PATHOLOGIC EFFECTS OF SOME THERAPEUTIC AGENTS ON ORAL MUCOSA

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INTRODUCTION

MUCOUS MEMBRANE lines the oral cavity where the food is masticated tasted and mixed with saliva thereby initiating the process of digestion. Like the skin the oral mucosa is composed of a surface epithelium and an inner connective tissue (Fig. 1). The epithelial layer is of ectodermal or endodermal origin whereas the deeper connective tissue is of mesodermal origin. Different areas of the oral cavity are seen to carry out different functions and the structure of the mucosa varies in an apparent adaptation to function. In the hard palate and gum cornified mucosa suitable for mastication is seen while the floor of the mouth, undersurface of tongue cheek, lip and soft palate have the simple lining mucosa. The epithelium is lubricated and protected continuosly by the small mucous glands situated away from the mucosa. Mechanical trauma, dietary deficiencies and certain toxic stimulation can stimulate mucosal reaction. Chronic irritation often leads to a thickening of the malpighian layer and development of non nucleated keratin layer which may appear clinically as a whitish or a gray-white patch described as leukoplakia. In addition to thickenings areas exposed to trauma demonstrate increased mitotic activity in the basal cell and malpighian cell layers. Deficiency of vitamin C and B can give rise to disease seen clinically with atrophy or inflammation in the region of highest metabolic and cellular activity.

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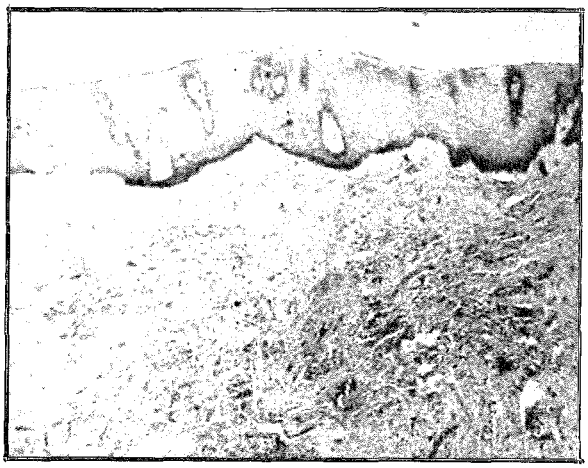

Fig. 1. Oral mucous membrane

EFFECTS OF ACETYLSALICYLIC ACID

Asprin, an analgesic medication is commonly used for the relief of headache, toothache or fever. Medications containing acetylsalicylic acid, phenacetin and other agents are considered to be safe and are available for purchase over the counter by the general public. It is now clear that prolonged use or abuse of this drug can lead to considerable amount of tissue destruction. Some toothache sufferers have the habit of placing crushed or intact tablets of asprin in the buccal sulcus along-side their painful tooth. This can lead to destruction of the mucosa and is probably responsible for the majority of mucosal burns (Fig. 2). In patients, where the contact between the caustic and soft tissues has been of short duration the removal of the cause will lead to normal healing whereas in cases of severe exposure risk of secondary infection is present. Gasterointestinal tissues, the renal system and the auditory system are found to be extremely susceptible to acetylsalicylic acid abuse and manifest early morphologic alteration (Najjar 1977). In addition it has been shown that

haemostatic mechanisms are affected by asprin abuse. Acetylsalicylic acid is a fairly strong acid with a pH of about 3.5. Effects on oral mucosa are mainly due to irritation which leads to protein coagulation. This leads to necrosis of tissues and clinically white surface mucosal slough is evident. In gastric mucosa several types of lesions caused by excessive ingestion of asprin has been observed (Thorsen *et al*, 1968).

Fig. 2. **Aspirin burn in buccal mucosa**

MONILIASIS FOLLOWING ANTIBIOTIC THERAPY

Oral moniliasis is caused by the yeast like fungus Monilia albicans and clinically presents as pearly white or bluish white lesions involving mucosal epithelial tissues of the mouth gastro-intestinal tract and vagina. Lesions of the mucous membrane are also called 'thrush' and it is a surface infection. Infections of the oral cavity either occur at the two extremes of age, infancy and old age or in persons who are debilitated due to some systemic disease like leukemia and diabetes. It may be seen in any part of oral cavity. Antibiotic treatment in some patients causes most of the oral bacteria to disappear leaving only fungus of the candida type. In moniliasis of the oral cavity, the tongue is generally affected first with the formation of creamy white spots which slowly enlarge and unite and this can be easily rubbed off leaving a raw red surface. Other areas that may be affected include gingiva, cheek mucosa, tonsils, pharynx and lips (Fig. 3). Laboratory aids are useful in confirmation of the diagnosis and some useful procedures include direct microscopic examination of material from the lesion, culturing and animal innoculation. Microscopic section shows a dense network of candida organisms in the form of hyphae and spores. The epithelium of the area of mucosa involved is either destroyed or densely infiltrated by the fungi and the underlying connective tissue is seen to show areas of oedema, presence of lymphocytes and plasma cells. Nystatin used topically helps in the cure of the condition and for the acute variety use of alkaline mouth wash is recommended.

Fig. 3. **Monilia of the lip**

ANTICONVULSANT DRUG THERAPY

An unfortunate side effect seen in the use of dilantin sodium as an anticonvulsant drug in the control of epileptic siezures is fibrous hyperplasia of the gingivae. It is observed that about fifty percent of patients receiving this form of therapy have this side effect. The mechanism by which sodium diphenylhydentoinate causes hyperplasia of gingival mucosa is not certain but a suggestion has been put forward that the drug has a degranulating effeet upon the gingival mast cells which leads to the liberation of cytoplasmic constituents that stimulate the surrounding fibroblasts to form connective tissue (Angelopoulos *et al*, 1972). In addition to the strength of the dilantin sodium administered presence of a local irritating factor such as chronic gingivitis is considered to be essential for the development of this pathologic effect. Clinically the initial changes seen is a painless increase in the size of the gingiva starting with the enlargement of one or two interdental papilla.

Surface shows an increased stippling and on palpation it is dense and insentitive with little tendency to bleed. Histologically the bulk of the tissue is made of large bundles of collagen fibres

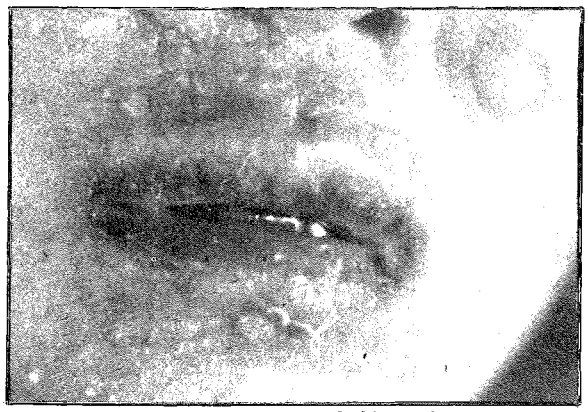

Fig. 4. Allergic hypersensitivity of skin and mucous membrane

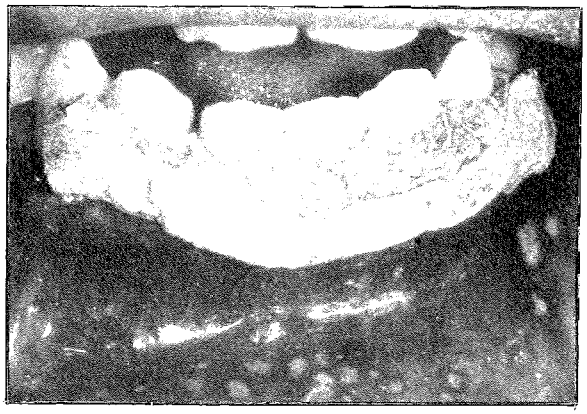

Fig. 5. Allergic reaction to periodontal dressing.

interspersed with fibroblasts and fibrocytes. Treatment is not indicated unless the enlargement becomes cosmetically objectionable.

CONTACT STOMATITIS AND CHEILITIS

In addition to primary irritation oral mucosa like skin is also subject to allergic sensitization. In contact dermatitis we observe symptoms and signs like itching erythema and eczematization (Fig. 4), whereas in contact stomatitis we observe burning sensation, loss of taste, numbness erosion and perleche. Often the sysptoms of the patient are more prominent than the physical signs. Some ingredients of dentrifices and mouth washes are capable of producing allergic stomatitis. Certain topical anaesthetic compounds and anaesthetic aerosol sprays had been known to produce allergic reactions. A variety of metals used in the dental surgery for filling and prostheses have been known to produce allergic rections (Fisher *et al.*, 1956). Allergic reactions of the oral mucosa may be produced by denture base materials or its constituents, denture cleansing materials or denture fixing preparations. Dressing materials used in periodontal surgery are seen to produce allergic reactions of oral mucosa (Fig. 5). Reports concerning the adverse effects of mouthwashes appear in the literature. Common pathologic effects include primary hypersensitivity stomatitis accompanied by erythema, ulceration or epithelial sloughing (Kowitz *et al.*, 1976). Excessive local application of listerine mouth wash was found to be connected with asymptomatic diffuse oral white lesions in few patients. Microscopical changes associated with wxcessive use of listerine mouth wash include hyperkeratosis, acanthosis and coagulation of epithelial proteins.

EFFECTS OF CANCER CHEMOTHERAPUTIC AGENTS

Chemotheraputic agents are used in the treatment of malignant conditions in some patients and the control of the cancer lies in the ability of certain compounds to interfere with the biochemical pathways involved in the formation of essential intracellular macromolecules. The majority of the drugs used in the treatment of cancer produce a non selective interruption of intracellular macromolecules and cell division not only in rapidly dividing neoplastic tissue but in rapidly dividing normal tissue as well.

A result of the above is toxic reaction to cells in various parts of the body. Bone marrow and oral mucosa are affected by this action in some patients giving rise to ulceration of oral mucosa (Dreizen *et al.*, 1975). Methotrexate has been found to produce ulceration of oral mucosa about a week following initiation therapy (Volger *et al.*, 1965). It is believed that the severe oral tissue destruction seen in some patients cannot be attributed solely to an inhibition of cell division. Some of the lesions may be due to direct action of the drug.

CONCLUSION

Oral mucosa like the skin can react to direct irritation at the local site and to allergic sensitization. Local tissue injury can occur as a result of the excessive use of mouth washes or tablets like asprin. The exact mechanism of action of some chemotheraputic agents on oral mucosa is not well understood at the present time.

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