Drug Rashes and immunology: a primer

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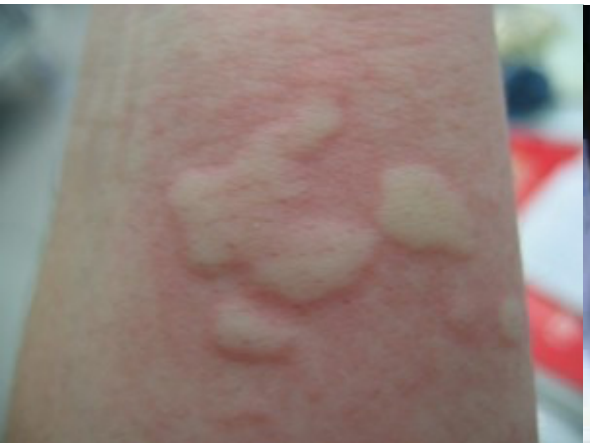
Disclosures

- I have nothing to disclose

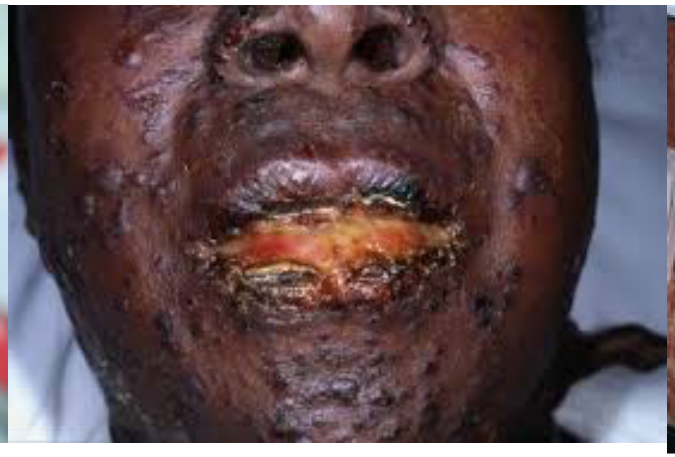
Learning Objectives

- Introduce Gell/Coombs classification of allergic reactions
- Focus on identifying Type I and Type IV reactions
- Become comfortable with identifying:
  - Hives/anaphylaxis/anaphylactoid type reactions
  - Stevens Johnson Syndrome
  - Delayed Maculopapular Exanthem
  - DRESS syndrome
  - Acute Generalized Exanthematous Pustulosis (AGEP)

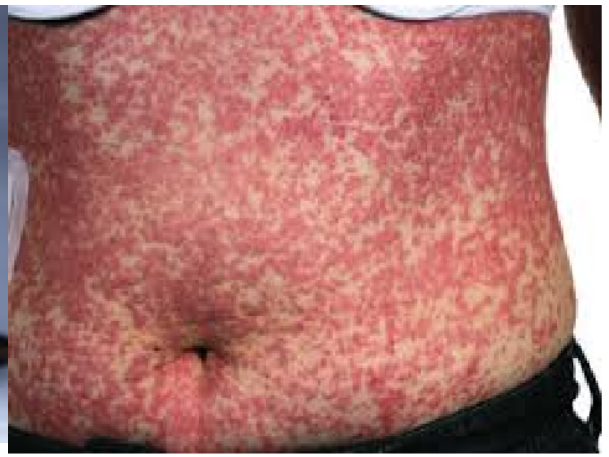
Learning Objectives



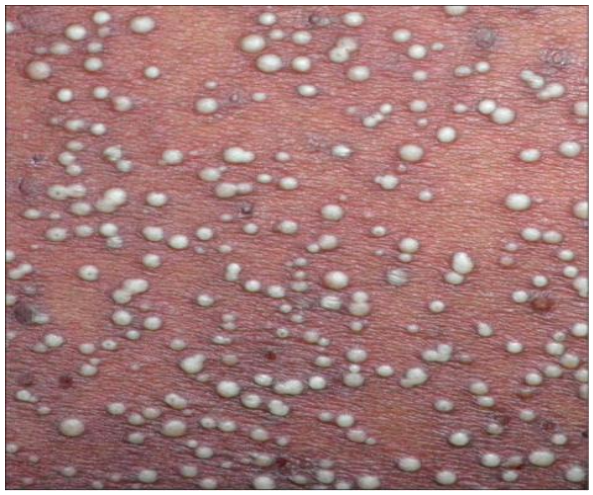
Urticaria



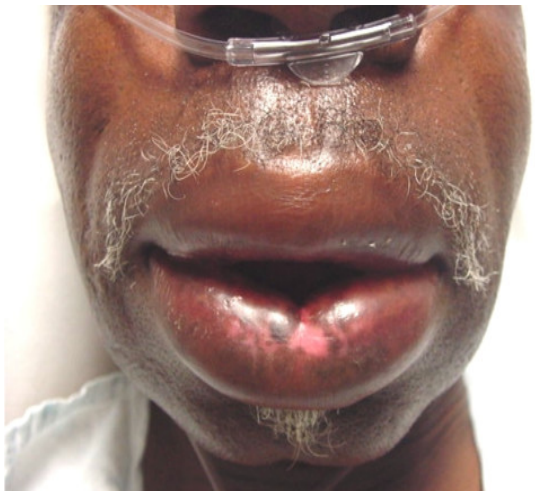
SJS/TEN



DRESS

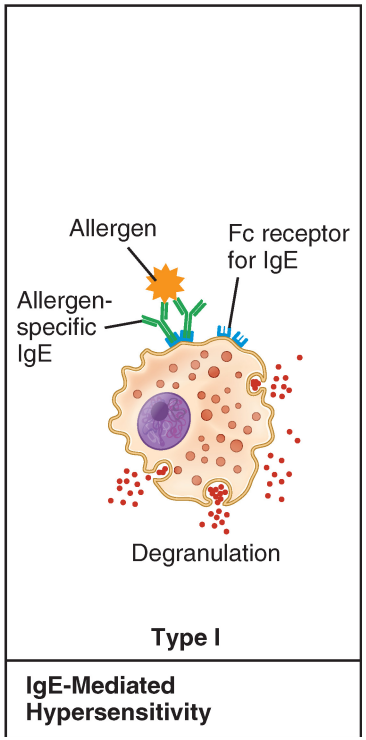


AGEP

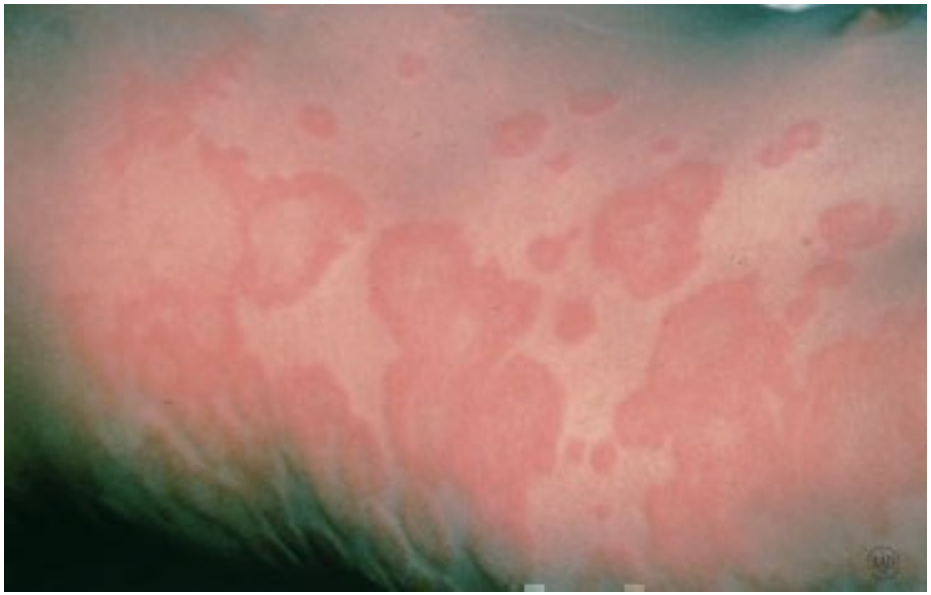


Angioedema

Gell/Coombs- A starting point to classifying allergic reactions



Rashes Caused By Mast Cells

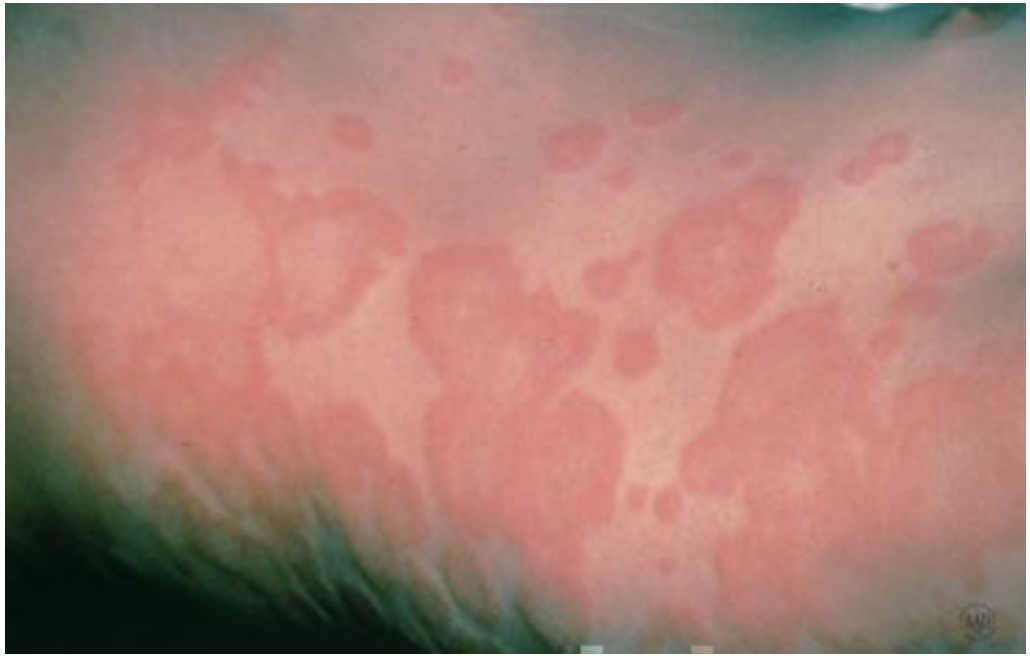


Hallmarks of Mast cell degranulation

- Fast-onset (within 1-2 hours, generally within 15 minutes)
- Itchy!
- Releases many chemicals (histamine)

Is it Urticaria? Are you sure?

- Quick onset
- Itchy
- “migratory”
- Generally antihistamine Responsive



Type I (IgE-Mediated) Hypersensitivity Reaction

- Two Exposures Required

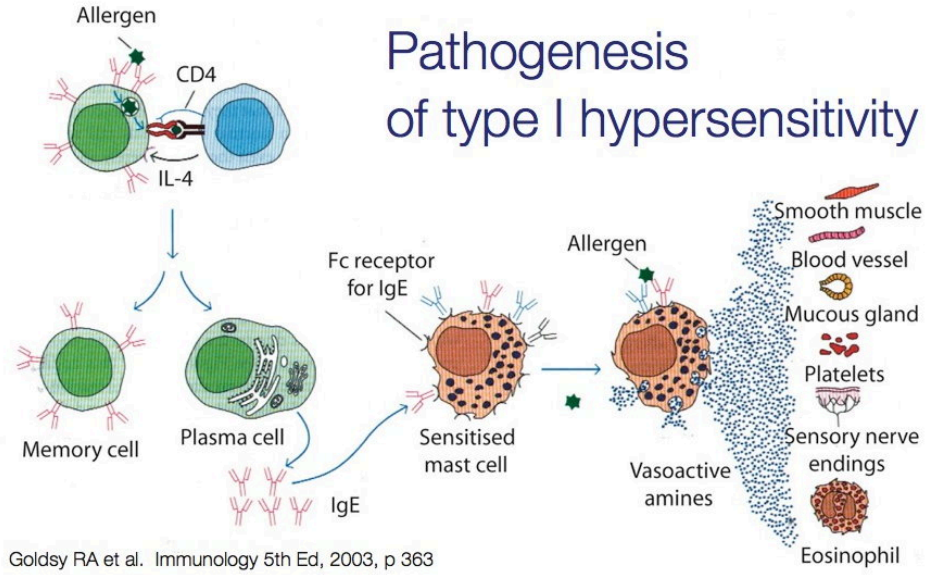
First Exposure

- Is NOT anaphylaxis

- The immune system, via T and B cells, creates IgE (allergy antibody)

Second Exposure

- Mast cell degranulation



Type I- Clinical Features

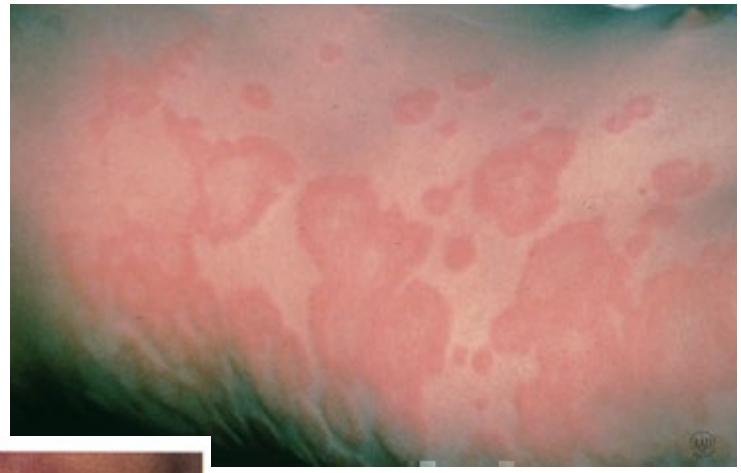
- Hallmarks of presentation

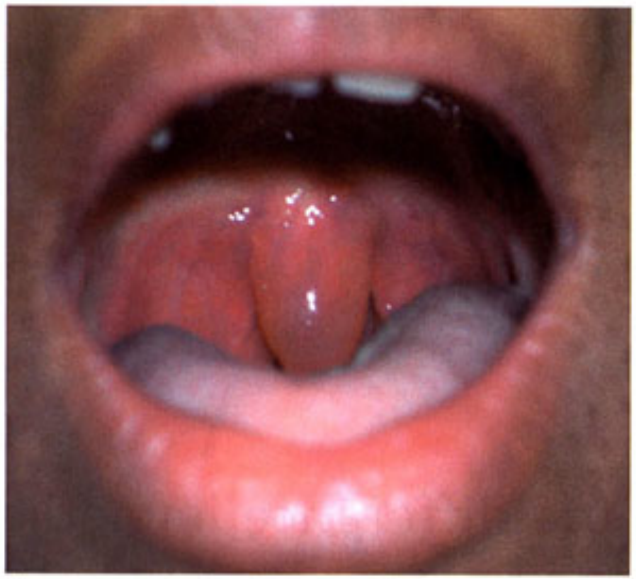
Increased Vascular Permeability

- Urticaria
- Palate and uvular swelling -> stridor
- Angioedema (hives of the dermis)
- Runny nose
- Abdominal pain or vomiting
- Hypotension

Increased Smooth Muscle Constriction

- Wheezing





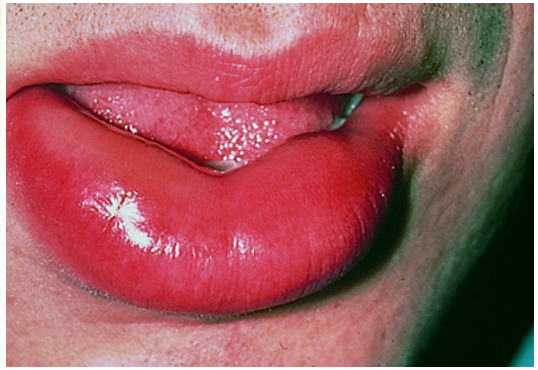
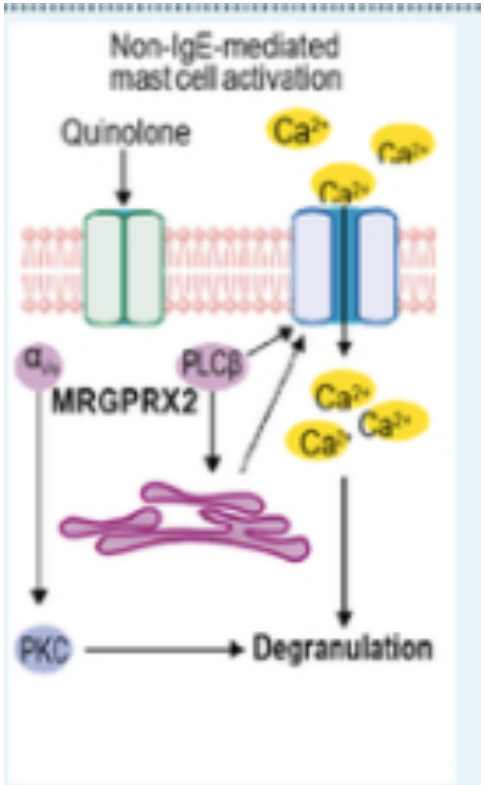
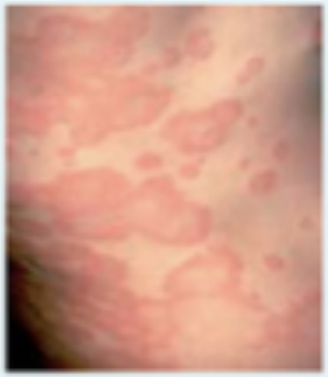


Figure. At presentation, the uvula is in the midline. The edema and erythema extend to the adjacent soft palate and tonsillar pillars.

Have you ever wondered why we don't rechallenge most drug "allergies" in the hospital but routinely do for vancomycin?





Fluoroquinolone urticaria

Non-IgE-Mediated Mast Cell Degranulation

- NO IgE
- Chemical property of medication leads to mast cell degranulation
- Allergy “look alike”
- Generally responds to a lower infusion rate and premedication of antihistamines

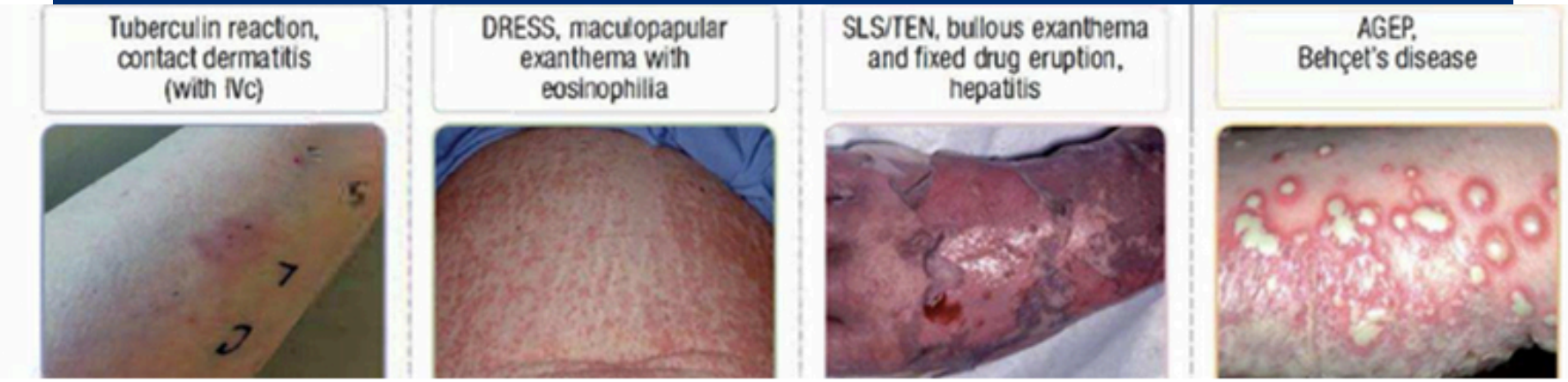
Lancet. 2019 Jan 12;393(10167):183-198. doi: 10.1016/S0140-6736(18)32218-9. Epub 2018 Dec 14.

Non-IgE mediated mast cell degranulation

- Vancomycin, opiates, contrast, fluoroquinolones, neuromuscular blocking agents

- Mast cell-mediated symptoms likely to be improved with premedication and lower infusion

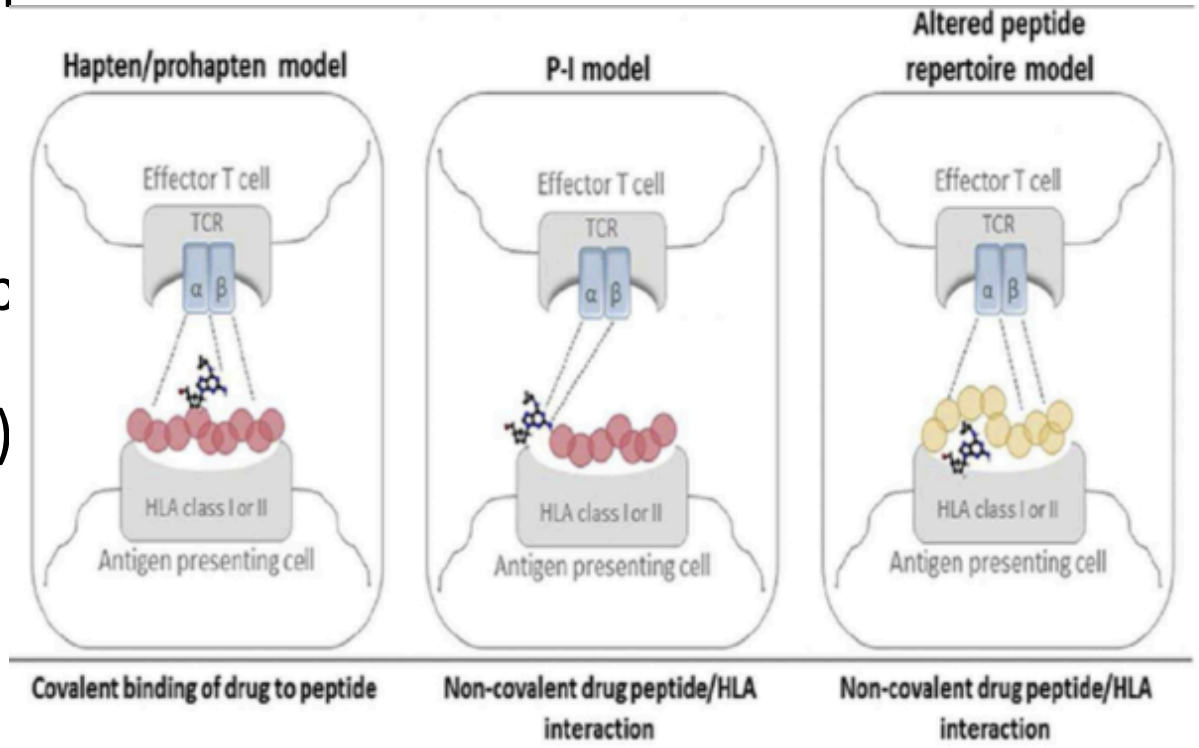
T-Cell Mediated Drug Reactions



J Allergy Clin Immunol. 2019 Jan; 143(1): 66–73.

What are T-Cells

- T-cells are the first step in creating a **specific** response towards fighting pathogens
- After being activated b presentation by dendritic cells (mainly) CD4+ T-cells release cytokines
  - Directs which cells become activated
- CD8+ T-cells directly kill infected human cells



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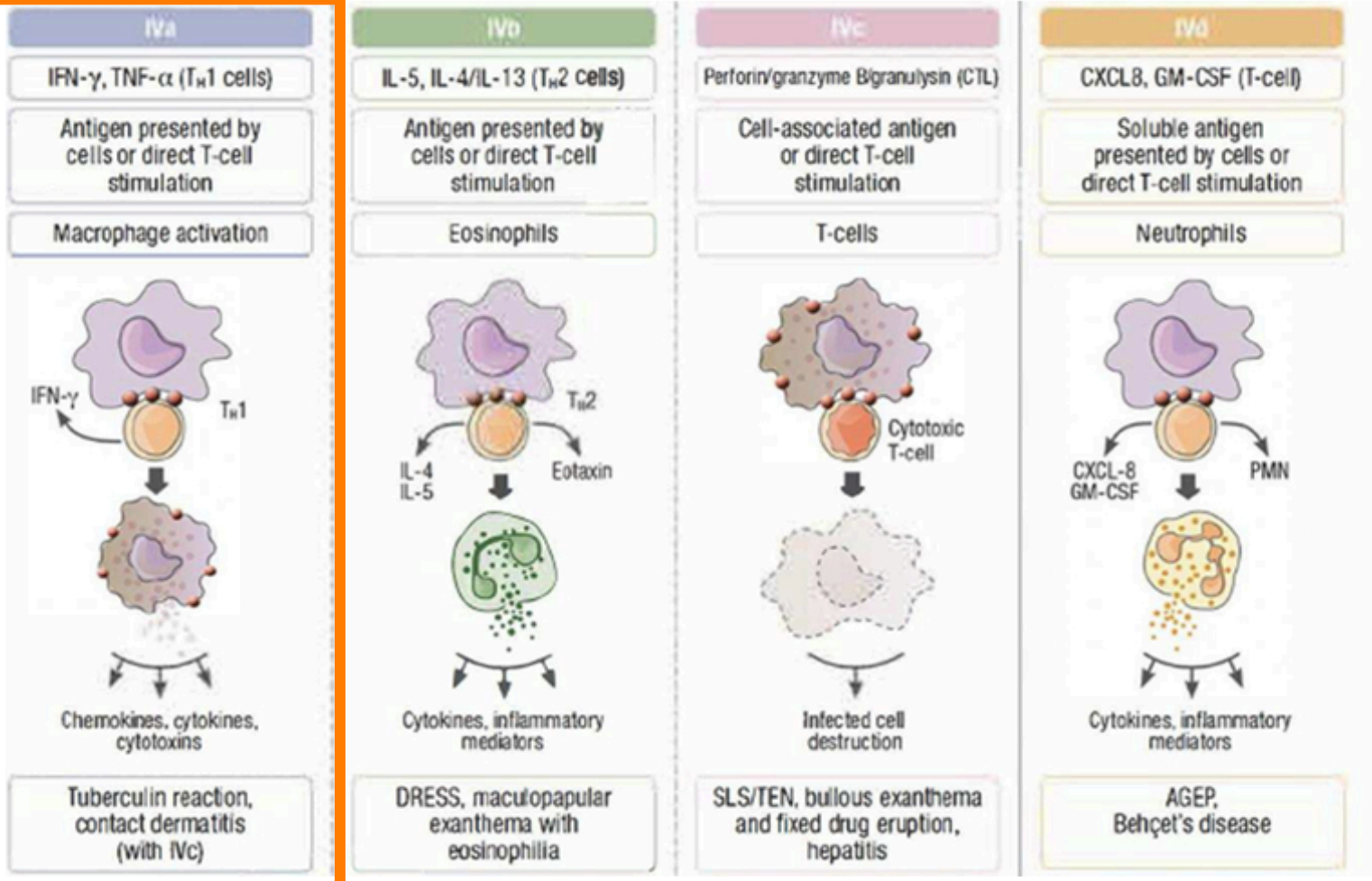
Hallmarks of T-Cell Mediated Reactions

- Slow Onset (variable, as quick as 2 days, but as late as 6 weeks after exposure)
- Can be itchy, but often burns
- Can be associated with damage to organs

Type IV Hypersensitivity Phenotypes



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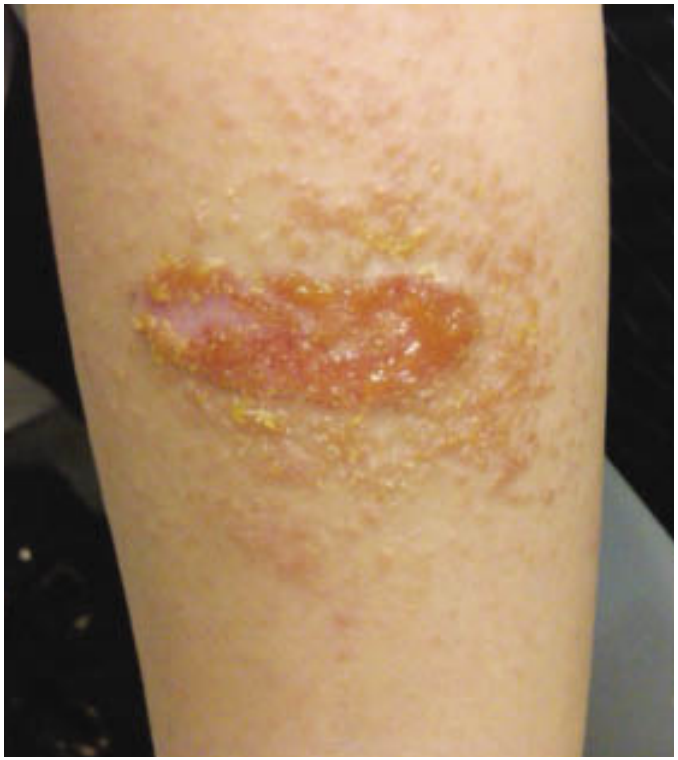
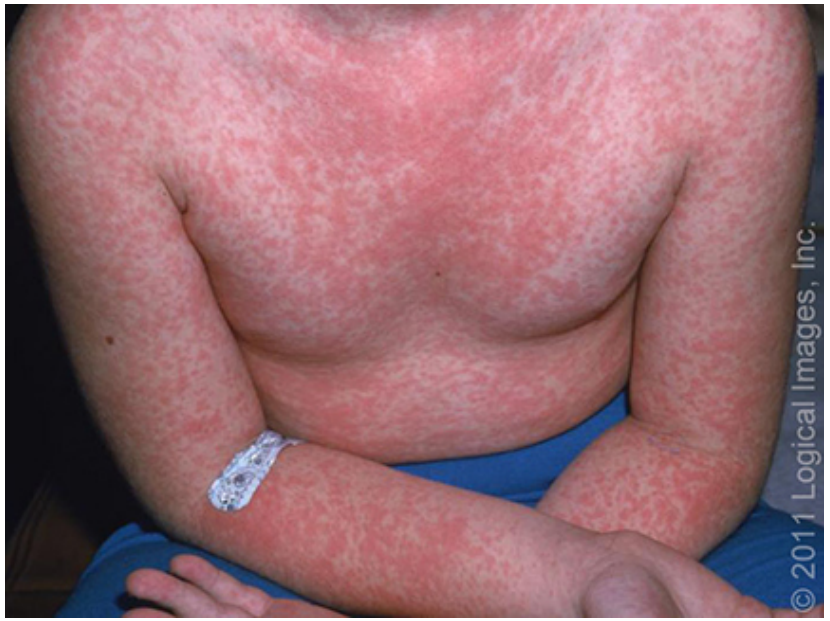


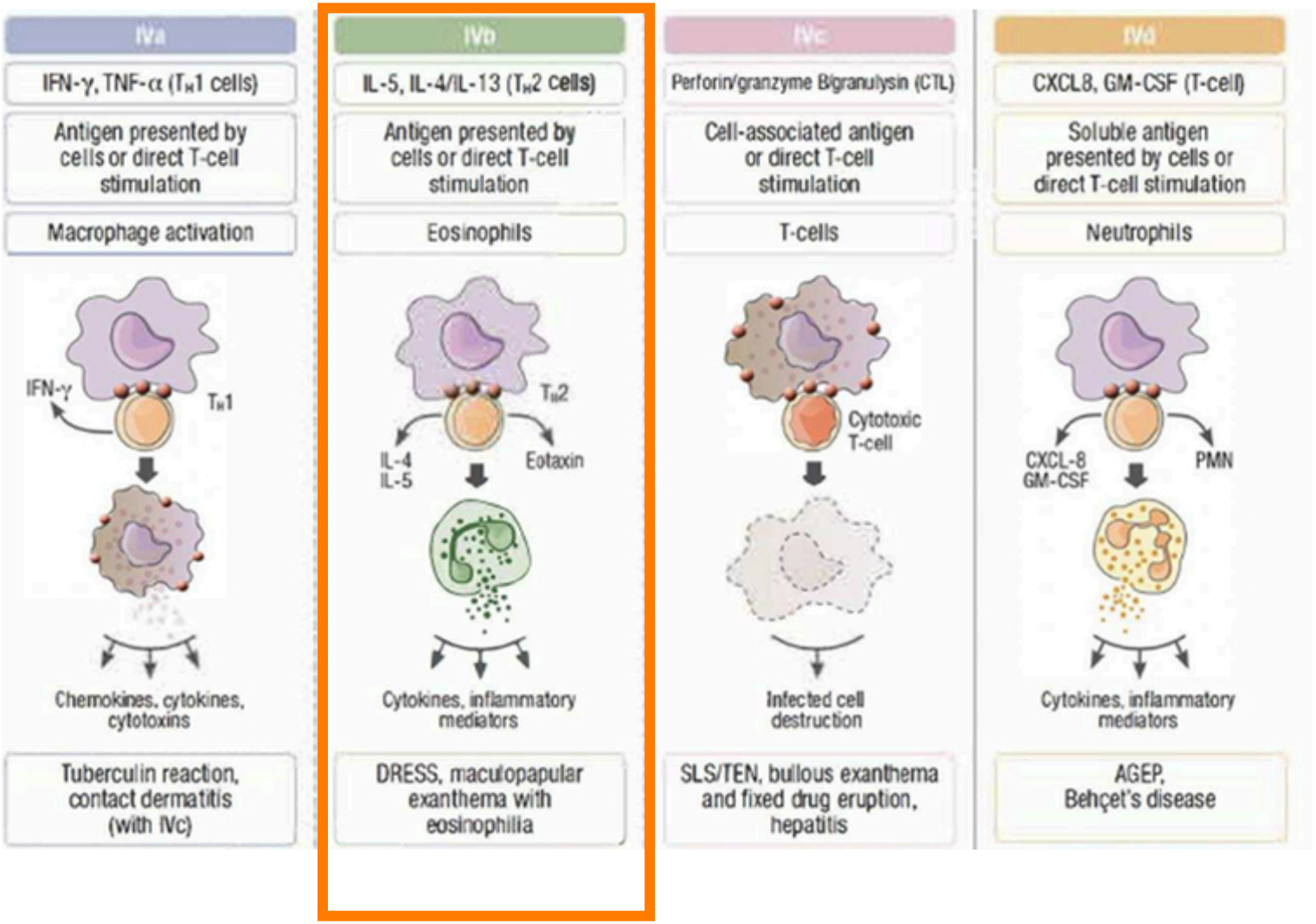
Contact Dermatitis



Maculopapular exanthem
"Drug Rash"

- Often self limited
- Often no associated organ damage
- Steroids will quicken the resolution

Type IV Hypersensitivity Phenotypes



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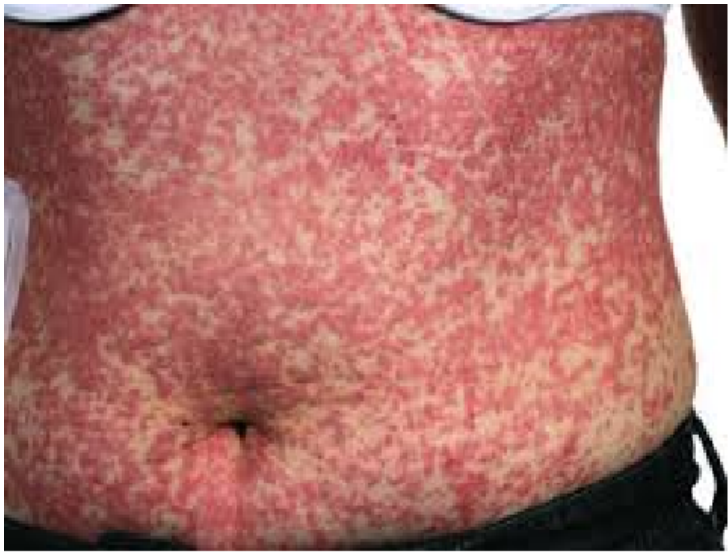
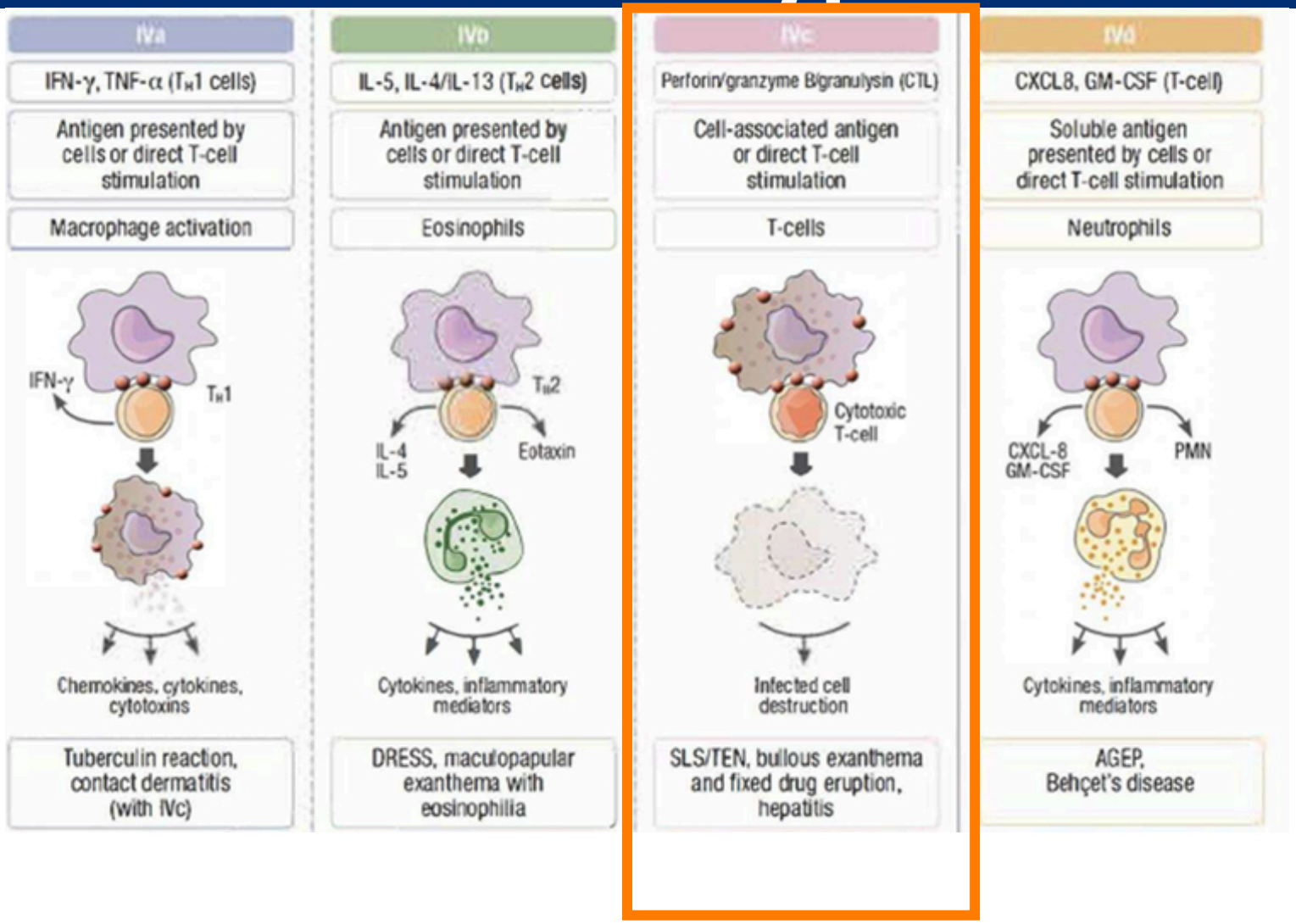
DRESS Syndrome

- Onset:2-4 weeks after starting med
- Clinical features: Rash (below), swelling (facial puffiness), fever, generalized lymphadenopathy
- Lab abnormalities: eosinophils, atypical lymphocytes seen on differential.
- End organ dysfunction: kidney, liver >>> thyroid, heart, CNS
- Treatment: Very high dose steroids, tapered slowly



Type IV Hypersensitivity Phenotypes



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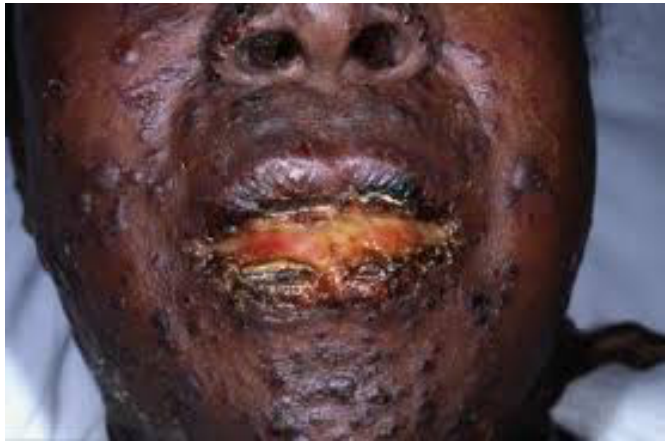
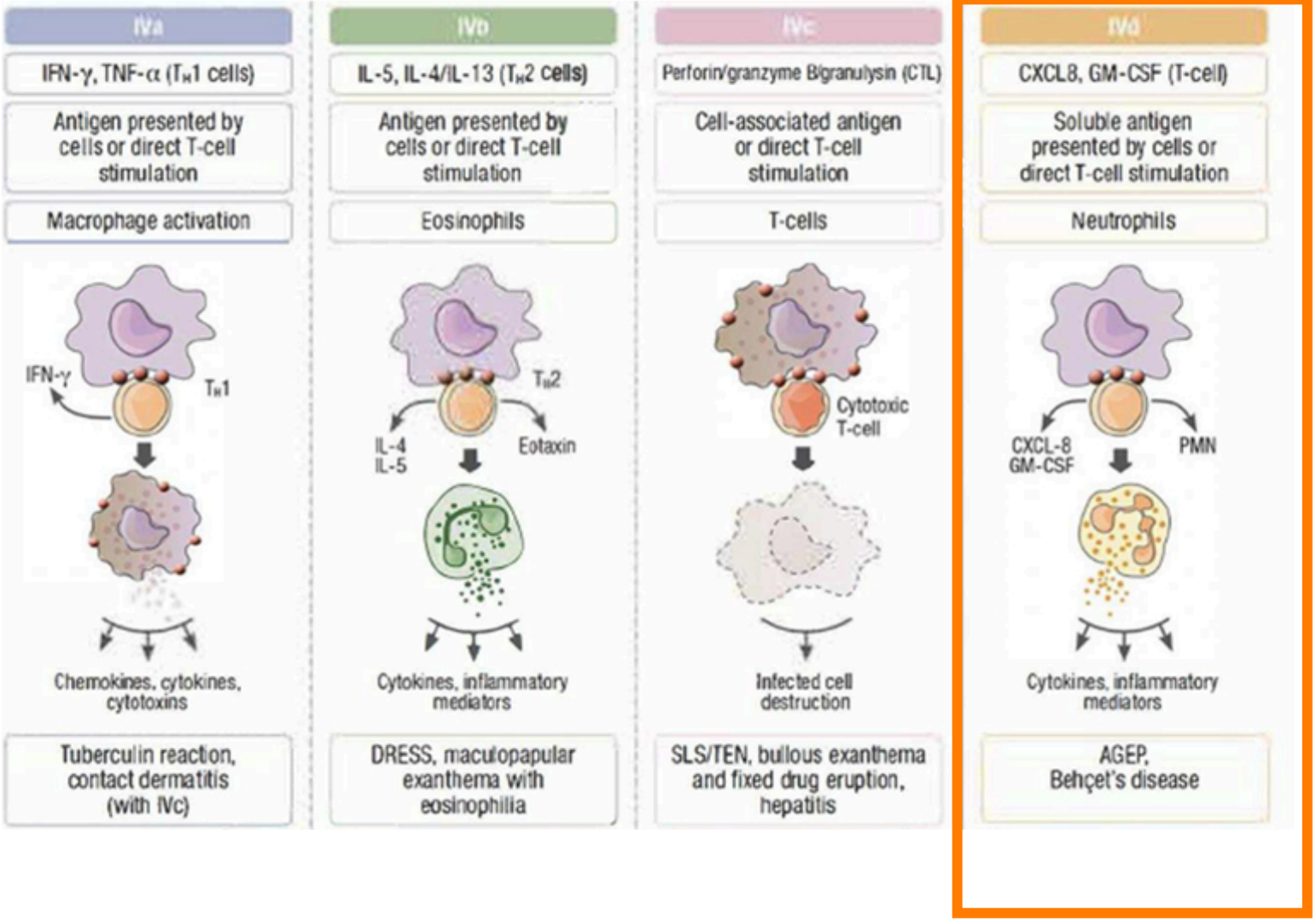
Stevens Johnson's Syndrome/ Toxic Epidermal Necrolysis

- Onset: <4 weeks, median onset around 1 week
- Clinical features: deep skin desquamation/mucosal erosion. Organ involvement common
- Lab abnormalities: infection common due to open skin, potential end organ dysfunction
- Treatment: transfer to skilled burn center



Type IV Hypersensitivity Phenotypes



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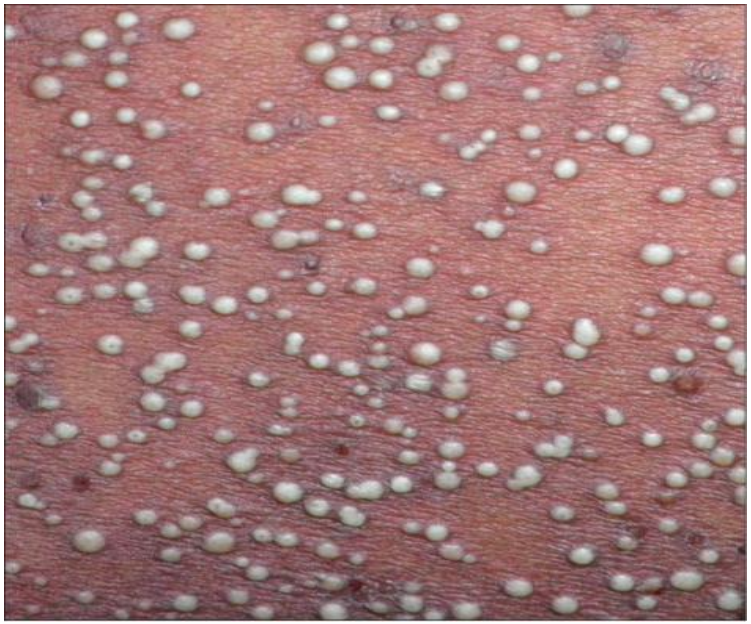
Acute Generalized Exanthematous Pustulosis (AGEP)

- Mean Onset: 1-2 days
- Clinical features: Skin with fine pustules. End organ dysfunction possible, but less common
- Lab abnormalities: neutrophilia
- Treatment: Topical or oral steroids, generally short course



T-Cell Mediated Skin Drug Reactions

- Morbilliform drug eruption
- Contact dermatitis
- DRESS Syndrome
- Toxic Epidermal necrolysis/SJS
- Acute Generalized Exanthematous Pustulosis (AGEP)
- T Cells, to the best of our knowledge, never forget… do not rechallenge DRESS, SJS/TEN, AGEP

Classes of drugs that are higher risk for T-Cell-mediated processes

- Note: any drug can theoretically cause this but these are higher risk:
  - Bactrim
  - Antiepileptics
  - Vancomycin
  - Allopurinol
  - NSAIDS
  - Lamotrigine

If you're not sure… we're here to help!

- Questions?

- Davidtc@uw.edu