Editor:
SAMUEL SELTZER, DDS
Department of Endodontology
School of Dentistry
Temple University
3223 North Broad Street
Philadelphia, Pennsylvania 19140

Age-related changes of the dental pulp complex and their relationship to systemic aging

Donald R. Morse, DDS, PhD,[a] Philadelphia, Pa.

TEMPLE UNIVERSITY SCHOOL OF DENTISTRY

The dental pulp and its associated structures, the dentin and the cementum, are discussed. Because many of the age-related pulpal changes have components considered in several of the current theories of aging, these theories are briefly reviewed. Part 2 describes the age-related changes of the dental pulp, the dentin, and the cementum (the dental pulp complex). An attempt is made to differentiate inherent aging changes from physiologic defensive changes and pathologic irritant-induced changes. Part 3 describes the relationship of age-induced changes in the dental pulp complex to components of the current aging theories together with a unified concept of the dental pulp complex aging. Part 4 considers whether dental pulp complex aging can be used as a biomarker for generalized aging. Whether age-related changes of the dental pulp complex can be altered by interventions is discussed.
(ORALSURG ORAL MED ORALPATHOL1991;72:721-45)

Although all dentists have learned dental anatomy and physiology in school, some readers may have forgotten certain details. To introduce the other aspects of this review and for nondental readers, the dental pulp and its associated structures are briefly considered.

The tooth is the hardest structure in the body. Enamel, which is 90% inorganic and 10% organic, is harder than bone. Dentin is similar to bone in composition, is 75% inorganic and 20% organic, and has a consistency similar to cartilage. Cementum is another bonelike substance.

Once formed, enamel does not show age-related changes except for a loss in permeability and an increase in brittleness. Other major changes are caused by fluoridation, normal function, diseases, and trauma. In a positive way, enamel can be remineralized by the addition of fluoride to drinking water, toothpaste, or mouthwashes, or as a supplement. The deleterious changes (loss of enamel) are related to biting and eating, dental caries, attrition, abrasion, erosion, trauma, and dental treatment. The remaining structures, dentin, cementum, and the dental pulp (the dental pulp complex), show age-related, physiologic, and pathologic changes. These changes reflect reactions in other parts of the body. This four-part article examines the age-related changes. First, a brief examination is given of the dental pulp and its associated structures. Because several of the dental changes are similar to those considered in some of the current aging theories, these theories are briefly reviewed. The age-related changes of the dental pulp, the dentin, and the cementum are thoroughly dis-

[a]Professor, Department of Endodontology.
7/15/28829

Fig. 1. Histologic sections of five stages in development of dental pulp complex. A, Late dental papilla (early bell) stage. C/, Cervical loop; *Dp,* dental papilla; *Id,* inner dental epithelium; *Me,* mesenchyme cells; *Od,* outer dental epithelium. B, Early dental pulp (late bell) stage. *Am,* Ameloblasts; *Dpu,* dental pulp; *Eo,* enamel organ; *Od,* odontoblasts. C, Formation of apical foramen *(arrowheads). Ab,* Alveolar bone; *Dpu,* dental pulp; *Od,* odontoblasts; *Pd,* primary dentin; *Pl,* periodontal ligament. *D,* Mature pulp stage. *Bv,* Blood vessel; *Cf,* collagen fibers; *De,* dentin; *Dpu,* dental pulp. E, Aged pulp stage with denticles *(Den)* and collagen bundles *(Cb). De,* Dentin; *Dpu,* dental pulp. (Original magnifications: **A,** X12; **B,** X35; **C,** X12; **D,** X54.) (Courtesy of Dr. S. Seltzer.)

cussed, and a succinct presentation of a unified concept of the dental pulp complex aging is then given. The possibility that dental pulp complex aging can be used as a biomarker for generalized aging is considered. Finally, the possibility of altering these age-induced dental pulp complex changes is examined.

PART 1: THE DENTAL PULP

The dental pulp, like other parts of the body, shows age-related changes. As elsewhere, these changes are difficult to separate from physiologic defensive changes and pathologic irritant-induced changes. In the early research on age-related changes of the dental pulp, aging, defensive, and pathologic changes were often examined together. Most of the teeth evaluated had been normally functioning, which made establishing whether the changes were related to aging, chewing, or disease difficult. However, recently, completely embedded (impacted) teeth have also been examined. Because these teeth are not functional, it was considered that a more realistic estimate of aging changes could be ascertained. Nevertheless, one may argue that because embedded teeth never erupt, they do not act as functioning teeth and changes detected may not reflect the normal situation. Primary teeth also show aging changes. In this review the findings of normally functioning permanent and primary teeth, as well as those of impacted teeth, are evaluated.

The dental pulp is a loose connective tissue encased in a solid wall of bonelike dentin and cementum.[1] During the formative stages of the tooth, the dental pulp begins as the dental papilla. The dental papilla is a diffuse collection of loose connective tissue that contains large, usually rounded, undifferentiated mesenchymal cells (Fig. 1, *A).* As the tooth forms and the root begins to develop, the cells of the dental papilla underlying the ameloblasts differentiate into odontoblasts, which are high and columnar close to the crown and become shorter and more flattened as they approach the root apex. The odontoblasts secrete a collagenous matrix known as predentin (uncalcified dentin). In time the predentin becomes mineralized and is then known as dentin. At this stage of tooth formation the dental papilla becomes the dental pulp (Fig. 1, *B* to *E,* and Fig. 2, *A).* As the root develops further, dentin deposition continues, together with the deposition of cementum outside the dentin along the root. These deposits result in the narrowing of the apical end of the root, which converges as the apical foramen (Fig. 1, C to £, Fig. 2, *B,* and Fig. 3).

Because odontoblasts develop from dental pulp

Fig. 1. Histologic sections of five stages in development of dental pulp complex. A, Late dental papilla (early bell) stage. C/, Cervical loop; *Dp,* dental papilla; *Id,* inner dental epithelium; *Me,* mesenchyme cells; *Od,* outer dental epithelium. B, Early dental pulp (late bell) stage. *Am,* Ameloblasts; *Dpu,* dental pulp; *Eo,* enamel organ; *Od,* odontoblasts. C, Formation of apical foramen *(arrowheads). Ab,* Alveolar bone; *Dpu,* dental pulp; *Od,* odontoblasts; *Pd,* primary dentin; *Pl,* periodontal ligament. *D,* Mature pulp stage. *Bv,* Blood vessel; *Cf,* collagen fibers; *De,* dentin; *Dpu,* dental pulp. E, Aged pulp stage with denticles *(Den)* and collagen bundles *(Cb). De,* Dentin; *Dpu,* dental pulp. (Original magnifications: **A,** X12; **B,** X35; **C,** X12; **D,** X54.) (Courtesy of Dr. S. Seltzer.)

cussed, and a succinct presentation of a unified concept of the dental pulp complex aging is then given. The possibility that dental pulp complex aging can be used as a biomarker for generalized aging is considered. Finally, the possibility of altering these age-induced dental pulp complex changes is examined.

PART 1: THE DENTAL PULP

The dental pulp, like other parts of the body, shows age-related changes. As elsewhere, these changes are difficult to separate from physiologic defensive changes and pathologic irritant-induced changes. In the early research on age-related changes of the dental pulp, aging, defensive, and pathologic changes were often examined together. Most of the teeth evaluated had been normally functioning, which made establishing whether the changes were related to aging, chewing, or disease difficult. However, recently, completely embedded (impacted) teeth have also been examined. Because these teeth are not functional, it was considered that a more realistic estimate of aging changes could be ascertained. Nevertheless, one may argue that because embedded teeth never erupt, they do not act as functioning teeth and changes detected may not reflect the normal situation. Primary teeth also show aging changes. In this review the findings of normally functioning permanent and primary teeth, as well as those of impacted teeth, are evaluated.

The dental pulp is a loose connective tissue encased in a solid wall of bonelike dentin and cementum.[1] During the formative stages of the tooth, the dental pulp begins as the dental papilla. The dental papilla is a diffuse collection of loose connective tissue that contains large, usually rounded, undifferentiated mesenchymal cells (Fig. 1, *A).* As the tooth forms and the root begins to develop, the cells of the dental papilla underlying the ameloblasts differentiate into odontoblasts, which are high and columnar close to the crown and become shorter and more flattened as they approach the root apex. The odontoblasts secrete a collagenous matrix known as predentin (uncalcified dentin). In time the predentin becomes mineralized and is then known as dentin. At this stage of tooth formation the dental papilla becomes the dental pulp (Fig. 1, *B* to *E,* and Fig. 2, *A).* As the root develops further, dentin deposition continues, together with the deposition of cementum outside the dentin along the root. These deposits result in the narrowing of the apical end of the root, which converges as the apical foramen (Fig. 1, C to £, Fig. 2, *B,* and Fig. 3).

Because odontoblasts develop from dental pulp

Fig. 2. Periapical radiographs of early stages in tooth development. A, Impacted maxillary right third molar with only crown formed *(arrow)*. Roots of second molar are almost completely formed *(arrowheads)*. **B,** Mandibular left first molar with partial development of roots (arrows/ Part of impacted early developing second molar can be seen *(arrowheads)*.

cells, predentin, dentin, and the dental pulp are logically considered one tissue. Therefore, when age-related changes are considered, all these structures are examined. There are several types of dentin. The dentin that is formed before the tooth erupts is known as primary dentin, and that which is elaborated after tooth eruption is known as secondary dentin. Secondary dentin also differs from primary dentin in that the contained dentinal tubules change their direction (Fig. 4). The major component of dentin is the centrally located dentinal tubule, through which the odontoblastic process passes with exchange of fluids and gases (inward from the outside of the tooth through the enamel and into the dental pulp, and outward from the dental pulp toward the exterior). Surrounding the dentinal tubule is the peritubular dentin, which is more calcified than the dentinal tubule. Between adjacent tubules is intertubular dentin, which is intermediate in calcification between the dentinal tubule and peritubular dentin. Secondary dentin is continuously deposited by the odontoblasts.

Interglobular dentin, found primarily in the crown of the tooth, is poorly mineralized (hypomineralized) and forms as a result of congenital disease and nutritional or hormonal deficiencies. A narrow layer of hypomineralized dentin that is found on the root is known as the Tomes granular layer, which may have a protective function. Sclerotic dentin is an overly mineralized (hypermineralized) form of primary dentin, also known as transparent dentin, that develops when calcium salts enter the dentinal tubules from the pulpal circulation. Sclerotic dentin is an aging change but can also occur as a reaction to irritants such as dental drilling. Reparative dentin (also known as irregular dentin, irritation dentin, and tertiary dentin) is deposited in response to irritants (e.g., dental caries, abrasion, attrition, erosion, dental drilling, and trauma). At times it is difficult to differentiate secondary from reparative dentin, although reparative dentin tends to be more irregular in appearance (Fig. 4).

Fig. 3. Histologic section showing apical part of pulp tissue *(Pu),* dentin *(De),* cementum *(Ce),* periodontal ligament *(Pl),* and alveolar bone *(Ab)*. (Original magnification, X54.) (Courtesy of Dr. S. Seltzer.)

Although cementum is not part of the dental pulp, it bounds the apical portion of the pulp, and its elaboration helps narrow the apical foramen. Cementum is formed from cells of the periodontal ligament, known as cementoblasts. The periodontal ligament fibers attach to the bone on one surface and to the cementum on the other surface (Fig. 3). Cementum is laid down continuously throughout life. Although there are three types of cementum—cellular, acellular, and intermediate—functionally they are the same.[2]

The dental pulp proper is a connective tissue consisting of cells, ground substance, fibers, bloodvessels, lymphatics, and nerves (Fig. 5). The primary cells of the pulp are fibroblasts. The young pulp has numerous fibroblasts as opposed to collagen fibers. As previously mentioned, odontoblasts are found in the periphery of the dental pulp. Other cells of the pulp are histiocytes (which convert into macrophages when needed), pericytes (in the walls of precapillaries and metarterioles), and undifferentiated mesenchymal cells (which can convert into macrophages, fibroblasts, odontoblasts, and dentinoclasts). Mast cells, lymphocytes, plasma cells, and eosinophils can be found in the dental pulp but usually only after

Fig. 4. Histologic section of dentin and pulp under mechanical (dentist-induced) exposure (Exp) of pulp *(Pu)* showing odontoblasts *(Od),* predentin *(Prd),* primary dentin *(Pd),* secondry dentin *(Sd),* and reparative dentin *(Rd).* (Original magnification, X96.) (Courtesy of Dr. S. Seltzer.)

Fig. 5. Histologic section of dentin *(De)* and pulp *(Pu)* showing blood vessels *(Bv),* collagen fibers *(CJ),* nerve fibers (TV/),and odontoblasts *(Od).* (Original magnification, X54.) (Courtesy of Dr. S. Seltzer.)

inflammation. The fibers of the dental pulp are collagenous (the principal type) and reticular (found around blood vessels and odontoblasts). The apical part of the pulp is more fibrous than the coronal region (Fig. 1, Cto£).

Similar to the ground substance of connective tissue elsewhere in the body, the ground substance of the dental pulp is composed of mucopolysaccharides (e.g., glycosaminoglycans, dermatan, and chondroitin sulfates) and glycoproteins. The blood, lymphatic, and nerve supply of the pulp enters the pulp mainly through the apical foramen. A minor supply comes through lateral and accessory canals and in molars through the furcation region (Fig. 6). Usually one pulpal artery, vein, and nerve enters through the apex. The principal blood vessels of the pulp are capillaries, arterioles, and venules (Fig. 7). Small lymphatic vessels are also found. The pulpal nerve that enters through the apex branches into cuspal nerves in the crown region (Fig. 8), which then divide into a network of small nerves (the plexus of Raschkow). A few nerve fibers enter the predentin and dentin.

PART 2: AGING THEORIES

Recently several current aging theories and their interrelationship were reviewed.[3,4] Because many of the concepts of these theories can be applied to the dental pulp, the highlights of these theories are briefly examined. The theories can be grouped into four types: (1) "biologic clock" (programmed) type, (2) immunologic, (3) DNA damage-related and (4) aging related to damage of other cellular components (OCC). Previously a critical review and a unified approach to aging was presented. [4] In this review, only the highlights of each theory are presented.

The *clinker theory,* related to OCC damage, considers that pigments (e.g., lipofuscin and ceroid) accumulate with aging. These inert, fluorescent brown substances slowly accumulate in the nondividing cells of the heart, brain, nerves, and a few other organs. These substances are considered to interfere with or choke off the activity of the involved cells.

The *falling domino theory,* related to OCC damage, states that certain toxic substances accumulate in cells. When one structure within a cell becomes inhibited or "falls," the other structures inside the cell tend to become inhibited. With each progressive fall the cell's ability to function normally is weakened that much more. As a person ages, the amount of inhibitory substances within the cells and in the intercellular spaces increases. Inhibited protein synthesis during aging is followed by a gradual decline of all the metabolic and biosynthetic processes.

Thermal denaturation, an OCC-damage theory, states that slow thermal denaturation immobilizes

Fig. 6. Histologic section of root of lower left first molar showing lateral canal *(Lc). De,* Dentin; *Fu,* furcation region; *Od,* odontoblasts; *Pu,* pulp. (Original magnification, X96.) (Courtesy of Dr. S. Seltzer.)

Fig. 7. Histologic section of dentin *(D)* and pulp *(Pu)* showing blood vessels *(Bv),* odontoblasts *(Od),* fibroblasts *(Fi),* and collagen fibers *(Of).* (Original magnification, X96.) (Courtesy of Dr. S. Seltzer.)

proteins. This in turn results in disruptions and eventually death of the involved cells.

The *cellular loss theory* involves DNA and OCC damage but focuses primarily on the latter. It considers that cell loss is one of the fundamental causes of human aging. Dividing cells found in the skin, mucous membranes, and gastrointestinal tract lining have the biologic potential to divide a maximum of 50 times and then die. Partially dividing cells, found in the liver and kidney, have a greatly reduced capacity to divide in advanced age. Of the nondividing cells, which include erythrocytes, neurons, cardiac and skeletal muscle cells, and bronchial cells, 40% are usually lost by 75 years of age. The cells are partially replaced by extracellular fluid and connective tissue. The loss of cells can result in decreased function and shrinkage of the involved structures.

The *enzyme/hormonal/ glycoprotein theory,* which involves OCC-damage and biologic-clock components, considers that the usual manifestation of aging is reduced enzyme, hormonal, and glycoprotein activity. Most of the reduced enzyme and coenzyme activity occurs within mitochondria. In contrast, lysosomal activity, with its destructive release of hydrolytic enzymes, increases with aging. Many hormones have decreased production and efficacy with aging. These include the sex hormones, adrenocorticosteroid hormones, thyroid hormones, pituitary hormones, catecholamines, thymic hormones, and the ubiquitous dehydroepiandrosterone. The proposed decreasing oxygen consumption hormone, which is considered by some to be an aging or "death" hormone, purportedly increases in advanced age. P-glycoprotein removes toxins from within cells. With aging, formation of P-glycoprotein is decreased, which could relate to cellular death.

The *genetic timetable* is a major biologic-clock theory, also known as the genetic-clock or ecologic-evolutionary theory. It states that for each species a specific genetically determined maximum life span exists. There is a definite time course and direction for the alterations in the various parts of the person. The sum total of these changes results in the failure of the person to withstand both external and internal stressors, and death occurs. Various types of aging genes have been proposed, including juvenescent genes (active during youth), senescent genes (active late in life), "shortevity" genes (genes for a short life), major histocompatibility complex aging genes (control DNA repair, antioxidant production, and cyclic nucleotide activity), longevity-determinant genes (yield pleitrophic genes producing advantageous changes in youth and deleterious changes in later life), and "restrainer" genes (keep deleterious genes in check early in life but later in life can no longer effectively control deleterious genes).

The *disposable soma* aging theory has biologic-clock and OCC-damage components. It is based on the concept of pleiotropic genes that allow for an optimum amount of energy to be available during a person's youth to maximize reproductive capability. The deleterious component is that once the reproductive period is over, the pleiotropic genes cause senescence to occur rapidly because sufficient energy is no longer available to ensure optimum performance.

DNA deterioration, a major DNA-damage theory,

Fig. 8. Dental nerve fibers. A, Histologic section of apical region of mature tooth showing entering nerve bundle *(Nb)*. Ce, Cementum; *De,* dentin; *Pu,* pulp. B, Scanning electron micrograph showing nerve fiber *(Nf)* in coronal region of pulp. (Original magnifications: A, X54; B, XI800.) (Courtesy of Dr. S. Seltzer.)

also includes OCC-damage, immunologic, and biologic-clock aspects. One possible cause for aging is that a cell multiplies a certain number of times and then dies because its DNA has deteriorated. Another possibility is that after a given period of time, the cell's DNA repair mechanisms no longer function effectively. With aging there are more DNA strand breaks, a decrease in DNA supercoiling, a steady loss of methylation of DNA bases, a haphazard falling apart of the differentiation mechanism (dysdifferentiation), an increase of migratory DNA (transposons or "jumping genes"), a dramatic increase in sister chromatin exchange, and either deterioration of the chromatin that prevents the repair enzymes from reaching the damaged lesion or the enzymes themselves go bad.

The *error theory* has DNA- and OCC-damage and biologic-clock components. It considers that flaws in the formation of proteins (including enzymes and hormones) can result from defects in any one or more of the many intermediary substances involved in making proteins. Hence errors could occur in either DNA, messenger RNA, transfer RNA, ribosomal RN A, or other aspects of protein formation. Defective enzymes could lead to an error catastrophe in the synthesis of proteins. The abnormal proteins that subsequently form could be a basic cause of aging.

Somatic mutation, a basic DNA-damage theory, considers that somatic cells (both dividing and nondividing) gradually accumulate defective genes by mutation, which causes the cells, and thus the person, to have decreased function. Most mutations are deleterious. Hence if the structures of older persons contain appreciable numbers of cells carrying mutations, the involved structure should function less efficiently than it would normally. When the somatic cells accumulate a specific number of mutations, senescence and death should follow.

The *radiation theory* has DNA- and OCC-damage components. It considers that aging is caused at least in part by harmful ionizing radiation from outer space, rocks, and soil. Ionizing radiation produces several changes comparable to those observed during normal aging. After radiation the number of viable cells in many tissues is reduced. These cells are often replaced by elements of connective tissue. Radiation can also cause DNA damage and somatic mutations, but radiation changes are seen primarily in dividing cells.

The *immunologic theory* has biologic-clock as well as immunologic components. It states that aging is caused at least in part by a progressive breakdown in the body's immunologic system that produces antibodies and lymphokines. It also involves an increased incidence of autoantibody reactions. The theory assumes that with aging the immunologic system becomes less capable of distinguishing normal proteins from foreign proteins and therefore normal beneficial proteins are destroyed.

It also considers that with aging the protective antibodies and the T lymphocytes become less able to perform their functions, and therefore infectious and malignant diseases become more prevalent. This theory is based on a genetic predisposition for the breakdown of the immune system, which results in a decreased number of immune cells and an increased number of poorly functioning immune cells.

The *nutritional theory,* an OCC-damage theory, considers that aging can result from the buildup of nutrient metal minerals such as copper, iron, manganese, zinc, and calcium, as well as toxic metals such as lead, aluminum, cadmium, tin, and titanium. It also considers that intake of polyunsaturated and saturated fatty acids promotes aging because of both lipid peroxidation and the development of obesity.

The *macrophage theory,* another OCC-damage theory, has an immunologic aspect as well. Metchnikoff believed that aging was related to increased activity of macrophages in the colon. 4 the co|on was considered to be the repository for bacteria and many noxious substances. It was postulated that toxic wastes from the colon passed into the bloodstream and ultimately debilitated the body cells. The macrophages then attacked the debilitated cells, and further damage occurred from the macrophages' released lysosomal enzymes. This theory is related to the former waste product theory, which stated that aging resulted from the accumulation of nonexcreted wastes.

The *watch-spring* theory is a biologic-clock theory that states that the human body, like a watch spring, gradually ceases to function because its stored energy

runs out. At first glance this theory appears realistic because older people usually have less energy than youngsters.

Redundancy is another biologic-clock theory that incorporates some components of DNA damage. In the genes repeated DNA nucleotide sequences function as a reserve of information for evolutionary change; a means of increasing functional expression; and, relative to this theory, a reserve mechanism for protecting vital information from random errors that occur in functioning DNA sequences. These repeated sequences are considered to have evolved for delaying the inevitability of failure by providing the redundancy needed for maintenance of vital information. This redundancy of genes leads to reserve capacity that ensures that systems will perform adequately for prolonged periods of time. Once reproduction (which is considered to be the main evolutionary reason for having these redundant copies of DNA) occurs, the various organ systems "coast" on the reserve capacity that was overengineered during the earlier developmental period. The various body tissues and cells are therefore stable for long periods of time, but eventually the overload of trauma is too great and the body begins to break down, resulting in aging. It is further proposed that these redundancy genes which allow for extra copies simultaneously have deleterious components that lead to the development of chronic diseases as one ages (e.g., malignancies, autoimmune diseases, cardiovascular diseases, diabetes mellitus).

The *wear-and-tear theory,* a combination DNA- and OCC-damage theory, also known as the accumulated pathology theory of aging, is based on the finding that all inanimate objects wear out. It states that aging is caused by some kind of wear or damage to the various body components, either by the use of the parts (wear-and-tear) or by injuries to the genetic or protein-forming mechanisms (biologic insults). The injuries can occur from physical stressors such as heat, light, oxidation, radiation, chemicals, drugs, pollutants, trauma, pressure, infection, diet, and noise.

Rate of living is a biologic-clock theory with some damage components. The concept is that the higher the metabolic rate per unit of body mass, the faster will be the rate of aging and the shorter will be the life span. In a general sense this is true because small animals with a rapid metabolism usually die sooner than large animals with a slower metabolism. For example, a mouse uses energy at 30 times the human rate and lives about one thirtieth as long as human beings. Excessive exercise, which increases the metabolic rate, reduces the life span of experimental animals. The metabolic rate of an average woman is 10% lower than that of an average man, and women live about 10% longer than men. Decreasing food intake, which increases life span, also decreases the metabolic rate per unit metabolic mass (but this has not always been confirmed).

Fig. 9. Intracellular sources of free radicals. (Adapted from Pollack RL, Morse DR. Int J Psychosom 1988;35:43-8.)

The *hypoxia* theory states that aging is mainly the result of lowered oxygen tension in critical areas of the body such as the brain. The decline in oxygen tension could relate to genetic factors, environmental traumas (e.g., diet-induced atherosclerosis that could impair circulation and reduce oxygen flow), or both.

Stress is a major OCC-damage theory closely related to the wear-and-tear theory and is known as the accumulated stress theory of aging. Basically, it states that stress per se causes aging. The concept is that an accumulation of environmental stressors, no matter how minor, can accelerate aging and result in death. Evidence shows that accumulation of lipofuscin pigments in neurons is accelerated by stress. Actuarial data indicate that with an increase in stressors to which a population of human beings is subjected the life expectancy decreases and thus aging is presumably accelerated. Adaptability to stress is decreased in the older person as compared with the young. Death is considered to be a stochastic event that results from

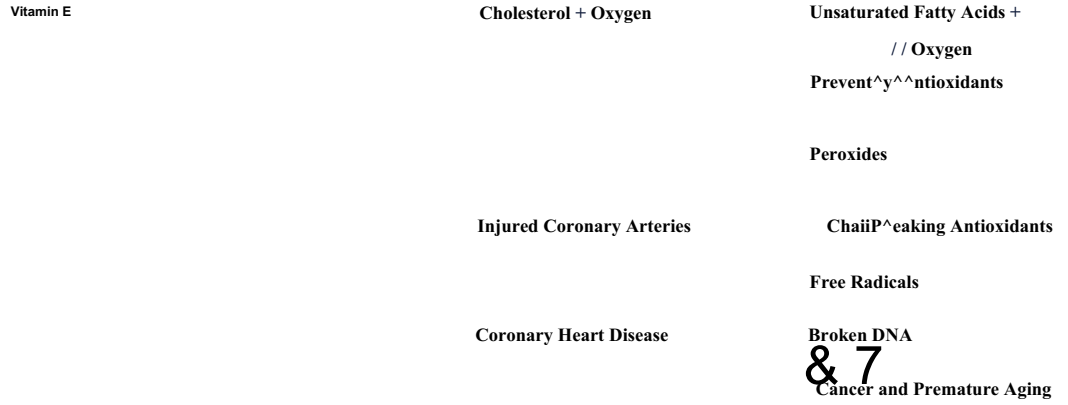

Fig. 10. Intracellular antioxidant protection. (Adapted from Pollack RL, Morse DR. IntJ Psychosom 1988;35:43-8.)

Fig- 11- Deleterious effects of oxidized lipids. (Adapted from Pollack RL, Morse DR. Int J Psychosom 1988;35:43-8.)

disruptive effects of stressors that would be tolerated at younger ages.

According to the *cross-linkage* theory, a major DNA- and OCC-damage theory, the chain of events known as aging starts with the formation of cross-linkages in proteins and nucleic acids. Cross-linkages can also occur between molecules of collagen, which makes it tougher and more rigid. This is purported to be the cause of aging of skin, tendon, bone, the dental pulp, blood vessels, lung tissue, and other body components. Cross-linked collagen is more readily infiltrated with calcium deposits. A previous aging theory known as the calcium theory linked aging to the gradual accumulation of calcium deposits throughout the body. Examples of the results of collagen cross-linkage are reductions in lung activity, transport of substances across cell membranes, and muscular activity. Elastin, another important proteinaceous fiber in connective tissues, especially blood vessels and lung tissue, becomes more cross-linked with aging. Other substances in the body can be cross-linked by intermediate molecules. Once a substance is cross-linked, it eventually loses its function. It is considered that cross-linkage prevents certain protein and nucleic acid molecules from being metabolized by the body's enzymes. These proteins then accumulate in the cells as "frozen metabolic pools," which clog the cells and eventually destroy them. The remaining number of active molecules is then gradually reduced and becomes progressively less adequate to cope with stressors.

According to this theory, with aging an increased accumulation of cross-linkage agents occurs. These can be derived from foods, drugs, and pollutants. Purported cross-linkage agents include acetaldehyde, formaldehyde, glyceraldehyde, malonaldehyde, pyruvic acid, citric acid, succinic acid, ubiquinone, orthoquinone, lipid peroxides and their derivatives, free radicals, silicon, lead, aluminum, copper, iron, manganese, cadmium, tin, titanium, calcium, and zinc. Glucose can attach to proteins and nucleic acids to form cross-linkage products. The formed substances are known as advanced glycosylation end products. Tobacco smoke contains acrolein and glycerin, which are considered to be cross-linkage agents. Cross-linkages can induce somatic mutations and protein degeneration, and can change the immunologic behavior of proteins, which appears to be a prelude to autoimmunity. It has been proposed that the principal phenomenon in atherosclerosis is cross-linkage. This could be the rationale for a previous aging theory known as the circulation deficiency theory. The concept for this theory might be that the accumulation of cross-linked collagen reduces the diameter of blood vessels, which in turn impairs circulation and eventually results in cell death.

The *free-radical* theory can relate to DNA damage, OCC damage, immunologic factors, and biologic-clock mechanisms. The free-radical theory is steadily gaining acceptance as a plausible explanation of primary chemical reactions involved in aging. Free

Fig. 12. Dental caries. A, Periapical radiograph of maxillary left canine showing dental caries *(arrow)* close to dental pulp *(arrowheads)*. **B,** Histologic section showing streptococci from dental carious lesion invading dentinal tubules. (Original magnification, X960.)

Fig. 13. Extensive attrition of maxillary anterior teeth as result of bruxism. (Courtesy of Dr. T. Simpson.)

radicals can propagate through hundreds of thousands of molecules and wreak havoc before they finally encounter another free radical and become neutralized. Free radicals have been called the "great white sharks of the biochemical sea of life."[5] If they are unchecked, free radicals can continue to create other free radicals from normal molecules, thereby disrupting vital functions. In this way free radicals can cause serious effects to cellular metabolism as a consequence of damage to DNA, RNA, enzymes, lipids, immune cells, and cell membranes. Free radicals are usually produced as unwarranted by-products of normal oxygen metabolism and lipid peroxidation of polyunsaturated fatty acids.

Free radicals can be formed endogenously and act either intracellularly or extracellularly (Fig. 9).[6] Endogenous free radicals are generated during normal metabolism of oxygen and iron, from the breakdown of the peroxidized fatty acids derived from the body's own fat stores, from the breakdown of leukocytes (free radicals are released with the disruption of the lysosomes), and during vigorous aerobic exercise. They can also be formed exogenously and then act within the body through either inhalation, injection, digestion, or absorption through the skin and mucous membranes. Exogenous substances producing free radicals include cigarette smoke, oxidized and polyunsaturated fatty acids, pollutants, radiation, ingested and injected drugs, and hyperoxic environments. Examples of free radicals include hydroxyl (which is produced by radiation and can be involved in arthritis formation), superoxide (which reacts with hydrogen peroxide to form hydroxyl radicals and is considered to downgrade collagen, damage DNA, destroy cells, inactivate enzymes, and oxidize polyunsaturated lipids), peroxides (which are involved in lipid peroxidation and can be active in the formation of aging pigments), hypochlorite, and alkoxyl.

With respect to aging, this theory states that oxygen-derived free radicals cause lipid peroxidation, which in turn damages cell membranes and other cellular structures. Mitochondria are the main source of free radicals. The body naturally contains antioxidant mechanisms (e.g., superoxide dismutase, a-tocopherol, ascorbic acid, 0-carotene, glutathione, glutathione peroxidase) that quelch free radicals (Fig. 10). With aging these mechanisms become less effective and more free radicals are generated. As a result of both occurrences, greater free-radical damage occurs.

Unsaturated fatty acids, which are essential components of cell membranes, are especially prone to lipid peroxidation by free radicals. Lipid peroxidation can result in the formation of toxic hydroperoxides, epoxides, aldehydes, and other deleterious substances. Structural proteins in the cell membranes can also be modified by free radicals and hydroperoxides. These altered proteins can form cross-linkage components with lipid peroxidation products. One of these cross-linkage components is malonaldehyde, which has been shown to form cross-linkage products with amines of proteins, phospholipids, and nucleic acids. Some lipid peroxidation products of free radicals become aging pigments, which accumulate in aged tissues and form cross-linkages.

Free radicals are capable of destroying immune cells. As a result, free-radical damage has been implicated in a number of chronic diseases that are

Fig. 14. Extensive erosion and attrition of anterior teeth from citrus fruit and diet high in abrasive foods. (Courtesy of Dr. T. Simpson.)

prevalent in older persons, including various malignancies, autoimmune diseases, cardiovascular diseases, and Alzheimer's disease (Fig. 11).

PART 3: AGE-RELATED CHANGES OF THE DENTAL PULP COMPLEX

Most teeth erupt, and human beings usually require them to eat, talk, bite, and perform other oral functions. These oral functions result in physiologic defensive pulpal, dentinal, and cemental changes. In Western countries dental caries is still prevalent even though its incidence has been greatly reduced because of fluoride treatment (Fig. 12). In other countries attrition from coarse, abrasive diets is frequent. In Western countries attrition is also common but is often stress related. This condition is known as bruxism[7] (Fig. 13). Erosion from ingestion of citrus fruits and juices was formerly fairly uncommon (Fig. 14). However, recently in Western countries, bulimia is becoming prevalent among young and middle-aged women. In this condition, in which vomiting is induced, the vomitus causes erosive effects on teeth. Abrasion, although not frequent, is seen most often in persons who brush their teeth too vigorously and eventually wear away the dental enamel (Fig. 15). Throughout the world periodontal disease is prevalent (Fig. 16) and tooth trauma (from blows, falls, objects, accidents, dental treatment) occurs frequently. As the result of trauma and disease, most people have pathologic changes induced in the dental pulp, dentin, and cementum of all or part of their dentition[8] (Fig. 12). Although relatively inherent aging changes can be found in impacted teeth, these teeth are nonfunctional. Hence both functional and nonfunctional teeth should be examined in the determination of dental-related aging changes. Aging-type dental pulp complex changes can be observed with genetic diseases

Fig. 1 5. Periapical radiograph showing marked abrasion of mandibular anterior teeth resulting from excessive horizontal toothbrushing. Root canals *(arrowheads)* show radiographic manifestations of premature aging (i.e., narrow, fine root canals). (Courtesy of Dr. T. Simpson.)

such as dentinogenesis imperfecta and progeria. Because many of the physiologic defensive and pathologic changes are similar in appearance to aging changes, at times it is difficult to differentiate them from each other. Nevertheless, an attempt will be made to differentiate inherent aging changes from physiologic defensive and irritant-based pathologic changes.

One purported means of differentiating aging and physiologic defensive changes from irritant-based pathologic changes is that teeth undergoing aging changes are symptomiess. Although patients can have a severe toothache from dental caries or a fracture into the dental pulp, many cariogenic teeth are asymptomatic. There is usually no pain associated with attrition, abrasion, erosion, and periodontal disease. Tooth trauma can also be asymptomatic. Hence symptomatology cannot be used to separate aging changes from physiologic and pathologic ones.

Another attempted means of differentiating aging and physiologic changes from pathologic ones is to pulp test the teeth. Teeth can be pulp tested by the use of hot, cold, and electric current. Teeth with necrotic pulps give no response to these testing modalities. A tooth having aging changes usually gives a partially vital response, but if the pulp is extremely aged, no response to the testing modalities may occur. Teeth having pulps with varying degrees of vitality can yield

Fig. 16. Periapical radiographs showing evidence of marked periodontal disease of mesial roots (i.e., periodontitis manifested by deep pocket) *(arrows).* Mesial root canals *(arrowheads)* show radiographic manifestations of premature aging (i.e., almost completely obliterated root canals). A, Mandibular right second molar, which also has periodontitis in furcation region. B, Mandibular left second molar with large amalgam restoration *(Am).*

pulp test responses that vary between a completely vital response to no response. Hence pulp test results cannot be used to separate aging changes from physiologic and pathologic ones.

Periapical radiographs can help in the differential diagnosis of age-related dental changes. Usually with inherent aging changes, dental caries, attrition, abrasion, periodontal disease, and tooth trauma are not evident (Fig. 17, *A).* However, the pulp can become necrotic as the result of a blow to the tooth that occurred years before. If the blow causes no external tooth damage, (which is often the case) then this tooth with a necrotic pulp will show no evidence of dental caries, attrition, abrasion, periodontal disease, or tooth trauma (Fig. 17, *B).* Hence radiography cannot be used to separate aging changes from physiologic and pathologic ones. Nevertheless, the periapical radiograph can give a strong clue to the presence of age-related dental changes, as discussed later.

Therefore, to adequately diagnose aging pulpal changes, tissue examination must be done. In this discussion the age-related changes of the dental pulp, the dentin, and the cementum are examined. Finally, the aging changes of primary teeth are considered.

Dental pulp changes

Compromised circulation and innervation. As discussed later, with aging the apical (root end) deposition of secondary dentin and cementum increases.[1,2] This tends to narrow the originally wide-open root apex. Because the blood, lymphatic, and nerve supply to the pulp comes through the apical foramen, as the apex narrows, these supplies can be compromised. In extreme old age the deposition of dentin and cementum can be so complete that the blood, lymphatic, and nerve supply to the pulp is almost completely shut off. Bloodvessels to the aged pulp undergo arteriosclerotic changes, resulting in a diminished blood supply to the pulp cells.[1] The arterial intima thickens, and the adventitia calcifies.[9] The lymphatics also show age-related degenerative changes. The pulpal nerve entering the aged pulp shows progressive mineralization of the nerve sheath and the nerve itself.[1] Although it has never been determined, this age-related interference in circulation and innervation may be the first step in the aging of the dental pulp.

Fig. 17. Periapical radiographs of dental pulps having aging changes and necrosis. A, Severely aged dental pulp in maxillary left lateral incisor. Tooth had no history of trauma, dental caries, attrition, erosion, or abrasion, and no dental restorations were present. Although root canal is almost completely obliterated *(arrowhead),* tooth still tested vital. In contrast, adjacent maxillary left canine had extensive dental caries (De) and pulp became inflamed and then necrotic. Internal resorption *(Ir)* of root canal is evident. **B,** Presence of pulpal necrosis in three mandibular incisors that had been traumatized many years before. Dental caries, attrition, abrasion, and dental restorations are not evident. Trauma resulted in premature aging of left central incisor. *Arrowhead* shows almost complete obliteration of apical half of root canal.

Fat droplet deposition. The first observable change within the dental pulp proper is fat droplet deposition. Although it has been reported as a definitive change,[10] recently it has been challenged and it may be a tissue-processing artifact.[1,11] According to the histologic description, fine droplets of fatty deposits are found in the odontoblasts, nuclei of pulp cells, and walls of pulp tissue capillaries. If this is a true occurrence, it must be differentiated from fat replacement

Fig. 18. Histologic section of root showing pulposis (fibrosis of pulp). *Ab,* Alveolar bone; *Ce,* cementum; *Pl,* periodontal ligament; *Pu,* pulp; *Rd,* reparative dentin; *Sd,* secondary dentin. (Original magnification, X54.) (Courtesy of Dr. S. Seltzer.)

(described later) and from fatty degeneration, which probably does not occur in the pulp.

Vacuolization of the odontoblasts. Vacuolization of the odontoblasts is another questionable change that may be an artifact.[1,9] Nevertheless, it has been described as the next sign of pulpal aging. The odontoblastic cells are pushed apart and separated from the dentin wall by the apparent pressure of an intercellular accumulation of tissue fluid.[10]

Reticular atrophy. Reticular atrophy has been considered an artifact by some authorities.[1,9,12,13] According to Kramer,[12] the appearance of reticular atrophy can be produced by incomplete elimination of the clearing agent and consequently imperfect infiltration of wax in preparation of the tissue slides. Nevertheless, histologically, [10] reticular atrophy is the next observable stage in pulpal aging. The tissue has a netlike appearance, which is apparently related to an abundance of intercellular fluid and a reduction in the number of pulp cells. Even if these first three histologic designations are artifacts, it is still likely that the pulp tissue goes through fat droplet deposition, intercellular fluid accumulation, and reduction in the number of pulp cells.

Fibrosis of the pulp. As the pulp aging process continues, there is a great decrease in the number of cells (odontoblasts, fibroblasts, and mesenchymal cells) and a corresponding apparent increase in the number of collagenous fibers (Fig. 18). The cell density of the pulp decreases by about half from 20 to 70 years of age.[9] The odontoblasts that remain become smaller and more flattened. With respect to the age-related increase in fibers, this may be more apparent than real. With the reduced size of the pulp (as the result of secondary dentin formation) and the decreased number of cells, the remaining pulpal space is filled more with fibers. However, because the number of fibroblasts is greatly reduced, more collagenous fibers cannot be produced.[14] Hence some of those fibers are remnants from previous production. There may also be an increase in polymerization and aggregation of previously existing smaller units of collagen.[15] In addition, the number of blood capillaries, lymphatics, and nerves decrease. They are encased in connective tissue sheaths. As the number of vessels and nerves decrease, their connective tissue sheaths remain. These connective tissue sheaths then become part of the remaining fibrous pulp. The reticular fibers (mainly around blood vessels) also increase with agmg.[16, 17]

In time the pulpal nerves become less sensitive. This is why aged teeth are frequently painless. Together with the cellular reduction, fibrous tissue accumulation, and decrease in circulatory and nervous elements, there is at first an increase (while the collagen is being formed) and then a reduction in the acid mucopolysaccharides. Eventually practically nothing remains in the pulp except fibrous tissue. This is now the stage known as fibrosis (fibrous degeneration) of the pulp (senile fibrosis, pulposis, atrophic pulp, senile pulp atrophy).[17] As previously mentioned, in this stage the pulp can show a decreased vitality response but clinically it functions normally. Pulposis should be differentiated from fibrous replacement. The latter process is the replacement of one tissue by fibrous connective tissue that contains viable fibroblasts. An example of this process is the replacement of infarcted heart muscle tissue by fibrous connective tissue. In pulposis there is no replacement, only degeneration. Eventually no viable fibroblasts but only the fibers remain.

These first four pulpal aging changes are actually only stages in the same process, and they differ only in degree.

Hyaline degeneration. Hyaline degeneration is usually an intermediate stage in the formation of pulp calcification. The pulp has only one blood circulatory system and no collateral circulation. Minor circulatory disturbances can often result in hyalinization of areas of the pulpal tissue.[11] Hyalinization denotes a

Fig. 19. Periapical radiographs showing denticles *(arrows)* in pulp chamber of molar teeth. *Am,* Amalgam restoration. A, Mandibular right first molar with dental caries *(De)* beneath and behind amalgam restoration. Mesial root canals show premature aging changes (i.e., almost completely obliterated root canals *(lower arrowheads)*. **B,** Mandibular left first and second molars with intact amalgam restorations. **C,** Maxillary right second molar with intact amalgam restoration.

change in the microscopic appearance of a tissue rather than the production of any specific substance. The change takes place within the intercellular fibers of connective tissues. It is usually a sequela to long-standing fibrous degeneration. In time this hyaline material and the spaces formed by the shrinkage fill with fat. This is the stage of fat replacement.[10]

Fat replacement. Under the light microscope in ordinary wax sections, fat replacement appears as circular spaces in the tissues, because the fat dissolves out in the preparation of the specimen. Although some investigators[1,11] consider this to be a tissue-processing artifact, others have found evidence of its existence. [10] Some investigators consider the presence of fat to be a replacement phenomenon, whereas others judge it to be a degeneration.[15,18] Stewart[18] isolated monoglycerides, diglycerides, phospholipids, lipoproteins, cholesterol, and cholesterol esters. Calcification commonly occurs in these fat deposits and can lead to the formation of pulp stones (denticles) and diffuse calcifications. [19] Before pulp calcifications are examined, two other changes are considered first.

Pulp "cysts. " Pulp "cysts" are related to pulp atrophy. Although they too may be a processing artifact,[1, 11] pulp cysts (pseudocysts) have been described in the pulps of sound teeth.[9,10] They are apparently spaces that are filled with fluid and surrounded by fibrous connective tissue. Pulp cysts have been considered to be the result of localized pulp atrophy with accompanying shrinkage of the pulp tissue.[10]

Mucoid degeneration. Mucoid lies in the interstitial spaces between the cells and the reticulum. It is a normal constituent of the pulp. With aging, mucoid increases and simultaneously the level of acid polysaccharides decreases. [9] Under pathologic conditions masses of mucoid can accumulate within the pulp. Together with the mucoid, degenerative changes, including a complete loss of embryonic connective tissue structure, occur.[20]

Calcifications. Calcifications can be classified according to size, structure, and position. By size they can be classified into denticles and diffuse calcifications. [9] Denticles are relatively large, well-defined, hard structures in the pulp cavity. If large enough, they can be visible on periapical radiographs (Fig. 19). By their internal structure these denticles can be divided into "true" and "false" types. True denticles, the rarer type, consist of an irregular kind of dentin with traces of dentinal tubules and odontoblasts. Usually they are found close to the apical foramen but can be in the wall or bottom of the pulp chamber. True denticles are rarely found free (Fig. 20, *A).* Epithelial cells from the inner enamel epithelium are needed for the differentiation of odontoblasts and the beginning of dentin formation. Therefore it has been hypothesized that true denticles form as the result of remnants of Hertwig's epithelial root sheath (an epithelial structure that helps in the development of the root of the tooth) becoming enclosed within the pulp because of a local disturbance. These remnants could then induce pulp cells to become odontoblasts and initiate dentin formation.[13]

False denticles are calcified structures in the pulp cavity that do not show the structure of dentin. They comprise most of the denticles found in human teeth. False denticles consist of concentric layers (lamellae) of calcified material surrounding a central nidus of necrotic and calcified cells (Fig. 20). The cells are derived from degenerated hyalinized pulp tissue. Once calcification begins, new layers are continuously laid

Fig. 20. Histologic sections of denticles. Blood vessels; *De,* dentin; *Fd,* false denticle; *Od,* odontoblast; *Td,* true denticle. A, Free true denticle. B, Attached false denticle. C, Attached false denticles. (Original magnifications: **A** and **B**, X96; **C**, X54.) (Courtesy of Dr. S. Seltzer.)

down, thereby increasing the size of the stone. One theory of the origin of these stones is that they are initiated by a calcification of thrombi in blood vessels (phlebolite).[13]

Denticles can also be classified according to position. Hence they can be free, adherent (attached), or interstitial (embedded). Free denticles lie unattached in the pulp tissue, not connected to the walls. Most free denticles are false denticles. Adherent denticles, attached to the wall of the pulp cavity, are also usually false. Interstitial denticles are those which have become embedded within dentin. They were originally free, lying close to the dentin surface. The continuous growth of the dentin caused them to become entrapped within its structure. With advancing age, denticles usually increase in size and number. They can also be found in functionless, erupted teeth and in impacted teeth.

Diffuse calcifications are calcific deposits that are fine, irregular, and fibrillar. They can begin in the wall of a blood vessel, in the connective tissue, surrounding a nerve, or following the course of blood vessels and nerves (Fig. 21). They can start as fine spicules, or by fusion they can develop into larger bodies. Denticles are usually found in the root canals, and they increase with advancing age. Diffuse calcifications have no definite structure (Fig. 21, *A).* Most authorities consider that diffuse calcifications invariably increase with age, whereas denticle increase is inconsistent.[9]

The association of calcifications with pathologic changes can occur as follows. Denticles often lie near nerve bundles. If they grow and exert pressure on these bundles, they can elicit a vague painful sensation. Denticles near blood vessels can cause pressure on them and thereby cause atrophy of the pulpal tissue.[13]

Metaplasia. Metaplasia is the change from one tissue type into another. Within the pulp this could be the transformation of the function of the odontoblasts from dentin formation to either cementum or bone formation. Mesenchymal cells, which would ordinarily form either fibroblasts or odontoblasts, probably change into cementoblasts or osteoblasts; hence this is not true metaplasia. A possible result of this admixture of cells is the formation of osteodentin and

Fig. 2 1. Histologic section of dentin and pulp showing dystrophic calcification *(Ca)* of collagen fibers *(Cj),* blood vessels *(Bv),* and nerve fibers *(Nj). De,* Dentin; *Od,* odontoblasts; *Pr,* predentin; *Pu,* pulp. A, Dystrophic calcification of collagen fibers. **B,** Dystrophic calcification of collagen fibers and blood vessels. **C,** Dystrophic calcification of nerve fibers. **D,** Enlargement of rectangular section in **C.** (Original magnifications: **A,** X54; **B** and **C,** X96; **D,** X960.) (Courtesy of Dr. S. Seltzer.)

osteocementum. This occurs more frequently as the result of trauma and probably is not a true aging change. Another metaplastic change that can occur in sound teeth is the proliferation and ingrowth of periodontal connective tissue through the apical foramen into the root canal. This is a substitution of the apical pulp tissue by periodontal connective tissue, which is more fibrous than the pulp tissue, and is not a metaplasia. Because cementoblasts are derived from periodontal tissue as the result of the ingrowth of periodontal tissue, cementum can be found in the apical portion of root canals.[9,10]

Summary of pulp changes. The aging changes of the dental pulp are usually sequential. Although some of the purported changes may be caused by processing artifacts, the changes that have been described are compromised circulation and innervation; fat deposits in the pulp cells, odontoblasts, and capillaries; vacuolization of the odontoblasts; reticular atrophy; fibrous degeneration; hyaline degeneration; fat replacement; pulp cysts; mucoid degeneration; calcifications, including denticles and dystrophic masses; and, rarely, metaplasia.

Dentin changes

With aging the pulp cavity gradually becomes smaller because of continuous secondary dentin deposition (Fig. 18).[1,19] As a consequence of this deposition there is a tendency toward eventual pulp obliteration. The pattern for the secondary dentin deposition varies among the different groups of teeth. In maxillary anterior teeth the greatest dentin deposition occurs on the palatal wall of the pulp chamber with subsequent deposition in the incisal tip and remaining walls of the pulp chamber. In molars the greatest dentin deposition is on the floor of the pulp chamber;

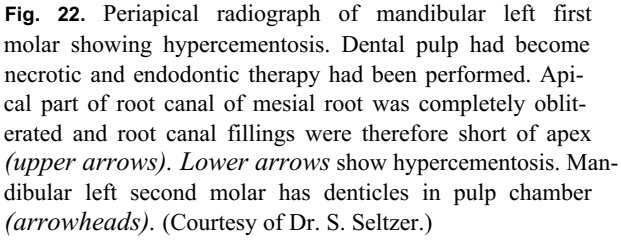

Fig. 22. Periapical radiograph of mandibular left first molar showing hypercementosis. Dental pulp had become necrotic and endodontic therapy had been performed. Apical part of root canal of mesial root was completely obliterated and root canal fillings were therefore short of apex *(upper arrows)*. *Lower arrows* show hypercementosis. Mandibular left second molar has denticles in pulp chamber *(arrowheads)*. (Courtesy of Dr. S. Seltzer.)

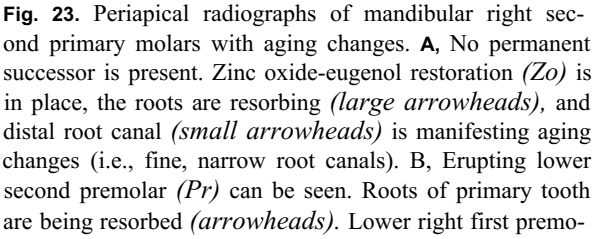

Fig. 23. Periapical radiographs of mandibular right second primary molars with aging changes. **A**, No permanent successor is present. Zinc oxide-eugenol restoration *(Zo)* is in place, the roots are resorbing *(large arrowheads),* and distal root canal *(small arrowheads)* is manifesting aging changes (i.e., fine, narrow root canals). B, Erupting lower second premolar *(Pr)* can be seen. Roots of primary tooth are being resorbed *(arrowheads)*. Lower right first premolar is beginning to close its apical foramen as result of deposition of cementum *(small arrowhead)*.

lesser amounts are deposited on the occlusal (biting) and lateral walls. In advanced age the secondary dentin becomes irregular and a gradual increasing loss of dentinal tubules occurs. With advancing age the odontoblasts undergo degenerative changes. In time the odontoblasts atrophy and disappear in most areas of the dental pulp.

Primary dentin is also affected by aging.[1,9] Increases occur in peritubular dentin (the most calcified type), and increased deposits of apatite dentin are found throughout the primary dentin. Ultimately the dentinal tubules are occluded. This condition is called sclerotic (transparent) dentin. This age-related accumulation of transparent dentin begins on the root(s) of the tooth and is evident by the third decade of life. The formation begins on the root apex and gradually advances toward the crown with age.[9] This has also been found in impacted teeth.[21]

In totally impacted teeth the age-related formation of secondary dentin is first seen in the apical region, from which it proceeds coronally.[21] As discussed previously, in functioning teeth secondary dentin begins in the coronal (pulp chamber) region. In impacted teeth a linear increase in the width of predentin is also seen.

Cementum changes

Studies of both erupted functioning teeth and impacted teeth have shown that with age the cementum widens.[2,9,21] This occurs primarily in the apical region and is known as hypercementosis (Fig. 22). With functioning teeth this may compensate for the loss of enamel on the biting surface as the result of normal biting, eating, and pathologic grinding (bruxism), toothbrushing (abrasion), and erosion.[2,8]

Aging changes of primary teeth

Unlike permanent teeth, primary teeth last only a few years unless there is no permanent successor (Fig. 23, ^4/ As the permanent tooth erupts, the root of the deciduous tooth resorbs until nothing is left except the crown of the tooth (Fig. 23, *B).* A recent study with transmission electron microscopy examined the dental pulp of both mature primary teeth and primary teeth with almost completely resorbed roots.[22] The results showed that the dental pulp of mature primary teeth contain cells and fibers that are characteristic of the pulp of fully developed permanent teeth, whereas the pulp of primary teeth with almost completely resorbed roots have many of the characteristics of the previously described aged pulps of permanent teeth. The investigators noted that the dental pulp of resorbing root primary teeth provide an excellent means to evaluate fibroblast aging.

Summary

The principal age changes of the dental pulp complex include increased mineralization of primary

dentin, accelerated formation of secondary dentin, decreased circulation and innervation, a marked reduction in cells, a relative increase in fibers, fat infiltration, and calcification. As the result of these changes the volume of the dental pulp is significantly reduced until eventually only a few shreds of calcified fibrotic tissue remain.

PART 4: POSSIBLE DENTAL AND SYSTEMIC INTERRELATIONSHIPS

> The nineteenth-century American poet John Saxe[23] told the following tale. Six learned blind men from Industan were asked to determine the nature of a certain creature. They each examined a different part of its body. For example, one touched the tail and thought it was "very like a rope" and another touched the legs and thought they were like tree trunks. In the end, they "disputed loud and long, each in his opinion stiff and strong, though each was partly in the right, and all of them were wrong." Of course, the creature was an elephant.
>
> A second tale concerns a wise old rabbi. He was asked to decide a case of marital nonbliss. The wife came in to see the rabbi and complained bitterly about her husband. The rabbi consoled and supported her. Soon afterward, the husband came in to see the rabbi. He, too, complained about how badly he was treated by his wife. The rabbi also comforted him and agreed with his viewpoint. Unbeknownst to the parties, the rabbi's wife had overheard both conversations. She thereby accussed the rabbi of being dishonest. "They can't both be right!" she exclaimed. "You know," answered the rabbi, "You're right, too."[24]

Although there is no consensus about which of the current aging theories correctly interprets aging changes, it is most likely that they all present some semblance of the truth. Therefore the dental pulp complex aging changes are evaluated with respect to how they relate to components of several of these aging theories.

Relationship of dental pulp complex aging changes to components of aging theories

Clinker theory. Age pigments such as lipofuscin and ceroid accumulate in nondividing neurons. In the dental pulp no neurons are present, only axons, because the neurons are in the trigeminal ganglion. Hence age pigments have not been reported in dental pulp nerves. However, as mentioned before, cholesterol deposits have been found in the pulp[18] and aging blood vessels show atherosclerotic changes.[1*16] Recently it has been found that atherosclerotic lesions in diseased coronary arteries contain the age pigment ceroid,[24] a complex of oxidized lipids and protein. Ceroid most likely results from the oxidation of low-density lipoprotein cholesterol. Hence, although this has not been determined in pulpal blood vessels, because the dental pulp contains both cholesterol and atherosclerotic lesions, aging pigments may also be present.

Falling domino theory. Certain dental pulp cells have been reported to show aging changes that could fit in with the gradual inhibition of cellular constituents aspect of the falling domino theory of aging. Older pulp fibroblasts show a reduction in size of the cells themselves and in most of their inclusions and organelles such as rough endoplasmic reticulum and mitochondria. The Golgi complex is rarely found in aged pulp fibroblasts. [1] The odontoblasts show a reduction in size and become more flattened. Intracellular and extracellular vacuoles are found in the aged odontoblastic layer.[9]

Thermal denaturation. There is no evidence that aged pulpal proteins are immobilized by slow thermal denaturation that leads to cellular disruption and death. However, dental drilling without adequate water spray can lead to thermal denaturation of pulpal proteins, resulting in necrosis of the pulp.[1]

Cellular loss. This theory is custom made for the manifestations of the aged pulp. There is a marked age-related loss of the dividing cells of the pulp, including fibroblasts, odontoblasts, mesenchymal cells, pericytes, and histiocytes. The theory states that the cells are replaced by connective tissue fibers (collagen and reticular types) and that there is shrinkage and loss of function of the involved structure. Once all the odontoblasts are lost, no more dentin can be formed. The tooth can still function, however, even with a pulp devoid of cells, viable fibers, nerves, blood vessels, and lymphatics, because the tooth is maintained in the jaw by the attachment of the periodontal ligament from the cementum of the root(s) to the surrounding alveolar bone.

Enzyme/hormonal/glycoprotein. The enzyme/hormonal/glycoprotein theory, which considers that the usual manifestation of aging is reduced enzyme and hormonal activity, has dental pulp components. Studies have shown that the fibers and ground substance of young pulps are readily digested by certain proteolytic enzymes, whereas the components of the aged pulp are highly resistant to the same enzymes.[17] According to this theory, the release of deleterious lysosomal enzymes increases with aging. These hydrolytic enzymes escape from dying phagocytic cells (usually polymorphonuclear leukocytes). The normal aged pulp does not contain polymorphonuclear leukocytes, but inflamed pulps invariably contain these cells (Fig. 24). Release of lysosomal enzymes is a ma-

Fig. 24. Histologic section of pulpal inflammatory reaction. **A,** *De,* Dentin; *Inf,* inflammation; *Pu,* pulp. **B,** Higher magnification of rectangular region. *Cap,* Capillary; *Ed,* edematous tissue spaces; *Pml,* polymorphonuclear leukocytes. (Original magnifications: A, X54; B, X960.) (Courtesy of Dr. S. Seltzer.)

jor cause of pulpal inflammation and necrosis.[1] Neurotransmitter hormones (e.g., norepinephrine, acetylcholine) have been found in the dental pulp in conjunction with action of blood vessels. As the blood vessels are reduced with aging, the output of these neurotransmitters is also decreased.

Genetic timetable. In an examination of aging changes in impacted teeth, Nitzan et al.[21] surprisingly found that the only statistically significant changes in aged teeth was an increase in the width of the predentin layer and an increased deposition of cementum. Other investigators[1,16,19,21] have found increased fibrosis, reduced cells, increased calcification, reduced circulation and innervation, and increased secondary dentin formation in both impacted and normally functioning, disease-free teeth. If the results of Nitzan et al. are verified by others, the genetic determinant of aging of the dental pulp complex may be limited to those two changes in nonfunctional teeth. However, in functional erupted teeth, all the previously described aging changes may have genetic determinants that require the environmental factors of salivation, biting, chewing, talking, and other oral functions, for the changes to be expressed. In vitro studies with dental pulp fibroblasts have shown that these cells follow the apparently genetically determined Hayflick limit (maximum of 50 divisions). Because dental pulp complex aging changes have been found in human beings and in other species (e.g., mice, rats, guinea pigs, dogs, cats, rabbits), genetic factors are apparently involved. In addition, in the genetically determined disease progeria, youngsters show most of the manifestations of premature aging.[1] The dental pulp complexes usually show aging characteristics, including fibrotic pulps, tremendous amounts of secondary dentin, flattened odontoblasts, and calcification of the blood vessels.

Disposable soma. Teeth are of maj or importance in digestion. Our group at Temple University completed a series of studies showing that significant digestion of starch (complex carbohydrate) occurs with deep relaxation and thorough chewing.[26] This can be related to the disposable soma theory of aging, in which pleiotrophic genes allow for optimal functioning during reproductive youth but for senescent changes in older age. To be reproductive, it is essential that persons stay healthy. One important component of health is nutrition. Hence people should eat well and thoroughly digest and absorb their food. Teeth are important in this respect. In older age many people lose their teeth because of periodontal disease, root caries, and attrition. The remaining teeth generally have fibrotic and calcified root canals. These teeth can still function, but not as well because with the decreased innervation and circulation, pain (a warning signal) can be absent when a disease occurs and the pulp's ability to defend itself against irritants is reduced because of the compromised circulation.[1]

DNA deterioration. Although DNA changes in the aged pulp have not been examined, because the pulp contains actively dividing cells (e.g., fibroblasts, odontoblasts, mesenchymal cells) that eventually die, DNA deterioration most likely occurs in the dental pulp.

Error. Although not examined in the dental pulp, flaws in the formation of proteins leading to errors can undoubtedly occur with dental pulp proteins.

Somatic mutation. The dental pulp contains dividing and nondividing cells that could accumulate deleterious mutations; however, this has never been examined.

Radiation. In experimental animal research, when teeth are irradiated, the odontoblasts become injured and osteodentin is formed. This change can occur with

dental aging. However, irradiation can cause pulpal necrosis, which does not occur with normal pulpal aging. In contrast to aging changes in which hypercementosis occurs, irradiation of teeth results in cementum destruction and root resorption. As in normal pulpal aging, irradiation of teeth can result in fibrosis and atrophy of the pulp.[1]

Immunologic theory. As mentioned before, lymphocytes and plasma cells are found in the pulp but usually only in inflamed pulps. Therefore the age-related breakdown of the immune system does not have a direct bearing on pulpal aging. However, with the compromised circulation and reduction in immune cells in the aged pulp, the defensive reaction to irritants is decreased and breakdown and necrosis are more likely.[1]

Nutritional theory. In the normal aging pulp the only nutrient-derived metal that can build up is calcium. Calcium is beneficial in the developing dental pulp complex (e.g., formation of dentin and cementum) but deleterious in the aging pulp (increase in denticles and dystrophic calcifications). ' Toxic metals can be found in the dental pulp but not as the result of nutrition. Rather, they can leak through pulpal exposures from dental amalgam fillings (which contain lead and mercury). Animal studies have shown that a vitamin C deficiency can result in excessive laying down of secondary dentin.[10] Intake of an optimal amount of vitamin C during tooth development appears to be important because it is necessary for collagen formation in the dental pulp.

Macrophage. The dental pulp contains histiocytes, which convert to macrophages in the presence of irritants. However, rather than increase with aging as is postulated in the colonic macrophage theory, pulpal histiocytes decrease with aging. With respect to the related waste product theory,[4] because the aged pulp has a diminished blood and lymphatic supply and a reduction in ground substance (all of which are involved in waste removal), accumulation of nonexcreted wastes can play a role in pulpal aging.

Watch-spring theory. Because the energy warehouses, the mitochondria, are greatly reduced in the odontoblasts and fibroblasts of the aged pulp, it is possible that the energy of the aged pulp is used up.

Redundancy. Dental pulp cells can be programmed by redundant genes that can allow for functioning odontoblasts and fibroblasts (and other cells) to work well during the reproductive life of the person, and eventually break down as the result of the overload of insults (e.g., physiologic biting, chewing, and talking and pathologic dental caries, attrition, abrasion, erosion, and trauma).

Wear and tear. Wear and tear is another aging theory that is tailor made for the dental pulp. Most functioning teeth show a perfect example of wear and tear. That is attrition, which results from chewing abrasive foods for many years. (As mentioned before, attrition can also result from stress.) Even normal chewing can cause the development of wear facets. Both these conditions, together with dental caries (infection), diet (e.g., citrus fruits resulting in erosion), and trauma (as from abrasion, dental drilling, and blows), can wear away the tooth surfaces and result in accelerated pulpal aging changes (marked fibrosis and calcification). Of course, these conditions can also lead to pathologic pulpal inflammation and necrosis.

Rate of living. Although human beings as a species has a slower metabolic rate than, for example, a short-lived mouse, the dental pulp has a faster metabolism during the growth and development of the tooth than when the pulp is aging.

Hypoxia. Studies have shown that the aged pulp has a lower oxygen tension than the mature pulp. Aged pulpal fibroblasts exhibit a reduced oxygen intake.[1, 19]

Stress. As mentioned before, a major stress-related disease is bruxism.[7] Bruxism causes a severe attrition, which in turn can accelerate pulpal aging changes (primarily fibrosis and calcification). Hence this is one example of an environmental stressor that can induce aging-type changes in the dental pulp.

Cross-linkage. Cross-linkages have been detected in the collagen of the aged pulp.[14] Cross-linked tissue is tough and rigid. As discussed before, there may not necessarily be more collagen in the aged dental pulp, but rather polymerization and aggregation of previously existing smaller units.[15] It has been shown that cross-linked dental pulp collagen is readily infiltrated with calcium deposits.[14] This can relate to the calcium aging theory, which links aging to the gradual accumulation of calcifications throughout the body. Another previous theory that can relate to collagen cross-linkages, the circulation-deficiency aging theory,[1] has an excellent model in the dental pulp, which shows both age-related collagen cross-linkage and impaired circulation.[14,28]

Free radical. Because mitochondria are the main source of free radicals and the mature dental pulp fibroblasts and odontoblasts have an abundant supply of mitochondria, it appears that oxygen-generated free radicals can be involved in the aging of the dental pulp.

Summary. Directly or indirectly, representations of the components of most of the various aging theories can be found in the dental pulp, dentin, and cementum of erupted, functional, and nonfunctional

impacted permanent teeth as well as of primary teeth. The most directly relevant aging theories for dental pulp complex representation are cellular loss, cross-linkage, calcification, waste product, wear and tear, clinker, circulation deficiency, and genetic timetable theories. Other aging theories that appear to have dental pulp complex representation are falling domino, enzyme/hormonal/glycoprotein, disposable soma, radiation, nutritional, watch-spring, redundancy, hypoxia, stress, and free radical theories. A case can also be made for dental pulp complex representation for the DNA deterioration, error, somatic mutation, and immunologic theories. There appear to be no dental pulp complex manifestations for the thermal denaturation, macrophage, and rate of living theories.

Can the dental pulp complex aging be used as a biomarker for aging in general?

The condition of horses' teeth is used as an indication of their age, because horses usually eat the same diet throughout their life and, as the result of their eating style, distinctive attrition-induced wear facets are found on their mandibular incisors. The wear patterns show specific age-related changes. These can be used as an estimate of the horse's age. In contrast, human beings do not eat the same type of diet and, not being exclusively herbivores, we do not show wear patterns solely on our mandibular anterior teeth. In addition, unlike horses, we have dental caries, toothbrush abrasion, bulimia-induced erosion, and stress-induced attrition. Hence a human being's age cannot be deduced by wear facets. Several attempts have been made to use dental components as a biomarker for systemic aging. The following changes in enamel have been considered:

- The nitrogen content of enamel increases with age.[29] This has been correlated with the increase in the amount and intensity of pigment, which causes a darkening of teeth in older age.[29] Changes in the refraction and absorption of light appear to be related to structural changes in the enamel and dentin.[31] However, tooth darkening depends on the original color, and teeth can darken from many local causes such as trauma, smoking, foods, and chewing substances such as betel nuts and tobacco.
- With the use of optical rotation measurements, aspartic acid in enamel has been found to exhibit increasing racemization with age.[32] This appears to be a promising method, but it requires specialized equipment.[33]
- An increase occurs in the fluoride content of enamel with age.[34] However, part of this may be related to water fluoridation and fluoride toothpaste, applications, mouthwashes, and tablets.
- The rate of enamel attrition has been considered as a possible method for determining systemic age,[36] but recently this method has been shown to be inaccurate because of the great individual variation in attrition related to different diets and stress-induced attrition (bruxism).[7,37]

The following changes in dentin have been considered:

- Although not all investigators agree on its accuracy, the age-related increase in transparent (sclerotic) dentin generally has been considered the best biomarker of systemic age.
- With the use of the scanning electron microscope, both Whittaker and Kneale[44] and our group at Temple University[45] found a reduction in the number of dentinal tubules with age. In our study the age-related changes were statistically significant. For example, the mean number of dentinal tubules was 242,775 in the 20- to 34-year-old group and 149,025 in the group 80 years and older. However, both changes can be evaluated or extracted only on avulsed teeth; therefore they cannot be used in intact teeth.
- The size of the dental pulp cavity is reduced with age, because of continuous secondary dentin deposition.[19] The pattern for this deposition varies among the different groups of teeth. For example, in maxillary anterior teeth the greatest dentin deposition occurs on the palatal wall of the pulp chamber, with subsequent deposition on the incisal tip and remaining walls of the pulp chamber. In molars the greatest dentin deposition occurs on the floor of the pulp chamber; lesser deposition occurs on the occlusal and lateral walls. In old age the secondary dentin deposition becomes irregular and an increasing loss of dentinal tubules occurs. The odontoblasts also undergo degenerative changes, and in time they atrophy and disappear from most regions of the dental pulp? These secondary dentin changes have not proven useful as a biomarker for systemic aging.

The following changes in cementum have been considered:

- A rhythmic increase in cementum deposition (annulations) occurs with age. This has been used to determine age in both domestic and wild animals.[33] Zander and Hurzeler[46] observed that the thickness of cementum in human beings was almost three times greater at age 76 years than at age 11 years. Although they used a small sample, Stott et al.[47] found that cementum annulations

counted from photographs of extracted teeth could be used as a method to estimate human age. However, with functioning teeth, cementum deposition can be a compensation for loss of enamel on biting surfaces as a result of both normal function and pathologic attrition, abrasion, trauma, and erosion.[2,8]

- Apical root resorption, which is primarily a loss of root end cementum, has been considered as a possible tooth-related aging biomarker.[36] However, this occurs primarily from local factors such as periodontal disease and trauma, and recent studies have shown that this method is inaccurate. [37]

All the above methods have some problems. Nevertheless, judging from the results of this review and my personal evaluation of the human dentition for 30 years, it appears that the condition of the dental pulp complex can be a biomarker for generalized aging. However, two conditions must be met:

1. The teeth to be evaluated must be in normal functional occlusion and cannot have any manifestation of pathologic insults such as dental caries, attrition, abrasion, erosion, trauma, or dental restorations.
2. The evaluation must be by the use of periodic periapical radiographs. A correlation must be determined between degrees of secondary dentin formation and pulpal fibrosis and calcification (as determined by root canal length and width relative to the overall length and width of the tooth), and a person's age. To do this many normal teeth must first be examined and correlated both with a person's age and current state of health. For example, it would be of interest to determine whether a person who did not exercise, was obese, and had angina would show accelerated dental pulp aging as compared with a person of the same age who was in excellent health. If a significant correlation is found between dental pulp complex aging and generalized aging, it may then be possible to determine by examination of a person's normal functioning teeth whether the physiologic age matches the chronologic age.

Our group is currently in the midst of such a study. Preliminary results have shown that from about the age of 21 years, the root canal of single-rooted teeth shows a radiographically determined loss in root canal length that averages about 0.21 mm per year. From the age of 60 years and up, the loss occurs at a rate of about 0.43 mm per year. When the study is completed, the results will be published. If the results are significant, in addition to its use as a biomarker for aging, x-ray evidence obtained from normal teeth may be useful in forensics and anthropology for identification of the approximate age of persons.

Fig. 25. Periapical radiograph of maxillary right first molar with fine, prematurely aged root canals that required nonsurgical endodontic (root canal) therapy because dental pulp subsequently became necrotic. A, Zinc oxide-eugenol temporary restoration *(Zo)* is in place. *Arrowheads* show aged root canals. B, Even though root canals were extremely fine and narrow, it was possible to clean them out and perform endodontic therapy *(arrowheads).*

Can dental pulp complex aging changes be altered?

First, it should be emphasized that, unlike the situation in the body as a whole, aging changes in the pulp do not necessarily result in death. It has never been proven that, even with absent circulation and innervation and no viable cells, the atrophic pulp becomes necrotic. However, even if that were to occur, the tooth could be maintained in good function (provided that severe periodontal disease was not present) if endodontic therapy were successfully performed. [8] Endodontic therapy (nonsurgical or surgical) can usually be completed on teeth having clinically calcified root canals (Figs. 25 and 26).

Even though the dental pulp is of major importance only during tooth growth and development, its premature aging or loss is detrimental because ionic exchanges can no longer occur between the outside of the tooth and the dental pulp.[1] This can lead to decreased moisture content, which makes the tooth with an aged pulp, a necrotic pulp, or a root canal filling more brittle and hence prone to fracture. The tooth with an aged pulp has a decreased ability to respond to irritants because of the compromised circulation. This means that the pulp is more likely to become necrotic from irritants such as dental caries, periodontal disease, attrition, abrasion, erosion, and trauma. In addition, the tooth with an aged pulp, be-

Fig. 26. Periapical radiograph of maxillary right first molar with fine, prematurely aged buccal root canals but with patent palatal root canal. Gold crown *(Gc)* is on tooth. Tooth required endodontic therapy because dental pulp subsequently became necrotic. It was possible to clean out and fill the entire palatal root canal, but buccal canals were so fine that they were nonnegotiable. Therefore buccal root canals were obturated surgically from apical end with gold foil. A, After palatal root canal has been filled *(large arrowheads),* buccal root canals appear obliterated *(small arrowheads).* **B,** Apexes of buccal root canals have been sealed with gold foil *(arrowheads).* (Courtesy of Drs. W. K. Kopp and H. Kresberg.)

Fig. 27. Periapical radiographs of two teeth that had endodontic (root canal) therapy *(arrowheads)* about 1 year before. Severe dental caries subsequently developed under gold crowns *(Gc). Arrows* show caries. A, Mandibular right canine; B, mandibular right first molar.

cause of the inhibited innervation, has a diminished ability to respond to hot, cold, and painful stimuli.[33] The affected person would not be aware that the pulp is inflamed or necrotic, and dental treatments could be delayed. This might cause the tooth to be severely undermined and could result in tooth loss. Endodontically treated teeth can still have dental caries. With the absence of a viable pulp the affected person would not have any painful warning that the tooth is being eaten away by decay, and this could result in tooth loss (Fig. 27).

As mentioned before, although aging occurs without any pulpal irritants, irritants such as dental caries, attrition, abrasion, erosion, and trauma can accelerate dental pulp complex aging changes (Fig. 28). In other words, the circulation and innervation can rapidly become compromised, reparative dentin can be laid down at an accelerated pace, and fibrosis and calcification can occur prematurely. Therefore the first intervention should be to prevent accelerated aging changes. Most of these are well known but are not necessarily well practiced. These include regular dental visits; routine toothbrushing with a soft, nonabrasive brush; routine dental flossing; avoidance of trauma (e.g., wearing seat belts, using mouth guards and face masks for contact sports); avoidance of abrasive foods; not sucking on citrus fruits; preventing or stopping bulimia; and preventing or stopping stress-induced bruxism.

With respect to reduction of innate aging changes of the dental pulp complex, to prevent excessive formation of secondary dentin and to allow for optimum production of collagen, it is important to have sufficient antioxidant nutrients (especially vitamin C), starting early in life. Once the permanent teeth erupt and are functional, it is advantageous to have the occlusion (bite) balanced by a dentist to prevent uneven pressure on any individual tooth. This can be done by having any occlusal interferences removed by selective tooth grinding and/or orthodontic tooth move-

Fig. 28. Periapical radiographs of dental pulp complexes show premature aging changes as result of irritants. *Arrowheads* show fine or invisible root canals. *Am,* Amalgam. A, Mandibular left second molar with occlusal dental caries *(arrow).* **B,** Maxillary right first and second molars with recurrent dental caries *(arrows)* beneath amalgam restorations. C, Maxillary left second premolar and first and second molars with intact extensive amalgam restorations. **D,** Mandibular right second premolar that sustained occlusal trauma. Notice that root canal is no longer visible because of extensive aging changes.

ment. During biting, chewing, talking, and other oral functions, excessive force should be avoided. Following these strategies can decrease trauma to the pulp. This can result in reduced formation of secondary dentin and cementum. The dental pulp circulation and innervation can stay intact longer, and functioning odontoblasts and fibroblasts can be maintained for many years. This outcome can occur, because teeth in nonagenarians and centenarians have been found with pulps that histologically have the appearance of those of a 3 0-y ear-old person.

If people take care of their teeth, will they live longer? There is no definite answer, but consider the following:

- In four studies at Temple University,[26] our group has shown significantly more digestion of starches occurred under deep relaxation and slow, thorough chewing than under stress and incomplete chewing.
- It has been observed that most of the centenarians in Soviet Georgia retained a majority of their teeth for a lifetime, had a relaxed and thorough eating style, and had practically no evidence of depression and colon cancer. Benet[49] states, "Food is taken in very small bites and is chewed thoroughly. It is considered to be boorish and unhealthy to eat fast. Mealtime is considered to be relaxed and pleasurable. When guests are present, meals often last several hours. Reading is discouraged during mealtime and quiet music is played. It is considered that the attention reading requires diverts nervous impulses from the digestive glands. Telling sad problems at the table is considered as bad manners."

- In a study conducted in India, it was shown that there was significantly less colon cancer in persons who thoroughly chewed their food as compared with those who did not chew thoroughly.[50]
- A recent study corroborated previous studies showing that diet-restricted rats live significantly longer than rats given free access to food.[51] The diet-restricted rats were given small amounts of nutrient-dense food. The other rats were allowed to eat anything they wanted at any time during the day. In the new study the diet-restricted rats ate fewer meals than did the unlimited eaters. However, the dietary-restricted rats spent more time eating each meal than did the unrestricted eaters. In other words, eating slowly contributed to the longer life of these rats. Applied to human beings, this appears to show that slow, relaxed eating, as we have advocated from our research, can help people live longer. Only with good, functional teeth can people eat well. Therefore, although the evidence is not substantial, it seems important to retain healthy, functional teeth.

In summary, the dental pulp complex manifests aging changes reflected in components of most aging theories. With proper care these changes can be reduced sufficiently so that a person can maintain healthy teeth for a lifetime. In fact, if people take care of their teeth, they can be assured that most of their teeth will outlive them (that is, until we find ways to substantially increase our present maximum life span).

I thank Drs. Ted Simpson and Sam Seltzer of Temple University, Philadelphia, for the clinical and histologic specimens. A special acknowledgement is given to Dr. Seltzer for his input during the last 20 years on dental pulp complex aging.

REFERENCES

1. Seltzer S, Bender IB. The dental pulp: biologic considerations in dental procedures. 3rd ed. Philadelphia: JB Lippincott, 1984:324-438.
2. Seltzer S. Endodontology: biologic considerations in endodontic procedures. 2nd ed. Philadelphia: Lea & Febiger, 1988:31-54.
3. Morse DR. Aging: causes and control. Int J Psychosom 1988;35:12-42.
4. Morse DR, Rabinowitz H. A unified theory of aging. Int J Psychosom 1990;37:5-24.
5. Smith RP, Quillen P. The La Costa prescription for longer life. New York: Fawcett Crest, 1985.
6. Pollack RL, Morse DR. Free radicals and antioxidants: diseases and aging. Int J Psychosom 1988;35:43-8.
7. Morse DR. Stress and bruxism: a critical review and report of cases. J Hum Stress 1982;8:43-54.
8. Morse DR. Clinical endodontology: a comprehensive guide to diagnosis, treatment and prevention. Springfield, Ill: Charles C Thomas, 1974:5-296.
9. Ketterl W. Age-induced changes in the teeth and their attachment apparatus. Int Dent J 1983;33:262-71.
10. Boyle PE. Kronfeld's histopathology of the teeth and their surrounding structures. 4th ed. Philadelphia: Lea & Febiger, 1955;75-1O7.
11. Bhaskar SN. Synopsis of oral pathology. 6th ed. St Louis: CV Mosby, 1961:154-6.
12. Kramer IRH. Pulp changes of non-bacterial origin. Int Dent J 1959;9:435-50.
13. Orban BJ. Oral histology and embryology. 4th ed. St Louis: CV Mosby, 1957:156-8.
14. Nielsen CJ, Bentley JP, Marshall FJ. Age-related changes in reducible crosslinks of human dental pulp collagen. Arch Oral Biol 1983;28:759-63.
15. Quigley MB. Functional and geriatric changes of the human pulp. ORAL SuRG ORAL MED ORAL PATHOL 1971 ;32:795-806.
16. Bernick S, Nedelman C. Effect of aging on the human pulp. J Endod 1975;1:89-94.
17. Bhussery BR. Modifications of the dental pulp during development and aging. In: Finn SB, ed. Biology of the dental pulp organ. Birmingham: University of Alabama Press, 1968:145-68.
18. Stewart JM. The possible significance of lipids in calcification. In: Finn SB, ed. Biology of the dental pulp organ. Birmingham: University of Alabama Press, 1968:249-63.
19. Seltzer S. Classification of pulpal pathosis. ORAL SuRG ORAL MED ORAL PATHOL 1972;34:269-87.
20. Bunting RW, Hill TJ. A textbook of oral pathology. 2nd ed. Philadelphia: Lea & Febiger, 1940:266.
21. Nitzan D, Michaeli Y, Weinreb M, Azaz B. The effect of aging on tooth morphology: a study on impacted teeth. ORAL SURG ORAL MED ORAL PATHOL 1986;61:54-60.
22. Dard M, Kerebel LM, Kerebel B. A transmission electron microscope study of fibroblast changes in the human deciduous tooth pulp. Arch Oral Biol 1989;34:223-8.
23. Saxe JG. The poetical works of John Godfrey Saxe. Boston: Houghton, 1892.
24. Barash DP. Aging: an exploration. Seattle: University of Washington Press, 1983.
25. YesilsoyC, Feigal RJ. Effects of endodontic materials on cell viability across standard pore size. J Endod 1985;11:401-7.
26. Morse DR, Schacterle GR, Furst L, Zaydenberg M, Pollack RL. Oral digestion of a complex carbohydrate cereal; effects of stress and relaxation on physiological and salivary measures. Am J Clin Nutr 1989;49:97-105.
27. Sayegh FS, Reed A J. Calcification in the dental pulp. ORAL SURG ORAL MED ORAL PATHOL 1968;25:873-82.
28. Walters C. Collagen crosslinks in human dentin: increasing content of hydroxypyridinium residues with age. Calcif Tissue Int 1983;35:401-5.
29. Bhussery BR, Emmel V. Changes in the nitrogen content of the enamel with age. J Dent Res 1955;34:672.
30. Brudevold F. Age changes in dental enamel. Forske Tannlageforenings Tidende 1957;67:451-8.
31. Dahlberg AA. Clinical aging patterns in teeth of different population groups. In: Symposium: Aging—some social and biological aspects. Chicago: American Association for the Advancement of Science, 1959:357-66.
32. Helfman PM, Bada JL. Aspartic acid racemization in tooth enamel from living humans. Proc Natl Acad Sci USA 1975;72:2891-4.
33. Altini M. Age determination from the teeth: a review. J Dent Assoc SAfr 1983;38:275-9.
34. Sognnaes RF. Forensic stomatology: part 2. N Engl J Med 1977;296:149-53.
35. Grahnen H, Myrberg N, Ollinen P. Fluoride and dental age. Acta Odont Scand 1975;33:1-4.
36. Gustafson G. Age determinations on teeth. J Am Dent Assoc 1950;41:45-54.
37. Will S. Tested accuracy of a decedent's age by teeth. J Ind Dent Assoc 1985;64:15-7.

38. Nalbandian J. Age changes in human teeth. J Dent Res 1959;38:681-2.
39. Nalbandian J, Gonzales F, Sognnaes F. Sclerotic age changes in root dentin of human teeth as observed by optical, electron and x-ray microscopy. J Dent Res 1960;39:598-607.
40. Miles AEW. Dentition in the estimation of age. J Dent Res 1963;42:255-63.
41. Johnson G. Transparent dentine in age estimation. ORAL SuRG ORAL MED ORAL PATHOL 1968;25:834-8.
42. Bang G, Ramm E. Determination of age in humans from root dentin transparency. Acta Odont Scand 1970;28:3-35.
43. Schwarz HR, Blick U, Liebhardt E. Age determination of teeth. Beitr Gerichtl Med 1978;36:369-72.
44. Whittaker DK, Kneale MJ. The dentine-predentine interface in human teeth. Br Dent J 1979;146:43-6.
45. Carrigan PJ, Morse DR, Furst ML, Sinai IH. A scanning electron microscopic evaluation of human dentinal tubules according to age and location. J Endod 1984;10:359-63.
46. Zander HA, Hurzeler B. Continuous cementum apposition. J Dent Res 1958;37:1035-44.
47. Stott GG, Sis RF, Levy BM. Cemental annulation as an age criterion in forensic dentistry. J Dent Res 1982;61:814-7.
48. Sperber GH. Clinical considerations of aging of the skull and dentition. Quintessence Int 1979;10:75-81.
49. Benet S. How to live to be 100: the life-style of the people of the Caucasus. New York: Dial Press, 1978.
50. Malhotra SL. Dietary factors in a study of cancer colon from cancer registry, with special reference to the role of saliva, milk and fermented milk products, and vegetable fibre. Med Hypotheses 1977;3:122-6.
51. Duffy PH, Feuers RJ, Leahy JA, Nakamura KD, Turturro A, Hart RW. Effect of caloric restriction on physiological variables related to energy metabolism in the male Fischer 344 rat. Meeh Ageing Dev 1989;48:117-33.

Reprint requests:

Donald R. Morse, DDS, PhD
Department of Endodontology
Temple University School of Dentistry
3223 N. Broad St.
Philadelphia, PA 19140