Malignant Melanoma

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- Originates from melanocytes
- Melanin producing cells
- Basal membrane, hair follicules

- 8 most common malignant tumor in CR
- In the last 30 years 4x increased incidence
- 2500 new cases per annum (450 deaths)
- Every 4 diagnosed patient <50r.
- Cca 25.000 patients with dg. MM in anamn.

- Malignant melanoma is usually diagnosed early approx. 85%
- High 5 year survival rate
- Stage I. 90/100 patients
- Stage IV. 15/100 patients

Characteristic horizontal growth phase
followed by penetrating vertical phase

Most cases Sweden, Estonia, Denmark, Holand and Australia.

Standardized mortality of MM per 100 000 capita



Genetics

- Mutation of CDKN2A, CDK4, MCN1
- Aneuploidia of chromosomes 1,6,7,9,10,11
- BRAF, N-RAS mutations
- Environmental factors (UVA, UVB)
 - Intermittent sun exposure (short but intensive) \uparrow
 - Long term sun exposure (slow but steady) \downarrow
 - Solariums +/-

Sensibilisation

- Plants (furocoumarines, lime)
- Tar
- Medication (furosemide, diclofenac, TTC, ketoprofen)

Imunosupression

- Transplanted patients
- Systemic treatment of autoimmune diseases

Ethnicity

- Pale skin (phototype I. a II.)Pigmented nevi
- $-\downarrow$ incidence in darker skin



Most common forms of MM

• Superficial spreading melanoma (SSM)

• Nodular melanoma (NMM)

• Acral lentiginous melanoma (ALM)

• Lentigo maligna melanoma (LMM)

Rarer types of MM

- Amelanotic melanoma
- Nevoid melanoma
- Malignant blue nevi
- Desmoplastic melanoma
- Mucous membrane melanoma
- Occular melanoma
- Juvenile melanoma

Superficial spreading melanoma (SSM)

- Most common form (approx. 70%)
- Often between 3 and 5 decade
- Women most often feet
- Men most often upper body
- Depigmentation (regression) signs of interaction with immune system

Superficial spreading melanoma (SSM)



Superficial spreading melanoma (SSM)



Nodular melanoma (NMM)

- 15-30% of all melanomas
- Often in 6 decade of life
- Chest, neck, face
- Blue or black nodules
- Often without horizontal phase

Nodular melanoma (NMM)



Acral lentiginous melanoma (ALM)

• Less common form of melanoma (5-10%)

 Most common form in asians and blacks (45%/70%)

• Palms, souls of feet, nails

• Due to location hard to diagnose

Acral lentiginous melanoma (ALM)







Acral lentiginous melanoma (ALM)





Lentigo maligna melanoma (LMM)

- Approx. 15% of all melanoma
- Locations of chronic sun damage
- Usually 7 decade of life
- Most often head, face and nose
- Differential diagnosis with sun damage

Lentigo maligna melanoma (LMM)







Amelanotic melanoma

- Rare form of pigmented
 - Approx. 2-20% of all diagnosed melanomas
- Often misdiagnosed (BCC, verruca, fibroma)
- Very hard to diagnose (3R method)
 - Raised
 - Red
 - Recent

Amelanotic melanoma



Diagnosis of MM

- Clinical image (ABCDEF rule)
- Medical history
- Dermoscopy

- Histological examination (excision/biopsy)
 - "When in doubt, cut it out"
- FISH detection of chromosomal aberrations

Non invasive diagnosis





Breslow scale

Breslow thickness is the measurement of the depth of the melanoma from the surface of the skin down through to the deepest point of the tumour. Stratum granulosum





Clark scale

- I. Only epidermis (Carcinoma in situ)
- II. down to papillary dermis
- III. papillary dermis involvement without reticular dermis invasion
- IV. reticular dermis involvement without subcutis invasion
- V. Da full monty

TABLE 1

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TABLE 2

STAGES OF MELANOMA				Stage	Description
Store	T	N	м	Tumor (T)	
Stage	Т	N	М	Тх	Primary tumor cannot be assessed.
0	Tis	NO	MO	TO	No evidence of primary tumor.
IA	T1a	NO	M0	Tis	Also known as "melanoma in situ," melanoma cells are found only between the outer layer (epidermis) and the inner layer (dermis) of skin and have not yet invaded these layers. This lesion is considered precancerous.
IB	T1b T2a	N0 N0	M0 M0	T1 T1a T1b	Melanoma is no more than 1 millimeter (mm) thick (about the thickness of a credit card). Melanoma is no more than 1 mm thick, without ulceration and a mitotic rate of less than 1/mm². Melanoma is no more than 1 mm thick, either with ulceration or a mitotic rate of 1/mm² or greater.
IIA	T2b T3a	N0 N0	M0 M0	T2 T2a T2b	Melanoma is thicker than 1 mm but not more than 2 mm thick. Melanoma is thicker than 1 mm but not more than 2 mm thick, without ulceration. Melanoma is thicker than 1 mm but not more than 2 mm thick, with ulceration.
IIB	T3b T4a	N0 N0	M0 M0	T3 T3a T3b T4	Melanoma is thicker than 2 mm but not more than 4 mm (about one-tenth of an inch) thick. Melanoma is thicker than 2 mm but not more than 4 mm, without ulceration. Melanoma is thicker than 2 mm but not more than 4 mm, with ulceration. Melanoma is thicker than 4 mm.
	140	NU	IVIO	T4a T4b	Melanoma is thicker than 4 mm, without ulceration. Melanoma is thicker than 4 mm, with ulceration.
IIC	T4b	NO	MO	Node (N)	
IIIA	T1-T4a	N1a	MO	Nx	Regional lymph nodes cannot be assessed.
	T1-T4a	N2a	MO	NO	No melanoma found in regional lymph nodes.
IIIB	T1-T4b T1-T4b	N1a N2a	M0 M0	N1 N1a N1b	Melanoma found in one lymph node. Microscopic metastasis found in one lymph node. Macroscopic metastasis found in one lymph node.
	T1-T4a T1-T4a	N1b N2b	M0 M0	N2 N2a N2b N2c	Melanoma found in two to three lymph nodes. Microscopic metastasis found in two to three lymph nodes. Macroscopic metastasis found in two to three lymph nodes. In-transit melanoma or satellite lesions are found, without metastasis to lymph nodes.
	T1-T4a	N2c	MO	N3	Melanoma is found in four or more lymph nodes, or in two or more lymph nodes that appear to be joined together (known as matted lymph nodes). Or, melanoma is found as in-transit lesions or as satellite lesions that have spread to the lymph nodes.
IIIC	T1-T4b T1-T4b	N1b N2b	M0 M0		
				Metastasi Mx	s (M) Metastasis cannot be assessed.
	T1-T4b	N2c N3	M0 M0	MO	No metastasis.
	Any T	IND CM	IVIU	M1a	Metastasis to skin, subcutaneous tissues or distant lymph nodes.
IV	Any T	Any N	M1	M1b M1c	Metastasis to lung. Metastasis to any other distant organs.

Metastasis

- Lymphogenic a hematogenic spread
- Most often lungs, liver, brain, bones

- Satellites (2 cm from tumor)
- Intransit (more then 2 cm from tumor)
- Nodal (regional lymph nodes)

Melanosis cutis diffusa

Metastasis



Primary therapy

- Wide excision (safety margin)
 - MM in situ 0.5 cm
 - MM up to Breslow 2 mm 1 cm
 - MM over Breslow 2 mm 2 cm

- Excision and sentinel lymph node extraction
 - Breslow over 1 mm
 - Breslow 0.8 mm and ulcerations

Adjuvant therapy

- Chemotherapy (Dacarbazine, Cisplatina)
- Interferon (Intron, Roferon)
- Cryosurgery (skin metastasis)
- Radiotherapy
- Targeted therapy (BRAF, MEK inhibitory)
- Imunotherapy (check point inhibition)
- Combination anti CTLA-4 + anti PD-1
- Therapy till progression or toxicity



SKIN CANCER

Nature's way of killing retards

There's no stronger sunscreen than sitting in a bar.



