Table I. Genodermatoses with known gene defects

Disease	Mutated gene*	Affected protein/function	Reference No.†
Epidermal fragility disorders			
DEB	COL7A1	Type VII collagen	6
Junctional EB	LAMA3, LAMB3, LAMC2, COL17A1	α3, β3, and γ2 chains of laminin 5, type XVII collagen	6
EB with pyloric atresia	ITGA6, ITGB4	$\alpha 6\beta 4$ Integrin	6
EB with muscular dystrophy	PLEC1	Plectin	6
EB simplex	KRT5, KRT14	Keratins 5 and 14	46
Ectodermal dysplasia with skin fragility	PKP1	Plakophilin 1	47
Hailey-Hailey disease	ATP2C1	ATP-dependent calcium transporter	13
Keratinization disorders			
Epidermolytic hyperkeratosis	KRT1, KRT10	Keratins 1 and 10	46
Ichthyosis hystrix	KRT1	Keratin 1	48
Epidermolytic PPK	KRT9	Keratin 9	46
Nonepidermolytic PPK	KRT1, KRT16	Keratins 1 and 16	46
Ichthyosis bullosa of Siemens	KRT2e	Keratin 2e	46
Pachyonychia congenita, types 1 and 2	KRT6a, KRT6b, KRT16, KRT17	Keratins 6a, 6b, 16, and 17	46
White sponge naevus	KRT4, KRT13	Keratins 4 and 13	46
X-linked recessive ichthyosis	STS	Steroid sulfatase	49
Lamellar ichthyosis	TGM1	Transglutaminase 1	50
Mutilating keratoderma with ichthyosis	LOR	Loricrin	10
Vohwinkel's syndrome	GJB2	Connexin 26	12
PPK with deafness	GJB2	Connexin 26	12
Erythrokeratodermia variabilis	GJB3, GJB4	Connexins 31 and 30.3	12
Darier disease	ATP2A2	ATP-dependent calcium transporter	14
Striate PPK	DSP, DSG1	Desmoplakin, desmoglein 1	51, 52
Conradi-Hünermann-Happle syndrome	EBP	Delta 8-delta 7 sterol isomerase (emopamil binding protein)	53
Mal de Meleda	ARS	SLURP-1 (secreted Ly-6/uPAR related protein 1)	54
Hair disorders			
Woolly hair, keratoderma, and cardiomyopathy (Naxos disease)	DSP, PG	Desmoplakin, plakoglobin	55, 56
Congenital atrichia	HR	Hairless (a transcription factor)	57
Monilethrix	hHB1, hHB6	Hair cortex keratins 1 and 6	58, 59
Familial cylindromatosis	CYLD1	Tumor-suppressor protein	60
Pigmentation disorders			
Albinism (different forms)	TYR	Tyrosinase	61
	P	Putative membrane transport protein	
	OA1	Member of G protein–coupled receptors	
	TRP1	Tyrosinase-related protein	
Chediak-Higashi syndrome	CHS1	Lysosomal trafficking regulator	62
Hermansky-Pudlak syndrome	HPS1	Putative transmembrane protein with unknown function	61
Piebaldism	KIT	Protooncogene, a transmembrane tyrosine kinase receptor for stem cell factor	63
Tietz syndrome	MITF	Microphthalmia-associated transcription factor	64
Waardenburg syndrome	PAX3, MITF	Transcription factors	64

(continued)

EB, Epidermolysis bullosa; *PPK*, palmoplantar keratoderma.

*For details of the genes, see Online Mendelian Inheritance in Man (OMIM) database, *www.ncbi-mim.nih.gov/Omim/*, or the references.

†If a recent, comprehensive review on the molecular genetics of the corresponding disease exists, the reference is included. In other cases, pertinent original publications are referenced.

‡Note that Williams syndrome is a contiguous gene deletion syndrome, including ELN.

Table I. Cont'd

Disease	Mutated gene*	Affected protein/function	Reference No.†
Porphyrias			
Congenital erythropoietic porphyria	UROS	Uroporphyrinogen III synthase	65
Erythropoietic protoporphyria	FECH	Ferrochelatase	65
Familial porphyria cutanea tarda	URO-D	Uroporphyrinogen decarboxylase	65
Variegate porphyria	PPO	Protoporphyrinogen oxidase	65
Multisystem disorders			
Trichothiodystrophy	XPB, XPD	Complementation groups B and D	66
Cockayne syndrome	CSA/CKN1, CSB	Transcription-repair coupling factors	67
Human nude/SCID	WHN	Winged-helix transcription factor	68
Fabry disease	GLA	Alpha-galactosidase A	69
Ataxia telangiectasia	ATM	Protein kinase	70, 71
Hereditary hemorrhagic telangiectasia	ENG ALK-1	Endoglin, activin receptor-like kinase 1	
Papillon-Lefévre syndrome	CTSC	Cathepsin C	72, 73
Haim-Munk syndrome	CTSC	Cathepsin C	74
Dyskeratosis congenita	DKC1	Dyskerin	75
Netherton syndrome	SPINK5	Serine protease inhibitor	76
Sjögren-Larsson syndrome	FALDH	Fatty aldehyde dehydrogenase	77
Refsum disease	PHYH	Phytanoyl-CoA hydroxylase	78
Hyperkeratotic cutaneous capillary-venous malformation	CCM1	KRIT1 (KREV1 interacting protein)	79
Milroy disease	VEGFR-3	Vascular endothelial growth factor	80
Waardenburg-Hirschsprung syndrome	EDN3	Endothelin-3	81
	EDNRB	Endothelin receptor B	82
	SOX10	Transcription factor	83
Cutis laxa	ELN	Elastin	84
Williams syndrome	ELN‡	Elastin	84
Pseudoxanthoma elasticum	ABCC6	MRP6, a multidrug resistance–associated protein	34
Ehlers-Danlos syndrome (different variants)	COL1A1, COL1A2, COL3A1, COL5A1, COL5A2, ADAMTS2 PLOD, B4GALT7	Type I, III, and V collagens, metalloproteinase, procollagen-lysine 2-oxoglutarate 5-dioxygenase (lysyl hydroxylase), xylosylprotein 4-beta-galactosyltransferase	8, 85
Menkes syndrome	ATP7A	ATP-dependent copper transporter	86
Occipital horn syndrome	ATP7A	ATP-dependent copper transporter	86
Werner syndrome	WRN	DNA helicase	67
Bloom syndrome	BLM	DNA helicase	67
Rothmund-Thomson syndrome	RECQ4	DNA helicase	67
Neurofibromatosis	NF1, NF2	Neurofibromins 1 and 2	87
Tuberous sclerosis	TSC1, TSC2	Hamartins 1 and 2	87
Griscelli syndrome	RAB27A, MYO5A	Ras-associated protein, myosin Va	88, 89
Wiskott-Aldrich syndrome	WAS	WASP (Arp2/3 complex interacting protein)	90
Ectrodactyly, ectodermal dysplasia, and cleft lip/palate syndrome 3 (EEC3)	TP63	Tumor protein p63	91
Hay-Wells syndrome (AEC)	TP63	Tumor protein p63	92
Hyperammonemia with reduced ornithine, citrulline, arginine, and proline	P5CS	Delta (1)-pyrroline-5-carboxylate synthase	93
Hereditary angioedema	CINH	C1 esterase inhibitor	94
Hidrotic ectodermal dysplasia	GJB6	Connexin 30	95
X-linked anhidrotic ectodermal dysplasia	EDA	Ectodysplasin A	96
X-linked anhidrotic ectodermal dysplasia with immunodeficiency (EDA-ID) and osteopetrosis and lymphoedema (OL-EDA-ID)	IKBKG	NEMO (modulator of NF-kappaB signaling)	97
Incontinentia pigmenti	IKBKG	NEMO (modulator of NF-kappaB signaling)	98
Cartilage-hair hypoplasia	RMRP	Endoribonuclease RNase MRP	99

(continued)

Table I. Cont'd

Disease	Mutated gene*	Affected protein/function	Reference No.†
Cancer disorders			
Cowden syndrome	PTEN	Phosphatase and tensin homolog	100
Bannayan-Zonana syndrome	PTEN	Phosphatase and tensin homolog	100
Basal cell nevus syndrome	PTC	Patched (drosophila homolog)	101, 102
Hereditary melanoma	CDK4, CDKN2A	Cyclin-dependent kinase 4, cyclin-dependent kinase inhibitor 2a	103
Muir-Torre syndrome	MSH2	Mismatch repair protein	104
Peutz-Jeghers syndrome	STK11/LKB1	Protein kinase	105, 106
Xeroderma pigmentosum (different complementation groups)	XPA, XPB, XPC, XPD, XPE, XPF, XPG, hRAD30	Complementation groups A-G, DNA polymerase η	66

zymes, such as lysyl hydroxylase or procollagen N–protease.[8,9]

At the same time, recent elucidation of the molecular bases of various genodermatoses has yielded a number of surprises. For example, the first attempts to disclose the molecular basis of Vohwinkel's syndrome revealed mutations in the gene encoding loricrin, an epidermal envelope protein, in a family with mutilating keratoderma with ichthyosis.[10] However, subsequent analysis of families with more classic forms of Vohwinkel's syndrome, keratoderma with hereditary deafness, revealed mutations in the *GJB2* gene encoding connexin-26, a cell-cell communication protein.[11,12] Furthermore, Hailey-Hailey disease and Darier disease have been shown to result from mutations in adenosine triphosphate (ATP)–dependent calcium transporter genes, *ATP2C1* and *ATP2A2*, respectively.[13,14] Quite recently, we and others have been able to disclose the genetic basis of PXE, a condition traditionally considered a prototypic heritable connective tissue disorder.[15-18] The gene harboring pathogenetic mutations in PXE, designated *ABCC6*, encodes a putative transmembrane transporter molecule, MRP6, with unknown substrate specificity. Surprisingly, this gene is expressed predominantly, if not exclusively, in the kidneys and the liver.

The progress made in individual diseases listed in Table I is detailed in the corresponding references. We will briefly illustrate the progress in molecular genetics of heritable skin diseases and its clinical implications by discussing two illustrative conditions, the dystrophic forms of epidermolysis bullosa (DEB) and PXE. A glossary of genetic terms can be found in the Appendix.

THE PARADIGM OF DEB

EB is a heterogeneous group of mechanobullous disorders manifesting primarily with fragility of the skin.[2,6] In addition, a variety of extracutaneous manifestations can be encountered, including corneal erosions, enamel hypoplasia, scarring alopecia, anonychia, esophagus strictures, pyloric atresia, and late-onset muscular dystrophy. EB is a disease of the cutaneous BMZ, and mutations have been identified thus far in 10 distinct genes expressed in the dermoepidermal junction[6] (see Table I).

An example of a variant of EB in which spectacular success has been recently made toward understanding the molecular basis of the disease is provided by DEB.[19] Just about a decade ago, relatively little was known about the molecular mechanisms leading to profound blistering and scarring in this group of diseases. In fact, early work suggested that proteolytic enzymes were somehow genetically activated, resulting in dissolution of the BMZ components in this and other variants of EB. However, careful ultrastructural and biochemical observations on the cutaneous BMZ provided the clues as to the candidate gene/protein system in DEB. Specifically, the diagnostic hallmark of the dystrophic forms of EB is an abnormality in anchoring fibrils, attachment structures that extend from the lower part of the lamina densa to the underlying papillary dermis. In DEB, the anchoring fibrils are morphologically altered, reduced in number, or entirely absent.[20] At the same time, biochemical analyses suggested that type VII collagen is the major, if not the exclusive, component of the anchoring fibrils.[21] Collectively, these two observations allowed us to propose the hypothesis that type VII collagen may serve as the candidate gene/protein system responsible for dystrophic EB.[5] To test this postulate, we cloned the entire human type VII collagen complementary DNA and elucidated the intron-exon organization of the corresponding gene, *COL7A1*, which turned out to be extremely complex, consisting of a total of 118 separate exons.[22,23] Nevertheless, cloning of the type

Disease	HLA
Addison's disease	Dw3
ALL	A2
Alopecia areata	DQB, DR4, DQB1
Ankylosing Spondylitis	**B27**
BCC	DR1, B27, DR7
Behcet's disease	**B5, B51**, B25
Celiac disease	B8, Dw3/DR3
Chronic hepatitis	B8, Dw3/DR3
CLL	B18
Congenital adrenal hyperplasia	B47
CTCL	DR5, DQB1
Dermatitis herpetiformis	B8, DQw2, DR3
EBA	**DR2**
Erythema multiforme (herpes assoc.)	**B15**, DQB1
Graves' disease	B5, B8, Bw35, Dw3/DR3
Hashimoto's Thyroiditis	Dw5/DR5
Hemochromatosis	A3
Hodgkin's disease	A1, A11, B8, B15
IDDM	Dw3/DR3, Dw4/DR4
Juvenile Rheumatoid Arthritis	B27, Dw5
Lichen planus	DR2, DR1, DR10, DRw9, Bw61
Melanoma	A2, DRB1, B13, B51, DQB1
Multiple Sclerosis	A3, B7, Bw2, Dw2/DR2
Pemphigus foliaceus	DRB1, DR1, DR4
Pemphigus vulgaris	Dw10, DR4, DRw6, DQB1
Psoriasis	A1, B13, Bw37, **Cw6**, DR406
Psoriatic arthritis	B27, B39, DQw3
Reiter's Syndrome	Dw8, **B27**
Rheumatoid Arthritis	**Dw4/DR4**
SCC	DR1, B27, DR7
Scleroderma	**DQA2, C4A**
Sezary syndrome	DQB1
Skin cancers	DR1, B27, DR7
SLE	C4A, DR2, DR3, DQA
Systemic Lupus Erythematosus	**Dw3/DR3**
Uveitis	B27
Vitiligo	**DR4**

Interleukins and Cytokines

Th1 cells primarily produce interferon (IFN)-γ and Interleukin (IL)-2, whereas Th2 cells produce IL-4, IL-5, IL-6, IL-10, and IL-13. The two helper T cell classes also differ by the type of immune response they produce. While Th1 cells tend to generate responses against intracellular parasites such as bacteria and viruses, Th2 cells produce immune responses against helminths and other extracellular parasites.[2,3] Interestingly, the cytokines produced by each Th subset tend to both stimulate production of that Th subset, and inhibit development of the other Th subset. That is, IFN-γ produced by Th1 cells has the dual effect of both stimulating Th1 development, and inhibiting Th2 development. Th2-secreted IL-10 has the opposite effect.

A large group of cytokines (IL-1 to IL-18) produced mainly by lymphocytes, although some are made by neutrophils, phagocytes, or by auxiliary cells. They have a variety of functions, but most are involved in directing other immune cells to divide and differentiate. Each IL acts on a specific, limited group of cells that express the correct Receptor for that interleukin.

Interleukin-1 (IL-1)

Produced by activated Macrophages, Endothelial Cells, B-Cells, and Fibroblast Cells. IL-1 induces Inflammatory responses, edema, promotes the production of IL-2, prostaglandins, and the growth of Lymphocytes. It also augments the release of corticosteroids, and induces fever. IL-1 is a protein (17 kD: 152 amino acids) secreted by macrophages or accessory cells involved in the activation of both T- and B-lymphocytes in response to antigens or mitogens, as well as affecting a wide range of other cell types. At least two IL-1 genes are active; a and b forms of IL-1 are recognized. There is an endogenous antagonist, IL-1ra that binds to the receptor but does not elicit effects. IL-1 a , IL-1 b and IL-1ra are remarkably different is sequence though similar in binding properties. See also catabolin, endogenous pyrogen.

Interleukin-2 (IL-2)

Also known as T-Cell Growth Factor (TGF), it is secreted by stimulated Helper T-Cells (CD4+), cytoyoxic T-Cells (CD8+), and Large Granular Lymphocytes (LGL). It promotes proliferation (clonal expansion) and differentiation of additional CD4+ Cells, B-Cells, and activates Macrophages and Oligodendrocytes. IL-2 is a cytokine (17 kD) released by activated T-cells that causes activation, stimulates and sustains growth of other T-cells independently of the antigen. Blocking production or release of IL-2 would block the production of an immune response

Interleukin-3 (IL-3)

Produced by activated T-Cells, it stimulates the proliferation of Precursors in all hematopoietic Cells (Red Cells, Granulocytes, Macrophages, and Lymphocytes). Product of mitogen-activated T-cells: colony-stimulating factor for bone-marrow stem cells and mast cells.

Interleukin-4 (IL-4)

Stimulates production of Antibody-producing B-Cells, leading to the production of IgG & IgE. It also promotes CD8+ Cell growth and promotes Th2 Cell differentiation. On Macrophages, IL-4 induces MHC Class II expression, but inhibits production of the pro-inflammatory cytokines (IL-1 and Tumor Necrosis Factor-alpha [TNF-]).

Interleukin-5 (IL-5)

Is chiefly a growth and activation factor for Eosinophils. A B-cell growth and differentiation factor; also stimulates eosinophil precursor proliferation and differentiation.

Interleukin-6 (IL-6)

Stimulates several types of Lymphocytes, and the production of Acute Phase Proteins in the Liver. It is particularly important in inducing B-Cells to differentiate into Antibody Forming Cells (Plasma Cells). IL-6 is a cytokine that is co-induced with interferon from fibroblasts, a B-cell differentiation factor, a hybridoma growth factor, an inducer of acute phase proteins, and a colony stimulating factor acting on mouse bone marrow.

Interleukin-7 (IL-7)

Is a T-Cell growth and activation factor, and a Macrophage Activation Factor. IL-7 is a single-chain 25 kD cytokine (20 kD) originally described as a pre-B-cell growth factor but now known to have effects on a range of other cells, including T-cells. Produced by monocytes, T-cells and NK cells.

Interleukin-8 (IL-8)

Is produced by most cells of the body, especially Macrophages and Endothelia Cells. It enhances Inflammation, by enabling Immune Cells to migrate into tissue, and is a powerful inducer of chemotaxis for neutrophils. One of the first chemokines to be isolated; one of the C-X-C family (8 kD). Secreted by a variety of cells and potently chemokinetic and chemotactic for neutrophils and basophils but not monocytes. Receptor is G-protein coupled.

Interleukin-9 (IL-9)

Up-regulates Th1 responses (Enhancing Inflammation) by inhibiting T-Cell apoptosis. IL-9 is a cytokine produced by T-cells, particularly when mitogen stimulated, that stimulates the proliferation of erythroid precursor cells (BFU-E). May act synergistically with erythropoietin. Receptor belongs to haematopoietic receptor superfamily.

Interleukin-10 (IL-10)

Down-regulates Anti-Viral Responses by inhibiting: the production of Interferon-gamma (IFN-), Antigen Presentation, and Macrophage production of IL-1, IL-6, and TNF-. IL-10 is also very important in B-Cell activation. Cytokine produced by Th2 helper T-cells, some B-cells and LPS-activated monocytes. Regulates cytokine production by a range of other cells.

Interleukin-11 (IL-11)

Pleiotropic cytokine originally isolated from primate bone marrow stromal cell line. Stimulates T-cell-dependent B-cell maturation, megakaryopoiesis, various stages of myeloid differentiation. Receptor shares gp130 subunit with other members of IL-6 cytokine family.

Interleukin-12 (IL-12)

Acts in a contrasting manner to IL-10; it promotes Th1 Type Response in Macrophages, NK Cells, and induces IFN- production. IL-13 is a heterodimeric cytokine (35 kD and 40 kD) that enhances the lytic activity of NK cells, induces interferon- g production, stimulates the proliferation of activated T-cells and NK cells. Is secreted by human B-lymphoblastoid cells (NC-37). May play a role in controlling immunoglobulin isotype selection and is known to inhibit IgE production.

Interleukin-13 (IL-13)

Has structural and functional similarities to IL-4 and promotes B-Cell differentiation. IL-12 is a Lackie Cytokine (12.4 kD) with anti-inflammatory activity. Produced by activated T-cells; inhibits IL6 production by monocytes and also the production of other pro-inflammatory cytokines such as TNF- α, IL-1, IL-8. Stimulates B-cells. Gene is located in cluster of genes on human chromosome 5q that also has IL-4 gene.

Interleukin-14 (IL-14)

Cytokine (53 kD) produced by T-cells that enhances proliferation of activated B-cells and inhibits immunoglobulin synthesis. Unrelated to other cytokines but has homology with complement factor Bb.

Interleukin-15 (IL-15)

Cytokine that has effects very similar to IL-2 but in addition potently chemotactic for lymphocytes. Levels are elevated in the rheumatoid joint. Receptor shares b and g subunits with IL-2 receptor but has unique a -subunit.

Interleukin-16 (IL-16)

Secreted from CD8+ cells and will induce migratory responses in CD4 + cells (lymphocytes, monocytes and eosinophils). May bind to CC-CKR-5 and contribute to the blocking of HIV internalization.

Interleukin-17 (IL-17)

Pro-inflammatory T-cell product (17 kD) that acts on receptors on a range of cells to activate NF k B. Induces expression of IL-6, IL-8 and ICAM-1 in fibroblasts and enhances T-cell proliferation stimulated by sub-optimal levels of PHA. Receptor is a Type I transmembrane protein, though a soluble form is also found, and has no homology with other known sequences.

Interleukin-18 (IL-18)

First isolated from liver of mice during toxic shock; has sequence homology with IL-1 b and IL-1ra and has also been designated IL-1 g .

Interferons

Interferon (IFN) was originally described more than 40 years ago by Isaacs and Lindeman as a substance that is produced upon stimulation of cells by viruses, and that has the ability to protect cells from infection with viruses. Interferons are proteins that elicit an antiviral activity that is not specific to a particular virus. This activity requires the new synthesis of RNA and proteins and is not observed in the presence of substances that inhibit RNA and protein synthesis. Apart from their antiviral activities, interferons also possess anti-proliferative and immunomodulating activities and influence the metabolism, growth, and differentiation of cells in many different ways. The three main human IFNs are known as IFN-alpha, IFN-beta, and IFN-gamma, although there are others (3). IFN-alpha, IFN-beta, and IFN-delta are also called Type-1 interferon. Interferon-gamma is designated as Type-2 interferon. Some older names of interferons such as leukocyte interferon (interferon-alpha), fibroblast interferon (interferon-beta), and immune interferon (interferon-gamma) can still be found in some publications.

The broad classes of action currently recognized for interferons are characterized as 1) antiviral, 2) antiproliferative, 3) regulator of differentiation, 4) modulator of lipid metabolism, 5) inhibitor of angiogenesis, 6) antitumoral, and 7) immunoregulator. Interferon effects include:

Monocyte and macrophage activation
Enhanced major histocompatibility complex (MHC) class I expression (IFN-alpha and IFN-beta)
Enhanced MHC class II expression (IFN-gamma)
Augmentation of natural-killer (NK) cell activity
Stimulation of proliferation and differentiation of B-cells
Increased cytotoxic T-cell activity

In general, IFN-gamma is a much more potent immunomodulator and IFN-alpha more effective antitumor agent in vivo.

TNF

TNF a or cachectin, originally described as a tumour-inhibiting factor in the blood of animals exposed to bacterial lipopolysaccharide or Bacille Calmette-Guerin (BCG). Preferentially kills tumour cells in vivo and in vitro , causes necrosis of certain transplanted tumours in mice and inhibits experimental metastases. Human TNF a is a protein of 157 amino acids and has a wide range of pro-inflammatory actions. Usually considered a cytokine. Soluble TNF a is released from the cell surface by the action of TACE (TNF a converting enzyme), a metalloproteinase. TNF b (lymphotoxin) has 35% structural and sequence homology with TNF a and binds to the same TNF receptors. Unlike TNF a , TNF b has a conventional signal sequence and is secreted from activated T and B cells.

GM-CSF

A cytokine that stimulates the formation of granulocyte or macrophage colonies from myeloid stem cells isolated from bone marrow.

Systemic Medication Summary (Dermatology)

GLUCOCORTICOIDS	Bind to glucocorticoid receptors (GCR) in cytoplasm; GC-GCR complex binds to DNA; regulates cytokines, adhesion molecules, interleukins, inhibit T cells (inhibit B cells at high doses); increase neutrophil demargination. Side effects include osteoporosis, Cushingoid habitus, hyperglycemia, and avascular necrosis of femoral head.
DAPSONE	Inhibits neutophil respiratory burst in lysosomes; inhibits neutrophil response to chemotactic stimuli; inhibits adhesion of neutrophils to endothelial cells. Also inhibits eosinophils. Side effects include agranulocytosis, methemoglobulinemia, neuropathy, and hemolytic anemia (in G6PD deficiency).
ANTIMALARIALS	Various immunosuppressive actions, anti-inflammatory actions; bind to DNA; effects on antigen presentation; inhibits TNF-alpha promoter. Side effects include retinopathy (esp. Plaquenil), lichenoid eruptions, and hyperpigmentation.
METHOTREXATE	Inhibits folate metabolism/cell division (S phase) – Inhibits dihydrofolate reductase (DHFR) (reversed by leucovorin). Also inhibits thymidylate synthetase (reversed by thymidine). Anti-inflammatory effects: Inhibits AICAR transformylase and methionine synthetase. Side effects include hepatotoxicity, cirrhosis, pancytopenia, radiation or UV recall, pneumonitis, and acral erythema.
AZATHIOPRINE	Purine analogue which inhibits DNA/RNA synthesis and repair. Immunosuppressive activity – inhibits T cells, B cells, APCs. Active metabolite is 6-thioguanine. Check thiopurine methyl transferase (TPMT) activity prior to use. Side effects include pancytopenia and increased infection risk.
HYDROXYUREA	Inhibits ribonucleotide reductase, thus preventing DNA synthesis/repair. Can lead to leg ulcers or a dermatomyositis-like eruption. Side effects include radiation recall, leg ulcers, dermatomyositis-like eruption, and onycholysis.
MYCOPHENOLATE MOFETIL	Inhibits DNA and RNA synthesis by inhibiting inosine monophosphate (IMP) dehydrogenase. Side effects include increased risk of zoster.
CYCLOPHOSPHAMIDE	Cross-links preformed DNA. Suppresses B Cells > T Cells; T suppressor cells > T helper cells. Causes hemorrhagic cystitis (prevented with Mesna) and sterility.
CHLORAMBUCIL	Cross-links DNA.Side effects include leukopenia, hepatotoxicity, mucosal ulcers, pulmonary fibrosis, aplastic anemia, and seizures.
CYCLOSPORINE	Inhibits production of IL-2 by inhibiting calcineurin (decr. NFAT-1). Inhibits IFN-gamma production by T cells. Binds to steroid receptor associated heat shock protein 56. Interacts with macrolide antibiotics, azole antifungals, and grapefruit juice through CytP450. Side effects include hypertension, hypertrichosis, renal dysfunction, gingival hyperplasia, and increased risk of infections.
TACROLIMUS	Similar effects as cyclosporine. Also inhibits IL-8 production. Side effects include immunosuppression and increased infection risk.
THALIDOMIDE	Hypno-sedative effects. Immunomodulatory/anti-inflammatory effects. Inhibits TNF-alpha. Inhibits IL-12. Promotes IL-4, IL-5, IFN-gamma; inhibits neutrophil chemotaxis/phagocytosis; inhibits monocyte phagocytosis. Side effects include teratogenicity (phocomelia), severe neuropathy, hypothyroidism, hypoglycemia, and leukopenia.
RETINOIDS	Activate nuclear receptors; regulate gene transcription. Immunologic and anti-inflammatory effects; effects on protein kinases; anti-keratinizing effects; anti-sebum effects; apoptosis/anti-neoplastic effects; anti-proliferative effects; effects on extracellular matrix; effects on embryonic development/morphogenesis; modulation of infections. Side effects include bone pain, hypertriglyceridemia, central hypothyroidism (bexarotene), pseudotumor cerebri, multiple osteophytes, mood changes, photosensitivity, and alopecia.

ACYCLOVIR	Inhibits viral DNA polymerase (must be phosphorylated by viral thymidine kinase, then phosphorylated by cellular kinases).
FOSCARNET	Non-competively inhibits viral DNA polymerase (does not require phosphorylation).
CIDOFOVIR	Competitively inhibits viral DNA polymerase (does not require initial phosphorylation by viral kinases).
INTERFERONS	Antiviral, anti-proliferative, immunomodulatory activity. Stimulates cytotoxic activity of NK cells, lymphocytes, macrophages. Enhances tumor-associated antigen and MHC class I expression. Inhibits growth of variety of malignant cells.
GRISEOFULVIN	Disrupts microtubule mitotic spindle formation, causing mitotic arrest at metaphase. Can cause photosensitivity.
AZOLE ANTIFUNGALS	Inhibit lanosterol 14-alpha demethylase (prevent conversion of lanosterol to ergosterol). Interact with numerous medications through CytP450.
TERBINAFINE (allylamine)	Inhibit squalene epoxidase (prevent conversion of squalene to 2,3-oxidosqualene). Allylamines are fungicidal.
PENICILLINS	Inhibit bacterial cell wall synthesis (inhibit penicillin-binding proteins).
CEPHALOSPORINS	Inhibit bacterial cell wall synthesis (inhibit penicillin-binding proteins).
TETRACYCLINES	Inhibit protein synthesis by interfering with 30S subunit of bacterial ribosomes.
MACROLIDES	Inhibit protein synthesis by interfering with 50S subunit of bacterial ribosomes.
FLUOROQUINOLONES	Inhibit DNA gyrase (topoisomerase II), which is involved in uncoiling DNA
TMP-SULFAMETHOXAZOLE	Inhibits tetrahydrofolate synthesis (disrupts folate metabolism)
UVB	UVB has shorter wavelength, more energy, less penetration. Affects keratinocytes and epidermal Langerhans cells. Causes mutations in p53, ras, GC > AT transitions.
UVA	UVA has longer wavelength, less energy, deeper penetration. Additionally affects dermal dendritic cells, fibroblasts, endothelial cells, T cells, and mast cells. Causes oxidative damage. UVB and UVA decrease ICAM-1 expression in keratinocytes. UVB decreases of IL-1 and TNF-alpha receptors. UV depletes epidermal Langerhans cells and induces T-cell apoptosis; inhibits epidermal proliferation. Psoralen forms 3,4- or 4',5'-cyclobutane addition product with pyrimidines creating crosslinked DNA. Also generates free radicals and leads to apoptosis.

Board Review Question Answers
2001

1. Methotrexate is associated with the flag sign.
2. Conception should be avoided for 90 days after discontinuation of Methotrexate in a male.
3. Doxycycline is the tetracycline of choice in acne patients with renal insufficiency.
4. Erythromycin estolate is associated with increased liver toxicity in pregnancy.
5. Itraconazole increases the blood levels of cyclosporine, digoxin, lovastatin, and cisapride.
6. Palmar-plantar erythrodysethesia is most commonly associated with 5-fluorouracil.
7. Hexachlorophene does not have good activity against Gram-negative organisms.
8. Doxycycline can increase the risk of cardiotoxicity in a patient on digoxin.
9. Radiation recall can be seen with methotrexate, bleomycin, hydroxyurea, and 5-fluorouracil.
10. Sulfonamides increase plasma level of Methotrexate due to increase displacement from proteins.
11. Chloroprocaine should be used for anesthesia in patients with cirrhosis.
12. Doxycycline dosage needs to be increased in patients on carbamazepine due to CytP450 induction.
13. Leucovorin rescue in methotrexate overdose should decrease levels below $1x\ 10^{-8}$ M.
14. Patients treated with at least 50 grams of cyclophosphamide should have annual urine cytology.
15. Acrolein is the metabolite of cyclophosphamide that causes bladder toxicity.
16. Cyclosporine should be discontinued if serum creatinine increases by at least 30%.
17. The risk of methotrexate-induced pneumonitis is idiosyncratic.
18. Dinileukin difitox targets cells expressing the IL-2 receptor.
19. Diabetic patients on sulfonylureas can have hypoglycemia when given bexarotene.
20. Bexarotene and gemfibrizol together cause increased bexarotene levels and hypertriglyceridemia.
21. Cyproheptadine can interfere with the effectiveness of fluoxetine (Prozac).
22. Patients on allopurinol should have their azathioprine dosages reduced to 25-30% of usual dose.

2002

1. Thalidomide is associated with severe neuropathy.
2. Cyclophosphamide is associated with hemorrhagic cystitis.
3. Terbinafine (Lamisil, an allylamine) is fungicidal.
4. Drug-induced Linear IgA dermatosis has been reported most frequently with Vancomycin.
5. Grapefruit juice inhibits the metabolism of cyclosporine.
6. Cyclophosphamide should be avoided in women of childbearing age due to infertility risk.
7. Thalidomide use in women requires 2 forms of contraception (i.e. tubal ligation and cervical cap).
8. Mycophenolate mofetil (CellCept) interferes with de novo purine synthesis (IMP dehydrogenase).
9. Methotrexate can cause radiation recall.
10. Birth control should be used until one month after discontinuing bexarotene.
11. Male patients on thalidomide need to use latex condoms until one month after discontinuation.
12. Warfarin levels are increased if erythromycin is used concomitantly.
13. Gingko Biloba, Garlic, and Ginseng all have anti-coagulant effects.
14. St. John's Wart and Green Tea can decrease effectiveness of OCPs due to inducing CytP450.
15. Women on Thalidomide need pregnancy tests weekly x 4, then q2w or q4w depending on regularity of menstrual cycle.
16. Hydrochlorothiazide increases methotrexate levels (displaces from proteins).
17. Infliximab targets TNF-alpha.
18. Psoriasis is mediated by Th1 cytokines.
19. Rifampin can decrease levels of dapsone due to induction of CytP450.
20. Griseofulvin can decrease levels of cyclosporine due to induction of CytP450.

Medication Review Questions 5/2002

1. Spironolactone can cause hyperkalemia and should not be used with Enalapril (ACE inhibitors).
2. Pimozide interacts with erythromycin but not with doxycyline.
3. Sumatriptan (Imitrex) interacts with SSRIs (sertraline).
4. Accutane (Isotretinoin) can cause periungual pyogenic granulomas.
5. Interferon alpha for infantile hemangiomas can cause spastic diplegia.
6. Jarisch-Herxheimer reaction (Syphilis Rxed with PCN) is treated with Ibuprofen.
7. Female patients should not become pregnant for 4 weeks after Thalidomide use.
8. PCN can treat blistering distal dactylitis (Staph/Strep).
9. Gentamicin can treat green nails due to pseudomonas.
10. Hydrochlorothiazide is most likely to cause a lichenoid photodermatitis.
11. Dexamethasone can cause steroid acne.
12. Benadryl is used for symptomatic relief in fire ant bites.
13. Itraconazole can be used to treat North American Blastomycosis.
14. Kawasaki's disease is treated with IVIG and aspirin.
15. Nicotinic acid can lead to acanthosis nigricans.

Substrates 1A2	Substrates 2C19	Substrates 2C9	Substrates 2D6	Substrates 2 E1	Substrates 3A4,5,7	
clozapine imipramine naproxen theophylline	Proton Pump Inhibitors: omeprazole lansoprazole pantoprazole	NSAIDs: diclofenac ibuprofen piroxicam	Beta Blockers: metoprolol timolol	acetaminophen chlorzoxazone ethanol	Macrolide antibiotics: clarithromycin erythromycin NOT azithromycin	Antihistamines: astemizole chlorpheniramine
	Anti-epileptics: diazepam phenytoin	Oral Hypoglycemic Agents: tolbutamide glipizide	Antidepressants: amitriptylline clomipramine desipramine imipramine		Anti-arrhythmics: quinidine	Calcium Channel Blockers: diltiazem felodipine nifedipine nisoldipine nitrendipine verapamil
	amitriptyline clomipramine cyclophosphamide progesterone	Angiotensin II Blockers: NOT candesartan irbesartan losartan valsartan	Antipsychotics: haloperidol risperidone thioridazine		Benzodiazepines: alprazolam diazepam midazolam triazolam	HMG CoA Inhibitors: atorvastatin cerivastatin lovastatin NOT pravastatin simvastatin
		celecoxib naproxen phenytoin sulfamethoxazole tamoxifen warfarin	codeine dextromethorphan flecainide ondansetron tramadol		Immune Modulators: cyclosporine tacrolimus (FK506)	
					HIV Protease Inhibitors: indinavir ritonavir saquinavir	buspirone haloperidol methadone sildenafil trazodone cisapride

Inhibitors 1A2	Inhibitors 2C19	Inhibitors 2C9	Inhibitors 2D6	Inhibitors 2 E1	Inhibitors 3A4,5,7	
cimetidine fluoroquinolones ticlopidine	fluoxetine fluvoxamine ketoconazole lansoprazole omeprazole ticlopidine	amiodarone fluconazole isoniazid ticlopidine	amiodarone chlorpheniramine cimetidine clomipramine fluoxetine haloperidol methadone mibefradil paroxetine quinidine ritonavir	disulfiram	HIV Protease Inhibitors: indinavir nelfinavir ritonavir saquinavir	amiodarone NOT azithromycin cimetidine clarithromycin erythromycin fluoxetine fluvoxamine grapefruit juice itraconazole ketoconazole nefazodone

Inducers 1A2	Inducers 2C19	Inducers 2C9	Inducers 2D6	Inducers 2 E1	Inducers 3A4,5,7	
tobacco		rifampin secobarbital		ethanol isoniazid	carbamazepine phenobarbital phenytoin	rifabutin rifampin troglitazone

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Table I. Examples of pharmacokinetic drug interactions

Mechanism	Interaction	Effect
Absorption	Calcium salts decrease GI absorption of tetracycline	Decreased plasma tetracycline
Distribution from binding sites	Sulfonamides displace metrotrexate from binding sites	Increased plasma methotrexate
Metabolism	Azole antifungal agents decrease hepatic metabolism of astemizole and terfenadine	Increased plasma astemizole and terfenadine
Excretion	Salicylates decrease excretion of metrotrexate	Increased plasma methotrexate

GI, Gastrointestinal.

Table II. Examples of pharmacodynamic drug interactions

Drug A	Drug B	Effect
Aspirin	Warfarin (Coumadin)	Increased anticoagulation activity
Alcohol	Antianxiety drugs	Increased CNS effects
Potassium-depleting diuretics	Digoxin	Decreased plasma potassium may induce digoxin-mediated cardiac arrythmia

CNS, Central nervous system.

Table III. Important hepatic enzyme inducers*

Carbamazepine
Phenobarbital
Phenytoin
Rifampin

*Blood level of the second drug is reduced.

Table IV. Important hepatic enzyme inhibitors*

Allopurinol	Erythromycin
Amiodarone	Isoniazid
Azole antifungal agents	Monamine oxidase inhibitors
Chloramphenicol	Serotonin reuptake inhibitors
Cimetidine	Sulfonamides
Disulfiram	Verapamil

*Blood level of the second drug is elevated.

Table V. Important drugs that are susceptible to hepatic enzyme inducers*

Chloramphenicol	Metronidazole
Contraceptives, oral	Mexiletine
Cyclosporine	Quinidine
Disopyramide	Theophylline
Doxycycline	Verapamil
Griseofulvin	Warfarin

*The blood level of the drugs listed is decreased.

as well as have their effects altered by other hepatic enzyme inhibitors.

Another aspect of the cytochrome P-450 enzymes is attracting considerable attention. It is now possible to subdivide the cytochrome P-450 enzymes primarily involved with drug metabolism into three gene families: CYP1, CYP2, and CYP3.[5] Although the CYP3 subfamily is involved most often in drug interactions in dermatology, some also occur with the other two. With these new developments, it is likely that drug interactions can be predicted before clinical trials.

This article discusses clinically significant drug interactions with a significance rating of 1 to 3, as well as less significant interactions that are controversial and of particular concern to the dermatologist.

In addition to the relatively large number of drug interactions to be discussed, the 10 most significant drug interactions for the practicing dermatologist are listed (Table VI). The list is based on both potential frequency and risk to the patient. Some well-known interactions (e.g., tetracycline and calcium salts) are not included. Of course, any drug interaction is significant if it involves a patient, especially our patient. All the drug interactions presented are clinically significant and

Table VI. Ten most significant drug interactions

Interacting drugs	Mechanism	Effect
Azathioprine*/Allopurinol	Decreased metabolism	Increased plasma azathioprine with pancytopenia
Cyprohepadine/Fluoxetine,* paroxetine*	Serotonin antagonism	Decreased antidepressant effect with possible suicide
Erythromycin*/Warfarin	Decreased metabolism	Increased plasma warfarin with increased anticoagulation and hemorrhage
Erythromycin,* clarithromycin,* troleandomycin*/Astemizole, terfenadine	Decreased metabolism	Increased plasma astemizole and terfenadine with cardiotoxicity
Erythromycin,* clarithromycin,* troleandomycin*/Cisapride	Decreased metabolism	Increased plasma cisapride with cardiotoxicity
Erythromycin,* clarithromycin,* troleandomycin*/Theophylline	Decreased metabolism	Increased plasma theophylline with seizures
Ketoconazole,* itraconazole*/ Astemizole, terfenadine	Decreased metabolism	Increased plasma astemizole and terfenadine with cardiotoxicity
Ketoconazole,* itraconazole,* fluconazole*/Cisapride	Decreased metabolism.	Increased plasma cisapride with cardiotoxicity
Methotrexate/Sulfonamides*	Methotrexate displaced from protein binding sites	Increased plasma methotrexate with methotrexate toxicity
Tetracycline HCl, doxycycline, minocycline/Digoxin	Increased absorption of digoxin	Increased plasma digoxin with cardiotoxicity

*Red flag drugs.

Table VII. Tetracyclines: Tetracycline hydrochloride, minocycline, and doxycycline may interact with the following:

Drug	Significance rating	Mechanism	Effect
Digoxin[a,b,c]	1	Increased GI absorption of digoxin	Increased digoxin toxicity
Methoxyflurane[a,b,c]	1	Unknown	Increased renal toxicity
Penicillins[a,b,c]	1	Decreased bactericidal action of penicillins	Decreased therapeutic effect of penicillins
Aluminum salts[a,b,c] (e.g., Rolaids)	2	Decreased GI absorption	Decreased plasma tetracyclines
Barbiturates[c]	2	Increased metabolism	Decreased plasma doxycycline
Bismuth salts[a,b,c] (e.g., Pepto-Bismol)	2	Decreased GI absorption	Decreased plasma tetracyclines
Calcium salts[a,b,c] (e.g., Oscal-500)	2	Decreased GI absorption	Decreased plasma tetracyclines
Carbamazepine[c]	2	Increased metabolism	Decreased plasma doxycyclines
Charcoal[a,b,c]	2	Decreased GI absorption	Decreased plasma tetracyclines
Food[a,b,c] (especially dairy products)*	2	Decreased GI absorption.	Decreased plasma tetracyclines.
Hydantoins[c]	2	Increased metabolism	Decreased plasma doxycyclines
Iron salts[a,b,c] (e.g., Fergon)	2	Decreased GI absorption.	Decreased plasma tetracyclines.
Magnesium salts[a,b,c] (e.g., Riopan, Phillips' Milk of Magnesia)	2	Decreased GI absorption	Decreased plasma tetracyclines
Rifamycins[c]	2	Increased metabolism of doxycycline	Decreased plasma doxycyclines
Urinary alkalinizer[sa,b,c] (e.g., Urocit-K)	2	Increased excretion	Decreased plasma tetracyclines
Zinc salts[a,b]	2	Decreased GI absorption	Decreased plasma tetracycline HCl and minocycline

GI, Gastrointestinal.

Interacting tetracyclines: a, Tetracycline HCl; b, minocycline; c, doxycycline.

*Decreased absorption of minocycline and doxycycline is not of clinical importance in most patients. It is still preferable to avoid milk with all tetracycline derivatives.

Table XVI. Miscellaneous reactions

Raynaud's phenomenon[35,345-349]	Bleomycin, bleomycin/vinblastine, bleomycin/vinblastine/cisplatin, bleomycin/etoposide/cisplatin, bleomycin/cisplatin/velban bleomycin/vincristine, bleomycin/vincristine/cisplatin, bleomycin/vincristine/doxorubicin, bleomycin/doxorubicin/dacarbazine/vinblastine, nitrogen mustard/vincristine/procarbazine/prednisone, vincristine
Scleroderma-like reaction[35,36,240,350-352]	Bleomycin, docetaxel
Folliculitis[2,35,36,353]	Dactinomycin, liposomal daunorubicin, fluorouracil, methotrexate
Exfoliative dermatitis[36,354,355]	Chlorambucil/busulfan, cisplatin, methotrexate, intravesical mitomycin C
Atrophic lichen planus-like eruption[36,152]	Hydroxyurea
Porphyria cutanea tarda[2,223,356,357]	Busulfan, cyclophosphamide, diethylstilbestrol, methotrexate
Porphyria[358]	Cisplatin
Acute intermittent porphyria[359]	Chlorambucil, cyclophosphamide
Fixed drug eruptions[152,360-362]	Dacarbazine, hydroxyurea, paclitaxel (bullous), procarbazine
Dermatomyositis-like reaction[363-367]	Long-term hydroxyurea, tamoxifen, tegafur
Keratotic papules[80,368]	Suramin
Capillaritis (purpura simplex)[369]	Aminoglutethimide
Leg ulcers[370-372]	Hydroxyurea, methotrexate
Lichenoid eruption[367,371]	Hydroxyurea, tegafur
Acne[139,373-375]	Dactinomycin, fluoxymesterone, medroxyprogesterone, vinblastine
Drug-induced lupus erythematosus[367,376-380]	Aminoglutethimide, diethylstilbestrol, hydroxyurea, leuprolide, tegafur
Erythema nodosum[296,381]	Busulfan, diethylstilbestrol
Telangiectasia[163]	Carmustine, hydroxyurea
Flare of dermatitis herpetiformis[382]	Cyclophosphamide/doxorubicin/vincristine
Bullous pemphigoid[383]	Dactinomycin/methotrexate
Hirsutism[296,373,384]	Diethylstilbestrol, fluoxymesterone, tamoxifen
Hair color change[139,225,239,259,359,385,386]	Bleomycin, bleomycin/cyclophosphamide/lomustine, bleomycin/doxorubicin/vincristine, cisplatin, cyclophosphamide, cyclophosphamide/doxorubicin/5-fluorouracil/vincristine, methotrexate, tamoxifen
Acanthosis nigricans[387]	Diethylstilbestrol
Furunculosis[373,388]	Fluoxymesterone, methotrexate
Pustular psoriasis[389]	Aminoglutethimide
Sticky skin (acquired cutaneous adherence)[390]	Doxorubicin/ketoconazole

the most dangerous cutaneous sequelae of chemotherapeutic treatment discussed herein, additional adverse cutaneous reactions have been reported (see Table XVI and Fig 12).

The cutaneous manifestations of chemotherapy are varied and range from benign to life-threatening. Furthermore, cutaneous reactions in the oncology patient may be a consequence of the chemotherapeutic treatment or may be a direct result of the patient's malignancy, ancillary therapy, infection, or hematologic status. Cutaneous reactions may manifest in immunosuppressed patients with life-threatening sepsis, in cutaneous metastasis, and in patients with GVHD. In addition, cutaneous injury may result from radiotherapy or from a multitude of other medications that oncology patients frequently require. Accurate diagnosis and subsequent appropriate treatment instituted in a timely fashion can reduce morbidity and mortality.

We are grateful to Dr Jonathan Sporn for his advice and guidance in the writing of this manuscript. In addition, we would like to thank the Yale residents for their generosity with the use of their slide collection.

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Table I. Genes associated with palmoplantar keratodermas

Function	Gene symbol	OMIM entry	Location	Protein	Inheritance	Disease	OMIM entry
Intracellular structural	LOR	152445	1q21	Loricrin	AD	Loricrin keratoderma (Vohwinkel's syndrome, ichthyotic variant; progressive symmetric erythrokeratoderma)	604117 602036
	KRT1	139350	12q13	Keratin 1	AD	Epidermolytic PPK	144200
					AD	Epidermolytic PPK with polycyclic psoriasiform plaques	139350
					AD	Diffuse nonepidermolytic PPK	139350
					AD	Ichthyosis hystrix of Curth-Macklin	146590
	KRT9	144200	17q12-q21	Keratin 9	AD	Epidermolytic PPK	144200
	KRT6a	148041	12q13			Pachyonychia congenita type I	167200
	KRT16	148067	17q12-q21	Keratin 16	AD	Focal nonepidermolytic PPK	600962
						Pachyonychia congenita type I	167200
	KRT6b	148042	12q13	Keratin 6b	AD	Pachyonychia congenita type II	167210
	KRT17	148069	17q12-q21	Keratin 17	AD	Pachyonychia congenita type II	167210
	KRT5	148040	12q13	Keratin 5	AD	Epidermolysis bullosa simplex with PPK	131800
	KRT14	148066	17q12-q21	Keratin 14	AD	Epidermolysis bullosa simplex with PPK	131800
Desmosomal	DSP	125647	6p24	Desmoplakin	AD	Striate PPK	148700
					AR	PPK, woolly hair, left-sided cardiomyopathy	605676
	DSG1	125670	18q12.1-q12.2	Desmoglein 1	AD	Striate PPK	148700
	PKGB	173325	17q21	Plakoglobin	AR	Naxos syndrome	601214
	PKP1	601975	1q32	Plakophilin	AR	Ectodermal dysplasia/skin fragility syndrome	604536
	EVPL	601590	17q25	?Envoplakin	AD	Tylosis with esophageal cancer	148500
Gap junction	GJB2	121011	13q11-q12	Connexin 26	AD	Vohwinkel's syndrome (classical variant)	604117
					AD	PPK with deafness	148350
	GJB6	604418	13q12	Connexin 30	AD	Hidrotic ectodermal dysplasia	129500
	GJB4	505425	1p35.1	Connexin 30.3	AD	Erythrokeratodermia variabilis	133200
	GJB3	603324	1p35.1	Connexin 31	AD	Erythrokeratodermia variabilis	133200
Enzymes	CTSC	602365	11q14.1-q14.3	Cathepsin C	AR	Papillon-Lefevre syndrome	245000
					AR	Haim-Munk syndrome	245010
	TAT	276600	16q22.1-q22.3	Tyrosine transaminase	AR	Richner-Hanhart syndrome	276600
Secreted proteins	SLURP-1	606119	8qter	SLURP-1	AR	Mal de Meleda	248300
Mitochondrial	MTTS1	590080	Mito 7445-7516	Serine tRNA	Mito	PPK with deafness	148350

AD, Autosomal dominant; *AR*, autosomal recessive; *Mito*, mitochondrial; *OMIM*, Online Mendelian Inheritance in Man; *PPK*, palmoplantar keratoderma.

carboxylic acid, which serve to filter ultraviolet radiation and to hydrate the stratum corneum.[5,6] The L granules are small round structures that release a cysteine-rich protein called *loricrin* that forms the major protein component of the CCE. Epidermal transglutaminases bind a number of structural proteins (including loricrin, involucrin, small proline-rich peptides, keratins, elafin, cystatin A, and desmosomal peptides) to the cell membrane, forming the highly insoluble proteinaceous component of the CCE at the inner leaflet of the plasma membrane.[7,8] The release of keratohyaline granule contents, the cleavage of profilaggrin into filaggrin, and the activity of transglutaminase are all calcium-dependent processes.

We review the molecular basis of PPKs by addressing each of the affected proteins. These pro-

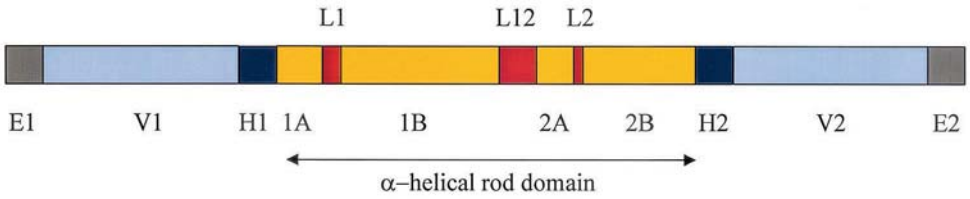

Fig 2. Keratin protein structure. E1 and E2 represent end domains, V1 and V2 represent variable regions, and H1 and H2 represent homologous regions (present only in type II keratins). The α-helical rod domain is composed of 4 α-helical domains (1A, 1B, 2A, and 2B), which are separated by nonhelical linker domains (L1, L12, and L2). The 2 ends of the α-helical rod domain include the highly conserved helix boundary sequences.

Table III. Keratin expression patterns and keratin-associated diseases

Type II	Type I	Major location of expression	Hereditary diseases
1	10	Suprabasal keratinocytes	Bullous congenital ichthyosiform erythroderma; diffuse nonepidermolytic PPK (keratin 1)
1	9	Palmoplantar suprabasilar keratinocytes	Epidermolytic PPK
2e	10	Upper spinous and granular layers	Ichthyosis bullosa of Siemens
3	12	Cornea	Meesmann's corneal dystrophy
4	13	Mucosal epithelium	White sponge nevus
5	14	Basal keratinocytes	Epidermolysis bullosa simplex
6a	16	Outer root sheath, hyperproliferative keratinocytes, palmoplantar keratinocytes	Pachyonychia congenita type I; focal nonepidermolytic PPK
6b	17	Nail bed, epidermal appendages	Pachyonychia congenita type II; steatocystoma multiplex
8	18	Simple epithelium	Cryptogenic cirrhosis

PPK, Palmoplantar keratoderma.

KERATINS

Keratins are members of the intermediate filament family and provide structural integrity to epithelial cells. Keratins are obligate heterodimers composed of one "acidic" (type I, keratins 9-20) and one "basic" (type II, keratins 1-8) keratin. Each heterodimer is tissue- and differentiation-specific (Table III).[25] The central α-helical rod domain is responsible for dimerization and higher-order polymerization and is composed of 4 domains separated by nonhelical linker domains. The helix boundary peptides that flank the α-helical rod domain show remarkable evolutionary conservation and are necessary for filament assembly. Finally, the head and tail regions consist of the 2 variable regions and end domains. Type II keratins also contain homology domains between their variable regions and the α-helical rod domains (Fig 2).[25] Keratins 1 and 9 are the predominant keratins of the differentiated palmoplantar epidermis, and mutations in these and other keratins have been found to be associated with hereditary PPK.

Disease associations

Epidermolytic PPK is an autosomal dominant skin disorder characterized by well-demarcated, nontransgradiens, symmetric hyperkeratosis of the palms and soles associated with histologic findings of hyperkeratosis and epidermolysis (ballooning degeneration) starting in the spinous layer. Ultrastructurally, there is vacuolization of the cytoplasm and an abnormal keratin filament network characterized by tonofilament clumping similar to that found in the Dowling-Meara variant of epidermolysis bullosa simplex.[26,27] Moreover, there is abnormal expression of filaggrin, loricrin, involucrin, and transglutaminase 1 in keratinocytes of the spinous layer in patients with epidermolytic PPK.[28] Epidermolytic PPK was initially mapped to 17q12-q21, the locus of the type I acidic keratin cluster.[29] Subsequently, different point mutations of the keratin 9 gene have been identified. These mutations generally affect the highly conserved coil 1A region of the α-helical rod domain of keratin 9, a domain thought to be important for keratin heterodimerization.[30-36] Mutations in

Table V. Diagnostic criteria for tuberous sclerosis

Primary features
- **Facial angiofibromas** (histology not required if clinically obvious)
- **Multiple ungual fibromas** (histology not required if clinically obvious)
- Cortical tubers (histology required)
- Subependymal nodule or giant cell astrocytoma (histology required)
- Multiple calcified subependymal nodules protruding into the ventricle (radiographic finding)
- Multiple retinal astrocytomas (histology not required if clinically obvious)

Secondary features
- **Shagreen patch** (histology not required if clinically obvious)
- **Forehead plaque** (histology not required if clinically obvious)
- Cardiac rhabdomyoma (histological or radiographic confirmation)
- Cerebral tubers (radiographic evidence)
- Noncalcified subependymal nodules (radiographic evidence)
- Other retinal hamartomas or achromic patch (histology not required if clinically obvious)
- Pulmonary lymphangiomyomatosis (histology required)
- Renal angiomyolipoma (histological or radiographic confirmation)
- Renal cysts (histology required)
- Affected first-degree relative

Tertiary features
- **Confetti macules** (histology not required if clinically obvious)
- **Hypomelanotic macules** (histology not required if clinically obvious)
- **Gingival fibromas** (histology not required if clinically obvious)
- Renal cysts (radiographic evidence)
- Randomly distributed enamel pits in deciduous or permanent teeth
- Hamartomatous rectal polyps (histology required)
- Bone cysts (radiographic evidence)
- Pulmonary lymphangiomyomatosis (radiographic evidence)
- Cerebral white-matter "migration tracts" or heterotopias (radiographic evidence)
- Hamartomas of other organs (histology required)
- Infantile spasms

Definite tuberous sclerosis complex
- One primary feature and two secondary features *or*
- One secondary feature and two tertiary features

Probable tuberous sclerosis complex
- One secondary feature and one tertiary feature *or*
- Three tertiary features

Suspect tuberous sclerosis complex
- One secondary feature *or*
- Two tertiary features

Adapted from Lindor NM, Greene MH. The concise handbook of family cancer syndromes: Mayo Familial Cancer Program. J Natl Cancer Inst 1998;90:1067. Recently, TS-associated skin findings have been reported in MEN1.

a large protein designated "hamartin" and, like tuberin, most alterations of hamartin result in a shortened protein.

Although chromosome 9q34 linkage and chromosome 16p13 each account for approximately 50% of TS kindreds, some studies have shown lower rates of mutations in *TSC1* compared with *TSC2*.[236,237] In a genetic analysis of 150 TS cases, Jones et al[238] detected mutations in 80% of the 150 cases, affecting *TSC1* in only 22 cases and *TSC2* in 98 cases.[238] Because of the large size of these genes, the exact frequencies of mutations may be inaccurate because of technical difficulties. The possibility also exists that other genes within the chromosome 9q34 region may be responsible for a subset of TS pedigrees linked to this region but lacking *TSC1* alterations.

The amino acid sequence of tuberin suggests that it also belongs to the family of GAPs.[239] Like neurofibromin, tuberin may thus down-regulate growth signals mediated by the *ras* family of proto-oncogenes. Although a part of hamartin appears to be transmembrane,[235] the function of hamartin is still largely unknown. Unlike tuberin, it bears no sequence similarities to any known enzymes or proteins.

Infections Diseases and Vectors

1st Disease	Measles; Rubeola virus (paramyxovirus, RNA)	
2nd Disease	Scarlet Fever; group A strep	
3rd Disease	German measles; Rubella	
4th Disease	Duke's disease; variants of rubella, rubeola, scarlet fever, exfoliative variants of *Staphylococcus aureus* infection, or viral exanthems of Coxsackievirus-Echovirus group	
5th Disease	Erythema infectiousum; human parvovirus B19	
6th Disease	Roseola infantum/Exanthem subitum; HHV-6/7	
Acrodermatitis Chronica Atrophicans	late sequel of *Borrelia Afzelii* (vector: *ixodes ricinus);* Europe	A354
Actinomycosis	*Actinomycosis israelii*	A.409,
Adult T-cell leukemia-lymphoma (ATLL)	HTLV-1	A520
Alterniosis	*Alternia alternatta*	A415
Amebiasis Cutis	*Entamoeba histolytica*	A526
Anthrax	*Bacillus anthracis*	323
Aplastic Crisis	Human parvovirus B19	H.358
Arthropod (misc)	Black widow: *Latrodectus mactans*; *Loxosceles reclusa* Tarantula: *Theraphosidae* Scorpion: *Centruroides sculpturantus* Fleas: human (*pulex irritans*), dog/cat (*Ctenocephalides felis/canis*) Mouse (*Leptosylla segnis*)	A571
Aspergillosis	disseminated: *Aspergillus fumigatus* primary cutaneous (rare): *A. fumigatus*, *A. flavus* (iv sites/wounds)	A414 L525
Atypical mycobacteriosis	Group I: photochromogens; *M. marinum, M. kansasii, M. simiae* Group II: scotochromogens: *M. scrofulaceum* Group III: nonphotochromogens; *M. avium-intracellulare complex* Group IV: rapid growers; *M. fortuitum, M. chelonei*	A426
Babesiosis	*Babesia microti* (vector: tick, *Ixodes dammini)*	353
Bacillary Angiomatosis	*Bartonella henselae (vector:* cat flea, *Lutzomyia verrucarum*) *Bartonella quintana* (vector: body louse, *pediculus humanus var. corporis*)	343
Bacterial vaginosis	*Gerdnerella vaginalis, Mycoplasma hominis, Mobiluncus,* others	
Bartonellosis (Oroya fever/ Verruga peruana)	*Bartonella bacilliformis* (vector: sand fly *Phlebotomus, lutzomyia*)	343
Bedbug Bites (Cimicosis)	*Cimex lectularius*;	A552
Bejel (Endemic Syphilis)	*Treponema pallidum subspecies endemicum*	468
Bilharziasis	visceral schistosomiasis	
Blastomycosis: keloidal	Lobomycosis: *Loboa loboi*	A408
Blastomycosis: North American (Gilchrist's dz)	*Blastomyces dermatitidis*	A398 L526
Blastomycosis: S. American	*Paracoccidiodes brasiliensis*	A400

Blistering Distal Dactylitis	*S. pyogenes, S. aureus*	
Boston exathem disease	Echovirus 16	A505
Botryomycosis	*S. Aureus*; *(*also: E. coli, Proteus, Pseudomonas, Bacillus, Klebsiella);	312,
Brucellosis (Undulant fever)	*Brucella melitensis* (goat), *suis* (pig), *abortus* (cow), *canis* (dog)	348
Bullous Impetigo	*S. aureus* phage II group 71	314
Buruli ulcer	*M. ulcerans* (group III)	A428
Carbuncle	*S. aureus*	
Cat bite	*Pasteurella multocida*	A341
Caterpillar Dermatitis	Gypsy moth, L*ymantria dispar*; Corn emperor moth, *Automeris io;* Puss caterpillar, *Megalopyge opercularis*	A551
Cat-Scratch Disease	*Bartonella henselae, Afipia felis* (less commonly); *(vector:* cat flea, *Lutzomyia verrucarum*)	343, L494
Cellulitis	*S. pyogenes, S. aureus, H. influenza* (esp. children), *V. vulnificans*	319,338
Chagas Disease	American Trypanosomiasis; *T. cruzi* (vector: *reduviid sp.*)	534
Chancroid	*Hemophilus ducreyi*	333
Chickenpox	Varicella-Zoster virus	
Chromobacteriosis	*Chromobacterium violaceum*	A339
Chromoblastomycosis	*Phialophora verrucosae, Cladosporium carrionii, Fonsecaea compacta, F. pedrosoi, Rhinocladiella aquaspersa*	A404 L533
Coccidiomycosis (Valley/ San Joaguin Valley Fever)	*Coccidiodes immitis*	A391 L535
Cryoglobulinemia	Hepatitis B infection (75%); also HCV	
Cryptococcosis	*Cryptococcus neoformans*	A396
Cysticercosis	*Taenia solium;* pork tapeworm	A540
Dengue Fever	Break bone fever; Arbovirus (RNA); vector: *Aedes aegypti* mosquito	A508
Dermatitis palaestrae limosae (Mud Wrestling dermatitis)	Enterobacteriaceae	
Diptheria (Desert Sore)	*Corynebacterium diphtheriae* (Klebs-Loeffler bacillus)	324
Dirofilariasis	*Dirofilaria tenuis* (US); vector: mosquito; *D. immitis*: dog heart-worm	L560
Dog bite	*Capnocytophagia canimorsus*	341
Dracunculosis (Guinea worm)	*Dracunculus medinensis* (vector: *Cyclops* copepods, water fleas)	A545
Duke's Disease	Fourth Disease (variants for rubella, rubeola, scarlet fever, exfoliative variants of *Staphylococcus aureus* infection, or viral exanthems of Coxsackievirus-Echovirus group)	H. 357
Dust mite	*Dermatophagoides pteronyssinus*	
Eaton Agent	*Mycoplasma pneumoniae;* cold agglutinins	A355
Ecthyma	Group A beta-hemolytic *S. pyogenes; S. aureus* or both	317
Ecthyma contagiosum (Orf)	Orf virus (parapoxvirus)	499
Ecthyma gangrenosum	*Pseudomonas aeruginosa* (most commonly)	330
Ehrlichiosis	rickettsial dz, *Ehrlichia canis, Ehrilichia chaffeensis*: (vector: tick)	A351
Endemic Typhus	Flea-borne or Murine typhus; *R. typhi (?R. mooseri)* (vector: rat flea; *Xenopsylla cheopis*)	349 H366
Epidemic Typhus	Brill-Zinsser Disease (recrudescent)***;*** *R. prowazekii* (vector: *pediculus humanus var. corporis*)	A349 H366
Ertyhema (chronica) migrans	Lyme disease; *B. Burgdorferi* (vector: deer tick)	

Erysipelas (St. Anthony's fire, ignis sacer)	Grp A beta-hemolytic *S. pyogenes,* also groups G and C (adults)	A318
Erysipeloid of Rosenbach (Fish handler's Disease)	*erysipelothrix rhusiopathiae*	A320
Erythema infectiosum	Fifth Disease (parvovirus B19)	A507
Erythema Multiforme (Eur J Ped 1999;158:929)	Children: infectious agent in 71% of cases: most commonly *Mycoplasma pneumoniae* (also URI and HSV)	
Erythrasma	*Corynebacterium minutissimum*;coral	327
Filariasis	*Brugia malayi* SE Asia); B. *timori* (Indonesia); *Wuchereria bancrofti (*Africa, Asia, S. America*); vector:* mosquitoes (*Culex, Anoph., Aedes)*	
Fire Ant Sting	Black fire ant, *Solenopsis richteri;* Red Fire ant, *S. invicta* family: *Formicidae*	A559
Fishtank granuloma	*Mycobacterium marinum*	
Folliculitis	mix of normal cutaneous flora (*S. aureus, P. orbiculae*)	
Fournier's Gangrene	Group A strep, mixed infection with anaerobes & enteric bacilli	A330
Frambesia ulcer	*Treponema partenue*	A326
Furuncle	*S. aureus*	
Gamasoidosis	Bird mites (*Ornithonyssus and Dermanyssus*)	A569
Gas Gangrene / Meleney's gangrene	*Clostridum perfringens*	A330
Gianotti-Crosti Syndrome	Hep B, EBV, coxsackie, CMV, RSV, vaccinia, rotavirus, poliovaccine virus, parainfluenza virus; papulovesicular; spares trunk	A494
Glanders	*Pseudomonas mallei*; farcy buds; horse (mules/donkey) handlers	A342
Gonococcemia	*Neisseria gonorrhoeae*	
Grain itch	Mites from grains; *Pyemotes tritici*	A569
Gram negative folliculitis	Enterobacter, Klebsiella, Proteus (deep, cystic lesions), Pseudomonas	
Granuloma annulare	associated with EBV and HIV	
Granuloma Inguinale	(aka: Donovanosis); *Calymmatobacterium granulomatis*	L491
Granulomatosis Infanti-septica	*Listeria monocytogenes*	freiden p142
Grocer's itch	Mites from prunes, figs, dates or cheeses (vs. grocer's eczema)	A569
Ground itch	Hookworm (*Necator americanus, Ancylostoma duodenale*) larvae	A542
Hand-Foot-Mouth Disease	picornavirus *(*coxsackievirus A 16)	H359
Herpangina	picornavirus group (coxsackieviruses and echoviruses)	H361
Herpesvirus misc	HSV-1: orolabial herpes, HAEM, Whitlow in children HSV-2: genital herpes (herpes progenitalis), ¾ of whitlow in adults VZV: zoster, varicella EBV: infectious mononucleosis, lymphoma (hodgkin's), OHL CMV: neonatal infxn, mono-like dz, oral/anal ulcers in HIV HHV-6/7: Roseola infantum/exanthema subitum/sixth disease HHV-8: KS, Castleman's dz, primary effusion lymphoma (B cell) *Herpesvirus simiae*; (B virus); macaques; fatal encephalitis in humans	L571
Histoplasmosis	*Histoplasma capsulatum; H. duboisii* (African)	A394
Hot tub folliculitis	*P. auruginosa*	332
Human bite	*Eikenella corrodens*	341

Human Papilloma Virus	Palmoplantar warts: HPV-1 (myrmecia); (2,4) HPV-60 (ridged wart, verrucous cyst) Verruca Vulgaris: HPV-2 (1,4, 7 and others) Verruca Plana (flat wart): HPV-3 (10, 27,41) Epidermodysplasia verruciformis: HPV-5,8,47 (9,10,12,14,15,17,19-25, 36-38) Giant condyloma acuminatum of Buschke-Lowenstein: HPV-6 (11) Condyloma acuminata: HPV-6,11 Butcher's warts: HPV-7 Bowenoid Papulosis: HPV-16,18 (31,33,51) Cervical CA: HPV-16,18 (31,33,51) Oral Focal Epithelial Hyperplasia/Heck's Disease: HPV-13 (32)	L578
Hyalohyphomycosis	*Fusarium, Penicillium, Paecilomyces*	
Hydatid disease	*Echinococcus granulosus*; reservoir sheep/dogs	A541
Impetigo of Bockhart	*S. aureus*	
Infectious mononucleosis	EBV (?CMV)	A491
Kaposi's Sarcoma	HHV-8	
Katayama fever	*Schistosoma japonicum*	
Larva currens	*Strongyloides stercoralis*	A545
Larva migrans	Creeping eruption; *Ancylostomoa braziliense* (dog/cat hookworm)	A543
Larva migrans profundus	Gnathostomoiasis; *Gnathostoma dolorosa* or *spinigerum* (Asia/sushi)	A544
Leishmaniasis Vector (Sandfly) Reservoir Cutaneous Mucocutaneous Visceral (Kala-Azar)	Old World / New World *phlebotomus spp.* / *Lutzomyia spp.* rodents, dogs / armadillos, rodents, dogs *L. tropica* (oriental sore) / *L. mexicana* (chiclero ulcer) / *L. Braziliensis* (Espundia) *L. donovani* (*donovani, infantum*) / *L. donovani chagasi*	A527 Katz182 L553
Leprosy (Hansen's Disease)	*Mycobacterium leprae*	L477
Leptospirosis	Pretibial Fever / Ft Bragg Fever; (anicteric leptospirosis: *Leptospira interrogans autumnalis);* urine/tissues of infected animals (dogs, rats) Weil's Dz (icteric leptospirosis: *L. i. icterohaemorrhagiae*)	
Loiasis	Loa loa (vector: mango fly, *Chrysops* spp.*)*	A547
Lupus vulgaris	*M. tuberculosis*	A421
Lyme Disease (NEJM Jul 01 p115)	*Borrelia burgdorferi* (vector: deer tick, *ixodes scapularis/dammini* in NE & Midwest, *I. pacificus* in NW); 10% also c babesiosis in N.E. *Europe: B. afzelli/ garinii; vector: I. ricinus* (Bannwarth's syndrome)	A352
Lymphogranuloma Venerum	*Chlamydia trachomatis* (L1,2,3)	L493
Malakoplakia	*E. Coli, S. aureus*; acquired defect in lysosomal action	
Malaria	*Plasmodium* spp. (vector: mosquito, *Anopheles* spp.)	
Mediterranean (Spotted) Fever	*Boutonneuse Fever, African Tick typhus, Kenya tick-bite fever;* Rickettsia cornorii *(vector: dog tick,* Rhipicephalus sanguineus*)*	A350 H368
Melioidosis (Whitmore's disease)	*Burkholderia pseudomallei*	A342
Molluscum Contagiosum	Poxvirus (MCV 1-4); MCV-1 in children, MCV-2 in HIV; inclusion bodies (molluscum or Henderson-Paterson bodies);	A501

Moth Dermatitis (Lepidopterism)	*Hylesia* moth venom	A551
Mycetoma (Madura foot)	Eumycetoma (true fungi, gram -): *Petriellidium* (Allescheria/*Pseudo allescheria) boydii* (US, white grain), *Madurella, Cephalosporium* Actinomycetoma (filamentous bact, gram +): *Nocardia brasiliensis* (most common)*, Streptomyces pelletieri* (pink grain), *A. israelii*	A407 L543
Myiasis (fly larvae)	Furuncular: Botfly, *Dermatobia hominis*; cattle grub (*Hypoderma lineatum*), rabbit botfly (*Cuterebra cuniculi*), Tumbu fly (*Cordylobia*) Traumatic/wound: screw worm (*Cochliomyia*), *Callitroga*, and black blowfly (*Phormia regina*); *Wohlfahrtia vigil* (infants only)	A556 L565
Nectrotizing fasciitis	*Type I: Bowel-associated infx (Enterobacteriaceae, Enterococci, B. fragilis* Type II: *S. pyogenes, Vibrio vulnificans* (rare)	
Nocardiosis	*Nocardia asteroides*	
Oculoglandular syndrome of Parinaud	*B. henselae* (cat scratch dz)	
Onchocerciasis	Onchocerca volvulus *(vector: black fly,* Simulium *spp.)*	A548
Oral hairy leukoplakia	EBV	
Orf	Ecthyma contagiosum; parapoxvirus	
Otomycosis	*Aspergillus* species	A415
Papular urticaria	(aka: lichen urticatus); hypersens. to mosquitoes, fleas, and bedbugs	L567
Paracoccidiomycosis	*Paracoccidiodes brasiliensis*	
Paronychia	Fungal, g(-) bacteria, herpes, *S. aureus, strep*	
Pediculosis capitis	*Pediculus humanus* var *captitis*	
Pediculosis corporis	*Pediculus humanus corporis*; Vagabond's disease	A554
Pediculosis pubis (phthiriasis)	*Pthirus pubis*	
Phaeophyphomycosis	*Exophiala jeanselmei* (most common in temperate climates A406) *Phialophora gougerotti* (most common subQ L529), *Alternia*	A406 L528
Piedra: Black	*Piedraia hortai* (tropical climates)	387
Piedra: white	*Trichosporon beigelii* (temperate climates)	387
Pinta	*Treponema carateum*	
Pinworm (oxyuriasis)	*Enterobius vermicularis*	
Pitted Keratolysis	*Corynebacterium minutissimum, Dermatophilus congolensis, Micrococcus sedentarius*	328
Plague, Bubonic	*Yersinia pestis;* vector: rat flea (*Xenopsylla cheopis); Pulex irritans*	A346
Portuguese man of war	*Physalia physalis* (atlantic), *P. utriculus* (pacific); neurotoxic venom	A536
Pox Virus	Smallpox: variola major (see below) Vaccinia: eczema vaccinatum, vaccinia necrosum, roseola vaccinia autoinoculation, generalized vaccinia, postvaccinial encephalitis Cowpox (orthopox bovis); vectors cats/rodents Parapox: milker's nodules/bovine papular stomatitis (cattle) Orf (ecthyma contagiosum): from sheep/goats Molluscum contagiosum: (see above) Human monkeypox: clinically similar to smallpox	 L574 L576 L578
Pretibial Fever	see Leptospirosis	

Prosector's Wart	Tuberculosis verrucosa cutis; *M. tuberculosis*	A419
Protothecosis	*Prototheca* wickerhamii*, P. zopfi*; (nonpigmented) algea	L546
Psittacosis	*Chlamydia psittaci*	
Purpura fulminans	Group A strep	
Pyomyositis	*S. aureus*	
Q Fever	*Rickettsia/Coxiella burnetti* (inhaled/ingested; only rickettsial disease not transmitted by vector)	
Queensland Tick Typhus	*Rickettsia australis* (vector: tick, *Ixodes*)	
Rat bite fever	*Spirillum minor* (sodoku)*, Streptobacillus moniliformis* (septicemia: epidemic arthritic erythema or Haverhill fever)	
Raw oyster septicemia	*Vibrio vulnificus*	A338
Reiter's Syndrome	*Chlamydia, Shigella, Salmonella, Yersinia, Campylobacter, Ureaplasma, Mycoplasma, Borrelia burgdorferi*	
Relapsing Fever (Tick Fever)	*Borrelia recurrentis, B. duttonii* (vector: tick, *Ornithodoros* spp.)	
Rhinoscleroma	*Klebsiella rhinoscleromatis* (?Frisch Bacillis)	L492
Rhinosporidiosis	*Rhinosporidium seeberi*	A409
Rickettsialpox	*Rickettsia akari* (vector: mouse mite*, Alodermanyssus (Liponys-soides?)* sanguineus; reservoir: ectoparasite of mouse, *Mus musculus)*	H366 A570
Rift Valley Fever	Phlebovirus-bunyavirus family (vector: mosquito, *Aedes caballus*)	
Rocky Mountain Spotted Fever	*Rickettsia rickettsii* (vector: wood tick, *Dermacentor andersoni* in West; dog tick, *D. variabilis* in East/South; Lone Star tick, *Amblyomma americanum* in Southwest)	H367, L490 A349
Roseola infantum	Exanthem subitum, Sixth Disease: HHV-6/7	
Rubella	German Measles (RNA togavirus)	H.355
Rubeola	Measles (RNA paramyxovirus)	H350
Sandfly fever	Papataci fever; Arbovirus (RNA); vector: *Phlebotomus papatasii*	A508
Scabies	*Sarcoptes scabiei var. hominis*	A563
Scarlet Fever	Group A strep (erythrogenic toxin)	H.352
Schistosomiasis (bilharziasis)	*Schistosoma haematobium, S. mansoni, S. japonicum;* snail vector	A539
Scrofuloderma	*M. tuberculosis*	A419
Seabather's eruption (salt)	Sea anemone, *Edwardsiella lineata*; Thimble jellyfish, *Linuche unguiculata*	
Seaweed Dermatitis (salt)	Toxins from blue-green alga, *Lyngbya majuscula Gomont* (Oahu)	
Smallpox	Variola (poxvirus variolae; genus *Orthopoxvirus*)	H363
Sporotrichosis	*Sporothrix schenckii*	A402
SSSS	*S. aureus*	
Strongyloidiasis	Cutanteous larva currens (*Strongyloides stercoralis*)	
Swimmer's Itch (fresh/salt)	Schistosome cercariae; snail reservoir; salt water (clamdigger's itch)	A538
Swimming pool granuloma	*M. marinum*	A426
Syphilis (Lues)	*Treponema pallidum*	A445
Tinea (Pityriasis) versicolor	*Malassezia furfur (*aka: *Pityrosporum ovale/orbiculare)*	
Tinea barbae	*T. verrucosum*(zoophilic, "cattle ringworm")*, T. mentagrophytes*	A364
Tinea capitis	US: *T. tonsurans* (*M. audouinii* is second)	A359

	Europe: *M. canis* Africa: *T. violaceum*; SE Asia: *M. ferrugineum*	
Tinea corporis	Adults: *T. rubrum* (anthropophilic); Children: *M. canis* (zoophilic)	A367
Tinea cruris	*T. rubrum*(majority)*, T. mentagrophytes, E. floccosum*	
Tinea facei	*T. rubrum* (majority)*, T. mentagrohpytes, M. canis (T. tonsurans* in infants)	A366
Tinea favosa (Favus)	*T. schoenleinii*	L518
Tinea imbricata (Tokelau)	*T. concentricum*	A370
Tinea nigra	*Exophiala phaeoannellomyces (*formerly *werneckii)* (dematiaceous)	A387
Tinea pedis/manum	*T. rubrum, T. mentagrophytes, E. floccosum*	
Tinea Unguium (onychomycosis)	Distal subungual: *T. rubrum* (most common by far) White superficial: T. mentagrophytes (leukonychia trichophyta) Proximal subungual: T. rubrum, T. megninii (may indicate HIV) Candidaonychomycosis: *Candida albicans*	A376
Tinea: Verrucous epidermophytosis	*Epidermophyton flocculosum*	A365
Toxic Shock Syndrome	*S. aureus* (TSS toxin-1, enterotoxin B)	
Toxoplasmosis	*Toxoplasma gondii*; reservoir: cats	A535
Trench Fever	*Bartonella quintana* (vector: body louse; *pediculosis corporis*)	
Trichinosis	*Trichinella spiralis*	A550
Trichomonas vaginitis	*Trichomonas vaginalis*	A527
Trichomycosis axillaris	*Corynebacterium tenuis*	A967
Trombidiasis	Chigger bites (*Parascoschoengastia nunezi)*; vector of scrub typhus	A568
Tropical Spastic Paresis	HTLV-1	A520
Trypanosomiasis	African: *T. brucei gambiense*(90%)*, T.b. rhodesiense* (vector: tse tse Fly, *Glossina* sp.) American (Chagas' disease): *T. cruzi* (vector: kissing bug, *Reduviida)*	A534 Katz170
Tuberculosis	*Mycobacterium tuberculosis*	
Tularemia	*Francisella tularensis* (vector: tick; *D. variabilis, Amblyomma americanum)* handling wild rabbits, rodents; ulceroglandular and typhoidal	L488, A347
Tungiasis	Burrowing flea/sand flea; *Tunga penetrans*	
Typhus	Endemic/Murine: *Rickettsia typhi* (vector: rat flea feces, *Xenopsylla cheopis, X. braziliensis*) Epidemic: *Rickettsia prowazekii* (vector: body louse feces, *Pediculus)* Scrub: *Rickettsia tsutsugamushi* (vector: red chigger/mite, *Trombiculid*);	
Vaccinia	Orthopox virus	
Vectors (general)	Lice: epidemic typhus, trench fever, bacillary angiomatosis Fleas: plague, endemic typhus, Dracunculosis (water flea), tungiasis Mosquitoes: yellow fever, malaria, dengue, filariasis, west nile fever, rift valley fever Ticks: rocky mountain spotted fever, tularemia, lyme, colorado tick fever, babesiosis, ehrlichiosis, mediterranean (boutonneuse) fever, queensland tick typhus, relapsing fever	

	Mites: rickettsialpox, gamasoidosis, grocer's itch, grain itch, trombidiasis, vanillism, copra itch, coolie itch, feather pillow dermatitis	
Virus: General	HSV: ds DNA, enveloped HPV: ds DNA, unenveloped Pox: DNA Parvo: ss DNA, unenveloped Rubella: ss RNA (togavirus family) HCV: ss RNA (flavivirus family) Measles: ss RNA (paramyxovirus family)	
Weil's disease	see leptospirosis	
West Nile Fever	Arbovirus; vector: *culex* mosquito	A508
Woolsorter's disease	Anthrax (*B. anthracis*)	323
Yaws	*Treponema pallidum* subspecies *partenue*	A466
Yellow Fever	Yellow fever virus (vector: mosquito, *Aedes aegypti*)	
Zygomycosis	*Mucormycosis:* Mucor, Rhizopus, Absidia *Entomophthoromycosis: conidiobolus coronats,Basidiobolusranarum*	A412 L526

DRUG ERUPTIONS

I. Drugs commonly associated with drug eruptions:
   a. Amoxicillin, Trimethoprim/Sulfamethoxazole, Cephalosporins, Anti-malarials, Gentamicin, Diuretics, Dapsone, Heparin, sulfonamides, Anticonvulsants, Quinolones, Tetracyclines, NSAIDs, Macrolides, AZT.

II. Drugs frequently associated with severe drug eruptions:
   a. Allopurinol, Anticonvulsants, sulfonamides, Furosemide, Penicillamine, Thiazide diuretics

III. Drugs associated with specific skin eruptions:
   a. Acne – corticosteroids, halogens (bromides/iodides), haloperidol, steroid hormones, isoniazid, lithium, phenytoin
   b. Acute generalized exanthematous pustulosis – Penicillins, Cephalosporins, macrolides, allopurinol, carbamazepine, tetracyclines, Calcium channel blockers, furosemide, hydroxychloroquine, imipenem, isoniazid, phenytoin, vancomycin
   c. Alopecia - Allopurinol, anticoagulants, azathioprine, bromocriptine, beta-blockers, cyclophosphamide, hormones, NSAIDs, phenytoin, methotrexate (MTX), valproate
   d. Bullous pemphigoid - penicillamine, furosemide, neuroleptics, penicillins, PUVA, sulfasalazine
   e. Erythema nodosum - Halogens, oral contraceptives, penicillin, sulfonamides, tetracyclines
   f. Erythroderma - Allopurinol, anticonvulsants, barbiturates, captopril, carbamazepine, chloroquine, chlorpromazine, Calcium channel blockers, lithium, sulfonamides
   g. Fixed drug eruptions - Anticonvulsants, aspirin, NSAIDs, barbiturates, benzodiazepines, dapsone, metronidazole, oral contraceptives, penicillins, sulfonamides, tetracyclines
   h. Hypersensitivity syndrome (Fever, adenopathy, elevated LFTs, and drug eruption) - Allopurinol, carbamazepine, dapsone, minocycline, NSAIDs, phenobarbital, phenytoin, sulfonamides
   i. Lichenoid reactions - Antimalarials, beta-blockers, ACE inhibitors, furosemide, gold, penicillamine, tetracyclines, thiazides
   j. Linear IgA dermatosis – Captopril, diclofenac, lithium, vancomycin
   k. Livedoid Eruption - Amantadine
   l. Lupus-like eruption – Hydralazine, procainamide, and minocycline, and hydrochlorothiazide, Calcium channel blockers, griseofulvin, terbinafine
   m. Morbilliform - ACE inhibitors, allopurinol, amoxicillin, ampicillin, anticonvulsants, barbiturates, carbamazepine, isoniazid, NSAIDs, penicillin, phenytoin, quinolones, sulfonamides, thiazides
   n. Pemphigus - Captopril, penicillamine, cephalosporins, penicillins, phenobarbital, piroxicam, progesterone, propranolol
   o. Photosensitivity - Amiodarone, chlorpromazine, furosemide, griseofulvin, lovastatin, piroxicam, quinolones, sulfonamides, tetracyclines, thiazide
   p. Pseudoporphyria - barbiturates, sulfonamides, isoniazid, NSAIDs, oral contraceptives, androgens, tetracyclines
   q. Psoriasis (Exacerbation) – ACE inhibitors, GM - CSF, lithium, gold, Beta blockers, antimalarial agents, interferon alpha, NSAIDs, clonidine, tetracycline, terfenadine
   r. Stevens-Johnson Syndrome - Allopurinol, anticonvulsants, NSAIDS, barbiturates, carbamazepine, codeine, diltiazem, furosemide, penicillins, phenytoin, sulfonamides, tetracyclines
   s. Toxic Epidermal Necrolysis - Allopurinol, anticonvulsants, NSAIDs, isoniazid, penicillins, phenytoin, sulfonamides, tetracyclines, and vancomycin
   t. Urticaria - ACE inhibitors. aspirin, NSAIDs, cephalosporins, opiates, penicillins, contrast dye, vaccines
   u. Vasculitis - Allopurinol, barbiturates, chlorpromazine, NSAIDs, gold, hydralazine, penicillins, phenytoin, propylthiouracil, quinolones, sulfonamide, tetracyclines, thiazides
   v. Vesiclobullous eruptions - NSAIDs, barbiturates, captopril, cephalosporins, furosemide, griseofulvin, penicillamine, penicillins, sulfonamides, thiazides

IV. Chemotherapeutic agents associated with specific morphologic patterns:
   a. Acneiform - Dactinomycin, vinblastine
   b. Alopecia - Alkylating agents, anthracyclines, bleomycin, doxorubicin, hydroxyurea, MTX, mitomycin, mitoxantrone, vinblastine, vincristine, cyclophosphamide
   c. Erythema multiforme - chlorambucil, cyclophosphamide, diethylstilbestrol (DES), etoposide, hydroxyurea, MTX, mitomycin C, paclitaxel
   d. Fixed drug eruptions - Dacarbazine, hydroxyurea, paclitaxel, procarbazine
   e. Hyperpigmentation - Busulfan, nitrogen mustard, cyclophosphamide, ifosfamide, BCNU, carmustine, fotemustine, cisplatin, thiotepa, fluorouracil, MTX, bleomycin, dactinomycin, daunorubicin, doxorubicin, mithramycin, mitoxantrone, hydroxyurea, procarbazine
   f. Lichenoid – Hydroxyurea
   g. Lupus - DES, hydroxyurea, leuprolide
   h. Morbilliform - Bleomycin, carboplatin, chlorambucil, cytarabine, DES, doxorubicin, etoposide, 5-fluorouracil (5-FU), hydroxyurea, MTX, mitomycin C, mitotane, mitoxantrone, paclitaxel, thiotepa
   i. TEN - Asparaginase, bleomycin, chlorambucil, cytarabine, doxorubicin, 5-FU, MTX
   j. Urticaria - bleomycin, busulfan, carboplatin, chlorambucil, cisplatin, cyclophosphamide, cytarabine, daunorubicin,

DES, doxorubicin, etoposide, 5-FU, mechlorethamine, melphalan, MTX, mitomycin C, mitotane, mitoxantrone, paclitaxel, pentostatin, thiotepa, vincristine

k. Vasculitis - Busulfan, cyclophosphamide, cytarabine, hydroxyurea, 6-mercaptopurine, MTX, mitoxantrone, tamoxifen

V. Cutaneous reactions to cytokine therapy:
   a. Granulocyte colony-stimulating factor (G-CSF) - Sweet syndrome, leukocytoclastic vasculitis, localized pruritus, localized erythema
   b. Granulocyte-macrophage colony-stimulating factor (GM-CSF) - Maculopapular eruptions, exfoliative dermatitis, urticaria, pruritus, purpura, alopecia, flushing, epidermolysis, localized erythema
   c. Tumor necrosis factor a (TNF-a) - Erythroderma and localized erythema
   d. IFN-a - Alopecia, pruritus, psoriasis, SLE
   e. IL-1 - Phlebitis, and mucositis
   f. IL-2 - Erythema, pruritus, desquamation, erythroderma, necrosis, urticaria, blisters, exacerbation of autoimmune skin disorders, flushing, telogen effluvium, cutaneous ulcers, erythema nodosum, TEN

VI. Nail changes associated with medications:
   a. Anonychia – oral retinoids
   b. Beau's lines – chemotherapy and other cytotoxic medications
   c. Splinter hemorrhages – tetracyclines
   d. Longitudinal pigmented streaks - bleomycin, busulfan, daunorubicin, nitrogen mustard, hydroxyurea, methotrexate, cyclophosphamide, 5-fluorouracil, psoralens (PUVA), zidovudine (AZT), gold, antimalarials, ketoconazole, tetracyclines, phenytoin, sulfonamides
   e. Blue nails - minocycline, bleomycin, zidovudine (AZT), antimalarials
   f. Terry's nail (Half-and-Half nail = Proximal white, distal pink) - prednisone, cyclophosphamide, methotrexate, doxorubicin, vincristine
   g. Onycholysis - bleomycin, doxorubicin, 5-fluorouracil, oral retinoids
   h. Photo-Onycholysis - tetracyclines, chlorpromazine, thiazides, PUVA
   i. Paronychia – oral retinoids

VII. Dermatological adverse reactions of commonly used classes of medications
   a. Beta Blockers – Pruritus (C), xerosis (C), alopecia (R), morbilliform drug eruption (R), lichenoid reaction (R), psoriasis (R), angioedema (U)
   b. Penicillins/Cephalosporins – Morbilliform drug eruption (R), fixed drug eruption (R), pemphigus (R), urticaria (R), acute generalized exanthematous pustulosis (U), angioedema (U), erythema multiforme (U), toxic epidermal necrolysis (U), Stevens-Johnson Syndrome (U)
   c. Tetracyclines – Fixed drug eruption (R), morbilliform drug eruption (R), photosensitivity (R), lichenoid eruption (R), angioedema (U), vasculitis (U), pseudoporphyria (U)
   d. ACE inhibitors – Alopecia (R), angioedema (R), morbilliform drug eruption (R), lichenoid reaction (R), psoriasis (R), urticaria (R), vasculitis (U)
   e. Calcium channel blockers – Acne (R), morbilliform drug eruption (R), lichenoid reaction (R), psoriasis (R), xerostomia (R), angioedema (U), vasculitis (U)
   f. Diuretics –lichenoid eruption (R), morbilliform drug eruption (R), photosensitivity (R), urticaria (R), acute generalized exanthematous pustulosis (U), bullous eruption (R), vasculitis (U), erythema multiforme (U), toxic epidermal necrolysis (U), Stevens-Johnson Syndrome (U), pseudoporphyria (U)
   g. Sulfonamides – Morbilliform drug eruption (R), photosensitivity (R), bullous eruption (R), vasculitis (U), erythema multiforme (U), toxic epidermal necrolysis (U), Stevens-Johnson Syndrome (U), erythema nodosum (U)
   h. Aspirin/NSAIDs – Alopecia (R), angioedema (R), bullous eruptions (R), fixed drug eruption (R), lichenoid eruption (R), morbilliform drug eruption (R), urticaria (R), acute generalized exanthematous pustulosis (U), erythema nodosum (U)
   i. Anti-convulsants (Phenytoin/Carbamazepine/Phenobarbital) – Acne (R), bullous eruption (R), gingival hyperplasia (R), lichenoid eruption (R), morbilliform drug eruption (R), urticaria (R), erythema multiforme (U), toxic epidermal necrolysis (U), Stevens-Johnson Syndrome (U), acute generalized exanthematous pustulosis (U), vasculitis (U)

VIII. Unique dermatological reactions associated with specific medications
   a. Bleomycin – Flagellate hyperpigmentation, radiation recall, Raynaud's phenomenon
   b. Penicillamine – Elastosis Perforans Serpiginosa
   c. Aspirin/NSAIDs – Pseudoporphyria
   d. Hydralazine – Lupus-like eruption
   e. Procainamide – Lupus-like eruption
   f. Methotrexate – "Flag" sign, radiation recall, UV recall, folliculitis
   g. Cytarabine – Acral erythema, neutrophilic eccrine hidradenitis, radiation recall, eccrine squamous syringometaplasia, leg ulcers
   h. Fluorouracil – Acral erythema
   i. Doxorubicin – Acral erythema, radiation recall, "Sticky" skin
   j. Dactinomycin – Radiation recall, folliculitis, Serpentine supravenous hyperpigmented eruption

k. Hydroxyurea – Dermatomyositis-like eruption, leg ulcers, lichenoid eruption
l. Vancomycin – "Red Man" syndrome, Linear IgA bullous dermatosis
m. Heparin – Heparin-induced thrombocytopenia
n. Warfarin – Skin necrosis
o. Captopril – Bullous pemphigoid, vasculitis, lichenoid eruption
p. Minocycline – Hyperpigmentation, acute generalized exanthematous pustulosis, Lupus-like syndrome, Sweet's syndrome, vasculitis
q. Phenytoin - Erythema multiforme, toxic epidermal necrolysis, Stevens-Johnson Syndrome
r. Phenobarbital - Erythema multiforme, toxic epidermal necrolysis, Stevens-Johnson Syndrome
s. Carbamazepine – Erythema multiforme, toxic epidermal necrolysis, Stevens-Johnson Syndrome
t. Sulfonamides – Erythema multiforme, toxic epidermal necrolysis, Stevens-Johnson Syndrome, vasculitis, Fixed drug eruption, Acute generalized exanthematous pustulosis
u. Progesterone – Autoimmune Progesterone dermatosis
v. Calcium channel blockers, Terbinafine, Furosemide, Hydrochlorothiazide – Acute generalized exanthematous pustulosis
w. Pravastatin, Simvastatin, Atorvastatin – Lichenoid eruption
x. ASA, NSAIDs, pseudophedrine, omeprazole, fluconzaole, sulfonamides, Protease inhibitors, Antibiotics – Fixed drug eruption
y. Amoxicillin – EBV-associated purpuric eruption, Flexural exanthem
z. Hydrochlorothiazide, Glipizide, Progesterone – Pigmented purpuric dermatosis

REACTIONS TO SYSTEMIC MEDICATIONS USED IN DERMATOLOGY

I. Immunosuppressive agents
   A. Azathioprine [Imuran]
      1. Contraindications – Pregnancy, Prior hypersensitivity, Active infection, Reduced activity of Thiopurine methyltransferase (TPMT), Drug interactions (Allopurinol, alkylating agents, captopril, coumadin, and pancuronium).
      2. Allergic (Immune-related) Reactions – Hypersensitivity (R)
      3. Pseudo-Allergic (Idiosyncratic) Reactions – Gastrointestinal distress (C), Immunosuppression carcinogenesis (R), Pancytopenia (R), Infection (R)
   B. Mycophenolate mofetil [Cellcept]
      1. Contraindications – Pregnancy, Prior hypersensitivity, Severe hepatic or renal disease, Drug Interactions (including azathioprine and cholestyramine)
      2. Allergic (Immune-related) Reactions – Hypersensitivity (R)
      3. Pseudo-Allergic (Idiosyncratic) Reactions – Gastrointestinal distress (C), Urinary distress (C), Headache (C), Infection (R), Carcinogenesis (U)

II. Injectable Agents
   A. Interferon-alpha [Intron, Roferon, Alferon]
      1. Contraindications – Prior hypersensitivity, Pregnancy (Relative), Cardiac arrythmias, Depression, Leukopenia.
      2. Allergic (Immune-related) Reactions – Hypersensitivity (C), Anaphylaxis (R)
      3. Pseudo-Allergic (Idiosyncratic) Reactions – Flu-like symptoms (C), Gastrointestinal distess (C), Depression (C), Cardiac arrythmia (R), Spastic diplegia (R), Rhabdomyolysis (U)
   B. Botulinum toxin [Botox]
      1. Contraindications – Prior hypersensitivity, Myasthenia Gravis
      2. Allergic (Immune-related) Reactions – Hypersensitivity (R), Anaphylaxis (U)
      3. Pseudo-Allergic (Idiosyncratic) Reactions – Ptosis (for peri-orbital injections) (R)

III. Miscellaneous
   A. Thalidomide [Thalomid]
      1. Contraindications – Pregnancy, Prior hypersensitivity, Women of childbearing potential, Severe hepatic or renal disease, Peripheral neuropathy, Congestive heart failure, Severe hypertension, Hypothyroidism, Drug interactions (including alcohol, barbiturates, and other CNS depressants)
      2. Allergic (Immune-related) Reactions – Hypersensitivity (R)
      3. Pseudo-Allergic (Idiosyncratic) Reactions – Sedation (C), Mood Changes (C), Brittle Nails (C), Increased appetite (C), Gastrointestinal distress (C), Peripheral neuropathy (C), Teratogenicity (C), Hypothyroidism (R), Hypoglycemia (R), Leukopenia (R), Erythroderma (U)
   B. Spironolactone [Aldactone]
      1. Contraindications – Prior hypersensitivity, Renal disease, Hyperkalemia, Pregnancy, Breast cancer, Gynecological malignancy, Drug interactions (including Potassium, Digoxin, and ACE inhibitors)
      2. Allergic (Immune-related) Reactions – Hypersensitivity (R)

3. Pseudo-Allergic (Idiosyncratic) Reactions – Gastrointestinal distress (C), Hyperkalemia (C), Teratogenicity (C), Gynecomastia (R), Breast or Gynecological malignacy (U)

C. Ortho-Tricyclen or other oral contraceptives
   1. Contraindications – Pregnancy, Drug interactions (including anti-convulsants, rifampin, and griseofulvin)
   2. Allergic (Immune-related) Reactions – Hypersensitivity (U)
   3. Pseudo-Allergic (Idiosyncratic) Reactions – Nausea (C), Breast tenderness (C), Weight gain (C), Headaches (C), Deep venous thrombosis (R), Thromboemboli (R)

D. Trental [Pentoxifylline]
   1. Contraindications – Prior hypersensitivity, Severe hepatic or renal disease, Pregnancy, Severe cardiac disease
   2. Allergic (Immune-related) Reactions – Hypersensitivity (R)
   3. Pseudo-Allergic (Idiosyncratic) Reactions – Nausea (C), Headaches (C), Dizziness (C), Gastrointestinal distress (C)

E. Methoxsalen [Oxsoralen] or other Psoralens
   1. Contraindications – Prior hypersensitivity, Pregnancy, Pemphigus, Bullous pemphigoid, Lupus erythematosus, Xeroderma pigmentosum, Photosensitivity, Personal or family history of melanoma, Severe cardiac, hepatic or renal disease, Concomitant use of photosensitizing medications (including tetracyclines, fluoroquinolones, and thiazide diuretics)
   2. Allergic (Immune-related) Reactions – Hypersensitivity (R)
   3. Pseudo-Allergic (Idiosyncratic) Reactions – Erythema (C), Gastrointestinal distress (C), Freckling (C), Photoaging (C), Non-melanomatous skin cancers (C), Pruritus (R), Photosensitive eruptions (R), Photoonycholysis (R), Hypertrichosis (R), Drug fever (R), Exanthem (R), Herpes simplex recurrences (R), Melanoma (R), Cataracts (R), Immunosuppression (R)

F. Finasteride [Propecia]
   1. Contraindications – Pregnancy, Prior hypersensitivity, Women of childbearing potential
   2. Allergic (Immune-related) Reactions – Hypersensitivity (R)
   3. Pseudo-Allergic (Idiosyncratic) Reactions – Teratogenicity (C), Loss of Libido (C), Erectile dysfunction (R), Gynecomastia (R), Myopathy (R)

IV. Psoriasis Medications

A. Cyclosporine [Neoral]
   1. Contraindications – Severe renal disease, Severe hypertension, Prior hypersensitivity, History of malignancy, Pregnancy (Relative), Immunodeficiency, Active infection, Drug interactions (including macrolide antibiotics, Azole antifungals, HIV protease inhibitors, Calcium channel blockers, H2-antihistamines, and diuretics, grapefruit juice).
   2. Allergic (Immune-related) Reactions – Hypersensitivity (R)
   3. Pseudo-Allergic (Idiosyncratic) Reactions – Gastrointestinal distress (C), Renal dysfunction (C), Hypertension (C), Hypertrichosis (C), Gingival hyperplasia (C), Metabolic abnormalities (C), Immunosuppression carcinogenesis (R), Infection (R)

B. Etanercept [Embrel]
   1. Contraindications – Prior hypersensitivity, Pregnancy, Active infection, Immunodeficiency
   2. Allergic (Immune-related) Reactions – Hypersensitivity (C), Anaphylaxis (R)
   3. Pseudo-Allergic (Idiosyncratic) Reactions – Flu-like symptoms (C), Headache (C), Infection (R), Immunosuppressive carcinogenesis (U), Multiple sclerosis (U)

V. Retinoids [Oral]

A. Isotretinoin [Accutane]
   1. Contraindications – Pregnancy, Hypertrigyceridemia, Uncontrolled Hypercholesterolemia, Severe Depression, Concomitant epilation or resurfacing procedures, Leukopenia, Hypothyroidism, Severe hepatic or renal disease
   2. Allergic (Immune-related) Reactions – Hypersensitivity (R), Anaphylaxis (U)
   3. Pseudo-Allergic (Idiosyncratic) Reactions – Teratogenicity (C), Cheilitis (C), Xerosis (C), Petechiae (C), Gastrointestinal distress (C), Bone Pain (C), Conjuctivitis (C), Hypertrigyceridemia (C), Hypercholesterolemia (C), Mood Changes (C), Photosensitivity (C), Depression (R). Pseudotumor Cerebri (R), Alopecia (R), Leukopenia (R), Myopathy (R), Agranulocytosis (U)

B. Acitretin [Soriatane]
   1. Contraindications – Pregnancy, Hypertrigyceridemia, Uncontrolled Hypercholesterolemia, Severe Depression, Concomitant epilation or resurfacing procedures, Leukopenia, Hypothyroidism, Severe hepatic or renal disease, Alcohol Use (In women, due to conversion to etretinate).
   2. Allergic (Immune-related) Reactions – Hypersensitivity (R), Anaphylaxis (U)
   3. Pseudo-Allergic (Idiosyncratic) Reactions – Teratogenicity (C), Cheilitis (C), Xerosis (C), Petechiae (C), Gastrointestinal distress (C), Bone Pain (C), Conjuctivitis (C), Hypertrigyceridemia (C), Hypercholesterolemia (C), Mood Changes (C), Photosensitivity (C), Depression (R).

Pseudotumor Cerebri (R), Alopecia (R), Leukopenia (R), Myopathy (R), Agranulocytosis (U)

C. Bexarotene [Targretin]
    1. Contraindications – Pregnancy, Hypertrigyceridemia, Uncontrolled Hypercholesterolemia, Severe Depression, Concomitant epilation or resurfacing procedures, Leukopenia, Hypothyroidism, Severe hepatic or renal disease
    2. Allergic (Immune-related) Reactions – Hypersensitivity (R), Anaphylaxis (U)
    3. Pseudo-Allergic (Idiosyncratic) Reactions – Teratogenicity (C), Cheilitis (C), Xerosis (C), Petechiae (C), Gastrointestinal distress (C), Bone Pain (C), Conjuctivitis (C), Hypertrigyceridemia (C), Hypercholesterolemia (C), Hypothyroidism (C), Mood Changes (C), Photosensitivity (C), Depression (R). Pseudotumor Cerebri (R), Alopecia (R), Leukopenia (R), Myopathy (R), Agranulocytosis (U)

VI. Sulfa Medications

A. Dapsone
    1. Contraindications – Prior hypersensitivity, Neutropenia, Glucose-6-Phosphate Dehydrogenase (G6PD) deficiency, Severe cardiac disease
    2. Allergic (Immune-related) Reactions – Hypersensitivity (C), Morbilliform eruption (C), Anaphylaxis (R), Toxic epidermal necrolysis (U), Exfoliative erythroderma (U)
    3. Pseudo-Allergic (Idiosyncratic) Reactions – Gastrointestinal distress (C), Methemoglobinemia (C), Peripheral neuropathy (R), Psychosis (R), Leukopenia (R), Hemolytic anemia (U), Agranulocytosis (U)

B. Sulfapyridine
    1. Contraindications – Prior Sulfonamide hypersensitivity, Neutropenia, Severe cardiac disease, Renal disease
    2. Allergic (Immune-related) Reactions – Hypersensitivity (C), Morbilliform eruption (C), Anaphylaxis (R), Toxic epidermal necrolysis (U), Exfoliative erythroderma (U)
    3. Pseudo-Allergic (Idiosyncratic) Reactions – Gastrointestinal distress (C), Peripheral neuropathy (R), Psychosis (R), Hemolytic anemia (R), Methemoglobinemia (R), Nephrotoxicity (R), Leukopenia (R), Agranulocytosis (U)

VII. Systemic Chemotherapy Agents

A. Methotrexate
    1. Contraindications – Pregnancy, Prior hypersensitivity, Leukopenia, Anemia, Thrombocytopenia, Active infection, Hepatic or renal disease, Alcohol use, Drug interactions (including NSAIDs, sulfonamids, phenytoin, tetracyclines, and dapsone).
    2. Allergic (immune-related) Reactions – Hypersensitivity (R), Anaphylaxis (U)
    3. Pseudo-Allergic (Idiosyncratic) Reactions – Nausea (C), Gastrointestinal distress (C), Dizziness (C), Hepatoxicity (C), Teratogenicity (C), Myelo-suppression (C), Pancytopenia (R), Pulmonary toxicity (R), Nephrotoxicity (R), Alopecia (R), Phototoxicity (R), Acral erythema (U), Epidermal necrosis (U), Vasculitis (U), Ultraviolet recall (U), Carcinogenicity (U)

B. Cyclophosphamide [Cytoxan]
    1. Contraindications – Pregnancy, Prior hypersensitivity, Leukopenia, Anemia, Thrombocytopenia, Active infection, Hepatic or renal disease, Drug interactions (including allopurinol, cimetidine, doxorubicin, and digoxin)
    2. Allergic (Immune-related) Reactions – Hypersensitivity (R), Stevens-Johnson Syndrome (U), Anaphylaxis (U)
    3. Pseudo-Allergic (Idiosyncratic) Reactions – Teratogenicity (C), Gastrointestinal distress (C), Leukopenia (C), Anagen effluvium (C), Hemorrhagic cystitis (C), Bladder toxicity (C), Thrombocytopenia (C), Anemia (C), Amenorrhea (C), Sterility (C). Diffuse hyperpigmentation (R), Nail ridging (R), Acral erythema (R), Carcinogenicity (R), Infection (R), Cardiomyopathy (U), Pneumonitis (U), Pulmonary fibrosis (U), Syndrome of Innappropriate secretion of Anti-Diuretic Hormone (SIADH) (U)

C. Chlorambucil
    1. Contraindications – Pregnancy, Prior hypersensitivity, Active infection, Hepatic disease
    2. Allergic (Immune-related) Reactions – Hypersensitivity (R), Morbilliform eruption (R)
    3. Pseudo-Allergic (Idiosyncratic) Reactions – Teratogenicity (C), Leukopenia (C), Thrombocytopenia (R), Anemia (R), Carcinogenicity (R), Gastrointestinal (R), Hepatotoxicity (R), Infection (R), Alopecia (R), Mucosal ulcerations (R), Peripheral neuropathy (R), Myoclonus (R), Tonic-clonic seizures (R), Aplastic anemia (U), Pneumonitis (U), Pulmonary fibrosis (U), Sterile cystitis (U)

D. Doxorubicin [Adriamycin]
    1. Contraindications – Pregnancy, Prior hypersensitivity, Active infection
    2. Allergic (Immune-related) Reactions – Hypersensitivity (R)
    3. Pseudo-Allergic (Idiosyncratic) Reactions – Alopecia (C), Stomatitis (C), Onychodystrophy (C),

Nail and acral hyperpigmentation (C), Chemical cellulitis or ulceration (R), Radiation recall (R), Palmoplantar dyesthesia (R), Neutrophil eccrine hidradenitis (R), Infection (R)

E. Dactinomycin
   1. Contraindications – Pregnancy, Prior hypersensitivity, Active infection
   2. Allergic (Immune-related) Reactions – Hypersensitivity (R), Erythema multiforme (U)
   3. Pseudo-Allergic (Idiosyncratic) Reactions – Acneiform eruption (C), Folliculitis (C), Radiation recall (R), Infection (R)

VIII. Antiparasitic Agents

A. Thiabendazole
   1. Contraindications – Prior hypersensitivity, Hepatic or renal disease
   2. Allergic (Immune-related) Reactions – Hypersensitivity (R), Stevens-Johnson Syndrome (U)
   3. Pseudo-Allergic (Idiosyncratic) Reactions – Nausea (C), Diarrhea (C), Tinnitus (R), Bradycardia (R), Leukopenia (R), Hematuria (R)

B. Diethylcarbamazine
   1. Contraindications – Prior hypersensitivity
   2. Allergic (Immune-related) Reactions – Hypersensitivity (R)
   3. Pseudo-Allergic (Idiosyncratic) Reactions – Nausea (C)

C. Sodium stibogluconate
   1. Contraindications – Prior hypersensitivity
   2. Allergic (Immune-related) Reactions – Hypersensitivity (R)
   3. Pseudo-Allergic (Idiosyncratic) Reactions – Nausea (C), Hemolysis (C), Anemia (C)

D. Pentamidine
   1. Contraindications – Prior hypersensitivity, Hepatic or renal disease
   2. Allergic (Immune-related) Reactions – Hypersensitivity (R), Toxic epidermal necrolysis (U)
   3. Pseudo-Allergic (Idiosyncratic) Reactions – Nausea (C), Diarrhea (C), Azotemia (R), Megaloblastic anemia (U), Acute pancreatitis (U), Leukopenia (U), Thrombocytopenia (U), Cardiac arrythmia (U), Hyperkalemia (U)

E. Ivermectin
   1. Contraindications – Prior hypersensitivity
   2. Allergic (Immune-related) Reactions – Hypersensitivity (R)
   3. Pseudo-Allergic (Idiosyncratic) Reactions – Headache (C), Dizziness (C), Nausea (C), Ataxia (R), Seizures (R)

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Von Gierke's disease	Glycogen storage disease/Glucose-6-phosphatase def./Xanthoma diabeticorum	668
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Whistling face syndrome	Microstomia/coloboma/flattened midface, nostrils/AD	731
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Sukhapakla	Ainhum/Linear constriction around digit leading to amputation of distal digit	767
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Gardner's syndrome	Osteomas, fibromas, desmoids, lipomas, fibrosarcomas, EICs, leimyomas/Colon polyposis, CA/APC gene/AD	789
Michelin Tire Baby syndrome	Folded skin with scarring due to smooth muscle hamartomas, nevus lipomatosis, or elastic tissue abnormalities	791
Becker's nevus	Acquired smooth muscle hamartoma on shoulder/M > F	793
Sister Mary Joseph nodule	Peri-umbilical metastasis	795
Bazex's syndrome	Acrokeratosis paraneoplastica (hands, feet, nose, ears) with aerodigestive cancer	797
Leser-Trelat sign	Eruptive seborrheic keratoses and gastrointestinal malignancy	797
Tripe palm	Acanthosis nigricans of the palms due to GI cancer especially esophageal CA	797
Trousseau's sign	Migratory thrombophlebitis associated with pancreatic cancer	797
ILVEN	Inflammatory Linear Verrucous Epidermal Nevus/Follows Blaschko's lines/Assoc. with CHILD syndrome	800
Schimmelpenning syndrome	Feuerstein and Mims syndrome/Solomon syndrome/Epidermal nevus syndrome	801
Schimmelpenning syndrome	Epidermal nevus syndrome/Sebaceous nevus, cerebral anomalies, coloboma, and lipodermoid of the conjunctiva	801
CHILD syndrome	Congenital Hemidysplasia, Ichthyosiform erythroderma, Limb defects/Verruciform Xanthoma-like epidermal nevi	802
Acanthoma cellules claires	Clear cell acanthoma of Degos and Civatte/Keratinocytes lack phosphorylase and accumulate glycogen	803
Degos' acantoma	Clear cell acanthoma of Degos and Civatte/Keratinocytes lack phosphorylase and accumulate glycogen	803
Degos and Civatte disease	Clear cell acanthoma of Degos and Civatte/Keratinocytes lack phosphorylase and accumulate glycogen	803
Flegel's disease	Hyperkeratosis Lenticularis Perstans/Psoriasiform plaques on insteps, dorsal feet, and lower legs	808
Ferguson-Smith syndrome	Multiple self-healing eruptive keratoacanatomas	817
Fibroepithelioma of Pinkus	Fibroepithelial tumor consisting of interlacing basocellular sheets and hyperplastic mesodermal stroma	823
Jacobi's ulcer	Rodent ulcer due to basal cell carcinoma	823
Bazex's syndrome	Follicular atrophoderma/hypohidrosis/hypotrichosis/BCCs/Autosomal dominant	831
Borst-Jadassohn epithelioma	Superficial basal cell carcinoma	831
Kangri cancer	SCC on abdomen in Kashmir when hot Kangri jar is carried chronically under clothing for warmth	833
Marjolin's ulcer	Skin cancer (usually SCC) arising in chronic ulcers, sinuses, scars, and burns	834
Bowen's diease	In-situ intraepidermal squamous cell carcinoma with full-thickness atypia	837
Erythroplasia of Queyrat	Bowen's disease of glans penis	840
Queyrat (erythroplasia)	Bowen's disease of glans penis	840
Zoon's Balanitis plasmacellularis	Balanitis plasmacellularis of glan penis	841
Paget's disease	Eczematous dermatitis due to adenocarcinoma, glandular carcinoma, or met.	842
Muir-Torre syndrome	Colon carcinoma, GU carcinomas, sebaceous adenomas/epith/CA, keratoacanthomas/hMSH2, hMLH1/AD	847
Eccrine poromatosis	On fingertips in Clouston's hidrotic ectodermal dysplasia	849

Schopf syndrome	Hydrocystomas of eyelids, hypotrich., hypodontia, onychodystrophy, palmoplantar eccrine syringofibroadenomas	853
Spiegler's tumor	Cylindroma	853
Calcifying epithelioma of Malherbe	Pilomatricoma	857
Malherbe's calcifying epithelioma	Pilomatricoma	857
Cowden's disease	AD/PTEN/Multiple hamartomas, trichilemmomas, oral papules, goiter, lipomas/Breast, thyroid, colon CA risk	859
Birt-Hogg-Dube syndrome	Trichodiscomas, fibrofolliculomas, achrocordons/Pneumothorax/Renal Cell CA, Colon CA, Medullary CA risk	860
Lhermitte-Duclos disease	Abnormal proliferation of neurons in cerebellum/Assoc. with Cowden's syndrome	860
Wen	Pilar (Trichilemmal) cyst of scalp	863
Pseudocyst of auricle	Localized degeneration of cartilage of ear due to trauma/Treat with drainage and compression	867
LEOPARD syndrome	Lentigines, EKG, Ocular hypertelorism, Pulmonary stenosis, Abnormal genitalia, growth Retardation, Deafness	871
Moynahan syndrome	Lentigines, congenital mitral stenosis, dwarfism, genital hypoplasia, mental deficiency	871
Myerson's nevi	Halo-like dermatitis around common nevus/Can occur from interferon alpha-2a in Behcet's syndrome	873
Sutton's nevus	Halo nevus	876
Spitz nevus	Epithelioid and spindle cell nevus of Spitz/Benign juvenile melanoma	879
Hutchinson's sign	Pigmented nail fold in acral-lentiginous melanoma	884
Ito's Nevus	Dermal melanocytosis on scapula and shoulder	891
Ota's Nevus	Dermal melanocytosis around eye	891
PNGD	Palisading neutrophilic and granulomatous dermatitis	893
Besnier-Boeck-Schaumann disease	Sarcoidosis	896
Boeck's sarcoid	Sarcoidosis	896
Leiker's granuloma	Granuloma multiforme	896
Meischer's granuloma	Annular elastolytic giant cell granuloma	896
Mkar disease	Granuloma multiforme	896
O'Brien's granuloma	Actinic granuloma	896
Darier-Roussy sarcoid	Subcutaneous nodular variant of sarcoidosis	900
Lofgren's syndrome	Fever, polyarthralgias, uveitis, bilateral hilar adenopathy, fatigue and erythema nodosum/Variant of sarcoidosis	901
Heerfordt's syndrome	Uveoparotid fever variant of sarcoid	902
Kveim-Siltzbach test	Test for sarcoid/Use sarcoid tissue to induce granulomas	902
Mikulicz's syndrome	Variant of sarcoidosis with enlarged lacrimal glands and salivary (parotid) glands	902
Uveoparotid fever	Heerfordt's syndrome (sarcoid)	902
Rosai-Dorfman syndrome	Sinus histiocytosis with massive lymphadenopathy/Emperipolesis (Phagocytosis of lymphocytes) on histology	911
CSHRH	Congenital self-healing reticulohistiocytosis/CD1a+, S100+	912
Hashimoto-Pritzker disease	Congenital self-healing reticulohistiocytosis/CD1a+, S100+	912
Hand-Schuller-Christian disease	Langerhans' cell histiocytosis	913
Letterer-Siwe disease	Langerhans' cell histiocytosis	913
Speigler-Fendt sarcoid	Idiopathic cutaneous B-cell lymphoid hyperplasia/Tattos, Borrelia	918
Ketron-Goodman Pagetoid reticulosis	Multiple lesion variant of pagetoid reticulosis (acral mycosis fungoides)	929
Woringer-Kolopp disease	Classic solitary lesion variant of pagetoid reticulosis (acral mycosis fungoides)	929
Sezary syndrome	Leukemic CTCL	930
LyP	Lymphomatoid papulosis (Ki-1+ = CD30+)	931
Hodgkin's diease	Lymphoma/Reed-Sternberg cells	937
Ophiasis	Confluent alopecia areata affecting the temporal and occipital scalp only	943
Sisaipho	Confluent alopecia areata sparing the temporal and occipital scalp only	943
Pohl-Pinkus constriction	Abrupt thinning of hair shafts at peak of anagen effluvium from chemotherapy	947
Pseudopelade of Brocq	Alopecia cicatrisata/Scarring alopecia which produces multiple round or irregular patches on scalp	949
Sperling's disease	Follicular degeneration syndrome/Hot comb alopecia/Central centrifugal scarring alopecia	949
IBIDS syndrome	Ichthyosis, Brittle hair, Impaired intelligence, Decreased fertility, Short stature	952
Marinseco-Sjogren's syndrome	Cerebellar ataxia, mental retardation, congenital cataracts, inability to chew, brittle fingernails, sparse hair	952
PIBIDS syndrome	Photosensitivity, Ichthyosis, Brittle hair, Impaired intelligence, Decreased fertility, Short stature	952
Crow-Fukase syndrome	POEMS/Polyneuropathy, Organomegaly, Endocrinopathy/M protein/(hyperpig., hypertrich., clubbing, angiomas)	953
Hallermann-Steriff Syndrome	Bird-like facies, beaklike nose, microphthalmia, micrognathia, cataracts, hypotrichosis	953
Klippel-Feil syndrome	Low posterior hairline, short neck, fused cervical vertebrae, strabismus, nystagmus, high cleft palate, bifid uvula	953
POEMS syndrome	Polyneuropathy, Organomegaly, Endocrinopathy/M protein/Skin changes/Glomeruloid/Microvenular hemangiomas	953
Tricho-Rhino-Pharyngeal syndrome	Fine sparse scalp hair, thin nails, pear-shaped broad nose, cone-shaped epiphyses of middle phalanges	953
McCusick's syndrome	Short-limbed dwarfism, and fine, sparse, hypoplastic, dysmorphic hair	954
Rothmund-Thompson syndrome	Poikiloderma, short, photosens., bone defects, hypogonadism, cataracts, sparse hair/DNA helicase defect	954
Werner syndrome	Progeria/premature aging due to helicase defect	954
Menkes' kinky hair syndrome	X-linked recessive/Pili torti, monilethrix, trichorrhexis nodosa/lethargy, seizures/Copper transport deficiency	957
Naxos disease	Variant of Woolly hair syndrome seen in Naxos, Greece	961
Brooke's disease	Keratosis follicularis contagiosa/Epidemic follicular keratoses affecting upper trunk	969
Kyrle's disease	Perforating disorder/Hyperkeratosis follicularis et parafollicularis in cutem penetrans	969
Ross syndrome	Segmental anhidrosis associated with tonic pupils (Holmes-Adie syndrome)	974
Fox-Fordyce disease	Follicular papules in apocrine areas (axilla, areola, umbilicus, groin and perineum)	975
Darier's disease	ATP2A2 mutation/Hyperkeratotic peri-follicular papules (Post-auricular, elbows, trunk)/Corp ronds/Corp grains	978
Lovidond's angle	Angle formed by nail plate and distal phalanx (Normal = 160, Clubbing > 180)	978
Cooks syndrome	AD/Nail hypoplasia of digits 1-3, anonychia of digits 4-5 of hands and all toenails, hypoplasia of distal phalanges	981
Beau's lines	Transverse furrows in nails due to childbirth, measles, paronychia, febrile illness, drug reaction or trauma	982
Mees' lines	White lines in nails/arsenic, thallium, sepsis, aortic dissection, parasitic infection, chemotherapy, renal failure	982
Muehrcke's lines	Paired white tranverse lines in nails due to hypoalbuminemia	982
Fong's syndrome	Hood syndrome/Triangular lunula/Lester iris/Radial head absent/Renal Insuff.	983
Lester iris	Hyperpigmented pupillary margin of iris/Seen in Nail-Patella syndrome	983
Nail-Patella syndrome	Fong syndrome/Hood syndrome/Triangular lunula/Lester iris/Radial head absent/Renal Insuff.	983
Terry's nail	Distal pink, Proximal whitening of nail plate due to cirrhosis, CHF, and DM	983
Trumpet nail	Pincer nail deformity	985
Yellow nail syndrome	Yellow nails due to lymphedema or impaired respiration (pleural effusions, chronic pneumonia, sinusitis)	989
Ascher syndrome	Inherited edema of lips and eyelids (blepharachalasis)	996
Melkerson-Rosenthal syndrome	Recurring facial nerve palsy, edema of lips, and scrotal tongue/Granulomatous cheilitis with lymphedema	996

Fordyce's disease (spots)	Ectopically located sebaceous glands on lips, cheeks, gums, areola, glans penis, or labia	997
Torus palatinus	Bony protuberance at midline of hard palate	997
Hunter's glossitis	Moeller's glossitis/Red, tender patches on tip and lateral aspect of tongue/Associated with pernicious anemia	1000
Moeller's glossitis	Hunter's glossitis/Red, tender patches on tip and lateral aspect of tongue/Associated with pernicious anemia	1000
Trumpeter's wart	Firm hyperkeratotic pseudoepitheliomatous nodule which is a callus on upper lip of trumpet player	1003
ANUG	Acute necrotizing ulcerating gingivitis/Bacteroides fusiformis and Borrelia vincentii co-infection	1004
Vincent's disease	Acute necrotizing ulcerating gingivitis/Bacteroides fusiformis and Borrelia vincentii co-infection	1004
Noma	Fusospirillary gangrenous stomatitis in children with poor nutrition/Leads to large ulcerations and necrosis	1005
Takahara's disease	Acatalasemia leading to gangrene of mouth and recurrent oral ulcers	1005
PFAPA syndrome	Periodic Fever, recurrent Apthous stomatitis, Pharyngitis, and Adenitis	1007
Behcet's syndrome	Uveitis, retinal vasculitis, oral ulcers, genital ulcers, erythema nodosum/HLA-B51	1008
Sutton's disease	Recurrent scarring aphthous oral ulcers	1008
Raynaud's disease	Raynaud's phenomenon assoc. with scleroderma, dermatomyositis, SLE, MCTD, RA, Sjogren's, PNH	1011
Raynaud's phenomenon	Vasospasm of digital arteries due to cold exposure (white -> red -> blue digits)	1011
Sneddon's syndrome	Livedo reticularis and cerebrovascular lesion/Anti-phospholipid ab + or anti-endothelial cell ab +	1013
PURPLE syndrome	Livedoid vasculitis/painful Purpuric Ulcers with Reticular Pattern on Lower Extremties	1015
Bier's spots	Marbled mottling of forearm when brachial artery occluded	1016
Marshall-White syndrome	Bier's spots, insomnia, and tachycardia	1016
Vibex	Linear purpuric lesion	1017
Werlhof's disease	Idiopathic (autoimmune) thrombocytopenic purpura/anti-platelet antibodies	1018
Moschcowitz's syndrome	Thrombotic thrombocytopenic purpura/strokes/schistiocytes/renal failure/ADAMST	1019
TTP	Thrombotic thrombocytopenic purpura/strokes/schistiocytes/renal failure/ADAMST	1019
Rumpel-Leede sign	Distal shower of petechiae on release of tourniquet in purpuric conditions	1022
Waldenstrom's macroglobulinemia	Lymphadenopathy, HSM, purpura, mucosal bleeds/Plasma cell dyscrasia with monoclonal IgM gammopathy	1022
Mondor's disease	Cordlike thrombosed vein on anterolateral chest wall due to thrombophlebitis	1026
Achenbach's syndrome	Paroxysmal hand hematoma due to spontaneous hemorrhage into palmar surface	1028
Gardner-Diamond syndrome	Autoerythrocyte sensitization/Painful bruising or purpura due to erythrocyte sensitization	1028
Gougerot-Blum syndrome	Pigmented purpuric lichenoid dermatitis/Rust-colored lichenoid papules and plaques on lower trunk and legs	1029
Majocchi's disease	Purpura annularis telaniectoides/Bluish-red annular macules with central red puncta	1029
Schamberg's disease	Pigmented purpuric dermatosis/Small reddish puncta in patches on legs	1029
Ducas/Kapatenakis' pigmented purpura	Scaly and papular pigmented purpura with spongiosis on histology	1030
Henoch-Schonlein purpura	Small-vessel IgA vasculitis/Arthralgias, abdominal pain, and renal failure	1031
Finkelstein's disease	Acute hemorrhagic edema of infancy/Acral edeme and annular purpura following upper respiratory infection	1035
Siedlmayer syndrome	Acute hemorrhagic edema of infancy/Acral edeme and annular purpura following upper respiratory infection	1035
Cogan's syndrome	Nonsyphilitic interstitial keratitis and vestibulo-auditory symptoms/Assoc. with PAN or Takayasu's arteritis	1039
Wegener's granulomatosis	Vasculitis, necrotizing granulomas/Sinusitis, glomerulonephritis, ulcers/c-ANCA/cytoxan	1040
Horton's disease	Temporal giant-cell arteritis/Assoc. with polymyalgia rheumatica/Scalp necrosis, retinal artery occ./prednisone	1042
Lethal midline granuloma	Ulcer on central face/Due to lymphoma, granulomatous tissue reaction, or Wegener's granulomatosis	1042
Degos' disease	Malignant atrophic papulosis/Fatal obliterative arteritis	1043
Takayasu's arteritis	Pulseless disease/Large artery vasculitis	1043
Buerger's disease	Thromboangiitis obliterans/Thrombosis and necrosis of distal fingers and toes/Smokers	1044
Kawasaki's disease	Fever, conjunc., desquam., LAN, acral edema, cheilitis, strawberry tongue, coronary art. aneursym/IVIG, Aspirin	1045
Huriez syndrome	Scleroatrophy, ridging or hypoplasia of nails, lamellar keratoderma of hands, poikiloderma, SCC	1049
Scleroatrophic syndrome of Huriez	Scleroatrophy, ridging or hypoplasia of nails, lamellar keratoderma of hands, poikiloderma, SCC	1049
Thomson's disease	Poikiloderma, short, photosens., bone defects, hypogonadism, cataracts, sparse hair/DNA helicase defect	1049
Nonne-Milroy-Meige syndrome	Milroy's syndrome/Hereditary lymphedema of lower legs	1054
L'oedeme bleu	Factitial purpuric lymphedema of dorsal hand or forearm caused by blunt trauma	1056
Secretan's syndrome	Factitial purpuric lymphedema of dorsal hand or forearm caused by blunt trauma	1056
Nelson's syndrome	Pituitary MSH-producing tumor causing hyperpigmentation in Cushing's syndrome treated by adrenalectomy	1058
Acropigmentation of Dohi	Reticulate pigmented and depigmented macules on extremities/Europe, India and Caribbean	1060
Dowling-Degos' disease	Reticular pigmented dark dots in flexures/AD	1060
Kitamura reticulate acropigmentation	Linear palmar pits and reticulate pigmented macules on dorsal hands and feet/AD	1060
Reticulate acropigmentation of Kitamura	Linear palmar pits and reticulate pigmented macules on dorsal hands and feet/AD/Japan	1060
Peutz-Jeghers syndrome	Melanotic macules on lips and oral mucosa and GI polyposis/STK11/GI, breast, and GU cancer risk	1061
Cronkhite-Canada syndrome	Melanotic macules on fingers and GI polyposis, hyperpig., alopecia, onychodys., enteropathy, hypogeusia/Japan	1062
Riehl's melanosis	Phototoxic dermatitis leading to melanosis/Japan	1062
Zebralike hyperpigmentation	Black male, ASD, dextrocardia, deafness, and bands of hyperpigmentation with increased melanocytes	1063
Vogt-Koyanagi-Harada syndrome	Acquired condtion with uveitis, vitiligo, alopecia, white scalp hair, poliosis, dysacousia	1068
Alezzandrini's syndrome	Unilateral retinitis and ipsilateral vitiligo and poliosis with or without deafness	1069
Prader-Willi syndrome	Hypotonic newborn, obesity, hypogonadism, small hands/feet, retardation/Paternal chromosome 15 deletion	1069
Chediak-Higashi syndrome	AR/albinism, immune deficiency/Lysosomal transport defect/Giant melanosomes fail to transfer to keratinocytes	1070
Cross-McKusick-Breen syndrome	Albinism, blond hair, small cloudy eyes, nystagmus, gingival fibromas, retardation	1070
Elejalde syndrome	Silvery hair, neural defects	1070
Griscelli syndrome	Partial albinism/recurrent infections/immunodeficiency/grey hair/NK cells defective	1070
Hermansky-Pudlak syndrome	Albinism/Puero Rico/Vesicle formation defects and platelel dysfunction	1070
Alport's syndrome	Collagen IV mutation associated with deafness and renal failure	1071
Angelman syndrome	Seizures, puppetlike ataxia, hand flapping, laughter, retardation/Maternal chromosome 15 deletion	1071
Bart-Pumphrey syndrome	Palmoplantar keratoderma with sensorineural deafness	1071
Bjornstad's syndrome	Pili torti, nerve deafness/recessive	1071
Brachmann-De Lange syndrome	Mental retardation, delayed growth, cutis marmorata, hypoplastic nipples and umbilicus	1071
Brooke-Spiegler syndrome	Cylindromas and trichoepitheliomas	1071
Cross' syndrome	Silvery hair, hypopigmentation, eye abnormalities, neural defects	1071
Delleman's syndrome	Orbital cysts, porencephaly, skull defects, eyelid colobomas, skin tags, aplasia cutis	1071
Ekbom's disease	Delusions of parasitosis	1071
Fisch's syndrome	Deafness, early graying of hair, partial heterchromia but no laterally displaced inner canthi	1071
Futcher's lines	Pigmentary demarcation lines	1071
Gorlin's sign	Ehler-Danlos (Tongue can touch tip of nose)	1071
Gorlin's syndrome	Basal cell nevus syndrome	1071

Grover's disease	Transient acantholytic dermatosis	1071
Herpes gladiatorum	Herpes on head and neck (wrestlers)	1071
Iso-Kikuchi syndrome	Congenital anonychia, micronychia, or polynychia of the index finger	1071
Johnston's syndrome	Hyperkeratosis, arthrogryphosis	1071
Kallmann's syndrome	X-linked/Anosmia and hypogonadotropic hypogonadism	1071
Kikuchi's disease	Benign form of necrotizing lymphadenitis of unknown cause, usually affecting young women	1071
Laugier-Hunziker Syndrome	Multiple acquired lentigines of oral mucosa, lips, palms and soles/No associated diseases	1071
MIDAS syndrome	X-linked/Micropthalmia, Dermal Aplasia, and Sclerocornea	1071
Nekam's disease	Keratosis lichenoids chronica	1071
Nicolaides-Baraitser syndrome	Mental retardation, sparse hair, brachydactyly	1071
Pallster-Killian syndrome	Mental retardation, high forehead, hypertelorism, characteristic facies	1071
Partington's syndrome	X-linked/Reticulate hyperpigmentation, failure to thrive, pneumonia, seizures, hemiplegia	1071
Rasmussen's syndrome	Trichoepitheliomas/cylindromas/milia/BCCs	1071
Rothman-Makai syndrome	Idiopathic self-resolving lobular panniculitis	1071
Rozychi's syndrome	Leukoderma, deafness, muscle wasting and achalasia	1071
Rubinstein-Taybi syndrome	Mental retardation/keloids/Broad thumbs/Beaked nose/Long philtrum	1071
Satoyoshi's syndrome	Early onset of alopecia areata	1071
Schopf-Schulz-Passarge syndrome	Palmoplantar keratoderma/eyelid cysts/hypodontia/hypotrichosis/BCC/SCC/poromas/renal tumors	1071
Shapira's syndrome	Brittle hair, short stature, developmental delay, mental retardation	1071
Steijlen's syndrome	Atrichia, palmoplantar keratoderma, loss of teeth, mental retardation/recessive	1071
Tokura-Ishihara Syndrome	NK cell lymphoma/EBV/Hypersensitivity to insect bites	1071
Voigt's lines	Pigmentary demarcation lines	1071
Wagner-Unverricht syndrome	Dermatomyositis	1071
Woolf's syndrome	Piebaldism with deafness	1071
Ziprowski-Margolis syndrome	X-linked recessive/deaf-mutism, heterchromic irides, piebald-like hypomelanosis	1071

MOPED CARS = Conditions associated with Elastosis Perforans Serpiginosa (EPS)
Marfans
Osteogenesis Imperfecta
Penicillamine
Ehlers-Danlos Syndrome
Downs Syndrome

Collagen Vascular Disorders/Cutis Laxa
Acrogeria
Rothmund-Thompson Syndrome
Scleroderma

CHADS KINKY WIFE LZ = X-linked disorders

Chondrodysplasia Punctata (Happle Syndrome/Conradi-Hunerman Syndrome)
Hunter's Syndrome
Anhidrotic Ectodermal Dysplasia (Ellis-Van Creuvald Syndrome)
Dyskeratosis Congenita
Schilder's disease (Adrenoleukodystrophy)

Menkes-KINKY hair sydrome
Wiscott-Aldrich Syndrome
Icontinentia Pigmenti
Fabry's Disease/Focal Dermal Hypoplasia (Goltz Syndrome)
Ehlers-Danlos (Type V and IX)
Lesch-Nyhan Syndrome
Ziprowski-Margolis syndrome (Waardenburg variant with Deaf-mutism/heterochromic irides/piebaldism)

Ehlers-Danlos Types

God Must Be A Man Or A Pretty Manly Female

1. Gravis
2. Mitis
3. Brevis
4. Arterial
5. X-linked
6. Ocular
7. Arthrochalasis/Dermatosparaxis
8. Periodontal
9. X-linked (Cutis Laxa)
10. Fibronectin

Disease	Protein/Gene	Location/Function	Pathogenesis
Bullous diabeticorum	N/A	Intraepidermal is most common, non-acantholytic; below DE jxn, destruction of anchoring fibrils; at LL, hemidesmosomes and anchoring filaments intact	Metabolic, associated with long standing diabetes
PCT	N/A	Subepidermal blister w/o inflammation; immunoglobulin binding to vessels and BMZ	AD and/or metabolic
Pemphigus Foliaceus	Desmoglein 1 (160 kd)/DSG1; plakoglobin (85 kd); Dsg1/plakoglobin complex (210 kd)	Transmembrane glycoprotein a/w desmosome, member of cadherin supergene family	autoimmune
Pemphigus Vulgaris	Desmoglein 3 (130 kd)/DSG3; plakoglobin (85 kd); Dsg3/plakoglobin complex	Transmembrane glycoprotein a/w desmosome, member of cadherin supergene family	autoimmune
IgA pemphigus (subcorneal pustular dermatosis variant)	Desmocollin 1	Neutrophils in upper epidermis only	autoimmune
IgA pemphigus (intraepidermal neutrophilic type)	Unidentified target antigen (may be Desmoglein 3)	Neutrophils throughout epidermis	autoimmune
Paraneoplastic pemphigus	Desmoplakin (250 kd), BPAG1 (230 kd), Desmoplakin II (210 kd), Envoplakin (210 kd), Periplakin (190 kd), Unidentified Protein (170 kd)	Members of the plakin gene family - intermediate filament-associated hemidesmosome proteins	autoimmune
Erythema multiforme major	Desmoplakin I, II (250 kd, 190 kd) in a subset of patients	Members of the plakin gene family - intermediate filament-associated hemidesmosome proteins	autoimmune
Bullous pemphigoid	BPAG1 (230 kd) - 100% of patients	Cytoplasmic component of hemidesmosome may bind K 4, 14; homology to desmoplakin I	autoimmune
Bullous pemphigoid	BPAG2 (180 kd)/COL17A1 - 50% of patients	Transmembrane component of hemidesmosome	autoimmune
Herpes gestationis	BPAG2 (180 kd)/COL17A1 - 50% of patients	Transmembrane component of hemidesmosome	autoimmune
Cicatricial pemphigoid	Laminin 6, laminin 5, BPAG1, BPAG2, Uncein, 168 kd mucosal target antigen are all targets	Separation within LL or below LD	autoimmune
Cicatricial pemphigoid (anti-epiligrin type)	Epiligrin = Laminin 5 (beta 3 subunit is target)	Glycoprotein in keratinocyte extracellular matrix at LL-LD interface	autoimmune
Lichen planus pemphigoides	BPAG2 (180 kd)	Separation in LL similar to BP	autoimmune
Dermatitis herpetiformis	Antibodies to reticulin and endomysium of smooth muscle correlate with GI dz; also anti-gliadin, antithyroid, ANA, and RF seen	Location of true antigen in skin unknown; IgA is deposited on microfibrillar components of elastin	autoimmune
Linear IgA	LABD97 = Ladinin (97 kd)/LAD-1; also subsets with BPAG1, BPAG2, collagen VII, and 200 kd antigen IgA autoantibodies	Upper LL, identical to extracellular domain of BPAG2; sub-LD	autoimmune
Chronic bullous disease of childhood	LABD97 = Ladinin (97 kd)/LAD-1; also subsets with BPAG1, BPAG2, collagen VII, and 200 kd antigen IgA autoantibodies	Upper LL, identical to extracellular domain of BPAG2; sub-LD	autoimmune
EBA	Type VII collagen (290 kd)	Sub-LD/major component of anchoring fibrils	autoimmune
Bullous LE	Type VII collagen (290 kd)	Sub-LD/major component of anchoring fibrils	autoimmune
Chan's disease	105 kd antigen; some also with BPAG1 antibodies	Separation within LL	autoimmune
200 kd antigen disease	200 kd antigen	Separation within LL	autoimmune
Ectodermal dysplasia/skin fragility syndrome	Plakophilin 1	Absence of plakophilin 1 in desmosomes	Unknown (described in 1 individual)
Hailiey-Hailey (Benign familial pemphigus)	Sarcoplasmic reticulum calcium pump/ATP2C1 gene	Acantholysis throughout spinous layer	AD
Darier's (keratosis follicularis)	SERCA2 calcium pump/ATP2A2	Intraepidermal acantholysis;Dyskeratotic keratinocytes;corp ronds and corp grains; split classically suprabasilar	AD

Epidermolytic hyperkeratosis (bullous congenital ichthyosiform erythroderma)	K1/10	Clear spaces within stratum spinosum and granulosum	AD
Epidermal nevi (EHK-type)	K1/10	Clear spaces within stratum spinosum and granulosum within lesional skin only	Somatic mosaicism; offspring may have EHK
Icthyosis bullosa of Siemens	K2e (granular layer)	Clear spaces within stratum spinosum and granulosum within, confined to extremities/flexures	AD
Epidermolytic palmoplantar keratoderma (of Voerner)	K9 (granular layer)	Clear spaces within stratum spinosum and granulosum within, confined to palms and soles	AD
Transient bullous dermolysis of the newborn	Type VII collagen (290 kd)	Sub-lamina densa/major component of anchoring fibrils	AR (abnormal secretion of collagen VII)
Lethal PA-JEB	alpha-6 integrin/ITGA6	Transmembrane molecule, anchors HD to BM	AR
L- and NL-PA-JEB	beta-4 integrin/ITGB4	Transmembrane molecule, anchors HD to BM	AR
NL-JEB	BP 180 (Collagen Type XVII)/COL17A1	Transmembrane molecule	AR
NL-JEB	Laminin gamma 2/LAMC2 (part of laminin 5)	Anchoring filament	AR
NL-JEB	Laminin beta 3/LAMB3 (part of laminin 5)	Anchoring filament	AR
Herlitz-JEB	Laminin alpha 3/LAMA3 (part of laminin 5)	Anchoring filament/mutation in any of the 3 subunits of Lam-5 results in lack of expression of Lam-5	AR
Herlitz-JEB	Laminin beta 3/LAMB3 (part of laminin 5)	Anchoring filament/mutation in any of the 3 subunits of Lam-5 results in lack of expression of Lam-5	AR
Herlitz-JEB	Laminin gamma 2/LAMC2 (part of laminin 5)	Anchoring filament/mutation in any of the 3 subunits of Lam-5 results in lack of expression of Lam-5	AR
GABEB (variant of JEB)	Laminin beta 3/LAMB3; Laminin gamma 2/LAMC2 (both part of laminin 5)	Anchoring filament	AR
GABEB (variant of JEB)	BP 180 (Collagen Type XVII)/COL17A1	Transmembrane molecule	AR
EBS-MD	Plectin/PLEC	Cytoplasmic plaque molecule	AR
EBS-Ogna	Loss of expression of Plectin; defect linked to ch. 8 (glutamic pyruvic transaminase)	Cytoplasmic plaque molecule	AD
EBS with severe mucous membrane involvement	Plectin/PLEC	Cytoplasmic plaque molecule	Unknown (isolated case)
EBS (Dowling-Meara variant)	K5/K14	Basal keratinocyte intermediate filaments/clumped tonofilaments in basal cells	AD
EBS (Weber-Cocakyne variant)	K5/K14	Basal keratinocyte intermediate filaments/no tonofilaments clumping	AD
EBS (Koebner variant	K5/K14	Basal keratinocyte intermediate filaments/no tonofilaments clumping	AD
Recessive EBS	K5/14	Basal keratinocyte intermediate filaments/complete absence of tonofilaments	AR (homozygous mutation in K14 or K5)
Dominant dystrophic EB (hyperplastic Cocayne-Touraine and albopapuloid Pasini variants	Type VII collagen (290 kd)	Sub-lamina densa/major component of anchoring fibrils/unstable anchoring fibrils	AD
Severe recessive dystrophic EB (Hallopeau-Siemens)	Type VII collagen (290 kd)	Sub-lamina densa/major component of anchoring fibrils/absent anchoring fibrils	AR
Recessive dystrophic EB (Mitis type)	Type VII collagen (290 kd)	Sub-lamina densa/major component of anchoring fibrils/functionally abnormal anchoring fibrils	AR

ANA	SLE/Dermatomyositis	2002, 2017	SLE/Dermatomyositis
ANCA (c)	Wegener's granulomatosis	2034, 2046	Wegener's granulomatosis
ANCA (p)	Microscopic polyangiitis (PAN)	1868	Microscopic polyangiitis (PAN)
Anti-cardiolipin	SLE vasculopathy	2002	SLE vasculopathy
Anti-centromere	Scleroderma	2023, 2031	Scleroderma
Anti-dsDNA	SLE	2002	SLE
Anti-endomysial	Gluten/Dermatitis herpetiformis	712	Gluten/Dermatitis herpetiformis
Anti-endothelial	Sneddon's syndrome	1952, 2049	Sneddon's syndrome
Anti-histone	Drug-induced LE	1596, 1994	Drug-induced LE
Anti-Jo-1	Dermatomyositis/Polymyositis	2011	Dermatomyositis/Polymyositis
Anti-La (SSB)	Sjogren's	2067, 2074	Sjogren's
Anti-PL	SLE vasculopathy	2008	SLE vasculopathy
Anti-reticulin	Dermatitis herpetiformis	712	Dermatitis herpetiformis
Anti-Ro (SSA)	Sjogren's/Neonatal LE	2067, 2074	Sjogren's/Neonatal LE
Anti-Scl	Scleroderma	2011	Scleroderma
Anti-Smith	SLE	2002	SLE
Anti-U1RNP	MCTD	2011	MCTD
CD105	Endoglin (Endothelial)	310	Endoglin (Endothelial)
CD11a	Component of LFA-1/Needed for diapedesis	410	Component of LFA-1/Needed for diapedesis
CD11a/CD18	LFA-1/Needed for diapedesis/Binds ICAM	410	LFA-1/Needed for diapedesis/Binds ICAM
CD13	Endothelial/Hematopoetic	310	Endothelial/Hematopoetic
CD14	Leu M3/APC marker	92, 311	Leu M3/APC marker
CD16	Fc gamma receptor III	411	Fc gamma receptor III
CD18/CD11c	Complement C3-mediated phagocytosis	410	Complement C3-mediated phagocytosis
CD1a	Langerhan cells	344	Langerhan cells
CD2	Cutaneous T Cell = CD2+, CD5+, CD7-	361	Cutaneous T Cell = CD2+, CD5+, CD7-
CD20	B cell marker	1250, 1259	B cell marker
CD26	Endothelial	310	Endothelial
CD27	CD27 ligand related to TNF	389	CD27 ligand related to TNF
CD28/B7	CD28 T cells, B7 APC = Activation	355	CD28 T cells, B7 APC = Activation
CD3	T cell marker (CD4/CD8)	1238	T cell marker (CD4/CD8)
CD30	Ki-1 (LyP + = good prognosis)	1236	Ki-1 (LyP + = good prognosis)
CD31	PECAM-1 (Endothelial adhesion)	309, 313	PECAM-1 (Endothelial adhesion)
CD32	Fc gamma receptor II	316, 411	Fc gamma receptor II
CD34	DF+, DFSP+, NFD+, LC-precursor+	346, 415	DF+, DFSP+, NFD+, LC-precursor+
CD35	Complement cascade receptor	424	Complement cascade receptor
CD4	T helper cell receptor	517, 2509	T helper cell receptor
CD40/CD40L	Costimulatory signal for T cell activation	355	Costimulatory signal for T cell activation
CD44	Hyaluronic acid receptor/LC homing	310, 349	Hyaluronic acid receptor/LC homing
CD45	Panhematopoietic marker	344, 346	Panhematopoietic marker
CD45RO+	Th1 memory cell marker	1449, 1450	Th1 memory cell marker
CD46	Membrane cofactor/Complement cascade	310, 424	Membrane cofactor/Complement cascade
CD49	alpha-integrin/Leukocyte diapedesis	313	alpha-integrin/Leukocyte diapedesis
CD5	Cutaneous T Cell = CD2+, CD5+, CD7-	361	Cutaneous T Cell = CD2+, CD5+, CD7-
CD54	Endothelial/Hematopoetic	310	Endothelial/Hematopoetic
CD55	Decay Acc. Factor/Complement cascade	310, 424	Decay Acc. Factor/Complement cascade
CD58	Endothelial/Hematopoetic	310	Endothelial/Hematopoetic
CD59	Endothelial/Complement cascade	310	Endothelial/Complement cascade
CD63	Weibel-Palade body (Endothelial)	309	Weibel-Palade body (Endothelial)
CD64	Fc gamma receptor I	411	Fc gamma receptor I
CD68	Macrophage+, Monocyte+	349, 354	Macrophage+, Monocyte+
CD7	Negative in Cutaneous T cells (lymphoma)	1238, 1239	Negative in Cutaneous T cells (lymphoma)
CD71	Brain endothelium	311	Brain endothelium
CD8	Cytotoxic T cell marker	1238, 1239	Cytotoxic T cell marker
CD80	B7, Engages CD28 on T cells to activate	353	B7, Engages CD28 on T cells to activate
CD86	B7, Engages CD28 on T cells to activate	353	B7, Engages CD28 on T cells to activate
CD9	Endothelial/Hematopoetic	310	Endothelial/Hematopoetic

LASER	WAVELENGTH (NM)	MODE	COLOR	TYPICAL APPLICATION
Argon	488-630	CW	Blue-Green	Vascular, light source for photodynamic therapy Target hemoglobin, adult only
KTP	532	QCW	Green	Vascular, epidermal pigment, red tattoos (adults>children), target Hgb
Nd:YAG (frequency doubled)	532	Q-switched 10 ns	Green	Vascular, epidermal pigment, red tattoos. Target foreign pigment melanin
Nd:YAG	1064	Long pulse, 5-50 ms	Invisible	1064 - QS: non-ablative dermal remodeling, nevus of Ota, black tatoos, hair removal in non-caucasians
Copper Vapor/bromide	512, 578	QCW	Yellow-Green	Vascular, epidermal pigment
Krypton	520, 568	CW/pulsed	Yellow-Green	520-pigment, 568-vascular (ophthalmology uses)
Flashlamp pulsed dye	585-600	Pulsed	Yellow-Green	Vascular, 550 red tattoos, target Hgb
Ruby	694	Q-switched, 20 ns Long pulse, 0.5 - 3 ms	Red	Epidermal/dermal pigmentation, nevus of Ota, tattoos (black, blue, green), hair removal. Target melanin - tattoos
Alexandrite	755	Q-switched, 50-100 micro seconds Long pulse, 10-50 ms	Infrared	Epidermal/dermal pigmentation, nevus of Ota, tattoos (black, blue, green), hair removal. Deliver at 10 pules/sec
Diode	800-1000	CW/pulsed	Infrared	Vascular, hair removal
Erbium:YAG	2940	Pulsed	Invisible	Rhytides, scars, photodamage, Targets water
CO2	10,600	CW, pulsed or scanned	Invisible	Vaporization/ablation rhytides, scars, photodamage, actinic cheilitis, ear lobe keloids, warts, targets water

TATTOO COLOR	ABSORPTION RANGE	LASER
Red	505-560 nm	Nd:YAG 532 nm Pulsed dye 510 nm
Green	630-740 nm	QS Ruby 694 nm QS Alexandrite 755 nm
Black	600-near infrared	QS Ruby 694 nm QS Alexandrite 755 nm Nd:YAG 1064

TATOO COLOR	PIGMENTS
Black	Carbon, Iron oxide, Logwood
Blue	Cobaltic aluminate (Azure blue)
Green	Chrome oxide (casalis green), Hydrated chromium sesquioxide (Guignet's green), Malchite green, Lead Chromate, Ferro-ferric cyanide, Curcumin green, Phthalocyamine dyes (copper salts with yellow coal tar dyes)
Red	Mercury sulfide (cinnabar), Cadmium selenide (Cadmium red), Senna (ochre-ferric hydrate and ferric sulfate)
Yellow	Cadmium sulfide (Cadmium yellow)
Ochre	Curcumin yellow
Brown	Ochre
Violet	Manganese violet
White	Titanium dioxide, zinc oxide
Flesh	Iron oxides

Disease	Associated cancers
Ataxia-Telangiectasia	Lymphoma, lymphocytic leukemia, gastric cancer, breast CA
Basal Cell Nevus Syndrome	BCC, medulloblastoma, ovarian CA, ovarian fibromas, fibrosarcoma, odontogenic cysts
Beckwith-Wiedemann syndrome	Wilm's tumor, cortical cancer, hepatoblastoma
Bloom syndrome	Sigmoid adenocarcinoma, lymphoma, leukemia, SCC (oral cavity and esophagus), lymphosarcoma
Chediak-Higashi Syndrome	Lymphoma-like phase (Lymphohistiocytic proliferation with infiltration of liver, spleen, and nodes)
Cowden's syndrome	Breast adenocarcinoma, follicular cancer of thyroid, fibroadenoma of breast, goiter, hamartomas of intestine
Down's syndrome	Acute myelogenous leukemia
Dyskeratosis congenita	Premalignant leukoplakia, SCC (tongue,oral,esophagus, cervix,skin), mucinous rectal carcinoma, rectal adenocarcinoma
Dystrophic EB	SCC
Ehler-Danlos syndrome	Molluscoid pseudotumors
Epidermal Nevus Syndrome	Lipodermoid tumors (eyes)
Epidermodysplasia Verruciformis	SCC, Bownen's, rhabdomyosarcoma, HPV 3, 5, 8
Fanconi syndrome	Myelomonocytic leukemia, SCC, hepatic tumors
Gardner syndrome	Colorectal adenocarcinoma, papillary adenocarcinoma of thyroid, osteomas, fibromas, lipomas, desmoid tumors, congenital hypertrophy of retinal pigmented epithelium (CHRPE)
Hermansky-Pudlak Syndrome	SCC
Howel-Evans Syndrome (PPK)	Esophageal cancer
Kleinfelter's syndrome	Breast adenocarcinoma, retinoblastoma, rhabdomyosarcoma
Maffucci syndrome	Enchodromas, chrondrosarcoma, angiosarcoma, fibrosarcoma, osteosarcoma, lymphangiosarcoma
MEN Type IIB	Medullary thyoid CA, pheochromocytoma, neuromas of tongue
MEN Type III	Medullary thyoid CA, pheochromocytoma, neuromas of tongue
Muir-Torre syndrome	Sebaceous CA, sebaceous adenoma, sebaceous epitheliomas, keratoacanthomas, colon adenocarcinoma, GU tract CA, lung, breast, and hematologic malignancies
NAME/LAMB Syndrome	Atrial myxoma, cutaneous myxoma, melanotic schwannomas, testicular sertoli tumors, thyroid tumors, pigmented nodular adrenocortical tumors, pituitary adenomas
Neurofibromatosis 1	Lisch nodules (iris hamartomas), chronic juvenile myelocytic leukemia/non-lymphocytic leukemia (JXG), vestibular schwannoma, neurofibromas, optic glioma, astrocytoma, menigioma, neurofibrosarcoma, rhabdomyosarcoma, pheochromocytoma, Wilm's tumor
Neurofibromatosis 2	Vestibular schwannomas, neurofibromas, astrocytomas, meningiomas, ependymomas
Peutz-Jegher syndrome	Ovarian CA, Breast CA, Pancreatic CA, GI polyps, odontomas
Porphyria Cutanea Tarda	Hepatocellular carcinoma
Proteus syndrome	Testicular tumors, lipomas, linear epidermal nevi
Rothmund-Thompson syndrome	Osteosarcoma, fibrosarcoma, SCC
Rubinstein-Taybi syndrome	Keloids, erythema, cataracts, osteosarcoma, fibrosarcoma, hypoplastic thumbs
Tubeous sclerosis	Rhabdomyomas, renal angiomyolipomas, pulmonary lympangioleiomyomas, phakomas, astrocytomas, subependymal hamartomas, collagenomas (Shagreen patch), periungual fibromas, angiofibromas (Adenoma sebaceum)
Tyrosinase- Albinism	SCC, BCC, melanoma
Tyrosinase+ Albinism	SCC, BCC, melanoma
Von Hippel-Lindau syndrome	Renal cell carcinoma, pheochromocytoma
Werner syndrome	10% chance of neoplasms: Fibrosarcoma, osteosarcoma, cutaneous CA, meningioma, adrenocortical CA
Wiskott-Aldrich syndrome	Lymphoreticular malignancies
Xeroderma pigmentosa	Melanoma, BCC, SCC

Bodies	Disease
Asteroid body	Sarcoidosis, Tuberculosis, Granulomatous infiltrate, Leprosy
Civatte body	Lichen planus, Lupus erythematosus, GVHD, Certain amyloidoses, Any interface dermatitis
Councilman body	Cytoplasmic inclusions containing condensed cellular remnants, Basal cell carcinoma
Cowdry type A body	VZV/HSV
Donovan body	Granuloma inguinale (represent parasitized macrophages)
Farber body	Farber's disease (EM)
Gaurnieri body	Vaccinia, Smallpox
Henderson-Paterson body	Molluscum contagiosum virus
Kamino body	Spindle and epitheloid nevus (Spitz nevus), melanoma
Michaelis-Gutman body	Malakoplakia
Mikulicz's cell	Rhinoscleroma
Molluscum body	Molluscum contagiosum virus
Odland body	Normal skin (EM)
Psammoma body	Nevocellular nevus, cutaneous meningioma
Pustulo-ovoid body of Milian	Granular cell tumor
Russell body	Rhinoscleroma, Syphilis, Any plasma-rich infiltrate
Schaumann body	Sarcoidosis, Tuberculosis, Granulomatous infiltrate, Leprosy
Verocay body	Neurilemmoma
Weibel-Palade body	Endothelial cells (EM)
Zebra body	Fabry's disease (EM)

Disease	Eye Findings	CNS Findings	Hair Findings	Nail Findings	Teeth/Bone Findings
Acrodermatitis enteropathica	photophobia				
Albinism/Hermansky-Pudlak/Chediak-Higashi syndromes	Nystagmus, photophobia, impaired visual acuity, strabismus, foveal hypoplasia, mis-routing of optic fibers, red reflex				
Alezzadrini's syndrome	unilateral tapetoretinal degeneration				
Anhidrotic ectodermal dysplasia			alopecia, thin eyebrows	dystrophy	peg teeth (incisors), molars with hooked cusps, anodontia, hypodontia
Ataxia-telangiectasia	Conjunctival telangiectases	Choreoathetosis, drooling, weak muscles, normal intelligence			
Bannayan-Riley-Ruvalcalba syndrome/Bannayan-Zonana syndrome		CNS vascular malformations			
Basal cell nevus syndrome (Gorlin syndrome)	hypertelorism, blindness, cataracts, colobomas, strabismus	Calcification of Falx cerebri, medulloblastoma			odontogenic jaw cysts
Biotinidase deficiency	optic atrophy				
Bjornstad's syndrome		deafness	pili torti		
Buschke-Ollendorf syndrome					osteopoikilosis
CHILD syndrome				severe nail dystrophy	
CHIME syndrome		Mental retardation, seizures			
Cockayne syndrome		Mental retardation, deafness			caries
Conradi-Hunerman syndrome	symmetric focal cataracts				
Crandall's syndrome		deafness, hypogonadism	pili torti		
Cutis marmorata telangiectasia congenita	glaucoma				
Darier's disease				red and white longitudinal bands, V-shaped nicks and/or splitting, subungual hyperkeratosis	
DDEB				dystrophy, absent nails	
Down's syndrome	Brushfield spots, epicanthic folds, strabismus				
Down's syndrome (Trisomy 21)		Mental retardation			periodontitis, dystrophic teeth
Dyskeratosis congenita	conjunctivitis, lacrimal duct obstruction with epiphora, ectropion			absent nails, dystrophy, vertical ridges, pterygium, atrophic nails	retained natal teeth
EBS (Dowling-Meara)				dystophy and nail shedding	
Ehler-Danlos type VI (ocular type)	ruptured globe, retinal detachment, intraocular hemorrhage, keratoconus, blindness				
Ehler-Danlos type VIII (periodontal)					periodontitis, premature loss of permanent teeth
Epidermal nevus syndrome	Extension of nevus to lid and conjunctiva, lipodermoid tumors, colobomas, nystagmus, blindness, corneal opacities				
Erythropoeitic porphyria (Gunther's disease)	photophobia, ectropion, conjunctivitis				Red-brown teeth that fluoresce red-pink under Wood's lamp
Fabry's disease (X-linked recessive)	corneal opacities with whorl-like configuration, lenticular opacity, dilated retinal vessels	Frequent febrile episodes, seizures, paralysis, psychosis, aphasia			
Familial dysautonomia (Riley-Day syndrome)	decrease corneal sensation, decreased tear flow with corneal ulcers				
Familiar hypercholesterolemia (type II)	arcus juvenilis				
Familiar lipoprotein lipase deficiency (type I)	lipemia retinalis				
Focal dermal hypoplasia (Goltz syndrome) (X-linked dominant mosaic)	coloboma, strabismus, microphthalmia	Mental retardation, seizures, hearing loss		dystrophy, absent nails	osteopathia striata, hypodontia, oligodontia, dysplastic teeth, dysplastic enamel
Fucosidosis		Mental retardation, weakness, spasticity, seizures			
Gardner's syndrome	Congenital hypertrophy of retinal pigmented epithelium (CHRPE)				supernumary teeth, odontomas
Gaucher disease	pingueculae				
Griscelli syndrome		Early severe neurologic defects			
Hemochromatosis				dystrophy, koilonychia (also in Plummer-Vinson syndrome)	
Hidrotic Ectodermal dysplasia (Clouston's syndrome)			alopecia, thin eyebrows	brittle nails, paronychia and/or nail matrix destruction, longitudinal striations, micronychia, convex nails	dystrophic teeth
Homocystinuria	ectopia lentis (downward), myopia, glaucoma				
Hyperlipoproteinemia (Type V)	lipemia retinalis				
Hypomelanosis of Ito	strabismus, hypertelorism				dysplastic teeth, anodontia
Incontinentia pigmenti (X-linked dominant mosaic)	strabismus, cataracts, optic atrophy, retinal vascular changes with blindness, retrolental mass	Seizures (13%), mental retardation, spastic paralysis		nail dystrophy (5-10%)	peg teeth (incisors), anodontia
Incontinentia pigmenti achromians	strabismus, cataracts, optic atrophy, retinal vascular changes with blindness, retrolental mass	Seizures, developmental delay		nail dystrophy (5-10%)	peg teeth (incisors), anodontia
JEB (Herlitz type)				dystrophy, nail plate shedding, non-healing granulation tissue of nail folds	dysplastic teeth with enamel pits/defects
KID syndrome	progressive bilateral vascularized keratitis	Neurosensory and/or neuromuscular changes		dystrophy	
Lamellar ichthyosis	ectropion			dystrophy with nail fold inflammation	
LEOPARD syndrome		deafness			
Lichen planus			scarring alopecia (lichen planopilaris)	longitudinal ridges and grooves, thinning of nail plate, pterygium	painful mucosal erosions
Lipoid proteinosis		Rage, seizures (rare), aymptomatic cancers above sella turcica (70%)			
Mal de Meleda				subungual hyperkeratosis, koilonychia, onychogryphosis	
Marfan syndrome	ectopia lentis (upward), myopia				
MEN type IIB	conjunctival neuromas, white medullated nerve fibers in cornea				

Menkes' kinky hair syndrome (X-linked recessive)		seizures, retardation	kinky (steel wool ivory) hair, trichorrhexis invaginata (bamboo hair)		
Monilethrix	cataracts		beaded hair, keratosis pilaris	Brittle nails	dystrophic teeth
Nail lines				Half and half nails (Renal), Muehrcke's lines (hypoalbuminemia), Terry's nails (Cirrhosis), Beau's Lines (illness), Mee's lines (arsenic)	
Nail-Patella syndrome	Lester iris (hyperpigmentation of pupillary margin of iris), heterochromia irides, cataracts			Triangular lunula, micronychia, vertical fissures	
Netherton's syndrome			trichorrhexis invaginata (bamboo hair)		
Neutral lipid storage disease		CNS abnormalities			
NF-1	Lisch nodule (iris hamartoma), glaucoma, choroidal nevi	Congenital absence of spenoid wing, meningiomas, acoustic schwannomas (90% in Type 2), ependymomas, learning disabilities, seizures			
NF-2	posterior subscapular cataracts	Congenital absence of spenoid wing, meningiomas, acoustic schwannomas (90% in Type 2), ependymomas, learning disabilities, seizures			
Niemann-Pick disease	cherry red spots on retina				
Ochronosis	pingueculae, Osler's sign (blue-grey pigment deposits in conjunctiva)				
Osler-Weber-Rendu syndrome	Telangiectases			subungual telangiectases	mucosal/gingival telangiectases
Osteogenesis imperfecta	blue sclera				dysplastic teeth (dentinogenesis imperfecta)
Pachyonychia congenita	cataracts, corneal dystrophy			Brownish-yellow nails, subungual hyperkeratosis, paronychia (commonly Candida or Staph), pincer nail deformity, distal elevation of nail plate	retained natal teeth
Papillon-Lefevre syndrome		Calcification of Falx cerebri			periodontitis, dystrophic teeth, bad odor, gingivitis
Peutz-Jeghers syndrome				pigmented macules	
Progeria (Hutchinson-Gilford syndrome)				dystrophic and thin nails	dystrophic teeth, delayed eruption of teeth
Psoriasis			scalp psoriasis	pitting, onycholysis, onychodystrophy, oil spots	
PXE	angioid streaks (Bruch's membrane)				
RDEB				dystrophy, absent nails	caries, dysplastic teeth
Refsum disease	retinitis pigmentosa with salt and pepper pigmentation	Cerebellar ataxia, peripheral neuropathy			
Richner-Hanhart syndrome (Tyrosinemia II)	keratitis with photophobia, corneal ulceration and neovascularization	Mental retardation			
Rothmund-Thomson syndrome	juvenile cataracts			dystrophy (25%)	dysplastic teeth
Rubinstein-Taybi syndrome	strabismus				
Rud's syndrome		Mental retardation, seizures, polyneuritis			
Sjorgen-Larsson syndrome	Atypical retinitis pigmentosa with glistening dots	Speech defects (95%), seizures (60%)			dysplastic teeth with enamel defects
Sturge-Weber syndrome	ipsilateral glaucoma				
Tay's syndrome		Mental retardation			
Trichorhinophalangeal syndrome (AD)		Mental retardation (in Type II)			
Trichothiodystrophy (BIDS)	cataracts, photosensitivity	Intellectual impairment, cerebellar ataxia	Tiger tail hair, trichoschisis, trichorrhexis nodosa		
Trisomy 13		Mental retardation			
Trisomy 18		Mental retardation			
Tuberous sclerosis	retinal hamartoma (phakoma)	Seizures (80%), mental retardation (60%), brain tumors (60%)			enamel pits, gingival fibromas
Turner's syndrome (XO)		Lower IQ		dystrophic, hyperconvex, hypoplastic, and deep-set nails	
Uncombable hair syndrome			pili triangulatiy et canaliculi (spun glass hair)		
Vitamin A deficiency	Bitot spots				
Waardenberg syndrome	dystopia canthorum, heterochromia irides	deafness	White forelock (poliosis)		caries
Watson syndrome (NF-1 with pulmonic stenosis)	Lisch nodule (iris hamartoma), glaucoma, choroidal nevi	Congenital absence of spenoid wing, meningiomas, acoustic schwannomas (90% in Type 2), ependymomas, learning disabilities, seizures, decreased intelligence			
Werner's syndrome (Adult progeria)	posterior subscapular cataracts			dystrophic and thin nails	dystrophic teeth, delayed eruption of teeth
Wilson's disease	Kayser-Fleischer rings (copper deposits in Descemet's membrane)			Bluish nails (rare)	
Xeroderma pigmentosa	lid papillomas, photophobia, melanoma				
X-linked ichthyosis	comma-shaped corneal opacities				
Ziprowski-Margolis syndrome (X-linked recessive)		deaf-mutism	White forelock (poliosis)		caries