13.1C: The 5 Classes (Isotypes) of Human Antibodies

Skills to Develop

1. State which classes (isotypes) of human antibodies possess the following characteristics:
   a. are monomers
   b. is a pentamer
   c. is a dimer
   d. activates the classical complement pathway by its Fc portion
   e. binds to macrophages and neutrophils by its Fc portion
   f. binds to NK cells by its Fc portion
   g. crosses the placenta
   h. functions as a B-cell receptor
   i. the first antibody produced during an adaptive immune response
   j. binds to components of mucous by its Fc portion
   k. found mainly in body secretions
   l. binds to mast cells and basophils by its Fc portion and promotes inflammation, coughing, sneezing, vomiting, and allergic reactions
   m. binds to eosinophils by its Fc portion and promotes the removal of parasitic worms and arthropods

2. Match the antibody isotype with its description.

There are five classes or isotypes of human antibodies:
IgG (Immunoglobulin G; 4 subclasses, IgG1-4)

IgG makes up approximately 80% of the serum antibodies. IgG has a half-life of 7-23 days depending on the subclass. IgG is a monomer and has 2 epitope-binding sites (Figure 13.3.1).

![IgG molecule diagram](image)

**Figure 13.3.1:** IgG. The Fab portion of the antibody has specificity for binding an epitope of an antigen. The Fc portion directs the biological activity of the antibody.

The Fc portion of IgG can activate the classical complement pathway (Figure 13.3.2). The Fc portion of IgG can bind to macrophage and neutrophils for enhanced phagocytosis (opsonization) (Figure 13.3.3).

![Classical Complement Pathway diagram](image)

**Figure 13.3.2:** Activation of C1 during the Classical Complement Pathway. The Fab of 2 molecules of IgG or 1 molecule of IgM bind to epitopes on an antigen. C1, consisting of C1q, C1r, and C1s then binds to the Fc portion of the antibodies. The binding of C1q to the antibody molecules activates the C1r portion of C1 which, in turn, activates C1s.
This activation gives C1s enzymatic activity to cleave complement protein C4 into C4a and C4b and complement protein C2 into C2a and C2b.

The Fc portion of IgG can bind to NK cells for antibody-dependent cytotoxicity or ADCC (see Fig. 4). The Fc portion of IgG enables it to cross the placenta. (IgG is the only class of antibody that can cross the placenta and enter the fetal circulation.) Feedback inhibition of B-lymphocyte activation. High levels of IgG feedback to B-lymphocytes to prevent their activation in order to turn off antibody production.

**Figure 13.3.3:** Opsonization (Enhanced Attachment). The Fab portion of IgG binds to epitopes of an antigen. The Fc portion can now attach the antigen to Fc receptors on phagocytes for enhanced attachment. This is especially important against encapsulated microbes. C3b and C4b from the complement pathways can also attach antigens to phagocytes.

For More Information: Classical complement pathway from Unit 5

For More Information: Opsonization from Unit 6

For More Information: Antibody-dependent cellular cytotoxicity (ADCC) from Unit 6

**IgM (Immunoglobulin M)**

IgM makes up approximately 13% of the serum antibodies and is the first antibody produced during an immune response. IgM is found mainly in the bloodstream rather than in the intracellular spaces of tissues where it can control infections in the blood. IgM has a half-life of about 5 days. IgM is a pentamer and has 10 epitope-binding sites (Figure 13.3.5).
IgM is a pentamer and, therefore, has 10 Fab sites.

The Fc portions of IgM are able to activate the classical complement pathway. IgM is the most efficient class of antibody for activating the classical complement pathway. Monomeric forms of IgM are found on the surface of B-lymphocytes as B-cell receptors.

**IgA (Immunoglobulin A; 2 subclasses, IgA1-2)**

IgA makes up approximately 6% of the serum antibodies where it has a half-life of approximately 6 days. IgA is found mainly in body secretions (saliva, mucous, tears, colostrum and milk) as secretory IgA (sIgA) where it protects internal body surfaces exposed to the environment by blocking the attachment of bacteria and viruses to mucous membranes. While only 6% of the antibodies in the serum are IgA, secretory IgA is the most immunoglobulin produced. IgA is made primarily in the mucosal-associated lymphoid tissues (MALT). IgA appears as a dimer of 2 "Y"-shaped molecules and has 4 epitope-binding sites and a secretory component to protect it from digestive enzymes in the secretions (Figure 13.3.6).
The Fc portion of secretory IgA binds to components of mucous and contributes to the ability of mucous to trap microbes. The Fc portion of secretory IgA can bind to macrophages and neutrophils for enhanced attachment (opsonization). IgA can activate the lectin complement pathway and the alternative complement pathway.

**IgD: (Immunoglobulin D)**

IgD makes up approximately 0.2% of the serum antibodies. IgD is a monomer and has 2 epitope-binding sites and is found on the surface of B-lymphocytes (along with monomeric IgM) as a B-cell receptor where it may control of B-lymphocyte activation and suppression. IgD may play a role in eliminating B-lymphocytes generating self-reactive autoantibodies.

**IgE (Immunoglobulin E)**

IgE makes up about 0.002% of the serum antibodies with a half-life of 2 days. Most IgE is tightly bound to basophils and mast cells via its Fc region. IgE is a monomer and has 2 epitope-binding sites. IgE is made in response to parasitic worms (helminths) and arthropods. It is also often made in response to allergens (allergens are antigens causing allergic reactions). IgE may protect external mucosal surfaces by promoting inflammation, enabling IgG, complement proteins, and leukocytes to enter the tissues, as well as by triggering coughing, sneezing, and vomiting for mechanical removal of microbes and toxins.

The Fc portion of IgE can bind to mast cells and basophils where it mediates many allergic reactions. Cross linking of cell-bound IgE by antigen triggers the release of vasodilators for an inflammatory response (Fig 7). The Fc portion of IgE made against parasitic worms and arthropods can bind to eosinophils enabling opsonization (Fig. 8). This is a major defense against parasitic worms and arthropods.

For More Information: IgE-mediated hypersensitivity (Type-I) from Unit 6

Each day an average adult produces approximately three grams of antibodies, about two-thirds of this IgA.

**Summary**

1. IgG makes up approximately 80% of the serum antibodies, is a monomer with 2 Fab sites. The Fc portion can activate the classical complement pathway, bind to macrophages and neutrophils to enable opsonization, bind to NK cells to promote ADCC, and can cross the placenta.
2. IgM makes up approximately 13% of the serum antibodies, is the first antibody produced during an immune response, is found mainly in the blood, and is a pentamer with 10 Fab sites. The Fc portion can activate the classical complement pathway. Monomeric forms of IgM are found on the surface of B-lymphocytes as B-cell receptors.
3. IgA makes up approximately 6% of the serum antibodies, is a dimer with 4 epitope-binding sites and is found mainly in body secretions as secretory IgA (sIgA) where it protects internal body surfaces exposed to the environment by blocking the attachment of bacteria and viruses to mucous membranes.
4. The Fc portion of secretory IgA binds to components of mucous and contributes to the ability of mucous to trap microbes, and can bind to macrophages and neutrophils to enable opsonization, and can activate the lectin complement pathway and the alternative complement pathway.
5. IgD makes up approximately 0.2% of the serum antibodies, is a monomer with 2 Fab sites, is found on the surface of B-lymphocytes as a B-cell receptor, and may play a role in eliminating B-lymphocytes generating self-reactive autoantibodies.

6. IgE makes up about 0.002% of the serum antibodies, is a monomer with 2 Fab sites, and is made in response to parasitic worms (helminths) and arthropods. It is also often made in response to allergens. The Fc portion of IgE can bind to mast cells and basophils (see Fig. 8) where it mediates many allergic reactions, and the Fc portion of IgE made against parasitic worms can bind to eosinophils enabling opsonization. IgE may also protect external mucosal surfaces by promoting inflammation.

Questions

Study the material in this section and then write out the answers to these questions. Do not just click on the answers and write them out. This will not test your understanding of this tutorial.

1. Match the class (isotype) of human antibody with its description.

   _____ are monomers (ans)
   _____ is a pentamer (ans)
   _____ is a dimer (ans)
   _____ activates the classical complement pathway by its Fc portion (ans)
   _____ binds to macrophages and neutrophils by its Fc portion (ans)
   _____ binds to NK cells by its Fc portion (ans)
   _____ crosses the placenta (ans)
   _____ functions as a B-cell receptor (ans)
   _____ the first antibody produced during an adaptive immune response (ans)
   _____ binds to components of mucous by its Fc portion (ans)
   _____ found mainly in body secretions (ans)
   _____ binds to mast cells and basophils by its Fc portion and promotes inflammation, coughing, sneezing, vomiting, and allergic reactions (ans)
   _____ binds to eosinophils by its Fc portion and promotes the removal of parasitic worms and arthropods (ans)

   a. IgG
   b. secretory IgA
   c. IgE
   d. IgD
e. IgM

2. Multiple Choice (ans)

Contributors

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