Symptoms of sicca (dry eyes and dry mouth) are common in the general population. They can result from a variety of benign conditions, including medication use or normal aging, or they can be a feature of an autoimmune disease.

The hallmarks of Sjögren’s syndrome (SS), a systemic autoimmune disease, are dry eyes and dry mouth. SS occurs at a rate of 1/1,000. It typically affects middle-aged women, with a female-to-male ratio of 9:1 and a mean age of diagnosis of 50 years. It takes an average of nine years for patients with SS to be diagnosed after the onset of sicca symptoms. It can be associated with serious complications, most notably, lymphomas.

Recently, a consensus group composed of American and European experts published revised classification criteria for SS.1 They defined ocular and oral symptoms as follows:

Ocular symptoms are characterized by a positive response to at least one of the following questions:
1. Have you had daily, persistent and troublesome dry eyes for more than three months?
2. Do you have a recurrent sensation of sand or gravel in your eyes?
3. Do you use tear substitutes more than three times a day?

Oral symptoms are characterized by a positive response to at least one of the following questions:
1. Have you had a daily feeling of dry mouth for more than three months?
2. Have you had recurrent or persistently swollen salivary glands as an adult?
3. Do you frequently drink liquids to aid in swallowing dry food?

Other common symptoms in SS include fatigue, dental caries, arthralgias/arthritis, parotid gland enlargement, Raynaud’s phenomenon, fever and dyspareunia.

When a diagnosis of SS is suspected, investigations fall into four categories: autoantibodies, ophthalmologic assessment, salivary gland testing and biopsy.\(^1\)

**Autoantibodies.** The ones used for classification purposes include anti-Ro/SSA and anti-La/SSB. Anti-nuclear antibodies (ANA) and rheumatoid factor (RF) are also commonly present.

**Ophthalmologic assessment.** Objective evidence of ocular dryness can be obtained by doing Schirmer’s test (a small piece of filter paper applied next to the conjunctiva should show less than 5 mm of wetness in five minutes) and rose bengal staining (showing increased uptake of dye by damaged corneal epithelium).

**Salivary gland testing.** Tests include unstimulated salivary flow (less than 1.5 ml in 15 minutes), salivary nuclear scintigraphy and/or parotid sialography.

**Biopsy.** A minor salivary gland, usually obtained by doing an inner lip biopsy, can show a characteristic lymphocytic infiltrate.

Finally, a number of conditions need to be excluded before diagnosing SS, such as sarcoid, human immunodeficiency virus (HIV) infection, hepatitis C infection, pre-existing lymphoma and use of anti-cholinergic drugs.

In general practice, a diagnosis of SS is made in the presence of sicca symptoms and positive serology, with or without a positive biopsy. Treatment is usually symptomatic and consists of artificial tears and pilocarpine, a cholinergic agonist, prescribed as 5 mg orally four times a day. Sweating...
occurs in about 50% of the patients on pilocarpine. Blurred vision, headaches and gastrointestinal symptoms are less common. Recent studies on cevimeline — a newer, selective cholinergic agonist — showed promising results in the treatment of both dry eyes and dry mouth in patients with SS. However, gastrointestinal side effects appeared common.

There are currently no medications that have been shown to alter the natural course of SS. Hydroxychloroquine, methotrexate and infliximab have been studied in small, open-label trials.

Is there evidence that NSAIDs affect cardiovascular risk?

Nonsteroidal anti-inflammatory drugs (NSAIDs) are commonly prescribed to treat osteoarthritis (OA) and rheumatoid arthritis (RA), which are two of the most prevalent joint disorders. OA increases with age and may co-exist with other age-related diseases, including cardiovascular disease. In RA, data suggest that the risk of cardiovascular disease may be increased. Thus, a large number of patients with arthritis who are exposed to NSAIDs may also have cardiac conditions.

These drugs have the potential to affect thrombosis in a number of ways: 

*Acetylsalicylic acid* (ASA) binds the cyclo-oxygenase-1 (COX-1) enzyme in platelets irreversibly, and interferes with thromboxane production and platelet aggregation. Low-dose ASA has been shown to be effective in the secondary prevention of cardiovascular disease.

*Non-selective NSAIDs*, by binding the COX-1 enzyme reversibly, have traditionally been perceived to be ineffective as anti-platelet agents.

*Selective COX-2 inhibitors*, by interfering with the production of prostacyclin, which has vasodilatory and anti-platelet function, have the potential to be pro-thrombotic.

The controversy over the effect of NSAIDs on the risk of cardiovascular disease erupted with the publication of the VIGOR (Vioxx Gastrointestinal Outcomes Research) trial. This was a large trial designed to assess the gastrointestinal safety of rofecoxib, a selective COX-2 inhibitor, compared to naproxen, a non-selective NSAID, in patients with RA. However, the authors reported that the incidence of myocardial infarction was lower among patients in the naproxen group than among those in the rofecoxib group (0.1% versus 0.4%).

The publication of this trial gave rise to an intense debate over whether the results were due to a beneficial effect of naproxen or a detrimental effect of rofecoxib. Subsequently, a large observational study involving 181,441
patients suggested that NSAIDs, including naproxen, were not cardioprotective. Yet, recent case-control studies suggest naproxen may have a cardioprotective effect. To add to the complexity of this debate, a recent paper examined the interaction of low-dose ASA and other NSAIDs and found that ibuprofen antagonized the platelet inhibition normally expected from ASA. A large, population-based cohort study on the interaction between ASA and NSAIDs in patients with previous myocardial infarction is ongoing.

In conclusion, heart disease is prevalent and NSAID use is common. Thus, the effect of NSAIDs on cardiovascular risk and the possible interaction between ASA and NSAIDs are significant public health issues and common clinical quandaries. For the time being, the authors recommend the safest approach is to assess each patient on an individual basis. Those who have indications for anti-platelet therapy should be treated with ASA. At this time, the non-selective NSAIDs, except possibly ibuprofen, are acceptable for patients who require treatment with an NSAID and ASA. Gastroprotection may be required in patients at risk of gastrointestinal toxicity. Further research will be needed to determine the safety of NSAIDs and selective COX-2 inhibitors in patients at risk of cardiovascular disease. In light of these issues, newer NSAIDs soon to be released will be expected to show both gastrointestinal and cardiovascular safety.

Practice Pointer

The effect of NSAIDs on cardiovascular risk and the possible interaction between ASA and NSAIDs are significant public health issues and common clinical quandaries. For the time being, it is recommended that the safest approach is to assess each patient on an individual basis.

“ADVAIL” is indicated for the maintenance treatment of asthma in patients, where the use of a combination product is appropriate. This may include patients on effective maintenance doses of long-acting β-agonists and inhaled corticosteroids or patients who are symptomatic on current inhaled corticosteroid therapy. “ADVAIL” should not be used to treat acute asthmatic symptoms.

“ADVAIL” DISKUS® contains lactose and is contraindicated in patients with IgE mediated allergic reactions to lactose or milk. In adolescents and adults, the most common side effects are throat irritation (2%), hoarseness/dysphonia (2%), headache (2%), and candidiasis (2%) which can be reduced by rinsing and gargling with water after inhalation; and palpitations (≤1%). In children aged 4 to 11, the only adverse event with an incidence of >2% was candidiasis.

HPA-axis function and hematological status should be assessed periodically. Height should also be regularly monitored in children and adolescents receiving prolonged treatment with inhaled corticosteroids.

“ADVAIL” is available in 2 dosage forms, “ADVAIL” DISKUS®, for patients 4 years and older and “ADVAIL” Inhalation Aerosol for patients 12 years and older.


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Osteoporosis is associated with significant morbidity and mortality as well as health care costs. Effective strategies exist to prevent osteoporosis and osteoporotic fractures. Screening all women with bone density measurements, however, is not a cost-effective approach to determine which women will benefit from these preventive tests.

Several practice guidelines and clinical decision-making algorithms have been designed to determine who should be screened. The National Osteoporosis Foundation (NOF) 1998 practice guidelines (revised in 1999) recommend that bone mineral density (BMD) screening be performed on:

- All post-menopausal women under age 65 who have one or more additional risk factors for osteoporotic fractures (besides menopause);
- All women aged 65 and older, regardless of additional risk factors;
- Post-menopausal women who present with fractures (to confirm the diagnosis and to determine disease severity);
- Women who are considering therapy for osteoporosis, if BMD testing would facilitate the decision; and
- Women who have been on hormone replacement therapy for prolonged periods.

Aside from female sex, age and menopausal status, other risk factors for osteoporotic fractures include: Caucasian/Asian race; personal history of a non-traumatic fracture as an adult; family history of osteoporosis; low body weight (less than 127 lbs); current cigarette smoking; estrogen deficiency; low calcium intake; heavy alcohol intake; and risk for falls.

In September 2002, the U.S. Preventive Services Task Force (USPSTF) published recommendations for screening for osteoporosis. They recommend that all women aged 65 years and older, and women aged 60 years and older who are at increased risk of osteoporotic fractures, should be routinely screened for osteoporosis.

A recent study found that the NOF guidelines had a 93.7% rate of sensitivity for identifying women with a T-score on BMD of less than -2, while still submitting 74.4% of women with a normal BMD to testing. Clearly, better decision-making tools need to be devised. In the future, decisions about screening may be facilitated by the availability of sensitive markers of bone turnover.
Raynaud’s phenomenon (RP) is a vasospastic disorder characterized by episodic attacks of colour changes with numbness and pain of the digits, usually on exposure to cold or to stressful situations. The prevalence of RP has been estimated at 3% to 5%. It is more common in young women and in patients with a family history.

Classically, RP consists of a triphasic colour change of some or all of the digits. It usually does not affect the palms. The patient reports that his fingers turn white (due to an initial vasospasm), then blue (due to stasis of deoxygenated blood) and then red (due to a reactive hyperemia when the spasm resolves). This classic triad may not be present in all patients.

RP may occur in isolation, in which case it is called primary, or secondary to an underlying condition. The underlying conditions associated with RP include systemic rheumatologic diseases (i.e., scleroderma, rheumatoid arthritis, fibromyalgia), occupation (i.e., drill or hammer operators), arterial occlusive diseases (i.e., atherosclerosis, thoracic outlet syndrome), hyperviscosity diseases (i.e., polycythemia, paraproteinemia) and drugs (i.e., ergots). A small percentage of patients with RP will develop a connective tissue disease. A meta-analysis of trials of primary RP found that 12.6% of patients developed a secondary disorder. The mean time to develop a secondary disorder was 10.4 years from the onset of RP and most of these were connective tissue diseases.12
The diagnosis of RP is made on history and usually does not require provocative testing. However, patients with atypical symptoms and signs, such as single-digit or asymmetric attacks, absent pulses, asymmetry of blood pressure or evidence of critical ischemia, should be suspected of having large artery disease and undergo further evaluation.

The initial goal in evaluating patients with RP is to exclude a secondary cause of disease. In addition to a thorough history and physical examination, nailfold capillary microscopy (NCM) and serology are useful adjuncts. NCM is performed by placing a drop of immersion oil on the cuticle of a finger and visualizing the capillary bed with an ophthalmoscope set at 10 to 40 diopters. Normal nailfold capillaries appear as fine and regular loops. However, dilated capillary loops or areas of avascularity are seen in RP secondary to an underlying rheumatic disease. Most patients with primary RP will have a negative ANA. However, the presence of disease-specific autoantibodies, such as anticentromere or anti-topoisomerase (anti-Scl70), is more suggestive of a secondary disease. The positive predictive value of NCM has been estimated to be 47%, while the presence of an ANA has been estimated to be only 30%.

Management of a patient with primary RP begins with lifestyle changes, including cessation of smoking or offending drugs, minimizing exposure to cold, adjusting office temperatures, wearing warm clothing and using warm packs inside gloves and boots. Patients who continue to have frequent, painful episodes or who develop evidence of digital ischemia (i.e., ulcers, pits, fissures or gangrene) may benefit from pharmacologic interventions. Calcium-channel blockers are the most commonly used drugs. Nifedipine XL 30 mg/d to 120 mg/d, amlodipine 5 mg/d to 20 mg/d or diltiazem CD 120 mg/d to 360 mg/d have all been reported to be beneficial in the initial relief of symptomatic RP.

Other drugs that have been shown to be of benefit include losartan and fluoxetine. Low-dose ASA and topical nitroglycerin ointments are occasionally recommended, but there is little data to support their use. Critical ischemia may require treatment with intravenous prostaglandins. Proximal and digital sympathectomy are reserved for patients with severe ischemia who fail to respond to medical treatment.
References


