Periodontal Diseases in Patients with Special Health Care Needs

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Abstract

A wide variation of people with an impairment or disability requires a “special care dentistry” once their general manifestations directly act in the oral cavity. This target public is inserted into the following categories: neuromotor disability, sensory disability, mental disorder, infecto-contagious diseases, chronic systemic diseases, and systemic conditions. Among the several oral illnesses found in these groups, periodontal diseases have been the most frequent, becoming a major challenge for the dental practitioners. Thus, we described the microbiological, histopathological, and clinical features of periodontal diseases in each “special health care needs” group. Advances in “Omic” technologies have suggested the application of molecular biology methods to assess the genomics (genes), proteomics (proteins), transcriptomics (mRNA), and metabolomics (metabolites) aspects of periodontal diseases. These researches aim to promote a better understanding of the mechanisms involved in the pathogenesis and in the identification of new biomarkers of periodontal diseases that help in diagnosis of periodontal diseases and in tissue responses after treatments of gingivitis and periodontitis. As an alternative therapy, some bioactive materials and photobiomodulation may be indicated once they strongly stimulate the periodontal tissue regeneration, attenuate the inflammatory processes, and/or promote the reconstruction of the microstructure of the periodontium.

Keywords: periodontal diseases, special health care needs, “Omic” technologies, bioactive materials, photobiomodulation
1. Introduction

The World Health Organization (WHO) estimates that there are more than one billion people in the world living with some form of impairment or disability, of whom nearly 200 million have considerable difficulties in functioning [1]. There is a growing proportion of people with disabilities worldwide, and these are vulnerable groups in both developed and developing countries.

Currently, the National Organization on Disability (NOD), a private and nonprofit organization, estimates that 54 million children and adults in the United States have one or more disabilities, with 35 million Americans being severely disabled [2–4]. The proportion of children with disabilities is estimated to be 12.5 million or around 18% [3–5]. According to the estimated data by National Health and National Health and Nutrition Examination Survey (NHANES), 46% of adults in the United States have periodontitis, and 8.9% have severe periodontitis [6].

The geopolitical and social plurality of states and regions in Brazil have shown the emerging need for effective public policies to meet the specific needs of this diversity. According to the Brazilian Institute of Geography and Statistics, 45.6 million Brazilian citizens (equivalent to 23.9% of the population) have some type of neuropsychomotor impairment as physical, sensory—visual and auditory—and intellectual disabilities. Among these, 17.7 million people (6.7% of the population) have severe disability. The majority of this target public is found in urban areas and is aged between 15 and 64 years; further, the northeastern areas have a higher number of cities with at least one person with disability [7]. Hence, oral health care needs should be emphasized mainly for this target public due to high susceptibility to infection risks and great vulnerability to develop illnesses. Mental disorders associated or not with disabilities must also be considered in these individuals. In this condition, the familiar influence shall be taken into account for these groups once their human development directly depends on the good relationship among them.

Regarding children with developmental disorders, especially the autism spectrum disorder (ASD), attention-deficit/hyperactivity disorder (AD/HD), or specific learning disorder (LD), the field of “special care dentistry” is rapidly gaining recognition as a necessary service once they require oral health care needs at all times [8]. According to American Psychiatric Association (APA) [9], these disorders have relatively been growing due to the increase in birth rates and life expectancy of these individuals. Another relevant factor would be the ability or difficulty to perform their self-care, in particular, in the mouth, resulting in a negative impact of precarious oral conditions. The main oral signs and symptoms found in this target public include poor oral hygiene, dental caries, and severity of periodontal diseases (PD). High incidence of dental hypoplasia, traumatic lesion (factitious, iatrogenic, and accidental), drug-induced gingival overgrowth, dental malocclusion, and tooth missing are also evidenced [8, 10]. It is important to highlight that the large dental loss of intact teeth is caused by the destruction of the collagen fibers of the periodontal ligament (PDL) and severe resorption of alveolar bone tissue from the persistent supra and subgingival and periopathogenic microbiota, recognized as periodontal disease [11]. Therefore, this disease is one of the most common oral chronic infections in people with special health care needs (SHCN), becoming an important dental public health problem.
Based on combined data from the literature and our scientific experiences, we discussed the microbiological, histopathological, and clinical features of PD in each “special care needs” group. Furthermore, we reported some advances in “Omic” technologies which are molecular biology methods used to assess the genomics (genes), proteomics (proteins), transcriptomics (mRNA), and metabolomics (metabolites) aspects of PD. These methods promote a better understanding of the mechanisms involved in the etiopathogenesis and in the identification of new biomarkers of PD that help in the diagnosis of PD and in tissue responses after treatments of gingivitis and periodontitis. In addition, alternative therapies to PD in patients with SHCN were recommended in order to aggregate new scientific knowledge, some of them being investigated at the Center of Biosciences Applied to Persons with Special Care Needs (CEBAPE) of the Institute of Science and Technology of the São Paulo State University (UNESP).

2. Special Health Care Needs (SHCN) in dentistry

The field of “special care dentistry” is rapidly gaining recognition as a service that should be provided to persons with physical, mental, or intellectual disabilities by general physicians, pediatric physicians, geriatric physicians, dental practitioners, and dental hygienists. Considering the limited opening of the oral cavity and the great difficulty of clinical procedure handling, the special needs patients may be treated under applying of psychological, physical, or pharmacological techniques in order to control their behavior and the voluntary or involuntary body movements. These patients may be affected by several comorbid physical illnesses including diabetes mellitus, cardiovascular diseases, respiratory illnesses as aspiration pneumonia, sleep disturbance as obstructive sleep apnea, malignant neoplasms, and so on. Extrinsic and intrinsic factors may corroborate to the installation and perpetuation of PD, as well as increase the susceptibility to supra and subgingival periopathogens in these individuals, even after oral hygiene promotion and/or intensive conventional mechanical treatment, combined or not with a supportive therapy. Concerning the main extrinsic factors, previous studies have considered oral mucositis-inducing chemotherapy drugs, saliva flow-reducing medications, respiratory disturbances as mouth breathing leading to oral hyperventilation and, as a consequence, dry mouth, motor deficit, cognitive impairment, learning difficulty and disability, crowded teeth, and inappropriate diet. The intrinsic factors include immune response deficiency, a high amount of periopathogens, sleep disorders such as obstructive sleep apnea, dysfunction of the oropharyngeal muscles resulting in severe dysphagia, and the risk of occurrence for aspiration pneumonia. Previous studies confirm the presence of respiratory pathogens in the oral cavity which may be aspirated into the lung alveoli due to severe dysphagia, developing aspiration pneumonia [12, 13]. This comorbidity may negatively influence the oral health homeostasis, aggravating the preexistent inflammatory processes, in particular, the PD.

Current researches confirm that the therapy applying neuromuscular electrical stimulation on the masticatory muscles was effective in adults with cerebral palsy. This biostimulating effect also reflected in the electrical activity of the oropharyngeal muscles, favoring their functional performance; then, a positive effect on the apnea and hypopnea index was found. These
episode cascades reduced the number of pathological respiratory events, promoting improvements in the quality of life for these patients [12–14].

Regarding the oral health status of these populations, the main oral manifestations are dental caries, dental hypoplasia, dental agenesis, orofacial traumas, drug-induced gingival overgrowth, and, in particular, PD [8]. Recent studies have shown that the presence of periodontopathic microbiota at the oral biofilm and/or spread throughout the saliva may explain the higher susceptibility to PD in this target public [15, 16].

According to the Joint Advisory Committee for Special Care Dentistry (JACSD), “special care dentistry” provides oral services for people with an impairment or disability including physical, sensory, intellectual, mental, medical, social, or a combination of one or more of these [17]. Several conditions, disorders, and/or disabilities lead these patients to the need of specialized oral assistance. In Brazil, the Federal Council of Dentistry has recognized the specialty of Dentistry for Patients with Special Health Care Needs as a dental service which has been assisting people with simple or complex disabilities, of acute or chronic nature, and temporary or permanent conditions or disorders. This target public is inserted into the following categories: neuromotor disability (1), sensory disability (2), mental disorder (3), infecto-contagious diseases (4), chronic systemic diseases (5), and systemic conditions (6).

The neuromotor disorders (1) include people with physical and intellectual disabilities which are from an unknown, environmental, and a genetic origin. These disorders consist of cerebral palsy, cerebrovascular disturbances (e.g., ischemic and hemorrhagic cerebral strokes), spinal cord injury, myelomeningocele, infectious disease (e.g., poliomyelitis or infantile paralysis), autoimmune diseases (e.g., myasthenia gravis and multiple sclerosis), muscular dystrophy resulting in muscle weakness and cellular degeneration, metabolic bone diseases (e.g., rickets or osteomalacia caused by genetic, nutritional and/or hormonal abnormalities affecting bone growth and remodeling), and bone genetic disorder (e.g., dysostosis, osteopetrosis and imperfect osteogenesis). The congenital and acquired abnormalities, resulting in craniomaxillofacial deformities, complex malformations, and syndromes are also included in the neuromotor disorders. It is important to emphasize that the intellectual disabilities may be associated with these conditions.

The sensory disorders (2) include the hearing and visual disabilities, generating immediate harmful effects as depression, isolation, dementia, and decrease of quality of life [18]. The severity of these impairments may result in the disruption of interpersonal relations and decrease of self-sufficiency in daily living activities, both of which are critical to the well-being of a person [19]. Hearing disability, with its resultant difficulties in communication function, pervades multiple domains of function in the individuals, decreasing activity, increasing depressive symptoms, and confounding assessment of cognitive ability. Although it is not curable, this impairment is often remediable with appropriate audiologic evaluation and the prescription of amplification devices. Visual disability also affects multiple domains of function, limiting the individuals’ ability and increasing the risk of falls, fractures, and morbidity. In order to attenuate the consequences of visual disability, the cause must be identified to obtain an effective treatment [20].

Conforming to the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) published by the American Psychiatric Association (APA) under coordination of the Division of Mental Health of the World Health Organization (WHO) and the National
Institute of Mental Health (NIMH), a mental disorder (3) is a syndrome characterized by clinically significant disturbances in an individual’s cognition, emotion regulation, or behavior which reflects a dysfunction in psychological, biological, or developmental processes underlying mental functioning [9]. Thus, mental disorders are usually associated with significant distress or disability in social, occupational, or other important activities. An expectable or culturally approved response to a common stressor or loss (e.g., the death of a loved one) is not considered a mental disorder [9]. For a better elucidation, the new North American classification of mental disorders is briefly mentioned in Figure 1.

Among the different groups of psychopathologies, it is worth mentioning the neurodevelopmental disorders which include intellectual disabilities (mild, moderate, and severe levels), autism spectrum disorder (ASD), attention deficit and hyperactivity disorder (ADHD), communication disorders (speech and language impairments), specific learning disorder, motor disorders (e.g., stereotyped movement disorder and tic disorders), and so on [9]. Children with neurodevelopmental disorders may experience difficulties with language and speech, motor skills, behavior, memory, learning, or other neurological functions [14]. While the symptoms and behaviors of neurodevelopmental disabilities often change or evolve as a child grows older, some disabilities are permanent. Diagnosis and treatment of these disorders may be difficult, frequently involving a combination of professional therapy, pharmaceuticals, and home- and school-based programs.

Considering the most common mental disorders including dementia, depression, generalized anxiety disorder, panic disorder, obsessive–compulsive disorder, posttraumatic stress, and phobias, the psychiatric patients have presented high susceptibility to PD. These illnesses have been caused by a set of processes such as the presence of oral microbial biofilm due to poor oral hygiene, psychotropic medication-induced dry mouth, and gingival hyperplasia [15, 21]. Mental health clinicians should also be aware of the oral consequences of prescribed medications, especially the antipsychotic drugs [15]. About this, the depression may dysregulate regulatory mechanisms within the brain involved in immune regulation, alter the immune system responses, and thereby influence the development and progression of infections and inflammatory diseases, including periodontitis [22]. As a support therapy, antidepressant drugs, such as fluoxetine, tianeptine (selective serotonin reuptake inhibitor), and venlafaxine (serotonin-norepinephrine reuptake inhibitor) are used; however, the side effects could affect the periodontal tissue health [23]. Current studies using animal models showed that the fluoxetine reduced the alveolar bone loss due to suppression of inflammatory response and protection against periodontal bone resorption and collagen fibers destruction of the periodontal ligament (PDL), while the tianeptine influenced the immune system, enhancing the plasma concentrations of pro-inflammatory and T regulatory cytokines and interleukins in response to the gram-negative bacterial lipopolysaccharide (LPS) antigen. As a consequence of these processes, there is an inhibition of the periodontal disease progression [24, 25]. On the other hand, the venlafaxine influenced the increase of alveolar bone loss, most likely due to its anti-inflammatory and immunoregulatory effects on the periodontitis once it is considered an inflammatory disorder and an immunologically compromised disease [22].

Therefore, an increased focus on the physical health of psychiatric patients should encompass oral health including closer collaboration between the dental practitioners and clinicians. Possible interventions must include the following approaches: to apply the best
| CATEGORIES OF MENTAL DISORDERS |
|-------------------------------|
| **1. Neurodevelopmental Disorders:** disabilities associated primarily with the functioning of the neurological system and brain (e.g. Autism Spectrum Disorder). |
| **12. Sleep-Wake Disorders:** insomnia, hypersomnia, and arousal disorder |
| **2. Schizophrenia Spectrum and Other Psychotic Disorders** |
| **13. Sexual Dysfunction** |
| **3. Bipolar and Other Related Disorders:** a psychological illness that causes severe changes in mood, energy, behavior and thoughts. People who suffer from this disease oscillate between periods of depression and periods of exacerbated mood and euphoria. |
| **14. Paraphilic Disorders** (i.e. feel personal distress about their interest, not merely distress resulting from society’s disapproval; or have a sexual desire or behavior that involves another person’s psychological distress, injury, or death, or a desire for sexual behaviors involving unwilling persons or persons unable to give legal consent). |
| **4. Depressive Disorders** (i.e. characterized by sadness severe enough or persistent enough to interfere with function and often by decreased interest or pleasure in activities). |
| **5. Anxiety Disorders** (i.e. defined as “a state of intense apprehension, uncertainty, and fear resulting from the anticipation of a threatening event or situation, often to a degree that normal physical and psychological functioning is disrupted”): separation anxiety disorder, selective mutism, specific phobia, social disorder, panic disorders, agoraphobia, generalized anxiety disorder, and substance-induced anxiety disorder. |
| **6. Obsessive-Compulsive and Other Related Disorders** (i.e. characterized by obsessions and compulsions that require a considerable amount of time, getting in the way of social activities and personal values; other related disorders are body dysmorphic disorder, trichotillomania or hair-pulling disorder, hoarding disorder, and excoriation disorder or skin-picking disorder. |
| **7. Trauma and Stress-Related Disorders** (i.e. outcomes of exposure to potentially traumatic stressful life events): reactive attachment disorder, disinhibited social engagement disorder, posttraumatic stress disorder, acute stress disorder, and adjustment disorders. |
| **8. Dissociative Disorders** (i.e. disruptions or discontinuity of consciousness, memory, identity, emotion, perception, body representation, motor control, and behavior). |
| **9. Somatic Symptoms and Other Related Disorders** (i.e. preoccupation with one or more distressing physical symptoms, resulting in disruption of daily life.) |
| **10. Feeding and Eating Disorders** (e.g. anorexia nervosa and bulimia nervosa) |
| **11. Elimination Disorders** (i.e. involuntary elimination of urine, enuresis, or defecation, encopresis, in inappropriate places or at inappropriate times by childhood or adolescence) |
| **12. Personality Disorders** (i.e. an enduring pattern that deviates from the expectations of the individual’s culture in two or more of the following areas: cognition; affectivity; interpersonal functioning; impulse control; the enduring pattern is inflexible and pervasive across a broad range of situations; and the enduring pattern leads to clinically significant distress or impairment). |
| **13. Substance-Related and Addictive Disorders** (i.e. marked by physiological dependence to substances, including alcohol, caffeine, cannabis, hallucinogens, inhalants, opioids, sedatives, stimulants, tobacco, and other, and, as a consequence, leading to a drug-seeking behavior, tolerance, and/or withdrawal. |
| **14. Neurocognitive Disorders:** dementia as Alzheimer’s disease, vascular dementia, and others. |
| **15. Gender Dysphoria** (i.e. very discomfort with the gender identity and, as a consequence, non-acceptance with the body which was assigned). |
| **16. Disruptive, Impulse-Control, and Conduct Disorders** (i.e. disruptive, impulse-control, and conduct disorders (i.e. characterized by a recurrent pattern of negativistic, hostile behavior and disobedience toward the societal standards and authority figures, and violation to the rights of others by physical and verbal aggression and destruction of property). |
| **17. Other Conditions that may be a focus of Clinical Attention** (i.e. affective problems including feelings of sadness, apathy, or anger about the other individual in the relationship). |
| **18. Drugs-Induced movement disorders** |
| **20. Other Adverse Effects of Drugs** |

Figure 1. Different condition groups of mental disorders described in the fifth edition of the diagnostic and statistical manual of mental disorders published by the American Psychiatric Association [9].
behaviors according to the difficulty levels of learning and the motor and cognitive dysfunction of each individual, and to perform periodic oral appraisals for necessary methodological adjustments in order to ensure the maintenance and the preservation of good oral health. Before introducing these procedures, the dental practitioner must comprehend the profile of each patient with SHCN, so as to know the physical and intellectual limitations, to identify the presence of comorbid diseases which may affect the overall health, and to assess the psychiatric behavior related to oral self-care. Surely, this systemic overview may favor the homeostasis of the stomatognathic system and improve the general health conditions, once these approaches can prevent the development of extensive and severe PD avoiding dental mobilities and/or loss.

The infecto-contagious diseases (4) is a subset category of highly dangerous transmissible diseases which include mainly infected patients with human immunodeficiency virus (HIV) infection and acquired immune deficiency syndrome (AIDS), patients with active tuberculosis disease, patients with viral hepatitis, and other such patients.

The chronic systemic diseases (5) are illnesses that spread throughout the body, affecting multiple organs and body systems, which may evolve into comorbidities, complicating the diagnosis and, consequently, influencing the prognosis. Considering this concept, the diseases imply juvenile rheumatoid arthritis, diabetes mellitus, congenital and acquired heart diseases, hematological diseases or disorders, chronic renal failure, autoimmune diseases (lichen planus, pemphigoid, pemphigus vulgar, erythema multiforme, lupus erythematosus, epidermolysis bullosa, etc.), vesiculobullous diseases, and so on.

The systemic conditions (6) are recognized as secondary factors that may modulate the disease initiation or progression rather than acting as primary etiological factors. These circumstances may affect the onset, progression, and treatment of such disease. Several patient types are included in these conditions, such as patients submitted to radiotherapy and chemotherapy in the head and neck regions, patients who received an organ transplant, patients with medication-induced immunosuppression, and similar others that may affect the general health conditions of the individual.

To better comprehend the relation among the environmental, genetic, and social effects and a person, a diagram was elaborated showing the occurrence of diseases, conditions, and/or disorders which may manifest during the life course of an individual. It is important to emphasize that these etiopathological factors may contribute to the development of one or more disabilities, leading to an acquired or congenital disability. On the other hand, an individual may be born with one or more disability and, concomitantly, develop diseases or disorders due to the high susceptibility to the environment and the different levels of disability complexity, characterizing the person with SHCN. It is noteworthy that the social impact resulting from precarious conditions of survival on the people with SHCN could explain the causes of health disparities or high occurrence of oral diseases (Figure 2). Socially disadvantaged groups have demonstrated poorer overall and oral health than the general population, becoming an aggravating factor, especially, in groups with SHCN. Therefore, a better attention to the public services in oral health for this population should be one of the main goals in government plans.
2.1. Types of periodontal diseases in patients with SHCN

Some case reports of patients with SHCN were briefly described in relation to their clinical, radiographic, histopathological, and laboratorial characteristics together with the oral manifestations, clinical procedures, and transdisciplinary approaches; then, we correlate them with the findings found in the literature. Furthermore, we mainly discuss the clinical management related to the PD. The additional commentaries are aimed to reinforce the importance of the early diagnosis and an appropriate dental treatment for each complexity of disability. Types of PD that were correlated with some categories of people with SHCN are depicted in the following section.

2.1.1. Case 1: chronic periodontitis associated with genetic disorder

A 14-year-old adolescent girl with Robinow syndrome had low stature, mild exophthalmos, hyperthyroidism, frequent thrombocytopenia, splenomegaly, and genital abnormality such as hypoplastic clitoris and small lips (a). Esophageal reflux was reported in the initial years of life. Using the Nicodemo et al. [26] and Grenlieh-Pyle [27] methods, dental and bone ages were 11.4 and 12, respectively. The intraoral examination showed mouth respiration, angular cheilitis, dental malocclusion, and ulcerated gingival surface (b and c) and accentuated alveolar bone loss (d), especially, at the region of mandibular incisors. Histologically, gingival tissues showed intense infiltration of mononuclear inflammatory cells diffusely spread throughout the connective tissue. Junctional epithelium hyperplasia with intense exocytosis (e) and extensive areas with no epithelium cover associated with infiltration of polymorphonuclear inflammatory cells into the lamina propria were also evidenced. In addition, presence of bacterial colonies (black arrows) and necrotic alveolar bone tissue fragments (blue arrows) was found (f and g). The diagnosis was chronic periodontitis with ulceration areas (Image 1).
2.1.2. Case 2: chronic gingivitis associated with genetic disorders plus uncommon abnormalities

A 19-year-old young man with Down syndrome associated with ectodermal anomalies. The extraoral features displayed dry skin and alopecia of eyelashes, eyebrows, and hair (a) while, the intraoral features showed dry mouth due to the severe reduction of saliva flow and mouth breathing, frequent angular cheilitis resulting from immune system deficiency, bilateral absence of the inner and upper third molars, presence of left upper and right lower deciduous canines, upper lateral incisors with microdontia, unerupted left upper permanent canine, generalized chronic gingivitis (a–d), and absence of caries. The recommended dental treatment was periodontal prophylaxis through the use of disclosing agents such as the scaling and root planning (e–g). It is important to point out that oral hygiene orientation and diet control must be continuously performed because of the neuromotor dysfunction of these patients, resulting in great understanding difficulties and difficulties in handling of cleaning devices and leading to a poor oral hygiene. Concerning dental education, we consider that the learning for repetition and use of ludic techniques or resources are effective strategies which must be implemented by dental practitioners. We also suggest the saliva analysis to assess their physicochemical properties, to determine the susceptibility to stress measuring the concentrations levels of salivary amylase or cortisol, and to identify the occurrence risk for aspiration pneumonia using as a biomarker the *Pseudomonas aeruginosa*. It is important to highlight that patients with Down syndrome present immune system disorders; therefore, oral infections must be avoided for general health balance and maintenance (Image 2).

2.1.3. Case 3: severe medications-induced gingival overgrowth

A 11-year-old female child with West syndrome had multiple epileptic spasms and, as a consequence, a severe neuropsychomotor impairment. The electroencephalography showed a hypsarrhythmia pattern confirming the diagnosis. The recommended treatment to this
condition has been the use of phenobarbital and/or valproic acid since birth. The intraoral features were drug-induced generalized gingival proliferative lesion with partial covering of the posterior teeth and gingival bleeding. Some permanent teeth were still impacted due to the presence of gingival fibrosis (a–c). The recommended dental therapy was the prophylactic periodontal treatment and gingivectomy (Image 3).

To illustrate this case, histopathological features were depicted in order to show the medication effects on the oral mucosa, in particular, on the gingival tissues (epithelium and connective tissue) (Figure 3).

2.1.4. Case 4: discreet chronic gingivitis associated with severe bruxism

A 7-year-old male child with spastic quadriplegic cerebral palsy, caused by hypoxic–ischemic brain damage, exhibited poor cognitive function and has been feeding on semi-solid food since 3 years of age. Ranitidine hydrochloride was used to treat gastroesophageal reflux, and botulinum toxin was never used to decrease the severity of the sleep bruxism. As a consequence, severe upper and lower teeth wear reaching the region of the dental pulp were evidenced (a).

This child was in primary dentition phase and exhibited discreet chronic gingivitis, mouth-breathing pattern, severe dysphagia, and involuntary tongue movements. First, oral hygiene orientation and diet control under supervision were done due to his severe neuromotor dysfunction. Posteriorly, we used a masticatory device denominated “hyperbola” to attenuate the sleep bruxism and, consequently, to improve the quality of his life. After the proposed therapy, we obtained satisfactory results, including reduction of the sleep bruxism and improvements of sucking-swallowing movements at meals. (Source: Giannasi, et al. [14]) (Image 4).
Image 3. Severe medications-induced gingival overgrowth.

Figure 3. Medication-related gingival hyperplasia. Photomicrography showing gingival hyperplasia characterized by the epithelium hyperplasia and proliferation of dense connective tissue. Epithelial crest projections were thin and long (blue arrows), interconnecting them (black arrows) (a). A lamina propria exhibited infiltration of mononuclear inflammatory cells, especially lymphocytes, plasma cells, and macrophages. Furthermore, scattered eosinophilic globules of gamma globulin, known as Russell bodies (b; square), were also seen (hematoxylin–eosin; bars = 200 and 50 μm).

Image 4. Discreet chronic gingivitis associated with severe bruxism. (Source: Giannasi, et al. [14]).
2.1.5. Case 5: chronic gingivitis associated with sensory disabilities and metabolic disease

A 9-year-old male child with visual disability resulting from the intracranial hypertension and/or alterations in the vascularization of the optical nerves which were caused by the cystic cranio-pharyngioma. Diabetes insipidus was developed as a complication of this disease, whereas, the motor functions, learning ability, memory, and mental health were preserved. The intraoral features showed generalized chronic gingivitis and deep caries, in particular, in the molar regions, resulting from poor oral hygiene. Considering that the periodontal disease is one of the main oral complications of diabetes, the oral health balance must be a major goal of the dentists once hyper-glycemic control in a diabetic child becomes is a great challenge for parents and doctor (Image 5).

2.1.6. Case 6: necrotizing periodontal disease associated with AIDS and metabolic disorder

A 59-year-old man with diagnosis of active positive-HIV had squamous cell carcinoma in the vestibular fornix region. In the clinical history, the patient was a smoker since the age 13 and had arterial hypertension, saphenous bridge, and type 2 diabetes mellitus. The diagnosis of positive-HIV was confirmed when the patient was 36 years old. To treat the malignant neoplasm, chemotherapy and radiotherapy were indicated by the oncologists; however, no emergency dental treatment was done before the recommended therapies in order to first eliminate the dentoalveolar infection foci. We imply that the severe periodontitis combined with periapical lesion caused by the presence of residual root, quickly evolves into an abscess with spontaneous extraoral suppurrative drainage. The neoplasm overgrowth and the indicated therapies with no support dental treatment surely influenced this infectious process (a and b). Severe candidiasis was spread on the hard palate and, in particular, superior alveolar ridge (c). The exfoliative cytology confirmed the diagnosis, showing a great amount of *Candida albicans* hyphae (d) and indicating a highly immunocompromised patient. As a consequence of the oral condition, this patient was with a severe malnutrition and cachexia resulting in hypoglycemic shock and, then, progressing to his death in 15 days. Most likely, there was no favorable response to the medical therapeutic protocols due to the severity of the immunosuppression and the presence of generalized acute oropharyngeal infections (Image 6).

2.1.7. Case 7: generalized chronic periodontitis associated with heart and metabolic diseases

A 61-year-old man had uncontrolled and insulin-dependent type 2-diabetes mellitus, arterial hypertension, ankylosing spondylitis, and hepatitis C. Regarding the diabetes control, the patient was treated with sinvastatina (10 mg), galvus (100 mg) and lantus (44 mL).
glycated hemoglobin (HbA1c) value was 9.1% (Reference values: normal: ≤5.6%, prediabetes: 5.7–6.4%, and diabetes mellitus: ≥6.5%, in accordance with the American Diabetes Association) [28]. In the intraoral features, generalized chronic periodontitis characterized by the clinical attachment loss and the periodontal abscess with suppurative drainage placed, in particular, at the right canine region were evidenced (a, b, c, and d). Oral hygiene was unsatisfactory, most likely because of the pain and the gingival bleeding stimulated by the use of cleaning devices. The periodontal treatment was done associated with prophylactic drugs as antibiotics. No local vasoconstrictive anesthetic agent was administered during the clinical procedures. (Courtesy: Professor Doctor Ana Cristina Solis) (Image 7).

Concerning the etiology of PD in patients with uncontrolled diabetes, the progressive attachment loss was detected due to the function and reduction of polymorphonuclear leukocyte chemotaxis leading to an increase in infection susceptibility, collagen synthesis and maturation reduction, increased collagenase activity, and the formation of advanced glycation end products (AGEs) that bind to the receptor for advanced glycation end products (RAGEs) in macrophages and monocytes. The effects of AGE accumulation increase tissue oxidant stress, alter the endothelial cell functions, elevate the activity of matrix metalloproteinases leading to the production of free radicals, and promote vascular dysfunction and cellular death. These factors may directly affect the migration and activity of inflammatory cells, impairing the mechanisms of defense against microorganisms and delaying the periodontal tissue repair processes, resulting in great losses of support structures [11].

To clarify these clinical findings, periodontal tissue alterations resulting from oral complications of diabetes were depicted, including intense alveolar bone resorption at the furcation region, proliferation of junctional epithelium (hyperplasia) toward the furcation, diffuse infiltration of mononuclear inflammatory cells which consisted of macrophages, lymphocytes,
and especially plasma cells. Numerous blood vessels were congested and the diapedesis mechanism (leukocyte extravasation into connective tissue) were well evidenced, justifying the great amount of inflammatory cells at the lamina propria (Figure 4).

2.1.8. Case 8: autoimmune disease associated gingivitis (desquamative gingivitis)

A 33-year-old woman with chronic mucocutaneous inflammatory disorder of immunological background showing aggressive and extensive oral lesions with erythematous, erosive and extensive areas, especially in the marginal and attached gingivae (a and b). Histopathological features showing a band of infiltration of lymphocytic inflammatory cells under the surface epithelium extending throughout the gingiva (c), besides hydropic degeneration and sharpness loss of the basal layer (d) (hematoxylin and eosin, 50× and 100×). The diagnosis was lichen planus. (Source: Gomes et al. [29]) (Image 8).

2.1.9. Case 9: gingivitis associated with hematological disorders

A 23-year-old young woman with Fanconi’s anemia had severe pancytopenia and a prolonged, long-term immunosuppression which resulted in the development of an abscess on the infra-orbicular region. This process progressed to phlegmon causing tissue necrosis of the nostrils, nasal septum, nasal fossa, and posterior orbit region of the right side (a). The etiologic agent of the phlegmon was Streptococcus parasanguinis. The myelogram shows moderately hypocellular bone marrow with cellular dysplasia involving the granulocytic, erythrocytic, and megakaryocytic (arrow) series (b). The intrabuccal examination showed abundant and spontaneous gingival bleeding, edema on the interdental papillae, hematomas on the superior and inferior lips, and inadequate oral hygiene (c and d). No caries, alveolar bone loss, and periodontal pockets were evidenced. No bone marrow transplant was performed due to incompatibility of donors; thus, the only available option was an alternative treatment through the erythrocytes and platelets-concentrated transfusion to prevent...
spontaneous hemorrhages and severe anemia. Oral exfoliative cytology was performed, showing superficial epithelial cells with nuclear and cytoplasmic alterations, erythrocytes, bacterial colonies (cocci), and numerous hyphae and spores of *Candida albicans* (e). Based on this, drug administrations, as antifungal medication and antibiotics, were also indicated to treat the oral acute inflammatory processes caused by bacterial and fungal infections. It is important to emphasize that the dental interventions were done together to the recommended medical therapy until the disease remission period. Initially, the periodontal prophylaxis was carried out by dentist and, posteriorly, the orientation and control of oral hygiene and diet accomplished by nurses and caregivers after adequate training in oral health. The health multiprofessional team, who may participate in this treatment process, corroborated in favor of supportive health care, leading to a quick recovery time of the patient (Source: Gomes et al. [30]) (Image 9).

**Figure 4.** Photomicrography showing chronic periodontitis related to Case 7 (Masson’s trichrome; bars = 1000, 200, 100, and 50 μm).

**Image 8.** Gingivitis associated with autoimmune disease (desquamative gingivitis) (Source: Gomes et al. [29]).

spontaneous hemorrhages and severe anemia. Oral exfoliative cytology was performed, showing superficial epithelial cells with nuclear and cytoplasmic alterations, erythrocytes, bacterial colonies (cocci), and numerous hyphae and spores of *Candida albicans* (e). Based on this, drug administrations, as antifungal medication and antibiotics, were also indicated to treat the oral acute inflammatory processes caused by bacterial and fungal infections. It is important to emphasize that the dental interventions were done together to the recommended medical therapy until the disease remission period. Initially, the periodontal prophylaxis was carried out by dentist and, posteriorly, the orientation and control of oral hygiene and diet accomplished by nurses and caregivers after adequate training in oral health. The health multiprofessional team, who may participate in this treatment process, corroborated in favor of supportive health care, leading to a quick recovery time of the patient (Source: Gomes et al. [30]) (Image 9).
2.1.10. Case 10: necrotizing ulcerative gingivitis associated with hematological disorder plus chemical and physical agents

A 14-year-old adolescent boy with Acute Lymphoblastic Leukemia (ALL) underwent the chemotherapy and radiotherapy on the region of the central nervous system for relapse prophylaxis of the primary disease (a). The myelogram before the medical therapies displayed hypercellular bone marrow composed exclusively by lymphoblastic cells with numerous atypical mitoses (square) (b and c). Extra and intraoral features of the patient, before the recommended dental treatment, were acute necrotizing ulcerative gingivitis, severe oral mucositis with areas necrosis associated to pseudomembranes, and facial asymmetry with signs of...
phlogistic processes (d and e). The exfoliative cytology of the hard palate and attached and free gingivae shows a great number of inflammatory polymorphonuclear and mononuclear cells, besides a great amount of *Candida albicans* hyphae confirming the diagnosis of candidiasis (f and g). The dental treatment protocol, inserted together to the medical therapies until the primary disease remission period, corroborated in favor of the patient’s general recovery time and of the elimination of the oral acute inflammatory process (h). The myelogram after the remission phase of the disease showed normal bone marrow (i and j). In extra- and intraoral features, the patient showed discreet facial asymmetry, discreet chronic gingivitis, and palate mucosa with normal features (l and m). Considering these clinical and histological findings, we dare reinforce that the insertion of a dental practitioner into the hospital transdisciplinary team is crucial to the medical therapy success and to the good quality of health services, in particular, for systemically highly compromised patients. (Source: Gomes et al. [31]) (Image 10).

3. **“Omic” technologies applied in periodontal diseases**

With advances in genomic (genes), transcriptomic (mRNA), proteomic (proteins), and metabolomic (metabolites) capabilities, an increased interest has emerged in the biologic system to define the complex regulatory networks that result in health or disease [32]. This implies a greater understanding of the data related to the etiopathogenesis of PD. These diseases are a multifactorial, highly complex disease involving some factors as host, environment, and microbiota. However, it is the host inflammatory response which may lead to the soft and hard tissue destruction. In severe diseases, this can lead to tooth loss [33]. The host response to the infections draws upon the innate, inflammatory, and adaptive immune systems which provide an appropriate response to the aggressive microorganisms. In some individuals and with some bacteria, this phenomenon will be an innate-only response, others will need to invoke the inflammatory response, and yet others will require the adaptive immune response (cellular, humoral, or both) in order to reduce the microbial activities [33, 34].

Although much of what Page and Schroeder proposed in 1976 has stood the test of time, advances in the fields of basic and periodontal immunology need a reassessment of their work, as well as their integration with emerging new concepts [35]. Major advances have been made regarding the cellular and molecular mechanisms underlying the induction, regulation, and effector functions of immune and inflammatory responses. Likewise, Kornman [36] described a new look of the PD pathogenesis when he reported the specific bacteria and immunoinflammatory mechanisms related to innate differences among individuals and changes in environmental factors. This fact may accelerate or attenuate these biochemical changes [37].

With emerging genomic, proteomic, and metabolomic data and tools of biology systems for interpreting data, it is now possible to start describing the basic elements of a new model of pathogenesis [36]. Stunning new findings have begun to clarify several complexities of the host-pathogen interaction of PD, pointing to key roles for microbial dysboiosis and immune imbalance in the pathogenesis of disease [34].

Regarding the genomic knowledge, inflammation, cellular infiltration, and expression of a complex array of cytokines, chemokines, and lipid mediators are key characteristics of PD. In
PD, the presence of elevated inflammatory cytokines, including tumor necrosis factor (TNF)-α, interleukin (IL)-1, IL-6, interferon (IFN)-γ, and IL-12, is considered a central force when coupled with cell activation and RANKL (receptor activator of nuclear factor kappa-B ligand) activation in driving pathogen elicited bone loss [38, 39]. In addition to pro-inflammatory cytokines, an array of chemokines including IL-8 and monocyte chemotactic protein (MCP)-1 and others are frequently elevated in PD [40]. Some examples of this type of interaction are described in the literature, for example, studies that reported a positive association between polymorphism of the IL-1 and PD [41, 42]. In addition, the presence of antiinflammatory and regulatory cytokines, such as transforming growth factor-beta (TGF-β), IL-10 and IL-4, has been reported [43, 44].

T lymphocyte cells (T cells) are well known as key regulating cells which orchestrate the host immune response. Considering the cells arise from the CD4+ population and are based on cytokine profiling, early studies showed that these cells were segregated into Th1 and Th2 populations. Modern cytokine profiling and transcription factor analysis have led to a much more detailed classification of Th cells and the emergence of the Th17, Treg, TFH, Th9, and Th22 subsets [45, 46]. More advances have been recognized in what concerns the Toll-like receptors (TLRs) and TLR signaling; TIR-domain-containing adapter-inducing interferon-β (TRIF), interferon regulatory factors and type 1 interferon, and other pattern recognition receptors and PD, including scavenger receptors (SRs) and nucleotide-binding-oligomerization-domain (NOD)-like receptors (NLRs) [34].

With a similar importance, the transcriptomics aspects are defined as gene expression profile and when altered may influence the microbiota composition of periodontal pocket, as observed by Papapanou et al. [47]. In the same way, recent studies started to use proteomic techniques, promoting high resolution in the evaluation of proteins and molecular pathways involved in gingival inflammation [48, 49].

The gingival fluid composition of inflamed sites of patients with generalized aggressive periodontitis was evaluated by Bostanci et al. [50], demonstrating the proportion of enzymes associated with neutrophils, metalloproteinase of matrix-8, catepsin G, mieloperoxidase in addition to bacterial, viral, and yeast proteins that were increased in aggressive periodontitis when compared to healthy sites of individuals without periodontitis. Cystatin B and defensins, defense proteins, were detected only in healthy individuals.

Proteins involved in immune response and antimicrobial function, such as α-amylases, calgranulin A, cystatin, C-lysozyme, and cathepsin G were regulated positively in the induction phase of gingivitis. In the resolution phase, several histones and neutrophilic proteins, including cathepsin G, myeloperoxidase, and defensin-1 had their production decreased [49].

Concerning metabolomic aspects, among the earliest host-response molecules found in response to infection are lipid mediators [51]. Resolution of inflammation involves the production of lipid mediators named immunoresolvents and includes the resolvins, protectins, lipoxins, and maresins [51, 52]. Functionally, resolvins limit inflammation in part through prevention of neutrophil penetration, limiting inflammation at the local level, and promote tissue regeneration. The reduction of inflammation, through the use of resolvin-based approaches, may represent a novel strategy to potentially augment PD treatment approaches [53].
New models in the next few years will be merely frameworks for integrating key knowledge as it becomes available from the “Omic” technologies for diagnosis, providing by identifying one or more biomarkers the detection of active disease, predict future progression, and evaluate the response to periodontal therapy, thereby improving clinical management through early diagnosis and intervention, especially in case of patients with SHCN.

4. Alternative therapy for periodontics

As an alternative treatment to obtain the regeneration of the periodontium, the photobiomodulation (PBM) and some bioactive materials may be indicated, once they strongly stimulate the periodontal tissue response, attenuate the inflammatory processes, and/or promote the microstructural reconstruction of the periodontium. However, in the indication of these therapies, PBM must be carefully studied, since it depends exclusively on the general and oral health status of each patient.

Concerning the patients with SHCN associated to immune system deficiency, the PBM, also known as low-level laser therapy (LLLT), has been largely used to promote therapeutic and biostimulating effects, such as analgesia, antiinflammatory action, angiogenesis, and mitogenesis [11]. Gomes et al. [11] assessed the impact of the GaAlAs diode laser on the periodontal tissues and investigated its effects on the alveolar bone remodeling process during orthodontic tooth movement in normoglycemic and diabetic rats. The authors demonstrated that the PMB strongly stimulated the alveolar bone remodeling and favored the continuous reorganization of the soft periodontal tissues, leading to the maintenance and the integrity of periodontal microstructures under orthodontic force, especially in uncontrolled diabetic rats (Figure 5).

Several bioactive materials have been used in the regenerative medicine, especially in patients with complex metabolic and cellular disorders. Among them, we highlighted homogenous demineralized dentin matrix (HDDM), amniotic membrane (AM) used as a biological dressing, and different types of platelet concentrates such as platelet-rich plasma (PRP) and platelet-rich fibrin (PRF). These biomaterials were applied in the craniomaxillofacial complex resulting in tissue regeneration and microstructural reconstruction due to their effective inductive and conductive properties. The HDDM, PRP, and AM in implantation sites may initiate an inductive cascade as chemotaxis

Figure 5. Low-level laser therapy applied on the periodontal tissues under orthodontic force (a) in a period of 21 days. Photomicrographs showing furcation region of the right mandibular first molar in diabetic rats: (b) diabetic rats with no laser irradiation displaying alveolar bone loss due to intense osteoclastic activity (square); and (c) diabetic rats with laser irradiation exhibiting suitable alveolar bone formation because of the intense osteoblastic activities (square) and the integrity of the periodontal ligament fibers (Source: Gomes et al. [11]).
of progenitor cells, mitogenesis, angiogenesis, and differentiation into a wide variety of cells. The cell recruitment, division rate, and differentiation of cell lines are under the direct control of several growth factors and stem cells which are found in these biomaterials [54–56].

In particular, the AM is a huge source for multipotent mesenchymal stem cells (MSCs) with the ability to differentiate into a wide variety of cells, such as chondroblasts, osteoblasts, adipocytes and fibroblasts, myocytes, endothelial cells, neuronal cells, and hepatocytes, leading to formation of cartilage, bone, connective tissue, muscle, blood vessel, nerve, and liver tissue, respectively [56–58]. This membrane acts as a barrier, preventing the entry of pathogens and toxins, preserving the tissue structures, and, consequently, reducing the levels of local pro-inflammatory cytokines [58, 59]. Thus, it could be largely used to selectively guide the tissue regeneration in the periodontium following destructive PD.

Regarding the second-generation platelet concentrate, the PRF clot forms a strong and dense natural fibrin mesh full of growth factors that can stimulate proliferation of PDL cells and osteoblasts; besides, it favors various cytokine entrapment and preserves the growth factors from proteolysis [60]. This concentrate is characterized by a high content of platelets and leukocytes that release an array of growth factors such as platelet-derived growth factor (PDGF), transforming growth factor-beta 1 (TGF-β1), insulin-like growth factor (IGF), vascular endothelial growth factor (VEGF), and the antiinflammatory cytokines [61].

Although the use of autologous platelet concentrates is not new to periodontics, current researches are strongly encouraging the combination of platelet concentrates, such as PRP, PRF, and concentrated growth factors, with bone graft materials, membranes for guided tissue regeneration and MSCs to stimulate the periodontal regeneration. Most likely, this pool has synergistic effects, favoring the environment and the development of desirable periodontal tissues which were seriously compromised by the periodontal disease.

5. Considerations

Considering the high susceptibility to PD in people with SHCN, it is important that the dental practitioners know the different levels of disability complexity and how the undesirable environment may impair the human and physical development, leading to temporary or permanent disorders and/or diseases. Among the most common oral diseases, periodontal disease is an inflammatory condition which has been identified as a potential risk factor for systemic diseases. Therefore, it must be continuously controlled by the dentists to maintain the general health status of this individual.

In addition, other treatments for oral rehabilitation may be indicated when the periodontium is healthy, such as orthodontics, dental implants and/or the use of dental prostheses, contributing to the balance of the stomatognathic system, the preservation of the general health, a better quality of life, and, consequently, social inclusion.

In search of alternative therapies for this target public, the photobiomodulation for periodontal tissue biostimulation and the reconstructive surgeries using bioactive materials may be recommended in order to favor the periodontal regeneration, to protect the periodontium
under daily actions of physicochemical agents and psychic conditions, and to restore lost periodontal microstructures.

Despite the entire scientific and technological development for people with SHCN, we may presume that the major challenges for health multiprofessionals are to promote the best transdisciplinary practices in oral healthcare on dental services and hospitals due to the high complexity of disabilities, conditions, disorders and diseases of these individuals; to perform people management focusing on the good interpersonal relationship among the health multiprofessionals, patient, family and caregivers; and to combat the several environmental and social factors that may strongly affect the decision-making power of the patient to carry out a satisfactory self-care.

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Conflict of interest

Authors have no conflict of interests.

List of abbreviations

| Abbreviation | Description                                      |
|--------------|--------------------------------------------------|
| ADHD         | attention-deficit and hyperactivity disorder     |
| AGEs         | advanced glycation end products                  |
| AIDS         | acquired immune deficiency syndrome              |
| AM           | amniotic membrane                                |
| ALL          | Acute Lymphoblastic Leukemia                     |
| APA          | American Psychiatric Association                 |
| ASD          | autism spectrum disorder                         |
| DSM          | Diagnostic and Statistical Manual of Mental Disorders |
| GaAlAs       | gallium-aluminum-arsenide                        |
| HbA1c        | glycated hemoglobin                              |
| HDDM         | homogenous demineralized dentin matrix           |
| HIV          | human immunodeficiency virus                     |
IFN interferon
IFN-γ interferon-gamma
IGF insulin-like growth factor
IL interleukin
IL-1 interleukin-1
IL-10 interleukin-10
IL-12 interleukin-12
IL-4 interleukin-4
IL-6 interleukin-6
IL-8 interleukin-8
JACSD Joint Advisory Committee for Special Care Dentistry
LLLT low-level laser therapy
LPS bacterial lipopolysaccharide
MCP-1 monocyte chemotactic protein-1
mRNA messenger ribonucleic acid
MSCs mesenchymal stem cells
NHANES National Health and Nutrition Examination Survey
NIMH National Institute of Mental Health
NLRs nucleotide-binding-oligomerization-domain (NOD)-like receptors
PBM photobiomodulation
PD periodontal diseases
PDGF platelet-derived growth factor
PDL periodontal ligament
PRF platelet-rich fibrin
PRP platelet-rich plasma
RAGEs receptor for advanced glycation end products
RANKL receptor activator of nuclear factor kappa-B ligand
SHCN special health care needs
SRs scavenger receptors
T cells T lymphocyte
TFH T-follicular helper cell
TGF transforming growth factor
Th cells T helper cells
Th1 T helper cell 1
Th17 T helper cell 17
Th2 T helper cell 2
Th22 T helper cell 22
Th9 T helper cell 9
TLRs Toll-like receptors
TNF tumor necrosis factor
TNF-α tumor necrosis factor-alpha
Treg regulatory T cell
TRIF TIR-domain-containing adapter-inducing interferon-β
VEGF vascular endothelial growth factor
WHO World Health Organization

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