M.Sc ZOOLOGY
SEMESTER 3
PAPER CC 10
HUMORAL IMMUNITY: 3

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Antibodies

Antibodies or immunoglobulins are the weapons of the humoral immune response and this response is defined by them.

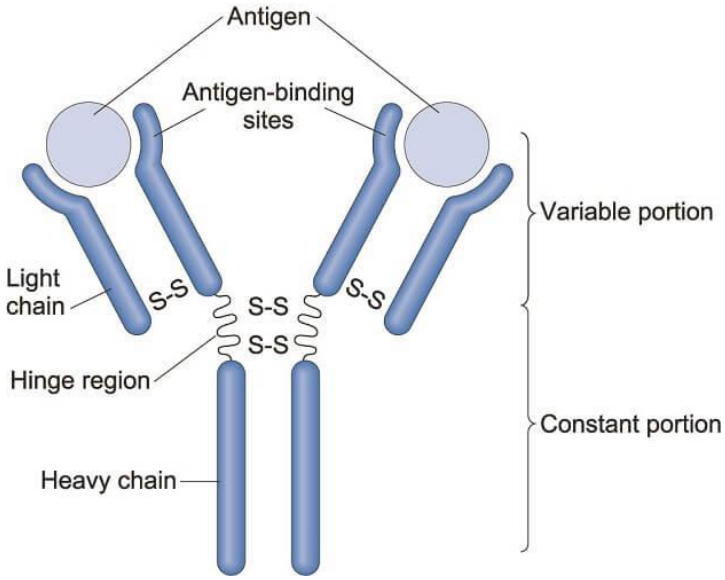
They work by attaching to a pathogen and breaking it down, stopping the microorganism from releasing toxins, or clumping the pathogens together. Clumping (aggregation) makes it easier for them to be destroyed by way of cell-mediated immunity (phagocytosis).

We have five types of immunoglobulin:

- IgM: encourages white blood cell phagocytosis and enables blood group determination
- IgA: clumps pathogens together, especially on mucous membranes
- IgD: helps initiate antibody production and is expressed very early on immature B cell membranes
- IgG: long-term protection
- IgE: not much is known about IgE immunoglobulins; they may be specific to parasites and hypersensitive allergic reactions

Each type is associated with one of the above methods of pathogen destruction. IgM antibodies are part of the initial humoral response to a first infection. IgG is the most common antibody but is not highly antigen-specific.

Antibodies have a known structure and are Y-like in form. The two arms of the Y feature antigen-binding sites. These sites differ in construction according to antibody type; part of this area is called the hyper variable region (HV) that binds to the epitope of a specific antigen.



Primary and Secondary Phases

In the primary phase of the humoral immune response that takes several days to take effect, the following occurs:

- First contact with a foreign pathogen by APCs
- Digestion of antigen by APCs and conversion of antigen fragments into MHC II surface proteins
- Recognition of MHC II surface protein by T helper cell
- Production of cytokines by T helper cell
- Naïve B cells activated by T helper cell cytokines
- Naïve B cells differentiate into plasma or memory B cells
- Plasma cells produce and secrete IgM antibodies; where necessary, IgG or IgA antibodies are secreted if the pathogen population remains active after peak IgM secretion.
- This process requires 7 to 10 days to produce peak antibody levels.

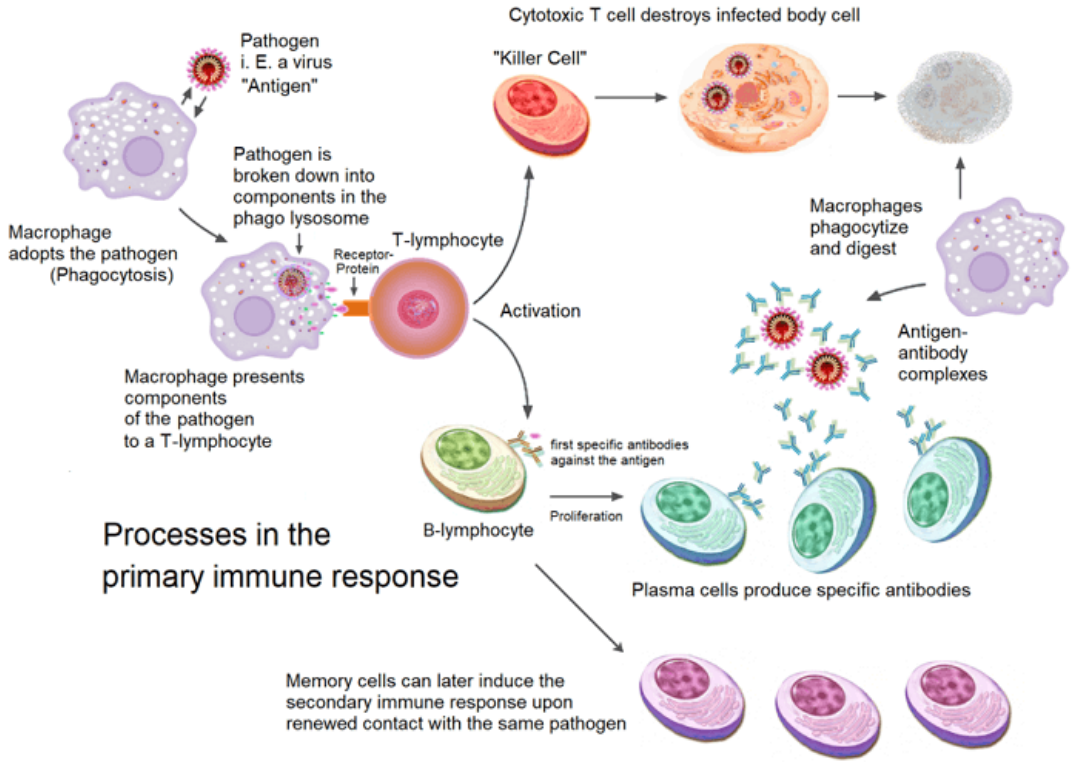
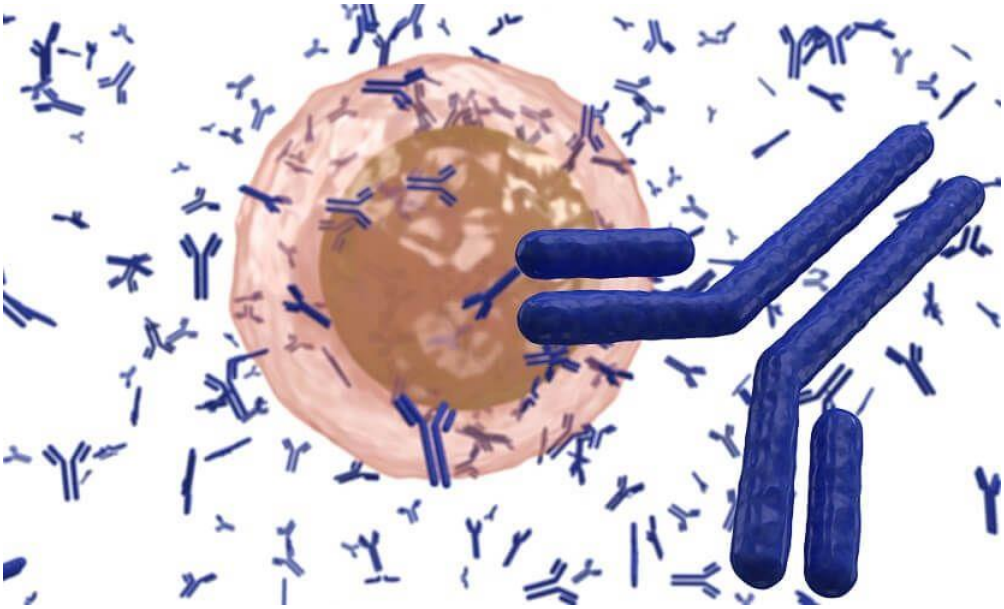


Fig: The primary humoral response

In the secondary humoral immune response, the body has previously been in contact with a specific pathogen and memory B cells produced during the initial attack are still present. Memory B cells can live for weeks, months, or even years.

The steps of the secondary phase only involve thymus-dependent antibodies (memory B cells):

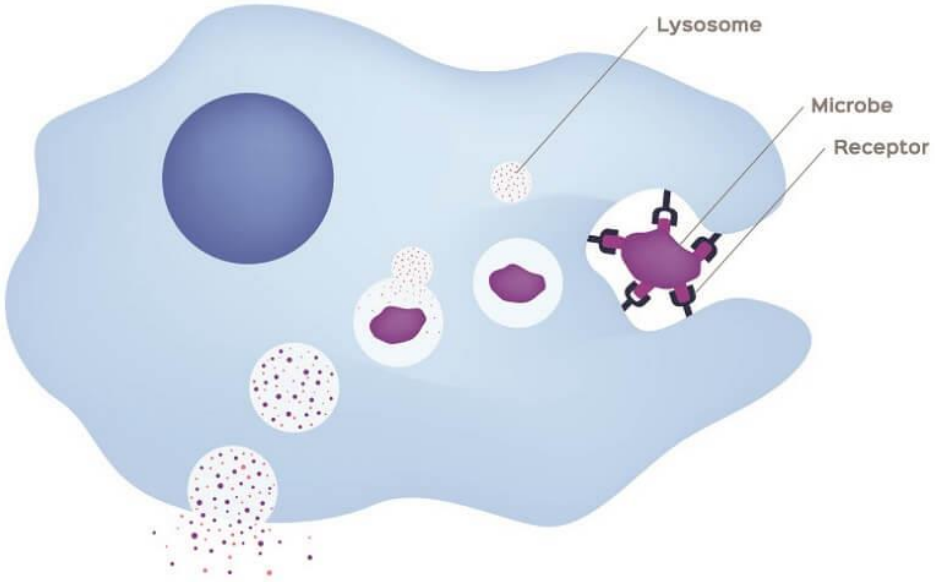
- Memory B cells recognize the antigens of the microorganism
- Memory B cells divide to produce highly-specific plasma cells
- Plasma cells produce primarily IgG but also IgM, IgA, and IgE immunoglobulins
- Antibodies are produced in quantities of over 1000 times the primary response
- Peak antibody levels are achieved within 3 to 5 days.



The secondary response produces many more antigen-specific antibodies

Humoral vs. Cell-Mediated Immunity

The difference between humoral and cell-mediated immunity is not always clearly defined. This is because the function of the T helper cell straddles the boundaries.



Phagocytosis steps within a phagocytic cell

The most obvious difference is antibody production. Cell-mediated immune responses do not produce antibodies. Instead, they use APC-activated T helper cells to secrete cytokines and these attract white blood cells. White blood cells (the cell-mediated part of this response) digest foreign particles via phagocytosis. Phagocytes are non-specific – they attack and digest any foreign particle they come across.

Of equal importance are cytotoxic T cells. These are also referred to as killer T cells and induce cell death in damaged or infected cells.

There are many similarities between humoral versus cell-mediated immunity, too. Both are part of both the innate and adaptive immune systems; both require antigen-presenting cells, lymphocytes, and cytokines to function.

Humoral Immunity Examples

Evidence of smallpox infection has been found in the 3,000 year-old mummy of Pharaoh Ramses V; the virus nearly wiped out indigenous populations in the Americas and Australia. It was finally eradicated across the globe at the

end of 1979. To date, only two viruses have been completely eradicated through vaccination.

It was Edward Jenner who first published his observations regarding the low infection rate of milkmaids during a time when smallpox was rife. Doctors were already using variolation – the deliberate infecting of healthy individuals with pus from dead or dying smallpox victims – to try to inoculate people. They did not understand the secondary phase of the humoral immune response but understood how a weak level infection could give rise to a stronger level of future protection.

When inoculated with smallpox pus, milkmaids rarely showed a response. Jenner removed pus from the sores caused by cowpox – a different but related infection – from a milkmaid called Sarah Nelmes and injected this pus into the arm of the young son of his gardener. The boy never contracted smallpox, even when in contact with the disease.

Moving on to the modern humoral immunity example, we can look at the recent race toward a vaccine against SARS-CoV-2. We do not know enough about the virus to justify injecting weakened or dead forms into the body. The Oxford-AstraZeneca vaccine uses a DNA template based upon a weakened chimpanzee cold virus known to generate a strong immune response. This virus was genetically engineered to not reproduce itself.

A COVID-19 surface membrane protein called the spike protein was then attached to the chimpanzee virus. This made the cold virus a viral vector. When injected, the vector virus enters the cell and injects its engineered DNA into the cell nucleus, as do all viruses. However, this virus will not replicate itself.

However, the gene for the production of the spike protein can.
Through protein synthesis, the foreign but harmless protein is manufactured inside the cell and released. This initiates the primary humoral response – APCs come into contact with the unknown protein and start the process that leads to antibody production.

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