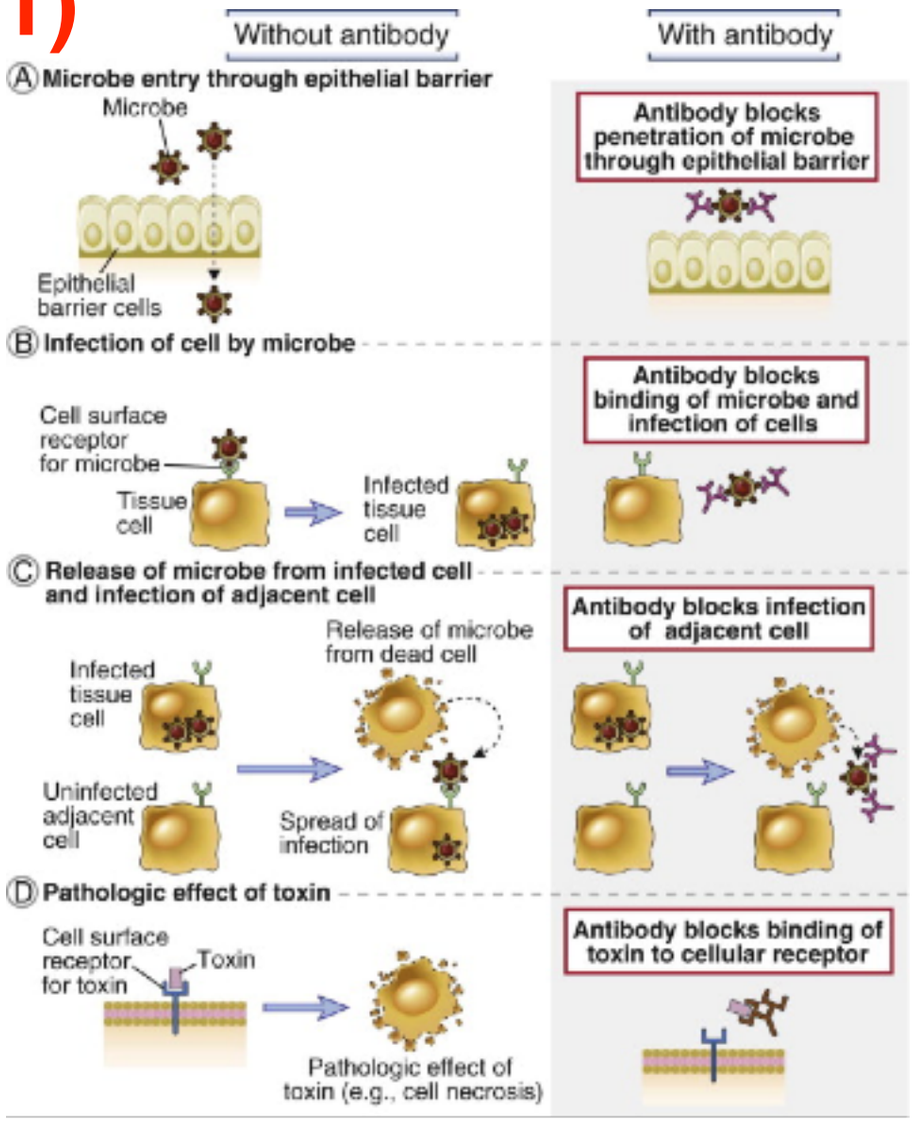
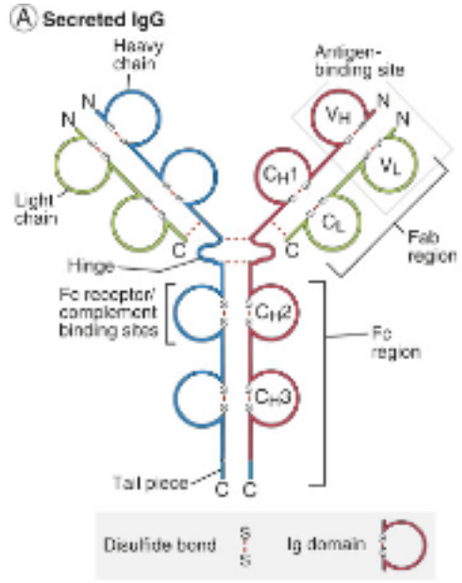
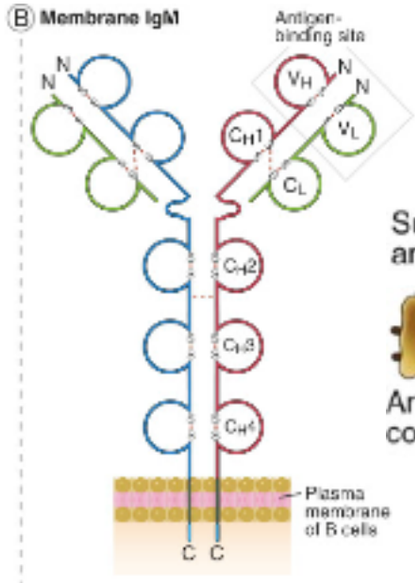
What do antibodies do?

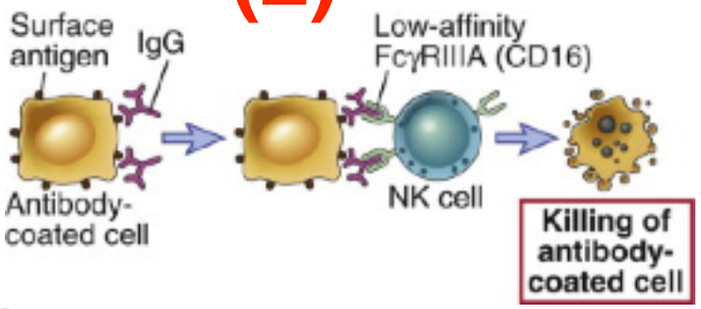
(1)



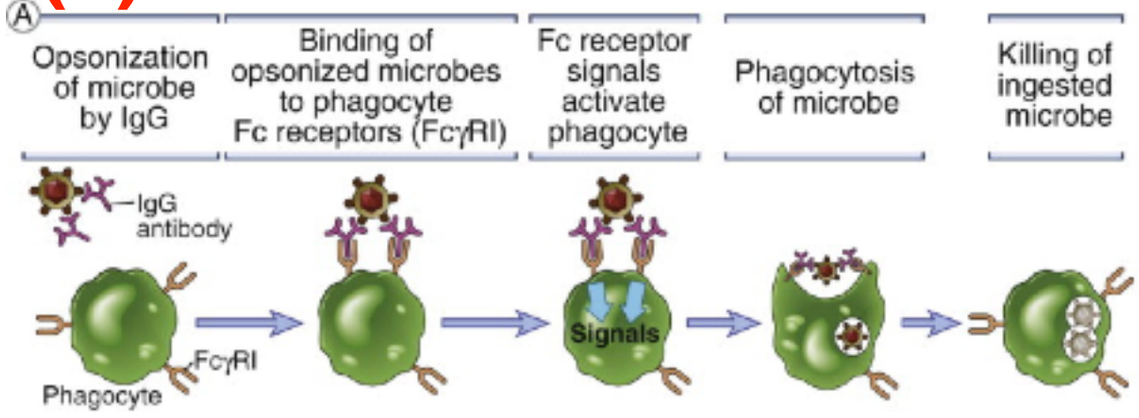




(2)



(3)



In response to specific antigen, activated B cells secrete antibodies (Abs) specific for that antigen, mediating humoral immunity. Abs can then work in several ways to enhance the effectiveness of the immune response.

(1) Ab can directly **neutralize** a toxin or pathogen by binding and blocking an important site either for toxin function or for infection of host cells. This occurs independent of the Fc region of the antibody.

(2) Ab can target a cell or pathogen for direct killing by macrophages, neutrophils or NK cells, via a process known as **antibody-dependent cytotoxicity (ADCC)**. This occurs via Fc recognition.

(3) Ab can **opsonize** a target Ag or pathogen, making phagocytosis much more efficient. In this case, the Ab-bound Ag/pathogen is efficiently engulfed by phagocytes expressing specific receptors for the constant region of Ig (these receptors are known as Fc receptors (FcR) and are specific for each Ig isotype).

(4) (not shown) Ab-bound antigen can activate the complement cascade that can then either a) promote opsonization via interaction with complement receptors expressed on phagocytes, b) promote an inflammatory response that recruits additional leukocyte effector cells, or c) directly induce the lysis of pathogens via the generation of the membrane attack complex, which creates pores in microbial cell membranes.

Why are there different isotypes?

The effector functions of Abs are regulated by the constant region, as determined by its genetic sequence, called an **isotype**. Each constant region exhibits a distinct type of effector function. Remember that binding of Ab Fc regions to FcR expressed on the surface of phagocytes and other cells occurs only when Ab has bound Ag (the exception being IgE binding to FcR of mast cells, which is why allergic IgE-mediated reactions occur so rapidly).

One important defense mechanism against the extracellular stages of most bacteria and viruses is to coat (opsonize) these microbes with antibodies and cause them to be phagocytosed by neutrophils and macrophages. This reaction is best mediated by antibody classes, such as IgG1 and IgG3 (in humans), that bind to high-affinity phagocyte Fc receptors specific for the γ heavy chain (**IgG**). Helminths, in contrast, are too large to be phagocytosed, and they are best eliminated by eosinophils. Therefore, defense against these parasites involves coating them with antibodies to which eosinophils bind. The antibody class that is able to do this is **IgE**, because eosinophils have high-affinity receptors for the Fc portion of the ε heavy chain.

Ⓑ Antibody isotype	Isotype-specific effector functions
IgG	Neutralization of microbes and toxins Opsonization of antigens for phagocytosis by macrophages and neutrophils Activation of the classical pathway of complement Antibody-dependent cellular cytotoxicity mediated by NK cells Neonatal immunity: transfer of maternal antibody across placenta and gut Feedback inhibition of B cell activation
IgM	Activation of the classical pathway of complement
IgA	Mucosal immunity: secretion of IgA into lumens of gastrointestinal and respiratory tracts, neutralization of microbes and toxins
IgE	Defense against helminths Mast cell degranulation (immediate hypersensitivity reactions)

The antibody isotype produced is also influenced by the site of immune responses. For example, **IgA** antibody is the major isotype produced in mucosal lymphoid tissues, probably because cytokines such as transforming growth factor (TGF)-β that promote switching to IgA are made in these tissues. The B cells activated in these lymphoid tissues are also induced to express chemokine receptors and adhesion molecules that favor their migration into the sites just below mucosal epithelial barriers. IgA is the principal antibody isotype that can be actively secreted through mucosal epithelia.

The diversity of pathogens is why an effective host defense requires that the immune system make different antibody isotypes in response to different types of microbes, even though all naive B lymphocytes specific for all these microbes express antigen receptors of the IgM and IgD isotypes. Thus, the nature of the **helper T cell response** to a microbe guides the subsequent antibody response, making it optimal for combating that microbe. This is how different components of the immune system are regulated coordinately and function together in defense against different types of microbes. It also explains why deficiencies in antibody production may be due to B cell or T cell defects.

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If you would like to learn more or review any particular topic, the links below will take you to a text-based review of these concepts, or to the correlating video. You may also skip ahead to the post-module assessment.