Top 5 Tips to be in the Know!

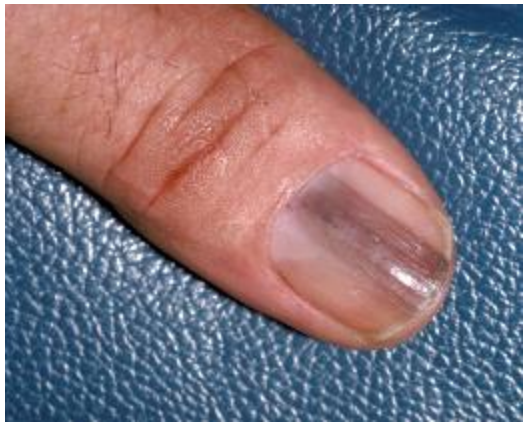
Dermatology Updates

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#5 – New Melanoma Guidelines

- The American Joint Committee on Cancer (AJCC) updated the staging system for classification of melanoma.
- 8th edition.
- Background: the AJCC is a classification system developed by the for describing the extent of disease progression in cancer patients. It utilizes in part the TNM scoring system: Tumor Size, Lymph Nodes affected and metastases.







AJCC Melanoma of the Skin Staging 8th Edition

Definitions

Primary Tumor (T)

- TX: Primary tumor cannot be assessed (for example, curettaged or severely regressed melanoma)
- T0: No evidence of primary tumor
- Tis: Melanoma in situ
- T1: Melanomas 1.0 mm or less in thickness
- T2: Melanomas 1.1 - 2.0 mm
- T3: Melanomas 2.1 - 4.0 mm
- T4: Melanomas more than 4.0 mm

NOTE: a and b subcategories of T are assigned based on ulceration and thickness as shown below.

T Category	Thickness (mm)	Ulceration Status
T1	≤1.0	a: Breslow < 0.8 mm w/o ulceration b: Breslow: 0.8-1.0 mm w/ ulceration or 1.0 mm w/ ulceration
T2	1.1-2.0	a: w/o ulceration b: w/ ulceration
T3	2.1-4.0	a: w/o ulceration b: w/ ulceration
T4	>4.0	a: w/o ulceration b: w/ ulceration

Regional Lymph Nodes (N)

- NX: Regional lymph nodes cannot be assessed (for example, previously removed for another reason)
- N0: No regional metastases detected
- N1-3: Regional metastases based on the number of metastatic nodes, presence of in-transit metastases, satellites without metastatic nodes, and presence of microscopic vs macroscopic disease

NOTE: N1 and N2 subcategories assigned as shown below.

N Category	# Nodes	Clinical/Occult/Microscopic/Imaging Status
N1	One node	a: clinically occult[1], no MSI[2] b: clinically detected[1], no MSI c: 1 node, MSI present[2]
N2	Two to three nodes	a: 2-3 nodes clinically occult[1], no MSI[2] b: 2-3 nodes clinically detected[1], no MSI[2] c: 1 node clinical or occult[1], MSI present[2]
N3	≥4 nodes	a: ≥4 nodes, all clinically occult[1], no MSI[2] b: ≥4 nodes, ≥1 clinically detected or matted, no MSI[2] c: ≥1 nodes clinical or occult[1], MSI present[2]

Distant Metastasis (M)

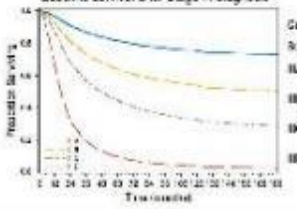
- M0: No detectable evidence of distant metastases
- M1a: Metastases to skin, subcutaneous, or distant lymph nodes
- M1b: Metastases to lung
- M1c: Metastases to all other visceral sites
- M1d: Metastases to CNS

NOTE: Serum LDH is incorporated into the M category as shown below.

M Classification	Site	Serum LDH
M1a-d	Skin/subcutaneous/distant nodal [a]; lung [b]; other visceral [c]; brain [d]	Not assessed
M1a-d(0)	Skin/subcutaneous/distant nodal [a]; lung [b]; other visceral [c]; brain [d]	Normal
M1a-d(1)	Skin/subcutaneous/distant nodal [a]; lung [b]; other visceral [c]; brain [d]	Elevated

ANATOMIC STAGE/PROGNOSTIC GROUPS

	Clinical Staging			Pathologic Staging[3]			
Stage 0	Tis	N0	M0	0	Tis	N0	M0
Stage IA	T1a	N0	M0	IA	T1a	N0	M0
Stage IB	T1b				T1b		
	T2a			IB	T2a		
Stage IIA	T2b	N0	M0	IIA	T2b	N0	M0
	T3a				T3a		
Stage IIB	T3b			IIB	T3b		
	T4a				T4a		
Stage IIC	T4b			IIC	T4b		
Stage III	Any T	≥N1	M0	IIIA	T1-2a	N1a	M0
					T1-2a	N2a	
				IIIB	T0	N1b/c	M0
					T1-2a	N1b/c	
					T3a-3b	N1b	
					T3a-3b	N1a-2b	
				IIIC	T0	N2b/c	M0
					T1	N2b/c	
					T1b-2b	N2a-2c	
					T2b-4a	Any N	
					T4b	N1a-2c	
				IIID	T4b	N2a-c	M0
Stage IV	Any N	Any M	M0	IV	Any T	Any N	M1



Conditional 5-year survival (%):

Stage	Baseline	5y survivors
IIIA	81.4	83.1
IIIB	64.0	76.0
IIIC	44.5	66.7
IIID	9.8	40.6

Notes

[1] Nodes are designated as "clinically occult/detected" if they are not pathologically examined and are confirmed by imaging (ultrasound, CT, PET, MRI) or clinical exam.

[2] MSI = microscopic satellite, in-transit, or regional metastasis.

[3] Pathologic staging is based on histopathologic examination of the primary melanoma and the regional lymph node dissection or biopsy. At least one lymph node must be examined to assign a pathologic stage. Pathologic staging is used to assign patients to adjuvant therapy trials.

[4] Gershenwald JE, et al. Journal of Clinical Oncology. 2016.

Produced by the 8th ed. AJCC Melanoma Staging Committee and the American Joint Committee on Cancer

Change in T1 classification of Melanoma

7th edition AJCC guidelines

- Melanoma is classified as T1 if:
  - Less than for equal to 1mm thickness
- T1a- nonulcerated and had a mitosis rate of less than 1/mm2
- T1b-ulcerated or had at least 1 mitosis/mm2

8th edition AJCC guidelines

- T1a - nonulcerated and less than 0.8 mm in thickness
- T1b - is 0.8-1.0 mm thick or less than 0.8 mm with ulceration
- Tumor mitotic rate has been dropped as a staging criterion for T1 tumors.

Example:

56 year old Asian American male with a 0.9 mm melanoma with no ulceration or mitotic figures on the back.

7th edition guidelines this would be: T1a

8th edition guidelines this would be: T1b

Updated 2017 NCCN guidelines: Sentinel Lymph Node Biopsy (SLNB)

- Not recommended in melanoma in Situ
- If 0.76-1.mm thickness without ulceration or mitotic rate of at least 1 per mm2 → discuss and consider SLNB
  - Evidence suggests that roughly 7% probability of positive result
- If 0.76-1.mm thickness with ulceration or mitotic rate of at least 1 per mm2 → discuss and OFFER SLNB
  - Evidence suggests that roughly 35% probability of positive result



New treatment options for melanoma stage III and IV

- Combination therapies – BRAF + MEK inhibitors work better than individual therapies (Dabrafenib + Trametinib)
- Immunomodulator drugs (CTLA4 and PD1 inhibitors) are most effective at treating melanoma (Combo>PD1>CTLA4)
  - CTLA4 inhibition (Ipilimumab), PD1 inhibition (Pembrolizumab)

Long G V, et al, Adjuvant Dabrafenib plus Trametinib in Stage III BRAF-mutated Melanoma, The New England Journal of Medicine. 2017; 377;19

Lancet Oncology, Vol 17, No 11, p 1558-1568, Nov 2016

#4 - Advances in Atopic Dermatitis (AD) Treatment

- Atopic Dermatitis aka: Eczema
  - Common skin disease affecting children and adults
  - Manifests as itchy red scaly patches on the cheeks of children, antecubital and popliteal fossae of children and adults
  - Part of the Atopy Triad: Atopic Dermatitis, Allergic rhinitis and Asthma






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Current Tx of Atopic Dermatitis

- Topical Treatments
  - Topical Steroids like Desonide (for use on the face or body fold areas), Triamcinolone (for use on the body), Clobetasol (for use on thick plaques)
  - Topical Calcinuerin inhibitors (Steroid Sparing medications) – Tacrolimus and Pimecrolimus
- Phototherapy
  - Most commonly Narrow Band UVB
- Immunosuppressants
  - Methotrexate, Mycophenolate mofetil, Cyclosporine, Azathioprine

New Medications for use in AD

- New non steroidal topical medication
  - Crisaborole approved late 2016
  - Topical PDE4 inhibitor
  - PDE4 is part of the inflammatory cascade
  - Approved for mild to moderate AD in ages 2 and up
  - Formulated as a 2% ointment applied BID with results seen in 28 days

New Medications for use in AD

- Dupilumab – First biologic medication approved for AD
- What is a biologic?
  - It's ALIVE!
    - Given IV or Injections – biologics are proteins derived from living tissue or cells cultured in a lab

Body contains interleukins (IL) that fight against viruses/bacteria as part of immune system but in AD these are overactive and they result in chronic inflammation

- Dupilumab blocks IL-4 and IL-13 from binding to their cell receptors limiting overreaction of the immune cascade and limiting inflammatory symptoms of AD

Dupilumab

- Loading dose two injections (600 mg)
- One injection (300 mg) every other week
- Most common adverse reactions: conjunctivitis, injection site reaction, cold sores
- Also note can cause transient elevation in eosinophils so good to have a baseline
- No starting or routine recommended lab testing

Drugs coming down the pipeline

- Nemolizumab – Phase 2b trials IL-31 blocker receptor A (Late 2019-2020)
- Tralokinumab – Phase 3 trials IL13 (Target) Launch 2020

#3 - Advances in Psoriasis Management

- Psoriasis
  - An immune mediated skin disease that causes raised red scaly plaques commonly on the extensor elbows, knees, scalp, lower back/buttock but can be on any body surface area.
  - Itchy
  - Associated with other conditions: diabetes, metabolic syndrome, heart disease, depression
  - Men and women can develop psoriasis in equal rates, all races
  - About 30% of people will develop psoriatic arthritis an inflammatory form of arthritis





Current treatment options

- Topical Treatments
  - Topical Steroids like Desonide (for use on the face or body fold areas), Triamcinolone (for use on the body), Clobetasol (for use on thick plaques)
  - Vitamin D topicals -> Calcipotriene
  - Vitamin A derivative → Tazarotene
- Phototherapy
  - Narrow Band UVB
  - Psoralens + UVA
  - Excimer Laser
- Immunosuppressants
  - Methotrexate, Cyclosporine, Azathioprine, Acitretin

New Oral Medication for use in Psoriasis

- Unlike traditional treatments for Psoriasis recent medications target specific parts of immune system pathways selectively

- Apremilast
  - Inhibits an enzyme known as phosphodiesterase 4 (PDE4) that controls inflammatory action within cells and effects inflammation
  - 30 mg twice daily dosing, after a 5 day start taper
  - Meant to be taken continuously to maintain improvement
  - Adverse effects: Diarrhea, Nausea, URI, Headache,
    - More rare depression, weight decrease
  - Think about using it in combination with phototherapy or topicals

New Biologics for use in Psoriasis

- What is a biologic?
  - It's ALIVE!
    - Given IV or Injections – biologics are proteins derived from living tissue or cells cultured in a lab



Treatment Comparison

6600 SW 92nd Ave., Suite 300 Portland, OR 97223
800-723-9166 education@psoriasis.org
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NATIONAL PSORIASIS FOUNDATION®

Biologic treatments

Treatment type	Indication	Mechanism of Action	Method of Delivery	Dosage and Frequency	Possible Side Effects*	Warning and Precautions**
Secukinumab	Psoriasis (Adults) Psoriatic arthritis (Adults)	Blocks interleukin 17 (IL-17)	Subcutaneous self-injection	Psoriasis and/or psoriatic arthritis: Week 0, 1, 2, 3 and 4, then every four weeks	Cold or flu-like symptoms Diarrhea Upper respiratory infection	Serious infection Tuberculosis (TB) testing before starting Cosentyx Inflammatory bowel disease (IBD) Serious allergic reaction
Etanercept Biosimilar to Etanercept	Psoriasis (People over 4 yrs) Psoriatic arthritis (Adults)	Blocks TNF-Alpha	Subcutaneous self-injection	Adult psoriasis: Twice weekly for 3 months, then once weekly Pediatric psoriasis: Once weekly Adult psoriatic arthritis: Once weekly	Infection Injection site reaction	Serious infection Fungal infection Nervous system problem Lymphoma New or worsening heart failure Low blood count Hepatitis B reactivation Serious allergic reaction Lupus-like syndrome
Adalimumab Biosimilar to Adalimumab Biosimilar to Adalimumab	Psoriasis (Adults) Psoriatic arthritis (Adults)	Blocks TNF-Alpha	Subcutaneous self-injection	Psoriasis and/or psoriatic arthritis: Once every other week	Infection (including upper respiratory and sinus) Injection site reaction Headache Rash	Serious infection Fungal infection Malignancies Serious allergic reaction Hepatitis B reactivation Nervous system problem Low blood count New or worsening heart failure Lupus-like syndrome

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Infliximab *Biosimilar to* Infliximab *Biosimilar to* Infliximab *Biosimilar to* Infliximab	Psoriasis (Adults) Psoriatic arthritis (Adults)	Blocks TNF-Alpha	IV infusion by a health care provider	Psoriasis and/or psoriatic arthritis: Week 0, 2, and 6, then every 8 weeks	Infections (including upper respiratory, sinus and throat) Infusion-related reaction Headache Stomach pain	Serious infection (especially when switching between biologics) Fungal infection Malignancies Hepatitis B reactivation Liver problem (including hepatotoxicity) New or worsening heart failure Low blood count Nervous system problem Lupus-like syndrome Special consideration when receiving a live vaccine Serious allergic reaction
Brodalumab	Psoriasis (Adults)	Blocks IL-17	Subcutaneous self-injection	Psoriasis: Week 0, 1, 2, then every 2 weeks	Joint pain Headache Fatigue Diarrhea Throat pain Nausea Muscle pain Injection site reaction Cold or flu-like symptoms Low blood count Fungal infection	Suicidal ideation and behavior Serious infection TB testing before starting Siliq Crohn's disease Special consideration when receiving a live vaccine

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Biologic treatments

Treatment type	Indication	Mechanism of Action	Method of Delivery	Dosage and Frequency	Possible Side Effects*	Warning and Precautions**
Ixekizumab	Psoriasis (Adults) Psoriatic arthritis (Adults)	Blocks IL-17	Subcutaneous self-injection	Psoriasis: Week 0 and every 2 weeks for 3 months, then every 4 weeks Psoriatic arthritis: Week 0, then every 4 weeks	Injection site reaction Upper respiratory infection Nausea Fungal infection	Serious infection TB testing before starting Taltz Serious allergic reaction Inflammatory bowel disease
Guselkumab	Psoriasis (Adults)	Blocks interleukin 23 (IL-23)	Subcutaneous self-injection	Psoriasis: Week 0 and 4, then every 8 weeks	Upper respiratory infection Headache Injection site reaction Joint pain Diarrhea Stomach flu Fungal infection Herpes simplex infection	Serious infection TB testing before starting Tremfya
Ustekinumab	Psoriasis (People over 12 yrs) Psoriatic arthritis (Adults)	Blocks interleukin 12 and 23 (IL-12/23)	Subcutaneous self-injection	Psoriasis and/or psoriatic arthritis: Week 0 and 4, then every 12 weeks	Cold or flu-like symptoms Upper respiratory infection Headache Fatigue	Serious infection (especially from mycobacteria, salmonella and Bacillus Calmette-Guerin (BCG) vaccinations) TB testing before starting Stelara Malignancies Serious allergic reaction Reversible posterior leukoencephalopathy syndrome

Hidradenitis suppurativa (HS)

- HS is a chronic inflammatory disorder of the apocrine glands
- Follicular occlusion leads to trapped follicular contents, rupture, inflammation of the dermis and superinfection
- Adalimumab has new indication to treat moderate to severe HS in people 12 years of age and older







#2 – New medication for the treatment of Urticaria

- Urticaria, Hives, are raised edematous wheals caused by histamine release from mast cells
- Triggers by a variety of mechanisms both allergic and non allergic – in half the cases the inciting factor never identified
- 40% associated with URI, 9% drug, 1% food
- Pruritus (itch), stinging, pain
- Acute (less than 6 weeks)
  - MC children
- Chronic (more than 6 weeks)
  - MC in women, middle aged
  - Resolves in 12 months in approx 50% of adults with idiopathic urticaria



Triggers for Urticaria

- Drugs
  - Aspirin, NSAIDs, morphine, codeine, PCN, Cephalosporins, Sulfa, Tetracyclines, blood products, radiographic contrast, Angiotensin-converting enzyme inhibitors,
- Infection
- Insect bits (papular urticaria)
- Pregnancy
- Foods
- Heat, cold, solar, pressure, water

Current Management/treatment of Urticaria: Things to consider

- Acute vs Chronic: → Acute usually resolves
- Is anaphylaxis present (hypotension, respiratory distress, throat scratchiness, swelling of mucous membranes (tongue, throat, lips))? → epinephrine
- Can we identify triggers→ if so avoid



Current Management/treatment of Urticaria

- Nonsedating H1 antagonists:
  - Cetirizine 10 mg QHS, BID
  - Fexofenadine 120 -180 mg
- Sedating Antihistamines:
  - Diphenhydramine 10-25 mg up to 4 times daily
  - Hydroxyzine 10-25 mg up to 4 times daily
  - Doxepin 10-50 mg up to 3 times daily
- Leukotriene inhibitors can be used in combination with antihistamines
  - Montelukast 10 mg daily

Omalizumab for Urticaria

- This is a humanized monoclonal IgG antibody against IgE
  - Approved for adults and children 12 and up for urticaria symptomatic on H1 antihistamines
  - 150 or 300 mg subcutaneous injections every 4 weeks
  - No routine baseline or monitoring labs
  - Commonly reported Adverse effects:
    - Headache, tired feeling, joint/muscle pain, rash, injection site reaction, hair loss, URI symptoms, dizziness

#1 – Topical prescription strength Retinol now available OTC

- Adapelene Gel 0.1% for over the counter use to treat acne.
- First retinoid approved for OTC use.
- Indications:
  - Comedonal acne (treatment of choice)
  - Fine line and wrinkle prevention, it decreases collagen resorption
  - Evens skin tone







Adapelene gel 0.1%

- Comparable to Tretinoin 0.025% cream in efficacy and slightly better than Tretinoin 0.025% in tolerability.
- Good for use in men and women all ages except women who are pregnant
- Common adverse effect: dryness, redness, peeling, photosensitivity → this can be alleviated by decreasing the amount used and applying moisturizer

Bonus: Sunscreen Primer

- What do you need to know about sunscreen?
- Broad spectrum → Protective against UVA and UVB
  - UVA → rays that cause tans, aging (brown spots, wrinkles),
  - UVB→ rays that cause burning
- SPF 30-50 – SPF 15 is not considered protective enough.
- Use daily on the face, neck, upper chest, backs of the hands