

IV. The Intestine as the battlefield

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Digestion

Digestion, distribution along the length of the gut, and depth of penetration within and across the wall of the gut, are all factors which influence whether a substance in food provokes an adverse reaction (Fig 1a).

With efficient digestion, antigenic materials and complex foods with toxic or pharmacological properties, are destroyed in the proximal small bowel, thus greatly limiting their potential for inducing harmful reactions. Gut secretions also have the benefit of diluting antigens and toxins (Fig 1b).

Partial digestion may reveal new antigenic epitopes, and also small molecular weight peptides

with potent local and systemic pharmacological properties (Fig 1c).

When there is failure of digestion and an individual is hypersensitive (allergic) to a food, the antigen is not only present in higher than normal concentrations in the proximal gut, but also, significant amounts of undigested food antigens are present throughout the small bowel and colon. This induces extensive and severe local hypersensitivity reactions all along the gut. One example is in celiac disease and other food sensitive enteropathies, which are much more severe clinically when there is coincident pancreatic insufficiency (Fig 1d).

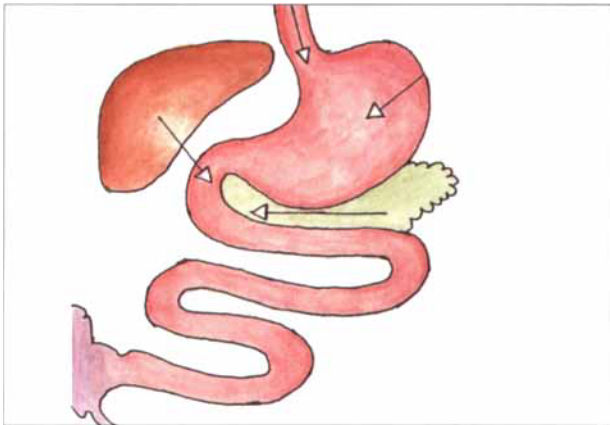


Fig 1a

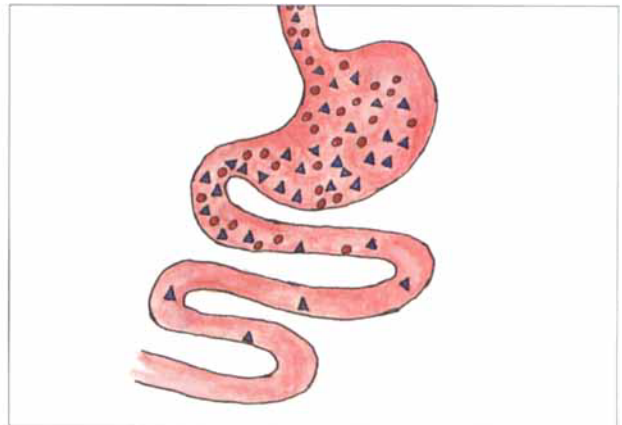


Fig 1b

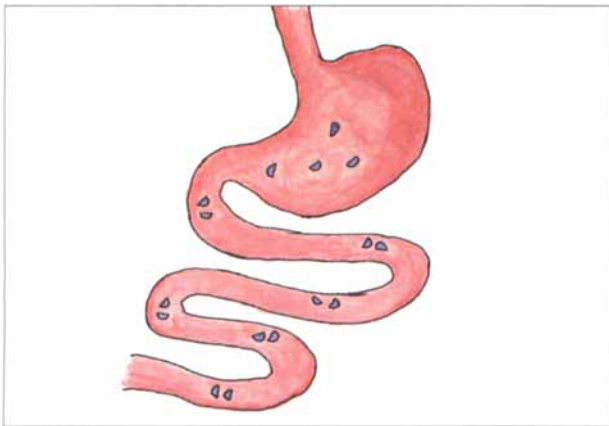


Fig 1c

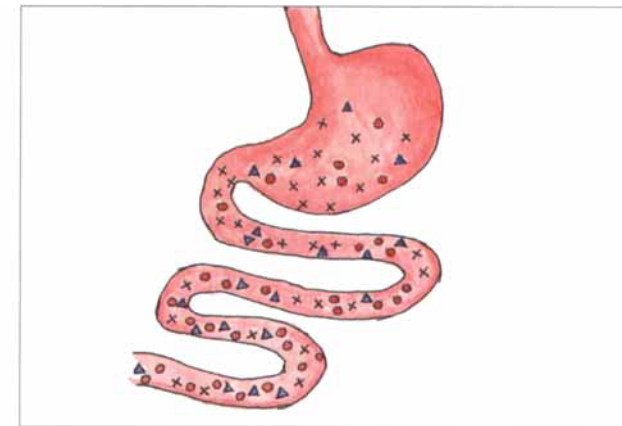


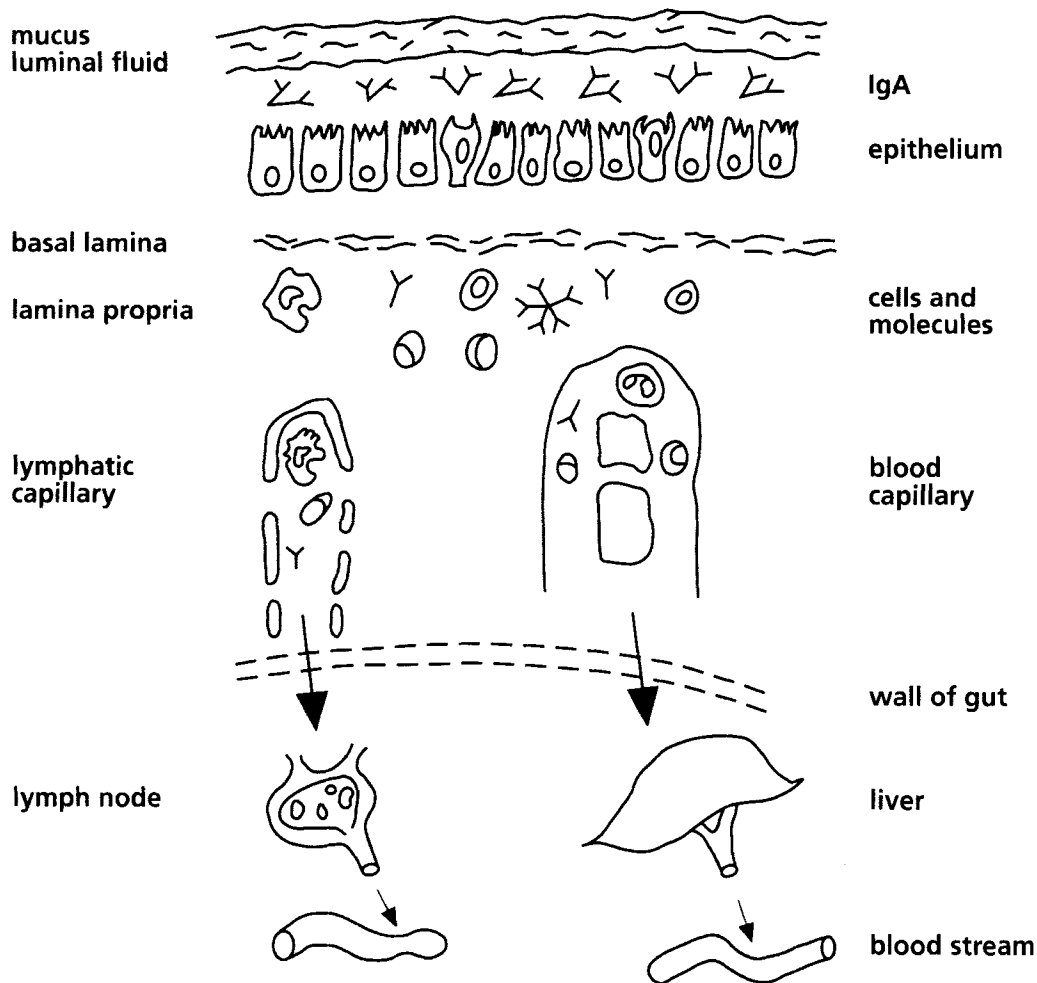
Fig 1d

Penetration of food substances into the intestinal mucosa

It seems likely that the multiple and overlapping protective mechanisms, which greatly impede access of particles and complex molecules into the body via the gut, have evolved to protect us from invasion of the tissues by gut bacteria and other micro-organisms. There are many specific and non-specific barriers to movement of the particles and large molecules, as well as specific antibodies, antigen reactive lymphocytes, and phagocytic cells

within the lumen, and in the lamina propria.

Substances which have penetrated the wall of the gut may either be phagocytosed and destroyed locally, or may leave the gut in the draining lymph or blood capillaries where they meet high concentrations of antibodies, cells and other inhibitors within the vasculature. Potentially harmful substances must traverse lymph nodes or liver before reaching the systemic circulation.



Potential functions of molecules and cells of the immune system within the gut

Immune responses may be host protective, e.g. conferring resistance to bacterial infection, neutralizing viruses or toxins; immune responses may occur but may be completely irrelevant to any protective or other function of the gut (as in most reactions between food antigens and IgA, IgG and

IgM antibodies); and from time to time the immune responses cause tissue damage, for example delayed type hypersensitivity reactions, IgG- or IgM-mediated complement fixing hypersensitivity, IgE- and mast cell associated allergic reactions.

Range of potential functions of molecular and cellular immune reactions in the gut

	Physiological	Potentially protective	Producing tissue damage
Immunoglobulins			
IgA	*	*	
IgM	*	*	*
IgG		?	*
IgE		parasites	*
Cells			
Delayed-type hypersensitivity		parasites	*
T cells		? cancer	
Other T effectors		*	?
Polymorphonuclears		*	*
Tissue macrophages (various subsets)	*	*	*
Molecules			
Immunoregulatory cytokines	*	*	
Inflammatory cytokines		*	*
Other molecular mediators e.g. prostaglandins	?	?	*

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Selected reference

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