

# Skin Manifestations of Internal Disease in Older Adults

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*In this article, we discuss skin findings affecting older adults, with a focus on pruritus, flushing, dermatitis, and ulcers, and consider related internal diseases. Our goal is to make this information readily transferable to the clinical setting for the non-dermatologist.*

**Key words:** dermatology, skin manifestations, older adults, pruritus, flushing, dermatitis, ulcers

## Introduction

Skin manifestations of internal disease is a broad, complex topic that is discussed in detail in specialized textbooks.<sup>1</sup> This paper highlights skin manifestations presentations that most commonly herald internal disease in older adults. The idea of the skin as an early warning system for internal disease is a useful concept to have in daily practice and should foster curiosity as to why a skin problem is occurring.

What do we mean by internal disease? This is becoming an increasingly complex question to answer. As we learn more about diseases once thought to be purely cutaneous, such as dermatitis and psoriasis, we begin to understand that the complex immunological processes in these diseases may involve other organs. For example, recent work on the elevated risk of cardiovascular disease in patients with psoriasis underscores the

multisystem nature of that disease.<sup>2</sup>

For the purpose of this article, internal disease will refer to diseases of non-cutaneous organs, such as the gastrointestinal or endocrine systems, that are associated with changes in the skin. Additionally, we will focus on the segment of those diseases that most often present in older adults. Thus, inherited conditions with skin manifestations (also called genodermatoses), usually diagnosed in children and young adults, are not considered in this article.

In this article, we will consider this topic from the point of view of a patient presentation that may be a harbinger of internal disease. The most common skin diseases diagnosed in older adults are dermatitis, pruritis, cutaneous ulcers and infections of various kinds (Figure 1).<sup>3</sup> As such, we will discuss these conditions as well as flushing because of its potential association with a rare but serious disease. This list represents a small number of possible skin presentations but provides a good introduction to the topic.

## Pruritis

The term *pruritus* is Latin for itch. Itch can be classified as generalized or localized, and with or without an associated rash. Many rashes, whether generalized or localized, are associated with itch. Consider localized contact dermatitis from poison ivy and other members of the *Toxicodendron* genus, which is usually extremely itchy. Similarly, widespread dermatitis, scabies infestation, and lichen planus are often extremely itchy rashes. In these cases where a rash is present, it is usually more useful to assess the underlying cause, as treatment of that cause will often reduce or eliminate the accompanying pruritus.

Cases of localized pruritus without an associated rash are usually neuropathic in origin. For example, *notalgia paresthetica*, the very common itch of the medial scapula found in up to 50% of the population, is thought to be a chronic sensory neuropathy.<sup>4</sup> Virtually any internal disease that causes a neuropathy, such as diabetes, stroke, or multiple sclerosis, can cause a localized neuropathy.

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Localized itch has also been linked to certain cancers. For example, itch of the nose has been reported in nasopharynx tumors and of the penis in penile cancer.<sup>5</sup> Pruritis has been reported in people with malignant tumours of the breast, colon, prostate, stomach, and uterus.<sup>6</sup>

Generalized pruritus without a rash is very common among older adults. It is estimated that at least 50% of the older adult population experience generalized itch, with 50% of those cases attributed to systemic disease.<sup>5</sup>

The investigation of generalized pruritus should seek to rule out disease of the hematopoietic, hepatobiliary, endocrine, and renal systems, as well as malignancies, HIV infection, and drug reactions. Table 1 identifies diseases associated with generalized itch without rash and recommends laboratory investigations.<sup>4,5,6</sup>

It is important to remember that the initial workup for internal causes of itch are falsely negative 10% of the time.<sup>7</sup> The combination of that false negative rate with the knowledge that itch may predate the onset of malignancy by a number of years underscores the need to continually

evaluate patients with chronic itch.

While the majority of cases of generalized itch without obvious internal cause are due to xerosis (i.e., dry skin) and can be handled by adequate skin barrier protection (e.g., emollient applied immediately after bathing and patting dry, as well as avoiding irritating soaps and fragrances), individuals with severe itch recalcitrant to topical and systemic measures should have continued monitoring for internal causes.

Flushing

Flushing is a sense of warmth accompanied by visible reddening of the skin. It is usually benign and is most commonly caused by emotion, temperature, food or beverage, fever, alcohol and rosacea, but can, on rare occasions, be a marker for serious internal diseases.<sup>8</sup>

Some tumours trigger factors that dilate blood vessels and mimic the flushing of rosacea. These include carcinoid tumors, pheochromocytoma and mastocytosis. In addition, tumours of the thyroid, pancreas, and kidneys can lead to flushing. Finally, neurological diseases,

such as Parkinson’s, multiple sclerosis, and peripheral nerve damage may affect the autonomic regulation of the cutaneous vasculature and lead to flushing. Diagnosis of these conditions is beyond the scope of this article, but interested readers can consult a recent excellent review article of this topic.<sup>8</sup> Table 2 presents a synopsis of the major entities that result in flushing and the basic workup involved for each.

Dermatitis and Other Eruptions

The eruption of a red, scaly rash in an older adult should prompt the clinician to ask a few pertinent questions. First, is the eruption generalized or localized? Answering this question requires gowning the patient to facilitate a thorough examination. For example, while a photodistributed rash may appear generalized when the patient is fully clothed, a thorough examination will often find that it is a localized rash. A generalized rash may have few random “islands of sparing” but will cover more than 90% of the body.

If the patient truly has a generalized

Table 1: Diseases Associated with Generalized Itch without Rash		
Disease	Prevalence of Pruritus	Laboratory Investigations
Polycythemia rubra vera	25–70%	CBC
Hodgkin’s disease	30%	CBC and imaging
Primary biliary cirrhosis	Nearly 100%	Liver function tests, imaging and newer serological markers
Cholestasis	25%	Imaging and liver function tests
Malignancy	May precede malignancy by several years	Age-appropriate screening
Hypothyroidism	80–90%	Thyroid function testing
Hyperthyroidism	4–11%	Thyroid function testing
Diabetes Mellitus	Varied	Fasting blood sugar and Hba1c
Renal insufficiency	25–86%	Renal function testing
HIV	Varied	HIV serology
Drug reactions	Unknown	History, CBC with differential for eosinophilia, liver function testing
Legend: CBC = complete blood count; HIV: human immunodeficiency virus Source: Ward J, et al., 2005 <sup>4</sup> ; Etter L, et al., 2002. <sup>5</sup>		

**Table 2:** Major Entities that Result in Flushing

Disease	Prevalence of Flushing	Laboratory Investigations
Carcinoid syndrome	95% at some point during disease	24-hour urine for 5-HIAA
Pheochromocytoma (chromaffin tumour)	Unknown	24-hour urine for fractionated metanephrines, norepinephrine, epinephrine, dopamine, vanillylmandelic acid
Mastocytosis	Unknown but correlated with mastocytosis in adults without urticaria pigmentosa	Serum tryptase persistently elevated; 24-hour urine for n-methylhistamine
Medullary carcinoma of the thyroid	Unknown	Calcitonin level; radioimmunoassay for calcitonin after intravenous calcium and pentagastrin
Pancreatic cell tumour	Rare	Elevated plasma VIP
Renal cell carcinoma	Unknown	Hematuria and imaging studies

Source: Izikson L, et al., 2006.<sup>8</sup>

red, scaly rash on 90% or more of the body, then he or she has an erythroderma. Common causes of erythroderma in older adults include drug reactions, dermatitis, psoriasis, viral exanthems (a widespread rash usually accompanied by systemic symptoms such as fever, malaise, and headache), and cutaneous T-cell lymphoma.<sup>9</sup> Rarely, an internal malignancy can give rise to widespread dermatitis-like rashes.<sup>10</sup> Such cases are often clarified by a careful history and, often, a skin biopsy read by an experienced dermatopathologist.

Because the frequency of adverse drug reactions increases with age,<sup>11</sup> it is important to question patients on drug intake when they experience such widespread rash. The timing of drug reactions can vary from having taken the drug only a few hours ago up to the patient having taken the drug for a number of years. Sullivan and Shear present an excellent in-depth review of this topic in older adults.<sup>11</sup>

If the rash is not truly an erythroder-

ma, then it often falls into a pattern of distribution. For example, a photodistributed rash is an important pattern that often heralds internal disease. It can be acute, similar to a sunburn, or chronic in nature. Acute photodistributed rashes are often due to phototoxic or photoallergic reactions to medications, most commonly to nonsteroidal anti-inflammatories (NSAIDs).<sup>11</sup> Less commonly, they may represent the initial manifestation of connective tissue diseases, such as systemic lupus and dermatomyositis.

Chronic photodistributed rashes of the sun-exposed face and dorsal hands may also result from connective tissue diseases or from porphyria, of which the most common variant is porphyria cutanea tarda (PCT). Often associated with underlying liver disease and hemochromatosis,<sup>12</sup> PCT is best diagnosed by specialized blood and urine testing for porphyrins. Such blood must be taken in light-protected tubes and is usually handled only by specialized lab-

oratories. Porphyria cutanea tarda usually manifests as sun-distributed scarring, milia, and hypertrichosis.

## Ulcers

Cutaneous ulcers should always prompt the primary care physician to consider the underlying cause. Traditional medical teaching emphasizes that ulcers often result from arterial, venous, and neuropathic origins. However, there are many other causes of a nonhealing ulcer that warrant attention.

Pyoderma gangrenosum, cutaneous tumors, and various cutaneous infections (such as mycobacterial and deep fungal infections) may all cause ulcers and can only be diagnosed by considering them in the differential diagnosis.<sup>13</sup> Pyoderma gangrenosum is usually clinically manifested as large ulcers with undermined (i.e., empty space) and "gun metal" grey borders at the sites of prior and ongoing trauma (a phenomenon commonly known as *pathergy*). It histologically shows large and dense infil-

**Table 3:** Some Internal Diseases with their Commonly Associated Skin Findings

Disease	Associated Skin Findings
Rheumatoid Arthritis <sup>14</sup>	Rheumatoid nodules, vasculitis, "granulomatous" dermatitis, splinter hemorrhages, pyoderma gangrenosum, Sweet's syndrome
Inflammatory Bowel Disease <sup>15,16</sup>	Pyoderma gangrenosum, erythema nodosum, oral ulcers, Sweet's syndrome
Diabetes <sup>17</sup>	Scleredema, diabetic foot, vascular and neuropathic compromise resulting in ulcers, granuloma annulare, necrobiosis lipoidica, diabetic dermopathy

Figure 1:  
**Skin Manifestations of Internal Disease**

### Ulcers

- may be caused by pyoderma gangrenosum, cutaneous tumors, and various cutaneous infections (such as mycobacterial and deep fungal infections)
- pyoderma gangrenosum is often associated with other internal diseases, including arthritis, AML and inflammatory bowel disease



### Flushing

- sense of warmth accompanied by visible reddening of the skin
- usually benign
- may be marker for tumours or neurological disease (Parkinson's, multiple sclerosis, or peripheral nerve damage)

### Pruritis

- generalized or localized itch
- with or without rash
- linked to neuropathies caused by internal disease (diabetes, stroke, cancer)



### Dermatitis

- red, scaly rash
- generalized or localized
- may be linked to erythroderma caused by drug reactions, dermatitis, psoriasis, viral xantheams, and cutaneous T-cell lymphoma
- photodistributed rash may be linked to connective tissue diseases or porphyria



## Key Points

The primary care physician should consider if a patient's skin issue might be a manifestation of underlying systemic disease. Without that consideration, the underlying cause will rarely be discovered.

Patients with ongoing pruritus should undergo surveillance for an underlying internal disease.

Flushing can be a marker of a cancerous tumour.

If an ulcer is not responding to usual treatments, then think malignancy or odd infections

Dermatitis—red, scaly (papulosquamous) rashes—have a wide differential. A skin biopsy and/or referral to a dermatologist may often help clarify the diagnosis. Patients with certain systemic diseases, such as rheumatoid arthritis and inflammatory bowel disease, are predisposed to develop skin manifestations of their diseases.

tration of neutrophils in the dermis, usually with an ulcer. It may be histologically confused with infections of the skin such as cellulitis, so an experienced dermatopathologist should interpret the biopsy. Pyoderma gangrenosum is also often associated with other internal diseases, including arthritis, acute myeloid leukemia (AML), and inflammatory bowel disease.<sup>13</sup>

## Common Internal Diseases and Associated Skin Findings

While we have approached the topic of skin manifestations of internal disease by starting with skin symptoms potentially associated with an internal disease, there are some common internal diseases that warrant special mention because they frequently incur skin manifestations. Table 3 presents a small selection of internal diseases with their commonly associated skin findings.

## Referrals

Generalized pruritus that is recalcitrant to routine antihistamines and emollients and dermatitis that does not respond to mild-to-moderate topical steroids should warrant a referral to a specialist for treatment, as should a new onset of a rash associated with a fever, arthritis, fatigue or other non-cutaneous symptoms. Nonhealing cutaneous ulcers may be neoplasms and atypical skin infections that require further investigation. A neuroendocrine tumour may at times be heralded by unexplained or widespread flushing and should be

explored by a specialist if suspected. Photodistributed rashes have a wide and specific differential that may benefit from specialist attention.

## Conclusion

This paper discussed potentially serious internal diseases associated with skin findings commonly seen in the elderly, and attempted to make the content clinically relevant and immediately useful for the non-dermatologist. Laboratory investigations were provided to assess the underlying reason for pruritis and flushing when more common causes are ruled out. Also, conditions that warrant a referral specialist were highlighted.



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## Clinical Pearls

In all cases of pruritis, maintenance of skin hydration is paramount. In mild cases, use of cleansers as opposed to soaps and application of emollients after bathing will help improve barrier function. Use of sedating and/or nonsedating antihistamines may be needed in more severe cases.

Many skin diseases can result from or be exacerbated by medications, with the onset of the skin disease occurring anywhere from minutes to many months after starting a new medication.