Systemic Diseases and Syndromes that Affect the Periodontium

This chart includes medical conditions known to impact periodontal health and that may be included in a differential diagnosis when periodontitis is detected in pediatric patients. Individualized at-home and professional preventive oral care interventions must be emphasized for these patients. A multidisciplinary approach may be indicated for safe and effective oral health care.

Disorder	General characteristics	Diagnostic criteria	Oral findings		Treatment considerations
			Clinical	Radiographic	
Chédiak-Higashi syndrome[1,2]	- Rare autosomal recessive disorder of the immune system - Mild 'atypical' phenotype: 10-15% of cases; 'classic' phenotype: 80-90%, progresses to accelerated phase (fatal without bone marrow transplant) - Characterized by reduced pigmentation, neurological deficits, fever, lymphadenopathy, anemia, neutropenia, hepatosplenomegaly thrombocytopenia.	- Microscopic analysis of WBCs - Genetic testing identifies mutations in the lysosomal trafficking regulator gene (LYST/CHS1)	- Severe gingival inflammation, swelling, and recession - Early onset periodontitis in primary and permanent dentitions - Premature tooth loss - Oral ulcerations may be present	Alveolar bone loss (localized or generalized)	- Immune status and transplantation dictate timing and precautions (e.g., antibiotics) - Supportive management of complications (e.g., antibiotics to treat bacterial infections) - Aggressive recurrent periodontitis may not respond to SRP or antibiotic treatment - For extractions/surgeries, consider adjunctive measures for hemostasis and avoid NSAIDs due to platelet dysfunction - Prosthetic therapy for lost teeth may be considered depending on patient's medical status
Diabetes mellitus[3,4]	- Metabolic disorder • Type 1: autoimmune reaction causes lack of insulin production; usually diagnosed in children and young adults • Type 2: insulin resistance; usually diagnosed in adults • Gestational: insulin resistance during pregnancy - Associated with increased inflammation, impaired immunologic response and wound healing, CV disease, retinopathy, nephropathy, neuropathy	- Glycated hemoglobin (A1C) - Other tests include: oral glucose tolerance tests, fasting plasma glucose test, random plasma glucose test	- Enlarged, erythematous attached gingiva - Dental/ periodontal abscesses - Increased clinical attachment loss and pathologic periodontal pockets - Severe periodontitis	Alveolar bone loss	- Assess level of disease control (e.g., compliance with diet and medications) • With uncontrolled diabetes, consider antibiotic prophylaxis for invasive oral procedures • Nonsurgical periodontal therapy (e.g., SRP and antimicrobial agents [chlorhexidine, antibiotics]) shows modest glycemic control improvement • Monitor for delayed healing
Haim-Munk syndrome[4,5]	- Rare autosomal recessive syndrome; a phenotypic variant of PLS with mutation to chromosome 11q14-q21 and loss of function of the cathepsin C gene - Milder periodontal disease and more severe dermatologic manifestations than PLS - Clinical manifestations • Dermatologic: palmoplantar hyperkeratosis; scaly patches on eyelids, lips, cheeks; skin infections • Skeletal: arachnodactyly, onychogryphosis, acroosteolysis, pes planus, muscle contractures, and destructive arthritis	Genetic testing for mutation of cathepsin C gene	- Rapidly advancing gingival inflammation and bleeding, deep periodontal pockets, gingival abscesses, periodontal destruction - Premature loss of all primary teeth by age 4-5; loss of permanent teeth by age 16 - After tooth loss, gingiva returns to healthy state	Generalized extensive alveolar bone loss with migration of teeth	- Treatment of oral manifestations depends on patient's age, psychological state, and tooth mobility - May include nonsurgical therapy (e.g., monthly SRP, systemic antibiotics) and/or extraction of hopeless teeth - Alveolar loss renders prosthetic rehabilitation challenging

Abbreviations in table: *BMI: Body mass index; CDC: Centers for Disease Control and Prevention; CV: cardiovascular; NSAIDs: nonsteroidal anti-inflammatory drugs; PLS: Papillon Lefèvre syndrome; SRP: Scaling and root planing; WBCs: White blood cells.*

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Hypophosphatasia[6,7]	- Rare genetic metabolic bone disorder characterized by impaired mineralization of bones and/or teeth - Mutations in the ALPL gene leading to low alkaline phosphatase activity - Wide-ranging severity (involving skeletal, renal, neurological, muscular, respiratory complications); six types based on severity and age of onset - Disturbed cementum formation; tooth loss is one of the first signs of the condition	- Serum alkaline phosphatase (ALP) levels - ALPL gene testing	- Premature exfoliation of primary teeth with little or no root resorption - Clinical inflammation milder than in other systemic diseases associated with periodontitis - Permanent dentition may be clinically normal in mild subtypes or prone to periodontitis and early tooth loss in severe cases	- Alveolar bone loss - Large pulpal chambers and root canals - Thin dentin	- Enzyme replacement therapy, a new disease-modifying treatment, has shown periodontal, tooth, and bone improvements - Caution with orthodontic management due to cementum dysplasia and impaired periodontal attachment - Prosthodontic therapy may include removable prostheses and possible implants to stabilize prosthesis in the permanent dentition for those skeletally mature
Langerhans cell histiocytosis[8]	- Rare cancer-like condition (inflammatory myeloid neoplasia) characterized by excessive proliferation/infiltration of histiocytes (Langerhans cells); form categorized as a single-system (single organ affected) or multisystem (several organs affected) - Mortality rate: <10% in single-system vs. 30-50% in multisystem - Average age of onset: 1-3 years; male predilection - Oral manifestations and pain can be the first signs of the condition	Clinical, microscopic, hematologic, and imaging examinations	- Gingivitis, bleeding, recession, mucosal swelling, periodontitis, ulceration - Excessive mobility of teeth, premature exfoliation - Oral pain	- Alveolar bone loss with distinct appearance of teeth floating in soft tissue - Unifocal or multiple lesions within the body of the maxilla and mandible	- Management of periodontal disease is not the first-line of treatment - Treatment of oral lesions depends on the type/extent of disease and may vary from observation to pharmacotherapy, surgical excision/curettage, and/or radiation therapy - Treatment should include basic periodontal therapy and extractions of hopeless teeth depending on immune status
Leukocyte adhesion deficiency syndromes[4,9]	- Rare autosomal recessive disorders - Primary immunodeficiency disorder involving both B and T cells - Impaired migration of WBCs to infection sites - Recurrent nonpyogenic bacterial and fungal mucosal infections - Compromised wound healing - Hematopoietic stem cell transplantation is the only curative treatment; high mortality rate	- Elevated WBCs (leukocytosis) - Genetic testing to identify mutations - Flow cytometry analysis to evaluate neutrophil expressions - Key clinical finding: absence of pus at site of infection	- Aggressive and severe gingivitis and rapidly progressive periodontitis - Persistent oral ulcers (gingivostomatitis) - Absence of pus - Premature exfoliation of primary dentition and early loss of permanent teeth	Alveolar bone loss	- Periodontal disease may be refractory to nonsurgical periodontal treatment and rigorous home care regimens - Prompt targeted antibiotic therapy - Adjunctive treatment may include granulocyte/thrombocyte transfusions, recombinant factor VIIa, and intravenous immunoglobulins - Prophylactic antibiotics prior to dental procedures
Obesity[10]	- Chronic complex multifactorial metabolic disorder presenting as excessive accumulation of fat - Etiologies: genetic, neuroendocrine, drug-induced, behavioral (diet and activity) - Comorbidities: diabetes, hypertension, CV disease, obstructive sleep apnea, systemic inflammation, some cancers	- Measured BMI • Ages 2-19: ≥95th percentile or ≥30 kg/m^2, whichever is lower based on age and gender using CDC growth charts • Adult: ≥30 kg/m^2 - Other measures include: waist/hip circumferences, waist to hip ratios	- Increased plaque index, bleeding on probing, periodontal pocket depth, clinical attachment loss - Mouth breathing	Alveolar bone loss	- Comorbidities may influence management - Dietary weight loss may reduce systemic inflammation and, in turn, enhance response to periodontal therapy

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Papillon Lefèvre syndrome (PLS)[11]	- Autosomal recessive disorder - Palmoplantar hyperkeratosis, nail dystrophy, pyogenic skin and other infections, intracranial calcification - Rapidly progressing periodontal manifestations beginning shortly after tooth eruption; occurs in primary and permanent dentitions - Etiology: alterations in the CTSC gene and, likely, neutrophil defects	- Urinalysis for cathepsin C activity - Genetic testing for mutation of cathepsin C gene - Key clinical finding: periodontal degeneration	- Rapidly advancing gingival inflammation and bleeding, deep periodontal pockets, gingival abscesses, periodontal destruction - Premature loss of all primary teeth by ages 4-5; loss of permanent teeth by age 16 - After tooth loss, gingiva returns to healthy state	Generalized extensive alveolar bone loss with migration of teeth	- Treatment of oral manifestations depends on patient's age, psychological state, and tooth mobility - May include nonsurgical therapy (e.g., monthly SRP, systemic antibiotics) and/or extraction of hopeless teeth - Alveolar loss renders prosthetic rehabilitation challenging
Periodontal Ehlers-Danlos syndrome[12,13] (Synonyms: Ehlers-Danlos syndrome VIII; pEDS)	- One of a group of hereditable connective tissue disorders; autosomal dominant - Characterized by varying features including tissue fragility with easy bruising, vascular complications, joint hypermobility and/or pain, pretibial discoloration/plaques, increased infection rate, hoarse voice - Predominant feature is severe early-onset periodontitis (mean age 14)	- Clinical examination and molecular genetic testing (variant in the genes C1R and C1S which play a role in innate immune system) - Complete lack of gingival attachment is considered pathognomonic - Most children identified through family history	- Severe gingival inflammation, loss of attached gingiva, and gingival thinning and recession - Rapid alveolar bone loss - Premature tooth loss	Alveolar bone loss	- May include nonsurgical therapy (e.g.,monthly SRP, systemic antibiotics) and/or extraction of hopeless teeth - Alveolar loss renders prosthetic rehabilitation challenging - Implants at high risk of peri-implantitis

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