

Quiz for launch of:
Ghadially's Ultrastructural Pathology of the Cell and Matrix, 5th ed
Chapter 12 Microtubules

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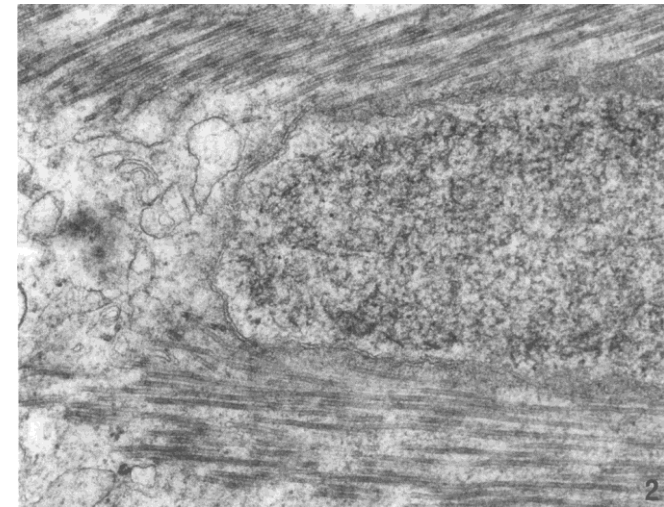
The 15th Joint Meeting of the BDIAP &
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the BELGIAN SOCIETY OF PATHOLOGY



BSP Belgian Society of Pathology



Pathological Society
Understanding Disease — Guiding Therapy



Q1: How can microtubules be recognized in TEM images?

Straight, un-branching cylinders of 22-27 nm in diameter. They are hollow, with an wall of 6 nm thickness.

Q2: Why should the temperature for glutaraldehyde fixation be 30 to 37 °C?

Low temperature, increased pressure, and various drugs are known to produce disassembly of microtubules or to prevent their formation.

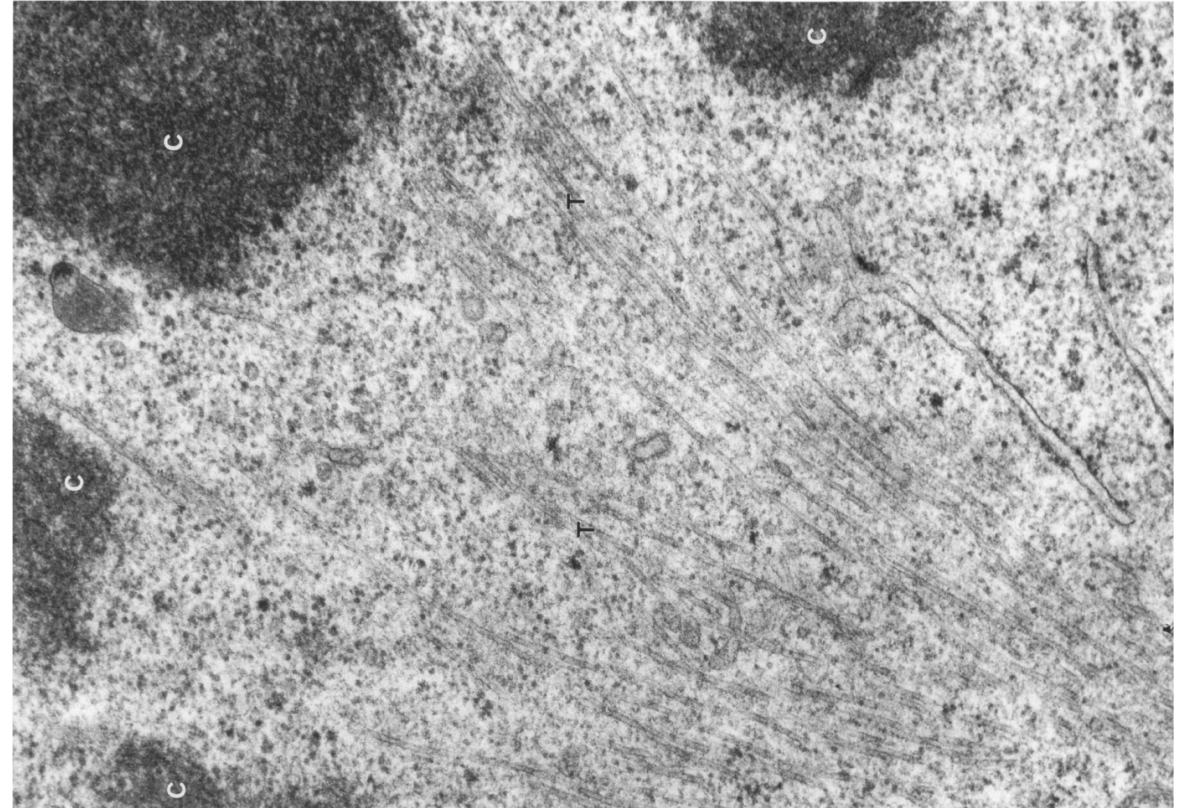


PLATE 12.2 Malignant melanoma. A neoplastic cell in mitosis showing chromosomes (C) and microtubules (T) of the mitotic spindle, $\times 56,000$.

See page 559 for answer and discussions

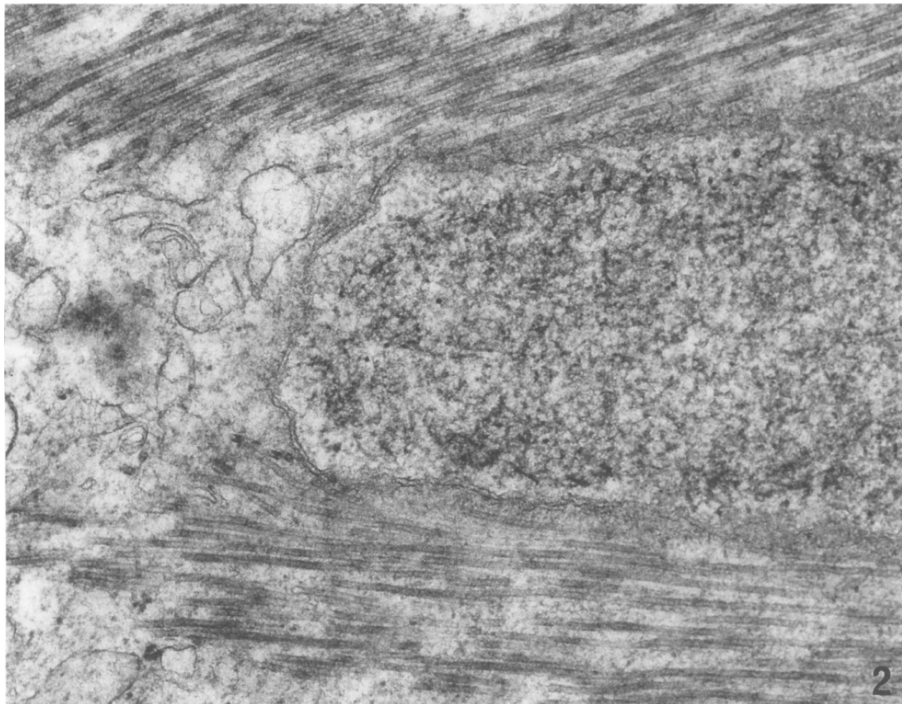
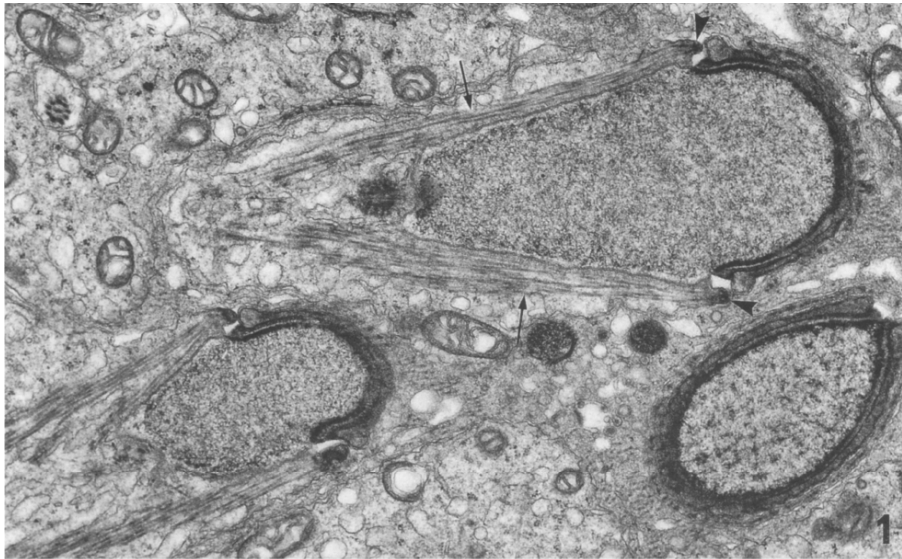


Plate 12.1.

Spermatids from a rat testis. The manchette comprises a cylindrical array of microtubules (arrows) extending caudally from a ring-like specialization of the cell membrane (arrowheads) near the posterior margin of the acrosomal cap.

Q3: What are microtubules made of?

Polymers of the globular protein tubulin (*α and β tubulin*) and of several types of microtubule-associated proteins (MAPs)

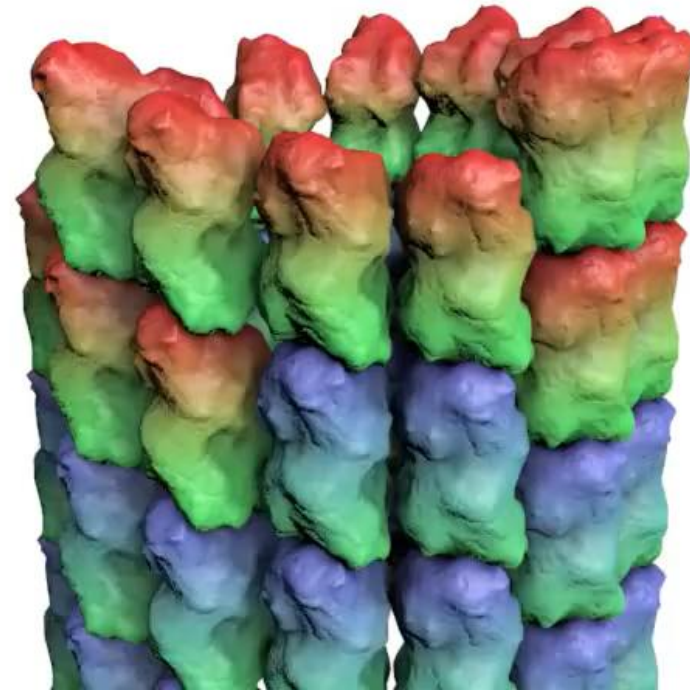
Q4: How do microtubules assemble?

Globular $\alpha\beta$ -tubulin heterodimers stack into a protofilament of 5 nm diameter (30 °C, tubulin has intrinsic GTPase activity, MAP assists); several protofilaments (usually 13) build a sheet that rolls into a cylinder.

See page 560 for answer and discussions

Eva Nogales lab,
University of California, Berkeley,
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Animation of the microtubule
dynamic instability:
Tubulin dimers bound to GTP (red)
bind to the growing end of a
microtubule.
Subsequently GTP hydrolyses into
GDP (blue) which is prone to
disassembly.



Q5: Where do we find “stable” and “dynamic” microtubules?

Stable: cilia, flagellae, axon and dendrites in neurons.

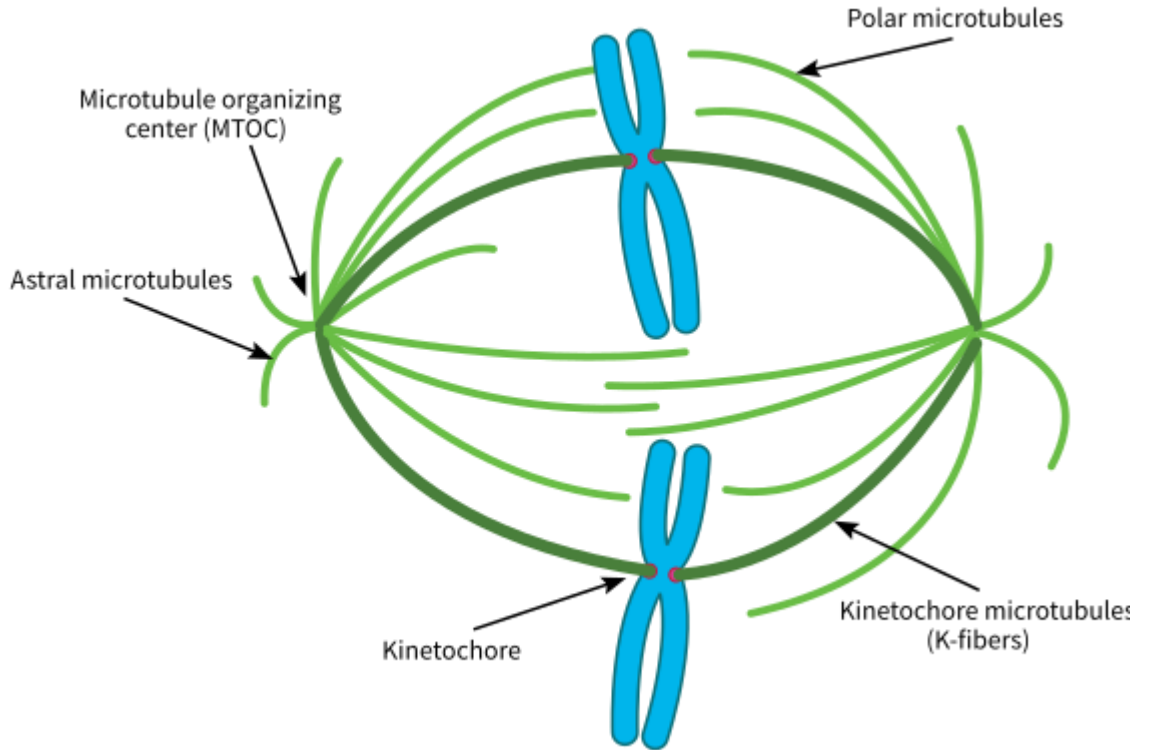
Dynamic: Mitotic spindles.

Q6: Where in the cell do microtubules assemble?

MT assembles preferentially at the centrosome and form the microtubule organizing center (MOTC). One end (the plus-end, capped by β -tubulin), grows quicker than the other (the minus end, α -tubulin).

The plus-end is usually oriented toward the cell membrane while the minus-end remains attached to MOTC.

See page 560 for answers and discussions.



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Diagram of a mitotic spindle with microtubules, microtubule organizing complex, and kinetochores labeled.

Q7: What substances affect the microtubules?

Colchicine and *podophyllotoxin* bind on the outer surface and impair microtubules growth. *Vinblastine*, binds along the inner lumen of microtubule and promotes formation of spiral aggregates of tubulin instead. *Taxol* and other drugs affect the lateral contacts between protofilaments, thus microtubules assembled in its presence are more resistant to ageing or low temperature. *Benzimidazoles* disrupt microtubules in helminths.

Q8: Why is this information relevant?

Anti-proliferation agents in malignancies, (auto)immune diseases, and anti-helminthics, but also have allowed for great progress in investigating the structure and function of microtubules.

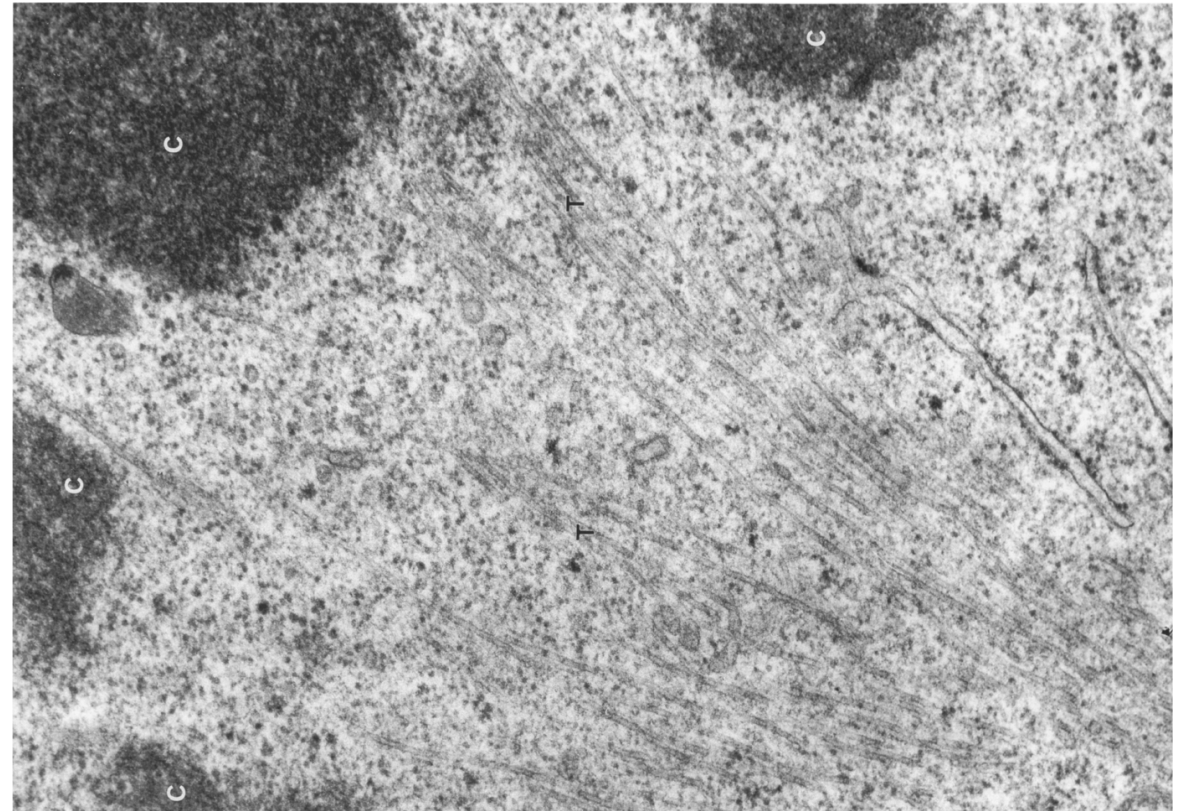


PLATE 12.2 Malignant melanoma. A neoplastic cell in mitosis showing chromosomes (C) and microtubules (T) of the mitotic spindle, $\times 56,000$.

Q9: What roles have the microtubules?

- Normal cell shape (pathologic spherocytosis)
- Intracellular transport
- Motility
- Migration
- Intraction with receptors, channels, signal transduction proteins, cytoskeleton, cellular membrane, nuclear membrane
- Free tubulin dimers in large amounts (malignancy) block channels in the mitochondria; switch towards glycolysis

See page 561 for answers and discussions.

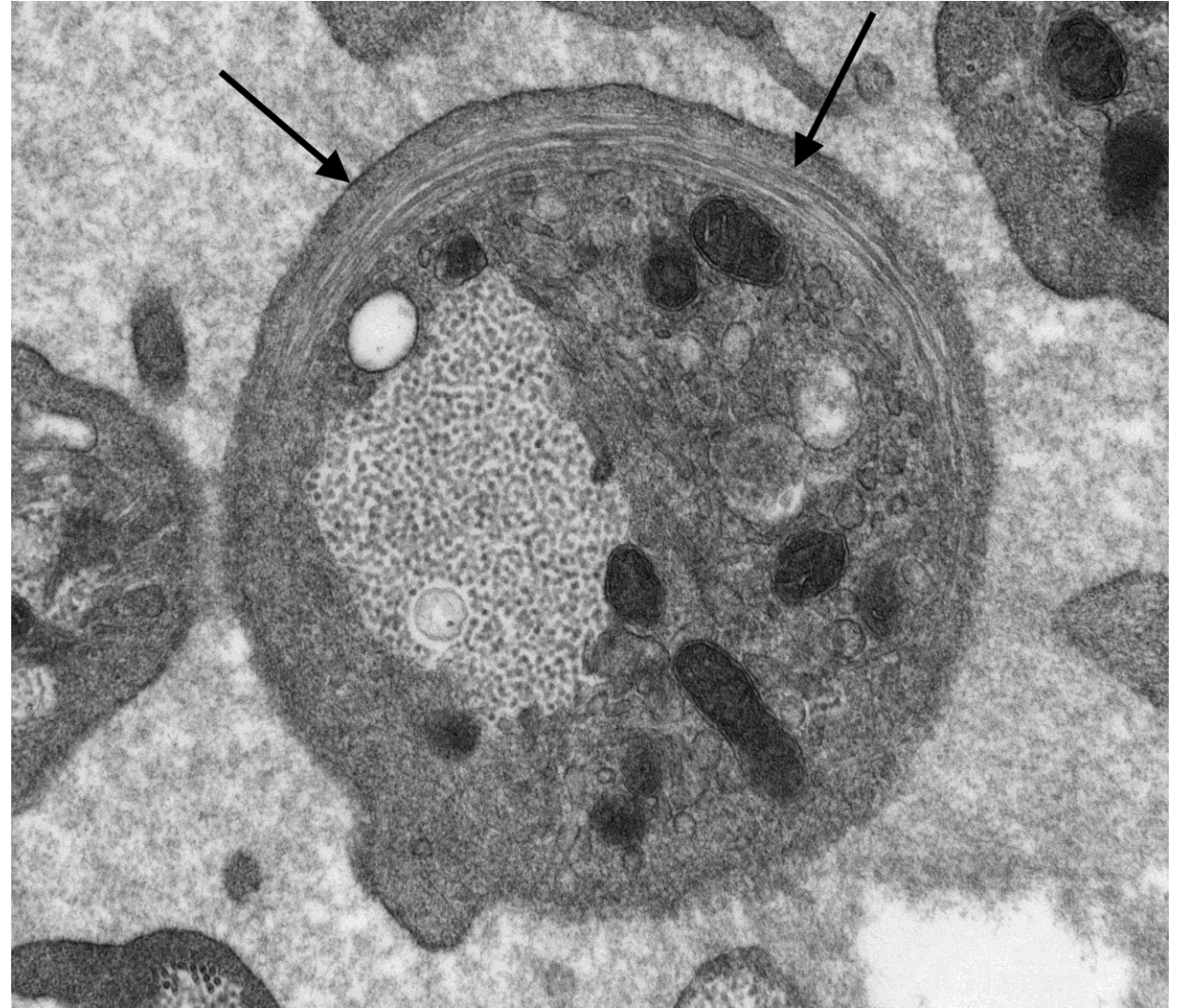
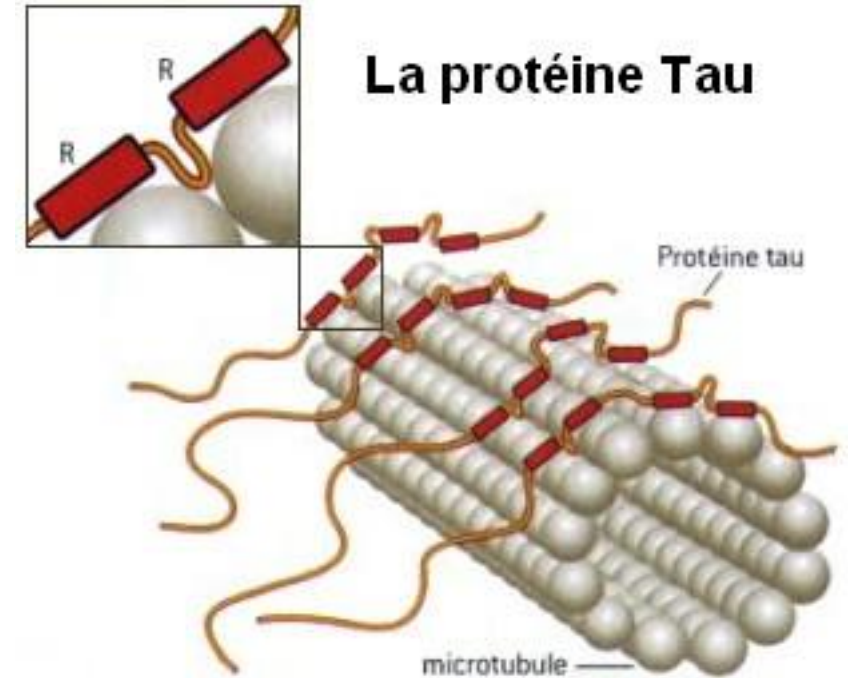


PLATE 12.3 Human platelet, showing a marginal band of microtubules (arrow). Original magnification, x 12,000. Electron micrograph courtesy of B. E. Wagner

Q10: What are microtubules associated proteins (MAP)?

MAPS are less conspicuous in TEM but important in stabilizing the microtubules or regulates its assembly/disassembly.

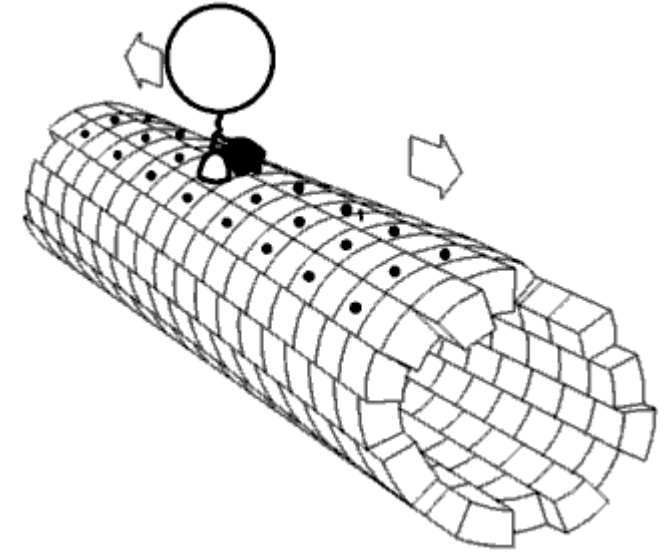
One of the most studied is the MAP2/tau family, which in neurons also interacts with Golgi and ER. Pathological accumulations of phosphorylated tau protein (so called tau tangles) are the hallmark of Alzheimer's disease and frontotemporal dementia.



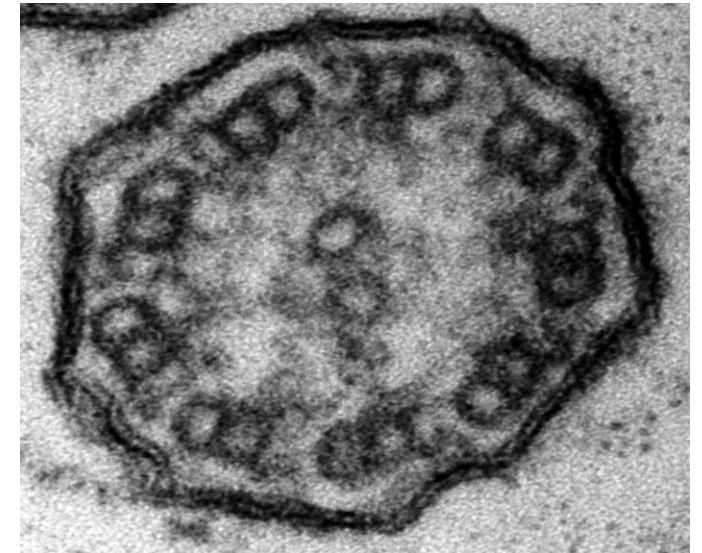
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Q11: What are kinesins and dyneins?

They are motor proteins which move in a walking-like manner along the microtubules in order to transport cargo (membrane bound vesicles, RNA, viruses), segregate chromosomes, move cilia and flagellae, but they can also affect the stability of the microtubules ends.



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See page 560 for answers and discussions.

Q12: Are microtubules of diagnostic importance?

They are common in ganglioneuroma and neuroblastoma. The presence of microtubules, intermediate filaments, and neurosecretory granules distinguishes these tumors from other tumors with which they may be confused, such as Ewing's tumor and lymphoma .

See page 561 for answer and discussions:

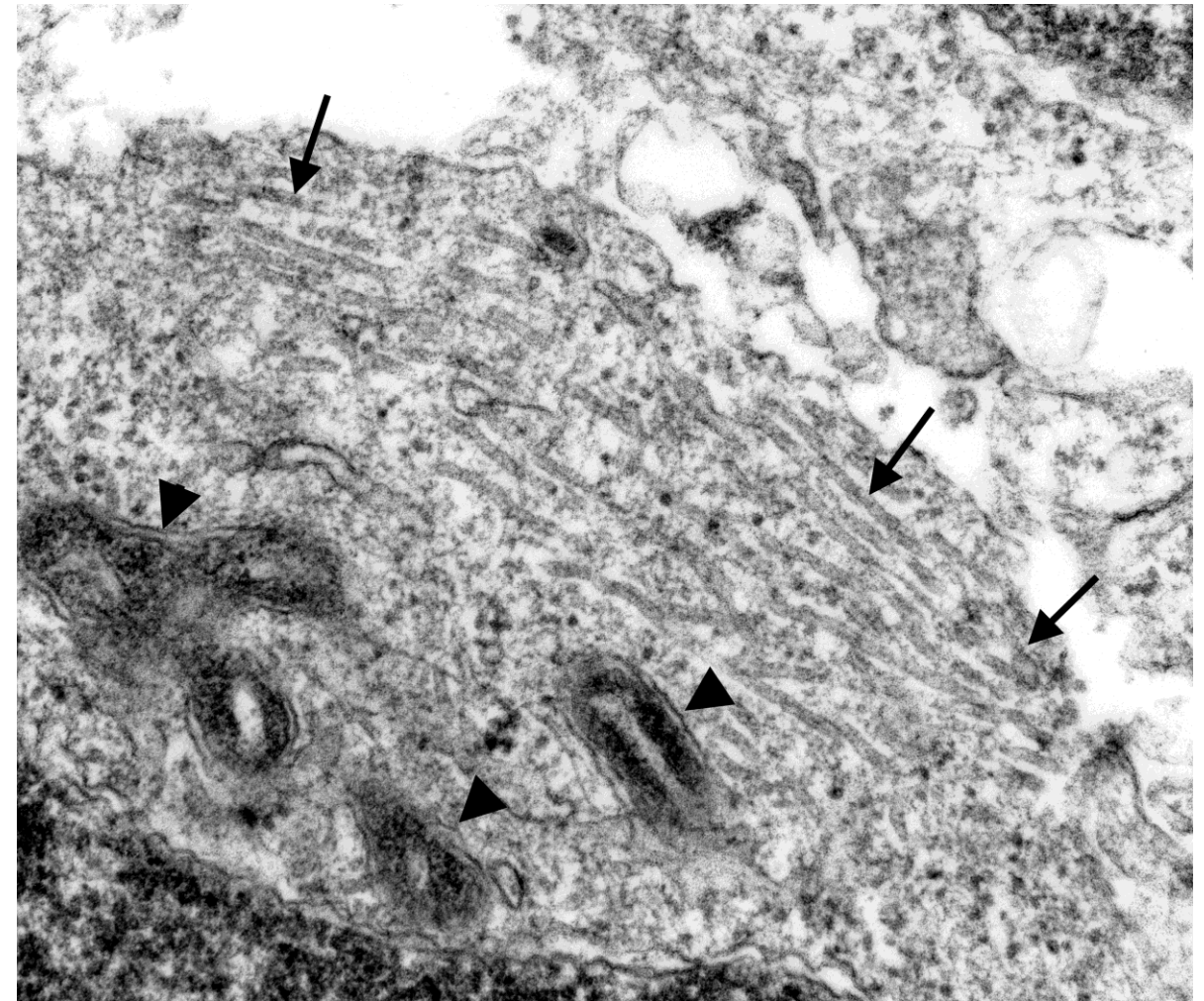


PLATE 12.4 Neuroblastoma. Tumor cells showing small mitochondria (arrowheads) and microtubules (arrows). Original magnification, x 46,000. Electron micrograph courtesy of B. E. Wagner

Q13: What happens to microtubules in virus-infected cells?

Viruses often exploit the host cell's microtubule network to navigate through the cytoplasm and reach replication sites, as well as to transport newly formed viral particles to the cell periphery for release. Kaposi's sarcoma-associated herpesvirus (KSHV), a large DNA virus, induces rapid cytoskeletal remodeling that includes MT stabilization. Chemicals that disrupt MT networks, still commonly used today, were reported to suppress virus infection.

See page 562-3 for answer and discussions.

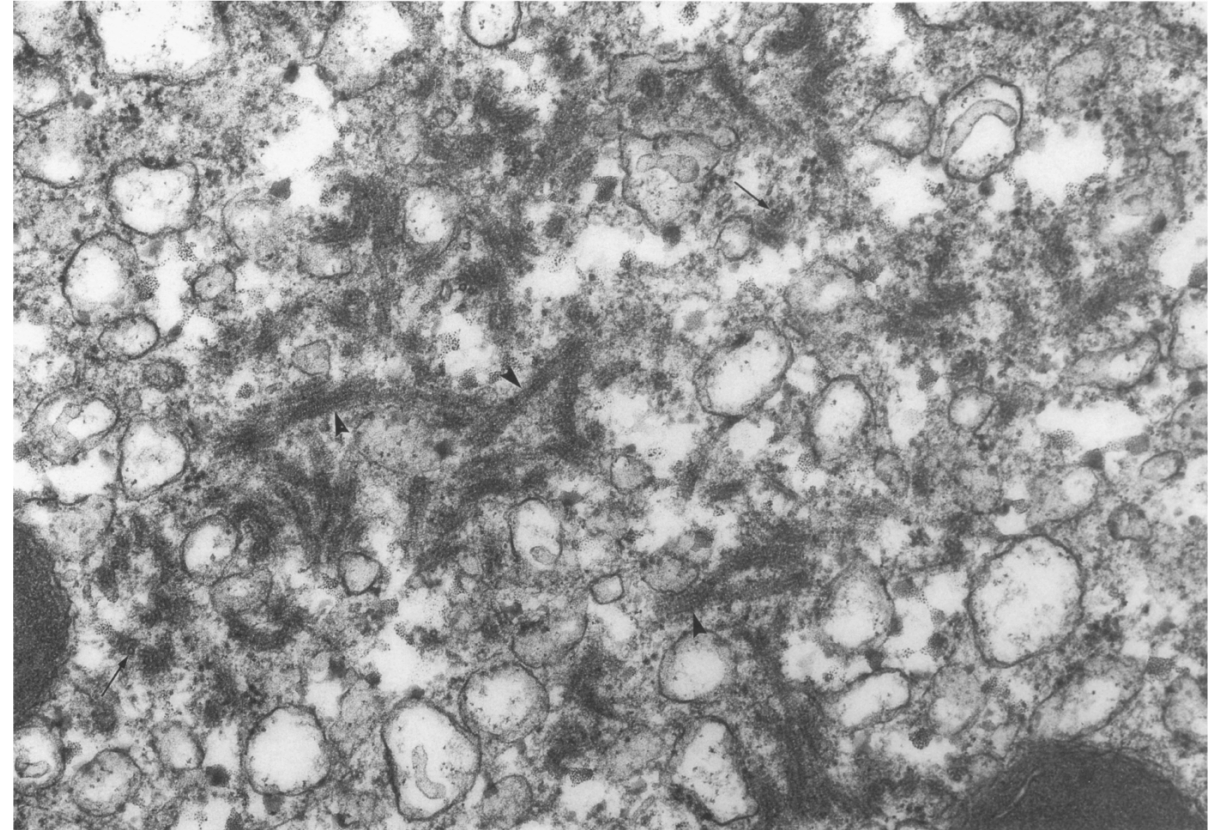


PLATE 12.5 Hepatocyte from a chimpanzee inoculated with serum from a patient with non-A, non-B viral hepatitis. Aggregates of microtubules (thick arrow) showing a faintly striated pattern are present. The expected circular profiles representing transverse sections through microtubules are also evident (thin arrows), $\times 122,000$ (electron micrograph courtesy of Dr H. P. Dienes).



Thank you!