

**Oral Biology**  
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**Lecture - 13**  
**Oral Defense Mechanisms**

Hi everyone, welcome to another interesting topic Oral Defense Mechanism.

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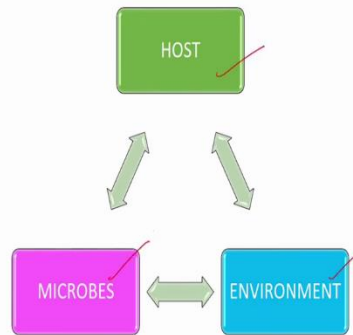
ORAL CAVITY & DEFENSE??



Oral cavity is the main entry point for various pathogens to enter into the body. Once the injury has been noted by the host cells, there will be more amount of the protective factors secreted by various lines of the oral cavity and it will diminish the invasion of the microbe and later helps in healing of the tissues promptly. So, yes, there is a relation between the defense mechanism and the oral cavity, that is the oral cavity has few defense mechanisms against various pathogens.

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## HOMEOSTASIS



Homeostasis is nothing but a balance. There should always be a balance between the living and also the functional organism. So, there should be a balance between the host, microbes and the environment of the body.

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## NON-SPECIFIC PROTECTION MECHANISM



- BACTERIAL BALANCE – Interference in binding, competition for nutrients, release of by-products
- SURFACE INTEGRITY – Continuous renewal + Desquamation
- SURFACE FLUIDS & ENZYMES – Attaching foreign objects
- PHAGOCYtic CELLS – Polymorphonuclear leukocytes + Macrophage
- COMPLEMENT SYSTEM – Immobilize the bacteria/toxin



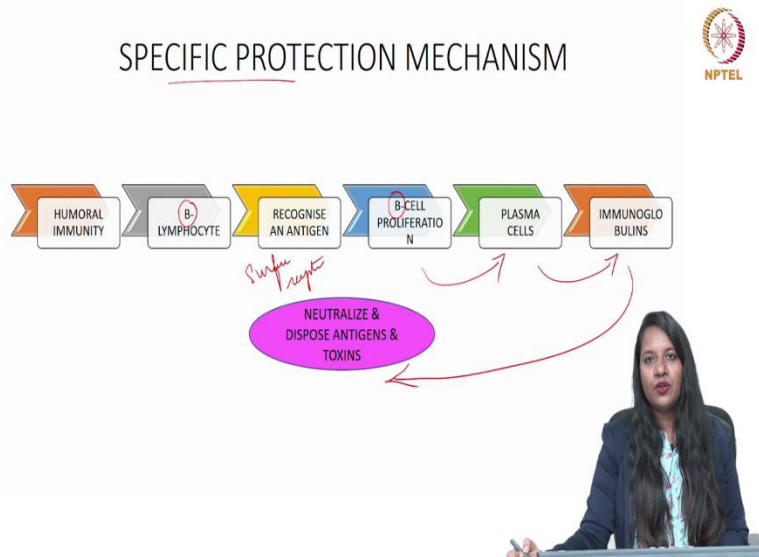
Non-specific protection mechanism - The first one being the bacterial balance; that is interference in binding, competition for the nutrients and the byproducts of one pathogen will be toxic to the other pathogen. So, by all these mechanisms there exists a balance between various species of the microbes in the body.

Surface integrity is nothing, but the continuous renewal and desquamation of the epithelial cells to maintain the surface integrity of the epithelium. Surface fluids and the enzymes - Any vital tissue

will have a fluid over it & it contains enzyme which can attach to the foreign objects and eliminates it from the body.

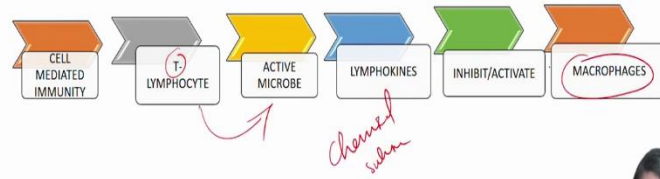
Phagocytic cells are nothing, but the polymorphonuclear leukocytes and the macrophages which help in the phagocytosis of the foreign bodies and thus eliminating it from the body. The complement system which enhances the phagocytosis by immobilizing the bacteria or the toxin. So, it makes sure that the entire foreign body has been eliminated from the body.

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Then comes the specific protection mechanism which is nothing, but the involvement of humoral and cell mediated immunity. Humoral immunity is mediated by the proliferation of B lymphocyte which recognize an antigen with the help of the surface receptor which leads to formation of B cell proliferation concomitantly plasma cell formation and the immunoglobulins. Finally, the immunoglobulins will neutralize and dispose antigens and toxins from the body.

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The second one being cell mediated, which is mediated by T lymphocytes which will capture the already active microbes present in the body and then it will release a chemical substance called lymphokines that will either inhibit or activate the macrophages leading to phagocytosis.

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### DEFENSE MECHANISM OF ORAL CAVITY

- SALIVA
- SULCULAR FLUID
- EPITHELIUM



A diagram of the oral cavity showing the tongue, throat, and gingiva. Various colorful cartoon microbes are depicted within the oral cavity. A small URL is visible at the bottom of the diagram: <https://www.healthline.com/health/oral-epithelial-barrier>



So, the defense mechanism of oral cavity starts from the saliva, gingival crevicular fluid or otherwise called as sulcular fluid and the epithelium of the oral cavity.

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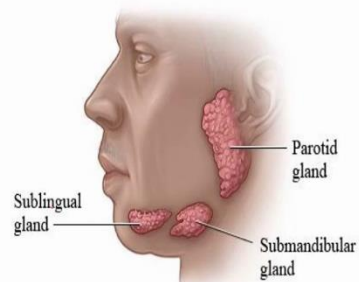
# SALIVA



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# SALIVARY GLAND



<https://www.ck12.com/head-and-neck/parotid-salivary-gland.org/salivary-gland/>



There are three major salivary glands - the parotid, submandibular, and sublingual along with numerous minor salivary glands.

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## COMPOSITION



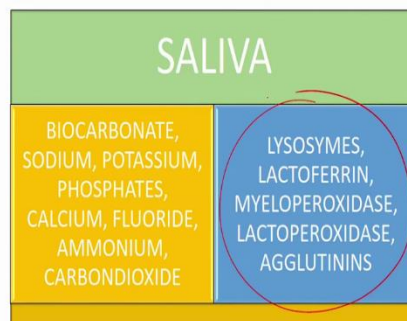
- WATER 99.5%
- ENZYMES – AMYLASE, LIPASE, MALTASE, PHOSPHATASE, CARBONIC ANHYDRASE
- INORGANIC SUBSTANCES – SODIUM, CALCIUM, POTASSIUM, BICARBONATE, BROMIDE, CHLORIDE
- ORGANIC SUBSTANCES – MUCIN, ALBUMIN, LACTOFERRIN, FREE AMINO ACIDS
- IgA
- BLOOD GROUP ANTIGENS



The composition of saliva includes 99.5 percent of water with 0.5 percent of other substances such as enzymes, inorganic, organic, immunoglobulins, blood group antigens, agglutinins, coagulation factors & various other factors.

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## ANTIBACTERIAL FACTORS



The anti-bacterial factors include bicarbonate, sodium, potassium, carbon dioxide and along with other major organic antibacterial factor such as lysozyme, lactoferrin, myeloperoxidase, lactoperoxidase and agglutinins.

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## ENZYMES



- PAROTID AMYLASE
- BINDS TO STREPTOCOCCI – BACTERIAL CLEARANCE AND ADHESION
- INCREASED CONCENTRATION OF SALIVARY ENZYMES – PERIODONTAL DISEASES
- PROTEOLYTIC ENZYMES – BOTH BACTERIA & HOST – CONTRIBUTORS TO INITIATION AND PROGRESSION OF PERIODONTAL DISEASE



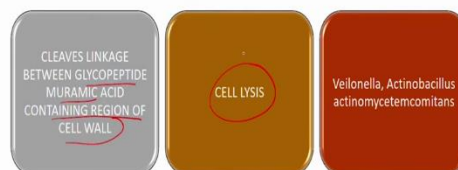
Moving to enzyme amylase which is the first enzyme secreted by the parotid that binds to streptococci and inhibits adhesion and further enhances bacterial clearance. There will be the increased concentration of enzyme in case of periodontal diseases and there are proteolytic enzymes which will be secreted by the host as well as the bacteria. So, those were the contributors to initiation and progression of periodontal disease.

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## LYSOSYME



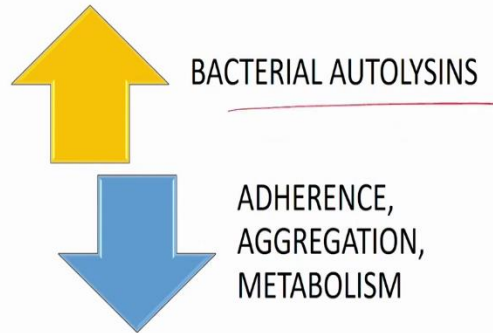
- HYDROLYTIC ENZYME



Moving to lysozyme, lysozyme is a hydrolytic enzyme which cleaves linkage between glycopeptide muramic acid containing region of cell wall, that leads to cell lysis mainly in the veillonella and actinobacillus actinomycetemcomitans.

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## LYSOSYME



So, it will enhance the bacterial autolysin, but it will inhibit its adherence.

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## LACTOFERRIN



- LINKS TO FREE IRON IN THE SALIVA
- BACTERICIDAL/BACTERIOSTATIC EFFECTS ON ORGANISM REQUIRING IRON FOR SURVIVAL
- FUNGICIDAL
- ANTIVIRAL
- ANTI-INFLAMMATORY
- IMMUNOMODULATION



Lactoferrin links to free ion present in the oral cavity. So, there are few pathogens which requires this ion for the survival. So, it will be either bactericidal or bacteriostatic to those pathogens. It will also be fungicidal, antiviral, anti-inflammatory and immunomodulatory.

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## PEROXIDASES



- LYSINE & GLUTAMIC ACID – BACTERIAL GROWTH
- LACTOPEROXIDASE-THIOCYANATE – BACTERICIDAL – PREVENTING ACCUMULATION OF LYSINE & GLUTAMIC ACID
- CATALYZE THE OXIDATION OF THIOCYANATE BY HYDROGEN PEROXIDE – OXIDISED FORM OF THIOCYANATE – TOXIC ACTION AGAINST MICROBE
- LACTOBACILLUS, STREPTOCOCCUS, ACTINOBACILLUS



Few pathogens need lysin and glutamic acid for their growth. So, the peroxidases will be bactericidal preventing accumulation of lysine and the glutamic acid, which catalyzes the oxidation of thiocyanide by hydrogen peroxide, oxidized form of thiocyanates are most toxic against various pathogens such as lactobacillus, streptococcus and actinobacillus.

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- MYELOPEROXIDASE – TOXIC OXIDIZED HALIDE DERIVATIVES/PROTECTIVE ROLE AGAINST OXYGEN FREE RADICALS
- COMBINATION – IgA + PEROXIDASE – ENHANCED ANTIMICROBIAL ACTION



Myeloperoxidase also produce toxic oxidized halide derivatives which have a protective role against oxygen free radicals, rather than being alone it combines with immunoglobulins to have an enhanced antimicrobial activity. The one such combination is the IgA and peroxidase which has the most enhanced antimicrobial action.

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## AGGLUTININS



- GATHERS UP UNATTACHED BACTERIA TO FASTEN THE CLEARANCE
- PAROTID – CALCIUM DEPENDENT
- SUBMANDIBULAR & SUBLINGUAL – CALCIUM INDEPENDENT



Salivary agglutinins are nothing, but gathering up of unattached bacteria to fasten their clearance. In parotid, it will be calcium dependent and in case of submandibular and sublingual, it is calcium independent.

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## STATHERINS



INHIBITS SPONTANEOUS  
PRECIPITATION OF CALCIUM  
PHOSPHATE SALTS

INHIBITS GROWTH OF  
HYDROXYAPATITE CRYSTALS

PREVENTING FORMATION OF  
CALCULUS

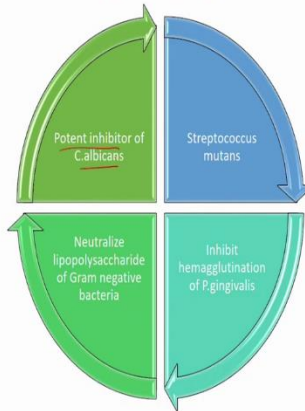


Statherins inhibits spontaneous precipitation of calcium phosphate salts thus it inhibits growth of hydroxyapatite crystals and thus preventing formation of something called calcific deposits – calculus, thus preventing further progression of periodontal disease.

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## HISTATINS



Histatins neutralize the lipopolysaccharide of gram negative bacteria. It is potent inhibitor of candida albicans and it also inhibits hemagglutination of P gingivalis.

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## CYSTATINS

- CYSTEINE CONTAINING PHOSPHOPROTEINS
- PROTEINASE INHIBITORS
- PROTECTS TISSUE FROM PROTEOLYTIC ATTACKS BY BACTERIA/VIRUS
- REGULATES ACTIVITY OF CATHEPSINS DURING INFLAMMATION
- CONTROLS PROLIFERATION OF CELLS



Cystitins are nothing, but cysteine containing phosphoproteins. They are also called as protease inhibitors - it inhibits or protects tissues from proteolytic attacks by bacteria or virus. It regulates the activity of cathepsins during inflammation and it also controls cellular proliferation.

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## DEFENSINS



- SUBFAMILY OF ANTIMICROBIAL PEPTIDES
- EXPRESSED IN GINGIVA, TONGUE, SALIVARY GLANDS & MUCOSA
- PRESENT IN ORAL INFLAMMATORY & ORAL CARCINOMA



Defensins are recently found in gingiva, tongue, salivary gland and mucosa which is a sub family of antimicrobial peptides. It is also present in oral inflammatory conditions and in oral carcinoma.

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## SALIVARY ANTIBODIES



- IMMUNOGLOBULINS
- IgA - MAJOR
- SMALL AMOUNT OF IgG & IgM
- IgA INHIBITS BACTERIAL ADHERENCE



Salivary antibodies which are nothing, but the immunoglobulins. IgA being the most important salivary immunoglobulin which will inhibit the bacterial adherence. IgG and IgM along with the peroxidases have an enhanced antibacterial activity.

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## SALIVARY BUFFERS & COAGULATION FACTORS



- THE MAINTAINENCE OF PHYSIOLOGIC HYDROGEN ION CONCENTRATION IN THE ORAL CAVITY – BICARBONATE-CARBONIC ACID SYSTEM
- COAGULATION FACTORS – FASTEN COAGULATION AND PREVENTS BACTERIAL COLONISATION & INVASION
- FIBRINOLYTIC ENZYME




The maintenance of physiologic hydrogen ion concentration in the oral cavity is brought by bicarbonate-carbonic and acid system and it also has various coagulation factors. Thus, it will fasten the coagulation and prevents the bacterial invasion and the proliferation or the colonization. Also, the saliva contains fibrinolytic enzymes as well.

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## SALIVARY ANTIOXIDANTS



- ANTICARCINOGENIC – INHIBITS INITIATION & PROGRESSION OF OC
- FIGHTS AGAINST REACTIVE OXYGEN & NITROGEN SPECIES – BY SMOKING, ALCOHOL, FOOD & DENTAL RESTORATIONS
- URIC ACID MOLECULE & PEROXIDASE
- PREVENTS CIGARETTE-INDUCED DNA DAMAGE 



Salivary antioxidants which are nothing, but anti carcinogenic that inhibits the initiation and progression of oral carcinoma. It fights against reactive oxygen species and reactive nitrogen species which are the byproducts of smoking, alcoholic beverages, food and dental restorations. Uric acid molecule and peroxidase were the most important salivary antioxidants. In recent studies, they have found that these salivary antioxidants prevent cigarette induced DNA damage as well.

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## LEUKOCYTES



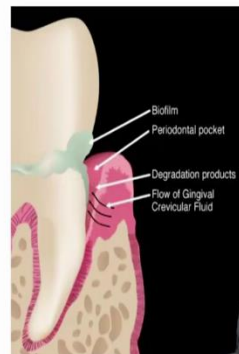
- SALIVA CONTAINS ALL FORMS OF LEUKOCYTES
- MIGRATE FROM THE LINING OF GINGIVAL SULCUS TO REACH ORAL CAVITY
- NEUTROPHILS – GINGIVITIS
- LIVING PMN IN SALIVA – OROGANULOCYTES
- PHAGOCTYIC ACTIVITY
- PREVENTS PLAQUE FROM REACHING GINGIVAL SULCUS



Moving to leukocytes; saliva contains all forms of leukocytes which migrates from the lining of the gingival sulcus to reach the oral cavity. So, the neutrophils will be seen in more number in case of gingivitis and living polymorph nuclear neutrophils in saliva is known as orogranulocytes which has a phagocytic activity and it prevents plaque from reaching the gingival sulcus.

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## SULCULAR FLUID



Moving to the sulcular fluid or gingival crevicular fluid.

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## GINGIVAL CREVICULAR FLUID



- SERUM EXUDATE SECRETED BY SULCULAR EPITHELIUM IN THE GINGIVAL SULCUS
- MORE DURING INFLAMMATION
- CELLULAR & HUMORAL IMMUNITY
- PRESENCE OF CYTOKINES - BUT NO RELATION EXISTS BETWEEN THE DISEASE AND ITS PRESENCE
- CREVICULAR CELLS (Neutrophils+Leucocytes) RESPOND TO CHEMOTACTIC SUBSTANCES, PHAGOCYTOSE MICROBES & GENERATE SUPEROXIDE RADICALS



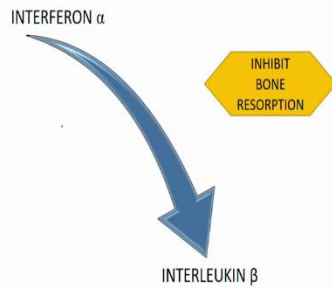
It is a serum exudate secreted by the sulcular epithelium in the gingival sulcus. So, the concentration increases during inflammation, it can either adapt cellular or humoral immunity to make the pathogens move out. There will be presence of cytokines during inflammation. The crevicular cells which is nothing, but the neutrophils and the leukocytes respond to chemotactic substances, phagocytose microbes and generate superoxide radicals.

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Interleukin alpha and interleukin beta will enhance the attachment of polymorphonuclear neutrophils and monocytes to the endothelial cells which will produce prostaglandins and thus responsible for the bone resorption.

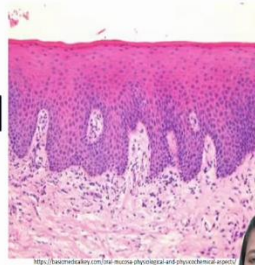
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However, we have interferon alpha which down regulates interleukin beta and inhibits bone resorption in case of periodontitis.

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ORAL EPITHELIUM



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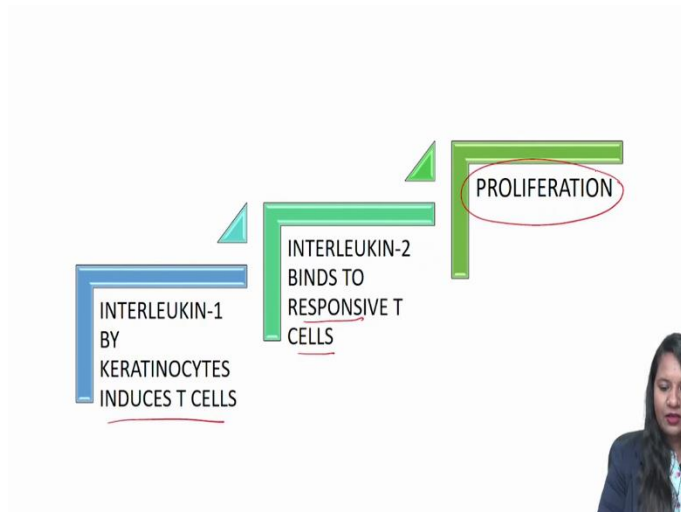


- ORAL MUCOSA HAVE AN EPITHELIAL IMMUNOLOGIC FUNCTION
- ACTIVELY RESPONDS TO INFECTION
- INTEGRATING INNATE & ACQUIRED IMMUNE RESPONSE
- DEGREE OF KERATINISATION AND TURNOVER RATE
- PROTECTION & DIFFERENTIATION – PROTECT DEEPER STRUCTURES FROM MASTICATION AND ABRASIVE NATURE OF FOODSTUFFS



Moving to the oral epithelium: Oral mucosa have an epithelial immunologic function which is very special. It actively responds to infection again just like crevicular fluid, it integrates both innate and acquired immune response. The main important factors were the degree of keratinisation and the turnover rate. So, there will be differentiation occurring in the oral cavity that will protect the deeper structures from mastication and abrasive nature of foodstuff.

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Interleukin-1 produced by the keratinocytes will induce the T cells and interleukin-2 will bind to the responsive T cells and thus leading to the proliferation of the epithelium.

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## EPIDERMAL CELL-DERIVED THYROCYTE- ACTIVATING FACTOR

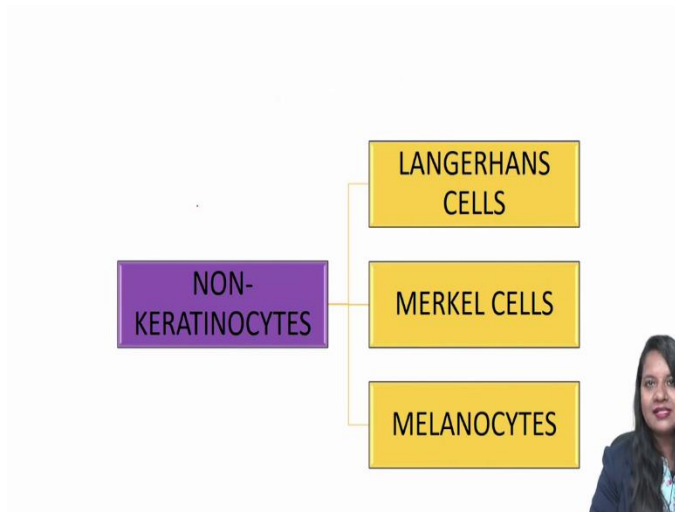


- SUBSET OF KERATINOCYTES
- ROLE IN CONTACT HYPERSENSITIVITY, ANTI-TUMOR IMMUNITY & GRAFT REJECTION
- SHUTTLE BETWEEN EPITHELIUM & REGIONAL LYMPH NODES



There is another factor named epidermal cell derived thyrocyte activating factor which is subset of keratinocytes. It has a role in contact hypersensitivity, antitumor immunity and graft rejection that shuttle between the epithelium and the regional lymph nodes.

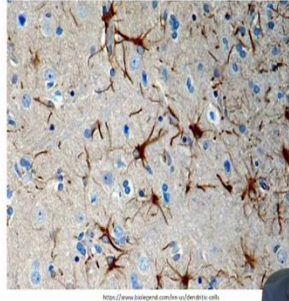
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Non keratinocytes includes Langerhans cells, Merkel cells and melanocytes.

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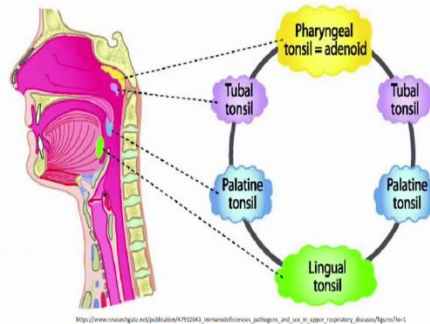
- LANGERHANS CELLS – SUPRA BASAL LAYER – PRESENT ANTIIGEN TO T-LYMPHOCYTES – EITHER LOCALLY/AT LYMPHNODE
- ANTIGEN PROCESSING/MODIFIED MACROPHAGES
- OM INTERACTS WITH ENTIRE LYMPHOID SYSTEM IN CONCERT WITH THE LANGERHANS CELLS TO HELP MOUNT AN IMMUNE RESPONSE



The Langerhans cells were present in the supra basal layer, they present antigen to the the lymphocytes either locally or at a lymph node. So, they are otherwise called as modified macrophages or antigen processing cells. So, the oral mucosa interacts with the anterior lymphoid system in concern with the Langerhans cells to help mount an immune response.

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### WALDEYER'S RING



Waldeyer's ring is nothing, but the lymphoid aggregates which is present in the oropharynx region to prevent the entry of microbes beyond that. So, it includes pharyngeal tonsils, tubal tonsil, palatine tonsil and lingual tonsil.

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## DEFENSE AGAINST INVASION DEPENDS ON FACTORS



- INTEGRITY OF MUCOUS MEMBRANE
- QUANTITY & COMPOSITION OF SALIVA
- QUANTITY & COMPOSITION OF GCF
- LYMPHOID AGGREGATES – WALDEYER'S RING
- BLOOD COMPONENTS TOWARDS SPECIFIC & NON-SPECIFIC IMMUNE REACTIONS
- SPECIALISED HOST CELLS TO RECOGNISE, TRAP & INACTIVATE FOREIGN MICROORGANISMS & CELLS



Though there are various defense mechanism which is present in the oral cavity, the defense against invasion depends on factors such as integrity of mucous membrane, concentration and quantity, quality and composition of saliva, quantity and composition of gingival crevicular fluid Waldeyer's ring, blood components towards specific and non-specific immune reactions and also to the inflammation specialized host cells to recognize, trap and inactivate foreign microorganisms and cells.

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## REFERENCES



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- G.S.Kumar. Orban's Oral Histology and Embryology. August 2015
- H C Girish et al. Oral Defense Mechanisms. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 2016. 1947-62



These are my references.

Thank you.