Gastrointestinal diseases (immune response)

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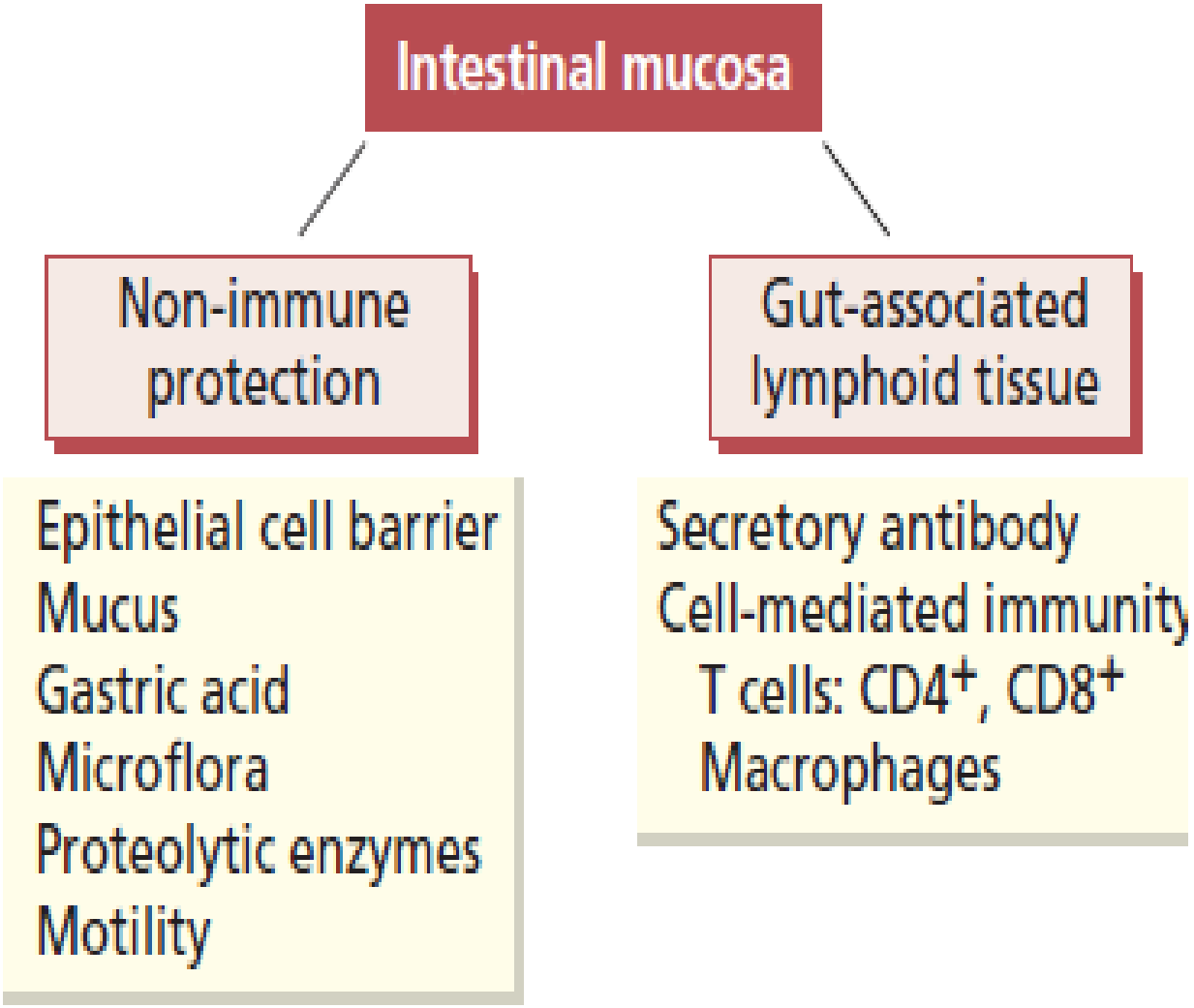
The gastrointestinal tract is the largest immunological organ in the body. Over 90% of the exposure of the human body to microorganisms occurs at the mucosal surface of the gastrointestinal tract and over 400 bacterial species inhabit the average human gut. The gut is protected by several non-specific mechanisms . Epithelial cells form an important physical barrier via their intercellular tight junctions and turn over rapidly (every 24–96 h).

Any injury to the epithelial barrier results in rapid migration of adjacent viable epithelial cells to cover the denuded area, a process called ‘restitution’, while lymphocytes and macrophages migrate out through pores in the basement membrane to provide temporary host protection. The acid pH of the stomach is a formidable chemical barrier to many organisms and bacterial overgrowth is a consequent complication in patients with a chlorhydria due to

atrophic gastritis.


Intestinal mucosa
Non-immune protection
Gut-associated lymphoid tissue
Epithelial cell barrier
Mucus
Gastric acid
Microflora
Proteolytic enzymes
Motility
Secretory antibody
Cell-mediated immunity
T cells: CD4+, CD8+
Macrophages

Mucosal immune responses involve the gut-associated lymphoid tissue (GALT). Lymphocytes are found at three sites within the mucosa :

- Organized lymphoid aggregates (Peyer's patches) beneath the epithelium of the terminal small intestine Lymphocytes within the epithelial cell layer (IELs)
- Lymphocytes scattered, with other immunocompetent cells, within the lamina propria.

GALT is divided into two functional compartments: an afferent arm – Peyer's patches – where interaction occurs between luminal antigen and the immune system; and an effector arm – the diffusely distributed intraepithelial and lamina propria lymphocytes.

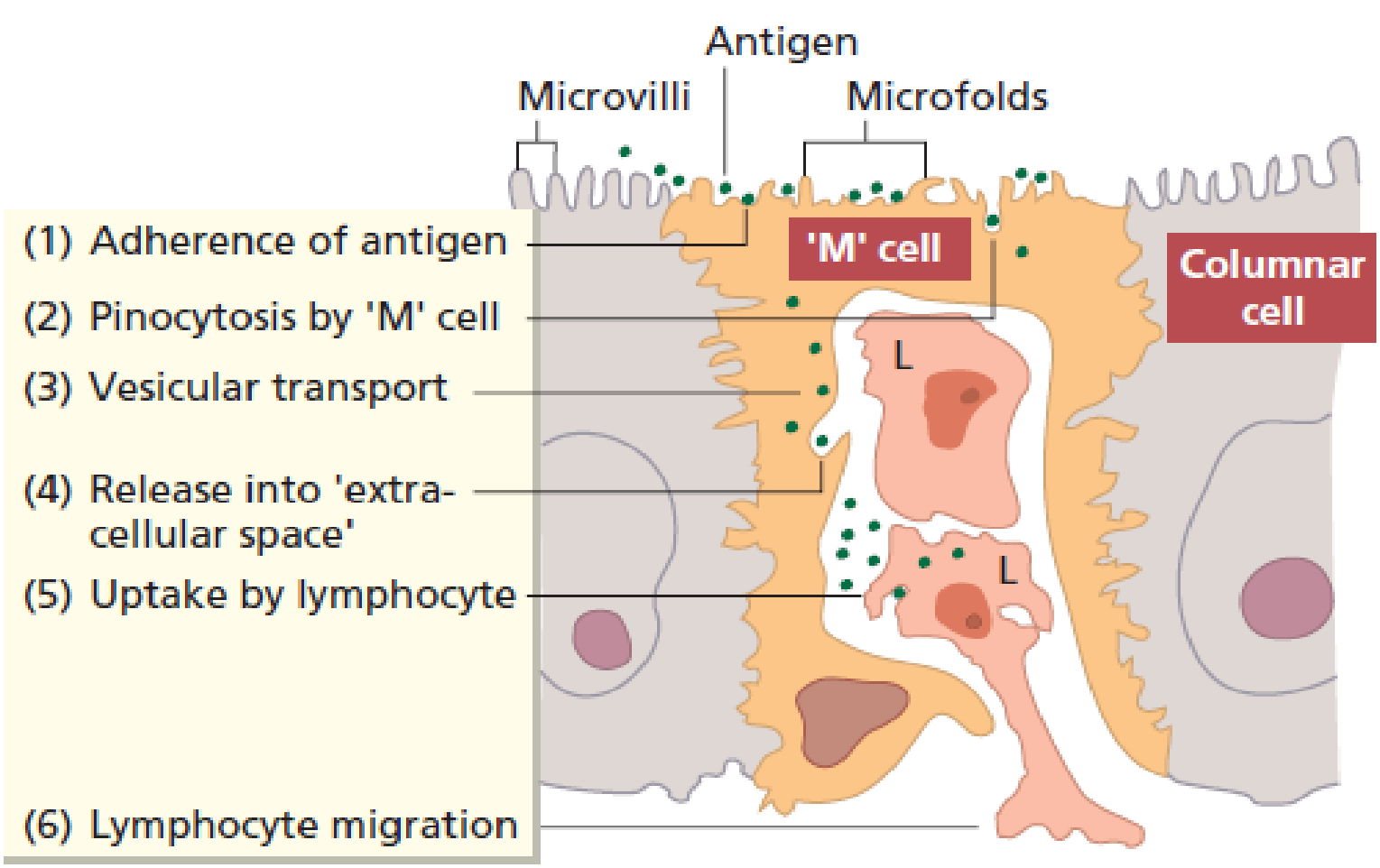
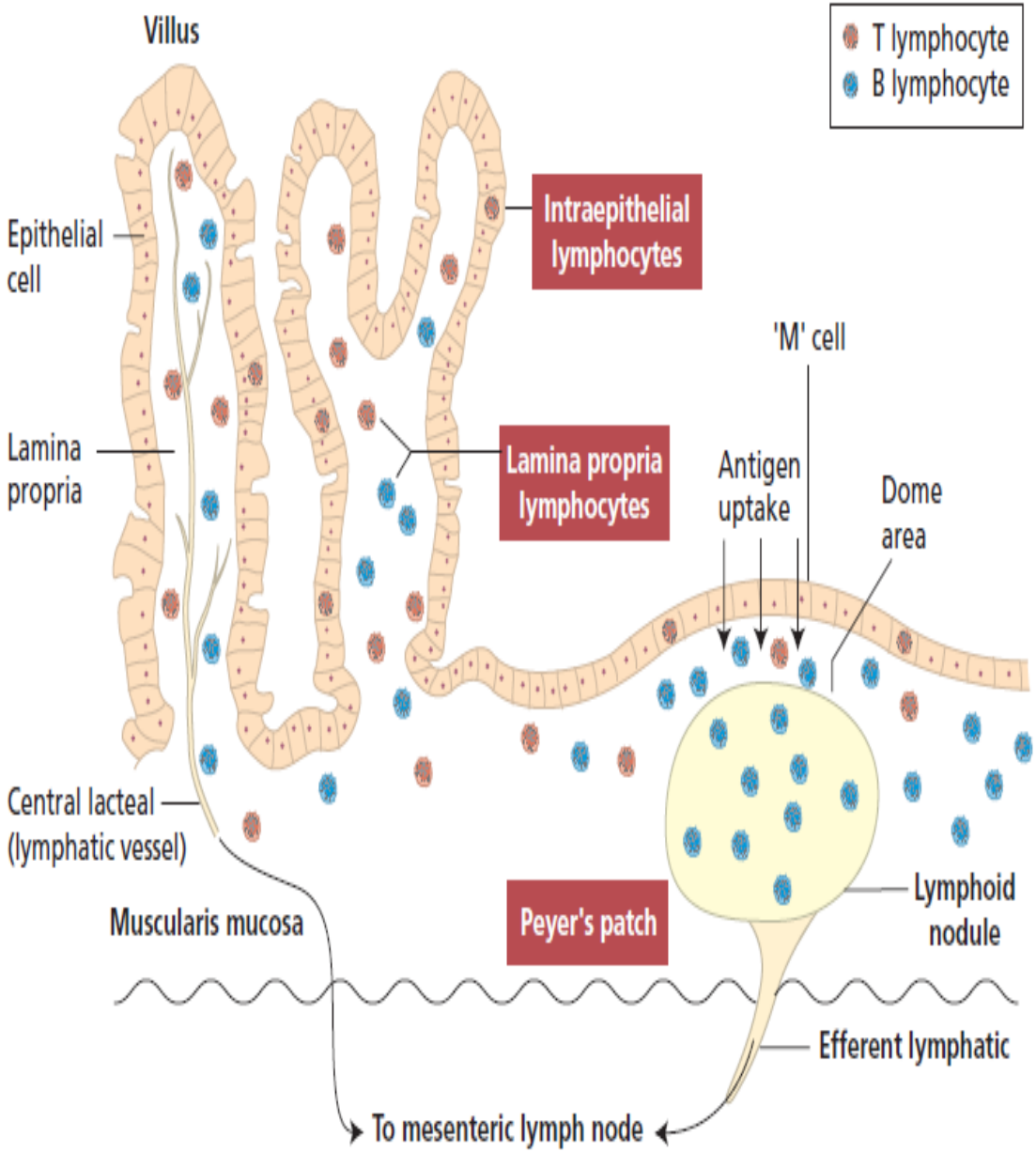


Fig. The stages involved in the transport of antigen by the M cell from the intestinal lumen into the extracellular space where it is taken up by dendritic cells and T lymphocytes (L).

Peyer's patches are covered by specialized epithelium (follicle-associated epithelium). Some of these epithelial cells have surfaces that seem folded under the scanning electron microscope . These microfold, or M, cells sample and actively transport particulate antigens from the lumen into the 'dome' area, where priming of both T and B lymphocytes occurs. Within Peyer's patches are specialized T cells that induce antigen-activated IgM bearing

B lymphocytes to switch isotype to IgA as well as immature IgA+ cells that are probably independent of T cells.


Villus
T lymphocyte
B lymphocyte
Epithelial cell
Intraepithelial lymphocytes
'M' cell
Lamina propria
Lamina propria lymphocytes
Antigen uptake
Dome area
Central lacteal (lymphatic vessel)
Peyer's patch
Lymphoid nodule
Muscularis mucosa
Efferent lymphatic
To mesenteric lymph node

Primed B lymphoblasts, committed mainly to producing IgA class antibody, migrate from Peyer's patches, via the lymphatics and mesenteric lymph nodes, to the thoracic duct and hence into the circulation . These cells return preferentially to the lamina propria, a process called 'homing'. Once back in the gut, they mature into IgA plasma cells and are responsible for local and secretory immune defences.

The number of IgA-producing cells in the lamina propria far exceeds the numbers producing IgM, IgG or IgE. *The IgA coating the epithelium is specially adapted for its function*. IgA plasma cells produce monomeric IgA, which is converted into a dimer by a smaller 'joining' peptide (J chain), also produced by the plasma cells. The polymeric immunoglobulin receptor is synthesized by epithelial cells and is essential for transport of secretory IgA into the lumen of the gut .

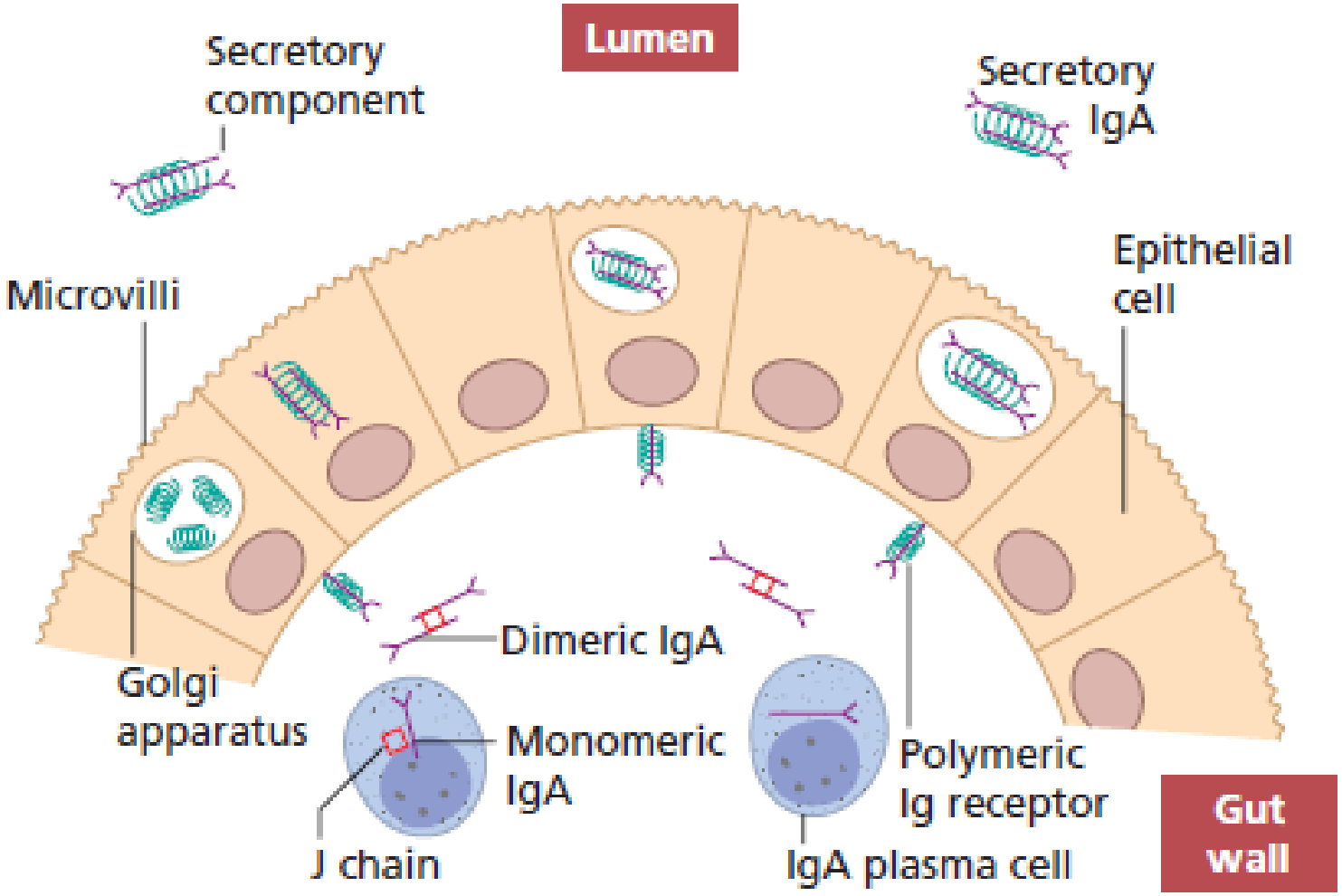


Fig. Synthesis and transport of secretory IgA through the gut epithelial cells into the gut lumen.