Photosensitivity Disorders

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Photosensitivity Disorders

Inherited photosensitivity disorders

Disease	Inheritance/ Mutation	Clinical features	Buzzwords/ Comments
Bloom Syndrome	AR BLM gene RecQL3 (DNA helicase) (RecQL2 by some sources)	- Skin: early-onset photo-induced erythema and telangiectasias in face, hands and forearms (photo-distributed poikiloderma), CALM's, dyspigmentation, hypertrichosis, cheilitis - Failure to thrive ("proportionate dwarfism"), distinct facies (small and narrow) with oversized ears, long limbs; immunodeficiency, increased risk of malignancy and type 2 DM	- Ashkenazi Jews - Associated malignancies: leukemia (most common before 20 y/o), lymphoma, GI adenocarcinoma, sarcomas (avoid treatment with alkylating agents and radiation) - Reduced serum IgM and IgA; early death from pneumonia - Quadriradial configuration in chromosomes is pathognomonic
Rothmund Thompson Syndrome (Poikiloderma congenitale)	AR RecQL4 gene defect (DNA helicase)	- Skin: early, acute PS results in poikiloderma of the face and extensor extremities; alopecia, nail dystrophy, premalignant acral keratosis, increased cutaneous malignancies: BCC, SCC, melanoma - Juvenile subscapular bilateral cataracts, radiologic bony abnormalities, osteoporosis, hypogonadism, cryptorchidism	- Hypoplastic thumbs, radii and ulna - Osteosarcoma (most common malignancy) may be multicentric and resistant to radiation. Recommended screening: baseline radiologic survey and by age 3 (and yearly if abnormal).
Xeroderma Pigmentosum (XP)	-All AR, (except XPB: AD) Multiple gene disorder- 7 nucleotide excision repair (NER) deficient complementation groups: -XPA -XPB/ERCC3 -XPC -XPD/ERCC2 -XPE/DDB2 -XPF/ERCC4 -XPG/ERCC5	-XPA: Most severe variant. PS, severe neurologic impairment, deafness, growth delay -XPB: PS, pigmentary retinopathy, basal ganglia calcification -XPC: At greatest risk for skin cancer (melanoma); rare neurological involvement -XPD: Poikiloderma, early onset skin cancer, decreased intelligence, ocular damage, neurologic impairment -XPE: Mildest skin/ocular PS; rare neurologic involvement -XPF: Mild PS, freckling, rare neurologic/ocular involvement -XPG: Mild skin changes, rare skin cancer, rare neurologic/ocular, except when XP/CS overlap - General skin findings: dry, atrophic, parchment-like texture with freckling, dyspigmentation/poikiloderma	- Groups A, B and C are most common: XPC in US/ Europe vs. XPA in Japan - Group A: AKA DeSanctis-Cacchione syndrome – severe neurologic abnormalities - XPV (variant): defective DNA polymerase (pol η) leads to increased risk of skin cancer; no neurologic abnormalities - PS is the most common presenting sign in all groups; excessive in groups: A, B, D, F, G, except C and E. - Up to 10,000x increase in risk of malignancies in anterior 2/3 of the tongue (SCC, angiosarcoma) XPC, XPD, XPA: associated with increased risk of cutaneous melanoma
Cockayne Syndrome (CS)	AR CSA/ERCC8 and CSB/ ERCC6 Defective transcription coupled repair subpathway of NER Unable to repair cyclobutene pyrimidine dimers	- Skin: PS, dry hair and skin, anhidrosis, acral cyanotic livedo, edema - Microcephaly, stunted growth, progressive neurological dysfunction due to leukodystrophy, mental retardation, basal ganglia calcifications, cataracts, dental caries	- Cachectic dwarfism: lipoatrophy of the face, sunken eye appearance, "bird headed facies, "Mickey mouse ears" -Salt and pepper retinal pigmentation - No increased incidence of skin cancer or sun induced pigmentation - Mutations in XPF may also cause CS and CS/XP/ Fanconi anemia phenotype. - XP/CS overlap syndrome with mutations in XPB, XPD and XPG have more neurologic, than cutaneous involvement typical for XP.
Cerebro-oculo-facio-skeletal (COFS) syndrome	AR Mutations in CBS, ERCC1, XPD, XPG	- Typical features of CS with hypotonia, impaired reflexes, poor vision and distinctive facial characteristics (small eyes +/- congenital cataracts, low set ears, small jaw)	- Arthrogryposis (congenital joint contractures) and microphthalmia differentiate from severe CS
Ultraviolet-sensitive syndrome (UVS)	AR Defective transcription coupled repair with mutations in 3 complementation groups (CSA, CSB and UVSSA)	- Skin: acute PS/ sunburn, dryness, freckling, photodistributed dyspigmentation, telangiectasia	- No increased incidence of skin cancer (normal global genomic repair)
Trichothiodystrophy aka "Tay syndrome," (PIBIDS)	AR Defective complementation groups in global and transcription-coupled NER subpathways (PS in XPD/ERCC2, XPB/ERCC3 and TTDA gene mutations)	- BIDS, IBIDS, PBIDS, PIBIDS: photosensitivity, ichthyosis, brittle hair (sulfur deficient trichoschisis), intellectual impairment, decreased fertility (+/- hypogonadism), short stature - Microcephaly, cataracts, hearing loss, recurrent infections/ hypogammaglobulinemia, osteoporosis, dental caries, nail abnormalities	- May present as collodion baby - Tiger-tail-like pattern of hair under polarized light. Also trichorrhexis nodosa, ribboning - Overlap with XPB, XPD
Kindler syndrome	AR KIND1 (AKA FERMT1) gene (encodes the focal adhesion protein fermitin family homolog-1)	- Skin: Congenital and neonatal blistering/ transient early-onset PS, progressive poikiloderma with marked cutaneous atrophy (cigarette paper-like atrophy), dental caries, nail dystrophy, palmoplantar hyperkeratosis - Ectropion, colitis, phimoses, pseudoainhum, digital webbing	Subtype of epidermolysis bullosa

Photosensitivity Disorders *(continued)*

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Acquired Disease/ Immunologically mediated

Disease	Epidemiology	Clinical features	Pathophysiology	Action Spectrum	Pathology	Treatment	Comments
PMLE	Women > Men 2nd and 3rd decades	Repeated outbreaks of lesions on sun-exposed skin during spring and summer Non-scarring, pruritic, erythematous papules, papulo-vesicles, vesicles or plaques Most common locations: upper chest, upper arms, back of the hands, the side of the face Onset minutes to hours from sun exposure and lasts for a few days	Delayed cellular hypersensitivity reaction to an undefined photo-induced antigen	UVB, UVA; rarely visible light	Epidermal spongiosis Superficial and deep, perivascular and periadnexal, lymphohistiocytic dermal infiltrate; may have eosinophils and neutrophils Significant papillary dermal edema	Mild disease: photoprotection Severe disease: hardening with NB-UVB phototherapy (initial dose 50-70% of MED) or PUVA Oral prednisone (<0.5mg/kg for 5-7 days during vacation Very severe disease: azathioprine or cyclosporine	Juvenile spring eruption is considered a clinical variant of PMLE in boys. Helices of the ear are the most common affected area. PMLE may be lifelong
Actinic prurigo (Hutchinson's summer prurigo)	Common in Native Americans (familial form), but can occur in all races Childhood onset (earlier than PMLE), most common in girls, often resolution by adolescence (may persist)	Erythematous papules or nodules, sometimes with hemorrhagic crust; marked pruritus May heal with fine linear or pitted scars Most common locations: face (including the nose) and distal limbs May have exudative cheilitis favoring lower lip or conjunctivitis	UVR exposure is the provocative factor Altered delayed immune response	UVB, UVA	Epidermal spongiosis, acanthosis, and dermal mononuclear cell infiltrate (occasional eosinophils) Papillary edema in early lesions	Photo-protection Mild disease: topical corticosteroids and topical tacrolimus Phototherapy with NB-UVB and PUVA (hardening) Resistant disease: oral thalidomide Other oral treatments: corticosteroids, azathioprine and cyclosporine	Association with HLA-DR4 (DRB1*0401) and subtype DRB1*0407
Hydroa vacciniforme (Hydroa = vesicles Vacciniforme = scarring)	Predilection for lightly pigmented individuals Childhood onset (boys>girls); resolves by adolescence	Symmetrical, clustered, pruritic or stinging erythematous macules Lesions can increase in size, become vesicular, umbilicate and progress with extensive crusting Healing over weeks: leaves varioliform scars Photo-distribution: face and dorsal aspect of hands Can be associated with general malaise (fever and headaches) May have ocular symptoms: photophobia, lacrimation, conjunctivitis or corneal lesions	Nature of the reaction is unknown. Summer sunlight generally provokes the eruption Epstein-Barr viral infection has been detected in a number of patients	UVA	Early: epidermal spongiosis with perivascular lymphohistiocytic infiltrate Prominent reticular keratinocyte degeneration; intra-epidermal vesicles with fibrin and acute inflammatory cells; confluent epidermal and focal upper dermal necrosis	Photoprotection Almost always refractory to treatment. Anecdotal treatments: BB-UVB, NB-UVB, PUVA, β -carotenes, antimalarials, azathioprine, cyclosporine, and thalidomide	Rare: finger, nose or ear disfiguration In Hydroa vacciniforme-like eruptions associated with systemic EBV-related disease (including lymphoma); the skin lesions are more severe and more widespread. Can also have facial swelling, ulcerated nodular lesions, high-grade fever, and hepatosplenomegaly.
Solar urticaria	Women > men 4th and 5th decade	Wheals limited to sun-exposed areas that appear a few minutes after exposure. Lesions resolve after 1 – 2 hours Anaphylactic shock may occur May last several years	IgE -mediated response against photo-induced, endogenous, cutaneous antigens	UVA, UVB, UVC, visible light	Mild dermal edema with perivascular mixed neutrophilic and eosinophilic infiltrate	Photoprotection Oral antihistamines Hardening with UVA or PUVA Refractory disease: plasmapheresis, omalizumab or IVIg	Fixed solar urticaria is limited to one area (mast cell alteration at that site)
Chronic actinic dermatitis	Most common in men over 50 years of age	Persistent, pruritic eczematous dermatitis with infiltrated papules and plaques located in sun-exposed areas (may extend to covered areas) Often spares: furrows, upper eyelids, finger webs, Nasolabial folds or post-auricular areas Patients can develop erythroderma Chronic lesions become lichenified Other findings: palmoplantar eczematous changes, loss of eyebrows or scalp hair from scratching	Delayed type hypersensitivity response (unknown endogenous, photo-induced, cutaneous antigen) Often patients have an existing allergic or photo-allergic dermatitis to exogenous sensitizer (plants or fragrances)	UVB, UVA, visible light	Epidermal spongiosis and acanthosis; lymphocytic exocytosis Superficial and deep dense dermal lymphohistiocytic infiltrate (may have eosinophils and plasma cells)	Strict photo-protection (including car window filters) Avoidance of relevant contact allergens Topical or oral corticosteroids, topical tacrolimus Refractory disease: low dose PUVA with initial high-dose steroids, azathioprine, cyclosporine, and mycophenolate mofetil	Lymphocytic infiltrate can mimic cutaneous T-cell lymphoma Chronic actinic dermatitis infiltrates are predominantly CD8+ cells

Abbreviations:

- PS: Photosensitivity
- CALMs: cafe au lait macules

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