Histopathology and the diagnosis of lysosomal storage disorders – part 1

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Lysosomal storage disorders

- Part one – blood and bone marrow
- Part two – NCL diagnosis and other tissues

Lysosomal storage disorders

- Group of 50 diseases
- Rare with a frequency of about 1:8000 live births
- Inherited in an autosomal-recessive fashion, exceptions X-linked
- Accumulation of waste products in lysosomes due to missing or reduced enzyme

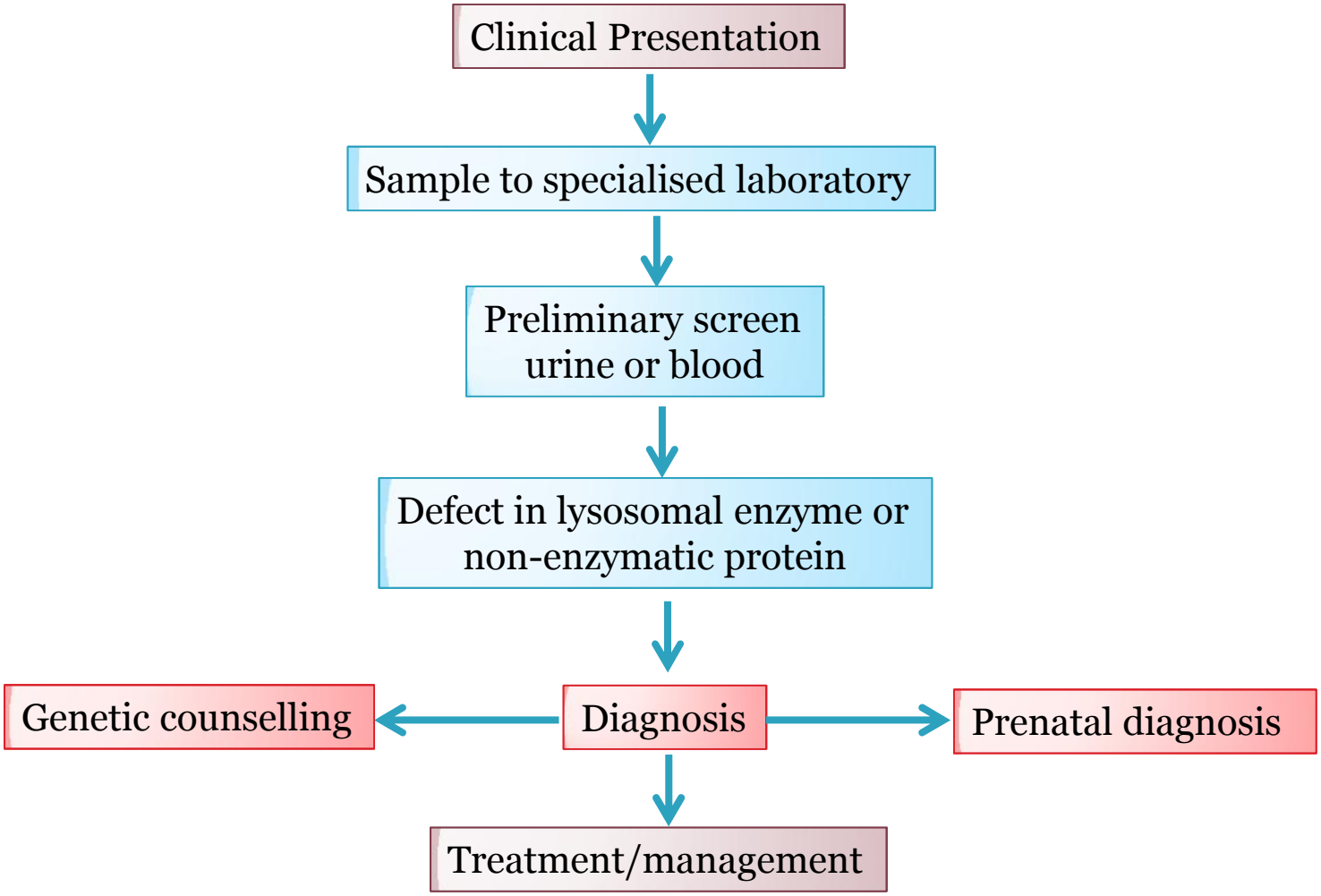
Clinical features - variable

- Appear normal at birth – progressive
- Failure to thrive
- Dysmorphic features
- Neurological symptoms – seizures, behaviour
- Organomegaly

Clinical features

- Visual problems – cherry red spot
- Skeletal dysplasia
- Muscle weakness including cardiomyopathy
- Loss of skills – speech and learning
- Many disorders can present in different forms – infantile, juvenile and adult
- Hydrops fetalis

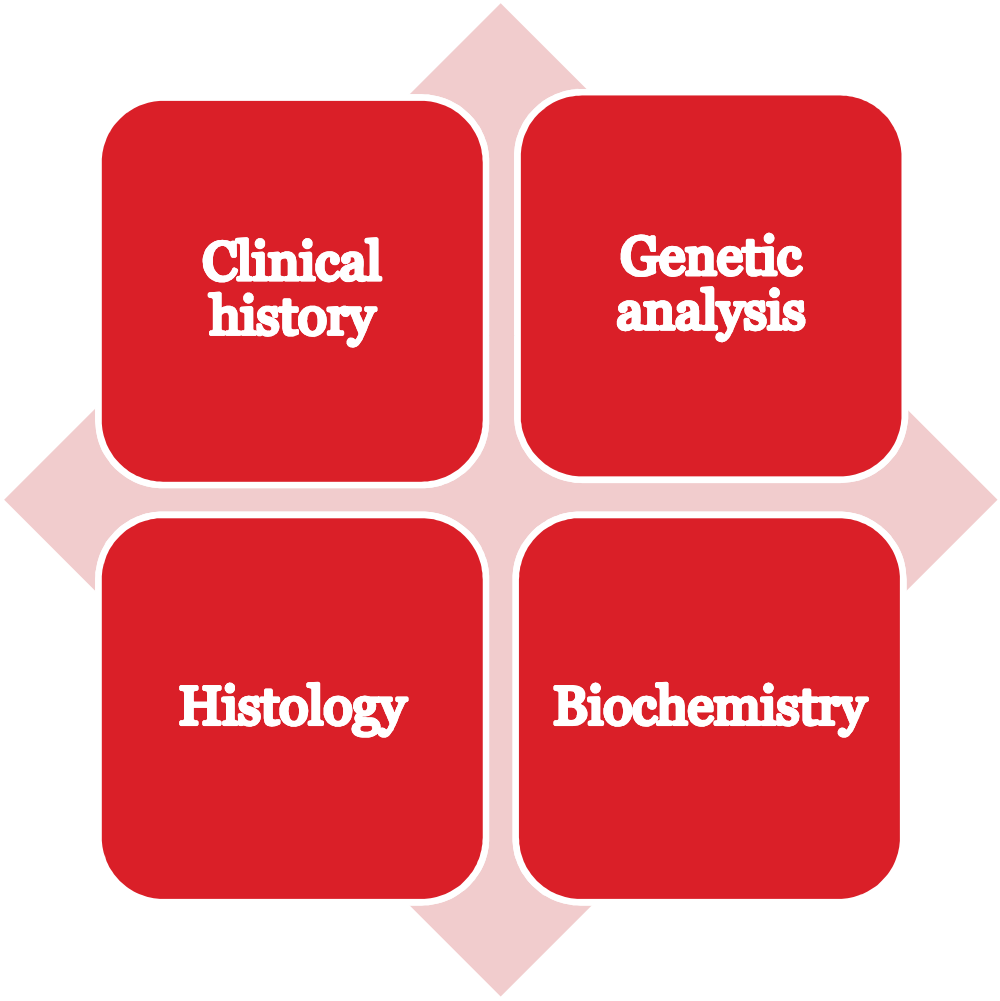
Algorithm for Diagnosis



LSD - classification

- Sphingolipidoses – GM1 & GM2 gangliosidosis, Fabrys, MLD, Gaucher, Krabbe, Niemann-Pick A & B
- Mucopolysaccharidoses – Hurler, Hunter, Sanfilippo, Morquio
- Glycoproteinoses (Oligos) – Mannosidosis, Fucosidosis, Sialidosis
- Other enzyme defects – Wolman, CESD, GSD II
- Neuronal ceroid lipofuscinoses – CLN 1-14
- Disorders of lysosome-related organelle – Chediak-Higashi, Griscelli, Hermansky-Pudlak
- Lysosomal membrane defects – Cystinosis, Sialic acid storage disease, Niemann-Pick C

Diagnosis of metabolic disorders



Morphological examination

- Light microscopy
  routine stains, lipid & enzyme histochemistry procedures

- Transmission electron microscopy

Blood

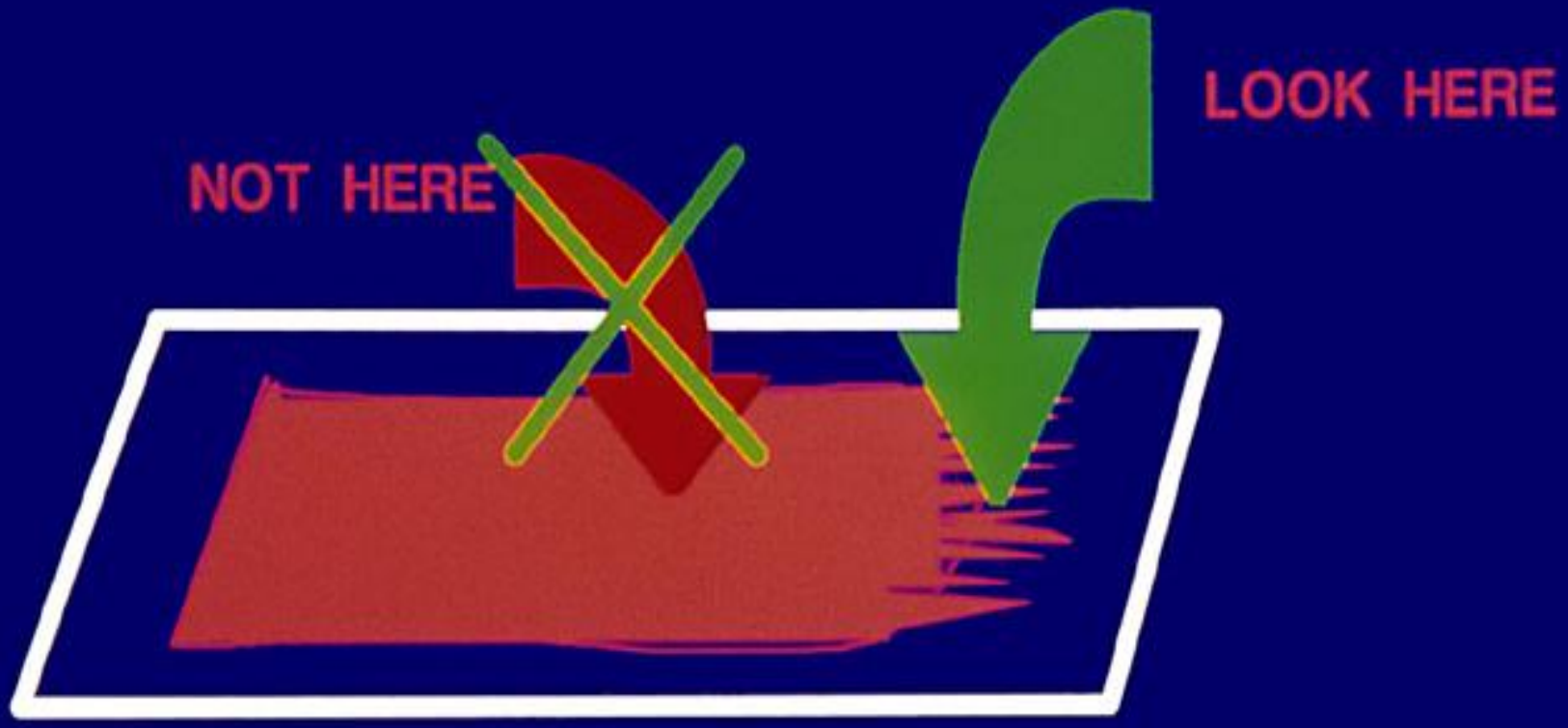
- Initial morphological screen
- Relatively non-invasive to obtain and transports well
- Films – MGG
- Whole blood – EDTA , buffy coat

Blood – film assessment

- Vacuolated lymphocytes
  (enlarged lyosomes)
  - small vacuoles
  - large vacuoles

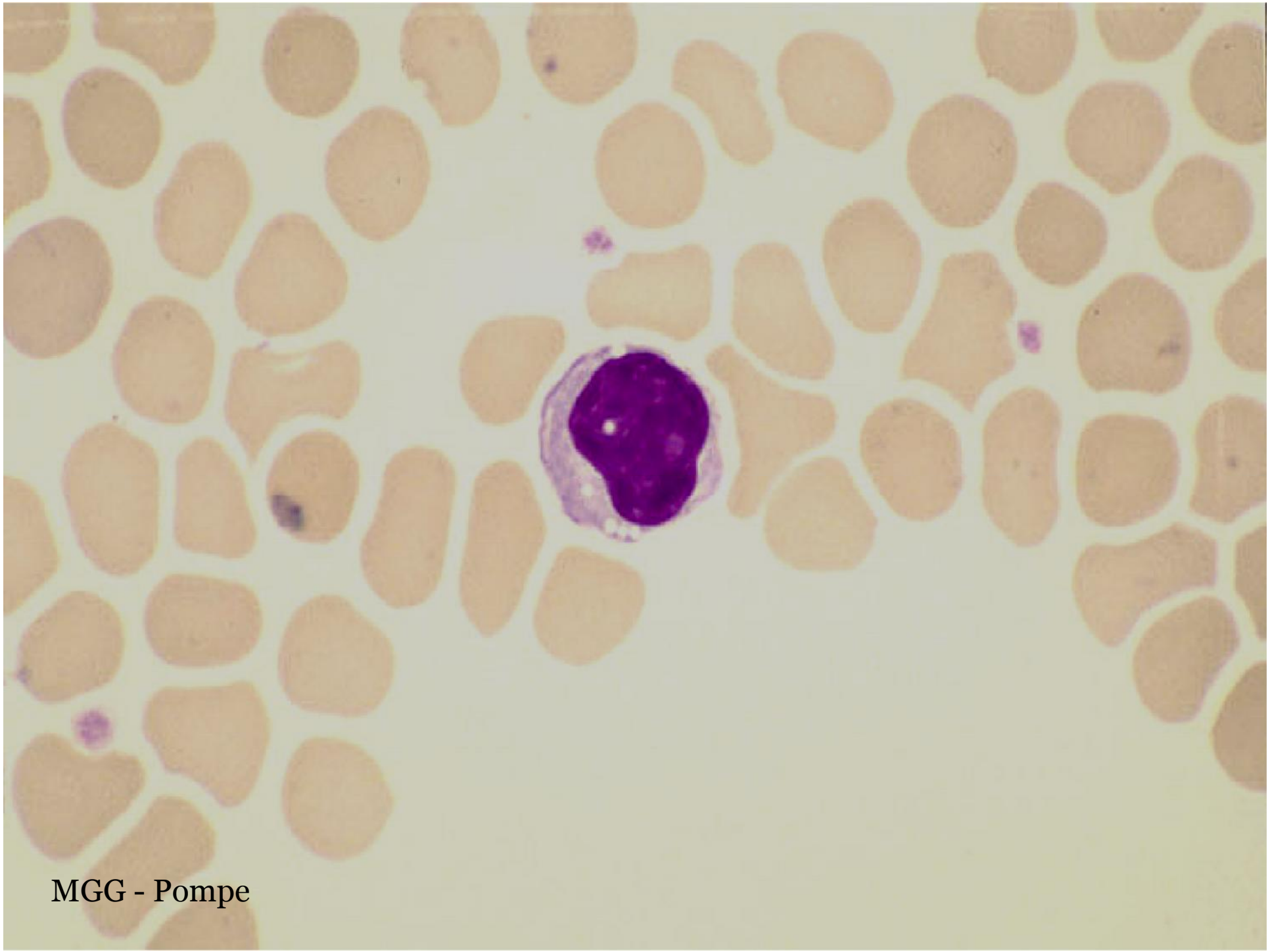
- Other white cells and platelets

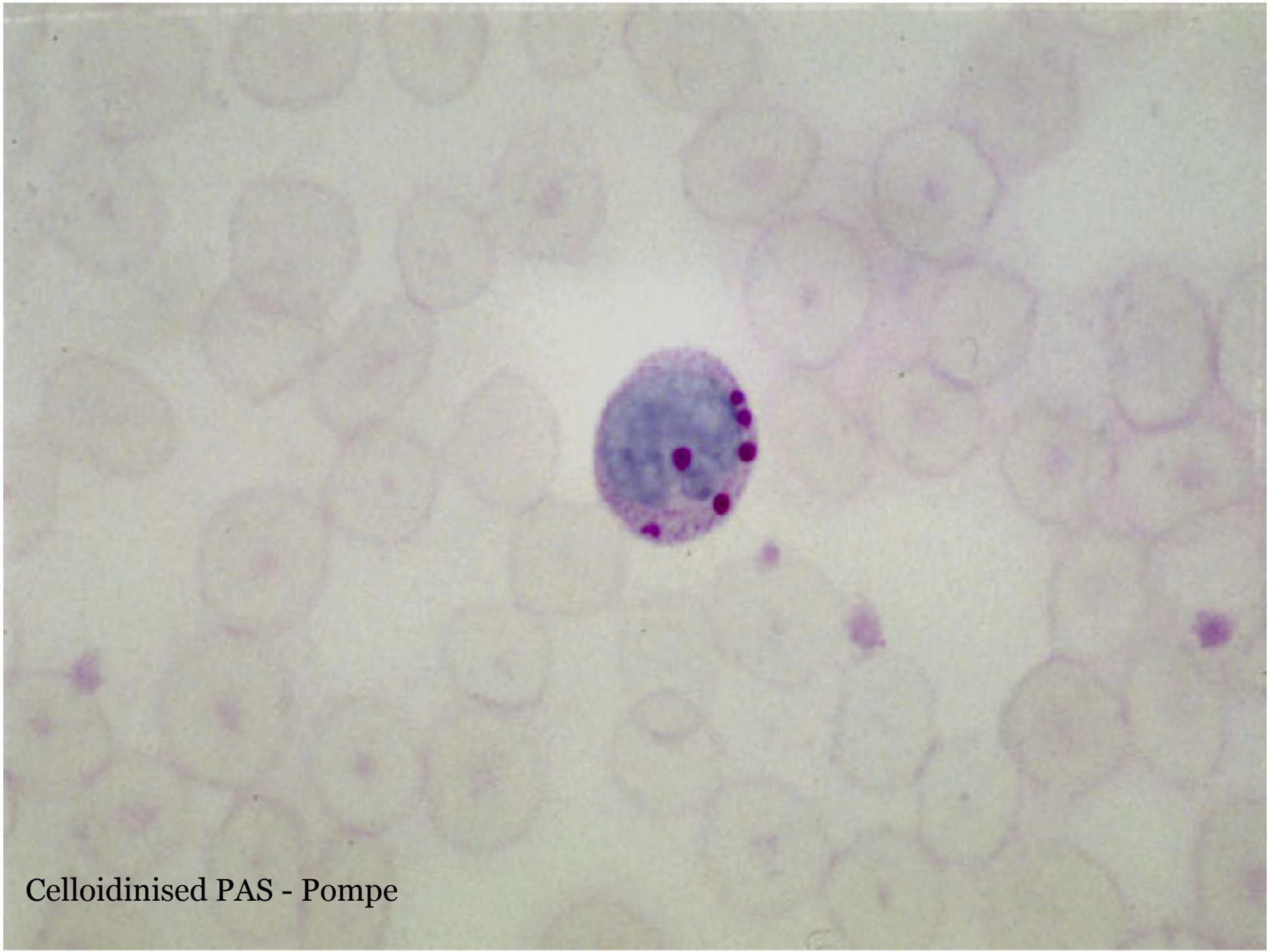
VACUOLATED LYMPHOCYTES ARE FOUND IN THE TRAILS OF THE BLOOD FILM



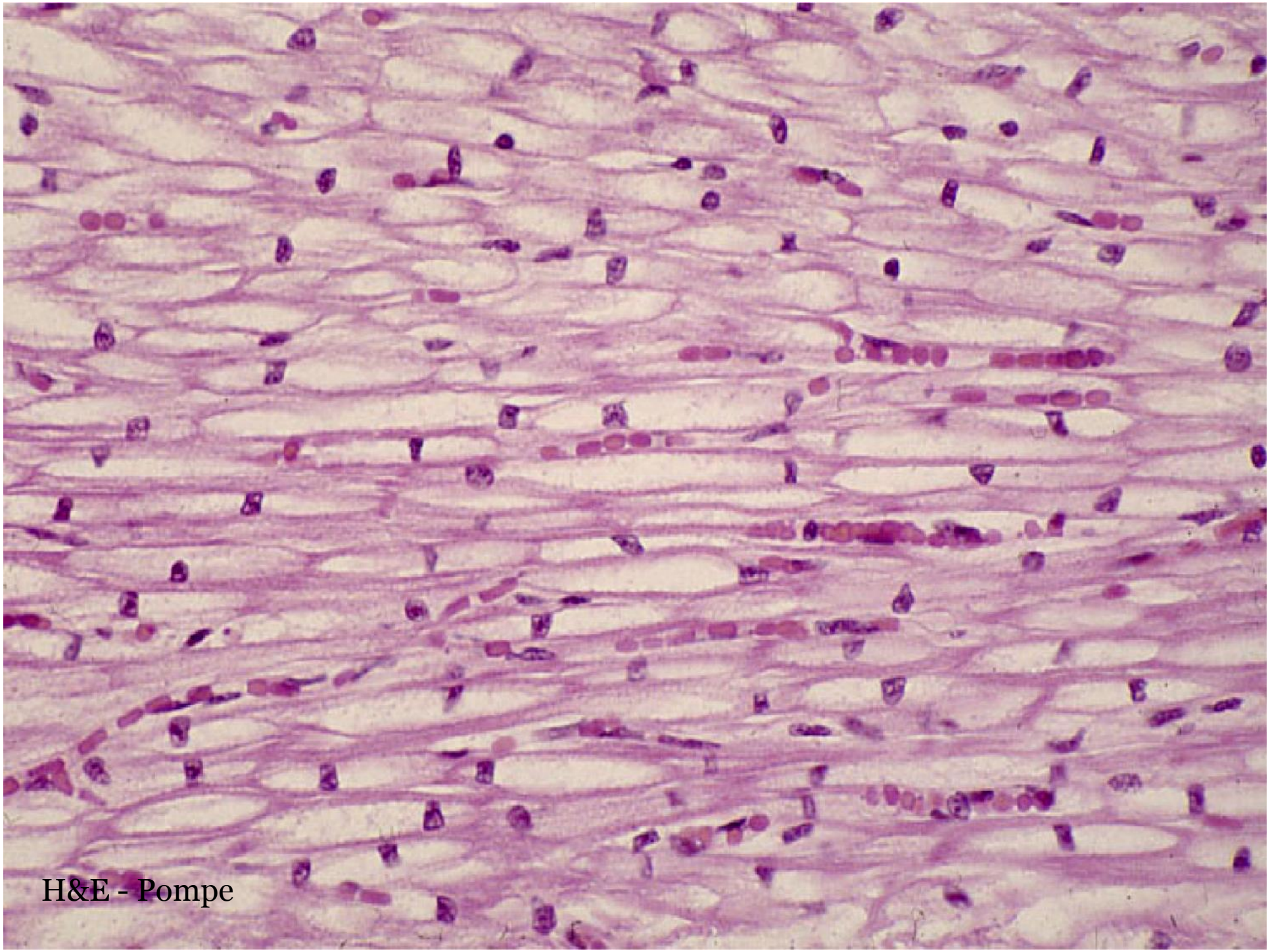
Small vacuolated lymphocytes

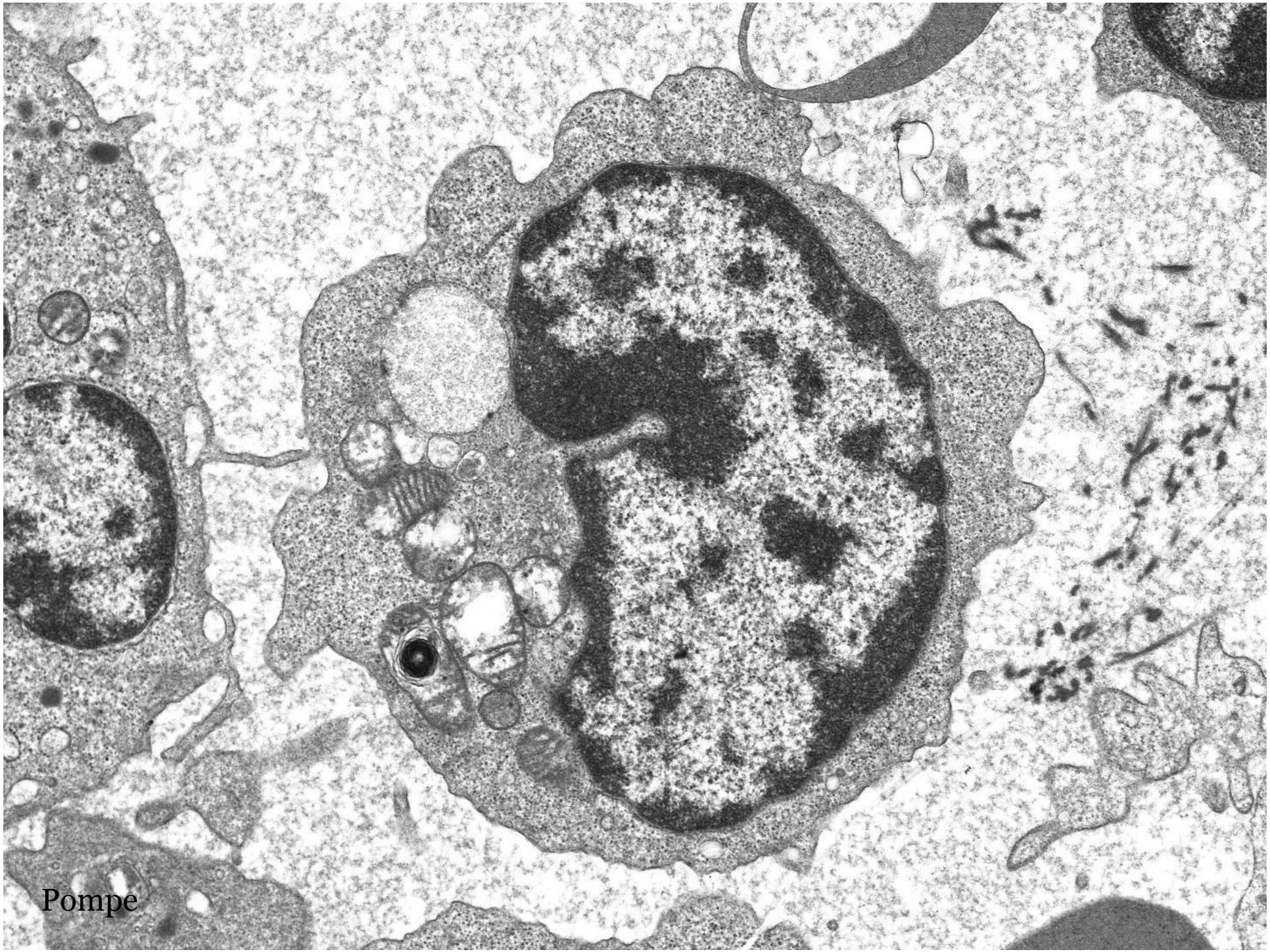
- Pompe disease – GSD type II
- Wolman disease
- Niemann-Pick type A

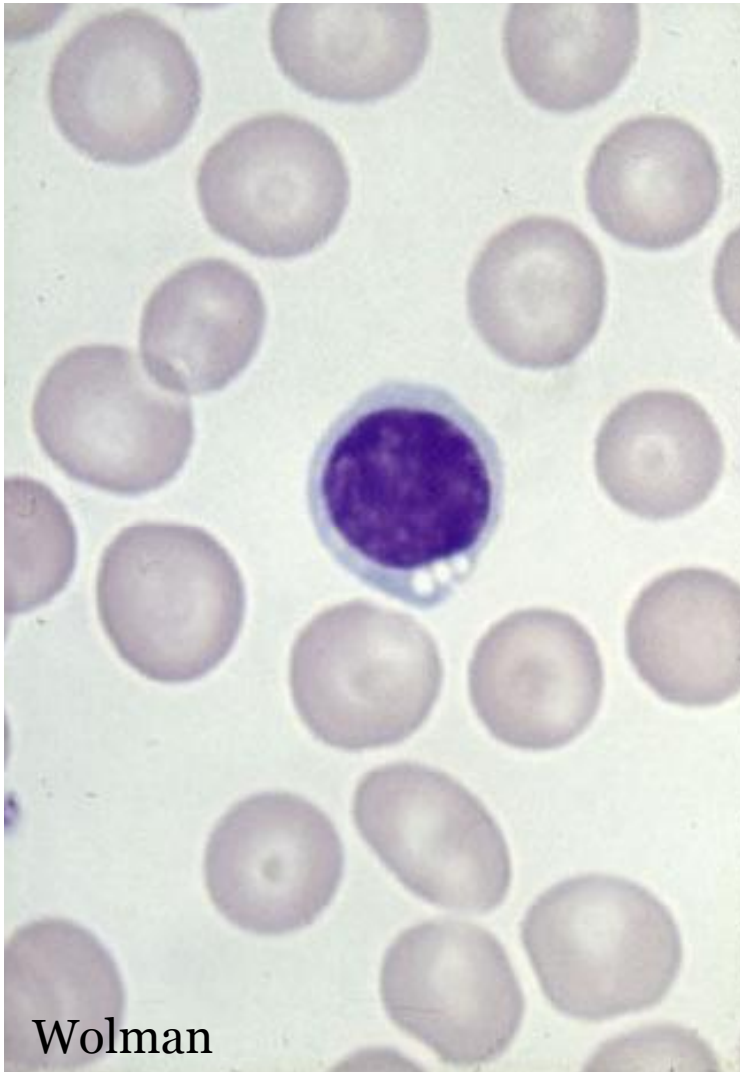

MGG - Pompe

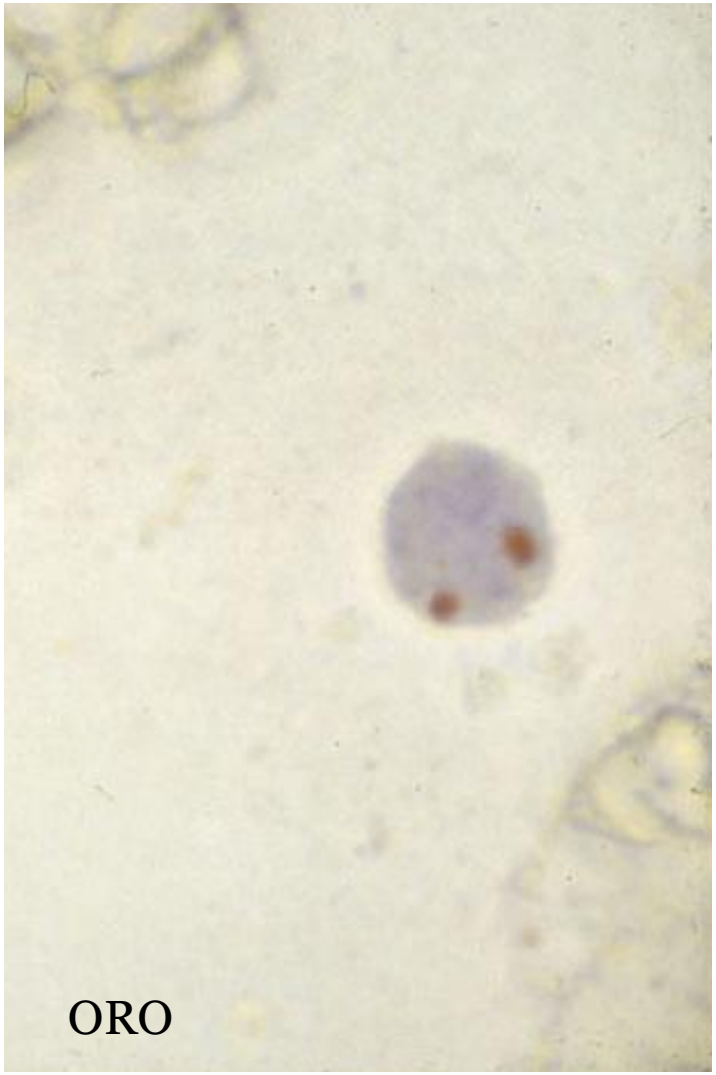


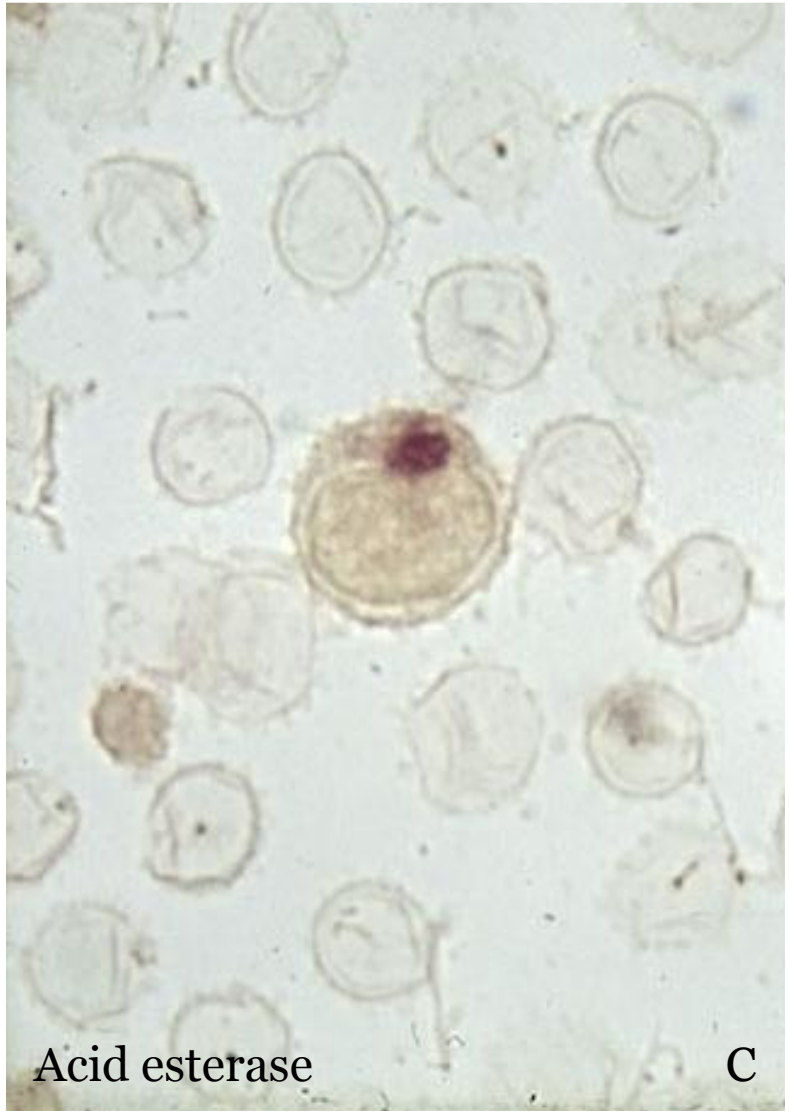
Celloidinised PAS - Pompe

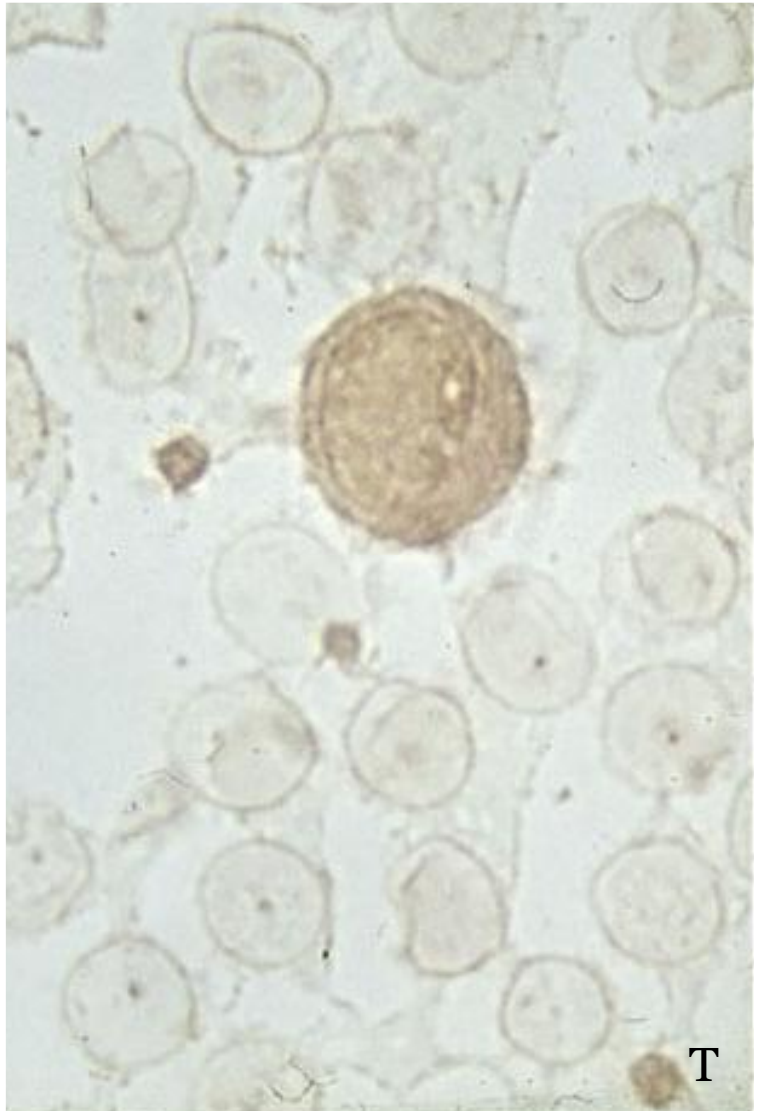

H&E - Pompe


Pompe


Wolman


ORO


Acid esterase
C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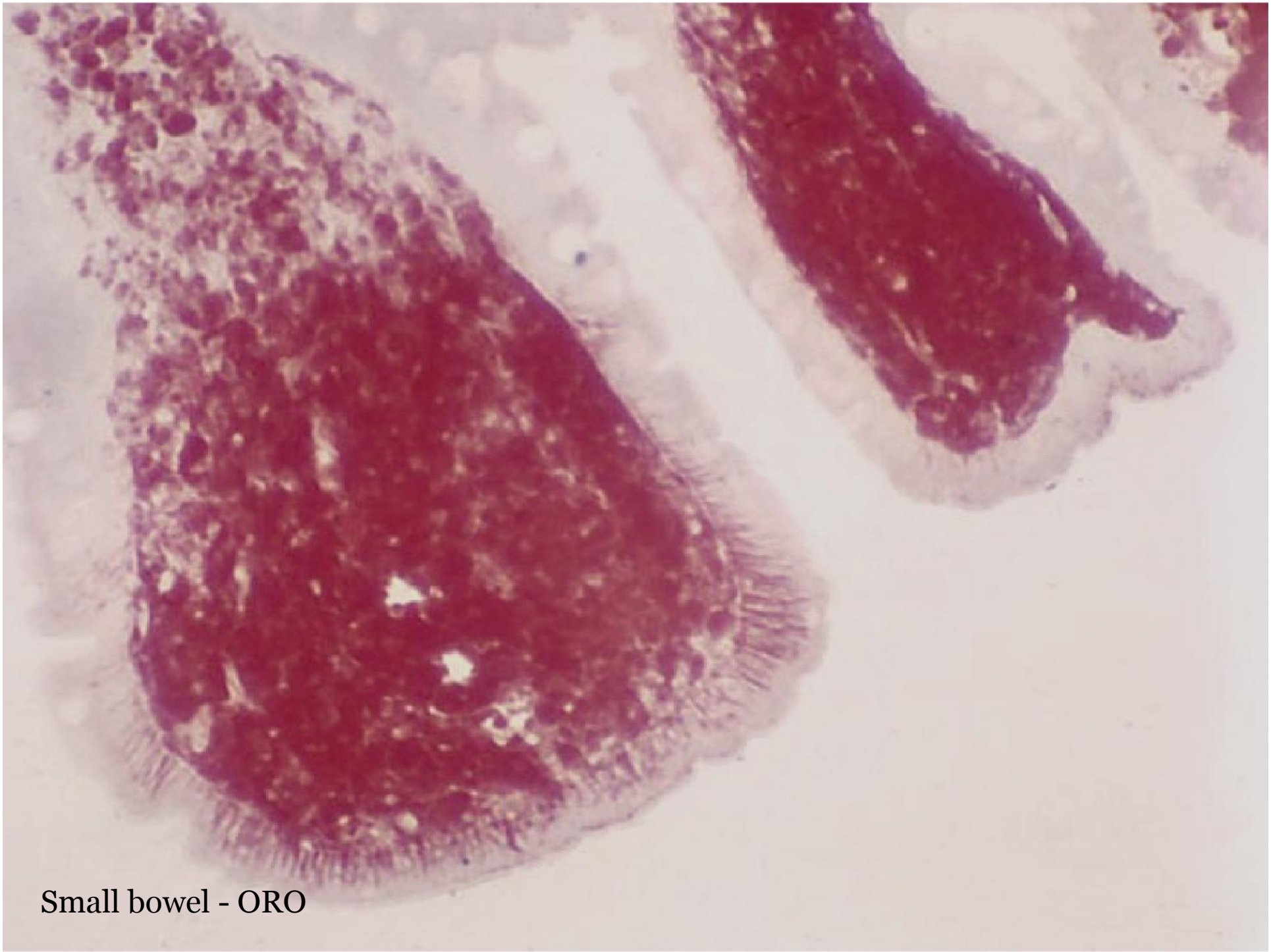
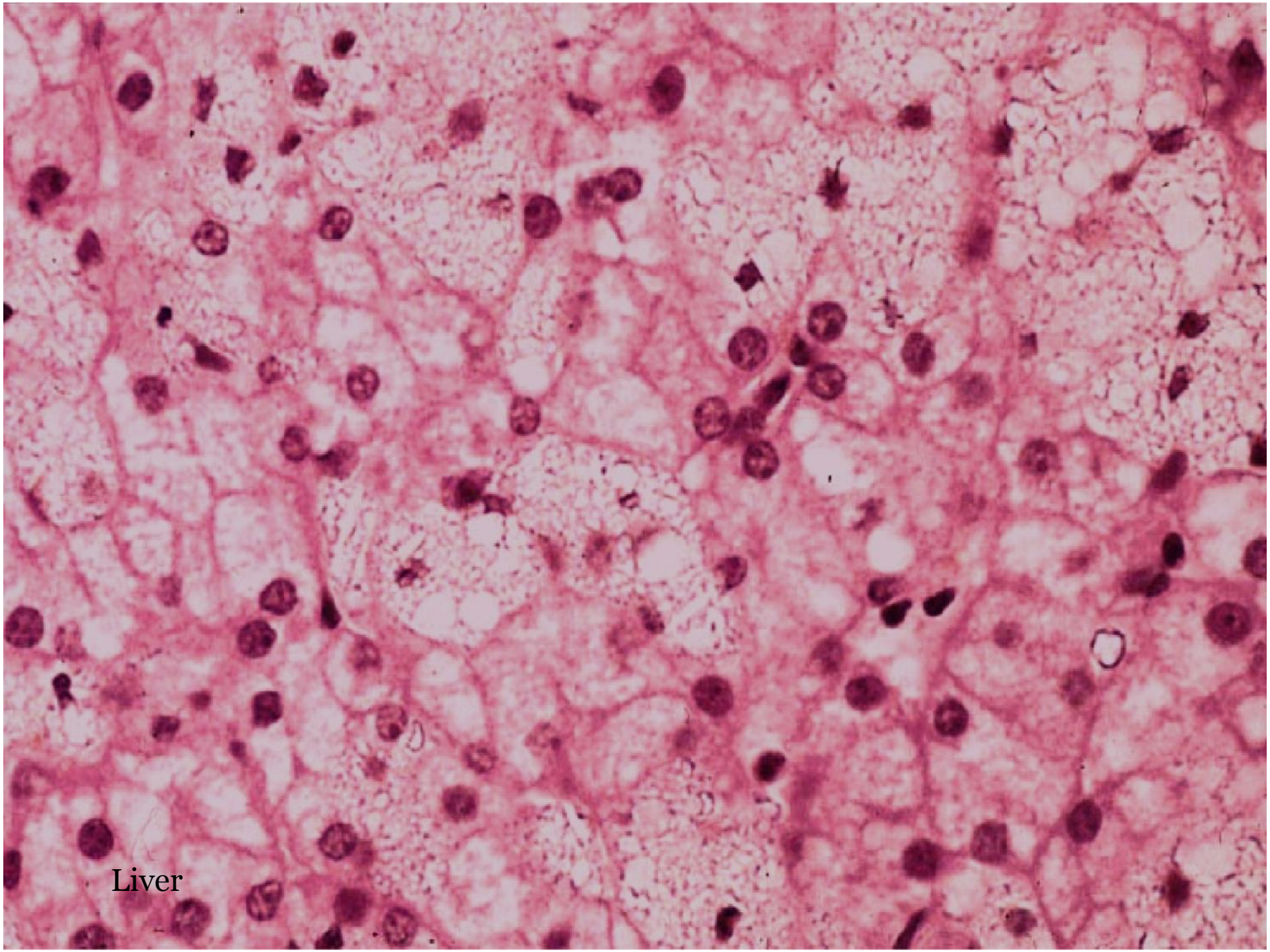
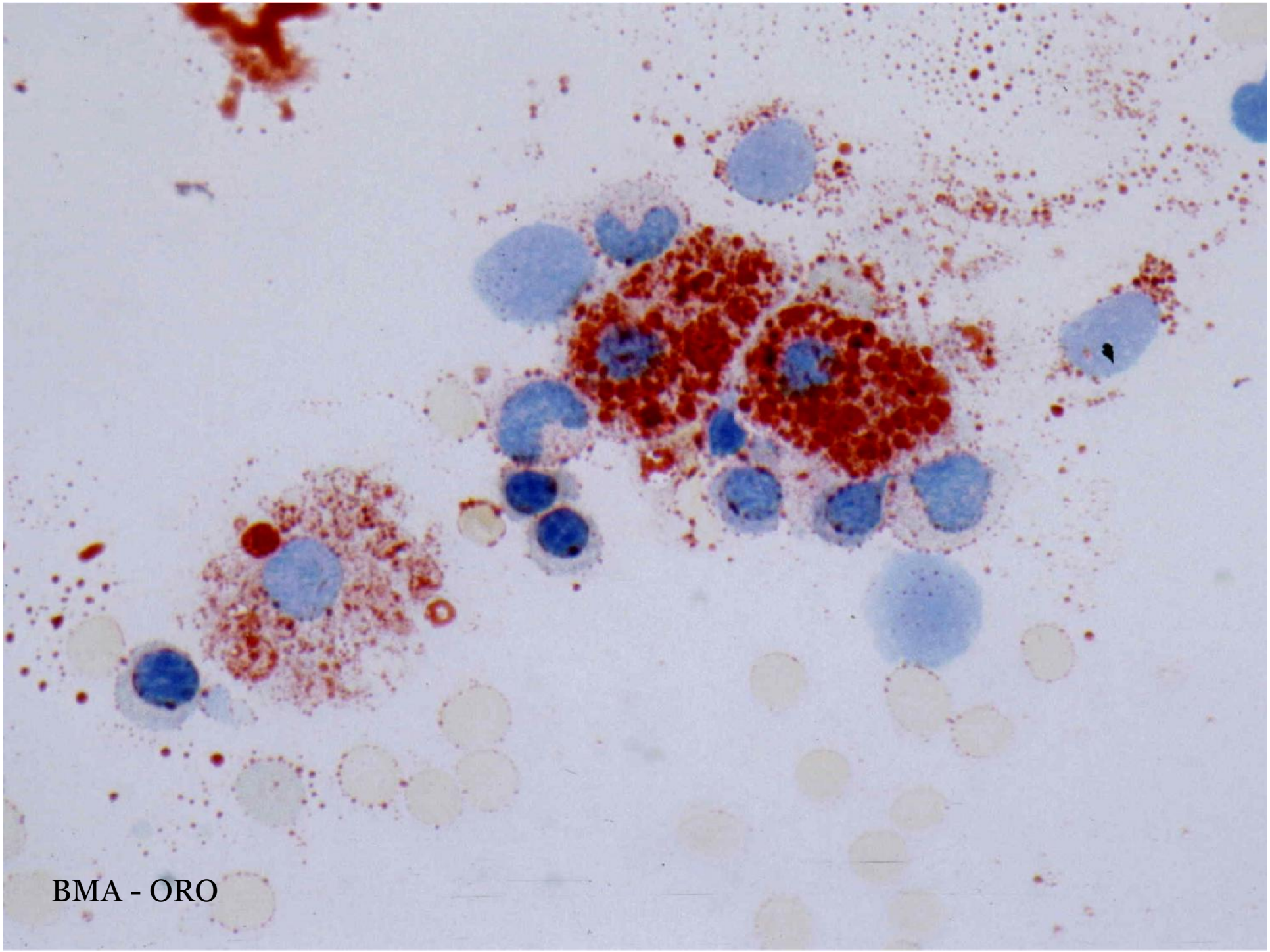
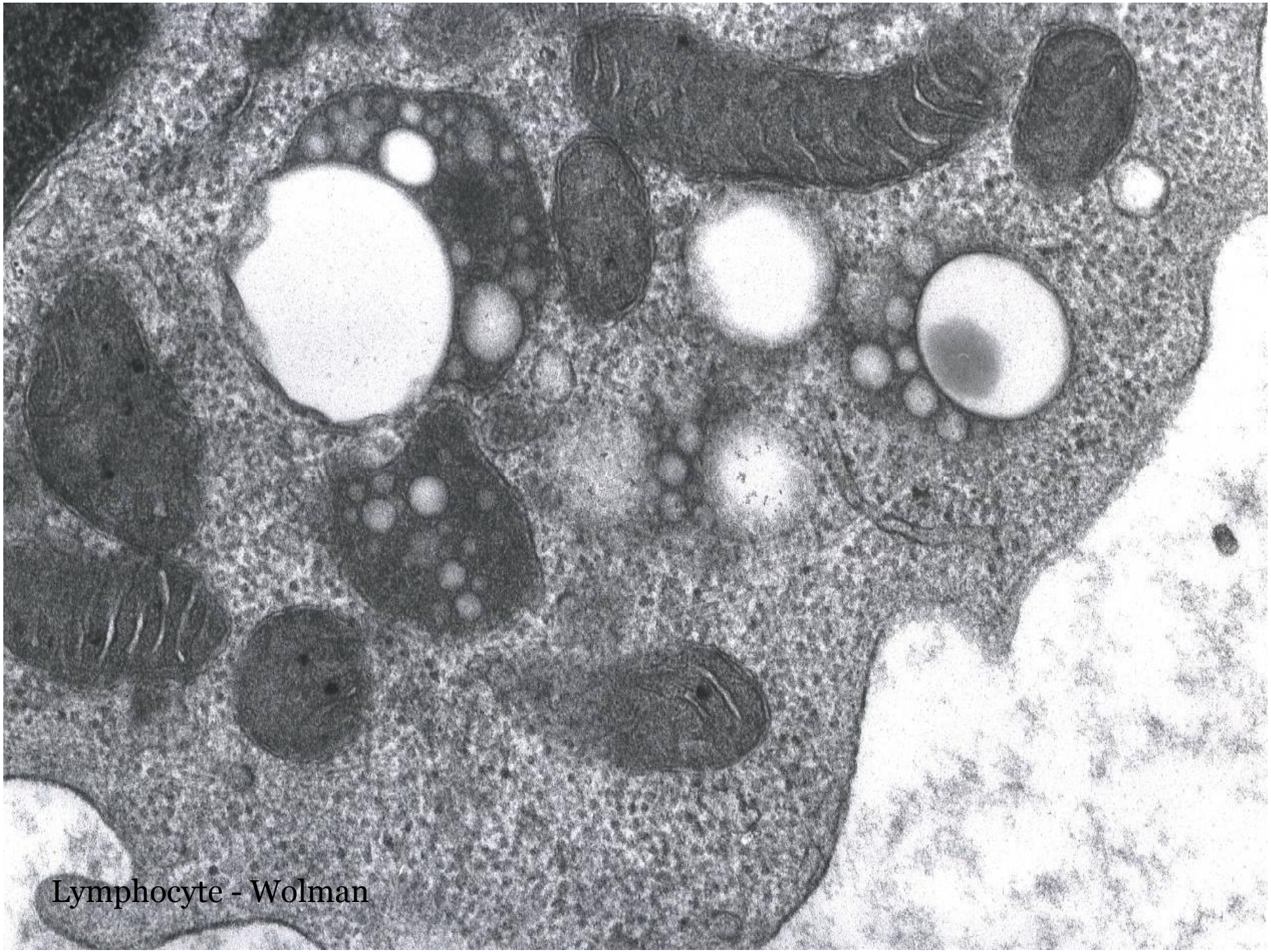


Small bowel - ORO

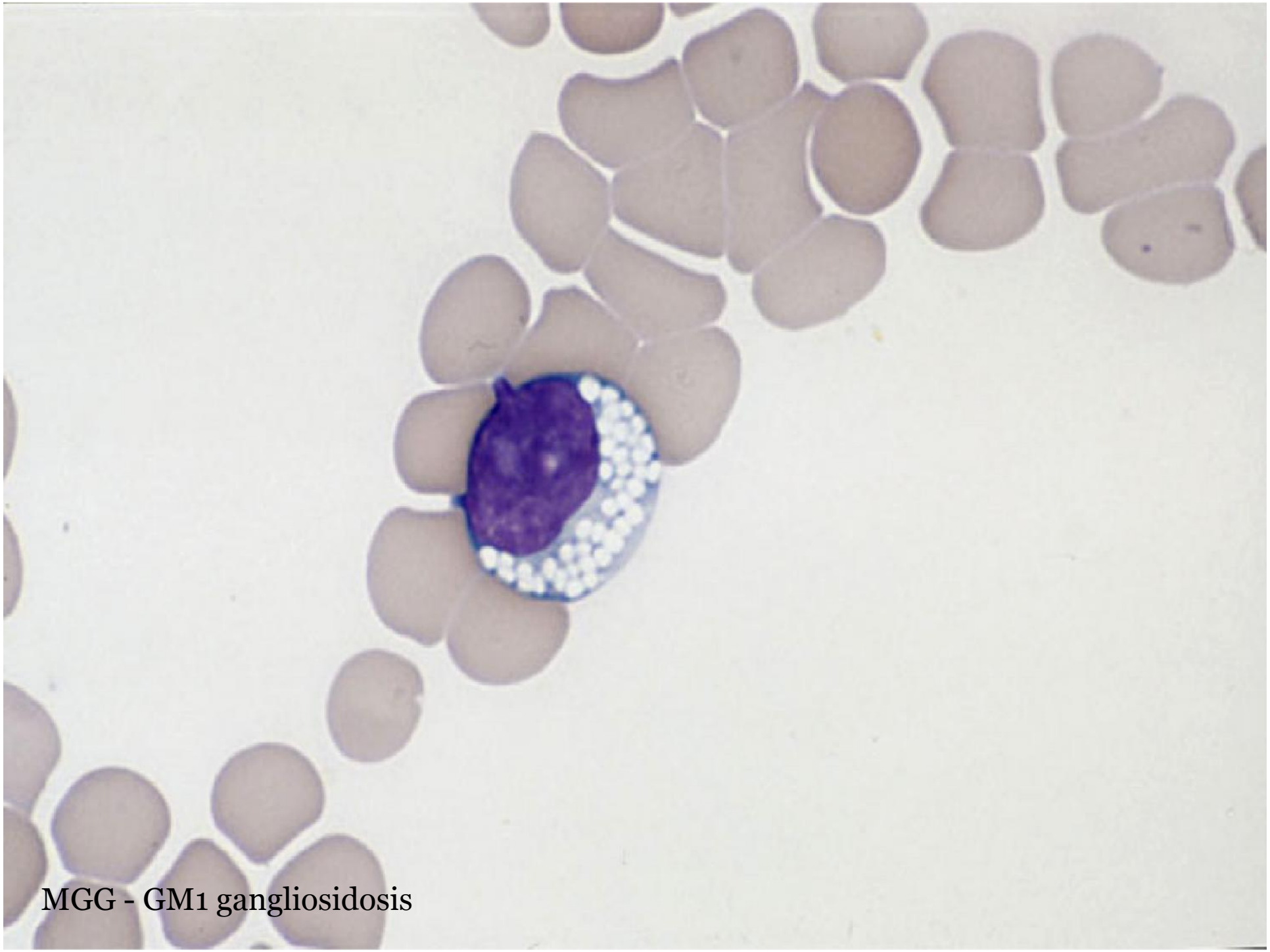

Liver


BMA - ORO

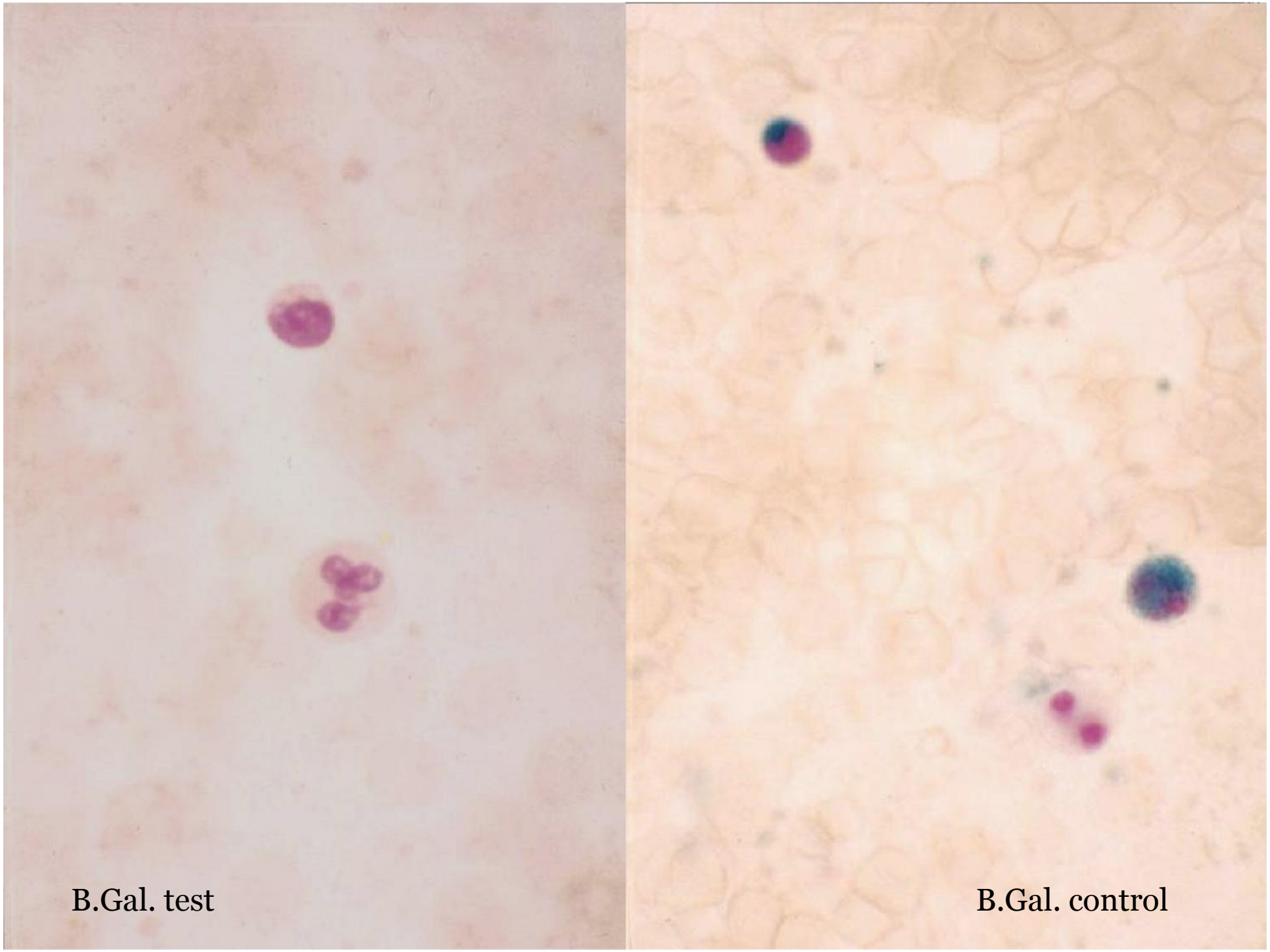

Lymphocyte - Wolman

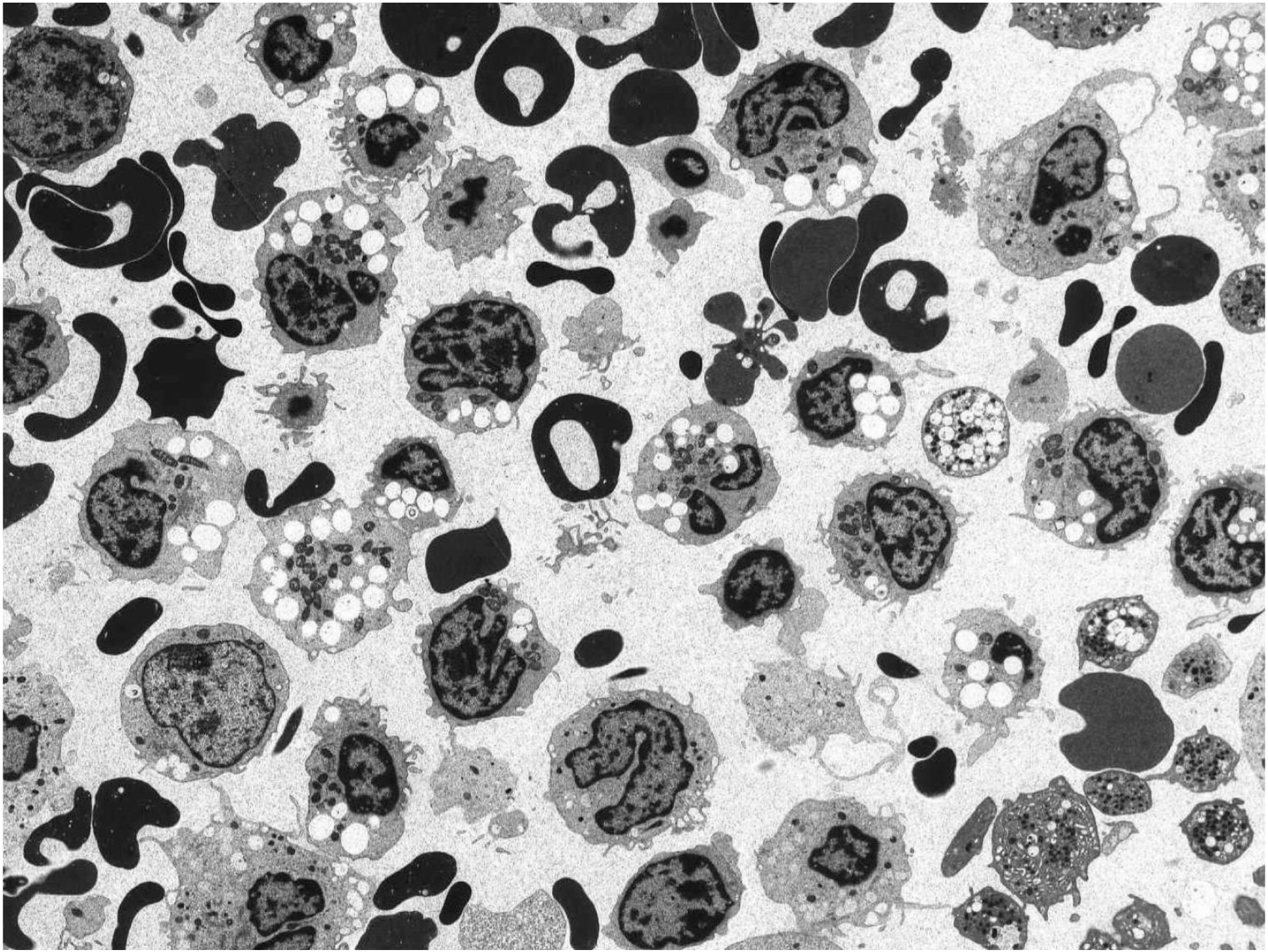
Large vacuolated lymphocytes

- GM1 gangliosidosis type I
- Juvenile Batten disease
- Mannosidosis
- Sialidosis
- I cell disease
- Sialic acid and Salla disease



MGG - GM1 gangliosidosis


B.Gal. test
B.Gal. control

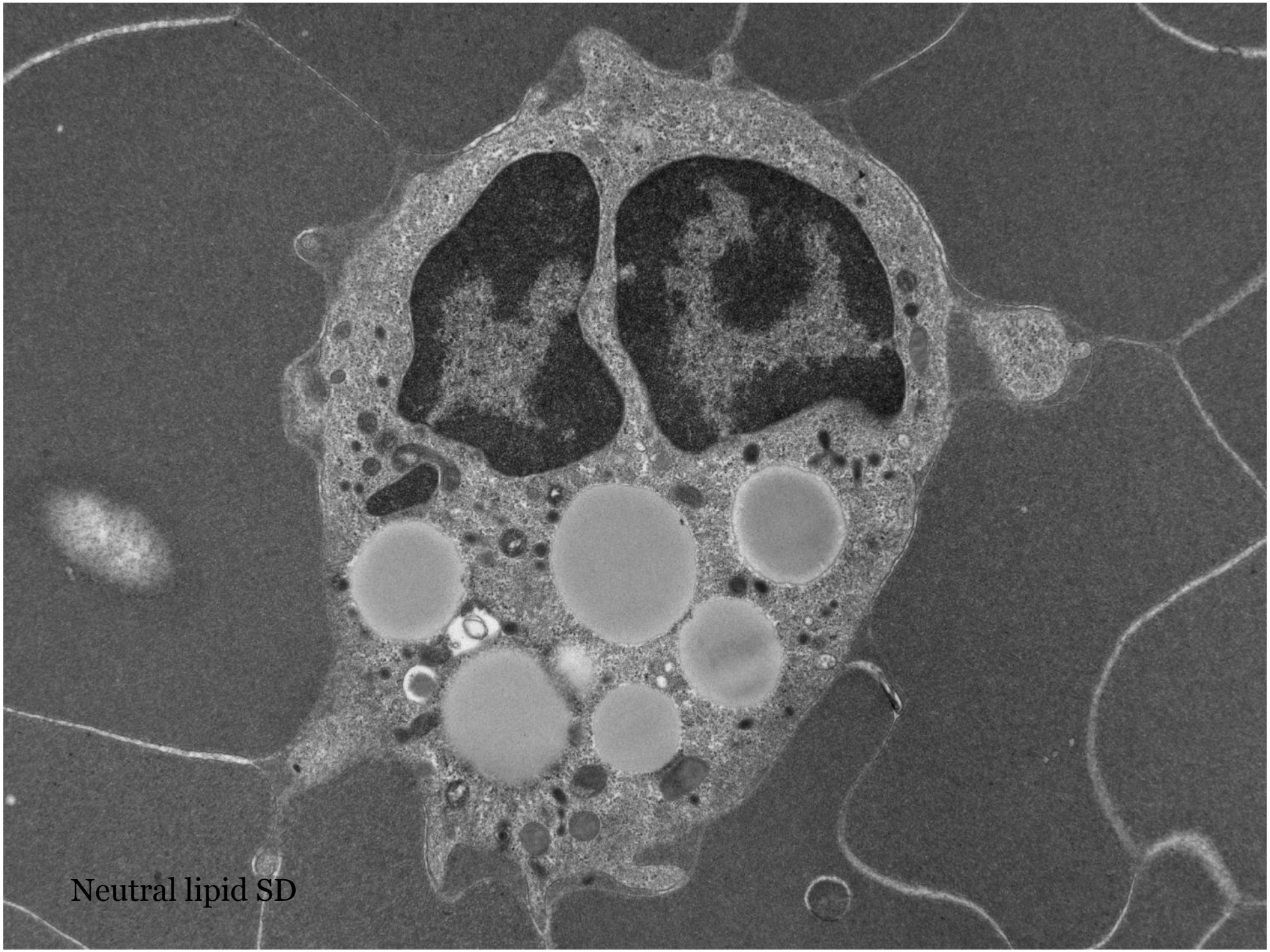


Lymphocytes - other inclusions

- Cytoplasmic inclusions – Chediak-Higashi, Gasser cells MPS
- Metachromatic inclusions – Sanfillipo MPS III

White cell changes - Neutrophils

- Vacuolation – nonspecific, neutral lipid storage
- Toxic granulation – inflammatory states ‘sepsis’
- Alder granulation – MPS
- Atypical granules – Chediak-Higashi


Neutral lipid SD

White cell changes - Eosinophils

- Atypical granulation – GM1, Sialic acid storage

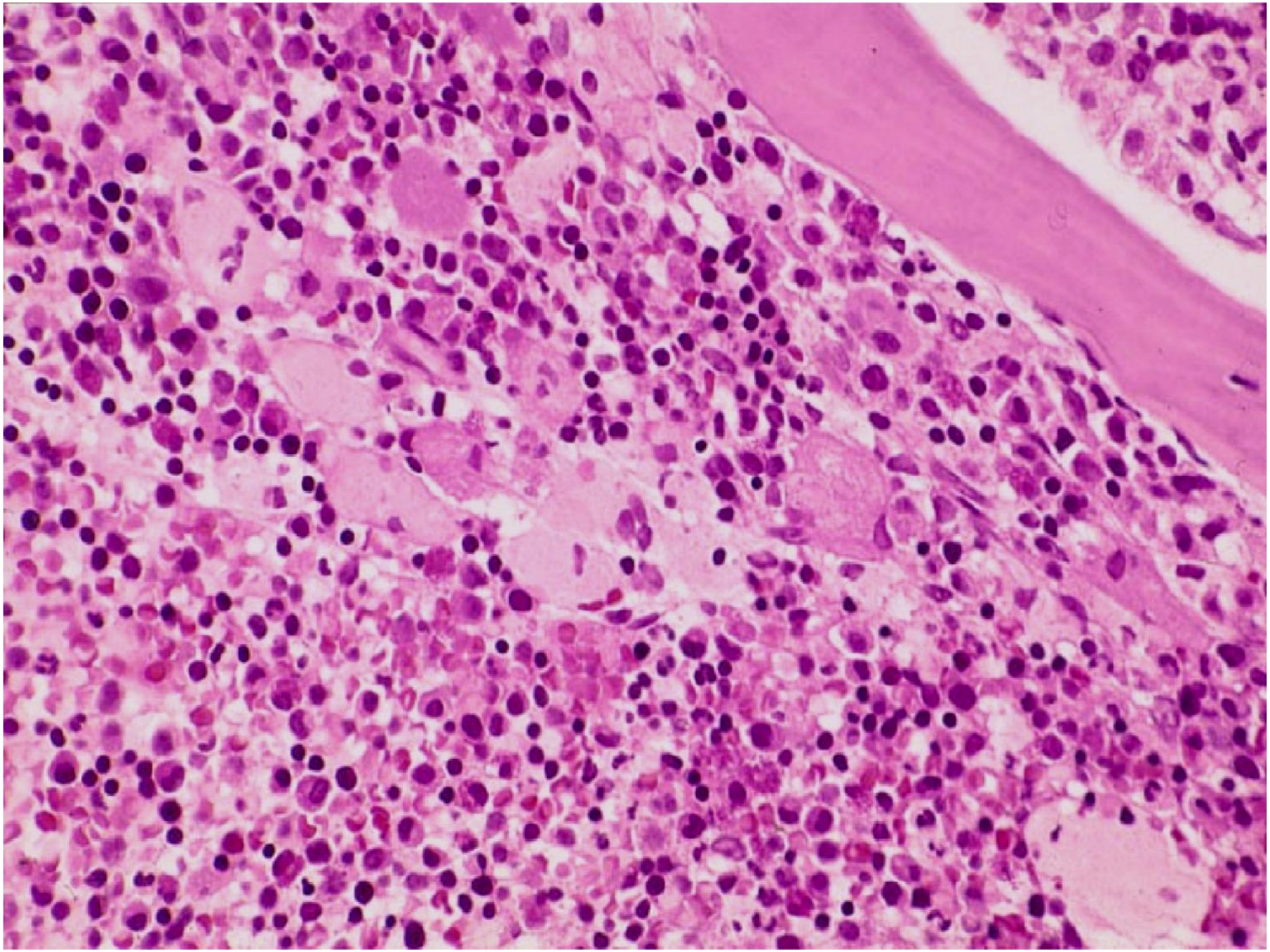
Bone marrow

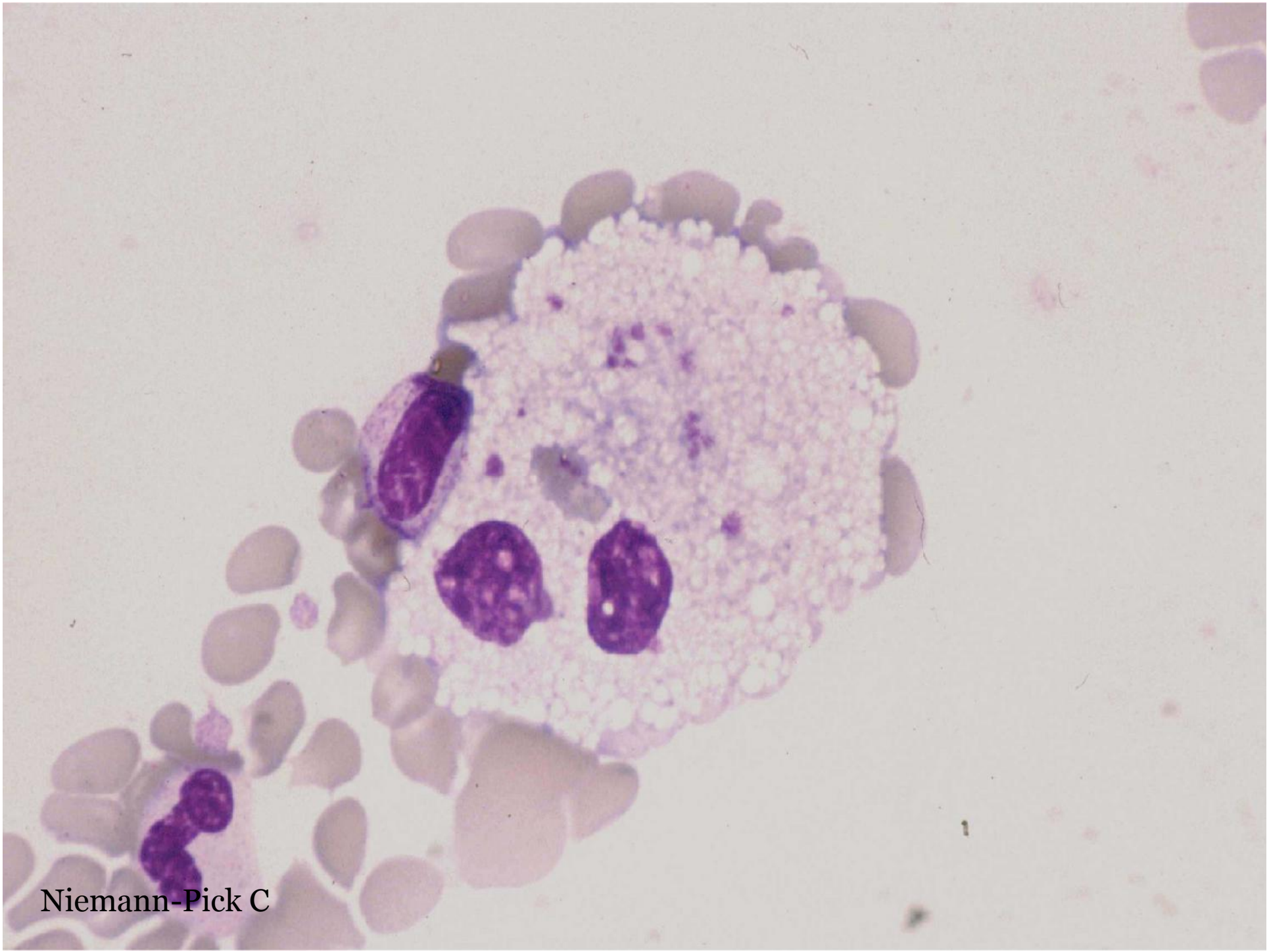
- Bone marrow aspirates
  - preferred
  - enzymes, lipids preserved
  - histochemical techniques, EM

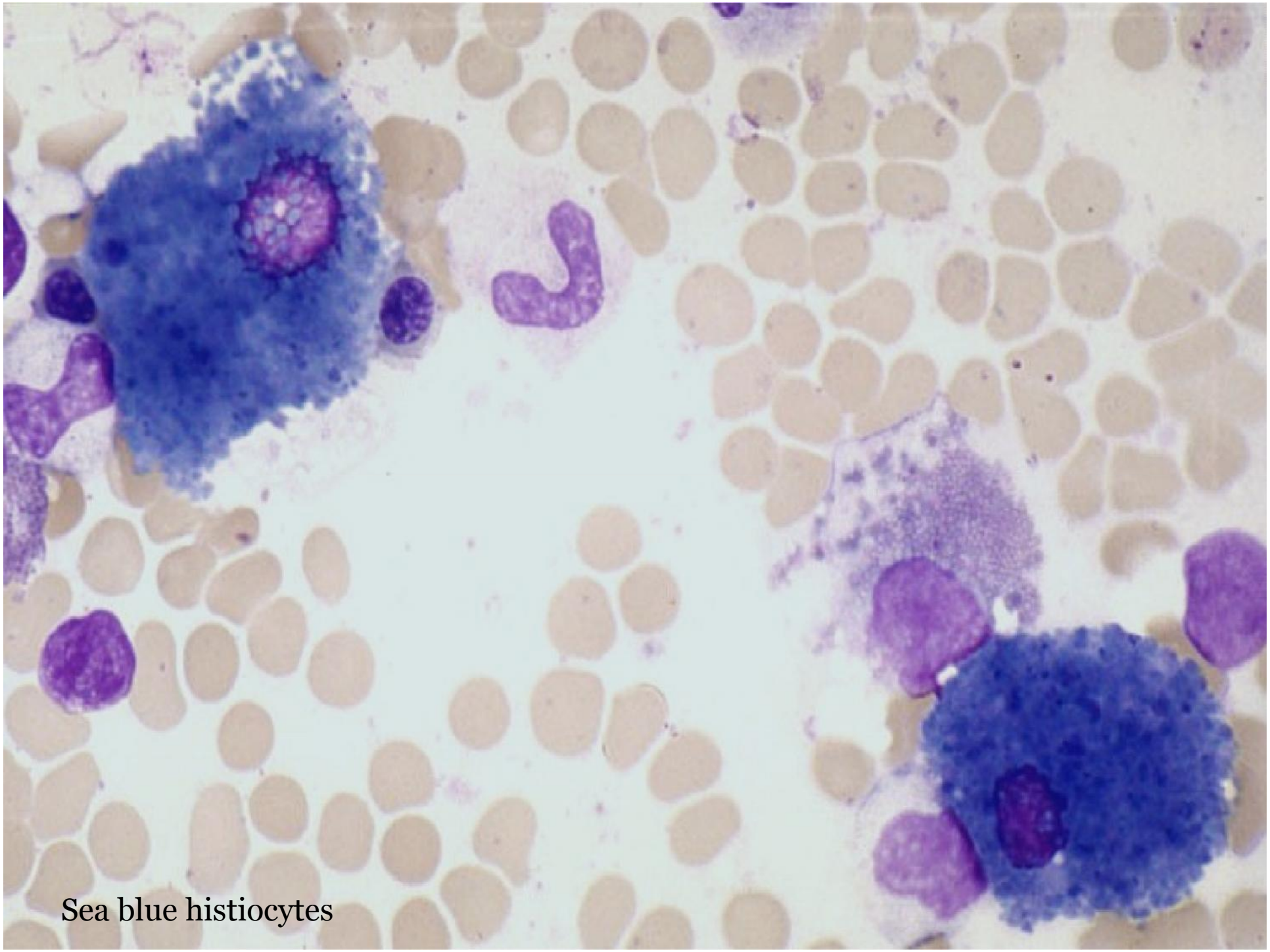
- Bone marrow trephines
  - more material
  - routine stains, immunocytochemistry, EM

Storage cells

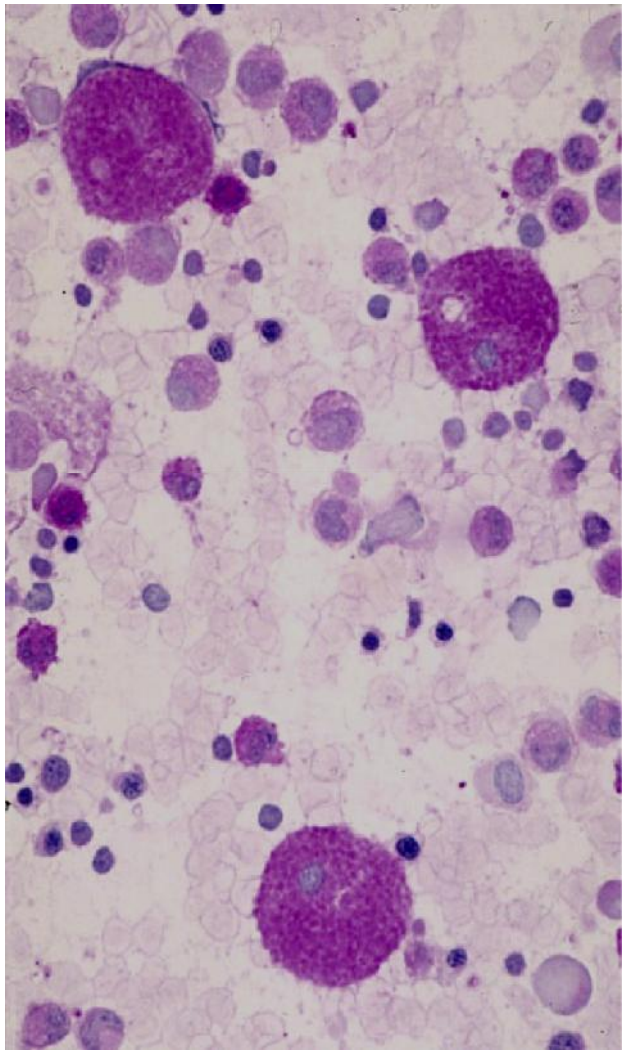
- Foamy cells
  - Niemann-Pick, Mannosidosis, Wolman
- Fibrillary cells
  - Gaucher, GM1 gangliosidosis type II



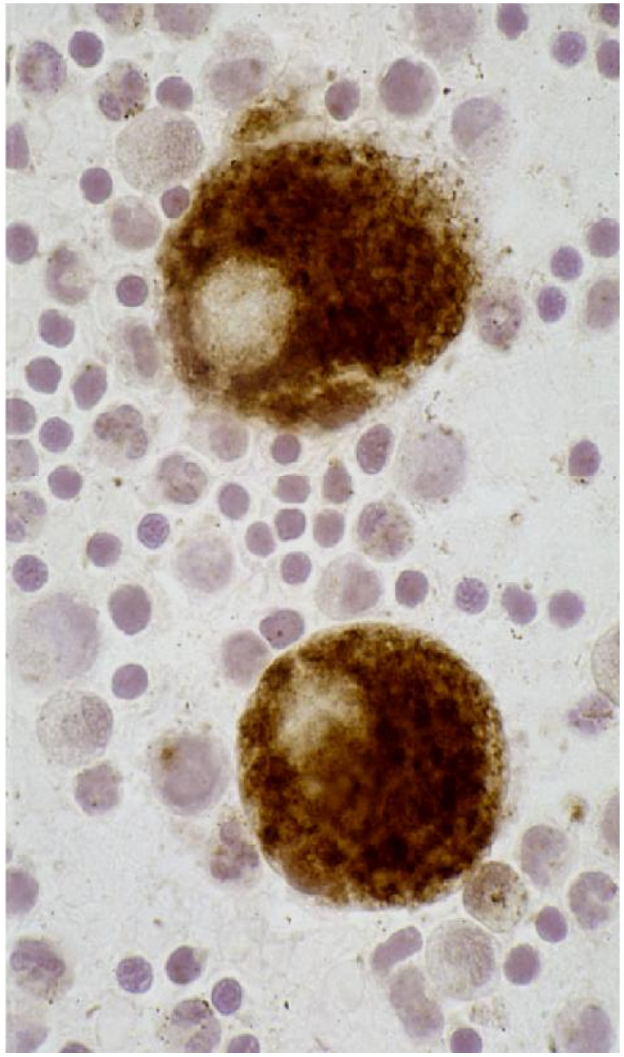

Niemann-Pick C



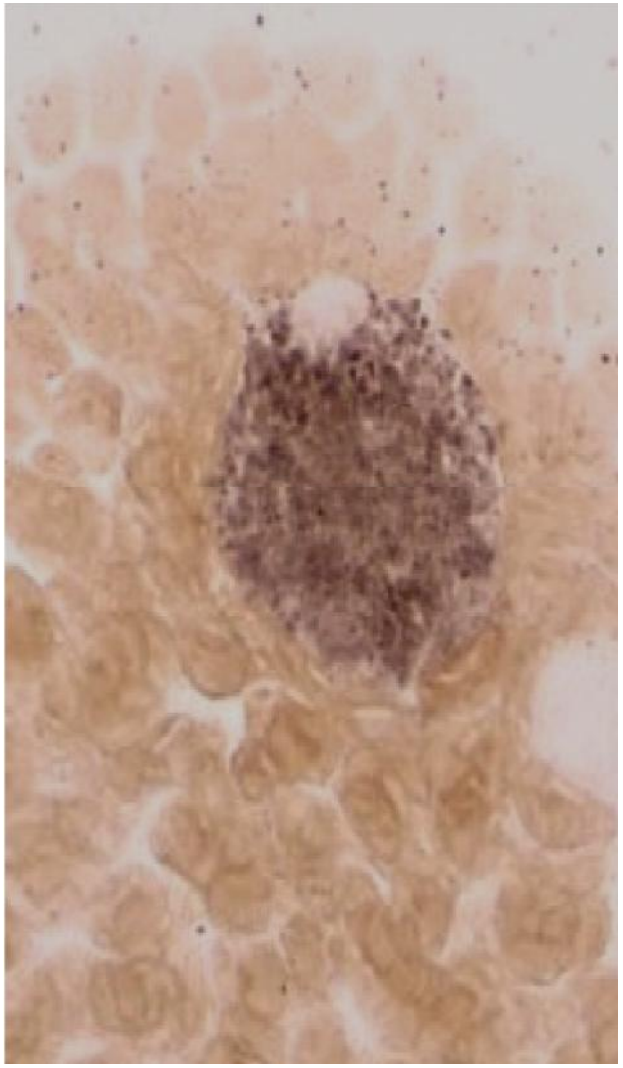
Sea blue histiocytes



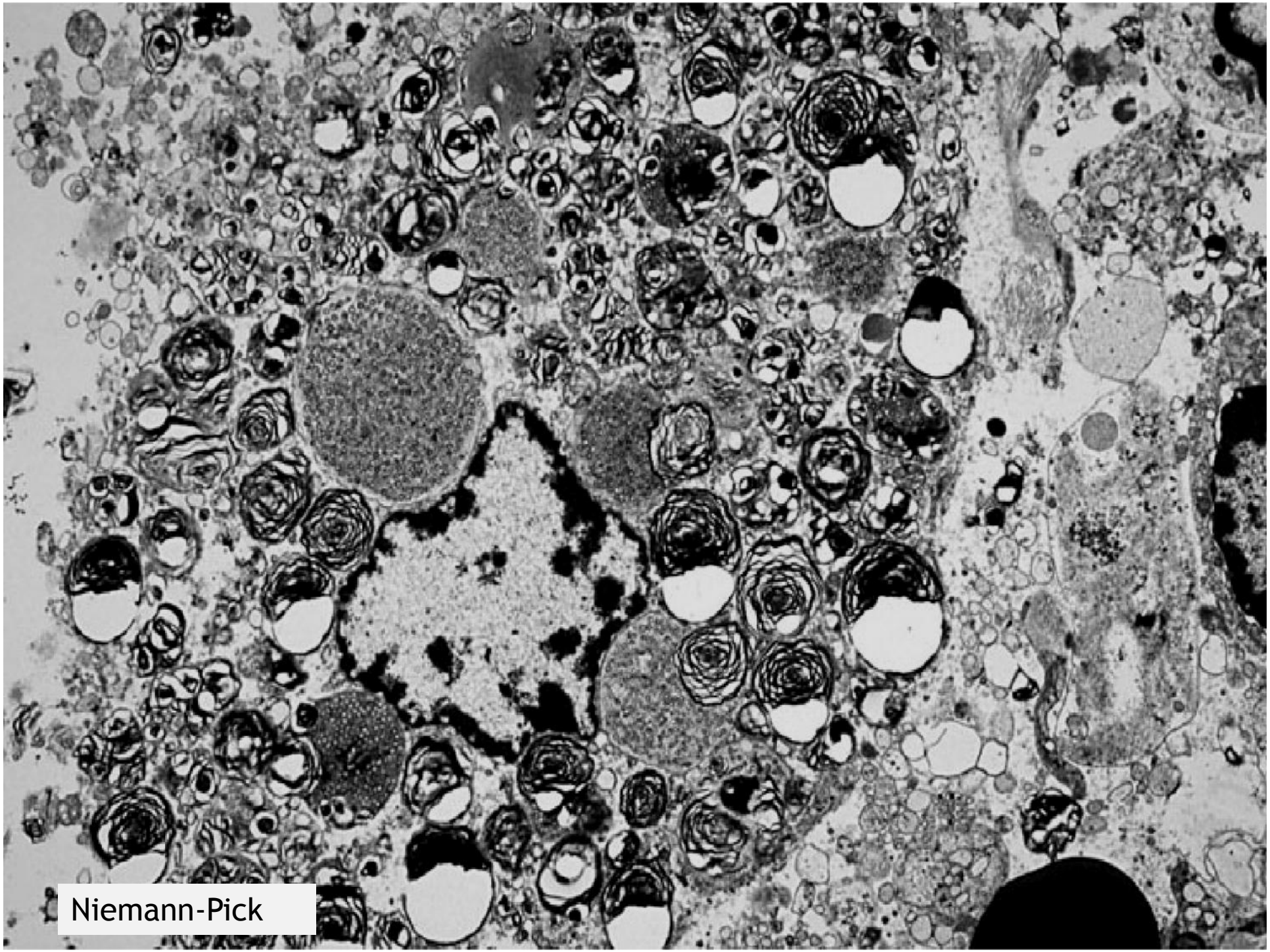
PAS

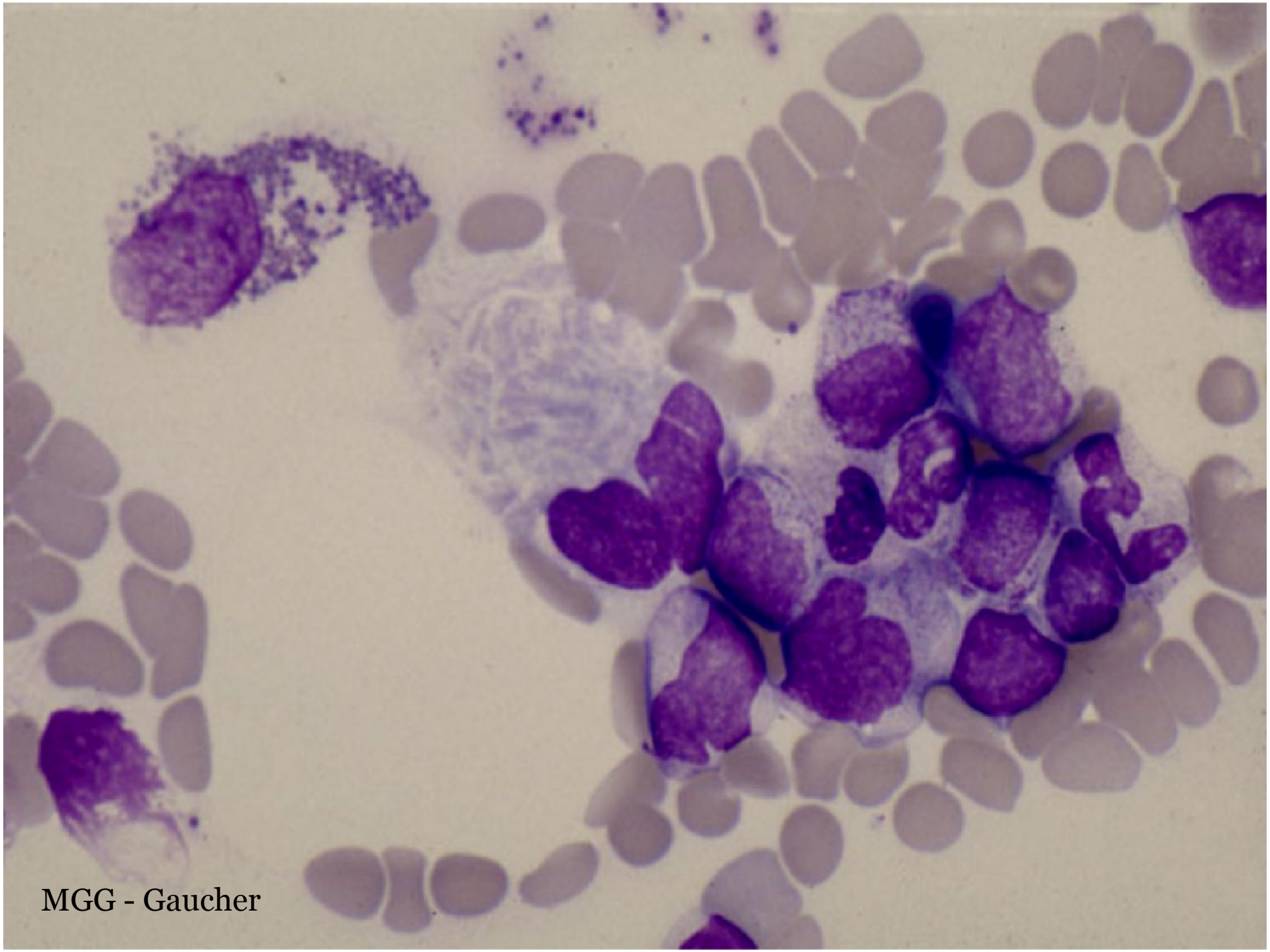


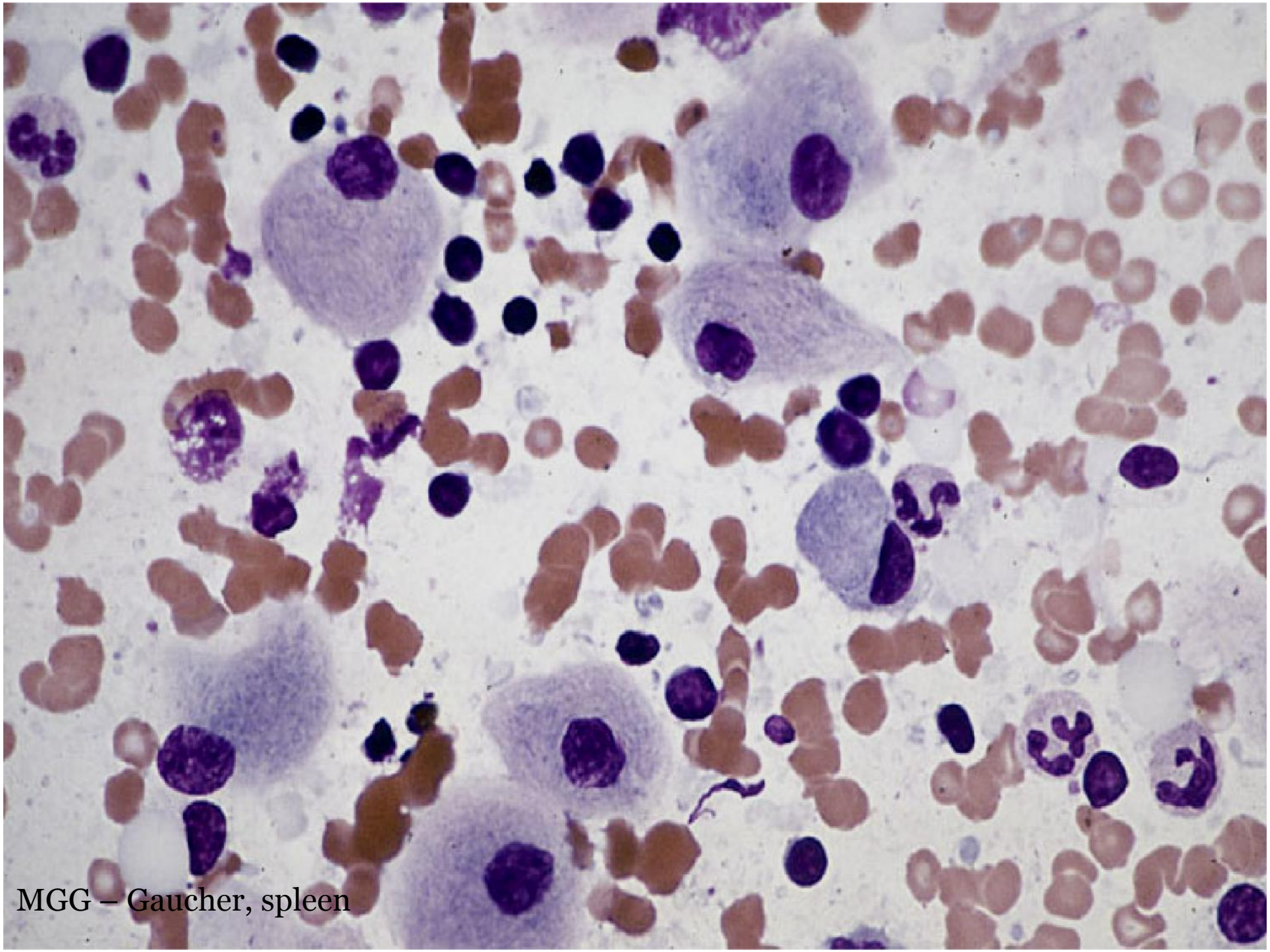
Acid phosphatase



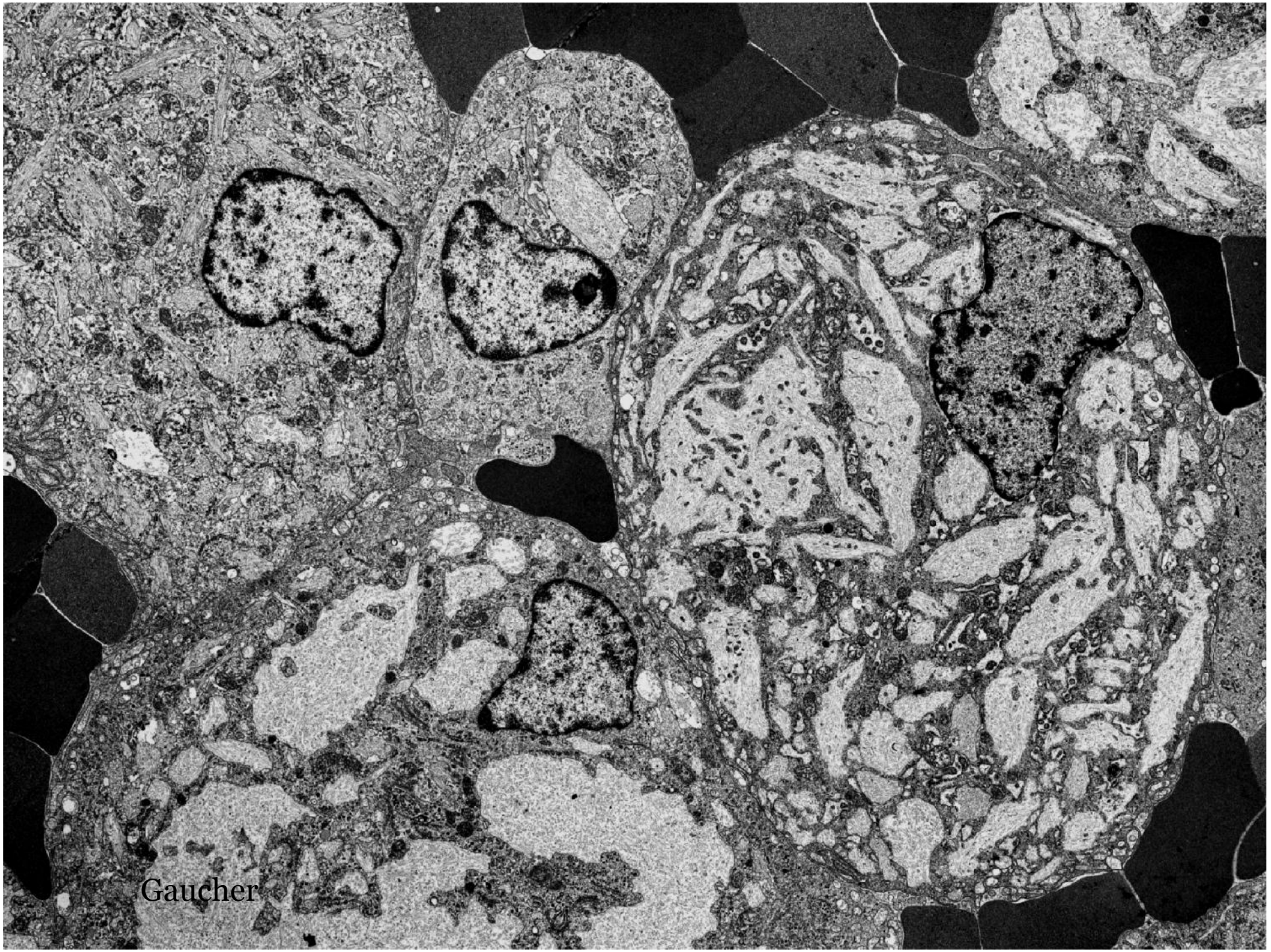
Sudan black

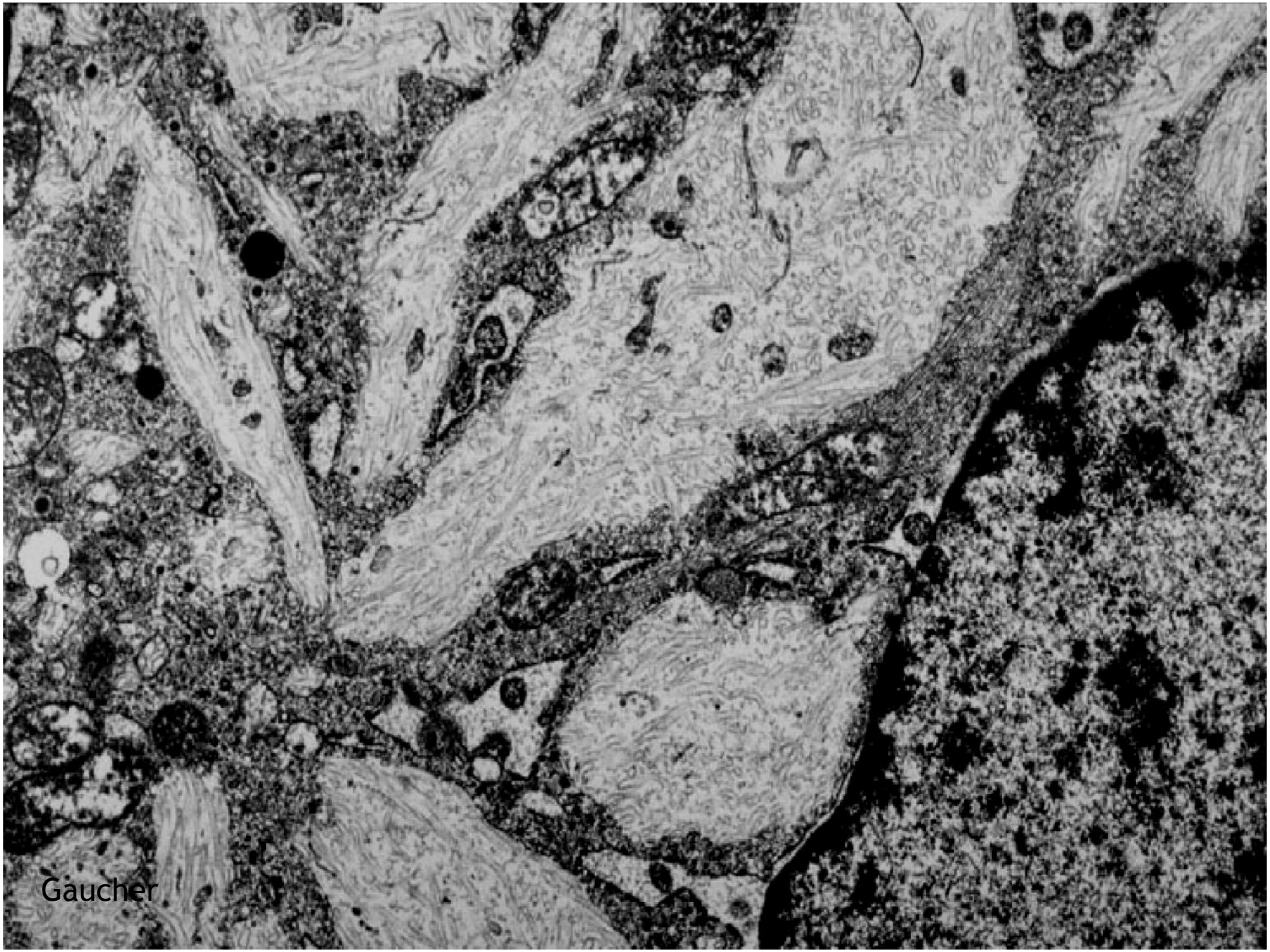

Niemann-Pick


MGG - Gaucher



MGG – Gaucher, spleen


Gaucher


Gaucher

Part 2 to follow.