## Melanoma

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### Melanoma

#### the most malignant skin cancer

Melanoma is responsible for the majority of deaths due to dermatological reasons

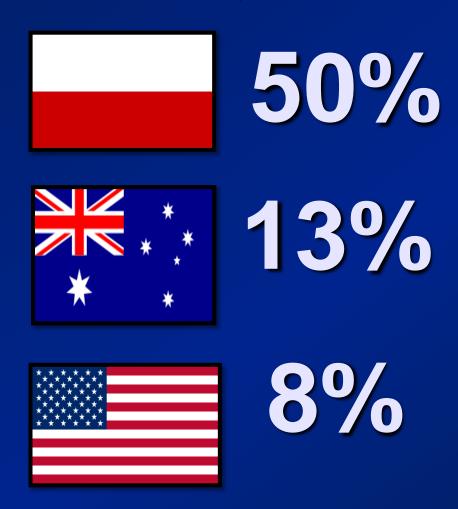


#### **Epidemiology**

- 1) incidence: 2500 persons annually in Poland
- 2) women: men 1:1
- 3) it affects mainly adults (at any age)
- 4) one of the the most common cancers in young adults
- 5) increase of incidence in the last few decades

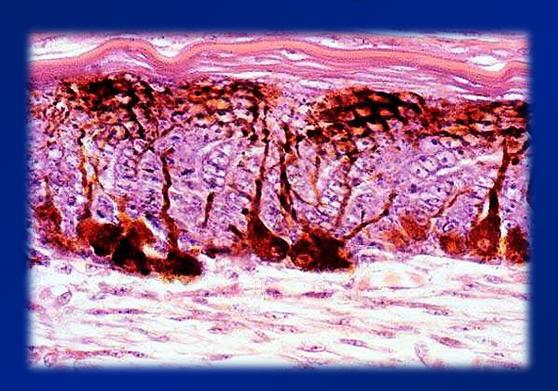
# Mortality to incidence ratio

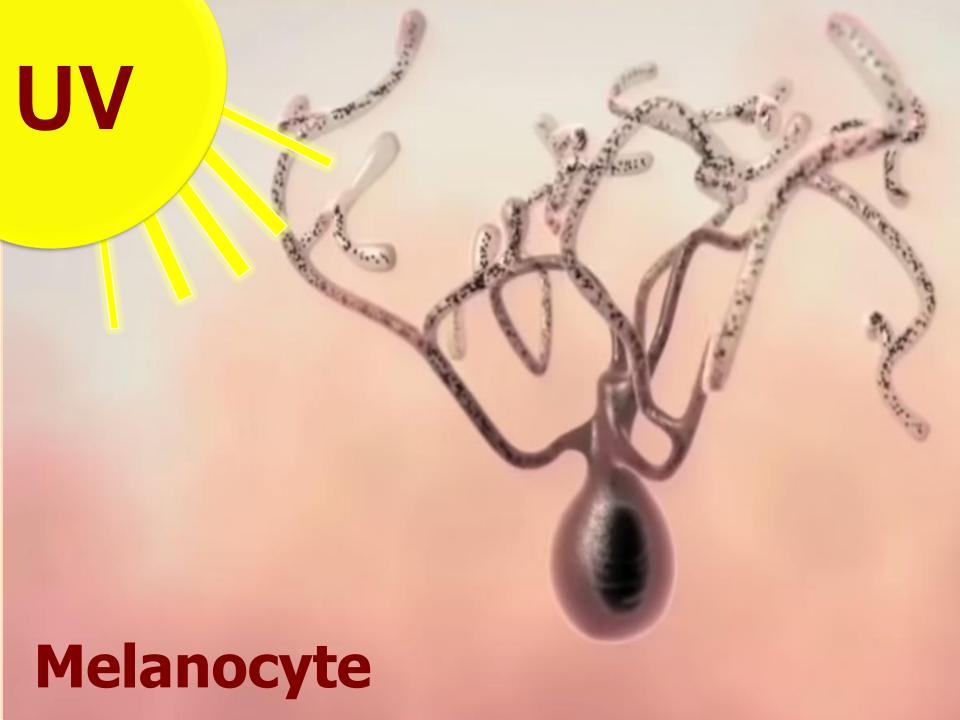
(the average values approximated on the basis of the most up-to-date available official data; 2011 – 2012)



#### **Pathogenesis**

# A cancer developing from melanocytes





#### keratinocytes



#### Melanoma: pathogenesis

genetic factors

plus

multiple overexposure to UVA

and UVB radiation

#### **Mutations**

The most important gene mutations in reproductive cells (approx. 10% of melanoma cases)

- **CDKN2A**
- -CDK4

The most important somatic mutations

- BRAF (approx. 40 50% of melanoma
- cases)
- c-KIT
- NRAS
- MEK

#### **UV** radiation

#### Sources

- Solar radiation
- Tanning lamps producing UV (solarium)

#### **Mechanism**

- Inducing mutations in melanocytes
- Immunosuppressive activity

The risk of developing melanoma

- increased
  - after burns
  - after numerous short-lasting episodes of exposure to intense UV radiation
- not increased in persons chronically exposed to UV (e.g. farmers)

# Melanoma in persons using tanning units which produce UV radiation (solariums)

Przegl Dermatol 2013, 100, 345-352

- Melanoma on average 9 years after the most intense exposure to UV in a solarium
- Numerous countries introduced restrictions on the use of solariums
- Brazil and Australia outlawed the operation of solariums

# Melanoma in persons using tanning units which produce UV radiation (solariums)



Przegl Dermatol 2013, 100, 345-352



The use of solariums banned for persons younger than 18

#### Risk factors

- Phototypes I and II
- Over 100 nevi
- Clinically "atypical" nevi
- Immunosuppression
- History of melanoma (past medical history or family history)
- History of intense exposure to UV radiation

#### Skin phototypes













the risk of melanoma

# Approx. 50% of melanomas develop from pigmented nevi

Approx. 50% develop de novo within the skin which seems healthy

#### Melanoma

- Most commonly asymptomatic
  - no pain
  - no pruritus

Rare pruritus or paraesthesia

#### Diagnosis of melanoma

clinical examination



dermoscopy



histopathology

#### Melanoma – how can we describe the lesion?



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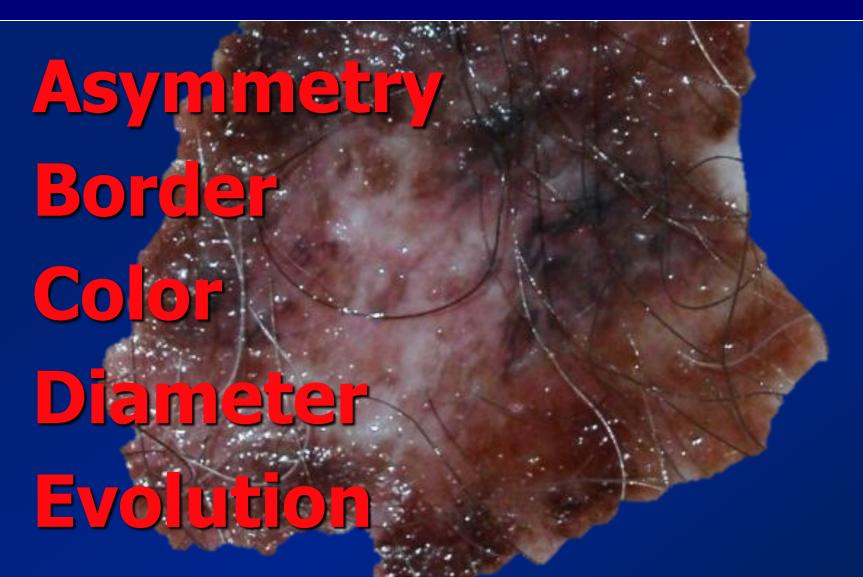
19

#### How can describe this lesion?

- black
- asymmetrical
- irregular border
- pink circumference



# Clinical ABCD(E) rules of melanoma diagnosis



A (asymmetry)





B (borders) – irregular borders





C (colors) 3 or more colors



Not every melanoma is black!















(diameter): over 5 mm



E (evolution) – change in the size or shape in the period of 3 months prior to the examination



approx. 50% of melanomas meet the ABCD(E) clinical criteria



Delayed diagnosis of melanoma

#### Melanoma - diagnosis

clinical examination

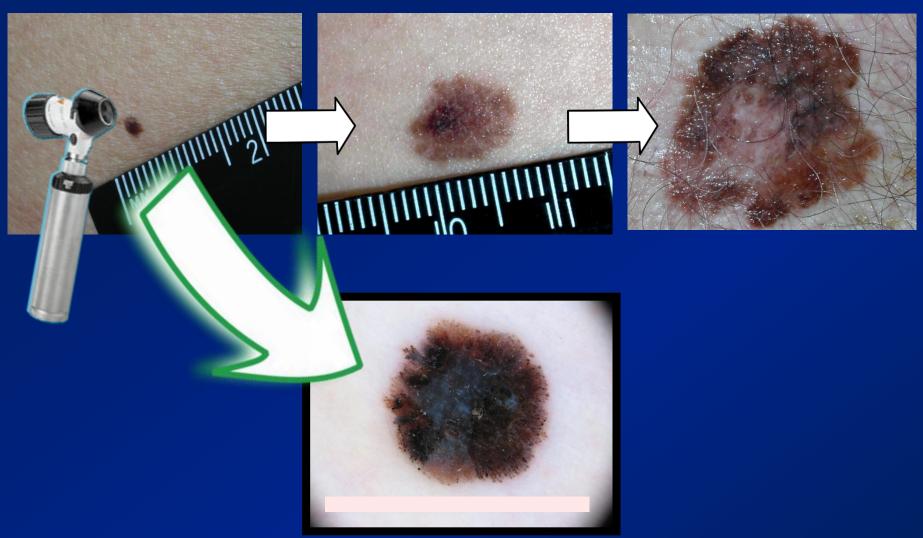


dermoscopy



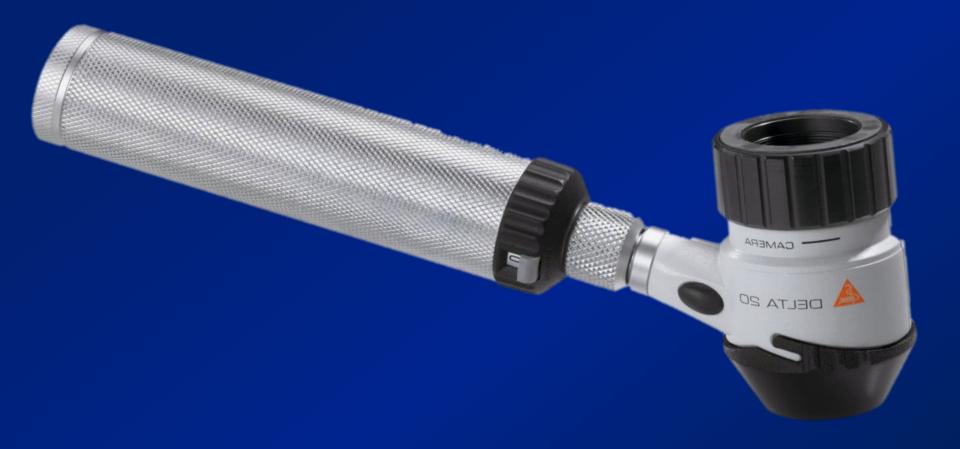
histopathology

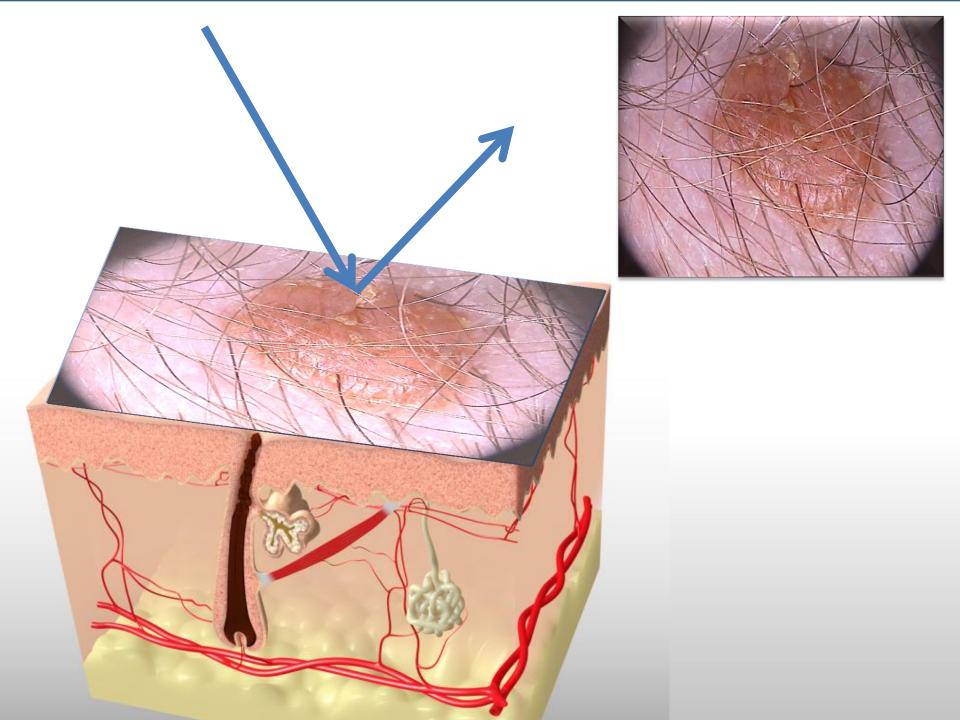
# Every melanoma used to be small

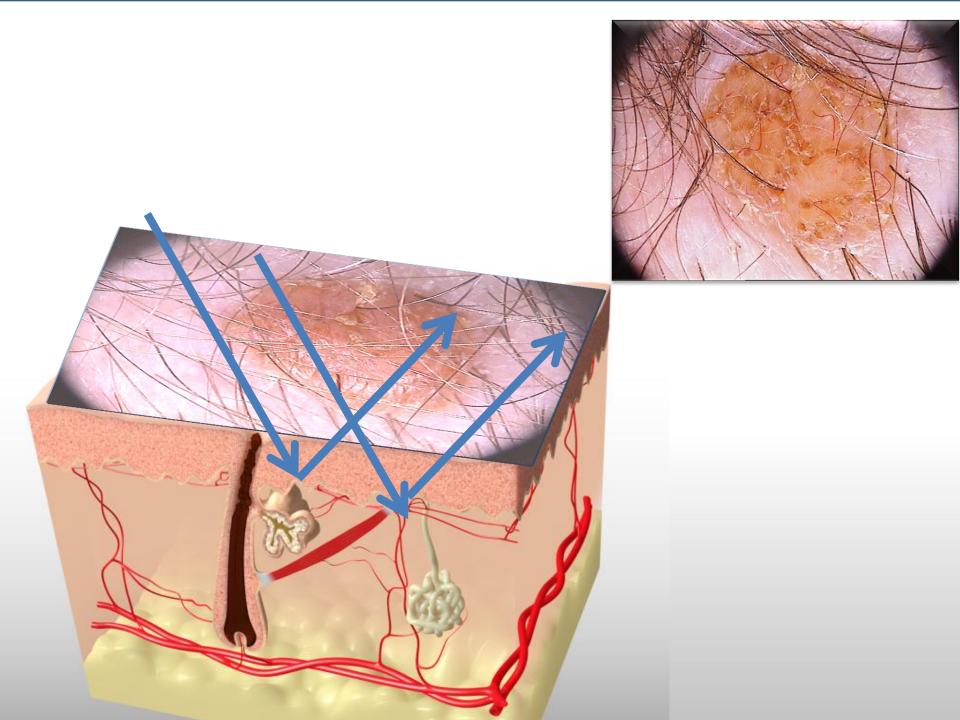


#### Dermoscopy

Magnification + side lighting



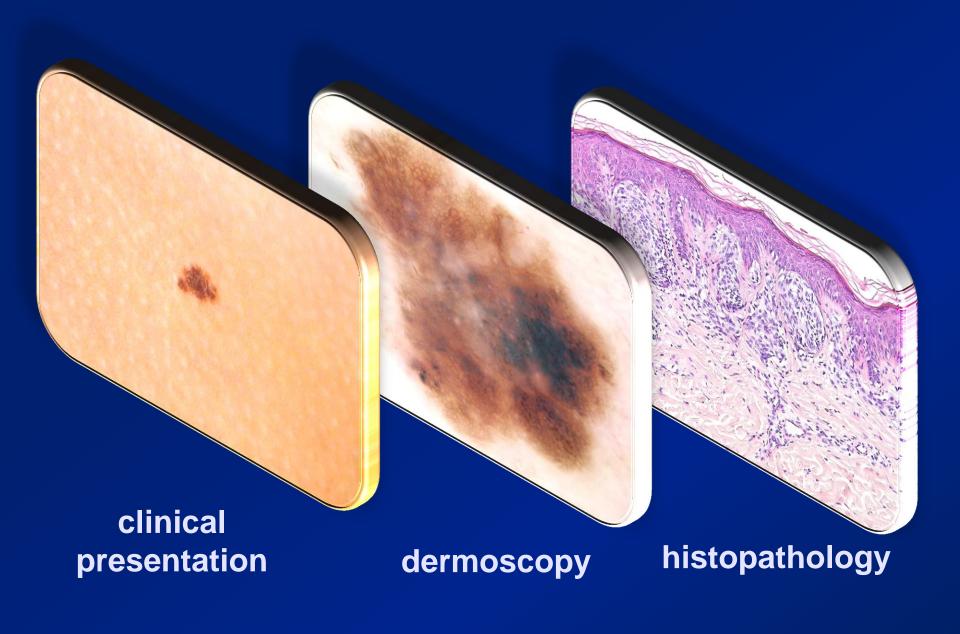






Clinical examination

Dermoscopy





#### September 2014 Volume 71 • Number 3



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Dermatoscopic features of central centrifugal cicatricial alopecia

Antibiotics vs oral contraceptives for acne

Hidradenitis suppurativa: Factors associated with disease severity

Omalizumab therapy for bullous pemphigoid

Tetracycline/niacinamide for pemphigus

Oral azole antifungal agents for head and neck dermatitis

A novel anti-CD6 monoclonal antibody for psoriasis

The role of skin trauma in the distribution of morphea

Acquired idiopathic anhidrosis

Health care accessibility and the prognosis of melanoma

Spitzoid melanoma

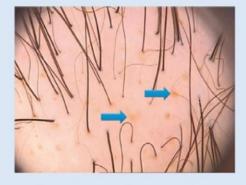
Risk of subsequent cutaneous SCC in patients with melanoma

Cancer and mortality in patients with mycosis fungoides and parapsoriasis

Bath PUVA for early mycosis fungoides

The "biker-glove" pattern of segmental infantile hemangiomas





#### Evaluation and diagnosis of the hair loss patient

Thamer Mubki, MD, Lidia Rudnicka, MD, PhD, Malgorzata Olszewska, MD, PhD, and Jerry Shapiro, MD Riyadh, Saudi Arabia; Warsaw, Poland; Vancouver, British Columbia, Canada; and New York, New York



#### **DERMOSCOPY**

Basic method of melanoma diagnosis prior to its removal and a histopathological examination

## ABCD(E) clinical rules



The ABCD rule of dermoscopy

## Dermoscopic algorithms

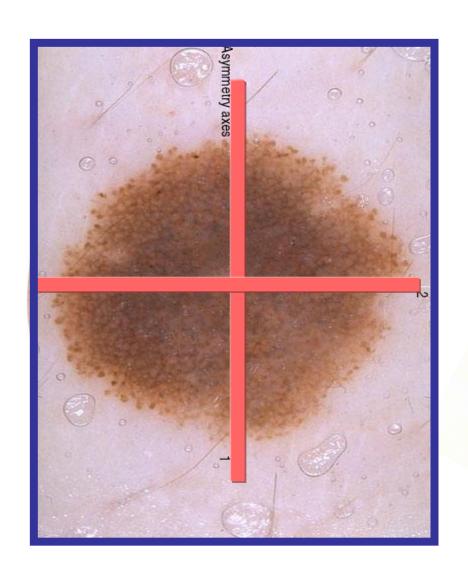
- The ABCD dermoscopy rule
- 7-point checklist (Argenziano)
- Menzies method
- CASH algorithm
- Pattern analysis
- 3-point checklist

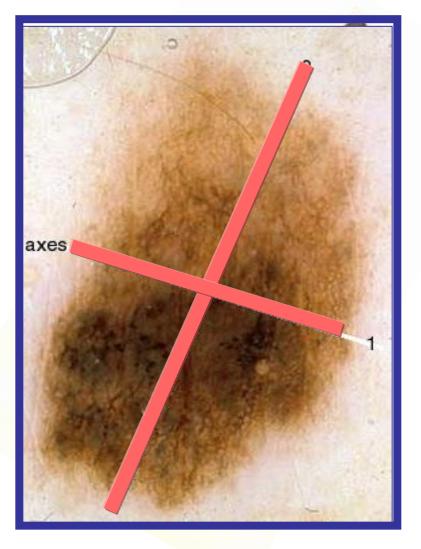
# 3-POINT CHECKLIST FOR MELANOMA

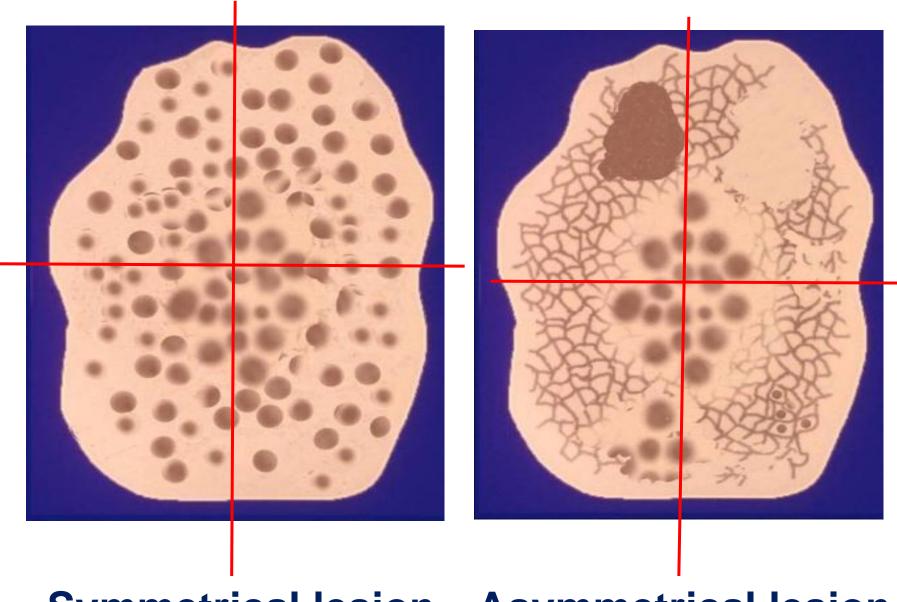
- 1. Asymmetry
- 2. Atypical pigment network
  - 3. Blue-whitish structures

2 features \to melanoma

## 1. ASYMMETRY





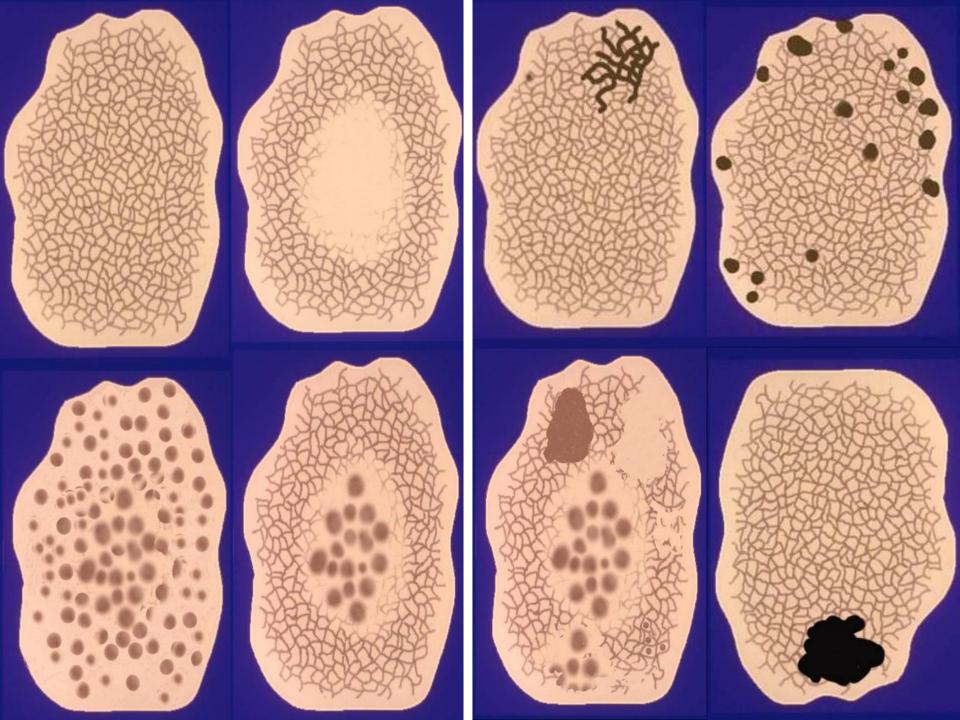


Symmetrical lesion Asymmetrical lesion

#### 2. Irregular pigment network





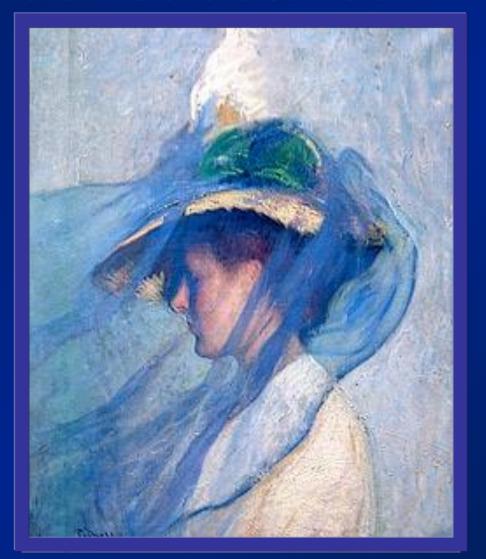






#### 3. Blue-whitish structures

Blue-whitish veil

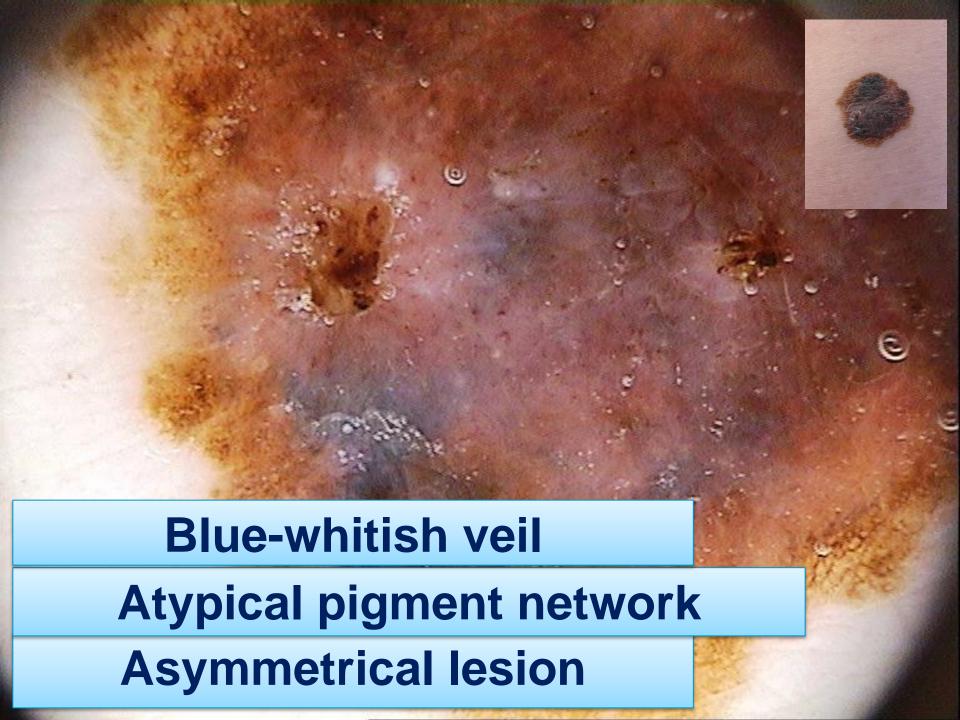


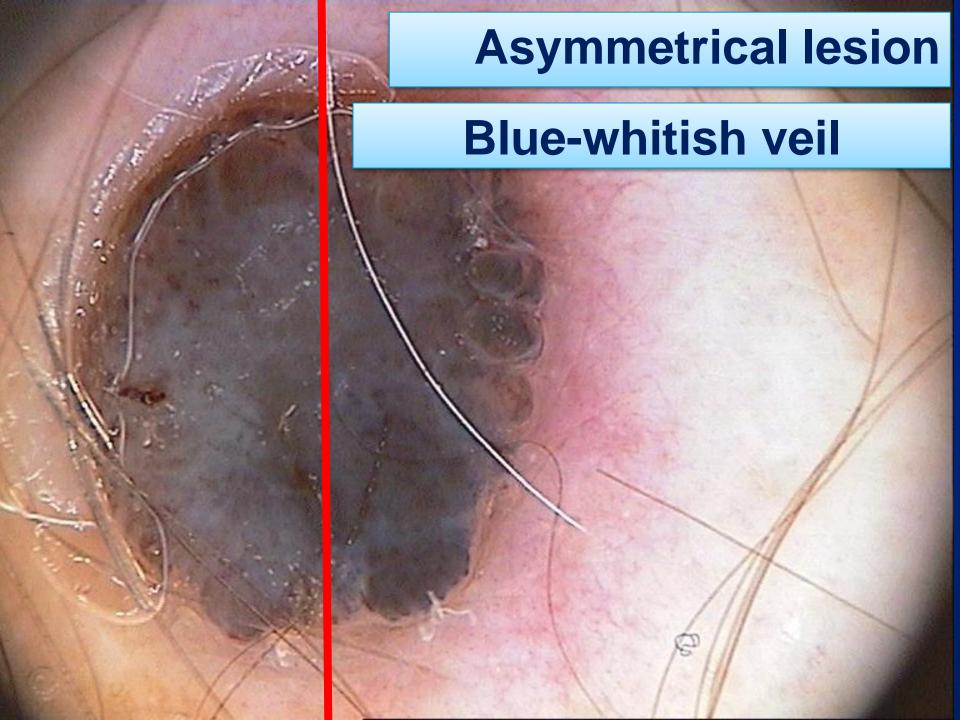


# 3-POINT CHECKLIST FOR MELANOMA

- 1. Asymmetry
- 2. Atypical pigment network
  - 3. Blue-whitish structures

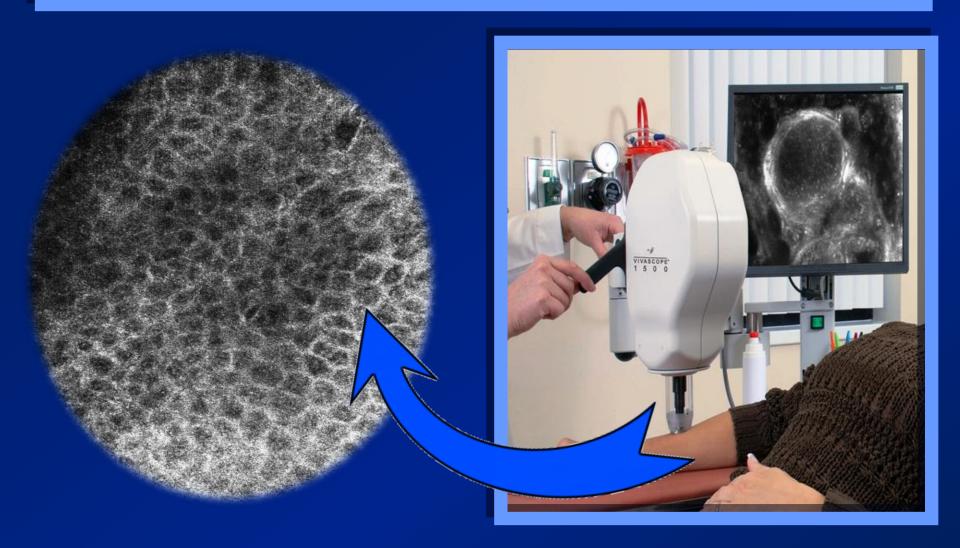
2 features \to melanoma



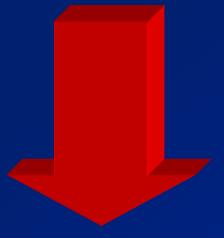


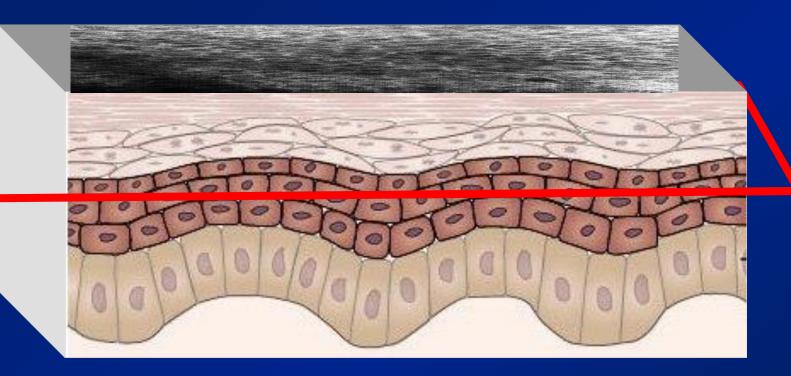
Reflectance Confocal Microscopy (RCM)

### Reflectance confocal microscopy



#### **RCM**



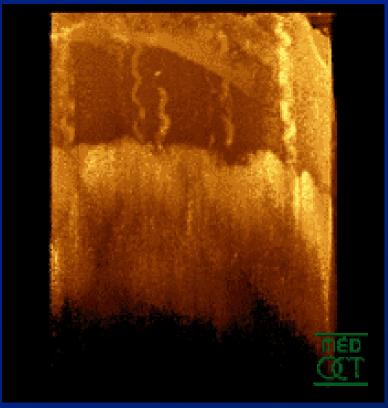


# 200-300 μm

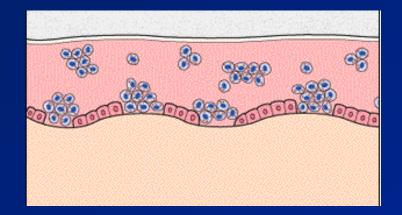
# Optical coherence tomography (OCT)

three-dimensional images with micrometre resolution

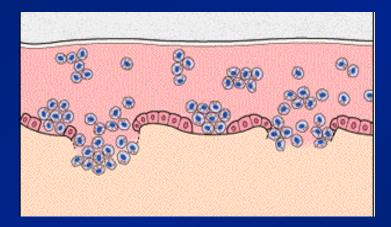




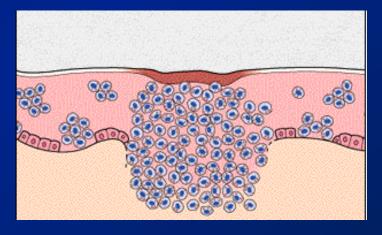
## In situ melanoma



# Horizontal growth



Vertical growth



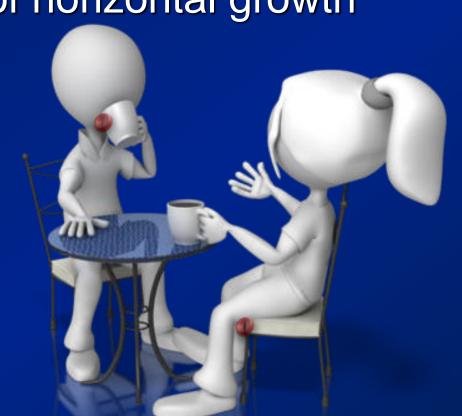
## The main clinical types of melanoma

- Superficial spreading melanoma
- Nodular melanoma
- Lentigo maligna melanoma
- Acral lentiginous melanoma

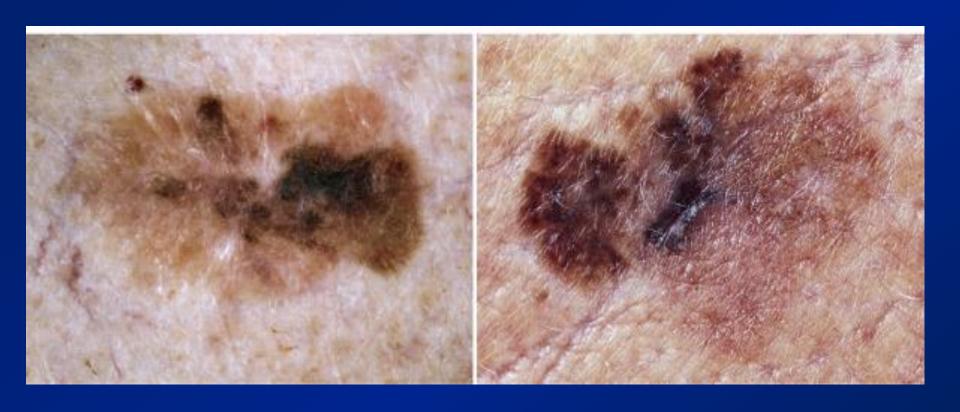
Amelanotic melanoma

#### Superficial spreading melanoma

- The most common type of melanoma
- Prolonged phase of horizontal growth
- Within a nevus or healthy skin
- Mainly young adults



#### Superficial spreading melanoma



#### Nodular melanoma

approx. 15% of cases

vertical growth is predominant

more common in men

over 50

diagnosed at a later stage of development



#### **Nodular melanoma**





#### Lentigo maligna melanoma

- lentigo maligna an in situ melanoma developing from UV-damaged skin
- 5% progression to an invasive melanoma
- slow horizontal growth
- most commonly occurs in persons over 60



#### Lentigo maligna

## Lentigo maligna melanoma





#### Lentigo maligna melanoma



#### Acral lentiginous melanoma



hands feet nails

#### Acral lentiginous melanoma









injury melanoma



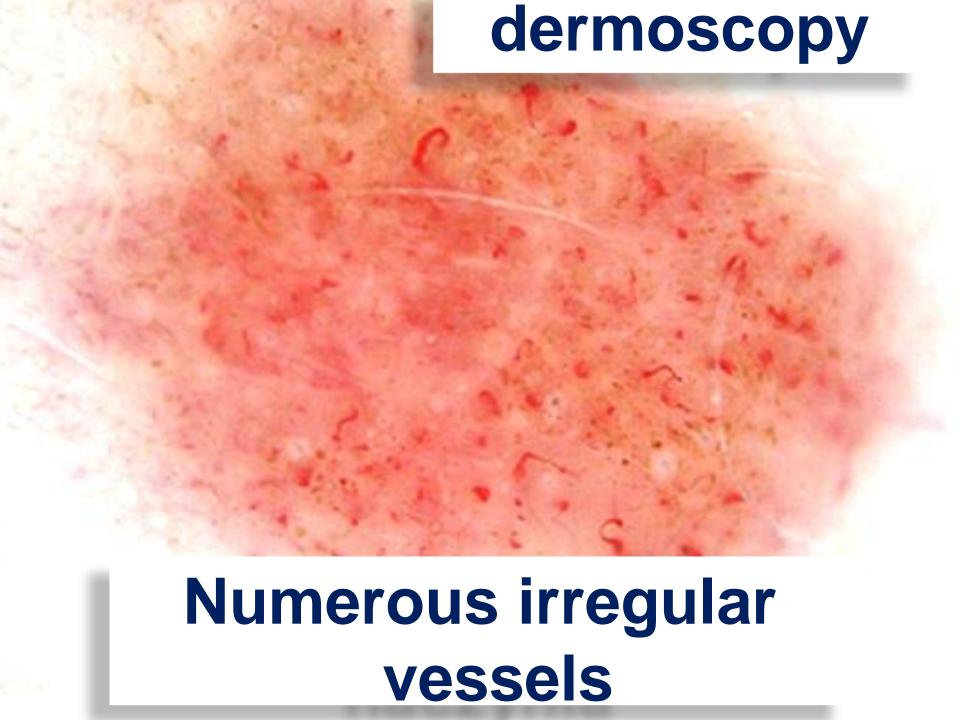
#### **Amelanotic melanoma**

- contains no melanin
- pink lesion
- late diagnosis















If melanoma is suspected, biopsy is not performed. The entire lesion is excised.

Excisional biopsy

## The suspicion of melanoma:

#### **Excisional biopsy**



minimum margin of 1-3 mm

#### The diagnosis of melanoma

clinical examination



dermoscopy



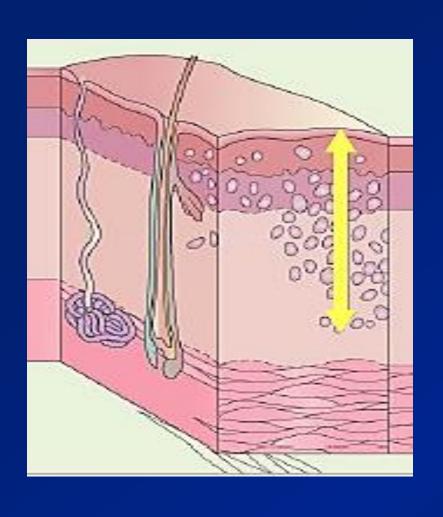
histopathology

## Histopathological confirmation



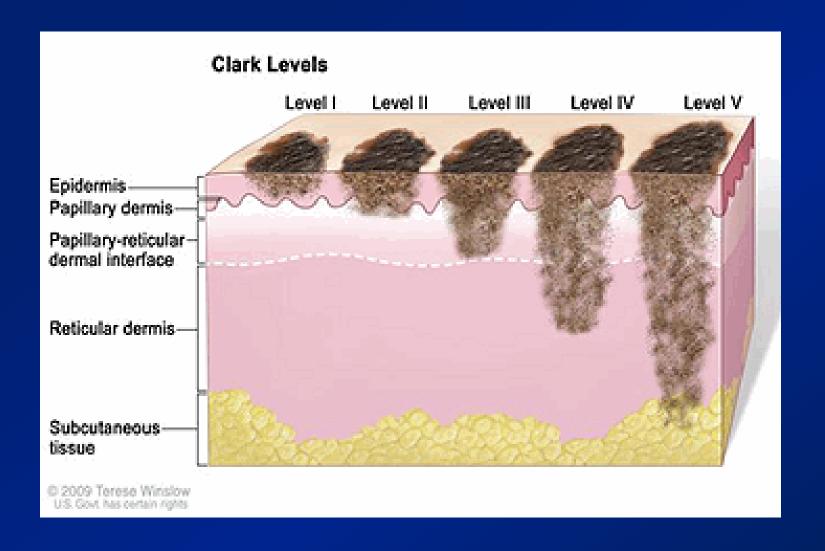
# analysis of local invasion stage

#### The Breslow scale



the thickness of the lesion in mm

## The Clark scale (used as additional information)



Level 1 – very superficial, in epidermis only

Level 2 – a little deeper, into the superficial layers of the dermis

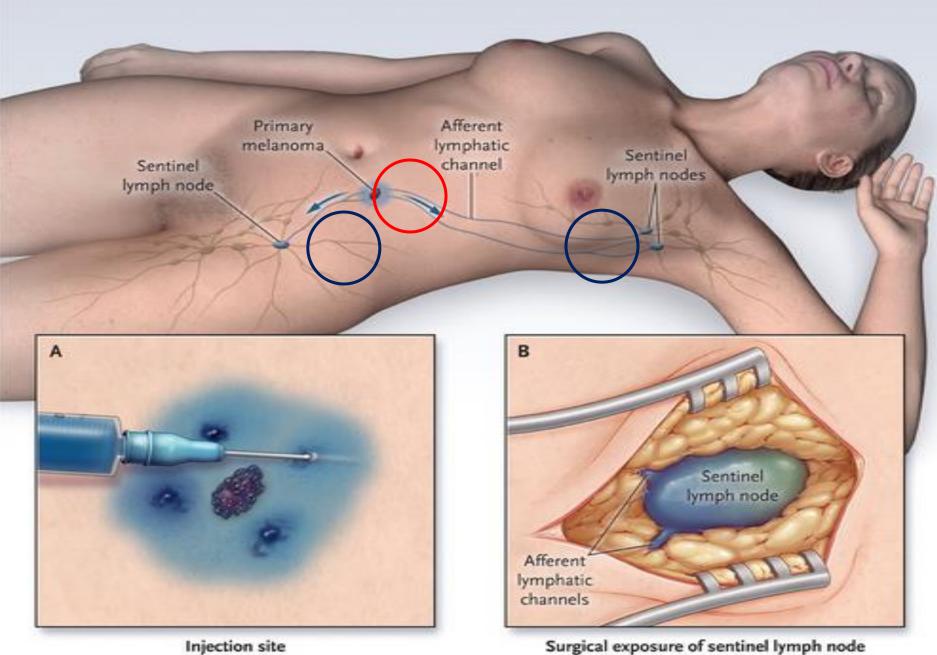
Level 3 – deeper yet, to the interface between superficial dermis and deeper reticular dermis

Level 4 – still deeper, into the reticular dermis

**Level 5** – into the subcutaneous tissues.

## Therapeutic decision (dependent on the stage of development)

- Widening the margin of excision
- The assessment of the sentinel lymph node
- Radiotherapy
- Hyperthermic isolated extracorporeal limb perfusion with melphalan
- Surgical treatment of metastases
- Systemic treatment



## Drugs in the treatment of melanoma

- ipilimumab (2011) immune activation via blocking CTLA-4
- vemurafenib (2011)
- dabrafenib (2013)
- pembrolizumab (2014)
- nivolumab (2014)

only for patients with the BRAF mutation

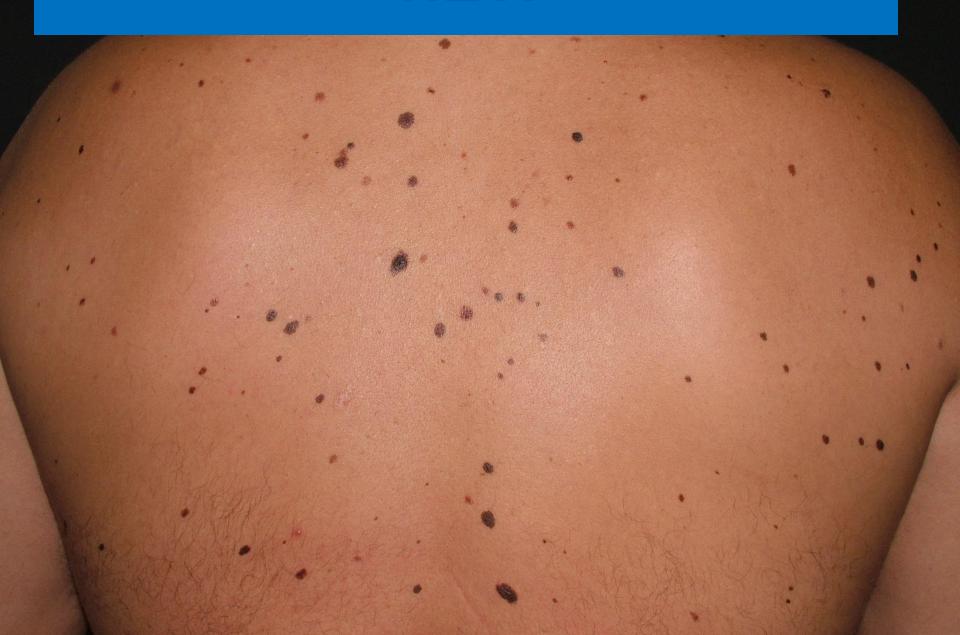
PD – 1 inhibitors



EMA (European Medicines Agency):

Ipilimumab and vemurafenib – first-line treatment in patients with metastatic melanoma or advanced unresectable melanoma

## NEVI



#### Pigmented nevi

- congenital
- acquired
- Sutton nevus (halo nevus)
- Atypical
- Spitz nevus
- Nevus coeruleus (blue nevus)

#### Congenital pigmented nevi

- •1/5000-1/20 000 births large nevi
- pathological migration of melanocytes during embryonic development
- dark, hairy, irregular surface

### **Congenital nevi**

Large/giant>20 cm

• Medium 1.5 - 20 cm

Small<1.5 cm</li>



## Congenital pigmented nevi





#### Congenital pigmented nevi

- 5-10% risk of melanoma development (large or giant nevi)
- the necessity of dermoscopic examination and photographic documentation

#### Nevus spilus

- congenital nevus
- cafe-au-lait spot with small pigmented nevi
- very low risk of melanoma development

## Nevus spilus



#### Acquired melanocytic nevi

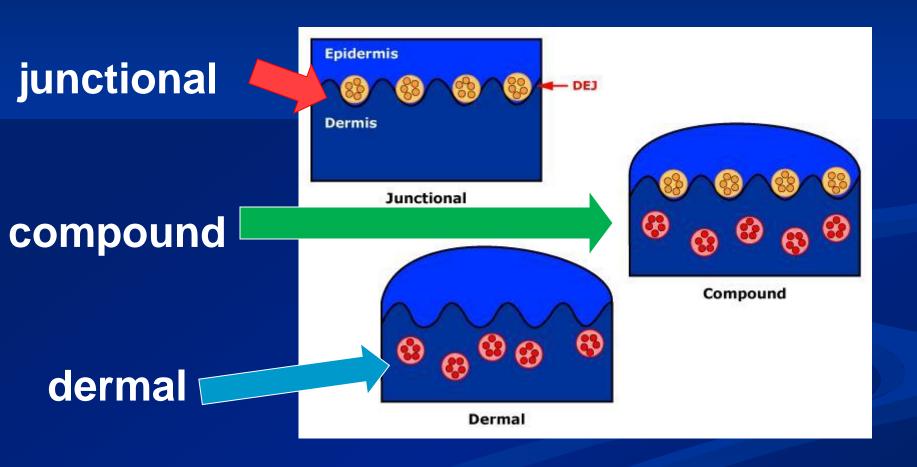
- developing most commonly between the ages 2-3 and 30 they may regress in elderly persons
- various colors and surface
- usually less than a centimetre in diameter

## Acquired melanocytic nevi





# Acquired melanocytic nevi. Histopathological types



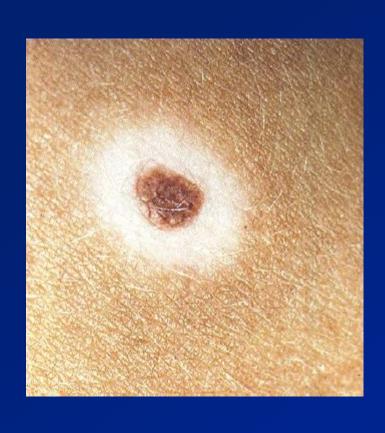
#### Acquired melanocytic nevi

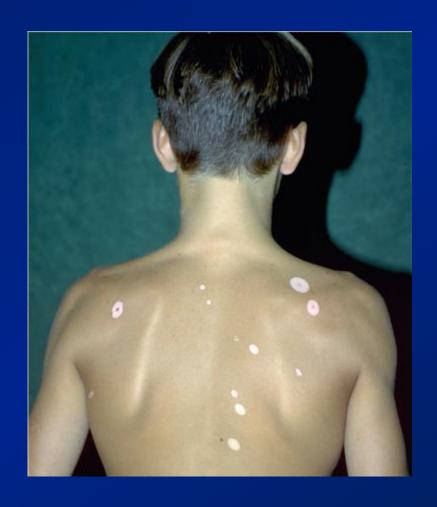
- \*numerous nevi a higher risk of melanoma development
- dermoscopic assessment
- surgical resection of nevi suspected of a cancerous transformation

#### Sutton nevus (halo nevus)

- melanocytes in and around the nevus are destroyed by lymphocytes
- a clinical pigmented nevus surrounded by a depigmented ring (halo)
- most common in young persons
- depigmentation subsides spontaneously

### Sutton nevus (halo nevus)





#### **Atypical nevi**

- a clinical term (controversial)
- frequent sporadic forms, infrequent inherited (familial) forms
- •irregular pigment distribution, asymmetrical shape, dynamics of development

## **Atypical nevi**





#### **Atypical nevus syndrome**

- numerous atypical nevi, possible higher risk of pancreatic cancer development
- sporadic or familial
- gene mutations, e.g. CDKN2A (p16)
- •increased risk of melanoma development
- dermoscopic assessment necessary,
   surgical resection possible

#### Spitz nevus

- a benign nevus commonly occurring in children
- •"melanoma juvenile"
- clinical presentation red-brown or greyblue nodules

## **Spitz nevus**



#### Nevus coeruleus (blue nevus)

- a solitary nodule
- a characteristic color: blue, blue-grey, blue-black
- rarely developing into melanoma

## Nevus coeruleus (blue nevus)



### Melanoma - summary

- a type of cancer developing from melanocytes
- frequently develops within nevi
- UV-exposure increases the risk of melanoma
- dermoscopy the basic method of clinical diagnosis
- early diagnosed melanoma is treated with excisional biopsy under local anaesthesia
- average risk of death in Poland due to late diagnosis: approx. 50%