The role of biology in the orthodontic practice

Orthodontic tooth movement results from forces applied to teeth that evoke cellular responses in the teeth and their surrounding tissues, including the periodontal ligament (PDL), alveolar bone and gingiva. It is advantageous for the orthodontist to know the details of the biological events that unfold during tooth movement because some of these details may differ from one person to another, owing to variables such as gender, age, psychological status, nutritional habits and drug consumption.

The purpose of this article is to emphasise that orthodontics is a field of endeavour in which mechanics and biology are integrated, and to stress the reality that tooth movement is conducted in individual human beings, each with a unique and intricate physiological system. Biological variations may be the foundation of the differences that are frequently observed in the outcomes of orthodontic treatment between patients with similar malocclusions treated identically.

Principles of orthodontic biomechanics are usually taught with the help of a typodont, consisting of artificial teeth embedded in wax. This set-up ignores entirely the biological aspect of tooth movement. In the clinical setting, living patients are encountered, and mechanical forces mobilise their teeth. These movements result from the development of strains in dental and para-dental tissues, followed by modelling and remodelling of these tissues.

In some patients, systemic conditions may exist, causing complications such as root resorption, dehiscences and fenestrations of the alveolar bone. Hence, clinical orthodontists must be viewed as a specialty staunchly entrenched in biology, all the way to the molecular level. As a clinical profession, it must be based on a commanding knowledge of mechanics, biology, physiology, and pathology. The goal of this article is to enhance the biological awareness of the orthodontic practitioner in order to minimise or avoid tissue damage during orthodontic treatment. It will demonstrate that this objective may be achieved by closely focusing on the nature of root movements, and avoiding the dogmatic following of "precription" methods that promise "automatic" correction of all malocclusions.

### Tissue remodelling and orthodontic tooth movement

The actual rate of tooth movement may depend on the rate of bone turnover. The latter was modified pharmacologically in rats undergoing maxillary molar mesial movement, by inducing either hypothyroidism or hyperthyroidism (Verna et al., 2000). In rats with high bone turnover, the rate of tooth movement was increased, while it was reduced in animals with a low turnover. Although all teeth had been moved in the same fashion (controlled tipping), the location of the centre of rotation differed, depending on the rate of bone turnover. Examination of histological sections from the jaws of these rats (Verna et al., 2005) showed that root resorption had occurred in both groups, as well as in the control group, but that it was more pronounced in the low bone turnover group.

Bone metabolism normally demonstrates measurable diurnal fluctuations that may affect the rate of tooth movement. Rats that were exposed to light for 24 or 12 hours per day for 21 days, and were subjected to orthodontic force only during the light period, presented doubling of the rate of tooth movement and bone remodelling, as compared with animals that received the force during the 12 hours of daily darkness (Miyoshi et al., 2001).

The realisation that tissue remodelling in orthodontics is mediated by a variety of cells, including fibroblasts, root and bone surface lining cells, endothelial, epithelial, and nerve cells, as well as different leukocytes, prompted clinical investigators to apply physical and chemical agents, concomitant with orthodontic forces in order to augment the effect of the mechanical forces. In this vein, Tweedle (1965) used local application of heat to para-dental tissues surrounding orthodontically treated teeth in dogs, Davidovitch et al. (1980) used minute electric currents, and Blechman (1988) advocated the use of static magnetic fields. Davidovitch et al. placed the electrodes much closer to the cat’s ca- nine, resulting in a significant enhancement of movement. Blechman hypothesised that magnets generate mechanical forces, as well as magnetic fields, and that this combination acts synergistically, causing the teeth to move faster. However, an experiment in rats (Tencu et al., 2000) revealed that magnets do not speed up the mesial movement of maxillary molars, and actually increase root resorption in the early phases of treatment.

Utilisation of chemical agents in attempts to increase the pace of tissue remodelling and tooth movement has been tested in various laboratories and clinics. Yamakawa et al. (1984) applied prostaglandin (PG) E1 into the gingiva of moving teeth in human subjects, resulting in rapid movement. Systemic application of minosprost, a PGF2 analogue, to rats undergoing tooth movement for two weeks increased the rate of movement significantly with out enhancing root resorption (Seki et al., 1996). Results were reported following intraperitoneal injections of PGF2 in rats (Seidi et al., 2005). Clumber and his co-workers injected indomethacin systemically, a PG synthetase inhibitor. Collins and Rubin (1986) used local applications of vitamin D, while Engstrom, Granstrom and Thilander (1987) observed increased bone metabolism in hypocalcaemic, vitamin-D-deficient, lactating rats. The bone matrix component osteocalcin was injected in rats into the palatal bifurcation of a tipping molar, causing rapid tooth movement owing to the attraction of numerous osteoclasts to this site (Hashimoto et al., 2001).

The reports cited above suggest that the effect of tissue remodelling and the rate of tooth movement can be significantly influenced by numerous factors that stimulate or inhibit para-dental cells. However, if our goal is to complete orthodontic treatment successfully and in the shortest possible amount of time, then we should avoid moving roots into areas from which they will have to be retrieved later.

When mechanical loads are applied to intact tissues in vivo or in vitro, the tissues usually become distorted (strained). In the case of the skeleton, loads like gravity prompt cells to arrange the architecture of the bony structures in such a way that will resist redundent loads. This phenomenon is known as Wolff’s Law, defined by Julius Wolff in 1892. However, when bone cells are subjected to non-redundent loads, such as orthodontic forces, the cells are activated, and remodelling of the alveolar process ensues, which facilitates tooth movement. In vivo applications of compressive loads to ulnae in turkeys and roosters by Lanyon and Rubin (1984) revealed that extensive osteogenesis can be evoked by short-term dynamic (intermittent) forces. In those experiments, the optimal load magnitude was 2,000 to 4,000 microstrain, and its daily duration was ten to 20 minutes. These findings suggest that orthodontic forces will be most effective when applied for brief periods, rather than continuously. This assumption was found to be correct in an experiment in rats by Gibson, King, and Keeling (1992). In that experiment, maxillary molars were subjected to mesially moving forces for one hour, one day, or 14 days. Teeth of animals one hour of force application continued to move mesially for 14 days, and achieved 35% of the movement reached by the teeth that had been subjected to orthodontic forces continuously for 14 days.

The age factor

The effect of age on the tissue response to orthodontic forces has occupied the minds of orthodontists...
patients since Hunter, in the 18th century, and probably earlier. Hunter observed that orthodontic treatment induces fewer complications in children. Studying histological sections of human teeth and their surrounding tissues, Britton concluded that the PDL is less cellular in adults than in children. Therefore, he recommended, when treating adults, to subject their teeth to light forces initially, in order to stimulate cellular proliferation, then to increase the force magnitude, in order to stimulate these cells to remodel the para-dental tissues. This observation implies that, in essence, the nature of the biological response to orthodontic forces is similar in young and adult subjects. This hypothesis was confirmed by Shimpo et al. (2005). These investigators moved molars bilingually in young (13-week-old) and old (60-week-old) rats, then studied their compensatory alveolar bone apposition under the lingual periosteum. They reported that in both age groups there had been vigorous compensatory alveolar bone growth. Thus, alveolar bone is successfully maintained, even in aged rats. Age can also refer to the duration of healing of a post-operative regenerate following distraction osteogenesis (Nakamoto et al., 2002). In an experiment on 15-month-old beagles, mandibular premolars were moved into a two-week or a 12-week regeneration period. The former consisted of immature, fibrous, and poorly mineralised bone, while the latter was composed of mature, well-organised and mineralised bone. Tooth movement was significantly faster in the “young”, immature regenerate, but this movement was accompanied by extensive root resorption that extended from the cemento-enamel junction to the root apex.

The effects of pre-existing medical conditions and the development of complications

It is estimated that 10 to 15% of all children under the age of 16 are affected by chronic, long-term medical problems. These problems may affect the outcome of orthodontic treatment (Burden et al., 2001). Common medical problems in this age group include infective endocarditis, bleeding disorders, leukaemia, diabetes, cystic fibrosis, juvenile rheumatoid arthritis and renal failure. An even higher percentage of adult patients may be affected by a variety of medical problems that involve one or more of the tissue systems. These conditions, and the medications used to treat them may have profound effects on the response of dental and para-dental cells to mechanical loading.

Endocarditis is a life-threatening condition requiring primary prevention in the form of administration of antimicrobial agents prior to certain orthodontic procedures. The orthodontist must weigh the risk of endocarditis against the risk of an adverse reaction to the prescribed antibiotic therapy. Fortunately, most orthodontic procedures do not cause bacteraemia. Lucas et al. (2002) obtained blood samples from children 50 seconds after taking dental impressions, separator placement, band placement and insertion of an adjusted arch wire. Significant bacteraemia was found only after separator placement.

Orthodontic braces, fixed and removable, can accumulate bacterial plaque that may be harmful to oral soft and hard tissues. This problem has been addressed by adding antimicrobial agents to bracket bonding materials, elastic bands and crown coating varnishes. The addition of benzalkonium chloride to a composite resin added antimicrobial properties to the compound without altering its mechanical properties (Othman et al., 2002). Likewise, coating teeth in orthodontic patients with a sustained-release chlorhexidine varnish decreases Streptococcus mutans levels in the patients’ saliva (Beyth et al., 2003).

Children treated for childhood cancers with both radiation and chemotherapy often exhibit disturbances in dental development, such as tooth agenesis, teeth with short roots or with no roots altogether. A retrospective analysis of treatment outcome in ten orthodontic patients with such a background revealed that five had been treated with lighter forces than usual, one displayed root resorption, and four achieved unsatisfactory results (Dahllof et al., 2001).

The development of inflammation in dental and para-dental tissues during the course of orthodontic treatment implies that circulating plasma and leukocytes migrate out of capillaries, and interact with native cells. The blood plasma may contain endogenous hormones produced by endocrine glands, as well as a variety of molecules derived from consumed drugs and nutrients. Some of these molecules may interact with para-dental target cells, augmenting or inhibiting the effects of mechanical forces on these cells.

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Periodontitis, acute or chronic, may be present before the onset of orthodontic treatment, or occur during the course of treatment owing to the accumulation of a bacterial plaque around the braces. Peripheral blood monocytes obtained from individuals with chronic periodontitis synthesized large amounts of pro-inflammatory cytokines when incubated in vitro with bacterial lipopolysaccharides. If such primed monocytes find their way into strained para-dental tissues, their increased production levels of cytokines may increase the risk of root resorption. An indicator of such an increased risk may be the concentration of cytokines in the gingival crevicular fluid. Previous studies reported on increased levels of cytokines, such as tumour necrosis factor- and interferon- in the gingival crevicular fluid of orthodontically treated teeth in humans (Kim and Park, 2000). The origin of these cytokines is most likely PDL cells.

Allergies and asthma are conditions involving periodic production of large amounts of pro-inflammatory cytokines in the airway mucosa and the skin. Primed leukocytes derived from these tissues may travel through the circulatory space of the tissues surrounding orthodontically treated teeth. Consequently, patients with a history of allergies and/or asthma appear to be at a high risk of developing excessive root resorption during the course of orthodontic treatment (Davidovitch et al., 1999). Hence, it is postulated that any inflammatory condition, such as gastro-enteritis, arthritis and rheuroidis, may increase the risk of orthodontic root resorption.

Allergy manifestations in orthodontics are infrequent, although the frequency of allergic diseases in the industrialised world is rising. The WHO reports that 15% of the population has had or will have an allergic disease. Allergic reactions to orthodontic materials can develop during treatment, manifesting as urticaria, angioedema, stomatitis and cheilitis (Beaudouin et al., 2005). Metals in orthodontic appliances that can induce an allergic reaction are nickel, chromium, cobalt and titanium. Other allergenic materials include latex, resins, adhesives and methyl methacrylates. When a reaction that appears to be allergy-related is detected in an orthodontic patient, there should be referral to an allergist for advice. Close collaboration between the orthodontist and the allergist is essential for each future stage of the orthodontic treatment in order to avoid further complications.

A method to detect patients sensitive to orthodontic alloys was developed in the form of an in vitro cell proliferation assay (Marigo et al., 2005). The best parameters for inducing the strongest cell proliferation response were 10 g/ml nickel sulphate, 10% fetal bovine serum, and 200,000 cells. With this method, it was possible to distinguish between nickel-sensitive and non-nickel-sensitive patients. Moreover, it was found that exposure to nickel alloys for periods longer than two years may lead to the development of oral tolerance mechanisms that modulate nickel sensitivity.

Consumption of low or moderate amounts of alcohol may have beneficial effects on the cardiovascular system, but chronic ingestion of large amounts of alcohol can on a daily basis have devastating effects on a number of tissue systems, including the skeletal system. Alcoholism may lead to severe complications, such as liver cirrhosis, nephropathies, osteoporosis, and spontaneous bone fractures. Circulating ethanol inhibits the hydroxylation of vitamin D3 in the liver, thus impeding calcium homeostasis. In such situations, the synthesis of parathyroid hormone is increased, tipping the balance of cellular functions towards enhanced resorption of mineralised tissues, including dental roots, in order to maintain normal levels of calcium in the blood (10 mg). Therefore, chronic alcoholism, or other conditions associated with an abnormally high incidence of trigeminal neuralgia. In multiple sclerosis, aberrant nerve fibres lose their myelin sheaths, leading to short circuits between axons. Such short circuits in the trigeminal nerve may precipitate trigeminal neuralgia. Oral-treatment evokes an inflammatory reaction in para-dental tissues, including painful sensations that travel in an an-tidromic fashion from strained para-dental sensory nerve endings. If areas of demyelinating are present along the way to the Gasserian ganglion, trigeminal neuralgia may ensue.

Psychological stress is a common component of everyday life. It may be found in patients prior to the onset of orthodontic treatment, or it may develop during the course of treatment owing to discomfort, resentment or other reasons unrelated to orthodontics. Psychological stress affects the hypothalamic-pituitary-adrenal (HPA) axis, and the immune system. Since osteoclasts and odontoblasts modulate the immune system, modification of their function by psychological stress may affect the process of root resorption. A recent survey showed that orthodontic patients with psychological stress were at a high risk of developing excessive root resorption during the course of orthodontic treatment (Davidovitch et al., 1999). Furthermore, patients who are non-compliant, poor co-operators and those who frequently break appointments and/or appliances do it most likely because of psychological stress. Often, these non-compliant individuals express their objection to orthodontic care that had been imposed on them by their parents through their behaviour. In these individuals, the rate of orthodontic root resorption was found to be significantly higher than in compliant patients.

Amongst the reasons for partial and total loss of scalp hair is psychological stress, probably through effects on the HPA axis. Davidovitch et al. (1999) reported a case of an adolescent orthodontic patient with alopecia totalis during orthodontic treatment. A review of the case revealed a normal medical background with the presence of a persistent psychological stress owing to exposure to orthodontic mechanotherapy. Consequently, the patient's paediatrician and the endocrinologist concluded that his alopecia had been most likely because of psychological stress. Often, these non-compliant individuals express their objection to orthodontic care that had been imposed on them by their parents through their behaviour. In these individuals, the rate of orthodontic root resorption was found to be significantly higher than in compliant patients.

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