Diseases of the Skin

Physiology & Function
- Protection
- Holds us together
- Water regulation
- Vitamin D
- Immune processing

Epidermis/Dermis Communication

Immune Processing
Basic Patterns

- Interplay between epidermis and dermis.
- Rash, reddened
- Changes in pigmentation
- Shape of isolated lesions
  - Macule: flat, close your eyes
  - Papule: raised
  - Vesicle: fluid filled

Rash

- Measles
- May be flat or raised

Macule

- A macule is flat
- Close your eyes and feel

Papule

- Raised lesion
- Maybe pigmented, maybe not

Vesicles

- Fluid filled
- Epidermal generally
Changes in Pigmentation

Vitiligo

Non-Proliferative Pigmented Areas
- Freckles
- Melasma
- Pregnancy mask

Proliferative Melanocytic Lesions
- Nevi
  - Benign growths of young melanocytes.
  - Born with them. We all have about 20
  - Not a freckle
- Dysplastic nevus
  - Abnormal maturation.
  - May become malignant
  - Malignant melanoma

Lentigo
- Linear proliferation of melanocytes along the basal layer of the epithelium
- Hyperplasia of melanocytes
- Older folks
- Sun exposed

Nevus
- ‘Mole’, benign proliferation of young melanocytes.
- Melanocytic embryonic rests
- Where are the nevus cells”
  - Epidermal
  - Dermal
  - Compound
- Spitz nevus
  - Young people.
  - Looks aggressive, but not.
  - Halo nevus (one undergoing regression)
Nevi

- Clusters of young melanocytes.
- Confined to dermis.
- Maturation from ‘surface to base’.

Dermal Nevus

Large Nevi

Halo Nevus

Dysplastic Nevus

- Abnormal maturation of nevus cells
- May proceed to malignant melanoma
- Sometimes part of a familial syndrome.
Malignant Melanoma

- Malignant melanocytic tumor
- Very unpredictable tumor
- Genetics
- Solar and UV exposure
- Ethnic
- Radial growth followed by
- Penetrating phase
- Metastasis
- Persistent
  - Transplant 15 years later died with it

Melanoma History

Superficial Spreading Melanoma

- Flag sign
- Nodular or vertical growth very important
- Depth >1.5 mm
  - Bad development
- Sites
  - Skin
  - Conjunctiva
  - Retina
  - Iris
  - Meninges

Nodular Malignant Melanoma

Study: Tanning beds as deadly as arsenic

International cancer experts have moved tanning beds and other sources of ultraviolet radiation into the top cancer risk category, deeming them as deadly as arsenic and mustard gas. A new analysis of about 20 studies concludes the risk of skin cancer jumps by 75 percent when people start using tanning beds before age 30. Experts also found that all types of ultraviolet radiation caused worrying mutations in mice, proof the radiation is carcinogenic. Previously, only one type of ultraviolet radiation was thought to be lethal. The research was published online today in the medical journal Lancet Oncology.
Malignant Melanoma
- Clusters
- Nucleoli
- Nuclear margins
- Lack of cohesion
- Depth

Depth of Penetration
- Clark’s level
  - I - IV
- Now use mm depth
- Depth in mm
  - <0.76 mm, low risk
  - 0.76 - 1.5 mm, intermediate risk
  - >1.5 mm, high risk

Measuring the Melanoma
- Measure from granular layer to the deepest extent of the dermal component
- Measure at right angles to surface of skin above tumor, avoid tangential sections
- Avoid hair follicles/adnexal structures
  - Atypical melanocytes in a column perpendicular to the epidermis are probably periappendiceal
- Take at least 3 measurements

Micrometer
Melanoma Mitotic Count

- Can metastasize widely
- Stay for years
- Transplant risk even 10-15 years later
- Other sites of origin
  - Meninges
  - Ocular
    - Retina (lever mets)
    - Iris
    - Conjunctiva

Ocular Melanomas

- Conjunctival
- Iris
- Retinal ->
- Histology
  - Spindle
  - Epitheloid ->
  - Bad
  - Liver mets

Tumors of Epithelial Origin, Overview and General Features

- Epidermis
  - Acanthosis
  - Perikeratosis
  - Hyperkeratosis
  - Varying degrees of pigmentation
  - Benign vs. malignant
  - Not sure of malignant potential

Epithelial Tumors

- Seborrheic keratosis
  - Older people
  - Pucker up big boy
  - Stuck on appearance
  - Greasy looking
  - Keratin rich
  - Benign
  - Epithelial proliferation
Acanthosis Nigricans
- Flexer areas
- Axillae
- Skin folds
- Thickened spinosum
- Hyperpigmentation
- Obesity
- Inherited
- Sometimes with underlying adenocarcinoma

Epidermal Inclusion Cyst (Wen)

Adenexal Skin Tumors
- Come from basal layer of epithelial appendage structures
- Cylindromas
- Apocrine
- Turban tumor
- Trichoepithelioma
- Hair shaft

Actinic (Solar) Injury

Actinic Keratosis
- Solar exposed skin
- Epithelial proliferation
- Dysplasia
- +/- malignant potential
Keratoacanthoma

- Now considered a low grade squamous cell malignancy
- Often will regress
- Solar exposed skin
- Rapidly growing
- ‘Cup or crater shaped’
- Epithelial proliferation
- Marked atypia

Squamous Cell Malignancies, Overview and general Features

- Actinic exposure
- Squamous origin
- Can arise from any layer of the keratinizing epi.
- All malignant cells look like the cell from which the cancer came

Squamous Cell Carcinoma

- Arises from differentiated squamous epithelium
- Sun exposed
  - UV
- Age of incidence is dropping
- Metastasizes

Squamous Cell Carcinoma

- Cells produce keratin
- Pearls
- Invade and spread
- High mitotic count
Squamous Cell Carcinoma

- Keratin Pearls

Basal Cell Carcinoma

- Arise from basal layer of epithelium.
- Clone
- No maturation beyond basal cell
- They look it microscopically
- Small clusters
- Peripheral palisade of cells

Basal Cell Carcinoma

- Arises from basal layer of epithelium.
- Invades locally
- Grows in clusters
- Peripheral palisade
- Sometimes adnexal skin structure differentiation

Basal Cell Carcinoma

- The most common malignancy we suffer from.
- Solar exposed skin.
- Pearly
- Raised edges
- Maybe central ulceration
- Stays at home, but
- Can locally invade and cause havoc.
Xanthomas

- Histiocytes containing lipid
- Around eyes
- Extensor surfaces of extremities
- Diabetes
- Liver disease
- Hyperlipidemia

Dermal Tumors

- Fibroma

Dermatofibrosarcoma Protuberans (DFSP)

- Fibrosarcoma
- Storiform pattern

Kaposi’s Sarcoma

- HIV & Herpes 8
- Vascular malignancy

Kaposi’s Sarcoma
Mycosis Fungoides
- Cutaneous T-Cell Lymphoma
- HTLV-1
- Sézary cells (cerebriform nuclear convolutions)

Sézary Cells in Mycosis Fungoides

Histiocytosis X
- One of several inherited histiocytic proliferative conditions
- Birbeck granules

Merkel Cell Carcinoma
- Neuroendocrine cell
- Behaves like a small cell cancer of the lung

Ichthyosis
- Autosomal dom
- Autosomal rec
- Disorder of maturation
- Defective desquamation
- Retention of cells
- Fish-like scales
Inflammatory Dermatosis

- Hives
- Urticaria (wheal)
- Generalized
- Allergic reaction
  - Bee sting
  - Medications
- IgE mediated
  - Histamine release
  - Vascular dilation
  - Fluid in tissues

Urticaria

Eczema, ‘Boiling Over’

- Contact dermatitis
- Local reaction to toxic agent.
- Epidermal spongiosis
- Vesicles
- Poison ivy

Spongiotic Dermatitis

Contact Dermatitis
Atopic Dermatitis

Eczematosus Dermatoses

<table>
<thead>
<tr>
<th>Type</th>
<th>Common or Pathognomonic Signs</th>
<th>Location</th>
<th>Atopic Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tarset dermatitis</td>
<td>Fatally applied antigen or sensory irritation</td>
<td>Face, forearms, arms, scalp</td>
<td>Irritated feeling, burning, or both requires attention, tension.</td>
</tr>
<tr>
<td>Atopic dermatitis</td>
<td>Uncommon, may be familial</td>
<td>Generalized dermatitis</td>
<td>Erythematous plaques in flexed areas, itching of arms, face, hands, feet.</td>
</tr>
<tr>
<td>Erythematous dermatitis</td>
<td>Subacute, sharply defined plaques or patches</td>
<td>Forehead, cheeks, ears, neck, arms, chest, anterior upper thighs</td>
<td>Increased natural immunity and eosinophilia.</td>
</tr>
<tr>
<td>Erythematosus erythema</td>
<td>Localized, itchy plaques on the scalp or face</td>
<td>Localized, itchy plaques on the scalp or face</td>
<td>Pustular nodules and pustules with urticaria.</td>
</tr>
</tbody>
</table>

Erythema Multiforme

- Red macule with darker center.
- Immunologic in most cases
- Degeneration of basal layer of epithelium with
- Lymphocytic infiltrate of dermis
- Rather nonspecific reaction

Stevens-Johnson Syndrome
Toxic Epidermal Necrolysis

- Erythema Nodosum

- Inflammation of fat and sub-Q tissues
- Immune complexes
- UC
Chronic Inflammatory Dermatoses

- Persistent
- Epithelial reaction characterized by increased turnover rate
  - Thickening
  - Scaling
  - Roughening
- Variable inflammation of dermis

Psoriasis

- Ag/Ab reaction?
- Knees, elbows, scalp, glans
- Whole body is pretty bad
- At areas of trauma
- Salmon skin

Psoriasis

- Acanthosis
  - Thickening of the epi
  - Long rete pegs
  - Thinned granulosa
  - Ag/Ab and C'
  - Microscopic abscesses in epi.

Lichen Planus

- Purple plaques
- Saw-tooth epidermis
- Band-like lymphocytic infiltrate in dermis
- Self-limiting but may last years
- Wickham’s striae
- Hypopigmentation when resolves

Lupus Erythematosis

- Autoimmune
- Two forms
  - Systemic ->
- Discoid (skin only)
- Systemic problems
  - Kidney failure
  - Vascularitis and DVT with emboli
  - Antibodies in serum
    - Anti-DNA
    - Other nuclear

Lupus Erythematosis

- Chronic inflammation
  - Derm/epi junction
  - Adnexal structures
  - Antibodies at derm/epi junction
Lupus Erythematosus
- Antihuman IgG
- Concentration at basal layer.

Discoid Lupus
- Confined to skin
- Few systemic problems
- No anti dsDNA

Blistering Conditions
- Pemphigus vulgaris
  - Ab against skin and basement membrane
  - Acantholysis
  - Suprabasilar cleft
  - Blisters with sloughing of skin
  - Pressure points

Pemphigus

Experimental Pemphigus
- 'Acantholysis'
- Mouse with no desmoglein 3 gene
- Blister forms because of absence of desmosomes
Cleft Position is Important

- Subcorneal: Impetigo
- Suprabasalar: Pemphigus vulgaris
- Subepidermal or basilar:
  - Bullous pemphigoid
  - Dermatitis herpatiformis

Bullous Pemphigoid

- Antibodies against hemidesmosomes.
- Hemidesmosomes anchor epidermis to basement membrane

Bullous Pemphigoid

- Note antibody staining along BM
- Antibodies against hemidesmosomes
- Epidermis lifts off the basement membrane

Dermatitis Heratiformis

- Not actually the virus herpes
- 'Herpes' describes radial spread of a lesion.
- In some the symptoms are associated with wheat products (gluten)
- IgA deposits in the tips of the dermal papillae
- Microabscesses in the dermal papillae

Epidermolysis Bullosa

- Inherited weak epidermal junctions
- Defect in keratin
- Defect in collagen
- Pressure separation
- Mild to severe
Porphyria
- Inherited varieties
  - Erythropoietic
  - Intermittent
  - Protoporphyria
  - Vampires
- Porphyrins absorb UV
- Cause profound solar damage
- Vesicular

Skin Infections

Acne
- Acne vulgaris
  - Males mostly
  - Testosterone
- Observations
  - Keratin plugging of hair shafts
  - Propionum bacteria grows
    - Breaks down sebaceous oils
    - Very reactive

Other Direct Infections of Skin
- Bacterial
- Abscesses
- Fungal
  - Ringworm
- Worms
- Viruses
- Smallpox
Gram+ Bugs

Viruses

Herpes
- Fluid filled
- Epidermal generally

Verruca Vulgaris

Molluscum Contagiosum
- Caused by a pox virus
- Self limiting
- Molluscum bodies

Tinea
- Note fungal forms in epidermis
Pediculosis

- Lice
- Head
- Pubic

Scabies

- Sarcoptes scabiei
- Burrows into the stratum corneum
- Interdigital skin
- Wrist
- Genital skin
- Very itchy dermatitis