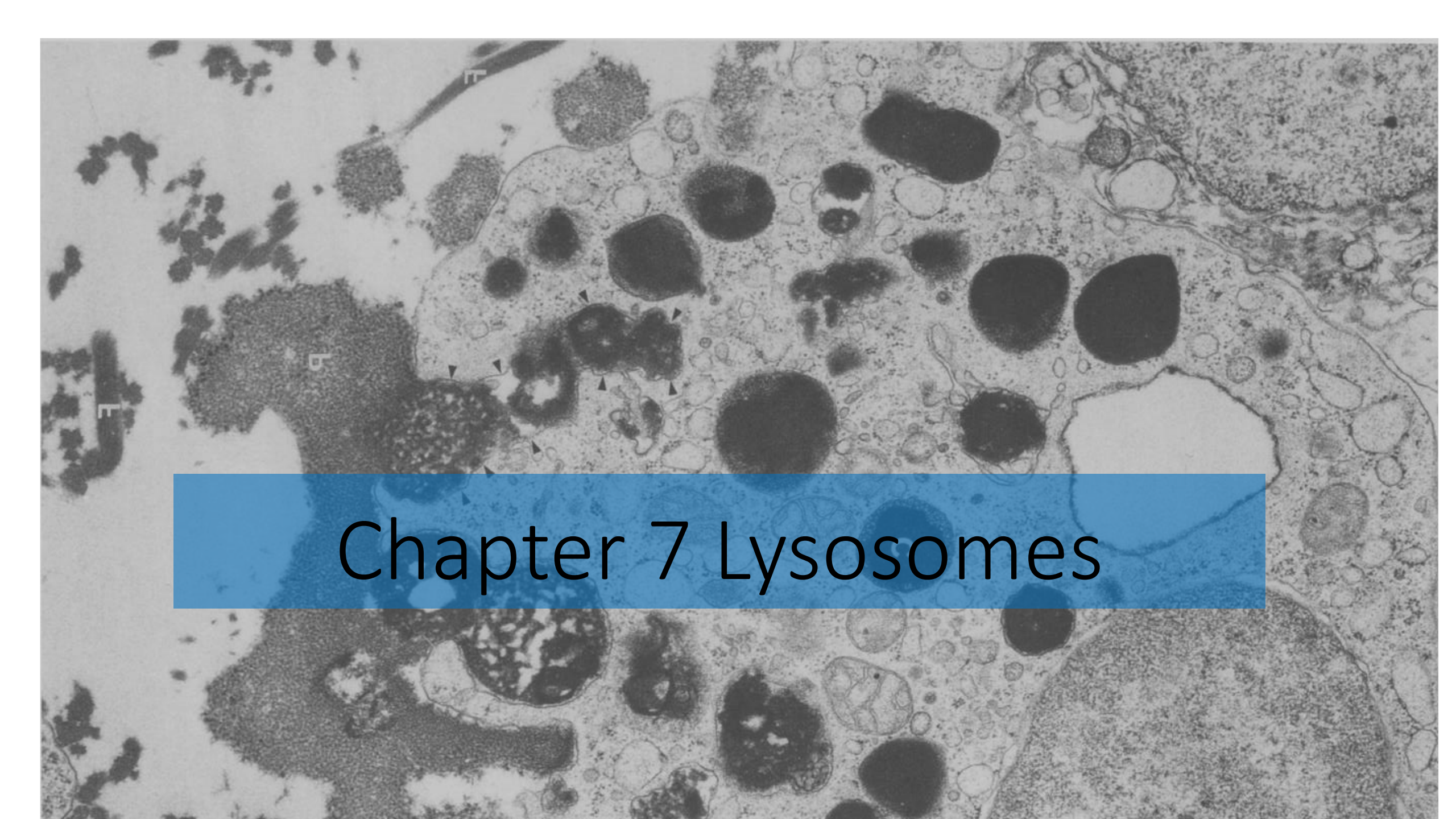


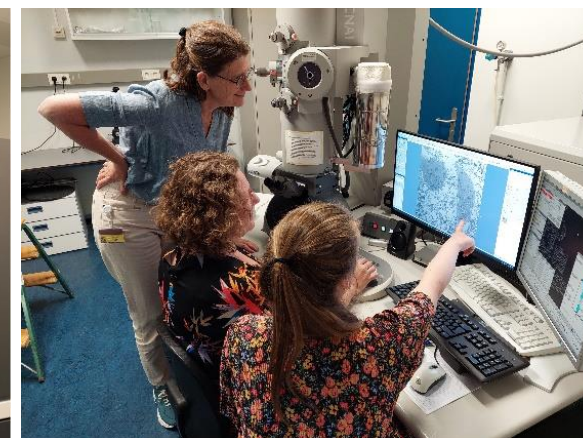
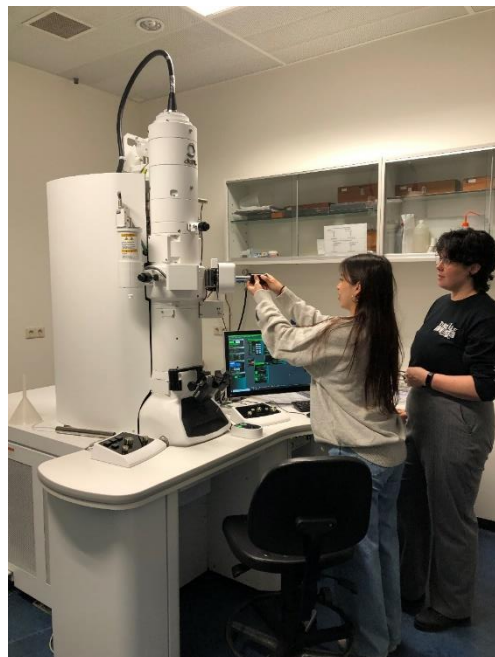
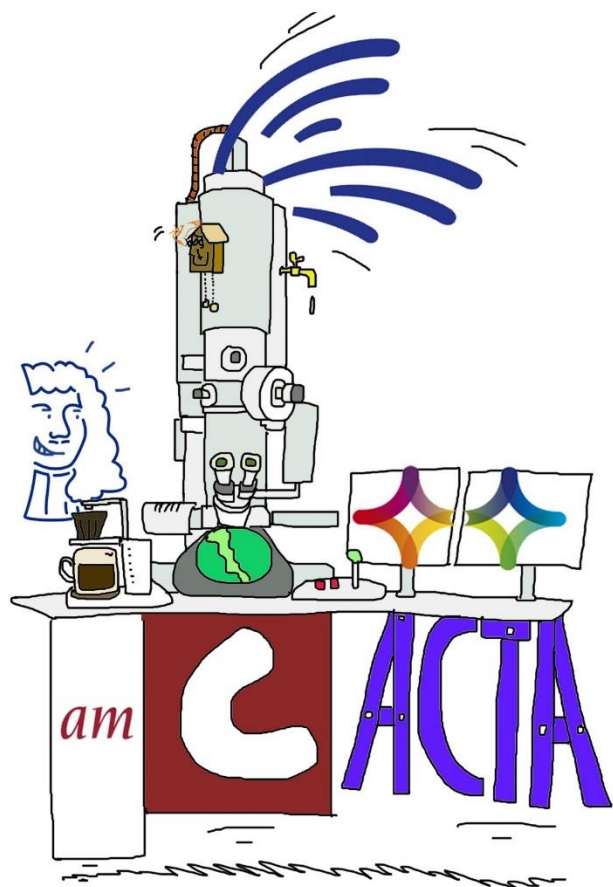
This is a transmission electron micrograph (TEM) of a cell. The image shows various organelles, including several large, dark, electron-dense lysosomes. Some of these lysosomes contain internal structures, possibly viral particles or other organelles. There are also smaller, lighter-colored vesicles and a large, irregularly shaped nucleus on the left side. The cytoplasm is filled with various proteins and other cellular components. A blue rectangular box is overlaid on the lower half of the image, containing the text "Chapter 7 Lysosomes".

# Chapter 7 Lysosomes



# Electron Microscopy Centre Amsterdam

## Nicole van der Wel



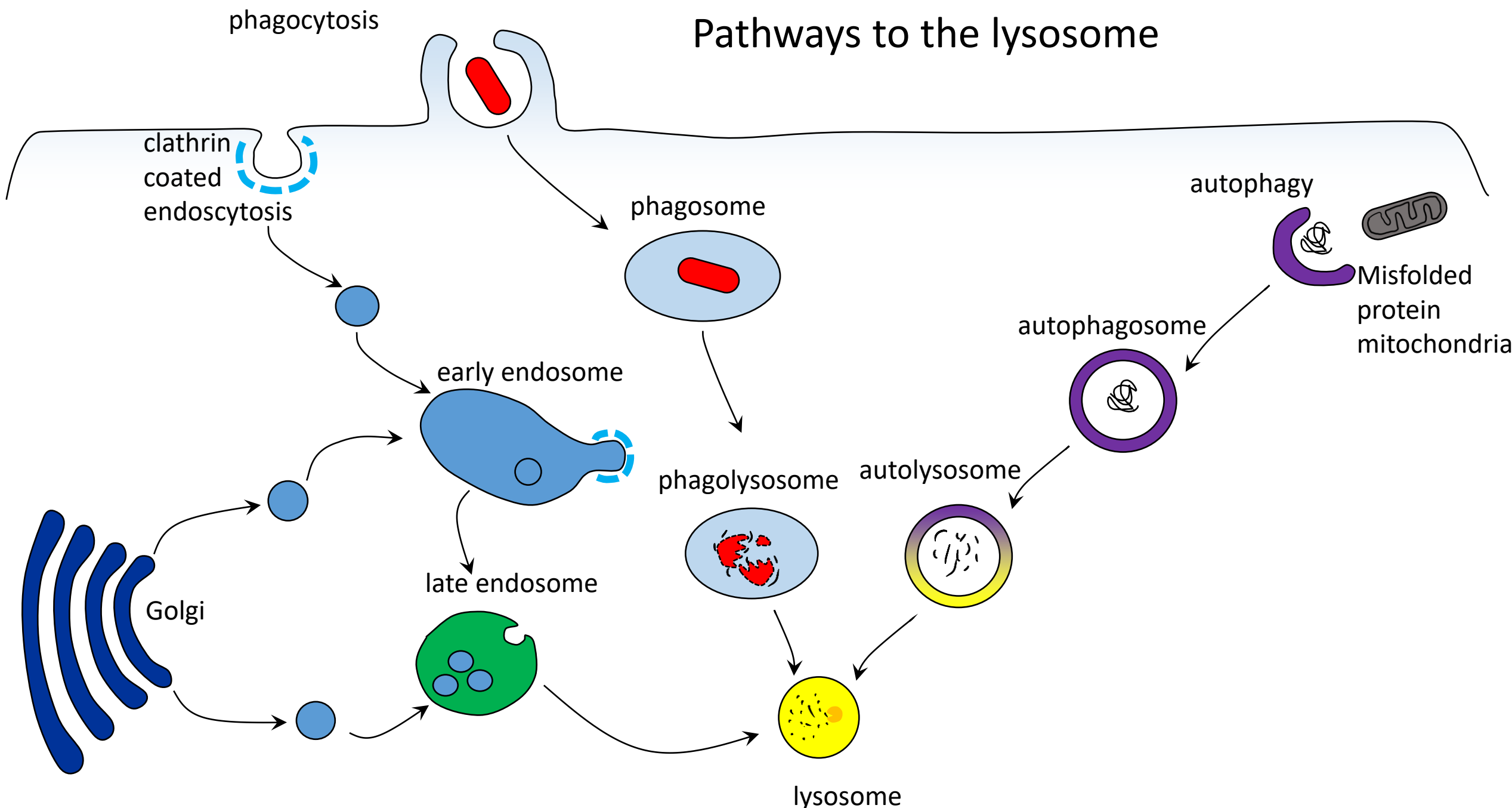
### Since opening:

800 projects have been processed  
EM operators from NKI, NIN, VUmc, ACTA, UvA  
100+ co-auteur on publications  
EMCA team 5 fte (2 pathology) EM technicians

### Our moto:

Sharing  
expertise and  
knowledge by  
bringing the EM  
operators  
together

# Pathways to the lysosome



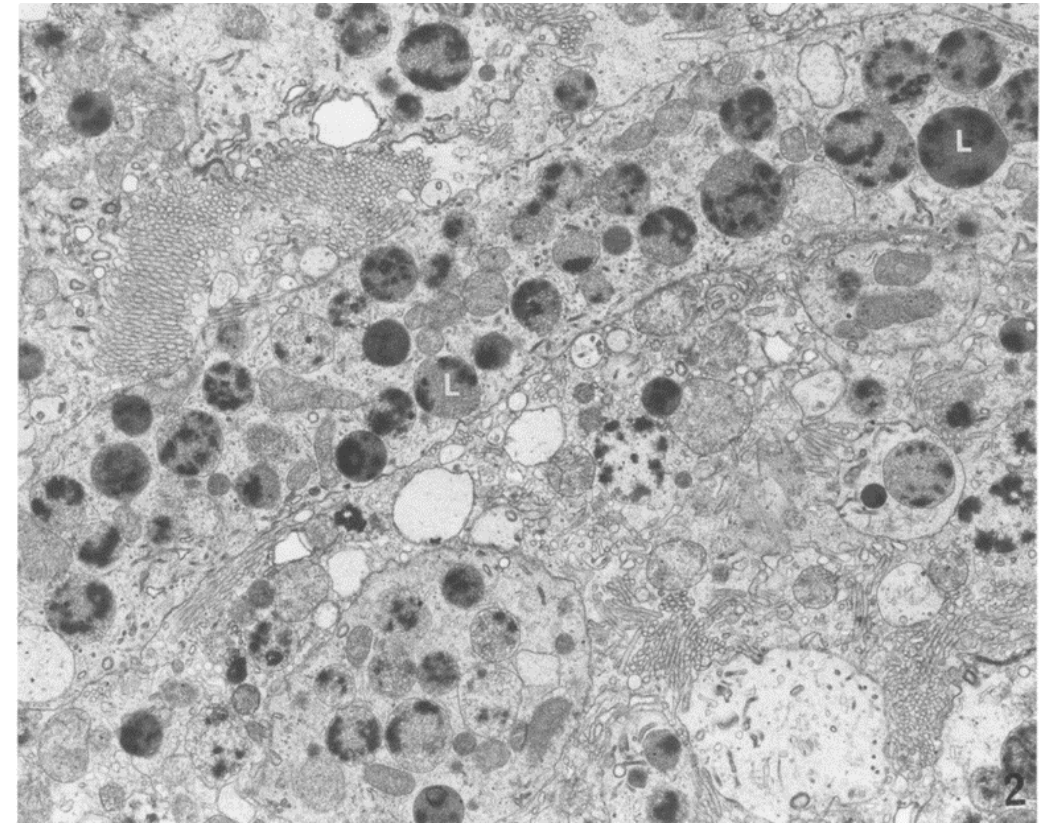
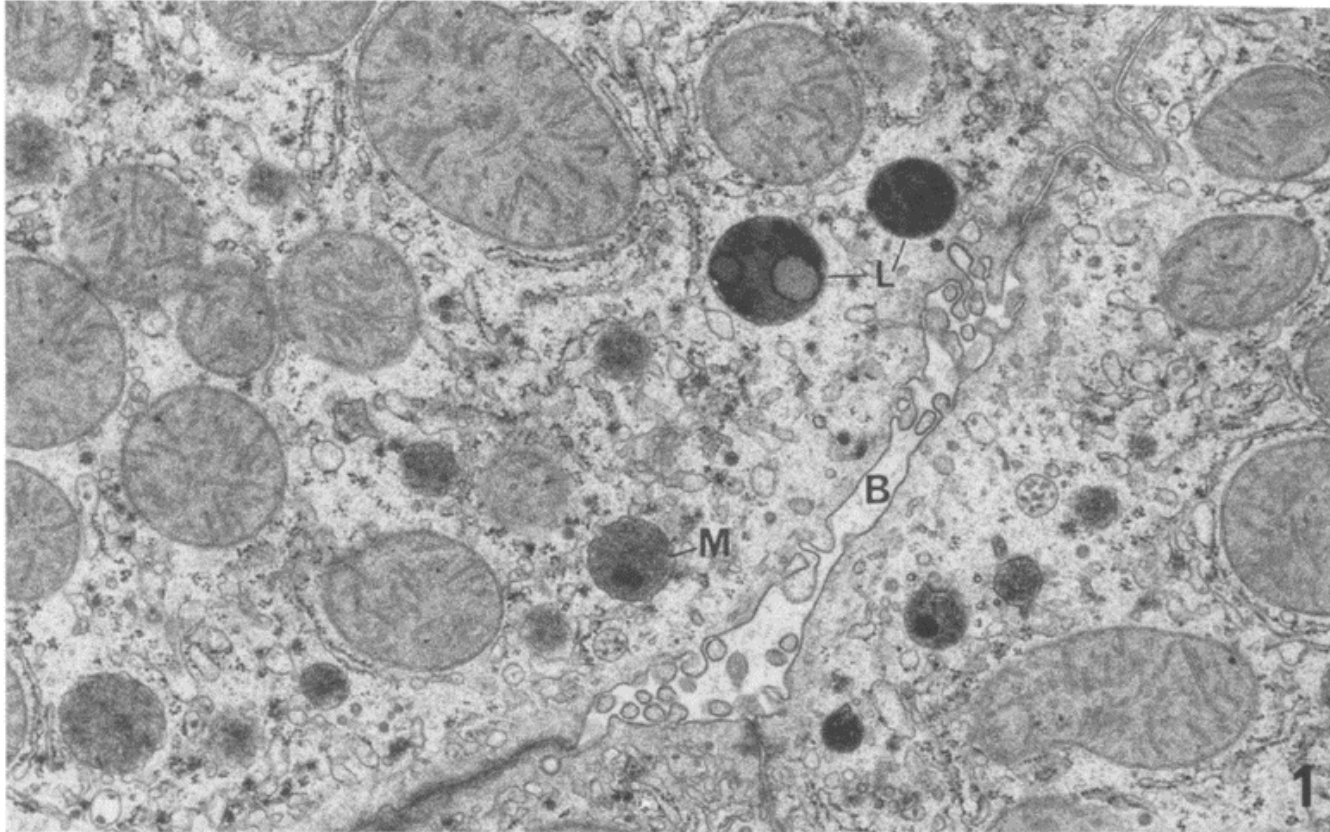


Plate 7.1

Question : what type of cells do we see in 1

Question : number of lysosomes are increased in....

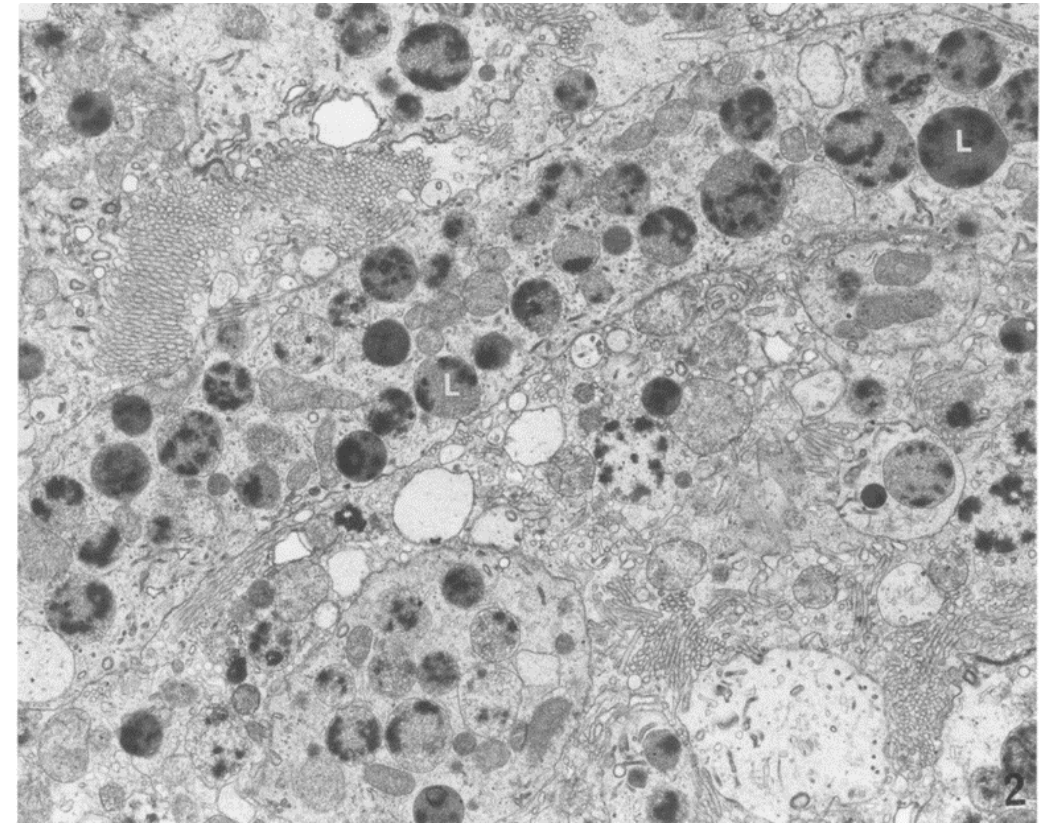
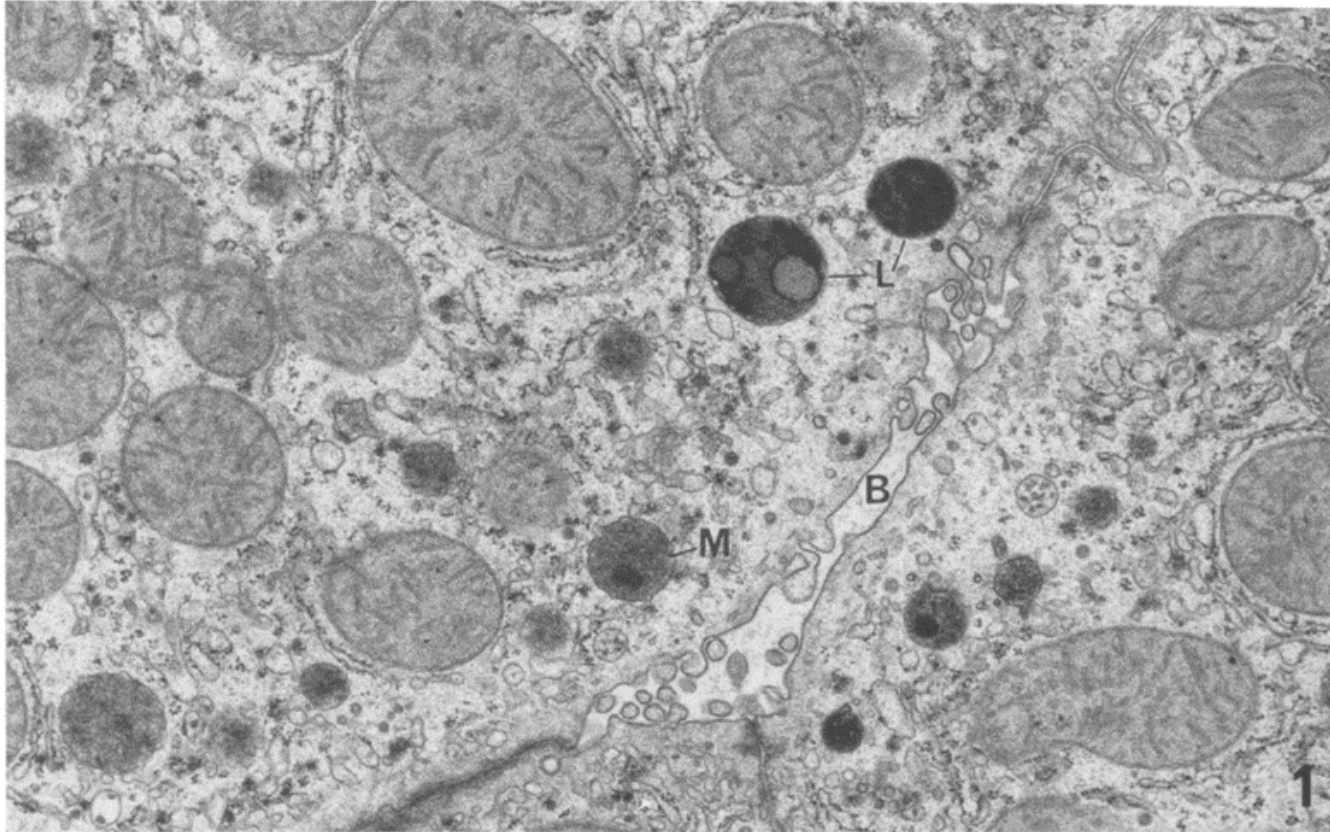


Plate 7.1

Figure 1. Normal rat **hepatocytes**, showing a bile canaliculus (B), some microbodies (M), and peribiliary dense bodies now known to be lysosomes (L).  $\times 21,000$ .

Figure 2. Disorganized tubular epithelial cells from **the kidney of a patient with systemic lupus** erythematosus, showing a markedly increased number of lysosomes (L). Similar but far fewer lysosomes are also found in the normal kidney.  $\times 8000$

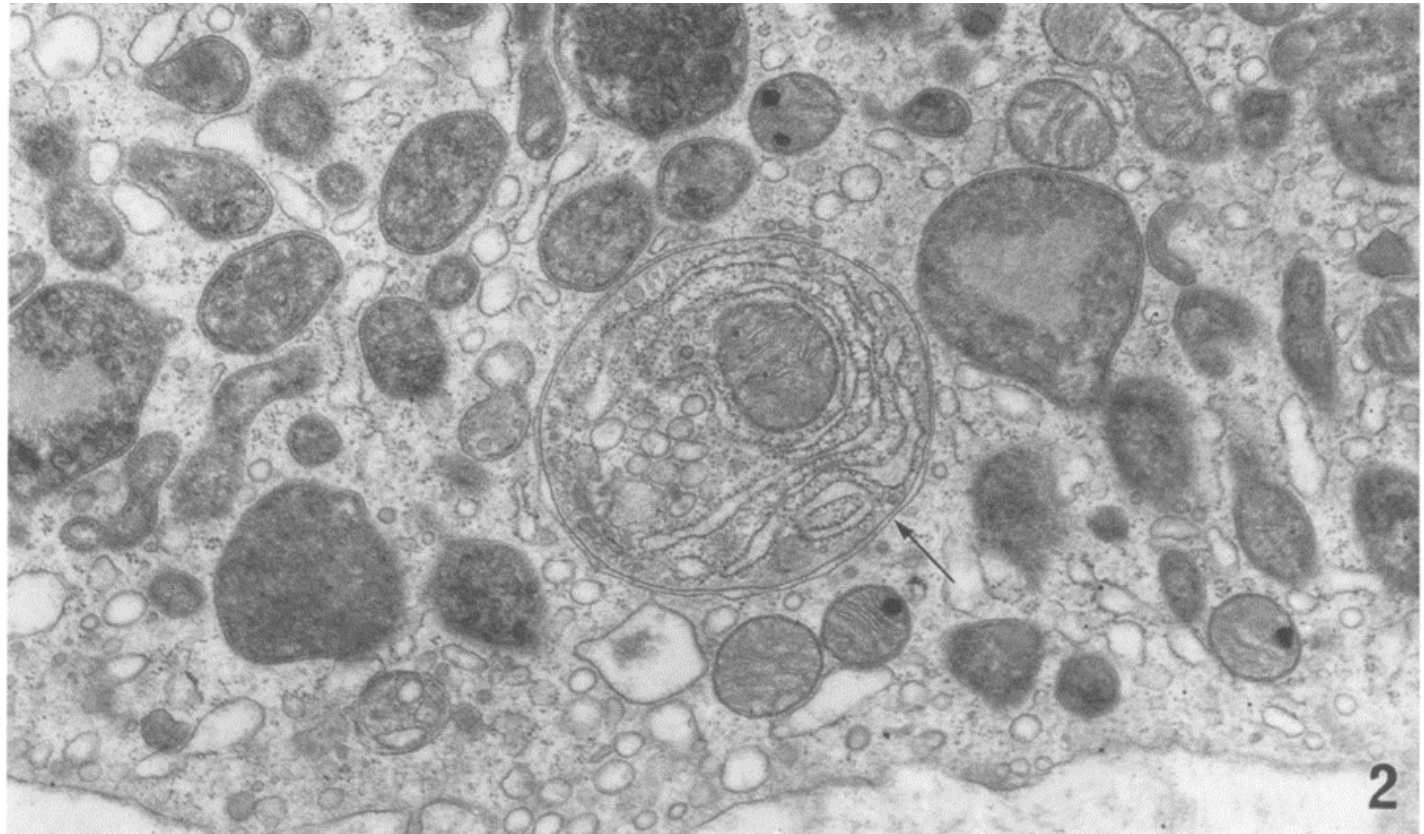
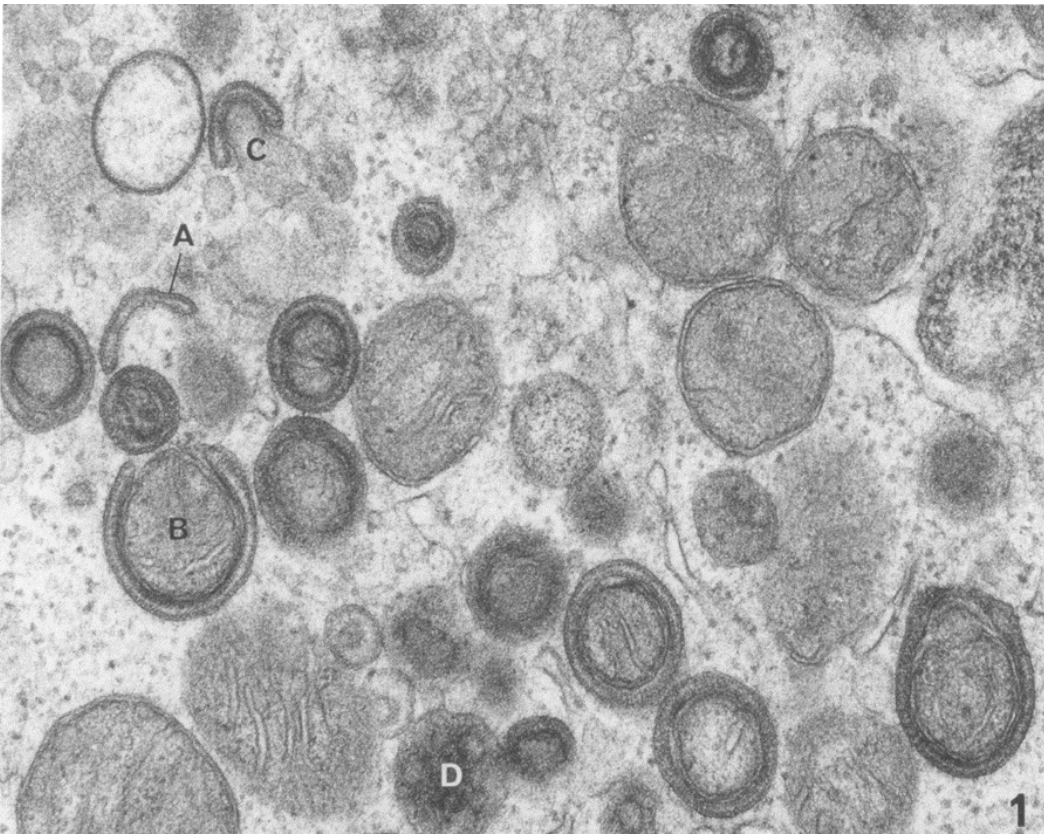
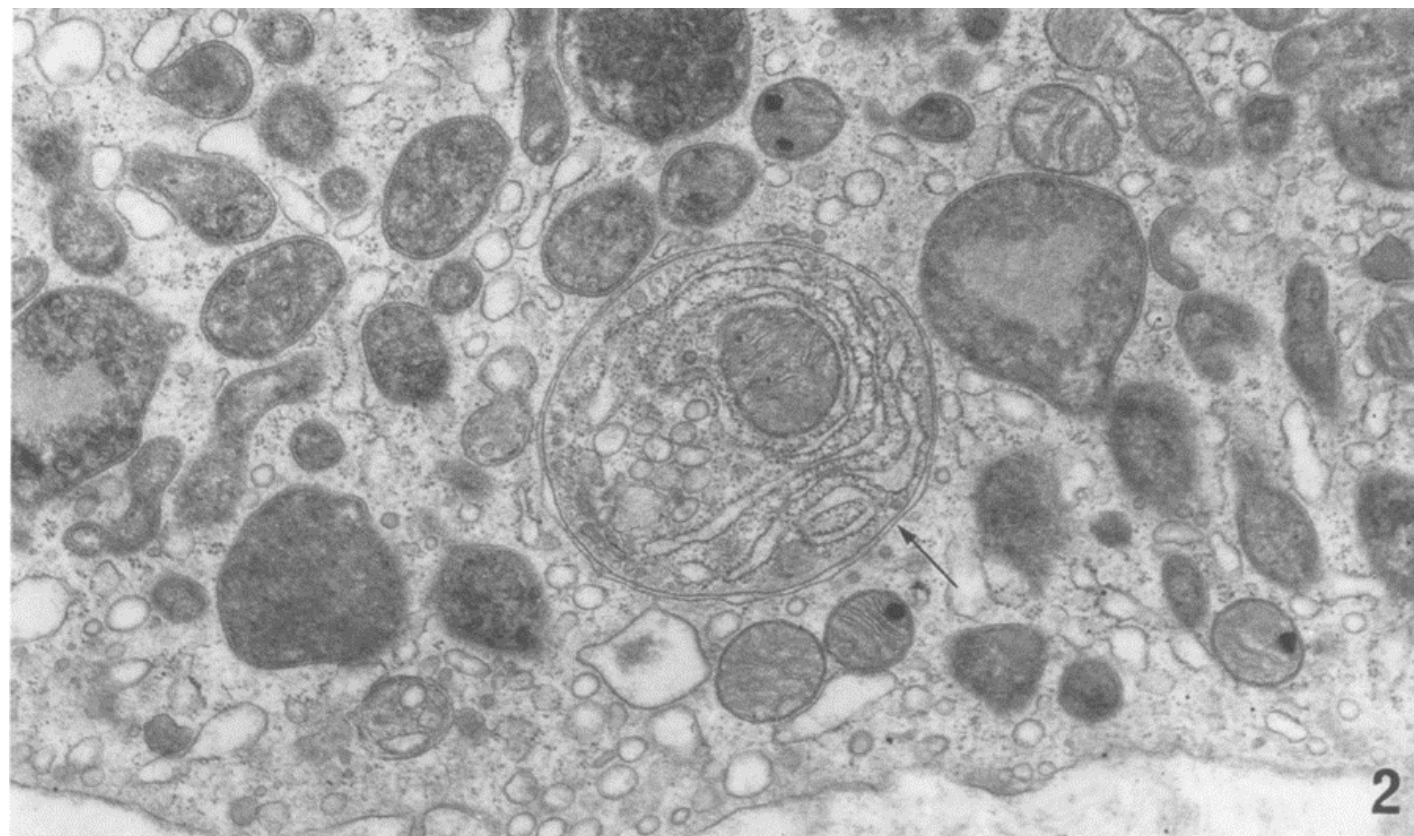
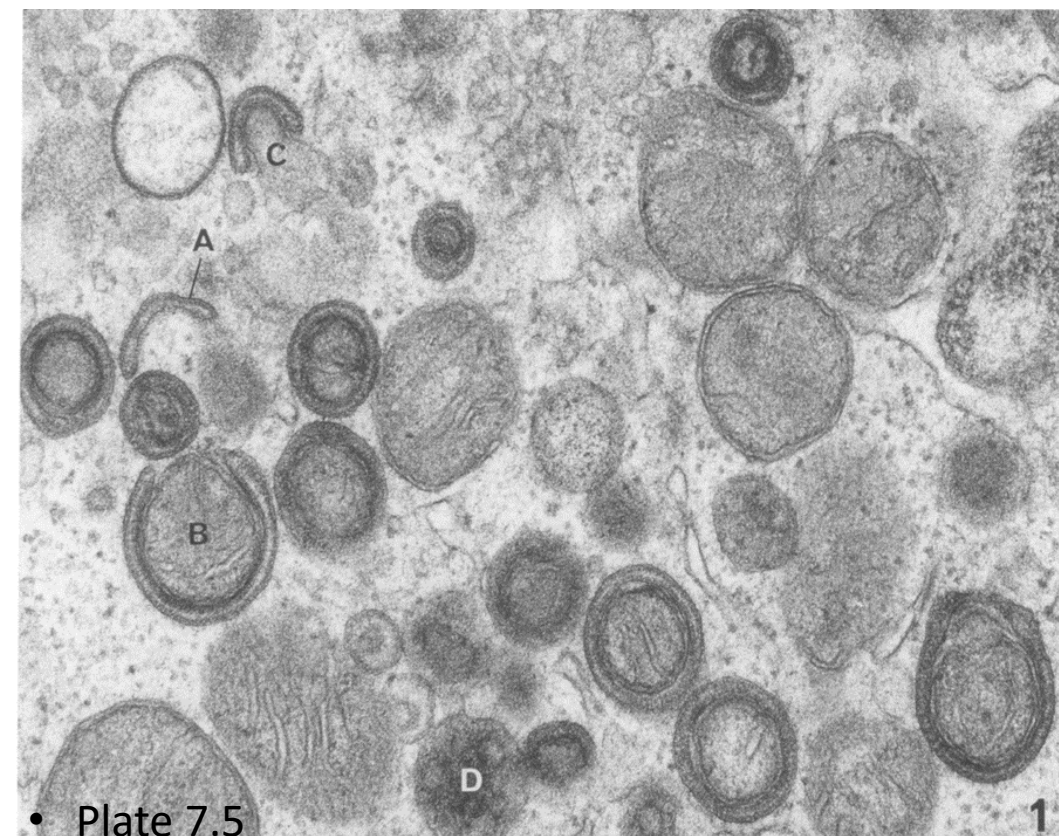


Plate 7.5

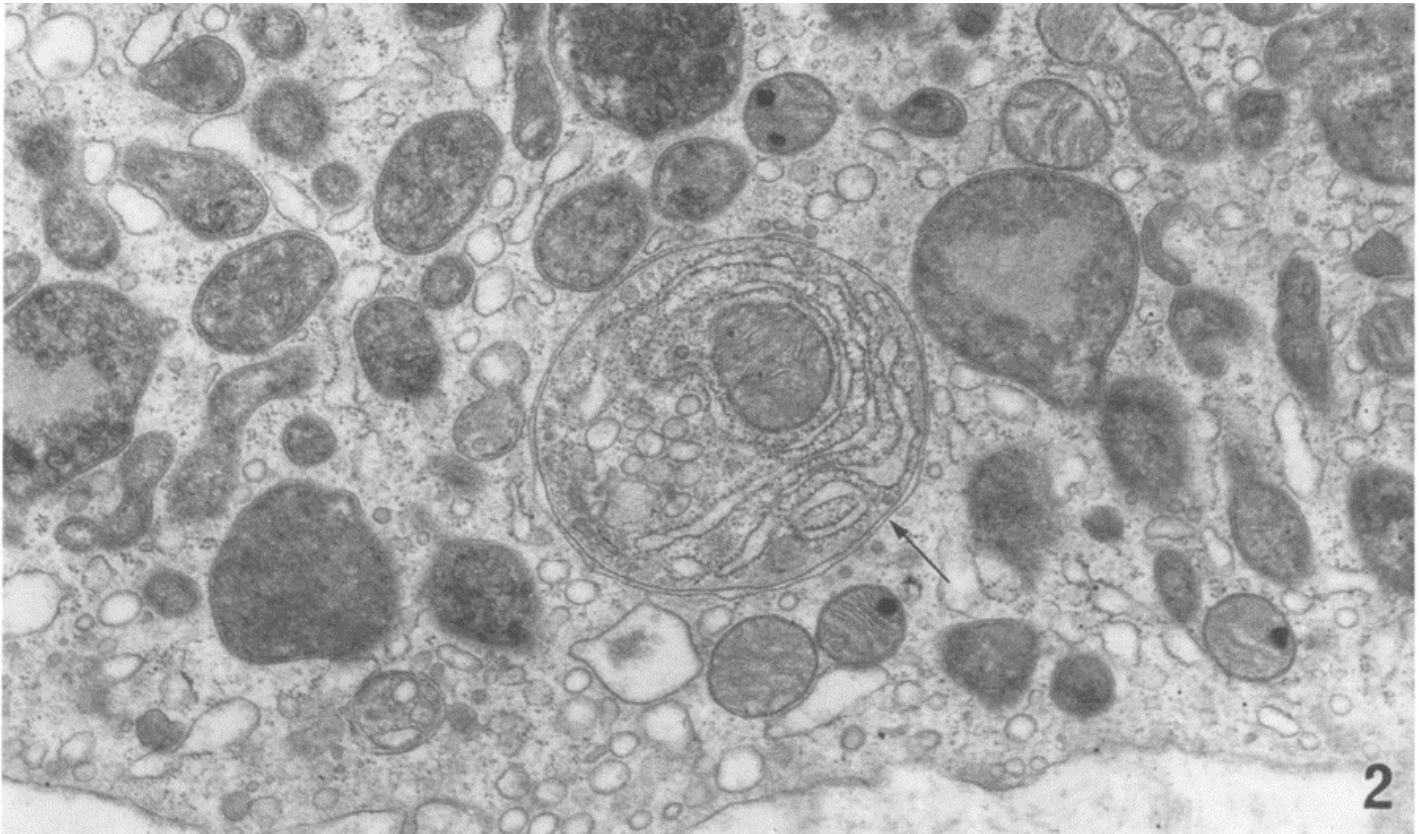
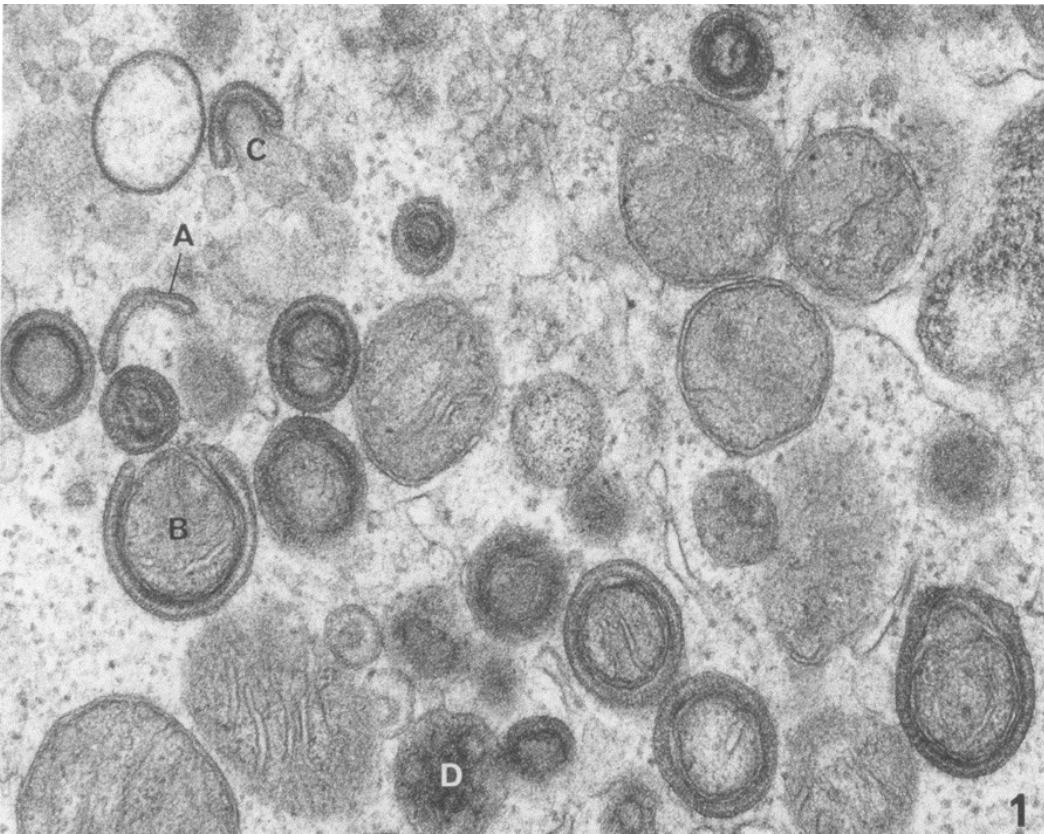
Question : what type of process do we see in 1

Question : what type of process do we see in 2



• Plate 7.5

- Figure 1. A probable mode of autolysosome formation is depicted here. Cup-shaped bodies (A) are seen lying free in the cytoplasm or wrapping around mitochondria (B) and other structures (C). Various images suggesting the breakdown of enclosed mitochondria and ultimate formation of single-membrane-bound dense bodies (D) are seen. From the megakaryocyte of a 6-month-old infant.  $\times 72,000$  (Ghadially and Skinnider, unpublished electron micrograph)



• Figure 2. A double-membrane-bound body (arrow) that may be interpreted as  
 (1) an early autolysosome,  
 (2) a phagocytosed cell fragment, or  
 (3) a finger-like evagination from an adjacent cell. From a case of melanosis coli.  $\times 29,000$  (Ghadially and Parry, unpublished electron micrograph)

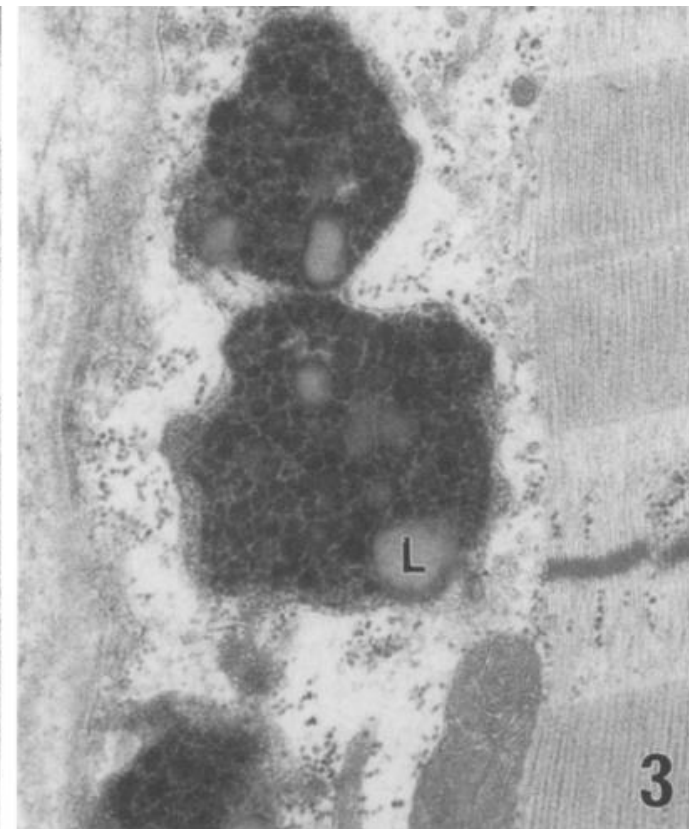
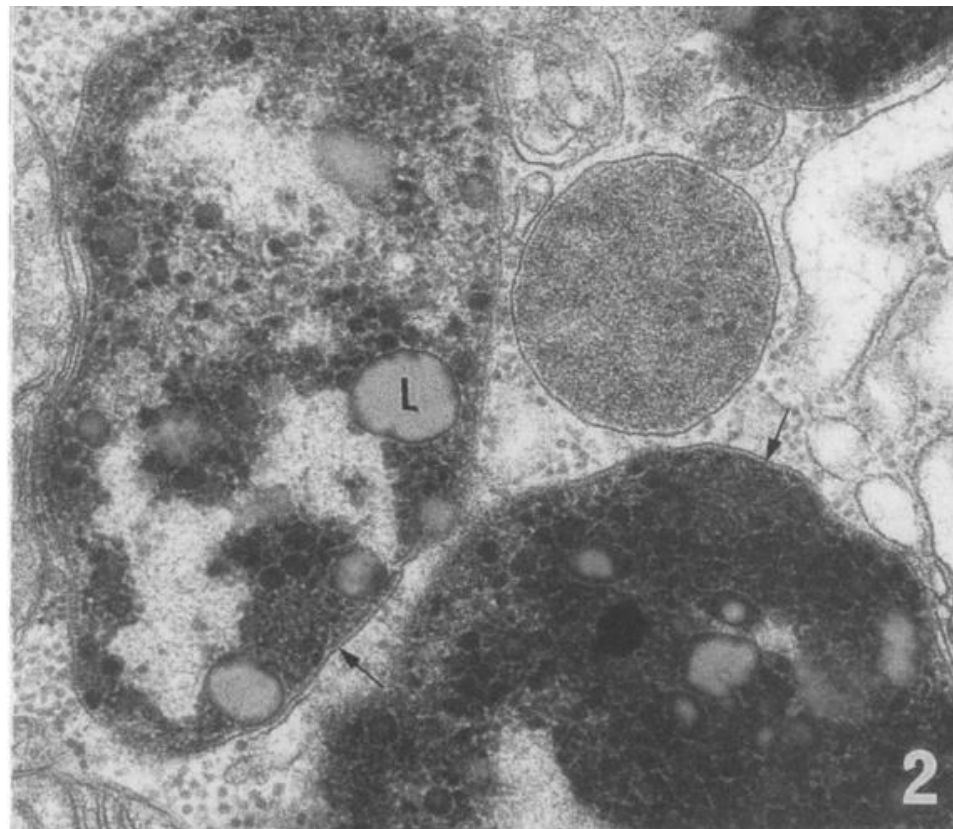
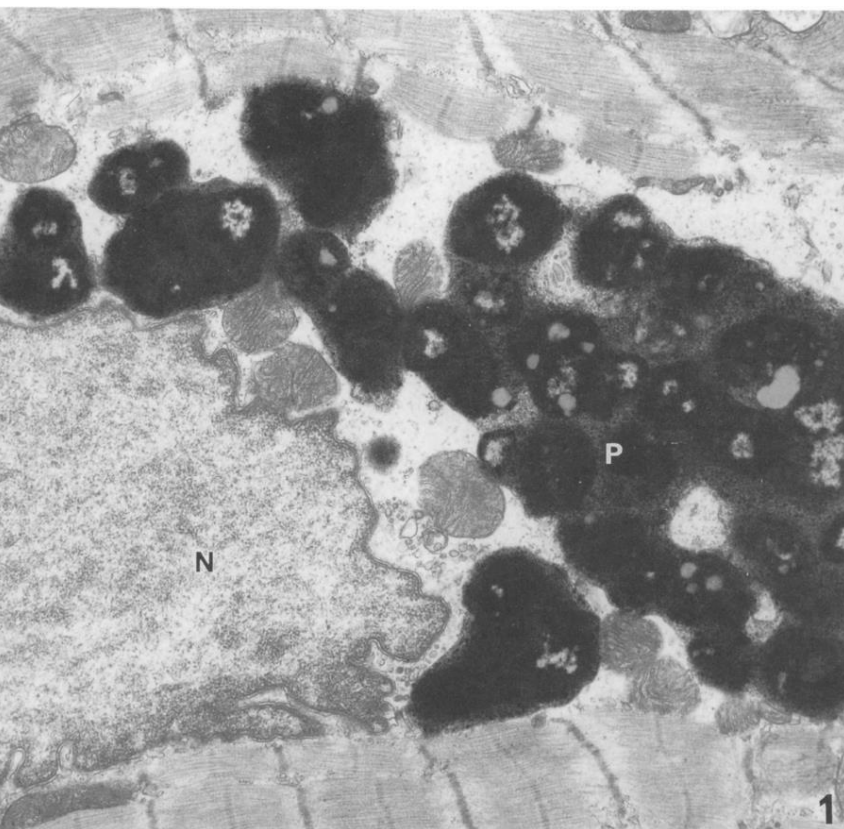


Plate 7.11

Question : what type of lysosomes are present in 1-3?

Question : what type is the content of these lysosomes?

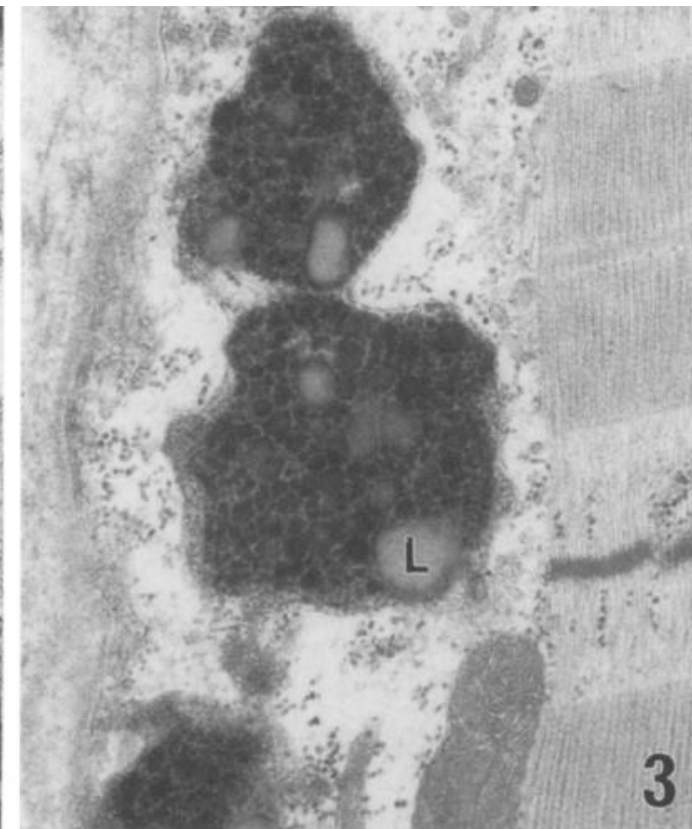
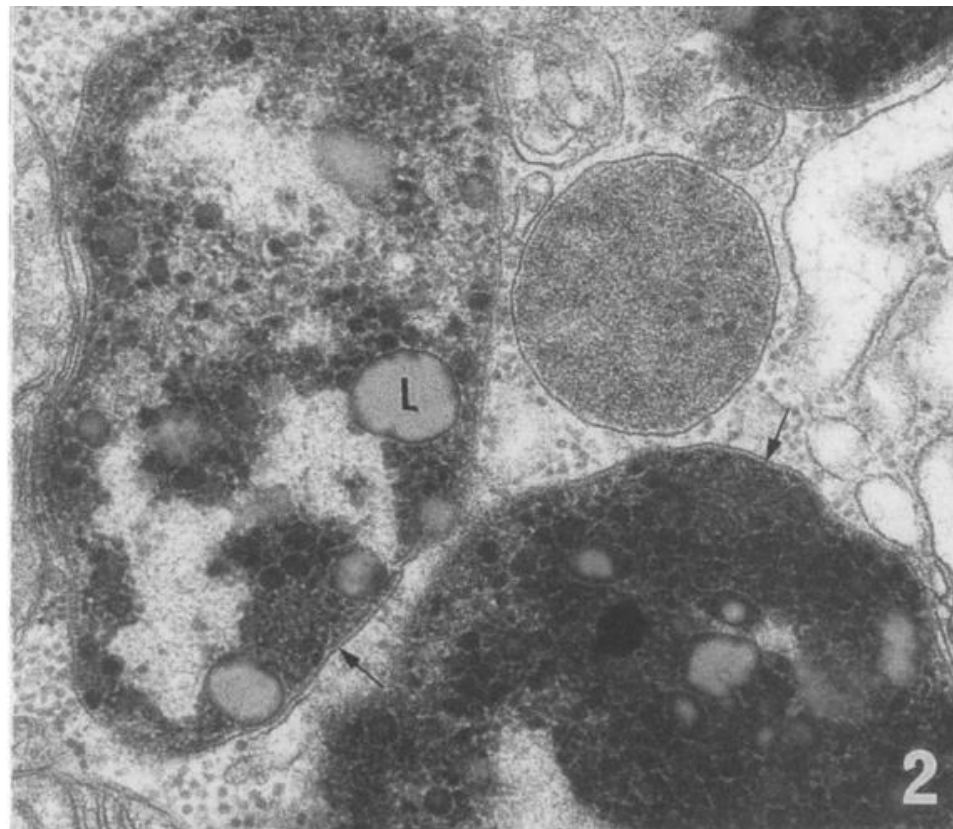
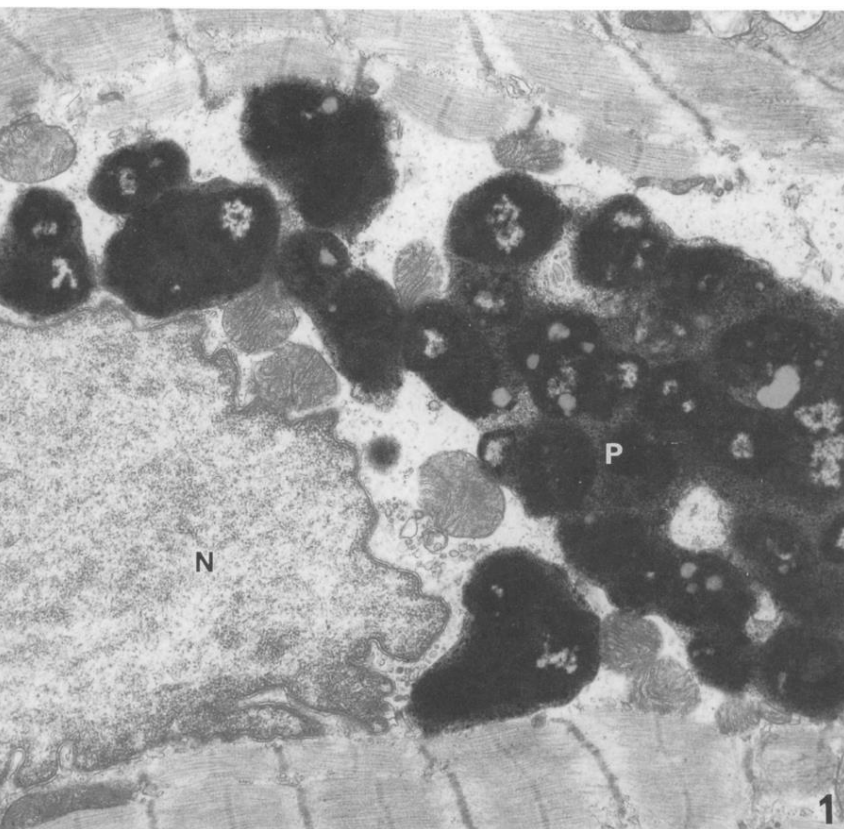


Plate 7.11

Figure 1. **Lipofuscin** granules found in the myocardium of an elderly man. In the condition called brown atrophy of the heart, such granules are abundant adjacent to the poles of the elongated nuclei of myocardial cells. This well-known relationship of the **pigment** (P) to the nucleus (N) is demonstrated in this electron micrograph.  $\times 18,500$

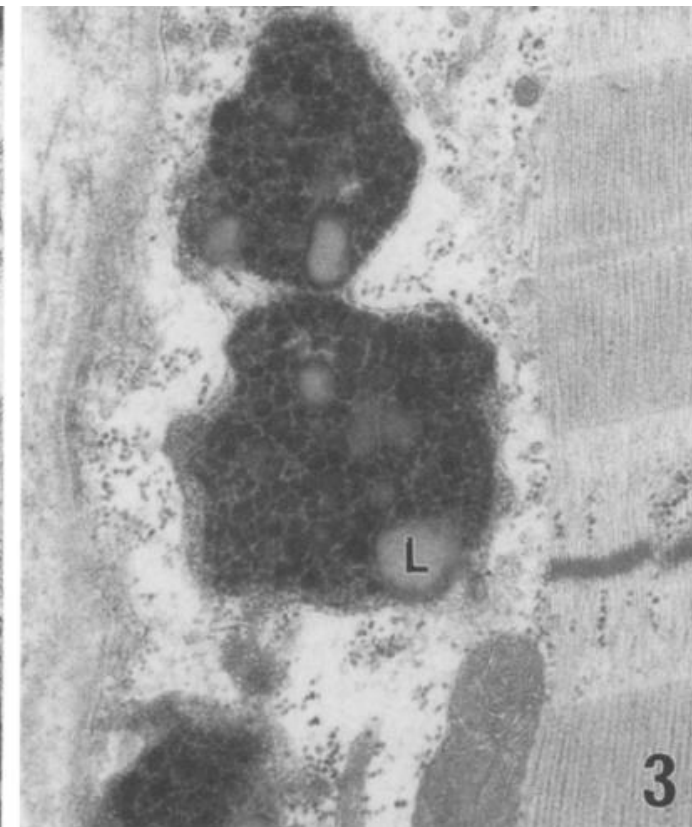
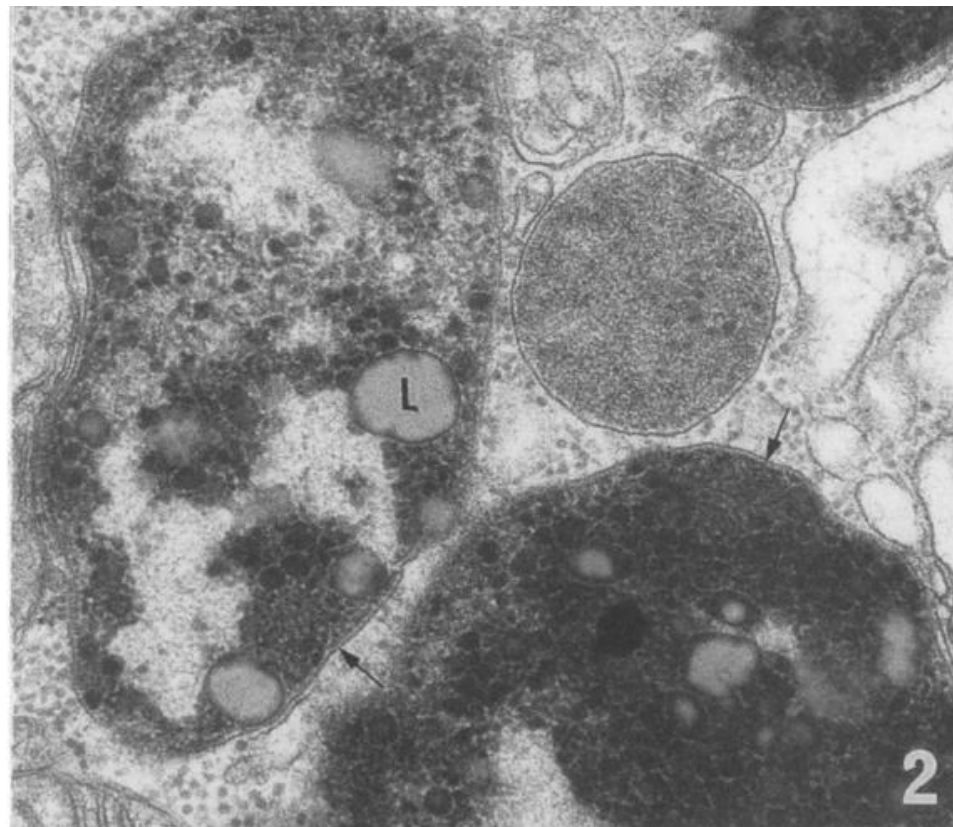
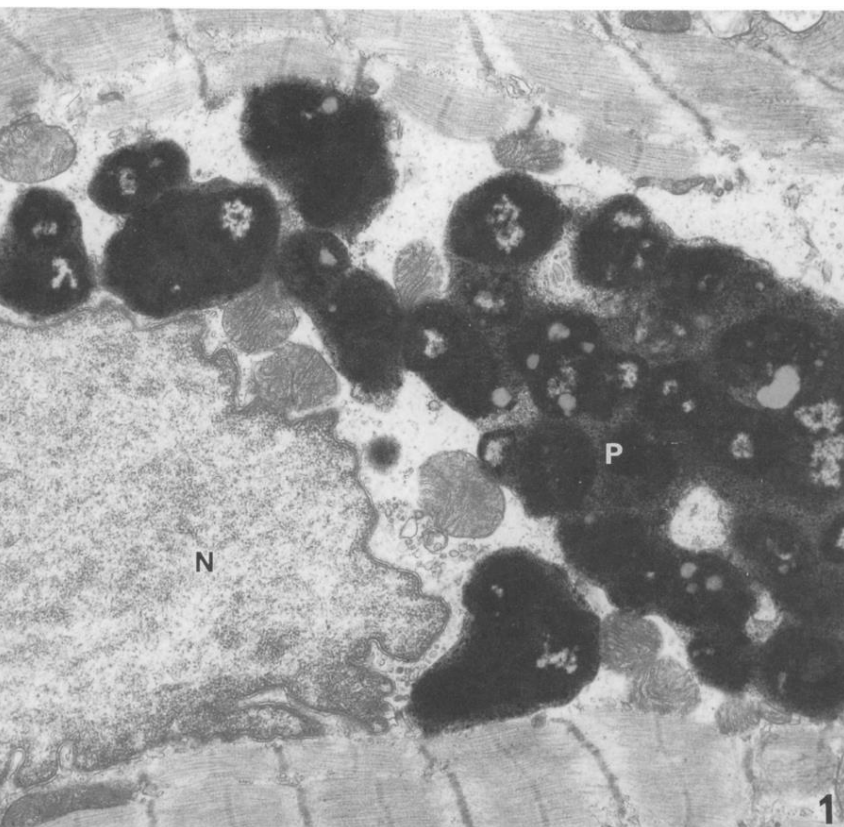


Figure 2. High-power view of lipofuscin granules from the same specimen as Figure 1. Note the characteristic dense granules, **lipid droplets** (L), and membrane surrounding the granules (arrows).  $\times 45,000$

Figure 3. Lipofuscin granules found in an atrophic deltoid muscle of man. Note once again the presence of dense granular material and **lipid droplets** (L).  $\times 23,000$

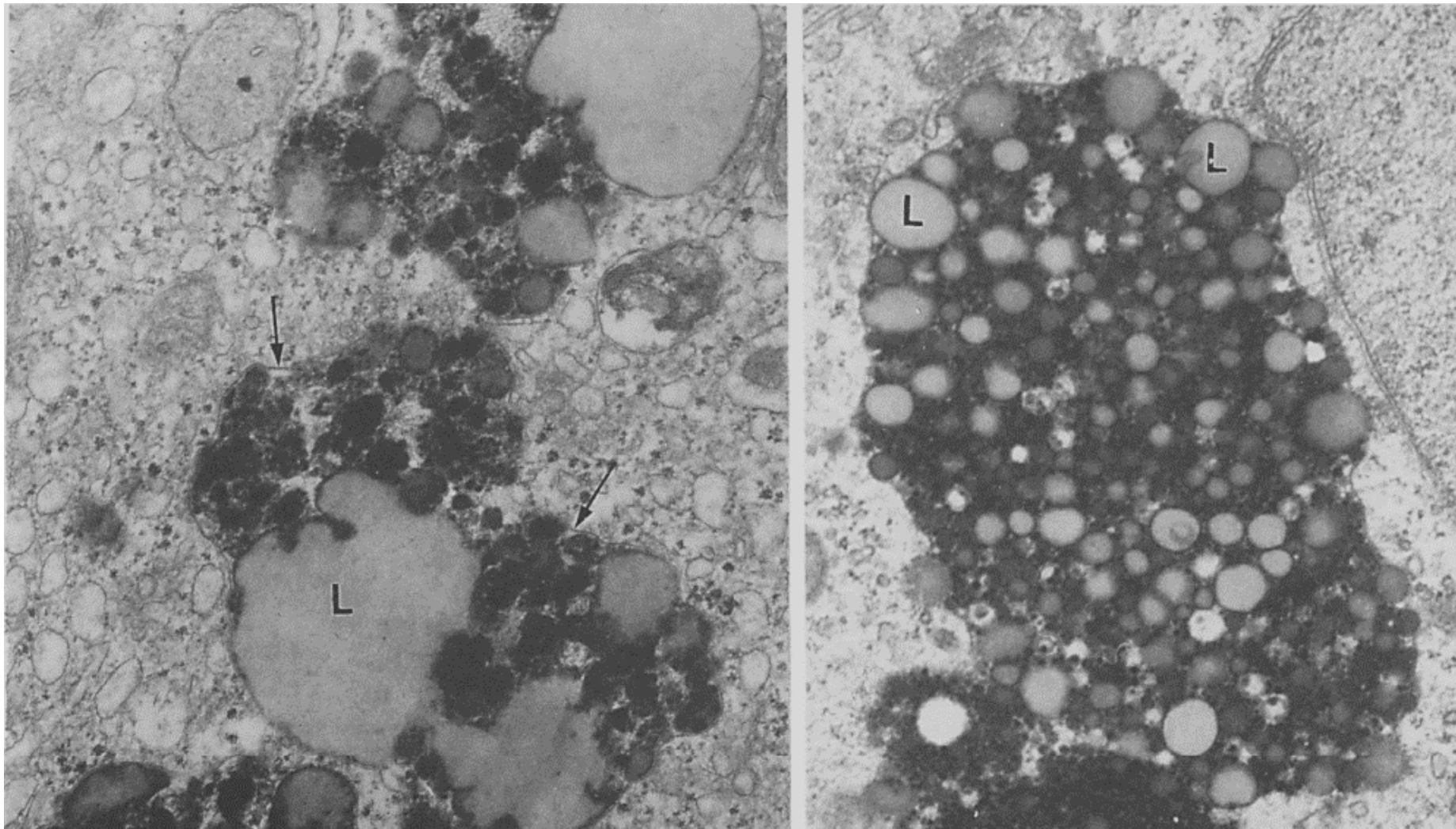


Plate 7.13

Figure 1. These lipofuscin granules, composed of numerous dense granules and **unusually large lipid droplets (L)**, were found in the liver tissue adjacent to a human hepatoma. The limiting membrane of these lysosomal bodies is discernible in some places (arrows).  $\times 27,000$  (From Ghadially and Parry, 1966a., Cancer 19:1989)

Figure 2. Lipofuscin granules in human gallbladder epithelium. Here the **lipid droplets (L)** are small and numerous.  $\times 26,000$

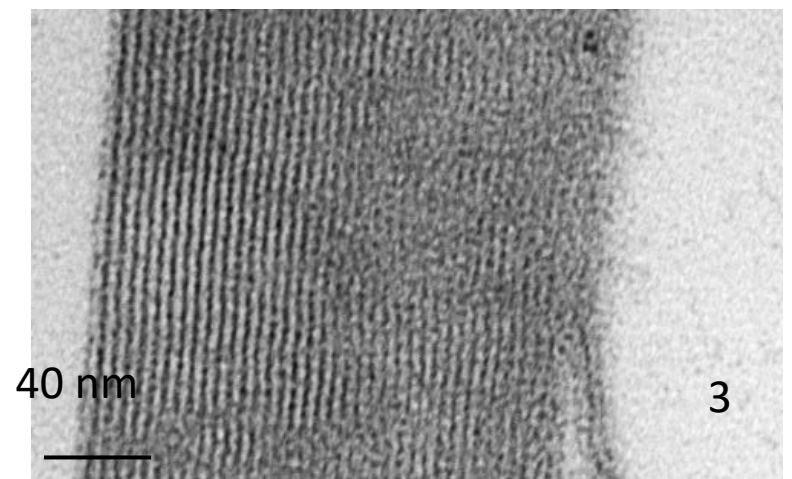
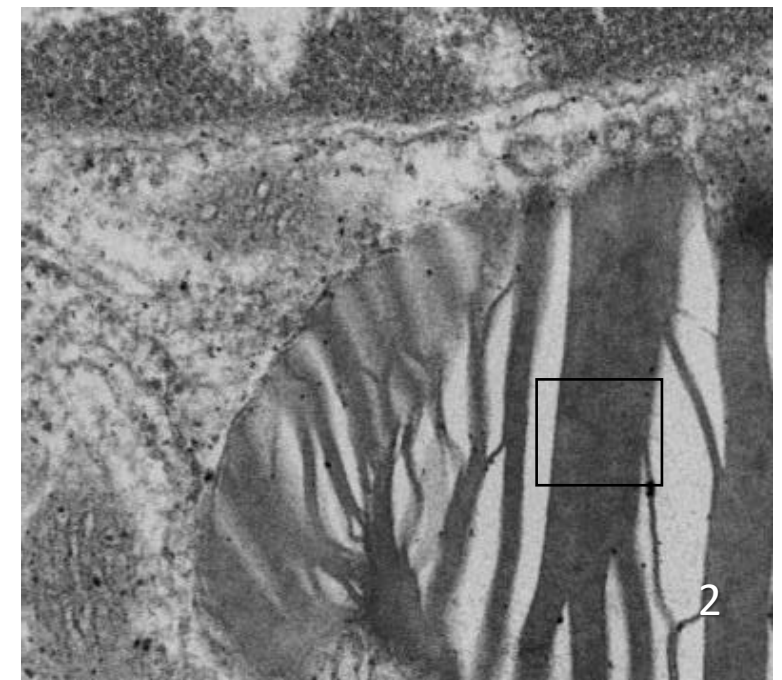
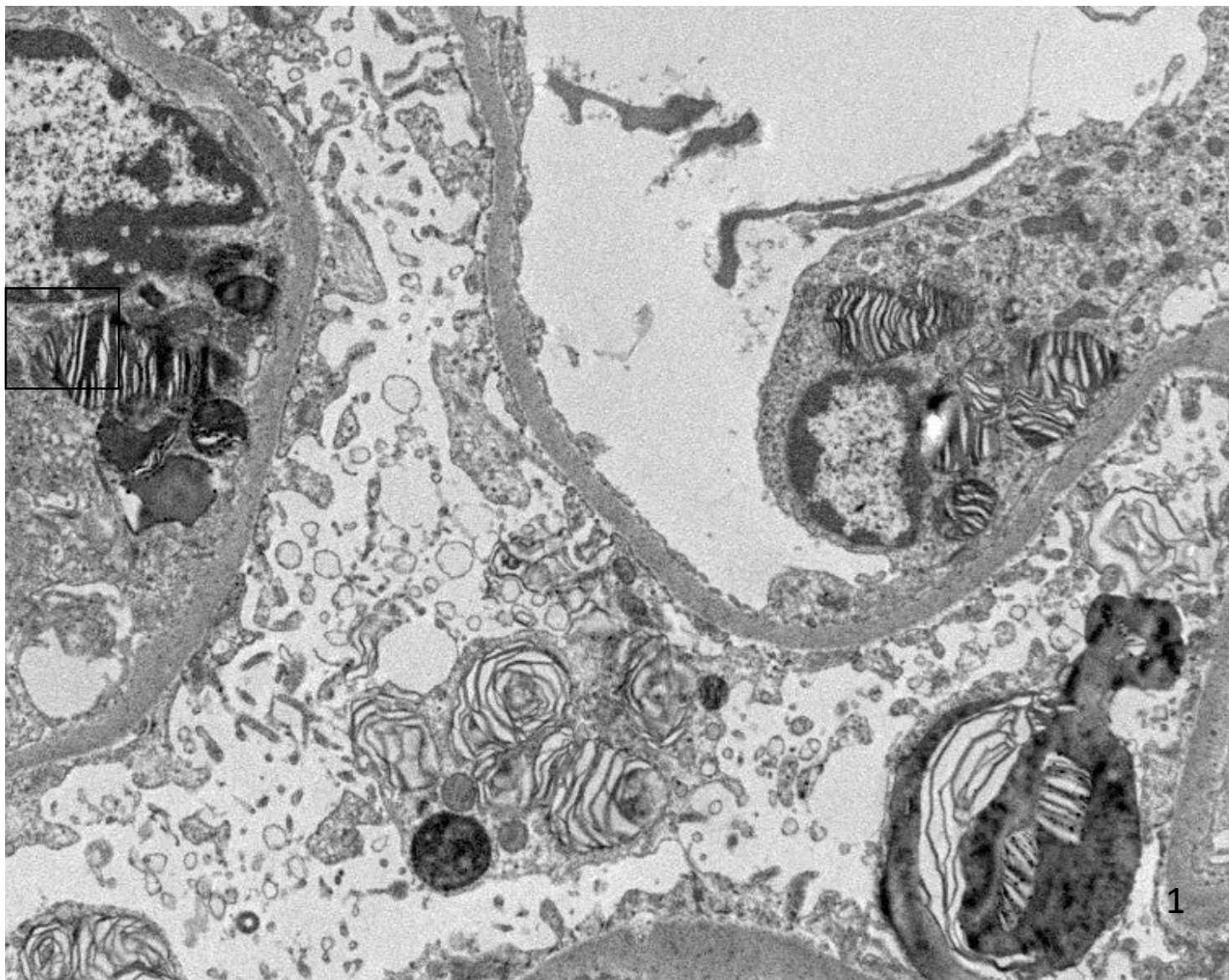


Plate 7.16

In which disease can be recognized by large multilamellar structures?

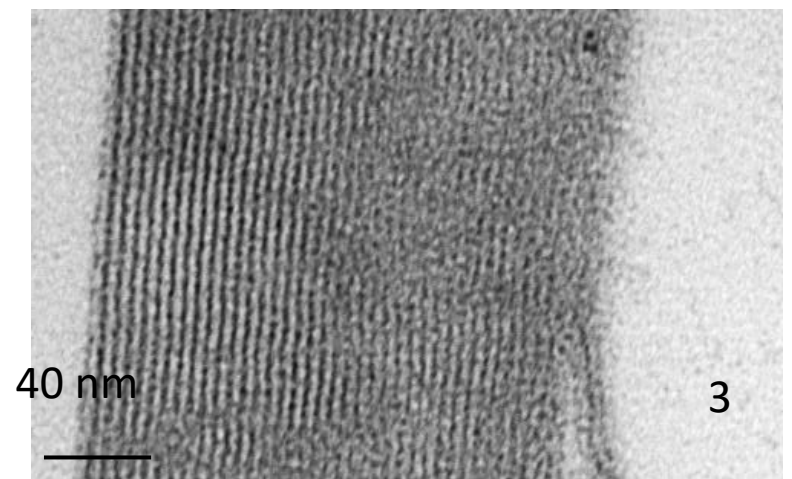
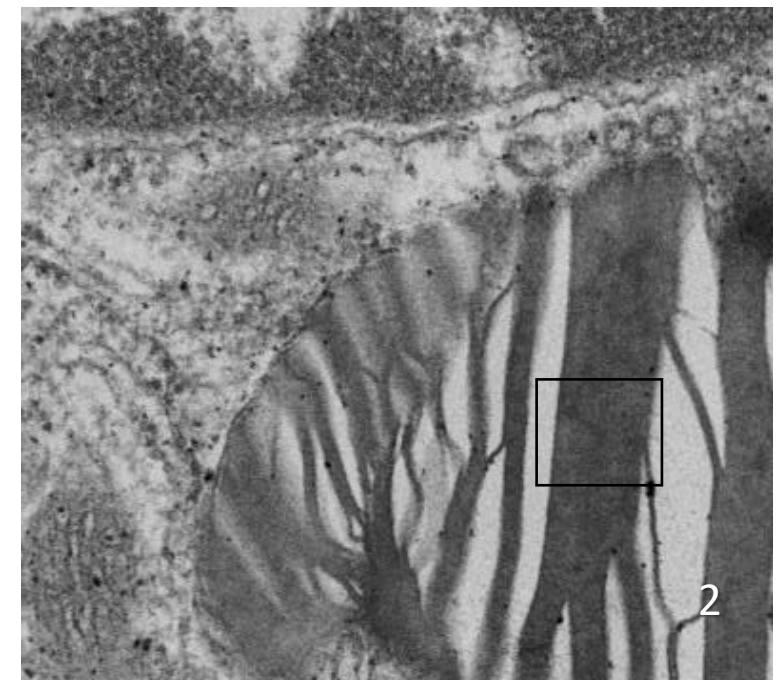
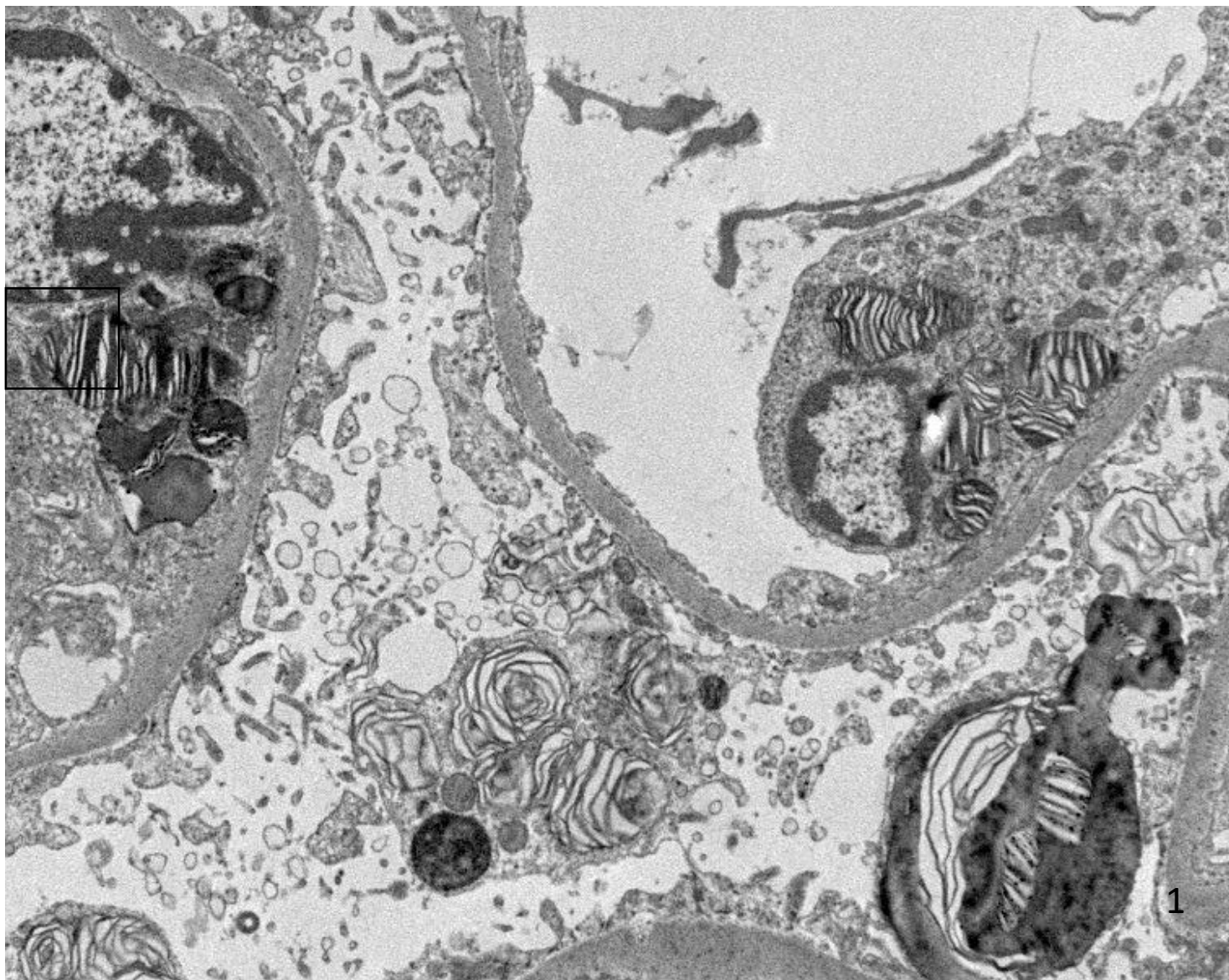


Plate 7.16

Figures 1-3. Electron micrograph showing multilamellar bodies on both side of the basal membrane in a kidney from a case of **Fabry's disease with renal involvement**. High magnification shows 6 dark and light layers over 30 nm so a periodicity of 5 nm. (Van den Bergh Weerman, Larsen, van der Wel unpublished from case described Eskes et al., 2021)

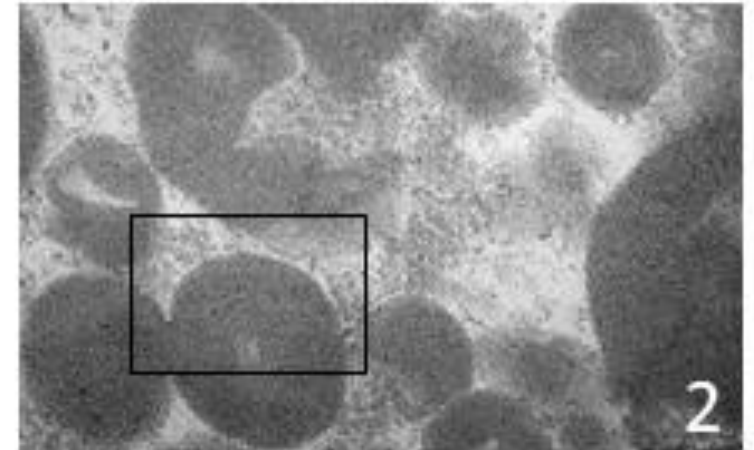
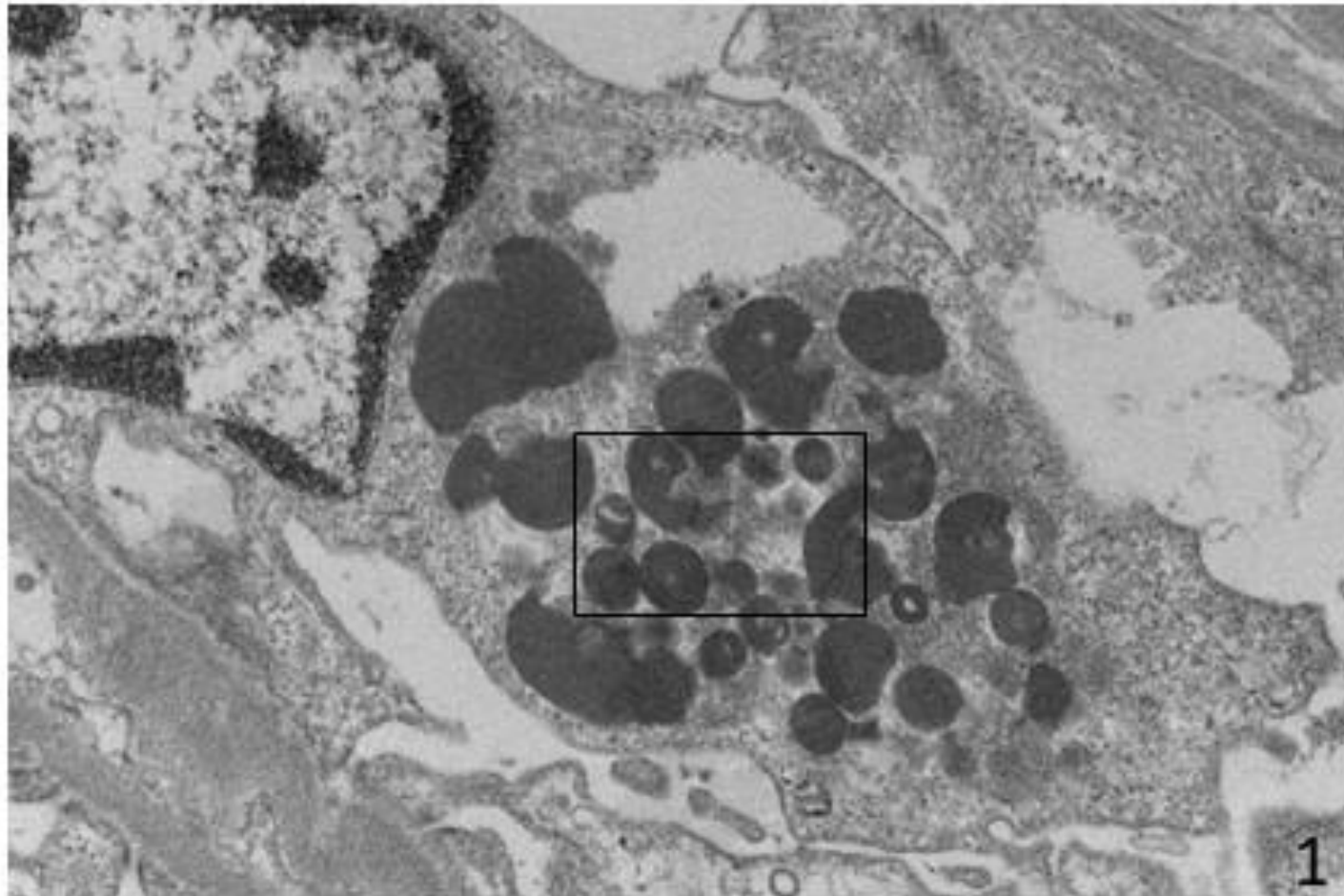


Plate 7.17

Which disease can be recognized by these multilamellar structures?  
 Which part of the human body is used to name these structures

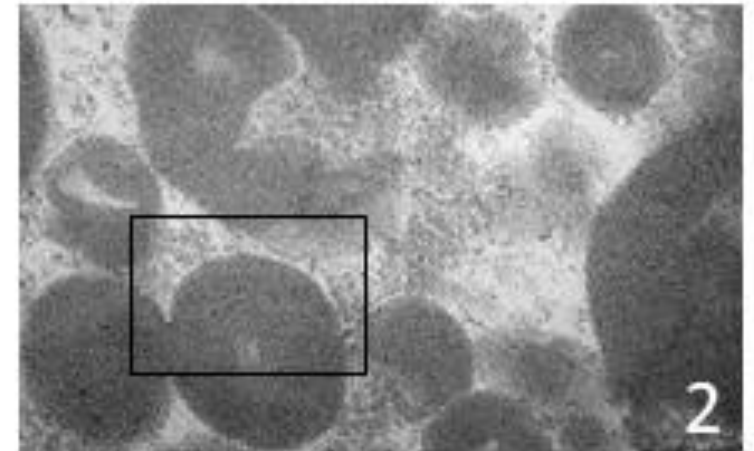
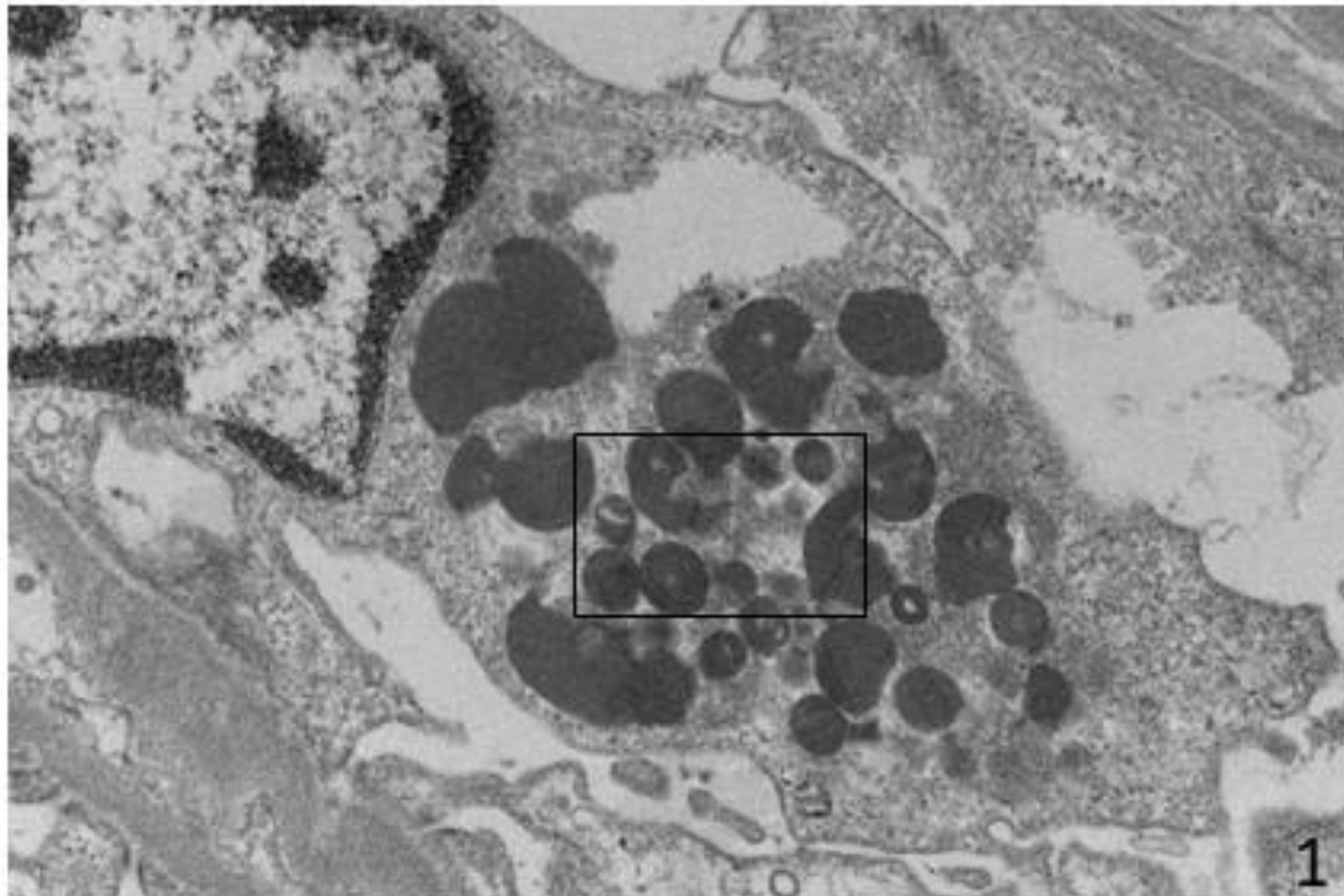


Plate 7.17

Electron micrograph showing both electron dense **fingerprints** (Figures 1,2 and 3) in a kidney from a case of Niemann-Pick disease with renal involvement.

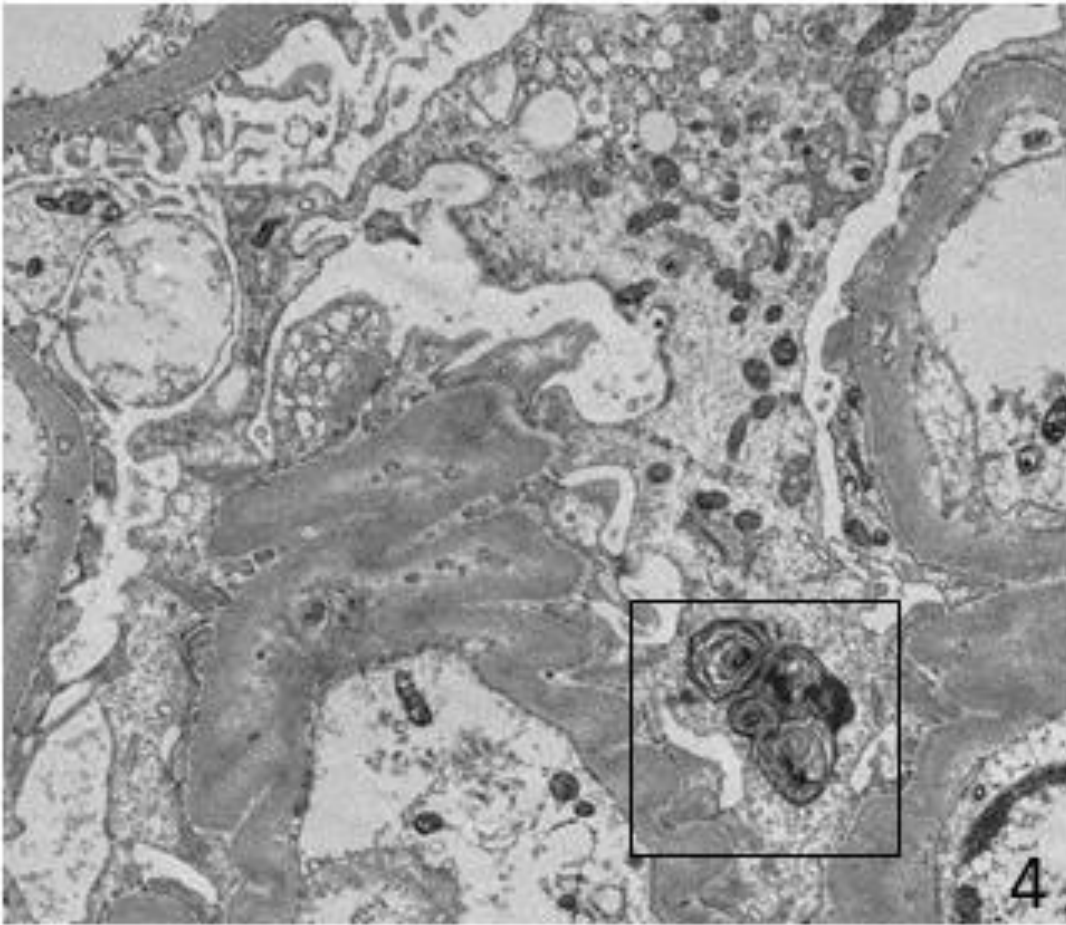


Plate 7.17

Which disease can be recognized by these multilamellar structures?

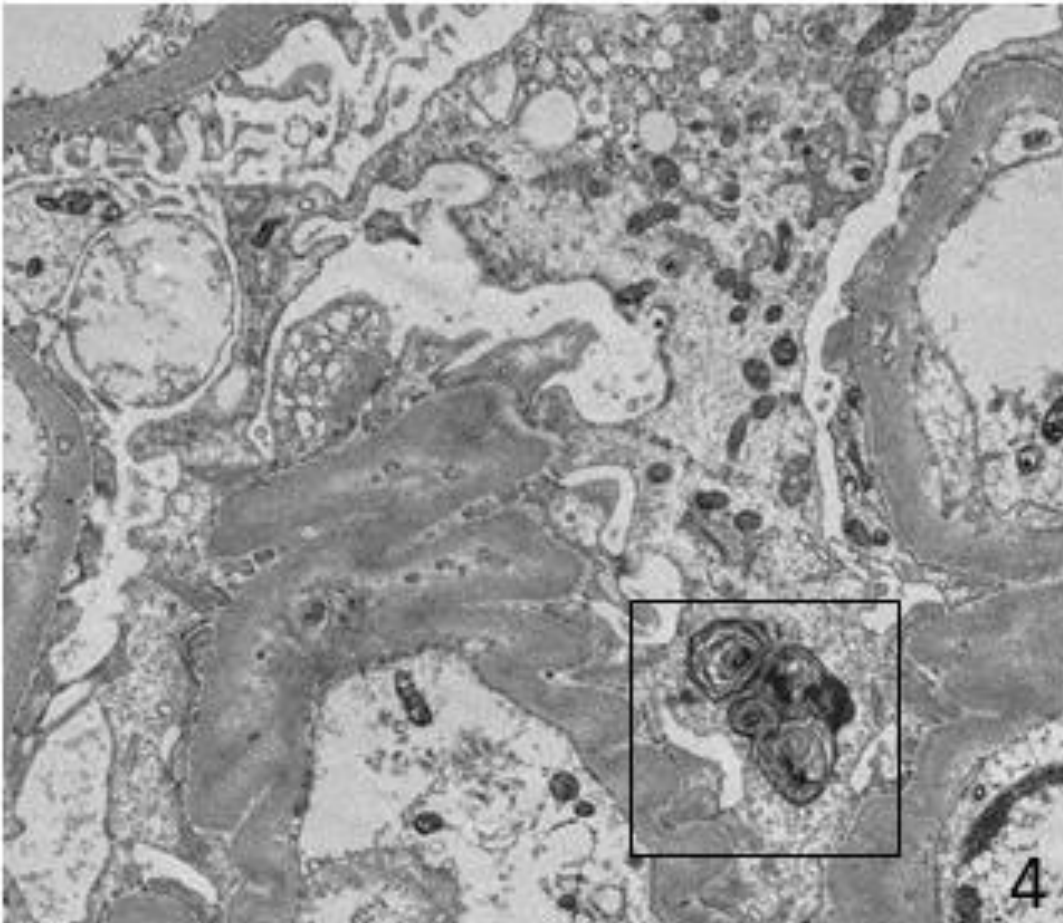


Plate 7.17

Figure 1-5. Electron micrograph showing both electron dense fingerprints (Figures 1,2 and 3) and multilamellar bodies (Figures 4 and 5) in a kidney from a case of Niemann-Pick disease with renal involvement. Figure 4:  $\times 6,800$  plus higher magnified inset Figure 5:  $\times 49,000$  (From Aten, Van den Bergh Weerman, Larsen, van der Wel unpublished data from case

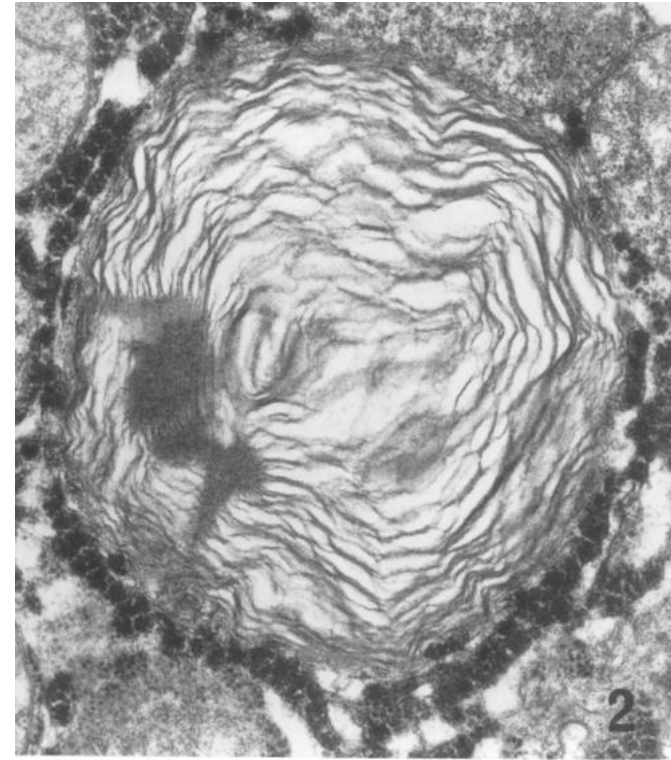
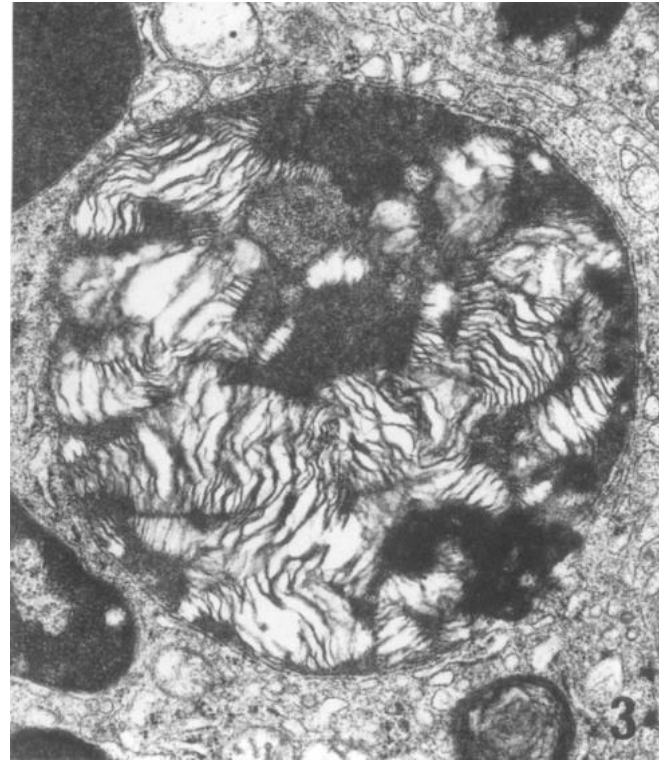
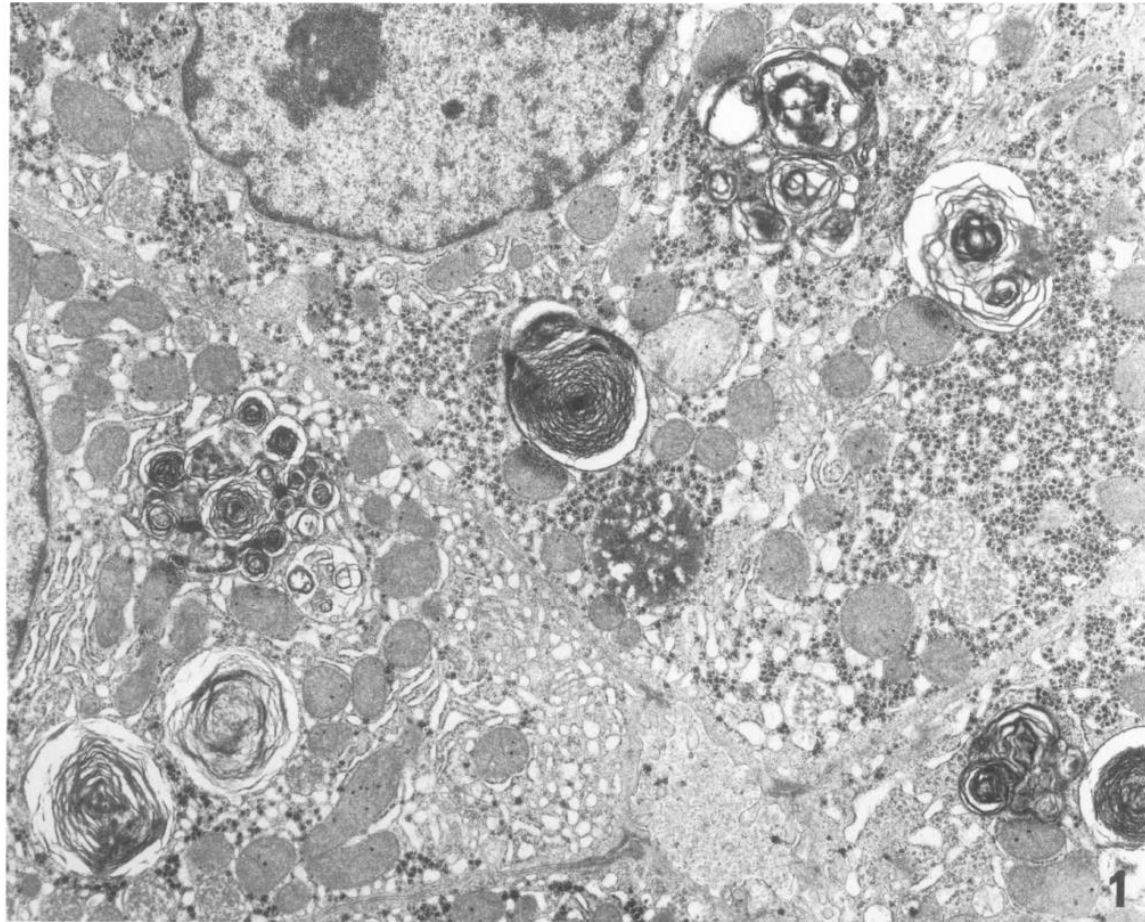
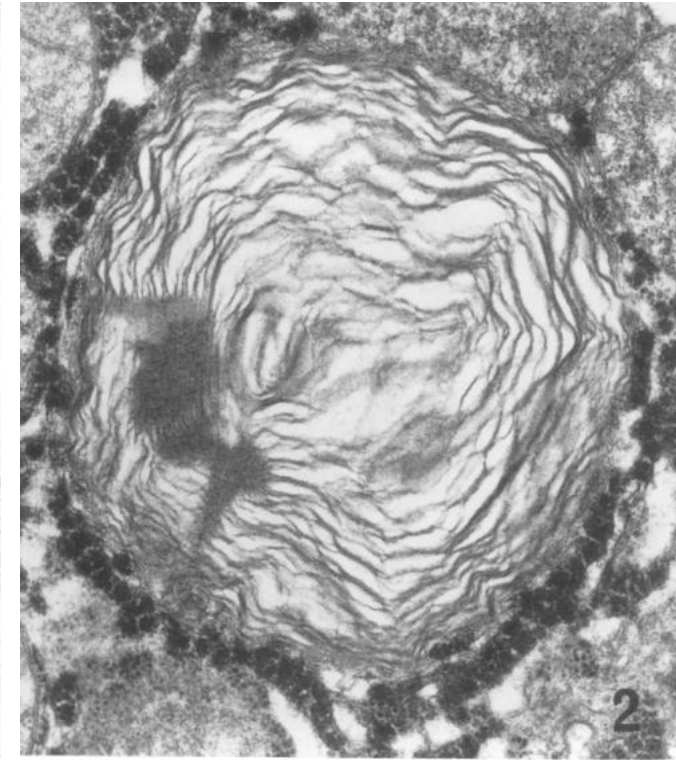
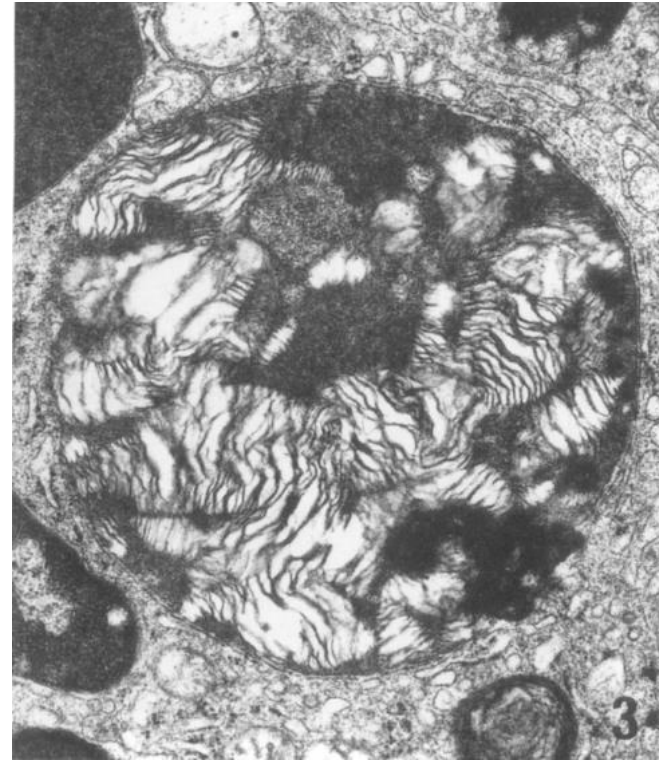
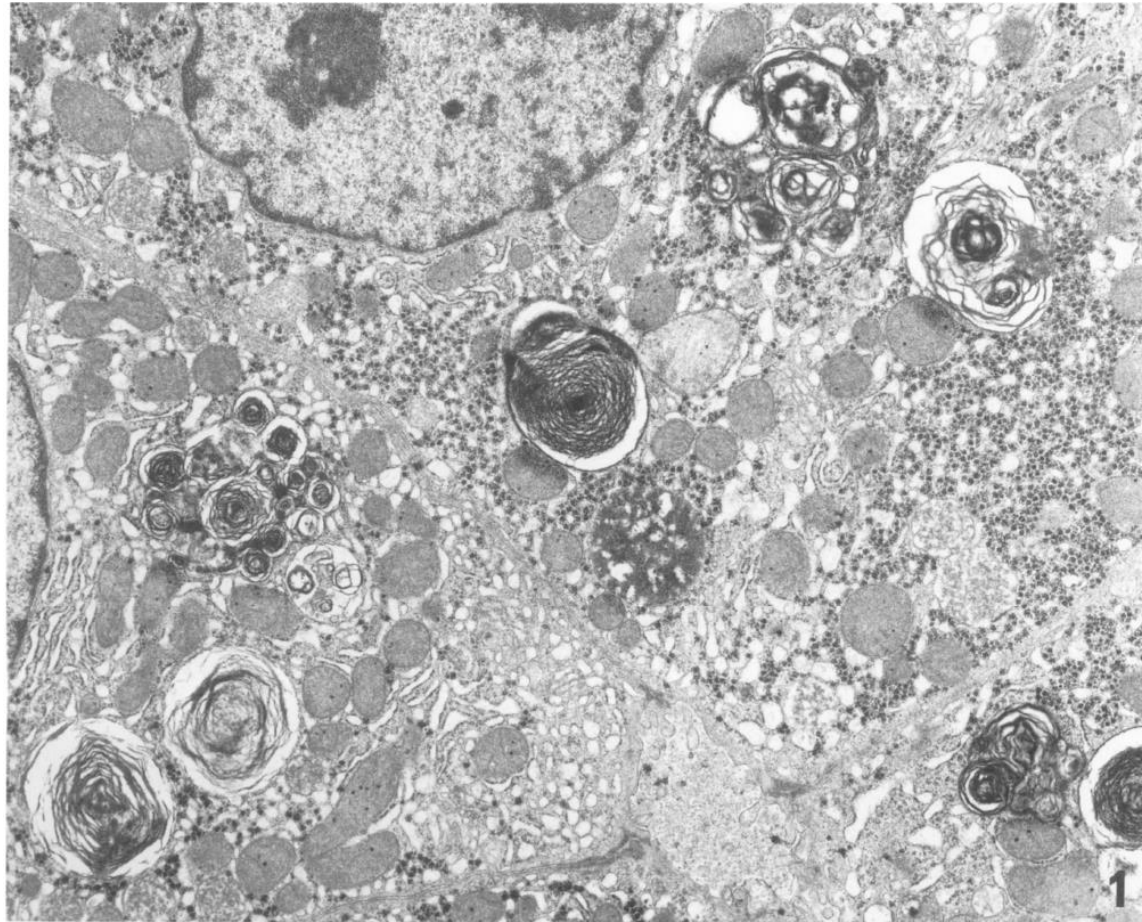


Plate 7.20

Which disease can be recognized by these large multi lamellar structures?



## Plate 7.20

Liver biopsy from a patient who had received **amiodarone** for 3.5 years.

Figure 1. Low-power view showing several **myelinosomes/multilamellar** bodies in hepatocytes.  $\times 10,500$

Figures 2 and 3. Higher-power view of myelinosomes or multilamellar bodies containing electron-dense masses and myelinoid membranes deployed in concentric and reticulated patterns.  $\times 27,000$ ;  $\times 20,000$

drugs that produce myelinosomes or multilamellar bodies are

amiodarone,  
chlorcyclizine,  
chloroquine,  
chlor-phentermine,  
clindamycin,  
diazcholesterol,  
4,4-diethylaminoethoxyhexoestrol,  
erythromycin,  
imipramine,  
norchlorcyclizine,  
paraquat,  
tripanol.

Ghadially was in favor of the term **myelinosomes**, but this term is not broadly adopted in the field. Therefore, we propose the more descriptive term **multilamellar** lysosome.

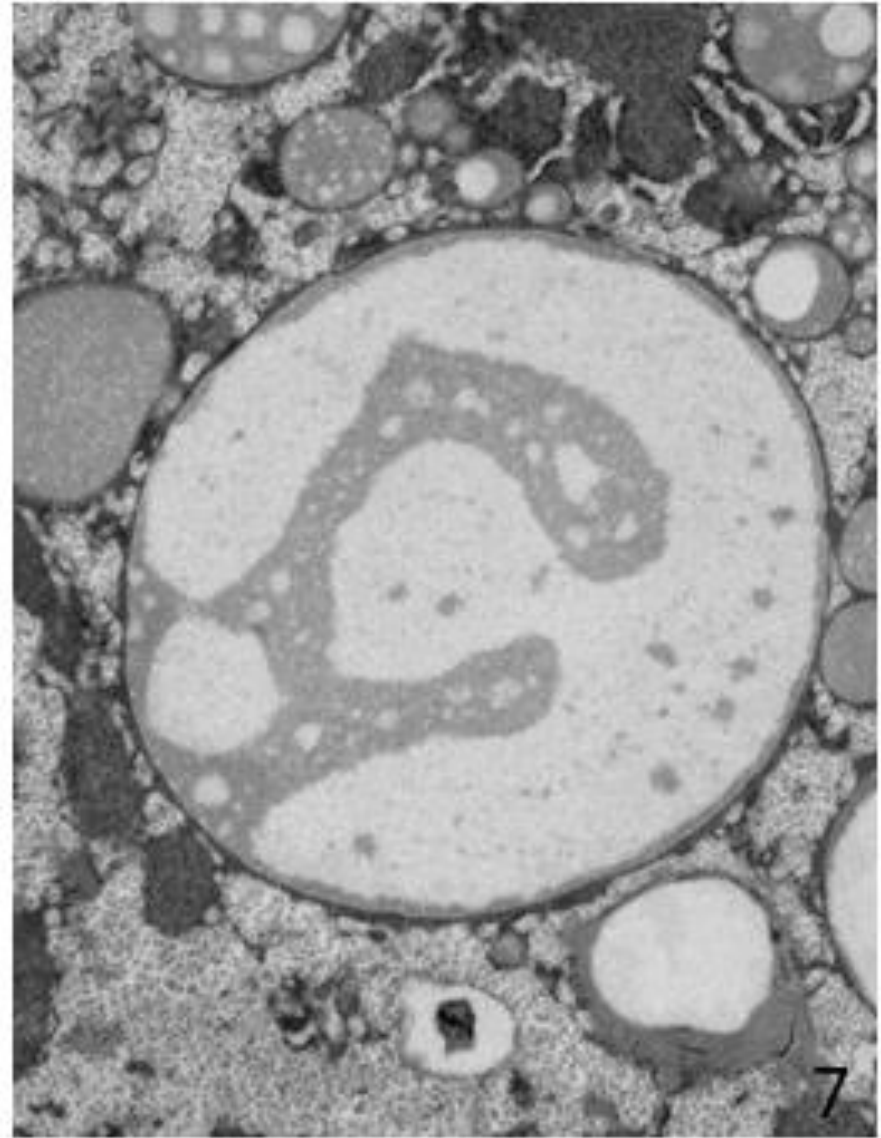
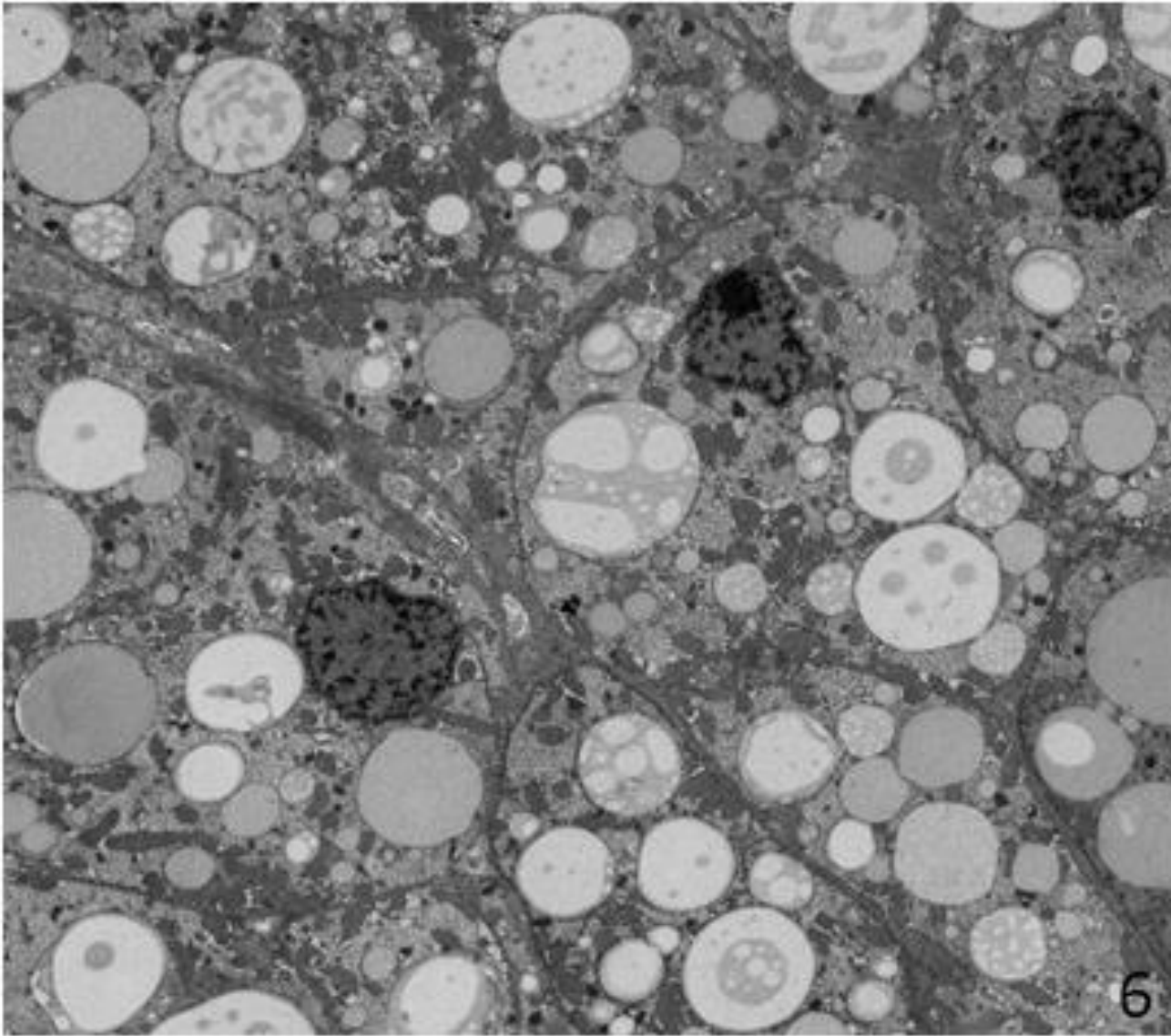


Plate 7.17

Which disease can be recognized by these large structures?

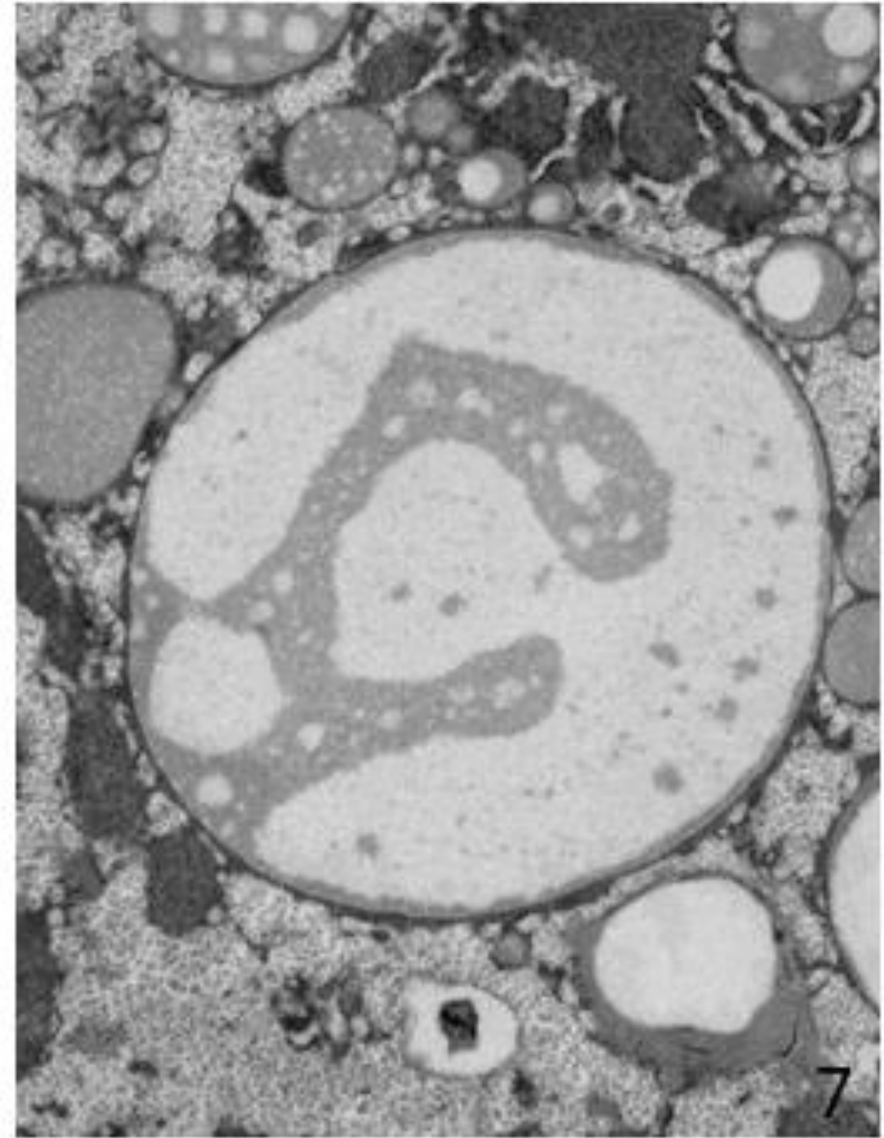
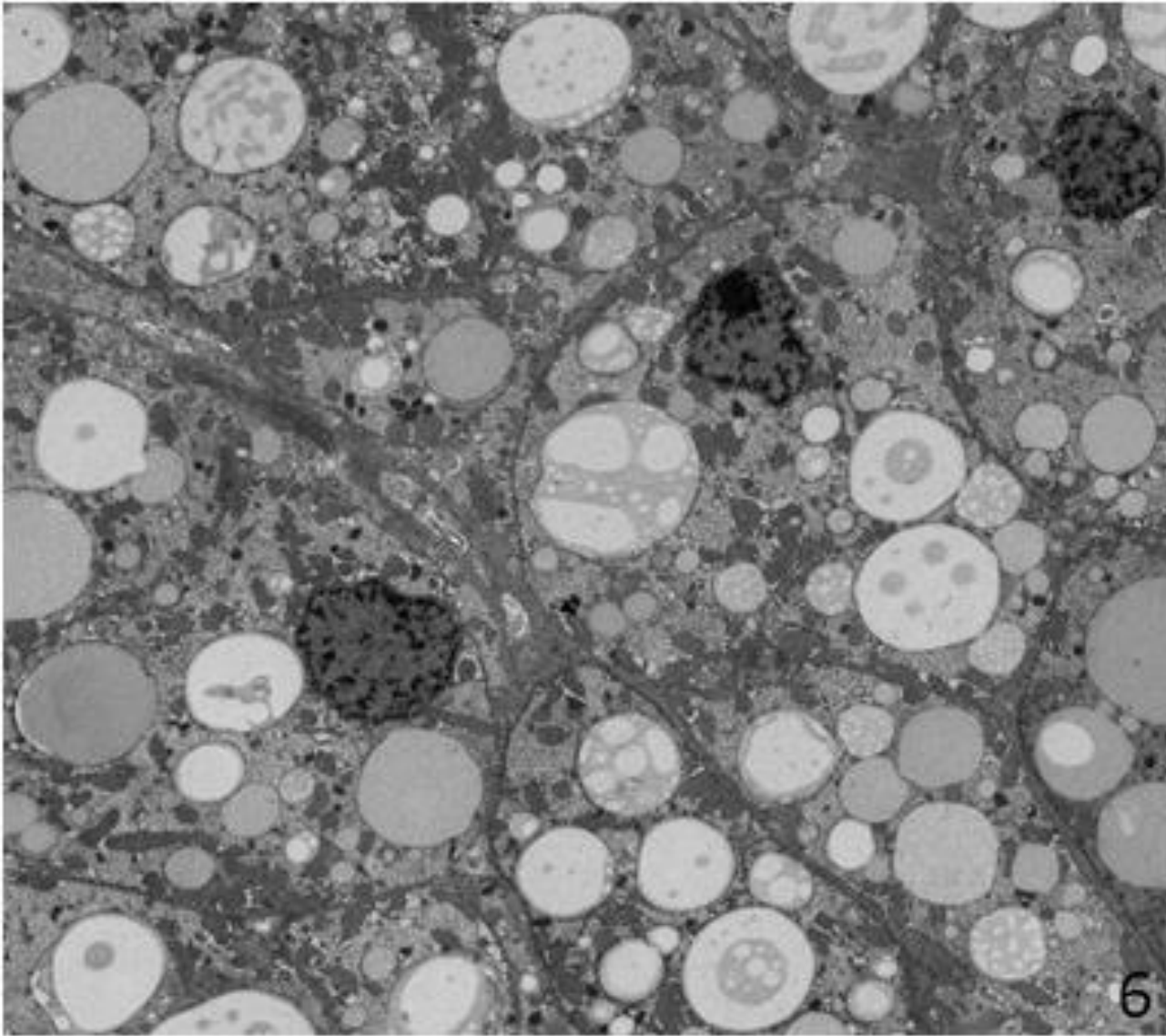


Plate 7.17

Liver tissue of a 5-year-old boy with **acid lipase deficiency (formally known as Wolman disease)** showing **lipid filled lysosomes** Magnification in Figure 6:  $\times 53,100$  and Figure 7:  $\times 251,000$ . (unpublished work and kind gift from B. Wagner)

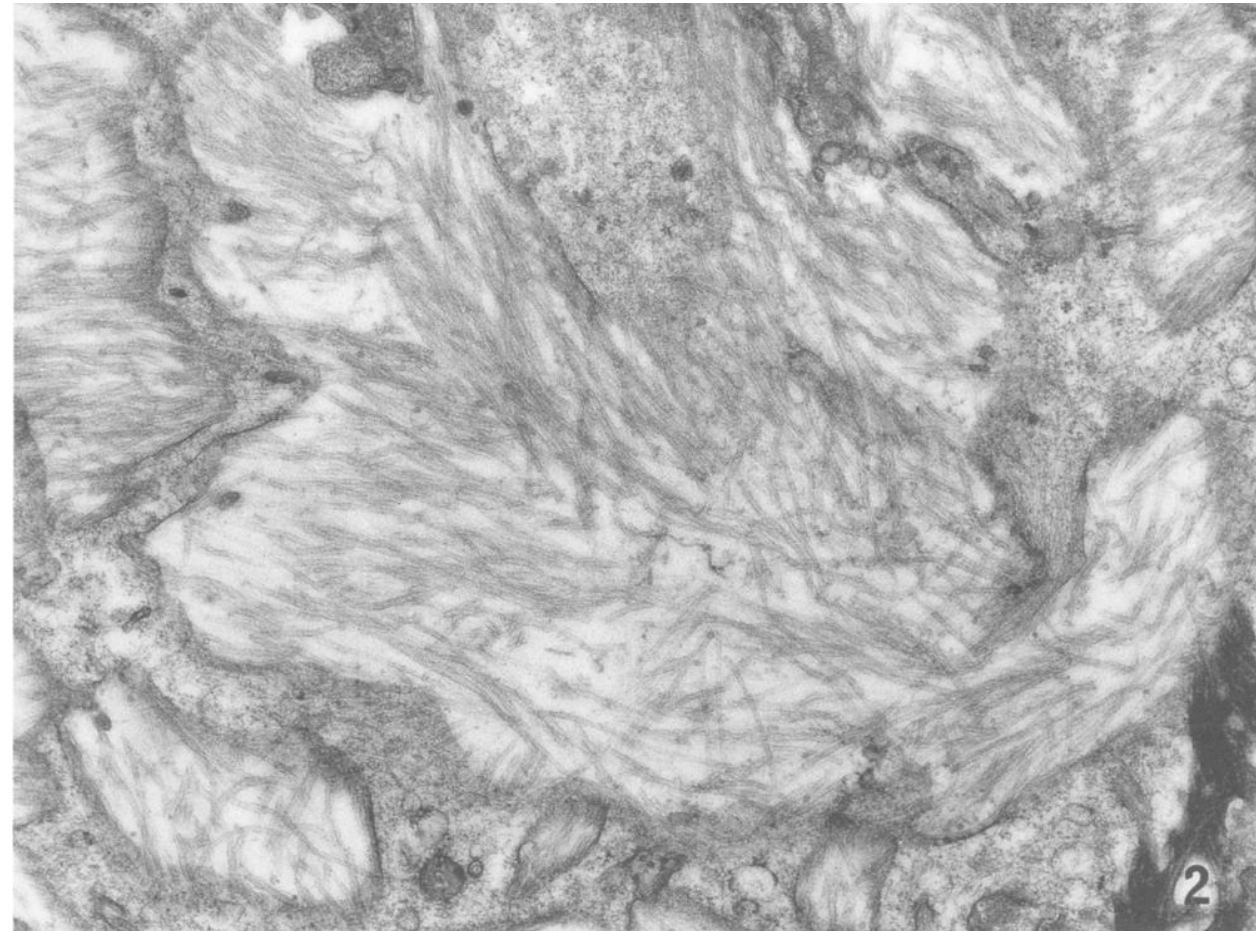
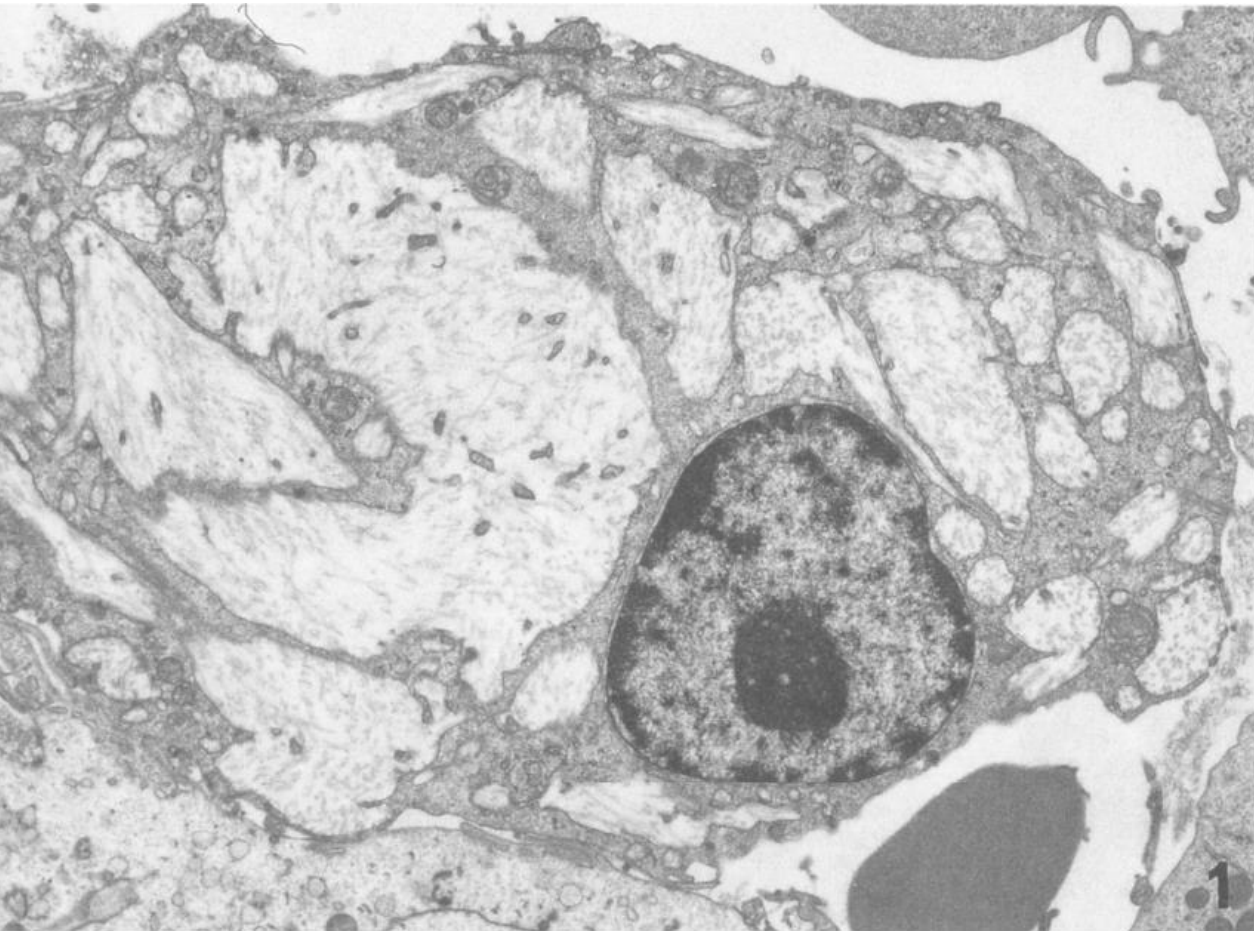


Plate 7.60

Which disease can be recognized by these large lysosomes?  
What is present in these large lysosomes?

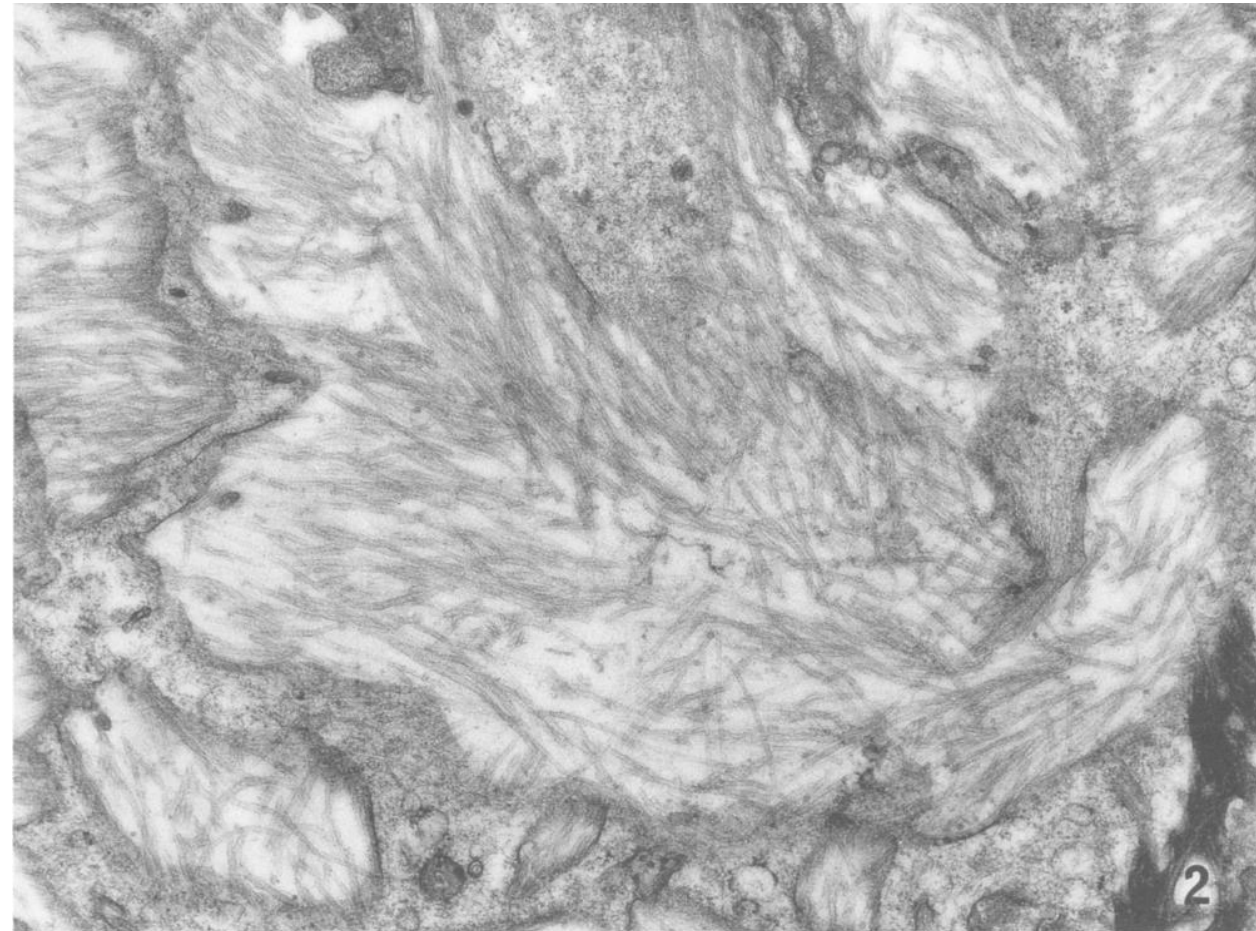
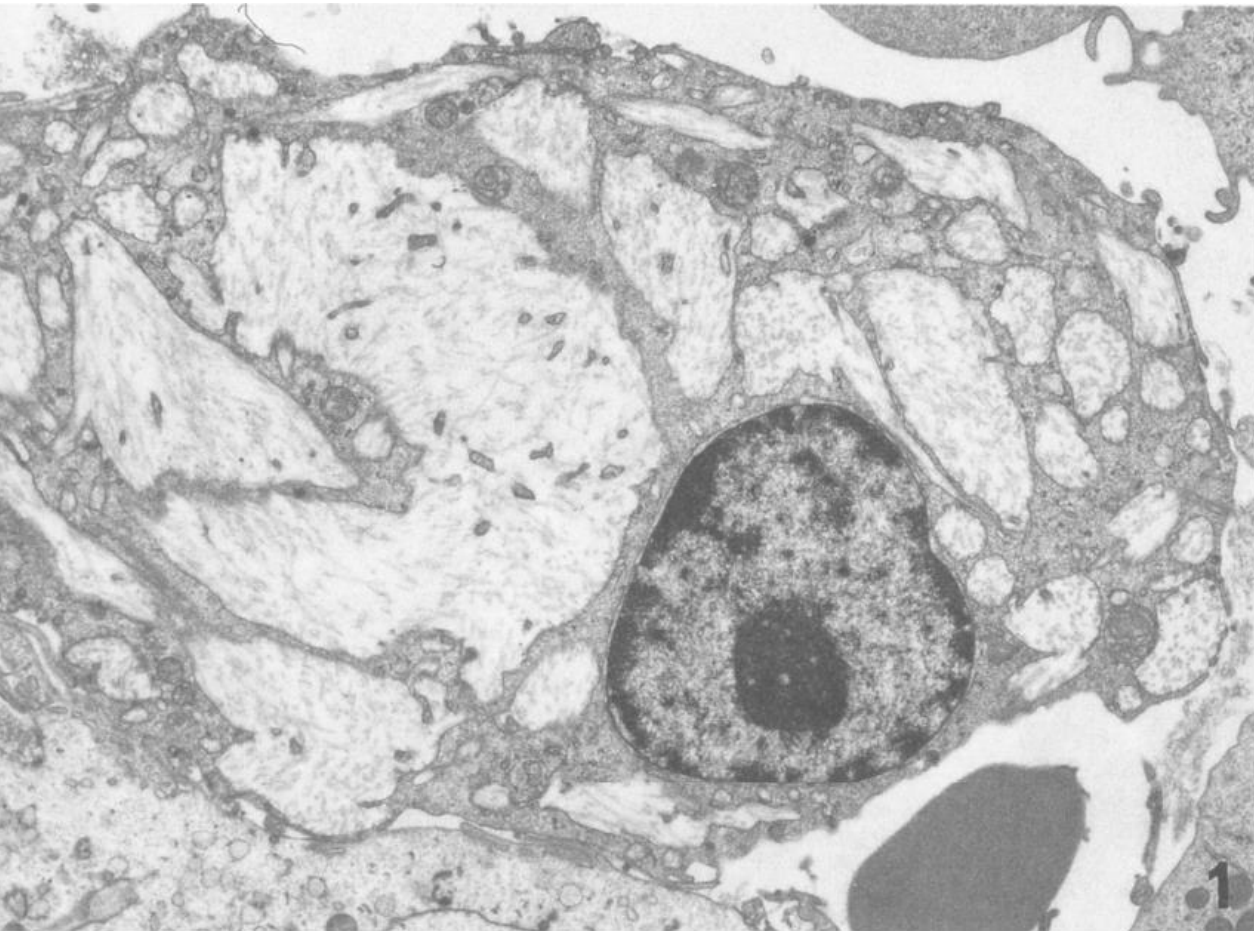


Plate 7.60

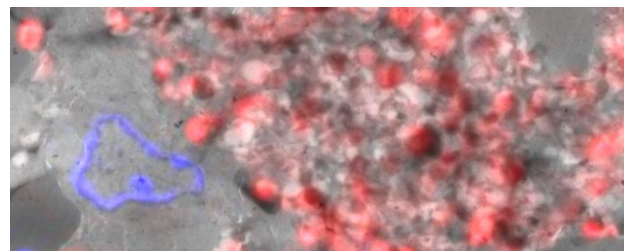
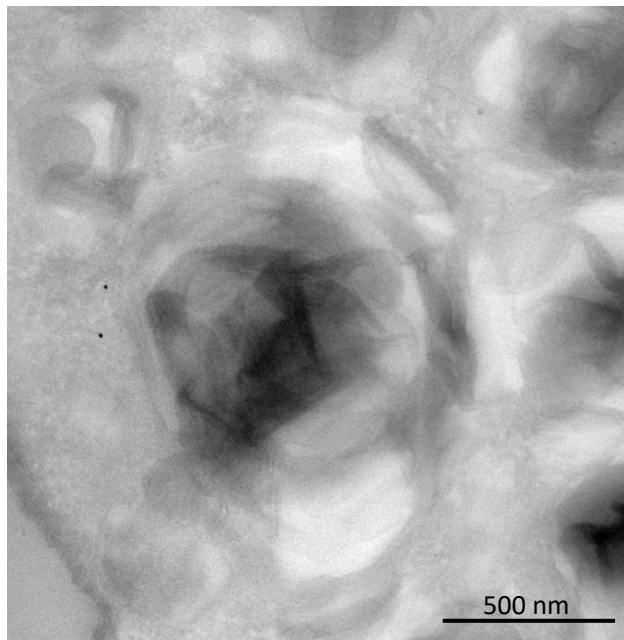
Gaucher's disease

the undigested **lipidic** residues (glucocerebrosides) constitute, or contribute to, the material in the **angulate** lysosomes

# Lipids are present in different shapes

Niemann Pick A/B  
Rose like membrane  
accumulations

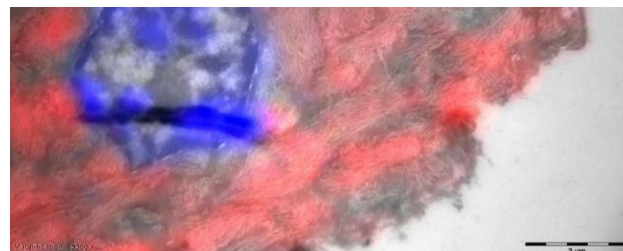
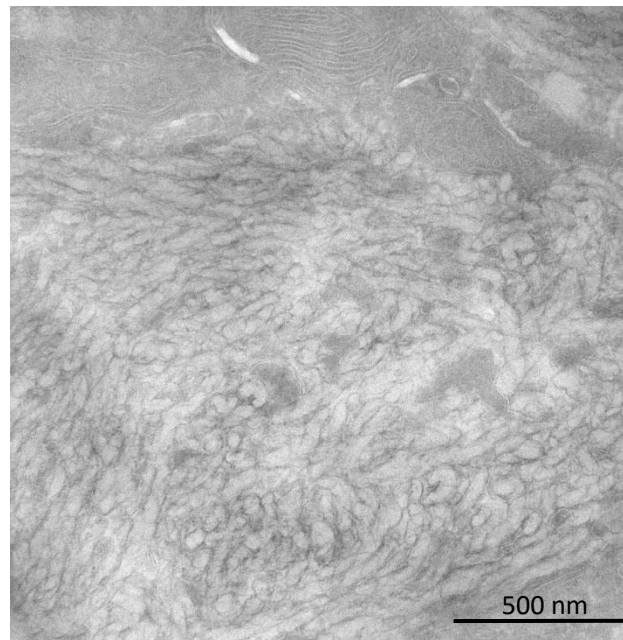
PLIN2-, LAMP1+



Martijn Van Lienden, Jan Aten, Sanne van der Niet in prep

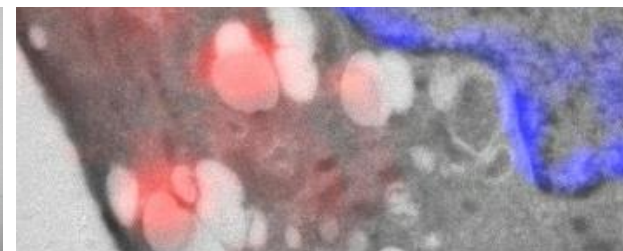
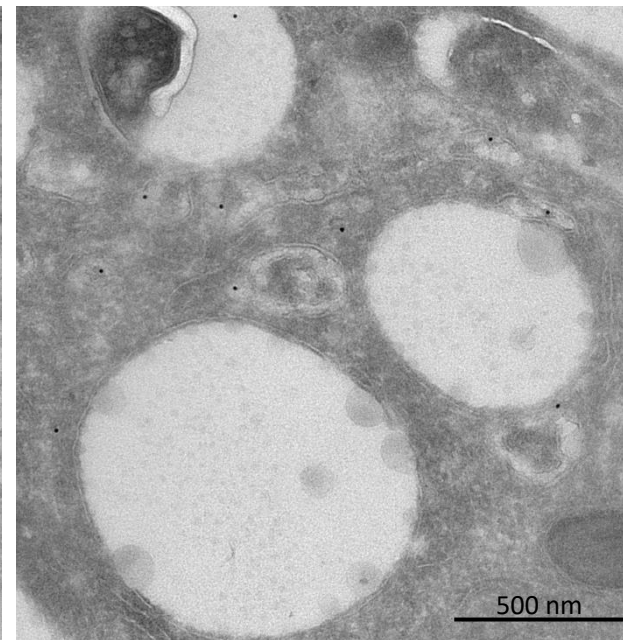
Gaucher disease  
Tubular structures

PLIN2-, LAMP1+



Mtb infection  
E-lucent, round, membrane  
enclosed compartments

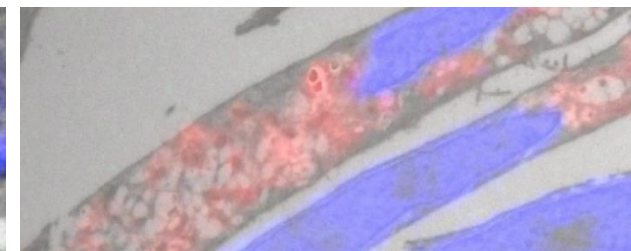
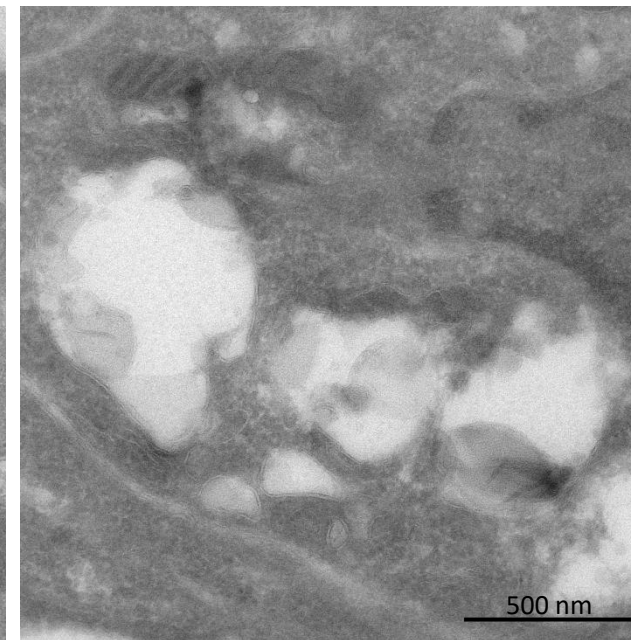
PLIN2-, sometimes LAMP1+



Bedard et al., JCI 2023

SARS-CoV-2 infection  
E-lucent, irregular, membrane  
enclosed compartments

PLIN2-, LAMP1-, viral protein+



Grootemaat et al., 2021, 2023

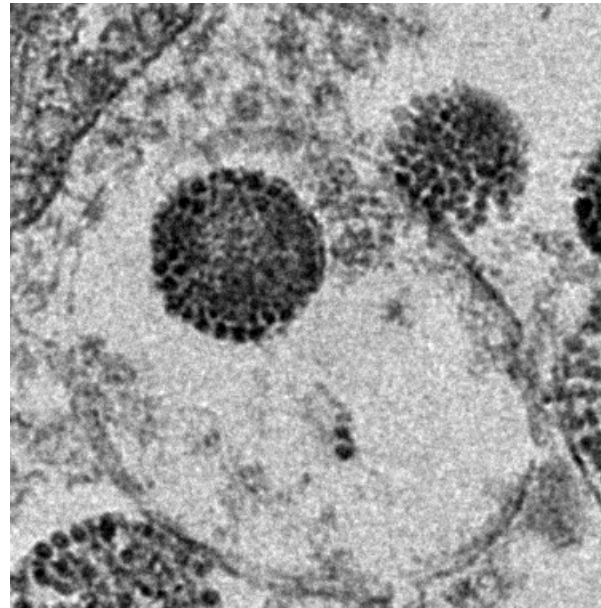
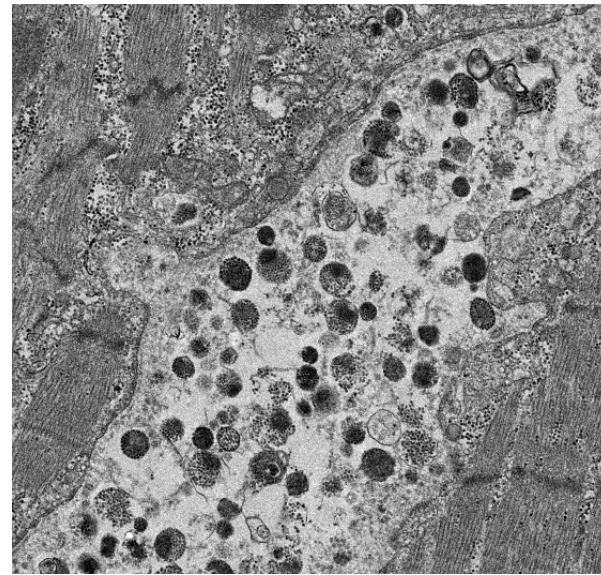
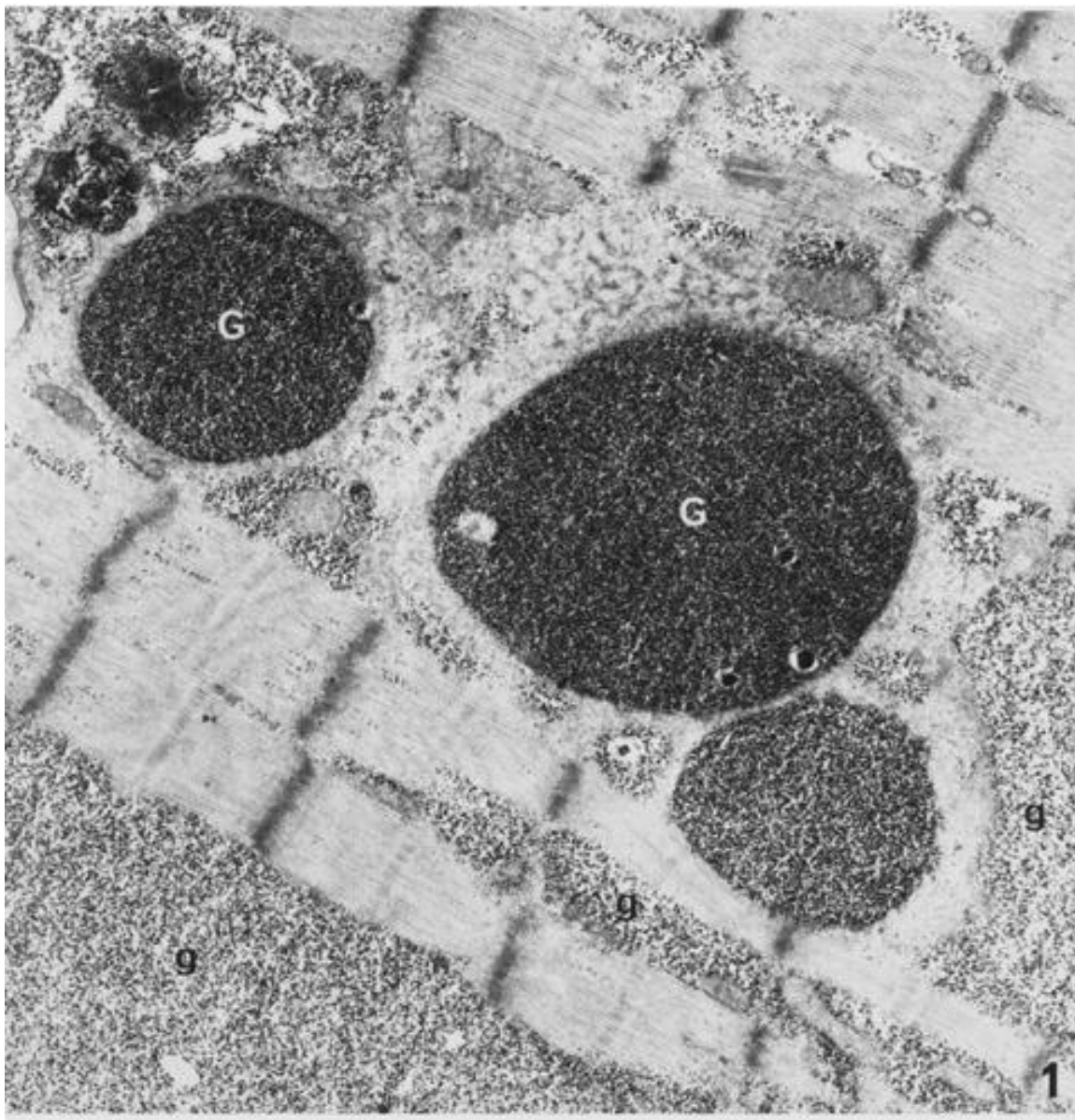
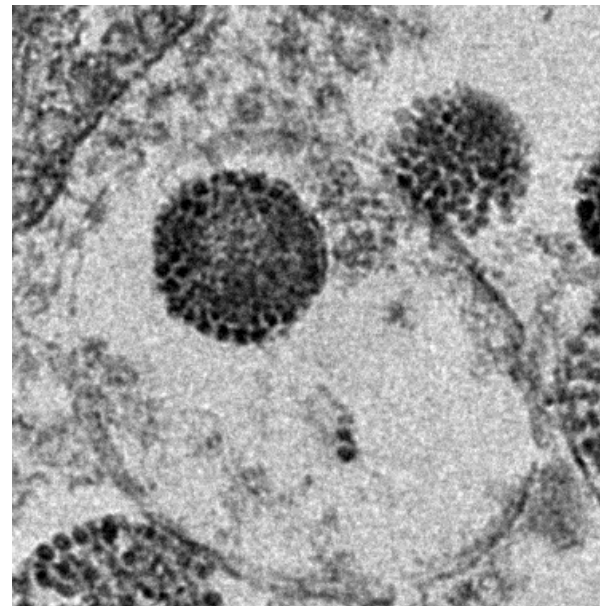
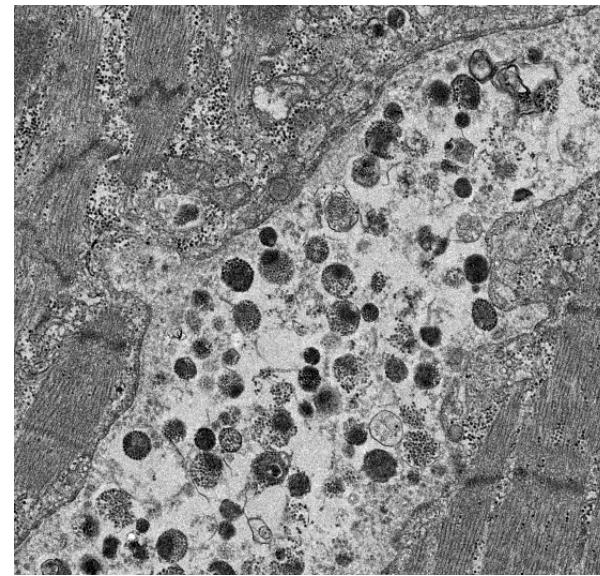
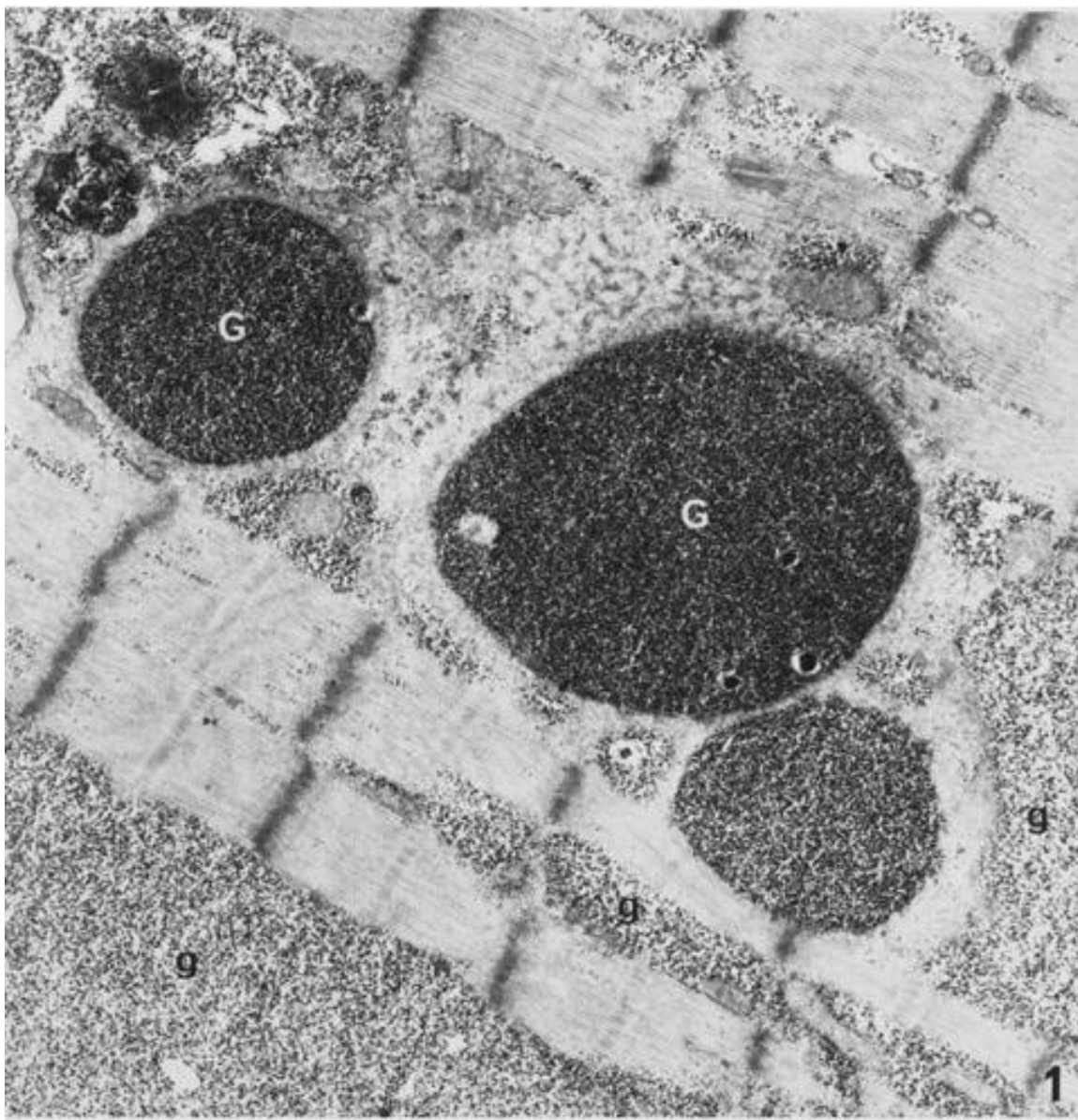


Plate 7.71

**Two** diseases can be recognized by these lysosomes, which?  
What is present in these lysosomes?



Left: Muscle biopsy from a case of **Pompe's disease**. (From Dr. Y. S. Lee) Figure 1. Glycogenosomes (G) and large accumulations of intracytoplasmic **glycogen** (g) are seen between the myofibrils.  $\times 23,000$

Right panel. Biceps brachii from a 13-year-old **Danon disease** patient (patient 2 in Nishino et al., 2000, a kind gift from Ichizo Nishino). **Glycogenosomes** (G) in between the myofibrils.

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Bastiaan Lodder

Meggie Hudspith

Enzo Scutigliani

Igne Kanopaite

Inssaf Darraz

**Sanne van der Niet**

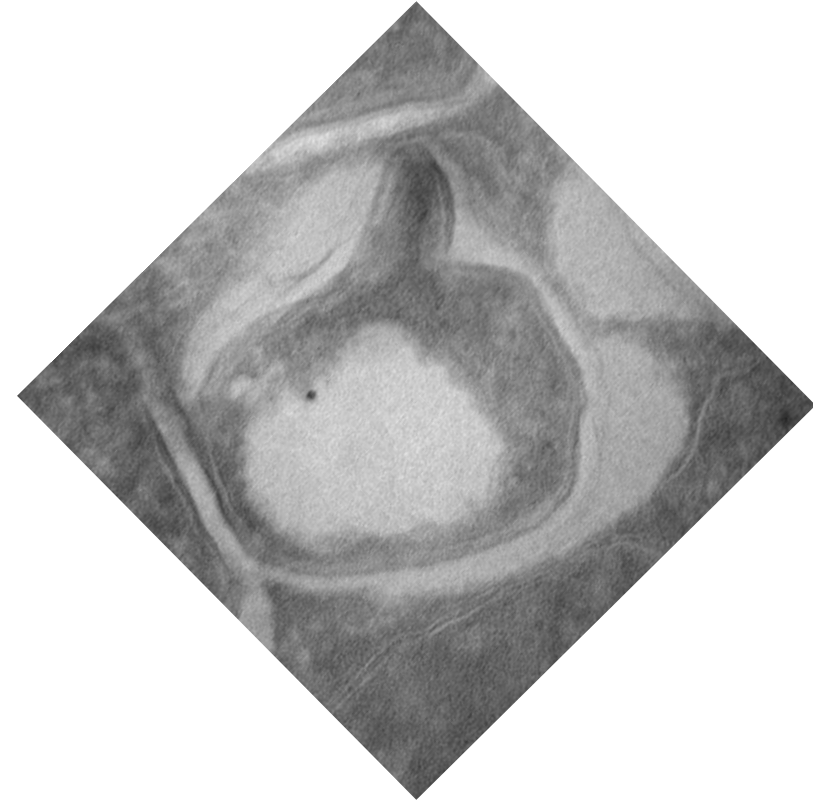
**Amsterdam UMC location AMC, The Netherlands**

**Shana Coley**

**Columbia University USA**

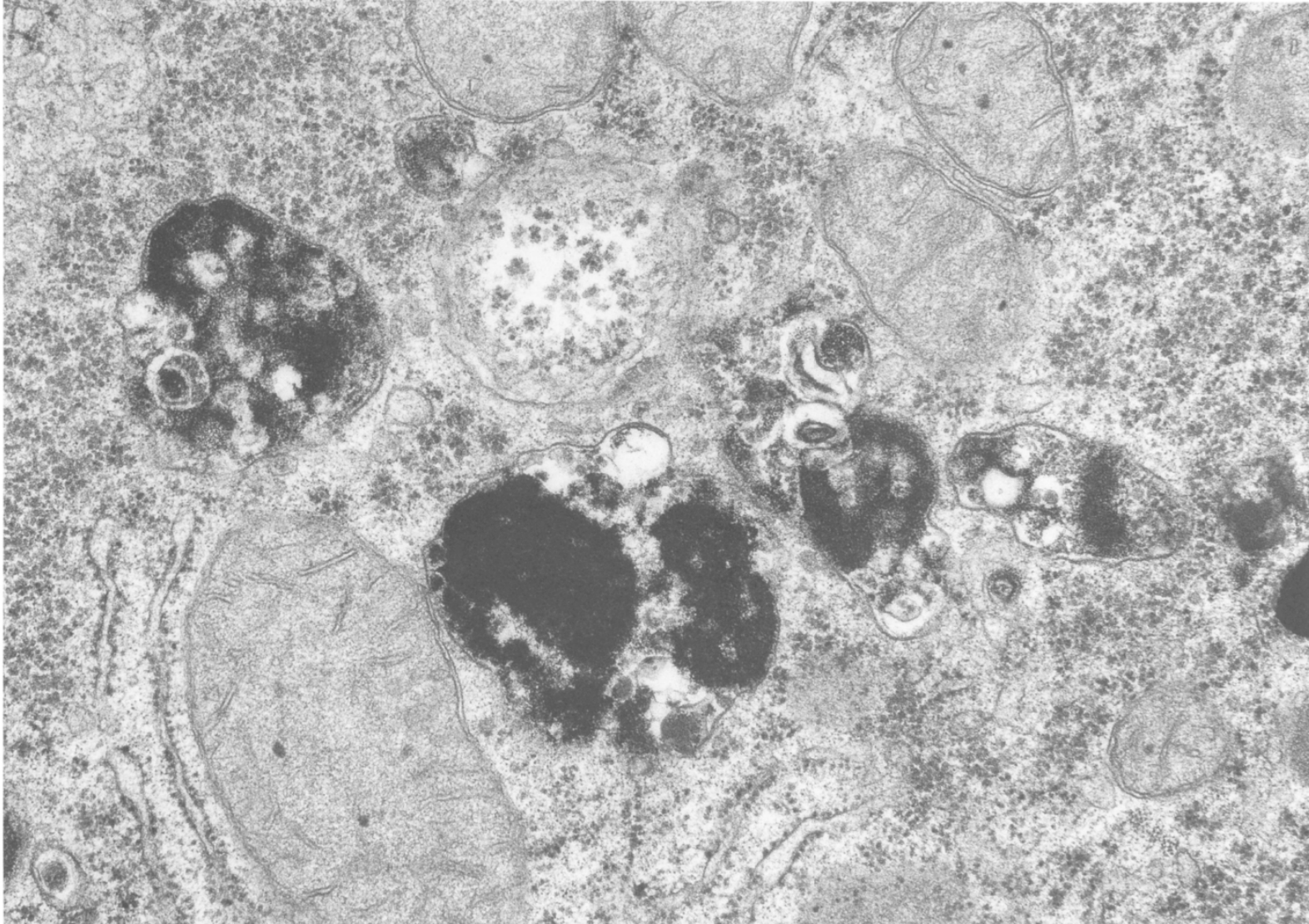
**Lucy Collinson**

The Francis Crick Institute London UK

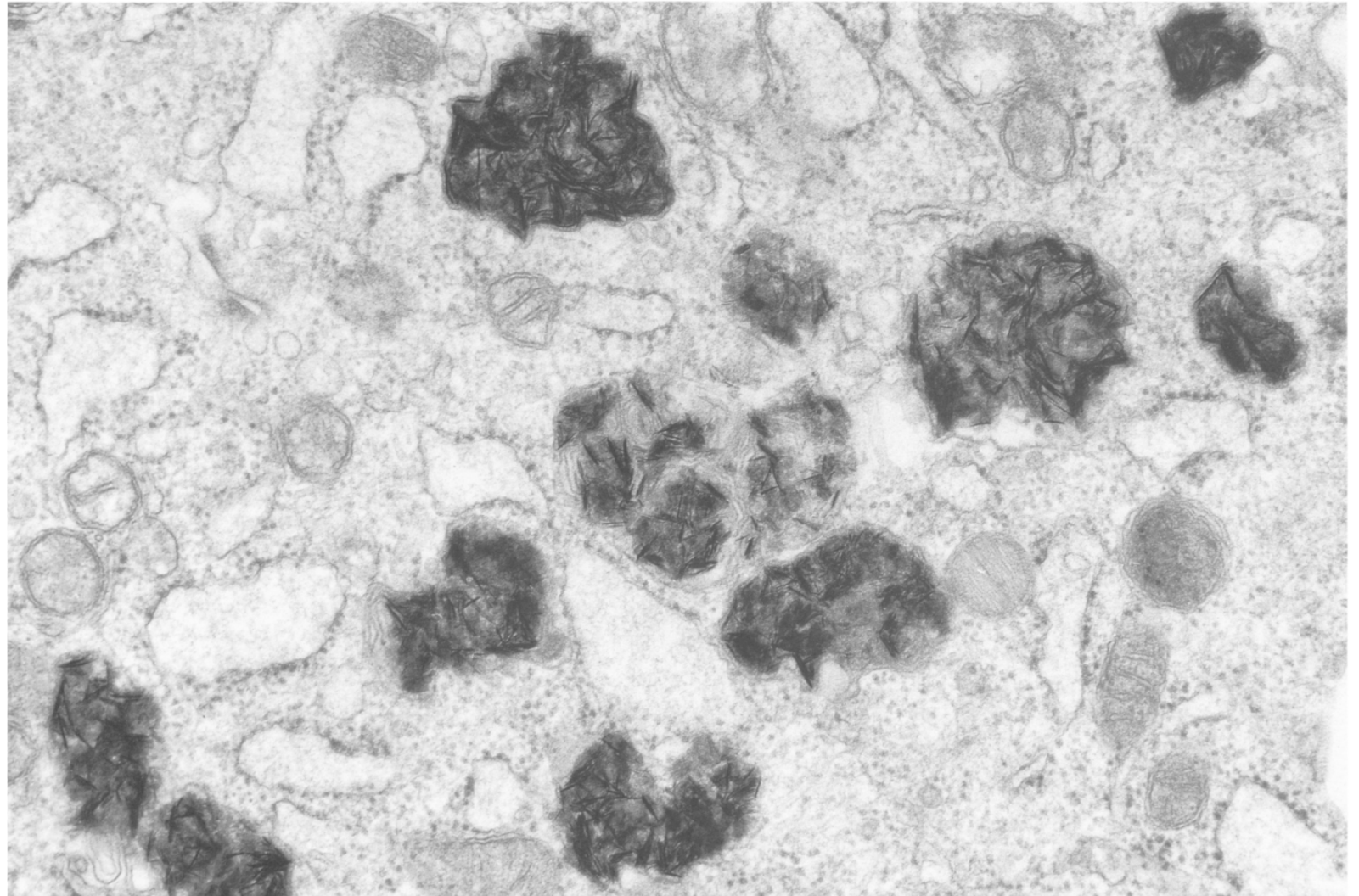
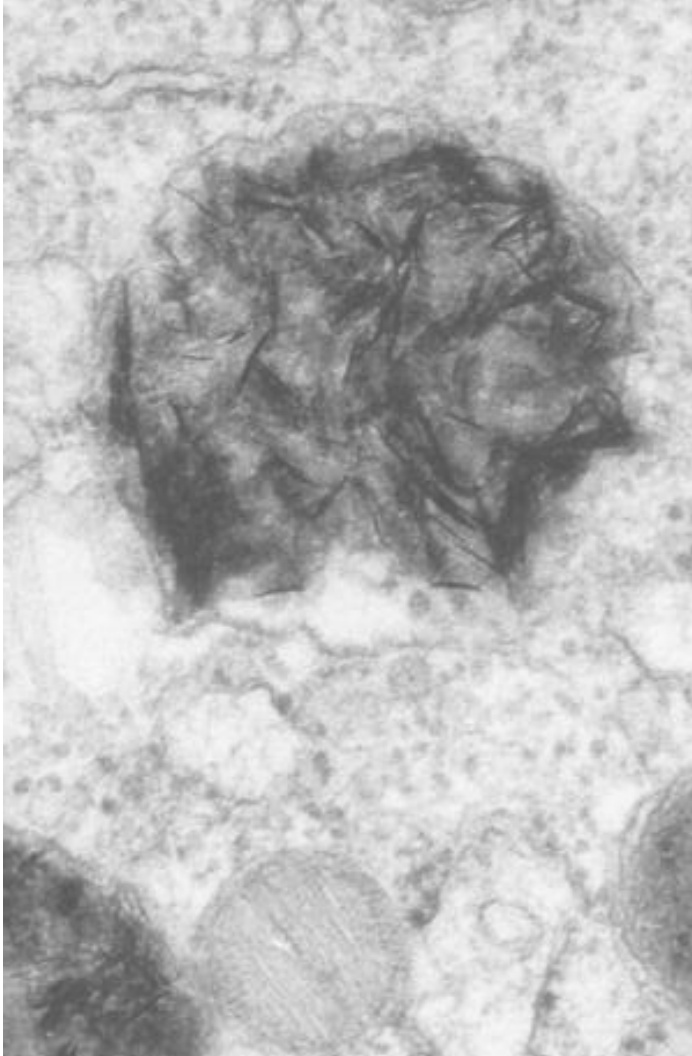


## Thank you

Iron-loaded, electron-dense lysosomes found in the liver of a rabbit that had received injections of iron dextran.  $\times 48,000$

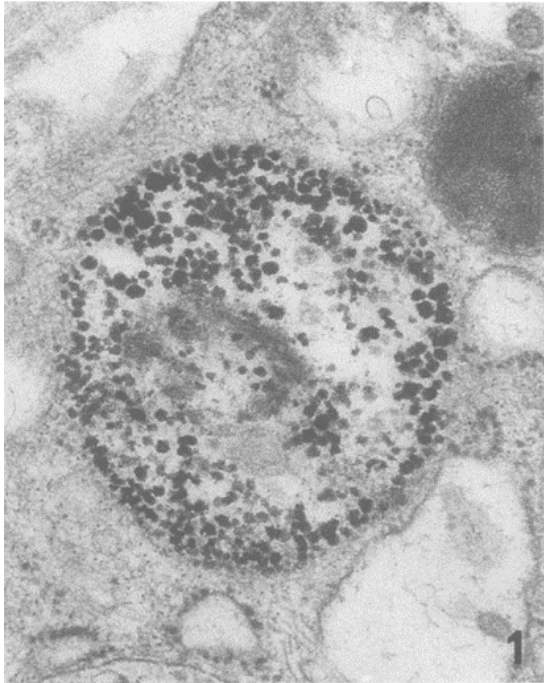


From a mouse spleen culture exposed to 25  $\mu\text{g}/\text{ml}$  of uranium acetate for 71.5 hours. Seen here is a cell showing single membrane-bound presumably lysosomal bodies (called uraniosomes) containing uranium crystals, which present electron-dense needle-like profiles.  $\times 53,000$  (*Ghadially and Yang-Steppuhn, unpublished electron micrograph*)

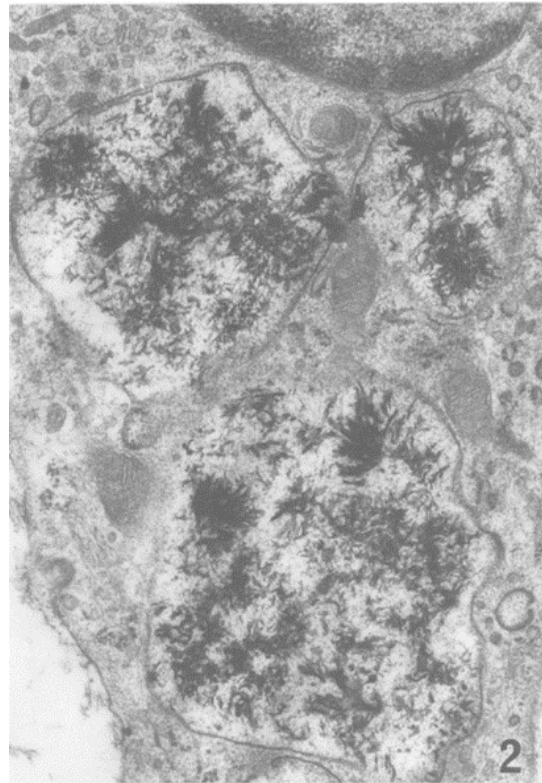


# Different times of incubation in mice:

• 4 hours



8 days



1 month



18 months

