

Malignant Melanoma

The Role of the Dermatopathologist

Presented to the Bread of Life Church
Torrance, CA

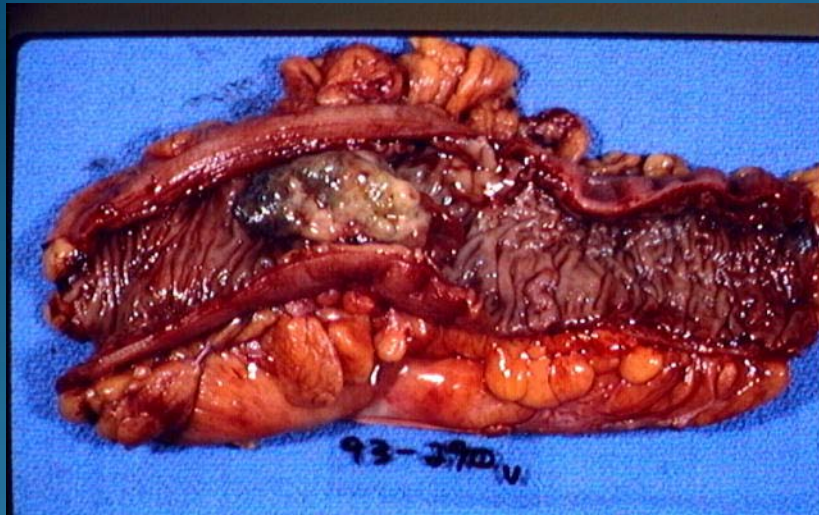
February 22, 2009

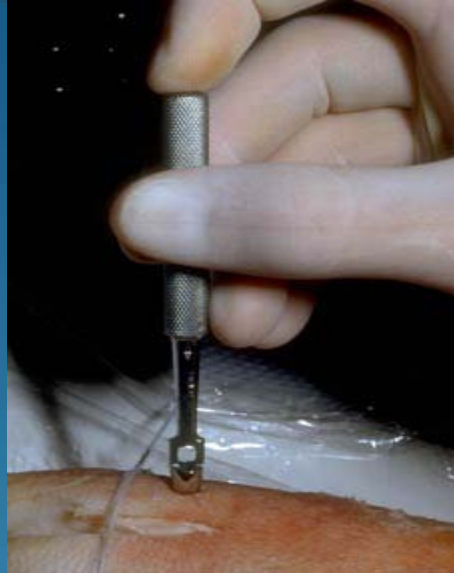
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David Geffen School of Medicine UCLA



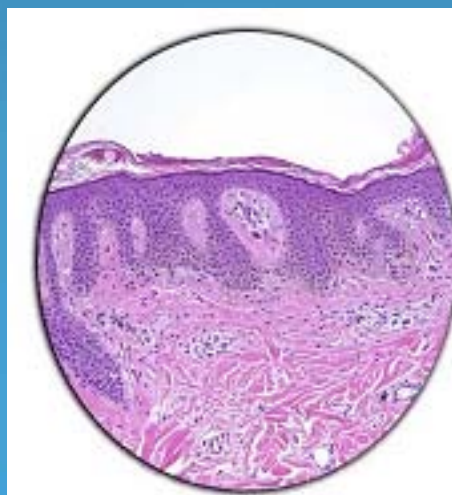


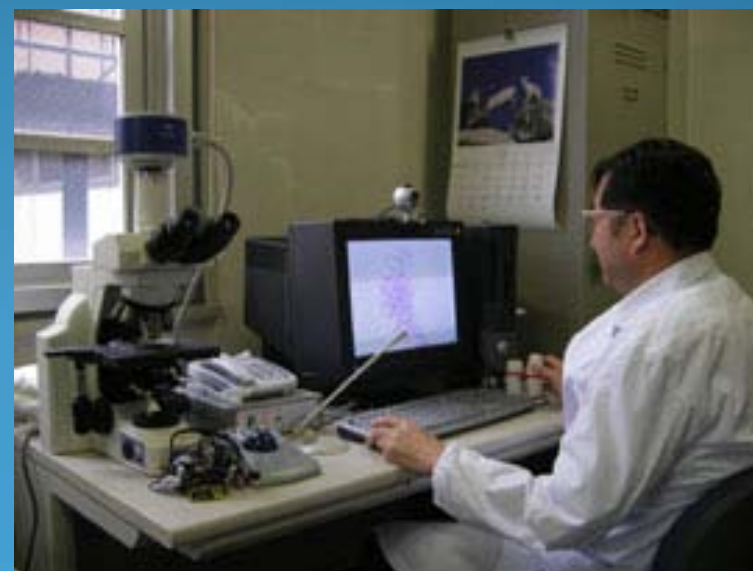






Dermatopathology









Epidemic

1. affecting or tending to affect a disproportionately large number of individuals within a population, community, or region at the same time
- 2 . excessively prevalent

Source: Merriam-Webster online

"...just one skin cancer cell was often enough to generate a whole new tumor."

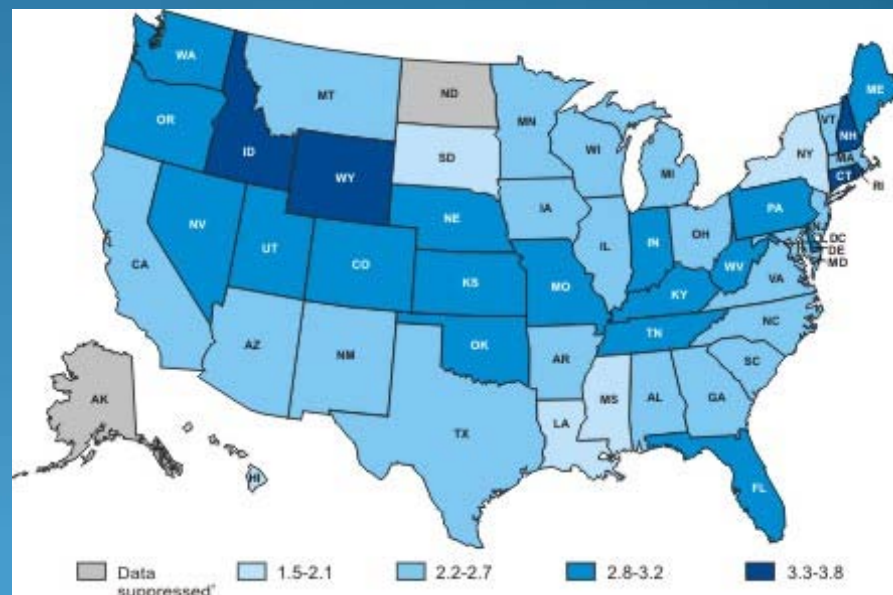
- Mice with weakened immune systems were injected with single melanoma cells
- Roughly one in four of these cells seeded new tumors

Sean Morrison, M.D.
Howard Hughes Medical Institute
Nature 2008 Dec. 4

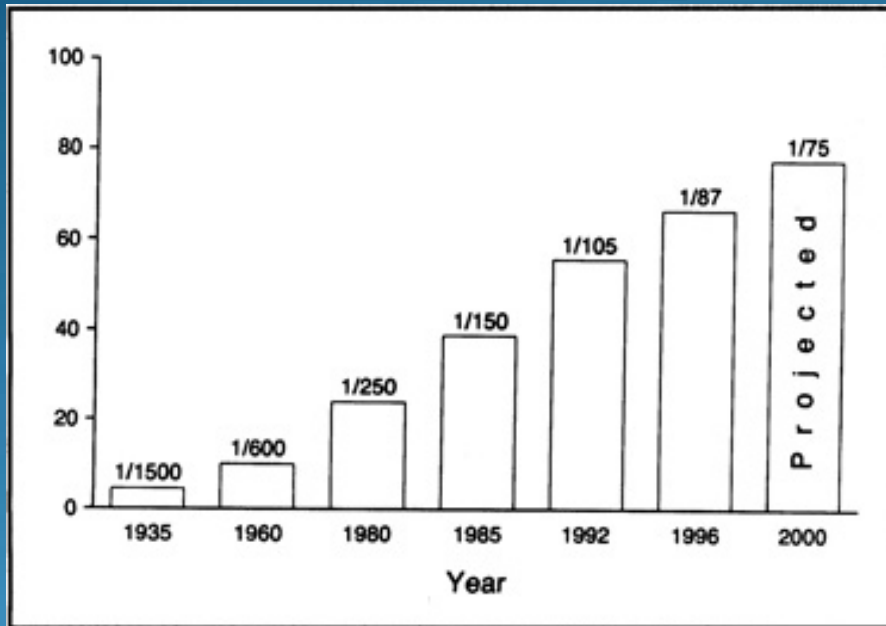


Is there an epidemic?

- 32,000 new cases/year
- Increasing 4-6% each year in U.S.
- 8th most common cancer
- Most common cancer in women between 25-39 years of age
 - Increasing faster than any other CA

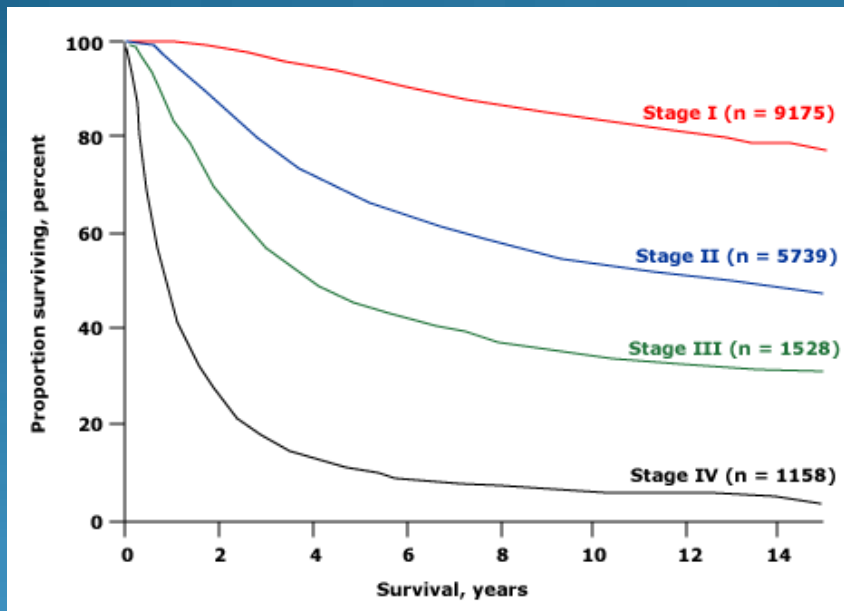


Is there an increase in melanoma?



- Increased awareness and surveillance
- Actual incidence is probably greater than reported
- Absolute number of melanomas has increased
- Death rate continues to increase in spite of earlier diagnosis
- 1/600 born in 1960
- 1/75 born in 2000-PROJECTED

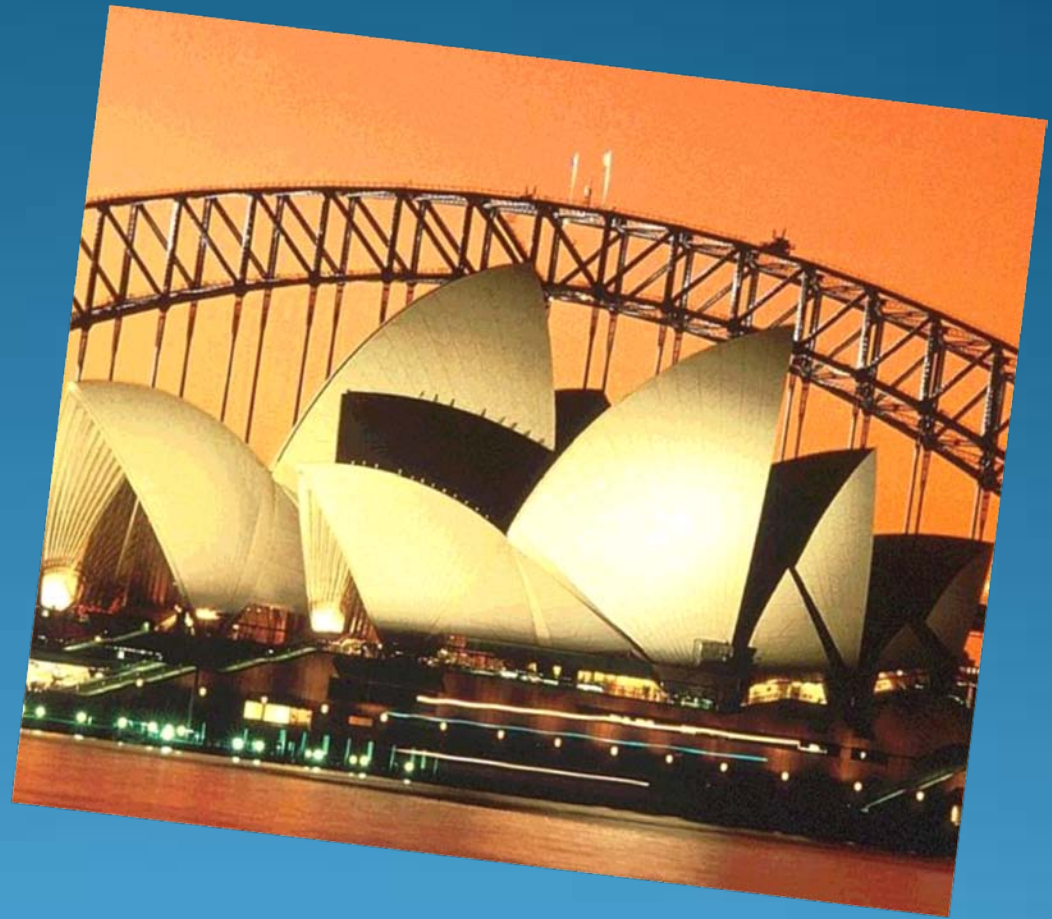
Melanoma Mortality



- 1973-1993
 - Incidence increased 110%
 - Mortality increased 34%
- 1997
 - 2.5/100,000
 - >7000 deaths/year

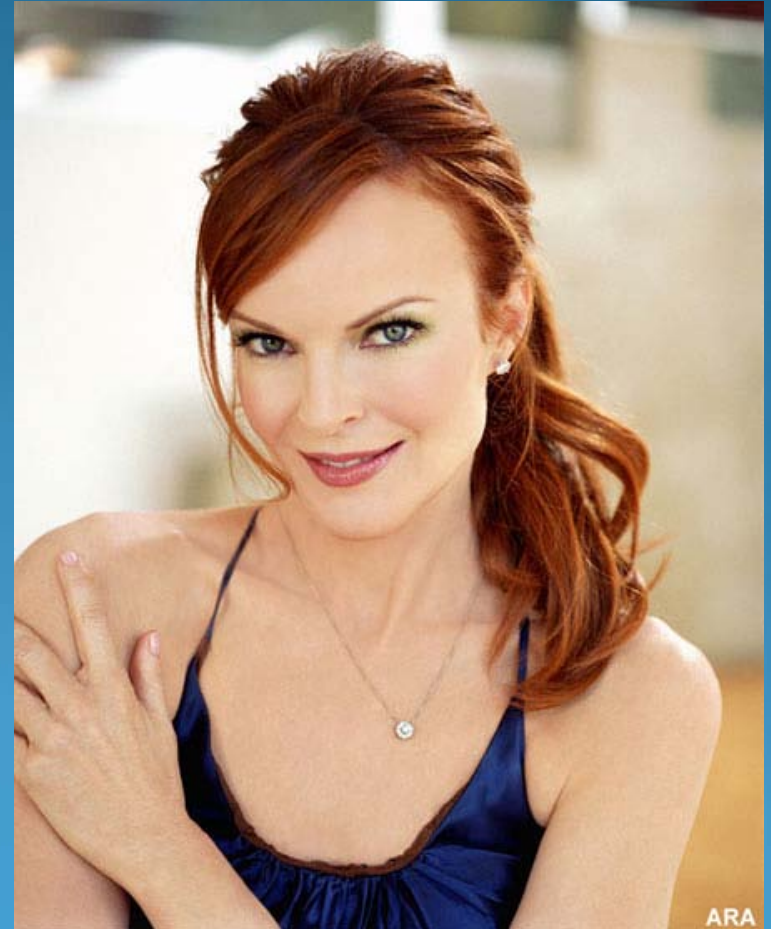
**U.K. passes
Australia in number
of annual
melanoma deaths**

- 9500 people in the U.K. a year are now being diagnosed with malignant melanomas
- 1,800 people die from that disease



Who is at risk?

- Atypical (dysplastic) mole syndrome
- Personal or family history of melanoma
- Phenotypic
 - Freckles, light skin, red or blond hair, blue eyes
 - Sunburns, sun exposure
- Immunosuppression



Estimation of risk



- One or two risk factors
 - 3-4 fold risk
- Three or more risk factors
 - 20 fold risk
- 8-24% of pts. with more than one melanoma have a family history

Tan Lines From Typical Summer Activities

Waterskiing



Mountain Biking



SCUBA Diving



Rollerblading



Computer Programming



Tennis



*Americans Know More
Than Ever Today About Sun
Safety-but Keep on Tanning*



- Survey of 8000 persons
- 94% concerned that sunlight increased risk of skin CA
 - 64% concerned that sun exposure could cause wrinkling
 - 88% more careful about sunlight exposure than 10 yrs ago
 - 88% used sunscreen at least some of the time

So why worry?

- 68% believed they looked better and healthier with a tan
- 55% actively sought a tan, some at tanning salons



Class 1 ("unconcerned and at low risk") were at least risk of skin cancer, intended to tan, and used the least amount of sun protection.



Class 2 ("tan seekers") had the second highest risk of skin cancer, had the highest proportion of women, became sunburned easily, intended to tan, had used tanning beds in past 30 days, and had the highest proportion of sunscreen coverage and the least clothing coverage.

Class 3 ("concerned and protected") had the highest skin cancer risk, the highest proportion of clothing coverage and shade use, and were more likely to be Hawaii residents.

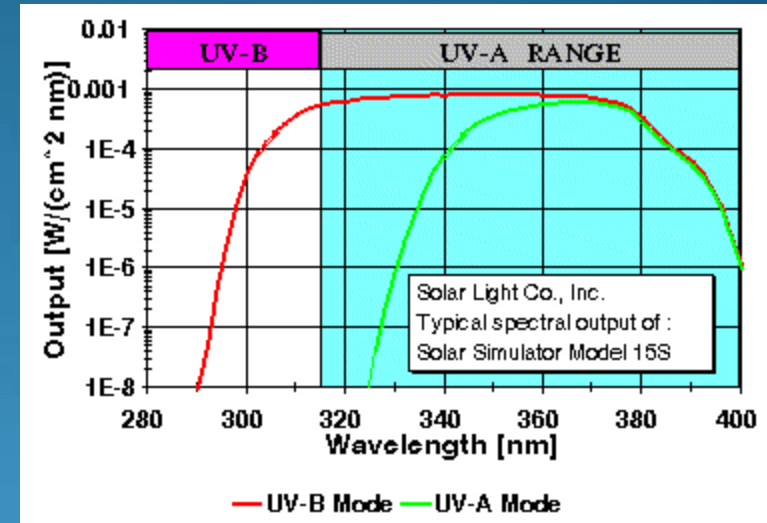
Tanning beds-Hotbed of Controversy?



- 75 % higher melanoma risk among individuals who started using sunbeds before age 35
- >18,000 tanning salons with >1 million people/day
 - Serious tanners 3x/week for >4yrs
- Tanning accelerators or enhancers (psoralens)

“We only use safe UVA tanning”

- UVB (290-320 nm)
 - Main cause of skin cancers
- UVA (320-400 nm)
 - Less likely to cause sunburn
 - Penetrates skin more deeply
 - Chief culprit in photoaging
 - Exacerbates UVB carcinogenic effect and may directly induce some skin CA including melanoma
- Exposure to total sunlight that incurs the risk
 - UVR does not equate with heat or warmth



“It’s windburn not a sunburn!”

- Water sports
 - Reflection and false sense of security with cooling
- Cloudy days
 - Reduced warmth not reduced UVR



UV exposure increases eight to 10 percent with every 1,000 feet above sea level

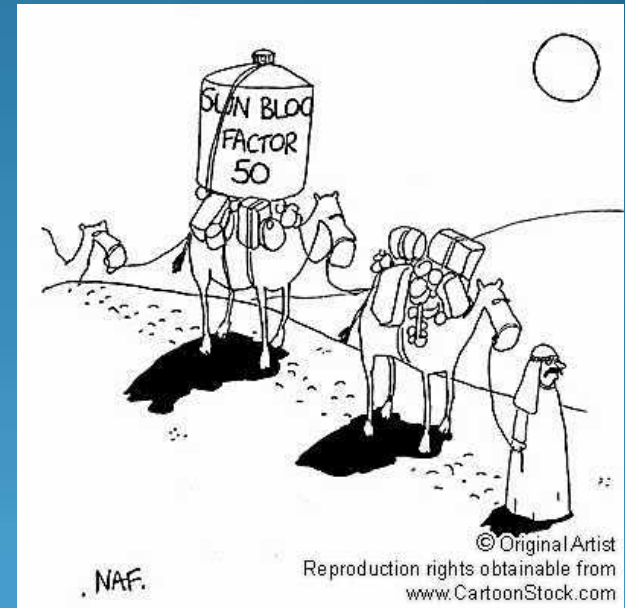


- Snow reflects 80% UV light=Double exposure
- SPF sunblock for skin and lip balm



Protect Yourself!

- Avoiding high exposure times
 - 11AM-3PM
 - 60% of total UVB
- Cover up
 - Broad brim hats
 - Densely woven clothes
 - Lighter color clothes
- Sunblocks



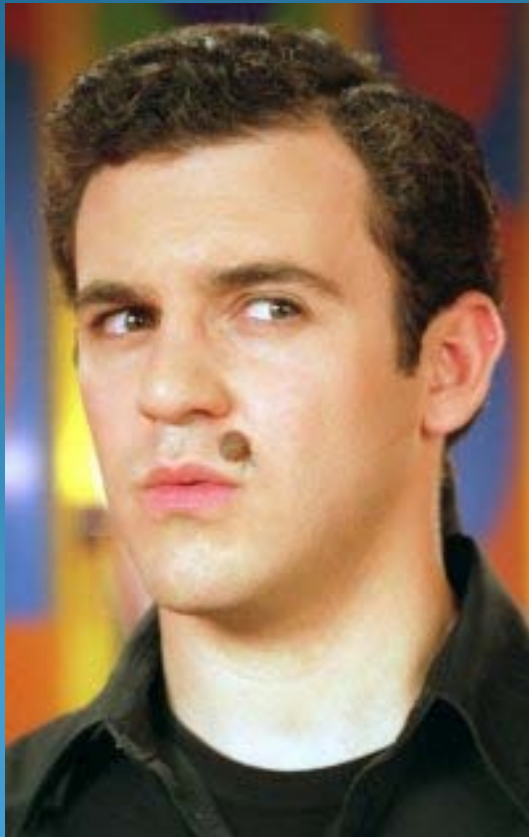
Increased awareness=Early Dx

- English Television show highlighted importance of skin examinations in the early diagnosis of melanoma
 - Melanoma cases increased 167% in 2 yr period
- Switzerland
 - Similar campaign doubled case number within 2 months





What is a mole?



- Benign proliferation of melanocytes
- Increases from 6 mo - 3rd decade
- Body site and rate of change partly due to UV exposure
- Nevus
 - Congenital
 - Acquired
 - Dysplastic
 - Other

What is a melanoma?

- Neoplastic (Cancerous) proliferation of melanocytes
- Arranged in the epidermis, dermis, or both
- Malignant with marked capacity to metastasize



The ABCDEs of Melanoma

- A Asymmetrical
- B Border irregularity
- C Color change
- D Diameter enlarging
- E Evolving





A, B, C, D, E's of Melanoma



What is a dysplastic nevus?

- Occurrence of MM in one or more first or second degree relatives
- Large number of dysplastic nevi (Usually >50)
- Characteristic histopathology



DN and the risk of melanoma

- No personal or family risk
 - 2-8x
- No personal but family history of melanoma
 - 148x
- Personal and family history of melanoma
 - 300-500x



What is melanoma in situ?

- Clinical appearance resembling a melanoma
- Histopathology
 - Atypical melanocytes confined to epidermis
- Prognosis
 - 100% cure with complete excision



©1994, Arthur C. Huntley, MD

I have a melanoma...now what?

- Complete skin examination
 - Dermatologist and self examination
- Regular skin examinations
 - Non-familial cases
 - 3% develop second melanomas within 3 years
 - Familial cases
 - 33% develop second melanomas within 5 years
- Lifetime surveillance

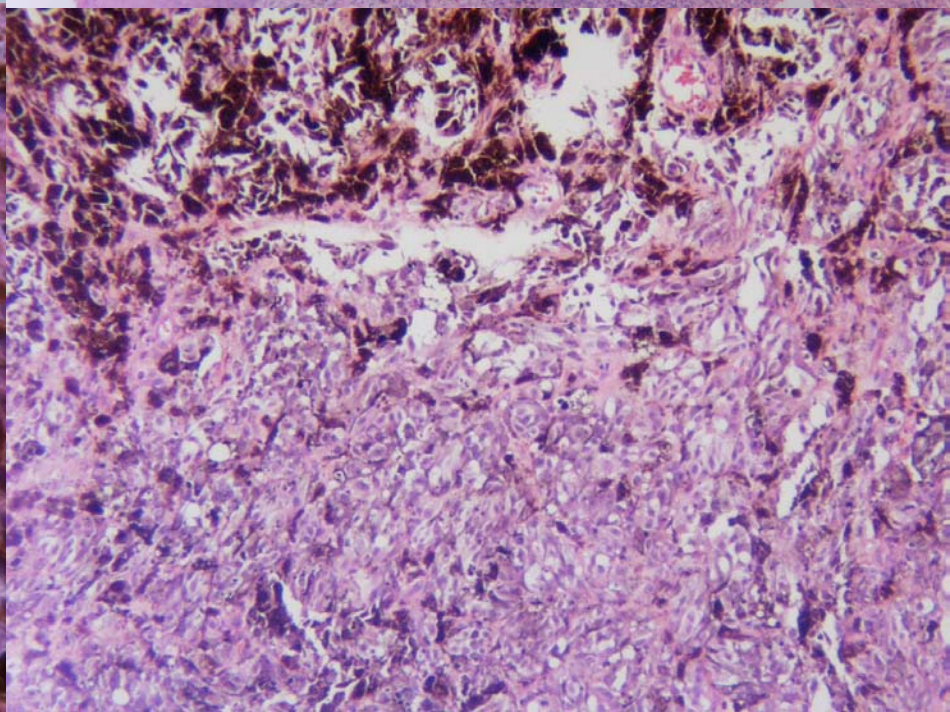
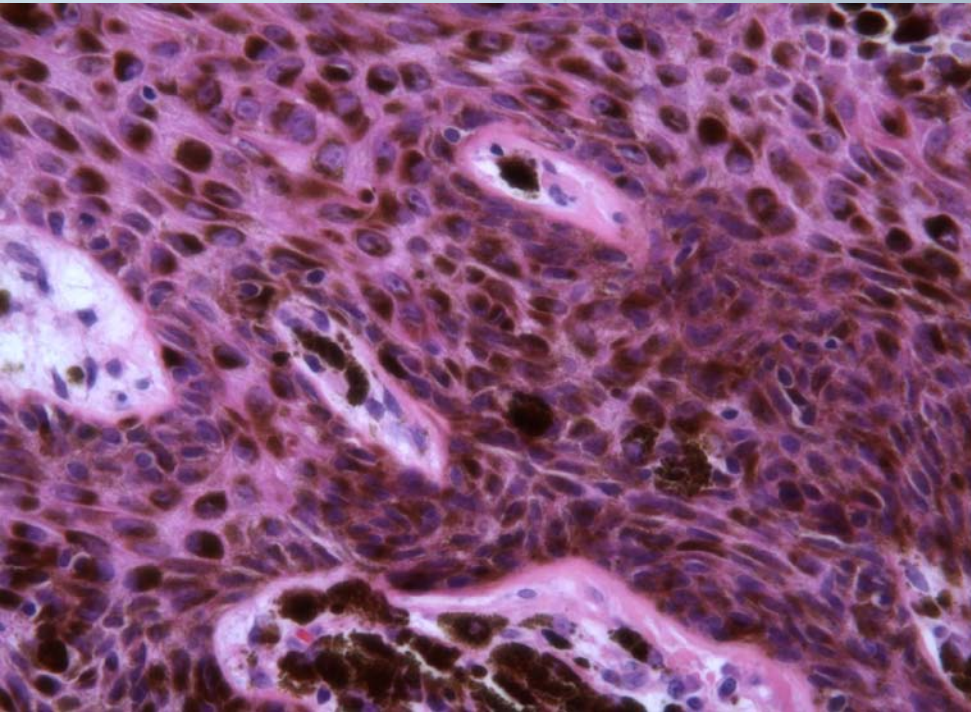
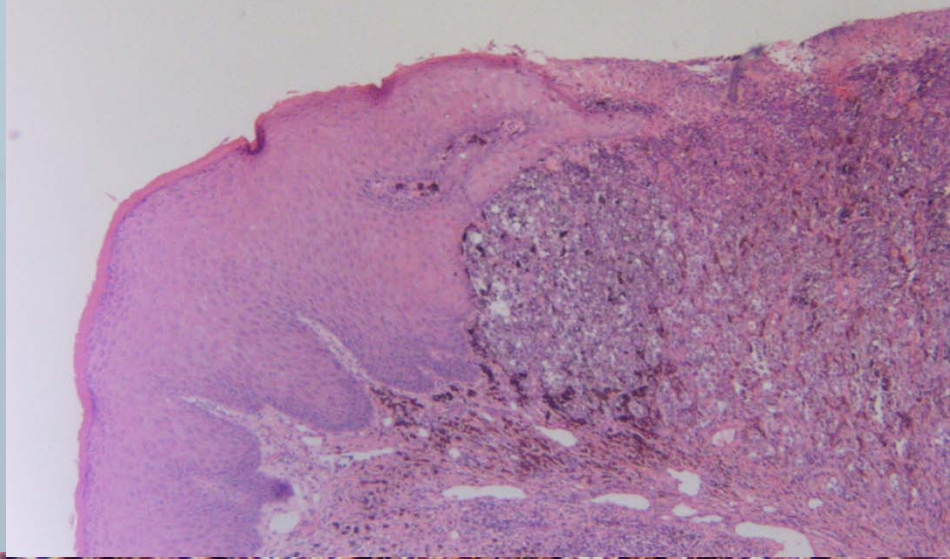
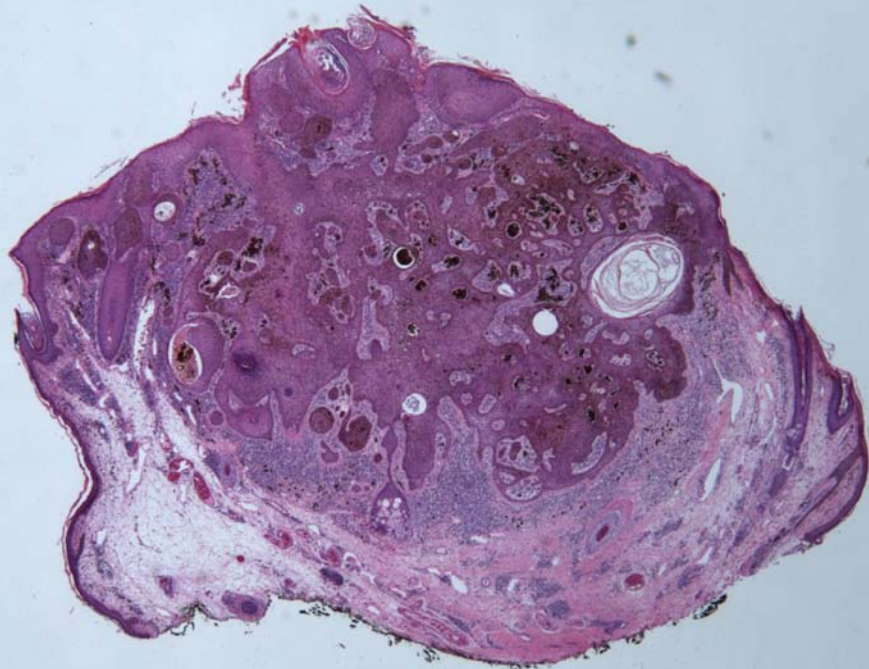




All Suspicious Pigmented Lesions Need to Be Biopsied!

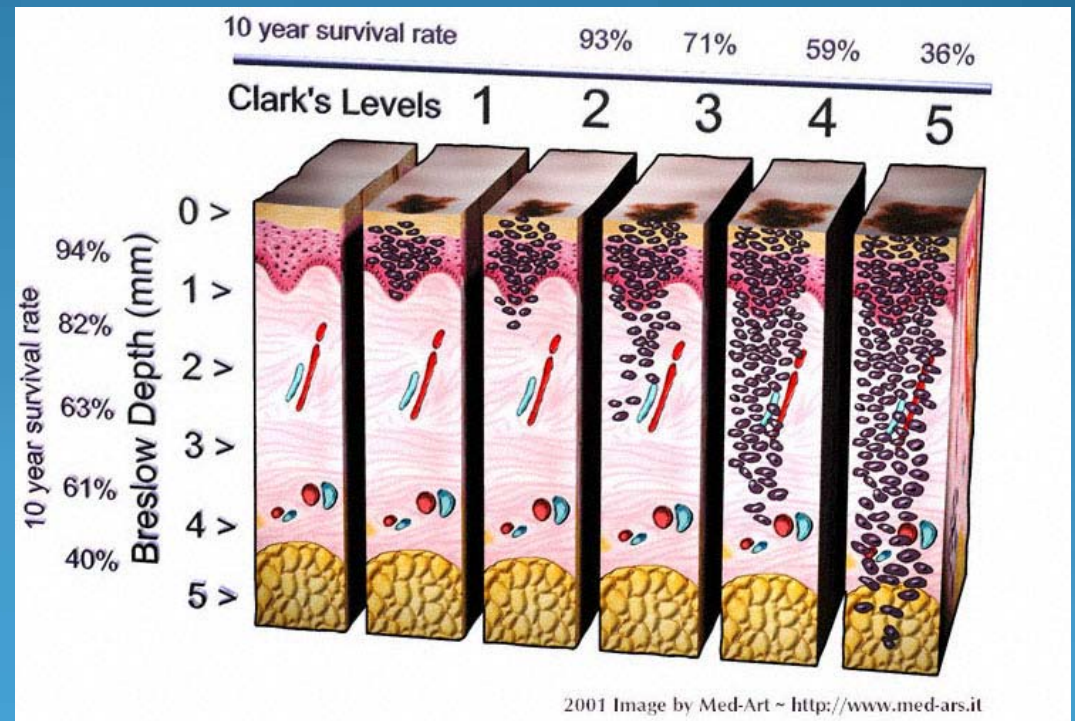


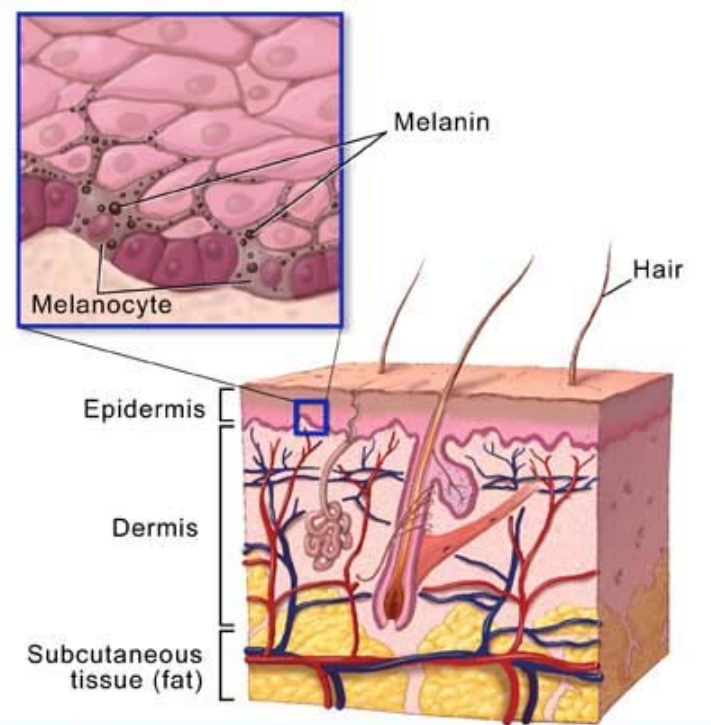
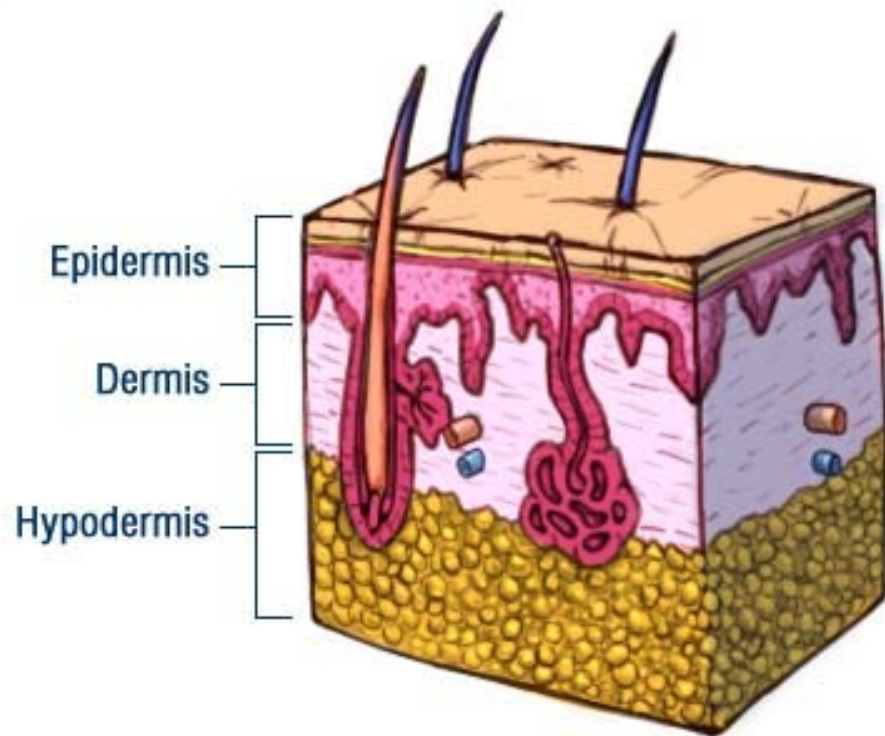




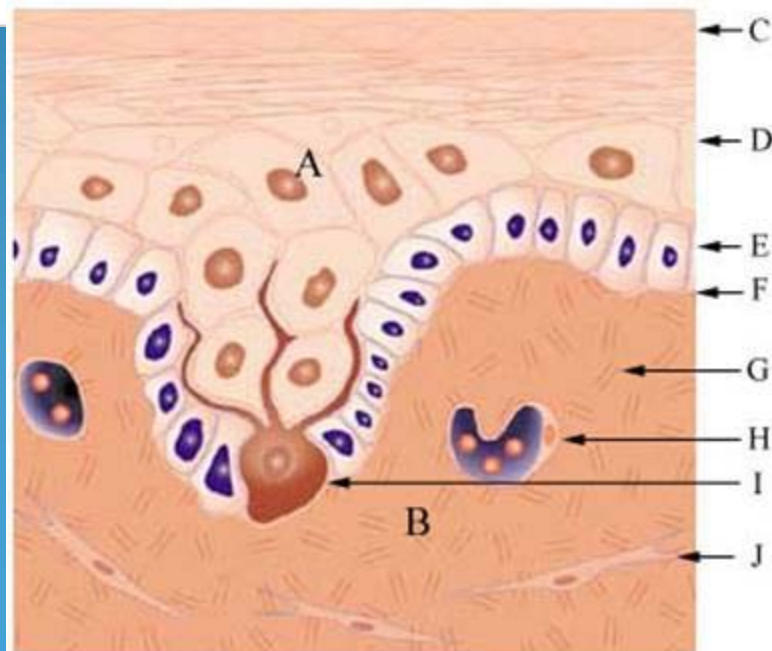
What the Dermatopathologist can tell you

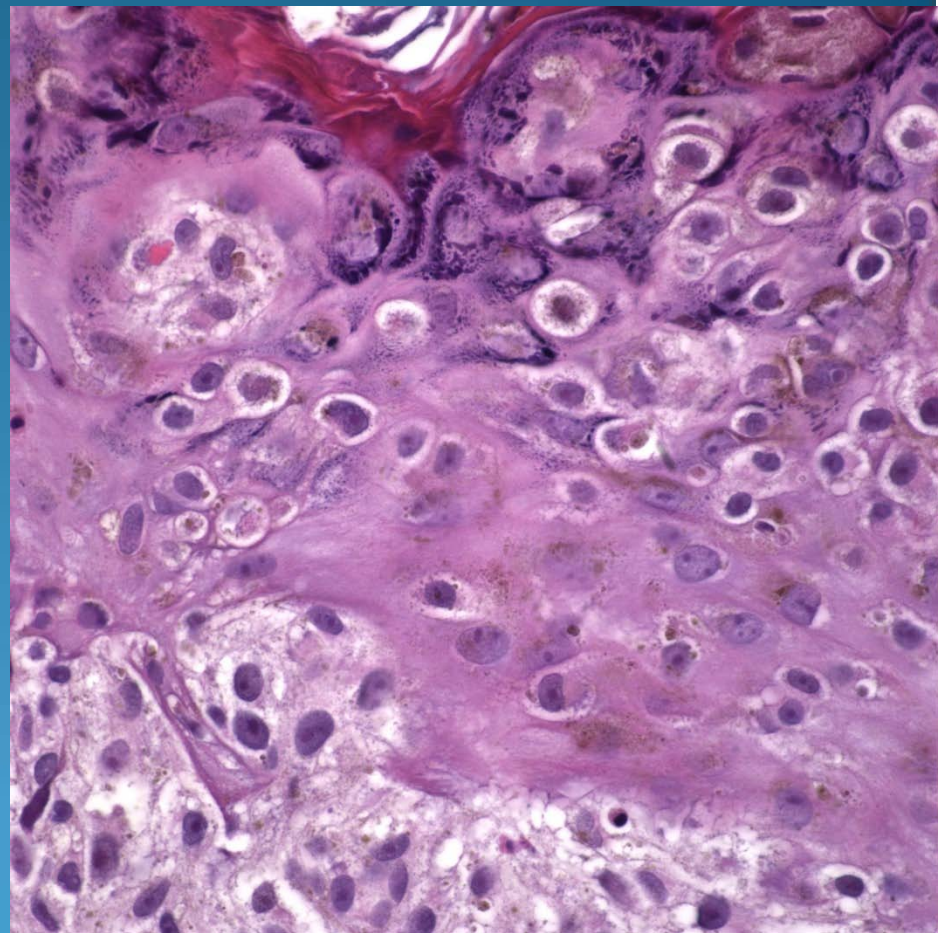
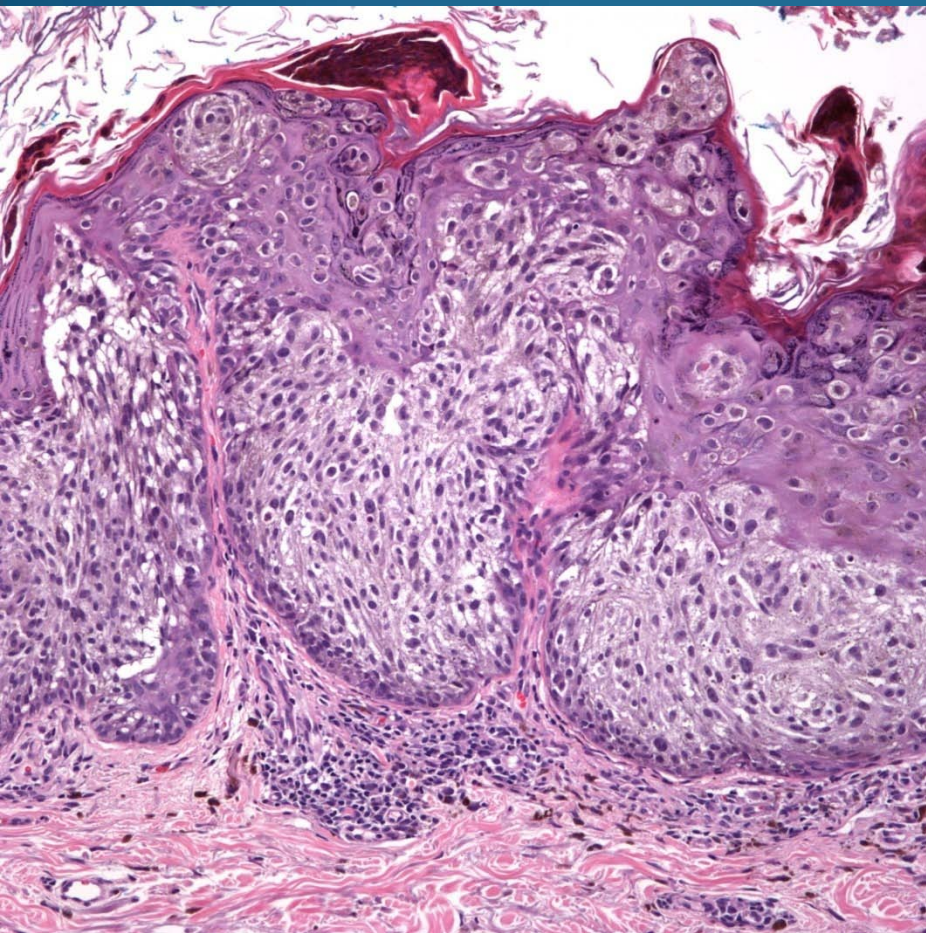
- Radial vs. vertical growth phase
- Thickness
- Depth of invasion

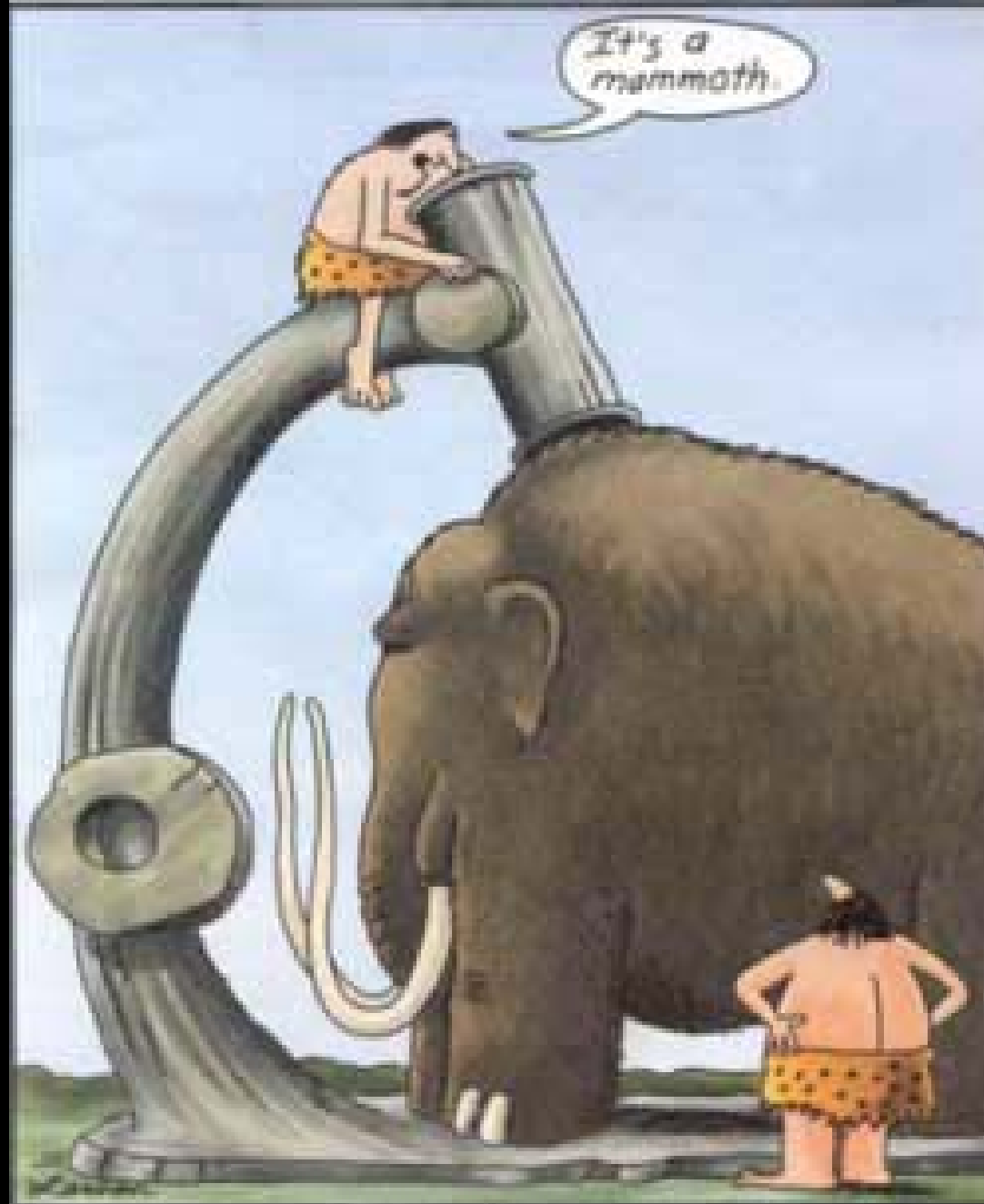




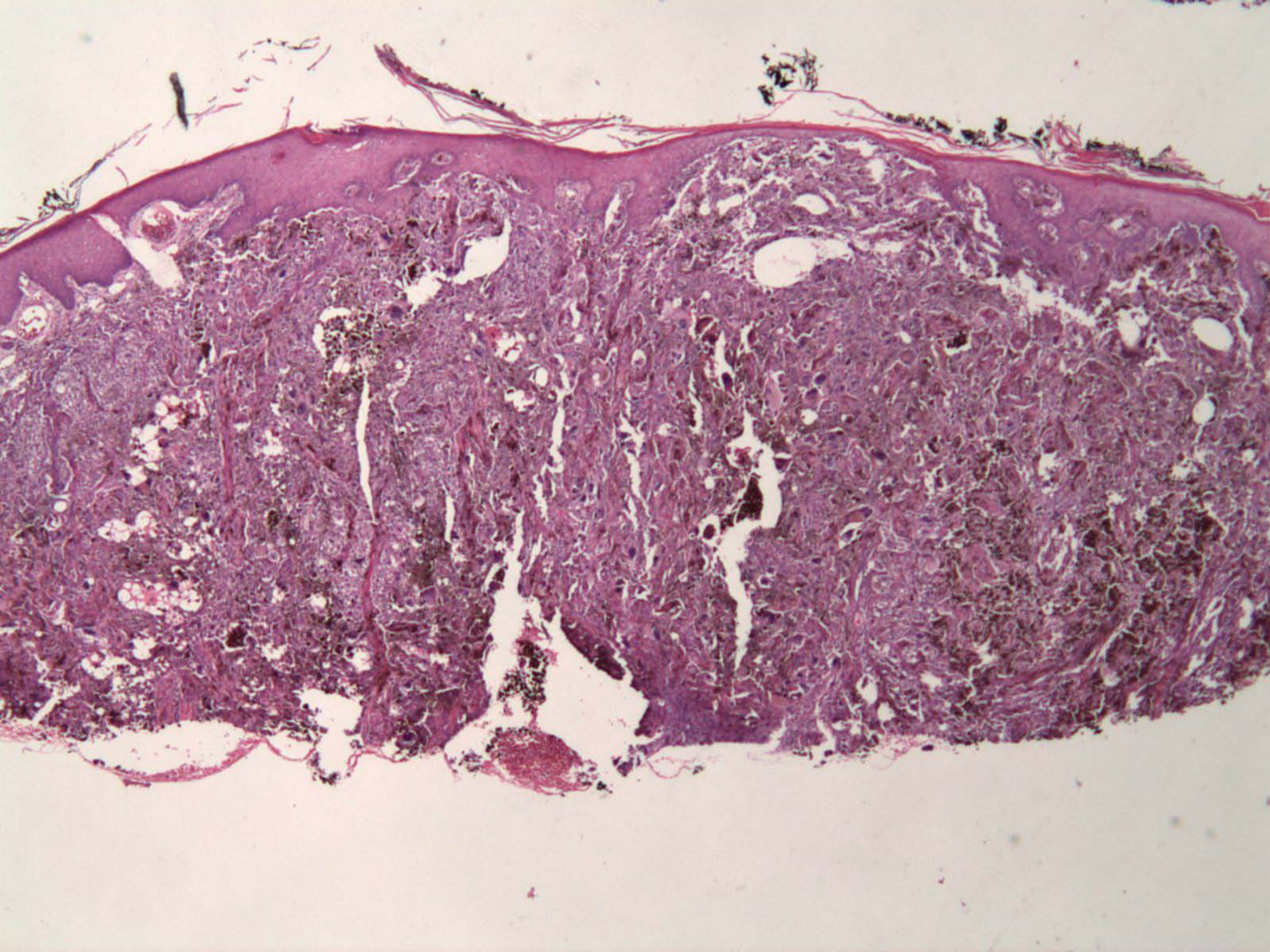
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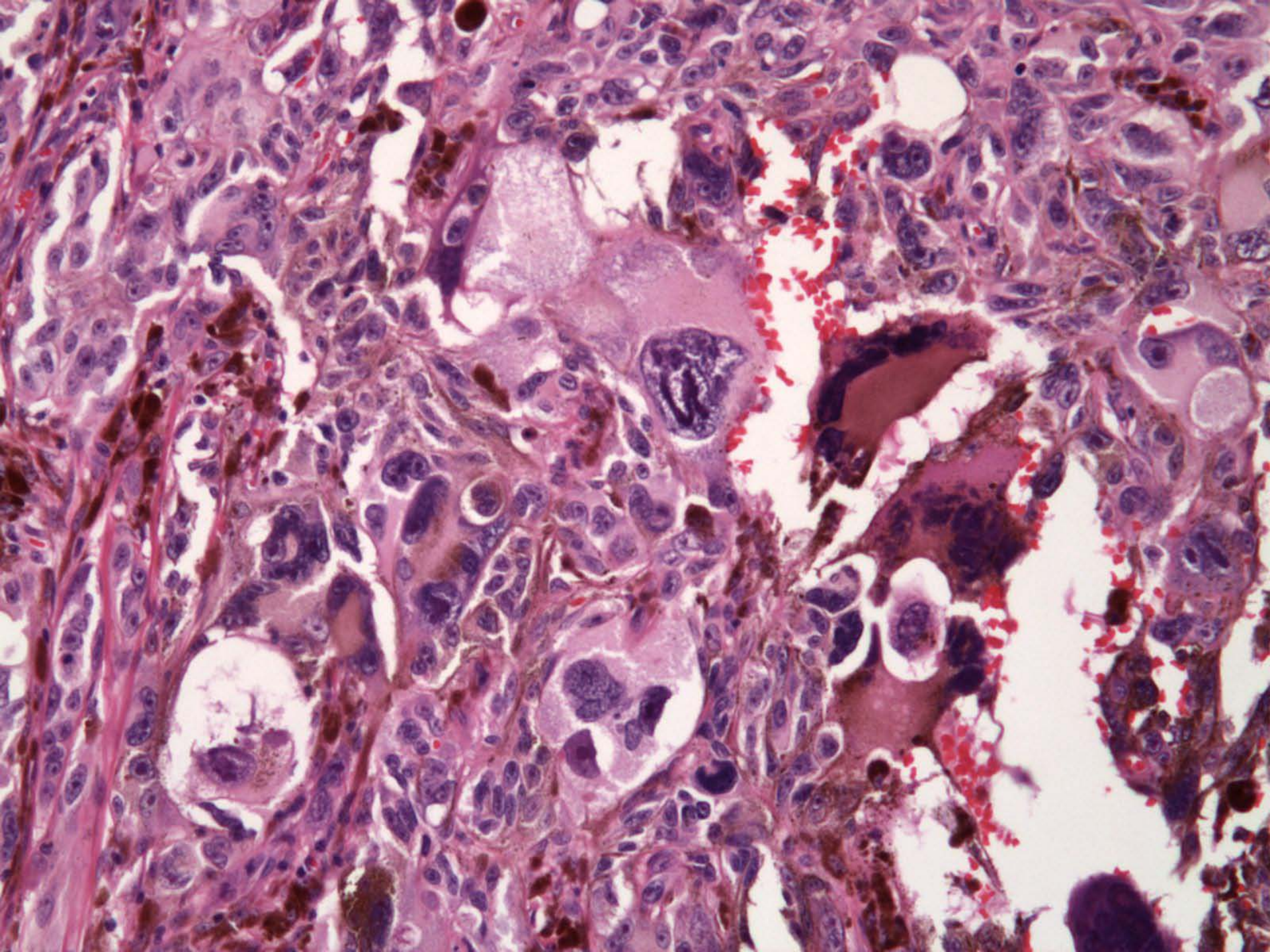


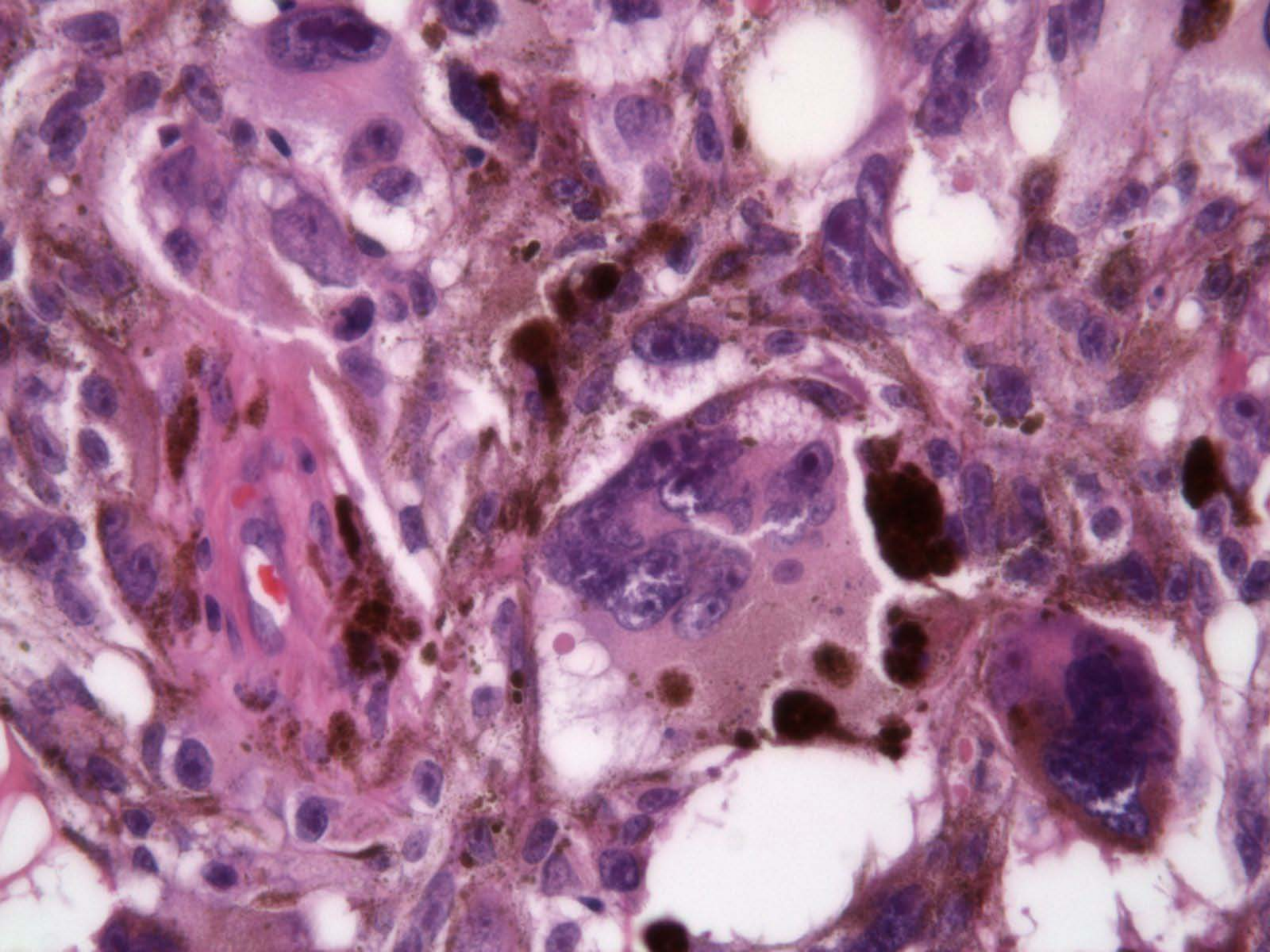




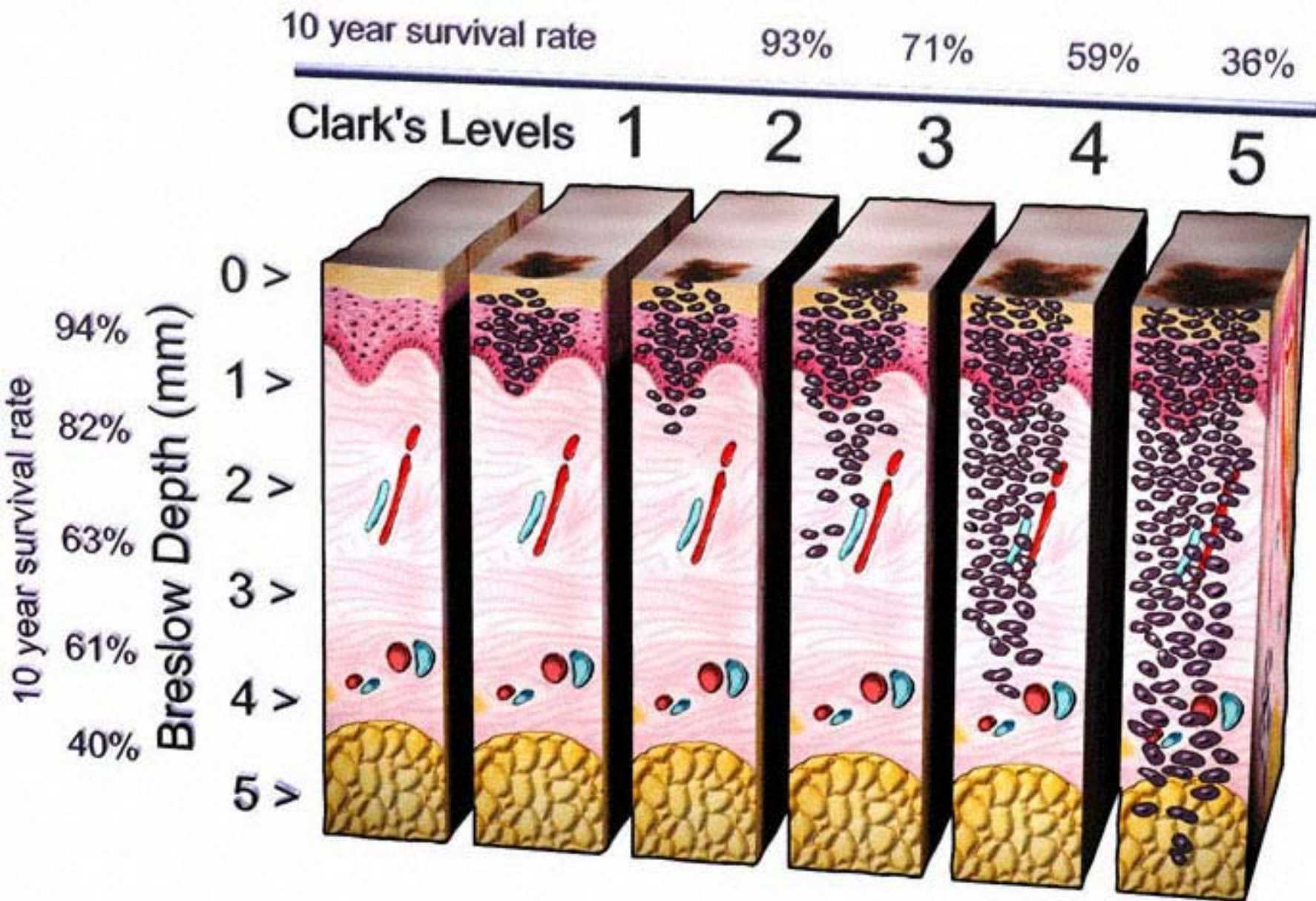
Early microscopes





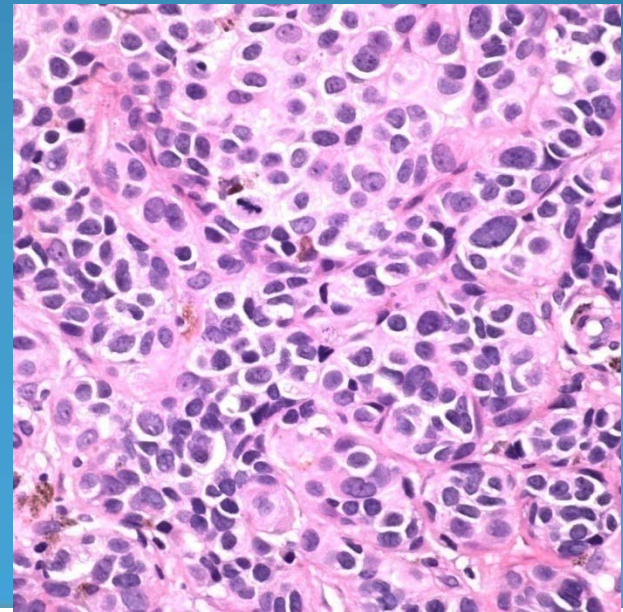
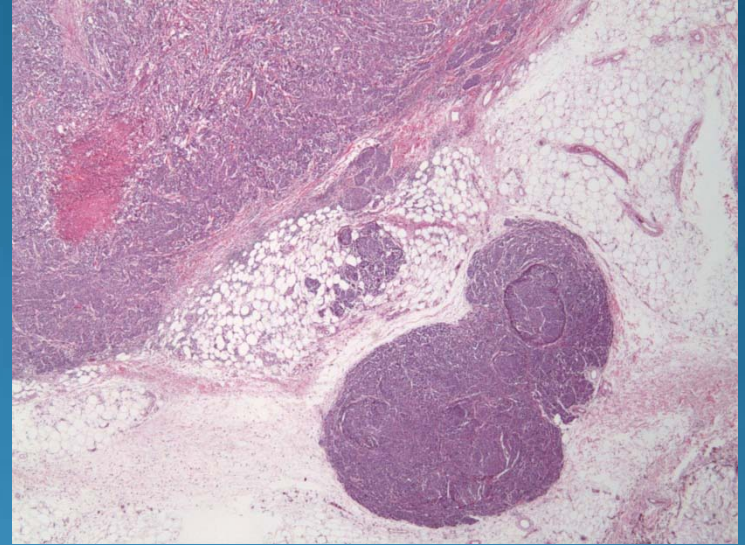


Malignant Melanoma
Clark's Level 4
Thickness 1.5 mm

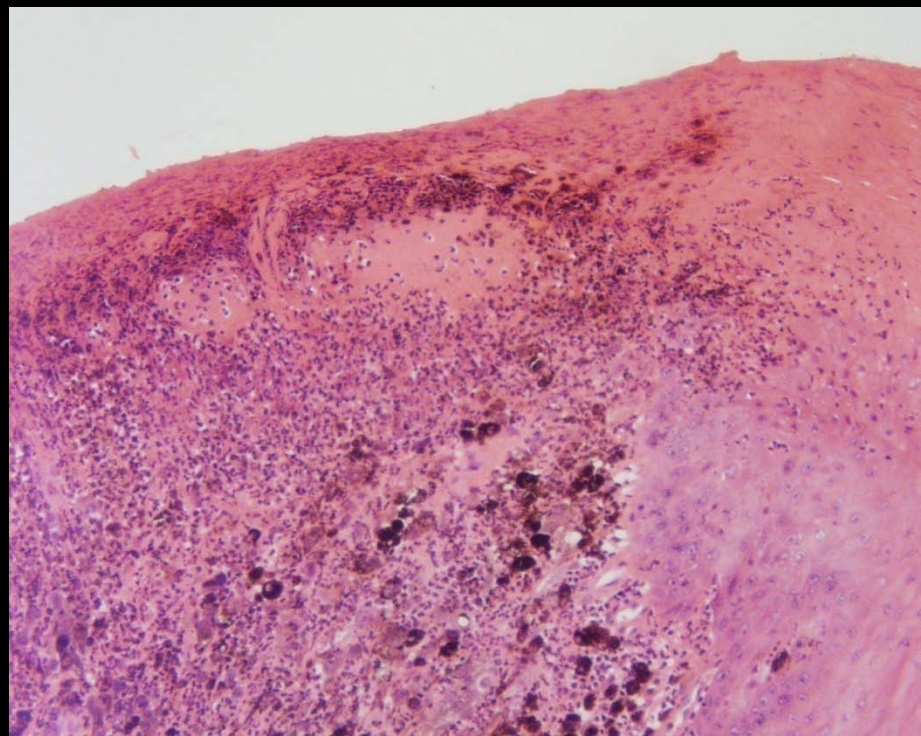


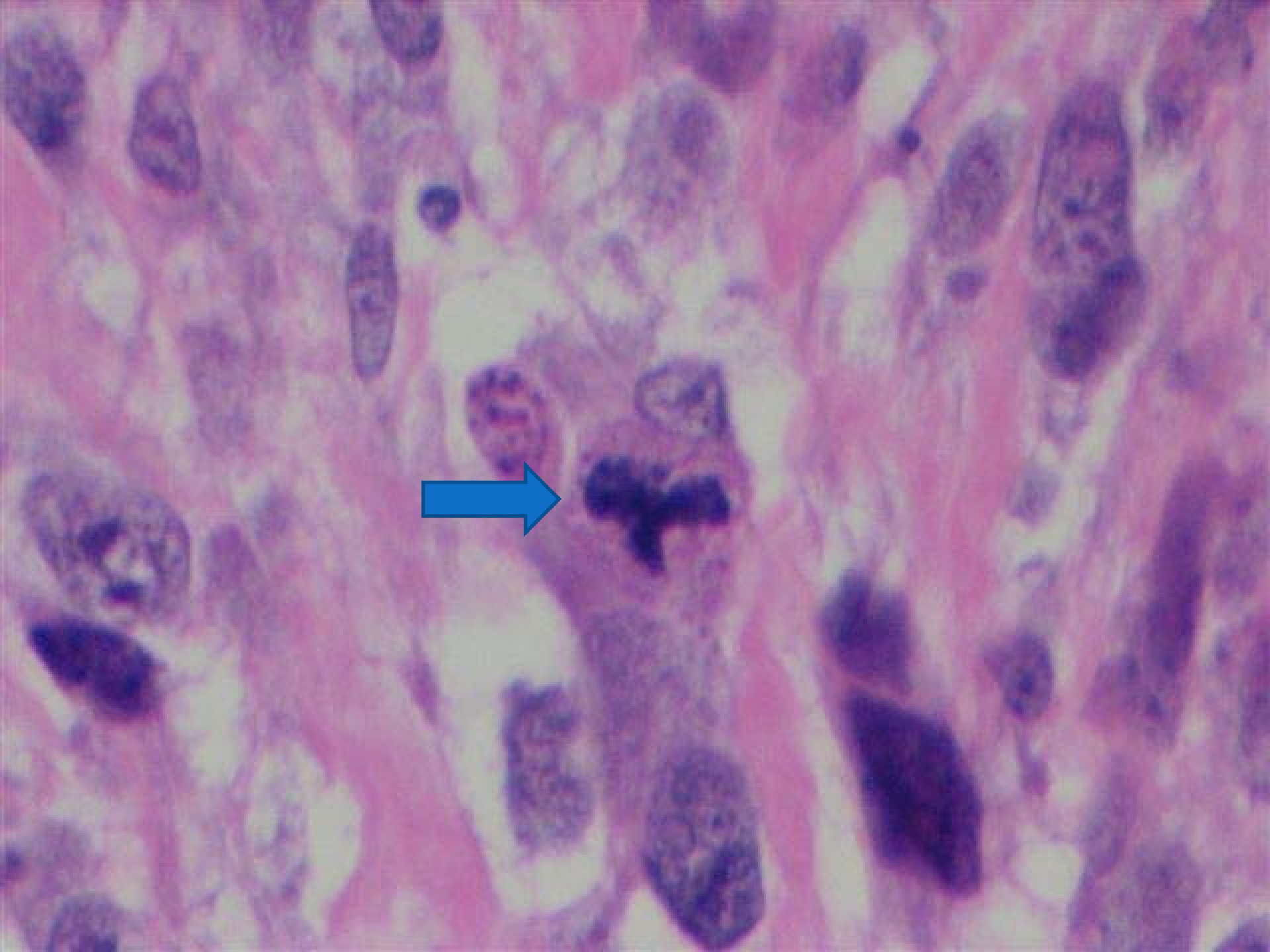
Other prognostic variables

- Ulceration
- Angiolymphatic invasion
- Satellitosis
- Mitotic activity
- Host response
- Regression



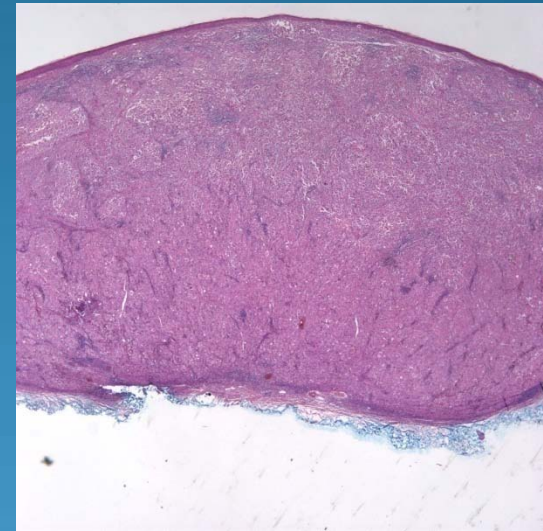


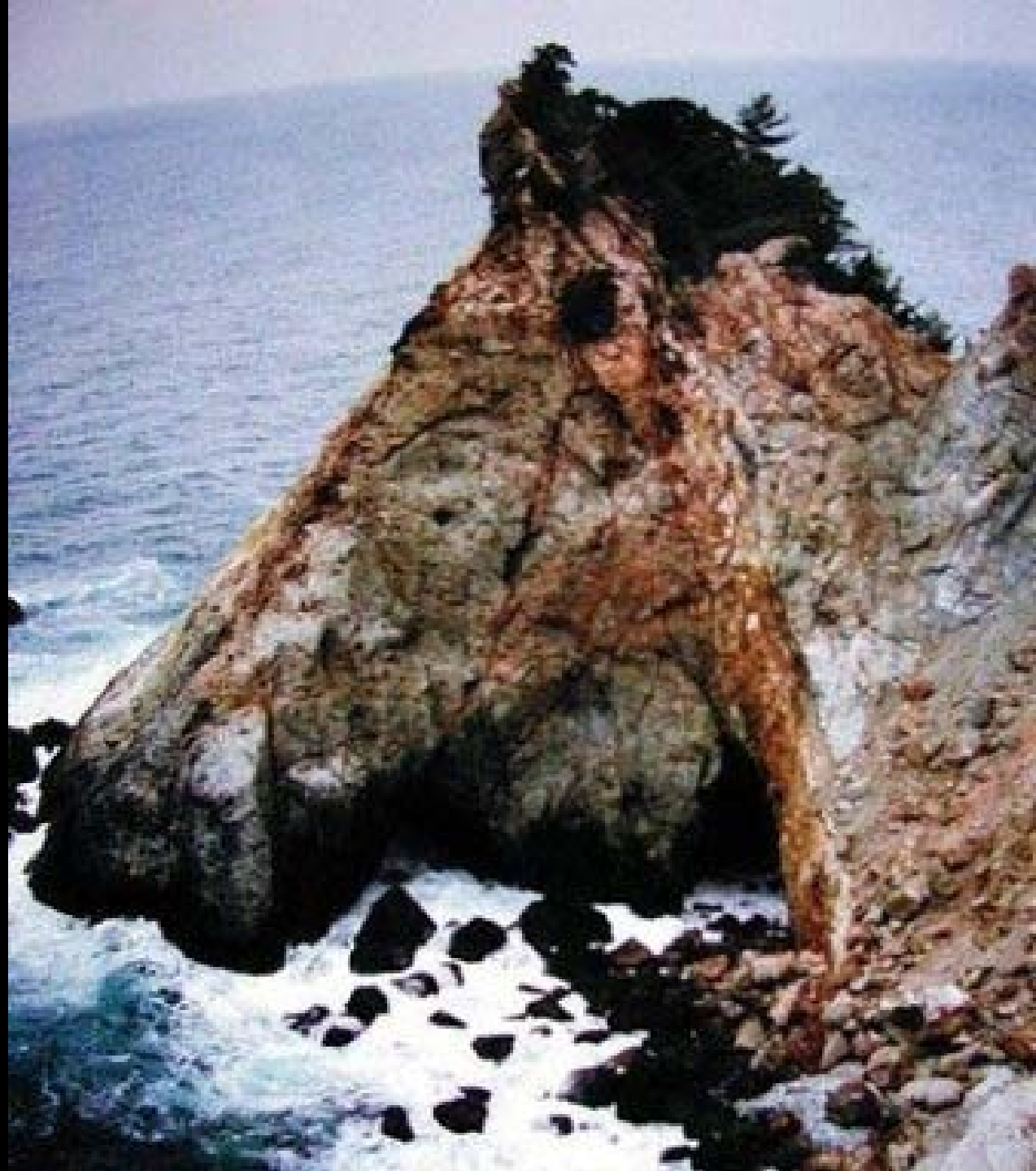


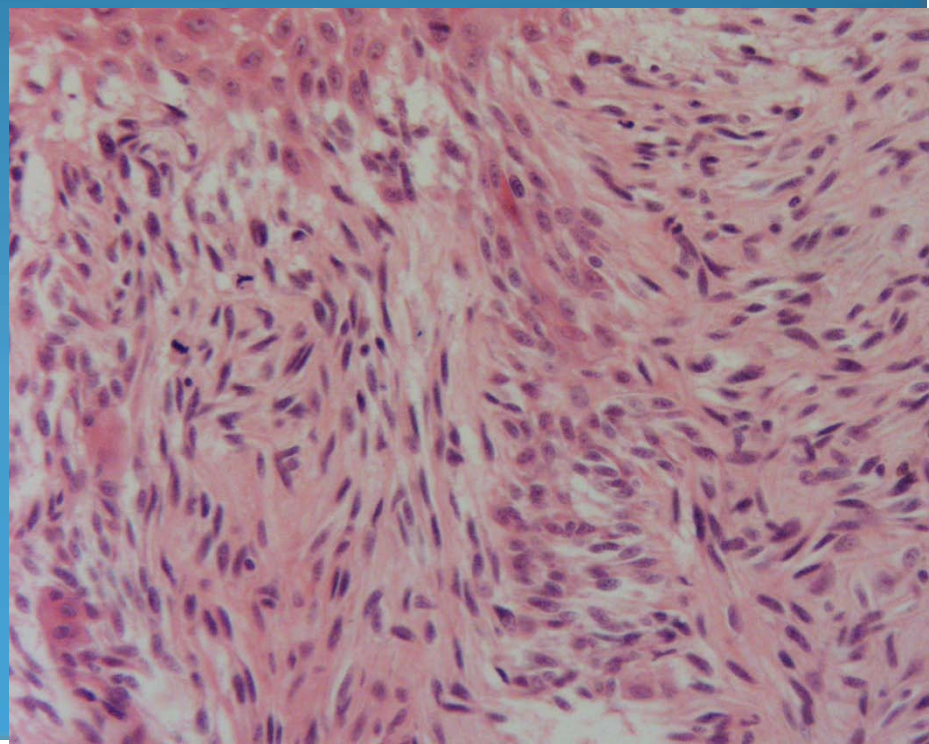
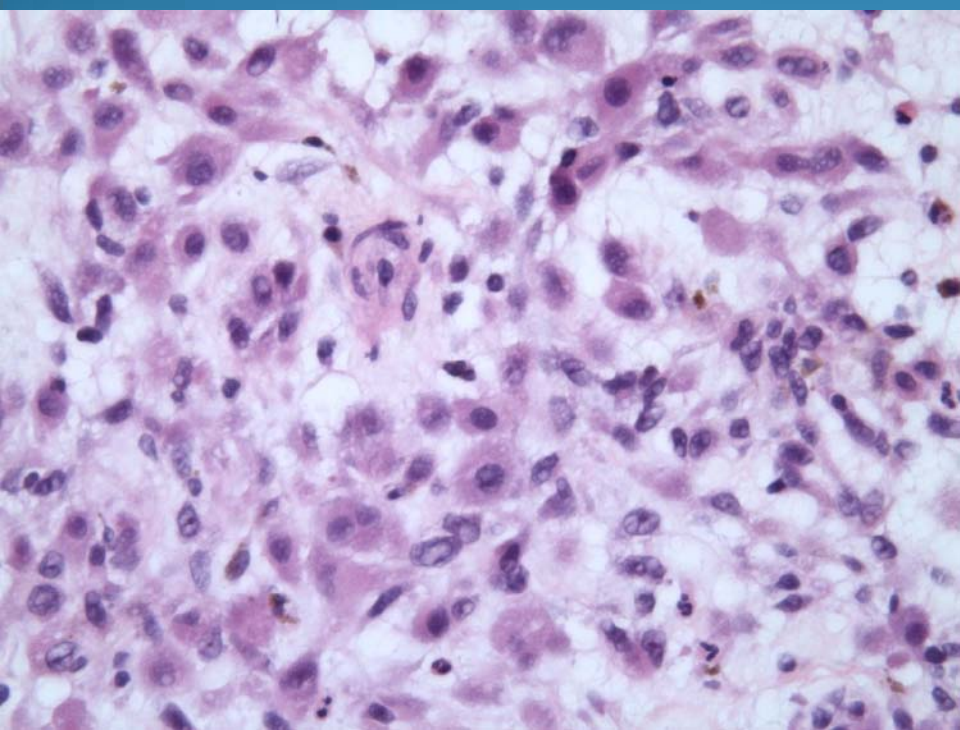
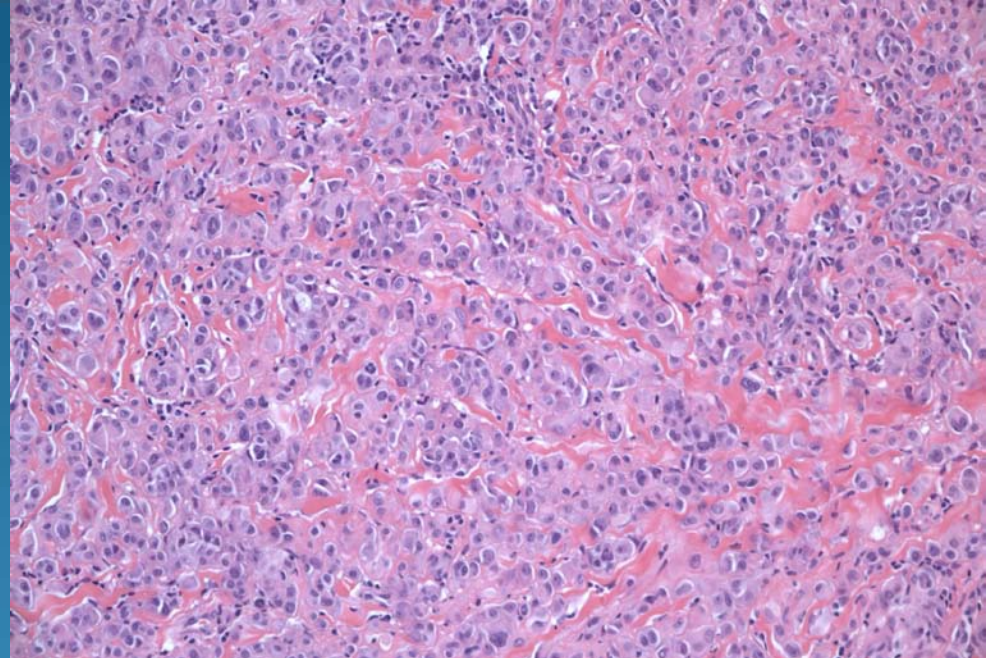
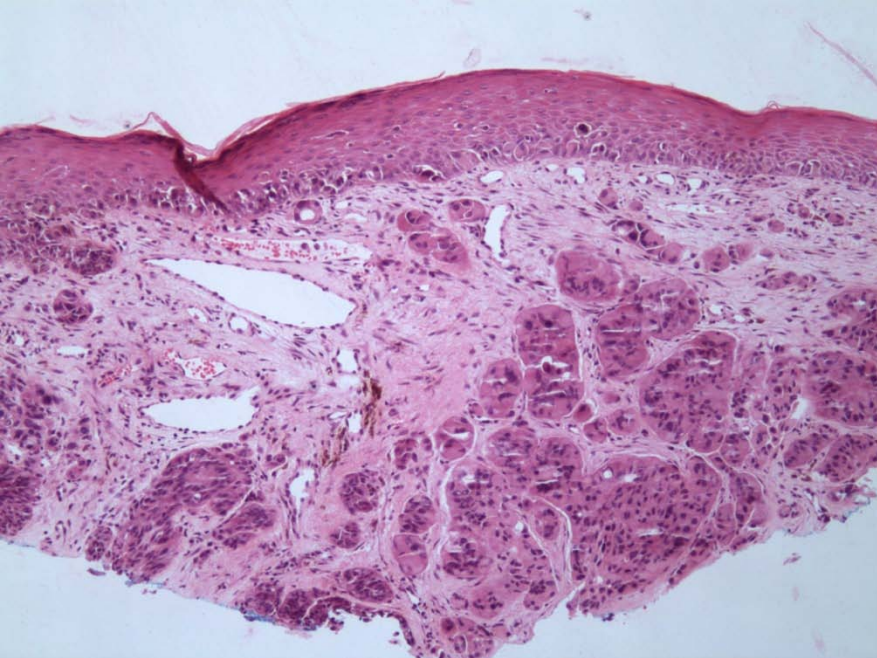


Increased awareness=Earlier Bx

- Review of biopsies and excisions of pigmented lesions from 1930-1990
- Cases from 1930's
 - All >0.75 mm
 - >5% thinner than 1.5 mm
- 1990's
 - >50% <0.75 mm
- Conclusion
 - Overall criteria had changed very little
 - Criteria applied to different set of pigmented lesions
 - Clinicians sampling different set of pigmented lesions

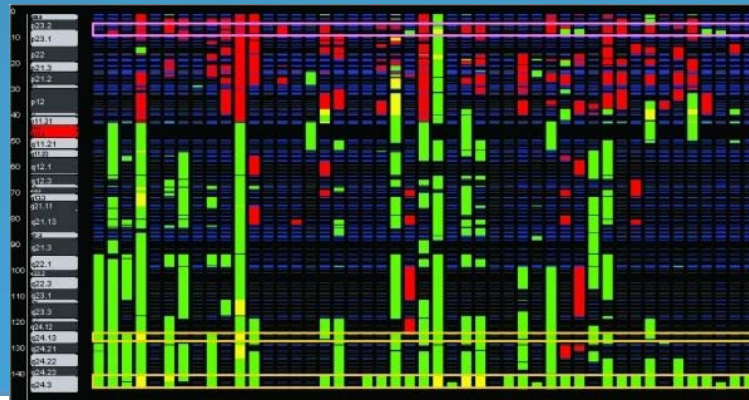
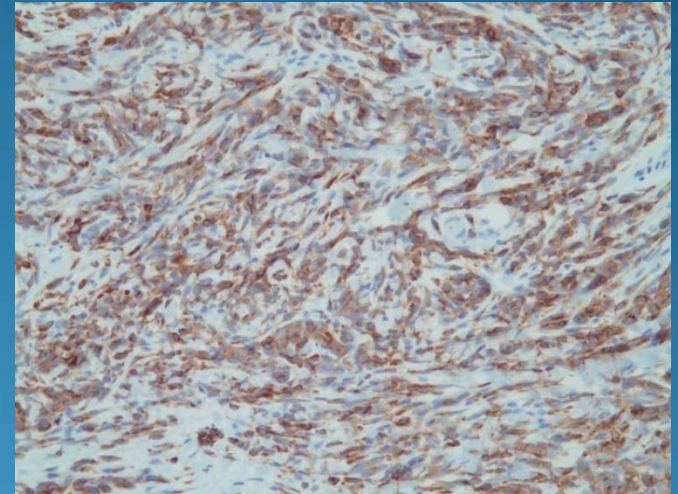


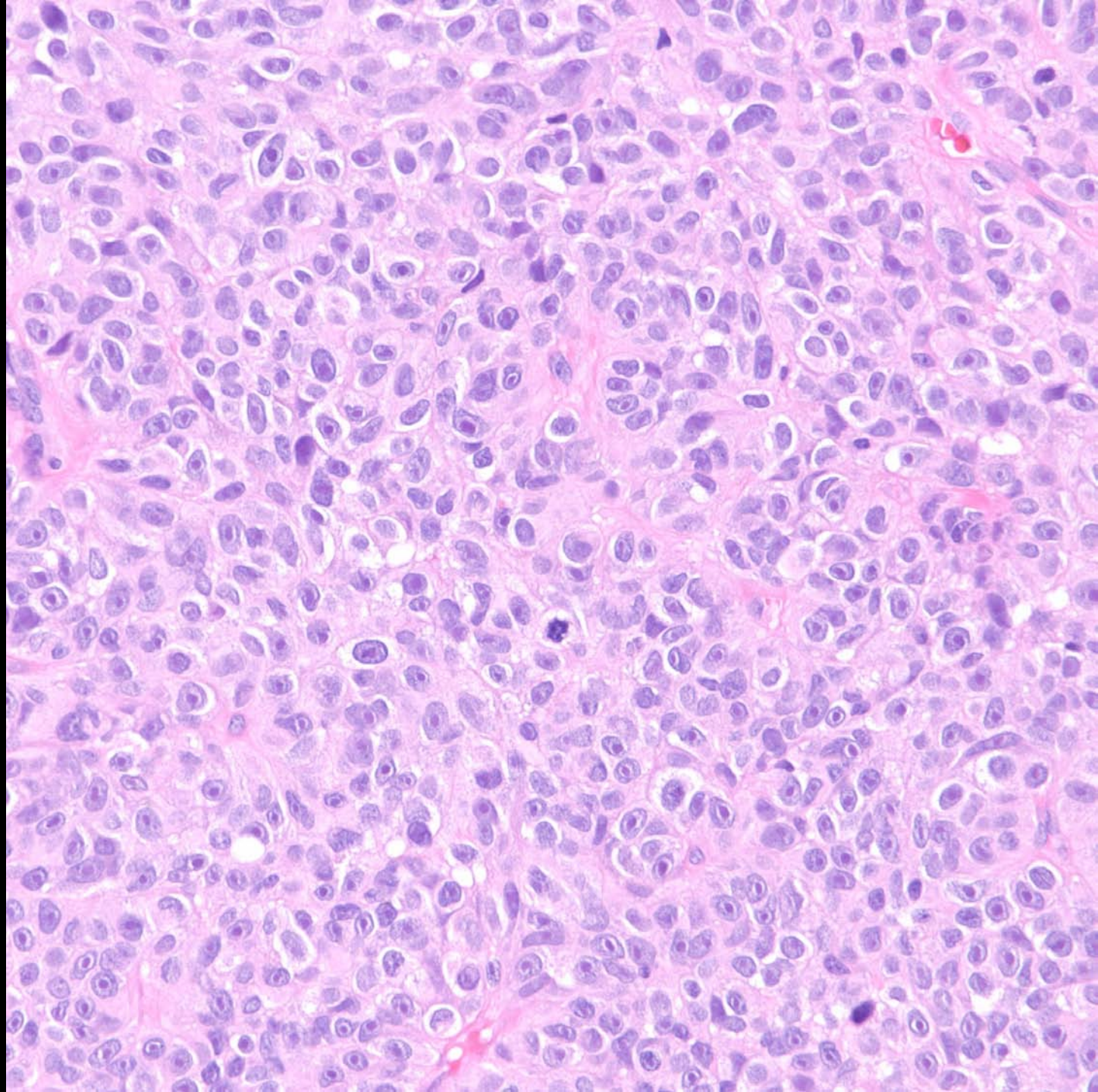




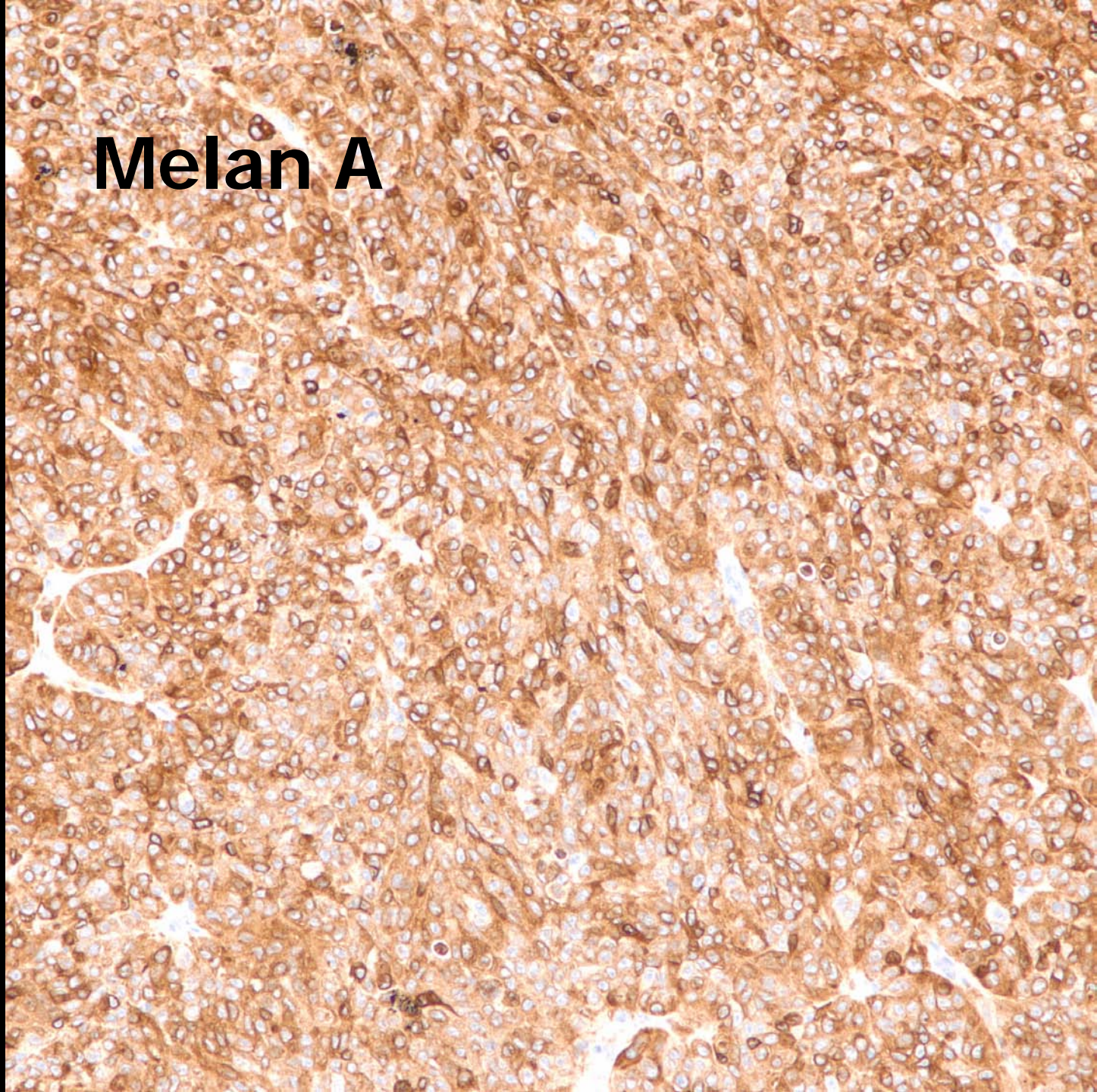
Melanoma- The Great Histopathologic Mimic

- Carcinoma
- Lymphoma
- Sarcoma
- May need adjuvant studies
 - Immunohistochemistry
 - Comparative genomic hybridization





Melan A



Chromosomal CGH / Matrix-CGH

Test-DNA (e.g. Tumor)

Reference-DNA

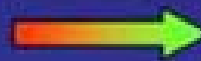
● = gain of genomic material

● = loss of genomic material

● = balanced status



Metaphase

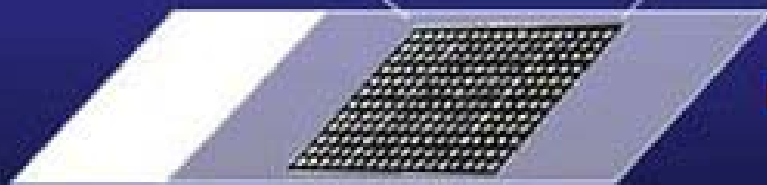
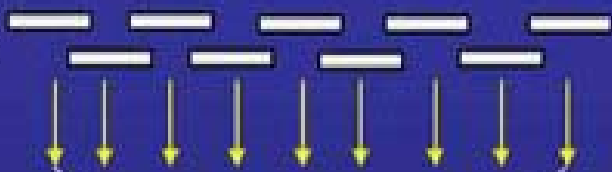


Chromosomal CGH

genomic DNA



DNA fragments



Matrix of spotted DNA fragments



Matrix-CGH



You Must Review Your Pathology Report!

Surgical Pathology Report	
Name: Jane Patient Age: 48 History: breast mass	
Diagnosis	Diagnosis Right breast lumpectomy: poorly differentiated infiltrating ductal carcinoma
Gross Description	Gross Description Received in formalin is a single piece of fibrofatty tissue measuring 4 x 5 x 6cm. Sutures mark the superior and inferior surgical margins. A central mass is palpable. Serial sections reveal a stellate tumor mass measuring 1.5 cm in greatest diameter. Representatively submitted in 5 cassettes.
Microscopic Description	Microscopic Description Sections reveal breast showing infiltrating ductal carcinoma. The tumor is composed of irregular nests of infiltrating cells with minimal gland formation. Individual cells have eosinophilic cytoplasm and irregular or round nuclei often containing a prominent nucleolus. Mitoses are abundant. The surgical margins are clear.
Comment	Comment Surgical margins are clear. Scarff-Bloom-Richardson score is 8 (poorly differentiated). TNM staging is T1, NX, MX.

Surgical Pathology Report

Name: Jane Patient

Age: 48

History: breast mass

Diagnosis

Diagnosis

Right breast lumpectomy: poorly differentiated infiltrating ductal carcinoma

Gross Description

Gross Description

Received in formalin is a single piece of fibrofatty tissue measuring 4 x 5 x 6cm. Sutures mark the superior and inferior surgical margins. A central mass is palpable. Serial sections reveal a stellate tumor mass measuring 1.5 cm in greatest diameter. Representatively submitted in 5 cassettes.

Microscopic Description

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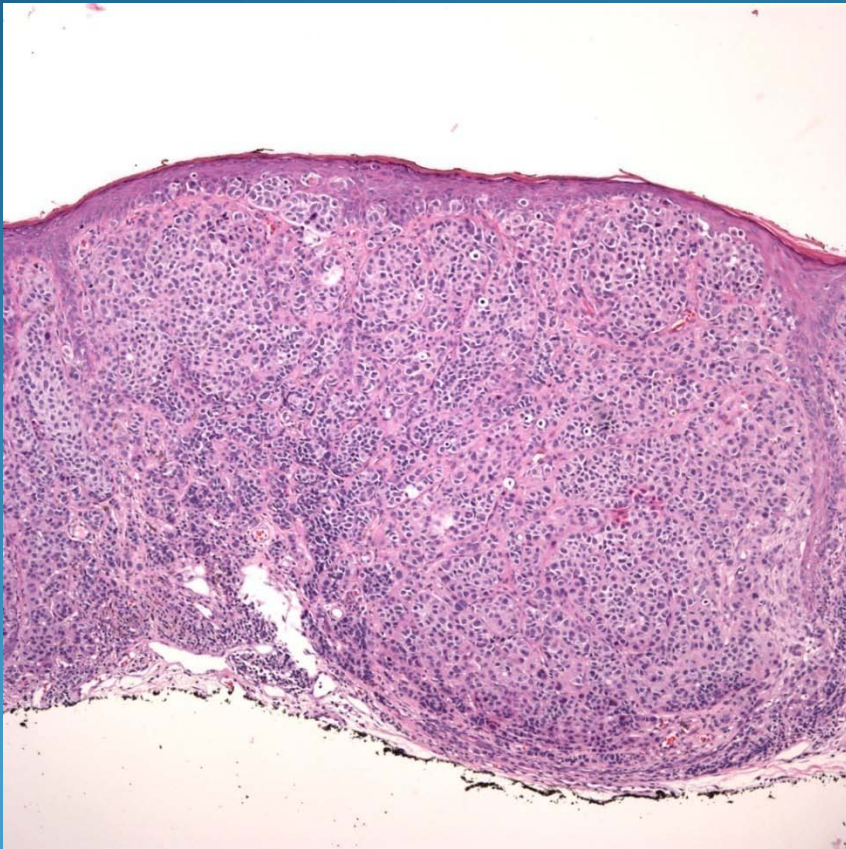
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Comment

Comment

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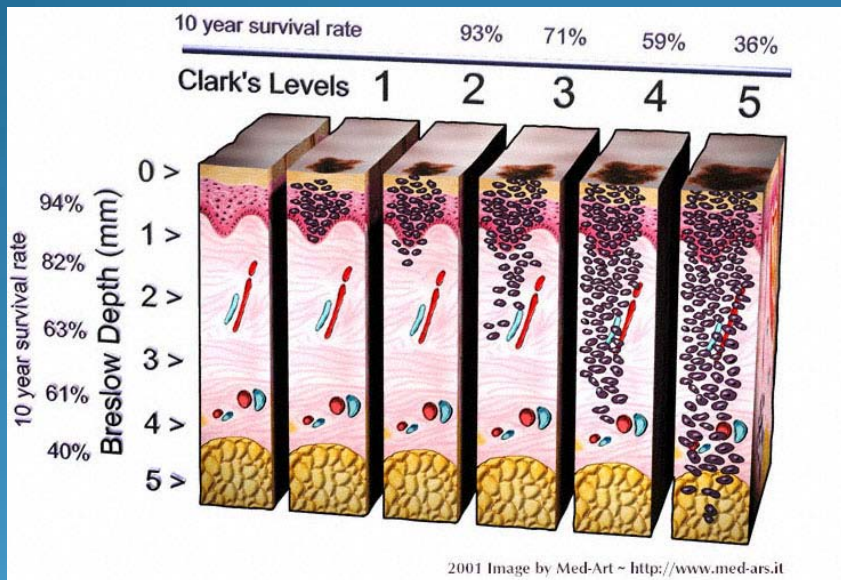
What Do I look For in My Report?



- Diagnosis
- Thickness
- Depth of invasion
- Margins
- Growth phase
- Ulceration
- Lymphovascular invasion
- Mitotic figures

Measurements

- Malignant Melanoma
 - Clark's Level III
 - Thickness 0.98mm

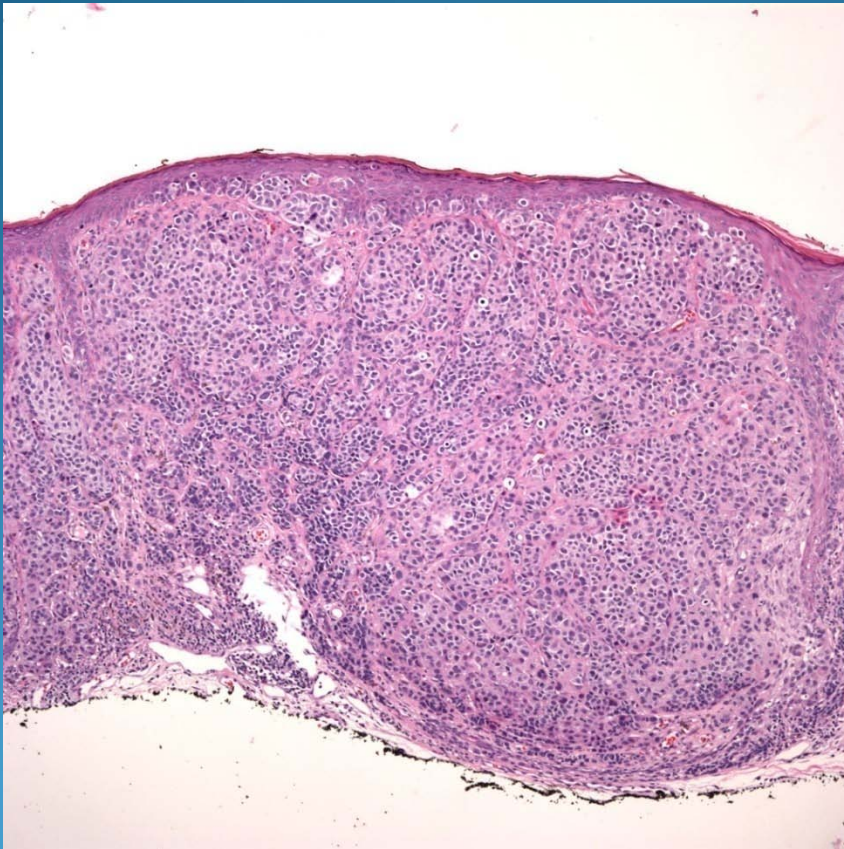


Margins

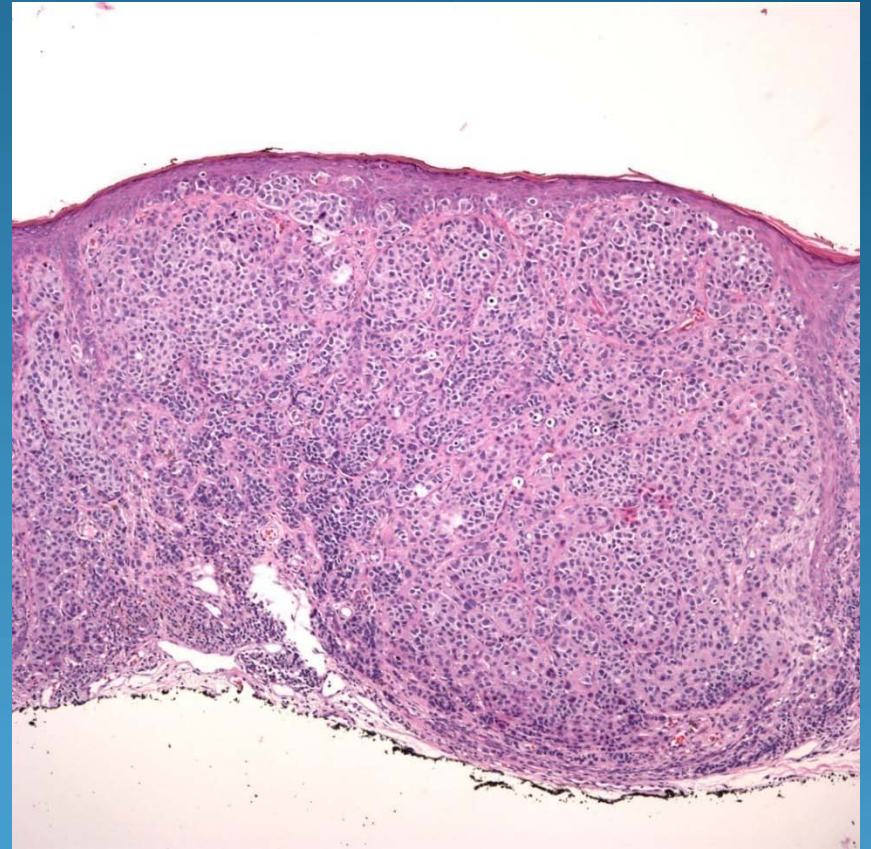
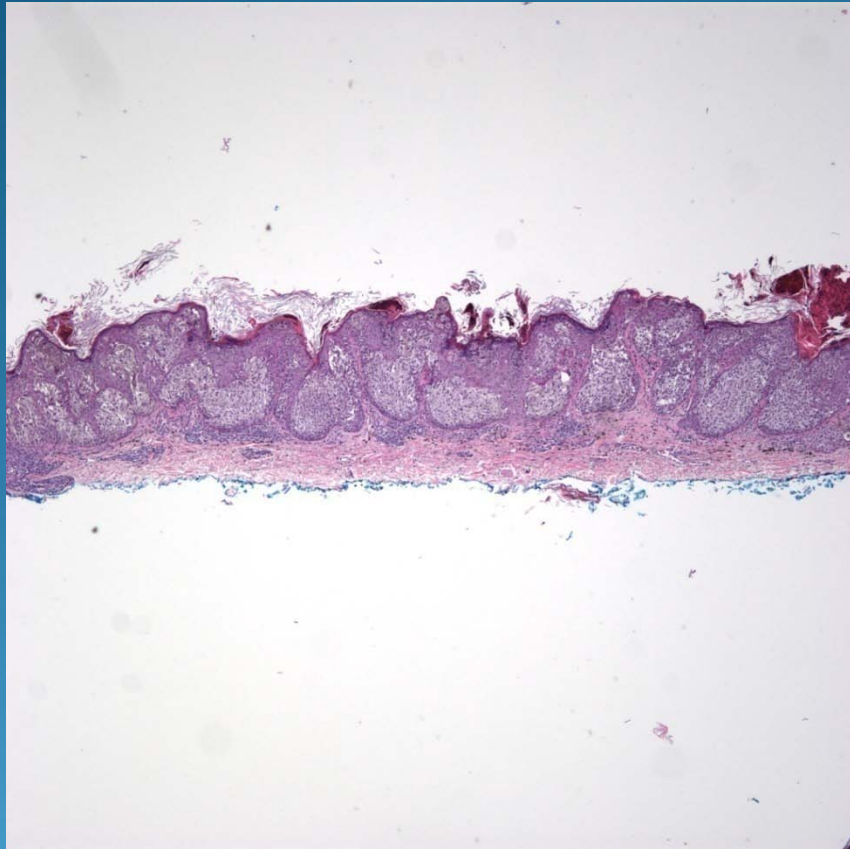


- Malignant Melanoma
 - Clark's Level III
 - Thickness 0.98mm
- Melanoma completely excised

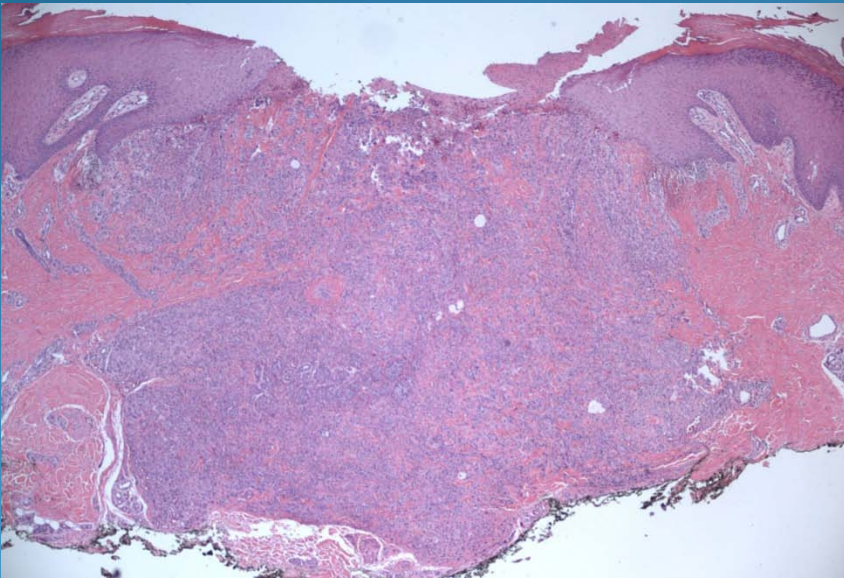
Growth Phase



- Malignant Melanoma
 - Clark's Level III
 - Thickness 0.98mm
- Melanoma completely excised
- Invasive growth phase identified

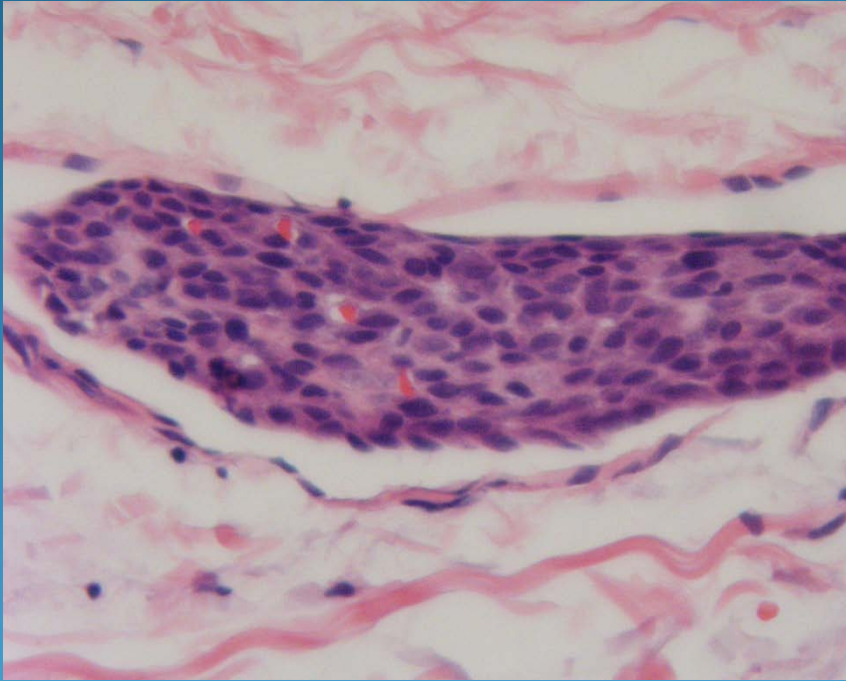


Ulceration



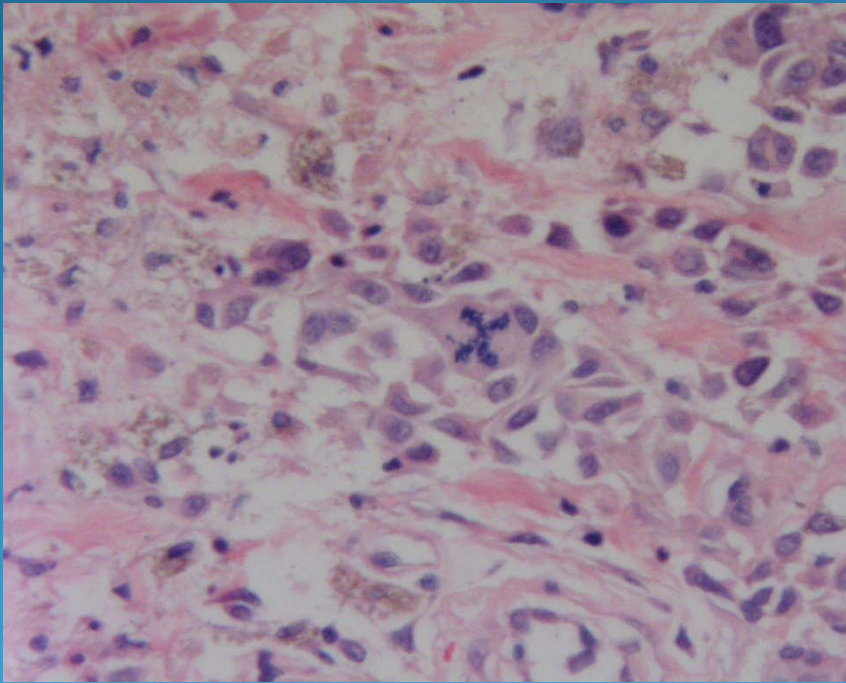
- Malignant Melanoma
 - Clark's Level III
 - Thickness 0.98mm
- Melanoma completely excised
- Invasive growth phase identified
- Ulceration present

Lymphovascular Invasion



- Malignant Melanoma
 - Clark's Level III
 - Thickness 0.98mm
- Melanoma completely excised
- Invasive growth phase identified
- Ulceration present
- Lymphovascular invasion present

Mitotic Figures

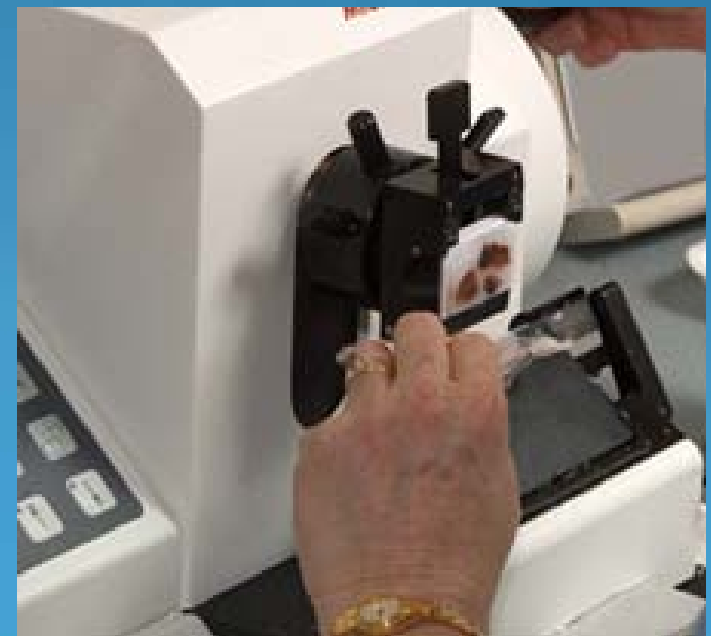


- Malignant Melanoma
 - Clark's Level III
 - Thickness 0.98mm
- Melanoma completely excised
- Invasive growth phase identified
- Ulceration present
- Lymphovascular invasion present
- Two mitotic figures/10 hpf

Surgical treatment

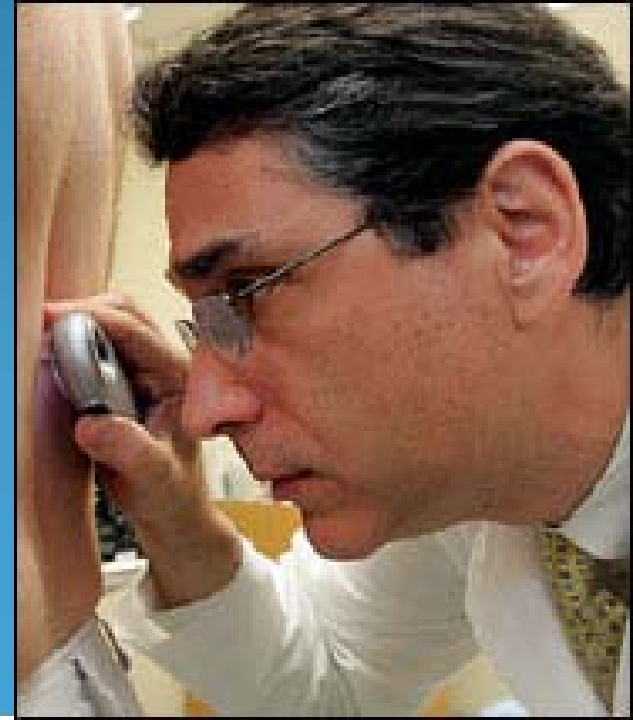
- Complete excision
 - In situ melanoma 0.5-1.0 cm
 - Invasive up to 1mm 1 cm
 - Invasive >1mm 2-3 cm
- Lymph node dissection
 - Traditional
 - Sentinel node dissection with
 - lymphoscintigraphy





Survival

- Early detection is the KEY
 - 100% cure with in-situ melanoma
 - 10YR cure rate 90% <1.5 mm in thickness
 - <50% survival with 3 mm in thickness
- Lifelong follow-up

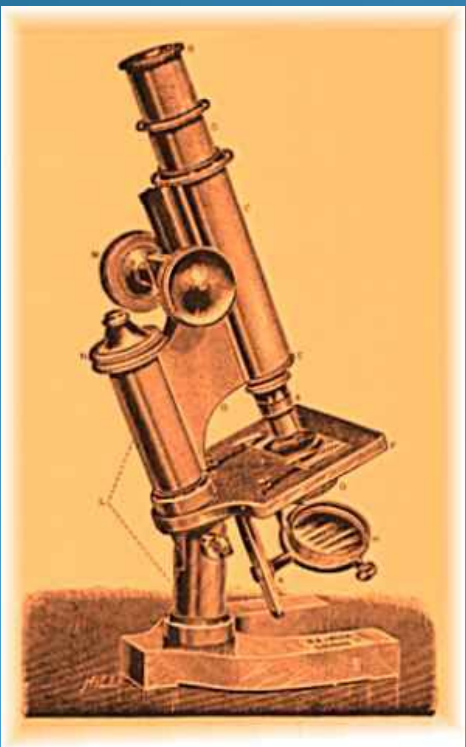


What can you do?

- Self-examination
- Yearly skin examination
- Preventive medicine
 - Sunscreens
 - Avoid high risk behavior







Questions?



Malignant Melanoma

The Role of the Dermatopathologist

Presented to the Bread of Life Church
Torrance, CA

February 22, 2009