2025 Rapids Clinical Insights

Thursday, April 10, 2025

Cytokines, Chemokines, Oh My… (Peter Lio, MD, and Douglas DiRuggiero, PA-C)

1. Cytokines are small secreted proteins released by cells that have a specific effect on the interactions and communications between cells. Autocrine (act on self), Paracrine (act on nearby), Endocrine (act on distant).

2. Cytokines are messenger proteins that tell other cells what to do, while chemokines are like shepherds that guide immune cells to their proper locations using chemotaxis.

3. Cytokines can be anti-inflammatory or pro-inflammatory

Yellow Brick Road to PsO/PsA - Why I Choose Which Path (Monica Richey, NP and Christopher Sayed, MD

1. Psoriasis comorbidities: cardiometabolic risks, mental health/suicidality, solid organ and lymphoma cancers, inflammatory bowel disease (IBD), and chronic obstructive pulmonary disease (COPD).

2. Psoriatic arthritis is one of the spondyloarthropathies: Ankylosing spondylitis, IBD, reactive arthritis, and spondyloathropathy.

3 Psoriatic arthritis in rheumatology follow GRAPPA guidelines as treating them is also trial and error and many times needs more than one medication to treat their disease.

Connective Tissue Diseases for the Derm Provider (Monica Richey, NP)

1. Systemic Lupus Erythematosus presentations can include malar rash, discoid, photosentivity (can be very severe), oral ulcers (could be just one), subacute cutaneous lupus (skin of color can look like psoriatic), lupus profundus/panniculitis, livedo reticularis

2. If you suspect bullous lupus, make sure you are doing DIF studies with a dermatopathologist to accurately differentiate between bullous pemphigoid and bullous lupus.

3. CREST: Calcinosis, Raynaud's Esophogeal dysmotility, Sclerodactyly, telangiectasias

4. While Scleroderma is angiopathy (problems with the blood vessels), dermatomyositis affects the muscles with elevated muscle enzymes.

<u>The Wizard of HS (Christopher Sayed, MD)</u>

1. Pathogenesis of HS: Chronic inflammatory disease of the follicles, Hyperkeritinization creates blockage of follicle, rupture and release of inflammatory debris into the dermis, then causes tunnels filled with debris.

2. Adaptive immune response is likely to blame. Gamma-secretase / notch signaling can be inflammatory through Th-17, JAK/STAT, and inflammasomes. SOX9 is a gene transcription factor that may be involved.

3. Pipeline of HS: Povorcitinib (oral JAK1 inhib), sonelokimab (IL-17A and IL-17F Nanobody), Remibrutinib (BTK inhibitor), Anakinra and MEDI8968 (IL-1 antagonist), Canakinumab (IL-1beta), Bermekimab (IL-1alpha…study was terminated), Orismilast and Apremilast (PDE4 inhibitor), IL-23s don't seem to be helpful, AND Complement C5a: vilobelumab, avacopan.

<u>Gut Skin Connection Part 1 (Douglas DiRuggiero, PA-C and Kimberly Orleck, PA-C)</u>

1. Our gut is a massive endocrine and immune organ that impacts illness development and the progression of disease.

2. The mesenteric (gut) epithelium should have tight junctions between the epithelial cells. In Leaky Gut Syndrome, the damaged junctions allow increased intestinal permeability, which leads to immune dysregulation.

3. The microorganisms that live inside and on humans are known as our microbiota. These microorganisms are estimated to outnumber human somatic and germ cells by a factor of ten.

<u>Gut Skin Connection Part 2 (Douglas DiRuggiero, PA-C and Kimberly Orleck, PA-C)</u>

1. IBD: Crohn's Disease and Ulcerative Colitis are chronic inflammatory autoimmune conditions of the GI tract. About 40-50% of these patients will have extra Intestinal manifestations like Erythema Nodosum, Pyoderma Gangrenosum, Sweets syndrome, Apthous ulcers, Cutaneous Crohns and of course Psoriasis

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2. ALL patients with IBD should have skin cancer surveillance, especially those with current or past thiopurine use.

3. 90% of patients with Dermatitis Herpetiformis have celiac disease, but only about 10-15% of celiac patients have DH (grouped papules and vescicles often on extesor surfaces caused by the deposit of IgA in the skin.

Friday, April 11, 2025

Type 2 Inflammation (Douglas DiRuggiero, PA-C)

1. IL-4 is involved in the immune response to parasitic Infections, and allergic diseases. IL-4 binds to Type 1 receptors on hematopoietic cells to convert Th0 cells into Th2 cells. Promotes B cells to switch class to IgE production. Enhances basophil cytokine production.

2. IL-13 increases mucous secretions, increases muscle contraction in the gut, and promotes epithelial barrier repair (enhances IgE, which increases allergic responses. IL-13 also drives M2 macrophages (which help contain parasites and promote tissue repair), enhances eosinophil & mast cell response, AND inhibits Type 1 Immunity (to prevent excessive inflammation- suppresses Th1 and IFN-gamma responses.

3. IL-31 induces itching (by activating sensory neurons), regulates inflammation in barrier tissues (by recruiting monocytes and T cells), and has a role in parasitic defense.

Atopic Triad - The Common Connection (Amanda Michaud, PA-C and Peter Lio, MD)

1. Patients with Atopic dermatitis will have another atopic condition: ⅓ of patients develop asthma, ⅔ develop allergic rhinitis. Atopic march can occur at any age.

2. Allergy can either be Immediate (IgE mediated = Type I) or Delayed (cell mediated = Type IV). IgE mediated reactions occur EVERY time the patient is exposed to the allergen, demonstrates IgE antibodies, occurs at a predictable time after exposure (usually 10-60min), and requires sensitization.

3. Allergy testing is NOT diagnostic; it stratifies risk. Testing includes: Intradermal testing / Skin Prick (intradermal exposure with allergens, most useful for lower potency allergens, look at the sections of reactions like environmental or drug/food); Immunocap / RAST (Specific IgE testing, when "high or very high" consider referral for immunotherapy)

HS Medical and Surgical Management (Christopher Sayed, MD)

1. Treatment of HS should be based on the Hurley Staging: Hurley stage I - Medical treatment, counseling on weight reduction, wound management, avoidance of triggers, tobacco cessation, etc. Hurley Stage II - Medical treatment with Biologics, NdYag laser, Deroofing/ surgical procedures, etc. Hurley Stage III - everything including wide local excision.

2. Aggressive medical therapy reduces pain, drainage, and new lesions, BUT tunnels do NOT resolve with medical therapy alone. So use medical management as a bridge to surgery.

3. If patients have localized disease, offer localized treatment with ILK and I&D without packing and deroofing. Providers may have to collaborate with Plastic surgeons, general surgeons, or reconstructive urologists for groin/genital lesions.

Beyond Antihistamines - Targeted Therapy in CSU (Amanda Michaud, PA-C)

1. Chronic Spontaneous Urticaria= non-inducible, recurrent wheals that last <24 hrs +/- angioedema >/= to 6 weeks

2. CSU pathophysiology includes Type 1 autoimmunity (autoallergy) driven by IgE antibodies and Type IIb autoimmunity (autoimmune) induced by IgG autoantibodies. This Type IIb autoimmunity leads to Type 2 inflammatory response, Mast cell and B-Cell activation. Other endotypes include concomitant type I and type IIb, and NON-type I/IIb.

3. Up to 30-60% of patients remain uncontrolled despite omalizumab. If they have elevated IgE, it is likely Type I (autoallergic) and will likely be responsive to omalizumab. If NO response to omalizumab within 6 months, cyclosporine 5mg/kg is recommended.

Inflammatory Cytokines in Acne and Rosacea (Hillary Baldwin, MD)

1. Etiologies are not fully understood, but both involve innate and adaptive immunity. IL-1beta and TNF-mediated inflammation activate Th1/Th17 cells and the resultant release of cytokines and activation of mast cells.

2. Rosacea triggers activate receptors (PAR2 and TLR-2 and channels on cells which lead to induction of the inflammasome and release of TNF-alpha, and IL-1.

3. Early acne= activated sebocytes,and keratinocytes upregulate IL-1b, IL-6(induce differentiation of Th17 cells), IL-12(drives Th1 differentiation) , and TGFb. Overproduction

of IL-17 and activation of Th17 cells have been shown to underlie the development of acne.

Itch Scratch Cycle - Neuro Immune Pathway (Peter Lio, MD)

1. There are two totally separate subtypes of itch-sensitive neurons: Histaminergic neurons and non-histaminergic neurons.

2. 4 categories of itch: Dermatologic (eczema, psoriasis), Neuropathic (brachioradial pruritis), Psychogenic (delusions of parasitosis), and Systemic (end-stage renal disease)

3. The treatment of itch should be based on etiology. The treatment ladder should include: Topicals, then "safe" systemics, then more powerful systemics, then alternatives (including accupressure, hypnosis, mindfulness, and cryotherapy, to name a few.

Phenotypes in Prurigo Nodularis (Douglas DiRuggiero, PA-C)

1. Prurigo Nodularis often has other related comorbidities, most commonly atopic dermatitis, due to the shared Th2 Cytokines: IL-4, IL-5, and IL-13

2. Prurigo Nodularis occurs in all age groups, but median age =62, NO gender predilection, but in the US, it is ~3 times more common in African Americans

3. The lesions CAUSE itch; they are NOT just the result of picking. There has been an increased number of nerve fibers found in the papillary dermis of PN lesions, and nerve growth factor (NGF) is overexpressed

Dermato-Allergy Panel - Cases from the Clinic (Marc Serota, MD, Peter Lio, MD, and Amanda Michaud, PA-C)

1. For patients with combined Atopic Dermatitis and Asthma, consider Dupilumab first since it has both indications…if not enough clinical improvement it is unlikely that the IL-13s will help. Consider switching to IL-31 or JAK inhibitors for a different mechanism of action.

2. There are now multiple 'non-steroidal' options for Mild to severe atopic dermatitis that can be used for flares or maintenance. Create an "Eczema Action Plan" with exact steps on when to apply what medications.

3. For patients with severe pruritis and increased eosinophils, consider HES: Hypereosinophillic Syndrome. About 50% of cases are idiopathic, but important to exclude secondary cases. Patients need treatment if symptomatic or have signs of end organ damage. Mepolizumab is an anti-IL-5 monoclonal antibody approved for patients with HES > 6 months for patients 12 and up.

Saturday, April 12, 2025

Pathophysiology and Impact of Alopecia Areata (Arash Mostaghimi, MD)

1. Pathophysiology of Alopecia areata: Cytotoxic (CD8+ + CD4+) T lymphocytes attack hair follicles, INF-gamma induces catagen, and IL-15 activates and maintains T-cell inflammation.

2. Evolved thinking in Alopecia is that the Th2 process may play a strong role since a common co-morbidity is Atopic dermatitis in 30-40% of patients.

3. Multiple comorbidities: Atopic Dermatitis, Autoimmune disease, Cardiac conditions, Cancer, Anxiety, Depression, Sexual side effects, bullying

All I Want to Do Is Grow My Patient's Hair (Arash Mostaghini, MD)

1. Beyond patchy disease…JAKs are the only good choice for treatment. Start baricitinib at 4mg, not 2mg. Stick with one of the JAKs and gain familiarity with it. The safety profile is good, but take a good medical history for malignancy risk and clotting risk.

2. For patchy disease, most are self-limited, with 30-50% spontaneous resolution at 1 yr. Follow the patient's lead on how/if they want to treat. Intralesional steroids are the standard of care for patchy disease, need repeated (4-6) treatments, 4-6 weeks apart, and can be combined with other meds.

3. Minoxidil data is limited, but it is inexpensive. Typical dosing is 2.5mg in men and 1.25mg in women. The major side effect is hirsutism and shedding with withdrawal.

Pediatric Management of Alopecia Areata (Lisa Swanson, MD)

1. Three possible courses for Alopecia Areata in kids: It's a one-time fluke, OR after regrowth, the hair is lost every few months or few years and cycles, OR Alopecia progresses to losing ALL of the hair = totalis or universalis (only 2% of kids with alopecia areata).

2. Treatment options in kids: Topical clobetasol + topical 5% minoxidil, Vitamin D3 and fexofenadine, Pulse Prednisone 5-10 MG/KG one weekend a month, low dose oral minoxidil, contact sensitizers like Squaric acid, and Oral JAK inhibitor-Ritlecitinib = 12 yrs and up.

3. Baricitinib and Deuruxolitinib are only indicated for age 18 and up

<u>Immunology of Vitiligo (Lisa Swanson, MD)</u>

1. The pathogenesis of Vitiligo is autoimmune. CD8+ T cells mediate the destruction of the melanocytes. INF-gamma, IL-2, and IL-5 all signal through the JAK/STAT pathway.

2. Vitiligo-associated conditions include Thyroid disease (Hashimoto's and Graves women), Morphea, Psoriasis, Atopic Dermatitis, Alopecia Areata, and Rheumatoid Arthritis.

3. It can be triggered by psychological stress, oxidative stress, toxins, chemical exposure, UV radiation, Medications, Viral infections/vaccinations, or a genetic propensity

<u>How I Counsel a Patient with Vitiligo (Lisa Swanson, MD and Stephaine Simmerman, NP)</u>

1. Assess the PATIENT'S wishes for treatment. Treatment goals=halt progression, re-pigment skin, maintain repigmentation, and make your patient happy.

2. Topical Ruxolitinib is the only FDA-approved topical treatment for ages 12 and up. It works best in sun-exposed areas. Takes time, so BE PATIENT! Combine it with Polypodium Leucotomas.

3. After repigmentation, there is a 30-40% chance of recurrence. Using tacrolimus 0.1% BID 2 days/week can reduce that to a 5-10% risk.

<u>Panel: JAK Inhibitors (Peter Lio, MD)</u>

1. JAK inhibitors present an alternative to Oral corticosteroids which are immunosuppressant. The JTF and AAD guidelines conditionally recommend AGAINST steroids because of a LOW certainty of evidence, and should only be used short term.

2. JAK Targets: Abrocitinib and Upadacitinib block JAK1, Baricitinib and Ruxolitinib block JAK1&2, Delgocitinib blocks JAK1, JAK2, JAK3, and TYK2.

3. Abrocitinib 200mg daily and Upadacitinib 30mg daily may be associated with better scores than Dupilumab (adult dose) in head-to-head trials.

Is There Still a Place for Traditional Immunosuppressants? (Jennifer Soung, MD)

1. Methotrexate Clinical Pearls: can be combined with biologics to reduce immunogenicity, caffeine can reduce adverse symptoms, dont forget folic acid supplementation

2. Cyclosporin Clinical Pearls: Limit use to SHORT periods for quick improvement; avoid using >2 years, which will increase the chance of kidney failure; NOT as safe as biologics

3. Absolute contraindications for Methotrexate: pregnancy, Nursing, Alcoholism, Immunodeficiency, severe anemia/leukopenia/thrombocytopenia/bone marrow hypoplasia.

RAPID Fire Clinical Pearls in Immuno-Dermatology (Peter Lio, MD)

1. A written EAP (Eczema Action Plan) had been proven better than the verbal instructions given for patient and parent education on AD, understanding the treatment regimen, and adjusting medications based on severity and anatomic location.

2. Patients want alternative treatments: Black tea compresses for facial dermatitis, Fish Oil for Psoriasis, and Garlic for Warts

3. The Mind/Body connection is strong: HRT=Habit reversal therapy for eczema, mitigating needle phobia with: distraction, relaxation, behavioral therapy, vibration, hypnosis or topical anesthetic

Sunday, April 13, 2025

What's on the Horizon: Other Potential Targets (Justine Love, PA-C and Jennifer Soung, MD)

1. There are many drugs currently in Phase 2 for AD, including two "Triple threat" tri-specific monoclonal antibodies…one targeting IL-4/13/TSLP and one targeting IL-4/13/33, plus ANti-OX40, TPD=targeted protein degradation, TSLP-epidermal cytokine, Anti-IL-22RA-1-IL-20 cytokine blockers, etc.

2. There are multiple ORAL drugs in Phase 2 and 3 for PsO: Oral TNFR1, Oral S1PR1-G proteins, Oral IL-23 receptor antagonist peptide, Allosteric inhibitor of TYK2, and Oral PDE-4 inhibitor.

3. CSU has a number or oral drugs in their Phase 2/3 development, including a few oral BTK inhibitors, JAK-1 inhibitor, and MRGPRX2-targeting Mast cells. Plus an Anti-KIT monoclonal antibody

<u>Obesity and Inflammatory Skin Disease (Jennifer Soung, MD)</u>

1. The GLP-1 agonists (Liraglutide, Semaglutide, and Tirzepatide) have been a game-changer in weight loss management. They mimic the incretin hormone which is released in the GI tract in response to eating to control appetite and metabolism.

2. Adipose tissue releases adipokines and pro-inflammatory cytokines that contribute to psoriasis development. Obesity increases the severity of PsO PGA or PASI.

3. Both Psoriasis and Obesity share the common pathways with overproduction of TNF-alpha, IL-17, IL-23, and IL-6. The GLP1-agonist Liraglutide has been shown to reduce the expression of IL-17, IL-23, and TNF

<u>Why is it Named That? What Can Drug Names Tell You? (Jennifer Soung, MD)</u>

1. Biosimilars are NOT just generics of the available Biologics on the market. Since they are manufactured from living systems, some inherent variation is expected within each lot.

2. INN (International Nonproprietary Names) nomenclature is changing and discontinuing the use of the stem "-mab" because the meaning was not always clear and being used for a variety of small immunoglobulins to large molecules.

3. The FOUR NEW stems are "-tug" for unmodified immunoglobulins, "-bart" for artificial immunoglobulins, "-ment" for immunoglobulin fragments, and "-mig" for multi-specific immunoglobulins

<u>Name That Cytokine - Kodachromes in Immunology Championship (Martha Sikes, PA-C)</u>

1. Psoriasis Gut Microbiome: Psoriasis patients have a higher abundance of Fimicutes, lower amounts of Bacteroidetes, higher E. Coli, and a higher prevalence of Candida. Patients can reduce Candida colonization with dietary coconut oil and high-protein, fatty acid, and amino acid diets.

2. In ‘Leaky Gut’ there is increased intestinal permeability and bacterial surface molecules, called endotoxin (LPS=Lipopolysaccharides), which result in increased IL-6, IL-1alpha, IFN-gamma, triglycerides, and insulin. This leads to Food Intolerance and Immune Dysregulation, which leads to an increased risk of a variety of chronic diseases.

3. Generalized Pustular Psoriasis is linked to a deficiency of IL-36 receptor antagonism due to IL-36RN gene mutation and can be linked to inflammatory liver, kidney, joint, and eye disease