 特別講演要旨

Gingival involvement in oral and general disorders

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Mr. President,
Mr. Chairman,
Ladies and Gentlemen!

At the beginning I have to say "thanks" to prof. Ichiro Matsue, President 22nd Annual Japanese Association of Periodontology Congress for his invitation to come to Japan. My invitation is an expression for a long lasting friendship between the Japanese and German Dental Societies. I hope that in future the intensive connections and friendship will increase more and more for the benefit of the Japanese and German Dental Societies.

In the past 40 years there have been considerable advances in the field of periodontology on both diagnostic and therapeutic levels. Clinical periodontology means today:

- The examination of occlusal relationships
- Exact probing of periodontal pockets
- Measuring of tooth mobility
- Estimation of bone destruction and bone loss
- Periodontal surgery with a broad pallet of different operation methods
- Mucogingival procedures

Although the dentist is a specialist of the oral cavity and the periodontium, he must understand the patient as a biologic entity with psychologic overlays affecting the course of disease. All the organ systems of the body play a role in the development of a clinical lesion in the mouth. The mouth serves as a mirror of systemic health and disease. Further, local lesions of the oral cavity have a direct effect on systemic health. There cannot be total health without oral health (SCOPP).

It is known that disease symptoms are seen by the practitioner only after the disease is well established on a cellular basis. Morely suppressing or eliminating clinical symptoms without interpreting the nature of the disease is no longer tenable for the alert diagnostician. Since the cell is the common point of origin of all diseases, reference to the basic sciences in order to explain the clinical phenomena and course of a disease. Clinical science can advance only by delving into the basic sciences for an explanation of clinical phenomena. Comprehending the nature of a disease means not only identifying and placing a label on a group of symptoms but also understanding the underlying mechanism of the disease and relation to the patient.

Apart from the gingivitis and periodontitis which to the periodontist is important in the therapeutic context, gingival diseases which occur side by side with diseases of the oral mucosa and the skin present an interesting challenge diagnostically. Therefore gingival involvement in dermatologic and oral disorders will be a field of interests in the future which should be understood and practiced by the periodontist.

Therefore differential diagnosis, cytopathology and clinical implications of frequently occurring ulcerative and dullous lesions will be the main topic of my paper.

Ulcerative lesions of the oral mucous membrane are common occurrences in patients. When observed in the mouth all these lesions have a similar appearance since they become secondarily infected and modified by the saliva and microorganisms in the oral cavity to nonspecific-appearing lesi-

ons. Despite their garden-verietty appearance the lesions have an individual pathology with varying origins and are symptoms of different disease entities that must be properly diagnosed in order to render correct treatment.

In the past the diagnosis of these lesions was often baffling and taxed the ingenuity of even the alert practitioner.

Terminology appropriated from the field of dermatology was often misleading. But during the past years advances have been made in the histopathology and histochemistry of mucous membrane diseases, in oral cytology, in microbiology, in immunology and in understanding the pathogenesis of viral diseases.

1. Recurrent aphthous ulcers

Aphthous ulcers are common, painful, ulcerative lesions of the oral mucosa cited in the literature by clinicians under a multitude of names. At least 9 synonyms for the condition have been recorded.

Clinical symptoms:

The ulcers are oval shaped and circumscribed and may occur as a single entity or as multiple ulcerations. They are generally red but at times have a necrotic covering and hence may look yellow or grey. The lesions starts with an erythematous macule, becomes necrotic, then forming a shallow ulcer with sharply defined margins. The ulcers are surrounded by a red indurated zone of inflammation and are always tender and painful.

Aphthous ulcers may be classified into 3 groups:

1. The first group may be seen here. Patients who experience recurrent crops of one to five ulcers affecting the nonkeratinising mucosa only and lasting from 7 to 14 days.

The ulcers may occur at approximately 4-weekly intervals. In women they occur predominantly in the luteal phase of the menstrual cycle. Similar ulcer of genital mucosa may occur.

2. Patients who have recurrent attacks with twenty or more ulcers at a time, which may be not confined to the mucobuccal fold but seen in all

parts of the mouth.

3. Patients who suffer recurrent attacks where there are usually one, two, three ulcers at a time. These ulcers are preferentially located at the soft palate. The ulcers are deep, destructive and may take 4 weeks to heal. This condition is described as periadenitis mucosa of the type "SUTTON".

Cytopathology

In smears of early aphthous ulcers we may see predominantly mononuclear cells. At a later stage polymorphonuclear leukocytes appear. The chances are that the mononuclear infiltrate consists of lymphocytes and monocytes. Pseudo-eosinophilia, vacuole formation, cytolysis and karyolysis are the most important criteria of exfoliated epithelial cells from aphthous lesions. These non-specific cell alterations are due to degenerative influences elicited by the inflammatory exudate.

Immunology

Recent investigations by the LEHNER and DOLBY-groups in the United Kingdom indicate that immunologic reactions play an important role. It was demonstrated quite clearly that the epithelial damage was consistently associated with an infiltrate of lymphocytes. When lymphocytes from patients suffering from recurrent oral aphthous ulcerations were brought together with oral epithelial cells in vitro a direct cytotoxic effect was visible. LEHNER supposed a breakdown in the normal tolerance of the immune system for self antigens in patients with recurrent aphthous lesions. A cross-reaction occurring between a foreign antigen such as bacterial or virus antigen and a previously non-antigenic self component of the oral mucosa may be possible.

2. Herpetic gingivostomatitis

Acute herpetic gingivostomatitis is an infection of the oral cavity caused by the herpes simplex virus. Secondary bacterial infection frequently complicates the clinical picture. Acute herpetic gingivostomatitis occurs frequently in infants and children below the age of 6.

Clinical features

The mucous membrane is extremely painful with aphthous ulcers occurring throughout the oral cavity and oral pharynx. The ulcers may be preceded by vesicles that break after a few hours and may become secondarily infected. Particularly the gingiva becomes inflamed and swollen and bleeds readily. Small blisters are found, rarely in the region of the marginal and attached gingiva, more frequently in the region of the mucogingival borderline and these will change into 2 mm sized ulcers of yellow or red surface with surface with serrated borders. Occasionally acute herpetic gingivostomatitis may occur in adolescents and adults. In these cases a herpetic involvement of the genital area may accompany the oral disease.

It is generally agreed that acute herpetic gingivostomatitis is not recurrent. However, activation of the virus lying dormant in the oral tissues or reinfection may provokes recurrent form of the disease. But this is clinically quite distinct from the primary infection and then usually localized to the mucocutaneous junction of the lips, called herpes labialis.

Cytopathology

In smears out of herpetic lesions one finds epithelial cells with typical changes in the nucleolus and cytoplasm. Enlarged nuclei, eosinophilic intranuclear inclusionbodies and margination of chromatin are observed. Frequently there are pictures of so-called bird-eyes 'or bulleyes' cells. Also observed are signs of degeneration where enlargement of nuclei, margination of chromatin occurs together with packing of parabasal or intermediary cell types forming multinucleated syncytia. The herpetic cytopathology is characterized by absence of intracytoplasmic inclusions. The complexes of epithelial cells are accompanied by dense leukocyte aggregates.

3. Benign mucous membrane pemphigoid and desquamative gingivitis

In contrast to the oral ulcerations occurring in aphthous ulceration the ulceration in these diseases is preceded by the formation of bullae. Benign

mucous membrane pemphigoid closely resembles desquamative gingivitis in the oral cavity. It is characterized by intense erythema of both the marginal and the attached gingiva with desquamation and may cause a generalized mucosal involvement. The skin and in particular the face and the genital region are involved in 20% of the cases. In 80-90% this disease starts in the oral cavity. Benign mucous pemphigoid occurs most often in females usually in the menopause. ZISKIN has suggested that the epithelial desquamation is a localized manifestation of disturbed sex hormone metabolism. It is becoming increasingly clear that desquamative gingivitis or gingivosis is part of the oral manifestation of benign mucous membrane pemphigoid.

Clinical features

Clinically an intense erythema of the marginal gingiva, attached gingiva and/or oral mucosa with painful desquamation may be observed. There is a tendency for the epithelium to detach from the underlying connective tissue, leaving red, raw surfaces that bleed easily when touched. Separation of the epithelium may be accomplished with the slightest pressure. Watery blisters may appear first. The desquamation of the epithelium occurs most commonly on the labial and buccal gingiva. In severe cases the surface epithelium becomes elevated and may peel with a blast of air or a spatula.

Cytopathology

Microscopically the epithelium appears in active stages of degeneration. There is an absence of keratin and the prickle-cell layer is thin and disturbed. There are areas of hydropic degeneration and disintegration. Between the basal cell layer and the underlying connective tissue arises a kind of "splitting". The subepithelial inflammatory infiltrate consists of lymphocytes, monocytes, macrophages and perigranulocytes. In exfoliative cytological smears cell forms from all epithelial layers are found. Smears from these lesions will rarely show degenerated forms. Bacterial colonisation is not found. The complexes of

epithelial cells are surrounded by neutrophilic granulocytes, macrophages and monocytes.

4. Pemphigus vulgaris

Pemphigus vulgaris is a grave systemic dermatosis in adults. Most often, the first signs of pemphigus are burning and painful erosions of the oral mucous membrane. These may continue for weeks before there are any cutaneous lesions, during which time the disease may remain undiagnosed. In 53% the oral cavity is the place of the first signs of this disease. So the patient may first seek the services of a dentist, and the alert dental practitioner should be aware of this.

Clinical features

The first symptoms may be painful and turning nonspecific erosions. The classical intraepithelial straw-coloured bullae are not generally found in the mouth because, just as soon as they erupt, they break down from the action of the tongue and cheek movements. Instead, one finds red, depressed and necrotic slough having the appearance of a curled-up, retracted egg-membrane. The erosions are discrete with irregular borders, but oddly enough do not exhibit an inflammatory reactions in or around the eroded area. A. NIKOLSKY sign can be elicited, in most cases by means of blast of air.

Cytopathology

The best results in histological and cytological investigations will be achieved in pemphigus, if an early bullae is examined before it has become secondarily infected. The first pathological changes are breaks in the lower aspects of the stratum spinosum of the epithelium caused by disintegration of the intercellular bridges. This acantholysis and a kind of intraepithelial splitting are pathognomonic of pemphigus. The cytological findings from newly opened bullae show hyperchromatic acantholytic so-called "TZANCK Cells". These isolated cells derive from the stratum apinosum where the breakdown of the intercellular substance starts.

Immunological abnormalities in gingivitis desquamative or benign mucous pemphigoid and in

pemphigus vulgaris.

The immunological findings in pemphigus are so striking as to lead to an immediate suspicion that they are causally related to the disease. In pemphigus there is a raised titer of antibodies of the IgG class of the intercellular substance of the epithelium. But the problem, whether pemphigus can be due to lymphocytotoxic mechanisms or to cell mediated immunity with the serum antibodies simply a secondary manifestation, has not yet been solved.

In cases of pemphigoid probably immunological reactions in the basal membrane region are responsible for the disease. Basement membrane material becomes antigenic. By engulfing chemotacting factors granulocytes release lysosomal material which may destroy the collagen anchoring fibrils. Thus a subepithelial splitting may arise which has been demonstrated morphologically before.

5. Mycotic infections

Specific infection diseases like those caused by tubercle bacteria, *actinomyces israeli*, *treponema pallidum* can lead to specific forms of stomatitis. In rare cases a specific gingivitis may result. The clinical diagnosis of such a specific gingivitis is difficult. The dark red to bluish colour of the gingival lesion and the ineffectiveness of conventional local therapy can point to a specific infection. The definite diagnosis is made through the further development of the disease clinically or through histological and bacteriological investigations.

Among the mentioned specific infections mycotic infections are of great clinical importance. *Candida albicans* certainly stands out as causing the most frequent type of mycotic infection of the oral mucosa. *Candida albicans* exists most commonly on normal and abnormal mucous membrane. When *candida albicans* multiplies in great numbers candidosis may result. Among the local factors contributing to candidosis are poor oral hygiene, diminished flushing action of the saliva and poor fitting of dentures. More often it is

the systemic factor that causes a proliferation of fungi. Immunodeficiencies in lymphocyte functions in cases of severe candidosis have been reported. Longterm large dosages of broad spectrum antibiotics and large dosages of steroids alter the ecology of the oral cavity.

Clinical features

The classical manifestation of the disease consists of creamy white patches often compared with milk-curd. They may occur on any area. The white patches are moderately adherent and strip away with some difficulty, leaving a bright erythematous base. In the last years an increasing number of patients with candidosis of the gingiva have been observed. The diagnosis of this special form of mycotic infection of the gingiva may be supported by the fact that conventional plaque reducing methods will not influence the clinical symptoms. In these cases the wornout tooth-brushes of the patient covered by *Candida albicans* may stimulate the lesions by means of inoculation. The culture of the tooth-brush bristles is strong positive in these cases.

The diagnosis of oral candidosis must be based on both clinical and laboratory-findings. The diagnosis may be established if the following 3 criteria have been fulfilled:

1. The presence of pseudomycelium and cluster of budding cells at the hyphal nodes in smears from suspected area.
2. A positive culture of the material
3. Typical creamy patches on the oral tissues with an underlying dark red underground.

Ladies and gentlemen, the general topic of this afternoon was selected to be: Future developments in Periodontology. In coincidence with the time available I have tried to stress some important aspects of oral mucous diseases. The final goal of my paper was, besides of presenting clinical interactions, to make the practitioner aware of the most important pathogenic directions. Due to this we find often very similar clinical pictures in the oral cavity: Firstly immunological disorders as in recurrent aphthous ulcerations, pemphigus

vulgaris and benign mucous pemphigoid. Secondly viral infections and here mainly herpetic diseases. Thirdly specific infections with special emphasis of candidosis.

For the practitioner the etiologic principles should be entirely clear because they are of most important significance for the therapeutic track to be followed. For example the application of corticosteroids seems to be most efficient and valuable in cases of immunological disturbances while we are knowing on the other side that locally applied corticosteroids have to be avoided completely in cases of viral and fungal infections.

The same should be related to antibiotics. They have no causal effect in viral and immunological disorders. The traditional antibiotics do not show any effect in mycotic infections. The fundamental knowledge of the individual form of disease should hereby determine the correlated therapeutic procedures and help to avoid failures.

In my personal view the future periodontist should be more aware of oral mucous diseases. Besides of his effective periodontal practice in diagnosing and curing periodontal lesions he should be most concerned of oral mucosal disturbances very often being located in the gingival area.

Every periodontist should have the obligation to establish and file a precise record of his findings in the oral mucous membrane. At the same time he should treat oral mucous lesions. In several cases a cooperation with the internal doctor and the dermatologist is highly recommended. The mucogingival junction should never appear to the periodontist to be an iron curtain. Research in periodontology follows already these outlines and has established milestones, in detecting inflammatory mechanisms and evaluating immunologic reactions, as speakers have mentioned yesterday. Modern periodontal textbooks contain already chapters dealing with mucous diseases.

Ladies and gentlemen, I have tried to pass on the message to the periodontist to keep in mind the general view for the various and widely structured aspects of his speciality.