Malignant skin tumors

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Precancerosis, CIS

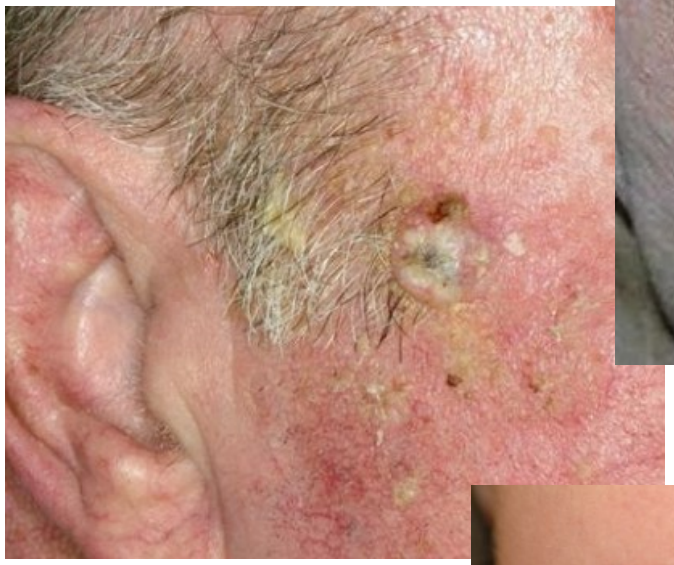
A) obligatory prec. -

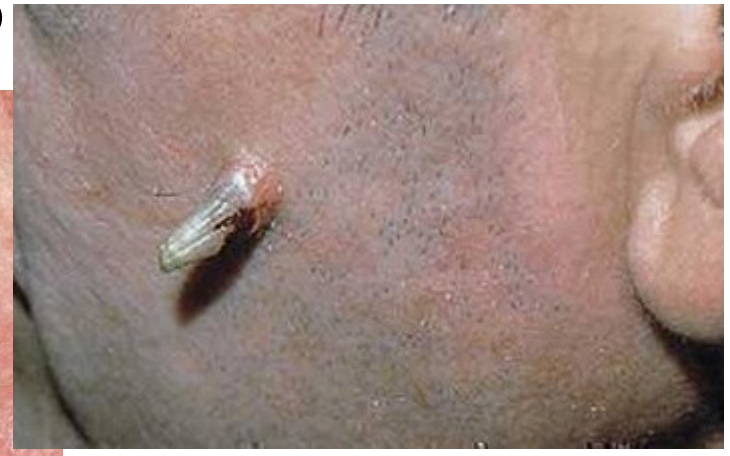
- are cutaneus lesions- from which can grow up malignant tumors after the years - obligatory precanc.

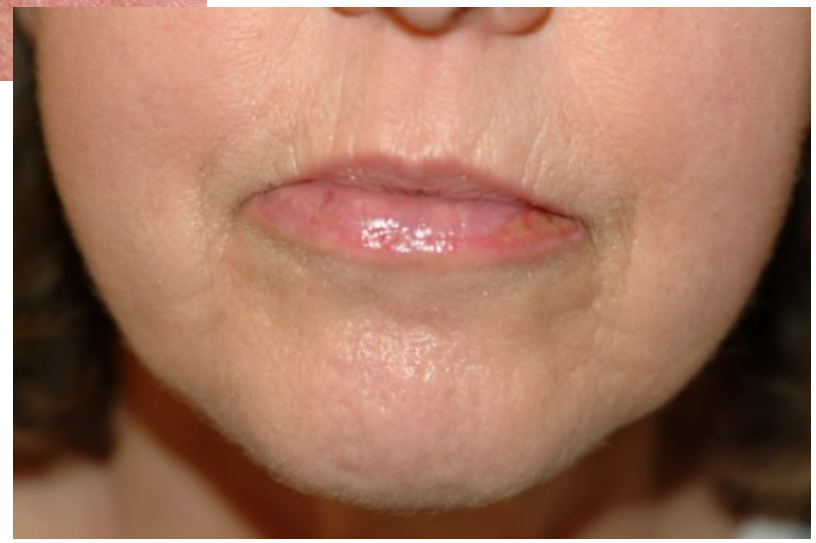
B) Facultative - in certain causes they can cause malignant tumor

- histological picture is variable - from inflammatory changes with epithelic hyperplasia to ca in situ

Precancerosis, CIS





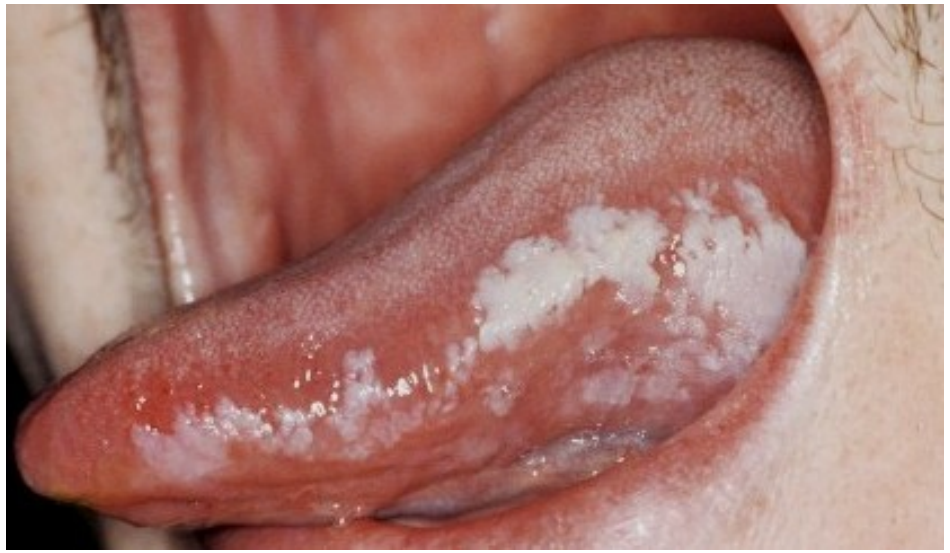


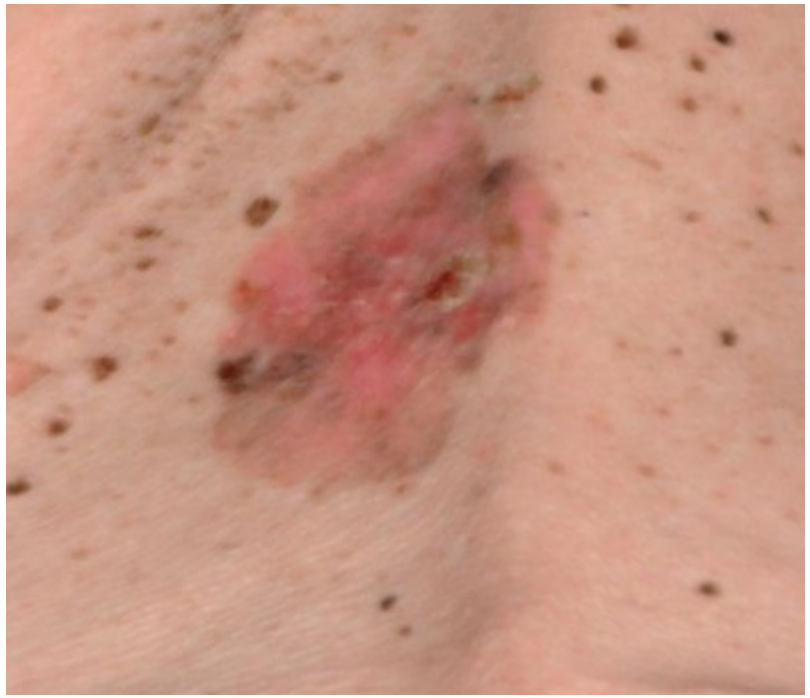
A) obligatory prec.- include:

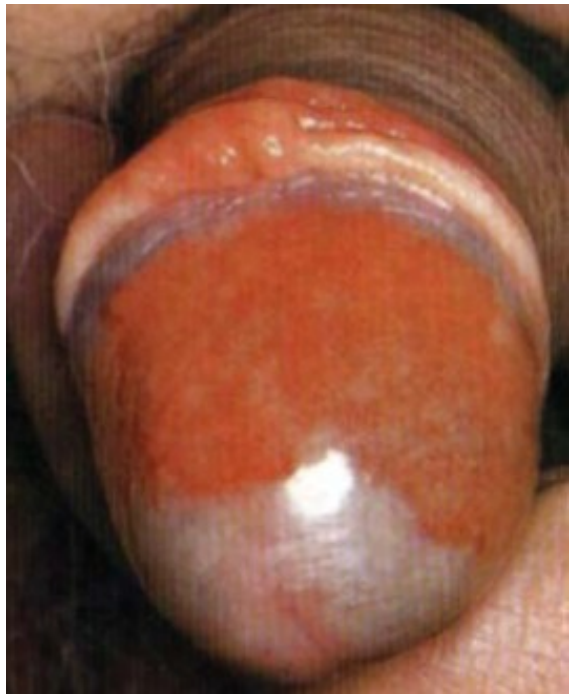
- Keratosis actinica
  - Spinalioma 15%
  - Cornu cutaneum
  - Actinic cheilitis
- Leukoplakia
  - Leukoplakia simplex, verrucosa, erosiva
- M. Bowen
  - Erythroplasia Quyerat
  - Bowenoid papulosis – HPV 16
- Lentigo maligna – melanosis circumscripta Dubreih
  - LMM

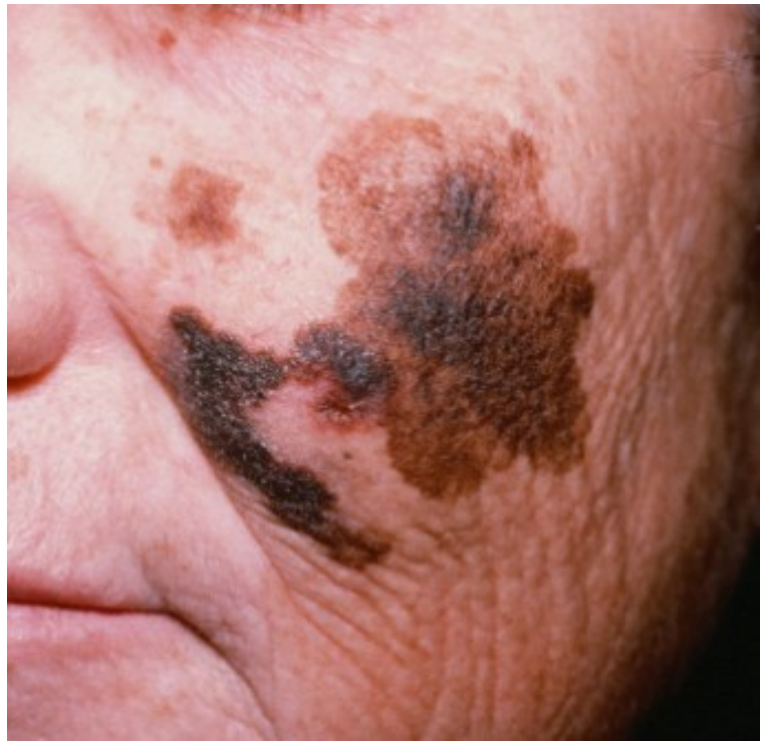
B) Facultative

- Chronic inflammation- ulcerations, scars – chronical iritation- growing granulation tissue- sometimes changes to spinalioma

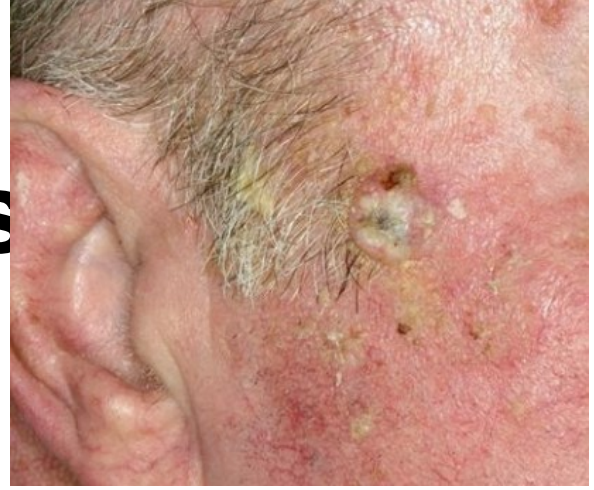








A) obligatory precancerosis



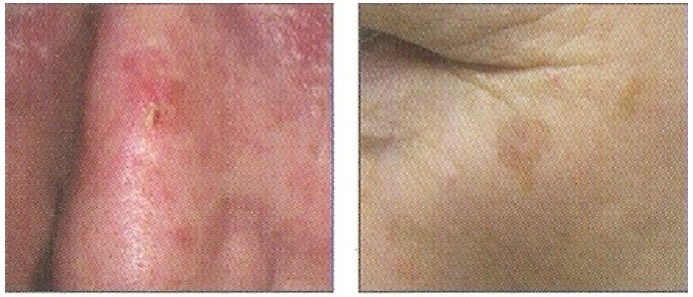
- **Actinic Keratosis**

- extremely common dysplazia of epidermis, especially in skin types I and II

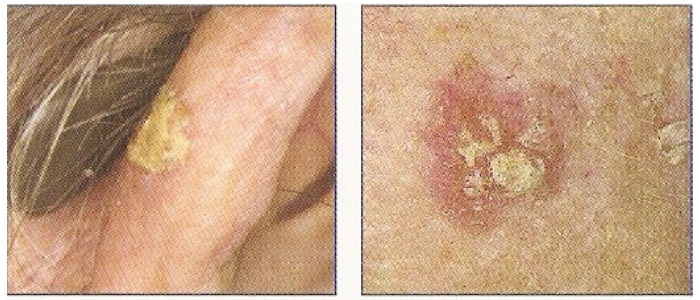
- It is a SCC in situ

- it is induced by chronical exposure to UV (UVB) irradiation (15 – 20 years after that), so we can find it at solar localization (forehead, bald scalp, cheeks, nose, ears, lower lip

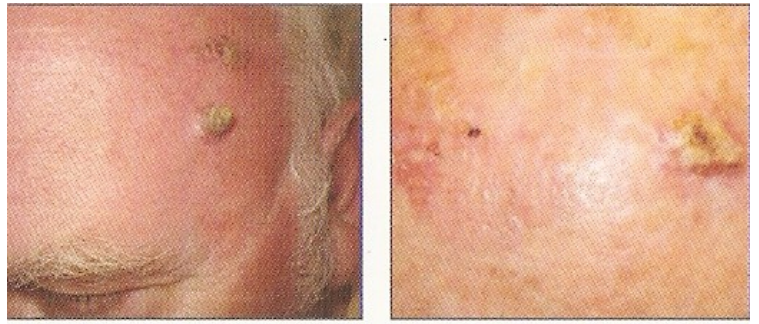
Classification of AK



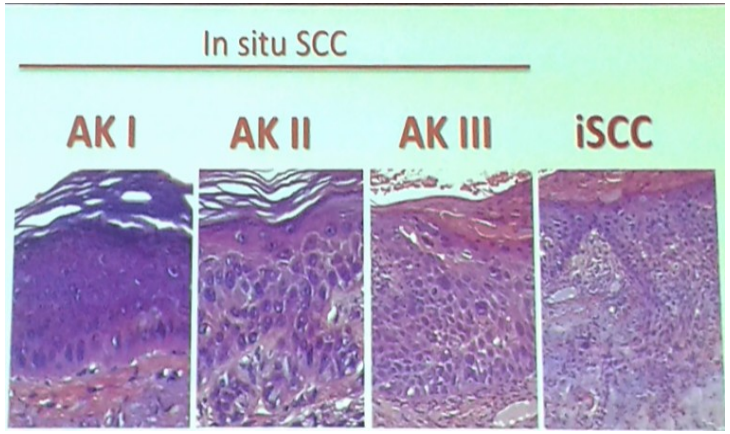
Grade I: Flat, pink maculae without signs of hyperkeratosis and erythema often easier felt than seen. Scale and possible pigmentation may be present



Grade II: Moderately thick hyperkeratosis on background of erythema that are easily felt and seen

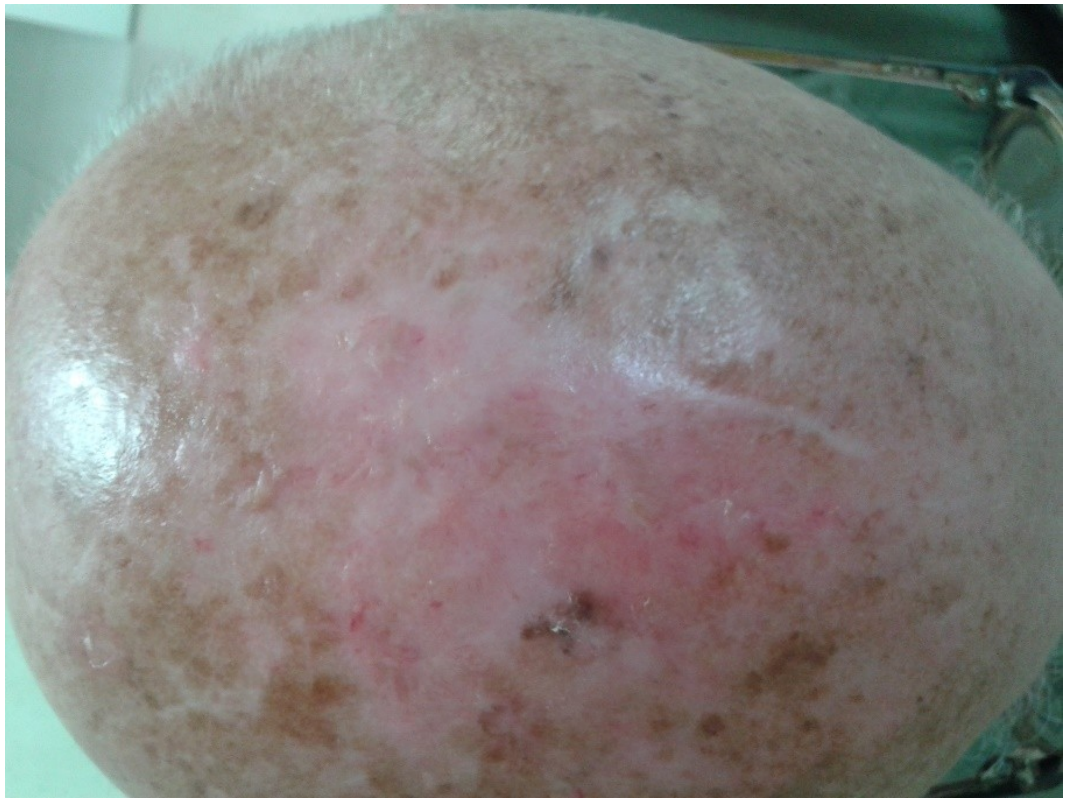


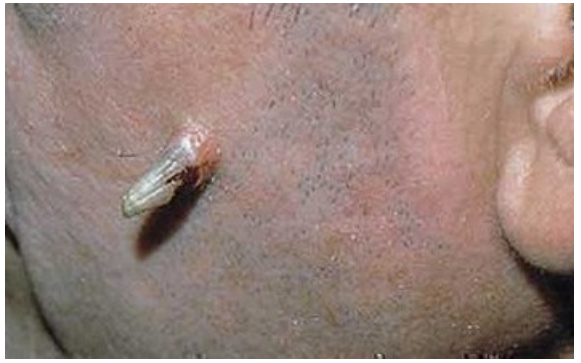
Grade III: Very thick hyperkeratosis, or obvious AK, differential diagnosis includes thick IEC (intra-epidermal carcinoma or SCC)



„Field cancerization“

- Some patients have a „field cancerization“ – effect with hundreds of AK
- Most common on bald scalp in elderly, imunosuppressed patients





- it can grows to
  - **spinalioma** (15-20%) after many years
  - **cornu cutaneum** - on the surface of the increasing lesion, the horn masses of cylindrical or conical shape resemble a horn
  - **actinic cheilitis** – white lesion with irregular surface on the muccose of the lower lip, with erosions or crack

- <u>Therapy</u> – superficial cryotherapy - quick, cheap, effective
  - curettage, shave excision or photodynamic therapy

- **M. Bowen**

  - it is intraepidermal ca (ca in situ), but not on sun – exposed skin, very often change to

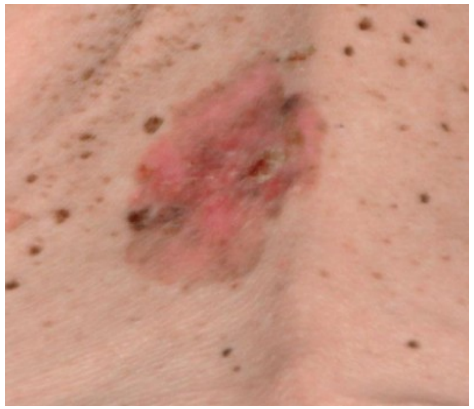
  spinalioma

  - localization- trunk, lower extremitas

  - etiology- arsenic exposure (in the past), human papilomavirus,

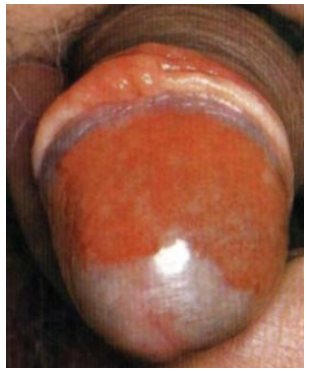
  - manifestation- oval red-brown patch or plague with variable scale

  - *therapy* – excision



- **Erythroplasia of Queyrat**

- Is SCC in situ on the transitional eithelium of the penis, female genitalia or mouth
- Red velvety patch with a sharp border
- Therapy - excision

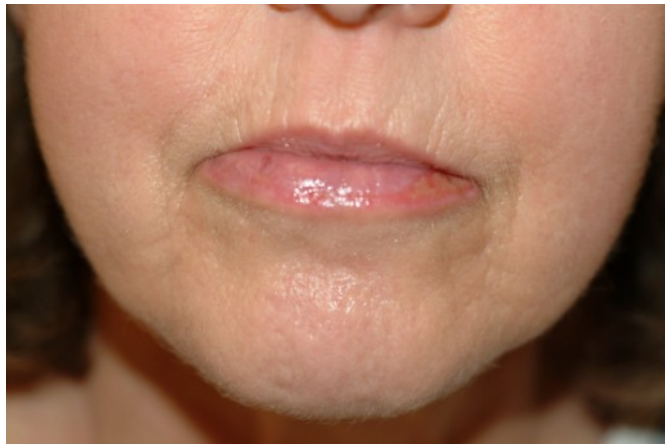


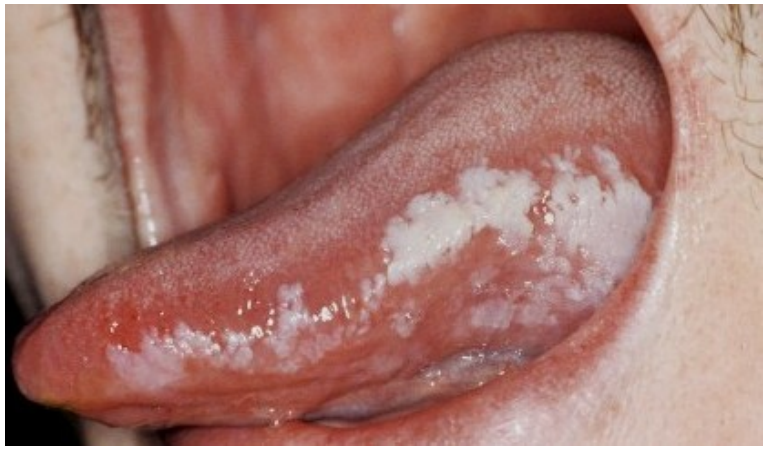
- **Leukoplakia**

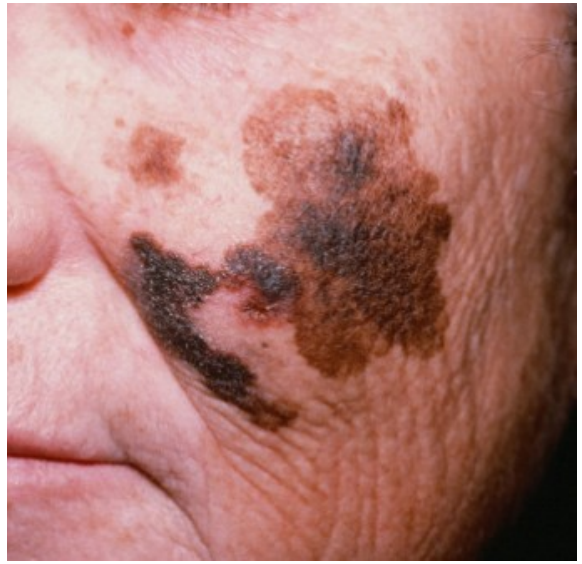
 - chronical white lesions on mucosa membranes – spinalioma of lip

- localization-mouth,genital

- it caused by exogenic irritation (mechnical, fyzical, chemical factors, smoking)







- **Lentigo maligna**

- it is induced by chronical exposure to UV irradiatio

- proliferation atypical epidermal melanocytes – it changes into melanoma

- appears- as irregularly shape and variable pigmented grey, brown and black patch spreads for many years

B) Facultative precancerosis

- Chronic inflammation- ulcerations, scars – chronical irritation - growing granulation tissue - sometimes changes to spinalioma

Malignant skin tumours - division into:

- **1. non-melanoma skin tumors (NMSC)**

- represent a large group of neoplasias that are found on the skin with the exception of melanoma

A) Epithelial malignant skin tumors = **carcinomas**

- Carcinoma basocellulare
- Squamous cell carcinoma
- Ca verrucosum

B) Mezenchymal malignant skin tumors

- Kaposi´s sarcoma

- 2. **Melanoma**

A) Epithelial malignant skin tumors = carcinomas

Basal cell carcinoma BCC (carcinoma basocelullare)

- Tu from basal cell layer
- Is the most common malignant tumor (80% of NMSC)
- It grows slowly and become localy destructive, but almost never metastasizes

Basal cell carcinoma - epidemiology

- The age peak is 60-80 years
- The incidence is increasing
- BCC is also 10 times more common than SCC
- The most common typ of malignant tumor in Europe, USA, Australia
- Twice as common in men

Basal cell carcinoma – risk factors

1. **UV radiation - chronic exposure, especially UVB radiation (280-320nm)**

- But UVA radiation also has a certain share in carcinogenesis - it is absorbed by skin chromophores, oxygen radicals are formed, DNA is damaged

- developing of BCC increases in direct proportion to the lifetime cumulative dose of UV radiation

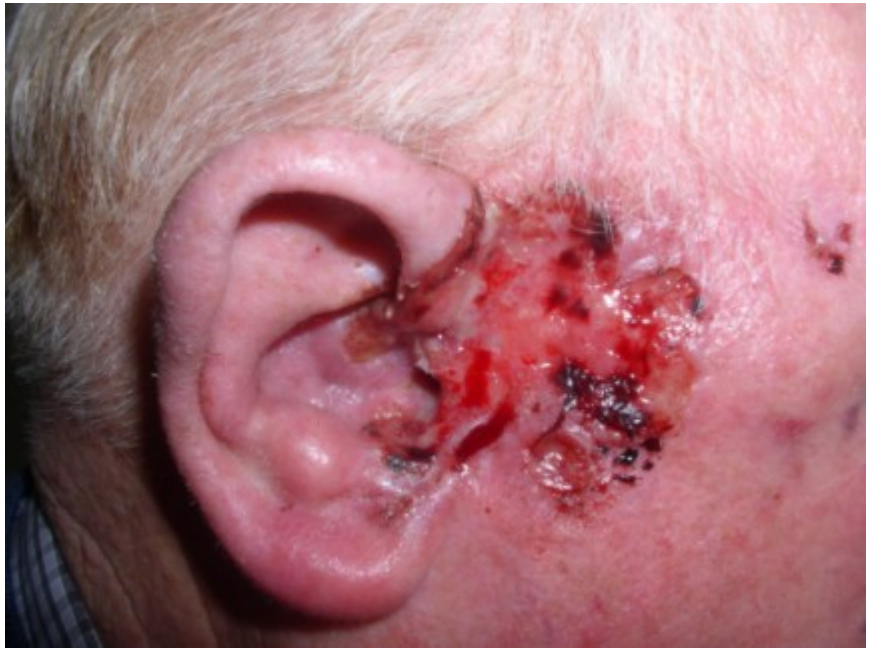
- Latency period after radiation therapy is - 15 to 20 years

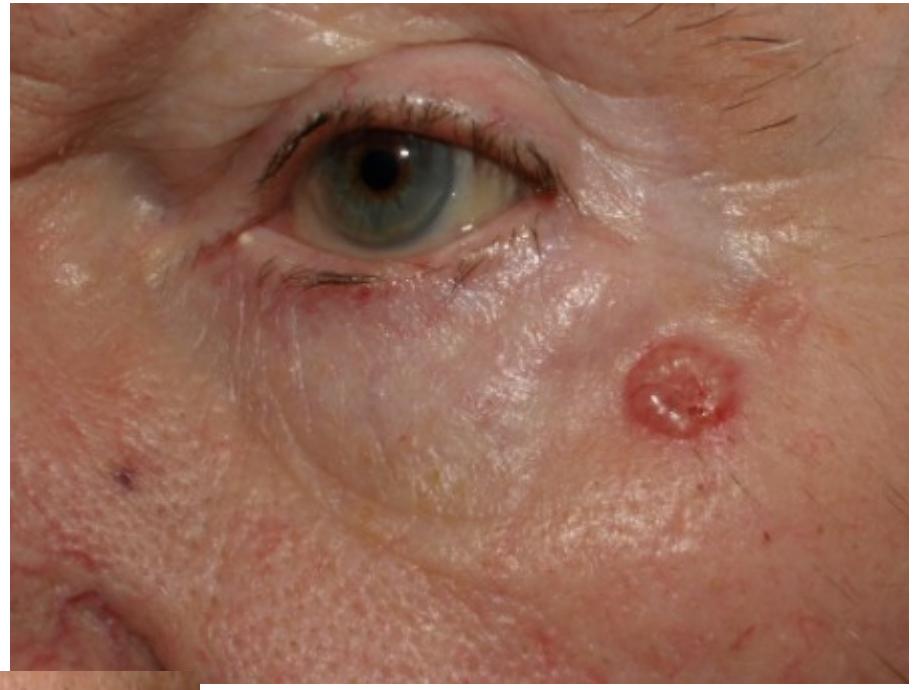
- Radiation sources: solar (recreational, at work), medical (NBUVB, PUVA?), Solariums

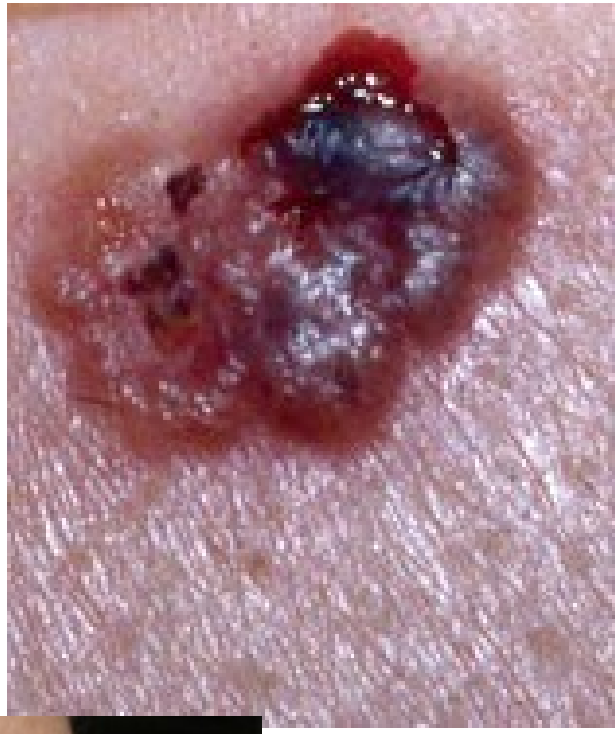
- Significantly increased risk of basal cell carcinoma - working outdoors (farmers, bricklayers, etc.)

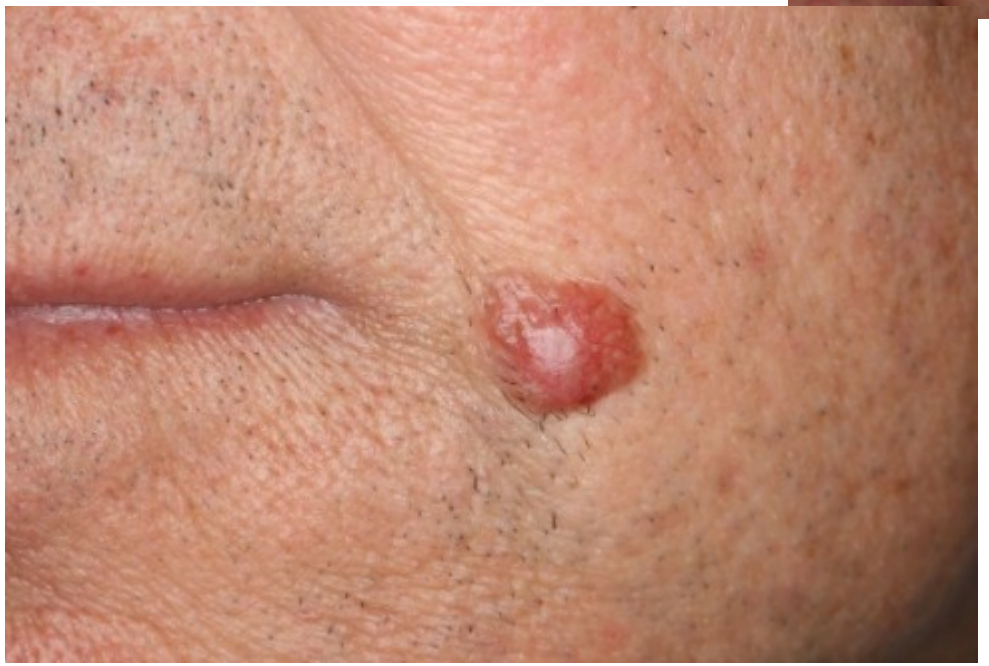
Basal cell carcinoma – risk factors

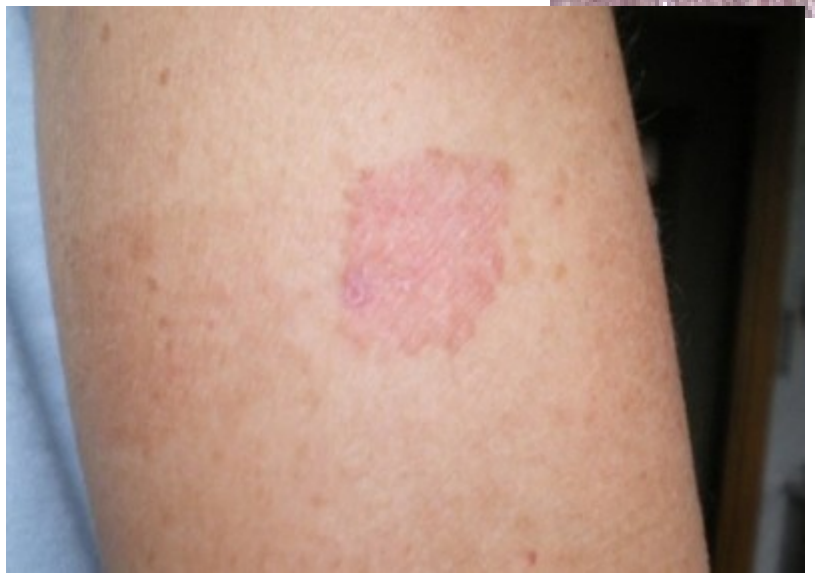
- **2. phototype** (lighter skin - higher risk), geographical location
- **3. immunosuppression** (transplant patients) - the risk of developing basal cell carcinoma is about 10 times higher than in the general population, especially after liver and kidney transplantation
- **4. genetic factors** - Gorlin's sy, Xeroderma pigmentosum
- **5. exposition of carcinogens (arsenic salts)**

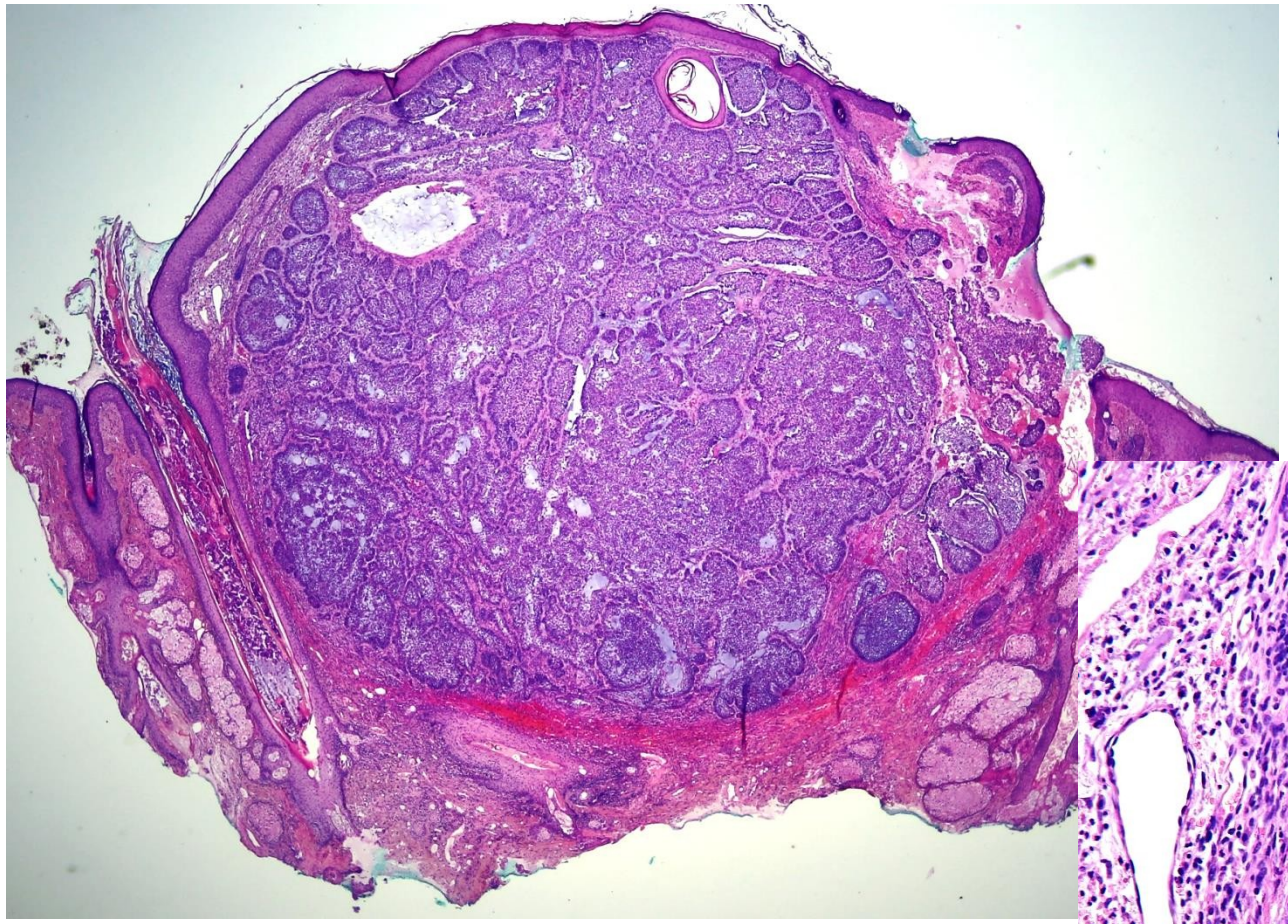


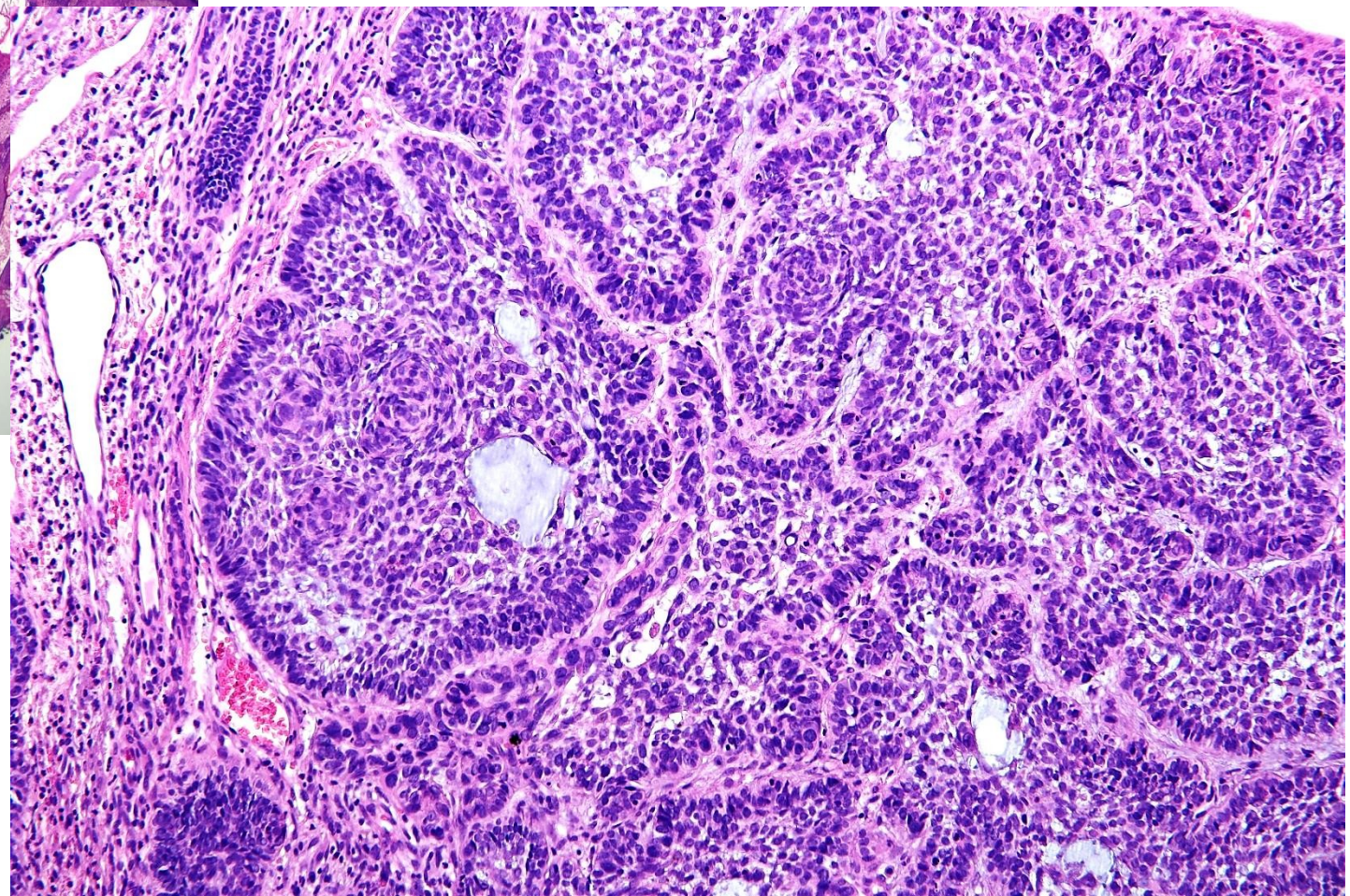










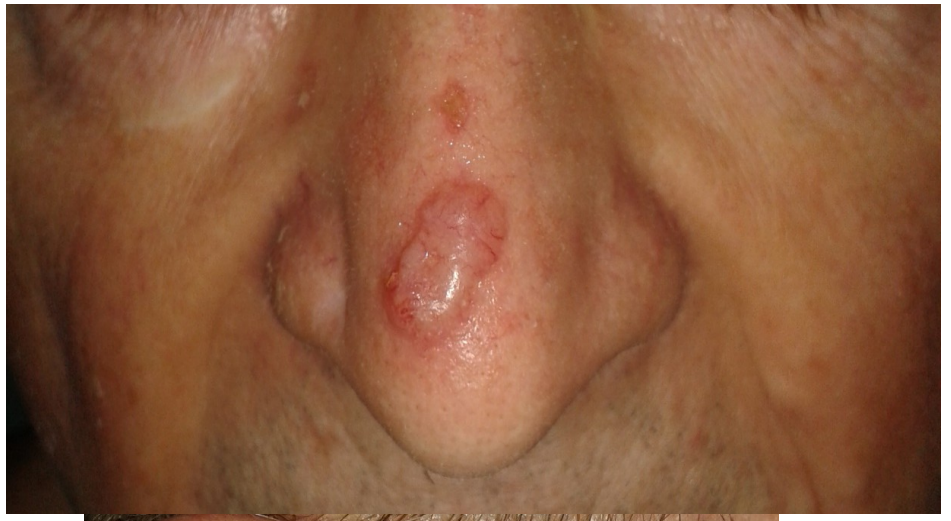


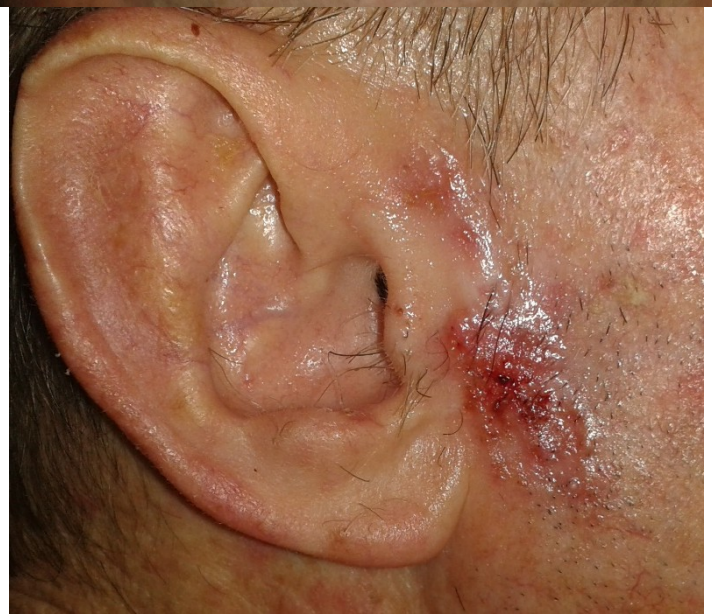
Basal cell carcinoma – clinical features

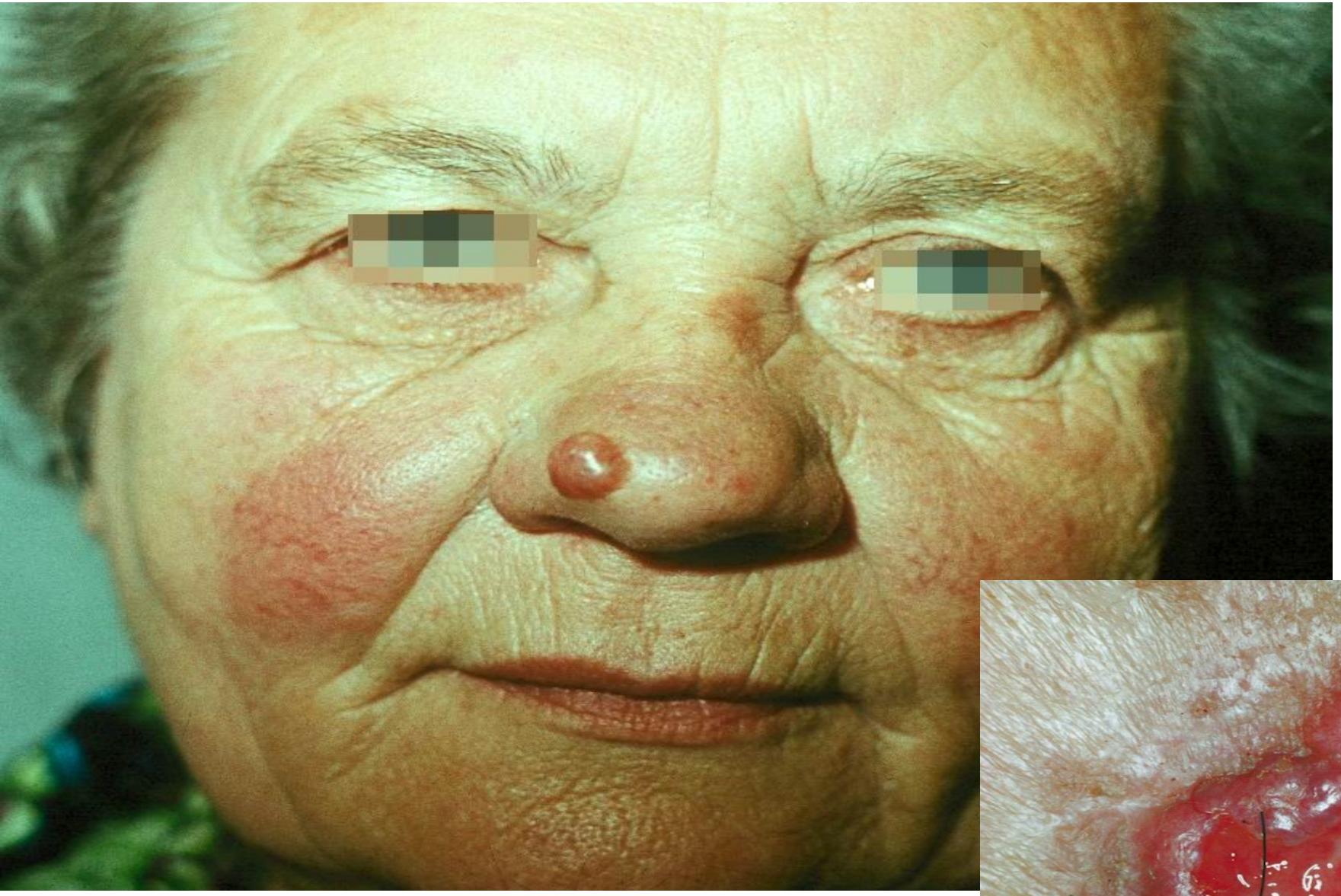
- **Nodular or solid BCC**

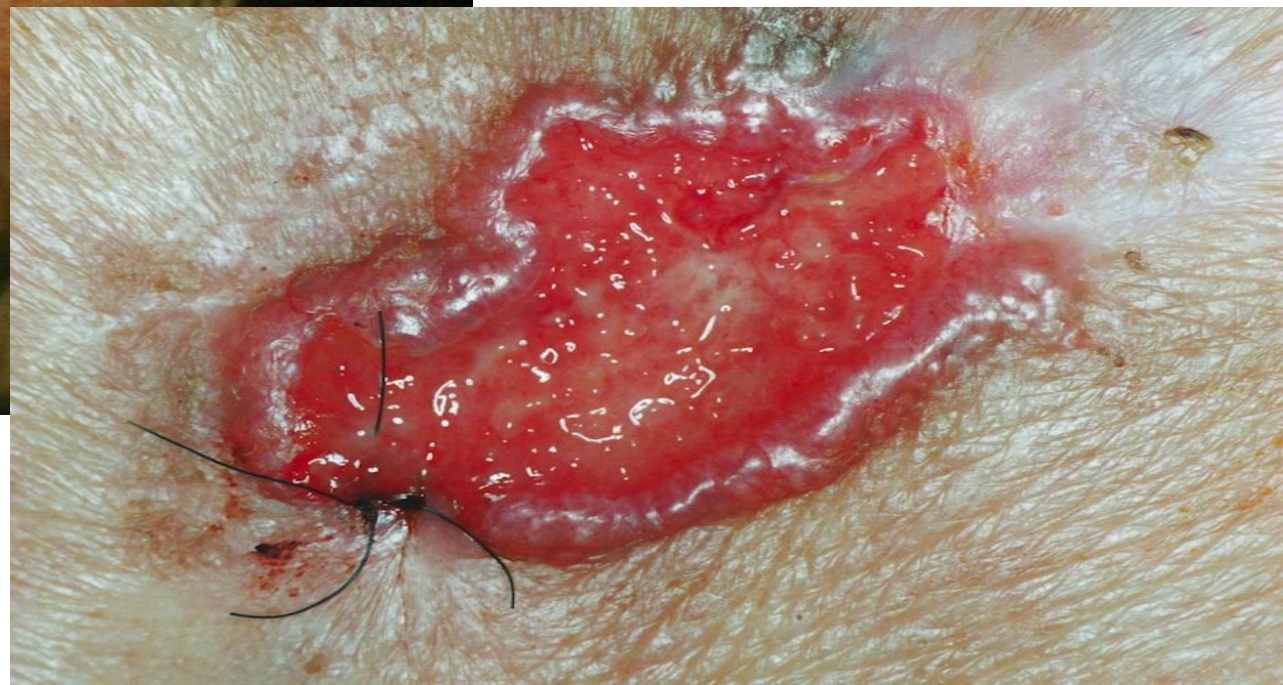
 - the most common variant (60%)

- localization: neck, head
- Irregular pink papule or nodule with telangiectases, pearlescent appearance
- During the time in the center of nodule arises central ulceration = (ulcus rodens)





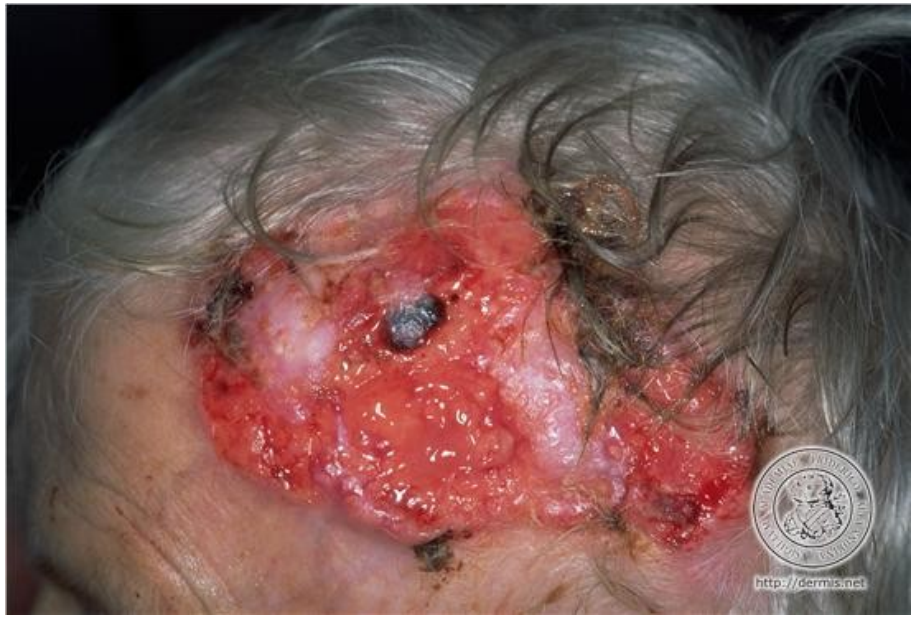




Basal cell carcinoma – clinical features

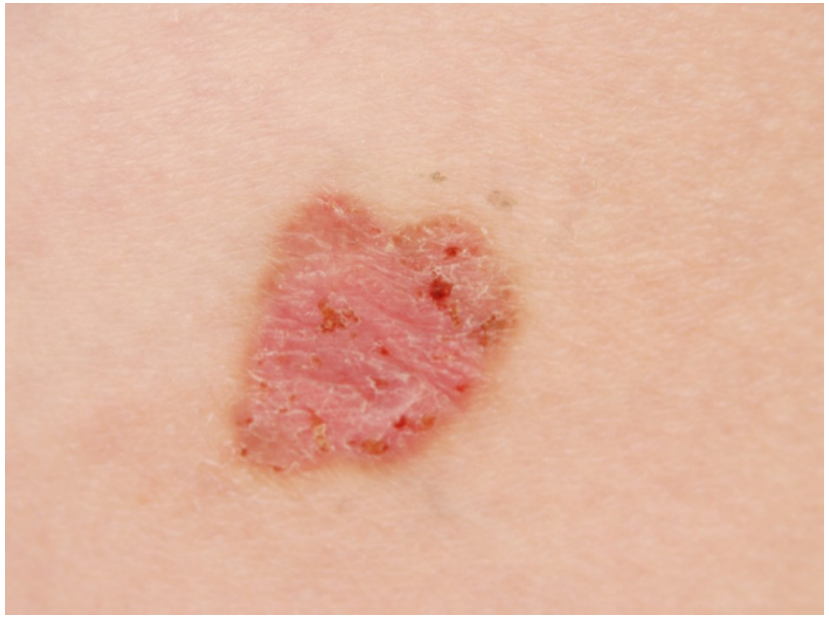
- Ulcus terebrans

 - with long-term growth, basal cell carcinomas can grow deeper, through cartilage or bone with the formation of a devastating granulating lesion



Basal cell carcinoma – clinical features

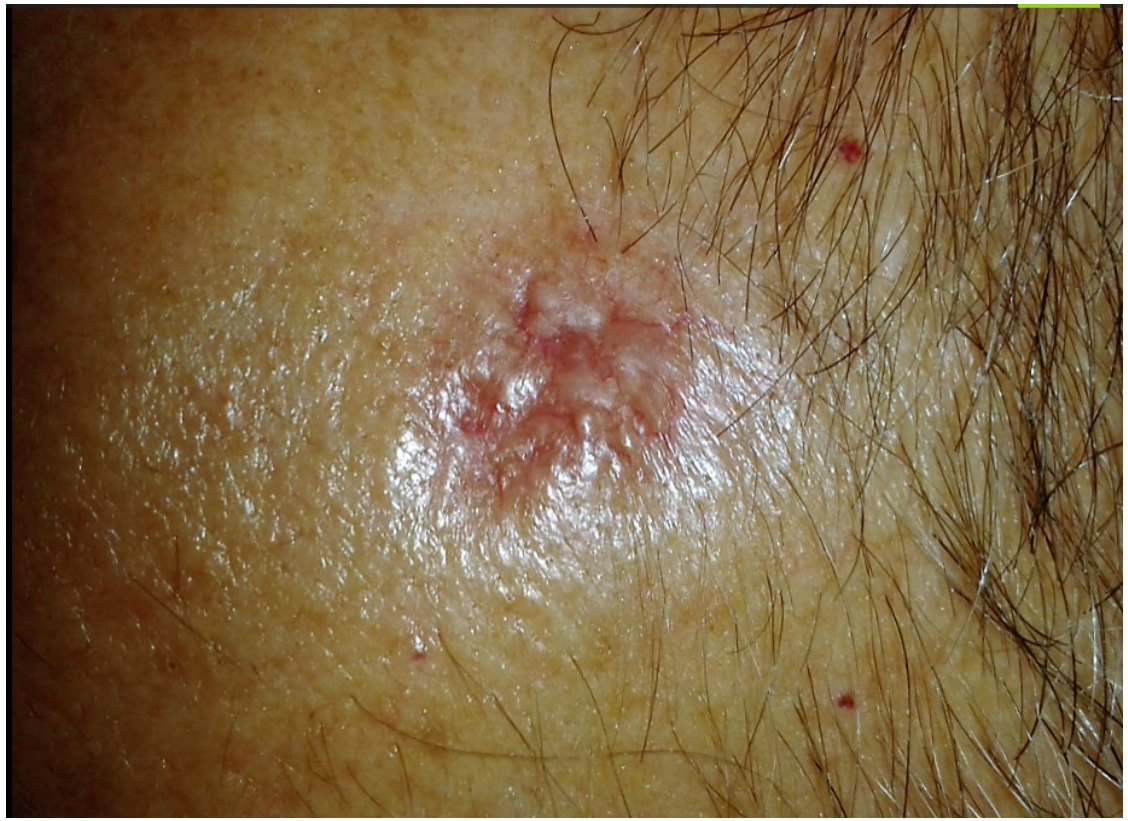
- **Superficial BCC** (15-30%)
- localization: trunk, limbs
- Red – brown macules and patches with scale and pearly border
- The most common type of BCC in arsenic toxicity

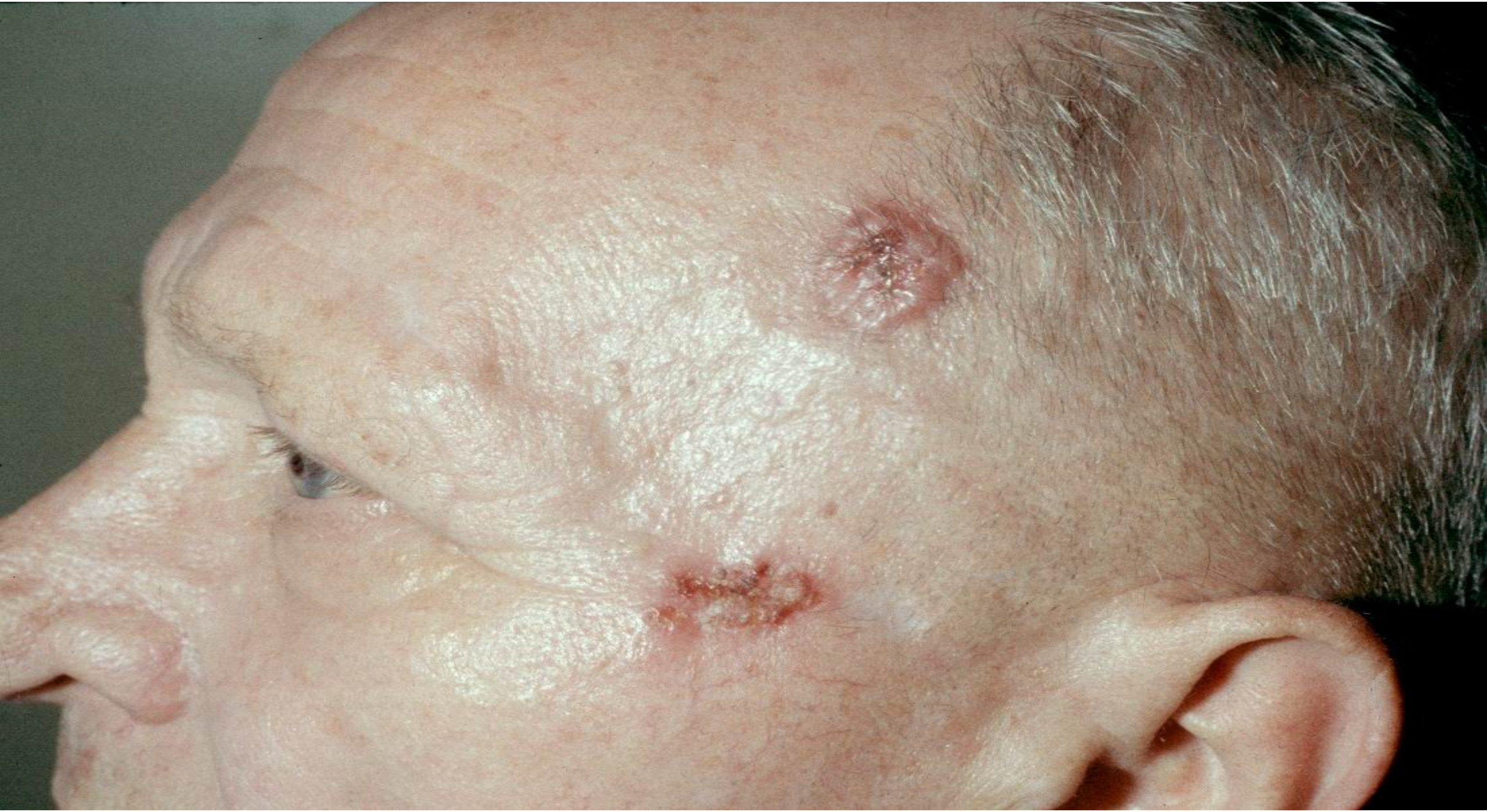


Basal cell carcinoma – clinical features

- **Sclerosing (sclerodermiform) BCC** 3%

- localization : head and neck
- this presents as indurated scar, smooth, slightly elevated lesion of yellow or whitish color, sometimes with crusts on the surface

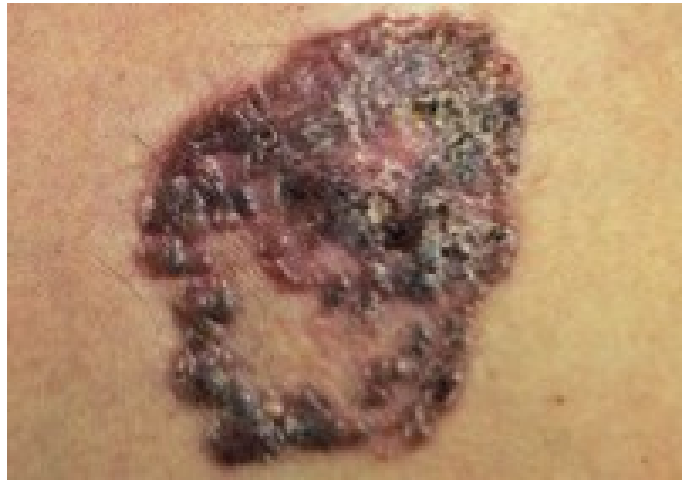


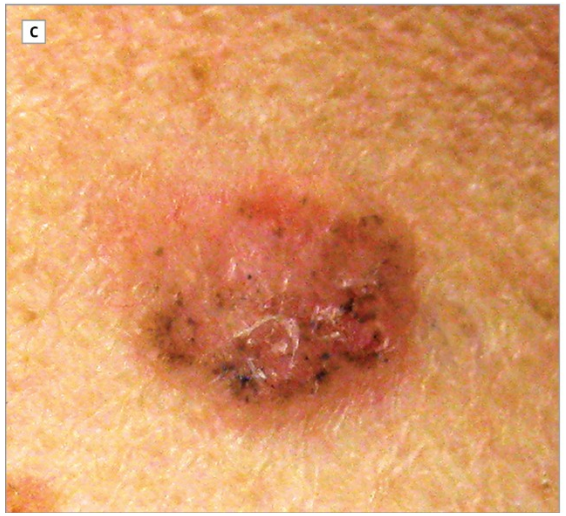


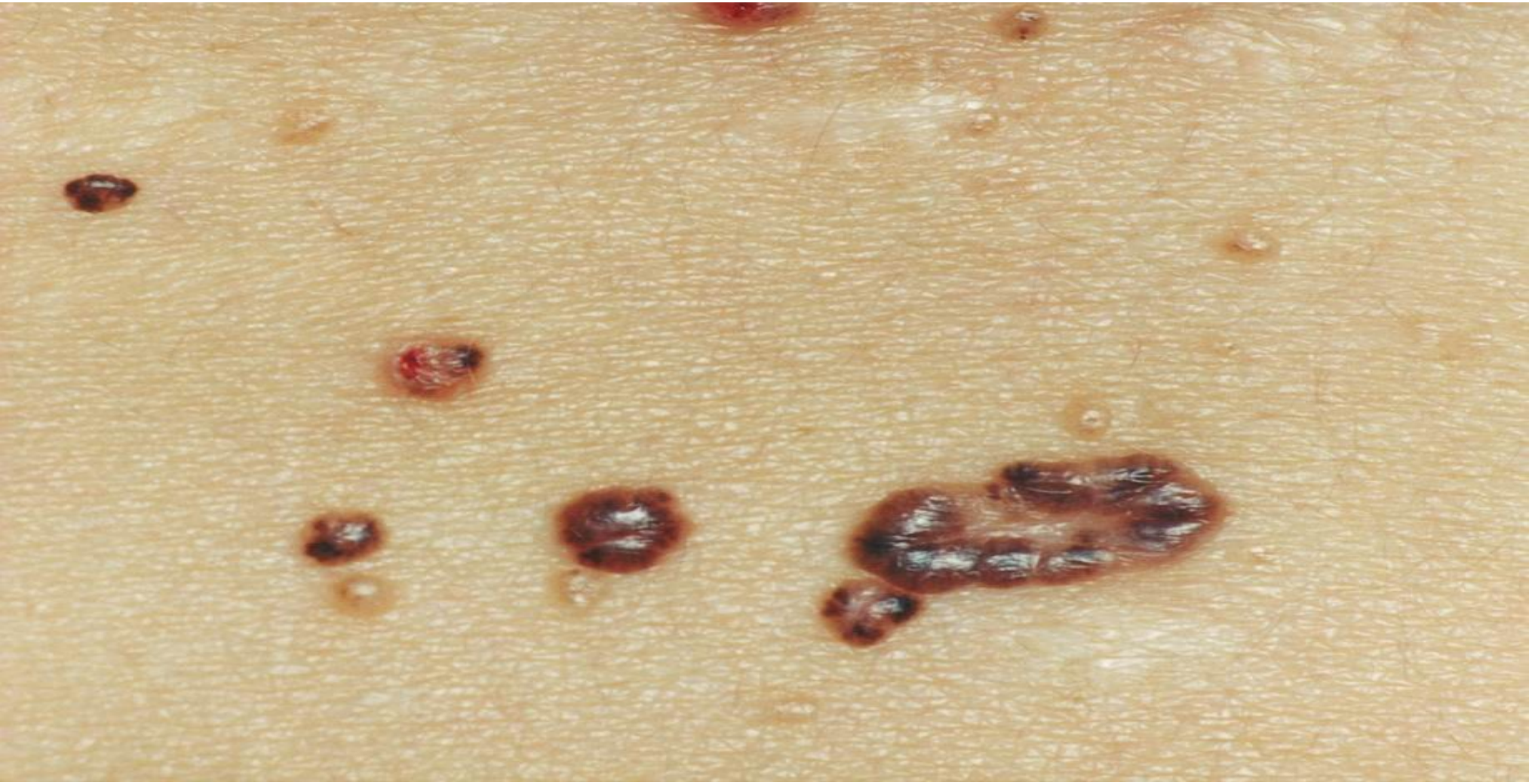
Basal cell carcinoma – clinical features

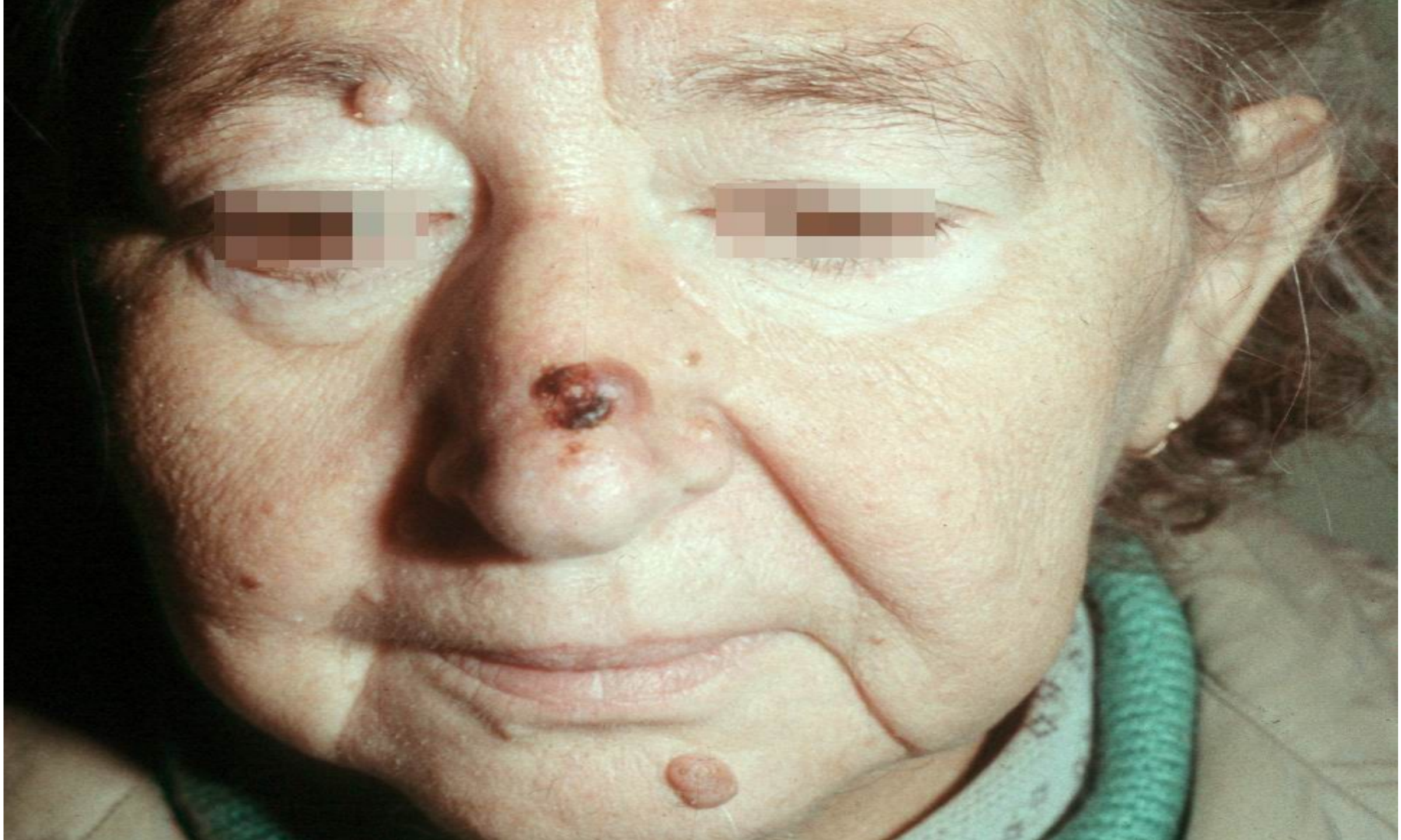
- **Basal cell carcinoma with pigment**

- easy confusion with melanoma







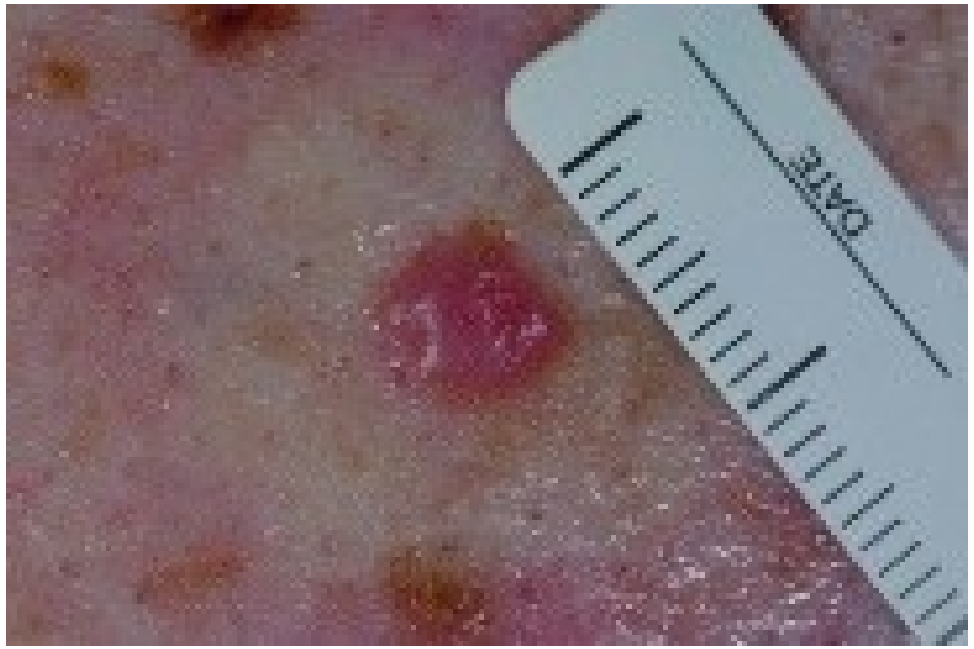


Basal cell carcinoma – clinical features

- **Fibroepithelioma (Pikus tumor)**

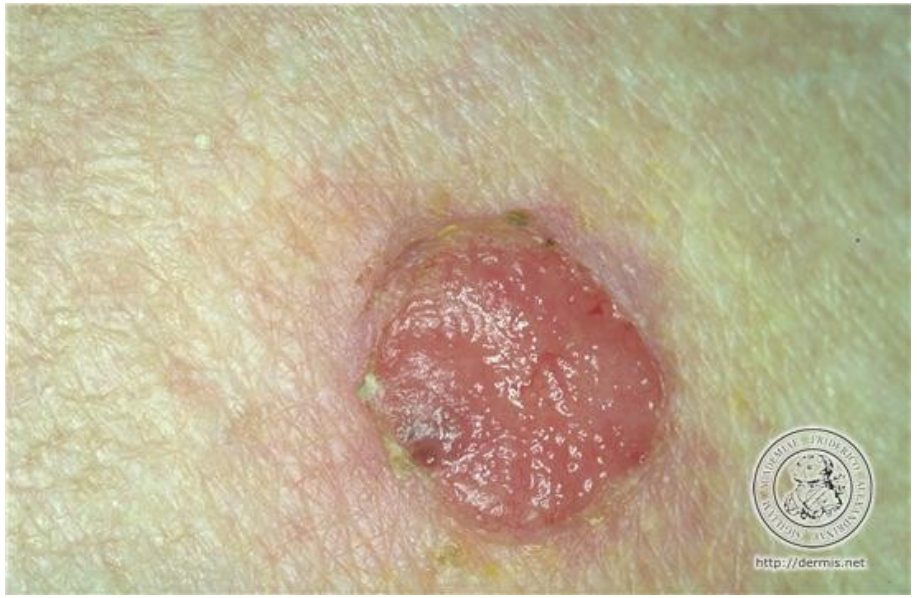
 - localization: trunk (lumbal region)

- Small smooth papule with pearls surface



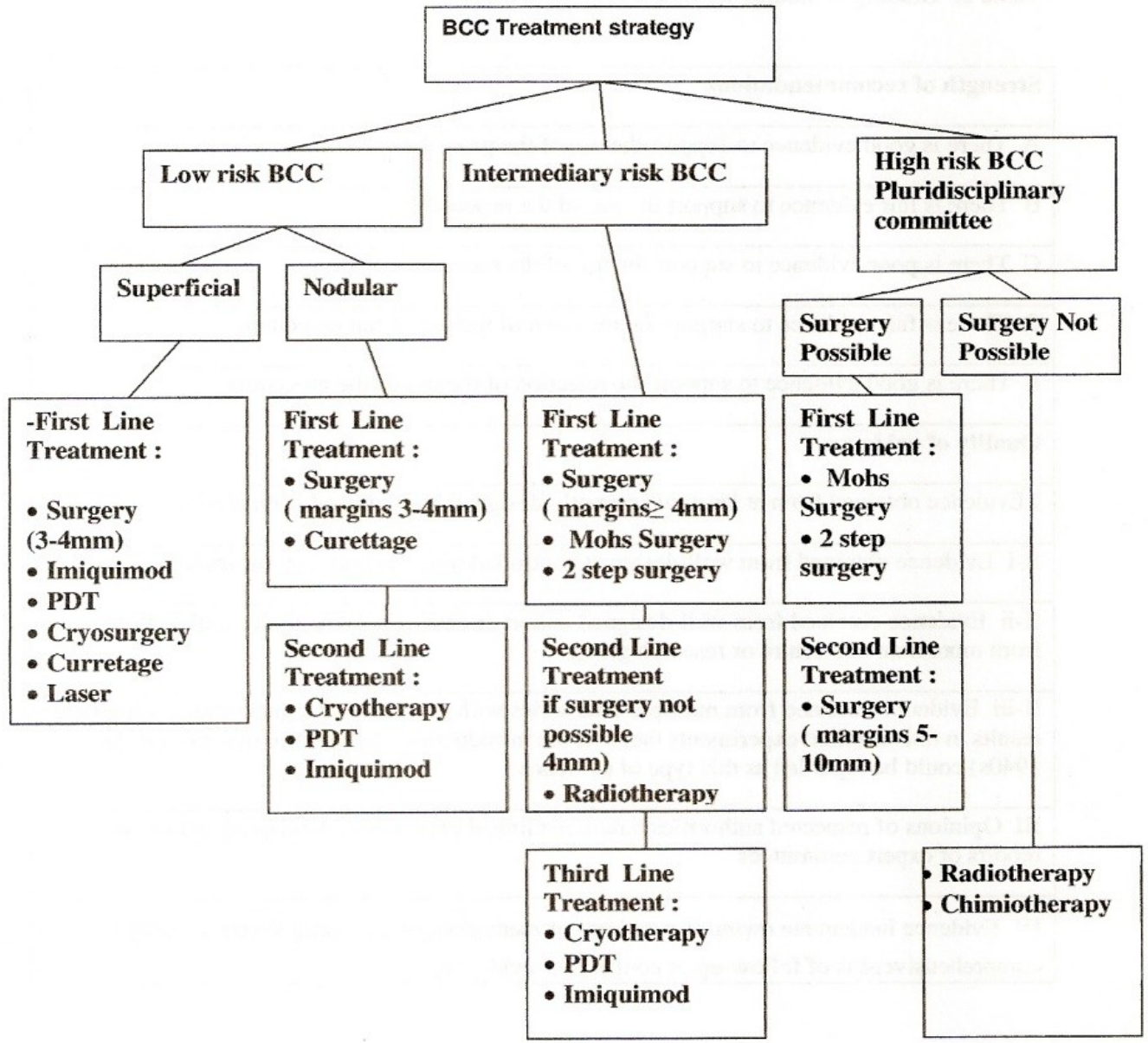
Basal cell carcinoma – clinical features

- **Bazosquamous basal cell carcinoma (metatypic basal cell carcinoma)**
- localization: head, neck
- histologically structures of basal cell carcinoma and squamous cell carcinoma
- faster and more aggressive growth



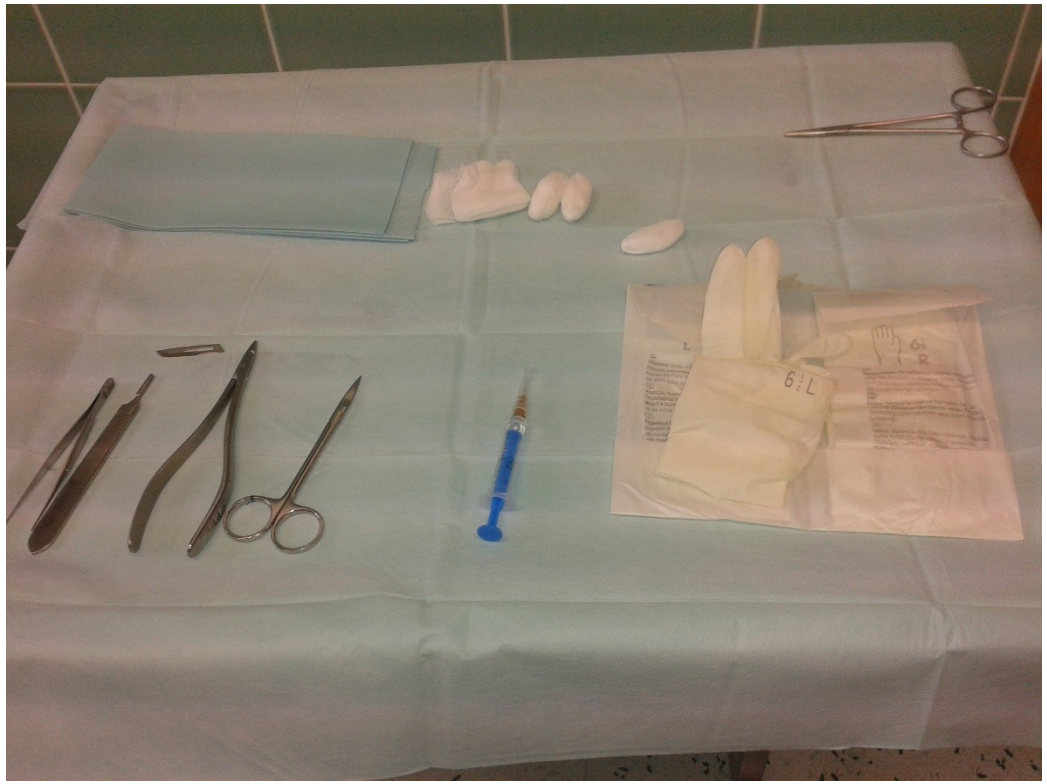
Basal cell carcinoma – therapy

- It depends on localization and size of tu
- Smaller tu – excision, bigger tu – radical operation, more superficial – cryotherapy
- Or laser, photodynamic therapy, 5% imiquimod, 5% fluorouracyl in special cases


BCC Treatment strategy
Low risk BCC
Intermediary risk BCC
High risk BCC Pluridisciplinary committee
Superficial
Nodular
Surgery Possible
Surgery Not Possible
-First Line Treatment :
• Surgery (3-4mm)
• Imiquimod
• PDT
• Cryosurgery
• Curretage
• Laser
First Line Treatment :
• Surgery (margins 3-4mm)
• Curettage
First Line Treatment :
• Surgery (margins≥ 4mm)
• Mohs Surgery
• 2 step surgery
First Line Treatment :
• Mohs Surgery
• 2 step surgery
Second Line Treatment :
• Cryotherapy
• PDT
• Imiquimod
Second Line Treatment if surgery not possible 4mm)
• Radiotherapy
Second Line Treatment :
• Surgery (margins 5-10mm)
Third Line Treatment :
• Cryotherapy
• PDT
• Imiquimod
• Radiotherapy
• Chimiotherapy

Basal cell carcinoma – therapy

- 1st choice method for all types of BCC - surgical excision
- Advantages: histological verification, high success rate - recurrences 2-8% after 5 years from the procedure
- Disadvantages: invasive, scars, problematic in elderly polymorbid patients, incomplete excision



Basal cell carcinoma – therapy

- **Cryodestruction**

 - suitable for low-risk basal cell carcinomas

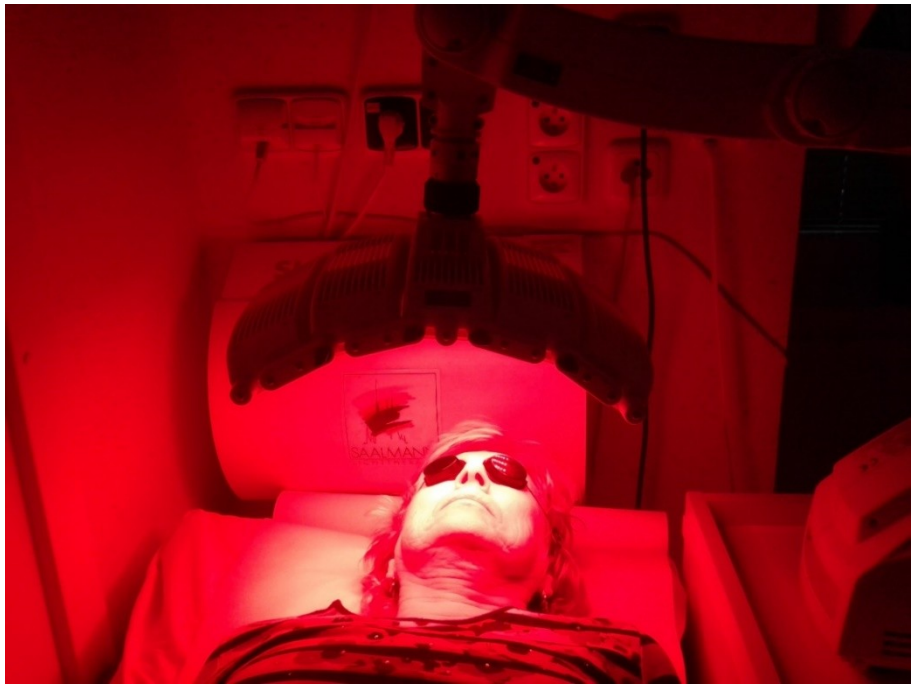
- Recommended exposure time - 2-3 repetitions for 10s,
- Advantage: fast, cheap method, repeated execution, high success rate 97%
- Disadvantages: there is no standardized method, hypopigmentation, according to the experience of the doctor recurrence - 8-40%

- **CO2 laser** - low-risk basal cell carcinomas

- Rather recommended in combination with PDT (nodular basal cell carcinomas)

Basal cell carcinoma – therapy

- **PDT (photodynamic therapy) -** targeted treatment using a photosensitizer - methyl ester of delta aminolevulinic acid, that we apply topically to the treated lesion (it is taken up preferentially by cells with higher metabolic activity) followed by irradiation with visible light in the presence of oxygen
- Indications: superficial AI and thin nodular basal cell carcinomas, especially for large or multiple lesions



Basal cell carcinoma – therapy

- **Radiotherapy**

- Indicated for medium and high-risk basal cell carcinomas as primary, more often adjuvant therapy, if excision is possible - always prefer a surgical solution

- histological verification is necessary before
- Indications: after incomplete excision, recurrence of BCC except recurrence after RT, BCC spreading to bone or cartilage, perineural spread of BCC

- advantages: can be used for KI surgical excision, especially for pac. older age, an efficiency around about 90% at 5 years of follow-up
- Disadvantages: going to the center, many visits, post-radiation dermatitis, alopecia

Squamous cell carcinoma SCC (carcinoma spinocellulare)

- The second most common type of skin cancer is 20% of all skin malignancies
- epithelial tumor which starts with intraepithelial growth, then after long time turns into a destructively growing tumor
- metastasizes predominantly by the lymphatic vessels (5-10%)
- localized in places exposed to sunlight, at the same time on the skin there are signs of solar damage
- 70% of spinaliomas - head, neck, 15% on the upper limbs
- occurrence in our population 11/100 000

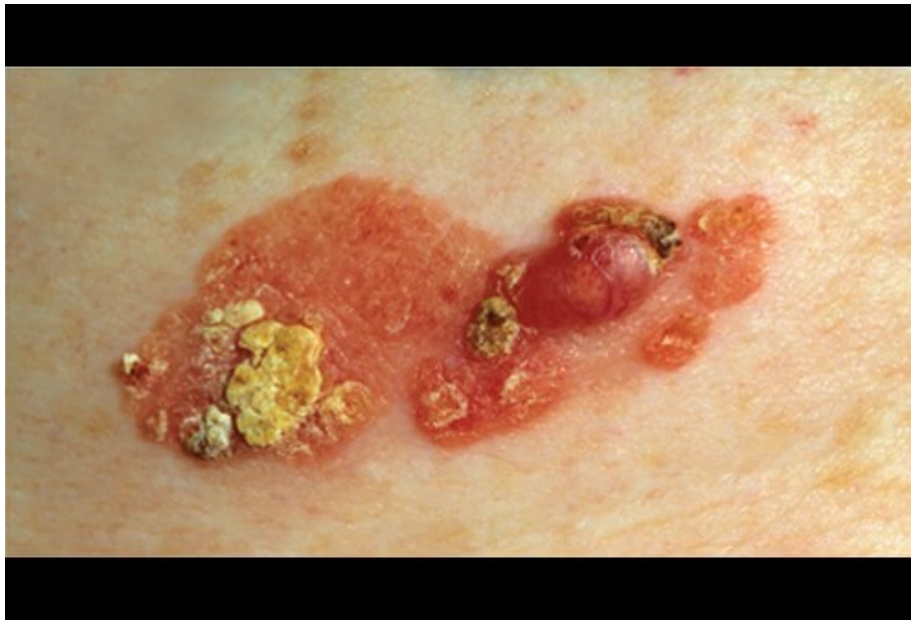
Squamous cell carcinoma – risk factors

- Age over 50 years
- Male gender
- Light skin, hair, low phototype
- UV exposure
- Chronic skin changes (scars, fistulas)
- Immunosuppression
- Human papillomavirus - HPV infection
- Chemical carcinogens (arsenic, asphalt)
- Ionizing radiation (medical, at work)

Squamous cell carcinoma – clinical features

- **diffusely infiltrating**

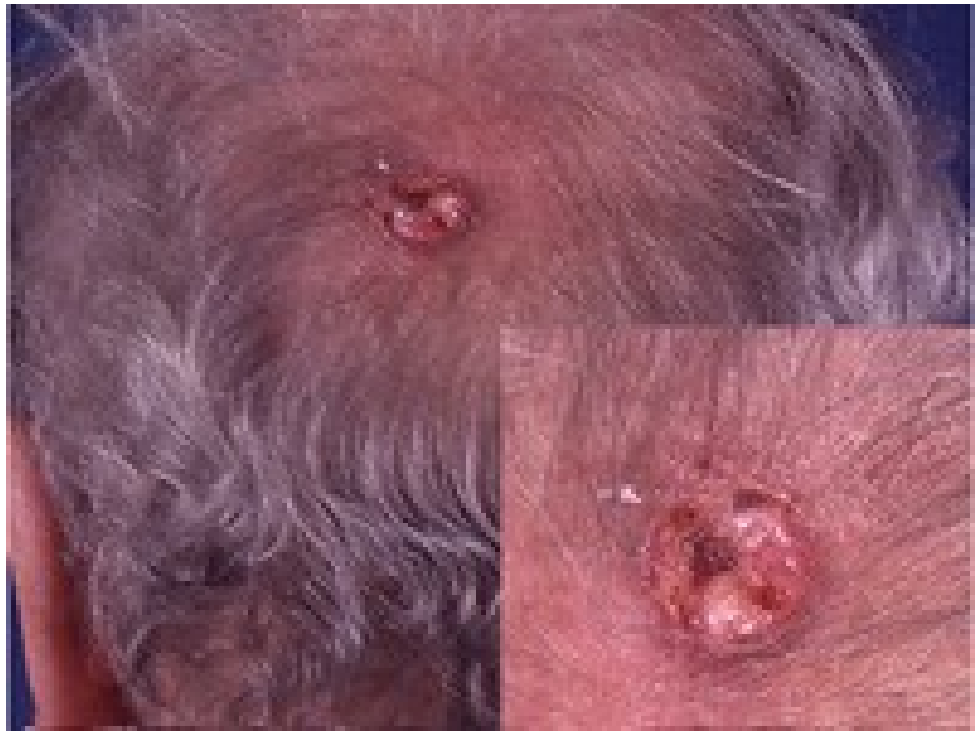
- Elevated hyperkeratosis or a solid infiltrated lesion with a nodular surface



Squamous cell carcinoma – clinical features

- **Ulcerative spinalioma**

- a chronic ulcer with rigid edges

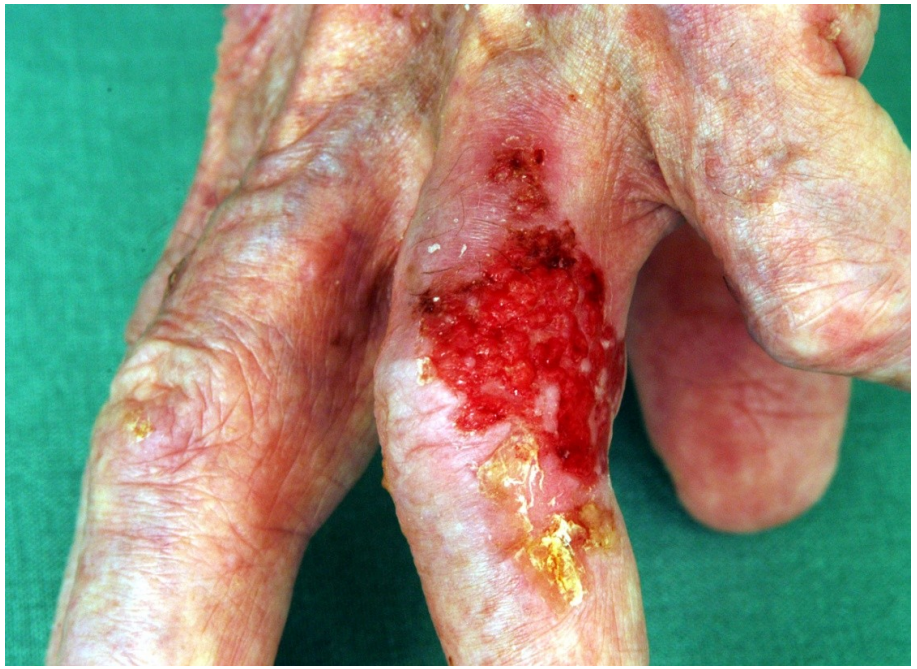


Squamous cell carcinoma – clinical features

- **Exophytic spinalioma**

- aggressive, rapidly metastatic form

- rapidly growing, soft, exophytic, bleeding and crumbling nodul

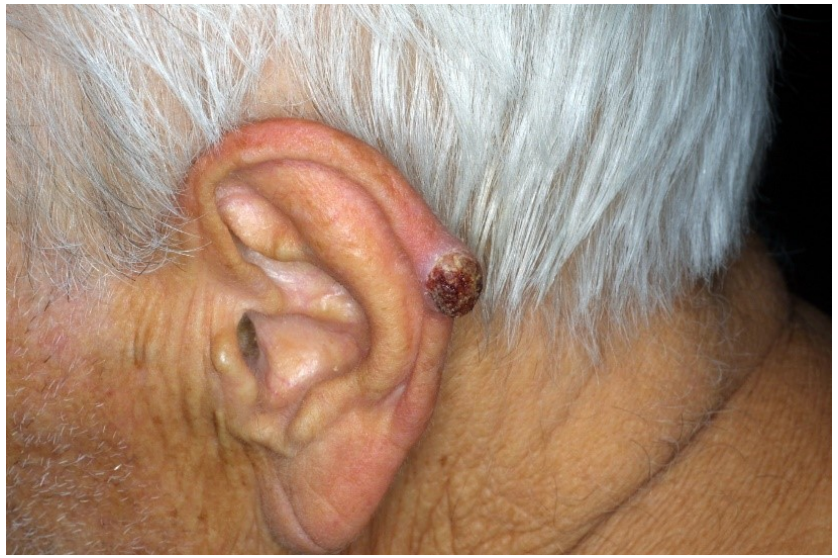


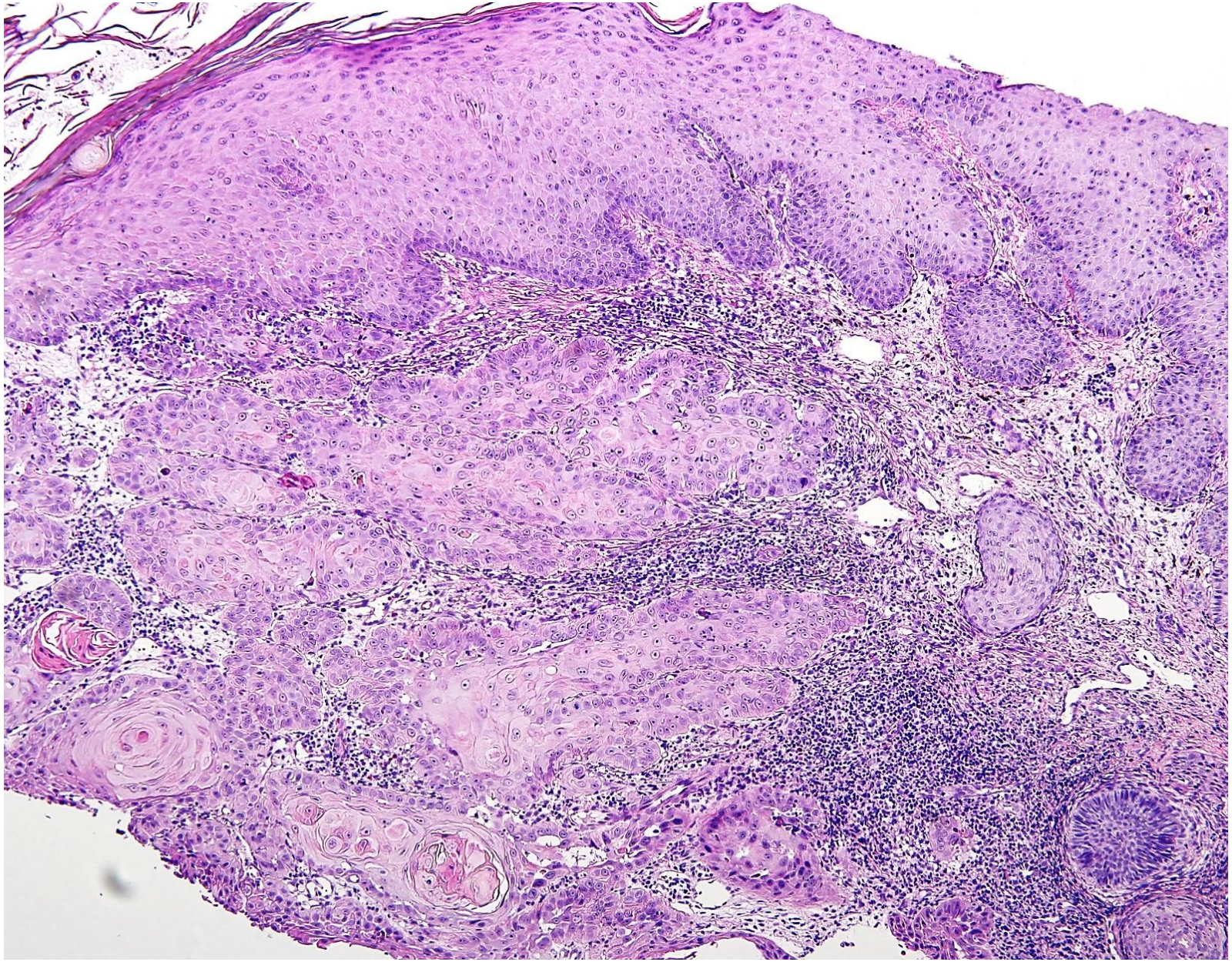
Squamous cell carcinoma - examination

- It is necessary histological verification
- invasive forms – we have to examine sentinel LU nodes (UZV, CT, MRI), in lymphadenopathy - thin aspiration

Squamous cell carcinoma - therapy

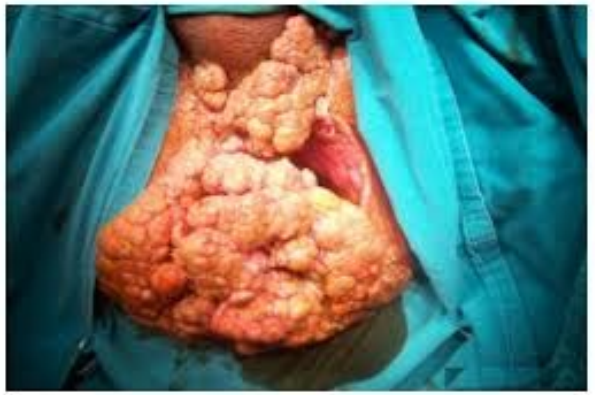
- Radical surgical excision
- Radiotherapy - especially in the elderly
- Chemotherapy - oral form of 5-fluorouracil - in inoperable or metastatic forms





Verrucous carcinoma (Ca verrucosum)

- Rare , highly differentiared spinoca with verrucous surface
- Invasive growth
- Lower tendency to meta
- HPV 6,11
- Epithelioma cuniculatum, papilomatosisi cutis carcinoides, florid oral papilomatosis, giant condyloma – BUSCHKE- LOWENSTEIN
- Therapy: excision, RT, laser; retinoids, INF, chemo



B) Mezenchymal malignant skin tumors

- **<u>Dermatofibrosarcoma protuberans</u>**
- Recurrent fibrous tumour, locally invasive growth, low tendency to meta, often reccurence after surgical excision
- Like a keloid
- CD34+ fibroblasts
- Therapy: wide and deep surgical excision (3-5cm, to fascia)

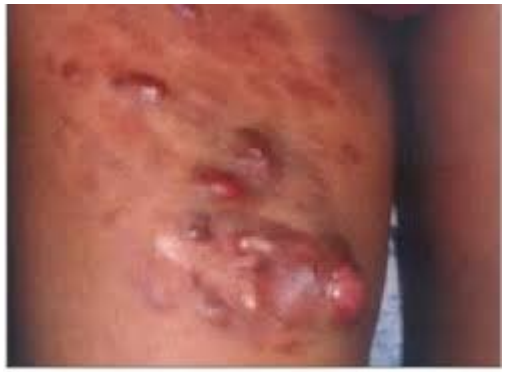
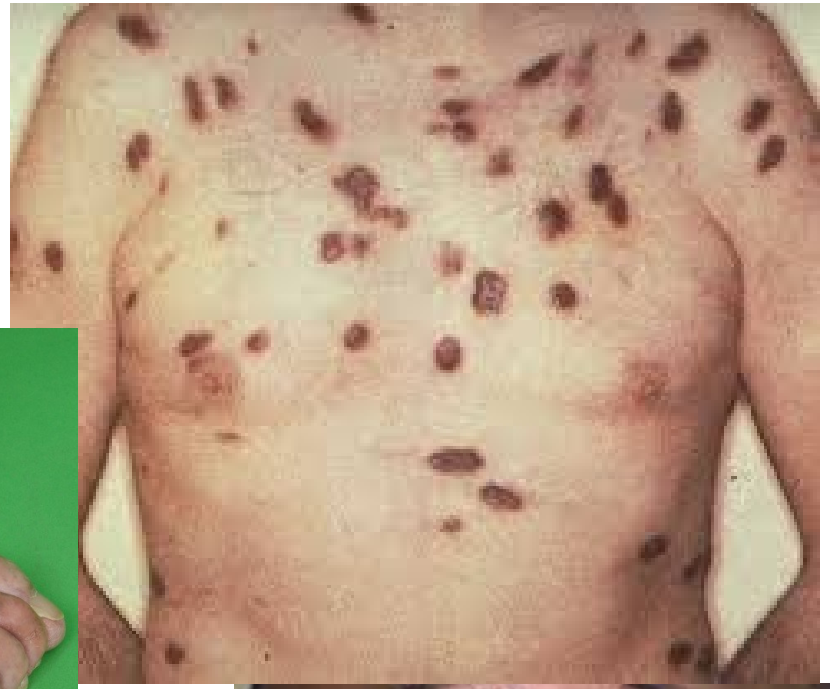
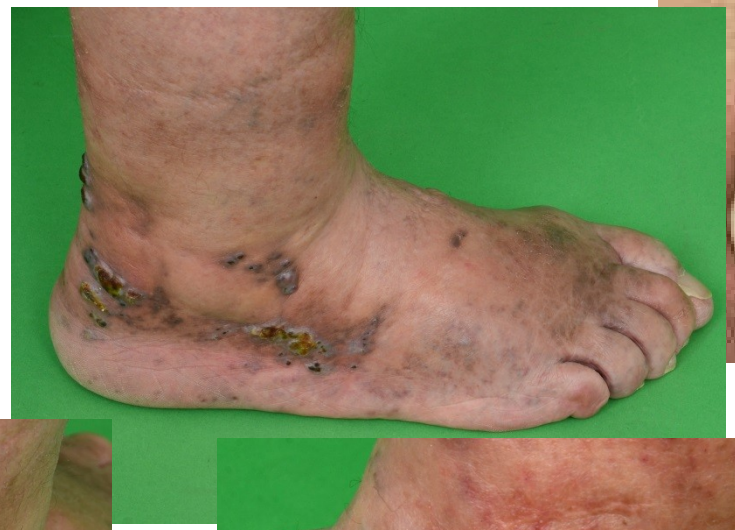
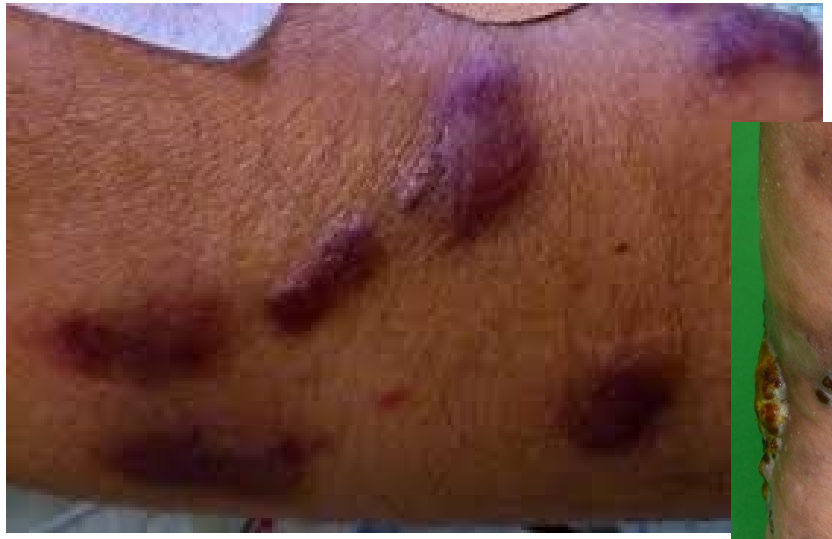
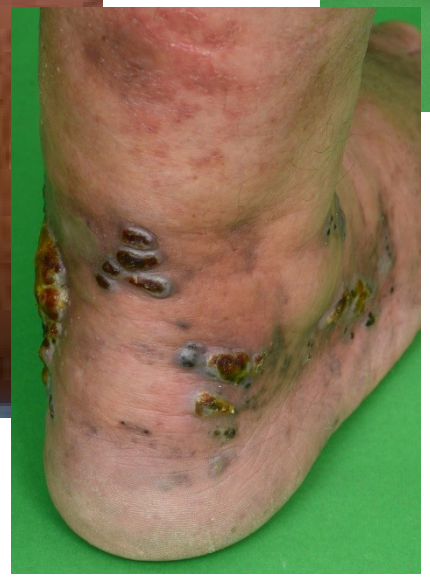
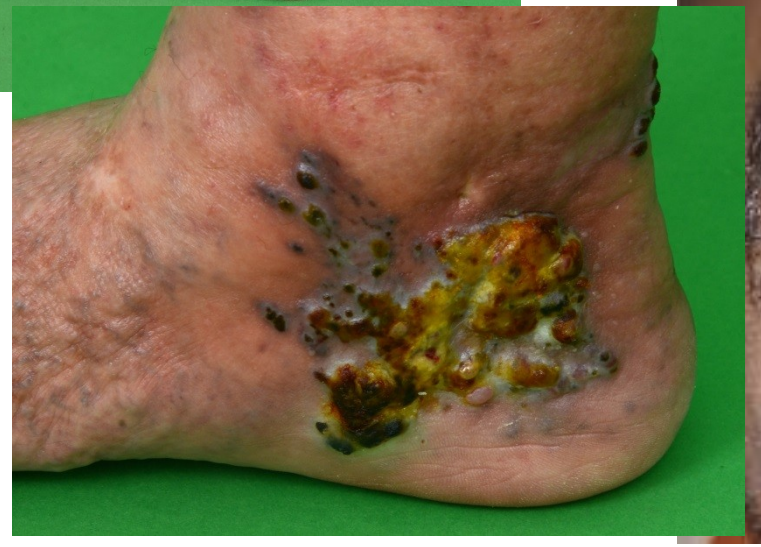
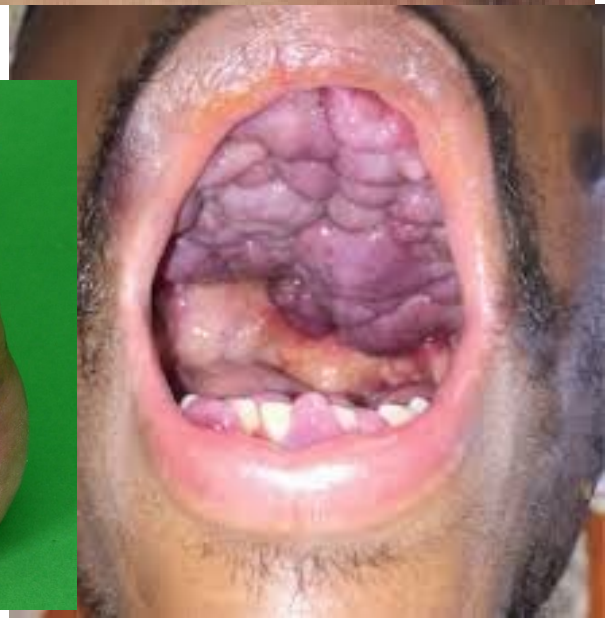


Figure 1: Atrophic and papulonodular lesions on the right thigh

- **Kaposi sarcoma**
- Malignant vascular tumour
- Risk f.: imunosupression, HHV 8
- types:
  - Classical – Europe, 50-80y, 15:1
  - Endemic – Africa, 25-40y, 17:1
  - Iantrogenic – imunos., 20-60y, 3:1
  - Epidemic – AIDS, 37 y, 106:1
- Clinical forms:
  - Classical – localised, nodular
  - Disseminated form (skin + mucosal. Mem, GIT)
- Stages:
  - Inicial- macula
  - Infitrated- macules
  - Tumorous – plaques, papules,nodules

- Therapy:
  - Surgical, kryo, PDT, RT, laser
  - INF alfa, chemo, antiretrovirotics- HIV +
- Prognosis:
  - Classical- great, indolent
  - Disseminated – fatal

2. Melanoma

- The most dangerous type of skin cancer
- Malignant tu. with high potential of mts
- Develops by neoplastic proliferation of melanocytes (pigment- containing cells) in the skin, eye, rarely occur in the mucose of the mouth, intestines, lungs….
- Develops from a mole (mark, nevus pigmentosus) or „de novo“
- It is more often among people of middle age
- In women – most commonly occur on the legs, in men on the back
- Prognosis: Breslow to 1 mm 10y ….93–99 %, 1,01–2 mm …. 70–92 %, 2,01–4 mm ……40–69 % over 4 15–39 % případů; + mitosisis, ulceration, meta!!!
- Follow up and prevention!

Risk factores of melanoma

1. Ultraviolet light exposure (especially sunburn in childhood with blisters, cumulative dose of UVB , be carefull about tanning devices)
2. People with many moles especially – dysplastic nevus syndrome
3. Phototype I, II (light skin, blond or red hair, blue eyes, or Snow White type with black hair, fine-bone white skin and blue eyes) – typically in Australia, New Zealand, Northern Europe

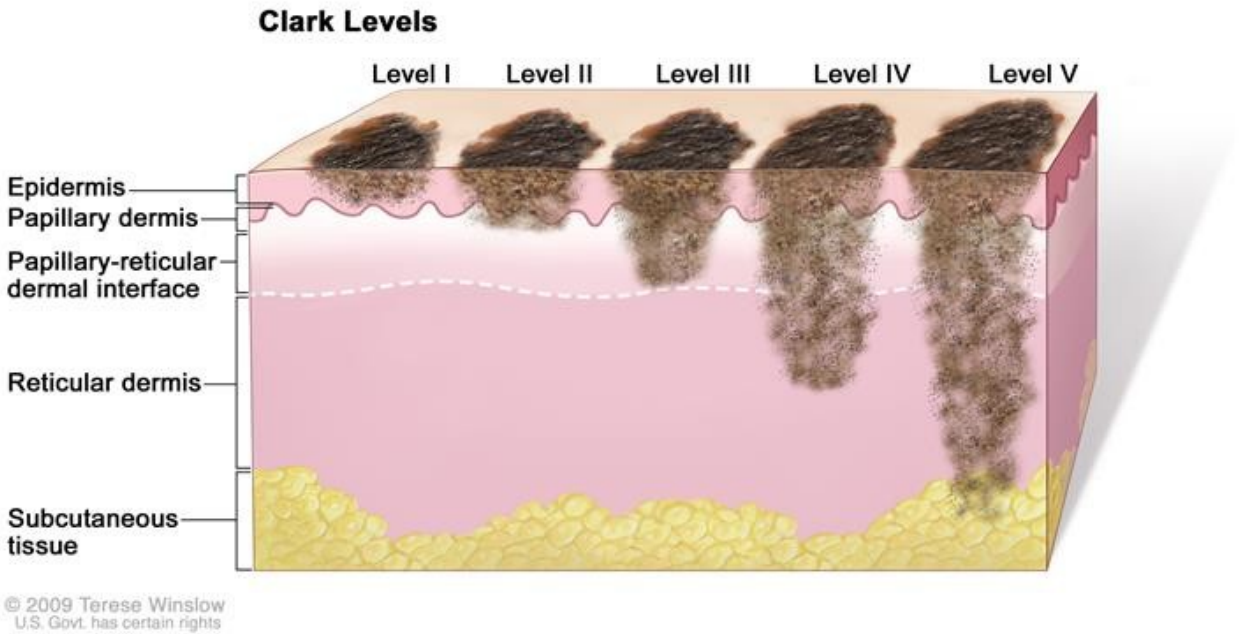
4. Genetic defects such as xeroderma pigmentosum
5. Immunosupression

Inicidence is rising - 15/100 000/y (Australia 60-70)

The growth of melanoma

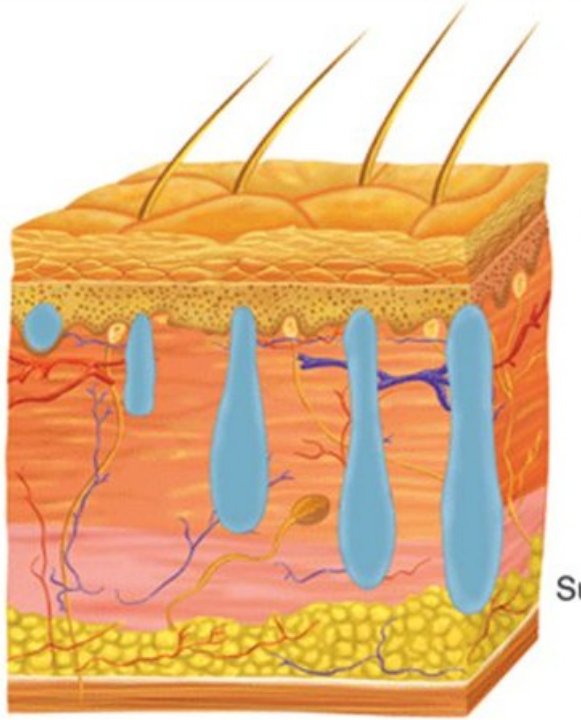
- **Radial growth phase** : melanocytes are found only in the epidermis, they spread into the higher layers of epidermis and then new clones with different speed of growth of malignant cells develope in the places far from the original, the tumor is less than 1mm thick
- **Vertical growth phase** : malignant cells spread deeper to papillary dermis, the tumor becomes able to grow into the surrounding tissue, can spread through blood or lymph vessels, the tumor is more than 1 mm thick
- The Breslows depth of the lession - the depth of invasion from stratum granulosum to the malignant cell , which is situated deepest

Growth of tumor



Breslow Thickness

Clark level	Breslow (mm)	AJCC T
I		
II	≤ 0.75	T1
III	0.76 – 1.50	T2
IV	1.51 – 4.00	T3
V	≥ 4.00	T4



Source: Brunicardi FC, Andersen DK, Billiar TR, Dunn DL, Hunter JG, Matthews JB, Pollock RE: *Schwartz's Principles of Surgery, 9th Edition:* http://www.accessmedicine.com

Malignant melanoma

4 Clinical forms:

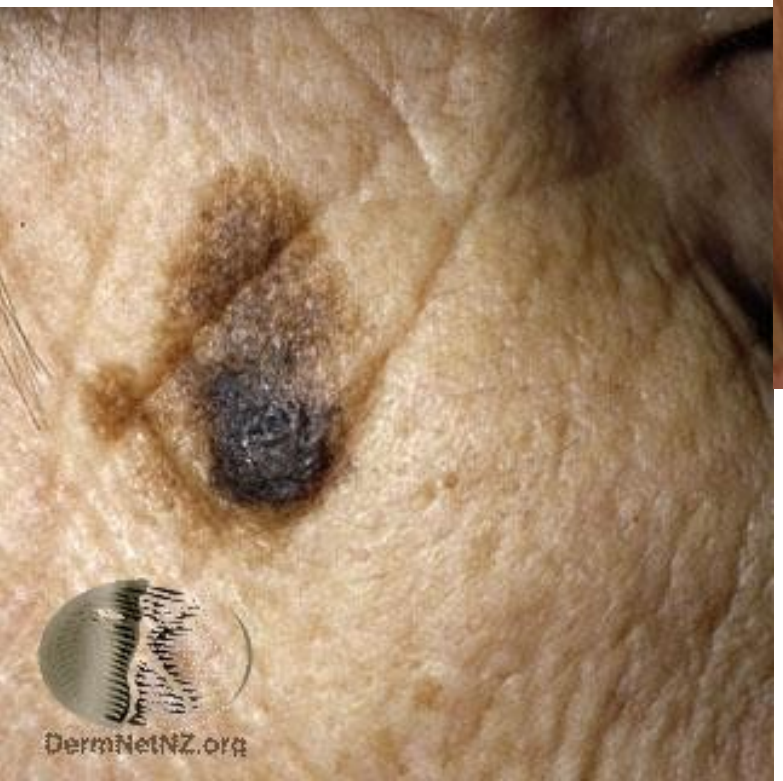
- Lentigo maligna melanoma – face – older patients
- Superficial spreading – most often
- Nodular – rapid metastases
- Acrolentiginous – often late diagnosis

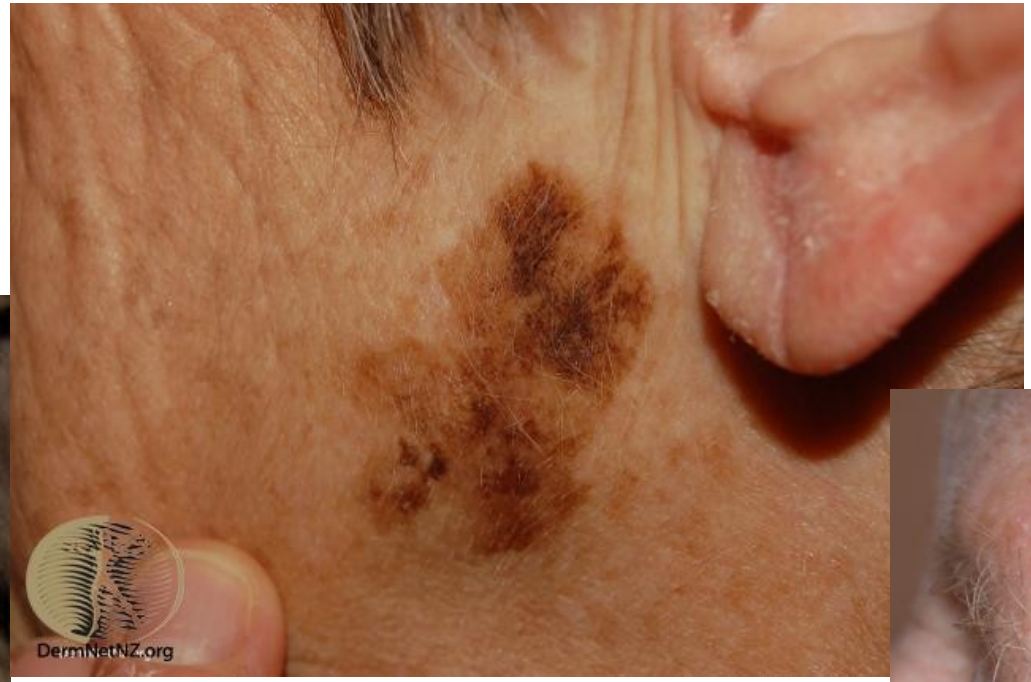
Melanoma – clinical features

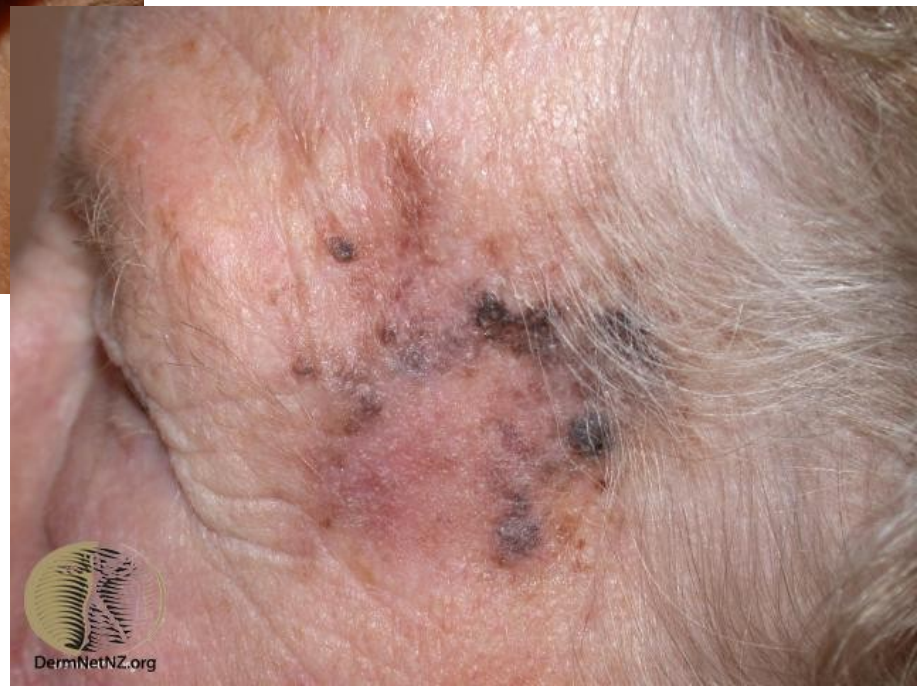
- **Lentigo maligna melanoma** – face and neck of older patients from previous lentigo maligna

- irregular edges and color, slowly increasing lesion (lentigo maligna), size of 5 or more cm, after several years of horizontal growing it starts vertical growing which ends in nodule pigmented knot or amelanotic knot develop (= transition to LMM)

LMM



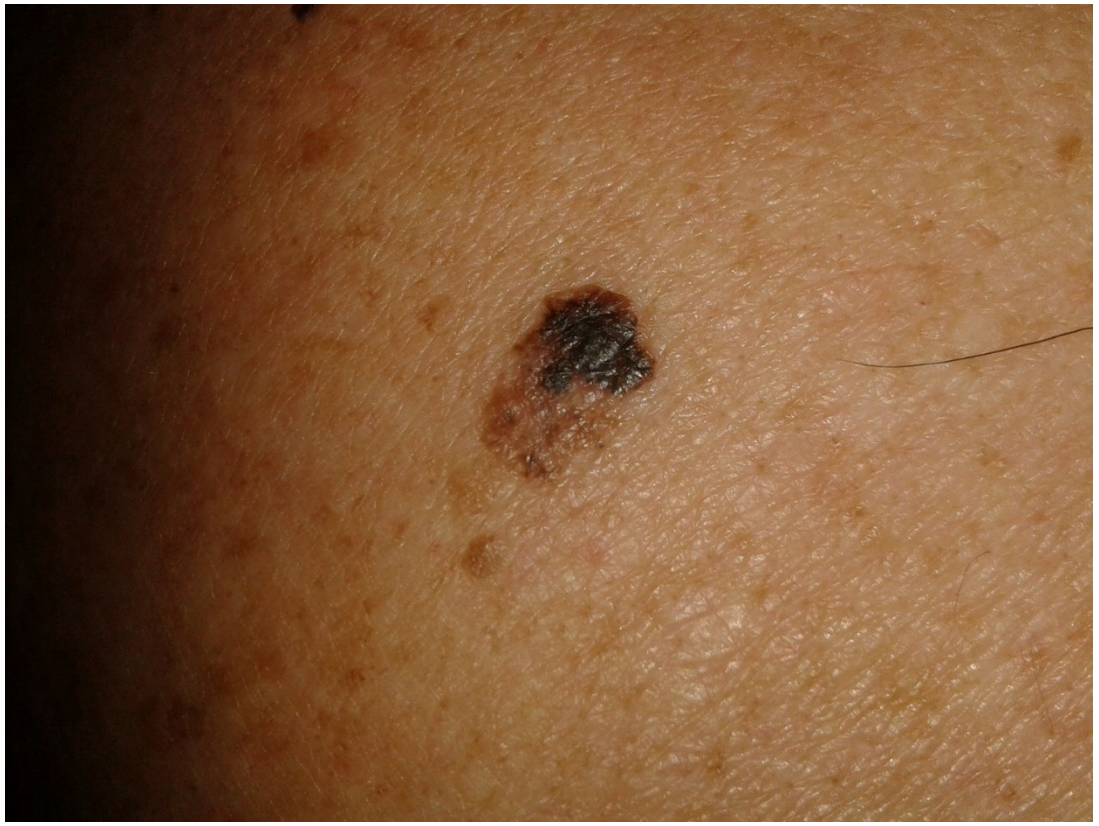


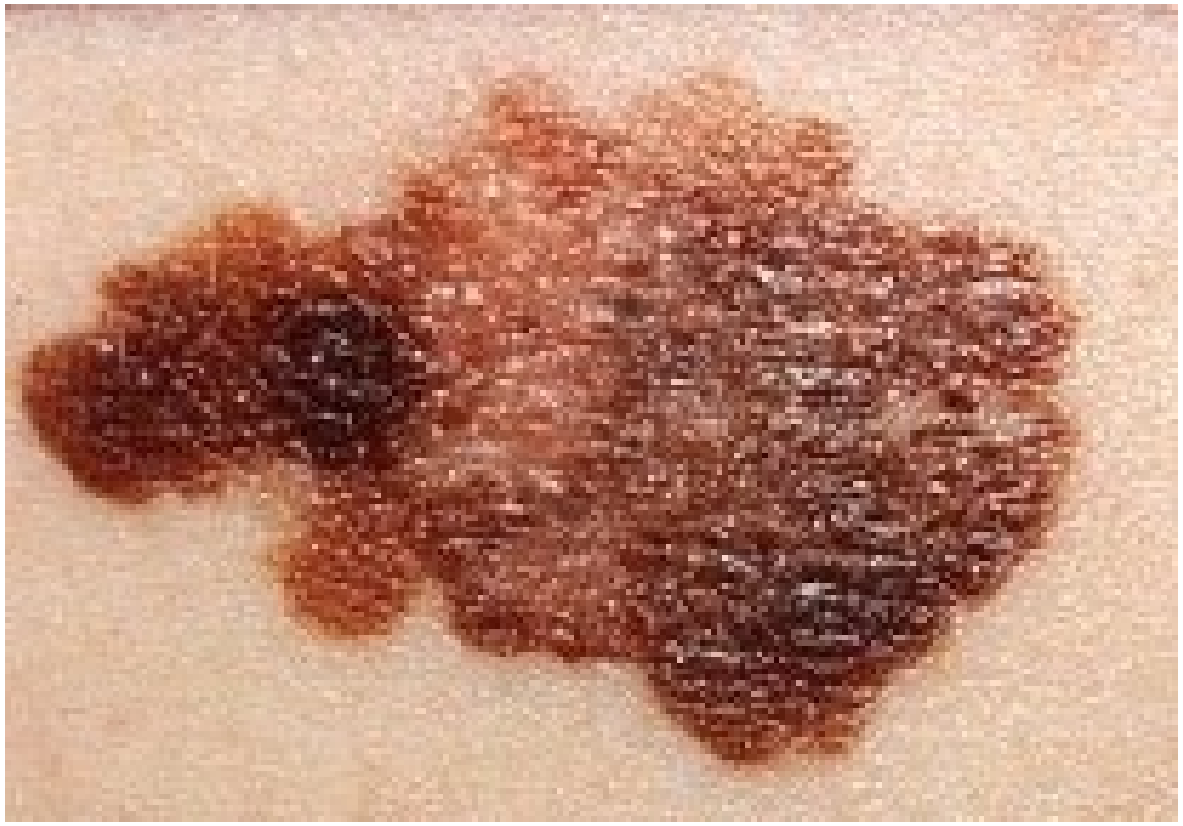


Melanoma – clinical features

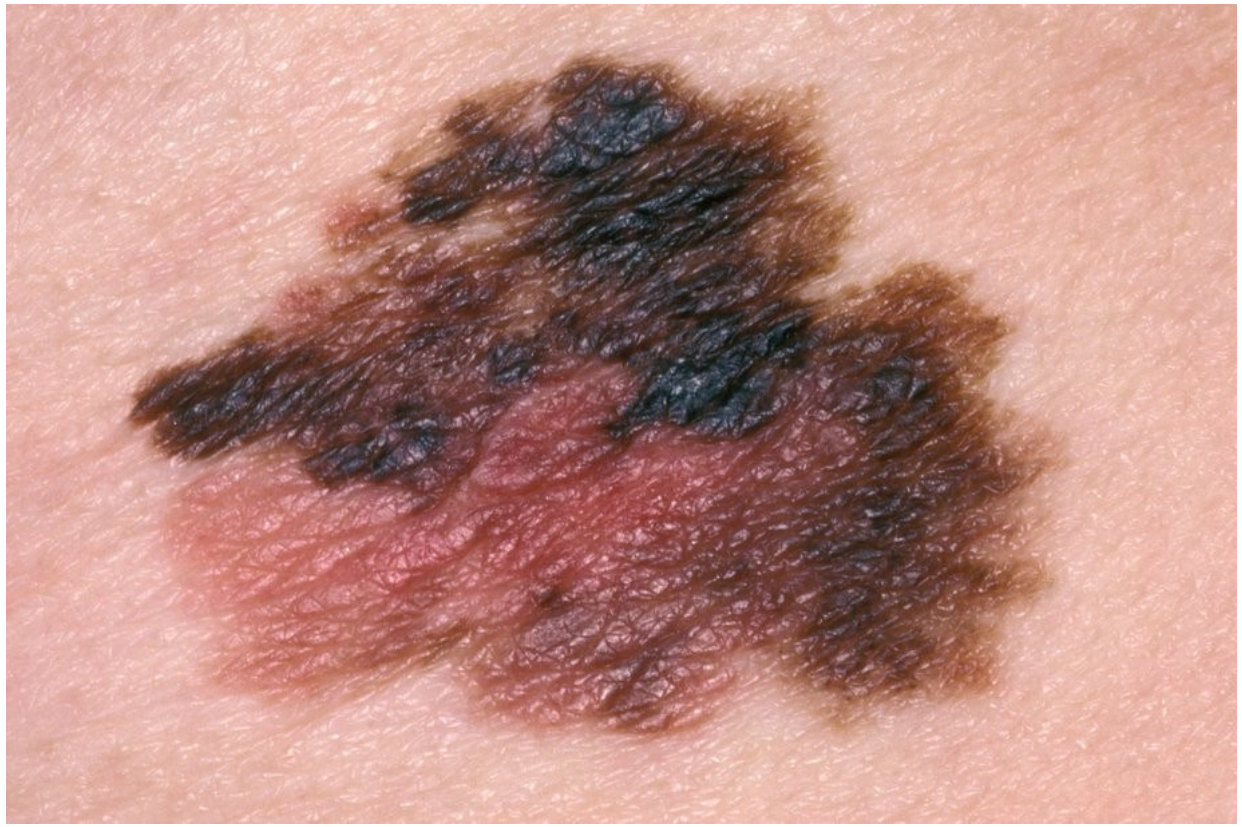
- **Superficial spreading melanoma**
- most often type (60-70%)
- At the beginning it grows slowly and symetrically, then it changed to nevus with irregular borders, it is slightly elevated than rest of the skin, it starts to change color from light to dark brown/black, some places spontaneous regreds or it could change their color to red
- **Secondary nodular melanoma** – the appearance of the nodule in the original lession, it is sign of vertical growth, worse prognoses

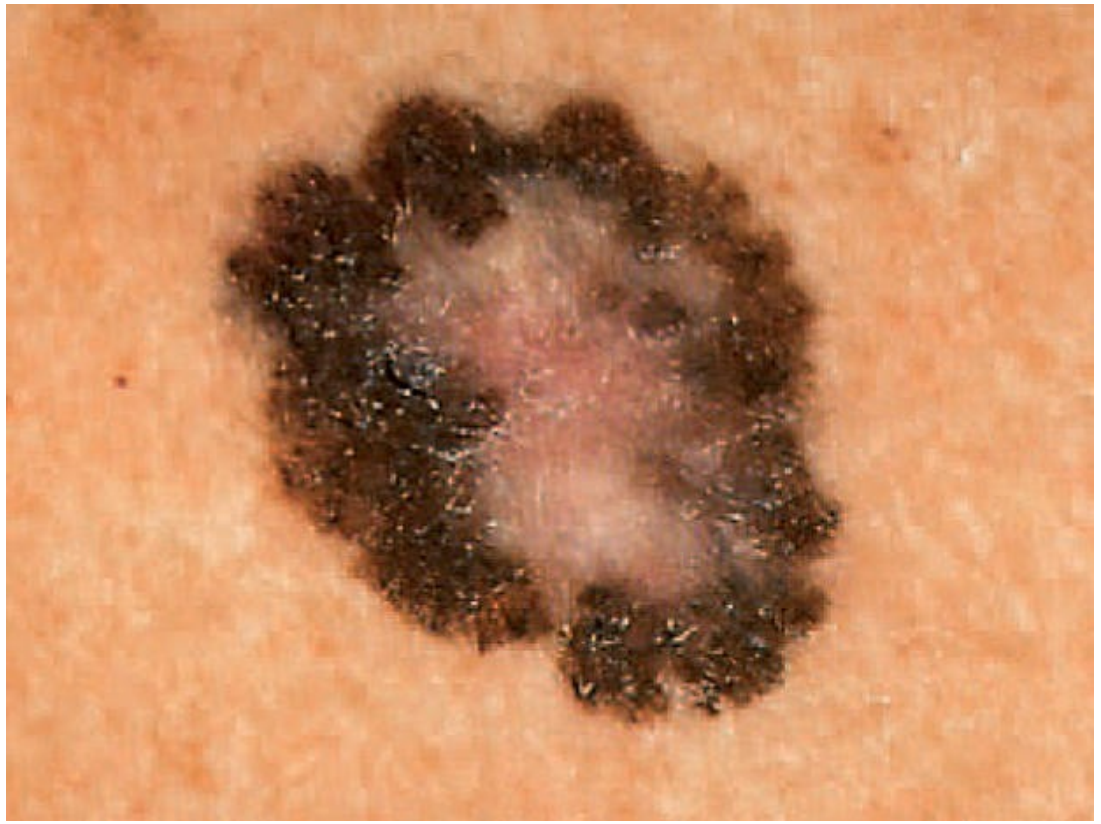
SSM





SSM





Melanoma – clinical features

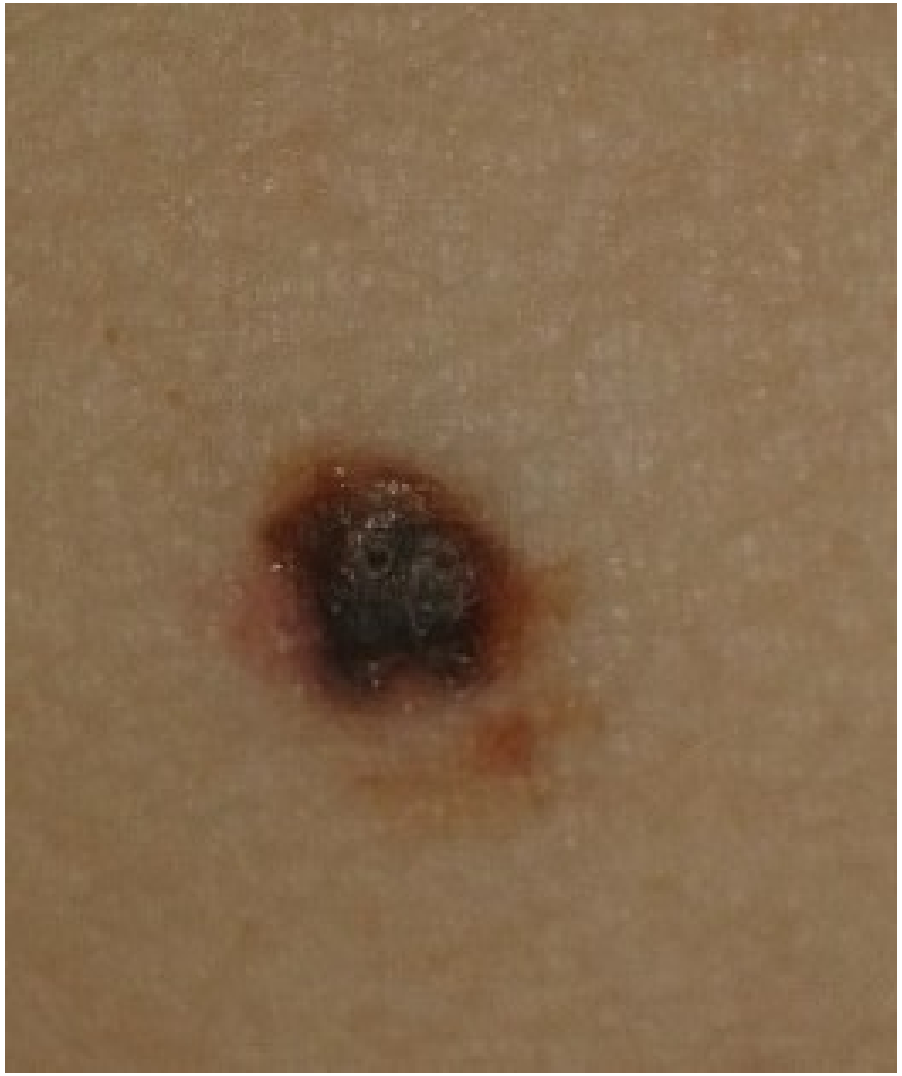
- **Nodular melanoma**

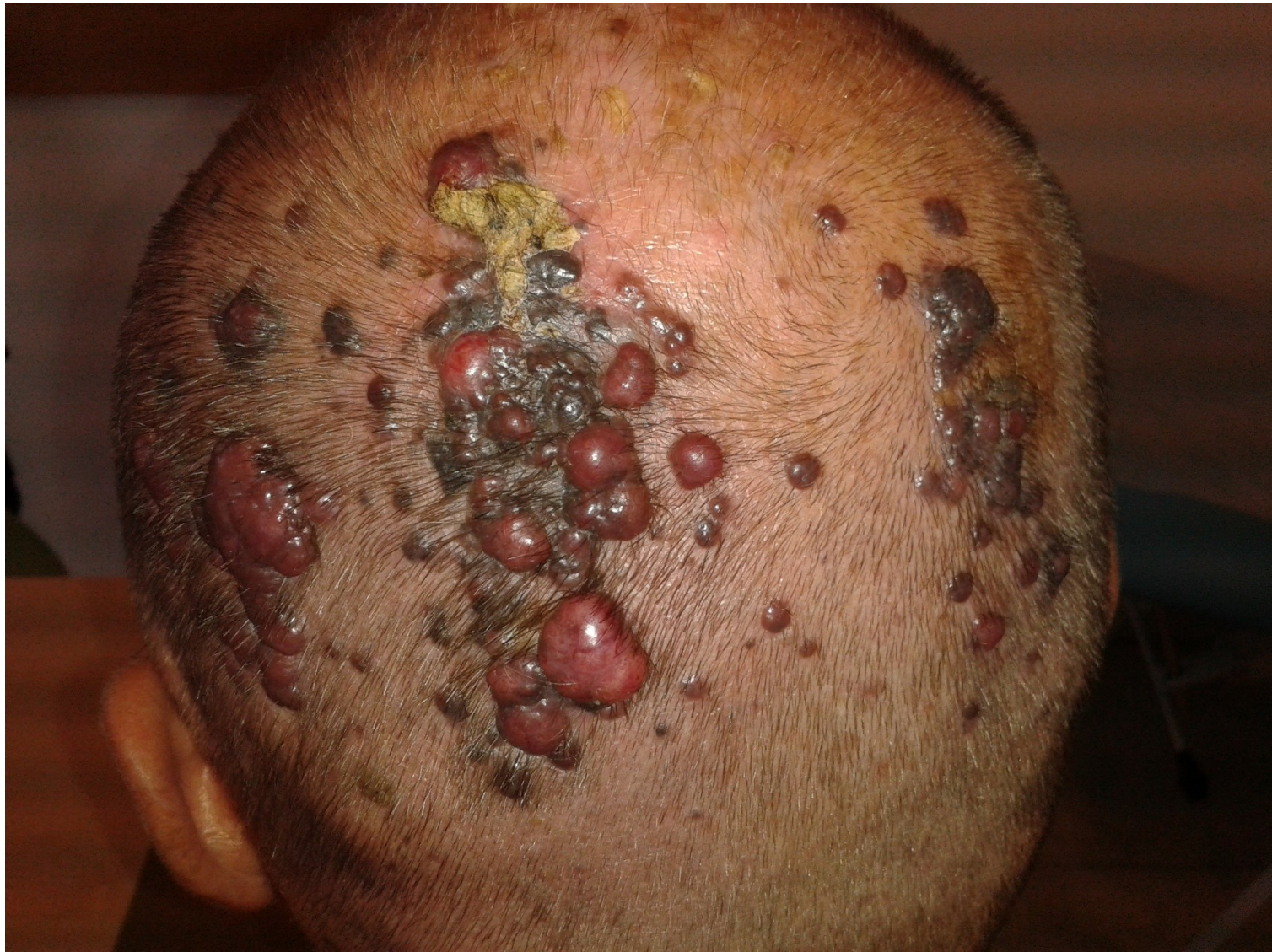
– the second most frequent type (15-30%)

- rapid becomes metastatic – developes skin local metastasis, metastases in brain, lymph nodes, liver, bones

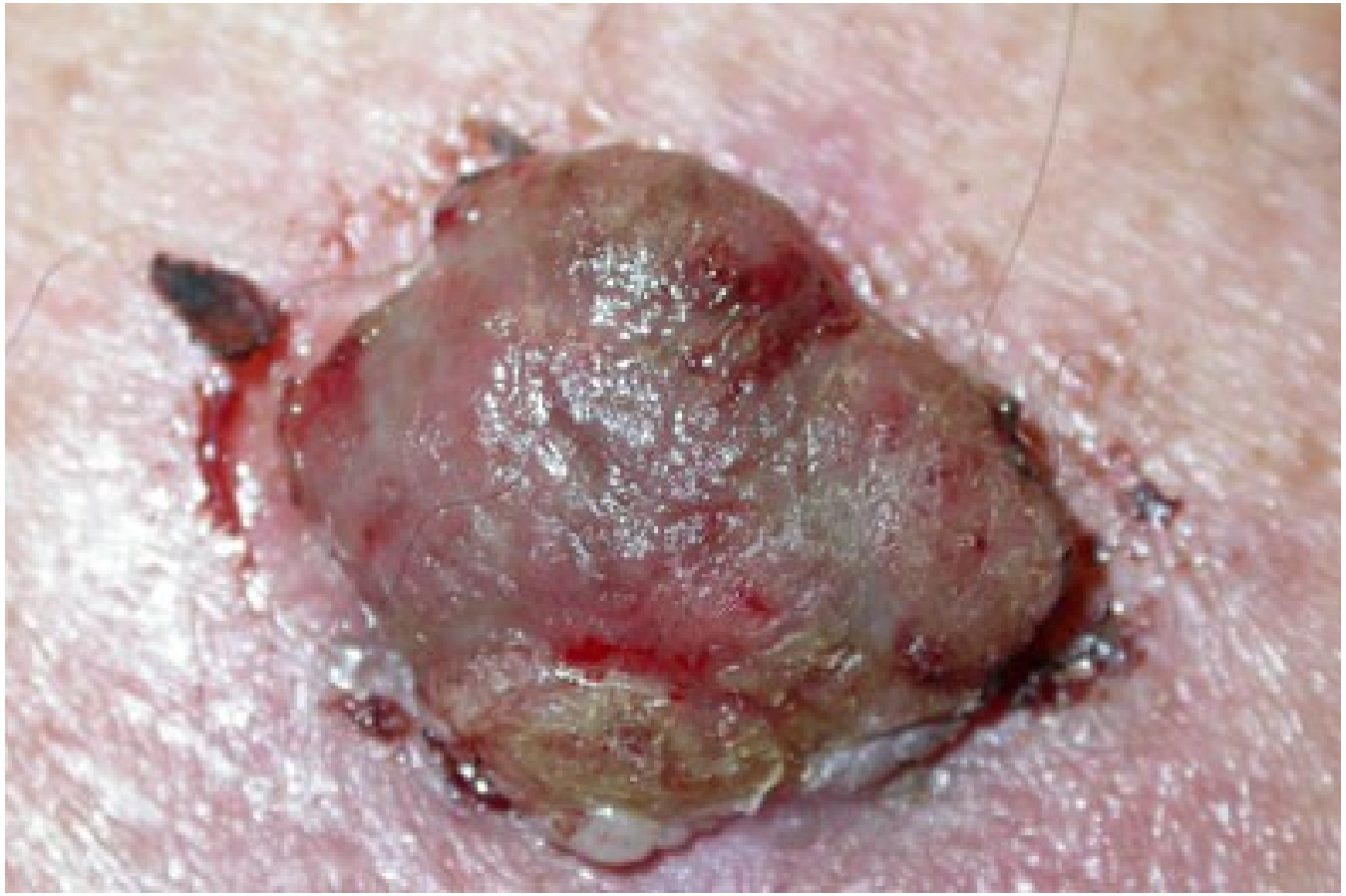
- Rapid growth, lump elevated above the skin surface, firm to the touch, with wide base, easily bleeding
- Amelanotic form – red lump with suppurating surface
- Bad prognose

NM





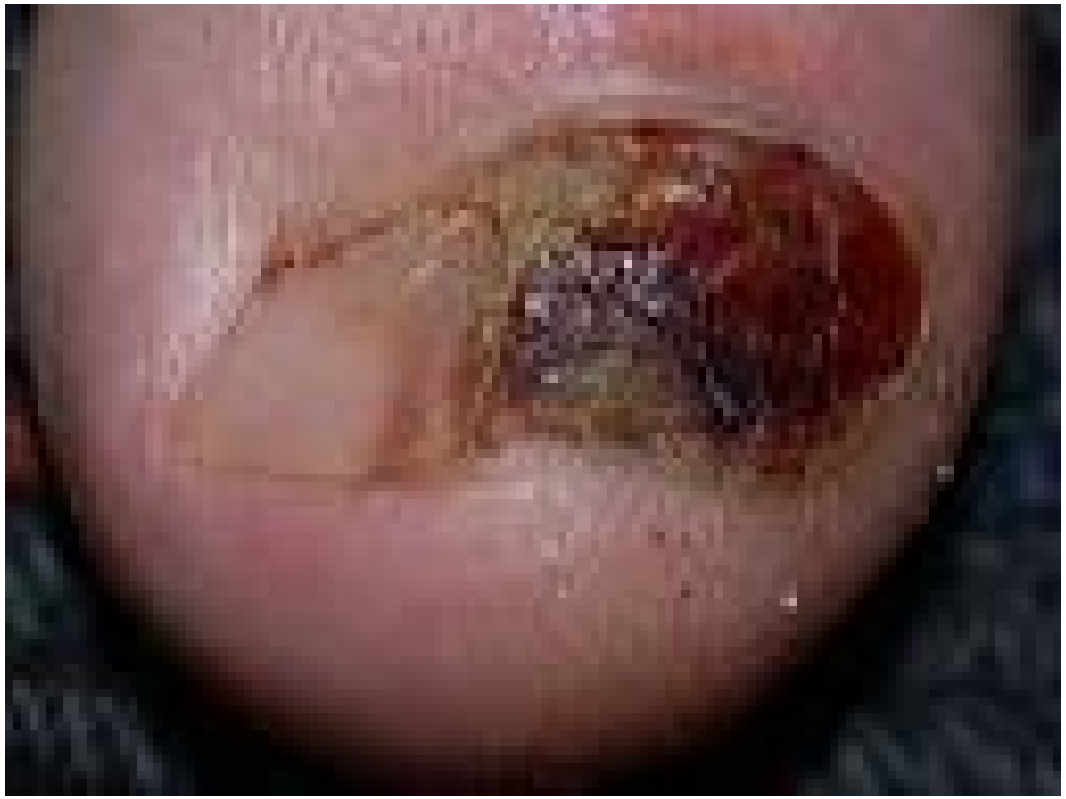
NM - amelanotic



Melanoma – clinical features

- **Acrolentiginous**
- often late diagnosis
- More frequent among dark skin people
- Localization – palms, soles, nails
- Irregular pigmentation of under the nail plate or red suppurating lump, with rest of pigmentation near the nail plate

AKL



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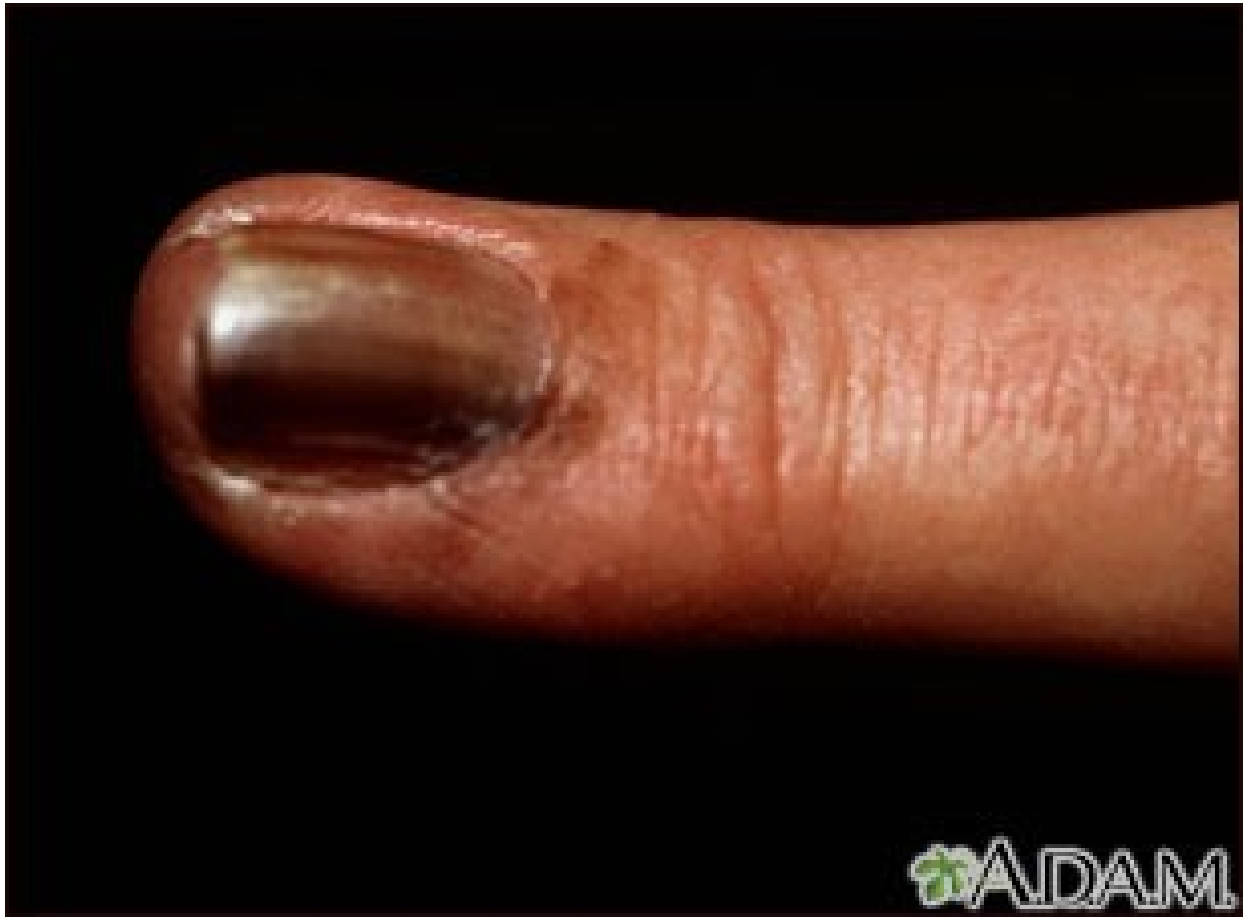


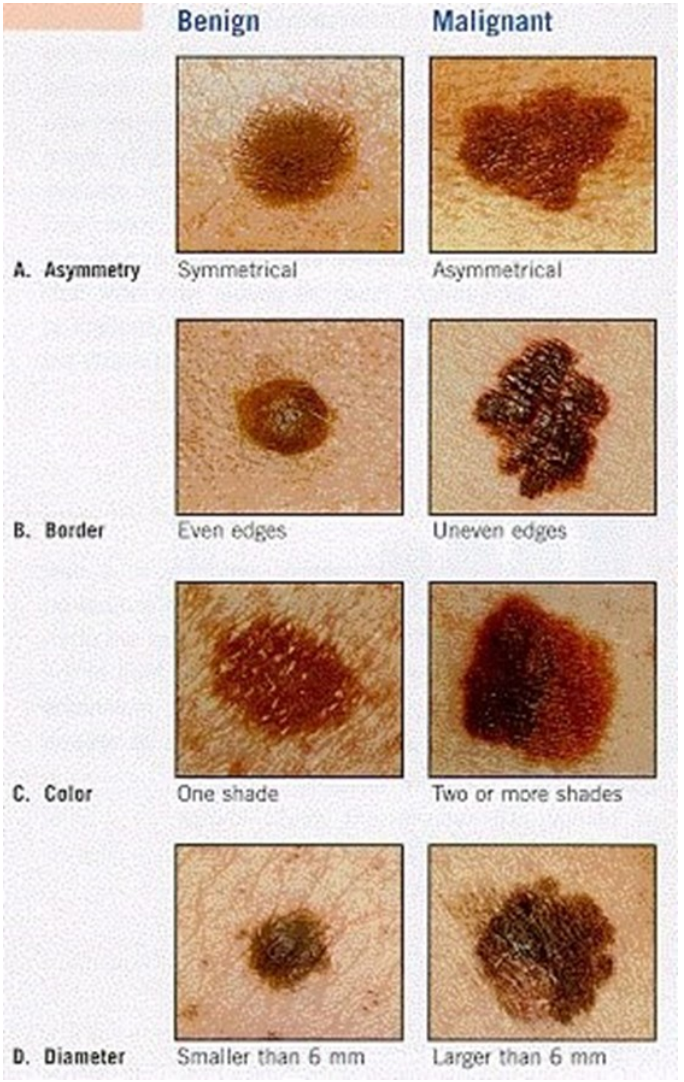
Diagnosis

- Visual inspection – typical signts of malign lesion - ABCDEF rule
- Dermatoscophy (manual or total body)
- Biopsy
- Sentinel lymph node biopsy
- Staging – chest X ray, CT, MRI, PET/CT

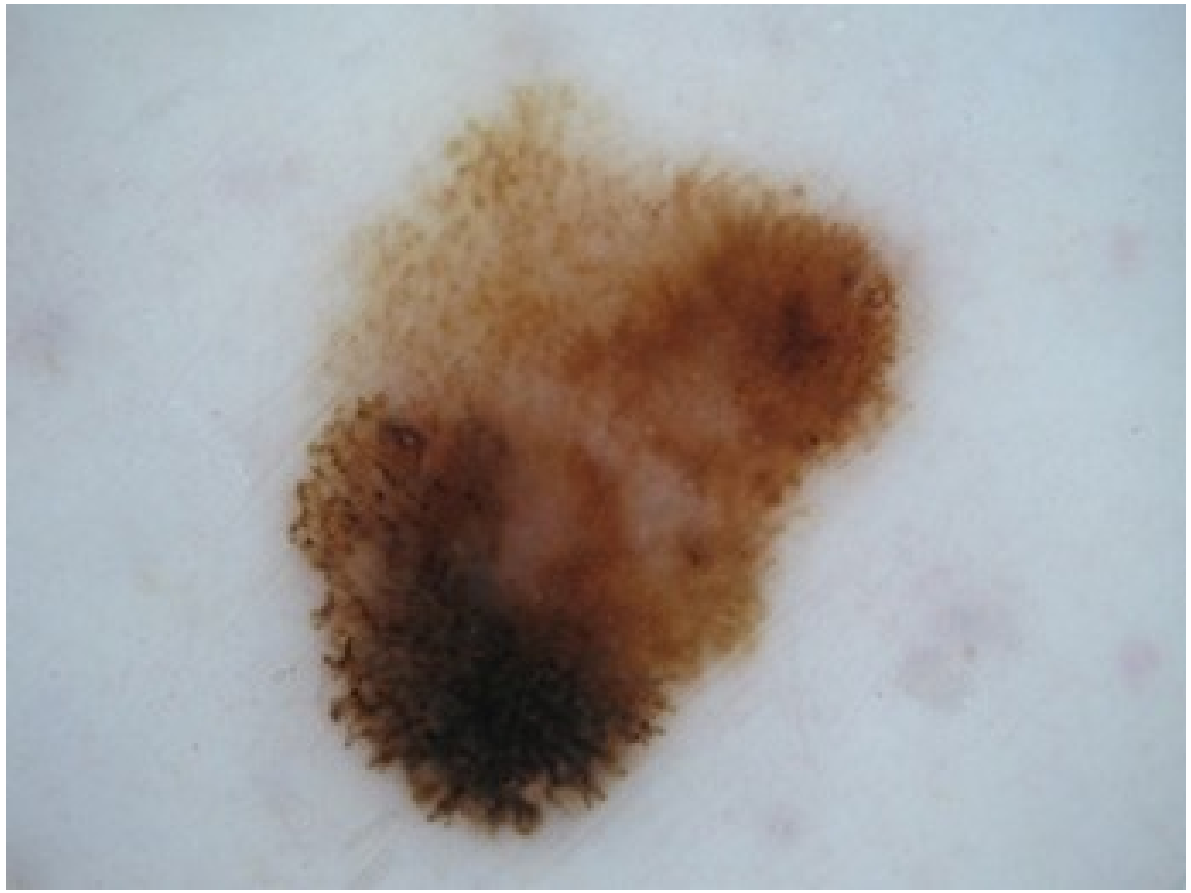
Malignant melanoma

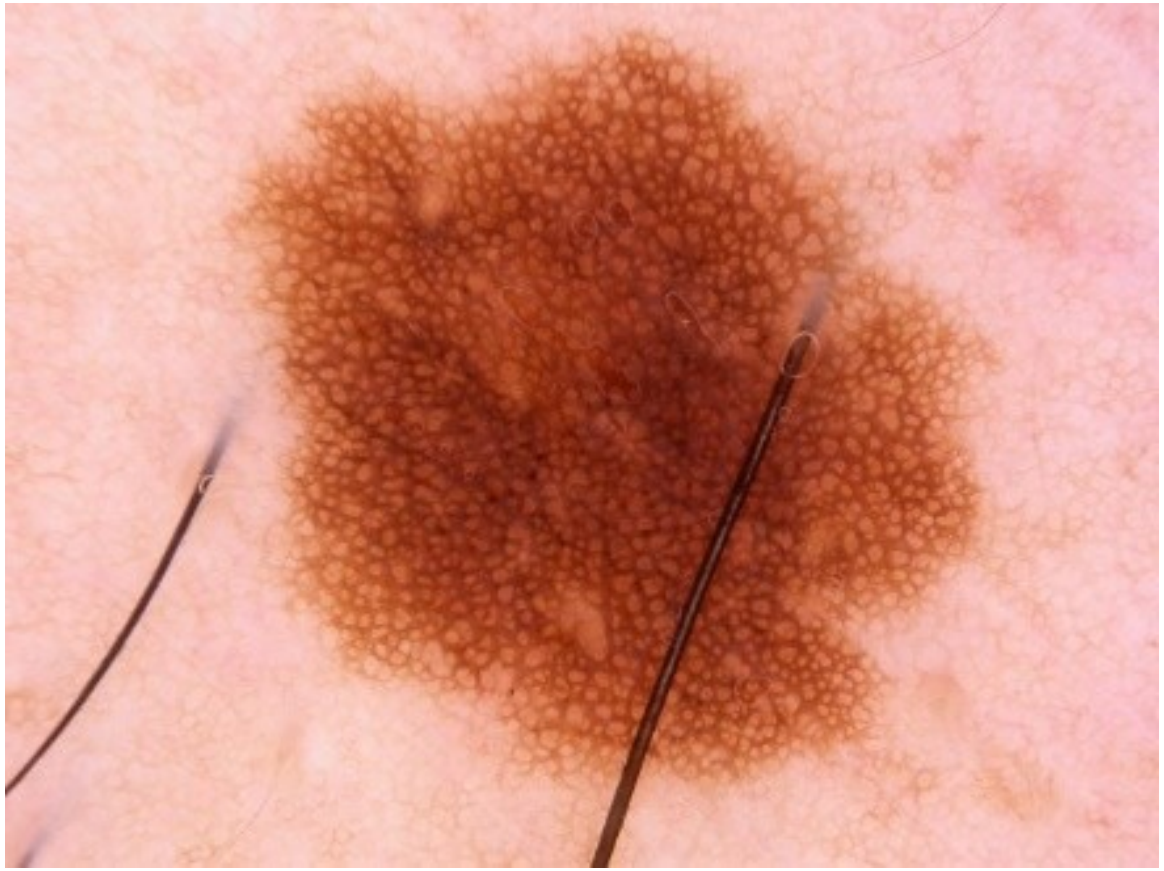
Rules for evaluation of pigmented naevi:

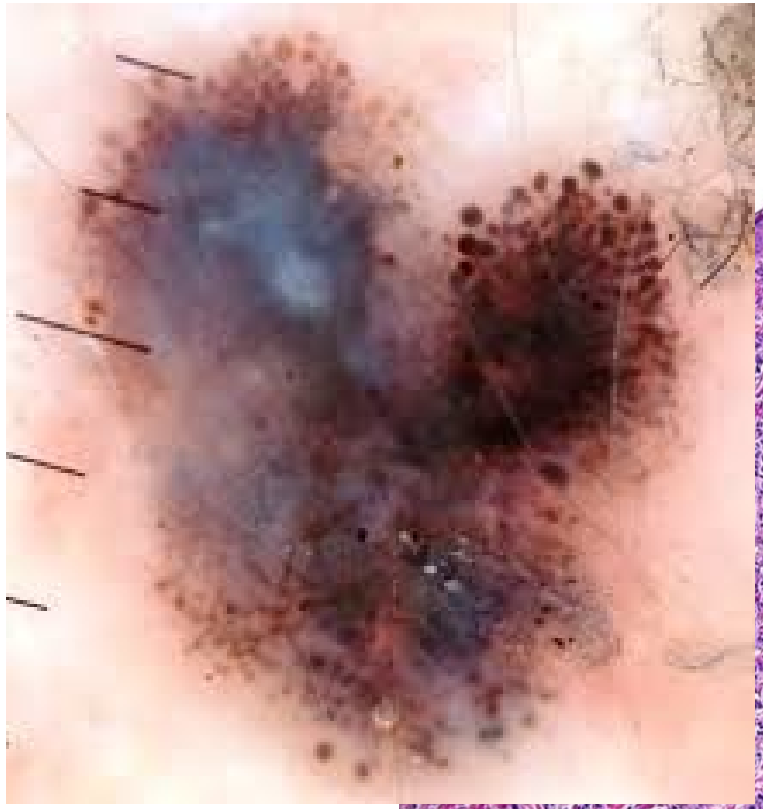
- Asymetry
- Borders
- Colour
- Diameter 5mm and more
- Evolution (bleeding, growth)

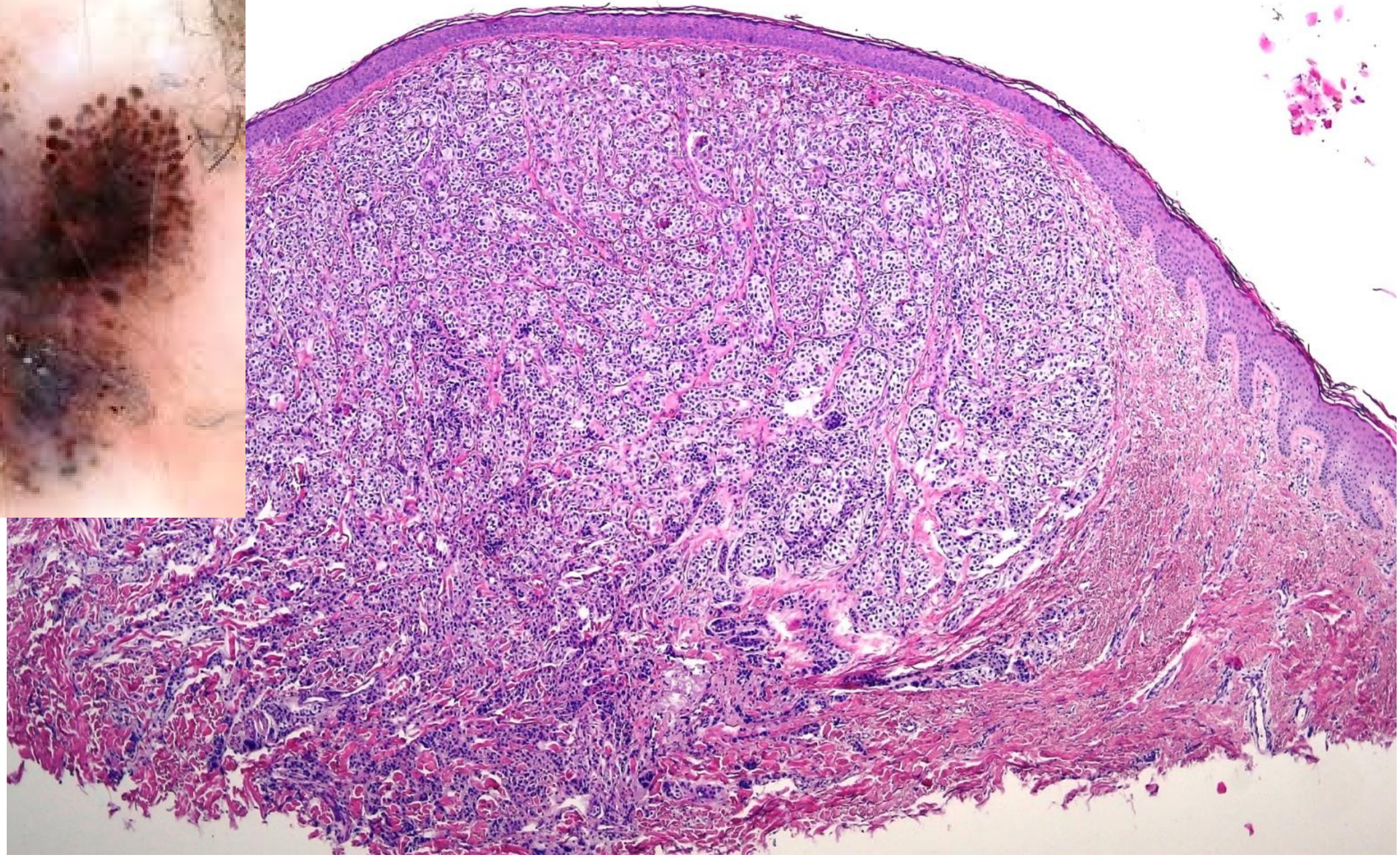


Dermatoscopy : MM x névus









Therapy

- Therapy:
  - Surgery- wide excision + sentinel LN extirpation
  - Adjuvant: RT (inoperable meta in LN), INF alfa
  - Organ meta: chemotherapy, biological therapy- dacarbazine (chemo), CTLR 4 inihibitors- ipilimumab, BRAF inhibitors- dabrafenibe, vemurafenib, EGFR inh,…..
- The effectiveness of treatment for metastatic melanoma is limited, the average survival time is 6-9 months !!!!!!!!
- The only reliable therapy for MM is early clinical dg. and early surgical removal.
- Follow up and prevention!

Prevention

- Limited excessive and intense sunbathing and skin burns in childhood and adulthood
- Search for risky pac. - with a high number of pigmented nevi and carriers of dysplastic nevi
- Public informations - early detection of MM - early excision - healing

Thank you for your attention