Chronic Itch: A Dermatology Perspective for Allergists

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Disclosures

Speakers' Bureau/Advisory Board:

- Arcutis (psoriasis), Dermavant (psoriasis), Galderma (acne), Incyte (atopic dermatitis), Pfizer (atopic dermatitis), Sanofi/Regeneron (atopic dermatitis).
- All relevant financial relationships have been mitigated.

Objectives

- Outline the pathophysiology of itch beyond histamine
- Apply a systematic approach to patients with itch but no rash
- Recognize dermatologic vs. systemic causes
- Implement evidence-based management strategies

Alex Honnold

Half Dome

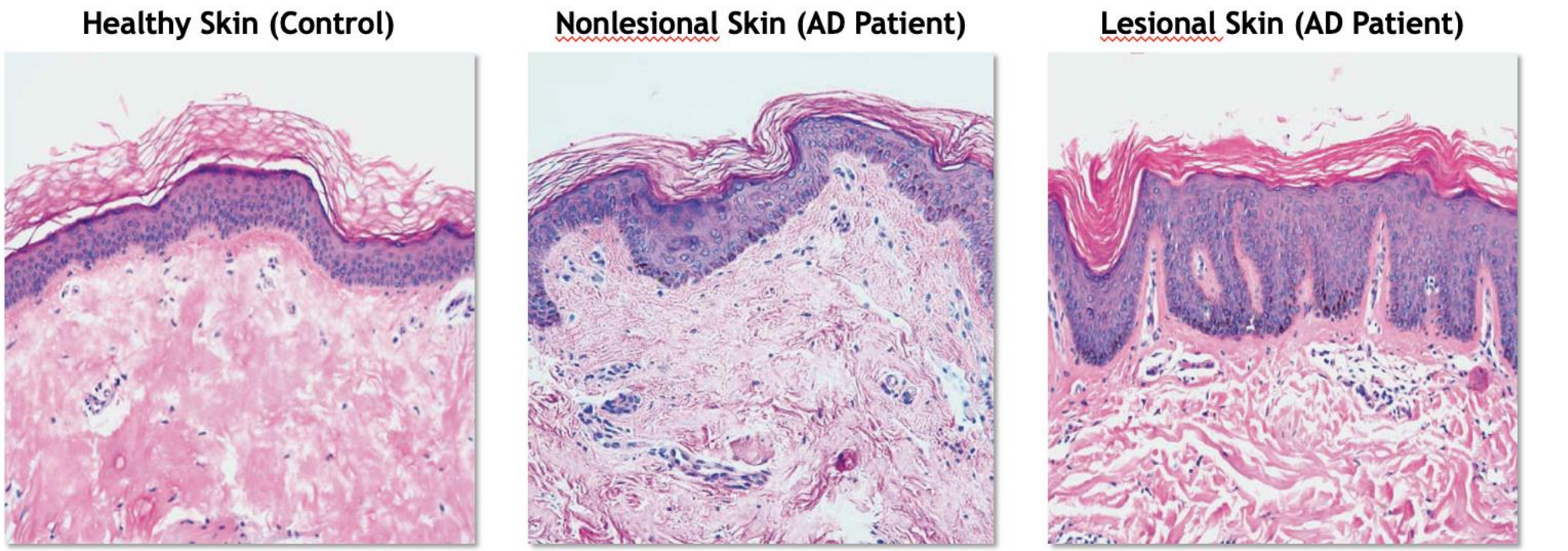
“I didn’t want to be a lucky climber, I wanted to be a great climber”
-Alex Honnold


El Capitan

Why It Matters!

- Itch without rash = diagnostic challenge
- May signal serious systemic disease
- Frustrating for patients, often misattributed
- Requires collaboration between dermatology & allergy

“Normal” Skin is not truly normal



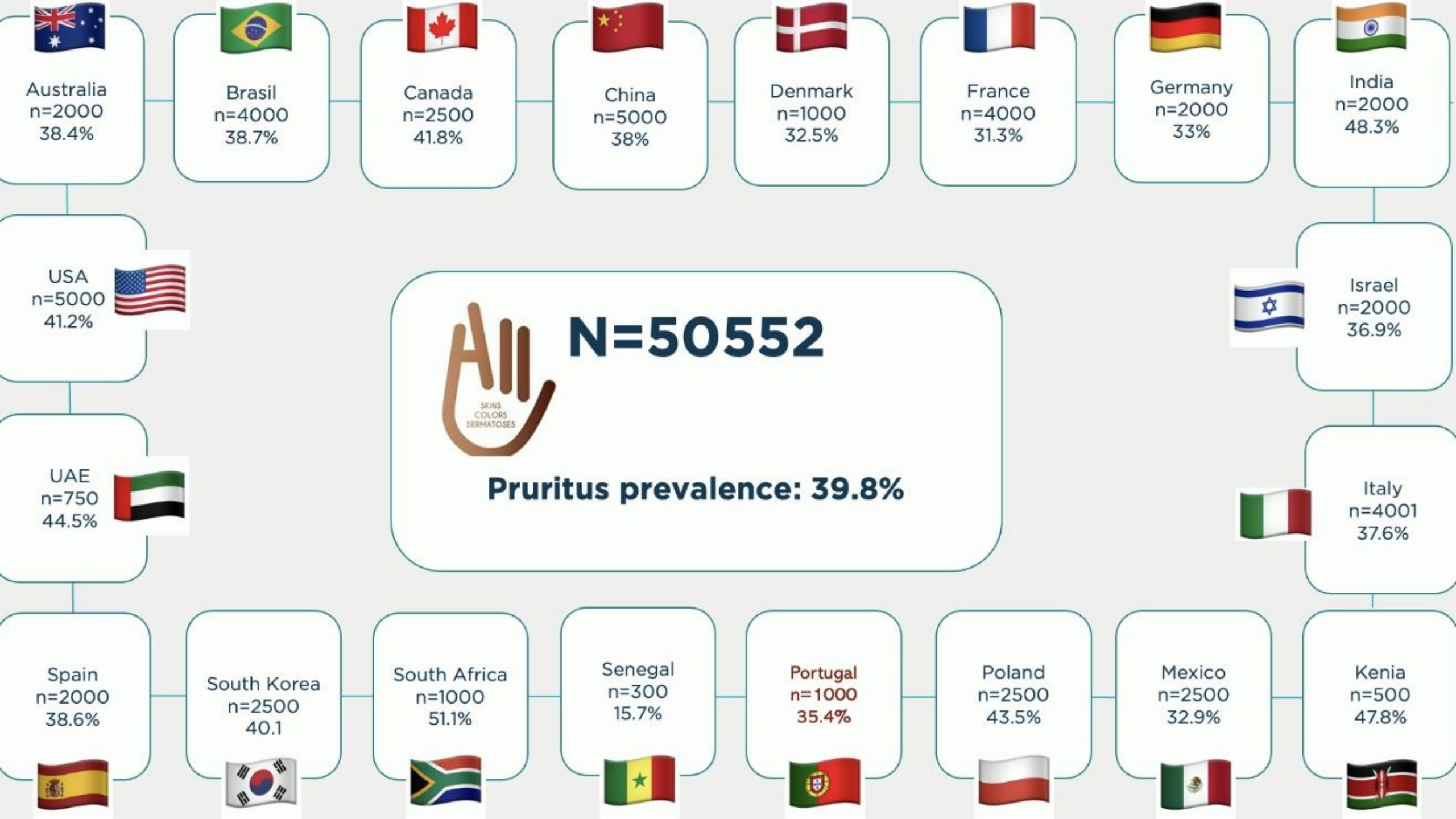
Esaki H, et al. J Allergy Clin Immunol. 2016: 138:1639-1651.

Perhaps the truest universal language is not words at all, but something as simple as an itch. Across every tribe, tongue, and nation, the gesture of scratching is instantly understood. Even in the most remote jungle, among people you've never met, one small scratch on your arm communicates perfectly.

Worldwide study on the prevalence of itch: examining itch as a global health problem

G Yosipovitch et al.

A Patient Centricity Study
by Pierre Fabre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SKINS
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N=50552
Pruritus prevalence: 39.8%
UAE
n=750
44.5%
Italy
n=4001
37.6%
Spain
n=2000
38.6%
South Korea
n=2500
40.1
South Africa
n=1000
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Senegal
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Portugal
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Kenia
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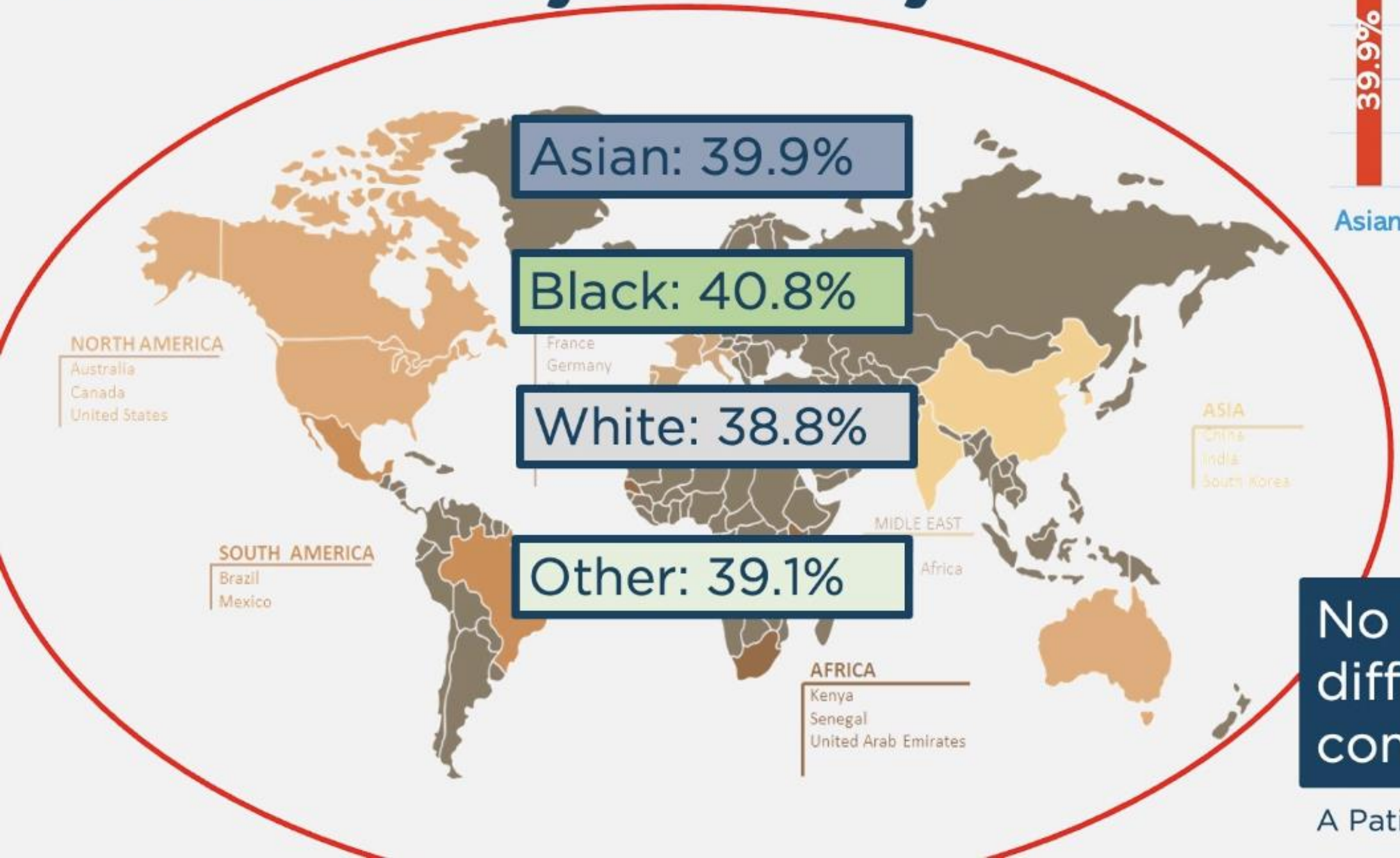
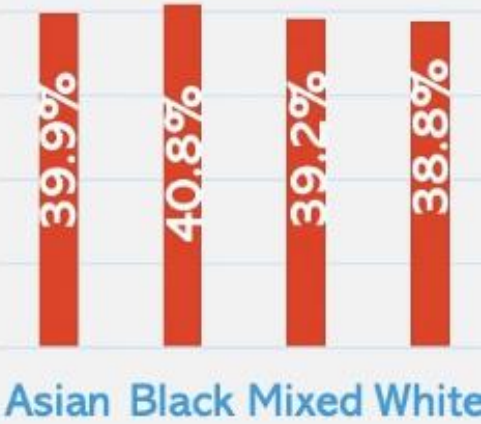
47.8%

Prevalence by Ethnicity





No significan
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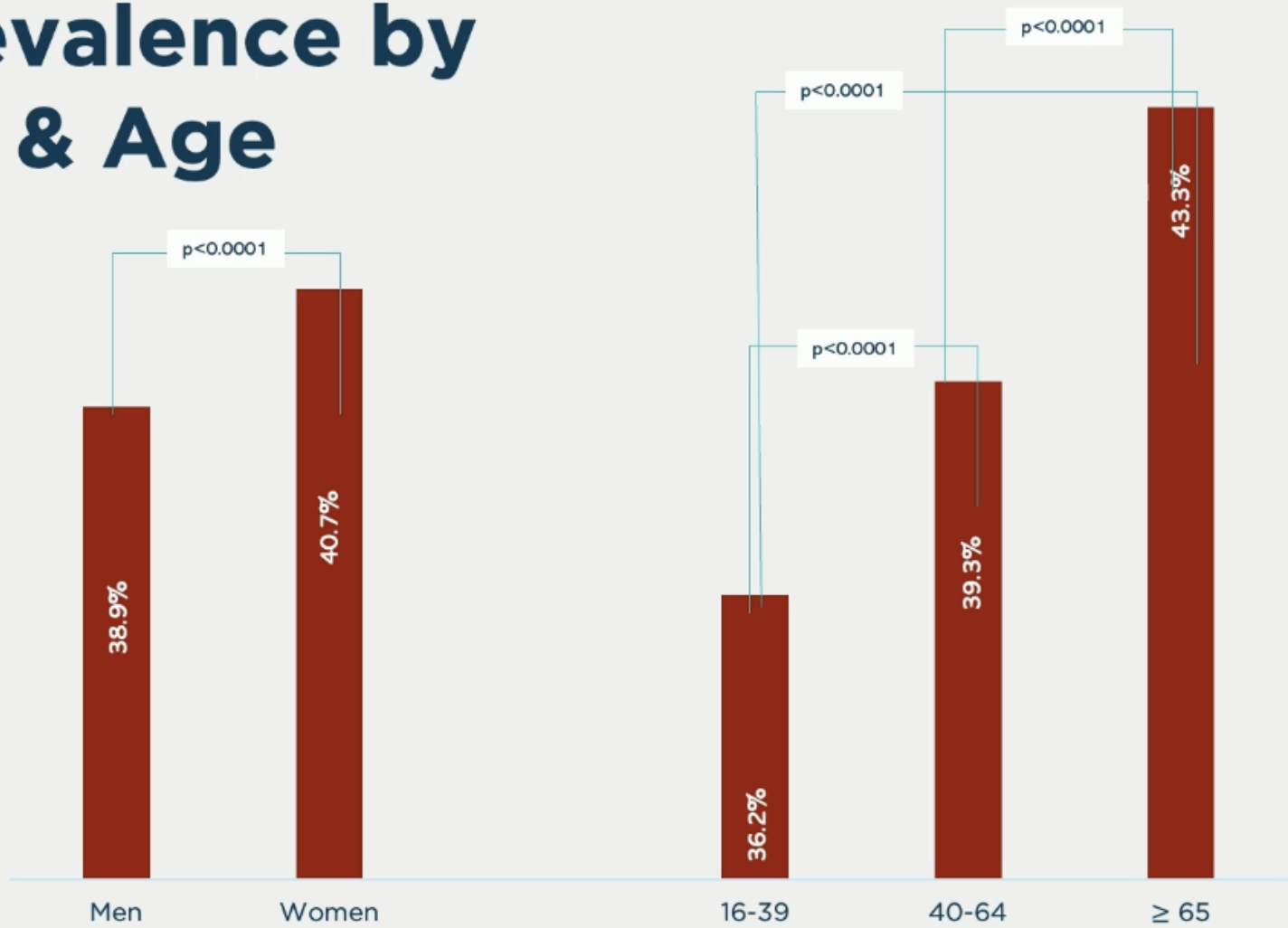
comparisons

A Patient Centricity St

Itch Prevalence by Gender & Age



Predictive sites of poor QoL in chronic itch patients

Itch in the **buttocks and upper limb** had the highest predictive value of poor QoL in chronic itch patients

Out of 16 total body sites: face, scalp, neck, shoulder, armpit, arm, forearm, hand, chest, abdomen, back, buttocks, groin, thigh, shin, and foot

Table 2. Predictors of itch-specific QoL – stepwise multivariable linear regression prediction model with backward deletion

Predictors[a]	Adjusted Beta (95% CI)[b] Adjusted R^2 = 0.21
Buttocks (vs none)	**0.24** (0.08, 0.40)
Arm (vs none)	**0.22** (0.04, 0.39)
Armpit (vs none)	**0.19** (0.02,0.36)
Forearm (vs none)	**0.24** (0.06, 0.41)
Hand (vs none)	**0.22** (0.06, 0.38)

[a] Variables included in the final prediction model
[b] The model was created using multivariable linear regression by including predictors stepwise. Positive beta represented poor QoL, and negative beta represented a good QoL

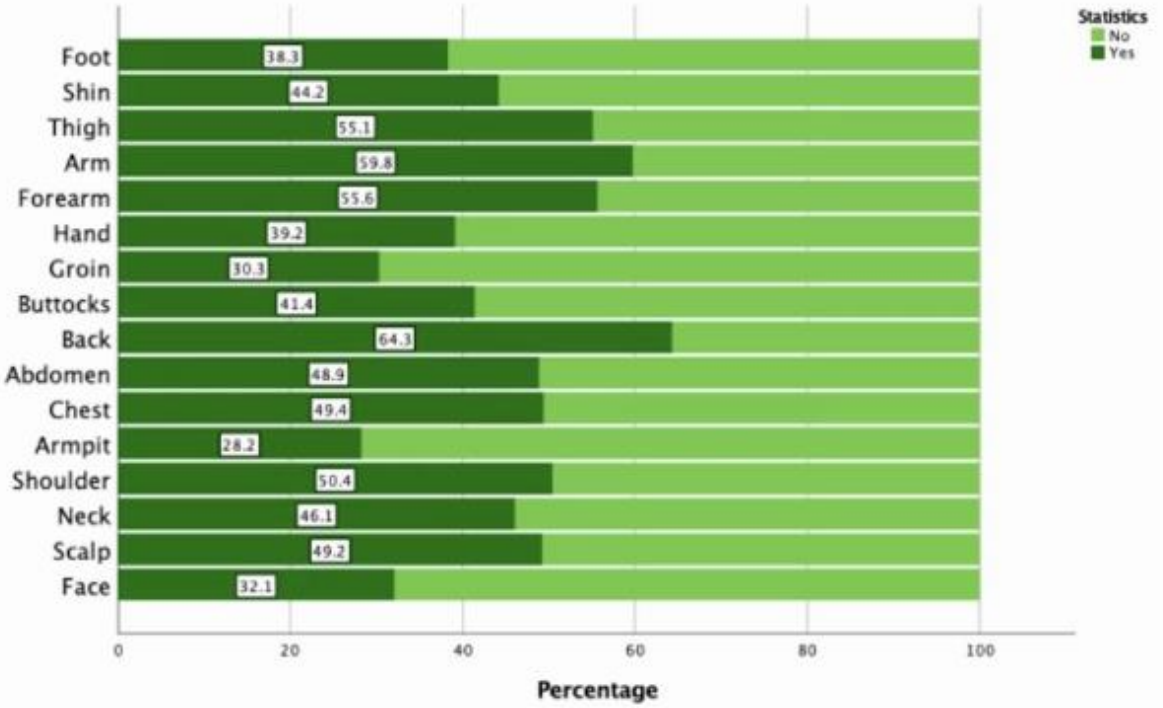
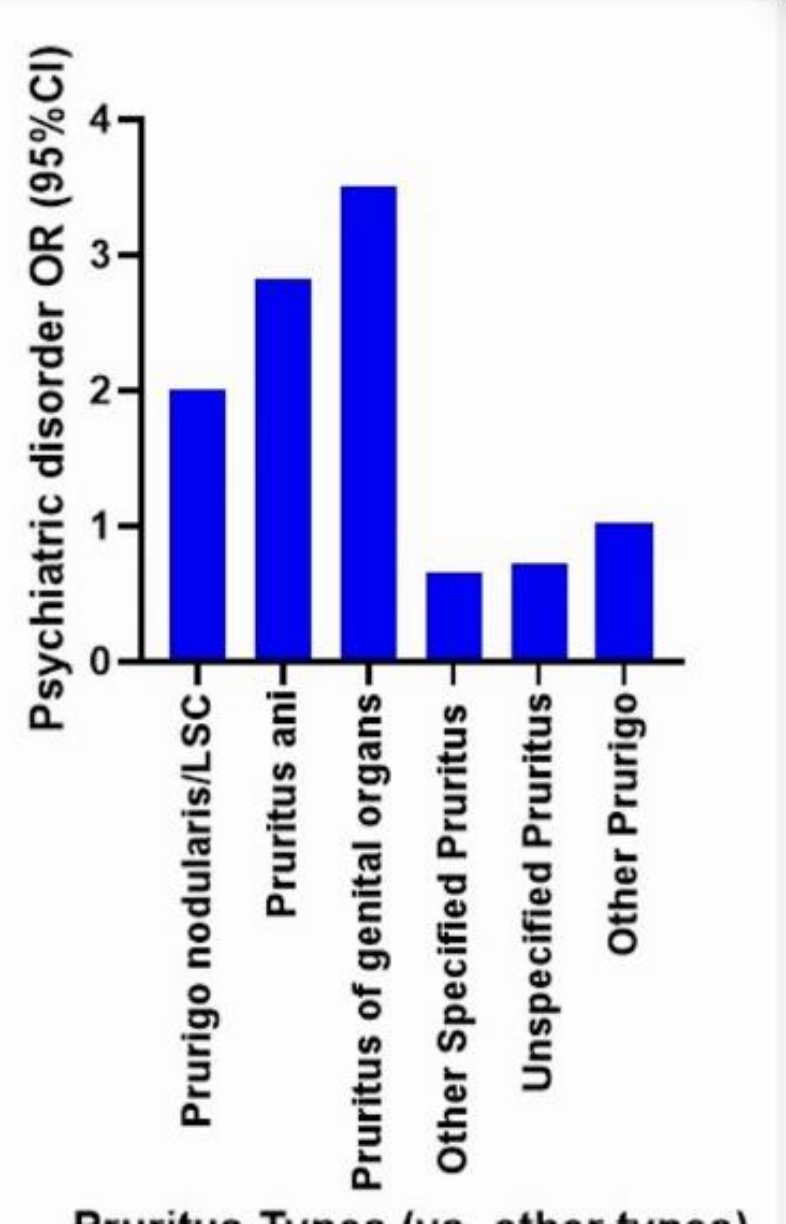


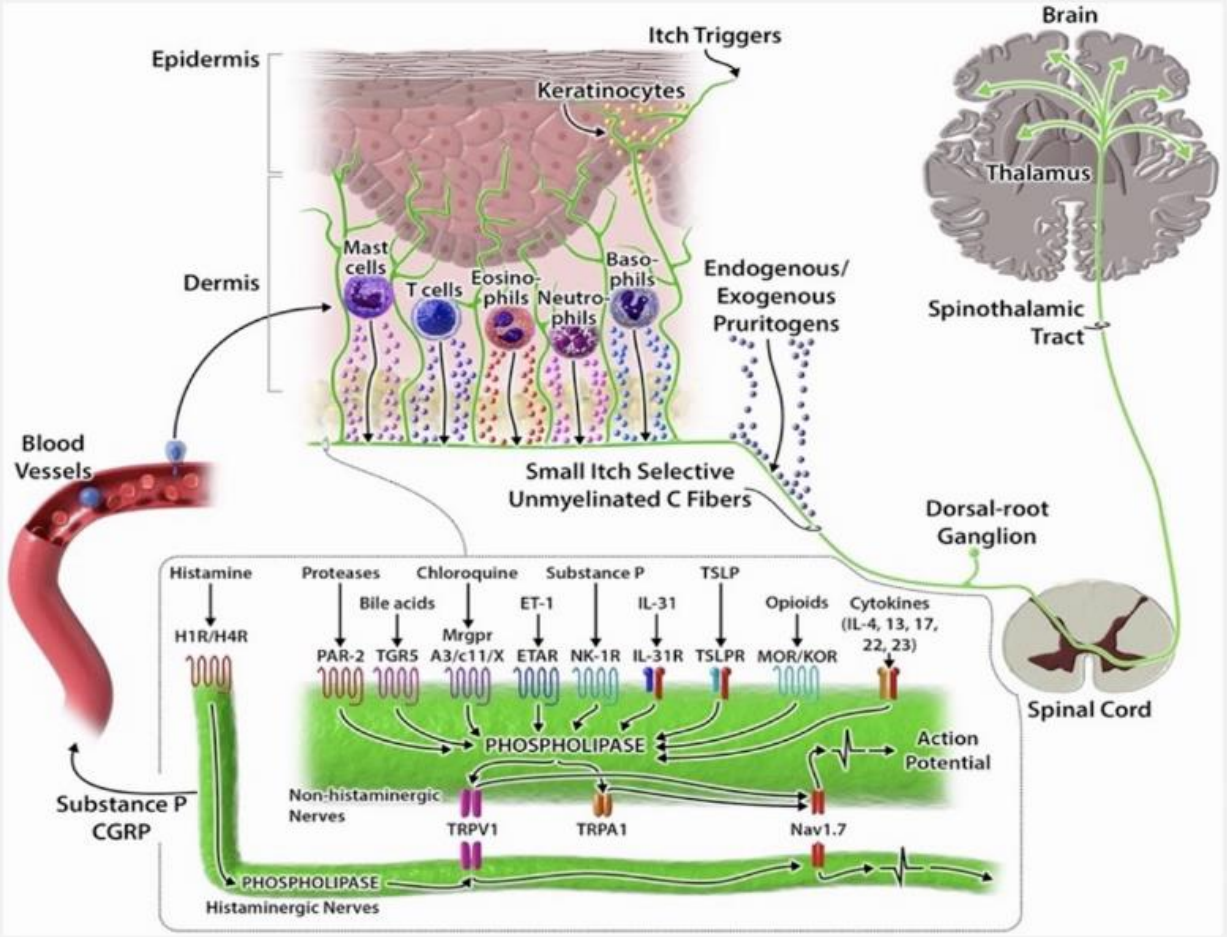
Figure 2. Frequency distribution of Sites of Itching

Genital Pruritus Impact on Patients Well Being

Genital pruritus is associated with longer hospital stays, higher costs, and increased odds of psychiatric hospitalization among inpatient adults with pruritus in the United States – National Inpatient sample (2012-2015)



Itch pathway



Skin

Nerves

Spinal cord

Brain

Clinical Pearl:

Antihistamines do not improve itching in majority of chronic itch

Patient #1: 55 year-old female

- Relentless, generalized itching for the past 6 months
- “Constant, gnawing, unbearable”
- Itch is worse at night, leaving her exhausted during the day

“I can’t focus while at work, I can’t sleep, and my whole life revolves around trying not to scratch”

How to Ask about Itch

pp-NRS (peak pruritus numerical rating scale)

- Rate your itch on a scale of 0-10, with 0 being no itch and 10 being the worst itch you can imagine
- Peak pruritus numerical rating scale from 0-10
  - 0-1: Normal person, no itch
  - 2-3: Mild itch
  - 4-6: Moderate itch
  - 7-10: Severe itch
- Might also hear about
  - WI-NRS (worst itch NRS)
  - Week-long average NRS
  - VAS (visual analogue scale)

…but insurance companies and payers are starting to ask for NRS scores!

Quantify Itch (According to Dr. Matt Zirwas)

Mild: Noticed occasionally; rarely a problem

- Comparable to one mosquito bite
- Impact: Minimal on daily activities
- NRS: ~2

Moderate: Present most of the time; sometimes interferes with activities

- Comparable to localized poison ivy or ~20 mosquito bites
- Impact: Can affect sleep or concentration on mundane tasks
- NRS: ~5

Severe: Persistent; affects most activities

- Comparable to rolling in poison ivy or hundreds of mosquito bites, worsening daily
- Impact: Disrupts sleep and daily functioning
- NRS: ~8

Why is itch worse at night?

- A 2024 study involving 241 adults found that itching was most frequent (74.7%) and intense (62.7%) between 8:00 PM and midnight.
- Cortisol, a natural anti-inflammatory hormone, dips in the evening and at night, reducing the body's anti-inflammatory response and potentially facilitating itch.
- Cytokines like IL-2 and IL-31—known itch promoters—increase at night, likely due in part to the reduced cortisol-mediated suppression.

History

- Duration & onset: acute vs. chronic (>6 weeks = chronic pruritus)
- Location: localized vs. generalized
- Exposures: new meds, supplements, environmental triggers, travel
- Associated symptoms: weight loss, night sweats, fevers, jaundice, neurologic symptoms, mood changes
- Systemic review: renal, hepatic, thyroid, hematologic, infectious, malignancy-related clues
- Medication review: opioids, antimalarials, antihypertensives(thiazides and calcium channel blockers common culprits)

Table II.

Initial history and physical examination for the assessment of itch

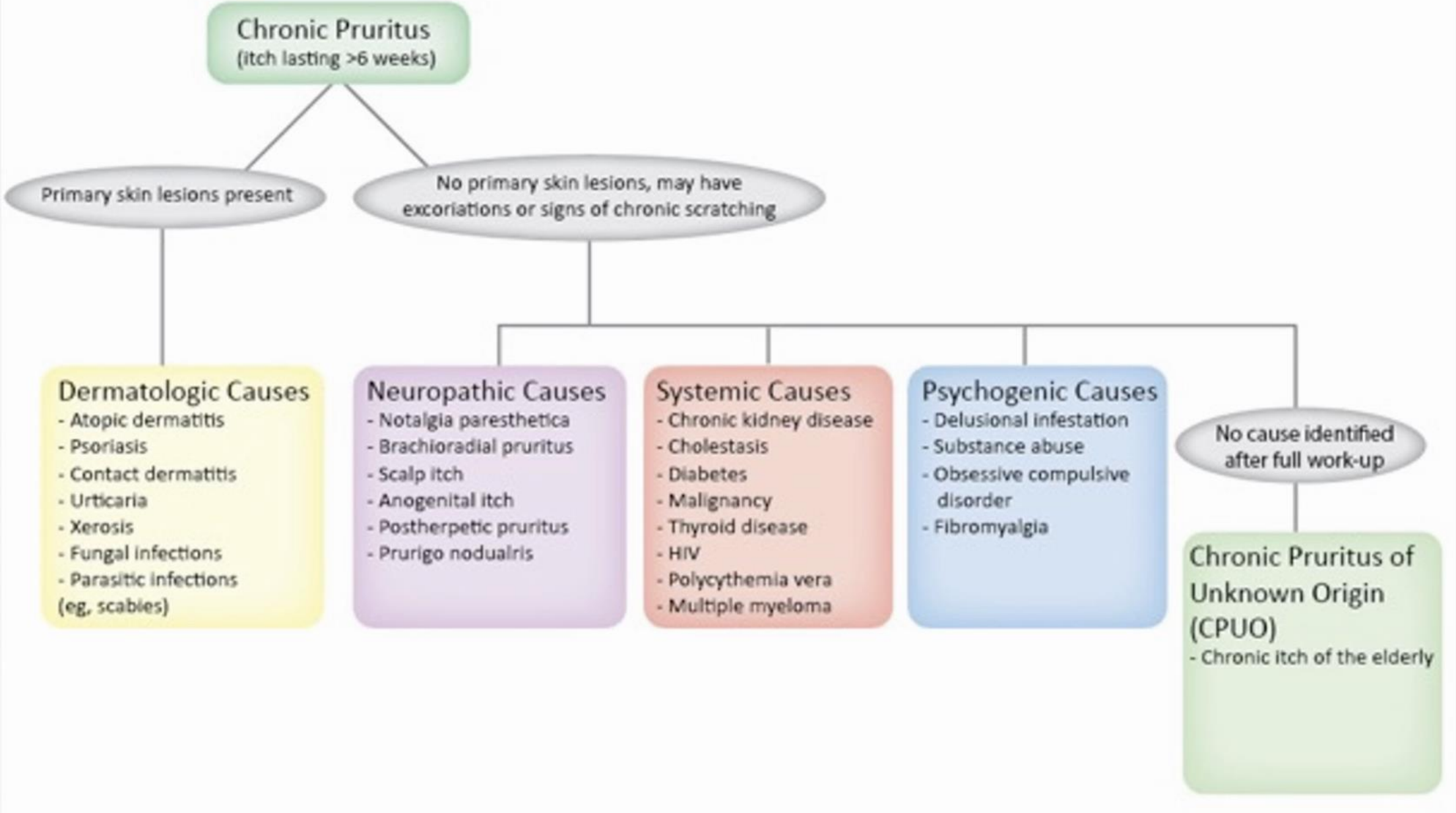
History	Physical examination
Duration	Skin examination
Localization of pruritus	Inflamed skin vs noninflamed skin
Timing and direction	Primary skin lesion
Worsen at night?	Secondary skin lesion (eg, excoriations)
Intermittent? Constant? Worsening?	Examples of other skin examination findings
Triggers	Dermatographism
Environmental exposures	Signs of atopy
Contact with water	Hyperlinear, thickened palms
Heat, exercise, sweating	Infraorbital Dennie-Morgan folds
Household members affected?	Track-like burrows between fingers
Pregnancy status	Erosions and scales between toes
ROS	Stigmata of liver disease
Constitutional B symptoms	Jaundice
Pain, paresthesia, heat intolerance	Ascites
Past medical history	Palmar erythema
History of atopic triad	Gynecomastia
History of neck or back pain	Thyroid examination
Recent medication change	Lymphadenopathy
Allergic history	Cachexia
Social history	Assessment of itch and its burden
Risk factors for communicable disease (HIV, hepatitis C, etc)	Itch NRS
	Scale of 0–10, 0 (“no itch”) and 10 (“the worst imaginable itch”)
Occupational exposure	
Risk factors of malabsorption	WI-NRS for 24 h
History of substance abuse	Scale of 0–10
Travel history	Verbal rating scale of itch on a scale of 0–4
Risk factors for infestation	No itch (0), mild itch (1), moderate itch (2), severe itch (3), very severe itch (4)

NRS, Numeric rating scale; *ROS*, review of systems; *WI-NRS*, worst itch numeric rating scale.

Roh YS, Choi J, Sutaria N, Kwatra SG, JAAD 2022;86(1):1

Physical Exam

- Get patient in a gown!
- Full skin exam (look for subtle primary lesions, excoriations, lichenification, dermatographism, xerosis)
- Do a lymph node exam
- Look for hepatosplenomegaly, thyroid enlargement
- Signs of systemic disease: jaundice, pallor, cachexia
- Don’t be fooled by scabies
- Lice nits are hard to see in grey hair


Chronic Pruritus
(itch lasting >6 weeks)
Primary skin lesions present
No primary skin lesions, may have excoriations or signs of chronic scratching
Dermatologic Causes
- Atopic dermatitis
- Psoriasis
- Contact dermatitis
- Urticaria
- Xerosis
- Fungal infections
- Parasitic infections (eg, scabies)
Neuropathic Causes
- Notalgia paresthetica
- Brachioradial pruritus
- Scalp itch
- Anogenital itch
- Postherpetic pruritus
- Prurigo nodularis
Systemic Causes
- Chronic kidney disease
- Cholestasis
- Diabetes
- Malignancy
- Thyroid disease
- HIV
- Polycythemia vera
- Multiple myeloma
Psychogenic Causes
- Delusional infestation
- Substance abuse
- Obsessive compulsive disorder
- Fibromyalgia
No cause identified after full work-up
Chronic Pruritus of Unknown Origin (CPUO)
- Chronic itch of the elderly

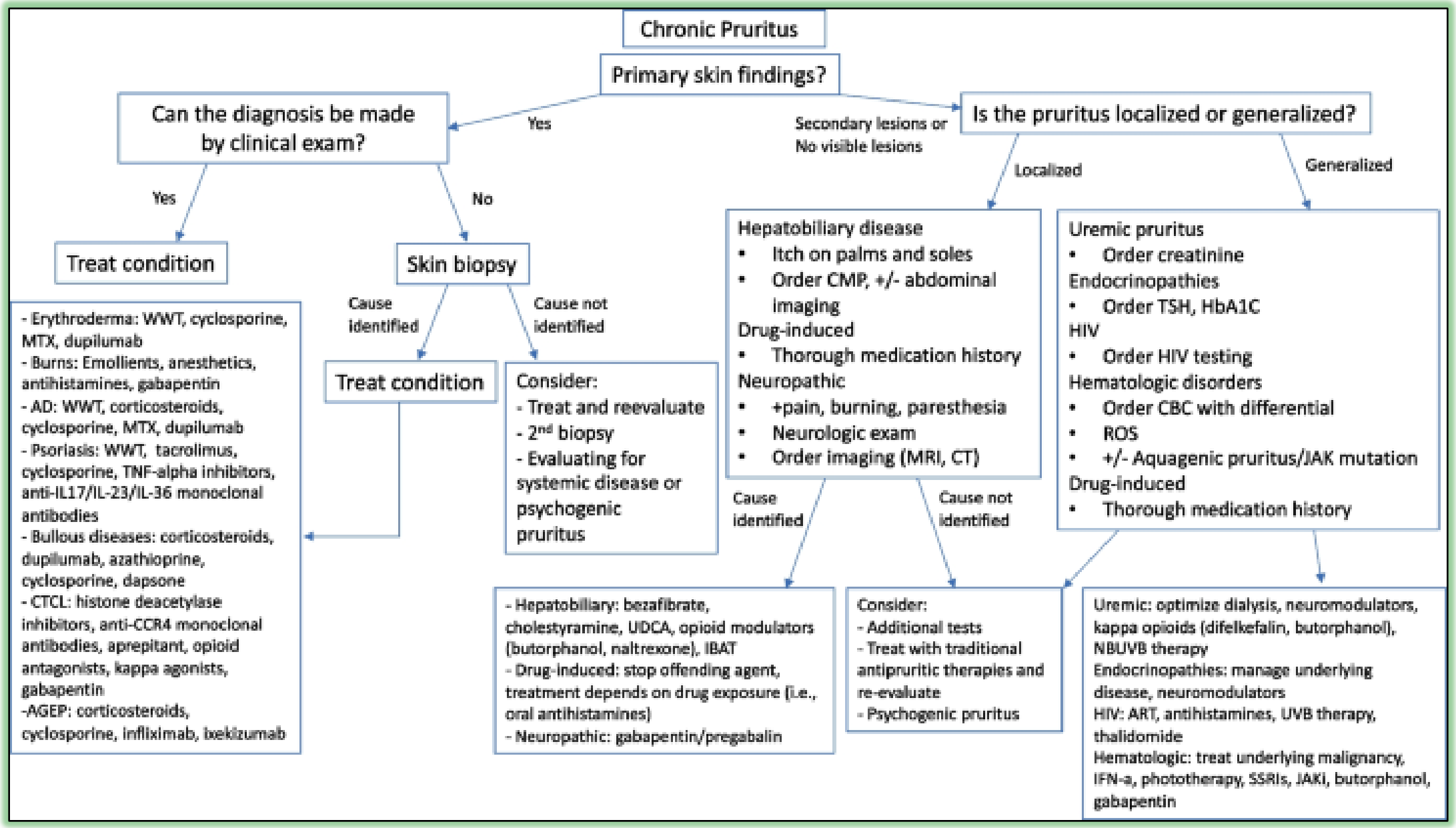
Systemic Diseases associated with Pruritis

- Diabetes mellitus
- Chronic renal failure
- Cholestatic Liver Disease
- Hyperthyroidism
- Cardiovascular disease
- Hepatitis B/C
- Gluten enteropathy
- Polycythemia vera
- HIV
- Myeloproliferative cancers
- Lymphoma
- Anxiety and depression

- CBC – sign. eosinophilia, think parasite
- CMP – creatinine
- Hem A1c
- Liver panel – bilirubin, bile acids, alk phos
- Thyroid Panel
- Hepatitis Panel
- IgE – atopy
- Gliadin antibody test – celiac
- Stool studies – travel or GI complaints
- HIV
- SPEP/UPEP
- CXR
- Age-appropriate malignancy screens
- Allergy testing largely useless
- Large ANA panels largely useless

Special Considerations

- Aquagenic pruritus: itch triggered by water → think polycythemia vera or myeloproliferative disease
- Neuropathic itch: post-stroke, multiple sclerosis, nerve compression
- Psychogenic itch: anxiety, OCD, delusional parasitosis



Soares, G.B., Yosipovitch, G. Pruritus: An Approach to Diagnosis and Management for the Inpatient Dermatologist. *Curr Derm Rep* **12**, 125–135 (2023).

Your next patient!


9/13/2022
14:12:22
DOB:
65.3 mm
72.6 mm
R
512 x 878
W:459 C:57
Series: 13 _ Image: 28/154

Pruritus of Unknown Origin: Zirwas & Seraly, JAAD 2001

- Retrospective review of 50 patients with unexplained itch.
- Goal: determine how often systemic disease explains pruritus without rash.
- Used chart review + patient interviews

Table II. Patients with likely systemic causes for pruritus

Patient No.	Sex	Age (y) at pruritus onset	Systemic diseases diagnosed before pruritus onset	Etiology of pruritus	Pruritus initial symptom of systemic disease?	Course and relationship of pruritus and systemic disease
1	M	68	None	Hypothyroidism	Yes	Hypothyroidism diagnosed during pruritus work-up; pruritus improved since thyroid replacement started
2	M	84	Adult onset asthma	Gastric cancer	Yes	Gastric cancer diagnosed 10 mo after pruritus onset
3	F	42	Iron deficiency anemia	Hepatitis C, diabetes mellitus	Yes	Hepatitis C[15,16] and DM type 2 both first detected during pruritus work-up
4	M	40	None	HIV	Yes	HIV diagnosed <1 y after pruritus onset
5	F	59	Breast cancer, hypothyroidism	Laryngeal cancer	Yes	Laryngeal cancer diagnosed 2 y after pruritus onset, pruritus cleared completely immediately after resection; breast cancer treated 7 y before pruritus onset, no evidence of recurrence at yearly checks; treated with levothyroxine sodium 6 y before pruritus
6	F	43	CML	Graft-versus-host disease	Yes	CML diagnosed at age 42, underwent bone marrow transplant at age 43; pruritus began after cyclosporine was discontinued; pruritus improved as graft-versus-host disease was controlled
7	M	81	Colon cancer, prostate cancer	CLL	Yes	CLL diagnosed 1.5 y after pruritus onset; patient died 2 y after CLL diagnosis
8	M	46	Alcoholic cirrhosis, iron deficiency anemia	Liver disease	No	Diagnosed with hepatitis C at age 48; underwent liver transplant at 49; pruritus improved after transplant
9	F	64	Uremia, on hemodialysis	Uremia/dialysis	No	Underwent kidney transplant at age 66; pruritus improved after transplant
10	F	81	Hepatitis C, lung cancer, hypothyroid	Hepatitis C	No	Persistent significantly elevated liver function studies during pruritus work-up; lung cancer treated 10 y before pruritus; no evidence of recurrence at yearly checks; treated with levothyroxine sodium for 30 y
11	F	36	DM type 1	DM	No	Blood glucose and hemoglobin a1c markedly elevated during pruritus; pruritus improved as blood glucose control improved

CLL, Chronic lymphocytic leukemia; *CML*, chronic myeloid leukemia.

Zirwas MJ, Seraly MP. JAAD 2001;45(6):892-896.

Key Findings

- 1 in 5 patients with unexplained itch may have systemic disease.
- Itch can precede diagnosis of cancer, infection, or endocrine disease.
- A structured workup is critical to avoid missed diagnoses.


IV CONT
A
DOB: 8/1
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44.9 mm

Pt presents with chronic, LOCALIZED pruritus with no primary skin lesions. What's next?

Neuropathic Itch

- Originates at any point along the afferent pathway as a result of damage to the nervous system
- Diseased or malfunctioning pruritic neurons firing action potentials without pruritogenic stimuli (an abnormal stimulus-response curve)

Localized itch disorders & neuropathic itch

- Scalp itch dysesthesia
- Brachioradial pruritis (BRP): cervical spine C4-C7 damage
- Notalgia parasthetica: impingement of T4-T10
- Meralgia parasthetica
- Vulvar and Scrotal itch

Prevalence

- Around 9% of patients with chronic pruritis
- Usually associated with other symptoms such as burning, stinging, pain, dysthesias, aloknesis, allodynia
- Can be first manifestation of spinal/CNS injury: subsequent evolution of neurologic signs
- Evolves on normal skin
- Secondary scratch lesions

Topical anesthetics for mild/moderate itch relief

- Pramoxine (1%)
- Lidocaine (2.5 to 5%)
- Prilocaine (2.5%)
- 5-10% Ketamine-5% amitriptyline- 5% lidocaine (Use up to 3 times a day on less than 30% BSA) Proposed to reduce hypersensitivity of peripheral nerve fibers through blockade of N-methyl-D-aspartate receptor and sodium channels.

Use for neuropathic itch, uremic pruritis, postburn pruritis, old-age immunosenescence itch, prurigo nodularis

Widespread Itch with Little-to-No Rash

- Other topicals to try
  - Mix 1 oz peppermint oil into 12-16 oz of cream
  - Mix 1.5 oz of pain/itch relief antiseptic liquid into 12-16 oz of cream
  - Mix 1 oz of capsaicin 0.1% into 12-16 oz of cream
  - Mix 50 mL of clobetasol scalp solution, along with one of the above, into 12-16 oz of cream
  - Use witch hazel topically (decent data to support it)
    - Can mix 50 mL clobetasol and/or 1.5 oz of pain/itch relief antiseptic liquid into 12-20 oz of witch hazel

Elsaie LT, et al. *Clin Cosmet Investig Dermatol*. 2016;9:333-338. Fazio SB, et al. UpToDate. Accessed June 20, 2025. https://www.uptodate.com/contents/pruritus-therapies-for-localized-pruritus/print.

Widespread Itch with Little-to-No Rash

- Strontium shown to work for
  - Histamine-induced itch
  - Non-histamine-induced itch
  - Burning/stinging from topical applications
- Works almost instantly
- Effect lasts for about 5 hours
- Often some brief stinging if applying to inflamed skin
- Available as a cream or scalp solution

Localized Pruritus

Brachioradial pruritus

- Any of the topicals listed previously
- Any of the orals listed previously
- Consider chiropractor or physical therapy
- Fluoroscopy-guided cervical epidural steroid injection by neurosurg or ortho spine

- Scalp pruritus
  - OTC strontium-based product is first-line agent for me
  - I regularly go to systemics for this
    - Same interventions as for brachioradial pruritus worth trying
      - Not as much info out there regarding chiropractic treatment, but still worth considering
      - Cervical steroid injections worth considering

Localized Pruritus

Anogenital pruritis

- Huge focus on keeping the anal area clean
- Both sweat and stool
  - May be unrecognized tiny amounts of leakage
- Have them clean with plain water and dry it
  - In bad cases, I recommend doing this AT LEAST every couple hours
  - Can try any of the agents listed previously
  - Good study showing 0.1% capsaicin diluted 1:20 is effective
- Lumbosacral epidural steroid injections
- Anogenital pruritus is most often a symptom of lumbosacral radiculopathy

Cohen AD, et al. *J Am Acad Dermatol*. 2005;52(1):61-66. Lysy J, et al. *Gut*. 2003;52(9):1323-1326.

Other Treatment Options

Accurate diagnoses lead to successful treatments
…and sometimes a treatment trail helps confirm diagnoses

- Topicals not working, add Systemics – but systemic side effects can be magnified in elderly and must watch out for drug interactions.
- I think mirtazapine/gabapentin/trazadone all work better for itch than doxepin & hydroxyzine
- Antidepressants (+/-)
- Injectables are rockstars for those “AD/non-specific pruritus” patients

Widespread Itch with Little-to-No Rash

- Mirtazapine
  - Pretty ineffective anti-depressant
    - Tell them you're not treating depression – that it is working on itch nerve endings
  - Start 15 mg qhs
  - Most effective oral medication I've found for itch
    - Very well-tolerated and very few drug interactions
  - Great sleep aid but RARELY can be AM "grogginess"
  - 10% of adults gain weight due to appetite increase
    - Warn them to be careful not to eat more

Yosipovitch G, et al. *N Engl J Med*. 2013;368(17):1625-1634

Widespread Itch with Little-to-No Rash

- Butorphanol (synthetic opioid pain medication)
  - Single most effective anti-itch treatment
    - Worked in at least 80% of patients with “intractable” itch who had failed multiple other therapies at Johns Hopkins itch clinic
  - Works in minutes, lasts about 6 hours
  - Theoretically does have abuse/dependence possibility, but seems to be MUCH lower than other opioids due to its unique mechanism of action and short half-life
  - Blocks Mu receptor and activates kappa receptor
    - Doesn’t make people feel good like other opioids do

Yosipovitch G, et al. *N Engl J Med*. 2013;368(17):1625-1634

Widespread Itch with Little-to-No Rash

- Butorphanol
  - Comes as a 2.5 mL bottle of nasal spray
    - Has about 15 “squirts”
  - It works so quickly that people use it prn after the itching has started – 1 spray up to bid prn
    - ONE spray, not 1 spray in each nostril
  - About 1 in 5 won’t like how it makes them feel, so have them be careful with first use
  - It is a controlled substance
  - Abuse or dependence quite rare, but not completely impossible

Yosipovitch G, et al. *N Engl J Med*. 2013;368(17):1625-1634.

Widespread Itch with Little-to-No Rash

- Gabapentin/pregabalin
  - Highly effective – works in almost every patient if you can get to a high enough dose, but sedation almost always makes it impossible
    - Gaba: Start 300 qhs (100 qhs in frail patients), titrate every 3-4 days to max of 1200 tid as tolerated
    - Pregaba: 25 bid to start, titrate up
  - Sedation, dizziness, “feeling like a zombie,” etc, that can be dose-limiting
    - Peripheral edema also possible

Yosipovitch G, et al. *N Engl J Med*. 2013;368(17):1625-1634.

In summary, pruritus without primary skin findings can be challenging to diagnose and manage, yet it often has a profound impact on a patient's quality of life.

Remember, above all, we are providers of hope—and that can be just as powerful as any treatment we offer.

Questions?

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