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The Clinical Conundrum of Pruritus

Victoria Garcia-Albea, Karen Limaye

ABSTRACT: Pruritus is a common complaint for dermatology patients. Diagnosing the cause of pruritus can be difficult and is often frustrating for patients and providers. Even after the diagnosis is made, it can be a challenge to manage and relieve pruritus. This article reviews common and uncommon causes of pruritus and makes recommendations for proper and thorough evaluation and management.

Key words: Itch, Pruritus

INTRODUCTION

Pruritus (itch) is the most frequent symptom in dermatology (Serling, Leslie, & Maurer, 2011). Itch is the predominant symptom associated with acute and chronic cutaneous disease and is a major symptom in systemic disease (Elmariah & Lerner, 2011; Steinhoff, Cevikbas, Ikoma, & Berger, 2011). It can be a frustration for both the patient and the clinician. This article will attempt to provide an overview of pruritus, a method for thorough and complete evaluation and possible treatment modalities.

The word pruritus stems from the Latin *prurire*, which means "to itch" (Merriam-Webster, 2009). Itch has been defined as an unpleasant feeling associated with the urge to scratch, exclusive to the skin (Stander et al., 2003). It can be induced by chemical mediators and by physical and thermal stimuli (Stander et al., 2003). Its biological purpose is likely to have originated from when pruritic agents were mainly parasites (Stander et al., 2003).

INCIDENCE

"Itching is the most characteristic and distressing symptom of diseases of the skin" (Bernhard, 1994, p. 37). Pruritus is also the most common symptom in dermatological disease and can be a symptom of several systemic diseases (Bernhard, 1994). The overall incidence of pruritus is unknown because there are no epidemiological databases for pruritus (Norman, 2003). According to a 2003 study, pruritus and xerosis are the most common dermatological problems encountered in nursing home patients (Norman, 2003).

ETIOLOGY

The skin is equipped with a network of afferent sensory and efferent autonomic nerve branches that respond to various chemical mediators found in the skin (Bernhard, 1994). It is believed that maximal itch production is achieved at the basal layer of the epidermis, below which pain is perceived (Bernhard, 1994). Autonomic nerves innervate hair follicles, pili erector muscles, blood vessels, eccrine, apocrine, and sebaceous glands (Bernhard, 1994). Afferent sensory nerves transmit noxious stimuli and cold (Stander et al., 2003). Roughly 10% of afferent C fibers respond to itch and thermal stimuli and not to painful or mechanical stimuli (Stander et al., 2003). Schmelz, Schmidt, Bickel, Handwerker, and Torebjork (1997) showed that there is one subset of primary afferent C fibers that is almost exclusively histamine sensitive and is probably the primary afferent nerve that carries the itch sensation.

A mediator of itch is any substance that causes the sensation of itching and the desire to scratch when introduced into the skin (Bernhard, 1994). A number of chemical mediators have been shown to induce pruritus and are, therefore, felt to play a role in various diseases that result in itch. Histamine is the best-known pruritogen. It was first described in the 1920s and is considered the "prototypic chemical mediator of itch" (Bernhard, 1994, p. 26). A biogenic amine, histamine is found in mast cells and keratinocytes and is activated by immunoglobulin E (IgE), cytokine 5a, substance P, immunoglobulin G (IgG), and nerve growth factor. Histamine produces itch primarily via the Histamine 1 (H1) receptor, and less so via the H2 and H3 receptors. Serotonin, another biogenic amine, is a weak pruritogen found in human platelets. Serotonin activates mast cells to release histamine.

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However, when injected into the skin, it causes a pricking, painful itch only in some people. Serotonin is involved in the central sensation of pruritus and the opioid neurotransmitter system (Bernhard, 1994).

Because nerves carry the itch sensation, researchers have studied the role of neuropeptides as itch mediators (Bernhard, 1994). Substance P, a neuropeptide, is found in the cell bodies of C neurons. It is transported toward the peripheral nerve terminals and released by depolarization to activate dermal mast cells to release histamine, cause vasodilation, and increase vascular permeability. Substance P is distributed all over the body, including the dermis and probably the epidermis. It is a potent itch inducer, whose pruritic effects can be blocked by proper administration of oral antihistamines (Bernhard, 1994).

Other chemical mediators involved in itch include acetylcholine, bradykinin, tryptase, endothelin, vanilloids, and proteinases (Bernhard, 1994; Stander et al., 2003). Prostaglandins, interleukins, and nerve growth factor all exaggerate existing itch (Bernhard, 1994; Stander et al., 2003). Opioid peptides modify the peripheral and central sensations of pruritus (Stander et al., 2003). Antagonizing endogenous opioids suppress localized and systemic pruritus (Stander et al., 2003). However, morphine, which is a powerful exogenous opioid analgesic, ironically can induce intractable itching (Bernhard, 1994). Morphine induces histamine release from mast cells, but antihistamines do not prevent or relieve morphine-induced itch (Bernhard, 1994).

Cannabinoid receptor agonists have been shown to reduce histamine-induced nerve excitation (Stander et al., 2003). Two cold receptors that act as desensitizers have been found. When skin temperature was reduced, the sensation of experimentally induced itch was reduced. Similar results, without a decrease in temperature, were achieved when topical menthol was applied to the skin (Stander et al., 2003).

TYPES OF ITCH

Pruritoceptive itch refers to sensations that arise in afferent C nerve fibers and are often due to inflammation, xerosis, or trauma in the dermo-epidermal junction surrounding the fiber tips (Bernhard, 1994). The sensation is then transmitted to the thalamus and sensory cortex via the spinothalamic tract. Neuropathic itch arises when a disease process involves the afferent pathway, such as in herpes zoster. Central or neurogenic itch is less well understood than other types of itch. It arises from a systemic etiology that may involve peripheral cutaneous mediators, such as in severe cholestasis (Bernhard, 1994).

PATTERNS OF ITCHING

The pattern of itch varies from person to person and can vary within an individual (Bernhard, 1994). Among aggravating factors, heat is usually a culprit, as is stress, absence of distractions, anxiety, and fear. Most patients with pruritus report that symptoms get worse at bedtime. Different body parts are disproportionately prone to itch; ear canals, eyelids, nostrils, perianal and genital areas are especially susceptible to pruritus (Bernhard, 1994).

EVALUATION

A thorough evaluation is necessary in identifying pruritic etiology, because it must be determined whether the patient's itch is due to a primary dermatological disease, systemic disease, or another cause (Bernhard, 1994). Particular attention must be paid to the onset, nature, duration, severity, location, relationship to activities, time relation, and precipitating, alleviating, and exacerbating factors (Table 1). Other pertinent information includes medications, allergies, atopic history, family history of atopy or skin disease, occupation, hobbies, social history, bathing habits, pets, travel history, and prior diagnoses (Table 1). Risk factors for human immunodeficiency virus (HIV) should be assessed, because itch can be an early sign of HIV infection. Complaint of interference with sleep patterns can be very helpful in making the diagnosis since some conditions, such as scabies infestation, can be

TABLE 1. History of Present Illness and Pertinent History for Patients With Pruritus (Bernhard, 1994)

Description of Itch	Pertinent History
Onset: sudden or gradual	Medications: prescription, herbal, over the counter, illicit
Nature: continuous, intermittent, burning, pricking	Allergies: medications, environmental
Duration: minutes, hours, days, weeks	Atopic history: asthma, allergies, eczema
Severity: does it interfere with normal activity	Family history of atopy or skin disease
Time relation: bedtime, cyclical	Occupation
Location: localized, generalized, unilateral or bilateral, scalp	Hobbies: chemical exposures
Relationship to activities: worse at work or when doing hobbies	Social history: personal contacts
Provoking factors: heat, exercise, water	Bathing habits: frequency, temperature of water, type of soap
Alleviating factors: distraction, antihistamines, cool compresses	Pets
	Sexual history
	Climate/season
	Travel history
	Prior diagnoses: by healthcare providers or patient's own theories
	HIV risk factors

worse at night, whereas psychogenic pruritus rarely interferes with sleep. Many medications have a potential to cause pruritus. Climate and heating systems should be taken into account; low humidity and cold weather can cause or exacerbate xerosis, which can trigger itch. Sweat retention caused by high humidity can lead to itch.

Bathing habits and chemical exposures at work or through hobbies should be assessed. Patients reporting severe itch within 30 minutes of water contact without visible skin lesions, which is called aquagenic pruritus, should be screened for polycythemia vera, myeloproliferative disease, histioycytic disorders, and physical urticaria, which usually presents with wheals. Travel history should be included because parasitic infections can present with pruritus. Patients reporting itch among family members and patients who are institutionalized should be evaluated for scabies. Recent life stressors or traumatic events may cause patients to experience pruritus; therefore, it is important to include a thorough mental and emotional evaluation on every patient.

Systemic signs and symptoms such as weight fluctuation, night sweats, fever, chills, lymphadenopathy, abdominal pain, fatigue, myalgias, and changes in bowel pattern should prompt further investigation for systemic etiology (Table 2; Bernhard, 1994). The patient's response to scratching may provide some information about the etiology of the itch. For example, in some diseases, scratching reduces pain, whereas in others scratching can increase pain (Bernhard, 1994).

TABLE 2. Review of Systems (Bernhard, 1994)

General health	Fever, chills, night sweats, weight loss, fatigue, anorexia
Skin	Rashes, pigmentation, jaundice, xerosis, sweating
Hair	Texture, growth, alopecia
Nails	Color change, grooves, lines, curvature, onycholysis
Eyes	Jaundice, exophthalmos
Endocrine	Temperature intolerance, polyuria, polydipsia
Hematopoietic	Anemia, bruising, bleeding, lymphadenopathy
Gastrointestinal	Nausea, vomiting, diarrhea, hematochezia
Genitourinary	Frequency, incontinence, color change
Neurologic	Headaches, neuropathy, visual disturbances
Mental status	Mood, hallucinations, sleep disturbances

Physical examination of the skin should focus on signs of possible dermatological disease (Bernhard, 1994). Xerosis may be present, in addition to primary lesions including wheals, papules, vesicles, plaques, patches, and nodules (Figure 1). The presence of secondary changes such as excoriations, crusts, fissures, ulceration, scarring, and lichenification are more commonly found in systemic etiologies of pruritus, or long standing dermatological disease (Figure 2). Involvement of the arms, legs, and anterior trunk with sparing of the upper midback is often associated with psychogenic pruritus. The presence of primary lesions on the upper midback, where it is difficult for the patient to reach, is more characteristic of true dermatological disease (Bernhard, 1994). A physical examination that reveals only secondary skin changes, such as excoriations, irregularly shaped ulcers, and hemorrhagic crusts, may indicate a self-induced etiology. In persons with good hygiene, scabies may be missed. Thus, thorough examination between the digits, in the axillae, waistline, wrists and groin is necessary, as it may reveal subtle papules or burrows. Examination of the lymph system and palpation for liver and spleen should be included to help rule out infectious and systemic etiologies. General physical examination may reveal an undiagnosed systemic disease (Bernhard, 1994).

Systemic disease has been shown to be associated with generalized pruritus in 16%–50% of patients (Bernhard, 1994). "Most systemic diseases, including underlying malignancy, will be detected… by history, physical examination, and the screening laboratory tests" (Bernhard, 1994, p. 343). Laboratory workup is directed by the clinical evaluation and may include complete blood count with differential, looking for eosinophilia, anemia, or evidence of myeloproliferative disease. Other relevant studies include measurement of thyroid-stimulating hormone and thyroxine, liver and renal function tests, stool for occult blood, viral Hepatitis B and C screening, serum glucose level, urinalysis, serum protein electrophoresis, and chest X-ray (Table 3). An antitissue transglutaminase antibody level should be performed if there is suspicion of dermatitis herpetiformis. A HIV antibody test is needed for patients with identified risk factors. In select cases, further laboratory evaluation is indicated, including serum iron and ferritin, skin biopsy for special stains and direct immunofluorescence, stool for ova and parasites, and additional radiologic studies (Bernhard, 1994).

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of an "itchy rash" is quite lengthy. Included on this list would be atopic dermatitis, psoriasis, scabies, lice, insect bites, allergic or irritant contact dermatitis, lichen planus, urticaria, pityriasis rosea, pityriasis rubra pilaris, drug hypersensitivity, folliculitis, Grover's disease, varicella, pityrosporum, mycosis fungoides, and many more (Bernhard, 1994). Persistent or

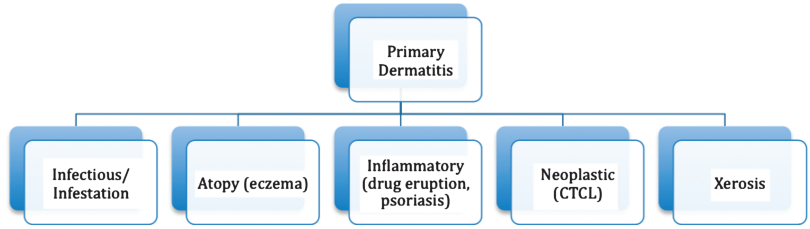

FIGURE 1. Evaluation of the patient with pruritus caused by a primary dermatitis (Bernhard, 1994).

recurrent pruritus of such severity to cause scratching and bleeding, with or without primary cutaneous manifestations is most often associated with lichen simplex chronicus, atopic dermatitis, nummular eczema, dermatitis herpetiformis, neurotic excoriations, eosinophilic folliculitis, uremic pruritus, subacute prurigo, prurigo nodularis, and scabies. History and physical examination can provide a variety of clues as to the diagnosis.

LOCALIZED PRURITUS

Localized pruritus is not usually due to a systemic etiology (Bernhard, 1994). Pruritus ani is the term used for perianal itch, although it can also involve the anogenital area. Pruritus ani affects 1% to 5% of the population, with men being affected four times more frequently than women. Manifestations mimic lichen simplex chronicus; the itch is characterized by intense bouts of burning pruritus, causing the patient to scratch until the skin bleeds. The most common causes are allergic contact dermatitis; irritant contact dermatitis due to fecal matter coming in contact with the skin, due to poor hygiene; episodic diarrhea, inflammatory bowel disease, or dietary causes, such as spicy foods; infectious etiologies such as gonorrhea, streptococcus, erythrasma, mycotic infections, parasites, or scabies; or skin diseases such as psoriasis, seborrheic dermatitis, lichen planus, or lichen sclerosis. Bowen disease or squamous cell carcinoma in situ is less likely to be intensely pruritic but is easily overlooked (Muehlbauer & McGowan, 2009). Squamous cell carcinoma in situ is diagnosed with a skin biopsy and should be considered if traditional therapy for other dermatoses fails to bring improvement. Effective treatment is dependent on the etiology of the itch. Itch secondary to irritation from fecal matter is ameliorated with proper skin hygiene and skin protection with barrier creams such as white petrolatum (Bernhard, 1994).

Pruritus scroti and vulvae are similar in clinical presentation, etiology, and treatment (James, Berger, & Elston, 2011). Genital itch induces psychosomatic overlay and vice versa (Bernhard, 1994). A report of sudden onset of genital itching and burning generates a differential diagnosis including candida infection, irritant contact dermatitis and allergic contact dermatitis, urinary tract infection, hemorrhoids, and pinworms (Bernhard, 1994).

Scalp pruritus is a common complaint, especially in older people. The most common cause is buildup of scale and hair products in people who do not wash their scalps often. Seborrheic dermatitis, folliculitis, atopic dermatitis, psoriasis, lichen planus, lupus, dermatomyositis, and some forms of alopecia can present with scalp itch. However, these skin conditions usually have characteristics accompanying dermatological manifestations that assist in diagnosis. It is important to recognize cicatricial (scarring) alopecia as a potential cause of scalp itch when it is accompanied by inflammation, indicating that it is new and, therefore, more responsive to treatment. Biopsy of refractory inflammatory scalp pruritus, leading to diagnosis and treatment, can be key to preventing permanent scarring alopecia. When no cutaneous findings are present, diagnosis and treatment can be especially challenging. Topical tar shampoos, salicylic

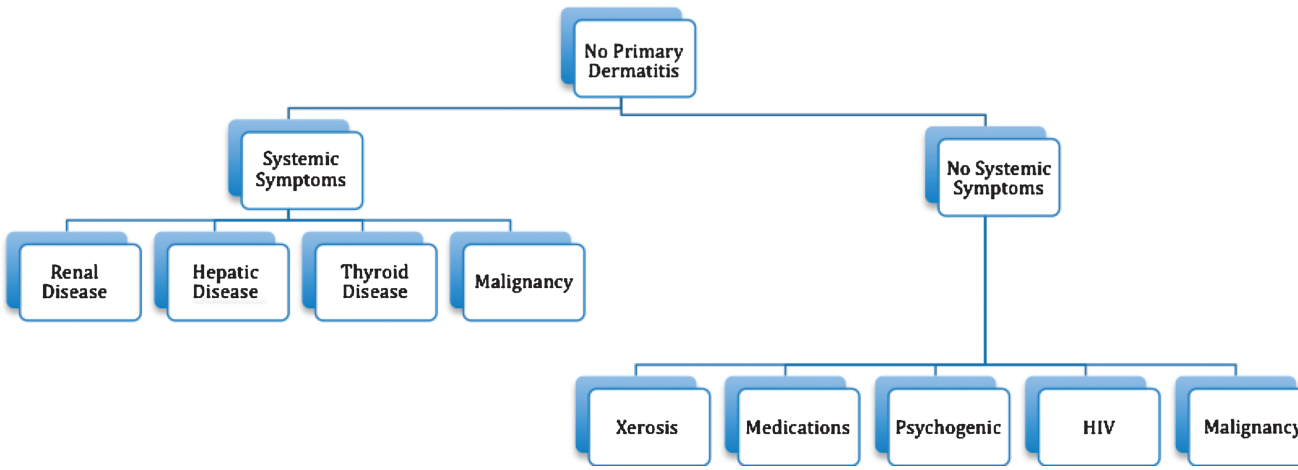

FIGURE 2. Evaluation of the patient with pruritus not caused by a primary dermatitis (Bernhard, 1994).

TABLE 3. Laboratory Evaluation for Patients With Pruritus (Bernhard, 1994)

Suggested initial screening to evaluate pruritus	Further laboratory evaluation for selected cases
Complete blood count with differential	Serum iron, ferritin
Blood urea nitrogen, creatinine	Serum protein electrophoresis, serum immunoelectrophoresis
Alkaline phosphatase, bilirubin	Skin biopsy for special stains (to exclude mastocytosis)
Thyroxine, thyroid-stimulating hormone	Skin biopsy for direct immunofluorescence (to exclude bullous pemphigoid, dermatitis herpetiformis)
Serum glucose	Stool for ova and parasites
Stool for occult blood	Additional radiologic studies
Urinalysis	
Chest X-ray	

acid preparations, and topical corticosteroid preparations usually provide some relief. Unfortunately, this relief is often temporary. In the case of scalp folliculitis, oral tetracyclines are often helpful (Bernhard, 1994).

ITCH DUE TO CUTANEOUS DISEASE

The most common cause of pruritus is xerosis or dry skin. It can be present with or without a rash and is most common in winter; it is also called "winter itch" (Bernhard, 1994, p. 56). It can be widespread but usually involves bilateral upper and lower extremities. Associated factors include a history of atopy, advanced age, hypothyroidism, anticholinergic medications, oral retinoids, frequent bathing with hot water and harsh soaps, forced hot air heating, and low humidity. Treatment consists of repairing the skin barrier to trap and retain moisture in skin with emollients and use of barrier creams. In severe cases, use of the "soak and seal" technique, which is often used in patients with atopic dermatitis, is helpful. In this method, the patient will soak the affected area in lukewarm water for 10 to 15 minutes. Before drying the area, an emollient or topical corticosteroid ointment is applied to the wet skin, locking in the moisture and providing a barrier at the same time (Bingham, Noble & Davis, 2007).

In patients who have a parasitic infestation, pruritus is a common complaint (Bernhard, 1994). The outstanding clinical feature of scabetic infestation is itching, primarily due to the dermal hypersensitivity reaction produced by the host. Any person can contract scabies, but it is most common in persons living in close quarters, such as college students, people who are incarcerated, or those living in assisted living facilities. The major symptom is severe pruritus, worse at night, accompanied by small, nondescript papules and eczematous changes found in the interdigital spaces, wrists, axillae, ankles, waistline, and genitalia. When correctly identified, the presence of burrows is pathognomonic for scabies, although well-formed burrows are not always present. The scabetic itch can persist for 2 to 4 weeks after successful treatment because mite parts, eggs, and feces remain in the skin. Pediculosis (lice infestation) is accompanied by itching of body regions with dense hair follicles. In pediculosis, itch is due to a delayed hypersensitivity reaction to the louse's saliva. Itch subsides with treatment (Bernhard, 1994).

Many inflammatory skin conditions present with pruritus (Bernhard, 1994). A review of all of them is beyond the scope of this article. Atopic dermatitis or eczema, the most common of these inflammatory skin conditions, is usually a clinical diagnosis, characterized by chronic recurrent courses of pruritic dermatitis with an early age of onset and a personal and/or family history of atopy (Bernhard, 1994).

Contact dermatitis refers to both irritant contact dermatitis and allergic contact dermatitis (Bernhard, 1994). Irritant contact dermatitis results when irritants, such as fragrances, chemicals, or harsh soaps directly cause damage to the skin, leading to the release of histamine and inflammatory mediators, resulting in itch. Allergic contact dermatitis is induced by an immune response (Bernhard, 1994).

Psoriasis is an autoimmune disease, characterized by a T-cell-mediated inflammatory response, with expression of multiple chemical mediators, including interleukin 2 (IL2), which is known to play a role in pruritus (Bernhard, 1994). Eighty percent of patients with psoriasis report itch. The best treatment for psoriatic itch is to treat and control the underlying psoriasis itself (Bernhard, 1994).

Lichen simplex chronicus is a chronic, localized dermatological disorder characterized by intense itch (Bernhard, 1994). The patient repeatedly scratches the affected areas, causing thickened, lichenified plaques that may develop into nodules, termed as prurigo nodularis or prurigo nodules. These prurigo nodules are itchy, so the patient continues to scratch, and the nodules persist. The primary etiology of lichen simplex chronicus can vary and may be associated with an underlying inflammatory disorder or psychogenic pruritus. Treatment focuses on breaking the itch–scratch cycle. Intralesional triamcinolone, topical fluorandrenolide tape, high-potency topical corticosteroids under occlusion, and Unna boots are effective.

Urticaria (hives) is a relatively common, transient, intensely pruritic dermatosis (Bernhard, 1994). Acute urticaria is usually allergic in nature. Chronic urticaria, defined as regular outbreaks of urticaria lasting for more than 6 weeks, may be the presenting feature in a systemic disease but is usually idiopathic (Bernhard, 1994).

Cutaneous diseases due to infectious etiologies can also present with itch as a symptom. The most common of these are dermatophyte (fungal) infections, which commonly present with annular red rings with active scaly borders and central clearing. A potassium hydroxide (KOH) mount or fungal culture will confirm the diagnosis. Itch will resolve when the infection is treated, usually with topical antifungal creams (Bernhard, 1994).

Other infectious etiologies include candidiasis, pityrosporum or bacterial folliculitis, and streptococcal skin infections, such as scarlet fever. Viral exanthems are not usually pruritic; those that are include varicella and parvovirus B19 (fifth disease). Patients with HIV are prone to many cutaneous problems, and pruritus is one of them. Patients with HIV may develop any cutaneous disorder that affects patients with an intact immune system. However, HIV patients have elevated IgE levels. Elevated IgE levels have been found in many pruritic conditions, including atopic dermatitis (Bernhard, 1994). This will be discussed further in the next section.

ITCH DUE TO SYSTEMIC DISEASE

Chronic renal failure is the most common internal systemic etiology of pruritus; this is termed uremic pruritus (Bernhard, 1994). Itch is not a symptom of acute renal failure (Bernhard, 1994). Uremic pruritus is usually generalized and is especially bothersome on the back (Bernhard, 1994). It primarily affects patients on hemodialysis and continuous ambulatory peritoneal dialysis (Bernhard, 1994). The etiology of the pruritus is multifactorial. The multiple side effects of renal failure, including xerosis, hyperphosphatemia due to secondary hyperparathyroidism, increased serum histamine levels, hypervitaminosis A, iron deficiency anemia, and neuropathy, likely contribute to the problem (Bernhard, 1994). The incidence of pruritus increases as renal function deteriorates (Bernhard, 1994). Treatment is often frustrating, with poor response rates to oral and topical medications (Bernhard, 1994; James, Berger, & Elston, 2011). Some success has been reported from narrow band Ultraviolet B (NB UVB) phototherapy, but recurrence is common with discontinuation. Renal transplantation is effective (Bernhard, 1994). Variable response rates have been reported with activated charcoal, cholestyramine, thalidomide, oral naltrexone, and oral ondansetron (James, Berger, & Elston, 2011).

Chronic liver disease, including viral hepatitis, cirrhosis, pruritus gravidarum (cholestasis of pregnancy), and drug-induced cholestasis, can be accompanied by obstructive jaundice and pruritus, termed as cholestatic pruritus (Bernhard, 1994). It is most commonly localized to the palms and soles, and around tight-fitting clothing (Bernhard, 1994; James, Berger, & Elston, 2011). Pruritus associated with liver disease spreads proximally, becomes generalized in 20% to 50% of patients with jaundice or impaired bile secretion, and is usually worse at night (Bernhard, 1994). Fifty percent of patients with primary biliary cirrhosis initially present with pruritus; 100% report pruritus at some point (James, Berger, & Elston, 2011). Pruritus is reported in 20% of patients with Hepatitis C (Mazoff, 2008). Pruritus from Hepatitis C may be localized to a specific body part, such as hands and feet, or generalized, involving the entire body (Mazoff, 2008). Some patients with Hepatitis C complain that their internal organs feel itchy (Mazoff, 2008). Etiology is related to the increased level of bile salts, elevated plasma and tissue levels of opioid peptides, and down regulation of opioid peptide receptors (James, Berger, & Elston, 2011). Hence, opioid receptor antagonists have been effective in many patients (James, Berger, & Elston, 2011). Cholestyramine and colchicines have also been effective in some cases (James, Berger, & Elston, 2011). Liver transplantation provides immediate and dramatic relief (James, Berger, & Elston, 2011). "Severe pruritus resistant to therapy has been accepted by the National Institutes of Health Consensus Conference on Liver Transplantation as a valid indication for the procedure" of liver transplantation (Bernhard, 1994, p. 239).

Pruritus has been reported as the presenting symptom of HIV infection; therefore, at risk individuals with pruritus should be screened. Persons with HIV are also at higher risk of pruritic disease secondary to immunosuppression and other complications of HIV. The most common causes of itch in patients with HIV are scabies, pediculosis, candidiasis, renal and/or hepatic dysfunction, and eosinophilic folliculitis (Bernhard, 1994).

Hypothyroidism is commonly associated with pruritus, as it causes the skin to be "cold, dry, pale, rough, and scaly" (Bernhard, 1994, p. 253). Xerosis is seen in 80% to 90% of patients with hypothyroidism. Correcting thyroid level imbalances and using topical emollients and dry skin care can treat this xerosis. Severe itch can be a presenting symptom of hypothyroidism. Thyroid hormones influence skin maturation, oxygen consumption, protein synthesis, skin thickness, hair formation, and sebum secretion. Itch in hyperthyroidism is possibly due to a reduction in the itch threshold caused by warmth and vasodilatation (Bernhard, 1994).

Pruritus in diabetic patients is less common now than in decades past, now occurring in about 3% of patients. The cause is not known, but it is thought to be related to diabetic neuropathy and autonomic dysfunction, resulting in anhidrosis and xerosis. It is possible that diabetic renal failure accounts for some cases. Pruritus ani and vulvae have been associated with poorly controlled diabetes (Bernhard, 1994).

Mastocytosis, in which the skin and internal organs exhibit an excessive number of mast cells, causes a variety of systemic and local cutaneous symptoms, including pruritus. Extreme temperatures, certain medications, and alcohol can exacerbate symptoms. Oral antihistamines decrease pruritus, flushing, bullae, and urticaria, which are often seen in mastocytosis (Alto & Clarcq, 1999).

Postmenopausal pruritus may be generalized or localized; the localized form usually affects the anogenital area (Bernhard, 1994). Generalized pruritus is frequently associated with hot flashes, which tend to be persistent but are not usually described as severe. Premenstrual pruritus can be caused by recurrent cholestasis. Pruritus due to cholestasis induced by oral contraceptives has also been reported. There are documented cases of recurrent premenstrual urticaria related to estrogen sensitivity. Autoimmune progesterone dermatitis can cause eczema, erythema multiforme (EM), and urticaria. This improves with administration of oral contraceptives (Bernhard, 1994).

Iron deficiency anemia is rarely associated with pruritus. Itch can be generalized or localized, especially in the perianal and vulvar areas. Complete relief is achieved once normal iron levels are restored (Bernhard, 1994).

PRURITUS-ASSOCIATED MALIGNANCIES

The most common malignancies associated with pruritus are Hodgkin's lymphoma, polycythemia vera, hematologic malignancies, gastric carcinomas, and mycosis fungoides. It is important to remember that the association of malignancy and generalized pruritus is rare, with the exception of Hodgkin's lymphoma and polycythemia vera. Pruritus is the presenting symptom of Hodgkin's lymphoma in 30% of patients and can precede development of other symptoms by several months or up to 5 years. The itch is described as burning and usually involves the lower extremities. Itch intensity increases with age and disease severity. Pruritus in Hodgkin's disease is resistant to all therapy, except treatment of the lymphoma (Bernhard, 1994),

Polycythemia vera, a disease of the bone marrow resulting in increased numbers of red blood cells, often presents with itch induced by a drop in temperature, such as after a hot bath or shower. This type of itch can last up to an hour. The etiology of this phenomenon is not understood, but the pruritus is intractable. As with the pruritus associated with many malignancies, itch can precede diagnosis by many years. Low-dose aspirin may provide immediate relief. Psoralen plus Ultraviolet A (PUVA), NB UVB, and oral paroxetine can also be helpful. Interferon alpha-2 has been shown to effectively treat the underlying disease and, therefore, reduce itch (James, Berger, & Elston, 2011).

Pruritus has been documented in approximately 2 to 3% of patients with non-Hodgkin's lymphoma at presentation. About 10% of non-Hodgkin's lymphoma patients will develop itch at some time during the course of disease. Pruritus is not common but has been described in chronic leukocytic leukemia and multiple myeloma (Bernhard, 1994).

Mycosis fungoides, the most common type of cutaneous T-cell lymphoma (CTCL), can present with pruritus before the onset of cutaneous findings. Early skin lesions are often subtle. Mycosis fungoides is commonly initially misdiagnosed as psoriasis or eczema. Whereas psoriasis and eczema are also itchy, mycosis fungoides patches, plaques, and tumors usually do not follow the patterns of distribution of psoriasis or eczema. In addition, mycosis fungoides tumors do not have the overlying micaceous scale of psoriasis and are usually more infiltrated and thicker than the characteristic plaques of eczema. It can be the "exasperating" nature of the itch that first awakens suspicion for CTCL (Bernhard, 1994, p. 300). Sezary syndrome, the leukemic variant of CTCL, is often characterized by significant generalized pruritus (Booher, McCann, & Tawa, 2011).

PSYCHODERMATOLOGY

Psychodermatoses can cause itch. However, this is a more difficult diagnosis to make, because it tends to be diagnoses of exclusion. Psychodermatoses may manifest clinically in many forms. Patients demonstrate secondary skin changes, with scattered excoriations and lichenified papules. Skin lesions usually occur on the extremities and always spare areas that are out of the patient's reach, such as the central back. Often a major life stressor or trauma precedes the onset of this condition (Bernhard, 1994).

Neurotic excoriations are self-induced, as an unconscious habit of picking, scratching, or rubbing. Most patients are aware that they are responsible for the lesions, but they cannot control their behavior. Patients cannot tolerate any imperfection in the smooth surface of the skin. The patient picks off the raised or altered skin, which results in more crusting, "and so the process become progressive" (Bernhard, 1994, p. 355). In some cases, pruritus is not a significant factor. For others, pruritic lesions such as papular urticaria or folliculitis attract attention, and therefore, the patient picks and scratches. Another scenario involves pruritic papules, which cause uncontrollable focal itch, leading to scratching, which causes prurigo nodules (Bernhard, 1994).

Lesions in patients with neurotic excoriations are polymorphous, with ulcers, excoriations, and lichenified papules and nodules. There will be evidence of older, healed lesions, with scarring and pigmentary alteration. The upper extremities and face are common sites of involvement; acne excoriee is a form of this condition. Most patients are normal, healthy adults. The most common psychopathologies seen in association with neurotic excoriations are depression, obsessive compulsive disorder, and anxiety. Treatment is difficult, often requiring collaboration with a therapist. Treatment with doxepin and various selective serotonin reuptake inhibitors has been effective (James, Berger, & Elston, 2011).

Delusions of parasitosis are firm beliefs in an individual's mind that he or she experiences an infestation (James, Berger, & Elston, 2011). Patients may also experience delusions that they can retrieve or express foreign material out of their skin (Bernhard, 1994). The patient will often bring pieces of skin, fibers, threads of clothing, and other materials to show the provider the

alleged insect, parasite, or expressed foreign material. Patients complain of pruritus, stinging, and the sensation of being bitten or of bugs crawling on the skin (James, Berger, & Elston, 2011). There is often a psychiatric history, most commonly depression, schizophrenia, bipolar disorder, or obsessive compulsive disorder (Bernhard, 1994). However, the absence of a pre-existing mental health problem does not rule out this condition (Bernhard, 1994). Development of delusions of parasitosis can precede the onset of other symptoms of mental illness (James, Berger, & Elston, 2011). Women are afflicted by this disorder twice as often as men, and patients are usually middle age or older (James, Berger, & Elston, 2011). Evaluation of these patients should focus on ruling out a true infestation and looking for systemic or drug-induced causes of itch (James, Berger, & Elston, 2011). Cocaine and amphetamine abuse are well-documented causes of delusions of parasitosis (James, Berger, & Elston, 2011). Referral to a psychiatrist is recommended; haloperidol, pimozide, or other antipsychotic medication is the recommended treatment (James, Berger, & Elston, 2011).

TREATMENT

The first step in treating any type of pruritus is to first make the correct diagnosis. However, symptomatic treatment is often required, regardless of the diagnosis. Bernhard (1994) identifies six main categories for symptomatic treatment: patient education; elimination of provocative factors; nonspecific topical preparations and skin hydration; chemical treatments, both topical and oral; physical modalities, such as phototherapy or counterstimulation; drastic measures, such as plasmapheresis; and understanding and support from healthcare providers, family, and friends.

Patient education should involve a clear explanation of the diagnosis, including exacerbating and triggering factors. Teaching about breaking the itch–scratch cycle is critical. Stress, fear, loss of sleep, and anxiety can make itch worse; therefore, every effort to alleviate stress is helpful. Psychiatrists, social workers, and counselors can help address stress at home and at work and can provide coping mechanisms for the patient (Bernhard, 1994).

Eliminating exacerbating factors includes avoiding dry skin, excessive bathing, low humidity, irritating fabrics and chemicals, contact allergens or irritants, alcohol ingestion, hot foods and liquids, stress and anxiety, excessive ambient temperature, dust and dust mites, fiberglass, and certain animal products (Bernhard, 1994). Patients should be encouraged to bathe in moderation, which will help maintain adequate skin hydration. Colloidal oatmeal products can be soothing when added to bath water. Bland emollients or bath oils applied after bathing can help hydrate the skin. Nonsteroidal topical emollients, such as menthol, tar, and salicylic acid, act as counterirritants to relieve itch through their cooling effect. Aloe vera, a popular favorite, may have bactericidal and antifungal effects but has been shown to cause allergic contact dermatitis. Vitamin E can also cause allergic contact dermatitis but is a popular home remedy (Bernhard, 1994).

Topical antipruritics include "caine" preparations, such as lidocaine, pramoxine, and prilocaine. These antipruritics may be useful for localized conditions. Capsaicin cream, which contains the naturally occurring alkaloid present in hot peppers, causes the release of neuropeptides, including substance P. Repeated application of capsaicin cream causes progressive depletion of substance P, which interferes with transmission of certain painful and itchy stimuli from the periphery to the central nervous system. Therefore, results are best in localized, chronic, pruritic disorders. Topical antihistamines, like doxepin 5% cream, block H1 and H2 receptors. These are useful antipruritics; however, percutaneous absorption leads to somnolence and limits widespread use (Bernhard, 1994).

Topical corticosteroids decrease itch by reducing inflammation and chemotaxis and by causing vasoconstriction. Therefore, they are most effective in pruritus caused by diseases of inflammation. Crotamiton is an older antiscabetic lotion that has been relaunched as an antipruritic. It is most useful for postscabetic itch and has shown mixed results in patients with other forms of pruritus (Bernhard, 1994).

Antihistamines are most frequently utilized by nondermatologists. H1 first generation antihistamines, such as diphenhydramine and hydroxyzine, may be helpful in nocturnal pruritus, primarily due to their side effect of somnolence (Bernhard, 1994). Unfortunately, their use as antipruritics has been disappointing. Oral doxepin is one exception. Doxepin is a more effective antipruritic, at doses of 10 to 25 mg up to four times daily, possibly because at higher doses it acts as an antidepressant (Bernhard, 1994). There is some evidence that selective serotonin reuptake inhibitor antidepressants, including paroxetine, fluvoxamine, fluoxetine, and sertraline, may ameliorate itch of a variety of causes (Hundley & Yosipovitch, 2004). There are anecdotal case reports of gabapentin decreasing itch in patients with liver disease, patients on hemodialysis, and patients with pruritus of unknown origin, but conclusive evidence is not published in the literature (James, Berger, & Elston, 2011). Nonsedating H2 antihistamines have been especially disappointing as antipruritics and are only effective in urticaria (James, Berger, & Elston, 2011). The opiate antagonists naloxone and naltrexone and the serotonin antagonist ondansetron have shown mixed efficacy in various studies (James, Berger, & Elston, 2011).

PUVA and NB UVB phototherapy have been shown to be efficacious in a wide variety of dermatological diseases and systemic etiologies of pruritus, including psoriasis, atopic dermatitis, pityriasis rosea, mastocytosis, renal itch, and polycythemia vera (Bernhard, 1994).

Recently, NB UVB has been shown to be as effective as PUVA in treating psoriasis (Amer, Tosson, Al Mokadem, & Nofal, 2007). Phototherapy can be used in conjunction with other agents, including oral antihistamines and topical corticosteroids (Borzova, Rutherford, Konstantinou, Leslie, & Grattan, 2008). However, use of phototherapy is limited by the frequency of visits required, potential side effects of oral psoralens, increased risk for skin cancer, and because symptoms frequently recur after therapy has been discontinued (James, Berger, & Elston, 2011).

Pruritus is reduced with thermal counterstimulation with heat or cold. This has been known for generations. The effects of heating the skin are less consistent than cooling the itchy skin. Heating can aggravate itch in about one third of patients (Bernhard, 1994).

Acupuncture, transcutaneous electrical nerve stimulation, and vibration provide counterstimulation and may reduce itch (Bernhard, 1994). In some studies, transcutaneous electrical nerve stimulation loses efficacy with continued use. However, these modalities have been shown to be effective beyond the placebo effect. "Drastic measures" are used in severe cases, when itch is causing significant reduction in quality of life (Bernhard, 1994, p. 376). These measures, including plasmapheresis, have been effective in specific situations. Providing understanding for an itchy patient makes that person more likely to comply with treatments and helps to reduce stress. Conversely, lack of understanding can further isolate the patient, causing more stress and self-aggression toward the skin. It is important to collaborate with the patient's family and friends to create a positive and supportive environment (Bernhard, 1994).

The difficulty in treating pruritus stems from the fact that pruritus, like pain, is a stimulus that cannot be measured directly and affects individuals differently. Most assessments measure pruritus by direct observation of scratching or by having patients rate itch on a severity scale, similar to a pain scale. A study by Desai et al. (2008) developed a pruritus-specific quality of life instrument that showed validity, reproducibility, and reliability with internal consistency. Hopefully, instruments such as these will assist in studying pruritus and lead to more effective treatment options.

Nursing implications for the pruritic patient include encouraging the patient to avoid triggering or exacerbating factors, maintaining proper skin hydration, using cool compresses on the skin, keeping the fingernails trimmed, and adequate adherence to the established treatment plan.

CONCLUSION

In summary, pruritus is a complex mechanism with numerous psychological and chemical mediators, many of which are not well understood or identified. The initial approach to the pruritic patient should focus on trying to identify or rule out primary dermatological disease. In patients without cutaneous findings, a thorough physical examination should be performed, looking for systemic disease. In the absence of skin findings, first-line therapy should include a short course of oral antihistamines, proper dry skin care education, and topical emollients and antipruritics. The patient should have a follow-up evaluation in 2 to 4 weeks. If there is no improvement or worsening of symptoms, consider laboratory evaluation for systemic disease. ■

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