APPROVED

Case Study

- 63-year-old woman with a blood alcohol level in the 190s fell and smashed her eyeglasses into her face

BAL 80 would be legally drunk...

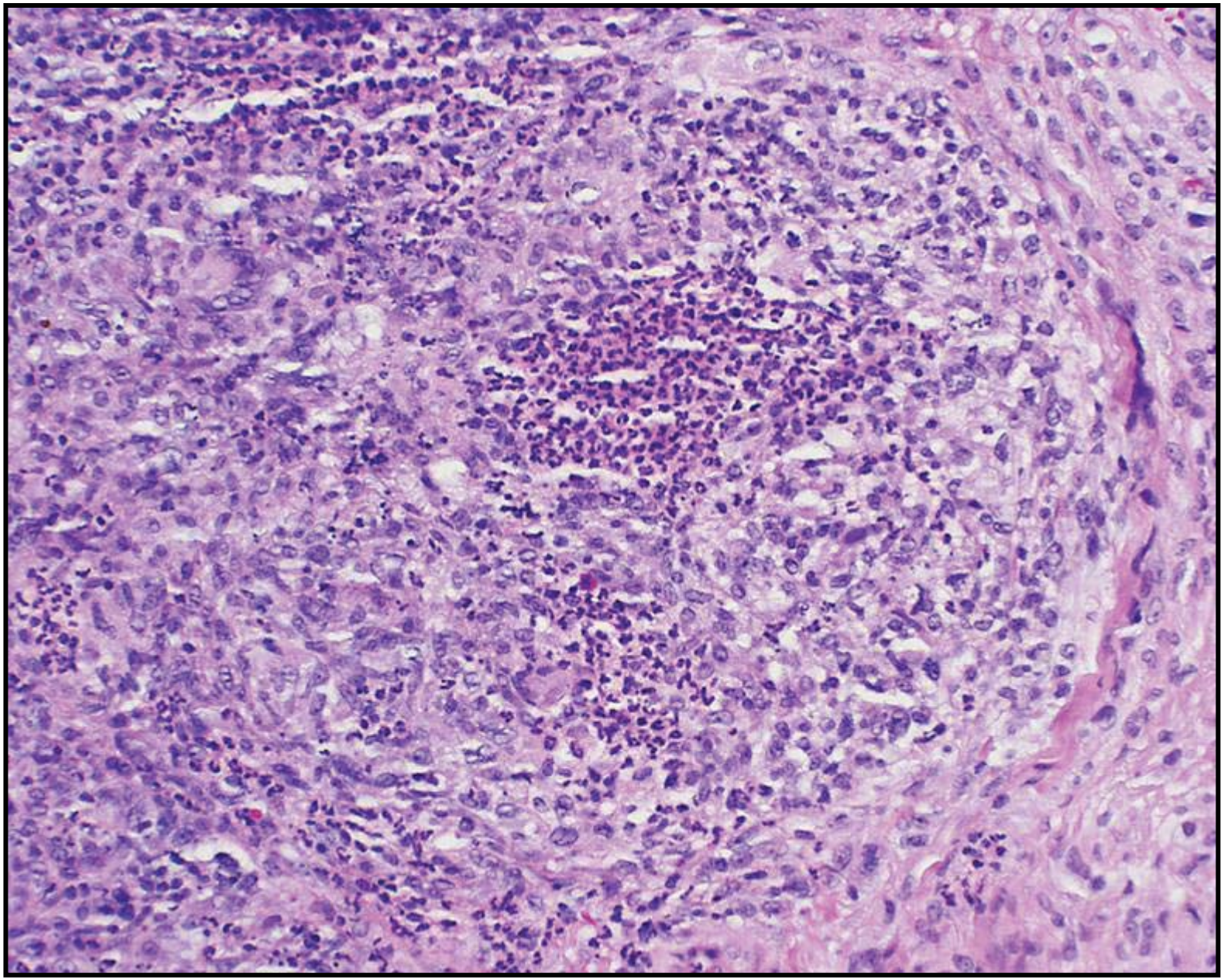
- Three months later she developed fullness under her right eyelid
- Incision and drainage led to no improvement so she underwent attempted excisional biopsy

Proia©/DUMC 194 May 19, 2002

Proia©/DUMC 195

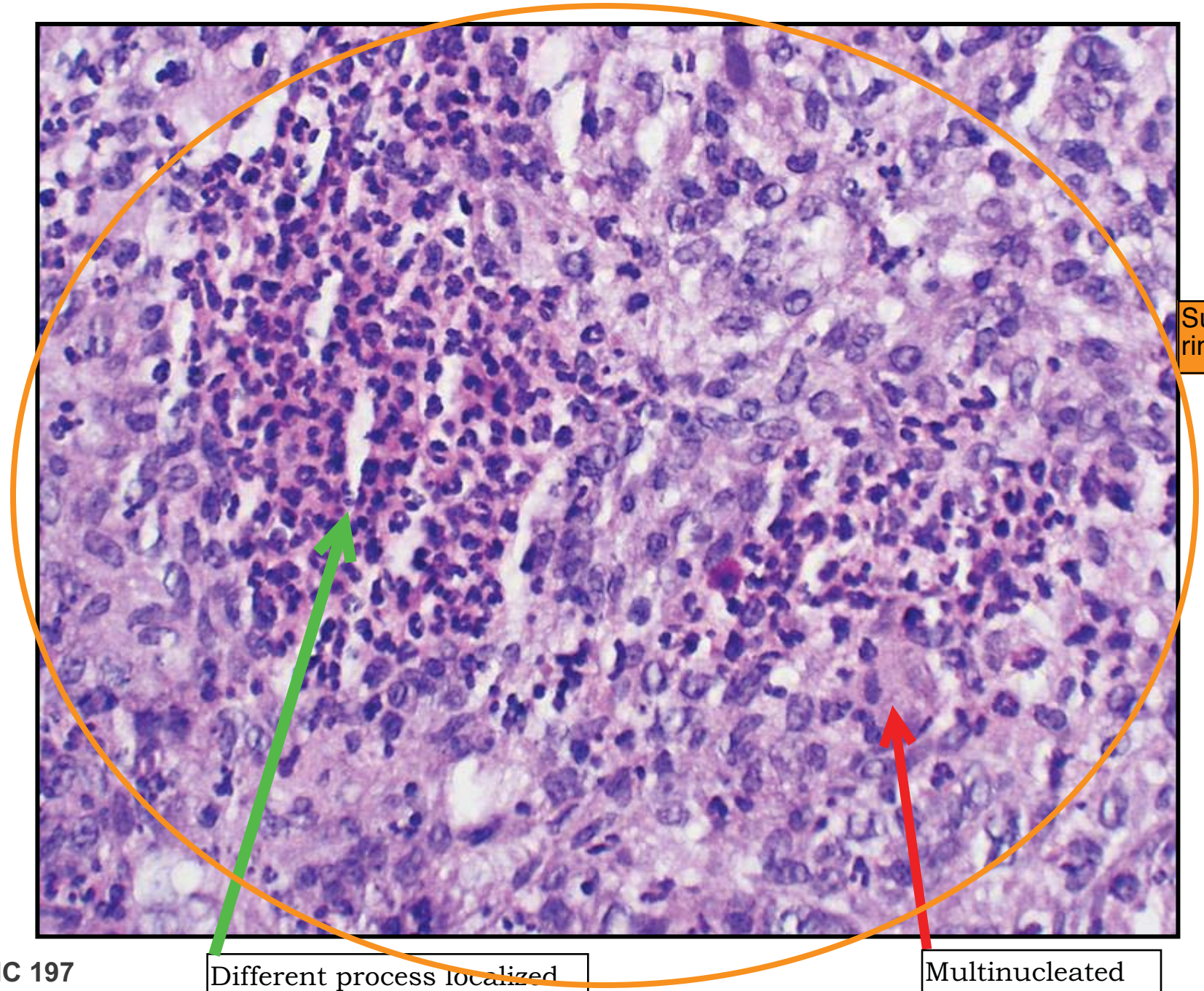
August 14, 2002

3 months later - fullness under eyelid not getting better



Proia©/DUMC 196

Circumscribed area, different from the ones we've seen...



Type of Inflammatory Response?

A) Acute

B) Chronic

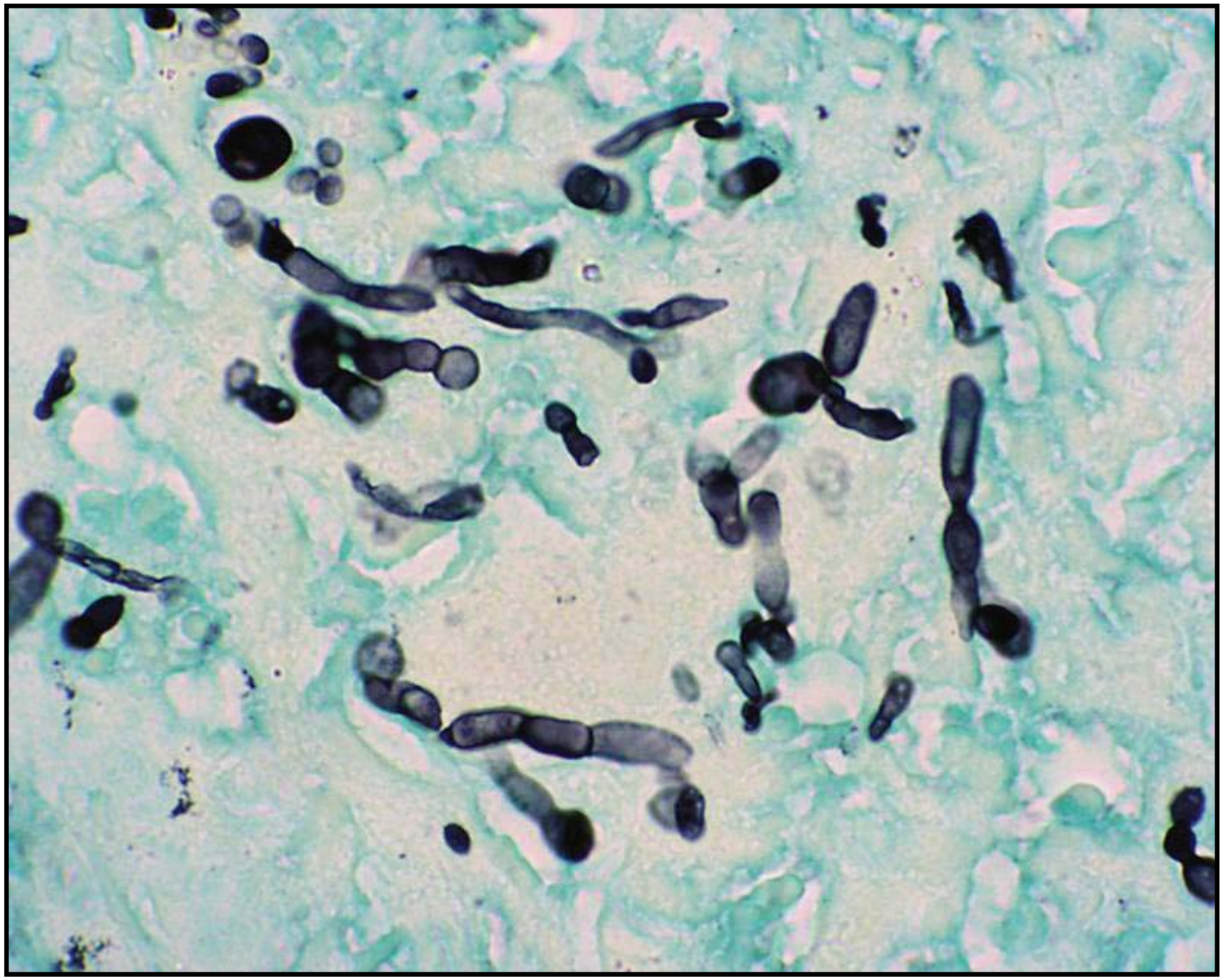
C) Granulomatous

D) Suppurative granulomatous

Not all processes are pure. In this case it's purulent inflammation surrounded by granulomatous inflammation

Granulomatous Inflammation

- **Presence of necrosis is a major clue to infection, most commonly tuberculosis or histoplasmosis in our patient population**
- **Acute inflammation in the center of a granuloma (suppurative granulomatous inflammation) may be a feature in other diseases**



Proia©/DUMC 200

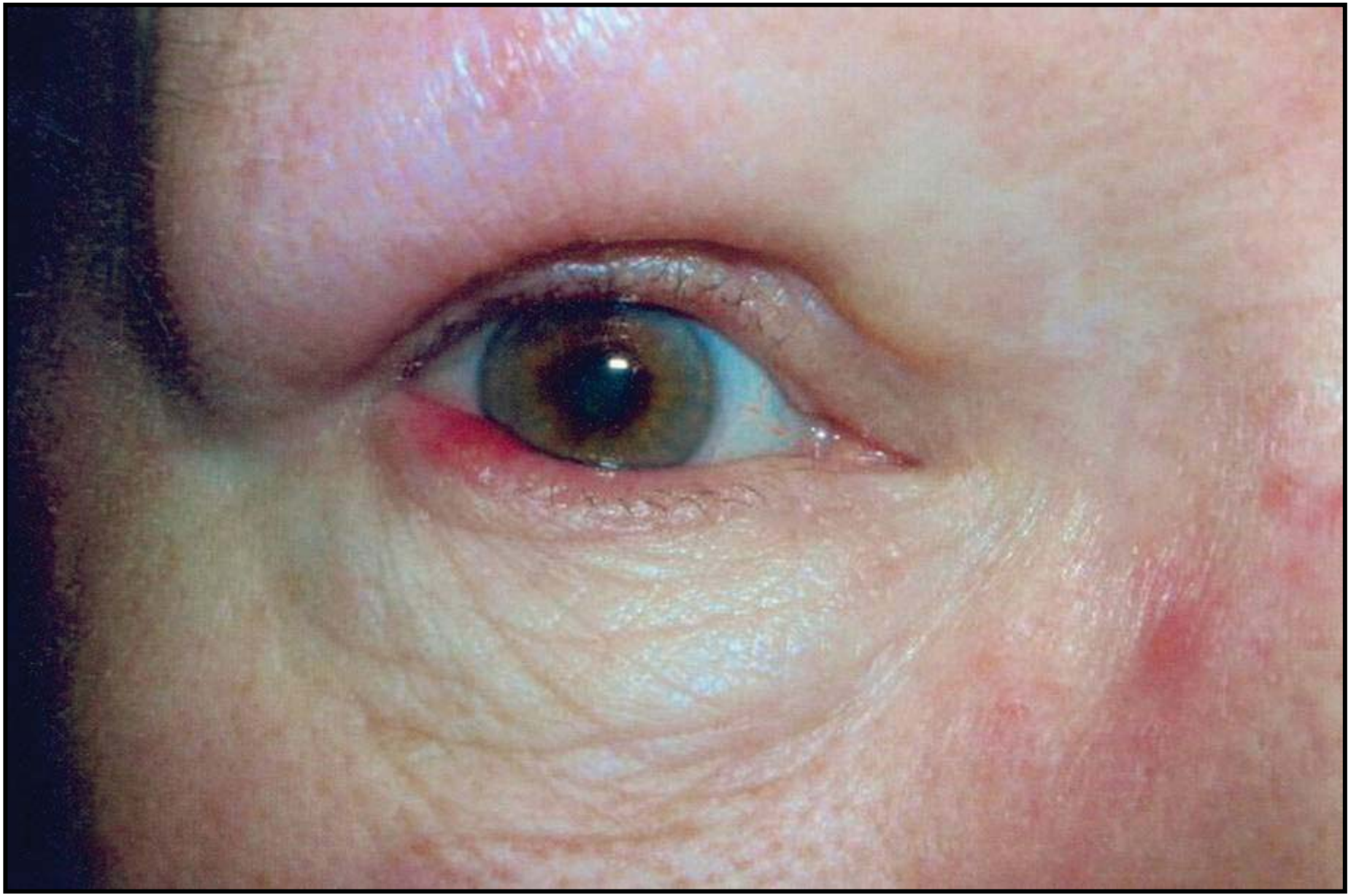
***Paecilomyces lilacinus* (methenamine silver)**

Fungus was the cause in this case

Case Study

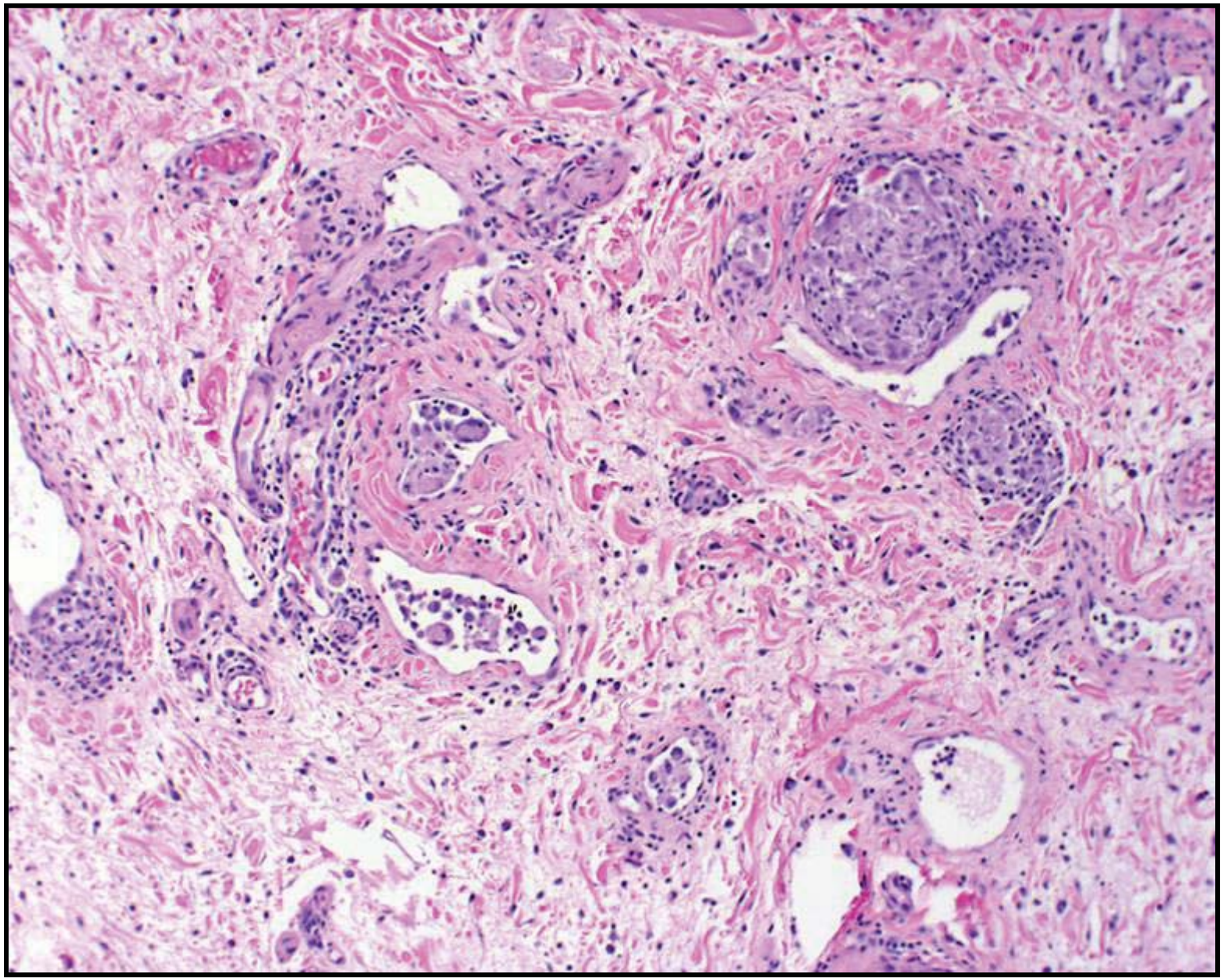
- 66-year-old woman with a history of unilateral right upper eyelid swelling for more than 1.5 years
- Submitted for a second opinion; outside diagnosis was sarcoidosis but extensive systemic evaluation normal

Proia©/DUMC 202



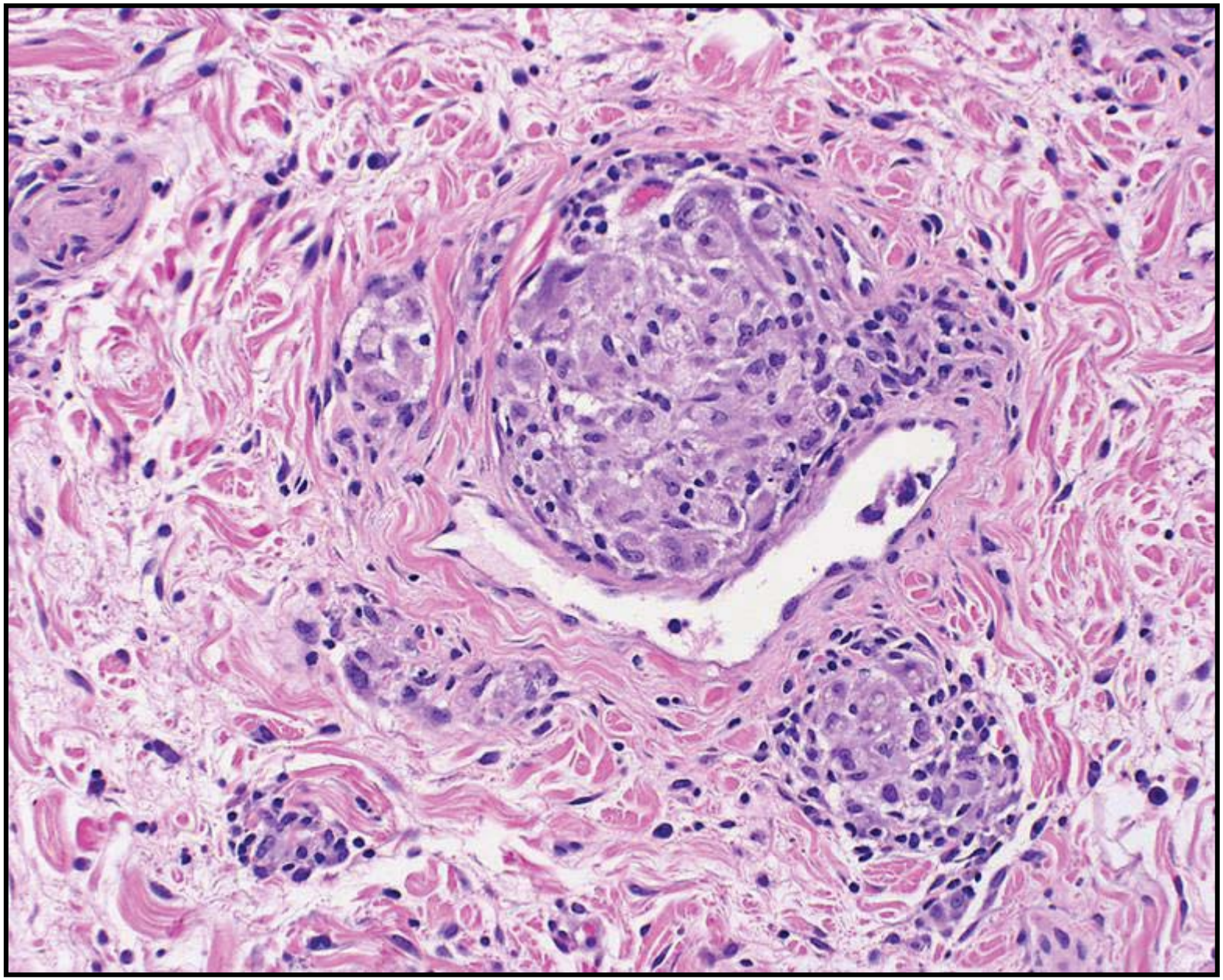
Proia©/DUMC 203

Several foci of inflammation in the dermis

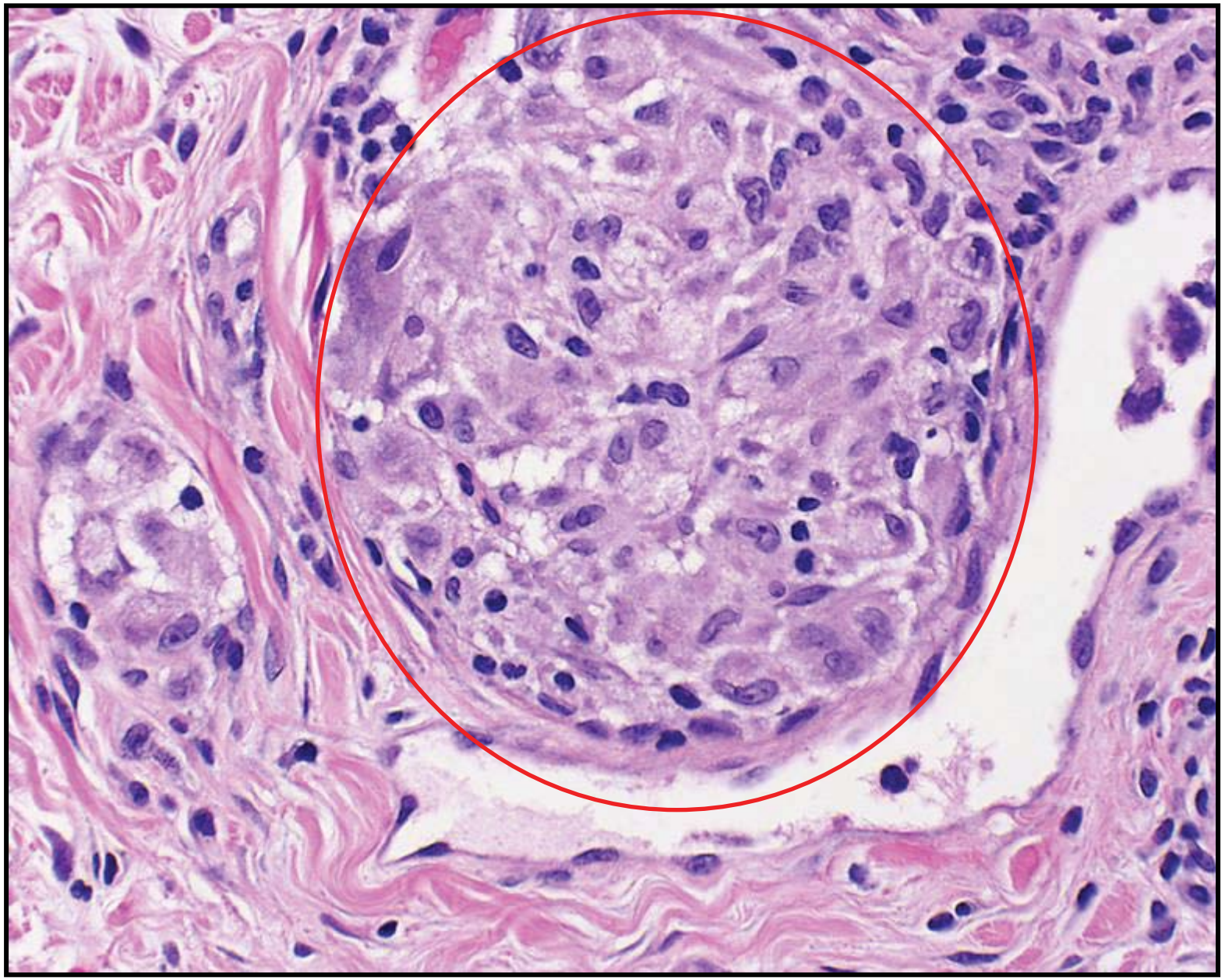


Proia©/DUMC 205

The key is not only to look at the type of inflammation, but also WHERE it occurs. This is a vascular process.



Proia©/DUMC 206



Proia©/DUMC 207

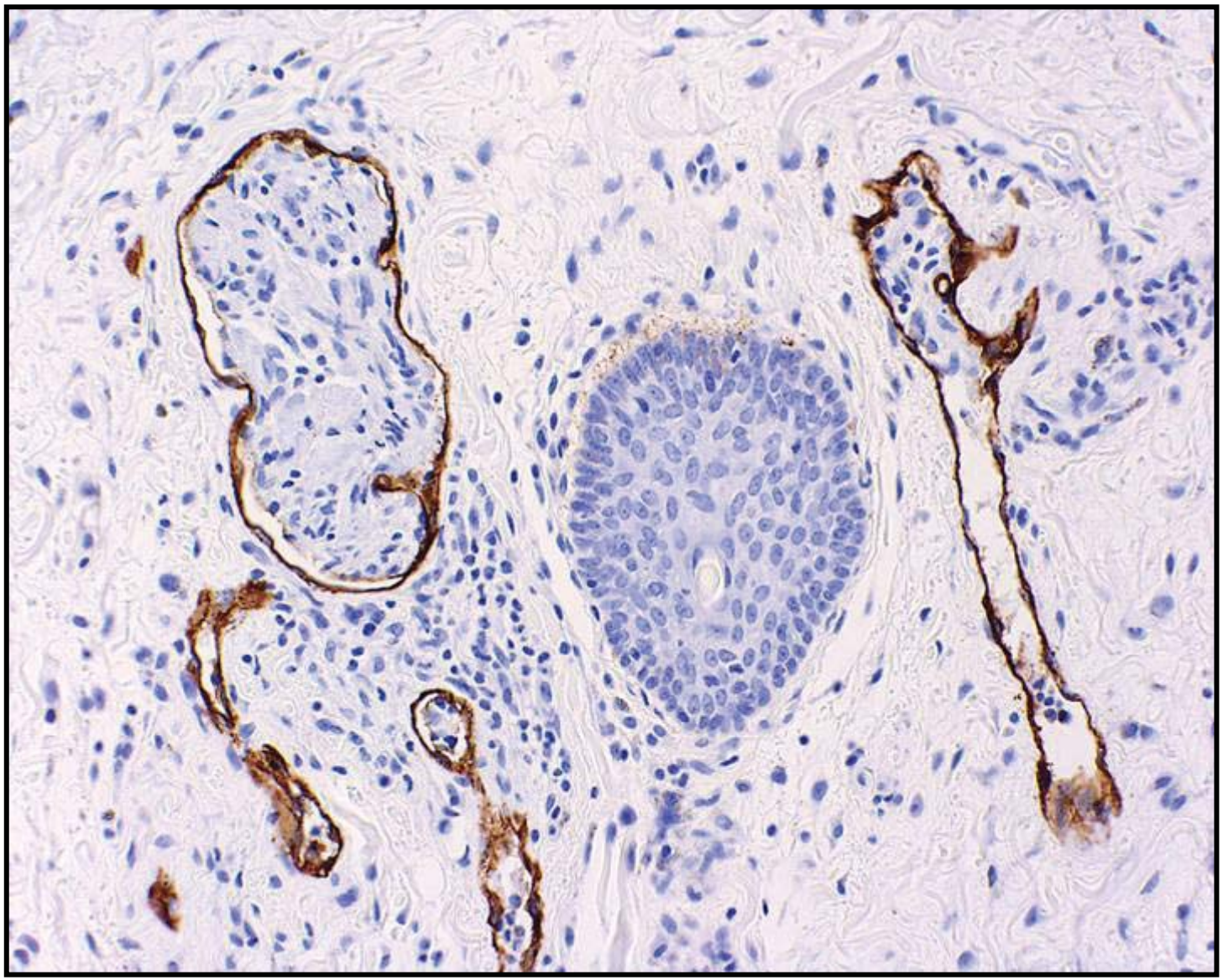
Circumscribed granuloma
with epithelioid cells

Type of Inflammatory Response?

A) Acute

B) Chronic

C) Granulomatous



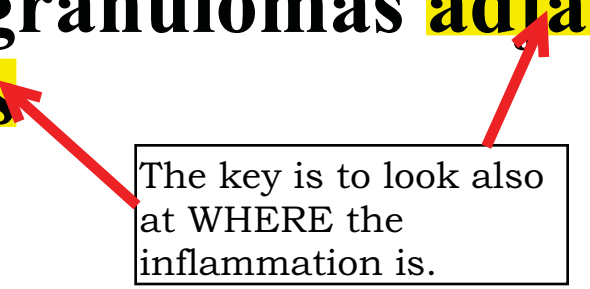
Proia©/DUMC 209

Immunostaining for lymphatics (D2-40)

Shown here to the left is a lymphatic with a circumscribed granuloma inside. To the right is a lymphatic with a granuloma inside and one adjacent to it

Orofacial Granulomatosis

- **Non-tender swelling and edema of the lips and/or face**
- **Melkersson-Rosenthal syndrome has the additional findings of facial nerve palsy and fissured tongue; present in 18-25% of people with orofacial granulomatosis**
- **Non-necrotizing granulomas adjacent to or within lymphatics**

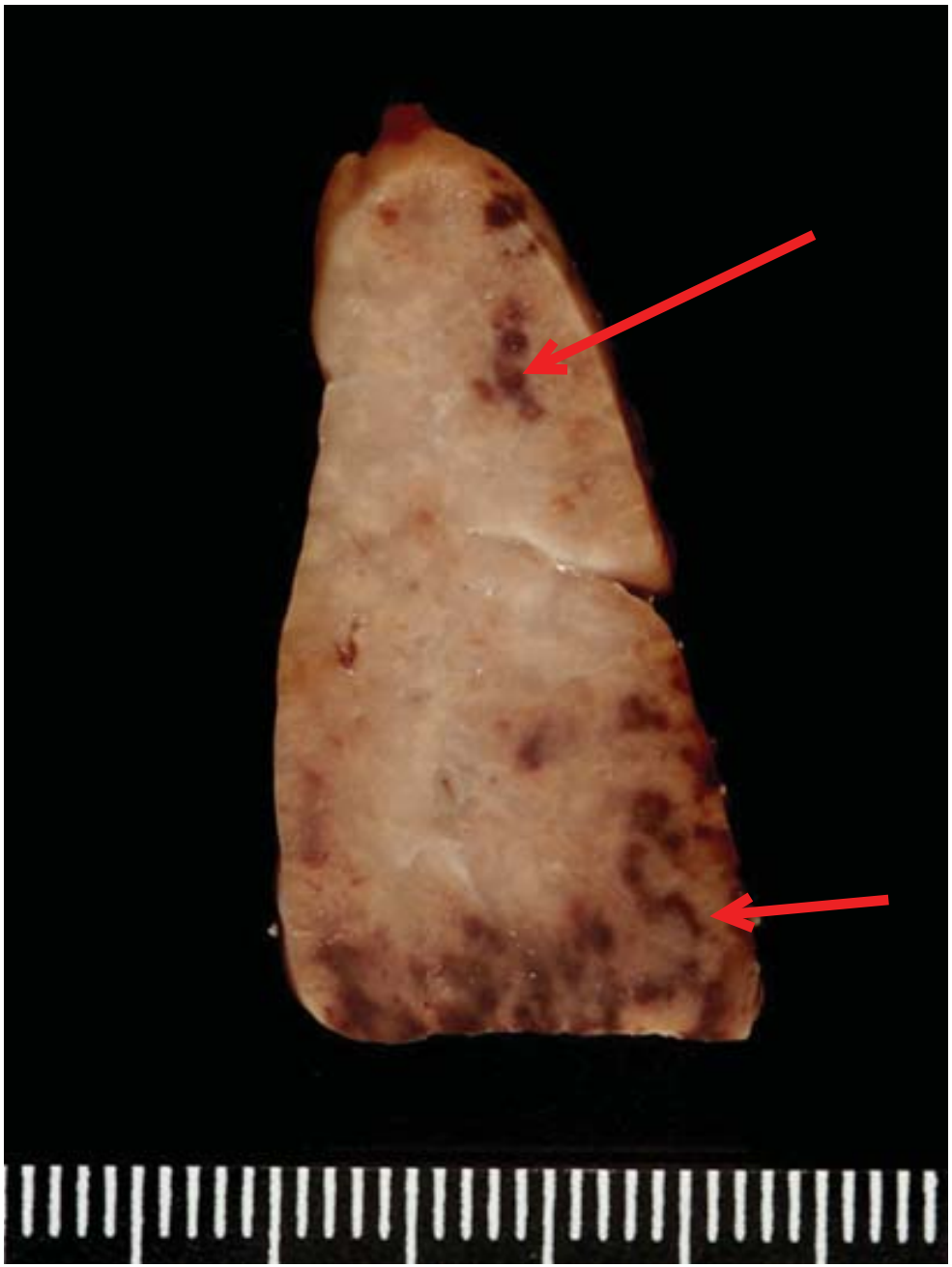


No treatment for this.

Case Study

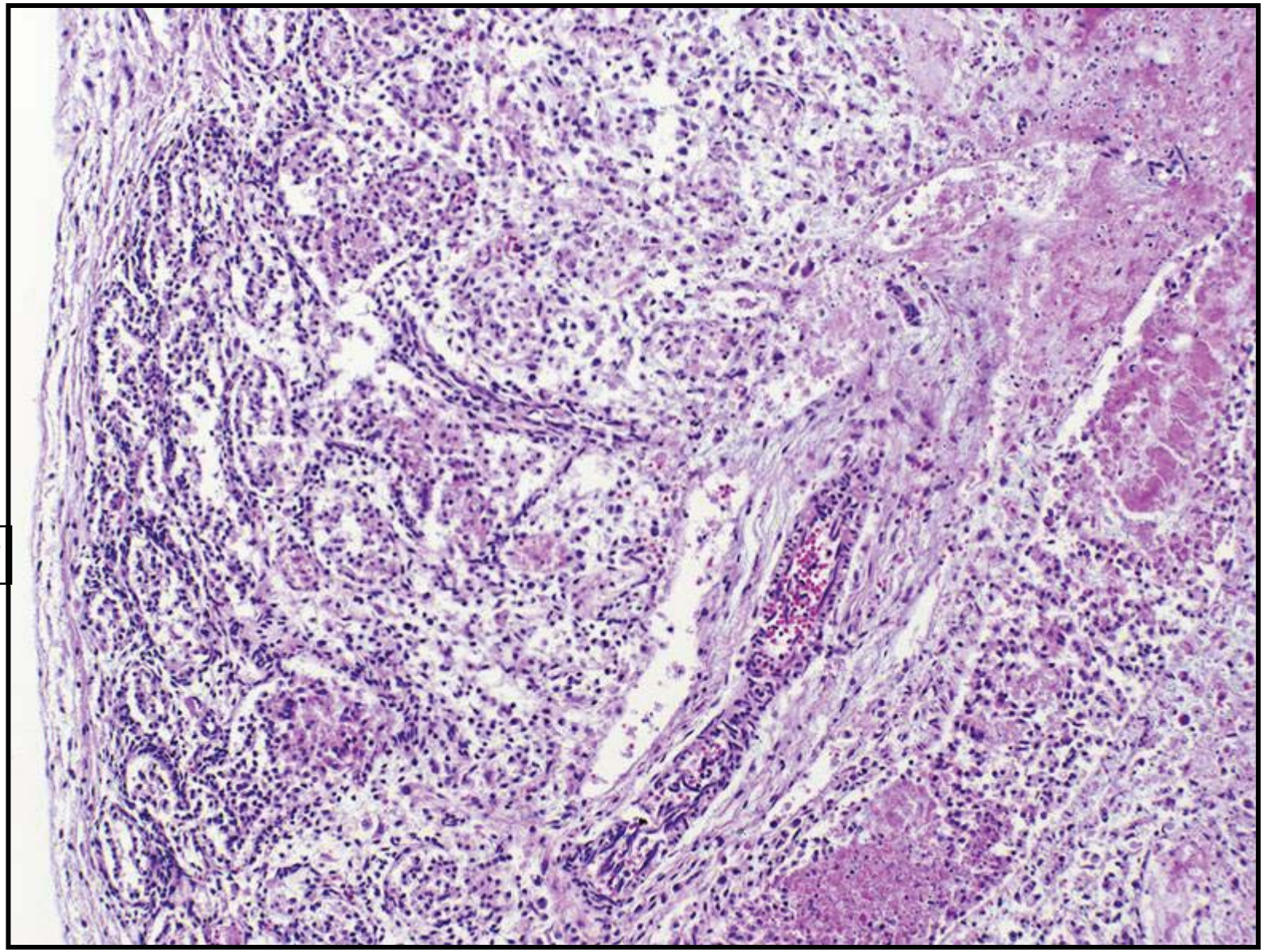
Male fetus.

- 19-week-gestation male delivered stillborn to an 18-year-old primigravida woman
- No abnormalities detected on ultrasound
- Laboratory tests including alpha-fetoprotein screen and serologies were negative
- Mother's medical history is significant for asthma and cigarette smoking

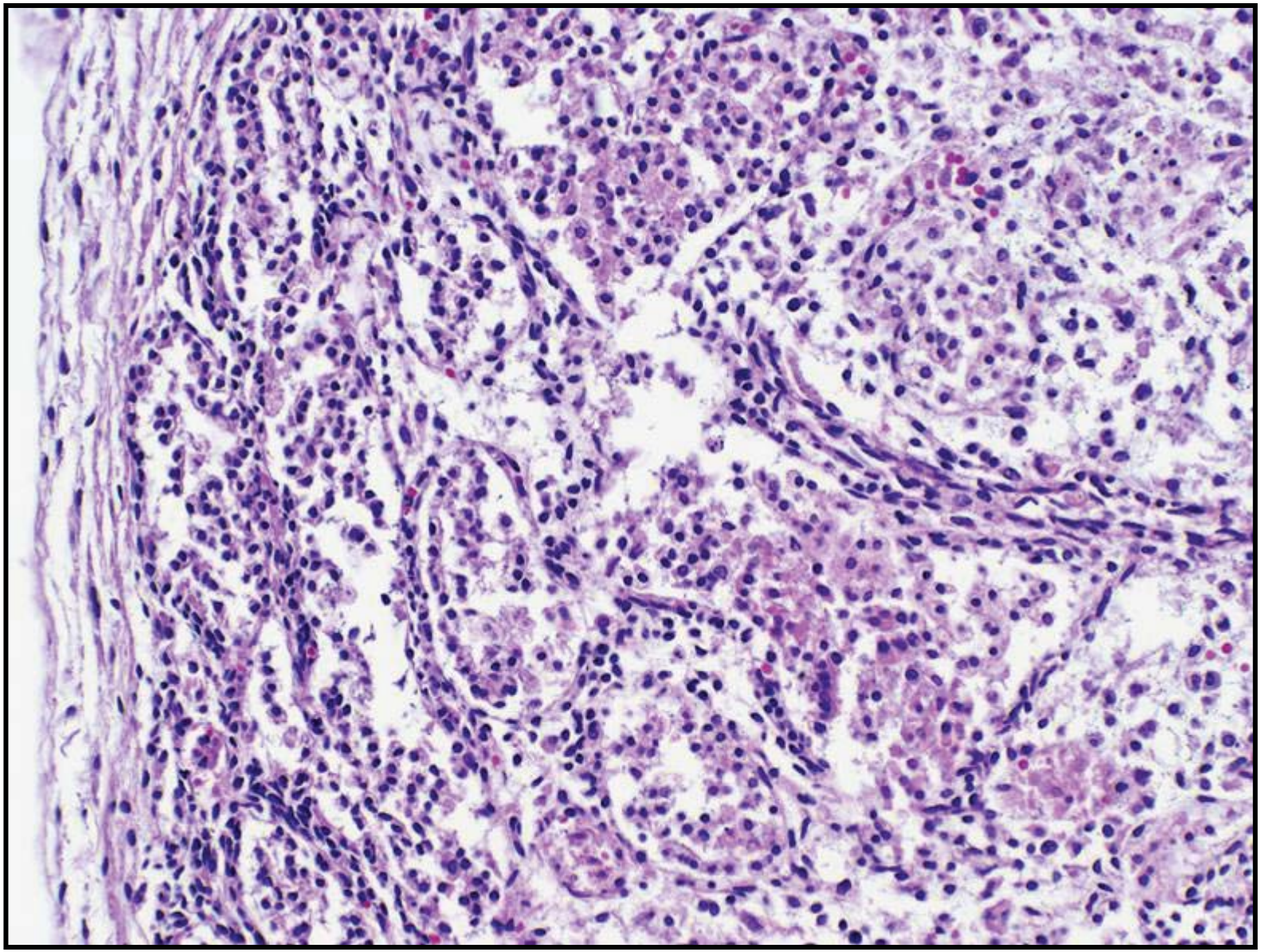


Fetal lung has abnormal motteling on the cut surface. Normally a fetal lung will look necrotic depending on how long the baby has been stillborn. Or it will look homogeneous. This motteling is abnormal

Lung



Immature **Lung**

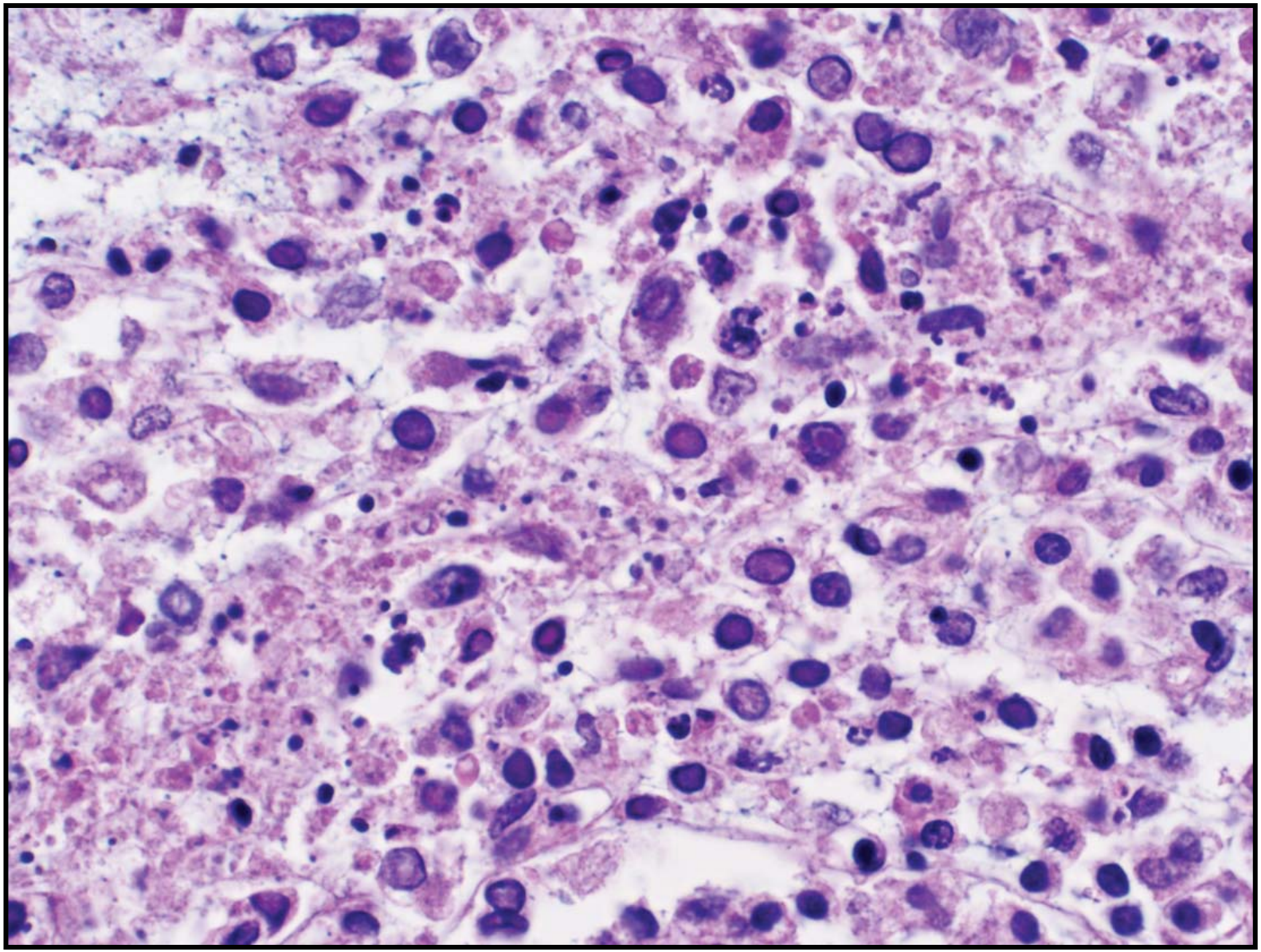


Proia©/DUMC 214

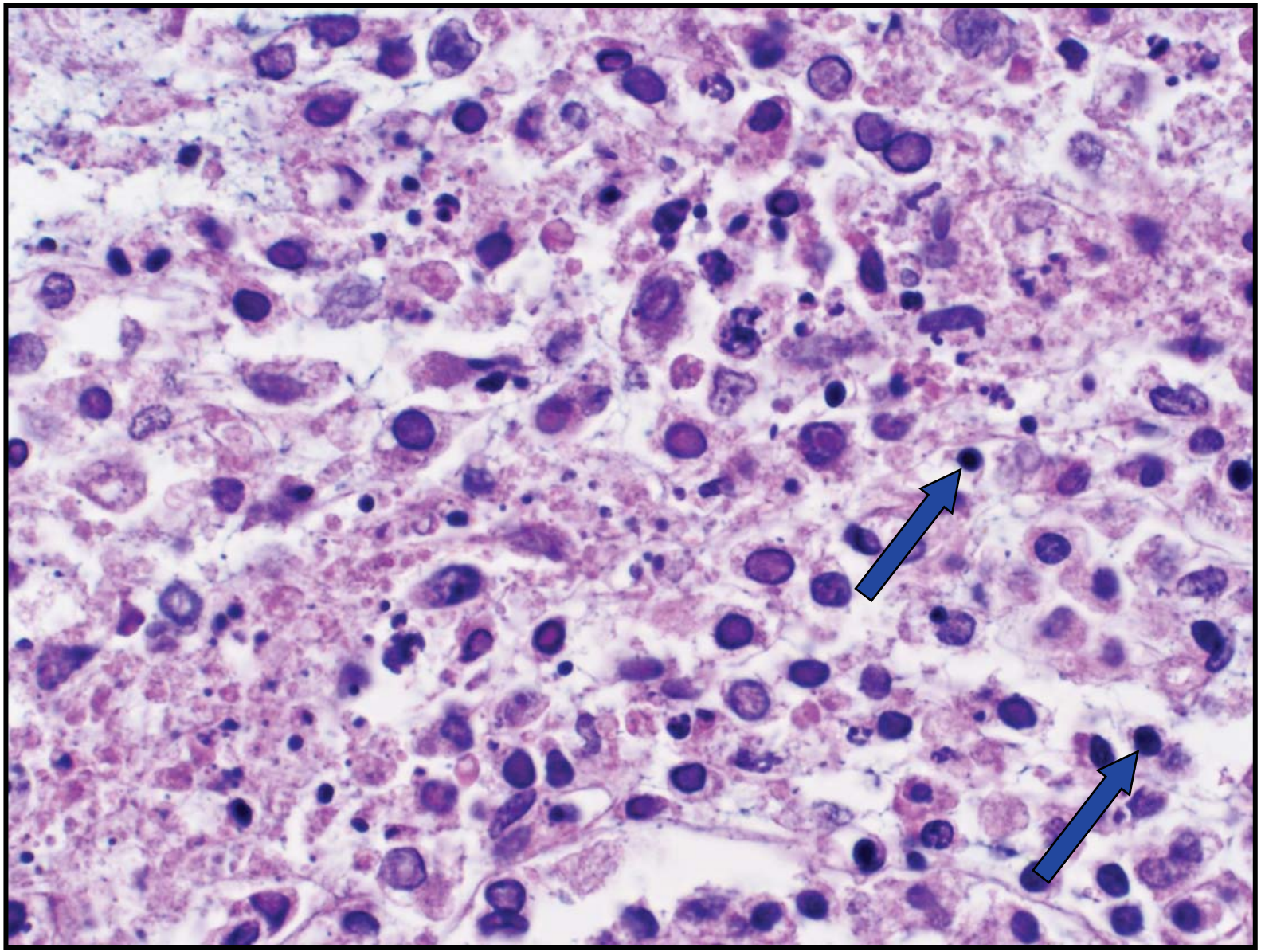
Lung

Observe the primitive alveolar sacs

Alveolar sacs filled with inflammatory cells. With viral change (red dots)



Lung



Proia©/DUMC 216

Lung

Inflammatory Cell Type?

A) Lymphocyte

B) Eosinophil

C) Plasma cell

D) Macrophage

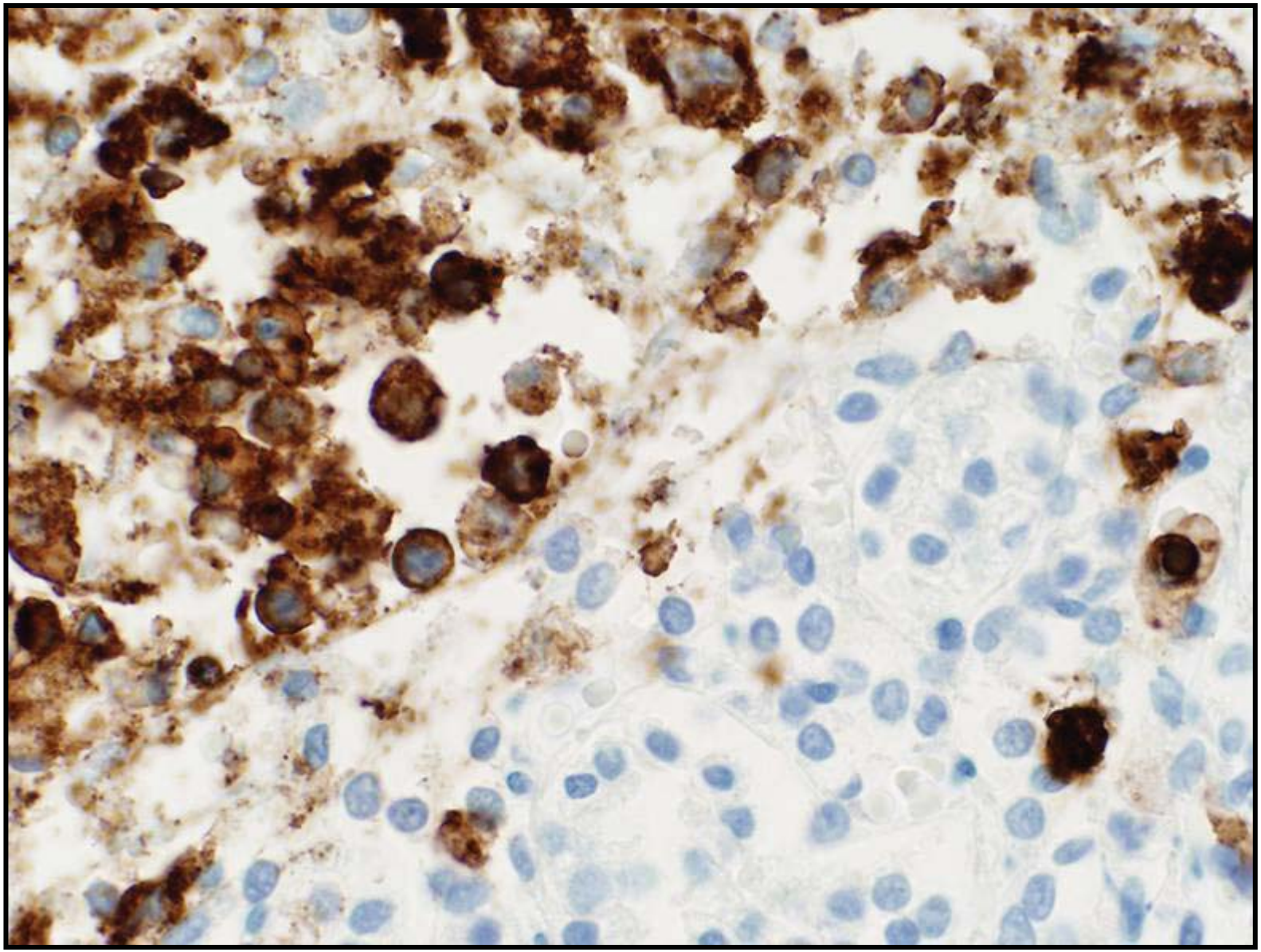
E) Neutrophil

Type of Inflammatory Response?

A) Acute

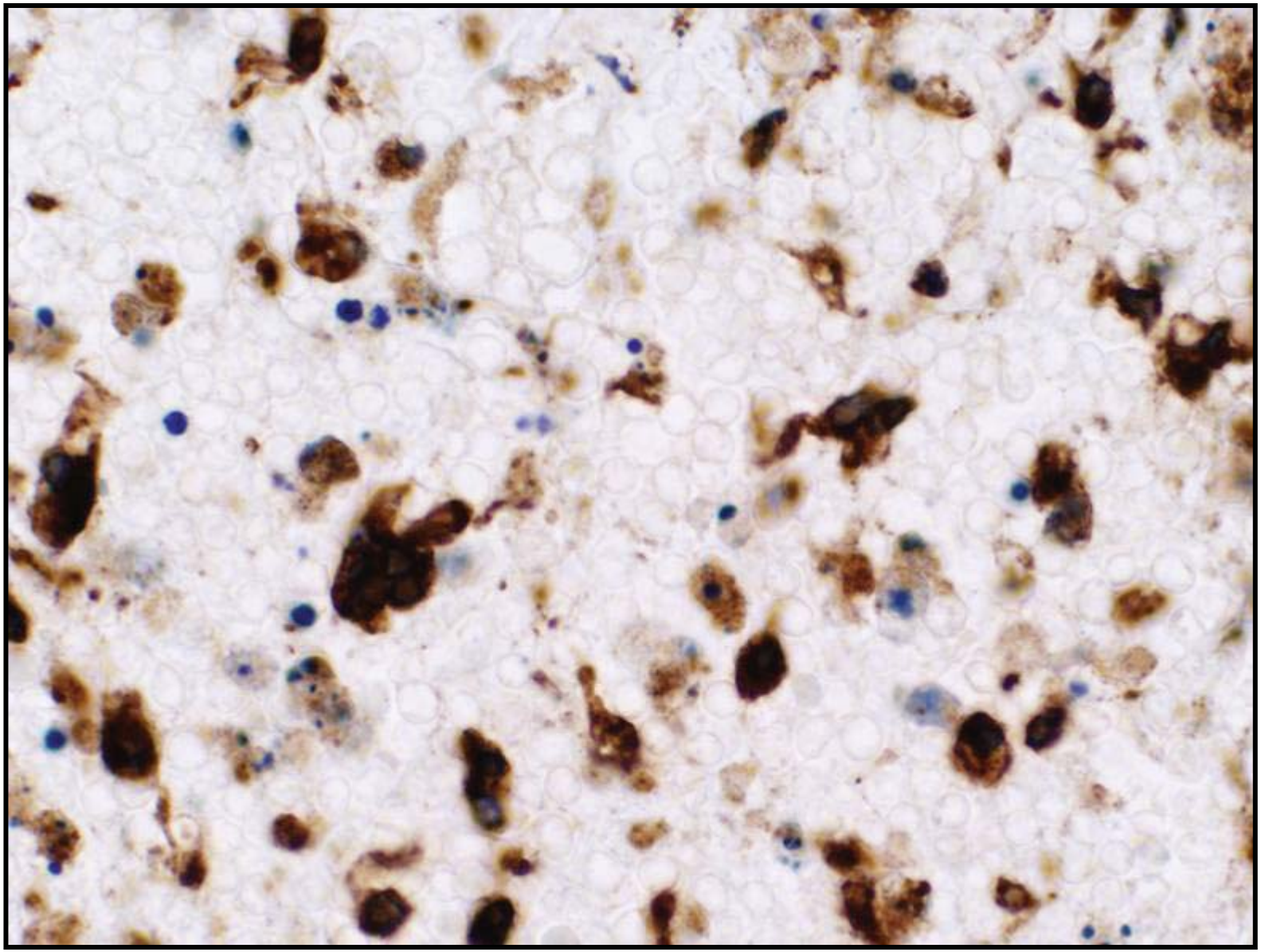
B) Chronic

C) Granulomatous



Lung – CD45 Immunostain

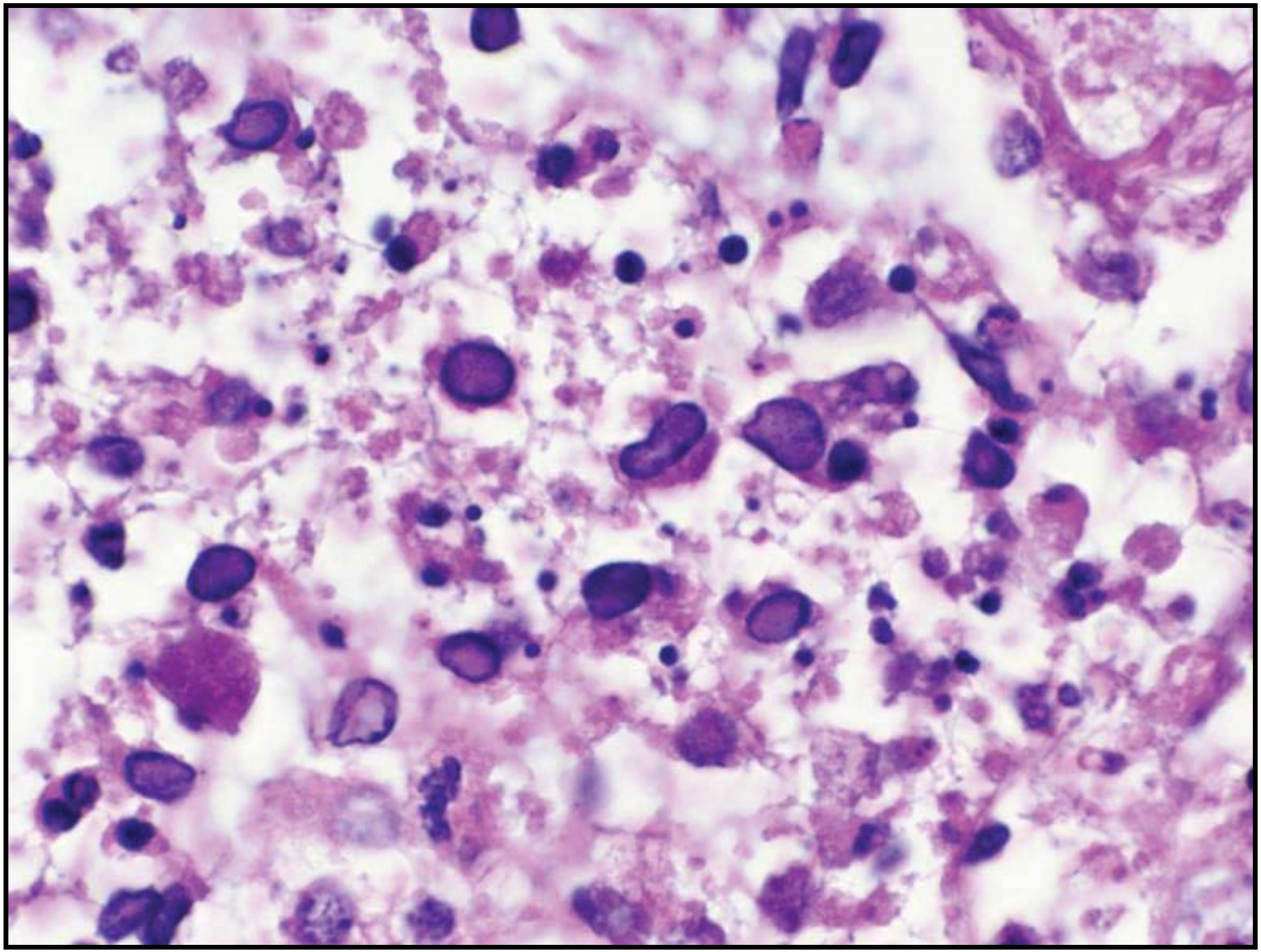
Proves the cells are lymphocytes



Proia©/DUMC 220

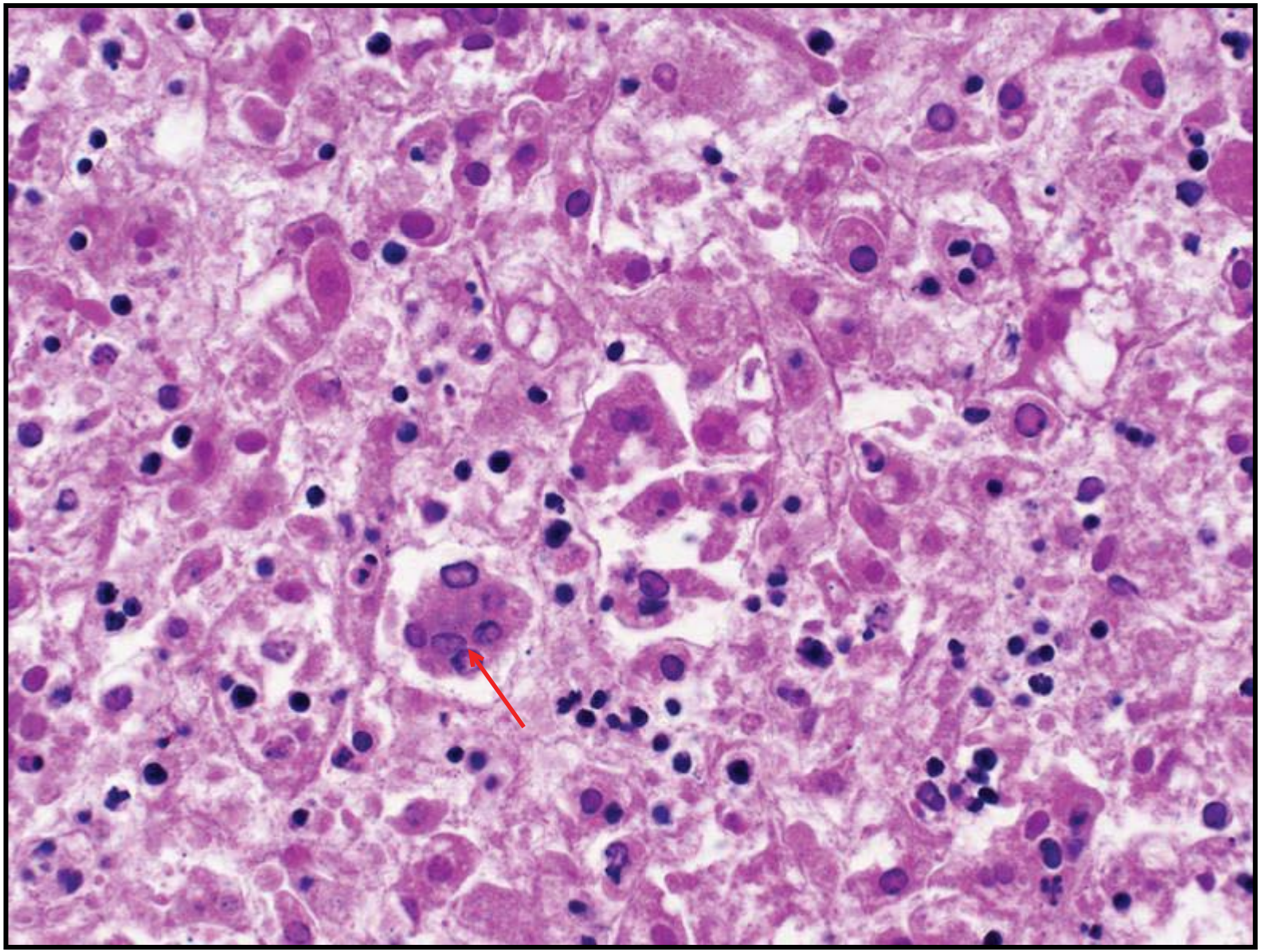
Lung – Herpes simplex virus Immunostain

Demonstrated the presence of the HSV antigen in the cells



Adrenal gland

Cells have a smudged red appearance because of viral inclusions bodies within the nuclei



Proia©/DUMC 222

Liver

Multinucleated cell with viral inclusions - HSV can cause this with infection. The difference is you can see viral inclusions so this is NOT GRANULOMATOUS inflammation

Herpes simplex virus

- Skin and mucous membrane infections common
  - » Fever blisters/cold sores (HSV-1)
  - » Gingivostomatitis (HSV-1)
  - » Genital herpes (HSV-2)
- Corneal infection (herpetic keratitis)
- Herpes encephalitis
- Disseminated and visceral infection
  - » Immunodeficient/immunosuppressed individuals
  - » Herpes esophagitis
  - » Herpes pneumonia and tracheobronchitis
  - » Disseminated infection

Implications

- **Mother will be given prophylactic antiviral medication during her next pregnancy**
- **Demonstrates the value of autopsy, even in cases in which the yield of "positive" results is low**
- **Demonstrates the importance of recognizing inflammatory patterns and knowing how to further characterize them**

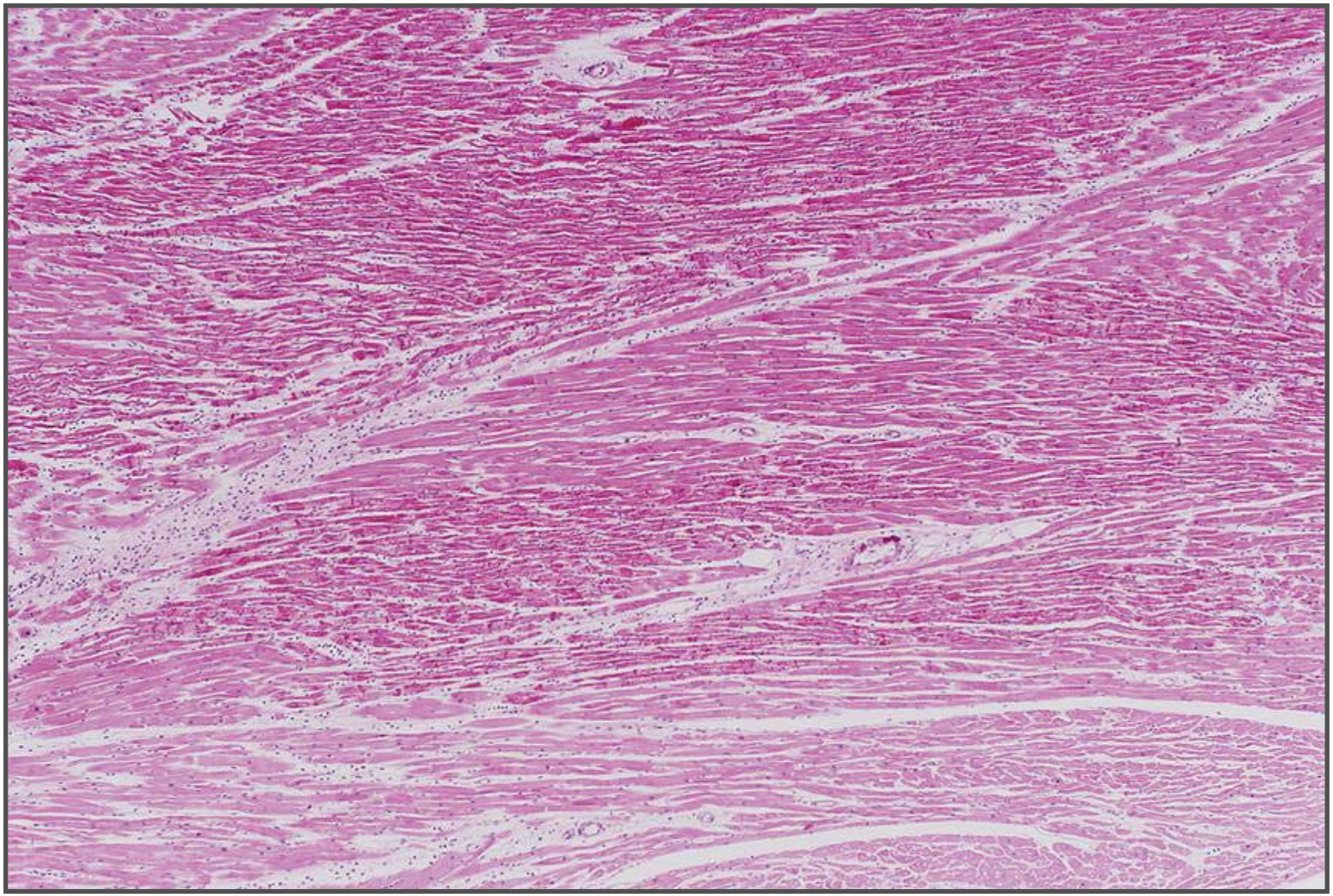
You have to recognize the viral inclusion to make the diagnosis of HSV!

Legal Case Study - 1

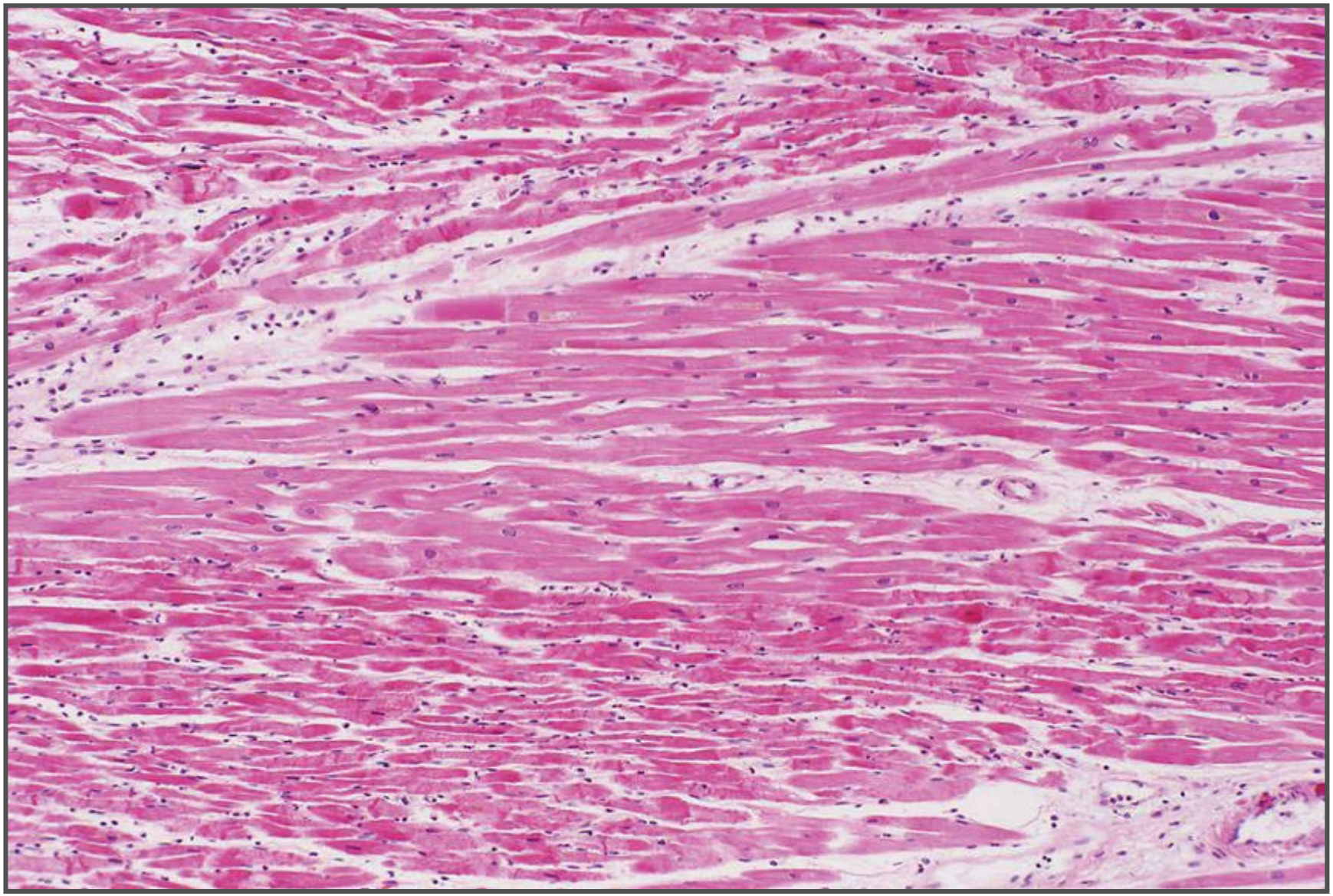
- 44-year-old man
- Driving from Virginia to Florida when he developed epigastric-chest pain; had to lay down in backseat of car
- ER: Given pain relievers since for "heartburn"
- Returned home later that evening
- Unwitnessed death in bathroom the next morning

Legal Issues

- **Was the patient having a heart attack when seen in the emergency room approximately 20 hours prior to death**
- **Did the ER treatment meet the "standard of care"** NO!

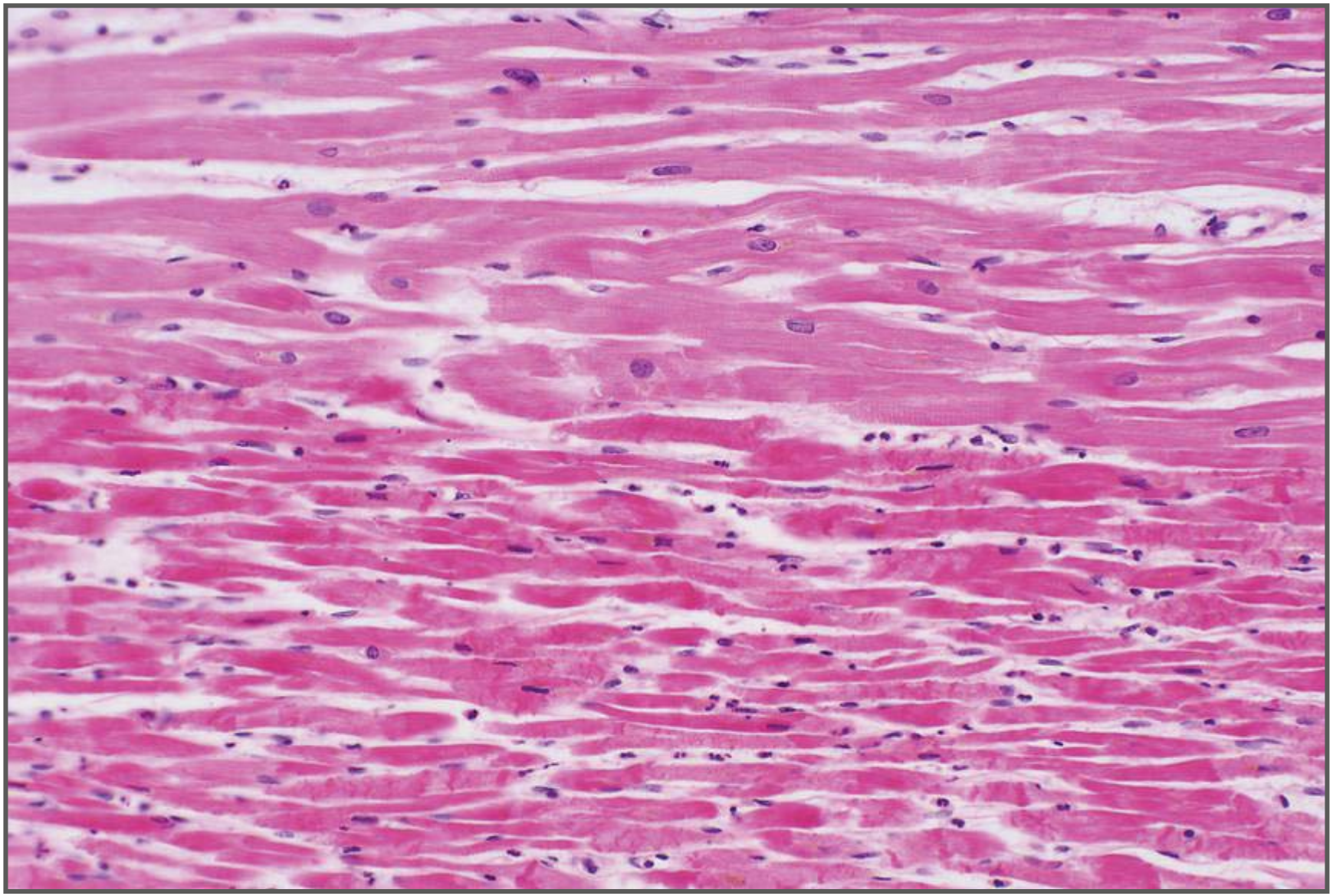


Low power of his heart muscle

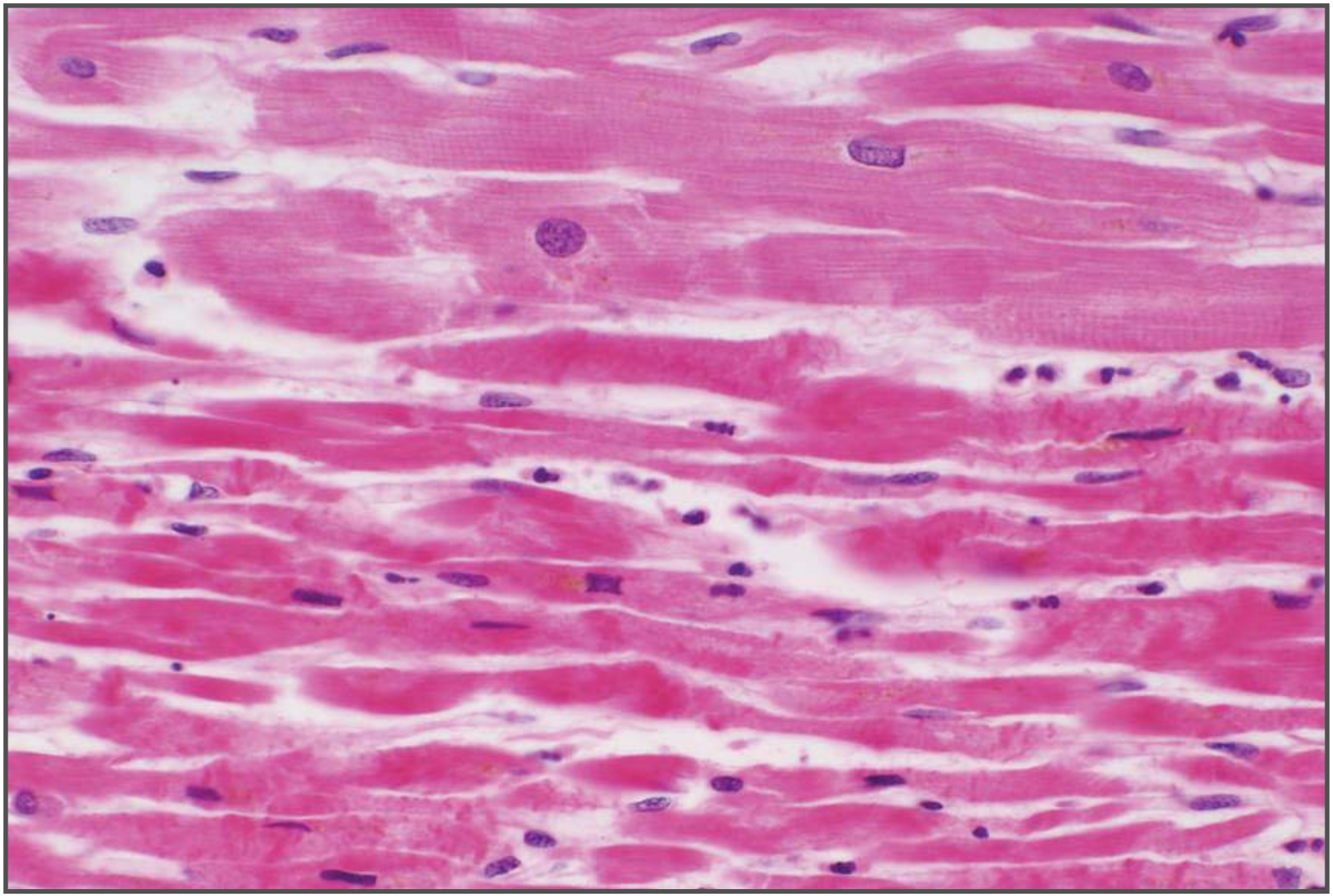


Proia©/DUMC 228

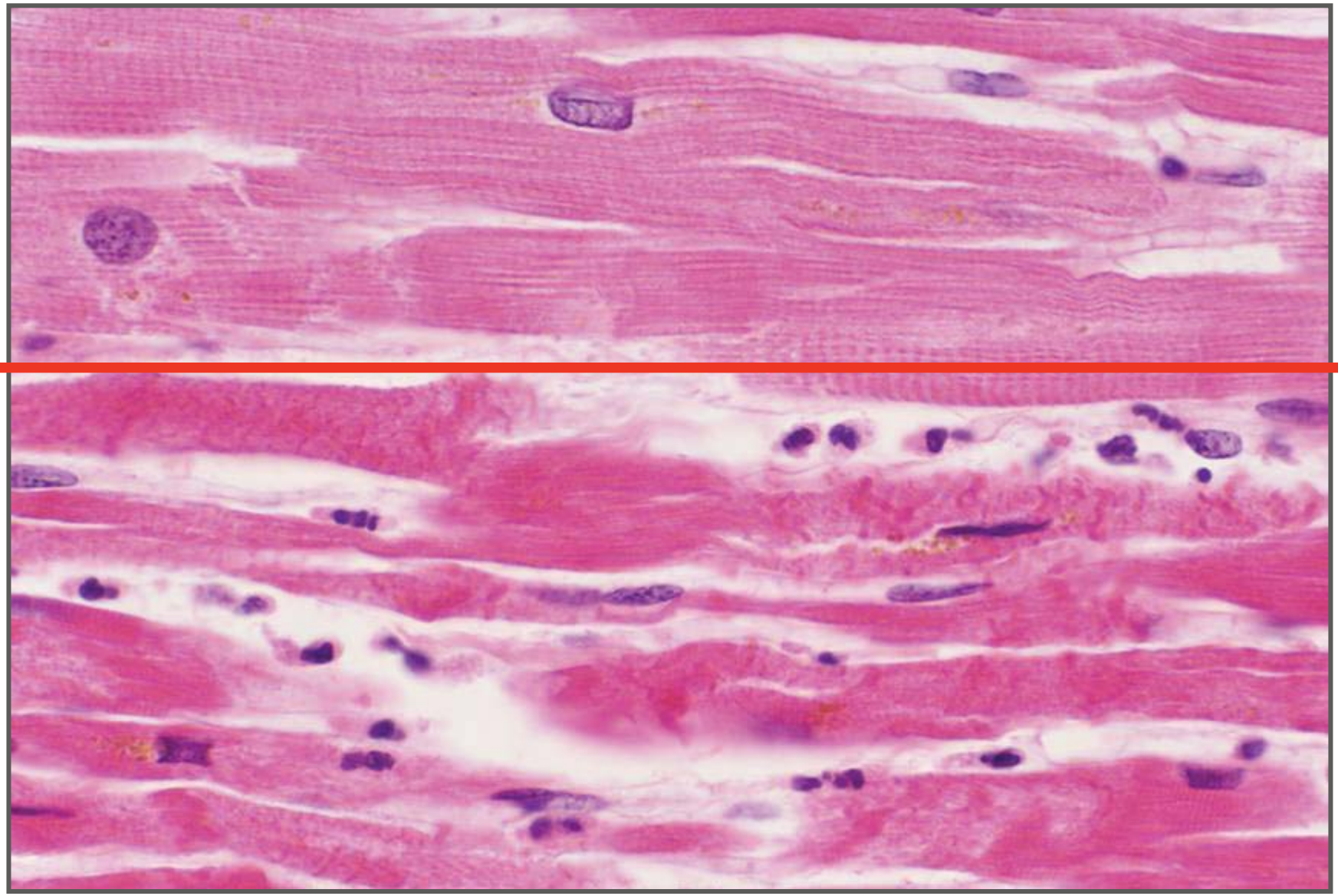
Area of infarct - dark pink



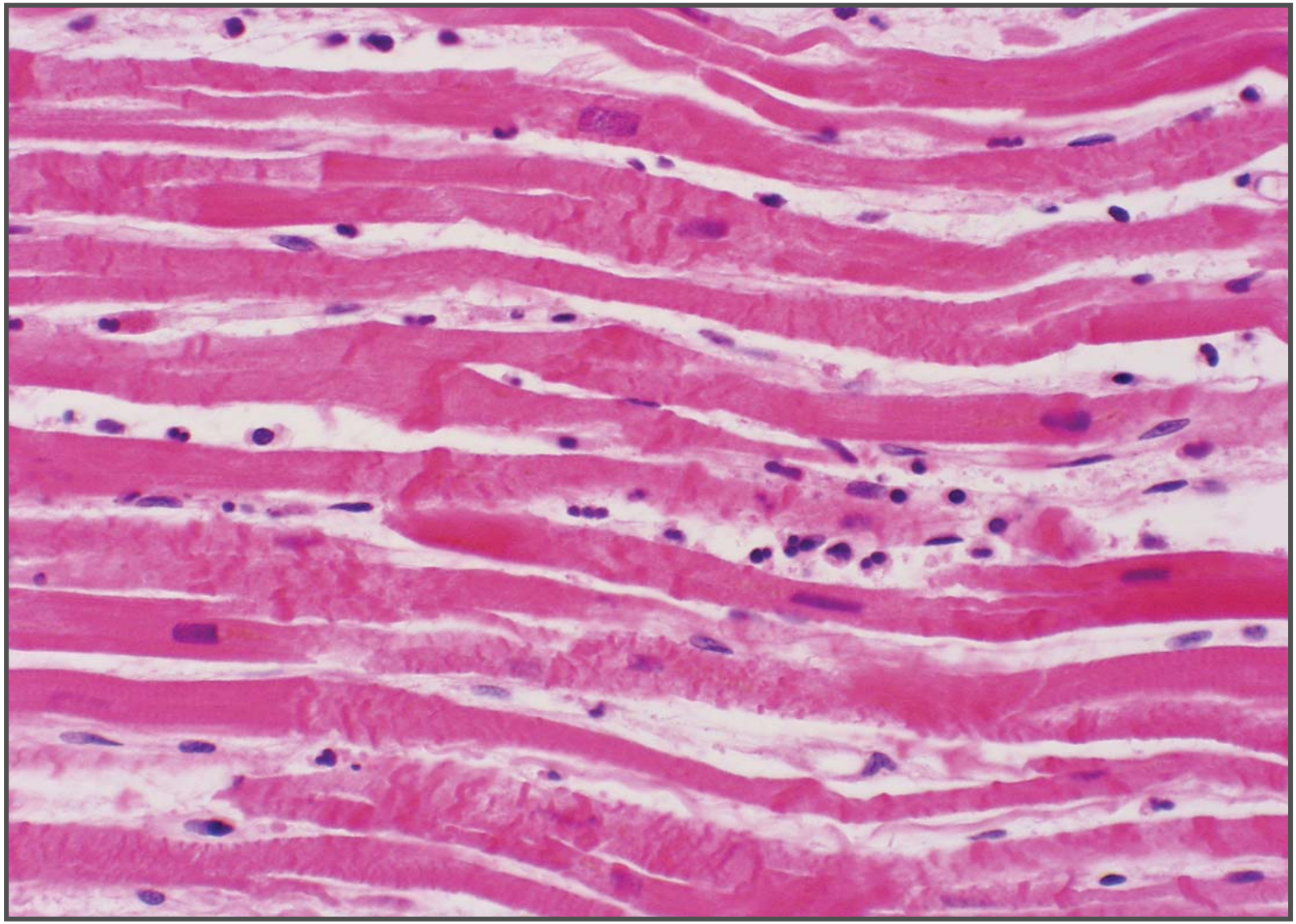
Proia©/DUMC 229



Lots of neutrophils and dying fibers



Proia©/DUMC 231



Proia©/DUMC 232

You still have nuclei in some of the cells so it's a reasonably early necrosis.

MI has very stereotypical process. Use this chart to date the MI, reasonably accurate up to about 7 days

Dating the Age of Myocardial Infarcts

Age	Necrotic Muscle	Neutrophils PMNs	Lymphs	Pigmented Macrophages	Collagen	Vasc. Prolif.
0-12 hr	0	0	0	0	0	0
1 day	++	+	0	0	0	0
2 days	++++	++	+1	0	0	0
3 days	++++	+++	+1	0 to +	0	0
4 days	++++	++++	+1	0 to +	0	0 to +
5 days	++++	++++	+1	0 to +	0 to +	+
6 days	++++	+++	+2	+	0 to +	++
7 days	+++(+)	++	+2	+ to ++	0 to +	++(+)
2 weeks	++	+	+3	+++	+	+++
4 weeks	+	+	+2	++++	++	++++
2 months	+	0	+1	+++	+++	++++
>2 months	+ to 0	0	+1 to 0	+++ to +	++++	+++(+)

Age of the Myocardial Infarct?

A) <12 hours

He was having an MI when he presented. If it had been less than 12 hours, you wouldnt have had that much inflammation.

B) ≈1 day

C) One week

you would have vascular proliferation - not seen in the histology

D) One month

Verdict

- Case settled in favor of plaintiff
  - » Patient was having myocardial infarct when he presented to emergency room
  - » ER doctors did not meet standard of care
    - – No electrocardiogram performed
    - – No cardiac enzymes monitored

Legal Case Study - 2

- **January 26, 2002: Emergency Room** 28 yo Female
  - » **Sudden onset of right flank pain about 1-1½ hours before arrival**
  - » **No fever or chills, dysuria, hematuria**
    - – **Temperature = 98.1°F**
  - » **Radiology: Right kidney stone with moderate to severe obstruction**
  - » **Urinalysis** NORMAL
    - – **pH = 5.0**
    - – **Blood: Negative**
    - – **Nitrite: Negative**
    - – **Leukocyte esterase: Negative**

Legal Case Study - 2

- **January 28, 2002, 2:07 p.m.: Emergency Medical Services**
  - » **Patient on floor, hot to touch, cyanotic with shallow rapid respiration**
  - » **Husband stated "…she was febrile last night"**
- **January 28, 2002: Emergency Room**
  - » **Septic shock: Temperature 105°F (40.6°C), blood pressure 40s/20s, heart rate 133 (5:30 p.m.)**

Neglected to take her to the ER at that time…

Legal Case Study - 2

- **January 28, 2002: Hospital**
  - » **Urinalysis**
    - – **pH = 6.5**
    - – **Blood: Positive**
      - **2-5 RBC**
    - – **Nitrite: Negative**
    - – **Leukocyte esterase: Positive**
      - **25-50 WBC**
  - » **Cultures of urine and blood positive for *Proteus mirabilis***
  - » **Dead at 10 p.m. from "overwhelming sepsis with septic shock"**

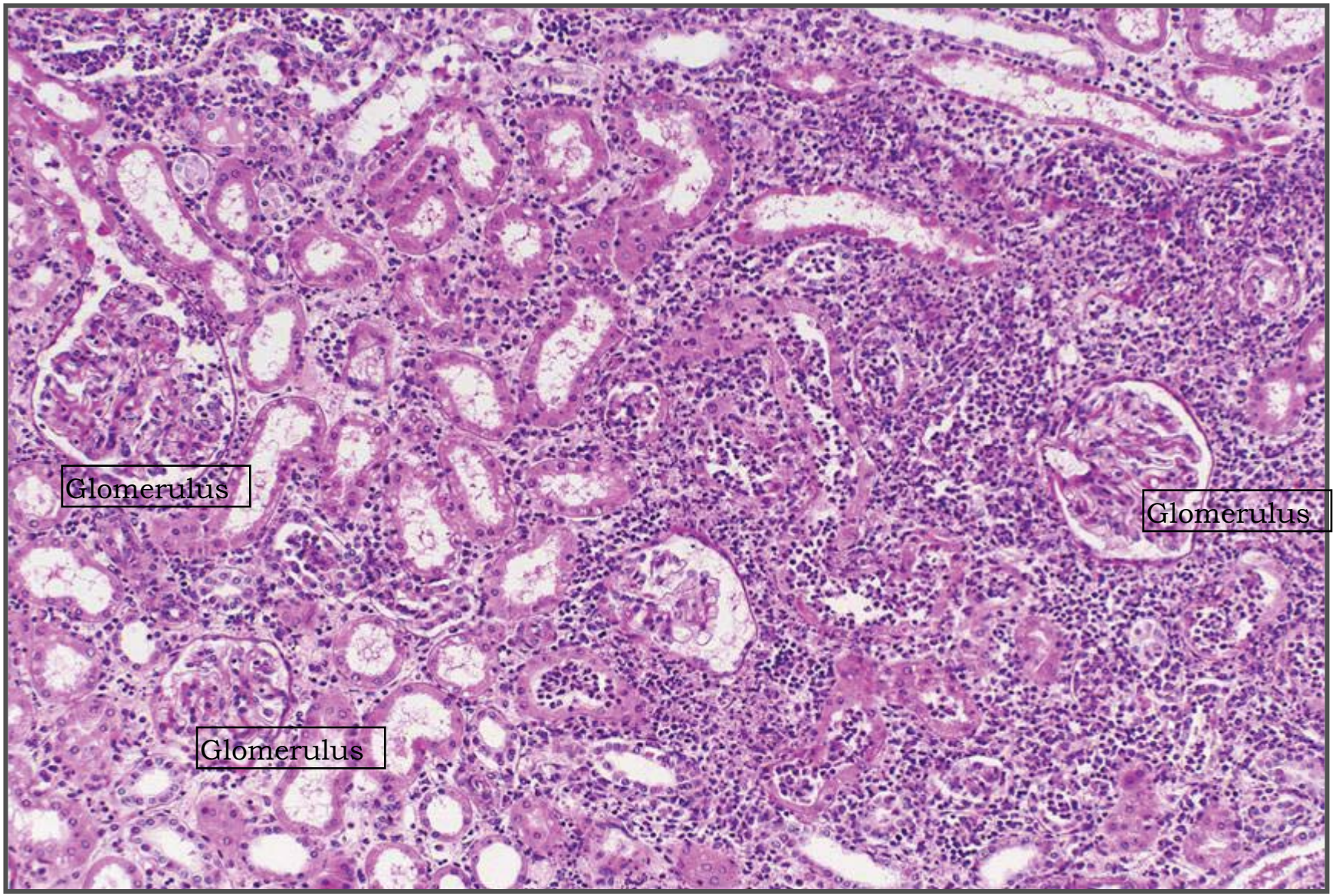
- **Urinalysis 01/26/2002**
  - » **pH = 5.0**
  - » **Blood: Negative**
  - » **Nitrite: Negative**
  - » **Leukocyte esterase: Negative**

- **Urinalysis 01/28/2002**
  - » **pH = 6.5**
  - » **Blood: Positive**
    - – **2-5 RBC**
  - » **Nitrite: Negative**
  - » **Leukocyte esterase: Positive**
    - – **25-50 WBC**

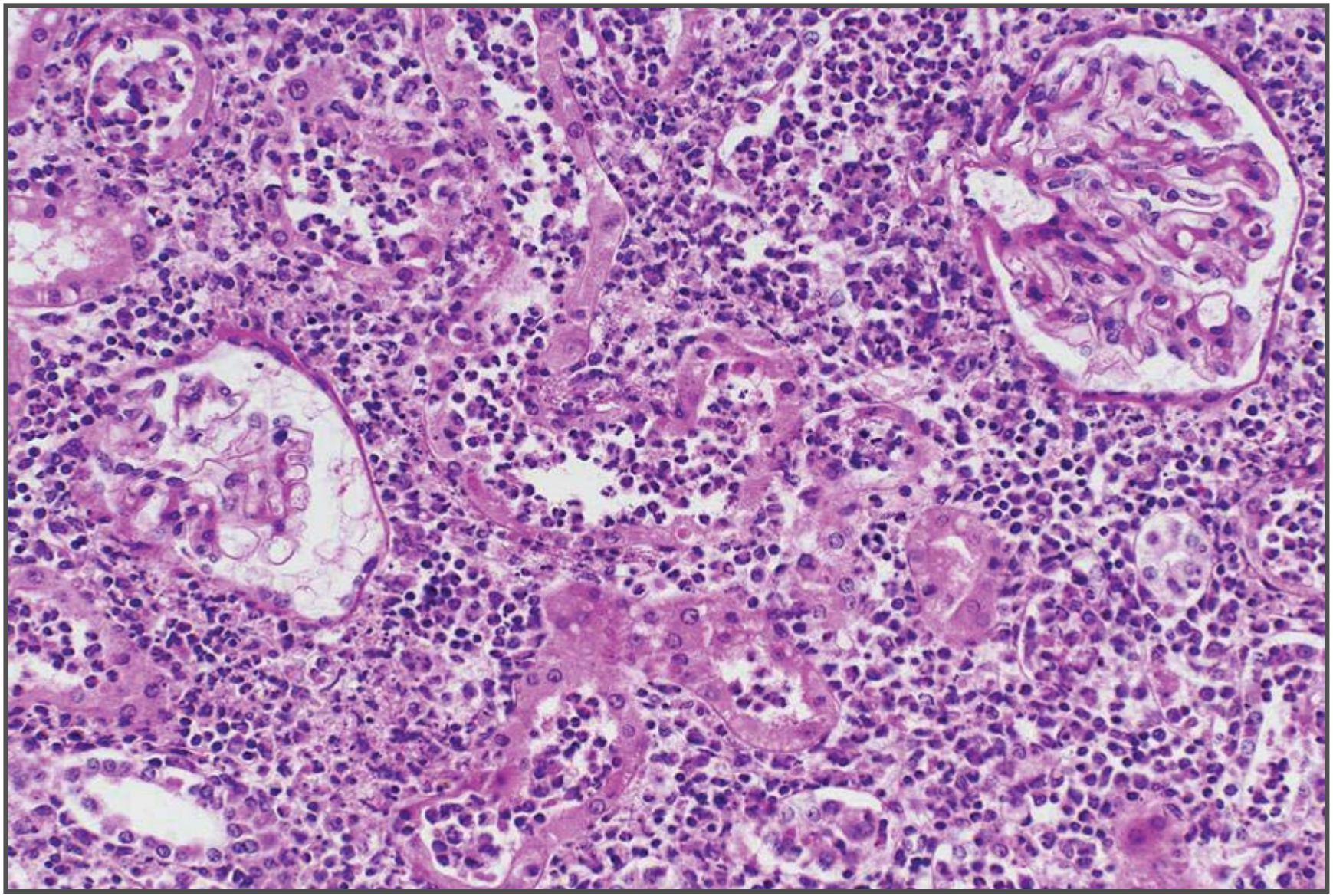
When she was in the ER earlier, she had a normal urinalysis. 2 days later her urine ph increased - typical of PROTEUS. She is also pyuric.

Legal Issues

- **Cause of death?**
  - » **Source of septic shock**
    - – **Urinary bladder**
    - – **Kidney infection (pyelonephritis)**
- **Did the patient have a kidney infection at the time of her emergency room visit on January 26, 2002?**

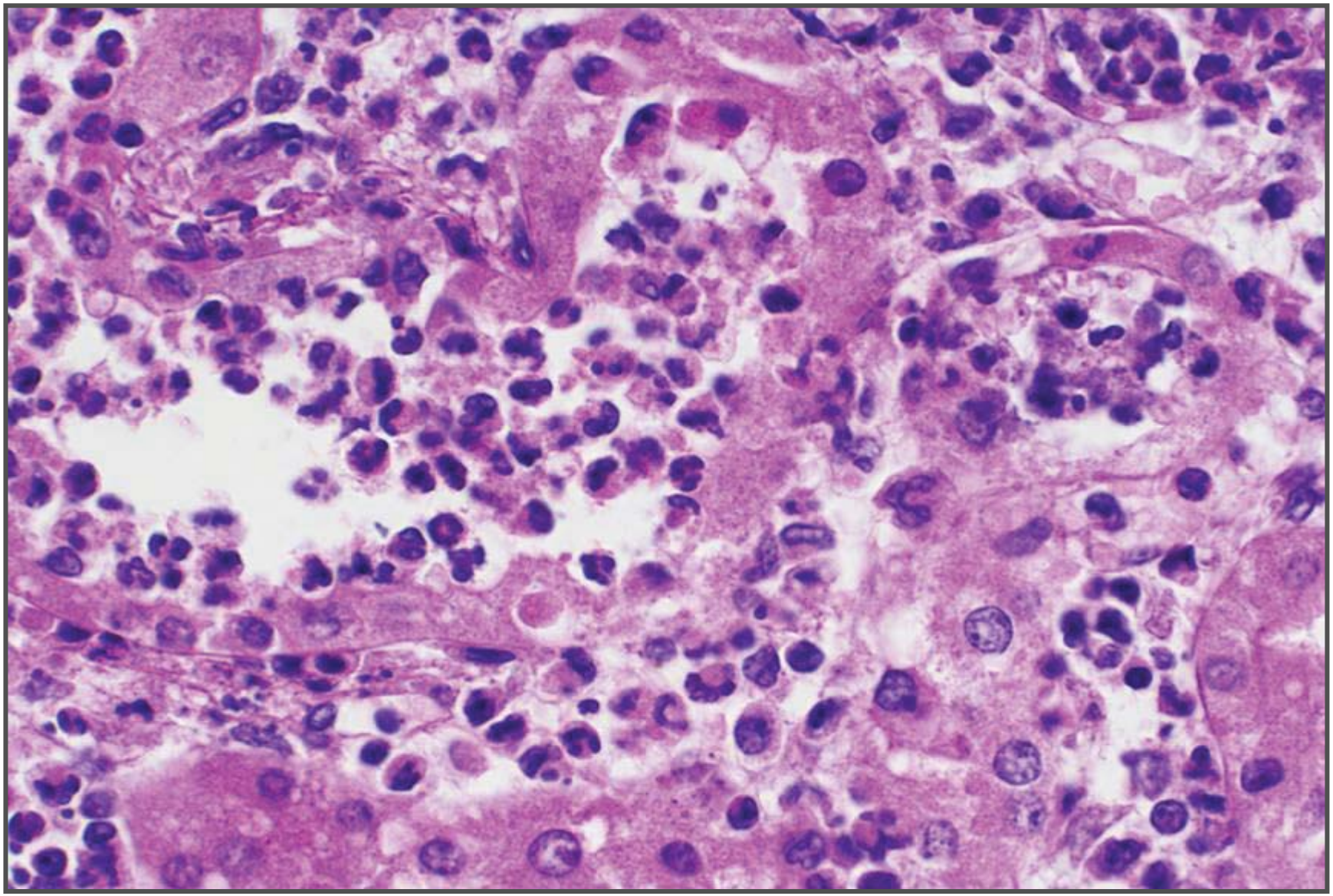


Her kidney. Inflammation all around



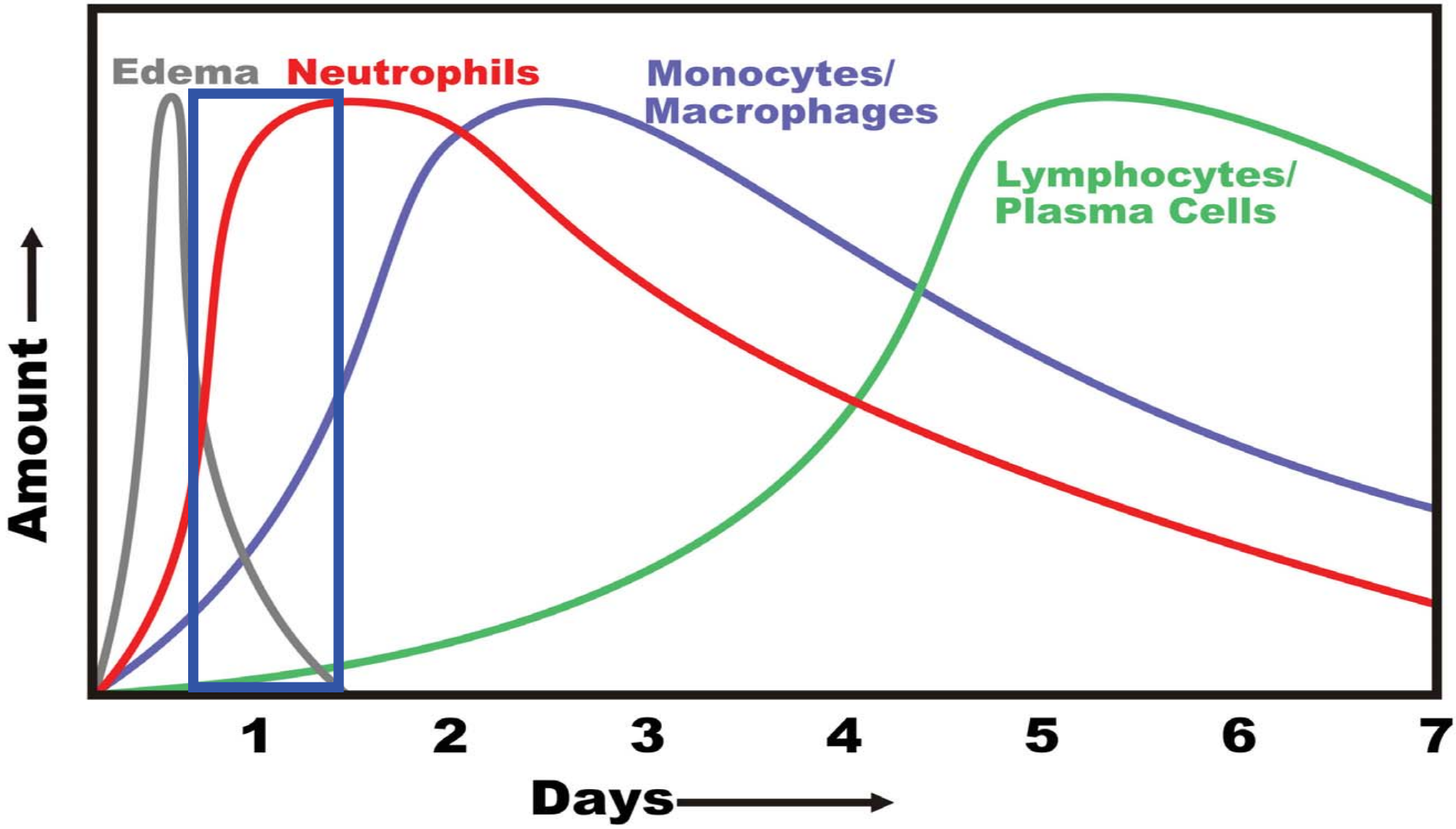
Proia©/DUMC 242

Tubules loaded with inflammatory cells - WHAT TYPE?



Proia©/DUMC 243

All neutrophils (many of them are breaking down)! Use this information to date the inflammation



Neutrophils predominate BEFORE day 2. So she did not have pyelonephritis when she presented. She had a stone, then developed pyelo

Age of the Pyelonephritis?

A) ≈1 day

B) 2 days

C) One week

My Conclusions

- The patient's death was the result of sepsis from acute pyelonephritis
- The pyelonephritis developed about one day prior to death, i.e., after her visit to the emergency room
  - » Development of fever the night before her death
  - » Normal urinalysis in ER
  - » Histology of kidney infection

Verdict

- **Jury awarded $2.88 million to husband**
  - » **Defendant doctor testified that he had changed his clinical practice after the patient's death**
    - – **De facto admission that he had rendered an incorrect clinical diagnosis**

If the doc hadn't said this, he wouldn't have lost - the evidence suggested that he was not at fault

Q/A - Sarcoidosis is a diagnosis of exclusion. Hylar enlarged nodes in the chest --> send pt to opthamologist because sarcoids usually occur in conjuctiva, easier to biopsy than chest. Pattern of granuloma, stain for microorganisms - presumptive diagnosis of sarcoidosis.

Triangle Christian Medical Fellowship

- Local branch of the Christian Medical and Dental Association
- Non-denominational
- Monthly meetings on Saturday at 6 pm, Mt. Moriah Baptist Church, Erwin Road (http://maps.google.com/maps?hl=en&q=Mt.%20Moriah%20Baptst%20Church)
- Next meeting – February 19, 2011: Dr. Alan Carlson, Duke Ophthalmology
- More information: http://www.trianglecmf.org/