


Oral Biology
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Lecture - 14
Mucosal and regional immunology

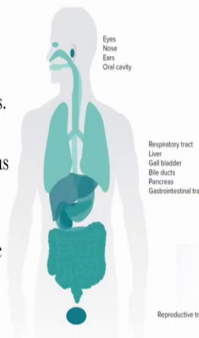
Welcome to the lecture cast on Mucosal and regional immunology. Mucosa represents the membrane that lines the inner surface of the body. Like skin, it forms a barrier between the internal and the external environment.

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Need for Mucosal Immunity



- With an area of 400 square metre, epithelium of adult mucosa represents the most frequent portal of entry for common infectious agents, antigens, and carcinogens.
- Highly efficient mucosal immunity - obvious need.
- Mucosal immune system(MIS) - Part of the immune system that responds and protects against microbes that enters the body through mucosal surfaces (gastrointestinal and respiratory tracts).




Picture courtesy: C E Wagner et al/AR CELL AND DEVELOPMENTAL BIOLOGY 2018



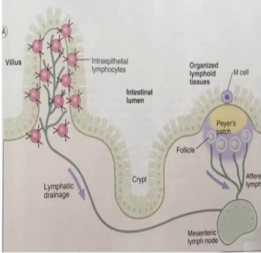
With an area of 400 square metre, the epithelium of adult mucosa represents the most frequent portal of entry for common infectious agents, antigens and carcinogens. Thus highly efficient mucosal immunity is of paramount importance. Mucosal immune system is defined as a part of the immune system that responds and protects against the microbes that enter the body through the mucosal surfaces.

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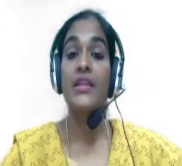
Mucosal immunity



- MIS - collections of lymphocytes and accessory cells in the epithelia and lamina propria of mucosal surfaces - large in numbers with their distinct phenotype and functional heterogeneity.
- Some of these organised into lymphoid follicle like structure called Mucosal Associated Lymphoid Tissues (MALT)
- Sites of adaptive immune responses to environmental antigens.
- Classified into
 - specialised aggregates like Payer's patches
 - scattered isolated lymphoid follicles.



Picture courtesy: Abbas, A. K., Lichtman, A. H. & Pille, S. (2007), Cellular and molecular immunology (8th ed.).



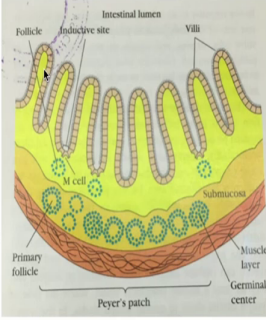
The mucosal immune system is provided with a rich collection of lymphocytes and accessory immune cells like IgE, IgA and macrophages. These are present in the epithelia and the lamina propria of the mucosal surfaces. You can see in the picture the collection of lymphocytes in the intraepithelial and subepithelial lamina propria. These cells are large in number with the distinct phenotype and functional heterogeneity.

Some of these cells are organised into a lymphoid follicle-like structure called mucosal associated lymphoid tissue. These are the sites of adaptive immune responses to the environmental antigens. The MALT tissues are classified into specialised aggregates (in Peyer's patches) or as scattered isolated lymphoid follicles.


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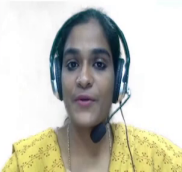
Mucosal associated Lymphoid tissue (MALT)

- GALT (Gut associated lymphoid tissue)
Payers patches
Appendix
Mesenteric lymph nodes (MLN)
Solitary lymph nodes
- NALT (Nasopharyngeal associated lymphoid tissue)
waldeyers ring (Tonsils and adenoids)
- BALT (Bronchus associated lymphoid tissue)
- Urogenital
- Exocrine glands - Salivary, lacrimal and mammary glands



Picture courtesy: Abbas, A. K., Lichtman, A. H., & Pillai, S. (2007). Cellular and molecular immunology (6th ed.).

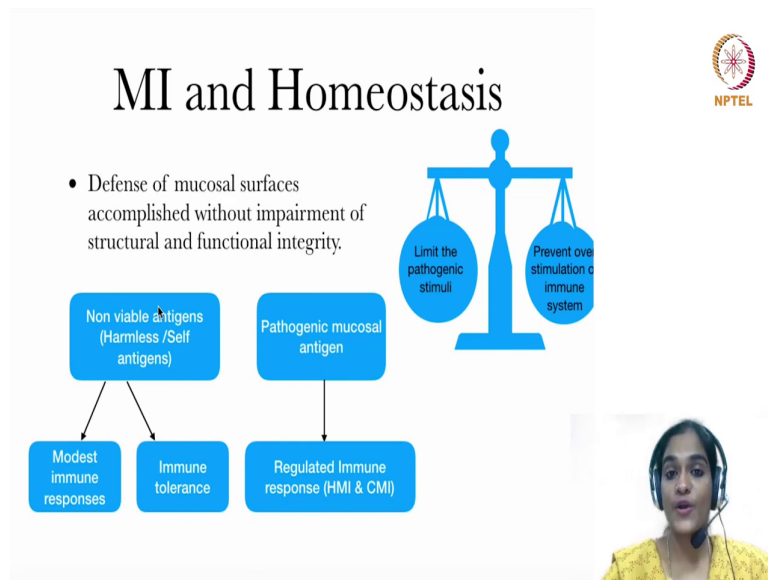




The MALT tissue is distributed all throughout different mucosal surfaces of the body. When they are present in gut they are called as GALT; Gut Associated Lymphoid Tissue. It comprises peyer's patches, appendix, mesenteric lymph nodes and solitary lymph nodes.

Those lymphoid tissue present in the nasopharyngeal area or the NALT tissue, the Waldeyer's ring including the tonsils and the adenoids form the component of the NALT tissue. Other lymphoid tissue associated with mucosa are BALT with the bronchial region, urogenital lymphoid tissue and those lymphoid tissue associated with the exocrine glands like salivary, lacrimal and mammary glands.

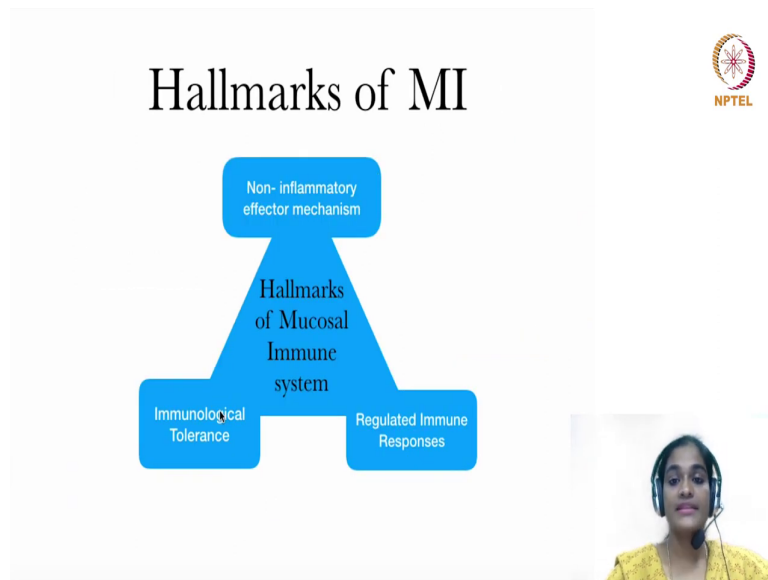
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The ultimate aim of mucosal immunity is to bring about the homeostasis that is the defence mechanisms of the mucosal surfaces should be established in such a way that there is no impairment of the structural and the functional integrity of the mucosa. The mucosal responses to the pathological stimuli should be limited to prevent the overstimulation of the immune system so that the integrity of the mucosa is preserved.

Against a nonviable antigen which is the potentially harmless or a self antigen, a modest to no immune response should be elicited. Against a pathogenic mucosal antigen, a regulated immune response is elicited. What do you mean by regulated immune response? The regulated immune response represents the heightening of the immune activity once the antigen is encountered. Following the elimination of the antigen, the immune system is brought back to normal sense.

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Thus, the hallmarks of mucosal immunity include the non-inflammatory effector mechanism by which the various immune mechanisms are mediated through a non-inflammatory process. There is immune tolerance against a self antigen or a potentially a harmless antigen and regulated immune response towards pathogenic stimuli.

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The slide is titled "Mucosal immunity". It lists two categories of mechanisms:

- **Non - Specific mechanisms**
 - Physical barriers provided by epithelial cells, and cilia
 - Mucus and other secretions
 - Antimicrobial peptides
 - commensal microbiota.
 - Pattern recognition receptors
- **Specific Mechanisms**
 - Secretory IgA and IgE
 - T Lymphocyte mediated immune responses
 - Mucosal B lymphocytes

In the top right corner of the slide is the NPTEL logo. In the bottom right corner, there is a small video inset of the same woman from the previous slide, wearing a headset and a yellow patterned top.

The various mechanisms of the mucosal immune system include non-specific mechanisms and specific mechanisms. Non-specific mechanisms include the physiological barriers as provided by the epithelial cells, cilia, mucus and other secretions those given by the

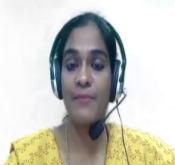

antimicrobial peptides, commensal bacteria and the pattern recognition receptors. Some of the specific mechanisms include those given by the antibody mediated cell mediated and humoral mediated responses.

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Antigen presentation in MI system

- **Specialised M cells** sample antigens - endocytosing bacteria, viruses and macromolecules.

Picture courtesy: Abbas, A. K., Lichtman, A. H., & Pillai, S. (2007). Cellular and molecular immunology (6th ed.).

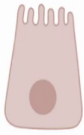


Before going into the details of the immune mechanisms of the mucosal immune system, let us see how an antigen is being presented to the mucosal surface. There are specialised M cells or the multi fold cells which are present on top of the mucosa associated lymphoid follicles. Over the GALT and NALT lies the M cells, which are the specialised epithelial cells. They do not have the microvilli.

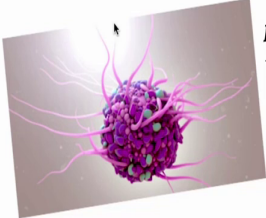
These take the antigen from the lumen to be processed by the lymphoid follicle. In the follicle there are presence of B cells which on encountering antigens get converted into specialised plasma cells. Those plasma cells produce the specific IgA or the immunoglobulin A to respond to the particular antigen. These are secreted through the lamina propria into the lumen, to encounter the specific antigen.

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Antigen presentation in MI system



Absorptive enterocytes
intracellular processing and presentation with surface class I or class II MHC antigens



Dendritic Cells protrude pseudopods into lumen to sample antigens, activate & regulate epithelial cells.



We have the epithelial cells (for example, the enterocytes). These take up the soluble antigen with the help of MHC class 1 and class 2. They process and present them to the underlying T cells or the intraepithelial T cells for the immune tolerance or immune stimulation.

There are dendritic cells which are present in the basal epithelial layer or they can also be seen in the lamina propria which protrude their pseudopods into the lumen to sample the antigen so that they activate and regulate the epithelial cells.

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Non specific barriers

- Epithelial cells - intercellular junctions and Keratin formation- prevent transit of antigens and pathogens encountered by the mucosal surface.
- Epithelium with stratification - Cell shedding from the surface layer of the oral epithelium minimizes the colonization of bacteria (Hovav, 2014).





Coming on to the mechanisms of the mucosal immune system, there are nonspecific barriers- most predominantly the epithelial cells play an important role. They have the intercellular junctions and the keratin formation which prevents the transit of antigens and pathogens into the mucosal surface.

Some of the epithelial cells which are labelled as type 2 epithelial cells - show stratification. they constantly shed their superficial layer. Because of the superficial shedding, there is no colonization of bacteria in the epithelial layer.

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Non immunologic barriers

- *Mucus production* by some epithelial cells- act as a vital physiochemical barrier.
- In respiratory & Genitourinary tract- beating *cilia* present.
- *Washing action* of tears, saliva and urine. peristaltic movements.
- *Bactericidal components* in secretions - eg. acids in gastric juice

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graph TD; Mucus --- BeatingCilia[Beating cilia]; Mucus --> MucociliaryBlanket[Mucociliary blanket]; BeatingCilia --> MucociliaryBlanket;
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The mucous production by some epithelial cells act as a vital physiochemical barrier. The mucus produced along with the beating cilia form the mucociliary blanket. This mucociliary blanket effectively traps the antigen and expels the same. So, in the various mucosal surfaces, you have secretions like tears, saliva and urine, which causes the washing action.

There are some of the reflexes like peristaltic movement, sneezing, coughing which helps to expel the antigens. There are bactericidal components in some of the secretions. Example: an acid in a gastric juice, lactozyme in tear saliva, lactoperoxidase in mammary secretions and spermine and zinc in sperms. These help to kill the microorganisms encountered by the mucosa.

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Mucosal Microbiota

- Resident microbiota has extensive and vital interaction with mucosa.
- **Microbial Antagonism**- Suppresses the growth of pathogens by competition for essential nutrients or by production of inhibitory substances.


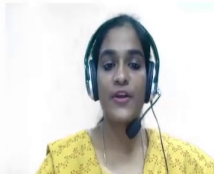
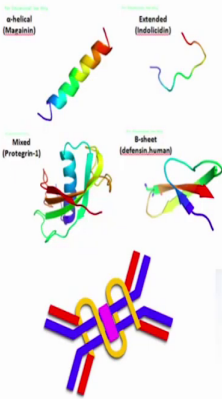


The residual microbial flora have an extensive and vital interaction with the mucosa. They produce the microbial antagonism. That is they suppress the growth of the various pathological bacteria and fungi, by competing for the essential nutrients and producing various inhibitory substances. For example, lactic acid produced by the vaginal flora helps to get rid of the pathogenic fungi colonization.

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Non-specific mechanisms

- **Antimicrobial peptides (AMP)** produced by mucosal epithelium - primary bacterial defence barrier. Group of AMP called defensins causes lysis of bacteria via disruption of their surface membrane.
- salivary antimicrobial components, such as lysozyme, histatins, α -defensins and the human cathelicidin LL37- exert their antibacterial function by affecting cell wall integrity and pore formation and indirectly by immune signalling (van't Hof et al, 2014).



The antimicrobial peptides produced by mucosal epithelium forms a primary bacterial defence barrier. There are groups of antimicrobial peptides called defensins. They get

inserted themselves into the bacterial membrane and cause the disruption of the same. Because of which, there is loss of cellular contents causing the lysis of the bacteria.


Similar mechanism is being shown by salivary antimicrobial compounds like lysozyme, histatin, beta defensin and human cathelicidin, which also affects the cell wall integrity and pore formation. Some of them also trigger the immune mechanisms that cause the elimination of the pathogen.


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Non-specific mechanisms

- Expression of range of **innate pattern recognition receptors** that recognise microbe-associated molecular patterns.
- Diverse source for cytokine network - influx, activation and differentiation of myeloid & lymphoid cells .

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graph TD
    OT[Oral tolerance] -- TGF- B, IL-10 --> EC[Epithelial cell]
    LTM[Local T cells & microbiota] --> EC
    EC -- Cytokines --> BCP[B cell/ plasma cell]
    BCP --> IgA[IgA secretion]
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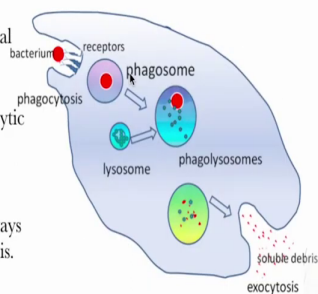
Some of the phagocytes and epithelial cells express the innate pattern recognition receptors. These receptors recognize the microbial associated molecular patterns. These patterns are nothing but lipopolysaccharide in case of a gram negative bacteria or a lipoteichoic acid in case of a gram positive bacteria and a glycolipid in case of the mycobacteria.

when the innate pattern recognition receptors combine with the microbial associated molecular patterns (also called as PAMP), there is an induction of diverse amounts of cytokines which causes influx, activation and differentiation of myeloid and lymphoid cells.

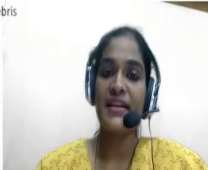

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Non- Specific mechanisms

- Phagocytes use PRR to recognise PAMP on microbial surface.
- Phagocytosis - Main phagocytic cells are neutrophils and macrophages.
- Activation of NF-KB pathways and initiation of phagocytosis.
- Microbicidal mechanisms follows using cytoplasmic granules of phagocytes.



The diagram illustrates the process of non-specific phagocytosis within a cell. A bacterium (red dot) is shown outside the cell, with receptors (blue Y-shapes) on the cell membrane. The process of phagocytosis is shown as the cell membrane engulfs the bacterium to form a phagosome (red circle). The phagosome then fuses with a lysosome (green circle) to form a phagolysosome. Finally, the phagolysosome undergoes exocytosis, releasing soluble debris (red dots) from the cell.



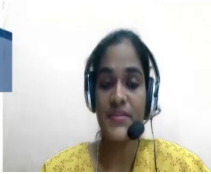

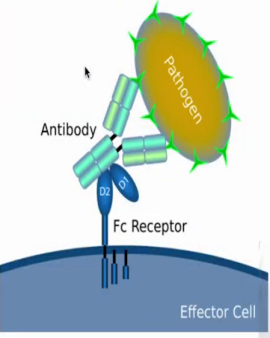
The other mechanism as soon as a PRR encounters the PAMP is that there is initiation of phagocytosis, that is after the PRR combines with the PAMP there is NF-kappa B pathway which gets activated because of which there is stimulation of phagocytosis. Thus, the phagocytes throw their pseudopods to engulf the antigen and form the phagosome.

And as soon as the antigen is internalized inside, these combine with the cytoplasmic granules of the phagocytes causing various microbicidal mechanisms like reactive oxygen and nitrogen mediated pathways. Soon soluble debris is being expelled after the lysis of the microorganism.

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Specific mechanisms

- Provided by Cell mediated, Humoral mediated and Antibody mediated mechanisms (IgA, Ig M, IgG and IgE antibodies).
- Most of the mucosal surfaces protected by IgA (exception : reproductive tissue has dominant isotope as IgG)

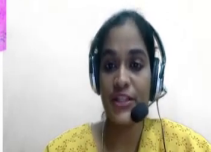




Various specific mechanisms are provided by cell mediated, humoral mediated and antibody mediated responses. The specific mechanisms of the mucosal immune system are mediated by the lymphocytes and antibodies. IgA is the dominant type of antibody, which is seen associated with a mucosal surface. More than the systemic circulation, it is commonly seen associated with the mucosa.

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Site of adaptive response

- MALT tissue like peyers patches, appendix, Pharyngeal tonsils.
- Central regions rich in B lymphocytes - *Germinal center* Produces various *Immunoglobulins* needed for adaptive immunity.
- CD4⁺ T lymphocytes found in inter follicular regions.



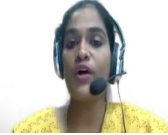

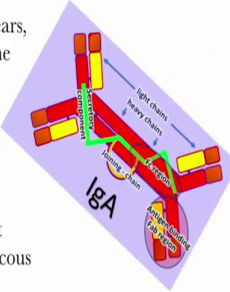
The appropriate site where the adaptive response or a specific response of the mucosal immunity occurs are the MALT or the Mucosal Associated Lymphoid Tissue. These MALT

tissues have follicles. The center of the follicle is B lymphocyte rich also called a germinal center. These are the sites where the antibodies specific to antigen are being produced. In the interfollicular region, the CD4positive T lymphocytes are seen and these are the sites of cell mediated immune responses.

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Role of IgA in mucosal immunity

- IgA antibodies - external body fluids, tears, saliva, nasal secretions, those bathing the surfaces of intestine and lung.
- Polymeric IgA has 4-8 antigen binding sites-enhanced avidity to antigens.
- Coats the bacteria and viruses - prevent adherence of the microorganisms to mucous membrane.
- IgA attaches to Fc receptor in macrophages and neutrophils - mediate phagocytosis.



Now, we will see the role of IgA in mucosal immunity. These IgA antibodies are seen bathing in the extracellular body fluids; tears, saliva, nasal secretions and also the intestine and the lung. These are polymeric. They have 4 to 8 antigen binding sites. Thus they have the enhanced avidity or attraction to the antigen. These coat the bacteria and the virus and various other microorganisms. They prevent the adherence of them to the mucosal membrane. These IgA attach to the Fc receptor in the macrophages and the neutrophils - mediating phagocytosis.

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Secretion of IgA - Expression of membrane receptors (pIgR) for IgA secretion

Co-operation between epithelial and lymphoid cells essential for selective transport of polymeric IgA. Epithelial cells of mucosal and secretory glands express pIgR - specific for J chain containing polymeric IgA (and IgM) - required for transcytosis of large quantities of IgA to form S-IgA.

Picture courtesy: Abbas, A. K., Lichtman, A. H. & Pille, S. (2007), Cellular and molecular immunology (8th ed.).

An IgA molecule is a dimer, which has been cross linked with the help of a J chain. These are produced in the lamina propria. They are being transported with the help of a poly IgA receptor on the cell surface of an epithelial cell. These receptor, combined with the IgA is transported through the membrane and finally, after the lysis (proteolytic cleavage) of the transporting molecule, the secreted IgA occurs in the luminal surface.

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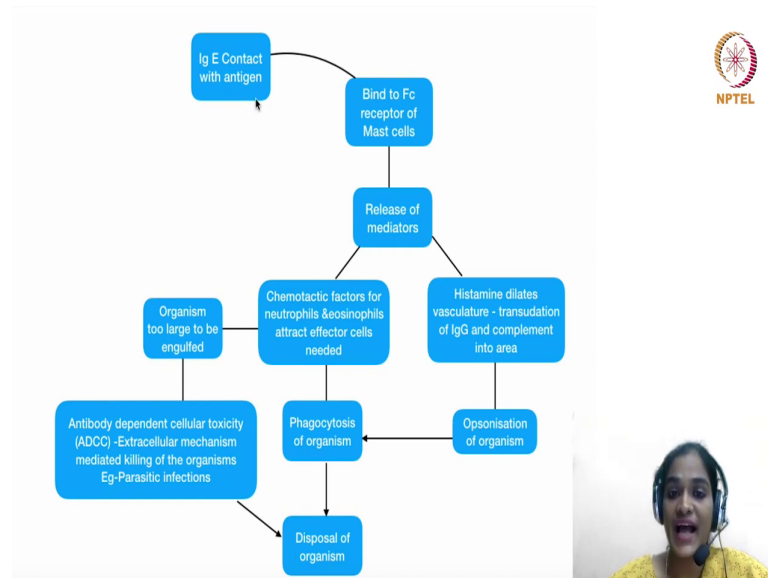
Role of IgE in mucosal immunity

- If micro-organisms succeeds penetrating IgA barrier, IgE forms the next line of defence.
- Complement derived anaphylotoxins and IgE utilise mast cells - cause local amplification of immune responses.

If the micro-organism succeeds in penetrating the IgA barrier, the IgE next comes into play. They are the next line of defence. The complement derived anaphylatoxins and the IgA

utilise the mast cells. They interact with the mast cells to cause the release of pre-secreted mediators of inflammation, which causes the local amplification of immune responses.

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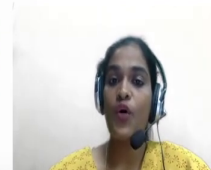
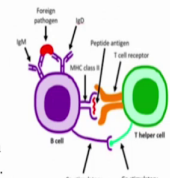
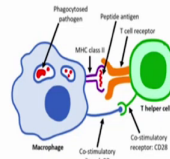
The IgA when it contacts with the antigen it binds to the Fc receptor of the mast cells due to t release the mediators. The histamine released dilate the vasculature causing transudation of IgE and complement into the area. These opsonize the organism causing the phagocytosis.

Some of the chemo factors released from the mast cells attract the neutrophils, eosinophils and other effector cells which causes the phagocytosis. Larger organisms are eliminated by means of an extracellular mechanism called antibody dependent cellular toxicity..(Refer Slide Time: 15:34)

Role of T lymphocyte in mucosal immunity



- Variety of T lymphocytes contained in mucosa- seen intra-epithelial, in lamina propria and in MALT
- Intraepithelial T cells - innate & adaptive cytotoxic mechanism.
- Majority are memory cytotoxic T lymphocytes - rapidly reactivated to provide immediate cytotoxic responses against infections.
- Th1 - rare - if present in association with MHC II - stimulation of cell mediated immune response. Th2 - activate B lymphocytes and antibody production.
- Th17 cells - cytokines IL17 & IL-22 - stimulate secretion of innate AMP - recruit neutrophils through chemotaxis.



Now, let us see about the role of T lymphocytes in mucosal immunity. The variety of T lymphocytes are contained in the mucosa. They are seen in the intraepithelial, subepithelial lamina propria and also associated with MALT tissue. The intraepithelial T cells are predominantly CD8 positive lymphocytes and also memory T cells.

The CD8 positive T cells or the cytotoxic cells cause the innate and adaptive cytotoxic mechanism. The memory T cells rapidly get reactivated to provide for the immediate cytotoxic responses needed for an infection. The lymphocytes are also present in the lamina propria, which are CD positive T helper cells.

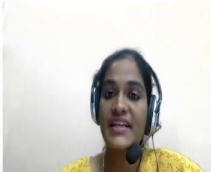

The T helper cells recognize and respond to the antigens in the lymph nodes draining the particular mucosal surface and migrate back to the mucosa to populate the lamina propria. These are predominantly Th2 type of lymphocytes. They activate B cells and antibody production.

Some of them are only Th1 type of cells that are associated with MHC class 2. They stimulate the cell mediated immune response, whereas some of the helper cells are Th17 type. Due to the stimulation of IL17 and IL22 they cause the secretion of innate antimicrobial peptide and also recruit the neutrophils through chemotaxis.

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Reactivity vs. Tolerance

- MI should distinguish between commensal microbiota and essentially harmless food antigen from pathogenic stimuli to prevent overstimulation of the immune system.
- **Nature of the antigen:** pathogen-associated molecular patterns (PAMPs) ligate pattern-recognition receptors on innate APC, **upregulating MHC** and co-stimulatory molecule expression.
- Replicating rather than inactive microbes are more likely to induce productive immune responses



Reactivity versus tolerance; how does a mucosal immune system distinguish between a self and a non-self antigen? They have to differentiate between the commensal microbiota and essentially harmless food antigen from a noxious pathogenic stimuli. How does a mucosal immune system distinguish between a self and a non-self antigen? They do this with the help of major histocompatibility antigen (MHC) and also the co-stimulation.

When a particular cell recognizes the pathogen associated molecular pattern, the MHC molecule co-stimulates; they get upregulated and there is also co-stimulatory molecule expression. Only after seeing the co-stimulation and molecular MHC upregulation there is activation of the immune response. When there is absence of the same, you have immune tolerance. Replicating rather than an inactive microbe is more likely to induce immune response.

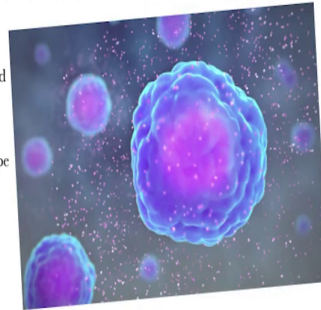
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Mucosal Immune stimulation

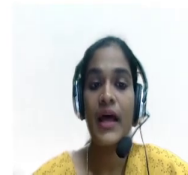


- **Mucosal cytokines:** mucosal 'accessory' cells release preformed mediators and cytokines on antigen stimulation, priming the micro-environment for a particular adaptive response shape

- DC antigen presentation and micro-environmental cytokines impact the immune response shape (Th1-type cell-mediated immunity, Th2-type antibody-mediated immunity, or Treg-mediated tolerance) and outcomes



- IL-12 and IFN γ from activated macrophages can break tolerance



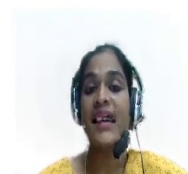
There are various cytokines and mediators which have been produced by accessory immune cells which primes the micro environment for a particular adaptive response. For example, if there is production of interleukin 2, 12, interferon gamma, Th1-type of cell mediated immunity gets activated. If there is interleukin 4, 6, 5 and 10 being produced, Th2-type of cell mediated immune response becomes activated. The interleukin 12 and interferon gamma break the tolerance state and reactivate the immune stimulation or heightened response.

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Mucosal Immune suppression

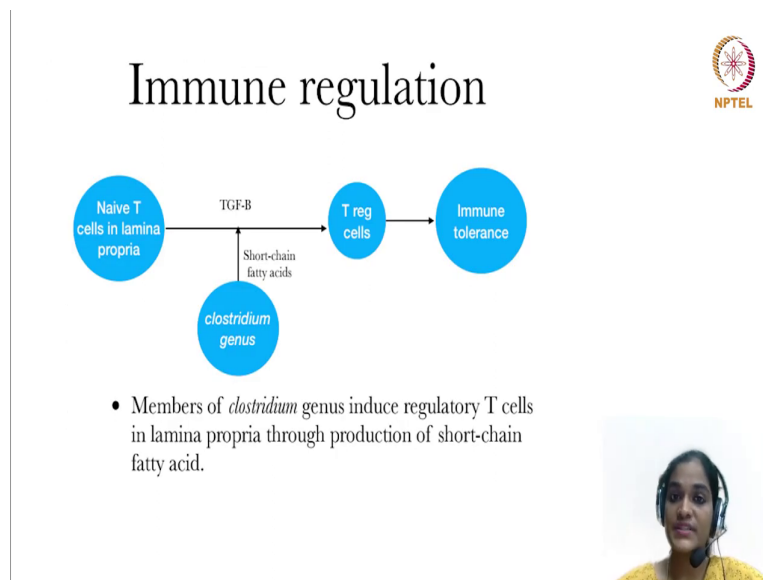


- Suppressor cytokines such as IL-10 and TGF β (e.g. [Peyer's patch](#) DC make IL-10 but little IL-12, leading to Th2-type responses)
- Regulatory cells operational in the mucosa, dampens or suppresses reactive antigen-specific cells.
- FOXP3 is the key regulatory gene in the development of CD25+ Tregs, which can be induced in the periphery, in presence of TGF- β .



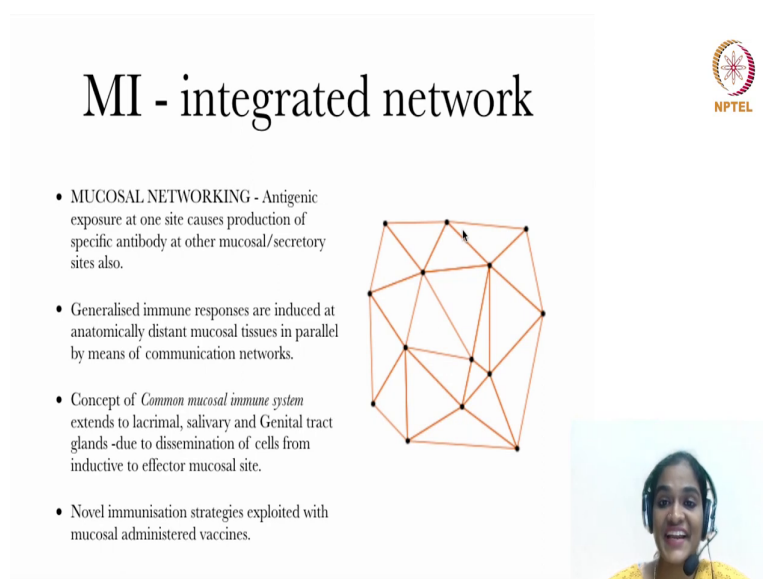
There are certain suppressor cytokines like interleukin 10 and TGF beta which cause the immune suppression or tolerance. The FOXP3 is a gene which converts the naive T cell into a T regulatory cell in presence of TGF beta. These regulatory cells are present in the mucosa. They dampen or suppress the reactive antigen specific cells.

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There is a particular contributory role which is shown by the intestinal microflora or mucosal microflora. These organisms, release the short fatty acid, which contributes to the conversion of naive T cell to a T regulatory cell ultimately leading to immune tolerance.

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The mucosal immune system acts as an integrated network. When there is an antigenic exposure to one particular site of the mucosa, there is production of specific antibodies at the other mucosal or the secretory sites also. How is it? These generalised immune responses are brought about by means of communication networks.


The concept of a common mucosal immune system also extends to the exocrine glands like the lacrimal, salivary and a genital tract glands also. These are brought about with the help of dissemination of cells from the inducers site to the effector site. This is a particular novel immunisation strategy, which has been much exploited with mucosal administered vaccines.

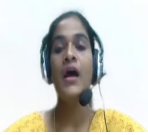
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Mucosal immunity in vaccines

- Most current vaccines administered by systemic route inadequately elicit protective immunity at mucosa.
- Mucosal route of delivery of vaccines/antigens utilised to produce secretory antibodies and mucosal effector T cells for desired responses.
- Mucosal immunisation reduces the carriage of pathogens at the mucosal surfaces - reduce the incidence of community acquired diseases - benefit even the unimmunized individuals on principal of herd immunity.









Most of the current vaccines which have been administered by systemic route do not adequately elicit the protective response from the mucosa. The mucosal route of delivery is being utilised to produce a secretory antibody and memory effector T cells for the desired responses. The mucosal immunisation reduces the carriage of pathogens at the mucosal surface. Thus they reduce the incidence of transfer of organisms in a communicable disease. Particular strategy is also being used by the principle of herd immunity.

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Conclusion

- Exploitation of MI system received increased attention.
- Attractive properties and advantages of mucosal vaccines resulted in establishment of several commercial institutions.
- Anticipated target vaccines- limited success in clinical trials.
- Efforts to exploit mucosal tolerance for clinical benefit are continuing and novel approaches like immunoregulatory cytokines, delivery systems, and adjuvants are pursued.
- Many mucosal diseases like asthma and Crohn's diseases are on rise.
- Understanding the homeostasis in MI system holds key to find the preventive strategies for these common diseases.





The exploitation of the mucosal immune system has received immense attention in recent years. The attractive properties and advantages of mucosal vaccines has resulted in establishment of several commercial institutions. Although the anticipated targeted vaccines have not achieved success in the clinical trials, various mucosal adjuvants are being tried as vehicles for the transport of mucosal immunity.

Efforts have been made to exploit the mucosal tolerance for clinical benefit. Novel approaches like immune regulatory cytokines, delivery systems and adjuvants are pursued. The many mucosal diseases like asthma and Crohn's disease are on rise. Understanding the homeostasis in the mucosal system holds the key to finding preventive strategies for these common diseases.

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References

- Holmgren, J., Czerkinsky, C. Mucosal immunity and vaccines. *Nat Med* **11**, S45–S53 (2005).
<https://doi.org/10.1038/nm1213>. *
- Mestecky, J., Strober, W., Russell, M. W., Cheroutre, H., Lambrecht, B. N., & Kelsall, B. L. (2015). *Mucosal Immunology*. Academic Press.
- Bellanti, JA (Ed). Immunology IV: Clinical Applications in Health and Disease. I Care Press, Bethesda, MD, 2012.chapter 20.



These are the references for further study.

Thank you.