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PUBLISHED: **JUNE 2024**
EXPIRES: **MAY 31, 2027**

ABSTRACT

Reported incidence and prevalence of connective tissue disorders (CTDs) are variable due to different study methodologies, surveyed to be present in 0.015%–3% of the population. CTDs include systemic lupus erythematosus (SLE), systemic sclerosis (SSc), rheumatoid arthritis (RA), Sjögren's syndrome (SS), inflammatory muscle diseases, and other overlap syndromes that cause inflammation, autoimmune processes, and/or systemic clinical phenotype involving several organs, as well as polymyositis and dermatomyositis. CTDs, although considered rare, are potentially life-threatening. Therefore, early diagnosis is essential if possible. Current classification criteria do not allow for convenient or proper diagnosis in all patients; nonetheless, they are supportive clinical tools to lead providers to proper diagnoses and to potentially save lives.

EDUCATIONAL OBJECTIVES

Upon completion of this course, the dental professional should be able to:

1. Outline prevalence and incidence of connective tissue disorders and the implications regarding periodontal conditions.
2. Illustrate the systemic signs and symptoms of connective tissue disorders.
3. Synthesize cotherapeutic management of connective tissue disorders and periodontal disease.
4. Elaborate counseling strategies for dental providers to translate to patients with connective tissue disorders.

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Autoimmune connective tissue disorder manifestations: Implications for the dental provider

A PEER-REVIEWED ARTICLE | by Katrina M. Sanders, MEd, BSDH, RDH, RF
Elizabeth A. Sanders, DPM, FACFAS, DABPM
Mark J. Mendeszoon, DPM, FACFAS, DABPM

Autoimmune diseases are characterized by the immune system attacking the body's own tissues. Increasing numbers of these conditions are affecting people all over the world, predominantly in women and Caucasians. Autoimmune diseases have been linked to genetic factors as well as environmental triggers. Still, little is understood about the exact etiology. These diseases occur in essentially all bodily systems, especially manifesting in the digestive tract, endocrine tract, neurological system, and connective tissue. The American Academy of Periodontology currently recognizes three specific diseases affecting connective tissues of the periodontium, including Ehlers-Danlos syndrome (types IV, VIII), angioedema (C1-inhibitor deficiency), and systemic lupus erythematosus (SLE).[1] These three systemic disorders are implicated in significant loss

of periodontal tissue and thus are classified as systemic disorders that have a major impact on the loss of periodontal tissue by influencing periodontal inflammation.

Not only do the disturbances in connective tissues affect the oral cavity, but there are direct implications on the musculoskeletal system that will impact joint mobility, joint stability, and human locomotion.

This article aims to assist the dental provider to better understand connective tissue diseases by describing the incidence and prevalence of connective tissue diseases, risk factors, signs and symptoms that health-care providers should be looking for, prevention and treatment strategies, and guiding the provider in oral management for patients with these ailments.

Prevalence of connective tissue diseases

The prevalence and incidence of connective tissue disorders (CTDs) have significant reported variability depending on study methodology.[2] Research currently indicates that up to 90% of undifferentiated CTDs occur in females, typically 32–44 years of age. With mild symptoms and early diagnosis, the progression of these disorders can be easily halted.[3] It is estimated that 72% of patients with undifferentiated CTDs are Caucasian. One population-based study in the United States found that CTDs occur in two people per 100,000 per year[4]; another study found a prevalence of 6.4 per 100,000.[5] Among CTDs, Sjögren's syndrome has an incidence of 0.5%–1% of the population, second only to the most common CTD, rheumatoid arthritis, which has an incidence ranging from 1% to 2% of the population.[6] Systemic lupus erythematosus (SLE) is estimated to be around 5.1 per 100,000 people in the United States, with a higher prevalence noted in the female population (8.7 per 100,000 women).[7] The prevalence of systemic sclerosis (SSc) varies among different countries. The prevalence of overlap syndromes, especially mixed connective tissue disease, is unknown. Polymyositis and dermatomyositis are regarded as very rare rheumatic diseases.

FIGURE 1: Beighton Score[7] offers a series of physical identifiers to identify joint hypermobility and thus assist in screening for connective tissue disorders. While many healthy people will have hyper-flexible joints, joint hypermobility syndrome may come from an underlying connective tissue disorder.

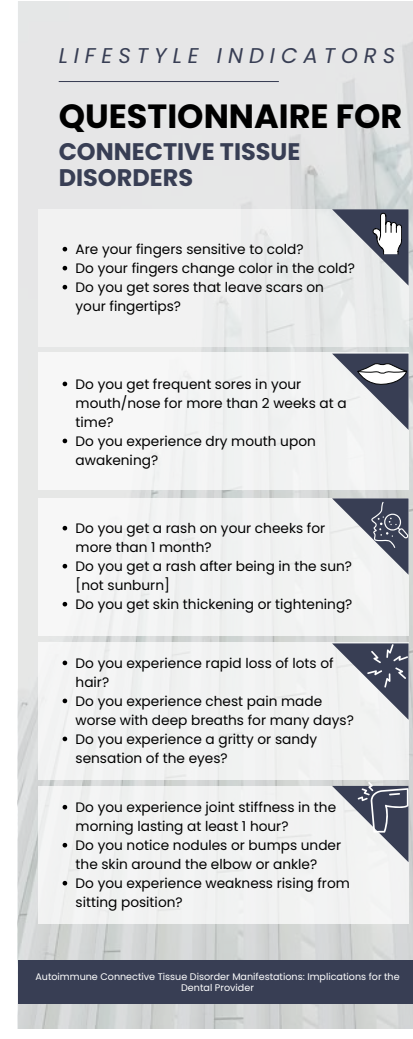

FIGURE 2: Lifestyle indicator[9] questions can provide an opportunity to screen patient-reported remarks as potential indicators of an underlying connective tissue disorder.

Signs, symptoms, and screening questions

While there is not one specific classification criterion to diagnose an individual patient with a CTD, there are signs and symptoms that the health-care provider can observe. The use of the Beighton score[8] **(figure 1)** indicates a nine-point scoring system implicated as a standard assessment for generalized joint hypermobility.[9] Lifestyle indicator questionnaires[10] **(figure 2)** are also beneficial in guiding the medical provider in a possible proposed diagnosis.

While oral manifestations commonly observed in individuals with CTDs do not directly indicate a CTD, they may point to an underlying and/or undiagnosed disorder. Therefore, the dental professional may play a role in early screening for unexplained

and unresolved oral manifestations that may provide key indicators for the need for advanced testing.

Risk factors

Risk factors for CTDs vary greatly based on the type of disease an individual may have, and these conditions are considered autoimmune in nature. Autoimmune diseases tend to have a genetic predisposition, which means one's risk is higher due to a genetic variation that impacts immune response.[11] The way that particular gene is expressed may be altered via the epigenome, a layer of chemical tags that sit on top of DNA.[12] When environmental triggers interact with the epigenome, they can activate or deactivate parts of the genome through complex chemical reactions. When one has been diagnosed with an autoimmune disease, there is greater risk of developing another. An accumulation of three or more autoimmune conditions is called multiple autoimmune syndrome, seen in 25% of patients.[13]

Another inherited risk factor includes being of the female sex,[14] as 78% of those affected by autoimmune diseases are female. This may be secondary to factors such as the additional X chromosome, hormonal changes, reproductive function, immune responses, and organ vulnerability. Certain noninherited risk factors may play a role in increasing susceptibility to autoimmune conditions as well, including:

- **Obesity:** Excess adipose tissue is associated with more than 10 autoimmune diseases[15] as it is involved in many physiological functions including metabolism and immune response. Excess adipose tissue leads to increased or dysregulated secretions of pro-inflammatory adipokines,[16] which threaten the healthy immune system. It may alter gut microbiota and lead to intestinal dysbiosis, leading to eventual organ damage, metabolic syndrome, and autoimmune conditions.
- **Tobacco:** Tobacco dependence impacts the immune system through various interactions, including inflammatory response, immune suppression, dysregulation of cytokines or signaling molecules involved in autoimmunity, and the development of autoantibodies.[17] Exposure to other toxins, such as air pollutants, ultraviolet radiation, and organic solvents, also poses a risk.[18] Moreover, toxic agents have the ability to alter gene expression, which may activate an otherwise repressed gene or deactivate an active one, leading to disease.
- **Pharmaceuticals:** Medications, such as those used for blood pressure, depression and anxiety, anticholesterols such as statins, and antibiotics, may have side effects that involve immune system function, leading to autoimmune reactions.[19]
- **Infection:** Early exposure to certain infections may increase susceptibility to autoimmune diseases. Epstein-Barr virus or *Streptococcus* Group A may interact with genetics to trigger an autoimmune reaction.[20,21] SARS-CoV-2 has been reported to trigger cases of Guillain-Barré syndrome, antiphospholipid syndrome, lupus, and other autoimmune diseases.[22]

Oral manifestations

Due to the rapid cellular turnover of the connective tissue lining the mouth, the oral cavity presents an optimal opportunity to observe abnormalities in the connective tissue and to detect symptomatic but undiagnosed CTDs. Oral manifestations can oftentimes provide some of the earliest signs, stages, or symptoms of an undiagnosed or underlying connective tissue disorder.

Most notably, xerostomia presents with difficulty in swallowing, speaking, eating dry foods, or wearing dentures. Additionally, patients may complain of oral manifestations such as burning, tingling sensations, dysgeusia, fissuring of the tongue, sores within the labial commissure observed as angular cheilitis, erosive lichen planus, corrugation or pale buccal mucosa, loss of papillae on the tongue, and/or erythematous candidiasis.[23]

Of note, the degree and magnitude of bone resorption associated with patients afflicted by connective tissue disorder pathologies are often recorded as early-onset observations and certainly increase with age. Specifically, the degree of periodontal destruction is classified as rapid, progressive, generalized, and severe in nature. Patients with CTDs often complain of bleeding gums, tooth mobility, and pain when eating or performing home care.

Finally, patients with autoimmune inflammatory diseases impacting the joints may experience temporomandibular joint (TMJ) involvement, noting TMJ ankylosis, retrognathic mandible, and malocclusion.[25]

Ehlers-Danlos syndromes (types IV, VIII)

Defined as an inherited group of CTDs, Ehlers-Danlos syndrome (EDS) is typically characterized by abnormal collagen synthesis that can impact the skin, ligaments, joints, vasculature, and other organs as well as delayed wound healing and hypermobility of the joints and skin. Hippocrates first described EDS, which is one of the oldest known causes of bruising and bleeding.[26]

EDS type IV represents approximately 5%–10% of cases of inherited CTDs[27] and is a vascular type, whereas EDS type VIII is a rare connective disorder that demonstrates both joint and skin abnormalities as well as periodontal conditions such as poor keratinization of the gingiva, causing premature dental loss.[28] As such, dental patients experiencing EDS routinely experience early severe periodontitis and gingival recession, as well as severe

gingival enlargement and localized periodontal breakdown around teeth with shortened roots.[29] Patients may also present with a severity of periodontitis that often leads to loss of all teeth.[29] Most notably, pediatric patients experiencing early-onset periodontitis or prolonged bleeding times may have undiagnosed EDS, and the unexplained sequelae of disease may warrant testing for diagnosis.[30]

Angioedema (C1-inhibitor deficiency)

Hereditary angioedema is quite rare and is typically demonstrated as recurrent episodes of edema that commonly occur in the skin, abdomen, and larynx.[31] These episodes, or "attacks," are a result of a decreased level or declined function of C1-inhibitor. C1-inhibitor is a protein within the blood, which is a component of the complement system responsible for providing immune support by removing dead cells and foreign material.[32] As such, individuals with a C1-inhibitor deficiency are prone to infection.

Oral manifestations of angioedema may include edema of the lips or oropharyngeal region, particularly noted during episodes. It is worth noting that upper airway or laryngeal edema attacks can be life-threatening.[33] Additionally, a few case reports notated patients with angioedema also had periodontal attachment loss or, in some cases, localized aggressive periodontitis.[34]

Systemic lupus erythematosus

Defined as a chronic, multisystemic autoimmune disease, SLE demonstrates a pathogenesis between genetics, hormones, and the environment. Of note, SLE presents with consistent patterns of clinical manifestations, and upward of 54% of SLE patients present with oral lesions.[35]

Oral manifestations may include atrophic or ulcerated lesions, "honeycomb plaques," intensely keratotic lesions, palatal or labial discoid lesions, lichen planus, erythematous-purpuric macules, palatal erythema, petechiae, ulcerations, secondary Sjögren's, and desquamative gingivitis.[36] Squamous cell carcinoma has also been known to arise in long-standing scarring lesions associated with SLE.[37]

Diagnosis of connective tissue disorders

There is no one specific classification criterion to diagnose a patient with a CTD, but a number of proposed diagnostic criteria have been published. One common agreement is that specific criteria are the most valuable tool for identifying patients with systemic rheumatic diseases such as CTDs.

A proper medical workup will include a physical exam, imaging, and laboratory testing.[38] Standard laboratory testing may include complete blood cell count (CBC); urinalysis; blood chemistry; erythrocyte sedimentation rate (ESR); C-reactive protein (CRP); antinuclear antibodies; muscle enzymes; anti-U1-ribonucleoprotein (RNP) antibodies; amylase and lipase to evaluate the pancreas; brain natriuretic peptide to evaluate pulmonary hypertension; fluorescent antinuclear antibody (FANA); anti-RNP antibodies, which may be the most sensitive with diagnosis; anti-U1-70 kd; antiphospholipid antibodies; rheumatoid factor; anti-double-stranded DNA antibodies; anti-centromere; anti-Scl-70; and anti-PM-1, C3, and C4 complement levels. Presence or absence of any of these laboratory values does not specifically indicate diagnosis of CTDs.

Imaging studies may also be indicated, including chest x-ray to evaluate pulmonary infiltrates or edema or cardiomegaly; echocardiography to evaluate for valvular disease or pulmonary hypertension; ultrasound or CT scan of the abdomen to rule out organ involvement; or MRI of the brain to assess neurological symptoms.[39]

Ancillary testing may also be required in the workup, including pulmonary function tests; electrocardiogram and/or cardiac enzymes; cerebrospinal fluid (CSF) analysis; cardiac stress test; or heart catheterization. Several sets of diagnostic criteria have been published to assist with diagnosis of CTDs, including the Sharp criteria, the Alarcon-Segovia criteria, the Kasukawa criteria, and the Kahn criteria.[40] In 1996, Amiques et al. performed a comparison study and determined that the Alarcon-Segovia performs the best with 62.5% sensitivity and 86.2% specificity.[41] These criteria are widely used because they contain five clinical symptoms, diagnostic when three or more are present: swollen hands, synovitis, biologically or histologically proven myositis, Raynaud's phenomenon, acrosclerosis with or without proximal systemic sclerosis, and anti-RNP positivity.[42]

In 2019, a consensus in Japan[43] revised the diagnostic criteria into four

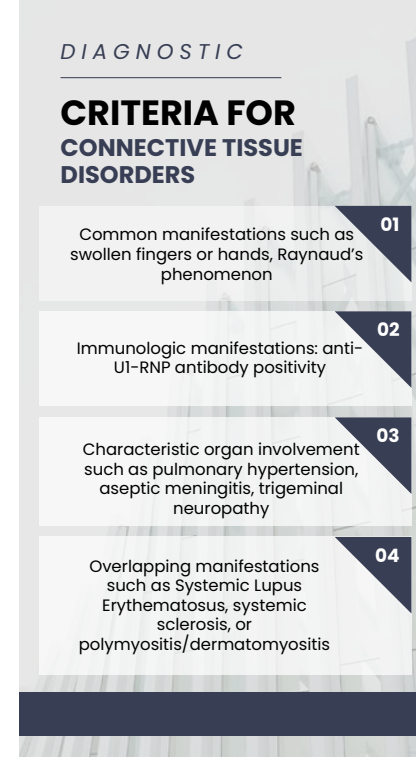

FIGURE 3: Diagnostic criterion[37] for considering an underlying connective tissue disorder.

categories **(figure 3)**. Most (90%) of patients who are ultimately diagnosed with CTDs are first diagnosed with other diseases that evolve into CTDs.[44]

Musculoskeletal manifestations

Patients with CTDs may experience skin disorders in which their integument is thin and fragile, with a higher risk for skin tears, lacerations, and either delayed healing due to compromised skin properties or risk of healing with disorganized scar tissues leading to hypertrophic scars or keloids.[45]

Patients with CTD may also experience stiffness or joint pain—for example, those with rheumatoid arthritis who experience this particularly in the mornings—which improves with activity.[46] Many note these findings upon waking or after sitting for a period of time followed by moving again. CTDs typically attack most of the joints throughout the body, including the upper extremities, fingers, lower back, hips, knees, and foot and ankle areas. Patients entering their fifth and six decades may also notice that they may be losing height and experience more stiffness or pain in the lower back.

Patients with CTDs may also have increased hypermobility of the joints.[47] Hypermobility and/or ligamentous laxity may put patients at higher risk for sprained joints, subluxations, or dislocations of joints in injury.

Many people with CTDs who have ligamentous laxity will experience a pes planovalgus, or flatfoot deformity, which can contribute to muscle imbalances that impact the soft tissue structures of the muscles, tendons, and ligaments.[48] Patients with hypermobile flat feet may develop conditions such as plantar fasciitis, posterior tibial tendonitis, Achilles tendinitis, hammertoe deformities, and long-term arthritis of the feet. These patients are at high risk for ankle sprains that can cause ankle instability and arthritis upon aging.

Persistent swelling in the lower legs can cause development of varicose veins that can ulcerate and cause pain due to significant problems with delayed healing.[49] Therefore, it is always important to inspect the feet and ankles daily, wear appropriate compression socks, apply lotion to the feet daily, and visit a foot and ankle specialist if there are major concerns **(figure 4)**.

Treatment and management

There is no one cure for patients who live with CTDs. The overall goals of therapy are to control the symptoms, maintain function, and reduce the risk of future disease consequences. Medical therapy may target the disease activity for specific organs. Monitoring and mitigating the risks of complications from the condition itself or the treatments is important.

After being diagnosed with a CTD, it is paramount that routine physician appointments be followed. Medications such as nonsteroidal anti-inflammatories, steroids, and biologic infusions may be instituted to help with the effects of the specific disease. Internists, family physicians, and rheumatologists are the experts to help with medical management of the conditions. Proper nutrition, hydration, anti-inflammatory diets, and various vitamins and supplements, such as vitamin C, D, B_{12}, zinc, turmeric, and garlic, may reduce some of the inflammatory symptoms of CTDs.[50]

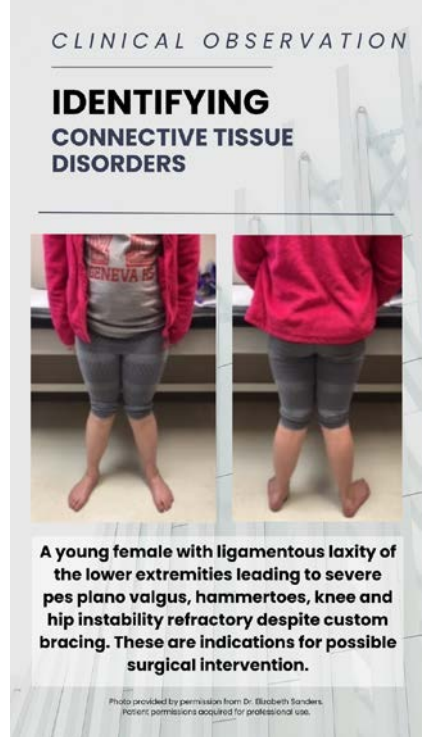

FIGURE 4: Clinical observation: Identifying connective tissue disorders

Treatments aimed at preventing injuries and sustaining a healthy lifestyle are essential. For patients with upper and lower instability, prefabricated or custom orthoses including bracing may be indicated. Use of high-top shoes may help patients with ankle instability if performing high-impact exercises that risk ankle sprains.

Little research has been performed regarding physical therapy treatment in patients with CTDs,[51] yet goals of therapy should include strengthening, mobility, and maintaining a regimen with specific intensity, duration, and frequency, which may be guided by a dedicated physical therapist.[52]

Surgical intervention may be required in patients with frequent lower extremity or upper extremity sprains and strains, which may include ligament or tendon repair, joint resections, joint replacements, joint arthrodesis, or fusions to provide a more functional extremity. However, patients with CTDs may not be ideal surgical candidates since they pose high risks for complications such as scarring, wound dehiscences, bleeding, blood clots, infections, problems with perioperative medication reconciliation, etc. The surgical candidate should be selected carefully and educated on the risks and benefits of both conservative and surgical options.

Biologic therapy is a revolutionary treatment of autoimmune diseases, designed to dampen the response of the

inflammatory cascade.[53] The first biologic therapies were approved years ago, but indications and new agents are challenging traditional treatment strategies for rheumatic diseases. In fact, biologics have also been used both on- and off-label for allergic disorders, oncology, neuroinflammatory disorders, inflammatory bowel disease, macular degeneration, and CTDs. Common biologics fall into two categories: cytokine inhibitors and lymphocyte-targeted therapies[54] **(figure 5)**. Finally, symptomatic therapy often involves addressing diminished salivary flow as well as the sequelae of xerostomia **(figure 6)**.

Preventive strategies

The outlook in preventing CTDs is highly variable on the etiology of disease. Several CTDs are inherited and, as such, complete prevention is impossible.

While EDS, angioedema, and SLE are inherited connective tissue diseases, it should be noted that many connective tissue diseases can also be caused or exacerbated by environmental factors. Environmental factors may include: exposure to toxic chemicals such as pollution or tobacco smoke, excessive exposure to ultraviolet light, poor nutrition noted in a lack of fat-soluble vitamin D and/or water-soluble vitamin C, or infections.[55] Thus, preventive strategies for CTDs may include a reduction in the exposure to environmental toxins and/or ample consumption of nutritional components aimed at preventing CTDs.

Lifestyle modifications, such as wearing gloves or taking other measures to prevent Raynaud's phenomenon, are important for preventing symptoms. Also important is avoidance of tobacco, which can vasoconstrict small arteries. Acute flare-ups may occur in times of stress; therefore, stress-reducing practices may help. Anti-inflammatories such as ibuprofen or naproxen can also help with symptoms. Other lifestyle adjustments such as consuming a low inflammatory diet can help lower inflammation and balance the gut bacteria, which may help reduce CTD symptom severity.[56] An excellent anti-inflammatory diet may include lean meats, fruits, vegetables, nuts, grains, seeds, healthy fats and oils, vitamins, and minerals. Adding prebiotic and probiotic foods, such as turmeric, ginger, fermented fruits and vegetables, isoflavones, bone broth, taurine, and fibers, may have added benefit as well. Iron and vitamin D deficiencies are also very common in patients with CTDs, so eating iron-rich and vitamin D-rich foods is recommended. Supplements such as bromelain may be considered to reduce arthritis pain and joint stiffness.

Additionally, nutritional counseling should consider eliminating or avoiding certain foods such as processed foods, sodium-rich foods, conventional dairy products, added sugars, sodas, caffeine, alcohol, omega-6 fatty acids such as canola oils and corn oils, as well as legumes or beans. A natural supplement, echinacea, which is intended to boost the immune system, may also cause flare-ups in patients with autoimmune disorders.[57]

Therapeutic strategies with controlled physical activity and regular exercise have been demonstrated to provide greater longevity and improve the quality of treatment and prevention of CTDs.[58] Because the aggressive effects of autoimmune diseases on the connective tissue of the locomotive apparatus directly affect the ability to perform physical exercise, the physical capacity of these patients is lower when compared to sedentary

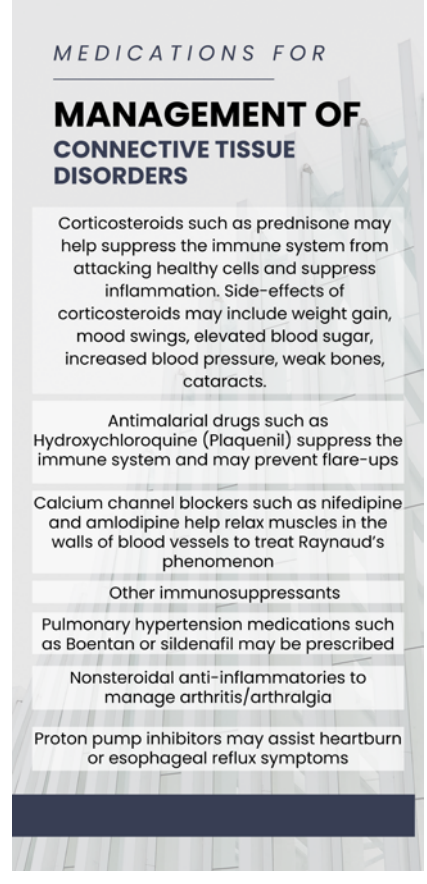

FIGURE 5: Common therapies for the control and management of various connective tissue disorders.[41]

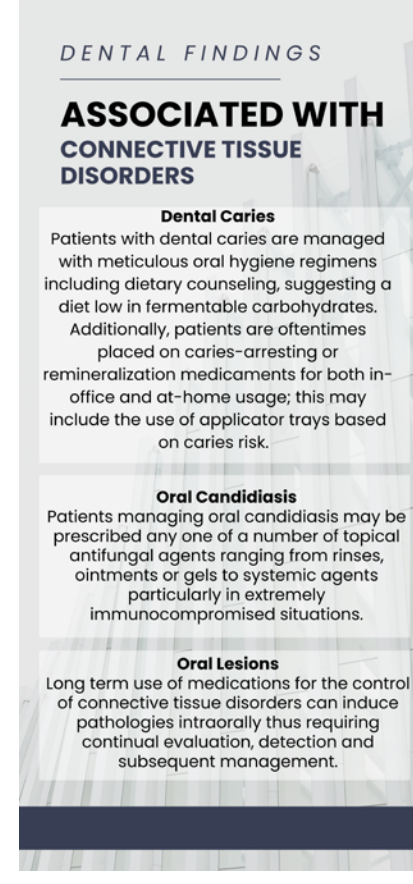

FIGURE 6: A compilation of common dental findings associated with connective tissue disorders.[22-24]

individuals who do not have any degenerative disease. This, along with fatigue, consequently makes physical activity a challenge. Regular routine exercise regimens performed at a specific intensity, duration, and weekly frequency managed by specialists may control the signs and symptoms of chronic progression of the disease process and interspace acute crises, making them less frequent.

Conclusion

Due to the wide array of symptoms, autoimmune CTDs may be difficult to diagnose. However, when the dental provider has a comprehensive understanding of the etiology, risk factors, symptoms, and oral manifestations that may indicate a diagnosis for patients with diagnosed or underlying CTDs, dental care for the patient becomes more comprehensive. The dental provider, thus, should understand the consequences of CTDs on a patient's dental care regimen and when to engage in a multidisciplinary approach to patient care.

Furthermore, for patients who have experienced complications with musculoskeletal issues that arise from CTDs, it is even more imperative that routine follow-ups, both with a musculoskeletal professional and a dental professional, be on a continual and routine basis for optimal disease management success.

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Katrina M. Sanders, MEd, BSDH, RDH, RF, is a clinical dental hygienist, author, and international speaker. She serves periodontal patients as the clinical liaison for Hygiene Excellence & Innovation for AZPerio and is the founder, CEO, and keynote speaker for Sanders Board Preparatory. Sanders is published in various publications including *RDH* magazine and Today's RDH and is an advisory member for *Modern Hygienist* and the Dental Academy of Continuing Education. Recently, she proudly accepted the 2023 Denobi Award for Clinical Excellence and Innovation in dentistry.

Elizabeth A. Sanders, DPM, FACFAS, DABPM, is a foot and ankle surgeon in Boston, Massachusetts, serving as assistant professor of surgery at Boston University School of Medicine. She completed surgical residency at Boston Medical Center, a fellowship in foot and ankle advanced reconstructive surgery in Ohio, and a mini-fellowship in external fixation at the Russian Ilizarov Scientific Center in Kurgan, Russia. She has given numerous lectures and presentations on innovative surgical techniques emphasizing limb salvage. Her research interests included reconstructive surgery, multidisciplinary medicine, and medical education.

Mark J. Mendeszoon, DPM, FACFAS, DABPM, is a foot and ankle surgeon practicing at Precision Orthopaedic Specialties in Chardon, Ohio. He is the director of the Advanced Foot and Ankle Fellowship in Ohio, clinical professor at Ohio University Heritage Medical School, sports medicine director at Kent State, and assistant professor at Iowa State University. He lectures nationally and internationally, has been published in several medical journals, and is a contributor to many health and wellness magazines including *Men's Health*. He also owns Achilles Running Shop in Ohio and Pennsylvania, the only known physician-owned specialty running store in the country.

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1. 72% of patients with connective tissue disorders are African Americans. Approximately 90% of undifferentiated connective tissue disorders occur in females.

A. The first statement is true; the second statement is false.
B. The first statement is false; the second statement is true.
C. Both statements are true.
D. Both statements are false.

2. A patient who experiences ___ when in the cold might have an underlying connective tissue disorder.

A. Finger sensitivity to cold
B. Fingers change color in the cold
C. Rapid tissue turnover of the fingers
D. A and B are both correct

3. Head and neck examination observations associated with an undiagnosed connective tissue disorder may include:

A. Frequent sores in the mouth for more than two weeks at a time
B. Dry mouth upon awakening
C. Thickening or tightening of the skin around the face
D. All of the above

4. Which of the following is false?

A. Autoimmune diseases tend to have a genetic predisposition.
B. Systemic lupus erythematosus (SLE) has a higher prevalence in the female population.
C. Sjögren's syndrome is the most common CTD documented.
D. Polymyositis and dermatomyositis are very rare rheumatic diseases.

5. The Beighton score evaluates joint hypermobility, assessing the ability to:

A. Passively oppose the thumb to touch the flexor aspect of the forearm
B. Passively hyperextend the elbow beyond 10 degrees
C. Passively hyperextend the knee beyond 10 degrees
D. All of the above

6. Lifestyle indicator questions that may indicate an autoimmune disease can include:

A. Nighttime aches and pains
B. Rash on the cheeks
C. Hair loss
D. B and C

7. Which of the following symptoms may indicate an autoimmune disease?

A. Cold sensitivity
B. Loose skin
C. Eye watering
D. B and C

8. Of the symptoms below, which finding might indicate an underlying autoimmune disease?

A. Increased chin hair growth
B. Morning joint pain that worsens throughout the day
C. Dry mouth
D. All of the above

9. Which can oftentimes provide some of the earliest symptoms of an underlying connective tissue disorder?

A. Oral manifestations
B. Headaches
C. Postnasal drip
D. Fatigue

10. Xerostomia may exacerbate oral manifestations such as:

A. Burning sensation
B. Dysguesia
C. Angular cheilitis
D. All of the above

11. Patients with autoimmune inflammatory diseases may experience ___ involvement.

A. Hypersalivation
B. Temporomandibular joint
C. Squamous cell carcinoma
D. None of the above

12. Risk factors for CTDs may include:

A. Genetic factors
B. Exposure to pollution
C. Using excess retinoids
D. A and B

13. Which of the following is considered an inherited risk factor for CTDs?

A. Female sex
B. Exposure to pollution
C. Obesity
D. Taking blood pressure medications

14. Which of the following is considered a noninherited risk factor for CTDs?

A. Female sex
B. Tobacco use
C. Having two X chromosomes
D. Family history of autoimmune disease

15. Which of the following is true regarding risk factors of autoimmune conditions?

A. Excess adipose tissue leads to increased or dysregulated secretions of pro-inflammatory adipokines.
B. Tobacco leads to inflammatory response, immune suppression, and dysregulation of cytokines.
C. Epstein-Barr virus, *Streptococcus* Group A, and SARS-CoV-2 have been linked to an increase in autoimmune conditions.
D. All of the above

16. The most significant laboratory value to assist with diagnosis of CTDs includes:

A. Anti-RNP positivity
B. Rheumatoid factor
C. C-reactive protein
D. Anti-Ro

17. Specific imaging may assist with CTD diagnosis. Which of the following is incorrectly matched with its purpose?

A. Chest radiography to evaluate cardiomegaly
B. ECG to rule out pulmonary hypertension
C. Ultrasound of the abdomen to look for neoplasms
D. MRI of the brain to evaluate neurological problems

18. Ancillary testing may be required in the work-up for CTDs and may include:

A. Pulmonary function tests
B. Cerebrospinal fluid
C. Cardiac stress test
D. All of the above

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19. Which of the following is true regarding the diagnosis of CTDs?

A. The Kasukawa criteria are regarded as the most specific for diagnosis.
B. Diagnostic criteria include swollen feet.
C. CTDs are typically one of the first considerations of differential diagnoses.
D. Anti-U1-RNP antibody positivity is highly suggestive of a CTD.

20. Which of the following is true regarding the diagnosis of CTDs?

A. Most patients who are ultimately diagnosed with CTDs are first diagnosed with other diseases that evolve into CTDs.
B. Diagnosis is frequently delayed with median time from first symptom to fulfillment of the criteria by 3.6 months.
C. Common initial symptoms include arthralgia.
D. A and C

21. Which is true about the diagnosis of CTDs?

A. At fulfillment of criteria, the most common manifestation is arthralgia.
B. CTDs frequently evolve to another CTD.
C. Mortality for patients with CTDs is significantly greater than the general population.
D. All are false.

22. Musculoskeletal manifestations of CTDs commonly may lead to all of the following except:

A. Ligamentous laxity
B. Tendinitis
C. High arch foot
D. Arthritis

23. Preventive strategies to avoid musculoskeletal complications in patients with CTDs may include:

A. Orthoses and bracing
B. Physical therapy
C. Surgical intervention
D. All of the above

24. Which of the following may make patients with CTDs poor surgical candidates?

A. Risk of scar tissue
B. Vascular disease leading to wound healing complications
C. Perioperative medication management
D. All of the above

25. Treatments for CTDs may include all of the following except:

A. Calcium channel blockers
B. Stimulants
C. DMARDs
D. Corticosteroids

26. Biologic therapy:

A. Is designed to enhance the response of inflammatory cascade
B. Is not yet approved as treatment for autoimmune diseases
C. Has been used both on- and off-label
D. Is not indicated for rheumatic diseases

27. Which of the following supplements is advised to be avoided in patients with CTDs?

A. Echinacea
B. Vitamin D
C. Vitamin C
D. Bromelain

28. What is considered part of an anti-inflammatory diet?

A. Omega-6 fatty acids and corn oils
B. Legumes and beans
C. Prebiotics and probiotics
D. Sodium-rich foods

29. Goals of physical therapeutic strategies in patients with CTDs include all of the following except:

A. Increased physical capacity
B. Decreased physical activity during acute flare-ups
C. Performance of physical activities at specified frequencies
D. Maintenance of regular routine exercise regimens

30. Which of the following is true regarding autoimmune CTDs?

A. Dental professionals should avoid asking their patients about CTDs and refer to a specialist immediately.
B. Patients with CTDs are not candidates for surgical intervention.
C. A multidisciplinary approach to managing patients with CTDs should be implemented.
D. Diagnosis of CTDs is straightforward and can be managed by any health-care professional alone.

PUBLISHED: **JUNE 2024**
EXPIRES: **MAY 31, 2027**

Autoimmune connective tissue disorder manifestations: Implications for the dental provider

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1. Outline prevalence and incidence of connective tissue disorders and the implications regarding periodontal conditions.
2. Illustrate the systemic signs and symptoms of connective tissue disorders.
3. Synthesize cotherapeutic management of connective tissue disorders and periodontal disease.
4. Elaborate counseling strategies for dental providers to translate to patients with connective tissue disorders.

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10.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	25.	Ⓐ	Ⓑ	Ⓒ	Ⓓ
11.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	26.	Ⓐ	Ⓑ	Ⓒ	Ⓓ
12.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	27.	Ⓐ	Ⓑ	Ⓒ	Ⓓ
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