# Melanoma

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# Introduction

- 82%-85% of patients present with localized disease,
- 10%-13% with regional disease, and
- 2%-5% with distant disease.

# Risk factors

1. UV exposure
2. Fitzpatrick type 1 and 2
3. Race : Risk is 10 to 20 times higher for whites than blacks. Prognosis in darker skin is worse because of delayed diagnosis.
4. Age
5. Previous hx
6. Family hx
7. Predisposing conditions

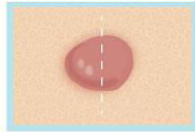
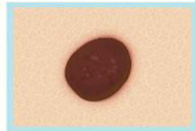
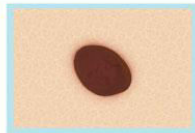
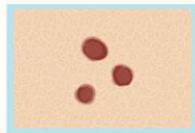
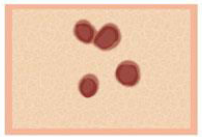
# Predisposing conditions

- Congenital nevus: 6% lifetime risk depending on size
- Typical moles: Increased risk if more than 50
- Lentigo maligna

# Benign vs malignant on examination

- A B C D E

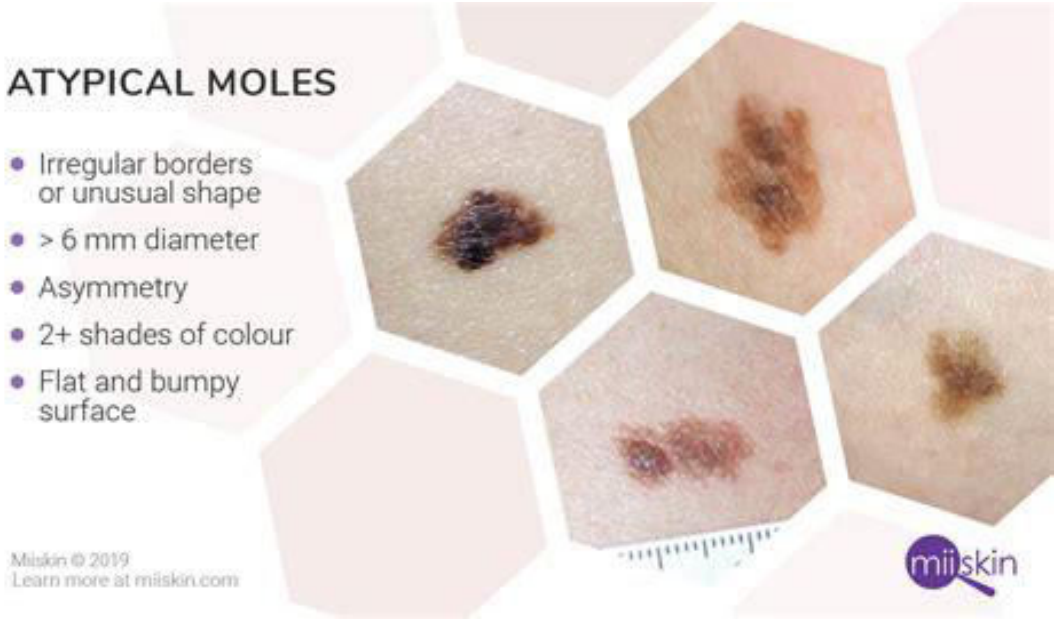
# ABCDEs MOLE OR MELANOMA?

| MOLE FEATURES | BENIGN | SEE DOCTOR |
| --- | --- | --- |
| **A ASYMMETRY** ONE HALF OF A MOLE DOES NOT MATCH THE OTHER. |  |  |
| **B BORDER** THE EDGES ARE IRREGULAR, RAGGED, NOTCHED, OR BLURRED. NORMAL MOLES ARE ROUND OR OVAL. |  |  |
| **C COLOR** THE MOLE IS NOT EVENLY COLORED. IT MAY INCLUDE SHADES OF BROWN OR BLACK, OR PATCHES OF PINK, RED, WHITE OR BLUE. |  |  |
| **D DIAMETER** THE SPOT IS LARGER THAN 6 MILLIMETERS ACROSS |  LESS THAN .25 IN |  GREATER THAN .25 IN |
| **E EVOLVING** THE MOLE IS CHANGING IN SIZE, SHAPE, OR COLOR. |  |  |

- Pigmented lesions could be:
- 1-benign
- 2-premalignant
- 3-malignant (melanoma)

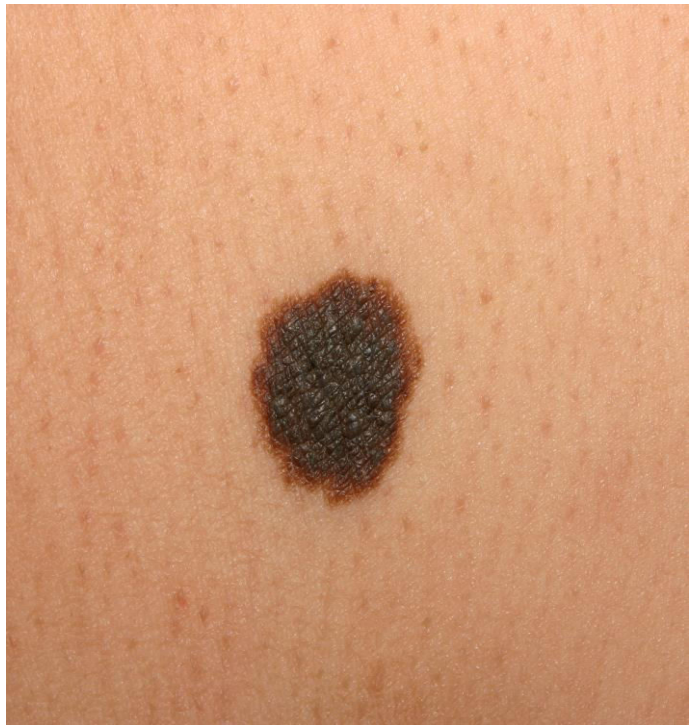
# Premalignant lesions

- Dysplastic nevi:
- A. have variegated color (tan to brown on a pink base)
- B. are large (5 to 12 mm)
- C. appear indistinct, with irregular edges
- D. have macular and papular components



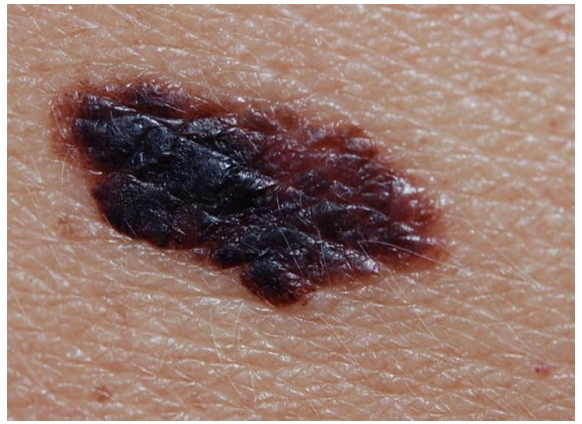
- Congenital nevi:

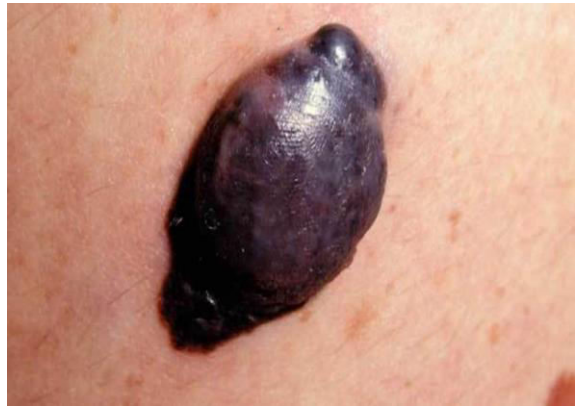
- are notable by their presence since birth and are commonly referred to as “birthmarks.” They can be premalignant: There is an increased risk of melanoma developing from these lesions, particularly for nevi greater than 20 cm in diameter.



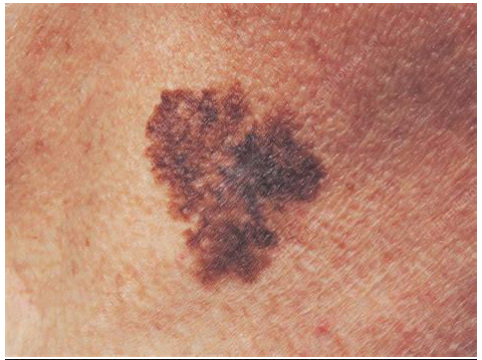
# Malignant lesions

- These are the melanoma spreading (growth) patterns.
- 1- Superficial spreading melanoma:
- Most common: 50%-70% •
- Usually arises from preexisting nevus
- 2- Nodular melanoma:
- 15%-30% of all cases
- most Aggressive due to its vertical spreading



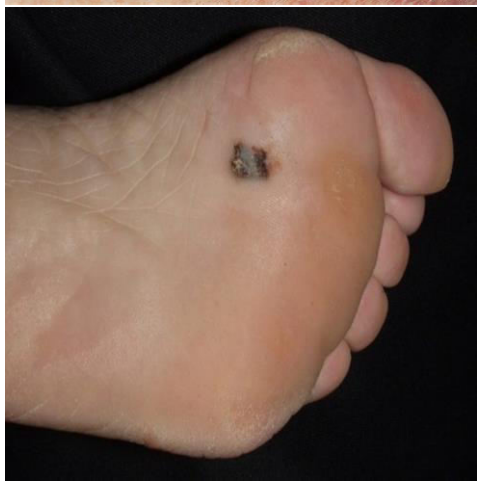


- 3- Lentigo maligna
- found on older patients as a large melanotic freckle on the temple or malar region known as Hutchinson freckle.



- 4- Acral-lentiginous melanoma:
- Usually on palms, soles of feet, subungual,

or sun-protected sites



# Melanoma Staging

Histologic analysis of full-thickness biopsy specimen is categorized by microstaging.

- Breslow thickness: Measurement of tumor thickness in millimeters
- Clark's level: Level determined by histologic invasion through skin layers

American Joint Committee on Cancer (AJCC) introduced revised tumor-node-metastasis (TNM) melanoma staging system in 2010

Tumor thickness (Breslow thickness) replaces level of invasion (Clark's level) as the most important prognostic variable of primary tumor invasion that best predicts survival.

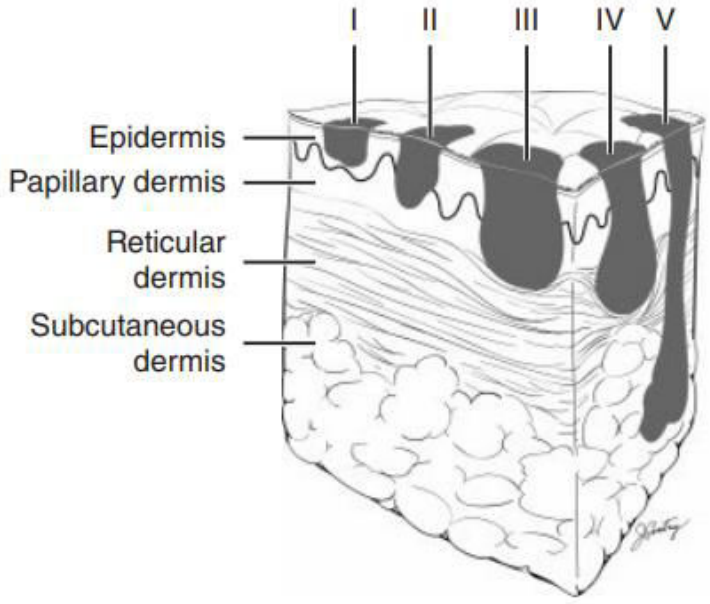



**Fig. 15-2** Levels of tumor invasion according to the Clark microstaging criteria.

- Ulceration of the primary tumor (microscopic histopathologic ulceration) upstages the disease to the next highest T substage
- Mitotic rate ≥1 per mm2 is independently associated with worse disease-specific survival, especially in tumors ≤1 mm thick.
- Number of metastatic lymph nodes replaces the size of lymph nodes in the N stage.
- Lymphatic mapping data (lymphoscintigraphy) and micrometastatic local regional disease within lymph nodes are incorporated in clinical and pathologic staging.
- Subcategorization of stage IV metastatic disease is based on anatomic site of the metastasis and elevated serum LDH.

**Table 15-3** *AJCC TNM Melanoma Staging Classification, 2010*

| Tumor Classification | Depth of Invasion |
|---|---|
| TX | Primary tumor cannot be assessed |
| Tis | Melanoma in situ |
| T1 | <1.0 mm |
| T2 | 1.01-2.0 mm |
| T3 | 2.01-4.0 mm |
| T4 | >4.0 mm |
| NOTE: a and b subcategories of T: a, without ulceration and mitosis $<1/mm^2$; b, with ulceration or mitoses $>1/mm^2$. | |
| **Node Classification** | |
| NX | Cannot be assessed |
| N1 | One node |
| N2 | Two to three nodes |
| N3 | Four or more nodes, matted, or in transit satellites with metastatic nodes |
| NOTE: a, b, and c subcategories of N: a, micrometastasis (diagnosed after sentinel lymph node biopsy); b, macrometastasis (clinically positive nodes); c, in transit satellites without nodes (N2 only). | |
| **Metastatic Classification** | |
| M1a | Metastases to skin, subcutaneous, distant nodes |
| M1b | Metastases to lung |
| M1c | Metastases to other viscera or any distant site combined with elevated serum LDH |

**Table 15-4** *Pathologic Staging*

| Stage | Tumor | Node | Metastasis |
|---|---|---|---|
| Stage 0 | Tis | N0 | M0 |
| Stage IA | T1a | N0 | M0 |
| Stage IB | T1b | N0 | M0 |
| | T2a | N0 | M0 |
| Stage IIA | T2b | N0 | M0 |
| | T3a | N0 | M0 |
| Stage IIB | T3b | N0 | M0 |
| | T4a | N0 | M0 |
| Stage IIC | T4b | N0 | M0 |
| Stage IIIA | T(1-4)a | N1a | M0 |
| | T(1-4)a | N2a | M0 |
| Stage IIIB | T(1-4)b | N1a or N2a | M0 |
| | T(1-4)a | N1b, N2b, or N2c | M0 |
| Stage IIIC | T(1-4)b | N1b, N2b, or N2c | M0 |
| | Any T | N3 | M0 |
| Stage IV | Any T | Any N | M1 |

Workup

- Obtain biopsy samples of lesion. Stage patient by evaluating lymph node status and imaging for metastatic disease.
- Obtain biopsy specimens of all suspicious lesions.
- • 5-7 mm punch biopsy is adequate but may miss thickest portion of tumor.
- • Obtain incisional biopsy for low-suspicion lesion or in cosmetically sensitive regions. Orient incision longitudinally in extremities.
- • Excisional biopsy with 1-3 mm margins is recommended.
- • Shave biopsy forfeits ability to stage on thickness.
- • Full-thickness biopsy is not required in subungual melanoma, because it offers no prognostic information.
- • Evaluate for Breslow thickness, ulceration status, dermal mitotic rate, deep and peripheral margins, microsatellitosis, Clark’s level, and desmoplasia.

- Imaging
- • Stages I and II: CT scan, PET/CT, MRI generally not recommended unless evaluating specific symptoms
- • Stage III: Can consider imaging, including CT chest, abdomen/pelvis, CT/MRI brain with or without PET/CT n CT pelvis in patients with inguinofemoral lymphadenopathy
- Stage IV: Confirm metastatic disease with FNA or open biopsy. Obtain baseline imaging as above

# Treatment

- Treatment of melanoma is mostly done by wide local excision with surgical margins based on tumor thickness.

- In situ: 0.5 cm margin
- 1 mm: 1 cm margin
- 1-4 mm: 2 cm margin
- 4 mm: 2 cm margin

**Depth of resection should not include fascial layer, because this increases risk of metastatic disease.

- A sentinel lymph node biopsy is done is stage IB melanoma or stage II
- It’s a staging procedure, not a therapeutic treatment
- A therapeutic lymph node dissection is performed in positive SLNB patients or clinically palpable disease.

- Immunotherapy is used in some cases, Vemurafenib and Dabrafenib *BRAF kinase inhibitors* have been approved to be used in stage IV patients with a mutation in the BRAF gene.