

# Systemic Medications

*Multidisciplinary Atopic Dermatitis Program (MADP) Clinic*

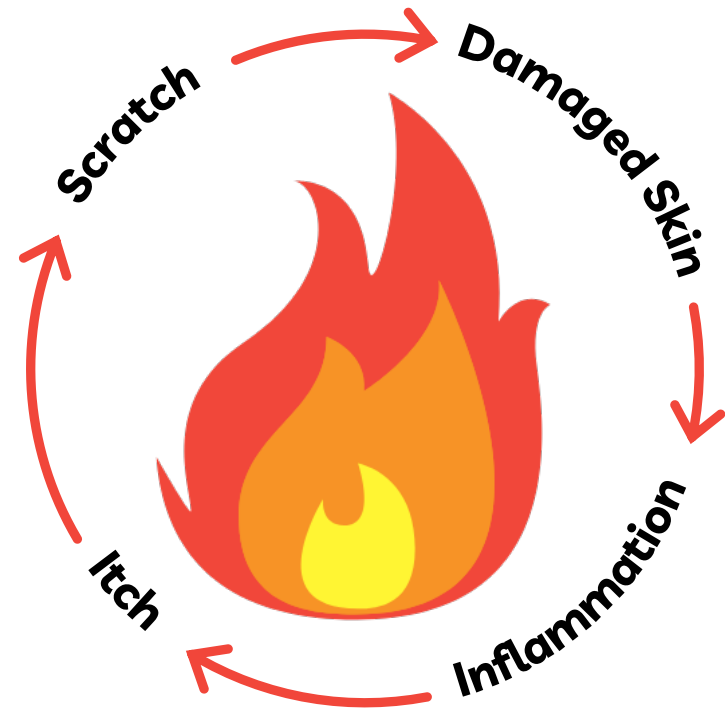
# What Are Systemic Medications?



- Medications taken by mouth or injected
- Used for more severe eczema
  - When creams/ointments not working well enough

# How Do They Work?

- In eczema, immune system overreacts and produces inflammation
  - Leads to itching, redness, and skin barrier problems
- Systemic medications help:
  - Decrease or suppress inflammation
  - Minimize itch-scratch cycle
  - Allow skin to heal
  - Decrease risk of skin infection





# Immune Suppressing Medicines

- For moderate to severe eczema
  - No response to topical therapy
  - Major impact on quality of life
  - Suppresses immune system
- Off-label use
  - Not FDA approved to treat eczema
  - Only short-term use, then taper off

## *Common Medications*

- Methotrexate (MTX)
- Cyclosporine
- Azathioprine (AZA)
- Mycophenolate Mofetil

## *Side Effects*

- Many including, but not limited to:
  - Nausea/upset stomach, high blood pressure, increased cholesterol, headaches, increased infections, etc.

## *Frequent Monitoring*

- Labs
- Blood pressure
- Drug interactions
- Harmful during pregnancy and breastfeeding

# Systemic Steroids

- For severe eczema flares
- Prescribed to control inflammation
- Oral or injectable
  - Example: prednisone
- Not commonly recommended
  - Symptoms may return worse after stopping
  - Long-term use of oral steroids (>1 month) can result in serious side effects

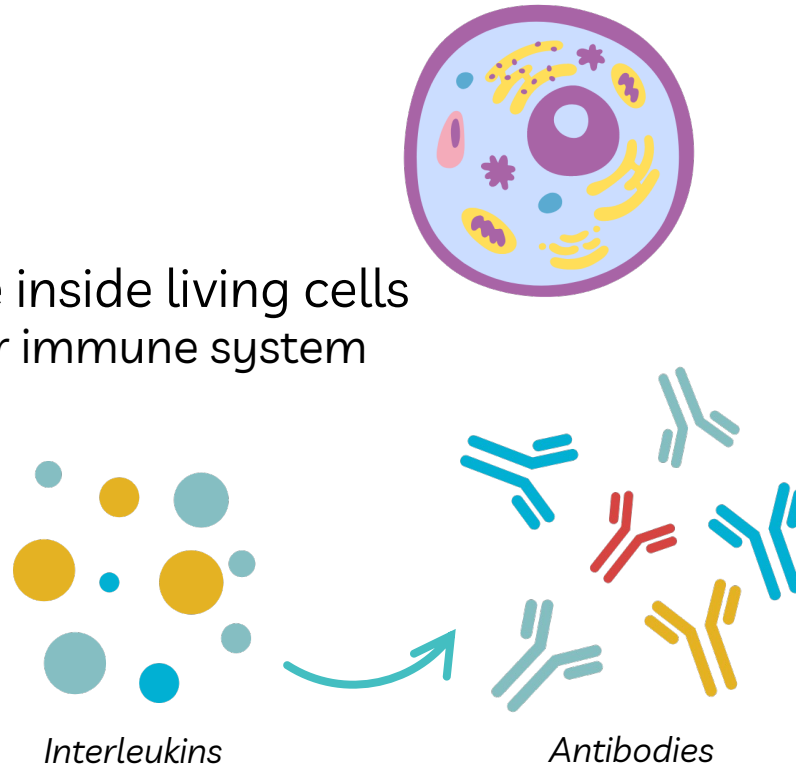


***Systemic steroids should be avoided if possible***

# Biologics

- **“Synthetic antibodies”** – made inside living cells
  - Targeted precision medicine for immune system
  - Injection

- **Interleukins (ILs)**
  - Signaling messengers in body
  - Helps with immune system



- **Eczema is an inflammatory disease**
  - Immune system overreacts → Triggers certain ILs to respond → ILs produce inflammation → Eczema

**Biologics calm immune system by blocking specific ILs**

# Dupilumab

- First biologic approved by FDA
  - For moderate to severe eczema
  - Available for 6 months and older
  - Injection every 2-4 weeks

## Clinical Trials

- Over 16 weeks of medication use
- Nearly half reported symptoms decreased by **75%**



*Dupilumab does not suppress the immune system*

# Dupilumab



## *Mechanism*

Blocks IL-4 and IL-13  
(Both contribute to eczema)



Limits immune system from overreacting



Decreases inflammation and eczema symptoms

- No bloodwork monitoring necessary
- Most common side effects include
  - Conjunctivitis
  - Injection site reaction



# Tralokinumab



- FDA approved for adults (18+ years)
  - December 2021
- Phase 3: 12 to <18 years
  - Long-term, open-label
- Phase 2: 6 to <12 years
  - Began September 2022
- IL-13 inhibitor
- Injection every other week (possibly transition to monthly injections)
- Used in combination with topical steroids

## Clinical Trials

- 75% improvement from start of trial
- Reduction in daily worst itch rating
- Improved sleep and quality of life

## Common Side Effects

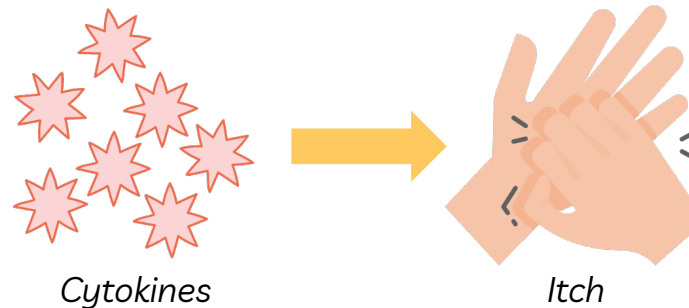
- Conjunctivitis
- Injection site reaction

# Janus Kinase (JAK) Inhibitors

- Topical or systematic (oral)
- Moderate to severe eczema treatment
- Blocks some itch signals
- Anti-inflammatory
- Work quickly
- Broader target range than biologic
  - Inhibit target inside cell

## Cytokines

- Immune system messengers
- Increased in blood and skin



Immune system overreacts → Body release cytokines → Activate JAK pathway → Abnormal immune response → Eczema

# Abrocitinib and Upadacitinib



- FDA approved for adults and +12 years

## Clinical Trials

- Higher score of clear to almost clear compared to placebo
- 75% improvement from start of trial
- Reduction of itch within **1-2 days** of first dose; improved nighttime itch
- Reduced skin pain rating (Upadacitinib)

- JAK1 inhibitor
- Once a day oral treatment
- Recommended if non-responsive to biologics
  - Cannot be taken with other JAK inhibitors, biologic, immunosuppressants

## Common Sides Effects

- Nausea
- Headache
- Herpes simplex (including cold sores)
- Acne

## Lab Monitoring

### Abrocitinib (Cibinqo)

Baseline labs; repeat 1 month after start and periodically

- Lymphocyte
- Neutrophil
- Red blood cell
- Platelet count
- Hepatitis (annual)
- TB (annual)

*Should not take abrocitinib if results are too low*

- Cholesterol

- Abrocitinib and upadacitinib may **increase** level of fat in blood - provider should check ~4 weeks after start

### Upadacitinib (Rinvoq)

Baseline labs; repeat 3 months after start and periodically

- Lymphocyte
- Neutrophil
- Hemoglobin
- Liver enzymes (elevated\*\*)
- Hepatitis (annual)
- TB (annual)

*Should not take upadacitinib if results are too low\*\**



# Black Box Warning

## JAK Inhibitors

### *Black Box Warning*

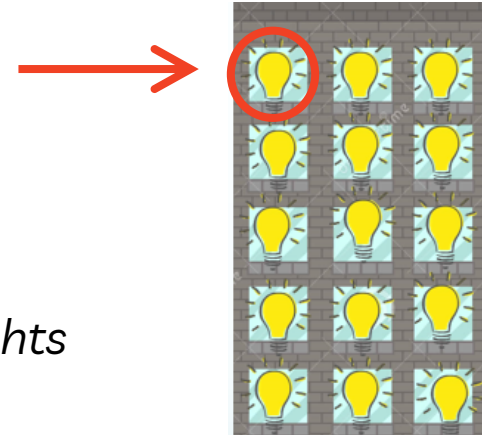
- FDA required for medication with serious safety risks
  - Cancer, major cardiac events, serious infections, blood clots
    - Actual rates are same or marginally higher than *not* being on the drug
- Based on studies in patients with rheumatoid arthritis on alternative JAK inhibitor not used in eczema
  - Older population (> 65 years) may have already had risk factors or other comorbidities
    - History of CAD, HTN, smoking increased risk of adverse events



# Medication Analogy

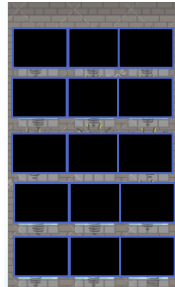
Building with all lights = overreactive immune system

- Eczema is one room
  - Want to turn off light in that room, *but not rest of the lights*



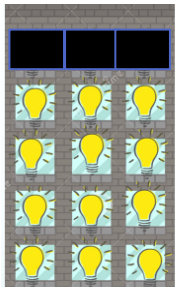
## 1. Systemic steroids

- Cut power to entire building
- Least specific



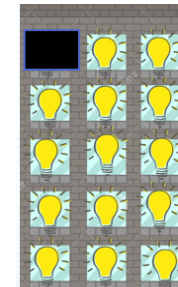
## 2. JAK Inhibitors

- Cut power to entire floor



## 3. Biologics

- Switch off light in room
- Most specific



# Emerging Therapies

Talk to your medical provider to see if it is appropriate and safe to participate in open clinical trials

- **Lebrikizumab**

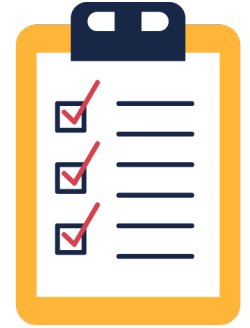
- Biologic
- IL-13 inhibitor injection
- Phase 3

- **Nemolizumab**

- Biologic
- IL-31 inhibitor injection
- Phase 3



# Key Points



- Systemic medications
  - Works on immune system to decrease inflammation
  - Reserved for moderate to severe eczema not responding to topicals
  - Not all suppress immune system
    - For example, dupilumab
- Biologics are most targeted therapy available
- JAK inhibitors
  - New “small molecule” agents: very potent, less side effects than older immune suppressing drugs
- New and emerging therapies are under investigation for moderate to severe eczema treatment



# Summary

- Goal:
  - Minimal eczema rashes
  - Less itch
  - Undisturbed sleep from itching or scratching
- Many ways to treat and control eczema
- Read more about eczema
  - [www.nationaleczema.org](http://www.nationaleczema.org)
  - Search “Rady” and “Eczema”
    - <https://www.rchsd.org/programs-services/dermatology/eczema-and-inflammatory-skin-disease-center>
- Reach goal by:
  - Using good skin care
  - Avoiding triggers
  - Using medicines regularly or as needed

**Eczema is complicated. Please reach out if you have any questions 😊**

