INTRODUCTION

Introduction

ANATOMY OF TONSILS AND ADENOIDS

I. Palatine tonsils :

They are two masses of lymphoid tissue, situated in the lateral walls of the oral part of the pharynx. Each tonsil is placed in the triangular recess (tonsillar sinus) between the diverging palatoglossal and palatopharyngeal arches. Its medial surface is free and forms a conspicuous projection into the pharynx. Its deep or lateral aspect extends upwards, downwards and forwards beyond the limits of the medial surface and is embedded below the level of the mucous membrane, Inferiorly, it extends into the dorsum of the tongue, superiorly, it invades the soft palate; anteriorly, it may extend for some distance embedded beneath the palatoglossal arch. The tonsil is variable in size and is frequently the seat of inflammatory changes.

The upper part of the tonsil contains a deep intratonsillar cleft, termed the supratonsillar fossa. This cleft does not lie above the tonsil, but actually in its substance, and its upper wall contains a quantity of lymphoid tissue which may reach a large size and extend into the soft palate. The mouth of the cleft is semilunar in shape and is parallel to the curve of the dorsum of the tongue.

The medial surface of the tonsil presents from 12 to 15 orifices leading into deep, narrow recesses, termed the tonsillar crypts, which penetrate nearly the whole thickness of the tonsil and from which numerous follicles branch out into the tonsillar substance.

The lateral or deep aspect is covered by a layer of fibrous tissue, termed the capsule. In most of its extent the tonsil and its capsule can easily be separated from the muscular wall of the pharynx, which is formed in this situation by the superior constrictor with the styloglossus laterally. In its antero-inferior part, the capsule is firmly connected to the side of the tongue, and behind this point it receives the insertion of some muscular fibers of the palatoglossus and palatopharyngeus muscles. In this situation the tonsillar artery, which is a branch of the facial artery, pierces the superior constrictor and at once enters the tonsil, accompanied by the venae comitantes. An important, and sometimes large, palatine vein (external palatine or paratonsillar vein) descends from the soft palate across the lateral aspect of the capsule of the tonsil before piercing the pharyngeal wall. This vessel is responsible for the excessive venous hemorrhage from the upper angle of the tonsillar sinus sometimes encountered in excision of the tonsil. The muscular wall of the

tonsillar sinus separates the tonsil from the ascending palatine artery and occasionally, from the facial artery itself, which, if very tortuous, may be extremely closely related to the pharyngeal wall opposite the lower part of the tonsil. The internal carotid artery lies 25 mm behind and lateral to the tonsil.

The tonsils form part of a circular band of lymphoid tissue (Waldeyer's ring) surrounding the opening into the digestive and respiratory tubes. The anterior and lower part of the ring is formed by the lingual tonsil; the lateral portions consist of the palatine and tubal tonsils; the ring is completed behind and above by the pharyngeal tonsil (adenoids). Smaller collections of lymphoid tissue exist in the interval between these main masses.

Vessels and nerves: The chief artery supplying the tonsil is the tonsillar branch of the facial artery. In addition, it may receive a few twings from the dorsal lingual branches of the lingual artery, the ascending palatine branch of the facial artery, the ascending pharyngeal artery, and the greater palatine branch of the maxillary artery.

One or more veins leave the lower part of the deep aspect of the tonsil and at once pierce the superior constrictor muscle to join the external palatine (paratonsillar),

pharyngeal or facial veins.

The nerves are derived from the pterygopalatine ganglion, through the lesser palatine nerves, and from the glossopharyngeal nerve. The latter, through its tympanic branch, also supplies the mucous membrane of the tympanic cavity.

II. Pharyngeal tonsil :

It is visible to the naked eye during the later months of fetal life and usually increases in size up to the age of six or seven years, after which it not infrequently begins to atrophy. In a child of eighteen months it forms a forwardly projecting pyramidal prominence, the apex of which is near the nasal septum, and the base at the junction of the roof and posterior wall of the nasal part of the pharynx. The prominence consists of a number of folds which radiate forwards and laterally from a median recess, termed the pharyngeal bursa, which runs upwards and backwards for some distance into its substance. The folds consist mainly of diffuse lymphoid tissue, but there are also some deeply placed mucous glands. The pharyngeal bursa lies in the base of the pharyngeal tonsil and presents the appearance of a blind recess. In the embryo, the notochord lies for a short distance inferior to the base of the skull,

in the region of the developing basilar part of the occiptal bone; here it is attached to the endoderm forming the roof of the primitive pharynx, and with subsequent growth of this region, the notchordal attachment draws out an angled recess of the endoderm (the pouch of Luschka) which forms the pharyngeal bursa. The lateral prolongation of the pharyngeal tonsil behind the pharyngeal opening of the auditory tube is known as the tubal tonsil. (Williams and Warwick, 1980).

HISTOLOGY OF TONSILS AND ADENOIDS

In the mucous membrane of the root of the tongue and of the neighbourhood of the fauces there are found accomulations of lymphoid tissue invaginated by the surface stratified squamous epithelium; these are easily seen as well-defined organs, the lingual and palatine tonsils and the median nasopharyngeal tonsil in the posterior wall of the nasopharynx.

Between the glossopalatine and the pharyngopalatine arches are the palatine tonsils, two prominent, oval accumulations of lymphoid tissue in the connective tissue beneath the mucous membrane. The overlying epithelium invaginates to form 10 to 20 deep tonsillar crypts. The stratified squamous epithelium of the free surface overlies a thin layer of connective tissue. The crypts almost reach the connective tissue capsule and are of simple or branching form.

The nodules with their prominent germinal centers are embedded in a diffuse mass of lymphoid tissue 1 to 2 mm. thick, and are usually arranged in a single layer under the epithelium. The epithelial crypts with their surrounding

sheaths of lymphoid tissue are partially separated from one another by thin partitions of loose connective tissue which invaginate from the capsule. In this connective tissue there are always numerous lymphocytes of various sizes, mast cells, and plasma cells. The presence of large number of polymorphonuclear leukocytes is indicative of inflammation which is very common in tonsils. Occasionally islands of cartilage or bone are found, which are probably late sequelae of earlier pathological processes in the tonsils. In the deeper portions of the crypts, the limit between the epithelium and the lymphoid tissue is obscured by an intense infiltration of the epithelium with lymphocytes. The epithelial cells are pushed aside and distorted, so that only a few recognizable epithelial cells remain on the surface. Plasma cells are common here.

The lumen of the crypts may contain large accumulations of living and degenerated lymphocytes mixed with desquamated squamous epithelial cells, granular detritus, and microorganisms. These masses may increase in size and form cheesy plugs, which are ultimately eliminated. If they remain for a long time, they may calcify. The microorgan-
are sometimes the

and carried to other parts of the body, they may be responsible for some general infections.

Many small glands are connected with the palatine tonsils. Their bodies are outside the capsule and their ducts open for the most part on the free surface. Openings into the crypts seem rare.

In the roof and posterior wall of the nasopharynx is the unpaired pharyngeal tonsil. The epithelium on the surface of this tonsil is the same as in the rest of the respiratory passages-pseudostratified cilisted columnar epithelium with many goblet cells. Small patches of stratified squamous epithelium are common, however. The epithelium is not invaginated to form crypts like those of the palatine tonsil but is plicated to form numerous surface folds. It is abundantly infiltrated with lymphocytes, especially on the crests of the folds. A 2 mm. thick layer of diffuse and nodular lymphoid tissue is found under the epithelium and participates in the formation of the folds. The lymphoid tissue of the tonsil is separated from the surrounding parts by a thin connective tissue capsule which sends thin partitions into the core of each fold. Outside the capsule are small glands of mixed character.

Their ducts traverse the lymphoid tissue and empty into the furrows or on the folds.

Unlike the lymph nodes, the tonsils do not have lymphatic sinuses, and lymph is not filtered through them. However, plexuses of blindly ending lymph capillaries surround their outer surface.

The pharyngeal tonsil is usually found in an atrophic condition in the adult, with its ciliated epithelium largely replaced by stratified squamous epithelium (Bloom and Fawcett, 1975).

CHRONIC TONSILLITIS AND ADENOIDITIS

Chronic tonsilitis represents chronic inflammation of the tonsils subsequent to recurrent attacks of acute or subclinical infections, the tonsils may or may not return to a state of complete health. In the latter event Hill showed (Hill, 1960), minute abscesses, having formed in the lymphoid follicles, may become walled off by fibrous tissues and surrounded by a zone of inflammatory cells. It is also possible for inflammatory debris to become trapped in crypts by fibrous occlusion of the openings, and for such debris to expand into neighbouring crypts. Germinal centers can become markedly heperplastic with notable thickening of fibrous septa.

It is possible for these histological changes to be found in tonsils which have not been associated with local symptoms of sore throat, and for there to be no direct relation between polymorphonuclear cell infiltration or fibrosis and the frequency or severity of clinical attacks of sore throat or tonsillitis. But the existence of the histological changes points to chronic infection in the tonsils through lowering of local tissue resistance as a probable cause of unusual susceptibility to acute tonsillitis. That it is indeed a principal cause has been

shown by the beneficial results of tonsillectomy in countless well selected cases (Mawson, 1977).

Stewart and lumsolen (1961), stated that minor symptoms of chronic tonsillitis are a bad taste in the mouth, discomfort in the throat and halitosis, all due to accumulation and discharge of infected cryptic debris. These symptoms alone in some cases have led to the designation of a chronic follicular (Lacunar) tonsillitis, specifically diagnosed by the demonstration of such debris in the crypts on inspection. Similarly when the tonsils are much enlarged giving rise to a thick voice and some embarrassment of respiration and deglutition with perhaps snoring and food faddism, the tonsillitis has been called chronic hypertrophic (parenchmatous) tonsillitis. But at the other end of the scale severe symptoms of sore throat and dysphagia may well be associated with small fibrotic tonsils, harmless in appearance, so called chronic fibroid tonsillitis.

Granulomatous diseases of the pharynx are more likley to be confused with chronic bacterial tonsillitis. These include tuberculosis, syphilis, pathogenic mycosis and collagen disease.

Pharyngeal tuberculosis is invariably secondary to active pulmonary disease, although bovine variants (from infected milk) can also cause primary pharyngeal infection. In this disease, the paryngeal mucosa will be found to have irregular shallow ulcerations. These contain pale granulations from which the acid-fast mycobacterium can be smeared or cultured. Involvement of the pharynx by lupus erythematosus is usually associated with facial or systemic disease and superficial ulcerations that heal by scar formation occur in the throat, although recurrence is possible. Pharyngeal gummas commonly form as painless swellings that later ulcerate before healing by scaring. Important sequelae are persistent perforations of the soft palate or tonsillar pillars. Leprosy produces pharyngeal nodules or ulcerations that subsequently heal with extensive tissue loss and scarring. Actinomycosis results in the formation of firm, painless mucosal swellings that may later ulcerate and suppurate. The organism can be demonstrated with the discharge by its characteristic sulpher granules. Among the mycoses, blastomycosis may produce irregular superficial pharyngeal ulcerations with soft granulated bases, whereas coccidioidal granulomas result in diffuse granular thickening of the soft palate and tonsillar pillars with superficial epithelial erosions

(Simpson et al., 1967, Beeson and Mc Dermott, 1975 and Kornblut, 1980).

Hyperkeratosis of the tonsils (keratosis pharyngeus):

It is characterized by the development of white horny projections on the lymphoid tissues of the pharynx as well as on the tonsils and adenoids. Debilitated patients, neurotic individuals and women may be predisposed to the condition. However, hyperkeratosis may be readily confused with chronic follicular tonsillitis.

The fungus leptothrix buccalis was formally considered to be the causative organisms, but this theory is now in doubt, as the fungus is known to be a common saprophyte of the oral cavity. Somehow lymphoid keratosis, which may be related to some metabolic disturbance, results from excessive cornification within the tonsillar crypts. Examination of the throat reveals multiple discrete, white, excrescent projections from the tonsillar crypts or other pharyngeal lymphoid tissue. Removal of the keratotic projections invariably leaves a bleeding base. (Hill, 1960 and Ballenger, 1969).

Tonsilloliths (Calculi of the tonsils):

Spiculated concentrations of varying size and consistency can form about or within the substance of the tonsils (Harding, 1962).

Repeated episodes of inflammation may produce fibrosis at the openings of the tonsillar crypts. Bacterial and epithelial debris then accumulate within these crypts and contribute to the formation of retention cysts. Calcification occurs subsequent to the deposition of inorganic salts, and enlargement of the formed calculus takes place gradually. This process may be stimulated by the oral flora, which may include fungi or actinomyces-like organisms. The resultant calculus may be quite large and may even ulcerate through the tonsillar surface (Samant and Cupta, 1975).

Direct examination of the throat invariable reveals the tonsillolith within the tonsil. Later on, inflammation may be present with enlargement of the tonsil (Kornblut, 1980).

Adenoidal Hypertrophy :

Enlargement of the nasopharyngeal lymphoid tissue or pharyngeal tonsil is relatively common in preadolescent children. The cause of this enlargement is unknown, but

it may represent a response to repeated infections or may only reflect generalized lymphoid hypertrophy (Handelman and Osborne, 1976).

Chronic Adenoiditis :

Chronic infection of the adenoids is commonly the end result of acute inflammation that have failure to resolve completely. This condition may follow recurrent purulent rhinosinusitis oftenly associated with chronic tonsillitis. Adenoidal hypertrophy may be the consequence, with the obstruction of the posterior nasal choanae and eustachian tube orifices.

Inflammation may be bacterial or viral in origin, although consideration should be given to other disease states that may cause adenoiditis e.g, tuberculosis, syphilis and other collagen disease and neoplasm (Hill, 1960).

Examination of nasopharynx reveals the presence of hyperplastic lymphoid tissue that is chronically inflamed. Purulent discharge of mucopus is frequently present (Kornblut, 1980).

FUNCTIONS OF TONSILS AND ADENOIDS

As Gray stated, (Gray, 1977) the functions of tonsils and adenoids are so closely interrelated, they should be thought of as a whole.

Tonsils :

The crypts of the tonsils tend to become filled with desquamated epithelial cells, food debris and bacteria. The lymphocytes move to and fro, from the germinal centers to the crypts. Each tonsil is embedded in the tonsillar fossa between the anterior and posterior palatine folds. With each movement of the palate, the tonsil is squeezed between these folds, thus tending to push the contents of the crypts into the lymphoid tissue (Fig.1). The alternate pressures by squeezing and relaxing, increase the lymph flow.

In very large tonsils (the allergic type) the crypts tend to be emptied medially into the mouth and these cases often take longer, clinically, to develop their resistance to infection than those with small tonsils.

Antistreptolysin, interferon and types of gammaglobulin (Wood, 1973) are produced, thus helping to combat and prevent infection. Tonsilsplay a part in specific cell-mediated

immunity and may also be a barrier to the development of certain kinds of malignancy (Hurtads, 1975). They also have considerable effect on the general resistance of the body as preventing Hodgkin's disease (Vianna et al.,1971), multiple sclerosis and septicaemia (Poskanzer, 1965). Indeed, it can be said that the function of the tonsils is to have tonsillitis which is the best way to stimulate antibody formation.

Adenoids :

They assist closure of the post nasal space, particularly in the wide square type (Maran et al., 1971). The atrophy of the adenoids by early teens is compansated for by the growth of the palate.

There is some immunity function, for lymphoid follicles are present, but there are only folds and no true crypts, so chronic infection rarely occurs.

CELL POPULATION OF TONSILS AND ADENOIDS

Electronmicroscopic studies of normal human tonsil have shown that its cell population consists of lymphoid cells (80-90%) in various stages of development, plasma cells (5-20%), and a small number of monocytes and polymorphonclear leukocytes (Zucker Franklin, 1972). Two populations of lymphocytes can be indentified :

The bone marrow derived or (bursa equivalent) thymic independent (B)-lymphocytes and thymic dependent(T)-lymphocytes.

The tonsil's B-lymphcoytes range in diameter from 4-8 u. The cells are generally spherical with numerous long microvilli. The cell membrane in some B-lymphocytes appear to be indulated with a relatively smooth surface harboring few short microvilli. The B-lymphocytes can be recognized by the presence of surface immunoglobulins and complement receptors and their ability to form rosettes with sheep erythorcytes in the presence of amboceptor and complement (EAC- rosette). B-lymphocytes are concerned with the synthesis of immunoglobulins (Morag, et al., 1975).

The T-lymphocytes are spherical in shape and range from 3-5u in diameter. Usually their surface is smooth with a few stud-like microvilli. These cells can be identified in the tonsils by their ability to form rosettes directly with sheep red cells, (E-rosette) (Lay,et al., 1971) and by the presence of human T-lymphocytes antigens (HTLA), subpopulation of T-lymphocytes are able to form high avidity E-rosettes and/or possess receptors for the (Fc) portion of IgG or IgM molecules (Brochier, et al., 1978). T-lymphocytes are responsible for cell-mediated immunity.

The ratio of B-lymphocyres to T-lymphocytes in the tonsils may vary form one individual to another (Zucker-Franklin, 1972). The distribution of T-and B-lymphocytes on tonsils varied according to the age of the donor, T-lymphocytes increase in number with age while B-lymphocytes decrease in number (Brochier, et al., 1978). Tonsillar lymphocytes of female patients showed higher values of T-lyymphocytes than those of male patients(Awad, et al., 1982).

Both populations on appropriate stimulation by antigen. proliferate and undergo morphological changes. The B-

lymphocytes develop into plasma cells series. The mature plasma cell is actively synthesizing, and secreting antibodies and has a well developed rough surfaced endoplasmic reticulum. T-lymphocytes transform to lymphoblasts shown by the electronmicroscope to be devoid of rough-surfaced endoplasmic reticulum although there are abundant free ribosomes, either single or as polysomes which are basophilic so that they show superficial resemblence to plasmoblasts in light microscope. These cells are concerned with the synthesis of lymphokines (Romagnani, et al., 1977). No antibody can be detected in T- lymphoblast cytoplasm using immunofluorescent staining methods.

Brocheir et al., (1978), found that the lymphocytes distribution in adenoid appear to be very similar to that from tonsils from the same age.

T-lymphocytes subpopulation :

T-lymphocytes upon stimulation with an immunogen give rise to several types of effector cells with different functions.

1/ TC-cells cytotoxic or killer cells : which eliminate foreign cells directly by lysis, (Greenberg, et al., 1973).

2/ TD- cells : which are responsible for delayed hypersensitivity. These cells release a variety of polypeptides called lymphokines (Schlossman and Hudson, 1973).

3/ TH-cells : which usually cooperate with B-lymphocytes in antibody formation (Lachmann, 1977). Specific TH-cells recognise and respond to antigens only when it is presented by macrophages (Turk, 1973).

4/ TS-cells : These specifically inhibit antibody production, they are believed to play an important role in regulating immune response and may be involved in the mechanism of tolerance.

5/ TA-cells : which serve the function of an amplifier in the maturation of antigen-specific killer TC-cells. TA cells apparently recognize a macrophage-processed or native cell surface antigen, and some how stimulate TC cells precursors that recognize other antigens on the same target cells to proliferate and differentiate to TC-effector cells, (Greenberg, et al., 1973).

IMMUNOLOGICAL ROLE OF TONSILS AND ADENOIDS

Faucial tonsils (tonsils) and pharyngeal tonsils (adenoid) are part of the complex lymphoid tissue encircling the pharynx referred to as Waldayer's ring. Both are part of the alimentary tract lymphoid tissue mainly concerned in the defence mechanisms of the body (Gray, 1977). The tonsils develop from the 2nd pharyngeal pouch in close proximity to developing embryonic thymus lymphoid cells which appear near the epithelial surface during the third month of gestation and organize as follicles after the six month. It has been suggested, due to the representation of the tonsillar structures, that tonsillar tissue may be more reactive immunologically than other developing lymphoid tissue in early weeks of life (Godrick, et al., 1971).

THE ANATOMICAL SITES OF LYMPHOCYTE POPULATION IN TONSILS:

a) B-lymphocytes area :

Curran and Jones (1977) demonstrated that the follicular aggregation of B-lymphocytes is a prominent feature of the cortex. In the unstimulated tonsil they are present as spherical collection of cells, termed primary nodules but after antigenic challenge they form secondary

follicles which consist of a corona or mantle of concentrically packed small B-lymphocytes surrounding a pale staining germinal center which contains large, often proliferating, lymphoid cells, scattered convential reticular macrophages and the specialized dendritic macrophages with elongated cytoplasmic processes and few if any lysosomes. Germinal centers are greatly enlarged in secondary antibody responses as if they are sites of B-lymphocytes memory. Following antigenic stimulation, differentiating B-lymphocytes appear and become plasma cells in the medullary lymphoid cords which project between the medullary sinuses.

Morag and Orga (1975),demonstrated that the majority of IgA forming cells are found close to the basement membrane of the tonsil, the glandular tissue in the epithelium, and in the glandular centers.

IgG and IgM containing cells are scattered throughout the lymphoid tissues, including the germinal centers. Most of IgD bearing cells are seen in the mantle zone surrounding the germinal centers,while cells containing IgE are seen frequently scattered throughout the tonsillar tissue.

b) T-lymphocytes area :

T-lymphocytes are largely confined to a region referred to the paracortical (or thymic dependent) area. If one looks to lymphatic tissue taken from children with selective T-lymphocytes deficiency or neonataly thymectomized mice, the paracortical region is seen to be virtually devoid of lymphocytes (Curran and Jones, 1977).

The secretory immune function of the tonsil :

The tonsils, Peyer's patches and the appendix constitute the subepithelial lymphoid system which lies immediately beneath the epithelial lining of the upper respiratory and gastro-intestinal tracts. This system is primarily concerned with the production of immunity by slow introduction of samples of the invading organisms into the lymphoid system (Wright, 1950, Meretey, et al., 1972).

Numerous investigators postulated an immunological function for the tonsil based solely on its lympho-epithelial structures and prediliction for infection (Wright, 1950, Chryssikos, et al., 1965 , Malcomson, 1967).

The tonsils have often been considered as the primary line of defence against respiratory infection because of their location at the portal of entry for many organisms (Oettgen, et al., 1966, Veltri, et al., 1972). The ability of the tonsils to capture a variety of inhaled and ingested antigens has been demonstrated by Merlier and Silberschrouit (1972), and Surjan and Surjan (1973). In this way Ransome (1973) suggested that the tonsils can be visualized as important sites of contact with external antigens which build up the immunological experience of the individual. In addition to this " gate keeper " site and function of the tonsils, the tonsillar tissue may be more reactive immunologically than other developing lymphoid tissues e.g, spleen and appendix, in the early weeks of life (Godrick and Patt, 1971).

Stewart and Lumsolen, 1961 stated that it appeared probable that the chief function of the tonsils was to promote immunity to infection during early access by the mouth. Later, Orga (1969) reported that the tonsils may be involved in production of antibodies which can provide local resistance to pathogenic organisms.

The tonsils may exert immunological functions in different ways. First, they may be important lymphoid

organ involved in development of B-lymphocytes system. Second, they may be important organs of contact between foreign material and lymphocytes, and hence, sites of clonal expansion and cellular differentiation.

Brandtzaeg, et al., (1978) provided supporting evidence for the latter possiblity and also reported that stimulated tonsillar lymphocytes are disseminated to other sites.

The tonsils were found to hold the complete set of cells necessary for primary antibody response (Watanabe, et al., 1974) and children who were previously exposed to antigenic stimulation via the tonsils, contain immuno-competent cells in their tonsils, that are capable of mounting secondary immune response (Platts-Mills and Ishizaka, 1975).

As stated previously both T and B-lymphocytes have been demonstrated in the tonsils(Rabellino, et al., 1971 Unanue, et al.,1971). Much evidence suggests that there are proportionately more B-lymphocytes in the tonsils than in peripheral blood (Delespesse, et al., 1976, Wilson, et al., 1976).

Differentiation of B-lymphocytes in tonsiller germinal centers was found to give rise, mainly, to immunoglobulin G (IgG)- producing plasma cells. However, heavy chain expression can switch in direction u (mu)→ (gamma) → (alpha), hence plasma cell precursors pass through a sequence depicted as IgM — IgG —— IgA cells (Cooper et al., 1972, Cooper et al., 1976). Gitlen and Saski (1969) identified surface IgG, IgA and IgM on tonsillar B-lymphocytes. However, surface IgG- carrying cells constituted the majority.

Delespesse et al. (1976), Ferranni et al. (1976) and Wilson et al., (1976) reported that distribution of immunoglobulin receptors borne by tonsiller B-lymphocytes have been inconsistent, especially with regard to IgG and IgA receptors, but IgM and IgD receptors are more frequently encountered.

The tonsils are at their most active stage of development and growth in early childhood when the need for immunity is greatest, then they stop their active growth at puperty and tend to atrophy in adult life when the need for immunity is least as the immunologiocal system of the

body has been developed fully (Wright , 1950). However, tonsillar capacity to produce IgA may be retained untill older age if there is relatively low serum levels of IgA (Brandtzaeg et al., 1978).

The tonsils have been shown to synthesize various types of immunoglobulins and specific antibodies in vivo and in vitro (Malecki, 1958, Gitlen and Saski, 1969, Orga, 1971, Peska, 1971, Ishikawa et al., 1972, Hoffmann et al., 1974, Platts-Mills and Ishizaka , 1975).

As there are no afferent lymphatics, microorganisms and other matters must reach and enter the tonsils some others way. Olah and Everett (1975), Curran and Jones (1977) and Owen and Nemanic (1978) reported that reticular crypts epithelium is the route of antigen transport into the tonsil.

Functions of the tonsillar B-lymphocytes system have been studied by localizing immunoglobulin-producing cells in tissue sections. (Chiappino and Corbetta, 1962),estimating the formation of immunoglobulins and antibodies in cultures (Sloyer et al., 1973, Platts-Mills and Ishizaka, 1975) and quantification of immunoglobulins in tonsillar extracts (Siegel and Wilke, 1976).

It has often been suggested that the cell population of each germinal center is monoclonal and may be monospecific with regard to the antigen stimulating its development (White, 1958, Sordet et al., 1970). Monoclonality can be demonstrated by showing that all cells arising from a single center are restricted to the production of a single type of antigen combining site (Wernet et al., 1972, Rudders et al., 1973). Although more than one type of immunoglobulin could be found within a germinal center, this does not exclude the possiblity of the immunoglobulins being monospecific with regard to the stimulating antigen (Curran and Jones, 1977).

Koburg (1967) studied the proliferation and migration of tonsillar B-lymphocytes and claimed that uncommitted small lymphocytes in germinal center respond to a particular antigenic stimulation in two ways. First, some of them might divide and become large lymphocytes (immunoblasts) which eventually begin to synthesize the immunoglobulins and become plasma cells. Second, other B-lymphocytes might undergo mitosis and migrate into the lymphoid follicle to constitute a pool of memory cells. Cells leaving the lymphoid follicle and entering the crypt epithelium would on meeting the appropriate antigen undergo a secondary immune response to synthesize the immunoglobulins.

Schmedtje and Batts, (1973) suggested that relatively few of the vast members of plasma cells in the epithelium emigrate into the crypt lumen. They also reported that aggregation of plasmocyte series containing either IgG, IgM or IgA, were present in the crypt epithelium. Mature plasma cells of the aggregation were found around the walls of blood sinusoid located under the epithelium which suggested secretion into these sinusoids. Some immunoglobulins secreted by plasma cells are released directly into the lumen of the blood sinusoids and indirect evidence has suggested that systemic immunity can originate and be boosted by reactions in tonsils (Parkinson, 1951).

Wood (1973) reported that immunological functions of the tonsils include, the production of interferon, thus they help to combat and prevent viral infection.

The tonsils are able to handle organisms and antigens in such a way that a suitable humoral or cell-mediated response ensues. The productive role of the tonsils exists only as long as they are not diseased. When they are chronically infected theirfunctions are likely to be lost or altered to the extent that it no longer exerts

any beneficial role, but they tend to serve as a nidus for discharge of infected material and to encourage infectious afflictions (Wood and Oberhand, 1972).

Immunoglobulin producing cells are present in all compartments of the tonsil : the germinal centers, mantle zone, extrafollicular areas and reticular parts of the crypt epithelium with general predominance of IgG producing cells, followed by IgA-, IgM- and IgD- producing cells. On the other hand, IgE- producing cells were lacking (Brandtzaeg, et al., 1978). Absence of IgE- producing cells was reported by other authers (Peska, 1971 Platts-Mills and Ishizaka, 1975). Conversely, Tada and Ishizaka (1970) and Ostergaard (1975) reported an astonishingly high percentage of IgE surface-bearing cells in the tonsils. Subsequent studies have indicated that mast cells, showing bright membrane fluorescent staining of IgE, may erroneously be taken as IgE- producing plasma cells when the immunofluorescent technique is used (Felt kap-Vroom, et al., 1975).

THE BODY REACTION TO VIRUS INFECTION

Viral infection in humans may be either asymptomatic or cause a clinical disease from which the individual fully recovers. As a rule, a virus gains entrance into the human by either the respiratory or the alimentary tract, less commonly by other mucous membranes or by the skin. If the virus causes disease it must replicate, spread and disturb or destroy enough cells to induce symptoms (Bellanti, 1971).

Direct virus effects upon immune reactivity:

Fulginiti (1978), reported that factors which influence the effect of viral infections in the immune systems are:

The nature of the virus-cell relationship.

The stage of development of the immune system.

The degree of involvement.

The extent of infection whether it affects one part of the immune system but spares others.

The capacity for repair in the infected cell

a) Extracellular (type I spread): Infectious virions are released from the cell to spread in the extracellular milieu. Many types of viruses spread by this route,at least some of the time.

b) Intracellular (type II spread): Virus spreads from cell to cell through desmosomes of intracellular bridges (cell fusion) without contact with the extracellular milieu. The surface of infected cells often contain viral antigens. The best examples are herpesviruses. Such viruses may spread by the extracellular (type I) route as well.

c) Nuclear (Vertical; type III spread): Viral genome is latent or integrated into host genome and is passed from parent cell to progeny during mitosis. Phenotypic evidence of viral presence may be striking (many virus-specific antigens on the cell surface) or absent, and the stability of integration is variable. C type oncornaviruses are the best example.

a) Local : Viral infection is largely confined to a mucosal surface or organ e.g, rhinoviruses (respiratory epithelium) and duoviruses (gastrointestinal epithelium).

b) Primary hematogenous : Virus is inoculated directly into the bloodstream, with subsequent organ dissemination. The best examples are arboviruses and hepatitis B virus.

c) Secondary hematogenous : Initial virus infection and replication occur on a mucosal surface, blood stream invasion occurs afterward by hematogenous dissemination to target organs. The initial mucosal phase is often relatively asymptomatic e.g, common viral exanthems, poliomyelitis, mumps.

Immunologic reaction involving viruses :

A variety of immunologic reactions involving viruses have been shown to occur in vitro, these may also be operative in vivo.

Humoral defense mechanism :

Antibodies probably constitute one of the more important mechanisms of host resistance to viral infection, and play a role in recovery from established infection. Virus-

antibody reactions that have been defined in vitro include neutralization (both with and without complement activation). Complement activation facilitate lysis of infected cells and opsonization and also virolysis. While complement-independent neutralization (Notkins, 1974) involves antibodies of the IgG, IgM, IgE and IgA classes which have been shown to neutralize the infectivity of virtually all known viruses, this is the most important virus-antibody interaction. The reaction is highly specific, as the antibody is synthesized in response to viral antigens. Viral spread by the type I route is most readily halted by neutralization. He studied also, that with viruses that spread from cell to cell by the type II route (e.g, herpes virus group), neutralizing antibody alone will be ineffective once infection is established, as it has no effect on the virus unless viral antigens are expressed on the cell surface. He explained that the mechanism of viral neutralization involves combination of antibodies with the virus coat proteins, thus blocking viral replication. In most cases the antibodies prevent cellular adsorption and penetration of the virus,but in some instance antibody coating of extracellular virus may interfere with subsequent intercellular events e.g, uncoating.

Oldstone (1975) reported that the exact mechanism of neutralization is unclear but presumably involves a change in the steric conformation of the virus surface or actual covering of receptor sites, either of which prevents the virus from gaining entry to the cells.

Donovan and Soothill (1973), reported that IgA often plays a role in viral infections which begin on or are confined to mucosal surfaces. In the case of rhinovirus infections and perhaps parainfluenza infections, where viral replication is confined to respiratory epithelium, resistance to infection is determined by surface IgA.

For viral infections which begin on a mucosal surface and then disseminate by hematogenous spread e.g, poliomylitis and measles local antibody may completely prevent infection. However, disease can also be prevented by serum antibody even though viral replication still may occur on the mucosal surface.

So, persons immunized parenterally with inactivated poliovaccine possess serum antibody to poliovirus but not local colonic or oropharyngeal secretory antibody(Orga, 1971).

Complement facilitated neutralization: In the case of some viruses with an outer lipoprotein coat (enveloped viruses), complement may enhance neutralization by antibody. The mechanism of this enchancement varies with virus type. In some instances, it may produce actual disruption of the lipoprotein coat, irreversible neutralization and loss of infectivity, in others, complement may enhance antibody induced-steric changes (Notkin, 1974).

Complement facilitated host cell lysis : The combination of antibody and complement may cause lysis of cells that have viral antigens on their outer membrane e.g. cells infected with herpesviruses (Ennis, 1973).

Opsonization : With a few viruses, antiviral antibody may promote phagocytosis by macrophages, with subsequent digestion of the virus in phygolysosomes i.e, it is opsonizing antibody (Winkelstein, 1973).

In the case of influenza,the virus has a surface protein, neuraminidase, that enzymatically cleaves the viral receptor (N-acetylneuraminic acid) from the host cell membrane. Neuraminidase has no known role in infection of cells but does function by facilitating release of progeny virus.

Antibody against neuraminidase has been shown to limit viral replication and spread but not to neutralize the virion. Presumably similar nonneutralizing antigen-antibody interaction may be found for other viruses(Drutz and Mill, 1978).

Cell-mediated defence mechanism ;

Delayed hypersensitivity to many viruses can be identified in the immune host using skin test reactivity e.g. mumps, or in vitro measures such as a blastogenic response of lymphocytes to viral antigens, leucocyte migration inhibition, and antibody dependent cytotoxicity (Abdel-Wahab, 1982, and Abdel-Wahab, et al., 1983). Some cell mediated reactions which appear to be important in host resistance to or defense against viral infection follow :

a) Lymphocyte cytotoxicity : Virus-infected cells are subject to lysis by sensitized lymphocytes. This is especially true to enveloped viruses, such as those of the herpesvirus group, where the infected cell membrane is often covered with viral antigens (Rand, 1977). However, it is also true of some nonenveloped viruses, such as those of the coxsackie virus group (Bendinelli, 1975).

b) Lymphokine production : Sensitized lymphocytes release lymphokines in response to viral antigens. The best characterized of these from a virologic standpoint is interferon.

c) Interferon : They are a family of low molecular weight proteins elaborated by infected host cells to facilitate protection of neighbouring noninfected cells from viral infections by direct spread. They may be produced in vitro by cultured cells or by intact animals in response to a variety of infected agents e.g, viruses, rickettsiae, protozoa as well as to bacterial endotoxins (Metz, 1975).

The gamma type of interferon is specifically released by sensitized T-lymphocytes upon rechallange with the same virus. Its action is very specific. Alpha and beta types of interferons are released from infected cells almost as soon as virus is produced, thus this is available much sooner than antibody (Isaacs,1961), but gamma type interferon is released from activated presensitized T-lymphocytes few days following infection.

of viral (but not host cell) messenger RNA. It does not block viral adsorption or cell penetration. Interferon is highly host-specific, but it is not virus-specific, having inhibitory activity against a wide variety of viruses . (Grossberg, 1972).

Ho and Armstrong (1975), first reported that, in addition to being released from epithelial and fibroblastic cells infected with virus, interferon is also released from lymphocytes, thus allowing it to be classed as one type of lymphokines with a wide range of activity.

d) Phagocytosis : Phagocytosis of viruses by macrophages or less commonly, by neutrophils (especially in the presence of antibody) may be responsible for resistance to infection and illness e.g, Enteroviruses (Stossel, 1975).

VIRUS INFECTIONS OF LYMPHATIC TISSUES OF UPPER RESPIRATORY TRACT

Viruses were first distinguished from other microorganisms on the basis of the size, as determined by filteration techniques. Most infectious virus particles, or virions,are smaller than any bacteria and are below the limit of resolution of the light microscope. The smallest virions are 20 to 30 nanometers in diameter (1 nanometer, nm=10^{-9} meter) and are the simplest agents known to cause infectious diseases in man. In addition to their size, virions may be distinguished from other microorganisms by the fact that they contain only a single type of nucleic acid, either DNA or RNA. RNA-containing viruses are unique in possessing this type of nucleic acid as their genetic material. Virions lack metabolic activity and do not possess ribosomes or many of the enzymes necessary for macromolecular synthesis, although they may contain certain specialized enzymes. As a consequence, viruses depend on the cellular processes for their replication and are obligate intracellular parasites. Their replication process involves intracellular dissolution of virions into their macromolecular components, followed by

synthesis of viral proteins and nucleic acid, whose structures are specified by the viral genome. The individual viral macromolecules are then assembled into progeny virions in yields as high as thousands of particles per infected cell. This type of replication cycle differs markedly from division by binary fission, which is the process by which bacteria multiply (Copan, 1981). The one feature common to all viruses is a conversion to a non-infective form during the process of multiplication, this non-infective " ectipse phase " is the essential difference between viruses and rickettsiae (Walter and Israel, 1974).

Klein, (1975) classified viruses isolated from tonsils and adenoids in into the following categories :

1/ Viruses that are well documented causes of pharyngotonsillitis or adenoiditis e.g, adenovirus, Epstein-Barr virus, group A coxsackie viruses and herpes virus hominis.

2/ Viruses that are frequent causes of diffuse upper respiratory infection including pharyngotonsillitis, e.g, respiratory syncytial viruses, rhinoviruses, and the

3/ Viruses responsible for systemic disease which may include inflammation of the tonsils and adenoids e.g, measles, hepatitis, herpes, and some arboviruses e.g, Sindbis.

Epstein-Barr virus infection :

Epstein-Barr virus (EBV), a member of the herpes group of viruses, is the cause of heterophile-positive infectious mononucleosis and of most heterophile-negative cases, and of occasional cases of tonsillitis and pharyngitis in childhood (Niederman, et al., 1968). Rarely it may involve the liver or central nervous system as primary site of infection. This virus is strongly implicated as having causal relationship to African Burkitt lymphoma and to nasopharyngeal cancer (Ziegler, 1981).

The route of natural transmission of EBV is not diffintely known, but the dominating role of close oral contact has been long suspected (Hoagland, 1955).

EBV is a lymphotropic virus, its transformed and infected cells are B-cells lymphocytes, which have EBV receptors on their surface (Jondal, and Klein, 1973, Pattengale et al., 1973, Epstein and Achong,1973, Klein, 1973, and Pattengale,et al., 1974). EBV has been regularly demonstrated in lymphocyte cultures from patients with acute infectious mononucleosis, where it may remain in a latent form for years and may be a source of transfusion mononucleosis (Diehl et al.,1968, Henle, et al.,1968,

Since the virus is lymphotropic, it can be postulated that lymphoid tissues in the oropharynx provide the source and a target of EBV, and this suggestion has been indicated by virus isolation from throat washing which indicate that the virus may replicate in lymphoid cells in this site (Chang and Golden, 1971, Golden, et al., 1971, Pereira, et al., 1972, Gerber, et al,1972, Miller, et al., 1973).

Yamamoto, (1976) reported that tonsil lymphocytes from children and adults can be transformed by EBV in vitro. So, he suggested that tonsil lymphocytes are targets to EBV.

Tischendorf, et al., (1970), was able to confirm a role for EBV in tonsillitis and he emphasized the inability of young children to develop hetrophil antibodies subsequent to EBV infections Jerner, et al.,(1972), using experimentally infected primates, implicate the tonsils as a primary focus of infection with EBV.

Veltri, et al., (1975), demonstrated a serological evidence of elevated IgM specific antibody titers to

the EBV-early antigen complex in patients with tonsillitis. The propensity of the virus for the palatine tonsils, a rich source of B-lymphocytes,was suggested.

Veltri, et al., (1976) and (1978) demonstrated the EBV genome in tonsil-derived lymphocytes of patient with exudative tonsillitis. They also reported that the tonsils may serve as a reservoir for EBV carrying lymphocytes and a basis for recurrent disease.

Goode and Coursey,(1976) suggested that the tonsillar lymphoid tissue serves as a reservoir and possible replicating milieu for the EBV. Epstein and Achong. (1973) reported that the EBV replicates in the oropharynx with the production of infectious virus particles into the buccalfluids. Niederman, et al., (1976), reported that EBV could be demonestrated in saliva and oropharynx specimens.

Veltri, et al., (1978), detected only the Epstein-Barr nuclear antigen,not early antigen,in the lymphocytes from the tonsils of recurrent exudative tonsillitis patients. Brichacek, (1981), found the Epstein-Barr genome in

exudative tonsillitis. Grandy, et al., (1982) reported that EBV is a significant causal or associative agent in acute exudative tonsillitis.

EBV infections of tonsils are acquired at any early age in lower socioeconomic groups; in economically privileged children infection is often delayed until adolescence and young adulthood(Sawyer, et al., 1971, Hallee, et al., 1974). In the general population, no distinct seasonal occurence of EBV infection has been reported (Heath et al., 1972, Henke et al., 1973).

Neiderman (1976), suggested that persistance of oropharyngeal virus for several months after acute illness appeared to be due to the presence of the agent in the saliva, rather than to its excretion from the posterior pharynx or tonsil, so he implicated the salivary glands as one of the sites of production of EBV. Morgan et al (1979) supported that suggestion.

Epstein-Barr virus infection is characterized serologically, by an elevated absorbed heterophile-antibody titer and the development of EBV immunoglobulin M(IgM)

et al., 1972, Schmitz and Scherer, 1972, and Nikoskelainen et al., 1974). Sumaya (1977), reported that, the EBV-specific IgM antibody has been included in surveys to identify recent infections.

Speirs, et al, (1982), studied immunoglobulins production by tonsil lymphocytes , before and after EBV transformation, he found that secreted Ig from tonsil lymphocytes was mainly IgA or IgG, after transformation IgM predominated with adult cell lines, and IgG or IgM, with cell lines from children.

High antibody titers against EBV are also present in 30-40% of cases of Hodgkin's disease in some patients with sarcoidosis, and in systemic lupus erythematosus (Evans and Neiderman, 1982).

Adenoviruses infection :

Adenovirsues derived their name from the fact that they were first isolated from adenoid tissues (tonsils) and have a certain affinity for lymph glands.

from surgically removed human tonsils and adenoids. In 1954, Hilleman and Werner, reported isolation of similar agents from military personnel who were ill with febrile respiratory disease. Several names were used for the new virus,but in 1956 the term adenoviruses was adopted (Enders, et al., 1956).

The frequent association of adenovirus with human tonsils and adenoids has long been known. Virus is present in these tissues without evidence of clinical illness and can be revealed by growing tissue fragments in vitro. Apparently, adenovirus may persist in tonsils and adenoids as a latent infection. There have been few investigations on the relationship of adenovirus to the tonsils and adenoids at the cellular level. In cultures of adenoids and tonsils, cytopathic effects characteristic of adenovirus are observed in epithelial and fibroblastic cells (Rowe, et al., 1955, Evans, 1958, Schlesinger, 1961, Israel, 1962).

Likhachev ,et al, (1972), found that adenoviruses have a role in the etiology and the pathogenesis of chronic tonsillitis and adenoiditis. Van der veen and Lambriex (1973), provided suggestive evidence that lymphocytes in

naturally infected tonsils and adenoids represent one of the cell types which may harbor adenovirus or viral precursor.

Strohl and Schlesinger (1965), reported extensive studies on the possible role of fibroblasts in the persistance of adenovirus infection. They suggested that fibroblasts might represent the major, if not the only susceptible cell type in primary cell suspensions prepared from tonsil and adenoids, implying that lymphocytic cells were refractory to adenovirus, so this suggests that the lymphocytes are not the principal cell type which determines the persistence of infection in vivo It is conceivable that the lymphocytes only play a role in initiating infection of tonsils and adenoids. Lymphocytes infected with virus at the primary site of infection would enter in the tonsillar and adenoid tissues. Virus would then be passed from these cells to other cell types. The continuous presence of a small number of infected lymphocytes in tonsils and adenoids might be explained by assuming that some cells may carry virus or viral percursor for a considrable time. Another possibility is that lymphocytes constituted the target of adenovirus produced by tonsillar

and adenoid cells. Studies of Nasz, et al., (1971) employing the immunofluorescent antibody technique, favor the hypothesis that adenovirus or adenovirus antigen may be present in lymphtocytes, at least temporarily. Kurian, (1961), and Kurian et al., (1962), in a limited series of cultures of tonsils and adenoids reported the presence of latent adenoviruses in these tissues.

The study of Devi,(1968) indicated that nearly 80% of tonsillar and adenoid tissue specimens collected,were positive for adenovirus complement fixing antigen. He also found that of the patients who yielded adenoviruses from their in vitro tonsils cultures, 75% showed adenovirsus antibodies, whereas of those who did not, only 44.4% had adenovirus antibodies in their sera.

In the respiratory tract, adenoviruses may cause a variety of clinical manifestations ranging from pharyngitis to bronchitis, croup and pneumonia. Adenovirus infections are widely distributed and common. Most infections occur

Other disease syndromes caused by certain specific serotypes of adenoviruses are pharyngoconjunctival fever (PCF) and epidemic keratoconjunctivitis (EKC). Several other disease syndromes that usually occur in children (Hemorrhagic cystitis, pertussis like disease, skin rashes have been associated with adenoviruses (Foy and Grayston, 1982).

Herpes simplex virus infection :

Herpes simplex viruses (HSVs) are among the most common infectious agents of man. There are two distinct serotypes,HSV type 1 and HSV type 2. They usually have different modes of transmission. HSV 1 is usually transmitted via a nongenital route, as it is chiefly spread by saliva which is likely to have been involved in the outbreaks of herpetic stomatitis. Spread via air droplet or via infected skin squames has not been well documented (Anderson and Hamilton, 1949, Hale, et al., 1963, Juretic, 1966 and Cesario, et al., 1969). HSV-2 is most often transmitted venereally or from a mother's genital infection to the newborn (Nahmias and Visintine, 1976, Corey et al., 1981 and Rawls and Campiane-Piccardo, 1981). HSV 1 infections occur most frequently during childhood and usually affect body sites above the waist. On the other hand, HSV 2 infection, occur most often during adolescence and young adulthood and involve body sites below the waist, primarily the genitals. Most infections in newborns are also caused by HSV-2 (Nahmias, et al., 1973).

pharyngotonsillitis, were associated with primary HSV infection. Because of the common presence of HSV in the mouth of asymptomatic subjects, it has been difficult to ascertain the etiological role of HSV in upper respiratory infections, such as rhinitis and pharyngotonsillitis, and the role of the virus as a cause of recurrent lesions inside the mouth. However, recent data strongly suggest that HSV is etiologically related to these clinical manifestations (Evans and Dick, 1964, Mufson et al., 1966, Lindgren, 1968, Dougles and Couch, 1970, Weathers and Griffin, 1970, Sheridan and Herrmann, 1971).

Glezen, et al., (1975) considered the herpes simplex virus type 1 a common non bacterial cause of inflammation of both tonsils and adenoids.

Young et al, (1978) recovered herpes simplex virus type 2 from the pharynx and identified the virus in a biopsy specimen of tonsillar tissue of a 25 years-old bisexual man . Notkin et al (1970) and Shore & Nahmias,(1981), reported that herpes simplex viruses enter lymphoreticular cells during pathogenesis and thereby induce immunosuppression.

Pelton, et al., (1977), reported that herpes simplex type 1 suppressed the induction of an antibody response to diphtheria toxoid in cultures of human tonsil cells, and that seemed to result from the infection of a small percentage of T-lymphocytes but B-lymphocytes appeared entirely non permissive for this agent. In 1980, Pelton's results, suggest that the immunosuppression is due to selective infection by the viruses of helper T-lymphocytes.

Measles virus infection :

Measles is a highly contagious, acute disease characterized by a general maculopapular eruption, it occurs most commonly in children. The disease is the result of infection with the measles virus which is morphologically a member of the paramyxovirus group but it lacks neuraminidase. The virus has a large single-stranded RNA genome and synthesizes shorter complementary RNAs during replication. The virion carries at least six different polypeptides the size and structure of which are quite similar to those of the proteins of other paramyxoviridae (Hall and Martin, 1973).

With the appearance of rash, both IgG and IgM antibodies become detectable by neutralization. IgM antibodies titers do not greatly exceed the IgG even in the early stages. Peak IgM titers are reached at about 10 days after rash, and they become undetectable again by about 30 days (Schluederberg, 1965).

IgG titers reach a peak at about 30 days, fall 2 to 4 fold during the ensuing 6 months, and then remain very nearly stationary for life. Little is known of IgA antibody or cellular responses (Bellani, et al., 1969 and Ultermohlen and Zabriskie, 1973).

White and Boyed (1973), demonstrated measles virus antigen in lymphoreticular organs of man and monkey during acute infection. Roberts (1975), reported a case of thymic dysplasia and recovered measles virus from slices of tonsils and lung with the implication that the cell mediated immune deficiency was responsible for virus growth in these tissues.

Measles virus infection in man has been known to induce transient impairment of cell-mediated immunity, since loss of tuberclin skin hyperensitivity during natural

measles virus infection was observed by Von Pirquet,(1908). One explanation for this phenomenon could be the direct infection of lymphoid cells, and subsequent studies have revealed the presence of measles virus in lymphocytes during acute infection judged by immunofluorescence (Osunkoya, et al., 1978).

Gallagher and Flanagan, (1975), reported that measles virus has been shown to grow in vitro in both T-and B-lymphocytes. However, Valdimarrson, Agnarsdottir and Lachmann, (1975) had attemps on human lymphocytes subpopulation which are susceptible to measles virus and they found that in vitro the majority of T-lymphocytes possess receptors for this virus. Other workers have shown that measles virus not only grows in cultured lymphocytes (Sullivan et al,1975a) but also depresses responsiveness to phytohemagglutinin (Sullivan, et al., 1975b, Whittle et al 1978). Mc Farland (1974) has suggested that measles selectively infects a functionally important subpopulation of lymphocytes. This suggestion is supported by Pelton, et al (1981),who showed that although measles virus grows in a small percentage of both human T-and B-lymphocytes of blood and tonsil, it will, like herpes simplex virus (HSV) only suppress the inductive stage of a specific antibody or

immunoglobulin response. Whittle et al., (1978), found out that the number and proportion of circulating T-lymphocytes was low during the acute stage of measles, and a small proportion of B-lymphocytes contain virus but their numbers did not alter during the infection.

Cytomegalovirus infections :

Cytomegalovirus (CMV) are a group of viruses within the herpes virus family with great structural and biologic similarities (Wildy, 1973).

Smith, (1956) isolated the virus from human salivary glands and Rowe, et al.,(1956) isolated the virus from cultures of adenoid tissues.

Stern and Elek, (1965) suggested that close or prolonged contact with playmates who are excreting virus is probably the most important method of spread of CMV among children and they discovered the high frequency of antibody among children in underdeveloped countries and in lower socioeconomic groups, probably because of crowding and poor sanitation.

Recurrence of excretion of human CMV in pregnancy, reactivation of CMV replication in immunosuppressed patients and the presence of infectious CMV in fresh blood donors strongly indicate the latency of human CMV infections, as found with other herpes group viruses (Diosi, et al., 1969 and Montgomery, et al., 1972).

Beutner, et al.,(1978), reported that over 75% of the seropositive subjects demonstrated cell-mediated immunity against one or more strains of cytomegalovirus in the tonsillar lymphocytes. In the lymphocytes transformation assay, no cross-reactivity was apparent between cytomegalovirus and herpes simplex type 1 , so they demonstrated in their studies the presence of strain specific systemic and mucosal cell-mediated immune responses to cytomegalovirus in humans. They noted that incidence of cytomegalovirus-specific antibody activity in tonsils and adenoids is notably greater than would be expected in children, so, they suggested that tonsils and adenoid patients may have an increased susceptibility to cytomegalovirus infection or that recurrent tonsillitis may be due to cytomegalovirus.

Waner,et al.,(1971) suggested that some individuals may experience repeated cytomegalovirus infection by different strains of cytomegalovirus, and these infections may at times be limited to the local mucosal tissue.