Objectives

- Identify the basic pathophysiology of itch
- Classify the chronically itching patient into one of four categories
- Devise therapeutic strategy, especially for the patient with itching of unknown etiology

Itch: Defined

- Itch (aka pruritus) is the unpleasant sensation which evokes the desire to scratch

Pathophysiology of Itching

- There are specific nerve fibers in the skin which transmit the sensation of itch (AP A6 & C)
- Itch is NOT a subset of pain; it is unique
- Itch is mediated by a host of molecules
  - Histamine
  - Neuropeptides (Serotonin, Bradykinin)
  - Proteases (Endopeptidases) and Cytokines (IL2, IL3)
  - Substance P (Mast cell activation)

Opioid receptors in the spinal column also transmit the sensation of itch
- Cannabinoid receptor activation blocks itch

Mediators of Itch
Scratch

- Physically scratching activates receptors and nerves which block itch sensation ("an"num inhibition")
- Scratching also sends an afferent signal to the CNS which activates pleasure centers (real-time MRI)
- Scratching an itch is like having sex: pleasurable

Montaigne 1533-1592

"Scratching an itch is one of nature's most wondrous things... and the closest at hand."

Itch-Sensitization

- Initial itch, then...
- Non-itchy stimuli are now perceived as itchy
- Itchy stimuli become even more itchy
- Both peripheral and central nervous systems involved

Net effect: Itching is a negative phenomenon that most people would rather not have!
Itching and the Elderly

- 50% of those 70 years old suffer from widespread and often intractable pruritus
- The majority of the elderly who itch, do so much more severely at night
Xerosis: Dry Skin

Causes inflammation: Xerotic eczema

Xerosis: Dry Skin

Inflammation associated with dry skin is xerotic eczema OR eczema craquele

Xerosis: Dry Skin

The most common skin disorder in the elderly
"Cracke le" means "Cracked" in French
Skin resembles cracked porcelain

Xerosis: Therapy

- Aged skin is dry (>50% over 65 have xerosis)
- Daily moisturizer, even if the individual was "oily" earlier
- Various formulations act as:
  - Humectant: draws water into skin: Lactic acid, Urea
  - Emollient: adds layer of oil: Dimethicone, Cyclomethicone, Jojoba
  - Occlusive: retains water in skin: Petrolatum, Carnauba wax, Mineral oil

<table>
<thead>
<tr>
<th>NAME</th>
<th>INGREDIENT</th>
<th>MECHANISM</th>
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<tbody>
<tr>
<td>AmLactin</td>
<td>Lactic acid</td>
<td>Humectant</td>
</tr>
<tr>
<td>Carmol 10120</td>
<td>Urea</td>
<td>Humectant</td>
</tr>
<tr>
<td>Nivea</td>
<td>Dimethicone</td>
<td>Emollient</td>
</tr>
<tr>
<td>Moisture!</td>
<td>Dimethicone Petrolatum</td>
<td>Emollient</td>
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<tr>
<td>Eucerin Cream</td>
<td>Dimethicone Petrolatum</td>
<td>Occlusive</td>
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<td>Lubriderm</td>
<td>Petrolatum</td>
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<tr>
<td>Keri</td>
<td>Lactic Acid Petrolatum Dimethicone</td>
<td>Combination</td>
</tr>
<tr>
<td>AI+ Defy &amp; Protect Therapy</td>
<td>Lactic Acid Dimethicone</td>
<td>Combination</td>
</tr>
<tr>
<td>Cerave Hyalatopic Plus</td>
<td>Hyaluronic Acid Ceramides</td>
<td>Combination</td>
</tr>
</tbody>
</table>

Why Ceramides Are Important: Illustrated

Comparison between normal and dry skins

Ceramide Products

- Cerave: Cream, Lotion, Wash
- Cure!: "Rough Skin Rescue Lotion"
- Cure!: "Advanced Ceramide Therapy" (FF).
- Eucerin: "Professional Repair"
- Cetaphil: "Restoradem"
- Aveeno: "EczemaCare"

Think about WHY the patient might be dry, aside from reduced sebum!

- Diabetes insipidus
- Diabetes mellitus
- Hypothyroidism
Scabies!

There are many other reasons for pruritus.

Scabies!

Scabies!

Scabies!

Scabies!

Permethrin 5%, applied twice 1-2 weeks apart (CDC, FDA)

Ivermectin 200ug/kg, oral twice, 1-2 weeks apart (CDC, Not FDA)

18 year old acne patient needs text + photo
“I am scratching my head raw. Can you see me soon?”
Scalp itching = Head Lice

DDx = Seborrhea, Psoriasis, Contact Derm

---

Scalp itching = Head Lice (pediculosis capitis)

DDx = Seborrhea, Psoriasis, Contact Derm

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Head Louse Treatments

<table>
<thead>
<tr>
<th>PRODUCT</th>
<th>AGE (Lowest)</th>
<th>APPLICATIONS</th>
<th>COST (AMP) 4oz</th>
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</thead>
<tbody>
<tr>
<td>Ivermectin Lotion 5%</td>
<td>6MONTHS</td>
<td>ONE</td>
<td>$300</td>
</tr>
<tr>
<td>Splnoid 0.5% Slns</td>
<td>6MONTHS</td>
<td>TWO (7 days)</td>
<td>$219</td>
</tr>
<tr>
<td>Benzalcohol 5% Lotion</td>
<td>6MONTHS</td>
<td>TWO (7 days)</td>
<td>$53</td>
</tr>
<tr>
<td>Pyrethrino Shampoo</td>
<td>2YEARS</td>
<td>TWO (7 days)</td>
<td>$50-80</td>
</tr>
<tr>
<td>Permethrin 1%</td>
<td>2MONTHS</td>
<td>TWO (7 days)</td>
<td>$80</td>
</tr>
<tr>
<td>Malathion 0.5% Lotion</td>
<td>6YEARS</td>
<td>TWO (7-9 days)</td>
<td>$300</td>
</tr>
</tbody>
</table>

Pediculosis capitis (Head lice)

- Collected head lice: 138 sites, 48 states
- Summer 2013-Summer 2015
- 96% of sites had 100% of all lice carrying resistance to pyrethroids
- 42 states had 100% resistance of all lice
- Correlates w/ Rid® & Nix® brand failures
“Natural” Therapy for Head Lice

- Wet combing, manual nit removal
- NUVO method w/Cetaphil® cleanser (QWk x 3)***
- Essential oil and botanical shampoos (USA)
  - ClearIce® Shampoo, Licefree Gel, Lice BeGone® Shampoo
  - Can be irritating, or allergenic
- Herbal shampoos (ex-USA, available online)
  - Wash-Away-Laus®, Nopycid Bio Citrus®
  - Can be irritating or allergenic

Head Lice in Young Adults!!!!!

- Abametapir = Xeglyze
  - Abametapir 0.74%
  - Blocks metalloproteinases
  - Prevents egg from opening (no nymphs)
  - Operculum

- Abametapir = Xeglyze
  - Abametapir 0.74%
  - Blocks metalloproteinases
  - Prevents egg from opening (no nymphs)
  - Interferes w/ several vital enzymes in adult
  - Ovicidal and Pediculocidal
  - Single 10 minute application
  - Operculum
Body Lice

Excoriation where clothes fit closely to skin (waist, axilla)
Lice don’t live on person, but rather in seams of clothes

“Seam squirrels”

Tinea pedis, cruris, corporis

Superficial fungal infection: foot, groin, trunk

Frequency increases with age
Diabetes, immunosuppression
Trichophyton rubrum
All forms itch
Tinea pedis probably first, then spreads to groin, trunk
ANY topical antifungal
Oral terbinafine 250mg/day

Tinea corporis = Ringworm

Tinea cruris = Crotch Rot

Tinea pedis = Athlete’s Foot
Tinea pedis, cruris, corporis
Superficial fungal infection: foot, groin, trunk

Therapy: Cutaneous Tinea
- Topical therapy: Many agents to choose from and all work; be aware of dosing, which varies from agent to agent
- Vehicle important (cream, gel, lotion, foam)
- Azole: clotrimazole, econazole, ketoconazole
  luliconazole, oxiconazole, sertaconazole
- Allylamine: butenafine, naftifine, terbinafine
- Olamine: ciclopirox

KOH+

Diagnostic: KOH prep
KOH the active border
Obtain scale for fungal culture
Tinea Rx: Luliconazole Cream OD x 7 days

Tinea faciei: Almost always means new pet (puppy, kitten) in household

Common Itchy Dermatoses

Psoriasis

Lichen Planus

Therapy: Cutaneous Tinea

Topical therapy: Many agents to choose from and **all work**; be aware of dosing, which varies from agent to agent
Vehicle important (cream, gel, lotion, foam)
- Azole: clotrimazole, econazole, ketoconazole
  luliconazole, oxiconazole, sertaconazole
  Allylamine: butenafine, naftifine, terbinafine
- Olamine: ciclopirox
- Butenafine = Lotrimin Ultra ($9.00 a tube)

Psoriasis and Itching

- 90% Psoriasis patient itch (3/4 daily)
- Often described as biting or stinging itch
- Worsened by: heat (81%), skin dryness (80%), sweating (65%) and stress (55%)
- Stress management
- Exercise (INSIDE): endorphins counteract itching
  Avoid hot baths/showers
- Regular moisturization
- **Pearl**: ASA helps w/pso riais!
Common Itchy Dermatoses

Pregnancy Rashes

Typically pruritic, but not dangerous

The Flaming Lips
1983 present

"And the summertime will make you itchy the mosquito bites"
- Buggin

Allergic Contact Dermatitis

Typically pruritic, but not dangerous

P/P/P. Pruritic Urticarial Papules and Plaques of Pregnancy

Don't forget the obvious! Insect bites
Classification of "Itchy Patient"

- Rash Present
- Rash Absent

Etiology
- Scabies incognito
- Atypical contact dermatitis, ID nm
- Unusual drug eruption,
- Prurigo nodularis, and
- "Unclassified Endogenous Eczema"

Scabies Incognito
Particularly in the Elderly

- Scabies Incognito

Scabies
- Suspect scabies: mineral oil prep; Likely negative
- Suspect scabies but prep negative....

EVERYELDERLYADULT
PRESENTING WITH NEWONSET
WIDESPREADITCH, NON-SPECIFIC RASH
SHOULD BE ASSUMED TO HAVE SCABIES
- Ivermectin 200ug/kg PO + permethrin 5% er
- Repeat in 1-2 week
- Treat close contacts with permethrin
- Address fabrics contacting skin/Contact way the disease is spread
- FROM: Nurse, Caregiver, Relative...••OR••
Itchy patient, Unclassifiable rash

- Occult or atypical contact dermatitis
- Allergic
- Irritant
- Wearing 100% soft, untreated cotton
- Apply desoximetasone ointment 3-4x/d OR
- Mix Cerave lotion (16oz) w/ betamethasone lotion (50cc)
- California Baby Shampoo + Body wash as soap OR
- Vanicream bar soap to wash, 3x weekly maximum
- Cerave moisturizer daily
- Double rinse all laundry
- Non-irritant laundry detergent {GreenShield, Eco-Me®}

Unclassifiable rash: ?Drugs

- Stop all meds where acute threat of death is not associated with discontinuation
- Duration of therapy does not preclude source*
- Blood pressure meds, particularly calcium channel blockers, oral anti-diabetic drugs and proton pump inhibitors likely
- Safer alternatives: ARBs, Insulin, Ranitidine (from skin rash perspective)
- May take 6 weeks for itch/rash to subside

Prurigo nodularis

- An itch that rashes...chronic pruritus leading to incessant scratching-picking which leads to nodules, some excoriated
- End stage of pruritus of unknown etiology
- Incidence/Prevalence unknown; F>M
- May need biopsy to R/0 KA, SCCA, H-LP
- Therapy:
  - Destruction: Cryosurgery, IL TAC, Cryo + IL TAC
  - nbUVB, PUVA
  - Topical Calcipotriol, Steroids, TCIs
  - Gabapentin & Pregabalin, MTX, Thalidomide

Prurigo nodularis
**Prurigo Nodularis: Pearl**

- Sometimes associated with:
  - Uremia
  - Anxiety

**Prurigo nodularis**

- Mediated by hyperactive CNS glutamate neurons
- Glutamate modifying drug: N-acetylcysteine (OTC)
- Releases free cystine, exchanged for glutamate
- Alters neuro milieu; Suppresses firing of the glutamate-mediated synapses
- DOSE: 500mg-600mg BID, titrating up to 4000-4200mg/day (divided dose)
- CHEAP: $0.4-0.7 per pill
- Nausea, vomiting, diarrhea, flatulence (all mild)

**"Endogenous Unclassified Eczema"**

- SYNONYMS: "Itchy red bump disease" and "Essential dermatitis"
- Dull red papules trunk and extremities
- Severe, persistent generalized itching
- Superficial to mid-dermal mild perivascular infiltrate admixed with eosinophils
- Nothing much helps except PREDNISONE (1mg/kg/day) and MYCOPHENOLATE (2000mg/day)

**"Itchy Red Bump Disease"**

- Nondescript dermal papulonodules

**HIV+ Patients and Pruritus**

- 45% HIV+ experience significant itching
- Usually itch hepatitis disease
- May just "itch" with no rash
- May itch due to eosinophilic folliculitis
- Rash above nipple line, particularly face/neck
- May itch due to pruritic papular eruption
- Rash on trunk and arms
- EF may actually = PPE
- Also think tinea and scabies
- Rx: Itraconazole, Doxycycline, UVB photoRx
Eosinophilic Folliculitis: HIV+

DDx includes Sarcoid and Syphilis

Gilda Susan Radner 1946-1989

"I base most of my fashion sense on what doesn't work."

Classification of "Itchy Patient"
Classification of "Itchy Patient"

- Renal failure, Hepatic failure
- Thyroid dysfunction, Sprue, Diabetes, Cancer, Low iron, Biliary tree obstruction, HIV Parasites, Drugs, Lymphoma

Itching and Systemic Disease

- OVERALL: Systemic disease etiology of itching in 13%-22% chronic pruritus patients
- OVERALL: Itch is presenting sign -65%
- Renal failure 15-90%
- Biliary cirrhosis 80%
- Polycythemia vera 30-50%
- Hodgkin's disease 30%
- Thyroid dysfunction 7-15%

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Itchy Patient with an Etiology

- Just because the underlying disease state is known does not mean we understand the precise pathophysiology of itching
  - Renal failure (as an example)
  - Dialysis often helps - why?
  - Pruritogen secreted from renal cells
  - Element of xerosis
  - Increased density of cutaneous mast cells
  - Increased parathormone
  - Abnormal Vitamin A concentration in skin

Drugs and Itching

- Those which induce cholestasis
  - Estrogens, Chlorpropamad, Ciprofloxacin
  - Those associated with hepatotoxicity
  - INH, Phenytoin, Sulfinpyrazone
  - Those which induce sebostasis and/or xerosis
  - Retinoids, Tretinoin, Neomycin
  - Those with presumed neurogenic effects
  - Morphine, Carbamazepine, Flunarizine, Canine
  - We have no idea
  - Chlorpropamid, Chlorpromazine
  - Clomipramine
  - Gabapentin
  - Lithium
  - Phenytoin (Fen-MOP)

Itchy Patient: Rash Absent

- CBC w/differential
- Serum iron, ferritin
- BUN, Creatinine (Ca, P)
- Fasting glucose, HbA1c
- TSH
- LFTs, incl bilirubin
- Chest x-ray
- HBV and ANA screen?
- Hepatitis serology?
- Stool for O&P

LABS

- Appropriate physical examination and laboratoriescreening for likely malignancy per age/gender
- Exam for enlarged lymph nodes in younger patients

Itchy Patient: Rash Absent

- CBC w/differential
- Serum iron, ferritin
- BUN, Creatinine (Ca, P)
- Fasting glucose, HbA1c
- TSH
- LFTs, incl bilirubin
- Chest x-ray
- HBV and ANA screen?
- Hepatitis serology?
- Stool for O&P

Appropriate physical examination and laboratoriescreening for likely malignancy per age/gender
Itching: Occult Malignancy?

- Overall: risk of occult internal malignancy with pruritus is very low

  Association greatest first 3 months of itch

  Lymphoreticular malignancy OR = 2

  CTCL, Hodgkin’s & NHL, Polycythemia vera

  Bile duct CA OR = 3.73

- Overall OR = 1: itching patient population (US & Danish studies)

Case

- 82 year-old female
- Resides at home
- Breast cancer (20 yrs earlier)
- Takes several medications, long-standing, for hypertension and cholesterol control
- Sudden onset of generalized itching

Case

- Another 80 year old. For comparison

Why is SHE itching? What would you do?

Classification of "Itchy Patient"

- Localized dysesthesias, Neuropathic, Psychiatric, Pruritis of Unknown Etiology

WHAT THE HELL IS GOING ON?
Itchy Patient Rash Absent
LOCALIZED

- Notalgia Paresthetica
  - Itch (Pain) interscapular back: Older
  - Degenerative disease Thoracic spine (T2-T6)

- Brachioradial Pruritus
  - Itch (Burn, Sting) arms: Middle-aged, Fair, Outdoor activities (golf, tennis, sailing)
  - May be associated with Cervical spine abn
    - Cervical vertebral osteoarthritis
    - Cervical rib
    - Cervical spinal tumor

THERAPY for both Notalgia Paresthetica and Brachioradial Pruritus
- Look for & correct gross vertebral spine defects
- Topical lidocaine
- Topical capsaicin cream 0.1% OTC, mixed in 1:4 ratio w/ any moisturizer, applied O/D, titrate
- TENS unit
- NB-UVB
- Systemic neuroleptic drugs (list later)
Excoriations in Nursing Home

Patient with dementia

itching CNS Diseases?

- Pruritus may accompany neuro-degenerative disorders, such as dementia, Alzheimer's, Creutzfeldt-Jakob Disease
- Pruritus may accompany brain tumors, brain abscess, stroke, multiple sclerosis
- ?? Loss of inhibitory pathways in CNS
- Concomitant: burning, stinging, tingling
- Excoriations only
- Still.....suspect scabies, but get Neuro exam

I don't know why you are itching!

- What the hell is going on?
- 30-50% of itchy patients!
- You've looked for answers; there are none
- The best you can expect is symptomatic relief
- Re-assess periodically for underlying cause
- Combination topical + systemic therapy

I don't know why you are itching!

- Avoid things which aggravate itch
- Avoid common soap (pH 11 aggravates itch)
- Avoid heat & wool; Converse: cool & cotton
- 1-2% Menthol lotion
- Topical: steroids, pramoxine, capsaicin
- NB-UVB phototherapy, Antihistamines

I don't know why you are itching!

- HOLISTIC APPROACH
  - Support groups/group therapy
  - Education
  - Behavior modification
  - Stress reduction training
  - Guided imagery
  - Therapeutic touch
  - Acupuncture
  - Progressive muscular relaxation

Intractable Idiopathic Itch

<table>
<thead>
<tr>
<th>DRUG</th>
<th>MECHANISM</th>
<th>Acts</th>
<th>DOSE</th>
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<tbody>
<tr>
<td>Naltrexone</td>
<td>1-Opioid receptor blockade</td>
<td>PNS</td>
<td>15mg QD</td>
</tr>
<tr>
<td>Butorphanol</td>
<td>1-Opioid receptor antagonist</td>
<td>PNS</td>
<td>2mg-4mg Q4-8hr</td>
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<tr>
<td>Paroxetine</td>
<td>SSRI</td>
<td>CNS</td>
<td>20mg QD</td>
</tr>
<tr>
<td>Sertraline</td>
<td>SSRI</td>
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<td>25-100mg QD</td>
</tr>
<tr>
<td>Mitrazapine</td>
<td>Norepinephrine enhancement</td>
<td>CNS</td>
<td>7.5-30mg QD</td>
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<tr>
<td>Gabapentin</td>
<td>Afferent blockade</td>
<td>CNS</td>
<td>300-2700mg QD</td>
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<tr>
<td>Thalidomide</td>
<td>Hypnosedative and anti-inflammatory</td>
<td>CNS</td>
<td>100-200mg QD</td>
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</table>
Intractable Idiopathic Itch

<table>
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<th>Mechanism</th>
<th>Acts</th>
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<tr>
<td>Naltrexone</td>
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<td>50mg QD</td>
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<td>Opioid receptor</td>
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<td>2mg PO</td>
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<td>Paroxetine</td>
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<td>100-200mg QD</td>
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</table>

Another Option?

Azathioprine and Chronic Itch

- May work: Mean maximum daily dose of 171mg
- Mean Rx duration: 16 mo
- VAS itch: 25>1.65
- Modestly priced
- QO dosing
- Measurable metabolite
- Pre-Rx TPMT
- Few drug interactions
- Well absorbed
- High risk AEs (2/3)
- GI, MT, Transamens
- High risk of cancer
- Risk lymphoma, NMSC

A New Approach to Chronic Pruritus

- Aprepitant: Neurokinin 1 inhibitor
- Anti-emetic in association with chemoRx
- 40mg BID
- Expensive (160 per pill)
- Serloputant: Coming!

Itching....

Ogden Nash (American poet)

Happiness is.....
Itching.....

Ogden Nash (American poet)

"Happiness is having a scratch for every itch."

THANKS FOR LISTENING