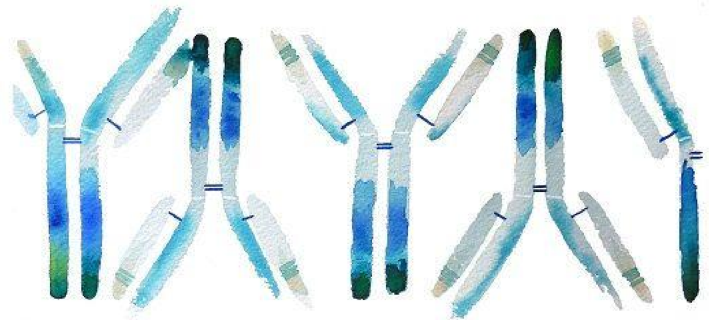


بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

Medical Immunology



Anas Abu-Humaidan
M.D. Ph.D.

Lecture 7

Antibodies and antigens

In this lecture we will discuss:

- Antibodies, their structure, types and function.

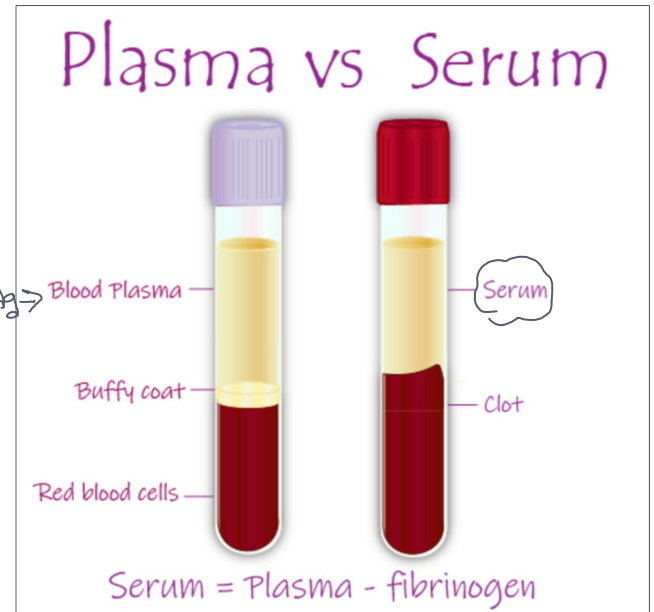
Very Imp molecules

اللهم صلّ وسلّم على نبينا محمد

Antibodies/ overview

لا حول ولا قوة الا بالله العظيم

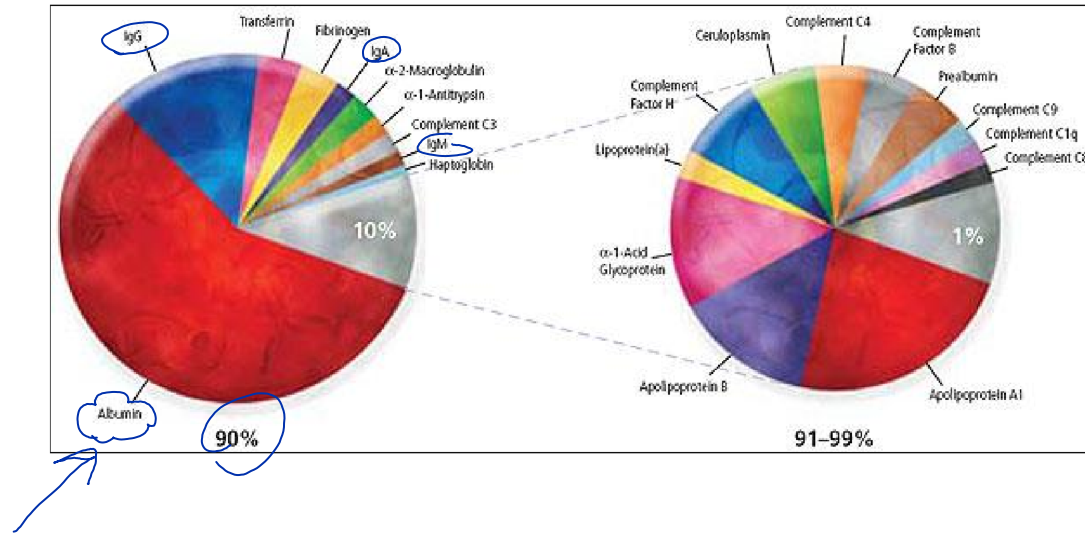
- The study of ^{all serum proteins} antibodies and their reactions with antigens is therefore classically called **serology**.
- **Serum** lacks coagulation factors but otherwise contains all the proteins found in plasma. Any serum sample that contains detectable antibody molecules that bind to a particular antigen is commonly called an **antiserum**.
- A healthy 70-kg adult human produces about 2 to 3 g of antibodies every day.



Antibodies/ overview

... فقد رُحِرَ عن سائر أَدْوِلِ الجَنَّةِ
فَقَدْ مَارَ ...
(آل عمران ١٨٥)

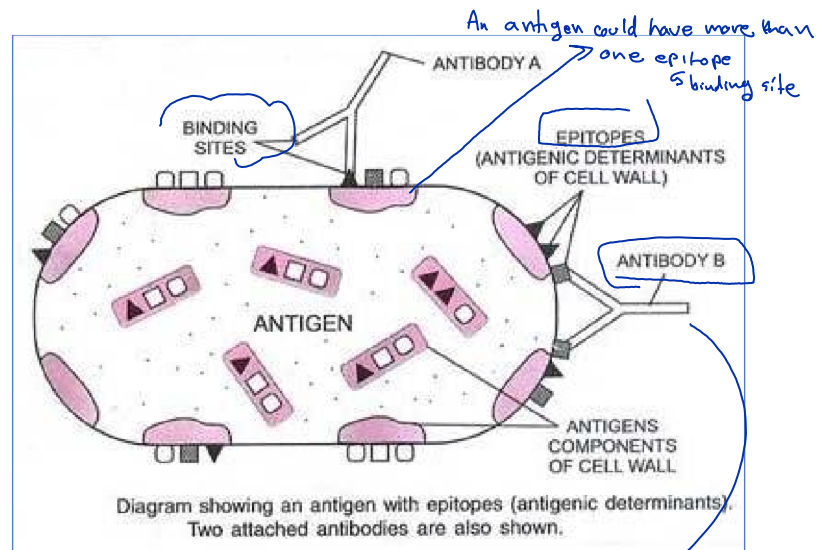
- Plasma proteomics holds great promise for the future of biomarker discovery, as well as *in vitro* diagnostics. Although plasma is readily accessible for analysis, the study of the plasma proteome is fundamentally limited by its vast dynamic range (10 orders of magnitude).



Antibodies and antigens

- **Antibodies** are circulating proteins that are produced in vertebrates in response to exposure to foreign structures known as **antigens**
- The **strength of the binding** between a single site of an **antibody** and an **epitope** of an antigen is called the **affinity** of the antibody.

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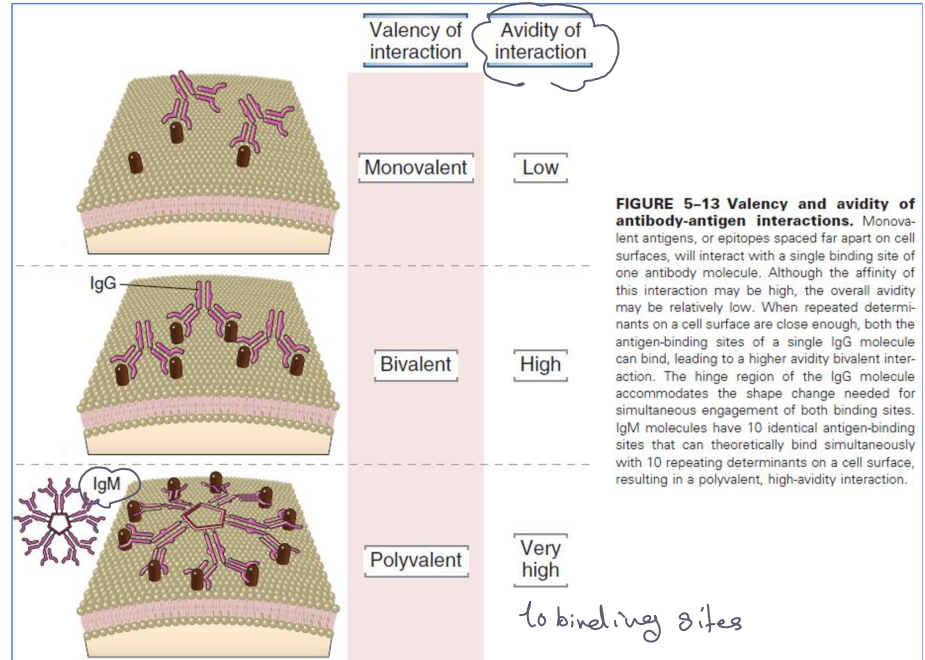


Antibodies and antigens

الاعتماد على بنية الجذر

- Because the **hinge** region of antibodies gives them **flexibility**, a **single antibody** may attach to a single multivalent antigen **by more than one binding site**. the **strength of attachment of the antibody to the antigen** must take into account binding of **all the sites to all the available epitopes**. This overall strength of attachment is called the **avidity**.

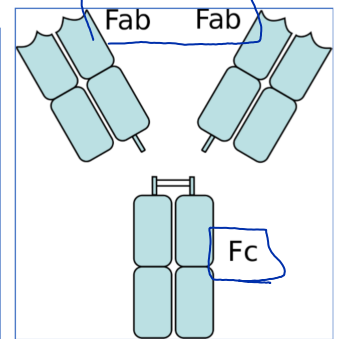
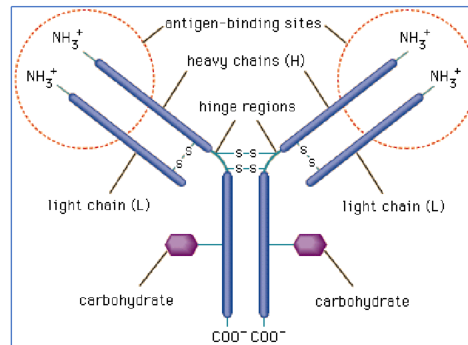
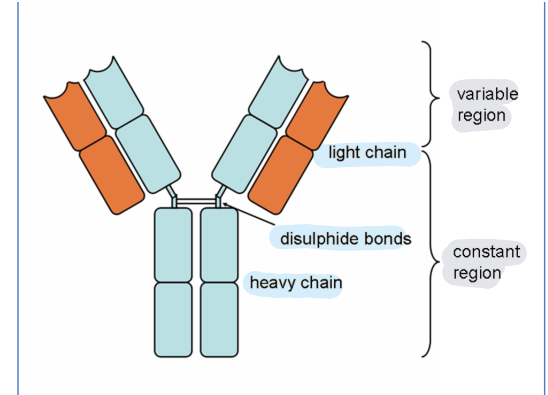
الاعتماد على بنية الجذر



Antibodies/ structure

- Antibodies (immunoglobulins) are made of 2 heavy chains and 2 light chains, those chains combined give us an antibody binding region (**Fab**) and the fragment crystallizable region (**Fc region**) which is the tail region of an antibody that interacts with cell surface receptors called **Fc receptors** and some proteins of the complement system.

↳ Fragment of Ag binding



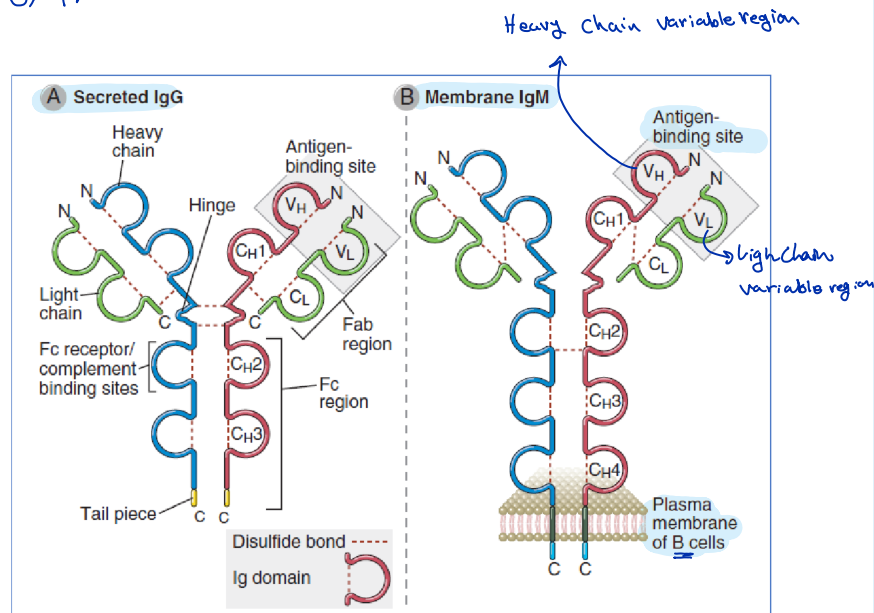
- Immunoglobulins are divided into different classes (isotypes).

like
macrophages

Antibodies/ structure

الاعمال هي وستم على بنينا محمد

- Antibodies can exist in two forms: **membrane-bound** antibodies on the surface of B lymphocytes function as receptors for antigen, and **secreted antibodies** that reside in the circulation, tissues, and mucosal sites
- Both heavy chains and light chains consist of amino terminal **variable (V)** regions that participate in antigen recognition and carboxyl-terminal **constant (C)** regions; the C regions of the heavy chains mediate effector functions.



Remember Igs are proteins so these are
poly peptide chains (2 light + 2 Heavy)

لله إنا لله

• Question: How many polypeptide chains make up a typical antibody molecule?

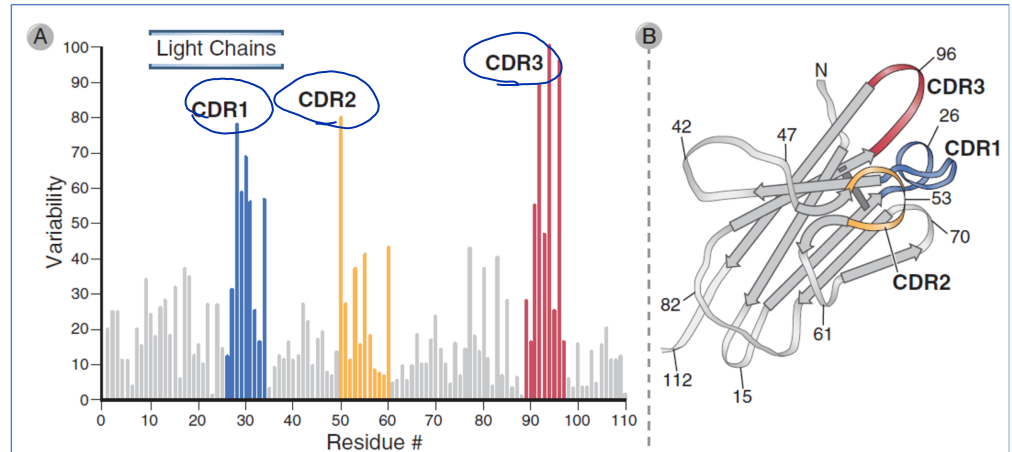
- a) 1
- b) 2
- c) 3
- d) 4

Antibodies/ structure

so 12 in each Ab

لا حول ولا قوة الا بالله العظيم

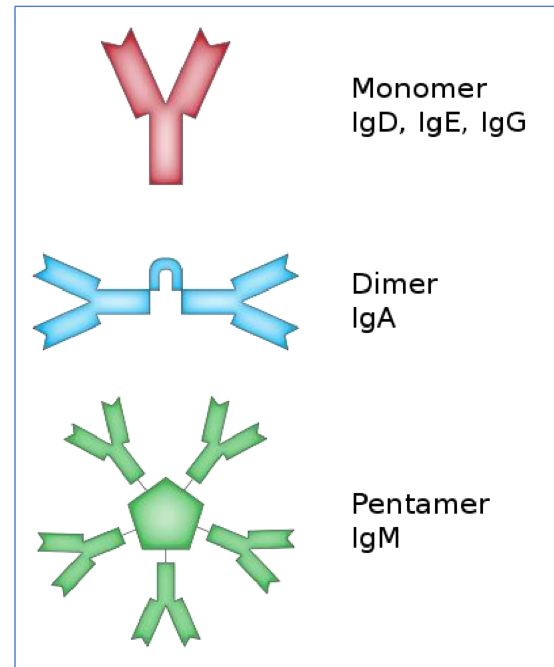
- Most of the sequence differences and variability among different antibodies are confined to **three short stretches in the V region of the heavy chain** and to **three stretches in the V region of the light chain**. These diverse stretches are known as hypervariable segments, Because these sequences form a surface that is complementary to the three-dimensional structure of the bound antigen, the **hypervariable regions** are also called complementarity-determining regions (**CDRs**).



Antibodies

لا إله إلا الله

- There are **five immunoglobulin classes (isotypes)** of antibody molecules found in serum: **IgG, IgM, IgA, IgE and IgD**. They are distinguished by the **type of heavy chain** they contain
- Antibodies of different classes **differ** in their **location** around the body, appear at **different stages of an adaptive immune response**.
di sf Functions
- The **heavy chain C** regions of all antibody molecules of one isotype or subtype have essentially the same amino acid sequence. This sequence is different in antibodies of other isotypes or subtypes.



Antibodies/ structure

Isotope of Antibody	Subtypes (H Chain)	Serum Concentration (mg/mL)	Serum Half-life (days)	Secreted Form	Functions
IgA	IgA1,2 (α 1 or α 2) <i>α</i>	3.5	6	IgA (dimer) Monomer, dimer, trimer <i>the most common form</i>	Mucosal immunity <i>in mucosal tracts</i>
IgD	None (δ)	Trace	3	None	Naive B cell antigen receptor
IgE	None (ϵ)	0.05	2	IgE Monomer	Defense against helminthic parasites, immediate hypersensitivity
IgG	IgG1-4 (γ 1, γ 2, γ 3, or γ 4) <i>Gamma 4 types</i>	13.5	23	IgG1 Monomer	Opsonization, complement activation, antibody-dependent cell-mediated cytotoxicity, neonatal immunity, feedback inhibition of B cells
IgM	None (μ) <i>ميو</i>	1.5	5	IgM Pentamer	Naive B cell antigen receptor, complement activation

لا حول ولا قوة الا بالله العظيم

لله الحمد لله

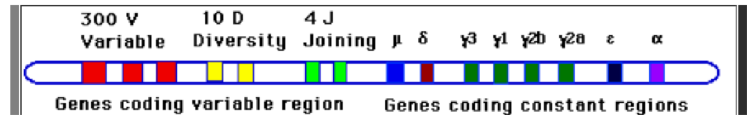
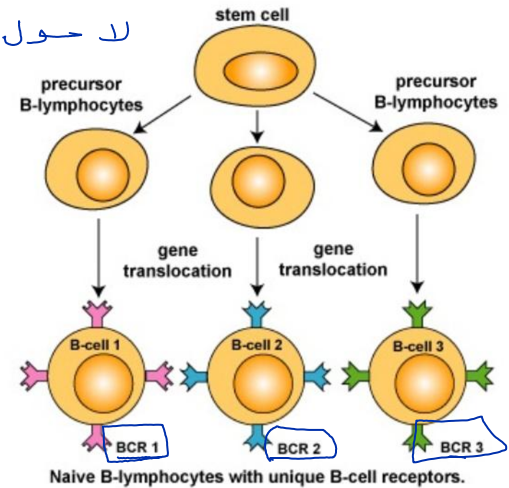
• Question: Which is the most abundant Ig class in serum?

- a) IgG
- b) IgA
- c) IgM
- d) IgE

B CELLS AND ANTIBODY RESPONSES

لا حول ولا قوة الا بالله العظيم

- B lymphocytes are the cells responsible for antibody responses.
- During its development, each B-lymphocyte becomes genetically programmed through a series of **gene-splicing reactions** to produce an antibody molecule with a **unique specificity**.
- It is estimated that the human body has the ability to recognize 10^7 or more different epitopes, due to the wide range of possible combinations during gene splicing.



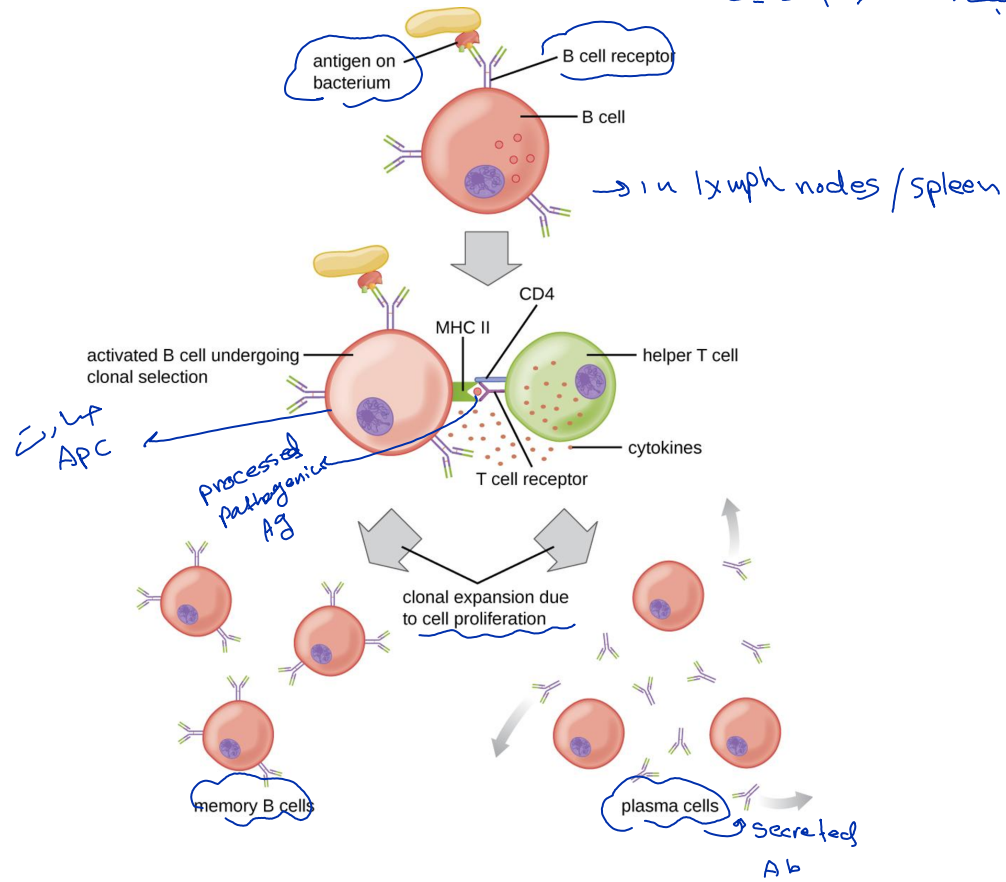
B Cell Activation

لله إله إن الله

- Resting B cells become activated by antigen **via binding to the BCR and internalization**.
- Once internalized inside the B cell, the protein antigen is processed and **presented with MHC II**. The presented antigen is then recognized by helper T cells specific to the same antigen.
- Once activated by linked recognition, **T-cells produce and secrete cytokines that activate the B cell and cause proliferation** into clonal daughter cells.
- After several rounds of proliferation, additional cytokines provided by the T-cells stimulate the differentiation of activated B cell clones into **memory B cells**, which will quickly respond to subsequent exposures to the same antigen, and **plasma cells** that lose their membrane BCRs and initially secrete pentameric IgM.

حسب الله ونعم الوكيل

B Cell Activation



Antibodies/ Antibody Production

في رسمه تستعمل المصروع بعد سلايين

كله مصروع

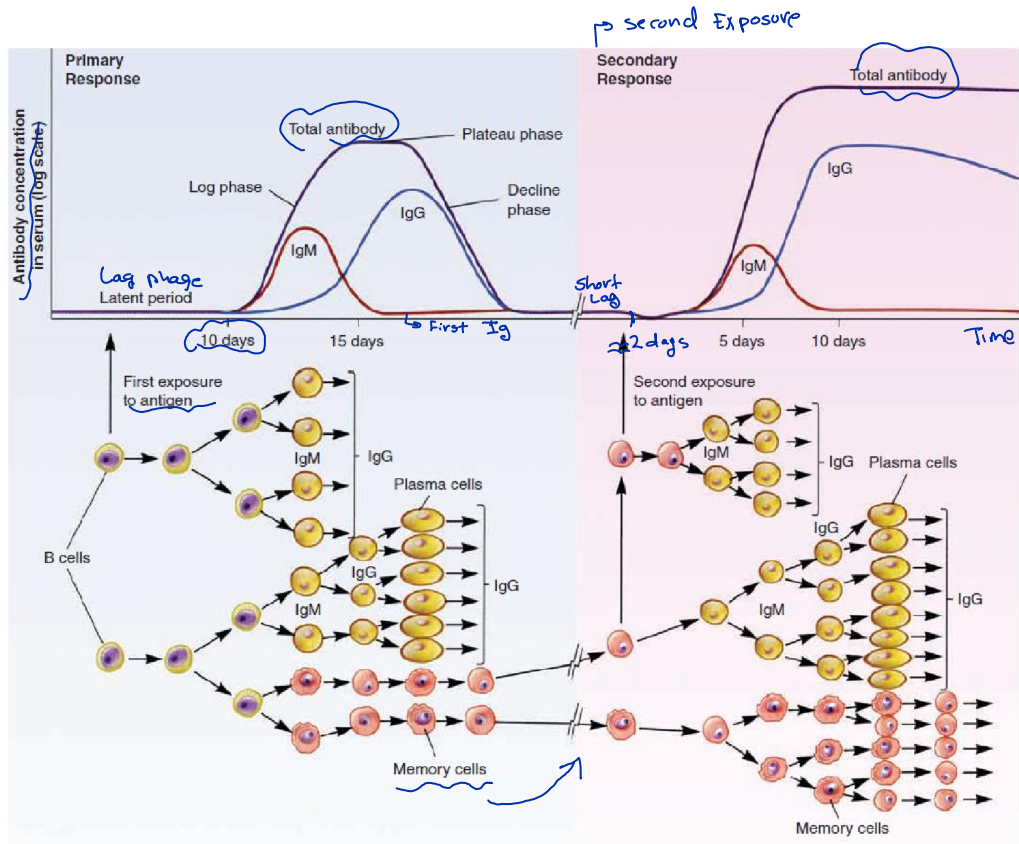
- Initial contact with a new antigen evokes the **primary response**, which is characterized by a lag phase of approximately 1 week between the challenge and the detection of circulating antibodies.
- Once antibody is detected in serum, the levels rise exponentially to attain a maximal steady state in approximately 3 weeks, then decline gradually with time.
- The **first antibodies** synthesized in the primary immune response are **IgM** and, then **IgG** antibodies arise and eventually predominate.

حسبنا الله ونعم الوكيل

Antibodies/ Antibody Production

السلام عليكم و عليكم بيوتنا خيرا

- كل ما ذكره
- After a subsequent exposure or booster injection of the same antigen, a different sequence called the **secondary response** ensues.
 - In the secondary response; العزوقاة
 - the **lag time** between the immunization and the appearance of antibody is **shortened**,
 - the rate of exponential increase to the maximum steady-state level is **more rapid**,
 - and the steady-state level itself is higher, representing a **larger amount of antibody**.
 - Another key factor of the secondary response is that the antibodies formed are **predominantly of the IgG class**.



سبحان الله وبحمده
سبحان الله العظيم

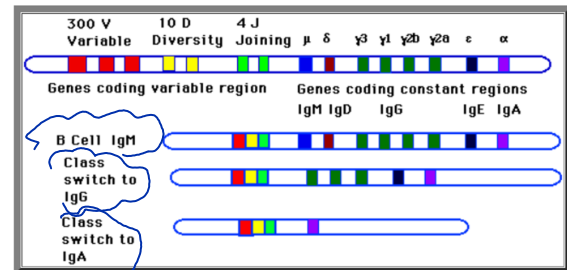
Antibodies/ Class switching

حسبنا الله ونعم الوكيل

- After initial secretion of IgM, cytokines secreted by T- cells stimulate the plasma cells to **switch from IgM production to production of IgG, IgA, or IgE.**
- This process, called **class switching** or isotype switching, allows plasma cells cloned from the same activated B cell to **produce a variety of antibody classes** with the same **antigen specificity.**
- Class switching is accomplished by **genetic rearrangement** of gene segments encoding the constant region, which determines an antibody's class. The **variable region is not changed**, so the new class of antibody retains the original antigen specificity.

Class switch

- DNA rearrangement changing the heavy chain constant gene in memory cells.



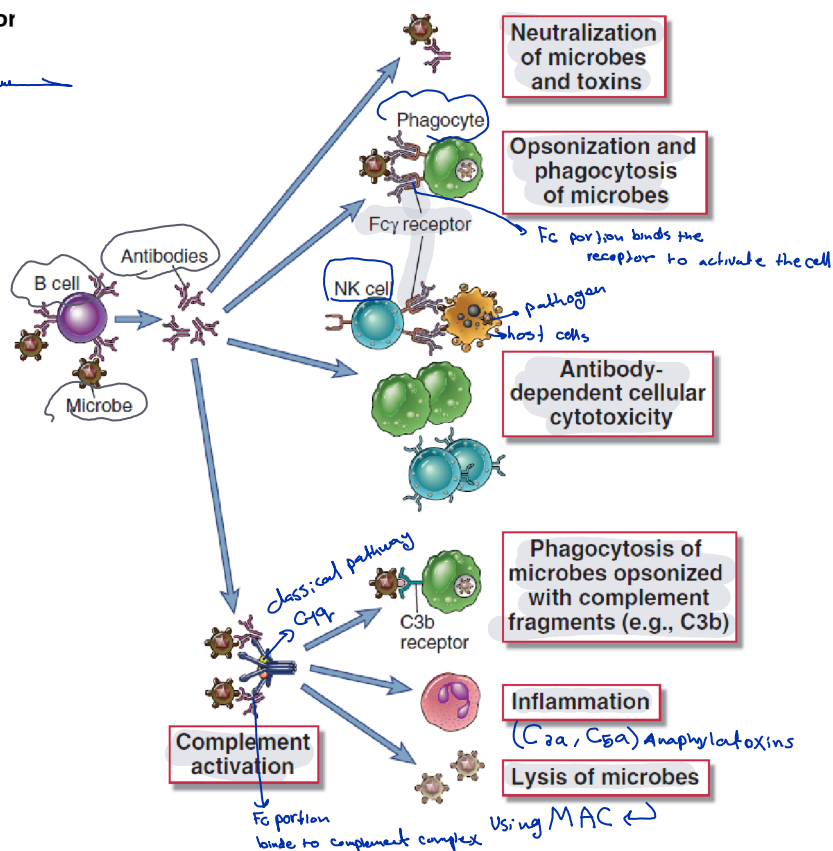
Antibodies and antigens

سبحان الله وبحمده
سبحان الله العظيم

- The **ability** of antibodies in any individual to specifically **bind a large number of different antigens** is a reflection of antibody **diversity**, and the total collection of antibodies with different specificities represents the **antibody repertoire**. The genetic mechanisms that generate such a large antibody repertoire **occur exclusively in lymphocytes**. This diversity is generated by **random recombination of a limited set of inherited germline DNA sequences** to form **functional genes that encode the V regions of heavy and light chains** as well as by the addition of nucleotide sequences during the recombination process.
- **Somatic mutation in antigen-stimulated B lymphocytes** ^{→ by making changes in the CDRs} that generates **new V domain structures**, some of which **bind the antigen with greater affinity** than did the original V domains. Those B cells producing higher affinity antibodies preferentially bind to the antigen and, as a result of selection, become the dominant B cells with each subsequent exposure to the antigen. This process is called **affinity maturation**.

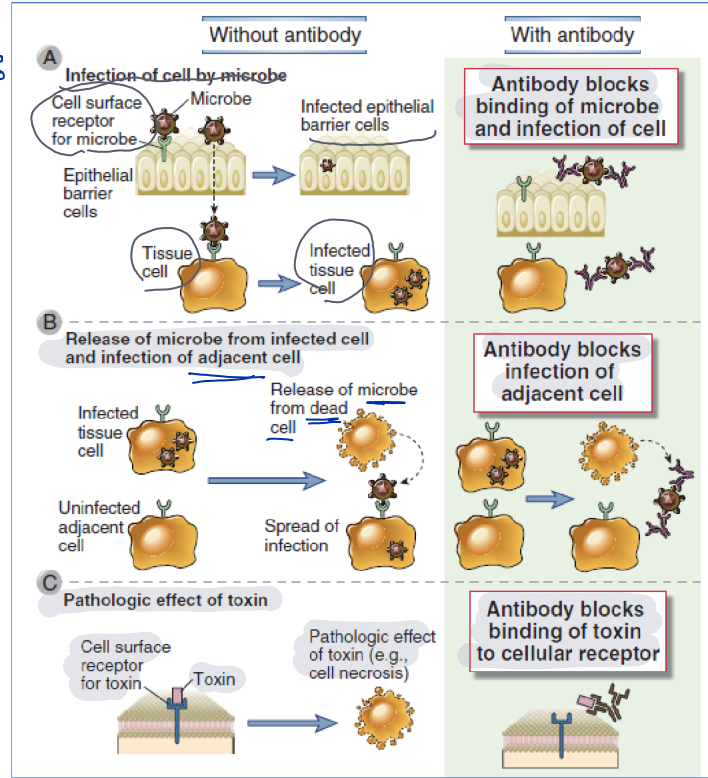
Effector mechanisms of humors

حسبنا الله ونعم الوكيل



Effector mechanisms of humoral immunity

Neutralization :
A B C

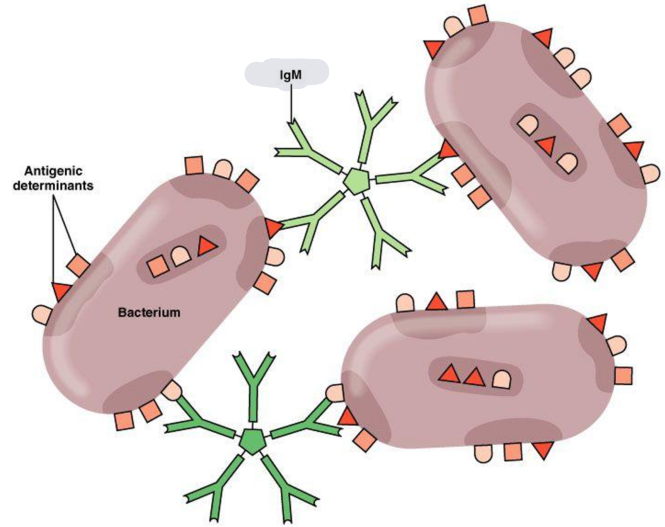


أستعمله الجسم بعد ما حلت وفل ما حلت

Antibodies/ IgM

لله في كل شيء وحده لا شريك له
 به العباد وله الحمد وهو على كل شيء قدير

- Because of its many specific binding sites, IgM is particularly effective in agglutinating particles carrying antigens against which it is directed.
- IgM is particularly active in bringing about complement-mediated cytolytic damage to foreign antigen-bearing cells.

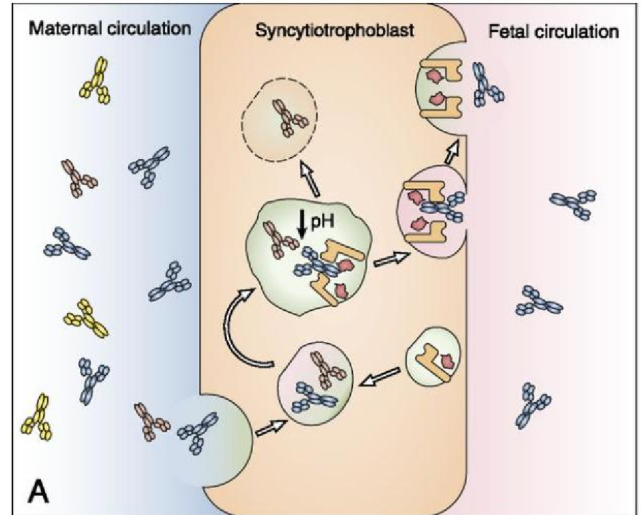


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Antibodies/ IgG

أَسْعَفُ الرَّائِيَةِ الْعَظِيمِ عِدَّةً مَحَلَّةً وَفَرْجاً مَحَلَّةً

- Immunoglobulin G (IgG) is **the most abundant immunoglobulin in health** and provides the most extensive and **long-lived antibody** response to the various microbial and other antigens.
- IgG antibody is characteristically formed in large amounts **during the secondary response to an antigenic stimulus**, and usually **follows production of IgM** in the course of a viral or bacterial infection.
- IgG is the only immunoglobulin class able to **cross the placental barrier** and, thus, provides passive immune protection to the newborn in the form of maternal antibody.

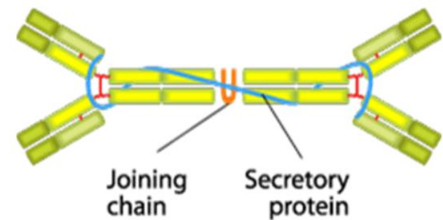
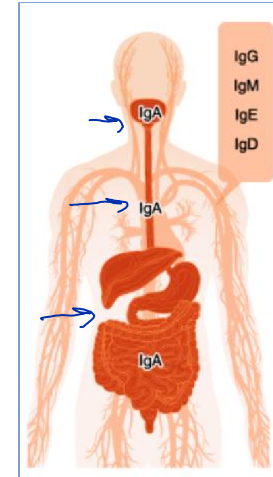


Antibodies/ IgA

سبحان الله وبحمده
سبحان الله العظيم

- Immunoglobulin A (IgA) has a special role as a major determinant of so-called local immunity in **protecting epithelial surfaces** from colonization and infection.
- At the epithelia, **two IgA molecules** combine with another protein, termed the **secretory piece**, which is present on the surface of local epithelial cells. The complex, then termed **secretory IgA (sIgA)**,
- The **major role of sIgA is to prevent attachment** of antigen-carrying particles to receptors on mucous membrane epithelia

ما تم : بيع الحصة قبل ان تصفح

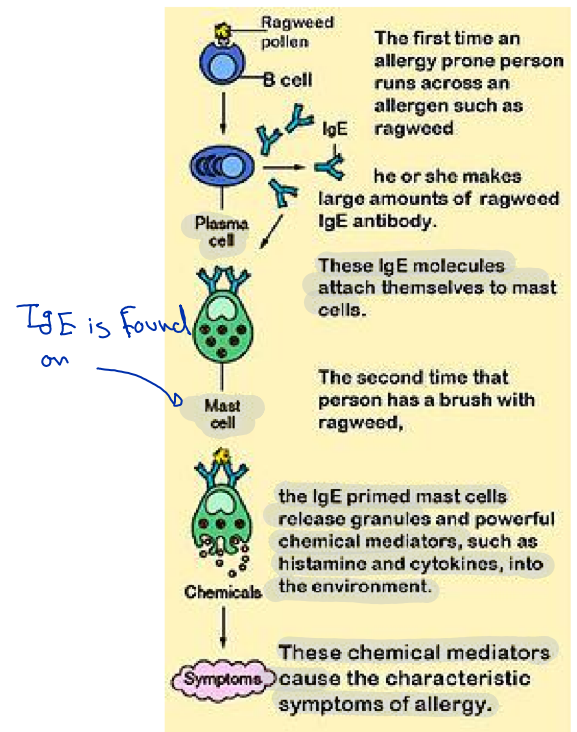


A dimer

Antibodies/ IgE

له حول ولا مَنوعة لآل بالله

- IgE not only provides protective immunity against **helminth parasites** but can also mediate the **type I hypersensitivity reactions** that contribute to the pathogenesis of **allergic diseases** such as **asthma, allergic rhinitis** and **atopic dermatitis**.

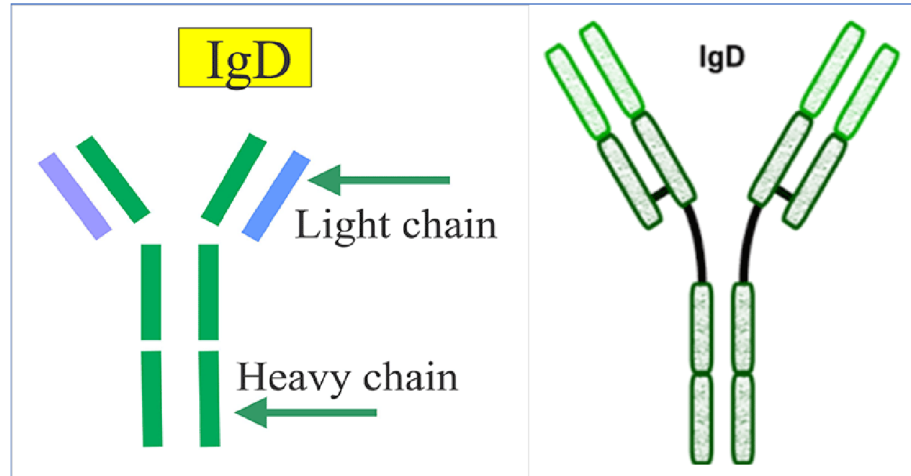


Antibodies/ IgD

أَسْتَغْفِرُ اللَّهَ الْعَظِيمَ كَدِّ مَاحِلَةٍ وَفَرْغِ مَاحِلَةٍ

- **IgD (IgD)** is a **monomeric** antibody isotype that is expressed in the plasma membranes of immature B-lymphocytes. **IgD** is also produced in a secreted form that is found in small amounts in blood serum.
- the function of IgD is to signal the B cells to be activated.

• It goes class switching to IgM, IgG, IgE



أَسْتَغْفِرُكَ اللَّهُ الْعَظِيمَ عِدَّةَ مَرَّاتٍ وَأَعْلَى حُلَّةٍ

[https://www.jacksonimmuno.com/secondary-antibody-resource/technical-tips/immunoglossary/#:~:text=Complementarity%20Determining%20Regions%20\(CDRs\)&text=An%20IgG%20antibody%20has%2012,each%20of%20the%20heavy%20chains.](https://www.jacksonimmuno.com/secondary-antibody-resource/technical-tips/immunoglossary/#:~:text=Complementarity%20Determining%20Regions%20(CDRs)&text=An%20IgG%20antibody%20has%2012,each%20of%20the%20heavy%20chains.)

Further reading:

- Cellular and Molecular Immunology. 7th Edition..
Chapter 5. Antibodies and antigens

للفائدة ولعلّها تكون سببًا في تعجيل النّصر أو
إزاحة الهموم عن إخواننا بإذن الله:
كان النبي صلى الله عليه وسلم يدعو في وقت
الأزمات والابتلاءات التي تصيب المسلمين بعد
القيام من الركوع الأخير في كلّ صلاة مفروضة
وهذا يسمّى القنوت ويستحب فعله في المساجد
فيدعو الإمام ويؤمّم المصلّون. **الدعاء يكون
في المصاب فيدعو للمسلمين المستضعفين
ويدعو على الظالمين ولا تشترط الإطالة في
الدّعاء