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Is hard tissue formation in the dental pulp after the death of the primary odontoblasts a regenerative or a reparative process?

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ABSTRACT

Objectives: Conceptually, two types of tertiary dentine may be produced in response to caries and environmental irritations: "reactionary dentine" that is secreted by existing primary odontoblasts and "reparative dentine", formed after the death of the odontoblasts by proliferation and differentiation of progenitor cells into odontoblast-like cells. Because histologic evidence for tubular dentine generated by newly differentiated odontoblast-like cells is lacking in human teeth, the present study examined pulpal cellular changes associated with caries/restorations, in the presence or absence of pulpal exposures.

Methods: Ninety-six extracted human teeth were histologically processed and serial sectioned for light microscopy: 65 contained untreated enamel/dentine caries; 20 were heavily restored and 11 had carious exposures managed by direct pulp-capping.

Results: Sparsely distributed, irregularly arranged dentinal tubules were identified from the tertiary dentine formed in teeth with unexposed medium/deep caries and in restored teeth; those tubules were continuous with the tubules of secondary dentine; in some cases, tubules were absent. The palisade odontoblast layer was reduced to a single layer of flattened cells. In direct pulp-capping of pulp exposures, the defects were repaired by the deposition of an amorphous dystrophic calcified tissue that resembled pulp stones more than dentine, sometimes entrapping pulpal remnants. This atubular hard tissue was lined by fibroblasts and collagen fibrils.

Conclusions: Histological evidence from the present study indicates that reparative dentinogenesis cannot be considered as a regenerative process since the so-formed hard tissue lacks tubular features characteristic of genuine dentine. Rather, this process represents a repair response that produces calcified scar tissues by pulpal fibroblasts.

Clinical significance: Formation of hard tissue in the dental pulp after the death of the primary odontoblasts has often been regarded by clinicians as regeneration of dentine. If the objective of the clinical procedures involved is to induce healing, reduce dentine hypersensitivity, or minimise future bacteria exposure, such procedures may be regarded as clinical success. However, current clinical treatment procedures are not adept at regenerating physiological dentne because the tissues formed in the dental pulp are more likely the result of repair responses via the formation of calcified scar tissues.

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1. Introduction

The dental pulp is a loose connective tissue enclosed within rigid dentine walls, with odontoblasts lining the predentine. Odontoblasts are neural crest-derived mesenchymal cells that are organised into a highly polarised, pseudostratified palisade along the dentine–pulp interface.[1] Similar to cardiac myocytes, and neurons,[2] odontoblasts are long-lived, terminally differentiated post-mitotic cells that are not replaced during the lifetime of the individual.[3] Apart from their more recently recognised roles as sensory and defence cells,[4–6] odontoblasts are secretory cells that are responsible for the synthesis and extracellular deposition of a type I collagen-rich matrix referred to as predentine; subsequent biomineralisation of this matrix produces mineralised dentine.[7] Unlike osteoblasts that are eventually encased within the osteoid to form mature osteocytes, the odontoblast cell bodies are never entrapped by the collagen matrix they secrete. Instead, the cytoplasmic processes of odontoblasts project into dentine matrix, secreting dentine-specific non-collagenous proteins such as glycoproteins, proteoglycans and dentine phosphoproteins, which are responsible for the biomineralisation of this matrix. The cytoplasmic processes produce dentinal tubules which are characteristic of circumpulpal and radicular dentine.

Primary dentine refers to the tubular dentine that is formed by actively secreting primary odontoblasts during crown formation. Secondary dentine is used for describing the physiological dentine that is continuously deposited after completion of root formation.[8] Following tooth eruption, the secretory function of the odontoblasts is tempered by autophagy,[9] a housekeeping process that degrades some of the secretory intracellular components to preserve the functionality of these long-lived post-mitotic cells and to ensure their survival during starvation, stress or cell injury.[10] The less actively secreting, mature odontoblasts that produce secondary dentine are characterised by the presence of autophagic vacuoles and increasing deposition of intracellular lipufuscin,[9] the latter being derived from autophagy of aged or damaged mitochondria.[2]

Unlike bone that continuously remodels throughout life, dentine does not remodel and once lost, cannot be replaced. Nevertheless, tertiary dentine may be formed focally along the pulpodentinal junction, in locations where dentinal tubules from the primary and secondary dentine are closest to the source of external insult. These insults may be in the form of heat, stress, cavity preparation, invasion of micro-organisms or intratubular diffusion of by-products derived from those micro-organisms.[11] Conceptually, two types of tertiary dentine may be produced in response to these irritations. Mild stimuli usually stimulate an increased rate of matrix secretion by existing odontoblasts, resulting in the accelerated formation of ''reactionary dentine''. Stronger stimuli would lead to the death of the primary odontoblasts. Under favourable conditions, it is believed that dental pulp stem cells differentiate into odontoblast-like cells to produce ''reparative dentine''. Reactionary dentinogenesis requires the interactions of dentine matrix-derived growth factors with existing odontoblasts for stimulation of additional matrix secretion, which will then be calcified.[12–14] For reparative dentinogenesis to occur, a cascade of events involving migration, proliferation and differentiation of dental pulp stem cells into odontoblast-like cells induced by dentine matrix-derived growth factors is required before secretion of dentine matrix can occur.[15–18] Growth factors are capable of affecting biological functions of cells such as activation or repression of gene transcription, or changing gene expression of stem/progenitor cells.

The notion of regenerating of ''new dentine'' by ''new odontoblasts'' differentiated from pulpal mesenchymal stem cells has been well-accepted by the dental community, and forms the basis of contemporary vital pulp therapy procedures.[19] This regenerative concept has also been ardently explored in tissue engineering, by deploying tooth-derived stem cells, scaffolds and appropriate signalling molecules for regeneration of new dentine–pulp complex in necrotic teeth following the death of the original dental pulps.[20,21] For management of carious pulpal exposures in vital pulp therapy,[22–27] it is commonly held that ''dentine-like tissues'' such as fibrodentine or osteodentine will be regenerated to replace the lost dentine: ''following pulp exposure and after placement of an appropriate biocompatible capping material, a dentine bridge is formed in a few weeks by new odontoblast-like cells''.[28] Histologically, formation of a dentine bridge with tubular dentine that is lined by odontoblast-like cells has only been shown in experimental pulp capping of intact, virgin animal teeth [27,29] or human teeth;[30–32] evidence of these features are lacking in human teeth after direct capping of carious pulpal exposures. In the absence of truly dentine-specific phenotypic markers to identify the exact origin of the newly formed calcified tissues, it is not known whether these tissues are really dentine, or simply ectopic intrapulpal calcifications in response to chronic inflammation. To date, interpretation of the identity of calcified tissues produced in the dental pulp after the death of the primary odontoblasts is largely based upon the conventional wisdom that mineralised tissues formed by undifferentiated mesenchymal cells derived from the dental pulp has to be ''dentine''.

Although examples of complete tissue or organ regeneration are replete in invertebrates, higher vertebrates such as amphibians demonstrate extensive but restricted regeneration, whereas mammals are severely limited in their regenerative capacity once their development extends beyond the gestation stage.[33] Regeneration and repair are two related but different processes.[33] Regeneration refers to the proliferation of cells and tissues to replace the lost or damaged cells and tissues, with restoration of normal tissue structure. Conversely, repair refers to a response to injury involving both wound healing and fibrosis, with permanently altered tissue structure. Repair in mesenchyme-derived tissues invariably involves an increase in collagen deposition to reduce the wound size by scar tissue formation. Dystrophic calcification of scar tissues is not infrequently observed, examples of which may be found in the lungs,[34] atherosclerotic plaques,[35] as well as in the form of pulp stones in the dental pulp.[36]

A review of the existing dental literature on the formation of the so-called tertiary dentine indicates that the distinction between the processes of regeneration and repair in tertiary dentinogenesis remains enigmatic. Thus, the objective of the present study was to examine, through analysis of clinical cases, the cellular and tissue changes that occurred during the