Keratinization of the Sulcular Epithelium—A Pointless Pursuit?*

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A considerable amount of effort has been directed at finding methods for modifying the nonkeratinized sulcular epithelium on the assumption that a keratinized surface may offer a better barrier to antigens and bacterial products present in the gingival sulcus. It is argued here that keratinization in itself may not confer greater impermeability, for nonkeratinized epithelia also have been shown to resist the penetration of certain substances. Moreover, few workers have considered the role of junctional epithelium in the initiation of periodontal disease although experimental evidence suggests that this may be a permeable tissue. As formation of a surface with barrier properties seems to be a concomitant of epithelial differentiation while attachment is a property of relatively undifferentiated epithelial cells, attempts to induce junctional epithelium to differentiate could result in a loss of epithelial attachment to the tooth. It is suggested that attempts to keratinize the sulcular region, on theoretical grounds, may be unjustified.

The region where the oral mucous membrane is penetrated by the erupted tooth is a unique site where two dissimilar tissues form a junction which, because of its structure and anatomic location, is subject to a variety of potentially damaging chemical and physical stimuli. From a biological point of view, this junction represents an unusual juxtaposition of hard and soft tissues with few parallels in mammals; clinically, the region has considerable importance as the site of development of the periodontal lesion.

Concepts of the etiology and pathogenesis of periodontal disease rely heavily on an understanding of the structure of the dentogingival junction. After more than 50 years of controversy as to the exact nature of the attachment of the gingiva to the tooth, ultrastructural studies1–2 have essentially resolved this problem. These studies have revealed that the attachment between the epithelium and tooth surface is mediated by a unique epithelium, derived initially from the reduced enamel epithelium and termed the "junctional epithelium" by Schroeder and Listgarten.7 Adjacent to this epithelium and lining the lateral aspect of the gingival sulcus is the nonkeratinized or parakeratinized oral sulcular epithelium, which is continuous with the keratinized gingival oral epithelium. Ultrastructural studies have shown that the cellular morphology of the junctional epithelium is quite different from that of any other stratified oral epithelium,8 whereas the oral sulcular epithelium is similar to nonkeratinized tissue elsewhere in the oral cavity. The juxtaposition of these three different epithelia, each continually proliferating while still maintaining a distinct pattern of differentiation, has prompted much speculation as to the biologic factors responsible for the determination and maintenance of these structures.9,10 Of similar interest is the observation that, after surgical removal of the junctional epithelium, a new attachment can be formed from the adjacent oral epithelium which is morphologically identical to the tissue which has been removed.11

In view of the considerable evidence that periodontal disease can be initiated by specific bacteria in the sulcular region,12–14 a primary concern has been the means whereby bacterial products gain access to the underlying tissues, i.e., the permeability of the gingival attachment region. Many investigations have concentrated on the role of the oral sulcular epithelium on the assumption that this epithelium, being nonkeratinized, is likely to be both more permeable and more susceptible to damage and breakdown than is the adjacent keratinized gingival oral epithelium.15 The role of the junctional epithelium in the initiation of disease, as Barnett15 recently pointed out, has been frequently ignored. The purpose of this paper is to question some of the prevalent assumptions concerning keratinization, permeability and the perceived need to modify the oral sulcular epithelium, and to consider the properties of the junctional epithelium in terms of such assumptions.

Much of the research on the differentiation and maintenance of oral sulcular epithelium has been justified in terms of ultimately achieving a keratinized sulcular lin-
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ing. Experiments involving the removal of the oral sul-
cular tissue and its implantation subcutaneously or
maintenance in vitro, the transplantation of oral sul-
cular tissue to different sites in the oral cavity, or the
oral tissue to different sites under certain circum-
cstances. Frictional stimulation of oral sulcular
epithelium by means of tooth brushing, either alone or
combined with antibiotic treatment, has suggested that
keratinization of this tissue is also possible in vivo. The
explanations for these results have differed considerably
however. Ten Cate supports the view that epithelial
differentiation in the sulcular region, as elsewhere, is
determined by the underlying connective tissue and
claims that beneath the sulcular epithelium this tissue is
"disturbed" as a consequence of the ever present inflam-
mation. Thus, it is this altered connective tissue which
prevents the epithelium from keratinizing as suggested
by the observation that transplantation of the epithelium
and connective tissue to sites where there is no inflam-
matory stimulus results in epithelial keratinization.
Although they do not cite any evidence for the assumption,
Caffesse et al. state that there is no difference in the
composition of the connective tissue underlying the oral
and sulcular epithelia and claim that the failure of the
sulcular epithelium to keratinize is due to the environ-
ment and, in particular, the contact with the tooth surface
and irritation of the epithelium by bacterial plaque and
its products. This, in turn, is thought to increase the
turnover and thus impede the differentiation of the
epithelium. Both points of view can be reconciled in
terms of the primary cause (inflammation) and the ultimate
effect (failure to differentiate into a keratinized
surface), so that only the intermediary events are contro-
versial. However, it is possible that these arguments are
largely irrelevant to the real problem, which is the perme-
ability of the denogingival tissue to sulcular substances.

Most workers assume that the oral sulcular epithelium,
because of the absence of keratin, is permeable, and that
changing this tissue to a keratinizing epithelium will
reduce its permeability thereby increasing resistance to
the initiation of periodontal disease. There is some evi-
dence that these assumptions may not be valid. Experi-
ments in vivo have suggested that uninfamed nonkerat-
inized oral epithelium may be almost as successful as
keratinized oral epithelium in resisting the penetratio-


certain tracer substances. Moreover, keratinization
does not always confer superior permeability properties; for
example epidermal callus is more permeable to water than
the thinner stratum corneum of normal skin while,
on the other hand, the nonkeratinized epithelium lining
the gut and the bladder are highly impermeable to
certain substances.

Other evidence comes from studies demonstrating the
development of periodontal disease in the rat despite the
presence of an orthokeratinized sulcular lining. However,
there are several experimental studies which can
explain these paradoxical findings. Listgarten has
shown microscopically that although the oral sulcular
epithelium of the rat does not resemble that of primates,
the epithelium joining this tissue to the tooth surface is
similar, i.e., there is a true junctional epithelium. Fur-
thermore, McDougall has demonstrated that an elec-
tron dense tracer instilled into the rat sulcus rapidly
appears in the subepithelial connective tissue and, con-
versely, tracer injected intravenously rapidly enters the
sulcus. In both cases electron microscopic studies re-
vealed that the tracer was present in the junctional, but
not in the oral sulcular epithelium. Similar results have
been obtained using tritiated hyaluronidase in rats and
labelled albumin in guinea pigs.

In spite of these findings, it is not justifiable to imply
that the primary oral sulcular epithelium necessarily
behaves as an impermeable lining since the presence of
inflammation may modify its properties. Treatment with
hyaluronidase, a likely product of dental plaque, has
been shown to alter the structural integrity of sulcular
epithelium and to increase its permeability. Never-
theless, the junctional epithelium by comparison may offer
a relatively unrestricted pathway for penetration and its permeable even when uninflamed. Thus, this suggestion
leads directly to the question recently posed by Barnett as
to whether junctional epithelium ought to be regarded as
different tissue from the oral sulcular epithelium and,
if so, whether we should not be trying to effect changes in this epithelium if we wish to decrease the diffusion of bacterial products into the gingival connective
tissue.

The evidence from ultrastructural studies, and in parti-
cular from quantitative (stereological) comparisons of
junctional epithelium with other oral epithelia described
below, indicates that the junctional epithelium, indeed,
is quite different. In both keratinized and nonkeratinized
regions of the oral epithelium there is a consistent pattern
of differentiation seen between the basal and superficial
cell layers; tonofilaments progressively increase in vol-
ume density while Golgi vesicles and rough endoplasmic
reticulum decrease in volume and surface densities as a
cell moves towards the epithelial surface. Another fea-
ture which seems to accompany differentiation in most
stratified squamous epithelia is a modification of the
intercellular substance in the most superficial layers,
which gives rise to a permeability barrier. Stere-
ological analysis of junctional epithelium shows it to be
a homogeneous tissue without any recognizable pattern
of differentiation. Cells of the junctional epithelium
when compared to the least differentiated cells of the
keratinized gingival epithelium (i.e., the basal and prickle
cells) have more cytoplasm, fewer desmosomes and a
smaller proportion of filaments, but comparatively larger
volumes of rough and smooth endoplasmic reticulum.
Thus, the junctional epithelium shows no evidence of
changes associated with differentiation in other epithelia.
This is not surprising for, as Schroeder and Munzel-
Pedrazzoli pointed out, keratinizing epithelium and junctional epithelium have different functions. The role of the junctional epithelium is to form a function between epithelium and a dissimilar tissue, the enamel, whereas the rest of the oral epithelial lining forms a protective surface barrier. The ability of epithelial cells to attach to surfaces other than those of neighboring cells in the epithelium appears to be inversely related to the degree of differentiation of the cells. Thus, if stratified keratinized squamous epithelium is disaggregated and plated it is only the basal-type cells which attach to the substratum and similarly, in wound healing it is cells derived from the least differentiated basal and parabasal layers which migrate and attach to the connective tissue wound bed to form a new epithelium covering. Thus, in a stratified squamous epithelium the formation of a surface with protective barrier properties seems to be a concomitant of differentiation whereas only undifferentiated epithelial cells maintain the ability to form an attachment to nonepithelial surfaces. Junctional epithelium is a tissue where attachment has taken precedence over differentiation and the formation of a surface barrier.

As attempts to modify the sulcular epithelium have occupied such a major position in periodontal research it is worth pursuing the point raised by Barnett and to ask whether alteration of the junctional epithelium is desirable. Differentiation of the junctional epithelium to form a keratinizing surface, if this could be brought about, would give rise to a tissue in which attachment to the enamel surface would be limited to the deepest and least differentiated cells. As Neidert has pointed out, the junctional epithelium is readily disrupted: if the epithelial attachment were mediated by only the deepest cell layers instead of the full length of the junctional epithelium (about 40 cell layers in man), then there would be virtually no resistance to separation. Thus, the mechanical seal between the epithelium and the tooth would be inadequate and a pathway between the enamel surface and the adjacent epithelium would exist through which material could still penetrate from the sulcus.

Such considerations suggest that it is reasonable to accept the junctional epithelium as a tissue which, by virtue of its adherent properties, is probably intrinsically permeable. This property presumably accounts for the invariable presence of an inflammatory infiltrate in the underlying tissues of clinically normal gingiva unless extraordinary prophylactic measures are undertaken. Indeed, unless all bacteria can be removed from the gingival crevice, there will still be the potential for reactions to antigens and bacterial products penetrating in small quantities. On the other hand, if the junctional epithelium was induced to keratinize, the effectiveness of the tissue as attachment would be drastically compromised. Furthermore, as Mackenzie has pointed out in a discussion of the keratinization of the oral sulcular epithelium, changes that have been brought about in this tissue in the direction of keratinization are probably the result of a reduced inflammatory status following removal of plaque rather than a reflection of the direct effect of mechanical stimulus. Therefore, the pursuit of keratinization per se in the epithelium lining the gingival sulcus may be a pointless task from the aspect of increasing host resistance. Efforts might better be devoted to mechanical or chemical procedures that minimize or prevent plaque accumulation.

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REFERENCES


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