

QUESTIONS

Select the single best answer.

1 A 55-year-old man from China presents with a 3-month history of scales on his skin. Physical examination reveals numerous scaly, pigmented plaques, which rub off easily. Biopsy of a plaque shows anastomosing cords of mature and stratified squamous epithelium, associated with small keratin cysts. This patient may have which of the following underlying conditions?

- (A) Acquired immunodeficiency
- (B) Basal cell nevus syndrome
- (C) Familial hypercholesterolemia
- (D) Human papillomavirus infection
- (E) Internal malignancy

2 An 18-year-old woman notes that one of her moles has increased in size and become darker. The patient has a family history of melanoma, and she is seen by her dermatologist regularly to "follow her moles." Physical examination reveals numerous, 5 to 10 mm, darkly pigmented, variegated lesions distributed primarily on her trunk but also involving non-sun-exposed skin. This patient may harbor a germline mutation in a gene that regulates which of the following proteins?

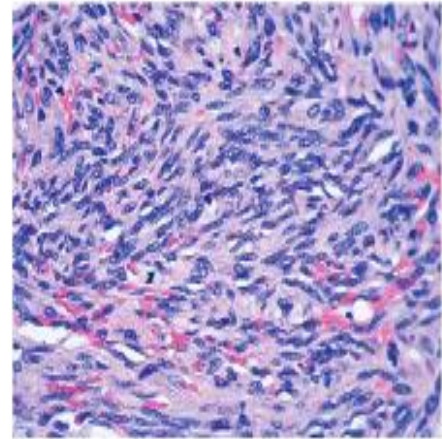
- (A) Caspase
- (B) Cyclin-dependent kinase
- (C) Epidermal growth factor receptor
- (D) Glycogen phosphorylase
- (E) Sodium-potassium ATPase

3 An 80-year-old farmer presents with a 1-cm, red, slightly raised plaque on his face. A biopsy of the lesion shows cytologic atypia and dyskeratosis limited to the basal layers of the stratum spongiosum, as well as hyperkeratosis and parakeratosis. This lesion is a precursor for which of the following dermatologic diseases?

- (A) Basal cell carcinoma
- (B) Erythema multiforme
- (C) Lichen planus
- (D) Malignant melanoma
- (E) Squamous cell carcinoma

4 A 45-year-old man presents with painful, purple nodules on the dorsal surface of his left hand that he first noticed 9 months ago. A biopsy (shown in the image) discloses a poorly demarcated lesion composed of atypical spindle-shaped neoplastic

cells and extravasated red cells. Similar lesions are found in the lymph nodes and liver. Which of the following viruses is associated with the pathogenesis of these skin lesions?



- (A) Cytomegalovirus
- (B) Epstein-Barr virus
- (C) Herpes simplex virus type 2
- (D) Human herpesvirus type 8
- (E) Human papillomavirus types 16/18

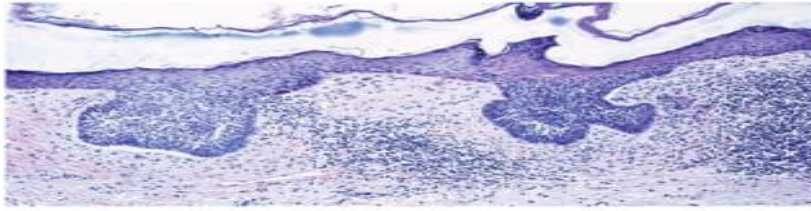
5 A 36-year-old woman presents with a pigmented lesion on the posterior aspect of her left calf (shown in the image). An excisional biopsy demonstrates a superficial spreading type of melanoma. Which of the following histologic features has the most important prognostic value in your evaluation of this patient?



- (A) Degree of melanocytic atypia
- (B) Degree of vascularity
- (C) Depth of dermal invasion
- (D) Extent of intraepidermal invasion by melanoma cells
- (E) Presence of variable melanin pigmentation

11

A 60-year-old former lifeguard presents with several small, pearly nodules on the back of her neck. A biopsy of one of the nodules (shown in the image) reveals buds of atypical, deeply-basophilic keratinocytes extending from the overlying epidermis into the papillary dermis. Which of the following is the appropriate diagnosis?



- (A) Basal cell carcinoma
- (B) Fibroepithelial polyp
- (C) Keratoacanthoma
- (D) Squamous cell carcinoma
- (E) Xanthoma

ANSWERS

1 The answer is E: Internal malignancy. Seborrheic keratoses are scaly, frequently pigmented, elevated papules or plaques whose scales are easily rubbed off. Microscopically, the lesions are composed of broad anastomosing cords of mature stratified squamous epithelium associated with small cysts of keratin (horn cysts). The sudden appearance of numerous seborrheic keratoses has been associated with internal malignancies (sign of Leser-Trelat), especially gastric adenocarcinoma. Papillomavirus infection (choice D) induces papilloma formation. Choices B and D do not lead to acute plaque eruption.
Diagnosis: Seborrheic keratoses

2 The answer is B: Cyclin-dependent kinase. Germline mutations in the *CDKN2A* tumor suppressor gene (also known as *p16*) have been found in some patients who have dysplastic nevus/melanoma and in their family members. This gene encodes an inhibitor of cyclin-dependent kinase that normally functions to suppress cell proliferation. Choices A, D, and E are not related to cell proliferation. Mutations in epidermal growth factor receptor (choice C) are involved in some malignant neoplasms but not dysplastic nevus/melanoma syndrome.
Diagnosis: Dysplastic nevus syndrome

3 The answer is E: Squamous cell carcinoma. Actinic keratoses ("from the sun's rays") develop in sun-damaged skin as circumscribed keratotic patches or plaques, commonly on the backs of the hands or the face. Microscopically, the stratum corneum is replaced by a dense parakeratotic scale. The underlying basal keratinocytes display significant atypia. With time, actinic keratoses may evolve into squamous cell carcinoma in situ and, finally, into invasive squamous cell carcinoma. However, most are stable and many regress. Basal cell carcinoma (choice A)

and malignant melanoma (choice D) also arise frequently in sun-exposed skin but are unrelated to actinic keratosis.

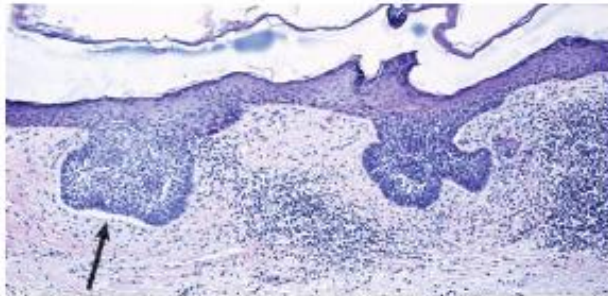
Diagnosis: Actinic keratosis

4 The answer is D: Human herpesvirus type 8. Kaposi sarcoma is a malignant tumor derived from endothelial cells. This vascular neoplasm is an important cutaneous sign in the AIDS pandemic. Human herpesvirus 8 (HHV-8) is thought to play a role in the pathogenesis of Kaposi sarcoma, however only a small percentage of HHV-8-infected individuals develop Kaposi sarcoma. These malignant tumors most often appear on the hands or feet but may occur anywhere. The histologic appearance of Kaposi sarcoma is highly variable. One form resembles a simple capillary hemangioma. Other forms are highly cellular and vascular spaces are less prominent. Epstein-Barr virus (choice B) is associated with Burkitt lymphoma in sub-Saharan Africa, and human papillomavirus types 16/18 (choice E) are associated with cervical cancer.
Diagnosis: Kaposi sarcoma

5 The answer is C: Depth of dermal invasion. Although choices A, B, and D may be factors in melanoma aggressiveness, the evaluation of tumor thickness is recognized as the single strongest prognostic variable for melanoma. Presence of variable melanin pigmentation (choice E) is not a predictor of melanoma growth or spread.
Diagnosis: Melanoma

11. the answer is A: Basal cell carcinoma (BCC). BCC is the most common malignant tumor in persons with pale skin. Although it may be locally aggressive, metastases are exceedingly rare. BCC usually develops on the sun-damaged skin of people with fair skin and freckles. The tumor is composed of nests of deeply basophilic epithelial cells with narrow rims of cytoplasm that are attached to the epidermis and protrude into the subjacent papillary dermis. Basaloid keratinocytes are rarely seen in squamous cell carcinoma (choice D) and are not encountered in the other choices.
Diagnosis: Basal cell c

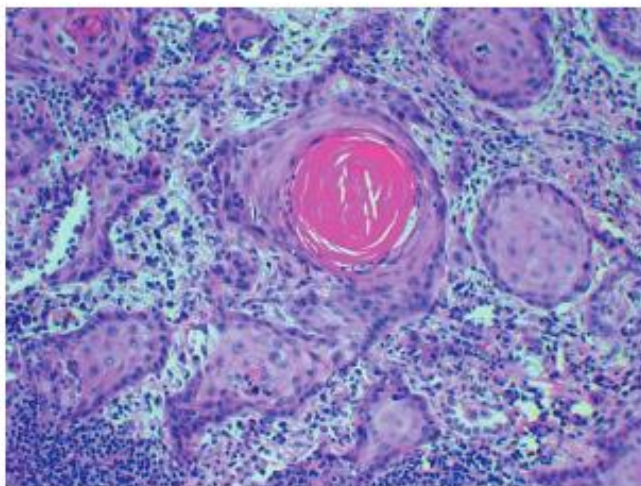
1. A 70-year-old retired farm worker is seen for evaluation of a pearly-appearing papule on the face just below and lateral to the left eye. The lesion is covered by small telangiectatic vessels. An excisional biopsy is performed, and the microscopic appearance is similar to that seen in the figure. Which of the following is characteristic of this disorder?



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- (A) Distal metastases common at the time of initial diagnosis
- (B) Frequent origin in a preexisting actinic keratosis
- (C) Hamartomatous non-neoplastic lesion
- (D) Most frequent occurrence is on head or neck

2. A scaling, ulcerated lesion develops on the forearm of a 45-year-old fisherman. Excisional biopsy is performed, and the histologic appearance is similar to that shown in the figure. Which of the following is most applicable to this lesion?



(Reprinted with permission from Rubin R, Strayer D, et al., eds.: *Rubin's Pathology. Clinicopathologic Foundations of Medicine*, 6th ed. Baltimore, Lippincott Williams & Wilkins, 2012, figure 5-19A, p. 168.)

- (A) Distal metastases almost always occur
- (B) Indicative of an underlying visceral malignancy
- (C) Predilection for sun-exposed areas
- (D) Uncommon skin tumor

6. An 80-year-old man presents with sharply demarcated, light brown, flat macules varying markedly in size. The lesions have the appearance of being “stuck on” or “pasted on,” and they are particularly numerous on the trunk. Microscopically, sheets of small basaloid cells with some melanin production are seen. Keratin production occurs at the surface, and numerous small keratin-filled cysts are apparent. Which of the following is the likely diagnosis?

- (A) Seborrheic keratosis**
- (B) Dermatofibroma**
- (C) Keratoacanthoma**
- (D) Actinic keratosis**
- (E) Acanthosis nigricans**

9. A 70-year-old man presents with a scaling, indurated, ulcerated nodule on the back of his left hand. He states that the nodule has been growing larger over time. The patient has had much direct sun exposure in the

past. Which of the following is the most likely histologic finding in this patient's skin lesion?

- (A) Invasion of the dermis by sheets and islands of neoplastic epidermal cells, often with “keratin pearls”**
- (B) Clusters of darkly staining basaloid cells, with a palisading arrangement of the nuclei of the cells at the periphery of the clusters**
- (C) Malignant melanocytes with numerous mitotic figures**
- (D) Abnormal proliferation of the connective tissue, with deranged arrangement of collagen fibers**

Answers:

1. **The answer is D.** The basal cell carcinoma shown in the figure has typical palisading of the nuclei of the cells at the periphery of the tumor cell clusters. Unlike squamous cell carcinoma, this tumor does not originate in preexisting actinic keratosis.
2. **The answer is C.** The lesion shown in the figure is a well-differentiated squamous cell carcinoma demonstrating sheets of neoplastic epidermal cells with keratin “pearls,” a very common skin tumor. There is a marked predilection for sun-exposed areas, and most lesions occur on the lower part of the face or the back of the hands. Metastasis occurs in fewer than 5% of cases, because most of these lesions are discovered early and are cured by ablative therapy.
or drugs, or to a concomitant connective tissue disorder or an associated malignancy.
6. **The answer is A.** Seborrheic keratosis is an extremely common benign neoplasm occurring in older persons. This neoplasm is manifested by sharply demarcated, raised papules or plaques with a “pasted-on” appearance on the head, trunk, and extremities.
9. **The answer is A.** This is a case of squamous cell carcinoma of the skin. Squamous cell carcinoma is a common skin tumor associated with excessive sun exposure. Clusters of darkly staining basaloid cells with a palisading arrangement of nuclei are characteristic of basal cell carcinoma. Malignant melanocytes are found in malignant melanoma. A keloid is a tumor-like scar resulting from abnormal proliferation of connective tissue with deranged arrangement of collagen fibers.