

Liver Forum 12

Disease Assessment Strategies to Accelerate Drug Development

Assessment of Inflammation: Portal/ Septal Inflammation vs. Lobular

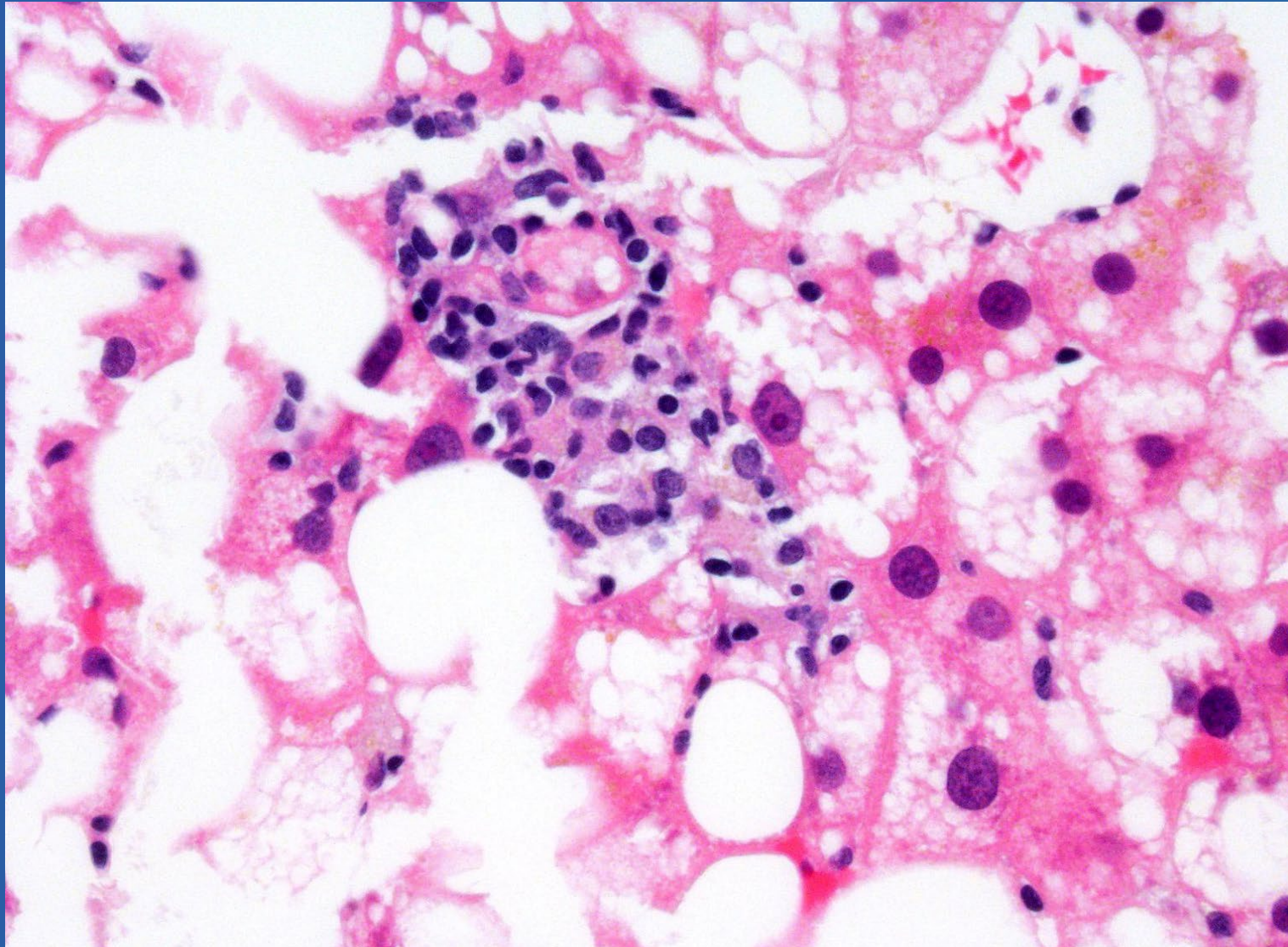
David E. Kleiner, MD, PhD

Laboratory of Pathology/Center for Cancer Research

Assessment of Lobular Inflammation



THE FORUM
For Collaborative ResearchSM



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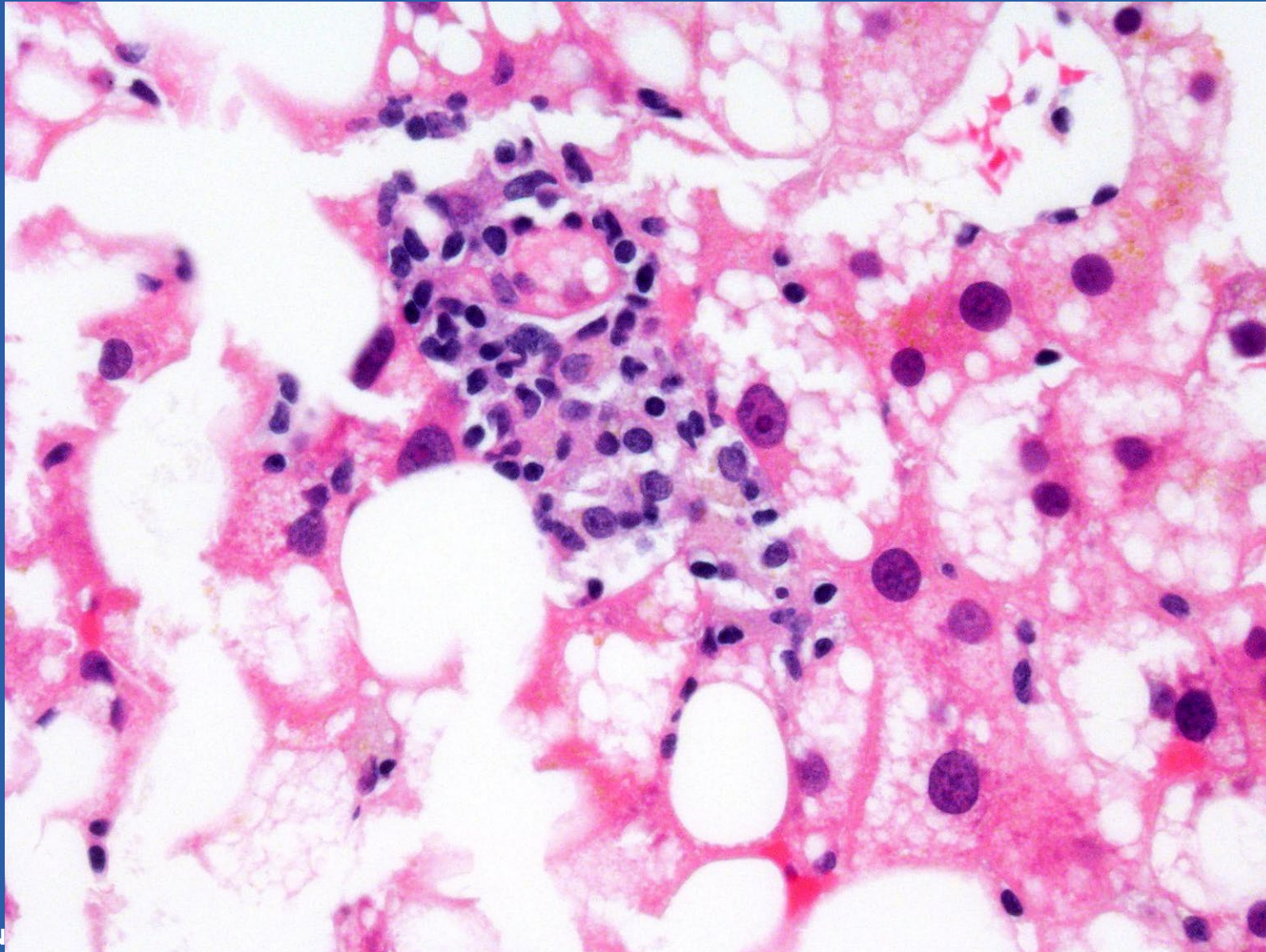
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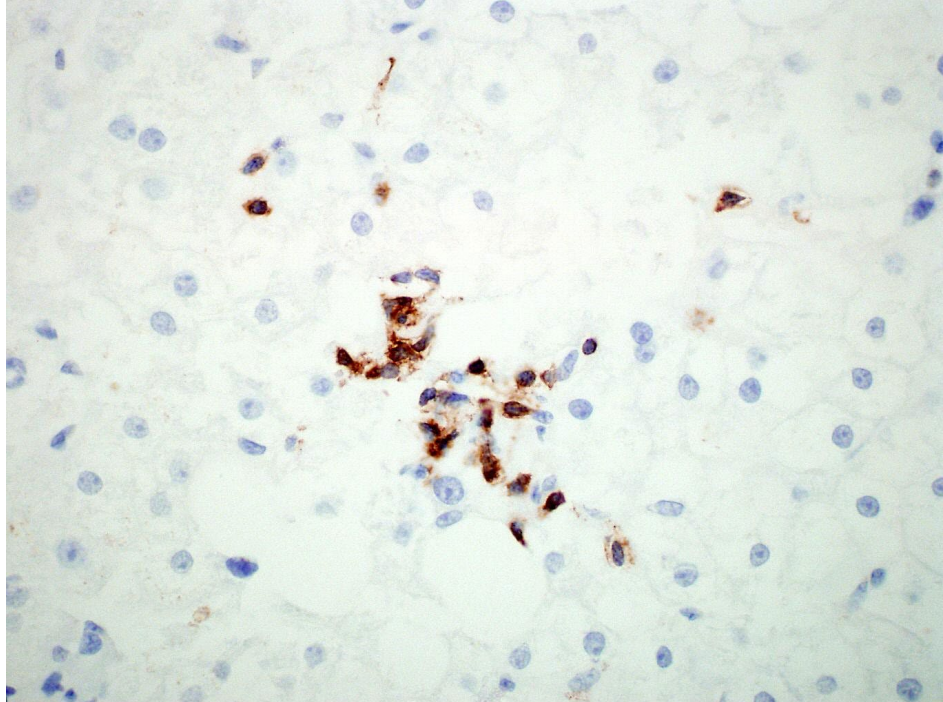


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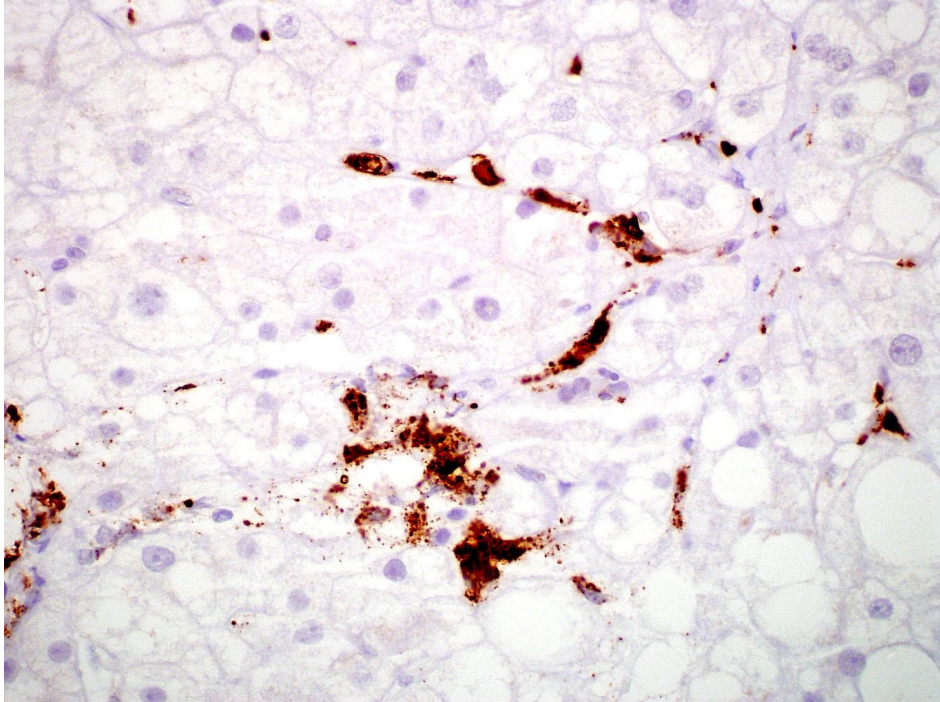




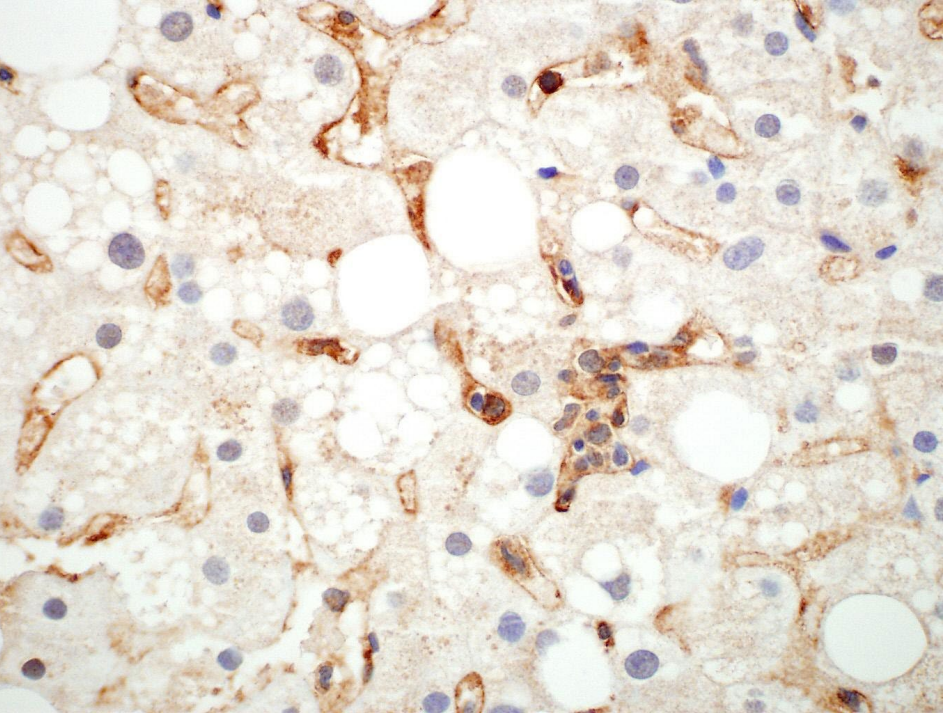
CD3



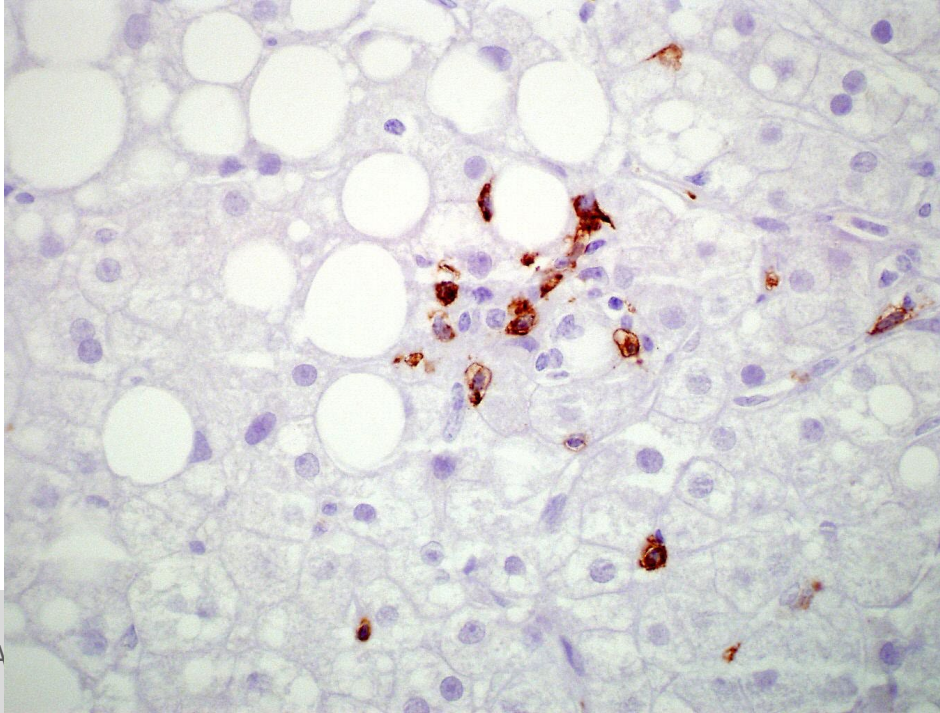
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Scoring methods for lobular inflammation

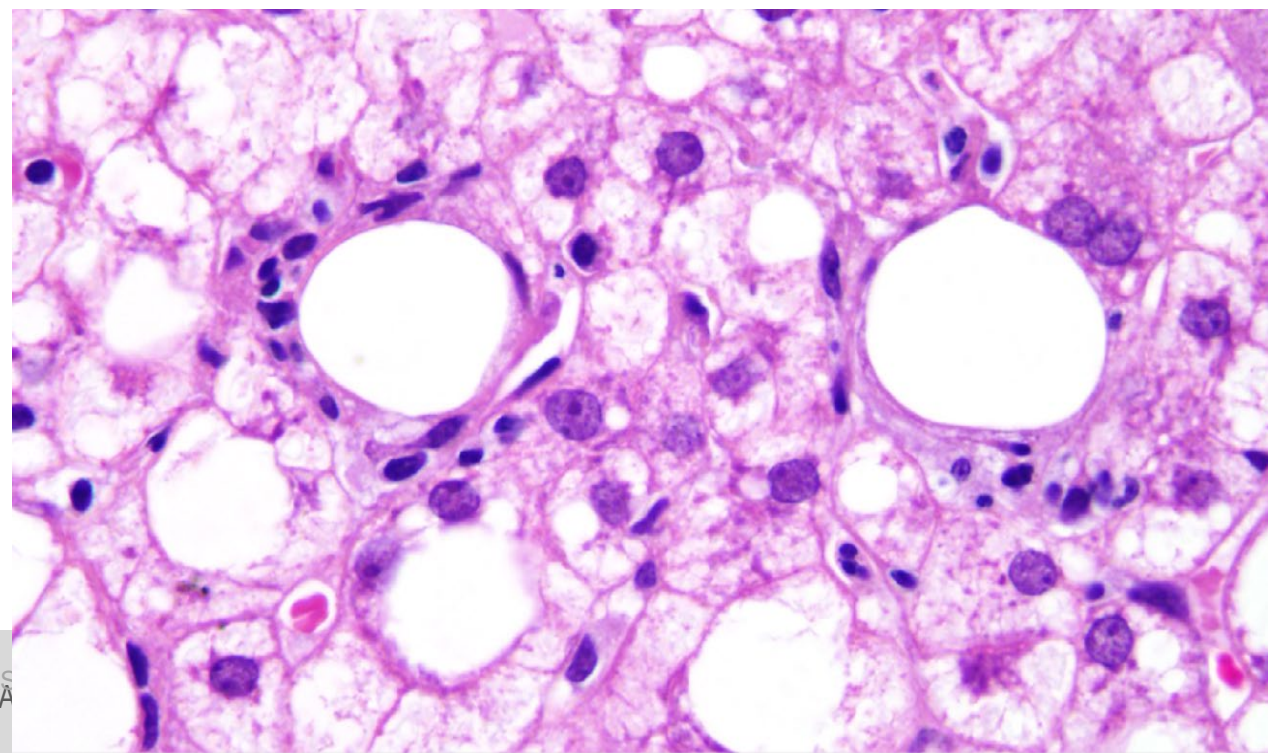
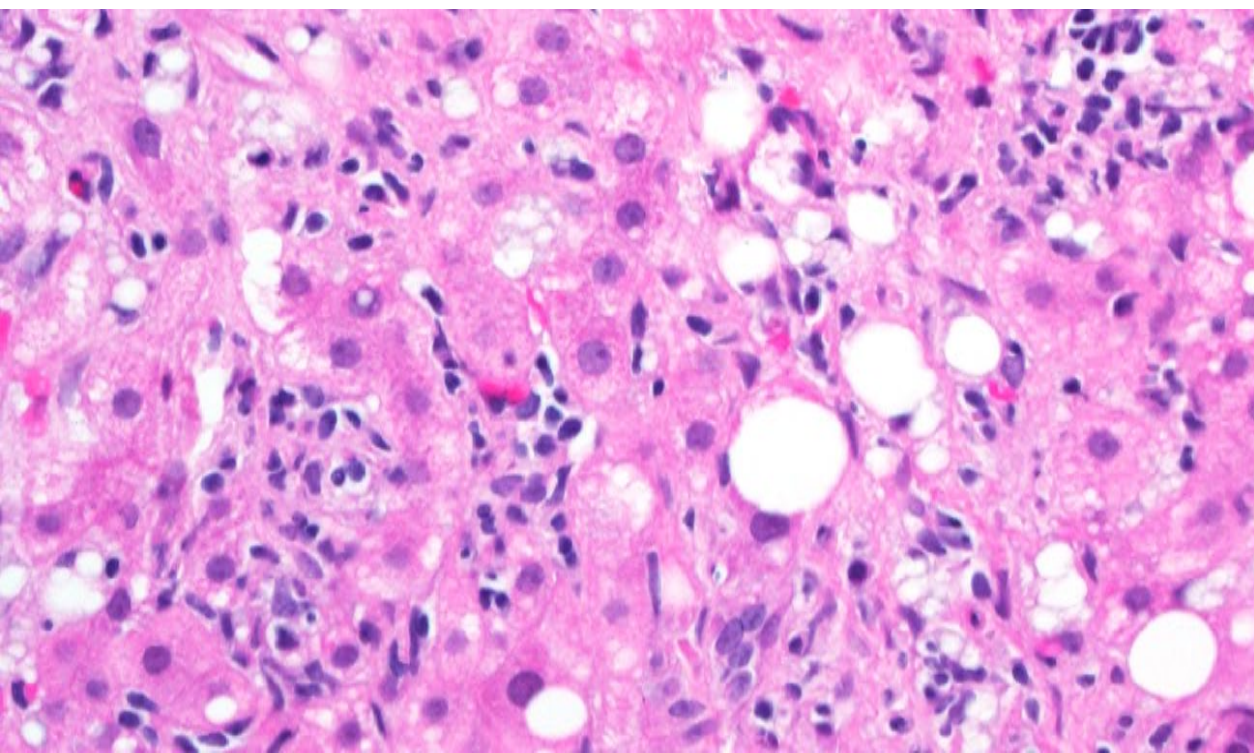
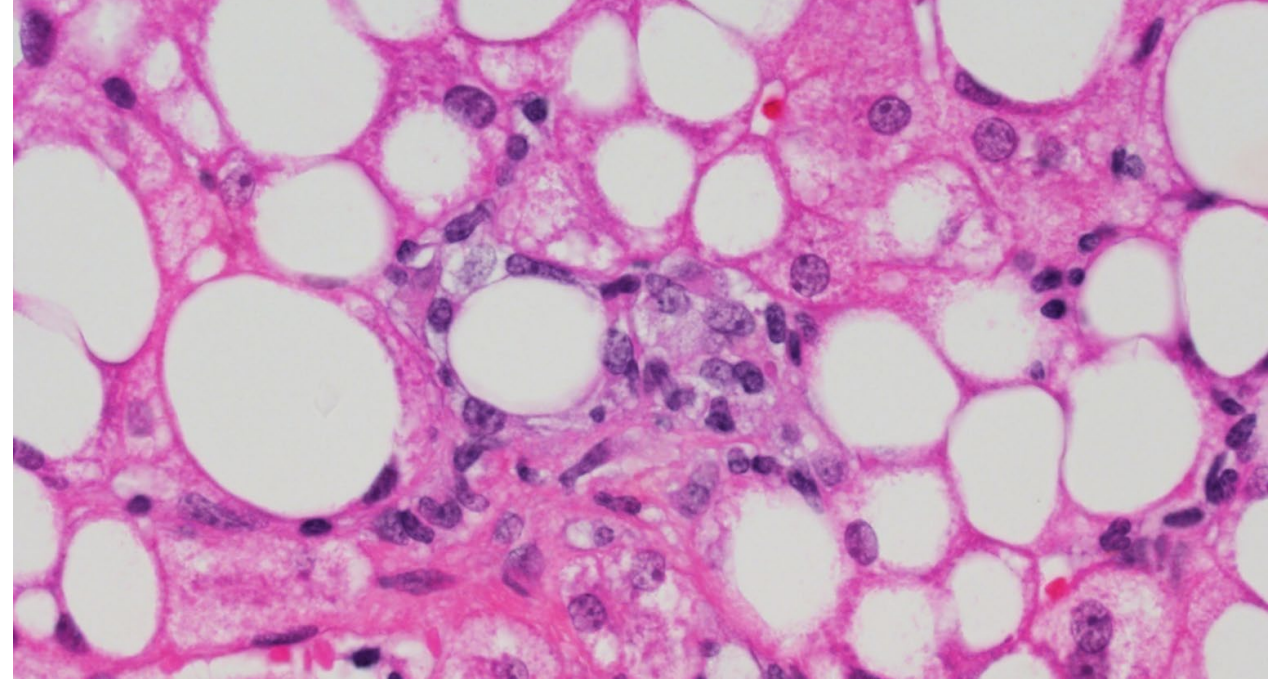
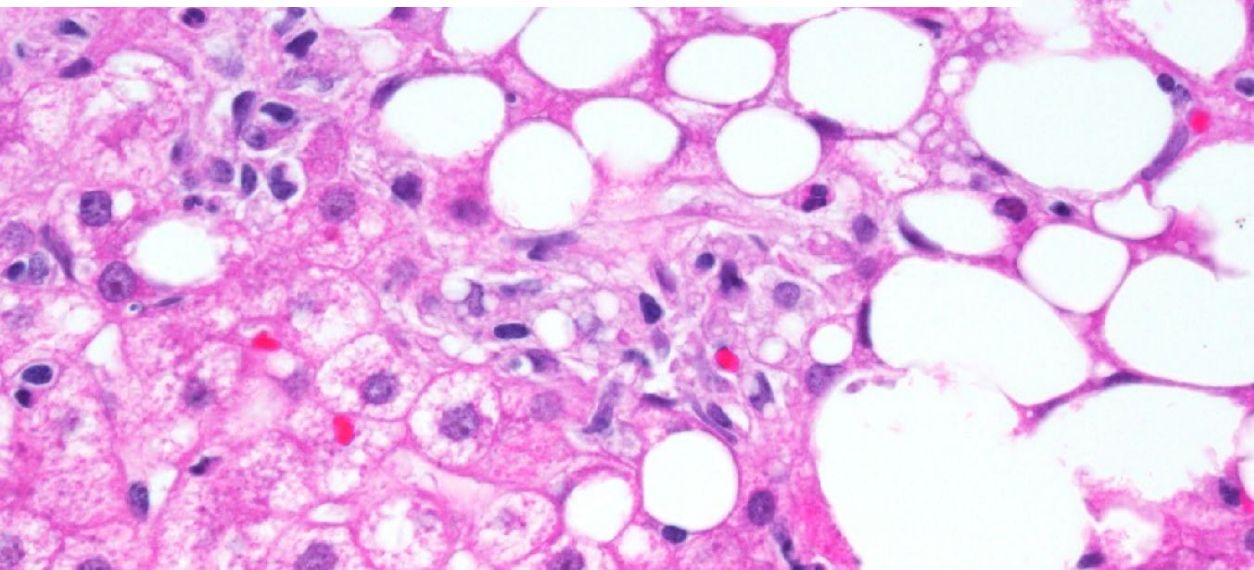
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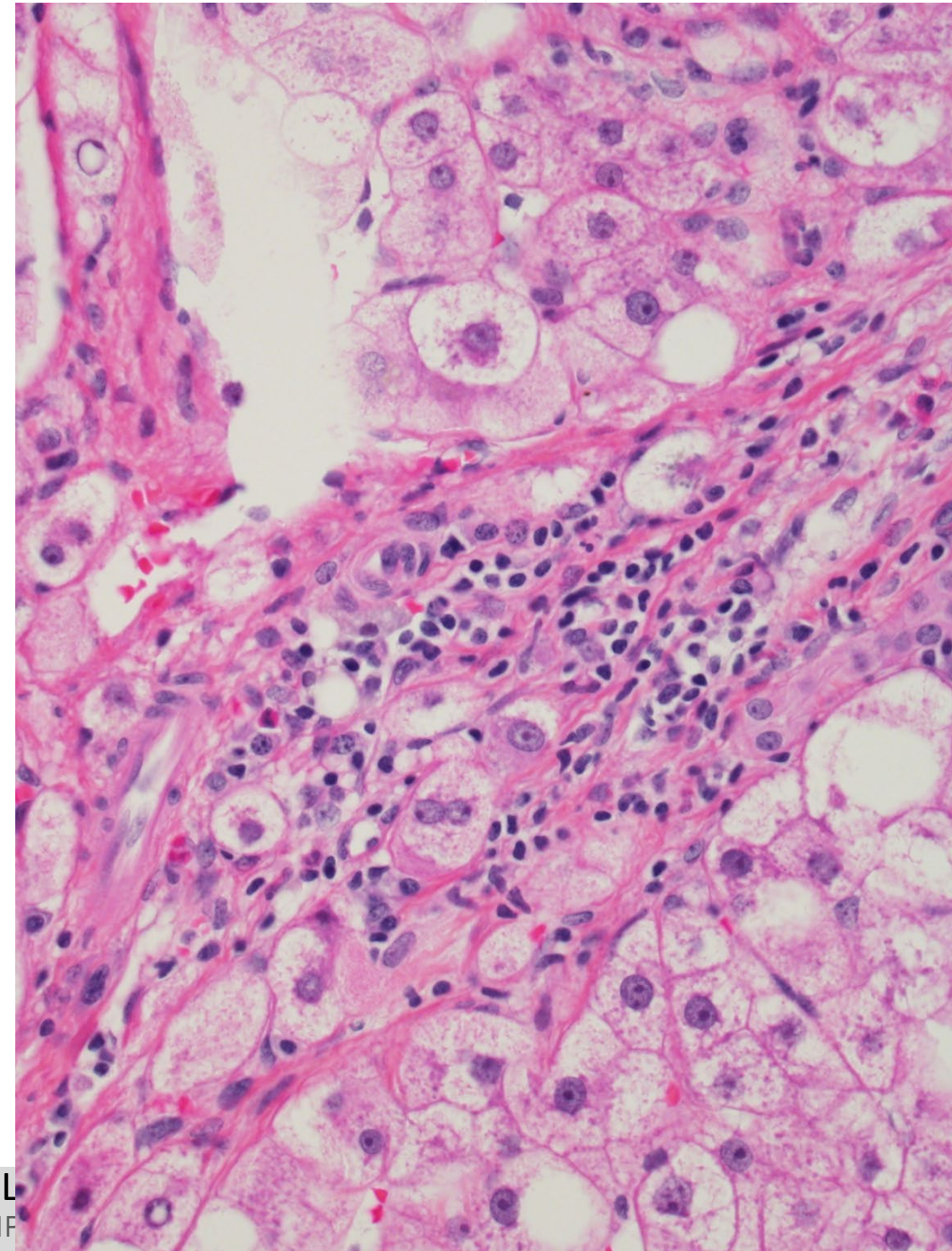
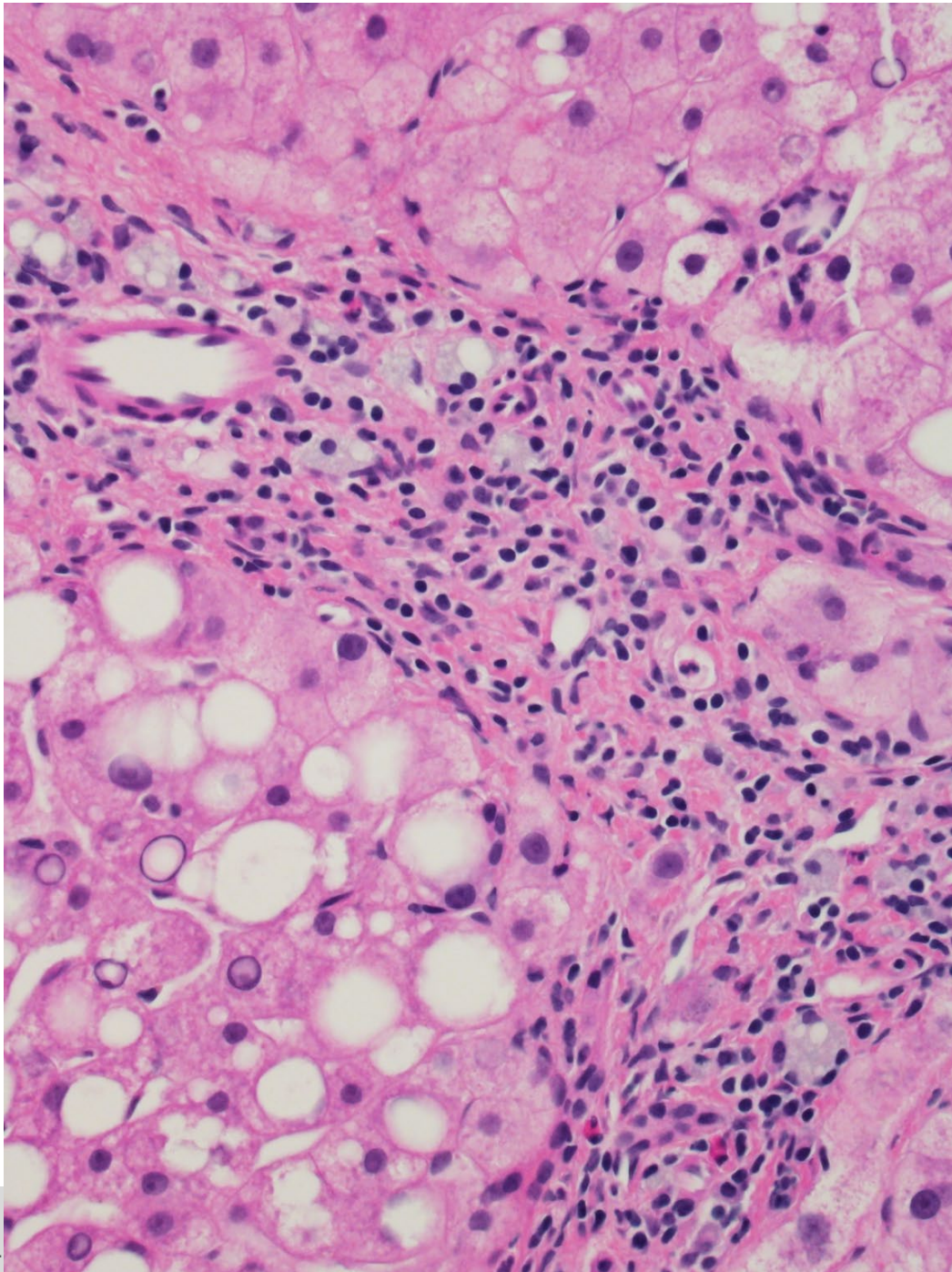
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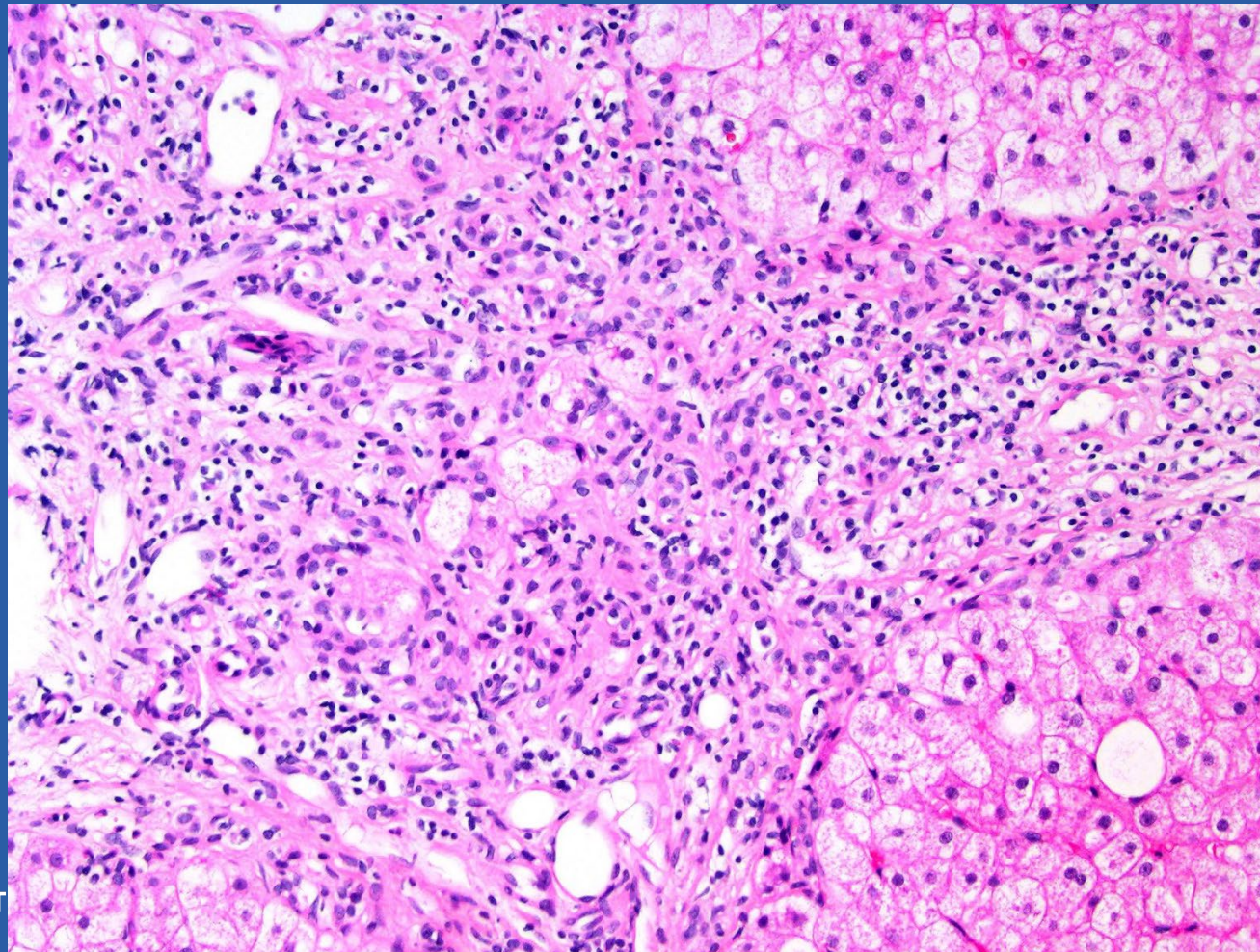
Lobular Inflammation



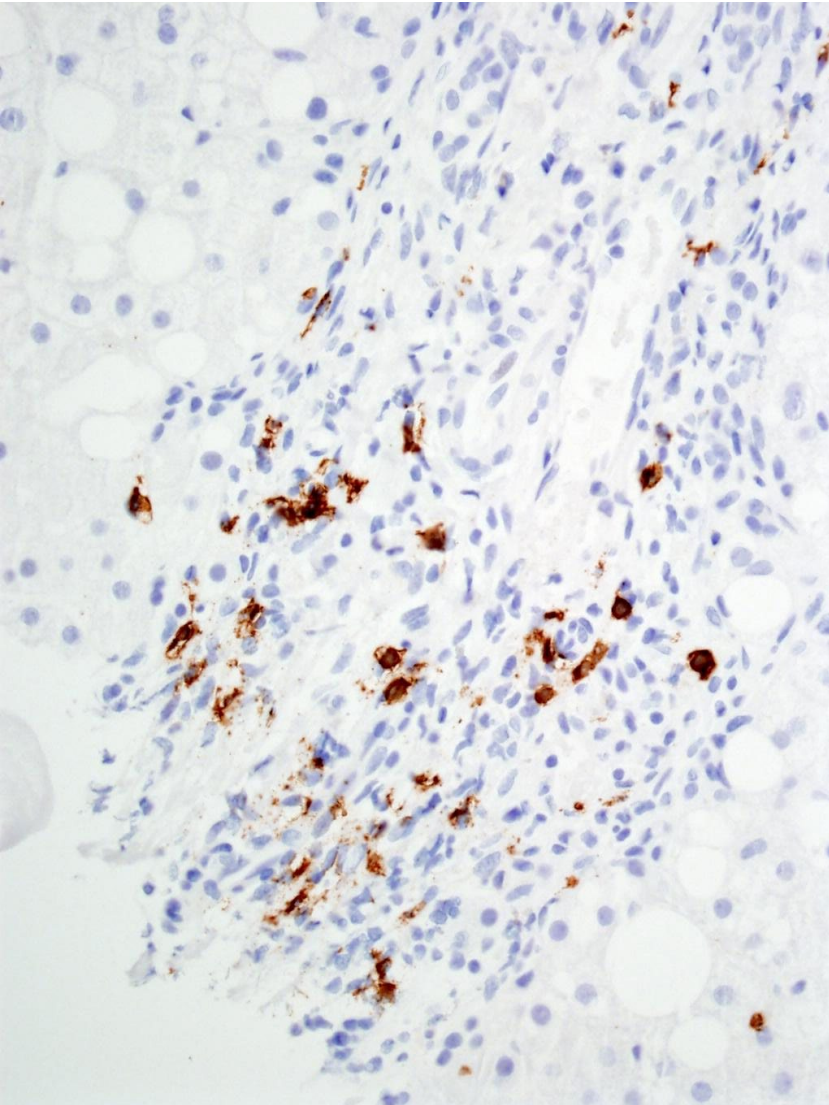
Zone 3
Parenchymal
Inflammation
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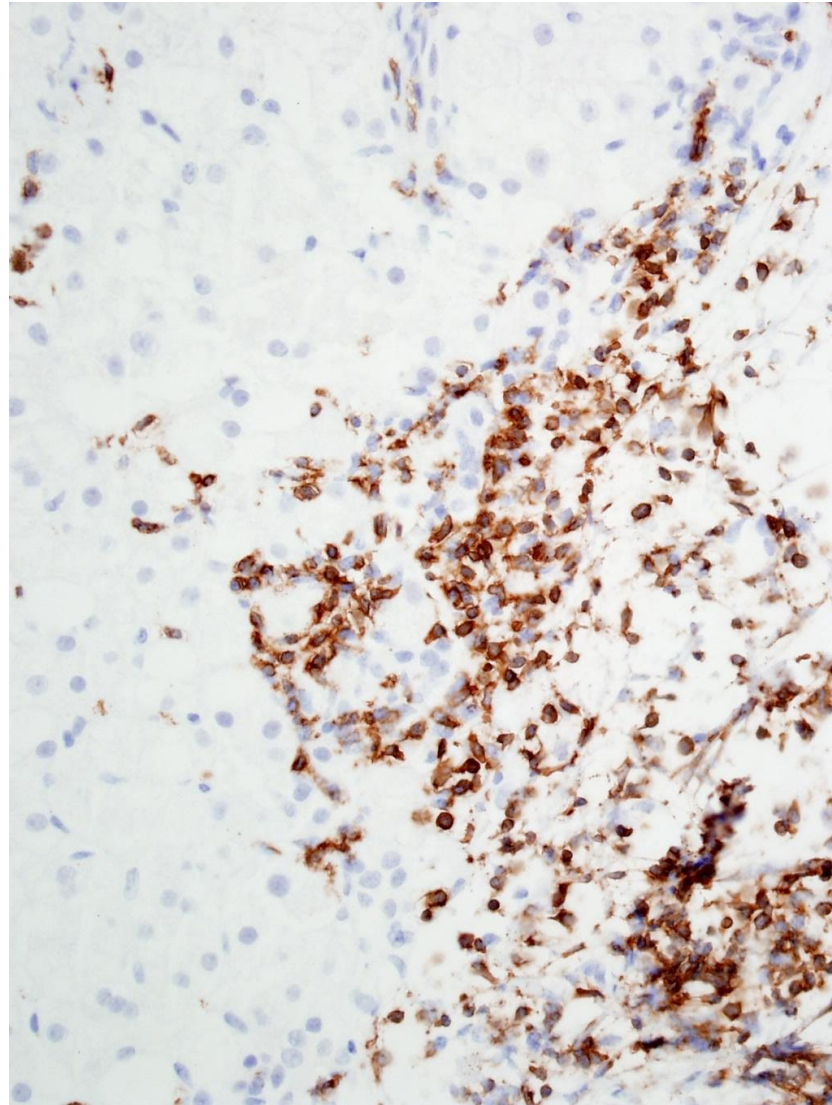
What About Portal Inflammation (and Interface Hepatitis)



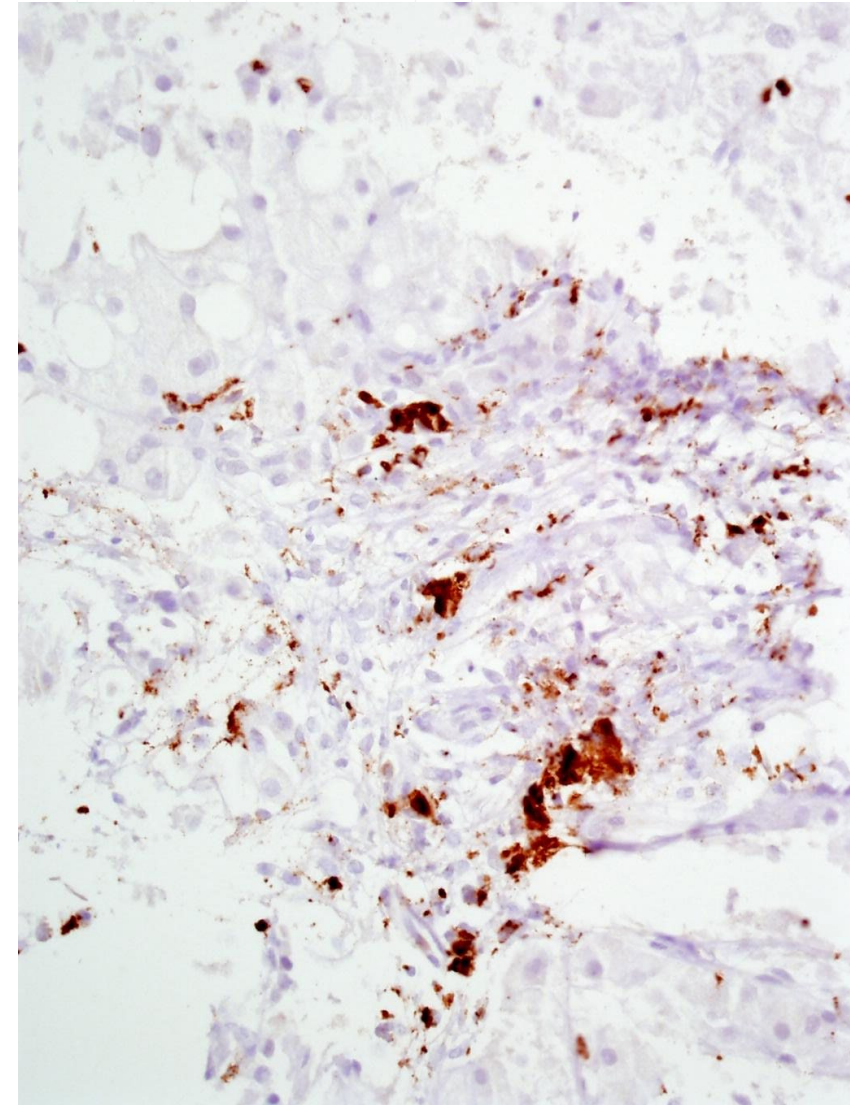
CD20



CD3



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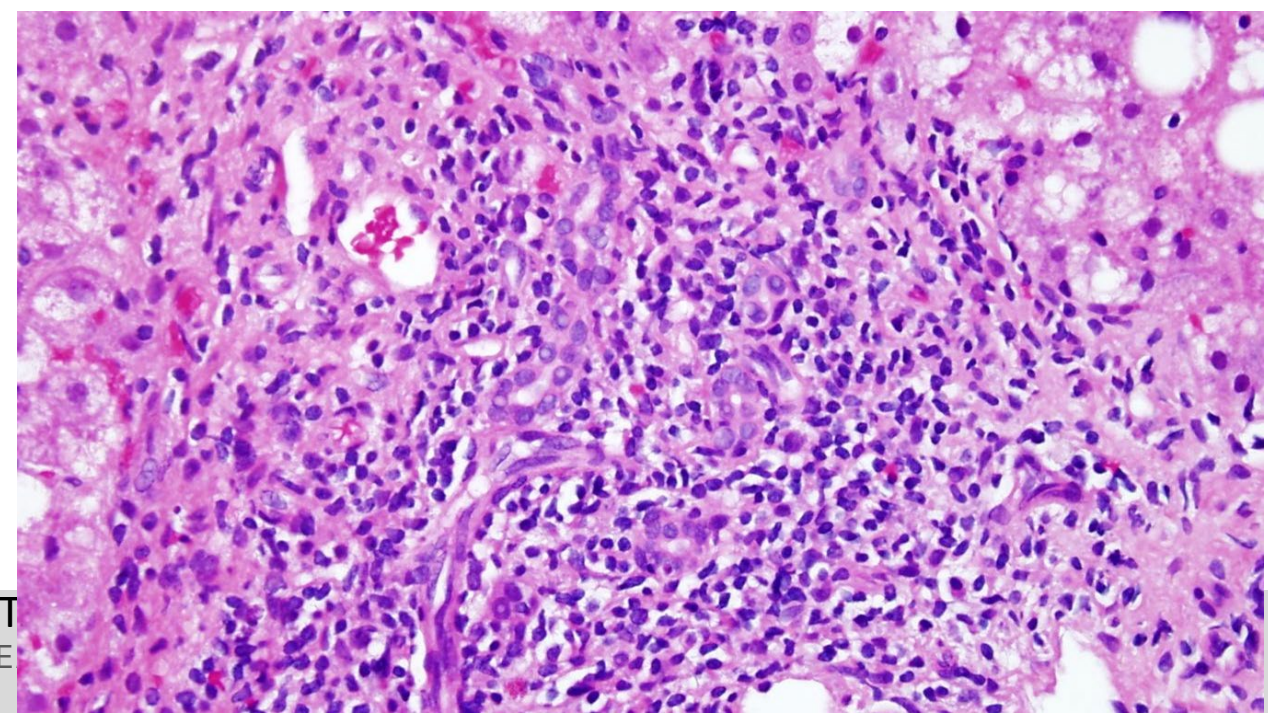
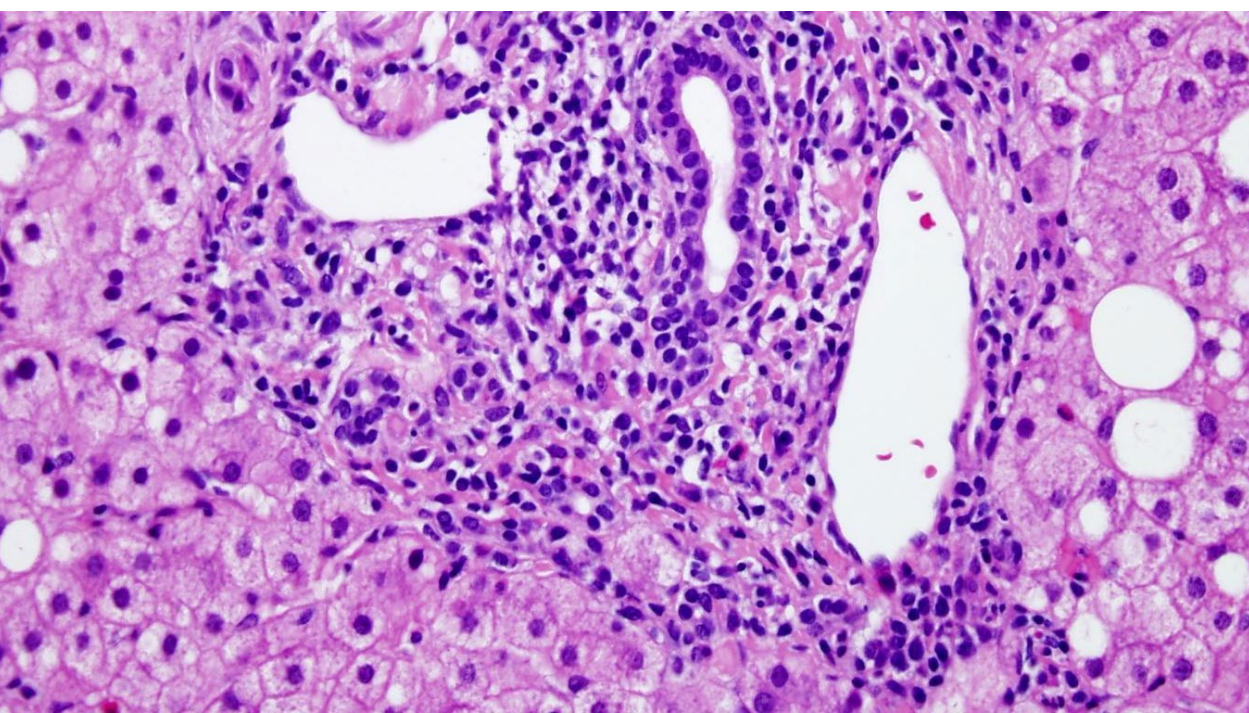
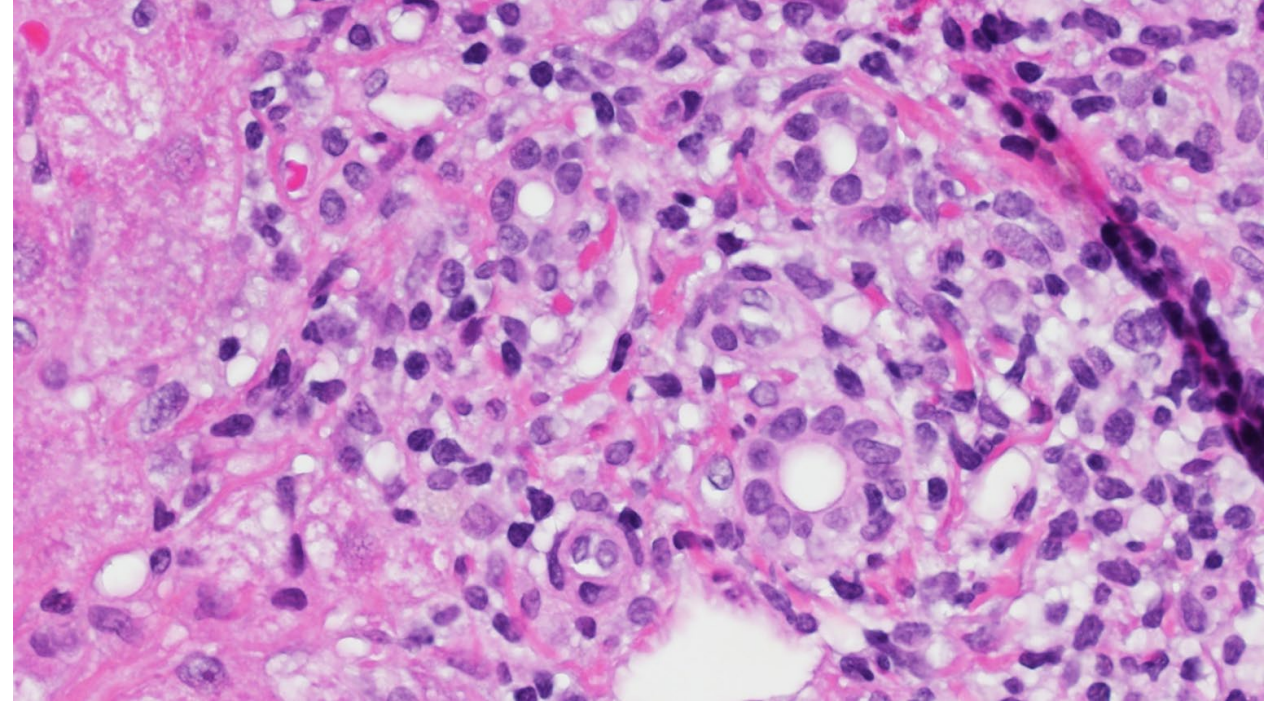
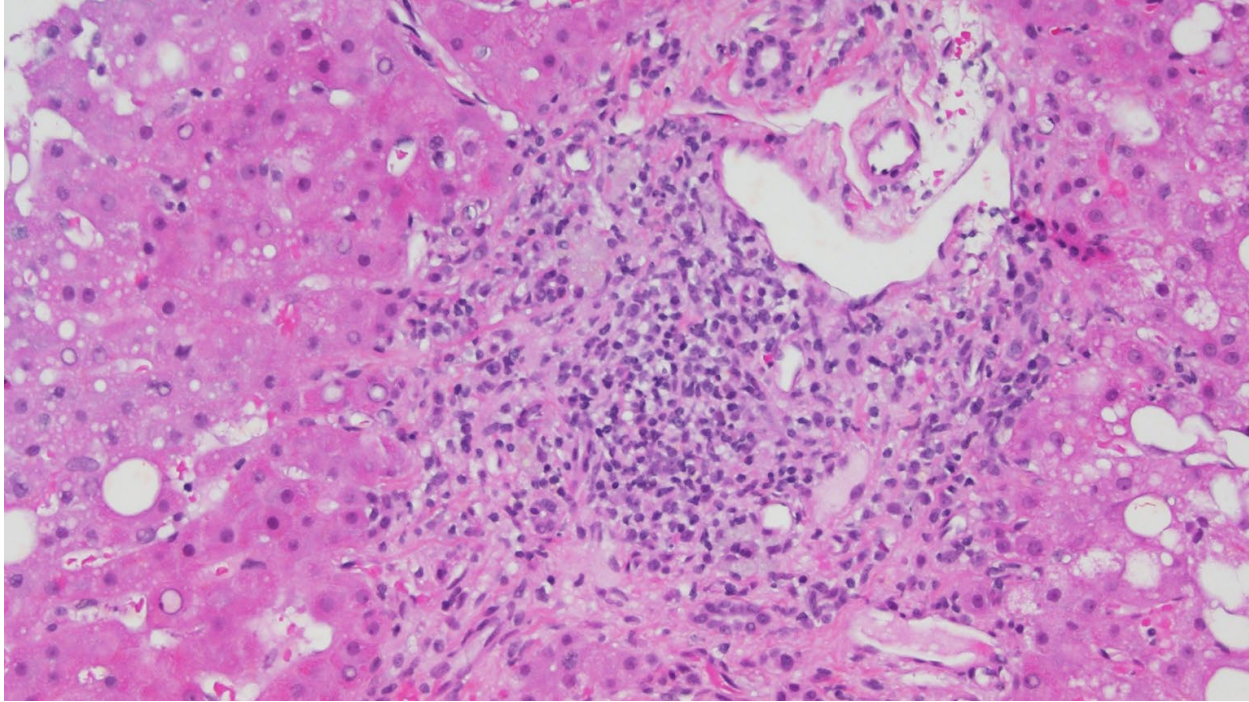
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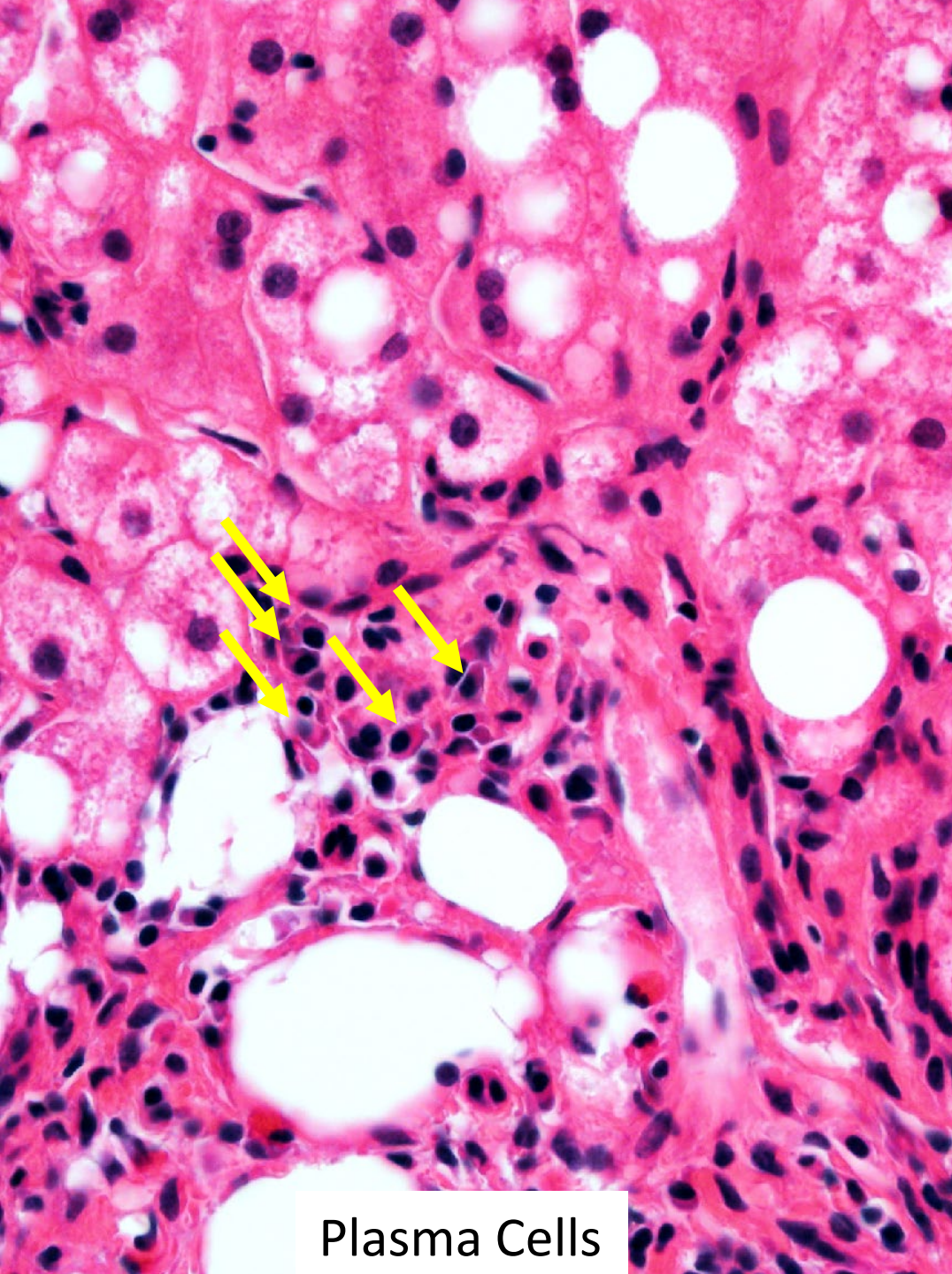
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Challenges and unanswered questions in assessing portal/septal inflammation

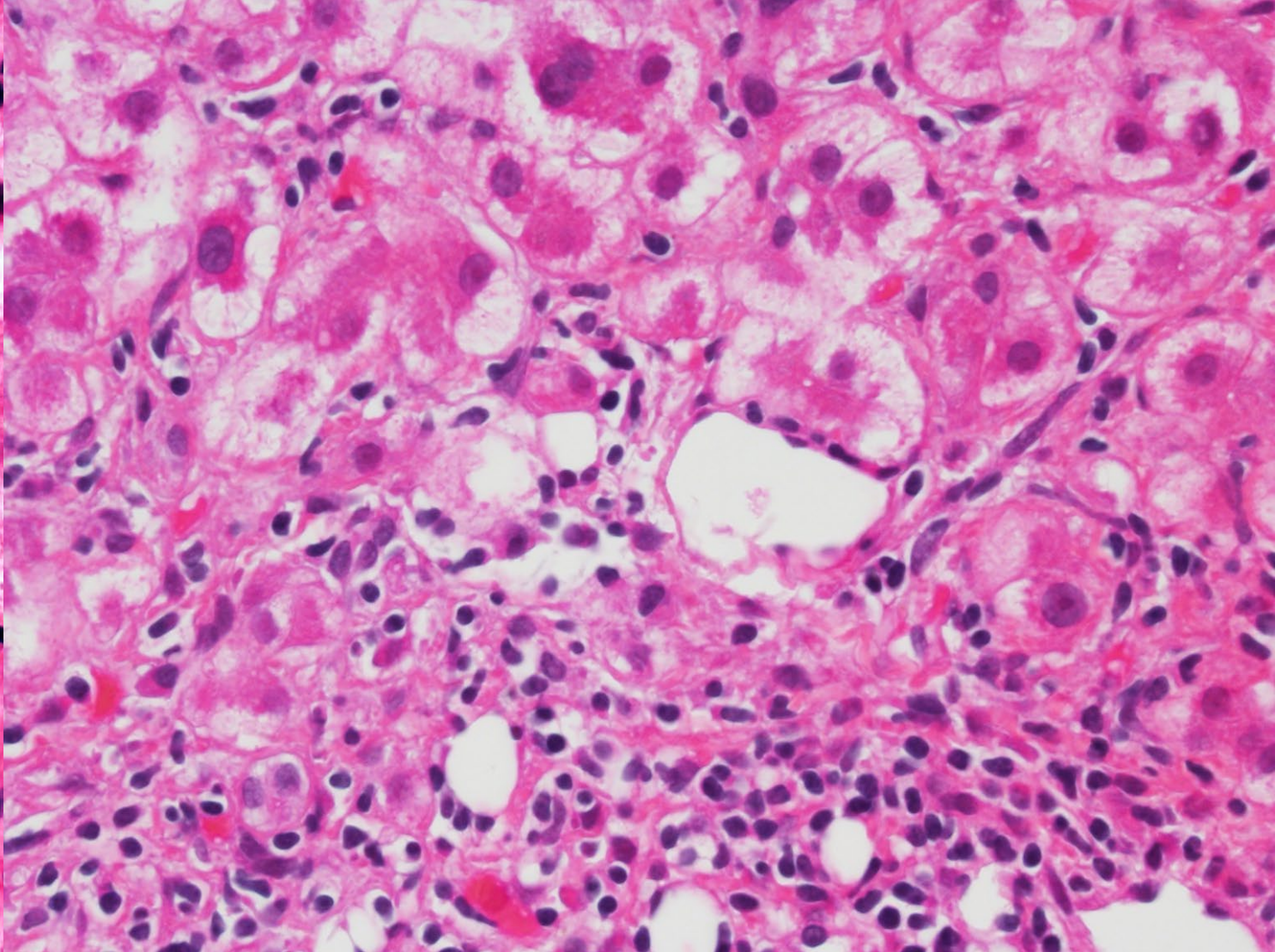
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ST
ESE



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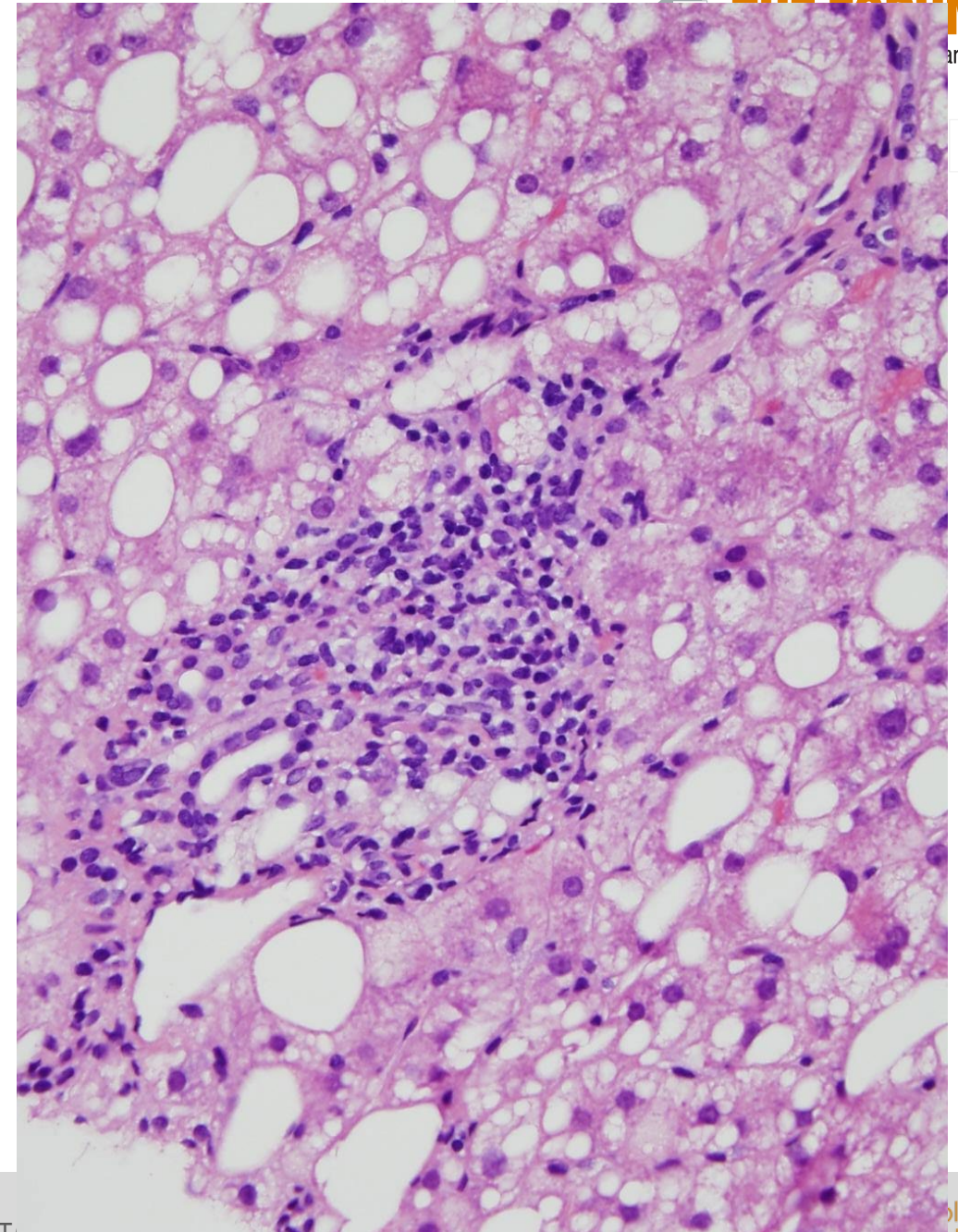
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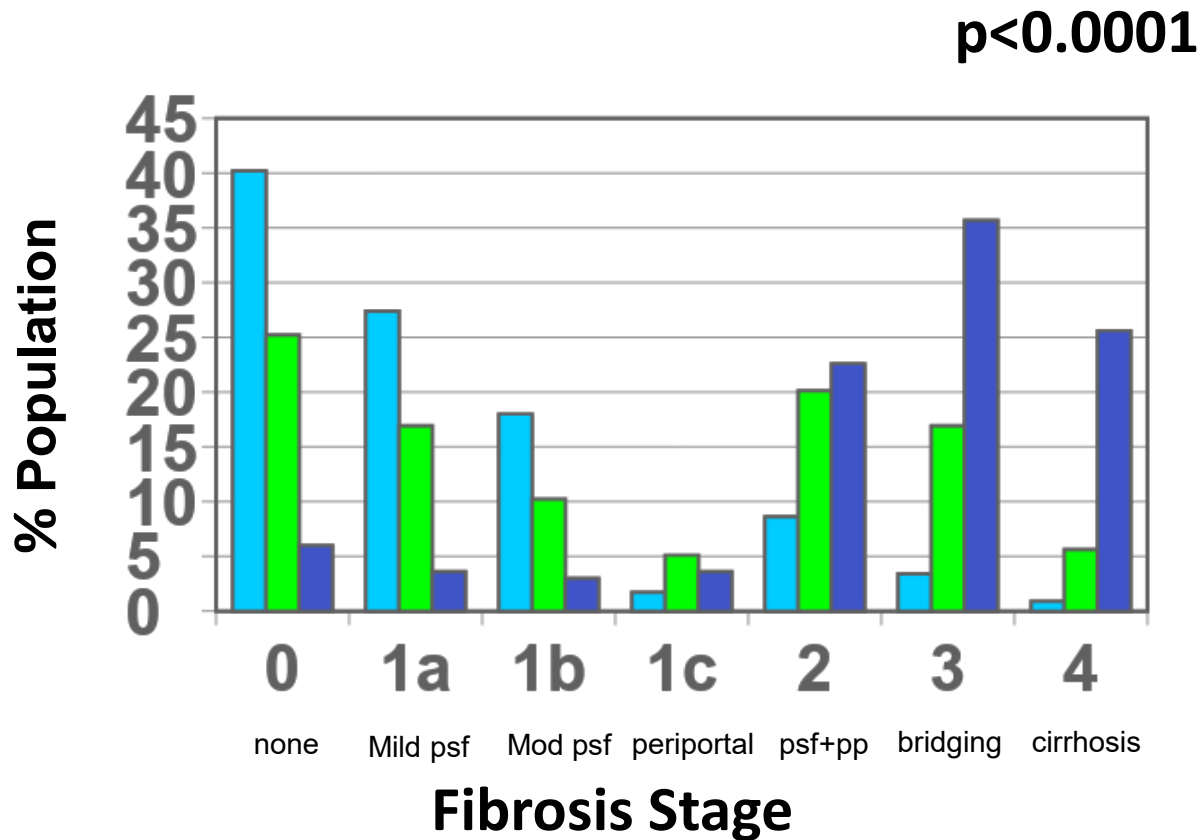
Hepatic Pathology among Patients without Known Liver Disease Undergoing Bariatric Surgery: Observations and a Perspective from the Longitudinal Assessment of Bariatric Surgery (LABS) Study

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Semin Liver Dis 2014;34:98-107





Hepatology 2009;49:809-820

Second Model: Histologic (n = 445) ^d				
Baseline				
Ballooning	0.6 (0.3-0.9)	.02	3.7 (2.2-6.0)	<.001
Portal inflammation	0.4 (0.2-0.8)	.007	4.0 (2.1-7.7)	<.001
Fibrosis stage	2.0 (1.5-2.8)	<.001	0.4 (0.3-0.5)	<.001
Change (last biopsy vs first)				
ΔSteatosis grade	0.6 (0.4-0.8)	<.001	0.8 (0.6-1.1)	.24
ΔBallooning	0.6 (0.4-0.8)	.002	3.0 (2.0-4.4)	<.001
ΔLobular inflammation	0.8 (0.6-1.2)	.33	1.3 (0.9-1.8)	.14
ΔPortal inflammation	0.5 (0.3-0.9)	.002	4.1 (2.3-7.3)	<.001
Years between biopsies	0.9 (0.9-1.0)	.24	1.1 (1.0-1.2)	.07

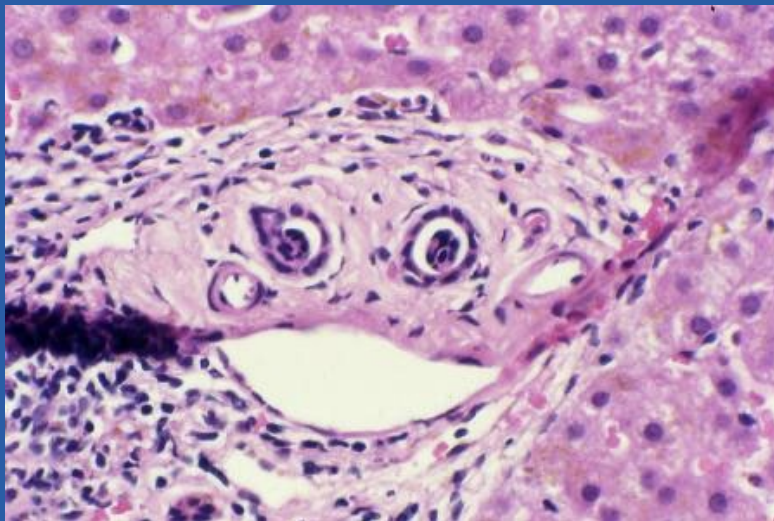
JAMA Netw Open 2019;2:e1912565

Summary

- Portal and lobular inflammation are difficult to define and quantify because the manifestations of inflammation in the liver are morphologically heterogeneous
 - Multiple cell types involved, multiple states within any one cell type
 - Infinite variety of organization and interaction with hepatocytes and other cell types in the liver
- This leads to variability in scoring, particularly for lobular inflammation
- Existing methods of assessment do not account for the variety of cell types and interactions

Where Do We Go From Here?

- NASH CRN and other groups are working to better understand and define the spectrum of portal inflammation and interface hepatitis in NAFLD/NASH
- International group organized to better define the various histological changes in NAFLD/NASH in order to improve scoring agreement for clinical trials
- Image analysis has the potential to better quantify portal and lobular inflammation, perhaps coupled with immunohistochemistry



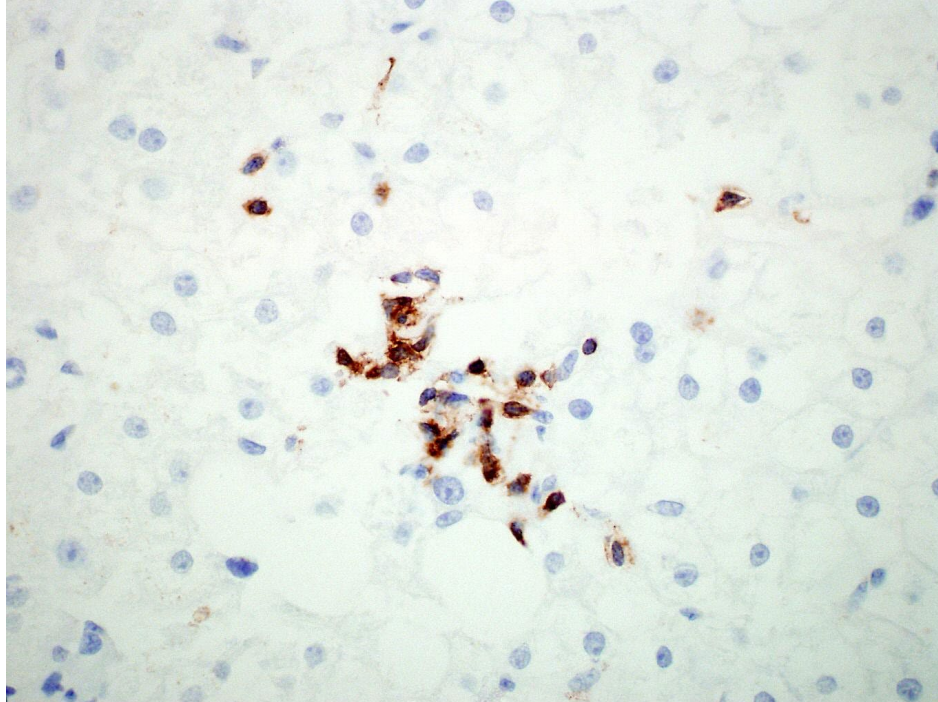
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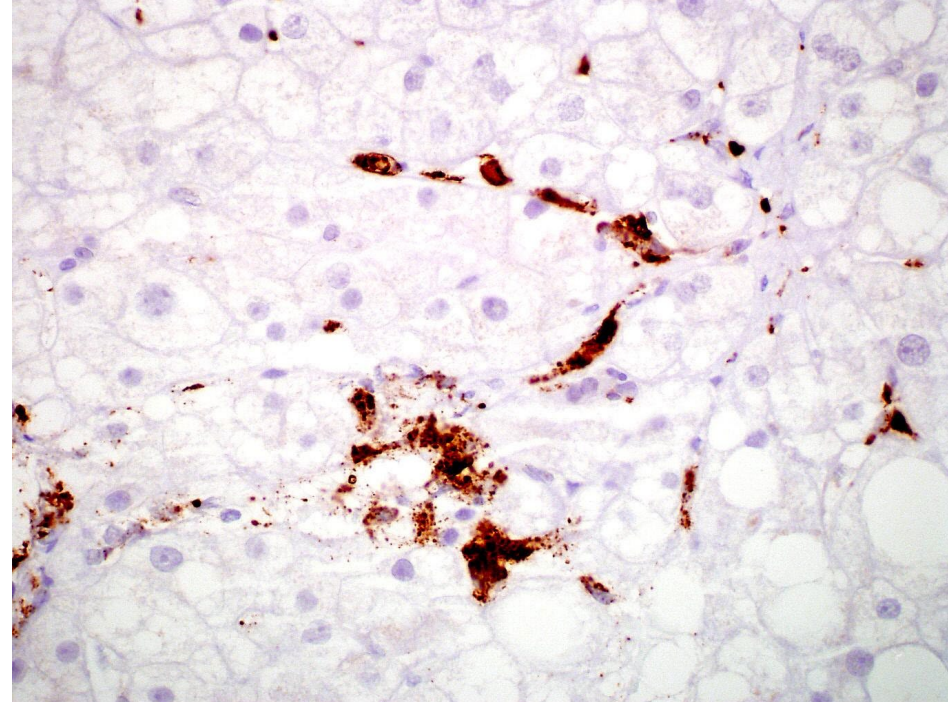
www.cancer.gov/espanol



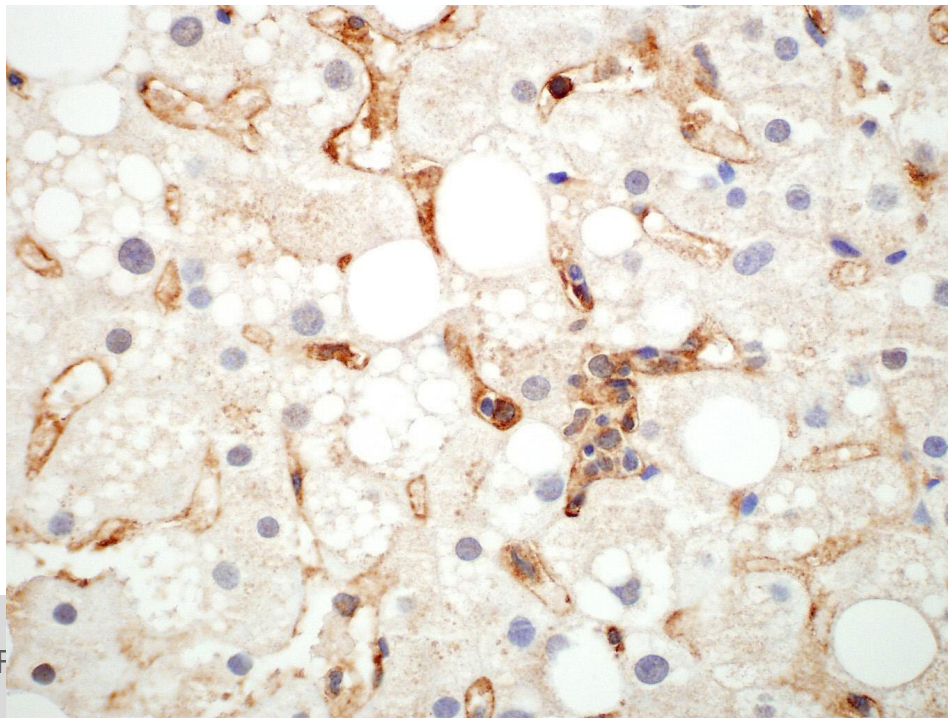
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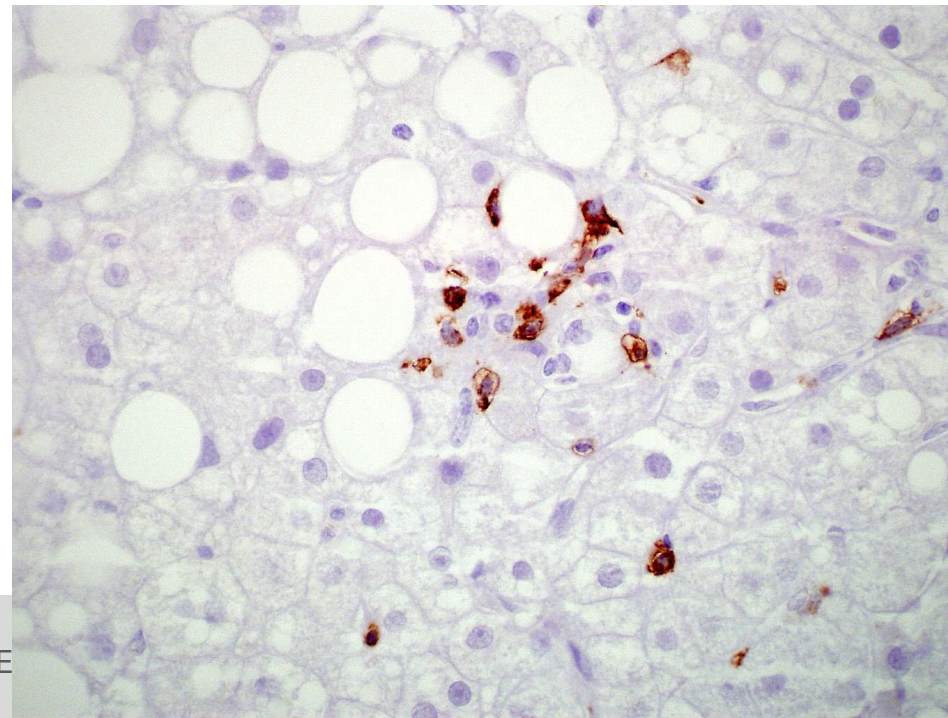
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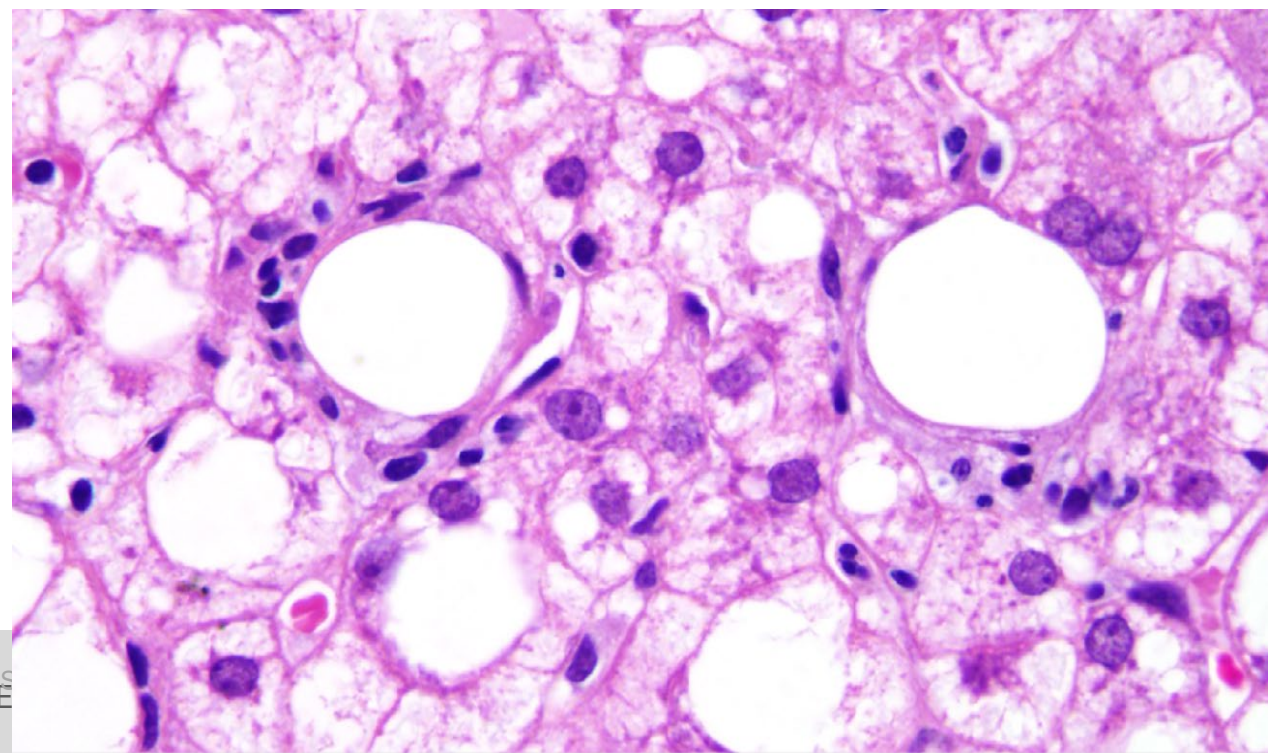
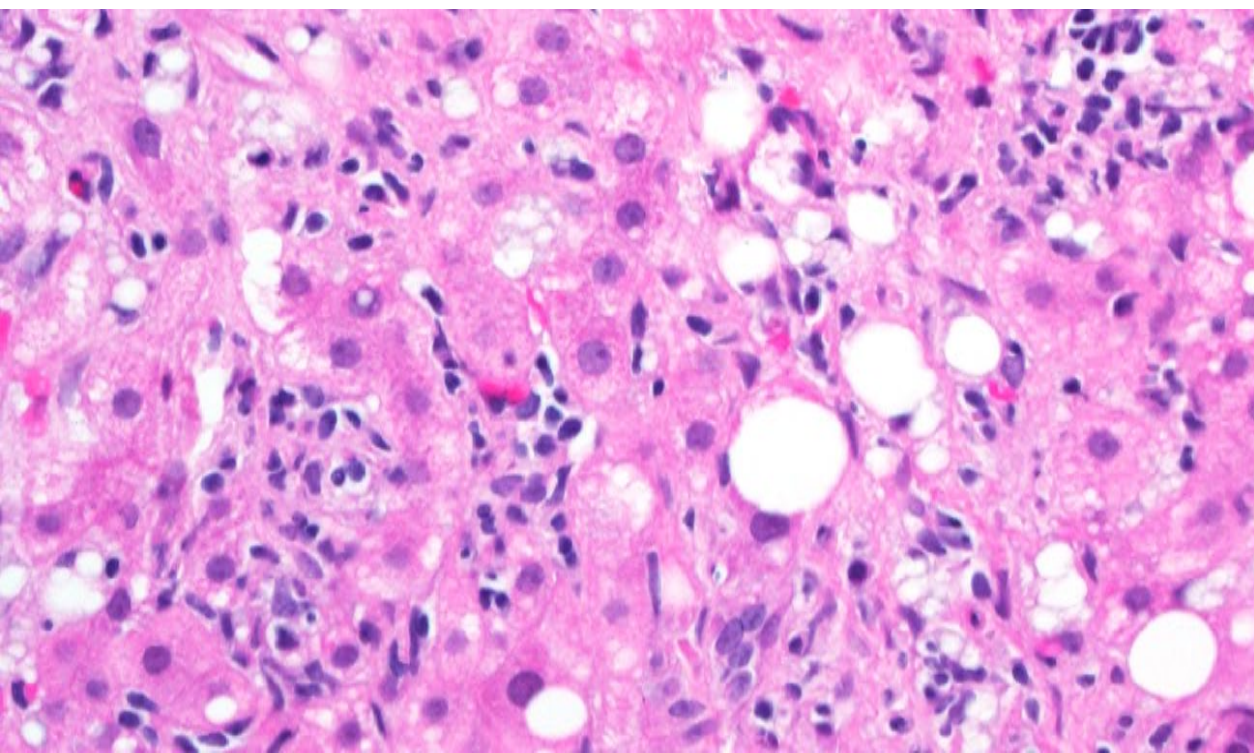
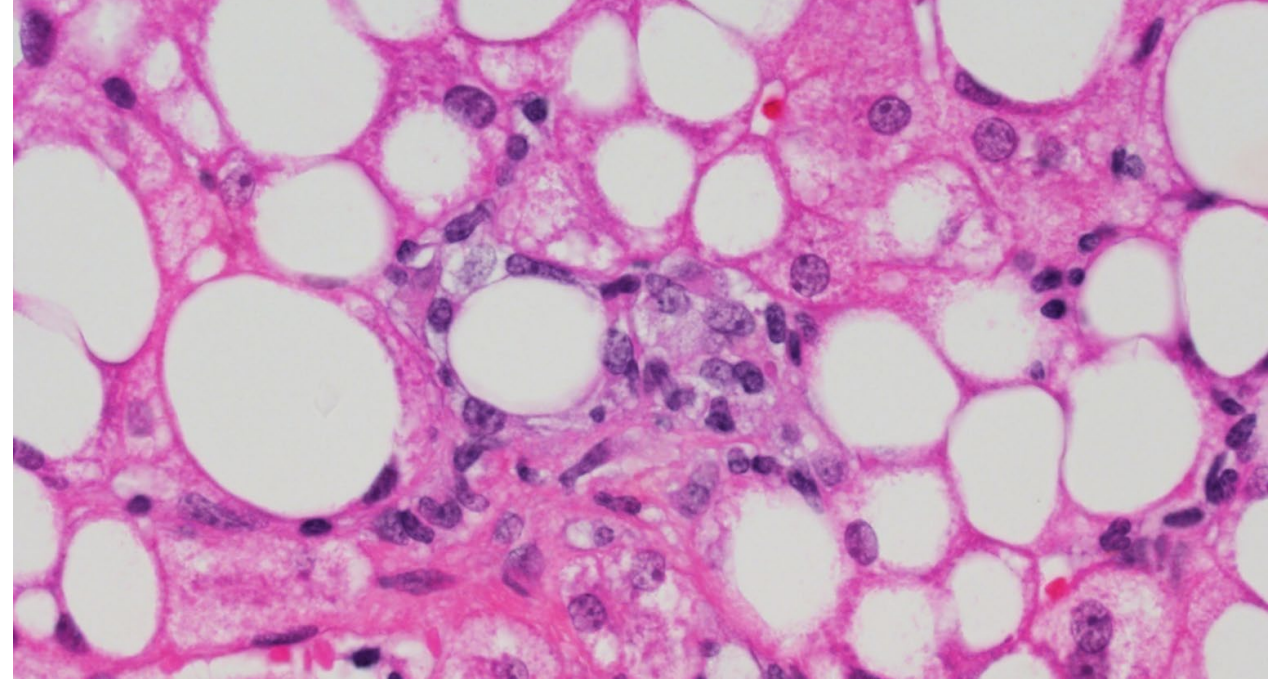
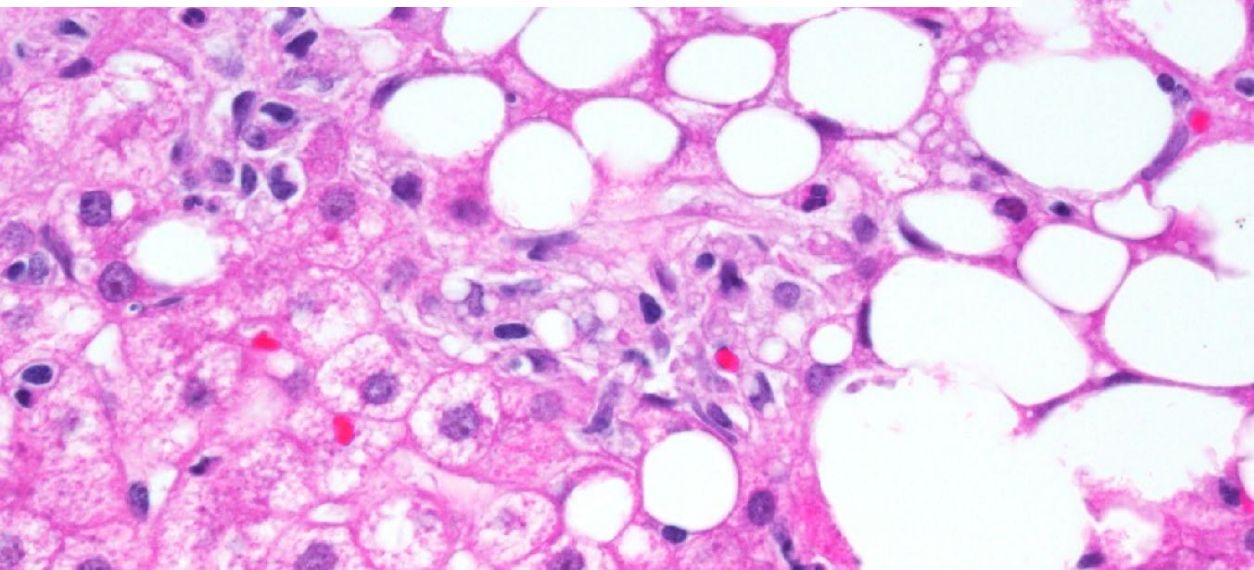
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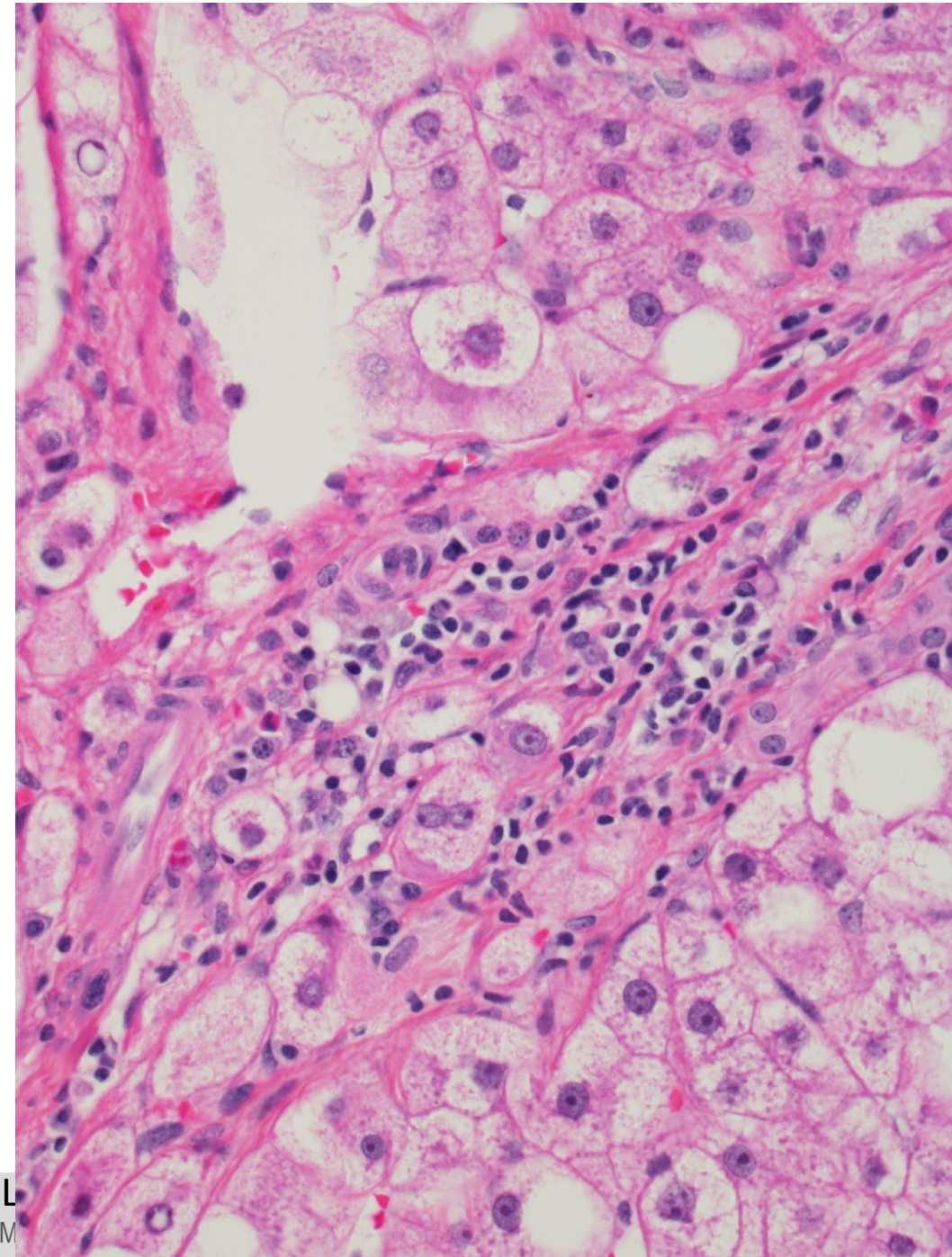
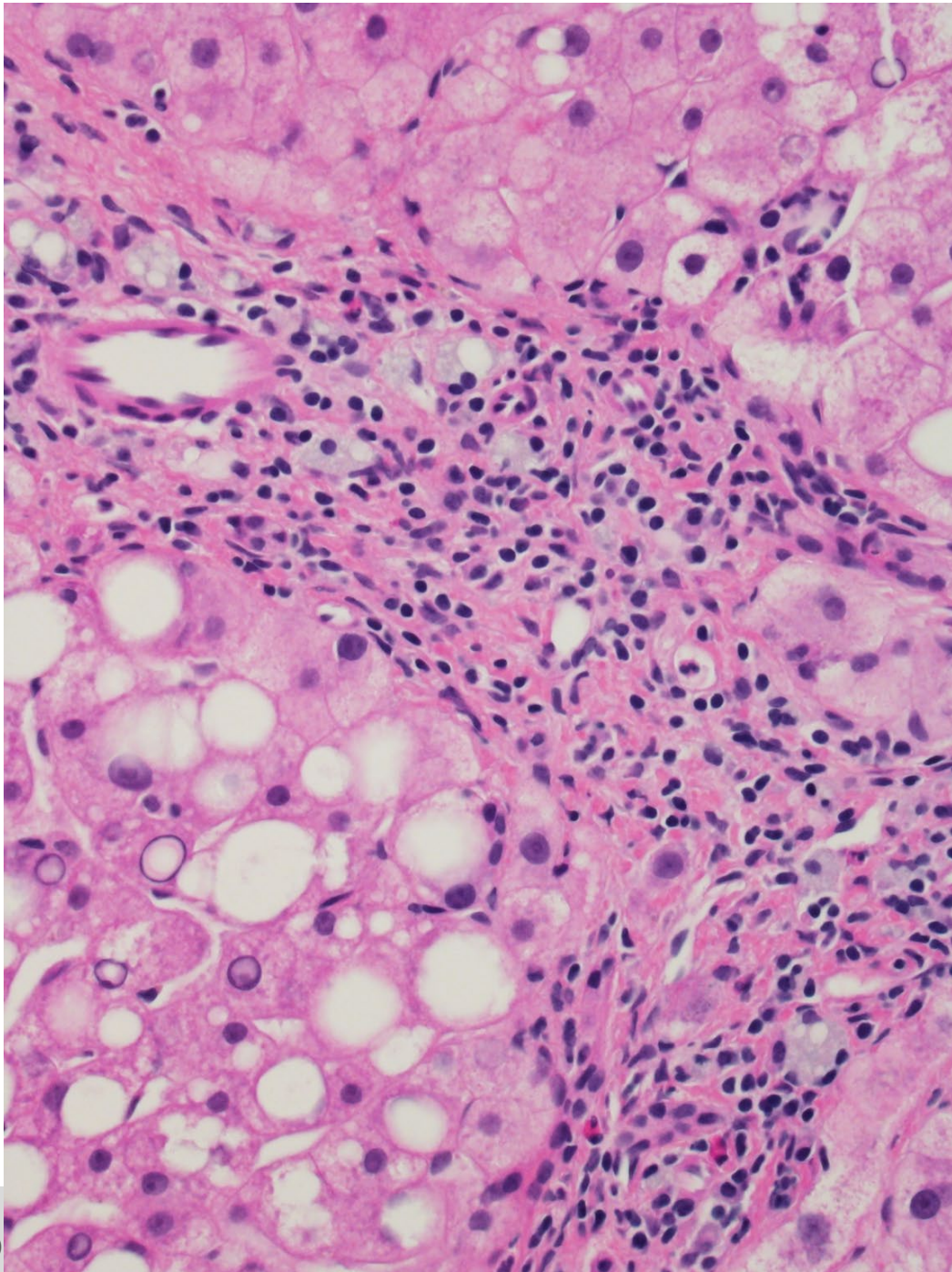
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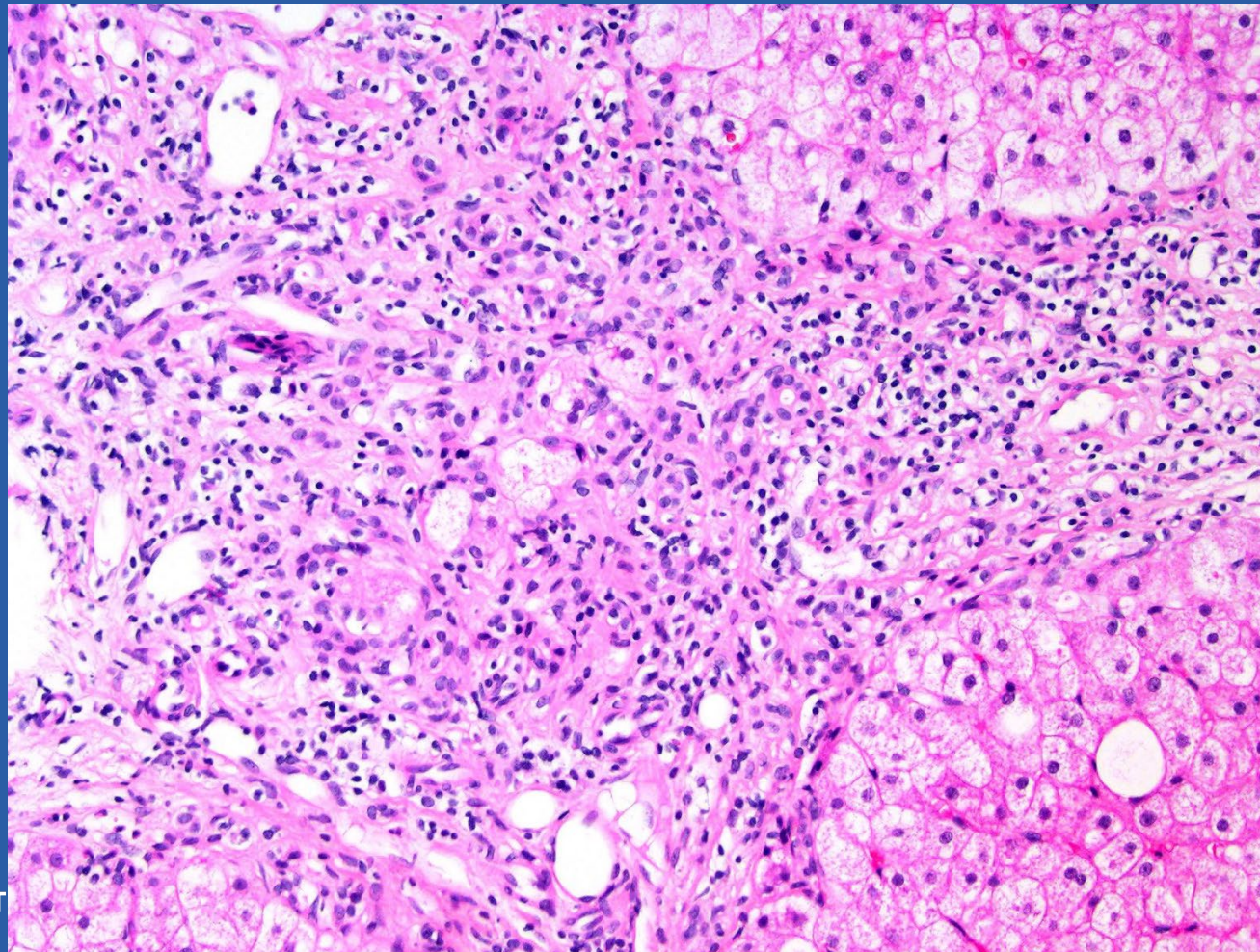
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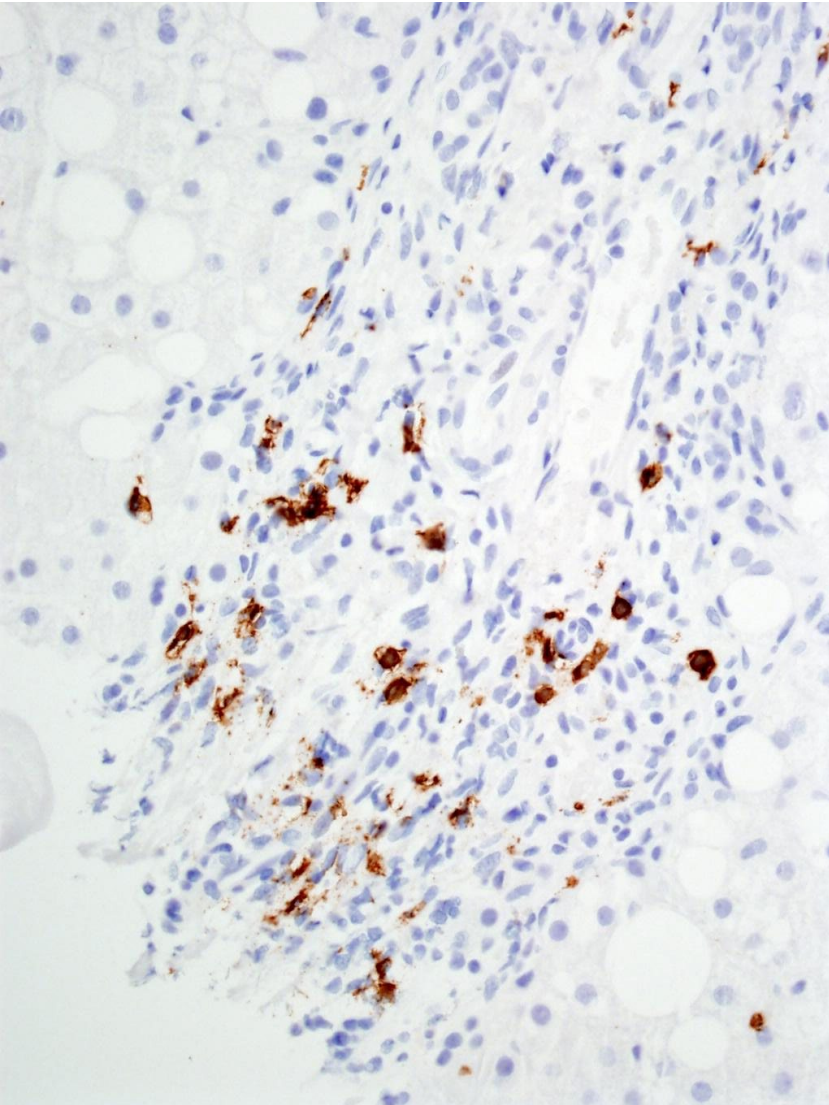
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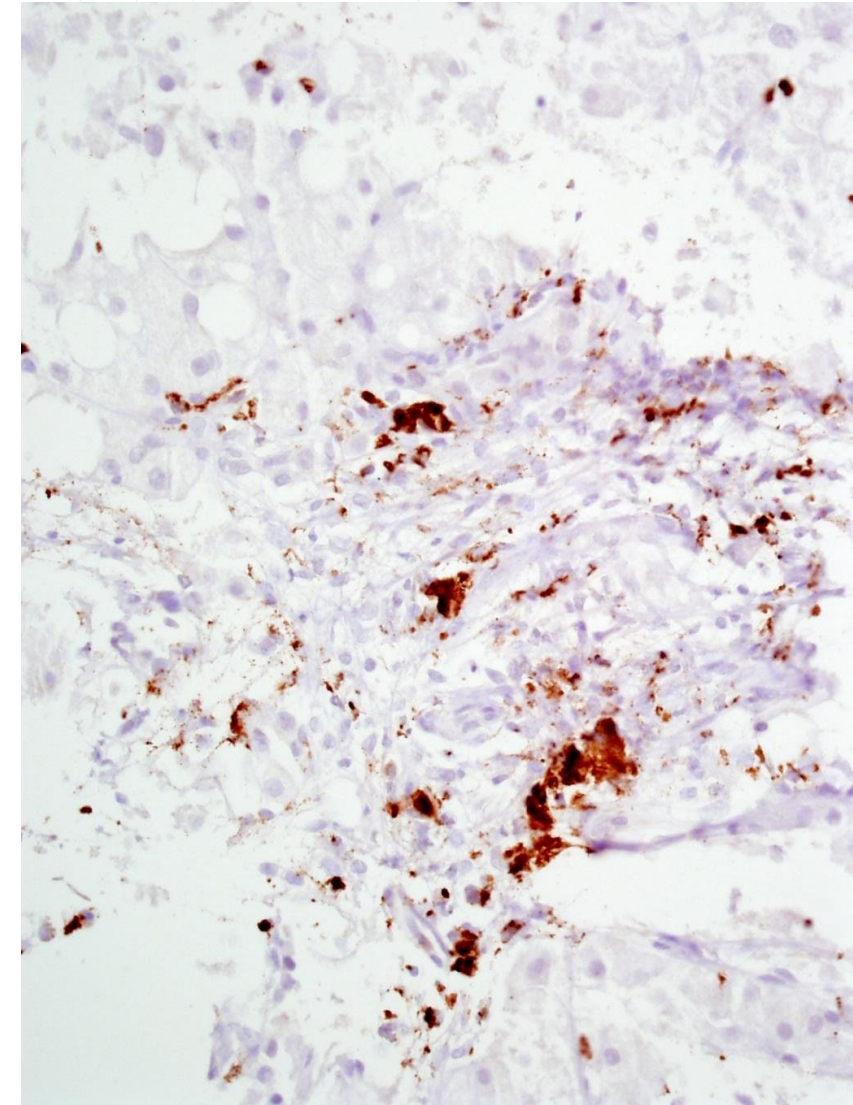
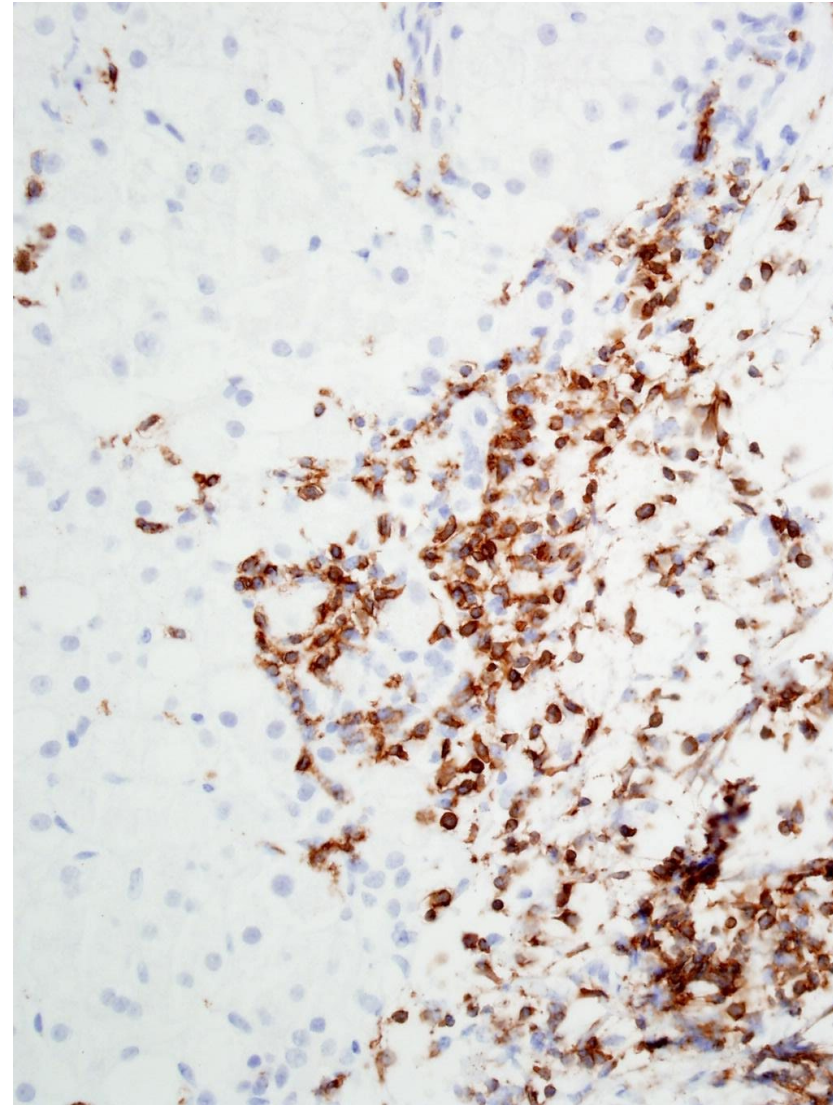
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CD20



CD3



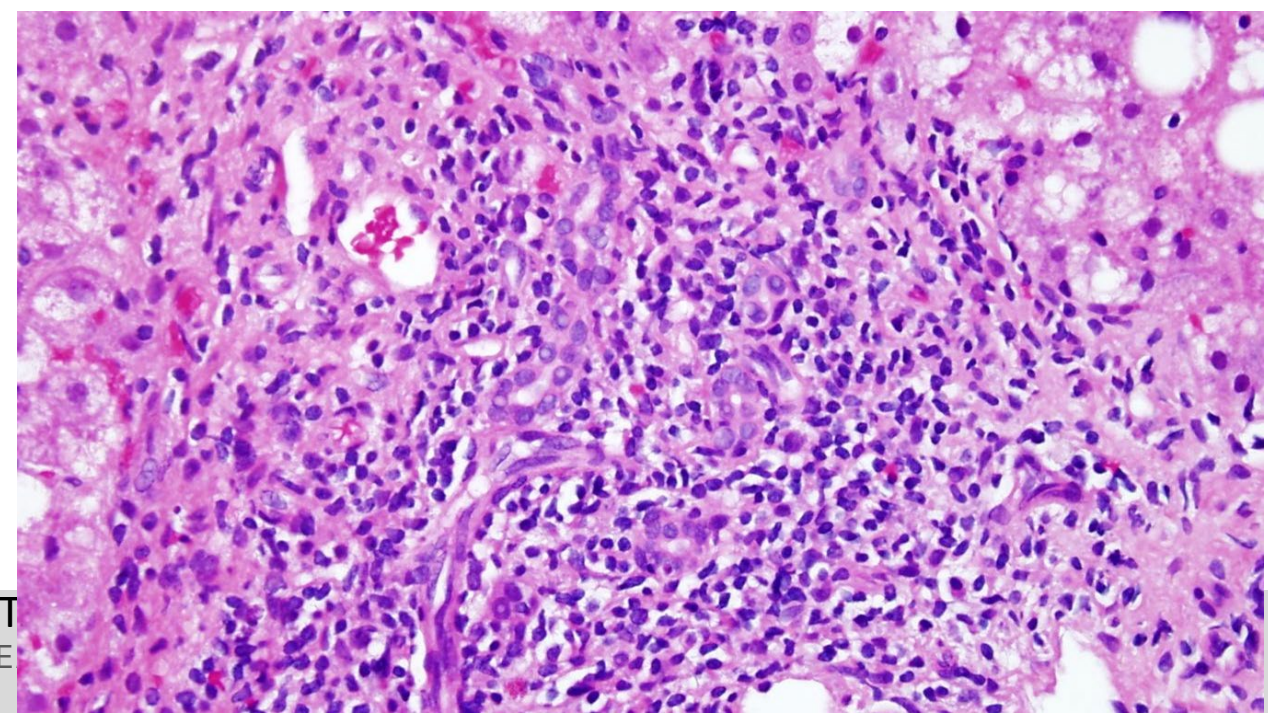
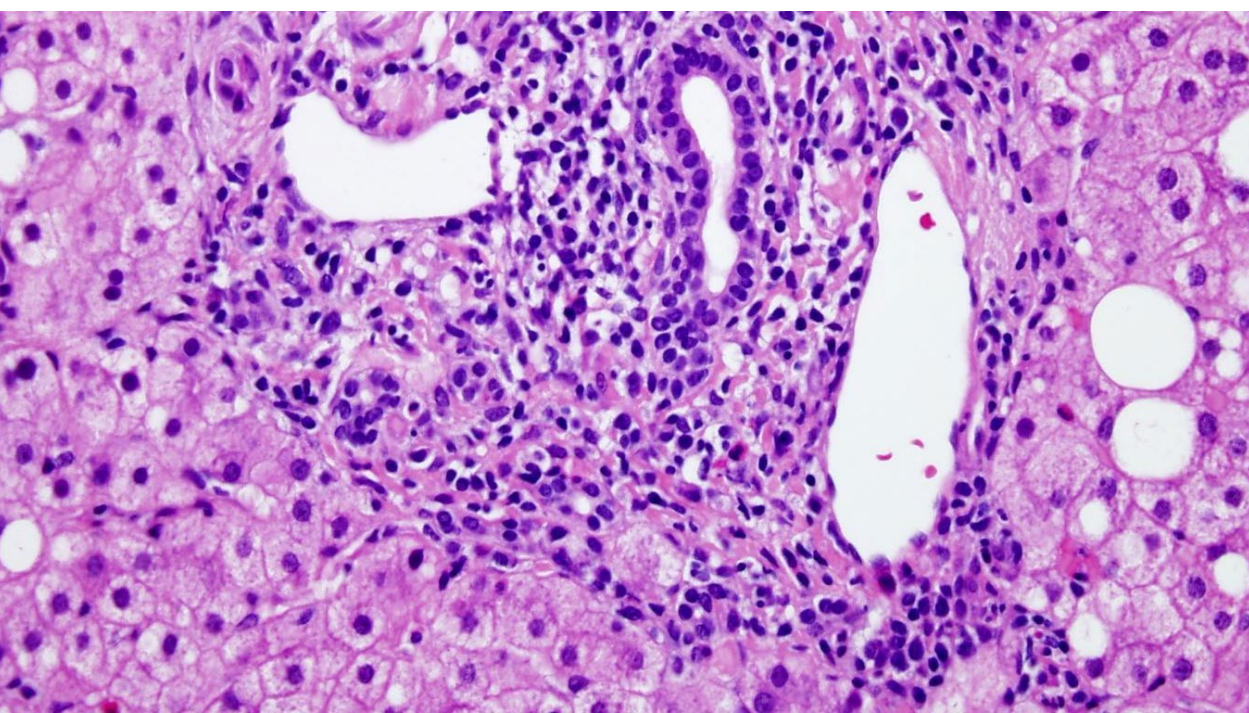
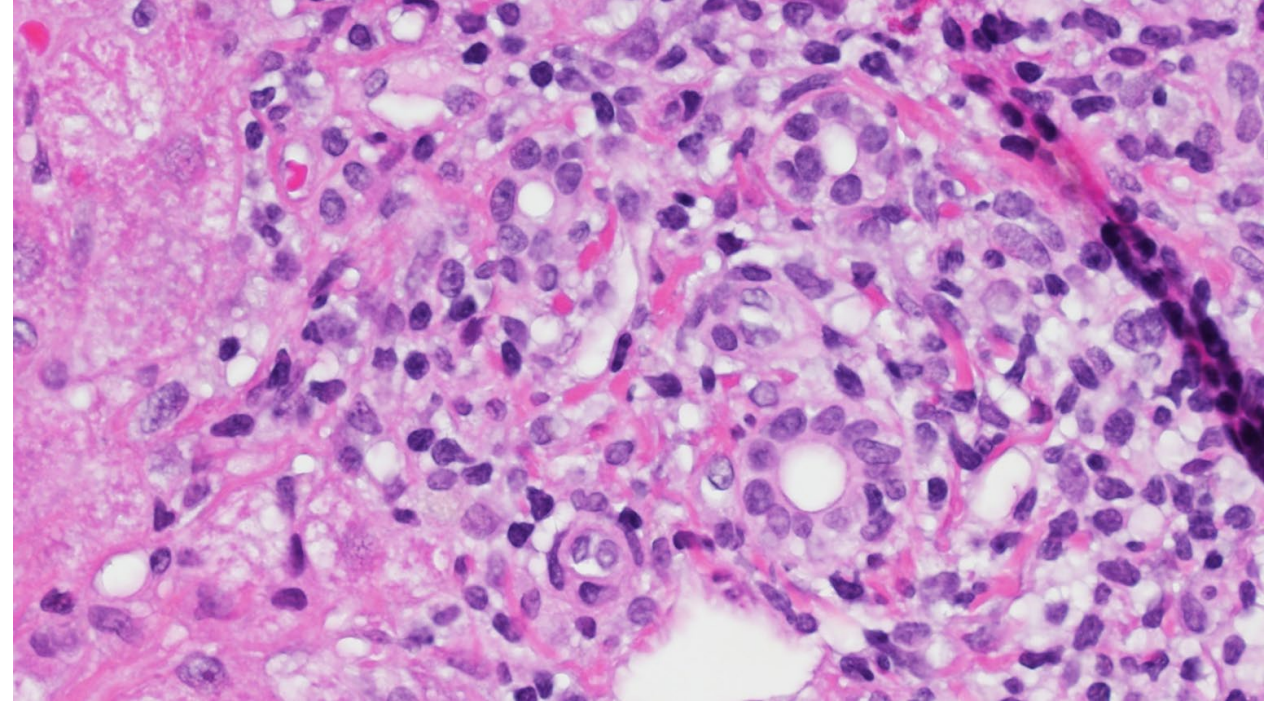
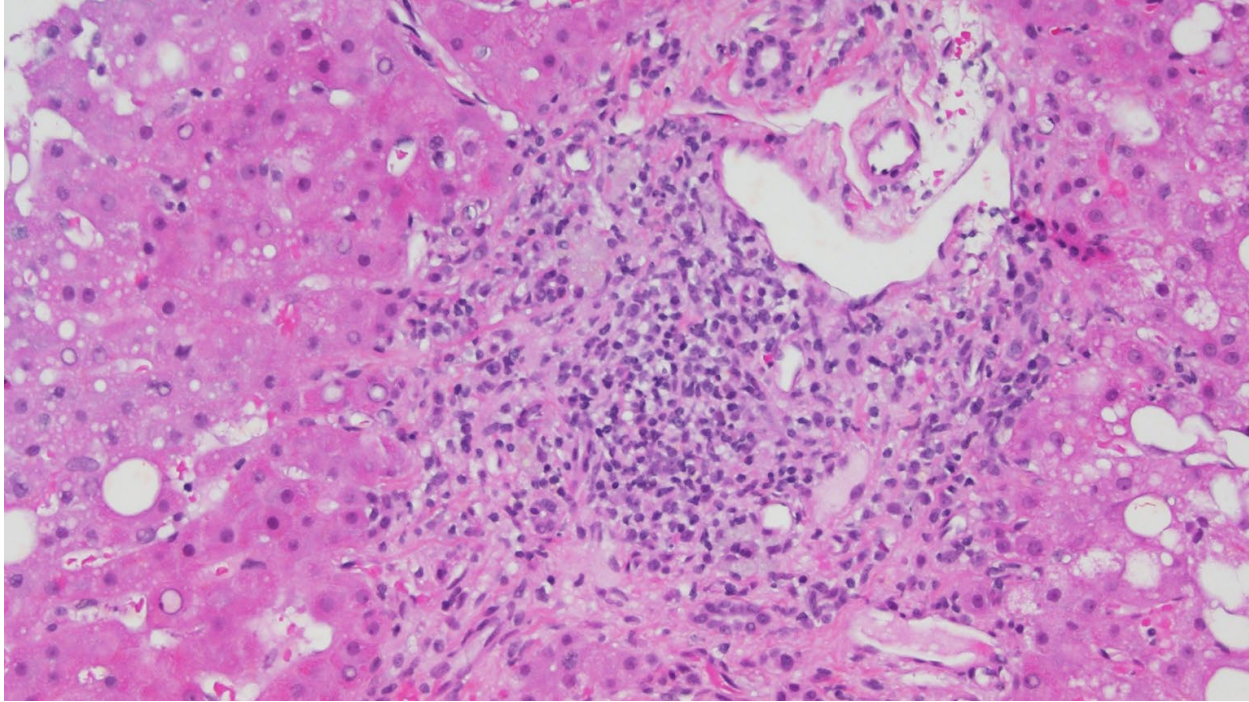
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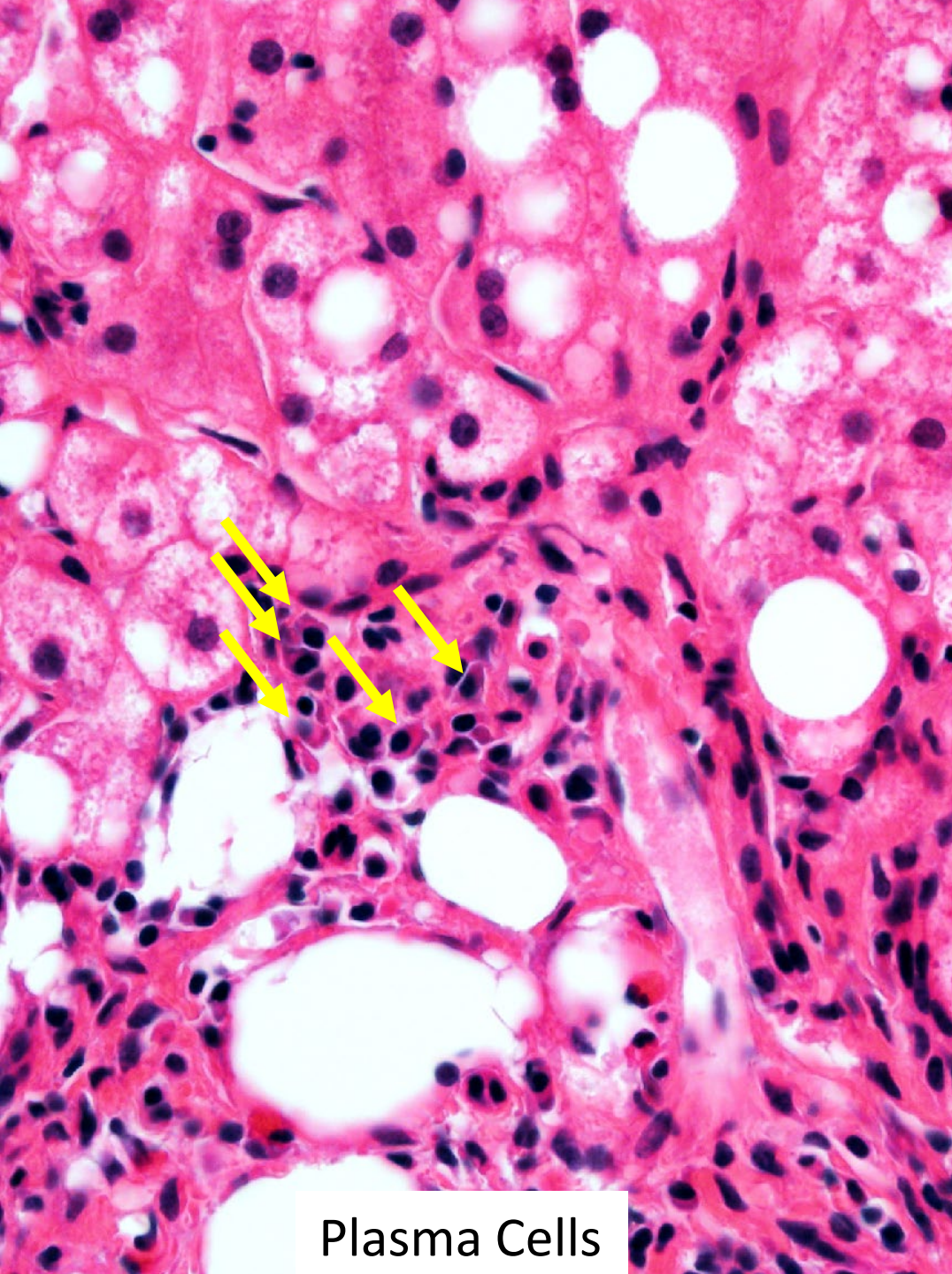
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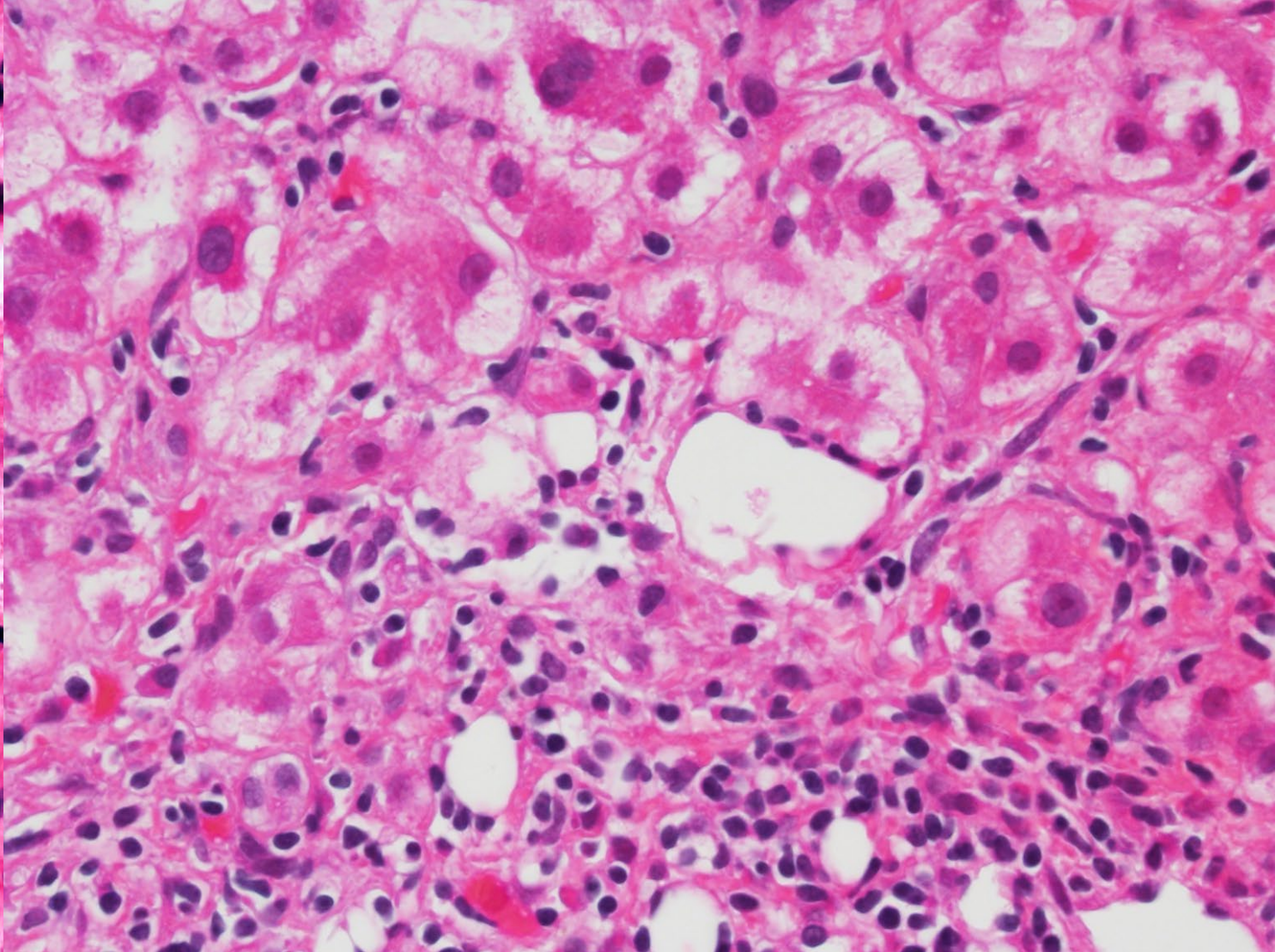
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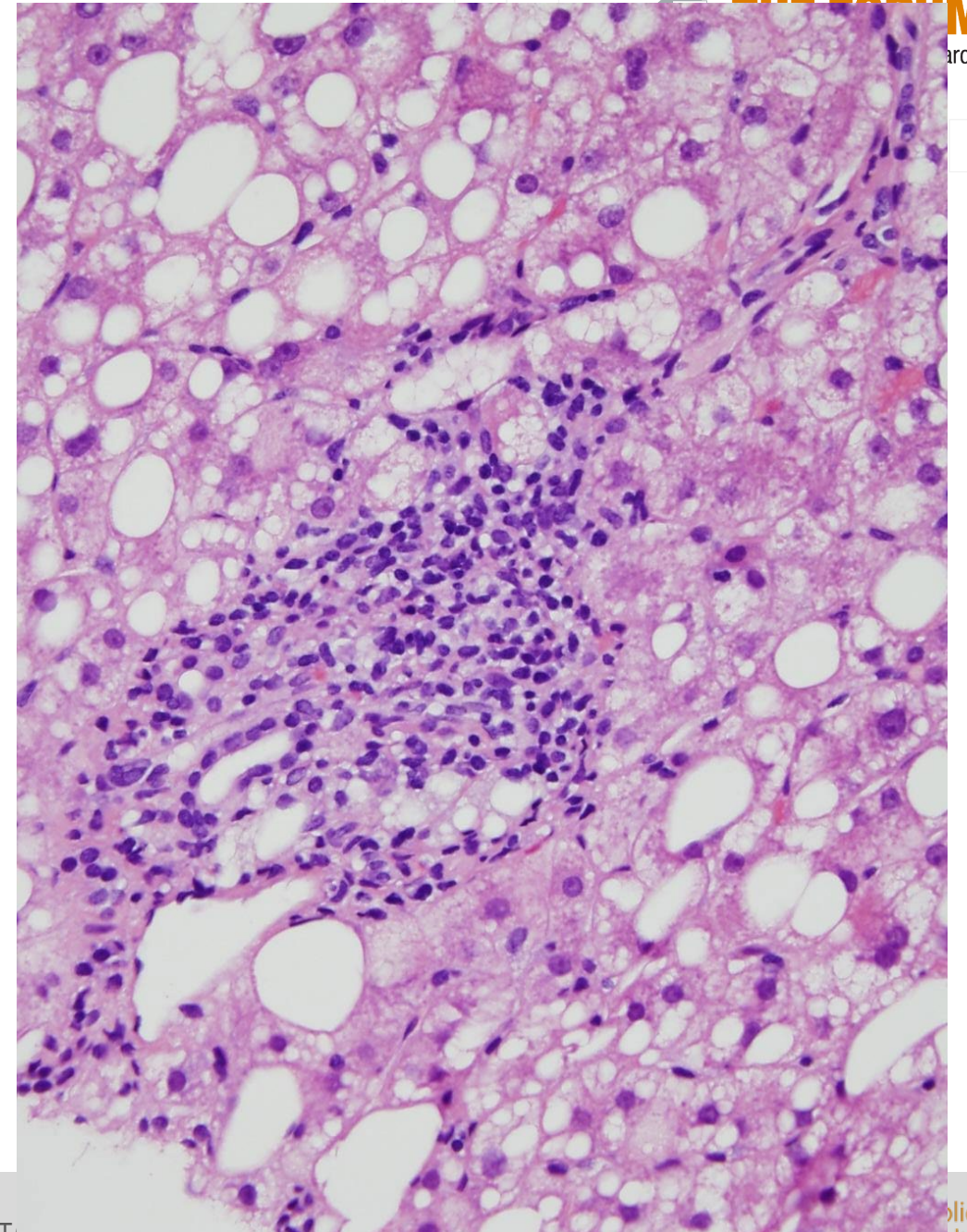
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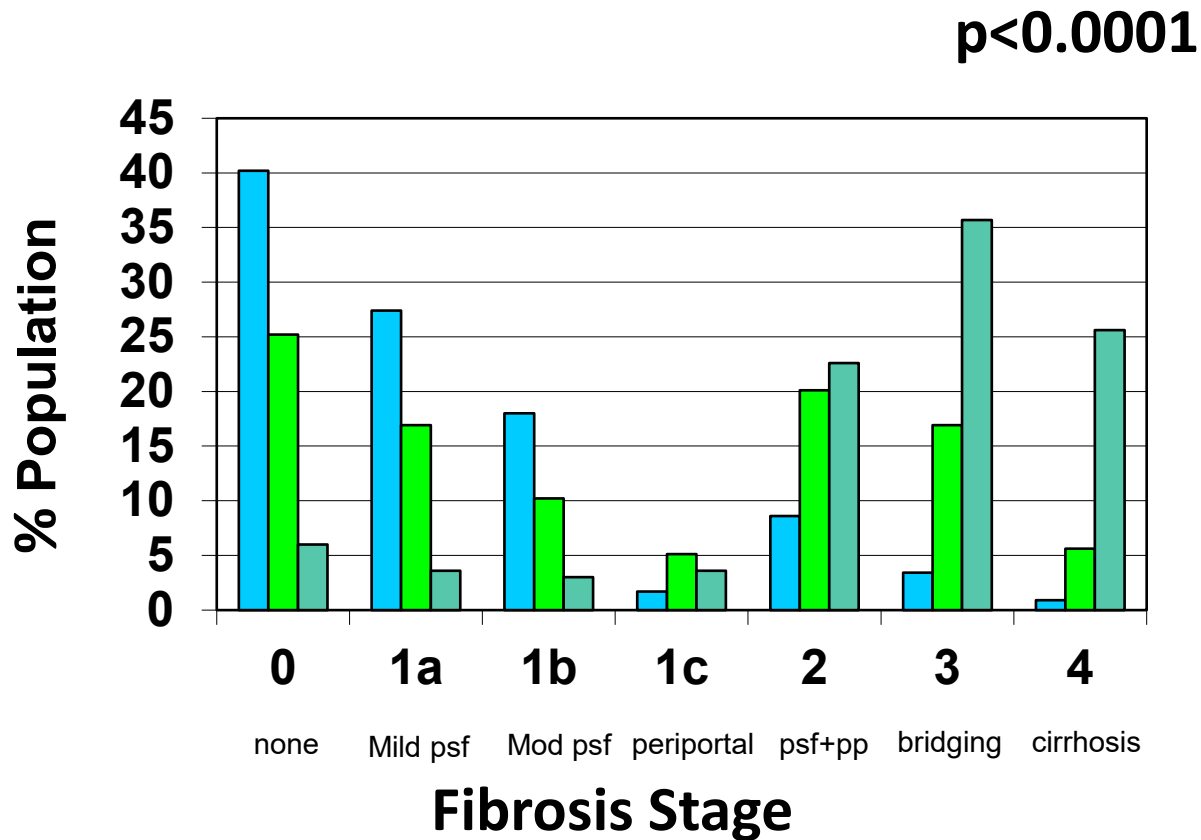
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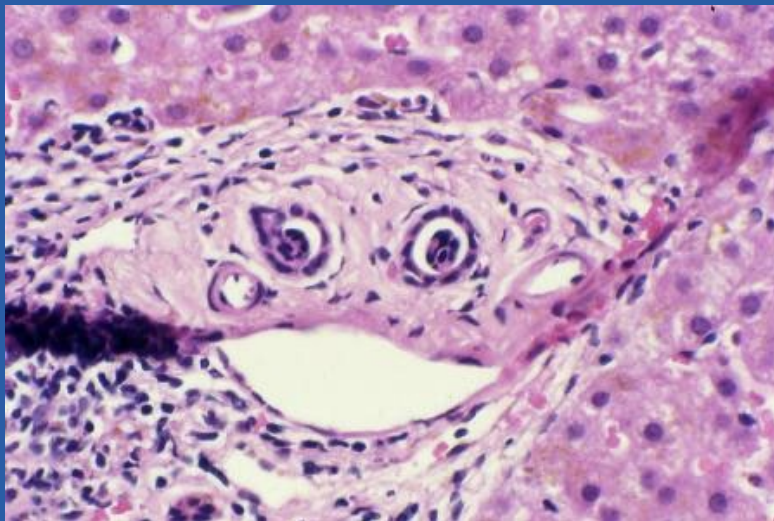
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