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The Junctional Epithelium: from Health to Disease Review

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ABSTRACT:

A structure that actively combats germs is necessary for periodontal tissues since they are continually in contact with them. Thus, the junctional epithelium is present at a critical junction between the bacterial-infested gingival sulcus and the periodontal soft and calcified connective tissues. The junctional epithelium can manage the ongoing microbiological challenge due to its usual structural and functional adaptability. The development of any gingival and periodontal lesions is not prohibited by the junctional epithelium's antimicrobial defence mechanisms. Recently, attention has been drawn to the transition from junctional to pocket epithelium, which is thought to be an authenticating mark in the onset of disease. The present review will cover some of the very important aspects of junctional epithelium from its development, anatomic structure, epithelial attachment, dynamic and molecular aspects to role of junctional epithelium in disease.

Keywords: Junctional epithelium, implant, periodontitis, epithelial attachment apparatus, dento-gingival unit

INTRODUCTION:

"Junctional epithelium (JE)" is the part of "dento-gingival unit". It is required for maintenance of healthy periodontium as it seals off the tissues of periodontium. JE is responsible for formation of gingival sulcus. It is attached to the tooth via internal basal lamina and to gingival connective tissue via external basal lamina. It has collar like band of stratified squamous non-keratinizing epithelium surrounding the cervical portion of tooth, approaching the cemento-enamel junction [1]. As the tooth erupts in the oral cavity the continuation of oral epithelial cells is altered and the tooth is adjoined by the gingival epithelium. Junctional epithelium (JE) then devoted to tooth by hemidesmosomes; front line

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of defence against periodontal disease [2,3]. There are 3 major zones of junctional epithelium:

Apical-germination

Middle- adhesion

Coronal- permeability

THE DEVELOPMENT OF THE JUNCTIONAL EPITHELIUM

Acccording to Orban`s the formation of JE begins with the union of oral epithelium and reduced enamel epithelium. The ameloblasts post the completion of primary enamel cuticle (thin membrane of ameloblasts on surface of enamel) shrinks and epithelial enamel organ gets reduced to a flat cuboidal cell layer resulting in formation of "reduced enamel epithelium (REE)". During the eruption of tooth, primary JE is formed by the "Reduced enamel epithelium (REE)" which is eventually replaced by "secondary Junctional epitheliumJE", derived from oral epithelium cells [4,5].

Once eruption initiates the transformation of Reduced enamel epithelium (REE) to Junctional epithelium occurs accompanied by following cellular changes:

- Cuboidal cells from ameloblasts become flat and get positioned parallel to tooth surface and start looking like junctional epithelium.
- These cells lose their ability to divide and exfoliate at the base of sulcus along with cells from stratum intermedium inhibiting proliferative capacity get transformed into Junctional epithelium.

The epithelium that envelops the tip of crown, disintegrates at center most point and this aperture becomes the location for crown to reveal from into the oral cavity.

The Reduced enamel epithelium remains in contact with the un-erupted part of tooth. After the tip of crown has emerged, Reduced enamel epithelium is called Primary attachment epithelium and gradually shortens.

Marginal gingiva is in continuation with the oral epithelium. Gingival sulcus develops at the junction of gingiva and surface of the tooth and extend around the circumference. Gingival sulcus is surrounded by the junctional epithelium at the base and by marginal gingiva laterally**. (Figure:1)** depicts the four stages of eruption along with development of Junctional epithel

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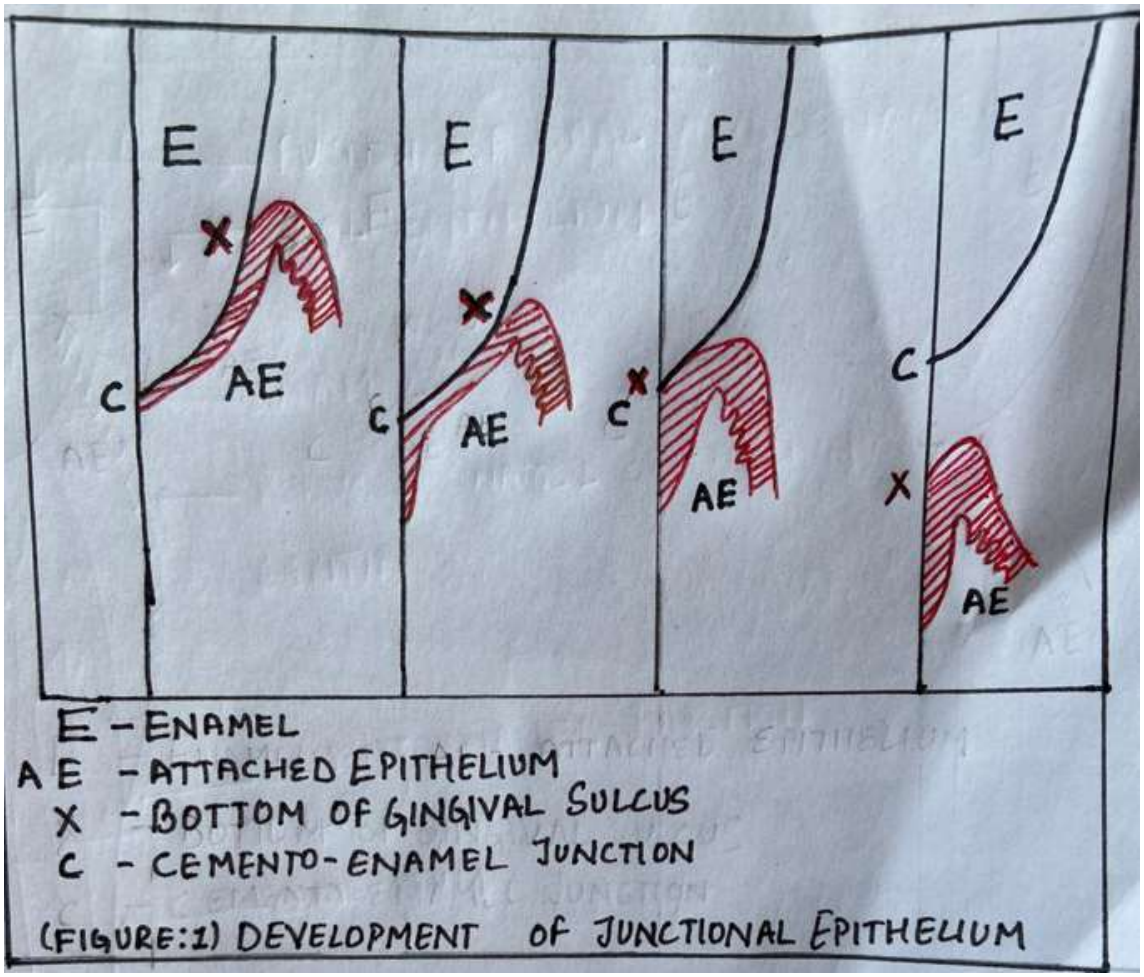

Figure:1 Development of Junctional Epithelium

Structure of Junctional Epithelium

Junctional epithelium is a stratified, non-keratinizing squamous epithelium that forms a collar-like ring around the edge of the tooth's cervical area. “The base of the sulcus is where the junctional epithelium's coronal end, which is a free surface, is located. Both Carranza and Gargiulo estimate the length of the junctional epithelium to be between 0.25 and 1.35 mm. Under sterile conditions, the epithelial seal has a 2mm height and extends from the cemento-enamel junction (CEJ) to the marginal gingiva. Internal basal lamina (IBL), which is regarded as a simple basal lamina, and external basal lamina (EBL), which is regarded as a real basal lamina, are used to link junctional epithelium to the tooth surface and to the gingival connective tissue, respectively. The lamina lucida is towards the basal keratinocytes and the lamina densa is toward the underlying connective tissue in the External basal lamina, which has features that are identical to those of a typical basement membrane. Directly attached to tooth (DAT) cells are the innermost suprabasal cells that are exposed to the tooth surface [6]. When compared to a typical basement membrane, the internal basal lamina's protein composition is significantly different. Laminin 111, Laminin 511, type IV and VII Collagens,

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and Perlecan are examples of typical basement membrane-forming proteins that are absent from the internal basal lamina [7]. Laminin 332 has been identified as the primary cell adhesion protein in the internal basal lamina. These results highlight the distinctiveness of Junctional epithelium and provide crucial details on the biological interaction between dental implants and the gingival epithelium to create an effective interface". [8,9] **(figure:2)**

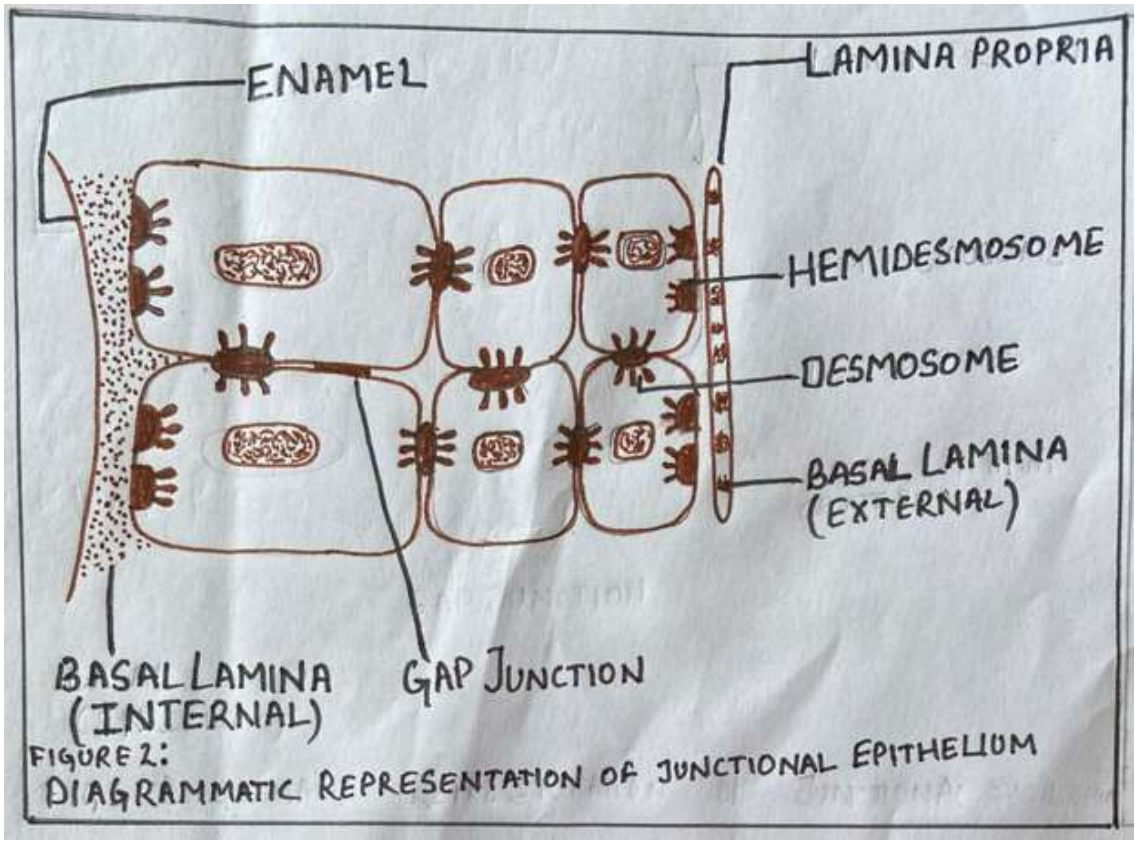

Figure:2 Diagrammatic representation of Junctional epithelium

Epithelial attachment

The epithelial attachment of junctional epithelium and tooth is because of *Epithelial attachment apparatus.*

"Epithelial attachment apparatus consists of:

- *Hemidesmosomes* of DAT cells (directly attached to tooth)
- *Internal basal lamina* on tooth surface which is basal lamina like extra cellular matrix".

Morphologically there are similarity between internal basal lamina and junctional epithelial "Directly attached to tooth (DAT cells)" and the enamels resembling "basement membrane between the epithelium and connective tissue". "Laminin and type V collagen" are present in the internal basal lamina and associated with hemidesmosomes [10].

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DYNAMIC ASPECTS OF THE JUNCTIONAL EPITHELIUM

"Its protective and regenerative capabilities depend on the junctional epithelium's cell and extracellular dynamics. According to Skougaard (1965, 1970), Demetriou (1972), and Ramfjord (1972), the junctional epithelium in primates is renowned for having a high rate of cellular turnover. Exfoliation of daughter cells occurs at the free surface of the junctional epithelium while cell mitosis occurs in the basal and potentially in certain Directly Attached to Tooth (DAT) cells (Salonen, 1994). (i.e., at the bottom of the sulcus and the interdental col). As a result, junctional epithelial cells move in a coronal direction toward the free surface, where they desquamate. Because the basal cells' surface area is greater than the sulcus bottom's, exfoliation must proceed at a very rapid rate (Löe and Karring, 1969, Listgarten, 1972b)". Directly associated to tooth (DAT) cells are also considered to move down toward the sulcus. A modification of the epithelial connection is necessary because the DAT cells are joined to the basal lamina by hemidesmosomes. The epithelial attachment is therefore typically dynamic rather than static. A passageway for fluid and migratory leukocytes is provided by the junctional epithelium's intercellular gaps. Approximately 30,000 PMNs move through the junctional epithelia of all human teeth and into the oral cavity per minute when there are no visible signs of inflammation (Schiött and Löe, 1970) [10]. The junctional epithelium allows the tissue fluid to transport a range of chemicals to the gingival sulcus' bottom. Together with leukocytes, these chemicals make up the host's defence mechanism against the bacterial threat. Since gingival fluid is an exudate that comes from the lamina propria's sub-epithelial blood vessels, the flow rate of this fluid reflects the degree of inflammation.

EXPRESSION OF VARIOUS MOLECULES AND THEIR FUNCTIONS

The preservation of typical tissue architecture and function is regulated by a large number of cell and extracellular molecules. The mechanisms that keep the epithelium attached to the tooth surface, the interface between the epithelium and connective tissue, and the spatial and interactive cell-to-cell relationships within the junctional epithelium itself are of particular interest. The significance of the epithelial attachment to the tooth surface has received a lot of attention recently. However, the extremely dynamic nature of the junctional epithelium suggests that the cells themselves play a considerably more significant role in the preservation of tissue integrity. Multiple cells are expressed by junctional epithelial cells. [10]:

"**Cell adhesion molecules (CAMs),** such as integrins for cell-cell and cell-matrix interaction and epithelial cadherins for intercellular adhesion and crucial for maintaining structural integrity. Carcino-embryonic Ag-related cell adhesion molecule 1(CEACAM1) for the adhesion between epithelial cells, they also contribute to guidance of PMNs through junctional epithelium and regulate the cell proliferation.

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Cytokines/chemokines like interlukins for chemotaxis; guiding PMNs towards the sulcus bottom and pro-inflammatory cytokines that contribute to the innate immune defense

Cell-membrane associated Blood group specific-carbohydrate like epidermal growth factor receptor for epithelial growth, differentiation and wound healing".

Molecular Factor	Location within the Junctional Epithelium	Suggested Functions
Cell Adhesion Molecules (CAMs)		
Integrins	Cell membrane of junctional epithelial cells	Mediate cell-matrix and cell-cell interactions
Epithelial cadherin (E-cadherin)	Epithelial intercellular junctions	Critical in intercellular adhesion and thus crucial for maintaining structural integrity
Carcino-embryonic Ag-related cell adhesion molecule 1 (CEACAM1)	Cell membranes of leukocytes and junctional epithelial cells	Adhesion between epithelial cells; contributes to the guidance of PMNs through the junctional epithelium; participates in the regulation of cell proliferation, stimulation, and co-regulation of activated T-cells; cell receptor for certain bacteria
Intercellular adhesion molecule-1 (ICAM-1 or CD54)	Cell membrane of junctional epithelial cells	Mediates cell-cell interactions in inflammatory reactions; guiding PMNs toward the sulcus bottom
Lymphocyte function antigen-3 (LFA-3)	Cell membrane of junctional epithelial cells	Mediates cell-cell interactions in inflammatory reactions; controls leukocyte migration to inflammatory sites
Cytokines/Chemokines		
Interleukin-8 (Il-8)	In junctional epithelial cells near the sulcus bottom	Chemotaxis; guiding PMNs toward the sulcus bottom
Interleukin-1α (Il-1α) Interleukin-1β (Il-1β) Tumor necrosis factor-α (TNF-α)	In junctional epithelial cells and macrophages in the coronal portion of the junctional epithelium	Pro-inflammatory cytokines that contribute to the innate immune defense
Cell-membrane-associated Blood-group-specific Carbohydrates		
N-acetyllactosamine	Cell membrane of junctional epithelial cells	Indicates a low level of cell differentiation
Growth Factors and Corresponding Receptors		
Epidermal growth factor (EGF)	In junctional epithelial cells	Mitogen that participates in epithelial growth, differentiation, and wound healing
Epidermal growth factor receptor (EGFR)	Cell membrane of junctional epithelial cells	Signal transduction
Proteases		

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Tissue plasminogen activator (t-PA)	In junctional epithelial cells	Serine protease that converts plasminogen into plasmin, which in turn degrades extracellular matrix proteins and activates matrix metalloproteinases
Matrix metalloproteinase-7 (MMP-7 or matrilysin)	In suprabasal junctional epithelial cells	Proteolytic degradation of the extracellular matrix
Natural antimicrobial peptides and proteins		
α-defensins	In PMNs and gingival crevicular fluid	PMN-produced antimicrobial substances that contribute to the innate immune defense
Human β-defensin-1 (hBD-1) Human β-defensin-2 (hBD-2)	Weak expression in junctional epithelial cells	Epithelially produced antimicrobial substances that contribute to innate host defense
Cathelicidin LL-37	In junctional epithelial and inflammatory cells	Antimicrobial and chemotactic substance produced by both PMNs and epithelial cells; contributes to the regulation of the innate immune defense

Junctional epithelium and Implants

"Always derived from oral mucosa epithelial cells is the junctional epithelium that surrounds implants. There are some similarities between the junctional epithelium that surrounds teeth and the peri-implant epithelium, but there are also some differences (Berglundh et al., 1991, Listgarten et al., 1991, Buser et al., 1992, Listgarten, 1996, Koka, 1998, Cochran, 2000). (Inoue et al., 1997, Ikeda et al., 2000, 2002, Fujiseki et al., 2003, Shimono et al., 2003). The peri-implant epithelium also expresses a few marker molecules that are involved in the defence mechanisms against the bacterial assault. Consequently, it has been observed that t-PA (Schmid et al., 1992), ICAM-1, and a cytokeratin profile similar to that of gingival junctional epithelium are present (Mackenzie and Tonetti, 1995). This means that when oral epithelia create an epithelial connection surrounding. This adaptive potential is also noticed in the regenerating junctional epithelium around teeth following gingivectomy". [10]

REGENERATION OF THE JUNCTIONAL EPITHELIUM

Accidental or deliberate trauma, tooth brushing, flossing, or clinical probing can all cause damage to the junctional epithelium. The junctional epithelium should therefore be able to handle such mechanical problems. The junctional epithelial cells from the tooth are mechanically damaged by clinical probing. Inadvertent trauma to the junctional epithelium may also be brought on by oral hygiene procedures. Dental floss use at premolars in 12-year-old people was the subject of Waerhaug's (1981) investigation into the healing of the junctional epithelium. After flossing stopped, cell detachment remained for 24 hours. Three days after flossing stopped, new attachment of junctional epithelial cells began. Studies demonstrate that the junctional epithelium is never entirely eliminated from the tooth since after two weeks, the cell populations on the experimental and control surfaces were once more indistinguishable from one another. However, the junctional epithelium would be

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entirely removed if gingivectomy procedures were used. The basal cells of the oral gingival epithelium must then divide to produce a fresh junctional epithelium (Listgarten, 1967; Innes, 1970; Frank et al., 1972; Listgarten and Ellegaard, 1973; Braga and Squier, 1980). In humans, a new junctional epithelium after gingivectomy may emerge within 20 days (Listgarten, 1972a, b; Schroeder and Listgarten, 1977). (Listgarten, 1972a, b; Schroeder and Listgarten, 1977). The junctional epithelium is therefore implied to be a highly dynamic and adaptive tissue with a rapid capability for self-regeneration [10].

Role of junctional epithelium in pocket formation

The conversion of junctional epithelium into pocket epithelium is considered as an authentication mark of beginning of periodontitis. The length of junctional epithelium in pocket is shorter than normal. There are two basic concepts in the attachment loss of junctional epithelium during pocket formation [11]:

Apical migration:

- Crestal collagen dis-integration results in loss of contact.
- Cytokine stimulates increased activity of EGF cells and its receptors

Coronal detachment:

- Coronal pooling of inflammatory cells
- Release of degenerating factors of cell adhesion molecule by inflammatory cells
- Gingipains (bacterial enzyme) destruct the complexes of cell adhesion.

These inflammatory cells in the junctional epithelium and the sub-epithelial region of the lamina propria should be viewed as a crucial component of proper homeostasis and the body's defence mechanism against ongoing bacterial warfare (for review, see Schroeder and Listgarten, 1997). In the junctional epithelium's coronal-most region, some studies have linked pocket formation to a loss of cellular continuity (Schluger et al., 1977; Schroeder and Listgarten, 1977). Therefore, the onset of pocket formation may be linked to the separation of DAT cells—tissue cells that are directly attached to teeth—from the tooth surface or to the emergence of an intraepithelial split. While researching pocket formation in humans, Takata and Donath (1988) observed declinatory alterations in the second or third cell layer of the DAT cells in the coronal region of the junctional epithelium toward the bacterial biofilm. In a dog model, similar findings were achieved (Hillmann et al., 1990). The focal breakdown of the junctional epithelium is thought to be caused by an increase in mononuclear leukocytes, specifically T- and B-lymphocytes and monocytes/macrophages with PMNs (Schroeder and Listgarten, 1997). Additionally, it is said that the host is the main cause of the elements that contribute to the breakdown of the junctional epithelium. However, other aspects must also be taken into account.

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Role of Junctional epithelium in Gingivitis

In the early lesion of gingivitis there is development of rete pegs and neutrophils densly infiltrate the junctional epithelium. Whereas in a well developed lesion of gingivitis, the intercellular spaces are widened due to flow of granular cellular debris, lysosomes derived from neutrophils, lymphocytes, monocytes. Destruction of basal lamina in some areas and formation of rete pegs, protruding into connective tissue.

Role of junctional epithelium in necrotizing ulcerative gingivitis

Destruction of junctional epithelium and replacement via meshwork of fibrin, necrotic epithelial cells, PMNs and neutrophil.

Edematous epithelium and intercellular spaces are infilterated by PMNs.

Role of junctional epithelium in Trauma from occlusion

Trauma from occlusion if leads to plaque accumulation then only junctional epithelium will undergo destruction.

Syndromes affecting junctional epithelium

Kindler syndrome: manifests due to loss of keratin-1 protein which is required for integrin activation. This syndrome leads to aggressive periodontitis. Failed attachment of junctional epithelium to tooth.

CONCLUSION:

The junctional epithelium is an idiosyncratic tissue that fulfills the challenging function at the border between the oral cavity, pioneer by bacteria, and the tooth attachment apparatus. It is very well adapted both structurally and functionally to control the constantly present bacteria and their products. However, its antimicrobial defence mechanisms do not signify the development of gingival inflammatory lesions. These defence mechanisms may be inundate by bacterial animus factors, and the gingival lesion could proceed to initiation of periodontitis. The transformation of the junctional epithelium to pocket epithelium is considered as an authentication mark in the development of periodontitis. Bacteria like e.g., P. gingivalis, may directly disturb the structural and functional integrity of the junctional epithelium. Recent studies have emphasised on the role of gingipains in the progression of pocket. This information may be useful in development of therapeutic strategies to counterbalance the deleterious effects of the cysteine proteinases.

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