1 Epidemiology, prevention, screening and surveillance of skin cancer

Epidemiology of malignant melanoma

Malignant melanoma (MM) arises from melanocytes responsible for pigmentation, which are located in the skin, mucosa, central nervous system or uveal tract of the eye.

Worldwide, cutaneous MM (cuMM) comprises 1.7% cases of all newly diagnosed primary malignant cancers (excluding non-melanoma skin cancer [NMSC]).

Incidence and mortality vary substantially between continents with low incidences in Asia and the highest incidences in Australia.

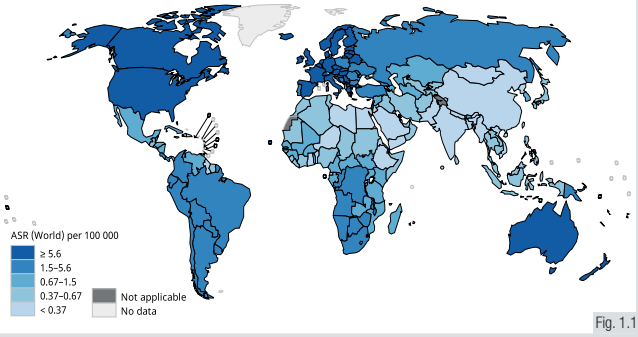


Fig. 1.1

ASR, age-standardised rate; cuMM, cutaneous malignant melanoma.

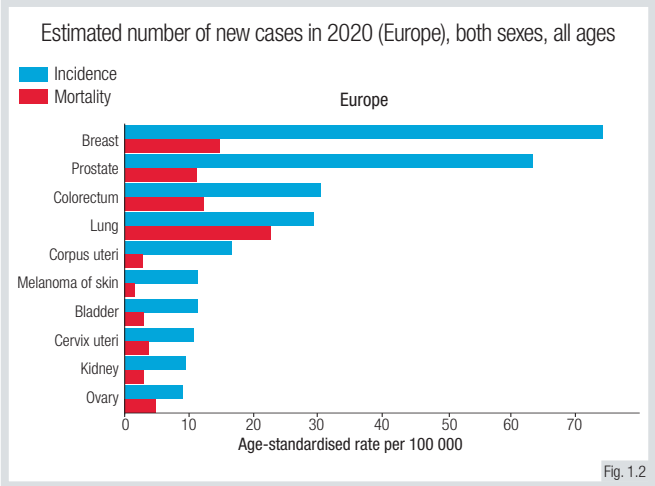


Fig. 1.2

In Europe, the overall incidence of cuMM is rising rapidly with highest rates in northern and north-western countries such as the UK, Ireland and the Netherlands, and lowest rates in Portugal and Spain.

Currently, cuMM is the sixth most common tumour in men and women in Europe across all malignancies (NMSC included in 'other cancers').

Although cuMM represents only 4% of all skin cancers (including NMSC), it is responsible for 80% of all skin cancer deaths.

During the last 20 years, multiple approaches have resulted in a better understanding of tumour immunology and the genomic characteristics of melanoma.

Survival for melanoma patients with metastases is significantly prolonged by new therapeutic options compared with chemotherapy.

Melanoma-specific survival of MM depends on the stage at initial diagnosis, comprising primary tumour characteristics, and local and distant metastasis status.

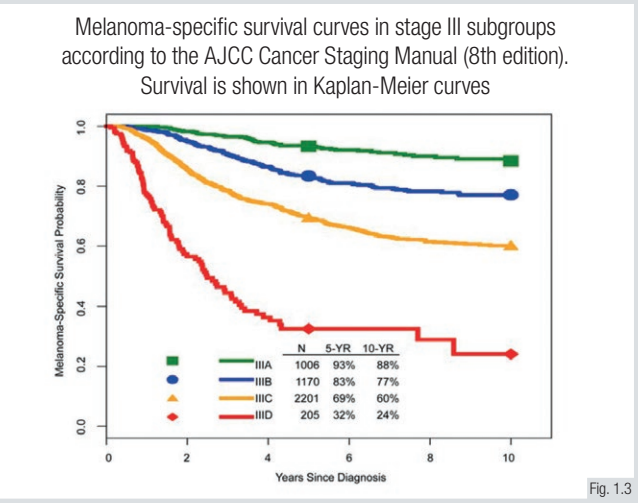


Fig. 1.3

AJCC, American Joint Committee on Cancer.

REVISION QUESTIONS

1. Where are melanocytes located?
2. Which countries have the highest incidences of melanoma?
3. What led to an increased survival of advanced melanoma patients?

Prevention of malignant melanoma

Persons with Fitzpatrick scale skin type I (fair hair, fair eyes, fair skin colour and freckles) have a higher risk of developing melanoma.

Well-known risk factors comprise ultraviolet (UV) radiation (sun exposure, tanning beds), sunburn, multiple or dysplastic naevi, and medical history of melanoma.

Inherited genetic mutations are possible, but rare, and should be considered if one person has multiple cuMMs, or several family members suffer from cuMM and/or associated tumour entities: FAMMM (familial atypical multiple mole melanoma) syndrome.

The Fitzpatrick scale of skin types is a numeric classification schema for human skin colour

Skin type	I	II	III	IV	V
					
Description	**Skin:** noticeably fair-skinned, pale **Freckles:** large number **Hair:** reddish **Eyes:** green, blue, seldom brown	**Skin:** somewhat darker than type I **Freckles:** seldom **Hair:** blonde to brown **Eyes:** blue, green, grey	**Skin:** light brown **Freckles:** none **Hair:** dark blonde, brown **Eyes:** grey, brown	**Skin:** brown **Freckles:** none **Hair:** dark brown, black **Eyes:** brown	**Skin:** dark brown, black **Freckles:** none **Hair:** black **Eyes:** brown

Fig. 1.4

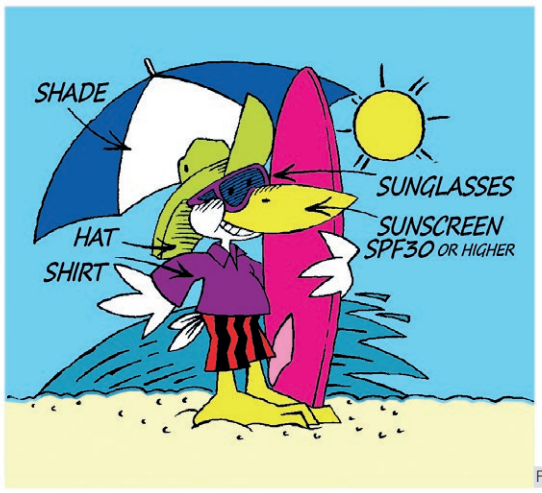


Fig. 1.5

Australia is one of the few countries where incidence has been decreasing since 2005, possibly reflecting an increased awareness due to primary preventive approaches.

National campaigns promoting physical and chemical sun protection support education from early childhood about acute and chronic sun damage and skin cancer.

In Europe, larger primary prevention campaigns were started in the 1990s, aiming to increase knowledge and awareness. Nowadays, broad campaigns and international, collaborative research projects to understand melanoma genetics and survival are funded by European institutions.

More common subtypes are superficial spreading melanoma and nodular melanoma, while rarer melanoma subtypes include melanoma of unknown primary (MUP), acrolentigious melanoma, mucosal melanoma and blue naevus-like melanoma.

Rare subtypes harbour a distinct mutation pattern and are assumed to be less UV-associated, which makes primary prevention in general more difficult.

Two to three percent of melanomas appear without a primary tumour, but with metastases. Possibly, the primary tumour has vanished by regression after recognition by the immune system or never existed in the first place.

Fig. 1.6

REVISION QUESTIONS

1. Which skin type has the highest risk for developing melanoma and why?
2. Name one measure which is used as primary prevention in melanoma.
3. What does MUP stand for?

Screening and surveillance of malignant melanoma

Awareness for self-examination of pigmented naevi using easily recognisable rules is underlined. One example is the ABCD rule for pigmented lesions: A-Asymmetry, B-Border, C-Colour, D-Diameter, helping to differentiate between benign and malignant lesions.

Patients at risk should be screened by total body skin examinations with a dermatoscope or comparable imaging technique (see Chapter 9).

Screenings should be performed by experienced physicians including mucous membranes and examination and palpation of lymph node stations.

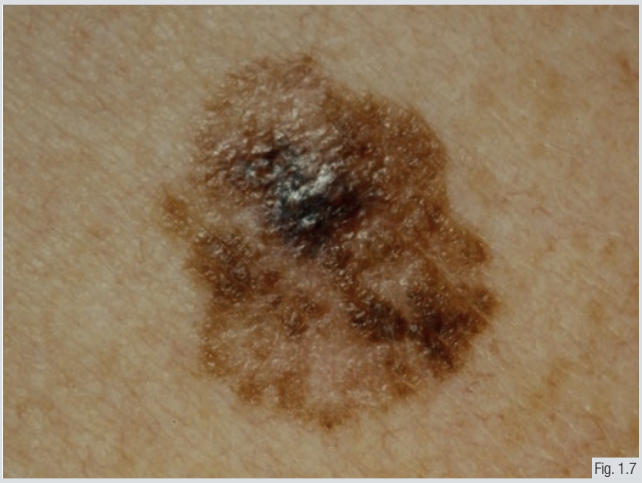


Fig. 1.7

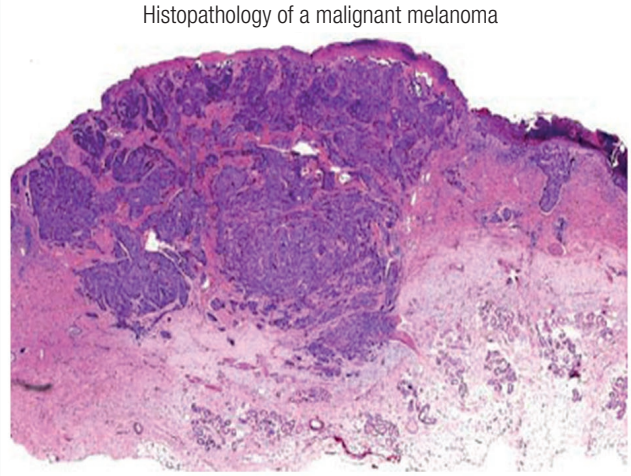


Fig. 1.8

Suspicious lesions should be excised completely and examined histopathologically. If a melanoma is confirmed, further diagnostics and therapeutic options should be initiated.

Secondary prevention is established by a regular follow-up schedule including clinical examination and ultrasound.

For higher tumour stages, imaging techniques should be used to detect disease progression early and thus increase disease-specific survival.

Regular screening can lead to early detection of skin cancer with lower invasion and depth of the tumour, which is known to be a risk factor for worse prognosis.

Skin cancer screening programmes vary between countries, with regular investigations every 2 years from the age of 35 in Germany to no general regular screenings in the USA.

So far, a decrease in mortality attributed to skin cancer screening has not been detected. Still, potential benefits might be relative to quality of life or aggressiveness of treatment.

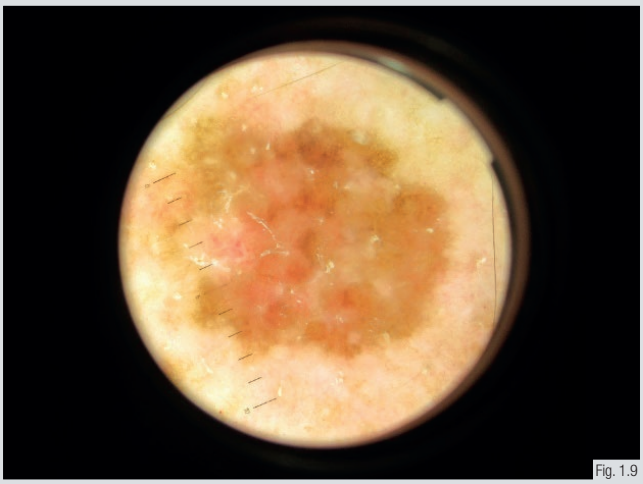


Fig. 1.9

REVISION QUESTIONS

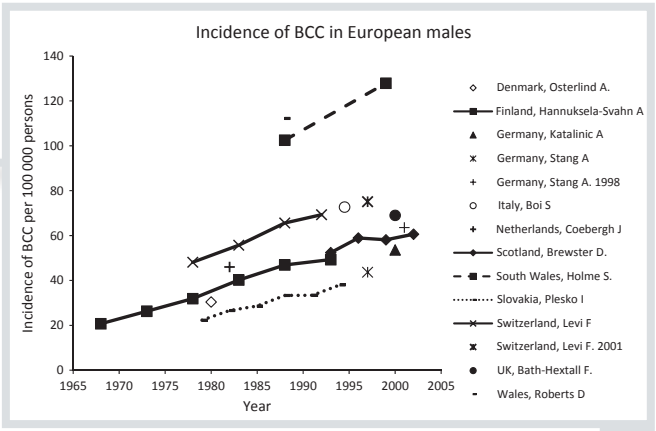
1. What does 'C' in the ABCD rule stand for?
2. What does regular screening consist of?
3. How is the diagnosis of melanoma confirmed and by whom?

Epidemiology, prevention, screening and surveillance of NMSC

NMSCs make up the greatest proportion of all human cancers, with an incidence of 8% worldwide.

Common NMSCs comprise basal cell carcinoma (BCC) arising from basal cells: 57%-80% of all NMSCs, and cutaneous squamous cell carcinoma (cSCC) arising from epidermal keratinocytes: 20%-25% of all NMSCs.

Rare NMSCs comprise Merkel cell carcinoma (MCC), cutaneous lymphomas, cutaneous adnexal tumours, Kaposi's sarcoma and others.



BCC, basal cell carcinoma. Fig. 1.10

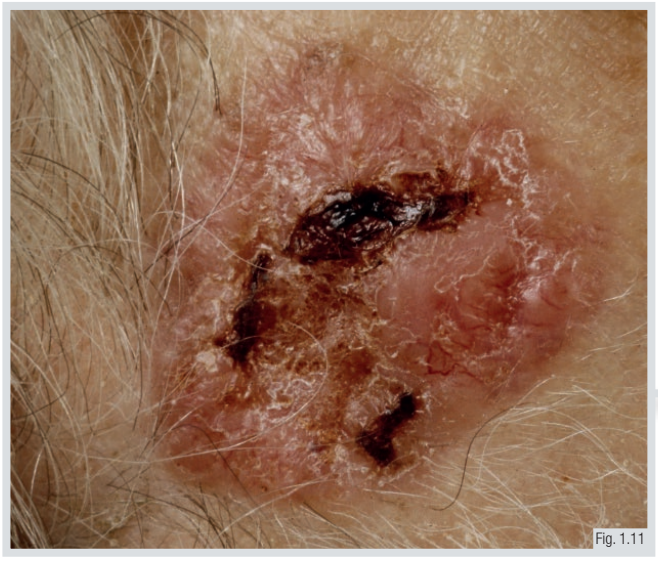


Fig. 1.11

BCC and cSCC show a low rate for distant metastases, but a higher risk for local recurrence. Major risk factors are chronic sun-damaged skin and immunosuppression.

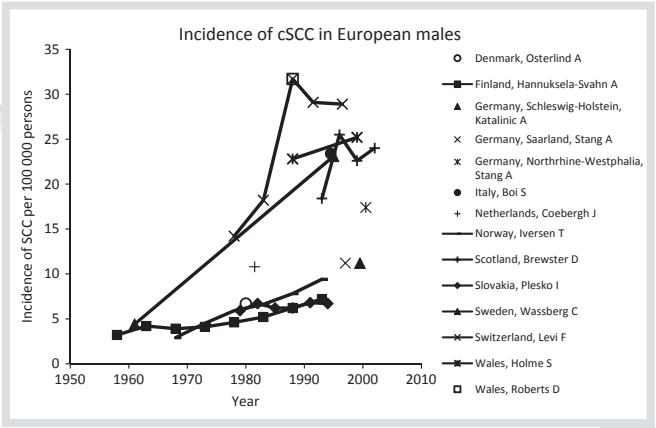
Risk factors for aggressive courses of cSCCs are immunosuppression (e.g. after solid-organ transplantation), high tumour thickness (>6 mm), poor differentiation and localisation (e.g. lips, ears).

BCCs more often arise in males (ratio 2.1:1) and elderly patients; the median age at diagnosis is 67 years. Around 80% of all BCCs are located in the head and neck region, followed, more rarely, by the hands.

cSCCs usually originate from precancerous lesions such as actinic keratosis, but they can also develop *de novo*.

Histology should always confirm the diagnosis of precancerous lesions before using any therapeutic modality other than surgery.

High-risk patients should be screened regularly with a whole-body examination, e.g. at 3-month intervals after organ transplantation or after previous high-risk NMSC.



cSCC, cutaneous squamous cell carcinoma. Fig. 1.12

REVISION QUESTIONS

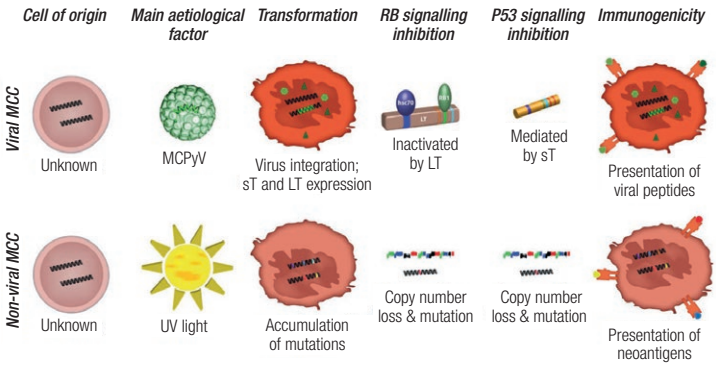
1. Which malignancies belong to common and which to rare NMSC?
2. From which cells does squamous cell cancer arise?
3. Name three risk factors for the emergence of cSCCs.

Epidemiology, prevention, screening and surveillance of NMSC (continued)

Risk factors for MCC are immunosuppression, older age and UV damage. The majority of tumours are associated with the Merkel cell polyomavirus.

Incidence is rising with approximately 2500 new cases per year in Europe (very rare), but its highly aggressive growth and disseminated spreading leads to a disease-specific mortality rate in the range of 25%-50%.

Screening is unwarranted due to the low incidence. Selection of immunosuppressive medication in dependant patients may be a crucial factor for prevention.



LT, large T antigen; MCC, Merkel cell carcinoma; MCPyV, Merkel cell polyomavirus; RB, retinoblastoma protein; sT, small T antigen; UV, ultraviolet. Fig. 1.13

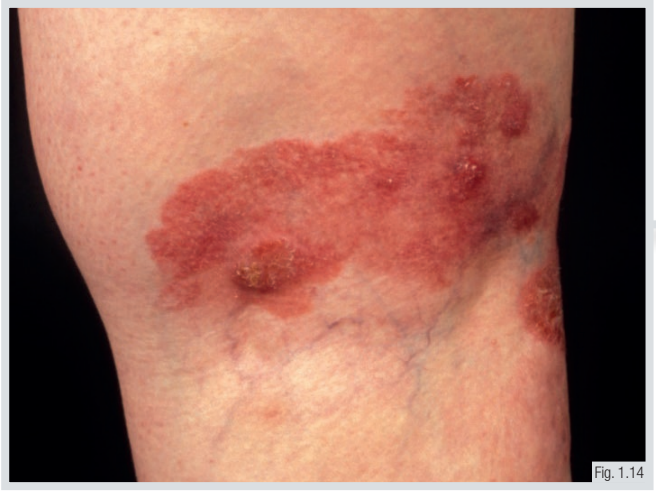


Fig. 1.14

Primary cutaneous T- (CTCL) and B- (CBCL) cell lymphomas are incurable, primary extra-nodal lymphomas of major T or B cells, respectively.

The most frequent CTCL is mycosis fungoides, which is a slowly progressing, low-grade lymphoma, clinically presenting with patches, plaques, nodules, ulcerations, but also potentially organ involvement and fatal outcome.

CBCLs are a rather rare entity with an overall incidence of 3.9/1 000 000 between 2006 and 2010. They present a heterogeneous group of malignancies, varying from slowly recurring courses to those with rapid courses.

Although rare in Europe, Kaposi's sarcoma is one of the most common neoplasms of people living with human immunodeficiency virus (HIV), with high incidences in some regions of Africa.

Overall, many patients show an immunosuppressed baseline status when developing skin cancer; this is also a risk factor for invasiveness and prognosis.

Increased awareness and regular screening of patients at risk may help to increase early diagnosis and improve outcomes in young and elderly patients.

Fig. 1.15

REVISION QUESTIONS

1. Name three risk factors for MCC.
2. From which cells do cutaneous lymphomas arise?
3. What different kinds of immunosuppression are known risk factors for skin cancer development?

Summary: Epidemiology, prevention, screening and surveillance of skin cancer

- There are great differences in incidence and mortality between countries internationally and also in Europe
- Survival for advanced melanoma patients has been significantly prolonged by new therapeutic options
- Risk factors for development of melanoma comprise UV radiation (sun exposure, tanning beds), sunburn, multiple or dysplastic naevi and medical history of melanoma
- Rising melanoma awareness among the population and protection from UV light has potentially led to a decrease in incidence in some countries (e.g. Australia)
- NMSCs make up the greatest proportion of all human cancers and include BCC, cSCC and further, rarer entities
- Major risk factors for NMSC are chronic sun-damaged skin and immunosuppression
- MCC is a very rare NMSC with a highly aggressive growth and a high disease-specific mortality rate
- Primary CTCLs and CBCLs are incurable primary extra-nodal lymphomas, which frequently show a rather chronic course of disease, but can also involve organs and show aggressive courses

Further Reading

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