



MSS

PATHOLOGY

11



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Before we start special thanks to Noor Kyatt for helping collect the important info! With that taken care of, let's get down to business.

MELANOCYTYC NEOPLASMS

Alright, we're going to have a chat about the fancy medical term for skin growths that come from melanocytes - the cells that give us our skin color. There are three types we'll be covering: Nevus (sounds like a Harry Potter spell, right? Ok, that was lame ik), Melanocytic, Dysplastic (fancy word for "atypical"), and finally, the big bad Melanoma (cue dramatic music! No? ok fine). So, let's dive in and learn about these skin growths that can be both fascinating and worrisome at the same time! But before that here's some light info that we will dive into deeper later on:

- **Nevus: a benign congenital melanocytic neoplasm**, pigmented melanocytic proliferation that is usually small, well-demarcated, and has no significant change over time. **NO MITOSIS!**
- **Melanocytic nevus: a general term for any melanocytic neoplasm**, which can be congenital or acquired.
- **Dysplastic nevus: a nevus with atypical features**, such as larger size (>5 mm), **loss of symmetry, fusion of junctional nests**, cellular and nuclear atypia, and lymphocytic infiltration. It has a higher risk of developing into melanoma than non-dysplastic nevi. **There is MITOSIS!**
- **Melanoma: a malignant tumor** arising from melanocytes that has the **potential to spread to other parts of the body**. Melanoma can arise de novo or from pre-existing nevi, including dysplastic nevi

** Note: Staining is commonly performed to differentiate melanocytic neoplasms from other tumors due to their similarities. **Sun damage is a major contributor** to the development of these tumors, and it is important to note that they can be present from birth (congenital) or acquired later in life.

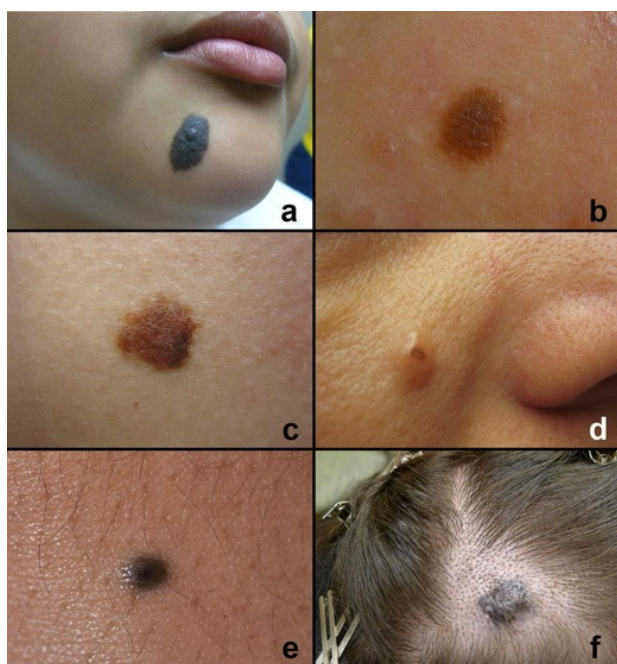
THE ORDER PROGRESSION IS IMPORTANT!!!

NEVUS → DYSPLASTIC NEVUS → MELANOMA

NEVUS

- Nevus is a **benign pigmented melanocytic proliferation**.
 - Not always pigmented, but most are.
- It is caused by a somatic gain of function mutation in the **BRAF or RAS genes**.
 - **These are the initial heads (early changes): BRAF & RAS (Extremely Important!)**
- This is followed by inactivity called "**Senescence**."
 - From the doctor: forget about it, it will only make you confused.
- Clinically, it appears as a **sharply demarcated, elevated and pigmented lesion**.
- Nevus is removed **surgically for cosmetic reasons**, irritation, and to rule out dysplasia or melanoma.
- There are three types of nevi: **Junctional Nevus, Compound Nevus, and Intradermal Nevus**.
 - **Junctional Nevus** occurs at the **junction** of the **epidermis and dermis**.
 - **Compound Nevus** involves **both** the **epidermis and dermis**.
 - **Intradermal Nevus** involves the **dermis only**.
- Most nevi are harmless and do not require treatment unless they change in size, shape, or color, which may indicate melanoma.
- **When there is Atypical cells and mitosis in the Nevus then you will get extremely concerned because it's a dangerous sign of Melanoma.**

BENIGN FEATURES OF NEVUS

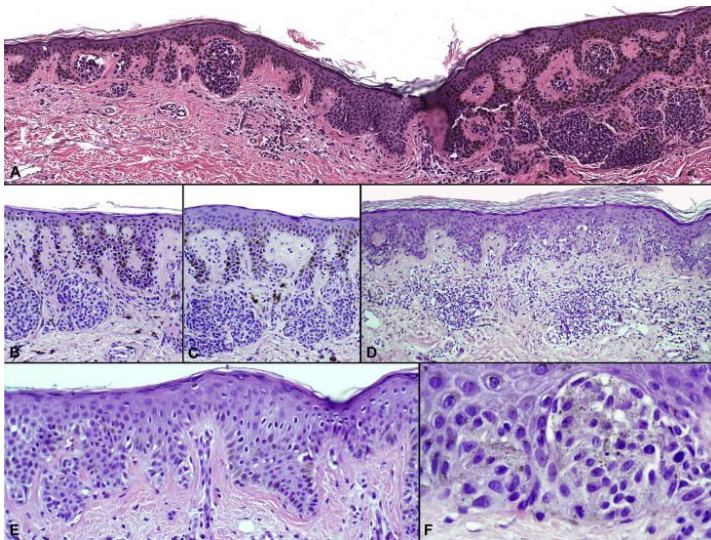


- It is characterized by **well-demarcated and sharp borders**.
- It usually **does not change** significantly over time.
- Histologically, it **exhibits symmetry and absence of atypia**, (including cellular enlargement, nuclear enlargement, nuclear chromatin abnormalities, prominent nucleoli, mitosis), and **maturation as you move deep into dermis which is a feature**.

DYSPLASTIC NEVUS

- Dysplastic nevi are moles **with atypical features**, which can include **irregular borders**, **uneven color**, and **larger size (>5 mm)**.
- They can occur sporadically or as part of a familial syndrome.
- They can **appear on both sun-exposed and non-sun-exposed** areas of the body.
- They can be single or multiple, especially in familial cases.
- Although **dysplastic nevi have a higher risk of developing into melanoma** compared to non-dysplastic nevi, the absolute **risk is still low** and most melanomas **develop without arising from a pre-existing nevus ("de novo")**.
- However, individuals with **familial dysplastic nevus syndrome have a higher lifetime risk of developing melanoma** and should undergo regular skin exams and surveillance.

HISTOLOGICAL FEATURES

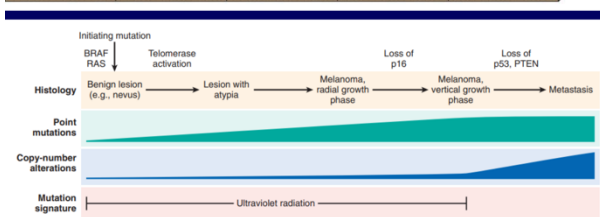
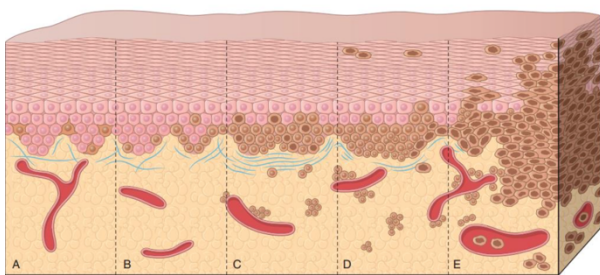


- **Loss of symmetry:** The nevus has an irregular shape and size.
- **Fusion of junctional nests:** The junctional nests (clusters of cells at the junction of the epidermis and dermis) are fused together.
- **Cellular and nuclear atypia:** The cells show signs of abnormal growth, with enlarged and irregular nuclei and abnormal cytoplasmic features.
- **Superficial dermal fibrosis:** The dermis (the layer of skin below the epidermis) shows fibrosis (the formation of excess connective tissue), especially near the surface of the skin. So, It means **collagen formation**.
- **Lymphocytic infiltration:** There are lymphocytes (a type of immune cell) present in and around the nevus.
- **Melanin incontinence:** Melanin pigment (the pigment that gives color to the skin) is dispersed within the dermis, indicating that melanocytes (the cells that produce melanin) are present and active within the nevus.

MELANOMA

- Melanoma is a type of skin cancer that arises from melanocytes, that is a **big mimicker and has a tendency to metastasize to the lymph nodes.**
- Melanoma **is less common** than squamous cell carcinoma, basal cell carcinoma, and nevi.
- Melanoma can be fatal if not detected and treated early.
- The incidence of melanoma is increasing, which is attributed to **more sun exposure, increased surveillance, and public awareness.**
- The most effective treatment for melanoma is **surgical removal of the tumor (WLE: Wide Local Excision).**
- Early detection is crucial for a better prognosis, and regular skin examinations are recommended for individuals at high risk of developing melanoma.
- Other treatment options may include chemotherapy, radiation therapy, immunotherapy, and targeted therapy depending on the stage and extent of the disease.

EVOLUTION OF MELANOMA (IMPORTANT!)

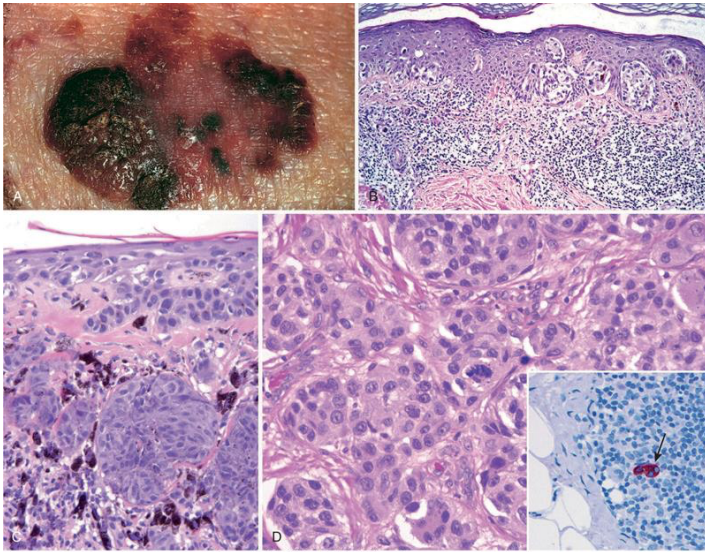


- **So we have multiple heads:**
 - the Initial head: **BRAF and RAS.**
 - The Middle head: **TERT**
 - The Later Heads: **TP53 and PTEN** which mainly involve the **Tumor Suppressor Genes!**
 - These Heads **are the target of treatment.**
- **First is Rapidly growth (radial growth)**

and then vertical growth.

- Melanoma **evolves from a nevus (mole).**
- The nevus progresses to become a dysplastic nevus.
- The dysplastic nevus can then progress to become an early melanoma.
- **Advanced melanoma can spread to other parts of the body, making it difficult to treat!**
- Regular skin exams and early detection are crucial for successful treatment.
- **Avoiding excessive sun exposure** and **using sunscreen** can prevent the development of melanoma.

PATHOLOGICAL FEATURES OF MELANOMA (IMPORTANT!)



Kumar et al: Robbins Basic Pathology, 9e.
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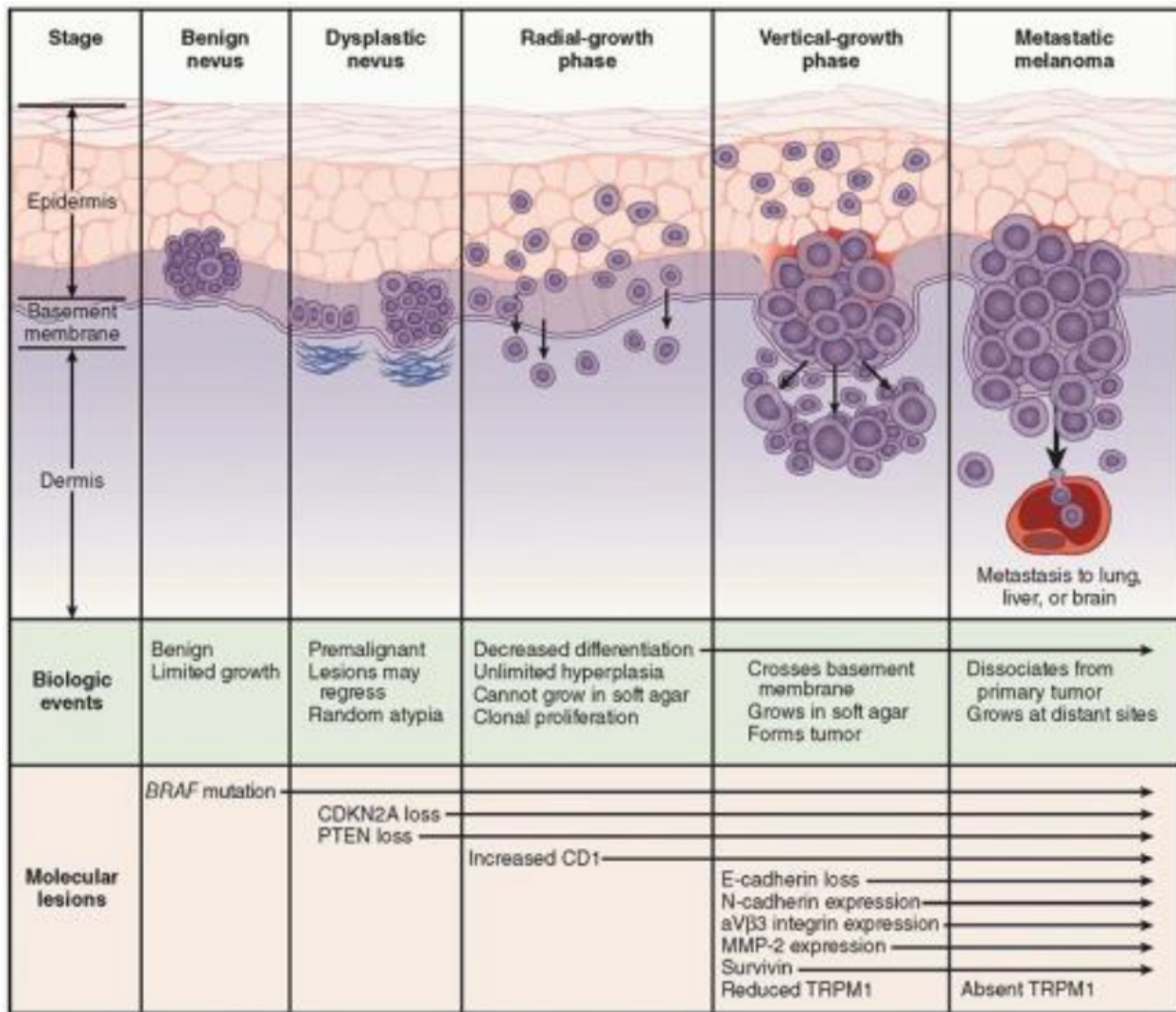
- Melanoma has **irregular borders and pigmentation (not always present)**.
- It shows **irregular nesting** with **increased numbers of single cells**.
- Melanoma exhibits **radial and vertical growth**.
- **The Deeper and thicker** it is, the **worse (prognosis)** it is because it can **metastasis**.
- The more **superficial and thinner** it is, the **better (prognosis)** it is.
- It has **increased thickness (Breslow thickness)!**
- **Deeper invasion** and **larger atypical cells** are also common.
- The nuclei in melanoma cells are larger and atypical with prominent **cherry-red nucleoli**.
- **Nucleus and cytoplasm are both enlarged**; **the ratio of nucleus to cytoplasm will not be high**, as both components are similarly enlarged

WARNING SIGNS OF MELANOMA

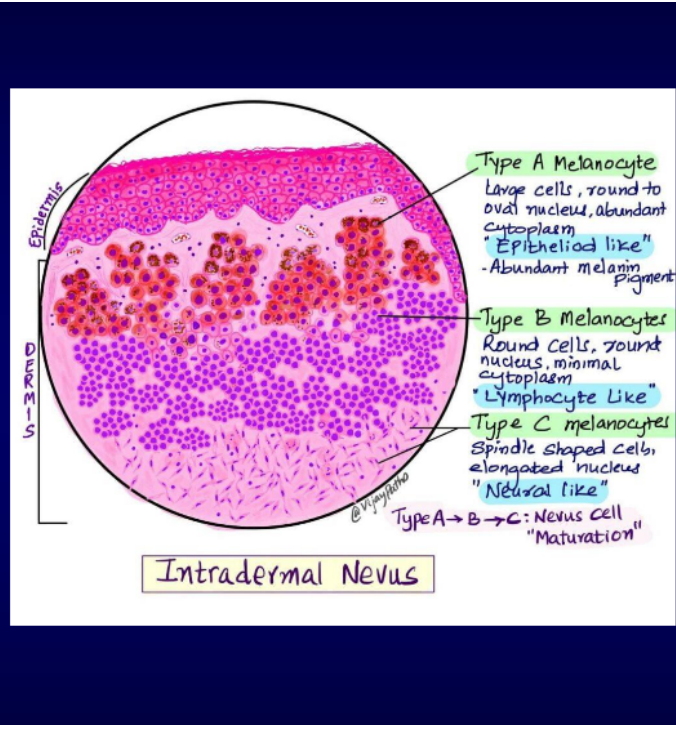
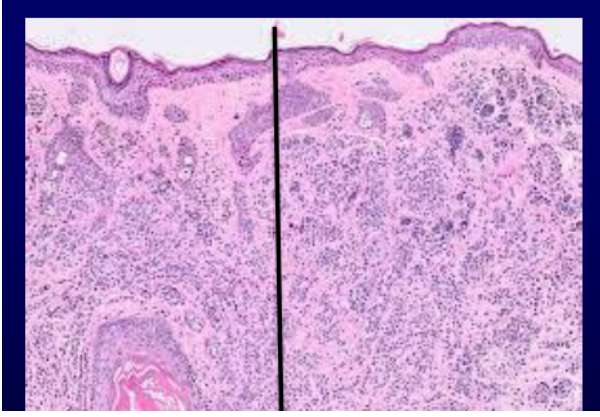
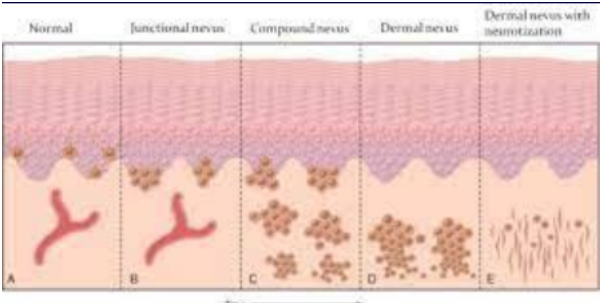
- **Rapid enlargement of a preexisting nevus**
 - A nevus is a mole or pigmented lesion on the skin.
 - If the size of the nevus increases rapidly, it can be a warning sign of melanoma.
- **Itching or pain**
- **New pigmented lesions development**
 - The development of new pigmented lesions on the skin, **especially in adulthood**.
- **Irregular borders of a pigmented lesion**
 - Melanoma often has an irregular or **asymmetrical shape with blurry or jagged edges**.
- **Variation of color within a pigmented lesion**
 - Melanoma often has a mix of colors or an uneven distribution of color.
 - Dark brown or black, red, white, or blue shades within a pigmented lesion can be warning signs of melanoma.

CLINICAL FEATURES AND PROGNOSIS OF MELANOMA

- Melanoma can be cured with surgery if detected early.
- **The stage of the melanoma is important** and is **determined by the depth of invasion**.
- Metastatic melanoma **has a poor prognosis**.
- "**Sentinel node**" evaluation can help determine the stage of the melanoma.
 - the sentinel node is the first lymph node that cancer is most likely **to spread to from the primary tumor**.
- Recent advances in treatment options include targeted therapies such as **Anti BRAF and KIT agents, and immune checkpoint inhibitors** that use T-cell mediated immunotherapy to target melanoma cells.
 - Targeted therapy targets specific molecules within the melanoma cells **to block their growth and division**.
 - Immune checkpoint inhibitors help the body's immune system to **recognize and attack** the melanoma cells.
 - **Combination therapy** with both targeted therapy and immune checkpoint inhibitors may also be used **to treat advanced melanoma**.



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1) EVOLUTION OF MELANOMA, 2) BENIGN FEATURES OF NEVUS.

TEST YOURSELF

Yes, those questions are made by yours truly 😊 enjoy!

1. What are the initial genes involved in the development of a nevus?

- a) RAS and TP53
- b) BRAF and RAS
- c) PTEN and AKT
- d) EGFR and HER2

Answer: b) BRAF and RAS

2. What is senescence in nevus?

- a) A stage of inactivity following a mutation in the BRAF or RAS genes.
- b) A stage of rapid growth before the nevus becomes benign.
- c) A stage of metastasis in nevus.
- d) A stage of cell division and proliferation.

Answer: a) A stage of inactivity following a mutation in the BRAF or RAS genes.

3. What are the benign features of a nevus?

- a) Symmetry, atypia, and cellular enlargement
- b) Sharp borders, absence of atypia, and does not change significantly over time
- c) Superficial dermal fibrosis, cellular atypia, and irregular shape
- d) Fusion of junctional nests, loss of symmetry, and mitosis

Answer: b) Sharp borders, absence of atypia, and does not change significantly over time

4. What are the histological features of dysplastic nevus?

- a) Superficial dermal fibrosis, lymphocytic infiltration, and melanin incontinence
- b) Loss of symmetry, cellular and nuclear atypia, and fusion of junctional nests
- c) Cellular enlargement, nuclear enlargement, and maturation as you move deep into the dermis
- d) Radial and vertical growth, irregular nesting, and increased numbers of single cells

Answer: b) Loss of symmetry, cellular and nuclear atypia, and fusion of junctional nests

5. What are the risk factors for developing melanoma?

- a) Smoking and alcohol consumption
- b) Family history of melanoma and dysplastic nevi syndrome
- c) Exposure to UV radiation and sunburns
- d) B & C

Answer: D) Family history of melanoma and dysplastic nevi syndrome, and Exposure to UV radiation and sunburns.

6. What is the most effective treatment for melanoma?

- a) Chemotherapy
- b) Radiation therapy
- c) Immunotherapy
- d) Surgical removal of the tumor

Answer: d) Surgical removal of the tumor

7. How does melanoma evolve?

- a) It progresses from a benign nevus to a dysplastic nevus and then to melanoma.
- b) It arises de novo without arising from a pre-existing nevus.
- c) It starts as a benign nevus and then rapidly progresses to melanoma without going through a dysplastic nevus stage.
- d) A & B

Answer: D) The evolution of melanoma can occur in two ways: either progressing from a benign nevus to a dysplastic nevus and then to melanoma or arising de novo without arising from a pre-existing nevus

8. What are the pathological features of melanoma?

- a) Sharp borders and absence of atypia
- b) Irregular nesting and increased numbers of single cells
- c) Superficial dermal fibrosis and melanin incontinence
- d) Fusion of junctional nests and loss of symmetry

Answer: b) Irregular nesting and increased numbers of single cells