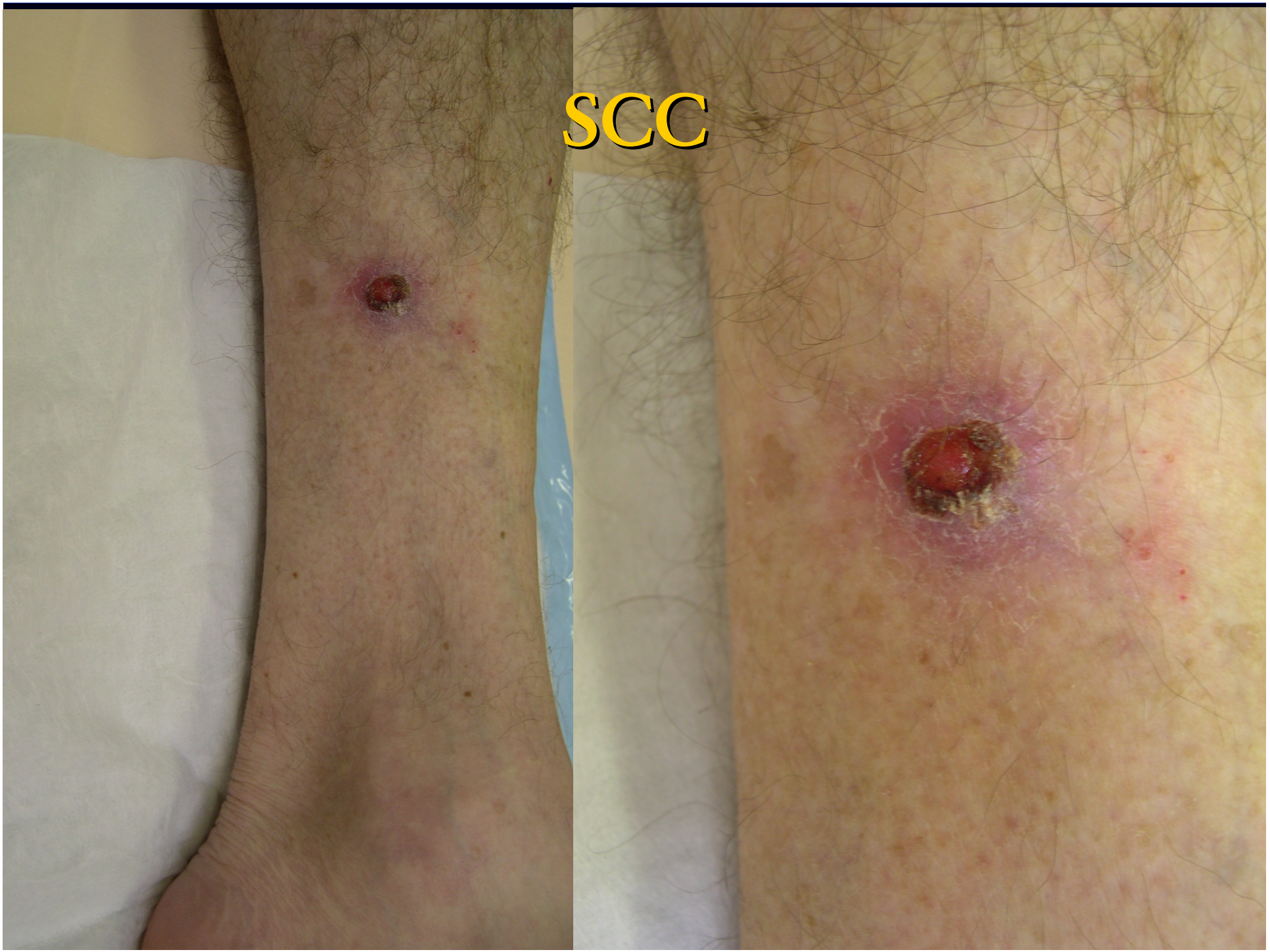
- <1cm
- Slow growing
- Sun damaged skin

high risk SCC

- >2cm
  - 2x risk recurrence
  - 3x metastatic risk
- Site: ear, lip, scalp, eyelids, nose
- Non-exposed sites
- SCC arising from scars, ulcers, injury
- Histology: depth, poor differentiation, perineural involvement

Non-surgical options

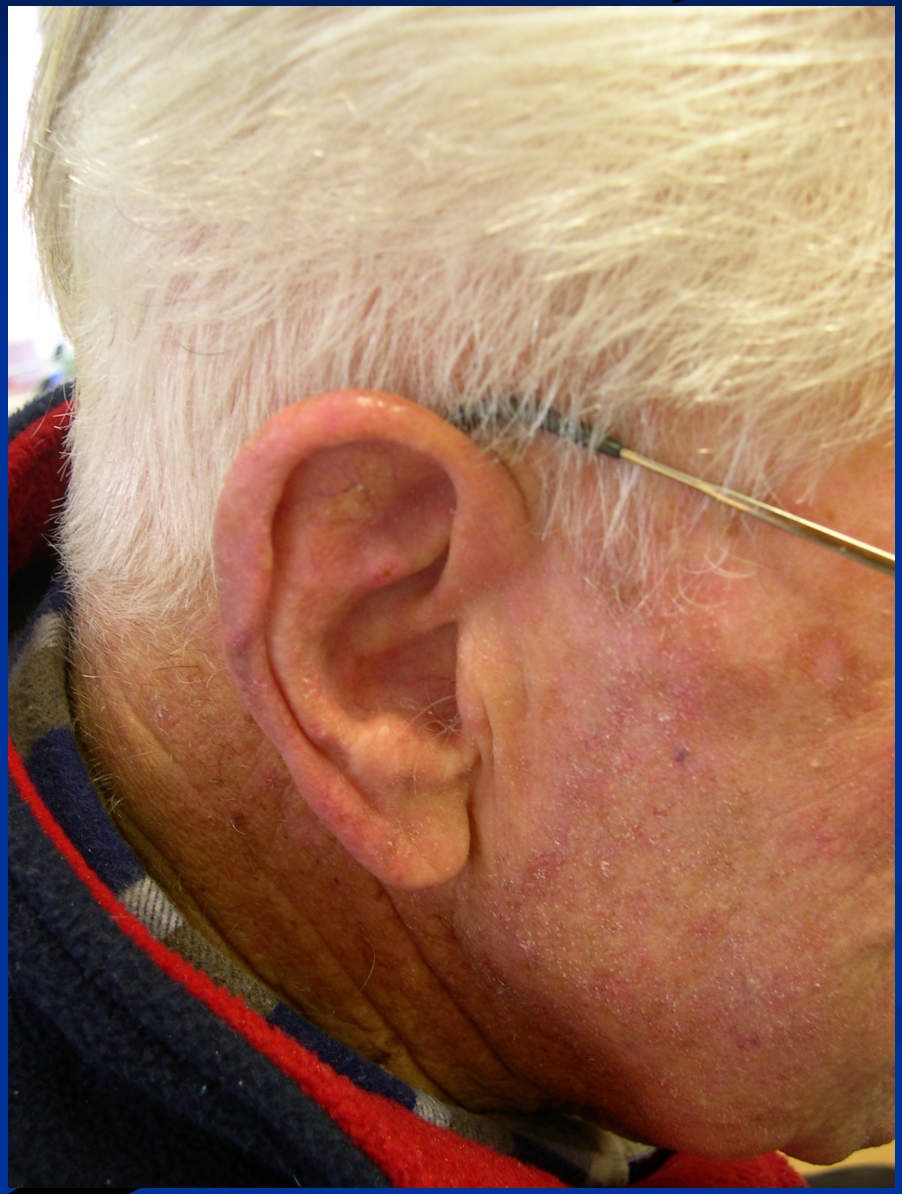
- For minor lesions
- When surgery contraindicated or declined!
- Other therapies:
  - Aggressive LN
  - Curettage and cautery
  - Photodynamic therapy (PDT)
  - Topical therapies e.g. imiquimod e.g. superficial BCC, Efudix, Diclofenac acid, future products e.g. Australian weed →Ingenol mebutate (PEP005)


SCC

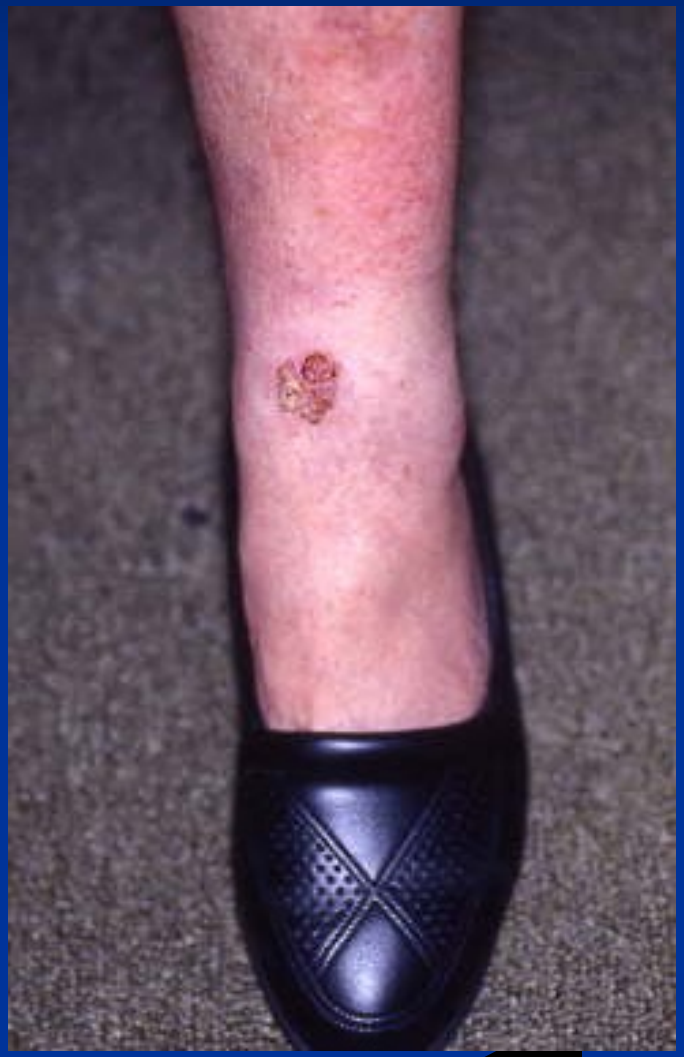
Pre-malignant lesions for SCC

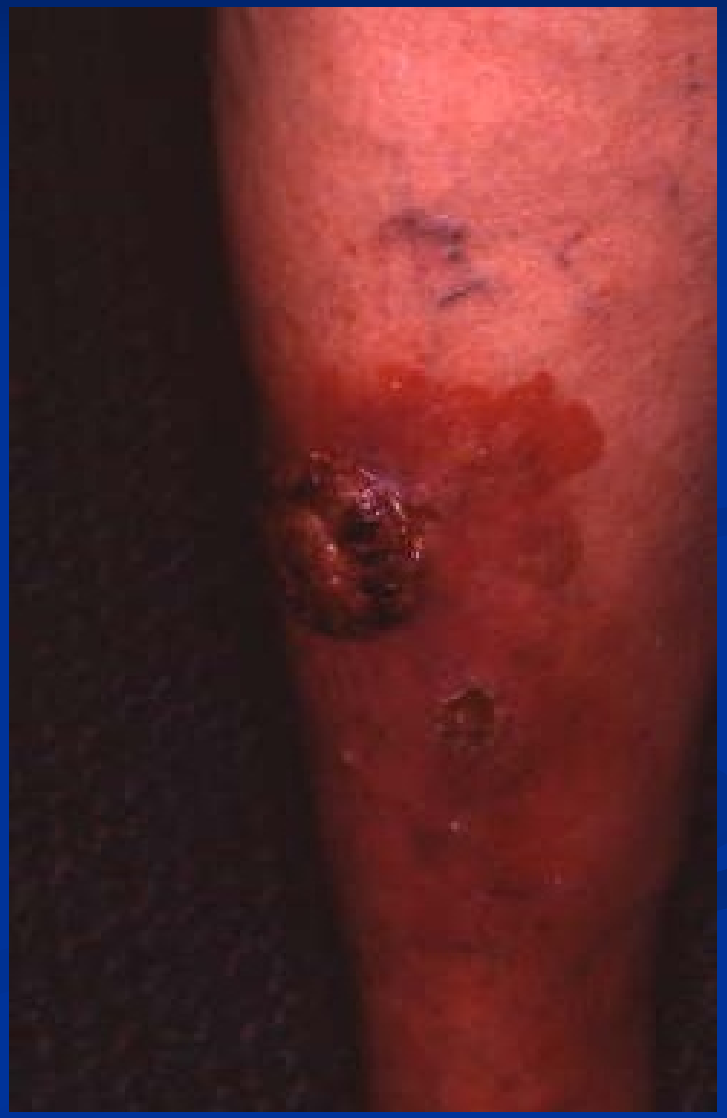
- Actinic keratoses NB if tender
- Bowen's disease
- Cutaneous horn from SCC, SCC-in situ, wart etc
- Actinic cheilitis vermillion border, dry scaling, fissures, adjacent atrophic changes, lip sunburn hx, smoking worsens, lipsticks prevent
- Intraepidermal carcinoma of eyelid margin
  - Looks like wart, eyelash loss, margin nodularity

Facial actinic keratoses, SCC ear

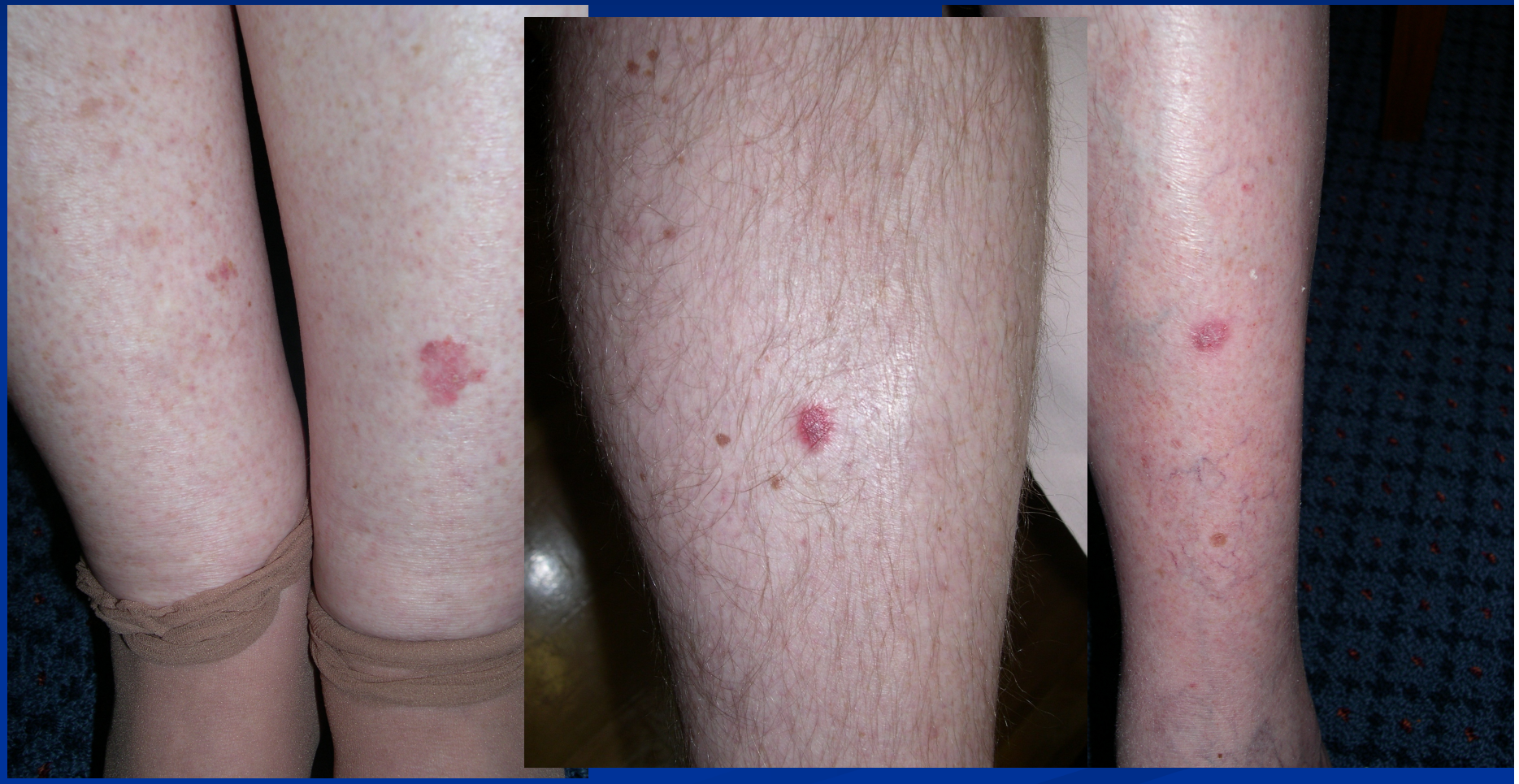


Bowen's disease and well differentiated SCC

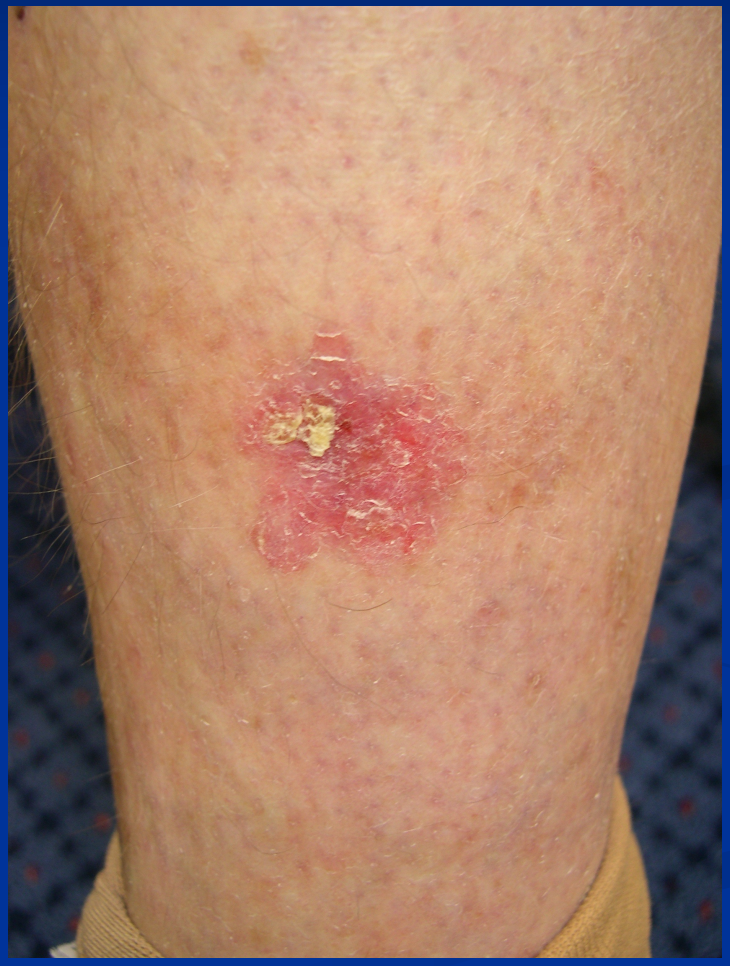




Bowen's disease



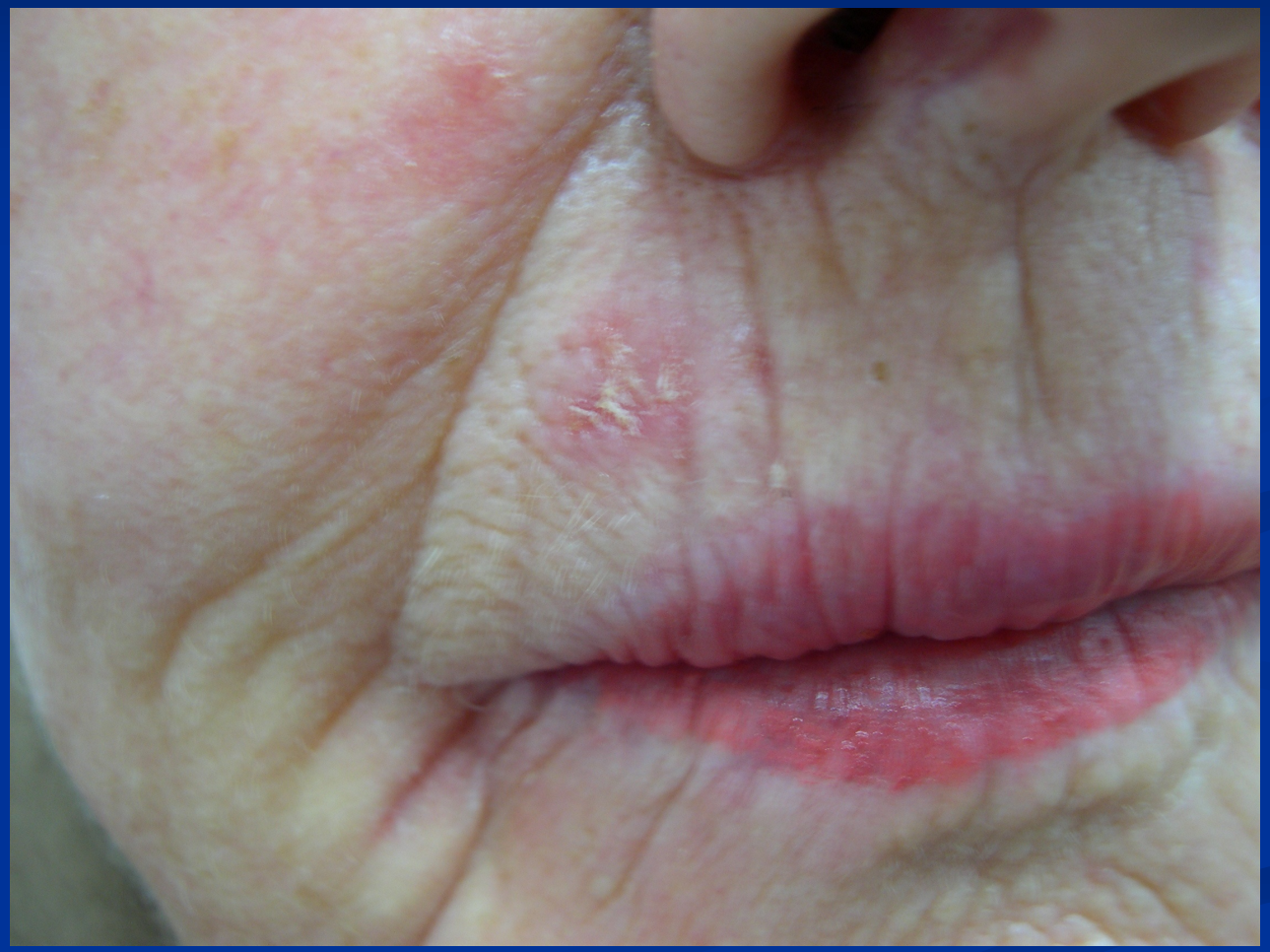
Bowen's disease

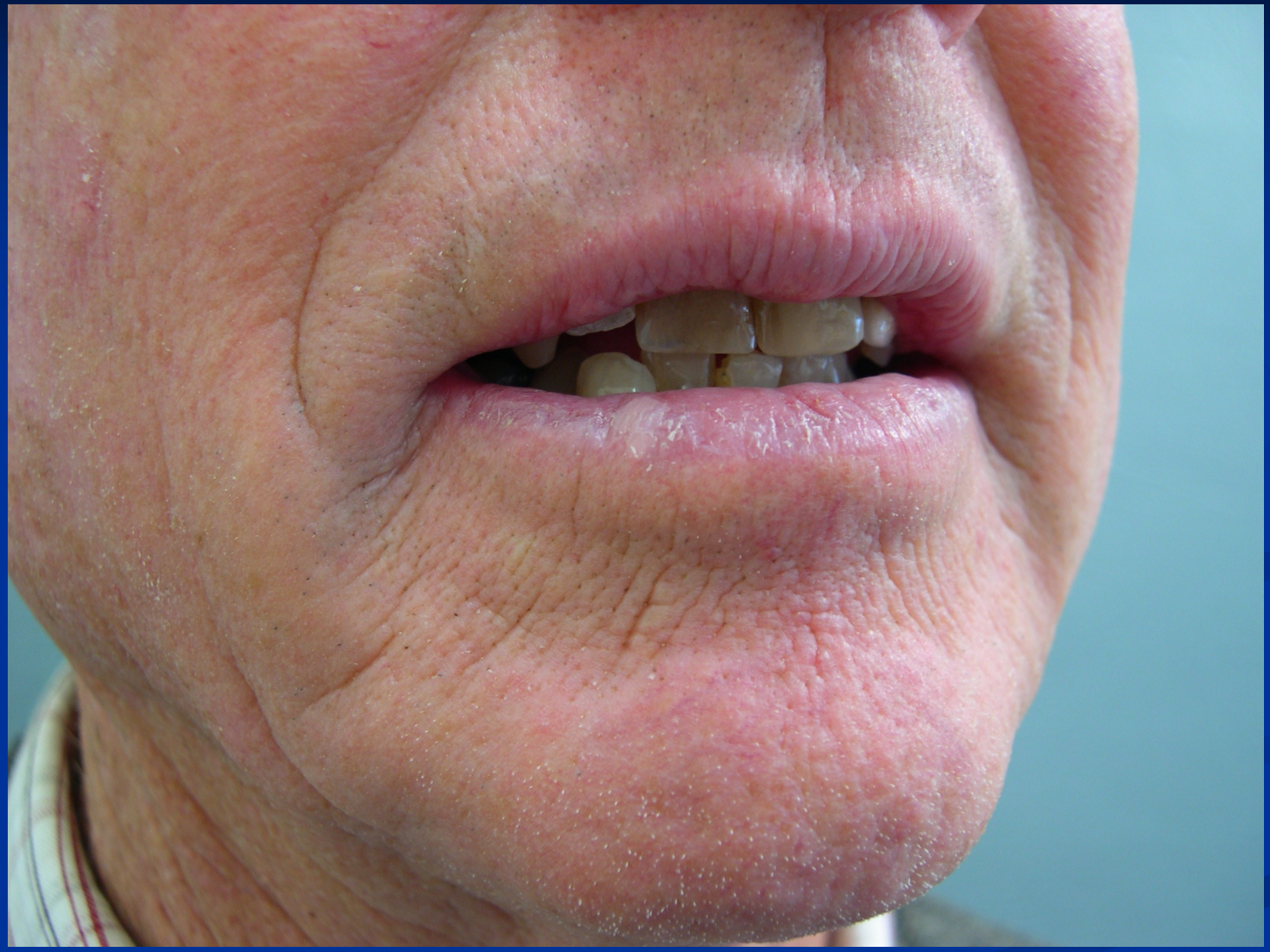


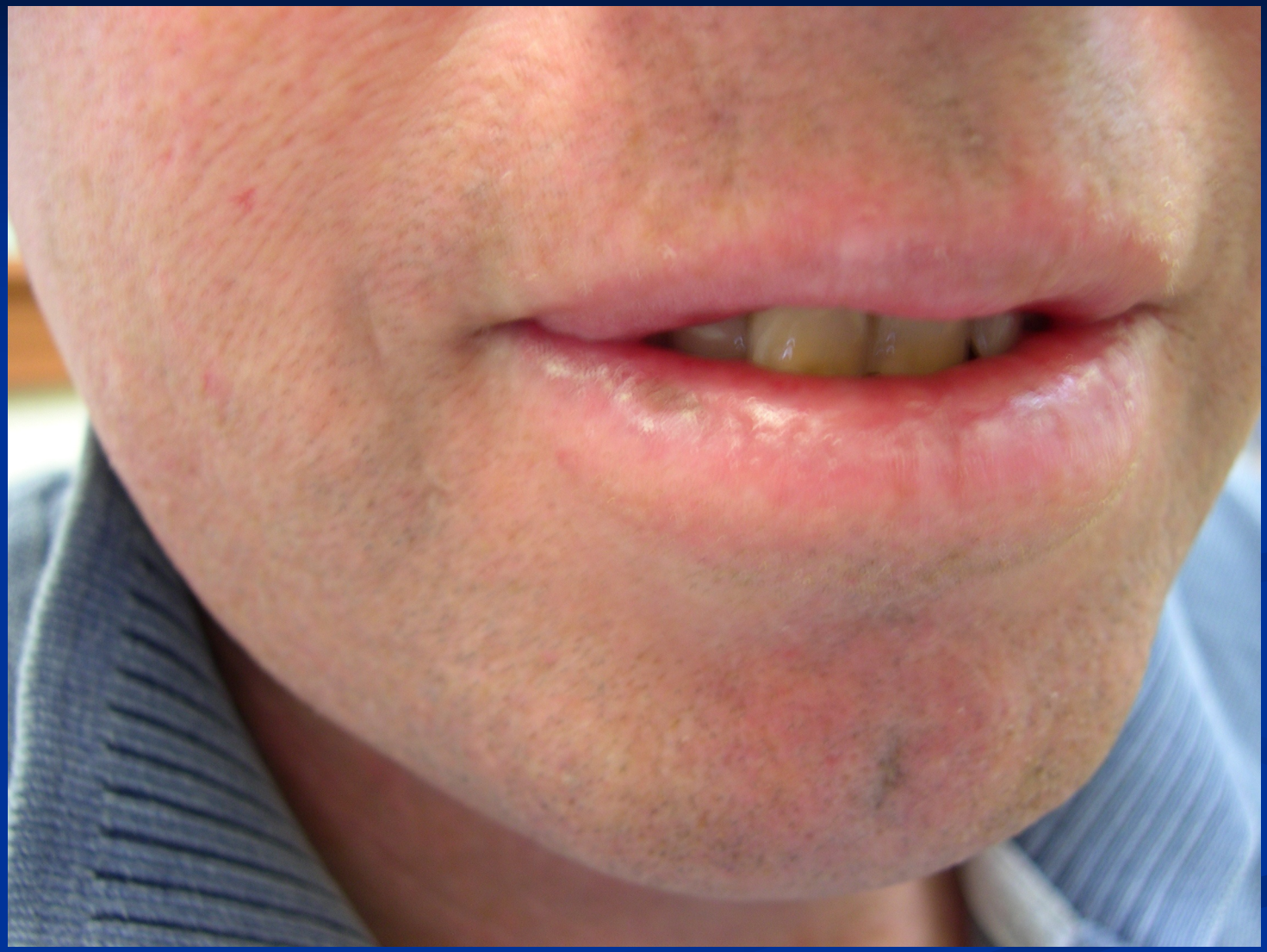
Photodynamic therapy

- Curettage lesion to thin
- Apply photosensitising drug / cream
- Wait, (usu. 3-6 hrs) to allow drug to concentrate in cancer cells
- Blue or Laser light shone on treated area
- ± 2nd cycle of treatment 7 - 10 days later
- Causes sunburn reaction, usu heals in 4-8 weeks

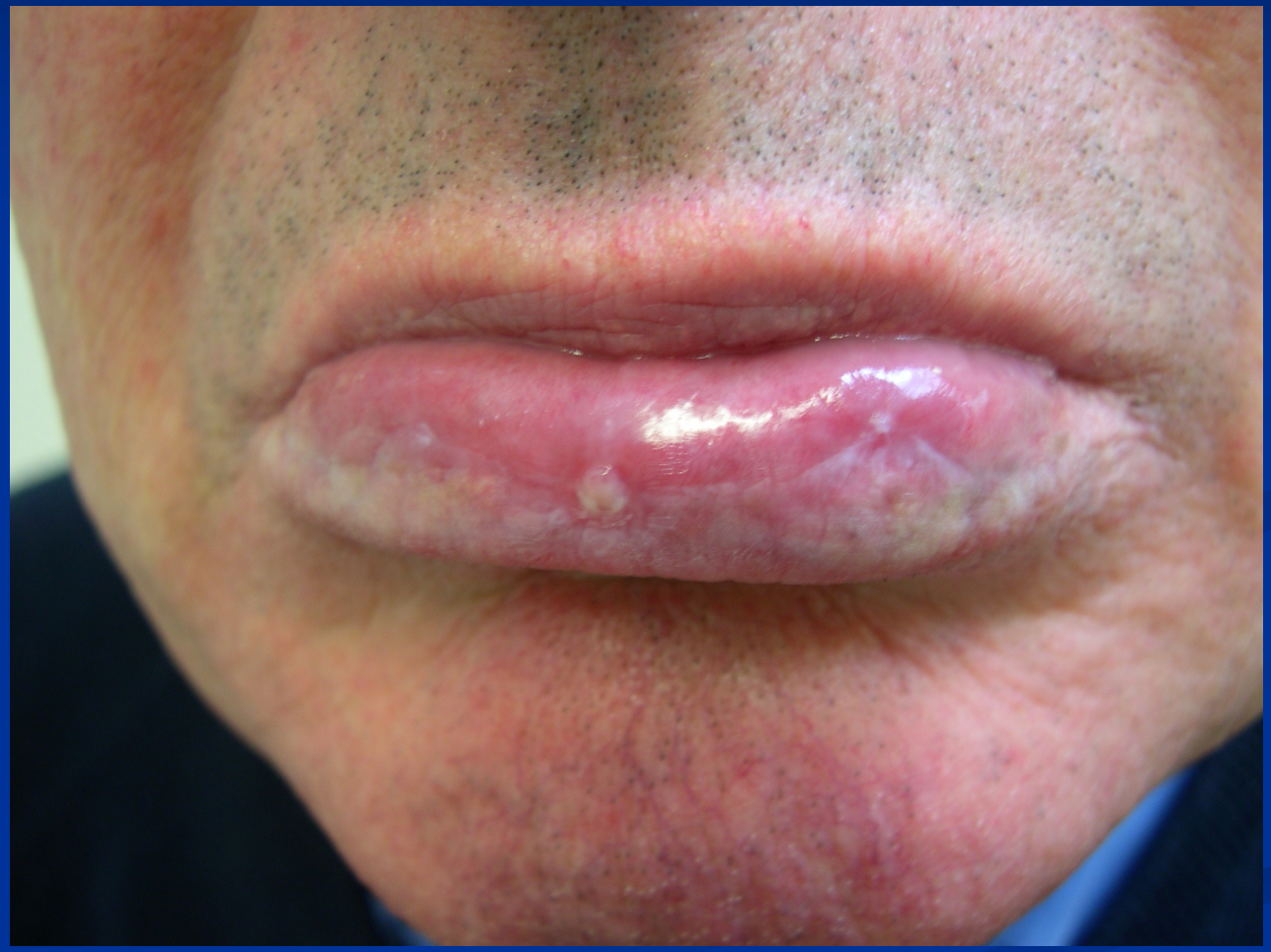
Actinic keratosis



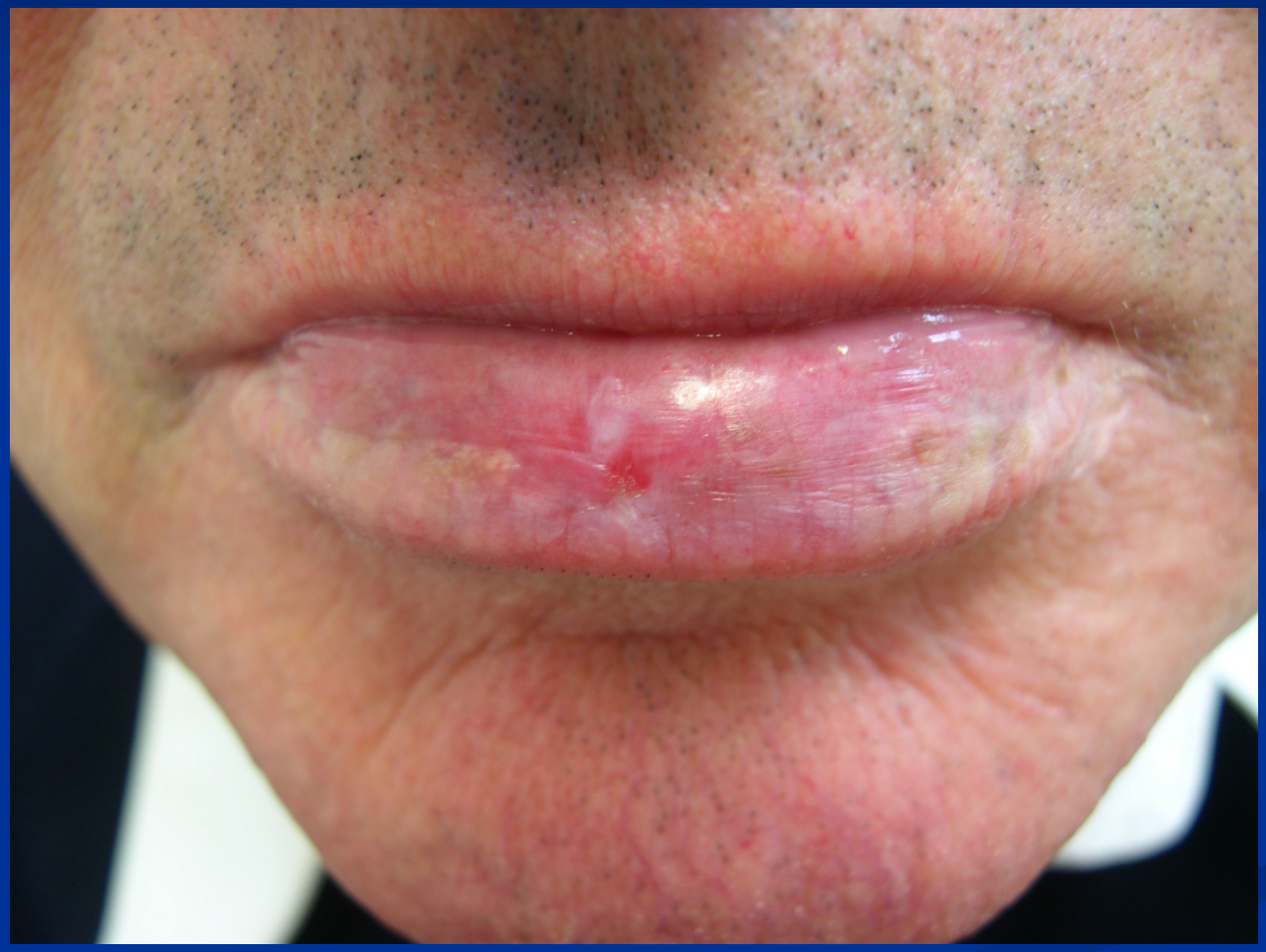




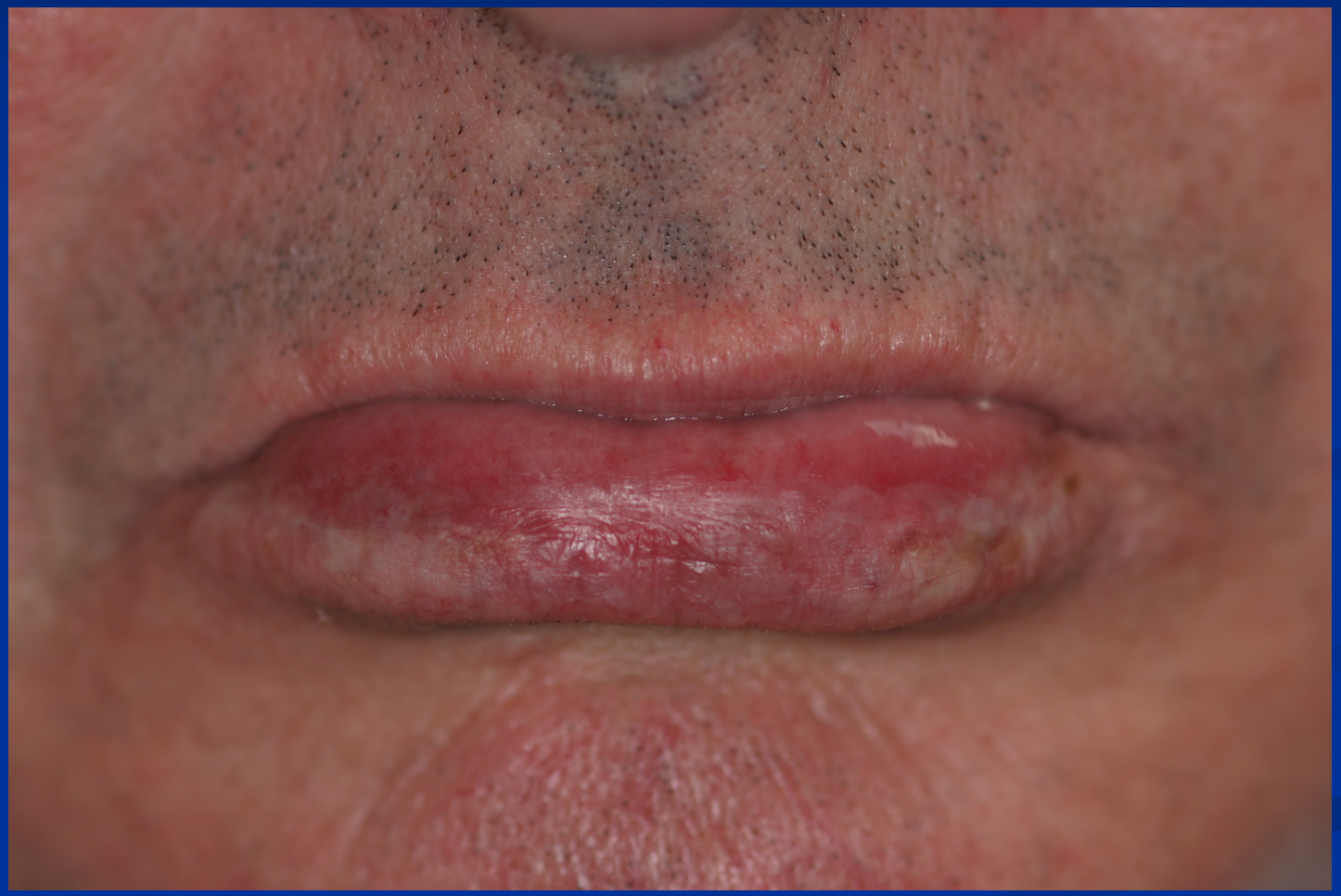
Actinic cheilitis pre treatment



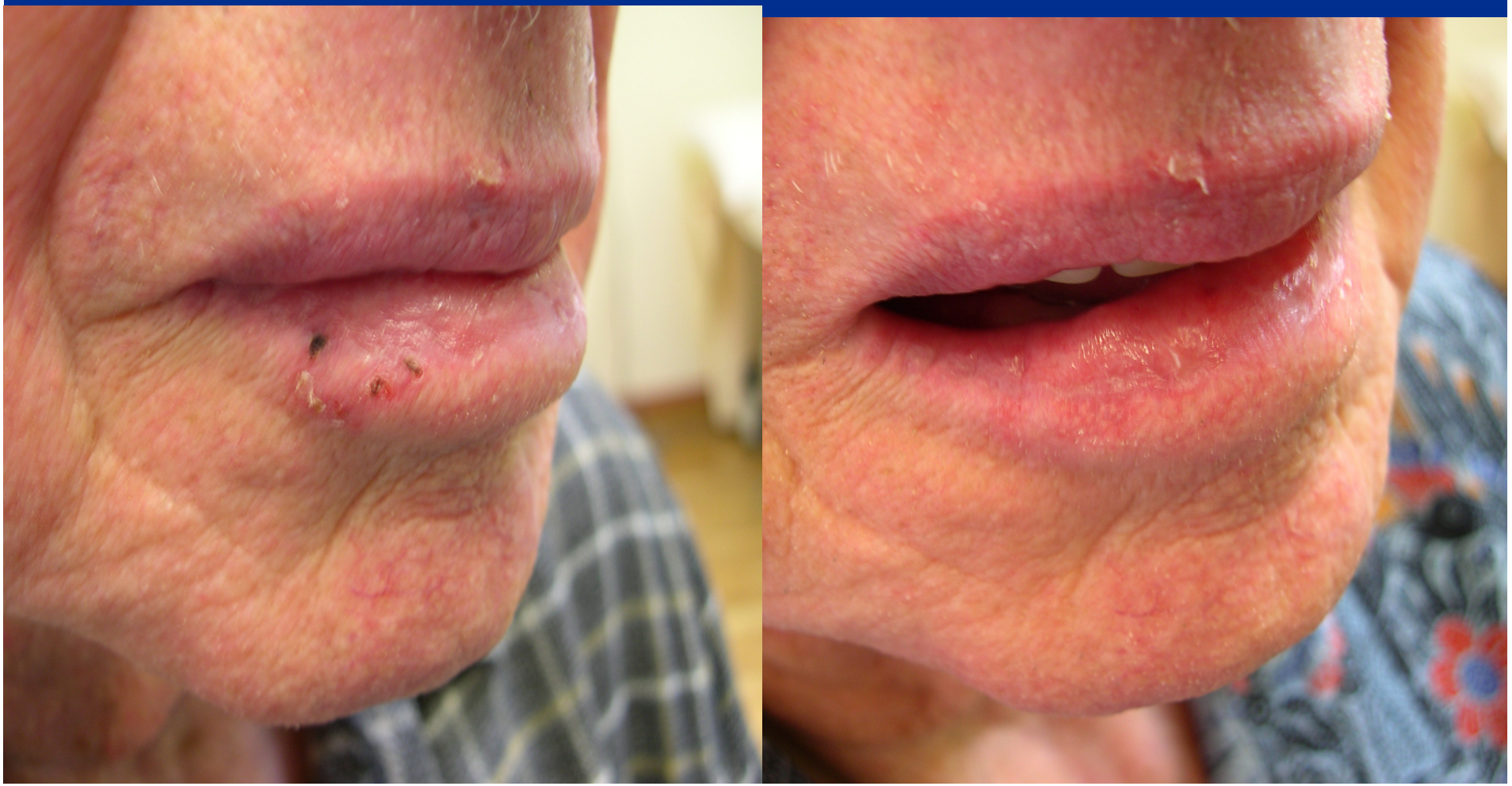
Actinic cheilitis during imiquimod therapy



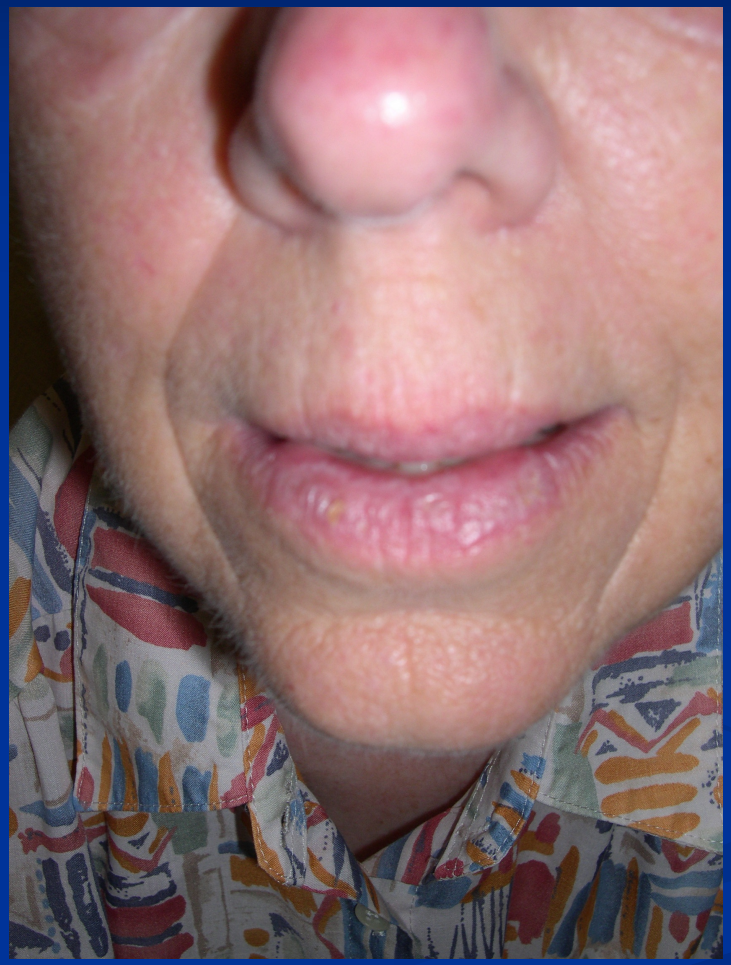
Actinic cheilitis resolved

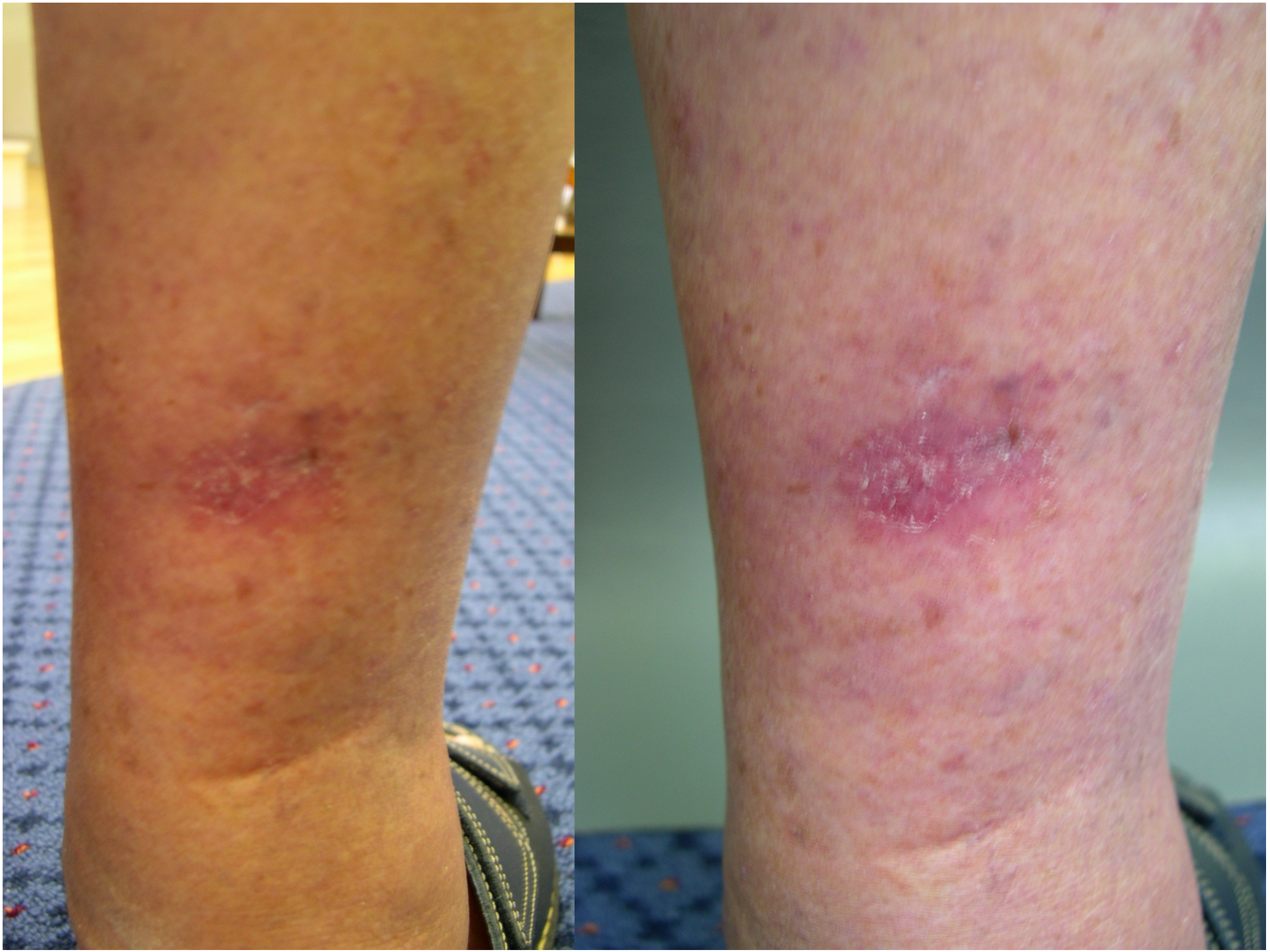


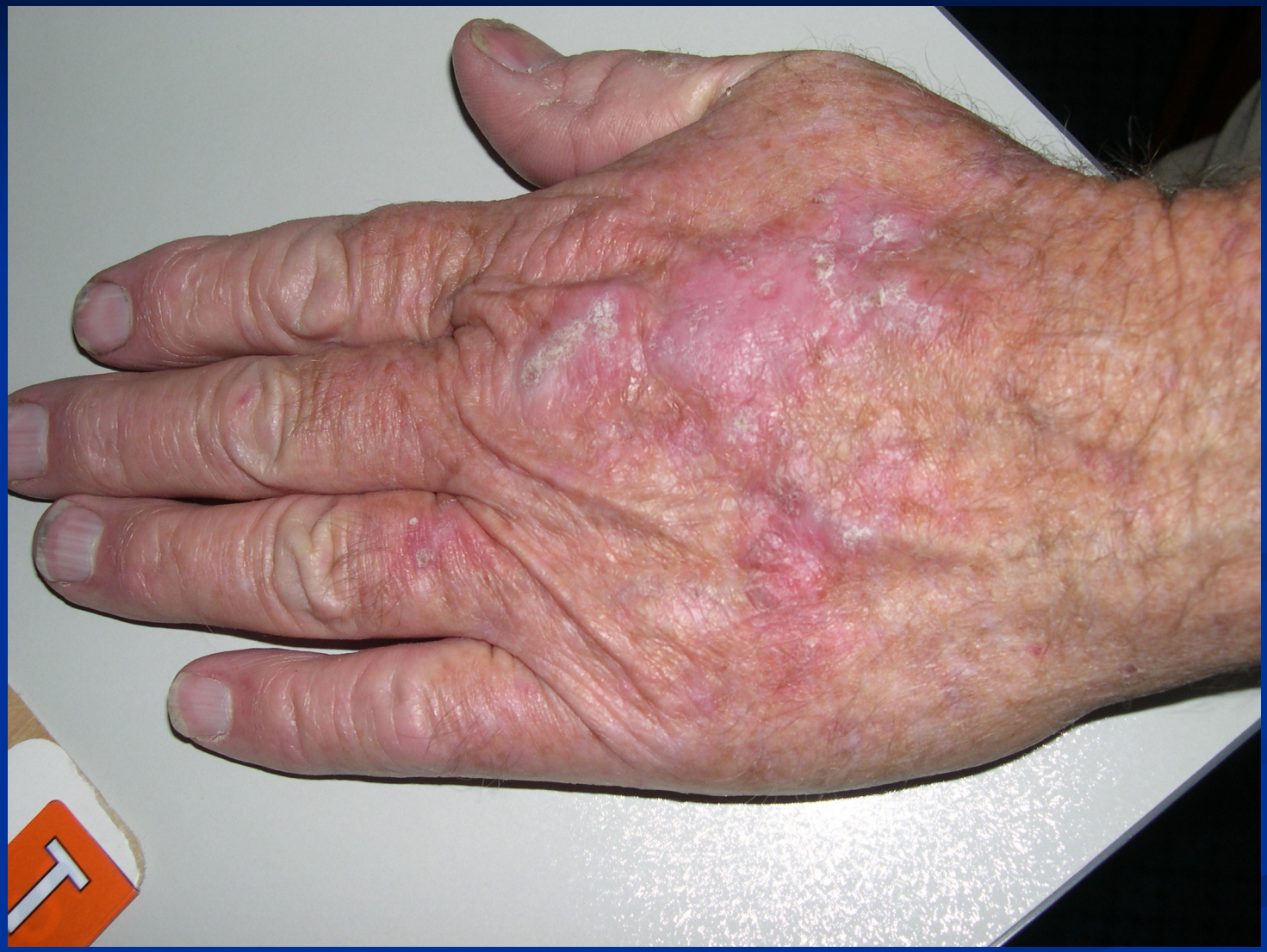
Pre and post actinic cheilitis treatment



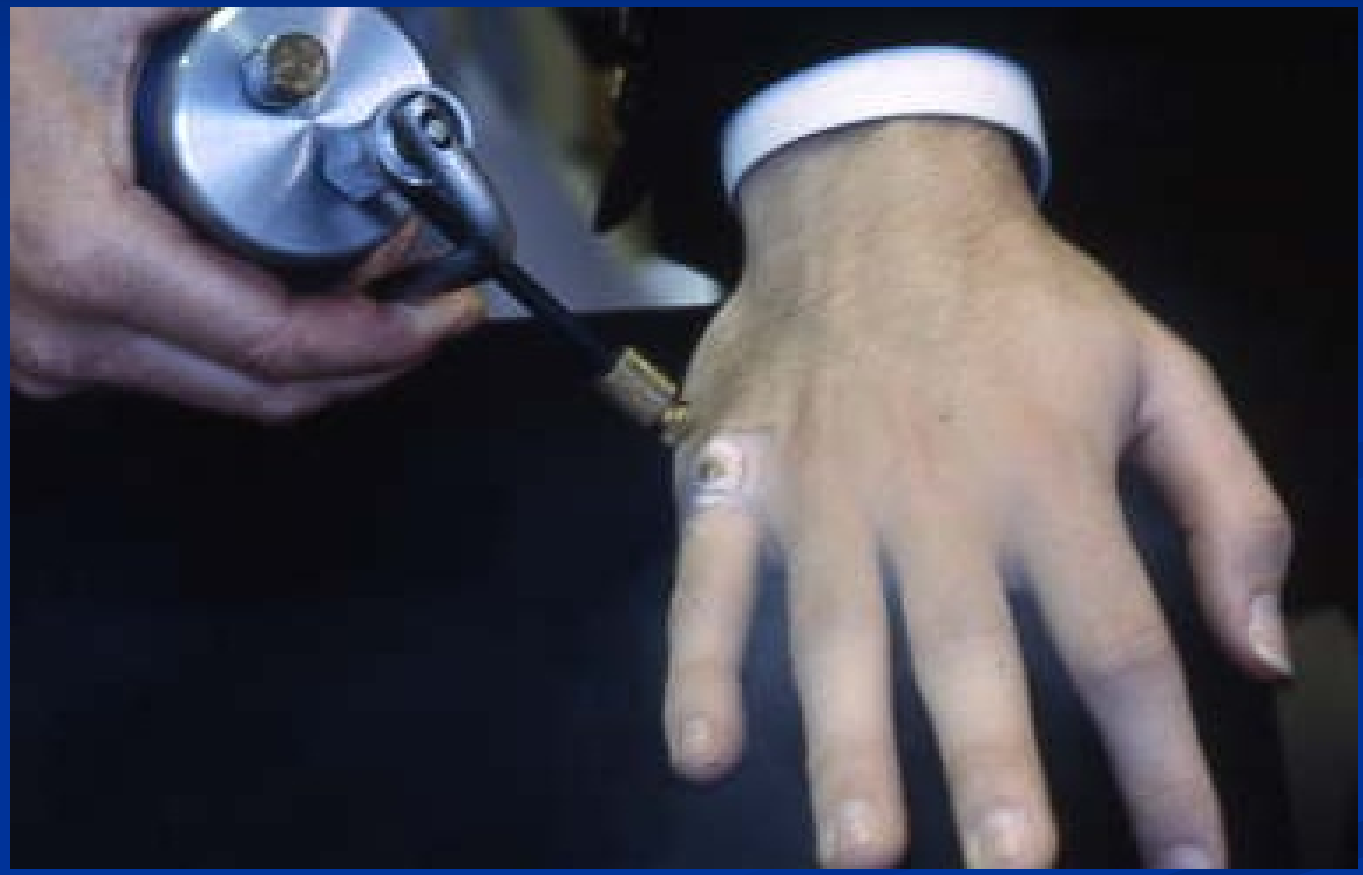
Lichenoid actinic cheilitis







Cryotherapy




voltaren®
Emulgel®
100 g Emulgel 1%
For external use only.
Dosage: Gently rub a small amount of gel onto the painful or swollen area 2 or 3 times daily.
Contains diclofenac sodium 1% w/w (as diclofenac diethylamine).
NOVARTIS
3M
Aldara™
Imiquimod
Cream 5% w/w
250 mg
Contains
1 Application
PRESCRIPTION ONLY MEDICINE
KEEP OUT OF REACH OF CHILDREN
Aldara™
Imiquimod Cream 5% w/w
3 x 250mg Single Use Sachets
For external use only
Physician's Starter Pack
AUST R 64798
3M

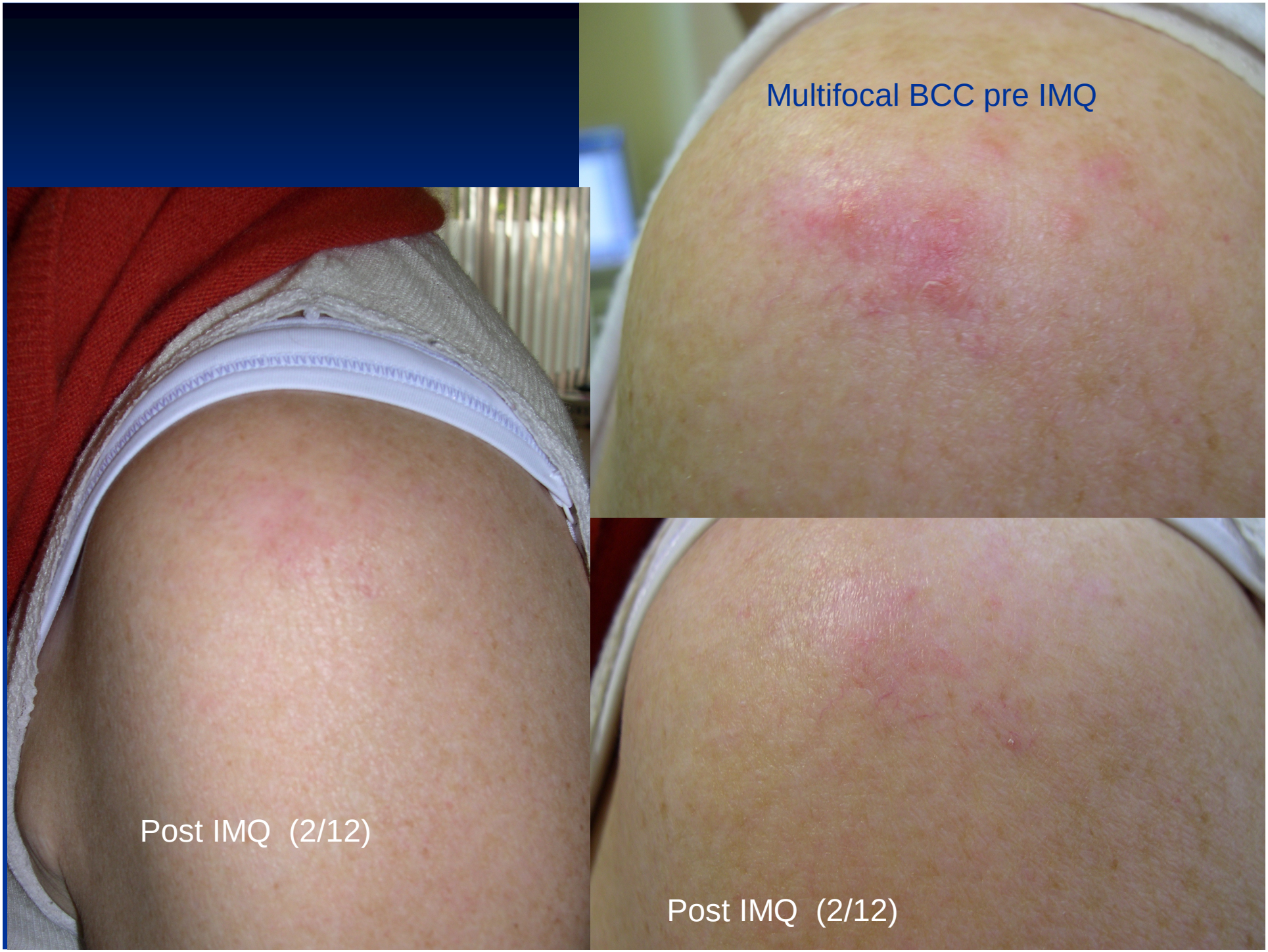
Imiquimod 5% cream

- is an immune response modifier (IRM)
- IRMs act by up-regulating the innate and cell-mediated immune response in the skin
  - stimulating natural killer cell activity
  - augmenting T-cell activity
- In addition, it induces interferon-α (IFN-α), tumor necrosis factor (TNF) and interleukins

Imiquimod cream 5%

- efficacious & well-tolerated for the treatment of AK
- Common reactions included erythema, edema / induration, erosion and crusting
- complete clearance ~85%
- Low recurrence rate, ≤10% clinically dx @ 1 yr


Pre IMQ Rx
Rx now stopping
2/12 post IMQ

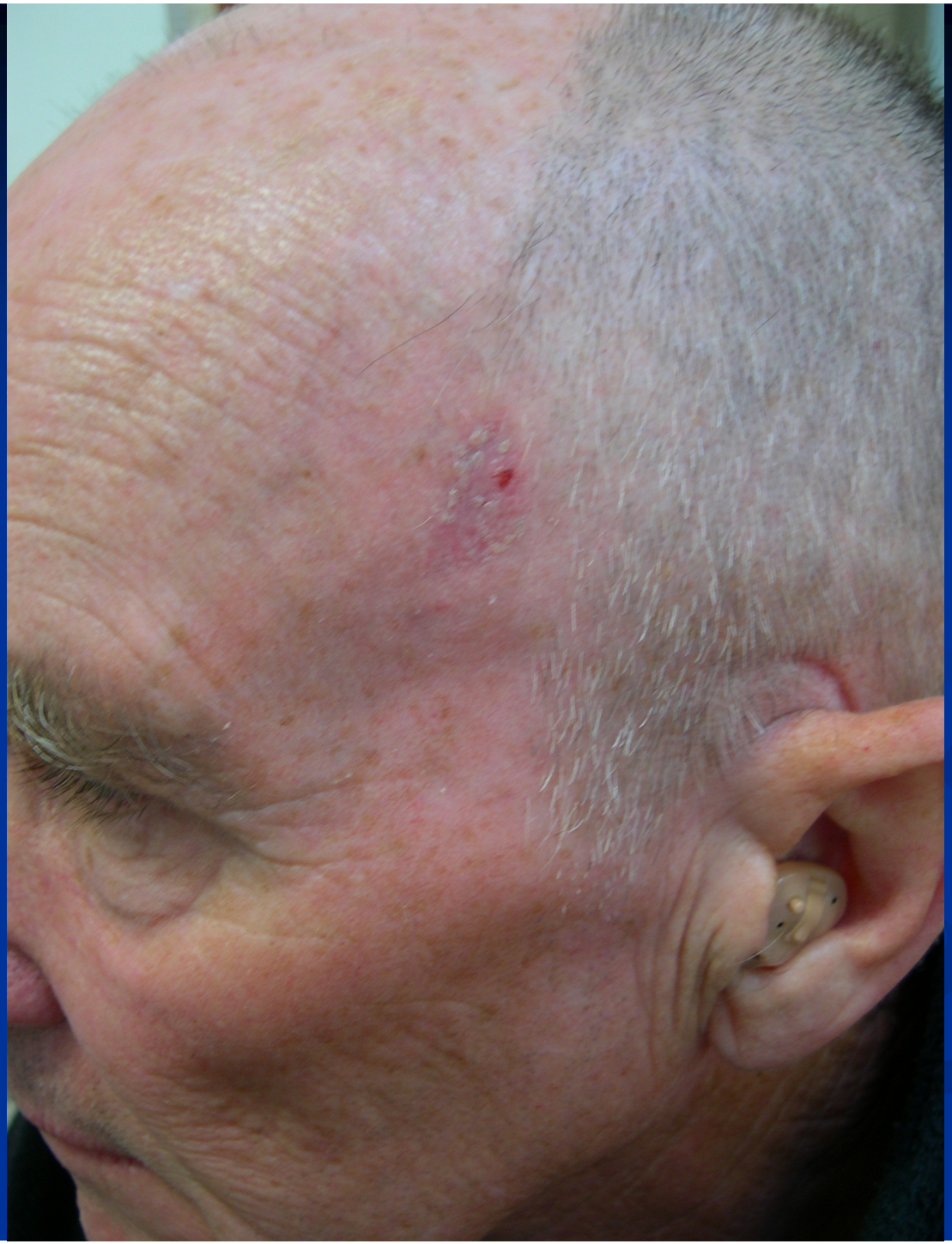

Multifocal BCC pre IMQ
Post IMQ (2/12)
Post IMQ (2/12)

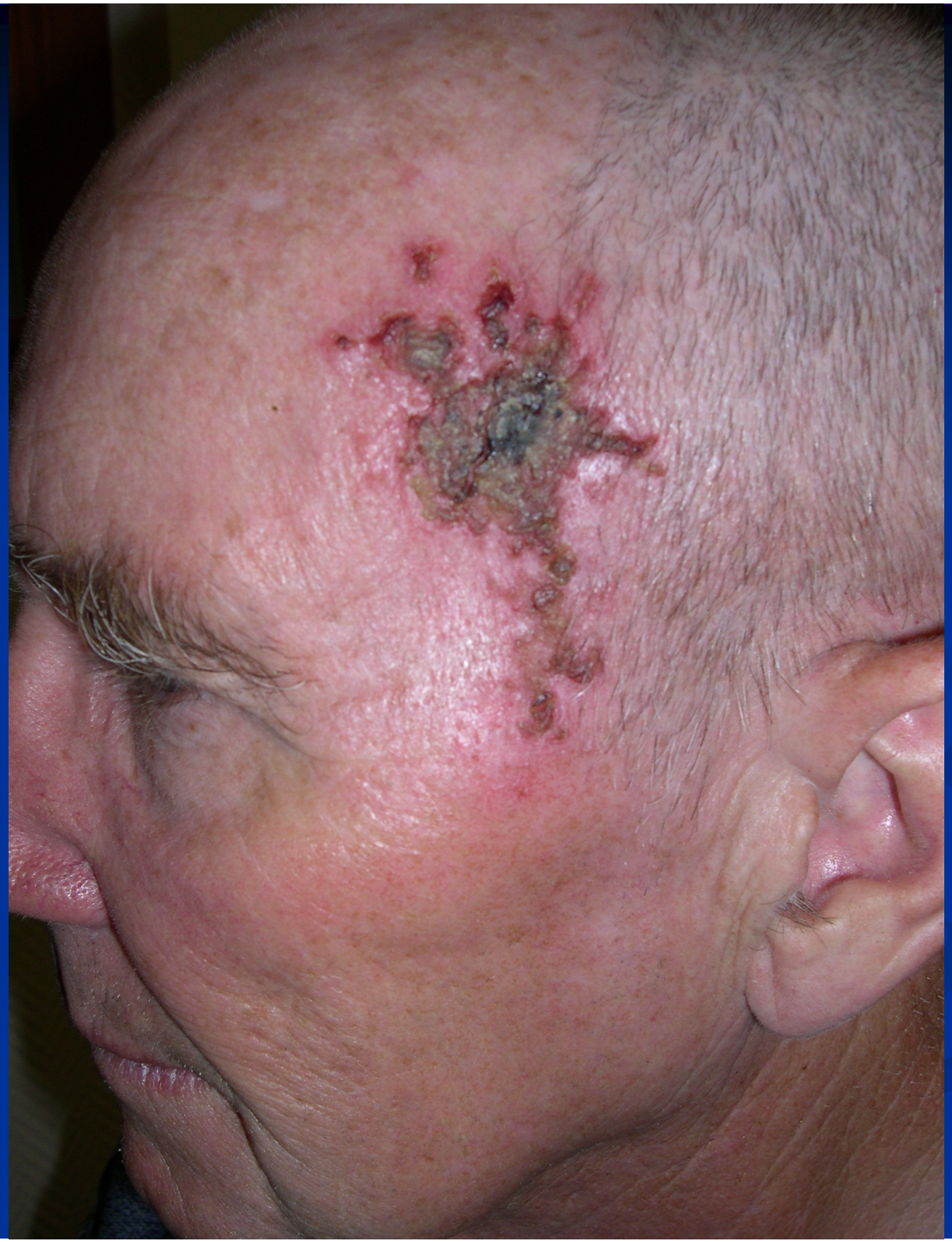
Imiquimod 5% cream for BCC

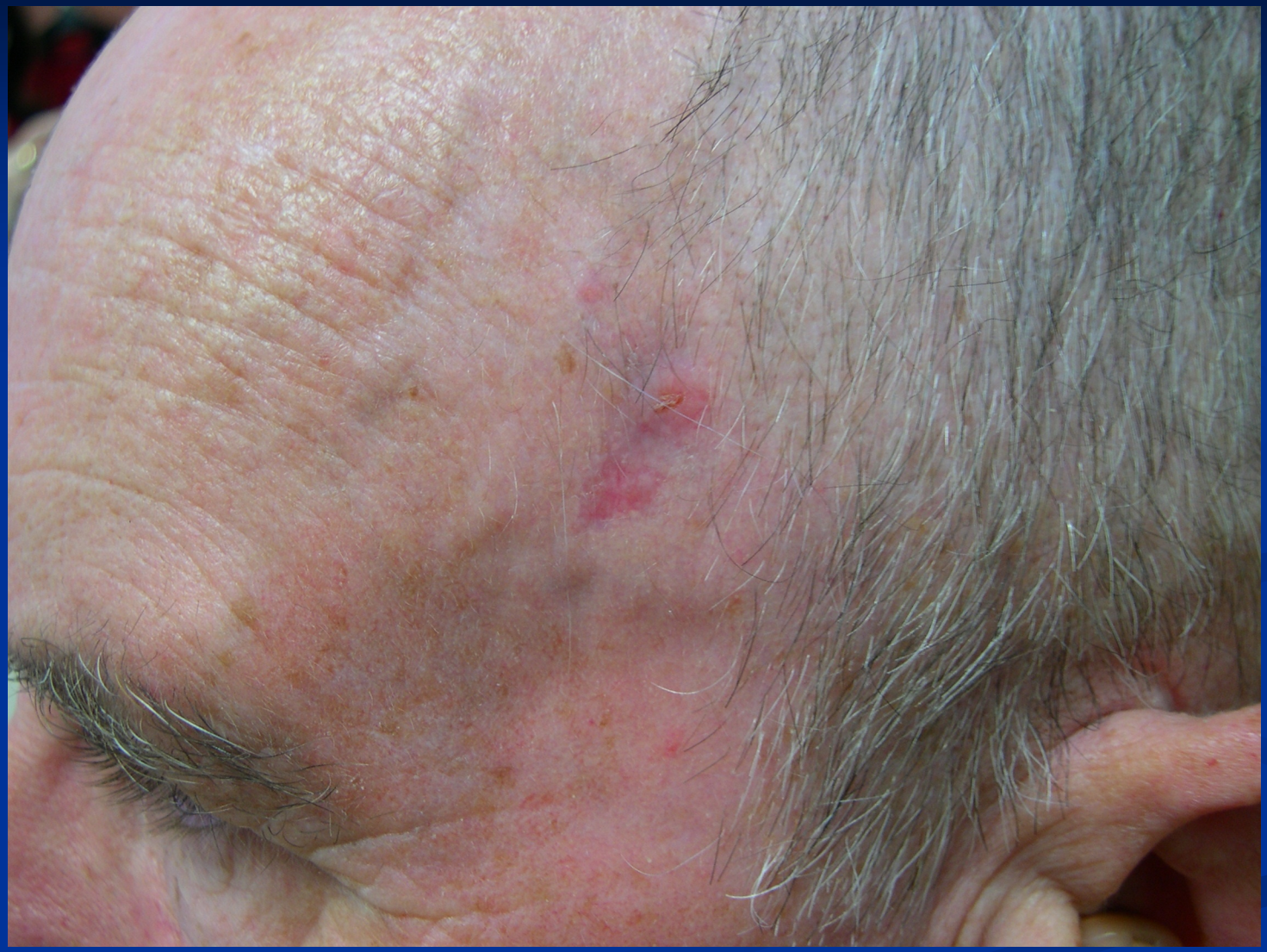
- safe and effective Rx option for sBCC
- safe & effective alternative treatment option for nBCC
- topically-applied 5 days per week, 6/52 →complete clearance
- ~ 90% for sBCC, ~70% for nodular BCC
- Cosmetic outcome excellent

- *current special authority Pharmac funding for superficial BCC

Superficial BCC treated with imiquimod cream







Regular use of Sunscreen

- reduces the rate of development of new actinic keratoses
- significantly reduce UV-induced skin damage, BCC and SCC skin cancers
- In 1st 18 years of life, effective SPF >7.5 can ↓ lifetime incidence of non-melanoma skin cancer by ~80%
- in early life, might reduce naevus counts and subsequent melanoma risk.

- Risk reduction for nonmelanoma skin cancer with childhood sunscreen use. Arch Dermatol 1986;122:537-45.
- Reduction of solar keratoses by regular sunscreen use. N Engl J Med 1993;1147-51

References re benefit of regular sunscreen use

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- Huncharek M, Kupelnick B. Use of topical sunscreens and the risk of malignant melanoma: a meta-analysis of 9067 patients from 11 case-control studies. Am J Public Health 2002;92:1173-7.
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Secondary prevention

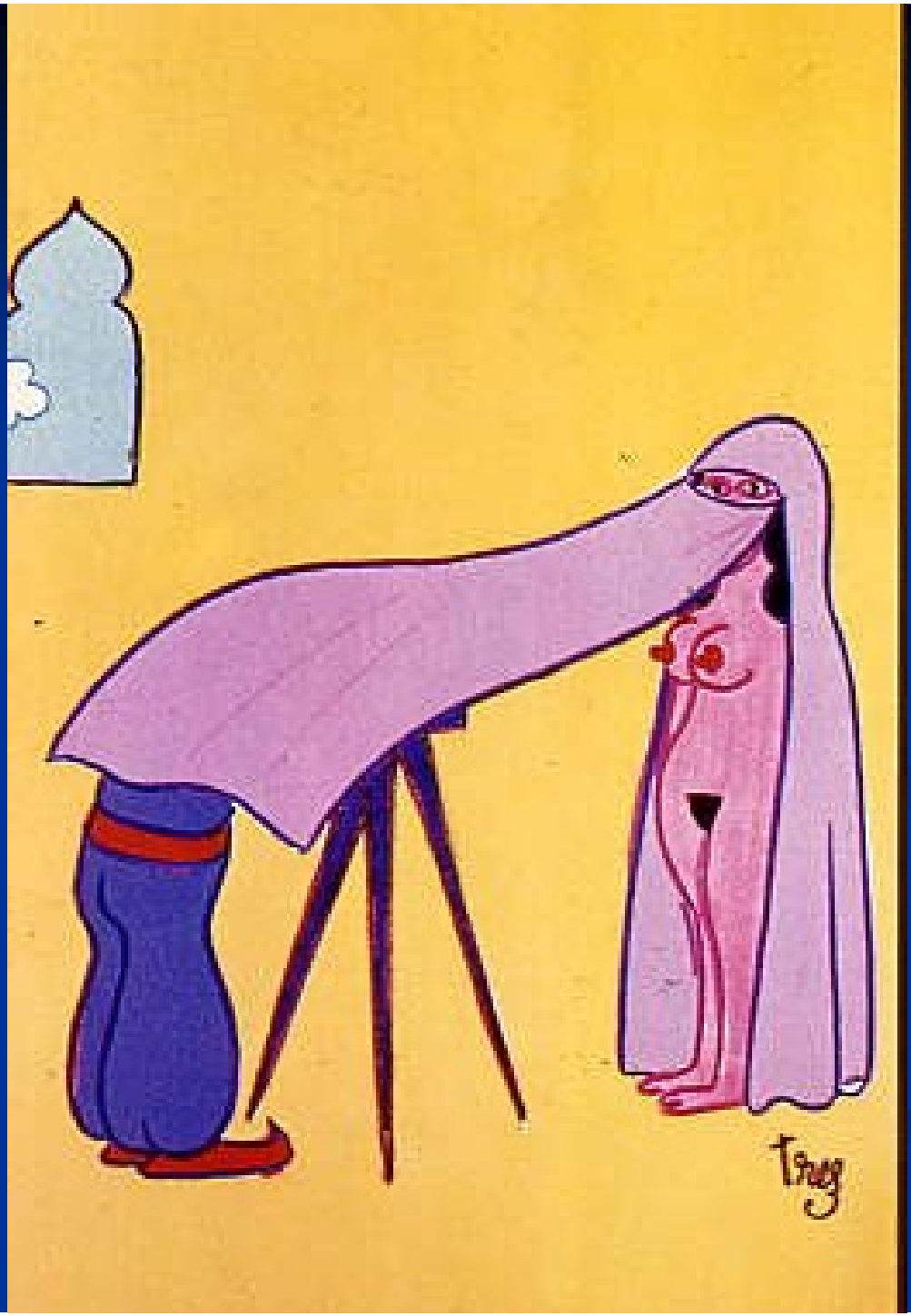
- Sun protection
  - Avoid peak sun exposure
  - Long sleeve shirts, long trousers, high UPF clothing
  - Hats
  - Wrap-around sunglasses
  - Broad spectrum sunscreen suited to skin type, activities,
  - Diet rich in antioxidants (fruit, vegetables, green tea etc)

Dietary antioxidant sources

- Dietary flavonoids & polyphenolic compounds
  - Fruit e.g. blueberries, grapes, tomatoes, oranges, other citrus fruits
  - Vegetables e.g. cucumber, broccoli, carrots
  - Oils e.g. olive
  - Beverages e.g. green tea, red wine, coffee

Early detection – surveillance

- Full skin examinations
- High risk patients
  - History of occupational / recreational sun exposure
  - High risk lesions
  - Immunosuppression
  - Skin type
  - Family history



Take home messages

- Skin cancer
  - common and expensive health problem in NZ
  - Excise if you can
  - When you can't excise
    - Refer on if large / awful (surgery, XRT, PDT)
    - Consider topical therapies (imiquimod, 5FU, etc)
  - Educate about secondary prevention
    - Holistic sun avoidance behaviours
    - Regular surveillance for high risk patients