

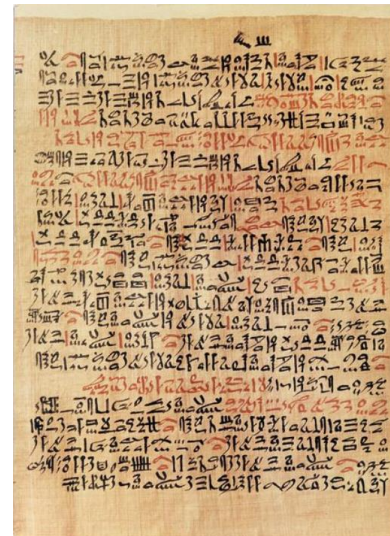
Dermatology training

14.6.2021

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The Ebers Papyrus documenting various skin conditions (exudative ulcers, rashes, tumors) and providing guidance on their treatment. A separate chapter is dedicated to aesthetic skin rejuvenation.

(circa 1550 BC, University of Leipzig)

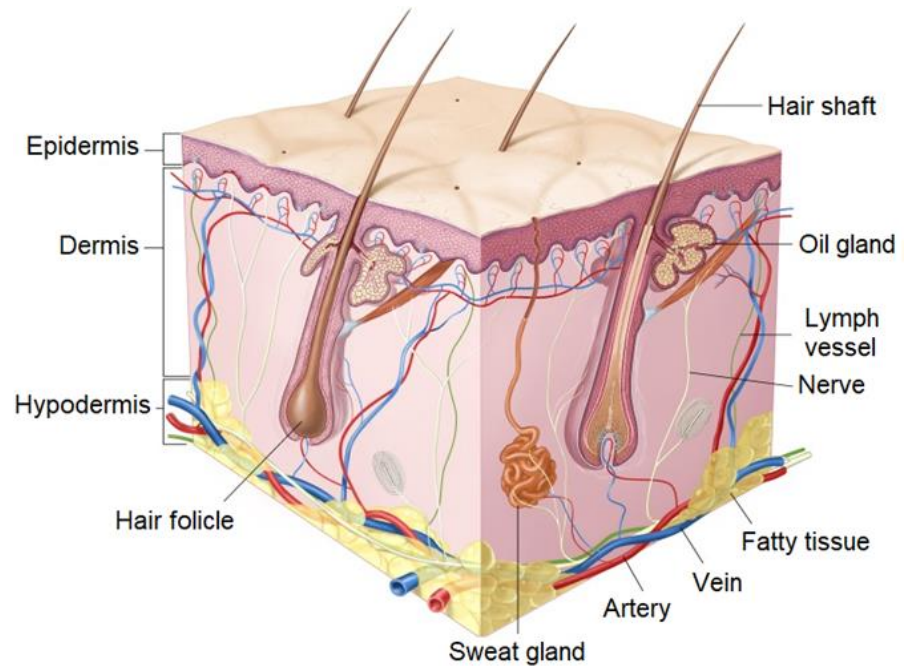


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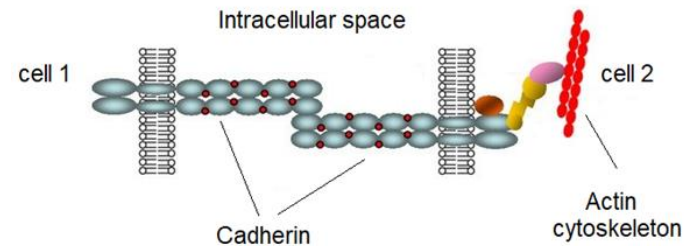
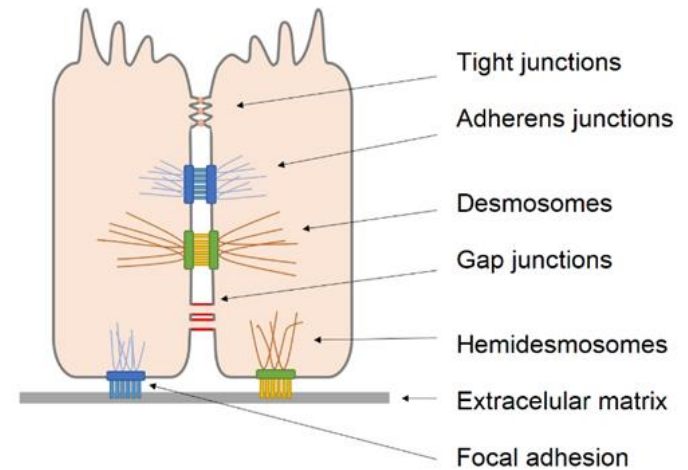
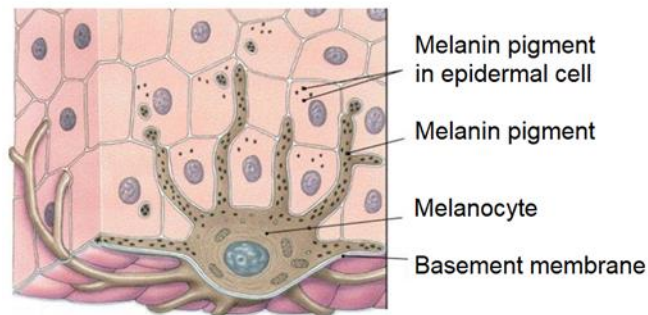
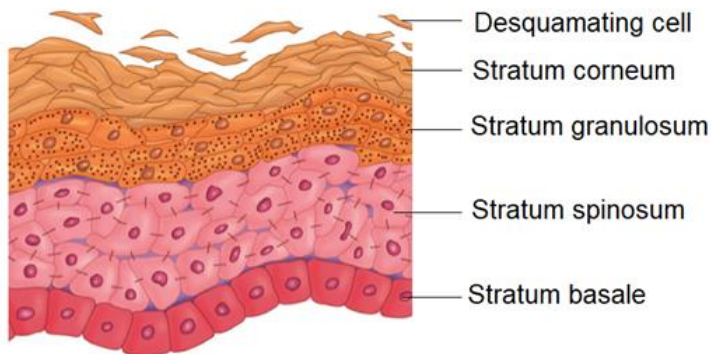
- second largest organ in the human body
- varies in pigmentation, thickness, dryness
- highly diverse microbiome
- a number of functions

- **epidermis**
(tightly packed cells)
- **dermis** and **hypodermis**
(extracellular matrix, connective fibers, glands, fat, nerves, circulatory vessels, fewer cells)



Epidermis

- 5 sublayers
- new cells are created in basal layer
- cells mature, they move up the layers
- keratinocytes, melanocytes
- specialized cell junctions



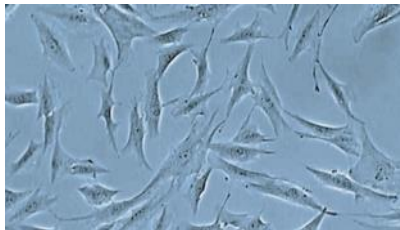
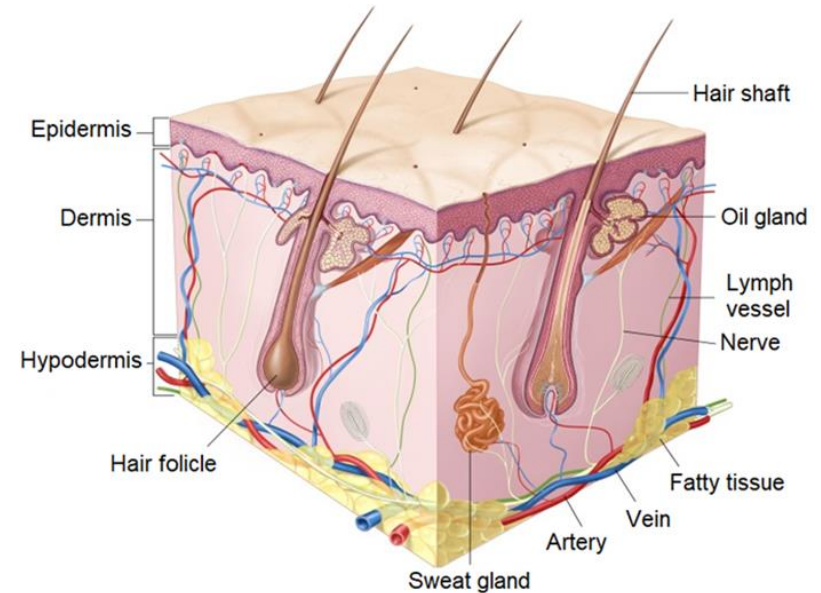
Dermis and Hypodermis

Dermis

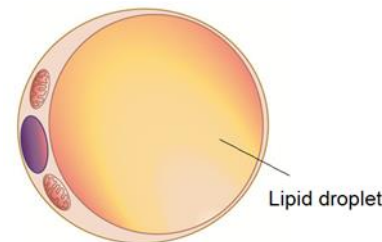
- papillary dermis and reticular dermis
- glycosaminoglycans, collagen, elastin, hair follicles, sweat and oil glands, nerves, blood and lymph vessels
- cells: fibroblasts, macrophages, mast cells

Hypodermis

- loose connective tissue
- adipocytes (fat)

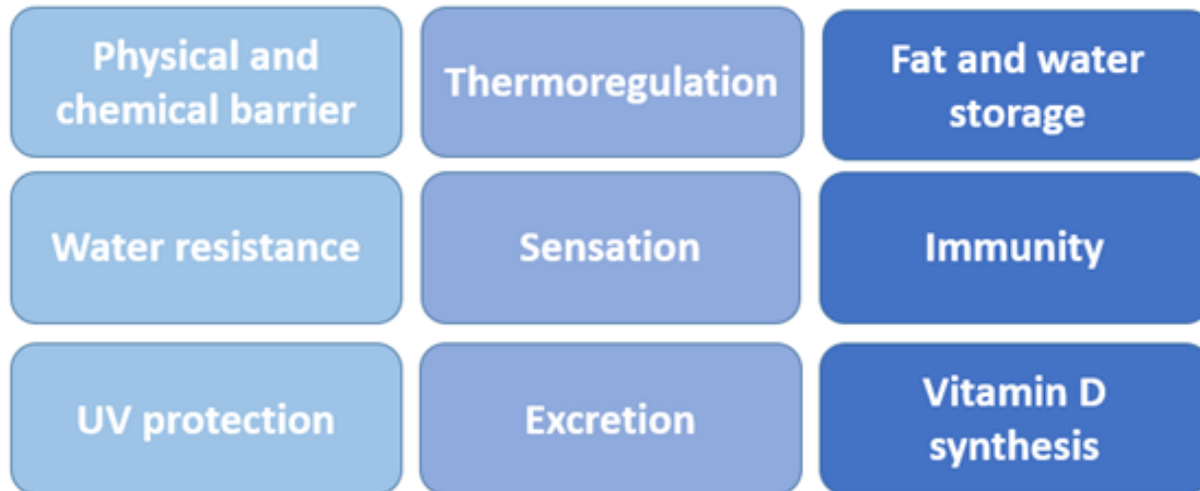


fibroblasts



adipocyte

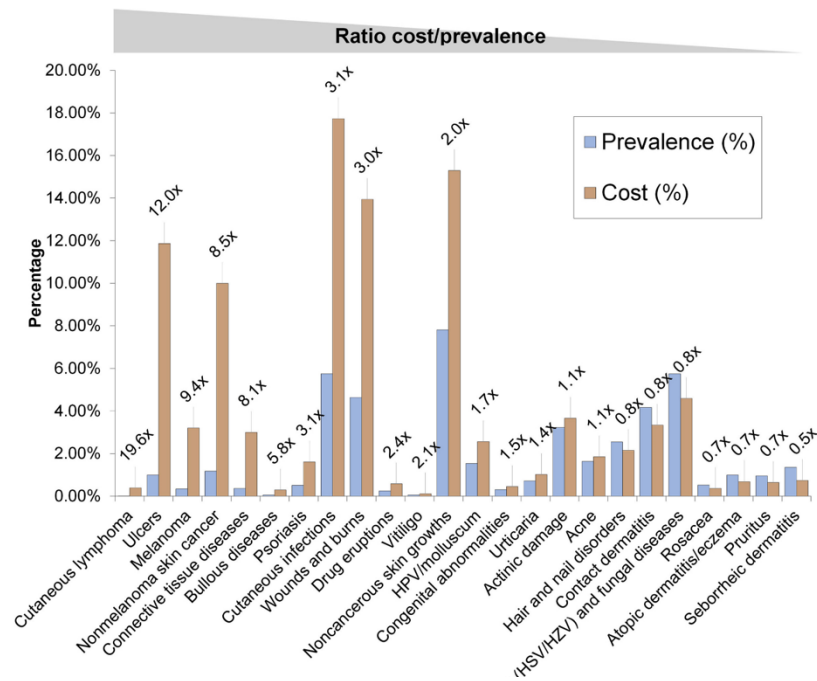
Functions of the skin



Skin conditions

- among most common health problems
- more than 2,000 skin disorders
- common: acne, shingles
- rare genetic skin disorders: elastoderma
- comparatively uncommon but with high healthcare burden: skin cancers, psoriasis, ulcers
- Infectious: scabies

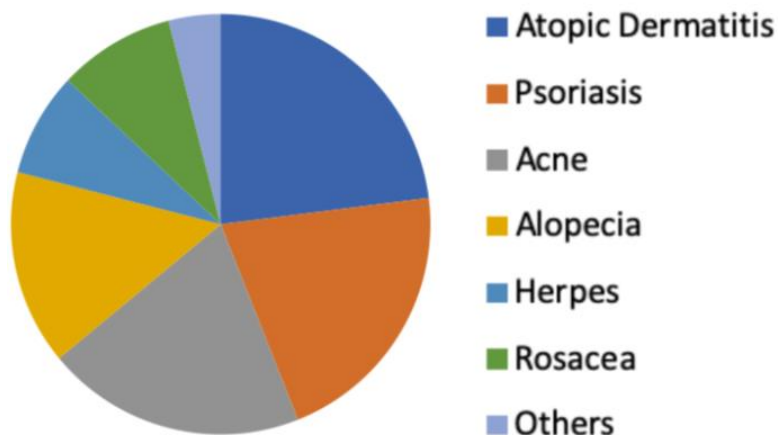
*Skin disease
medical costs
versus
prevalence
(2013, US)*



argyria

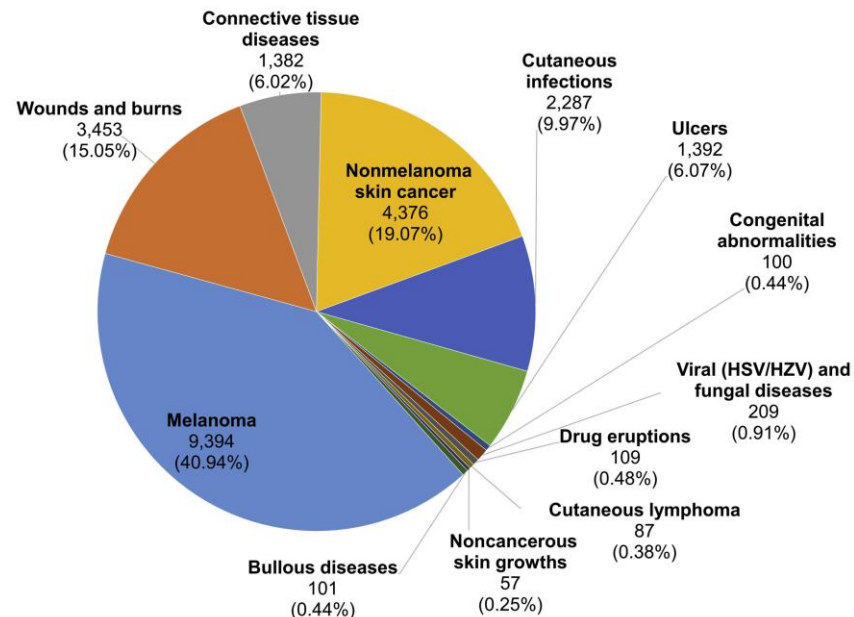
<https://doi.org/10.1016/j.jaad.2016.12.043>

Skin conditions



*Global dermatology drug market
by condition*

<https://www.datamintelligence.com/research-report/dermatology-drugs-market>



*Deaths related to skin disease
(2013, US)*

<https://doi.org/10.1016/j.jaad.2016.12.043>

Dermatology in clinical trials

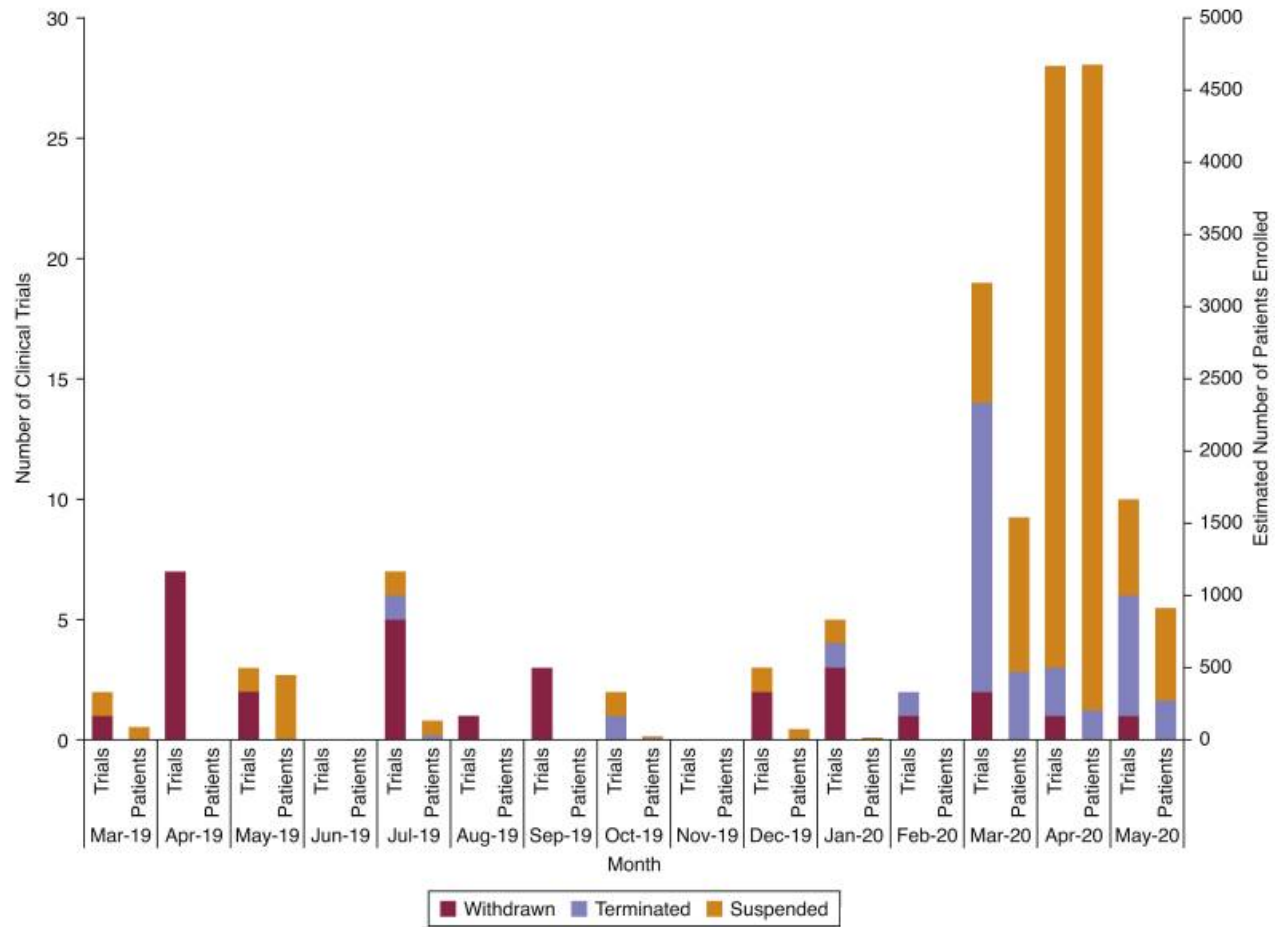
Skin condition	Active clinical trials	Completed
Melanoma	271	1139
Psoriasis	82	1130
Atopic dermatitis (eczema)	42	594
Lupus Erythematosus	37	382
Leg Ulcer	29	452
Acne Vulgaris	16	473
Urticaria (Hives)	9	199
Herpes Simplex	8	177
Warts (genital, anal, oral, hand)	8	115
Pruritus (Itching)	7	288
Neurodermatitis	0	13
Scabies	0	19

Numbers of active clinical trials (not recruiting), as well as all completed trials, per skin condition. Clinicaltrials.gov, accessed March 2021.

- * In total 17,525 active (not recruiting) Clinical Trials in March 2021**
 - around 500 of them in dermatology (200,000 patients)
 - 479 of them for COVID-19

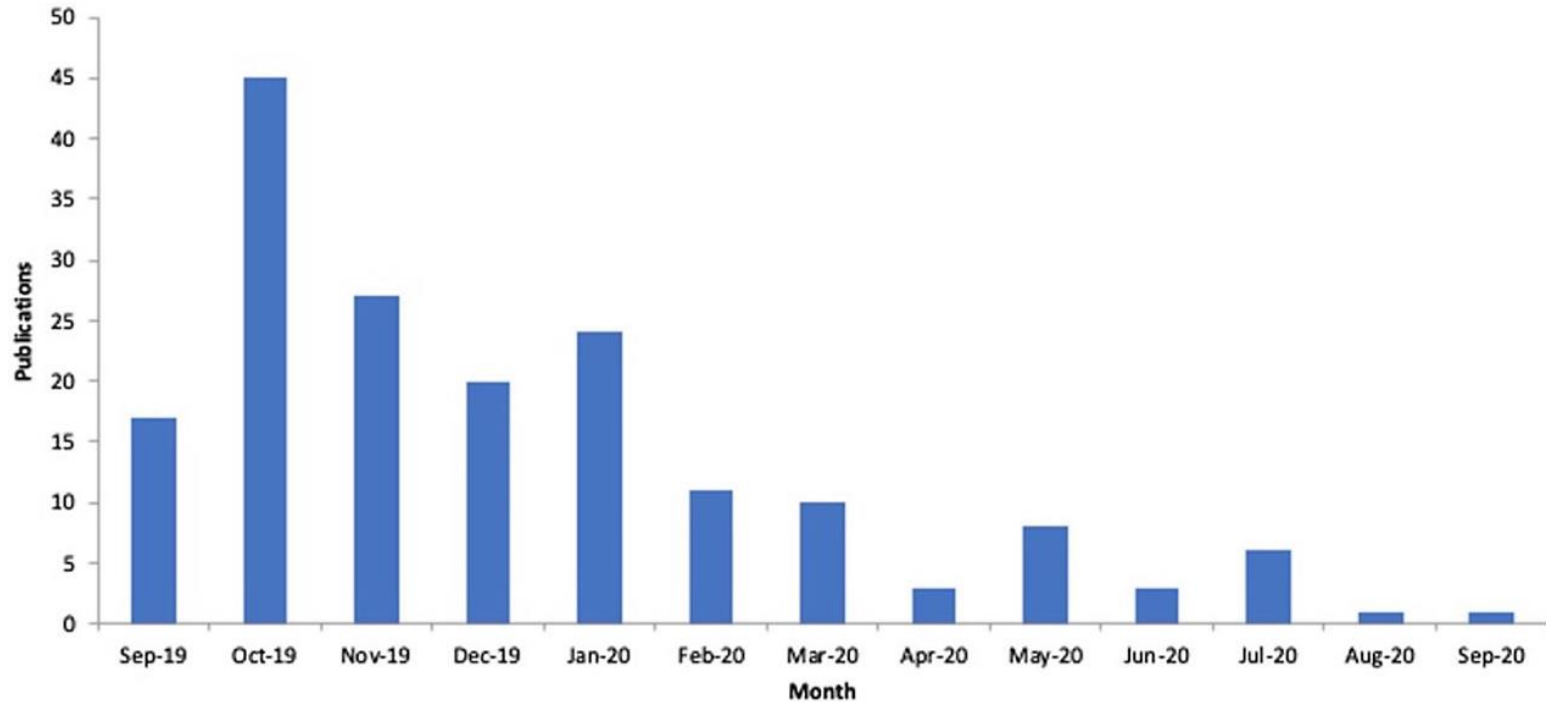
Impact of COVID-19 on dermatology trials

Dermatology trials that were suspended, withdrawn, or terminated (April 2019- April 2020)



doi: 10.1016/j.jid.2020.06.032

Impact of COVID-19 on dermatology trials



Publication frequency from dermatology clinical trials (September 2019- September 2020)

doi: 10.1111/ijd.15355

Psoriasis

- noncontagious autoimmune disease, skin cells multiply
- painful, itchy red bumps covered with white scales
- chronic
- cause unknown (genetics, infection, stress)
- feed-forward activation of adaptive immune system
- no cure
- treatment: moisturizing and steroid creams, phototherapy, biologics
- mental issues
- most common in north Europe

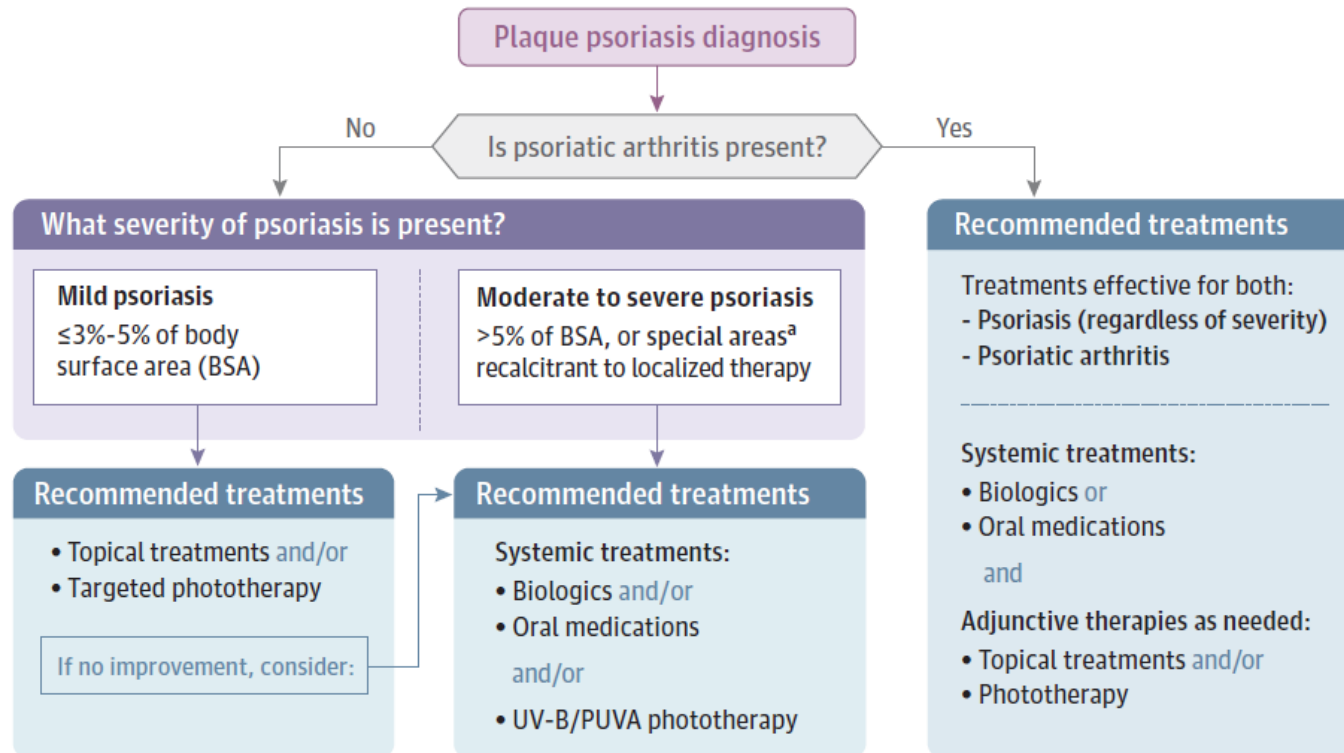


Psoriasis



Psoriasis affecting different areas

Psoriasis- treatment approach



-Stelara (IL-12,23 inhibitor)- J&J's top drug by sales- \$7 billion annual sales, potential future megablockbuster

-Humira

- redness, thickness, and scaliness (0- 4 scale)
- % of affected body area (0- 6 score)
- x 0.1, 0.2, 0.3, and 0.4 for head, arms, trunk, and legs
- sum up for final score (0-72)

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Assessment of psoriasis

Dermatology Life Quality Index (DLQI)
 questionnaire (10 questions, 30 points)

- | | | |
|----|---|--|
| 4. | Over the last week, how much has your skin influenced the clothes you wear? | Very much <input type="checkbox"/>
A lot <input type="checkbox"/>
A little <input type="checkbox"/>
Not at all <input type="checkbox"/> |
| 5. | Over the last week, how much has your skin affected any social or leisure activities? | Very much <input type="checkbox"/>
A lot <input type="checkbox"/>
A little <input type="checkbox"/>
Not at all <input type="checkbox"/> |
| 6. | Over the last week, how much has your skin made it difficult for you to do any sport ? | Very much <input type="checkbox"/>
A lot <input type="checkbox"/>
A little <input type="checkbox"/>
Not at all <input type="checkbox"/> |

Body surface area (BSA)

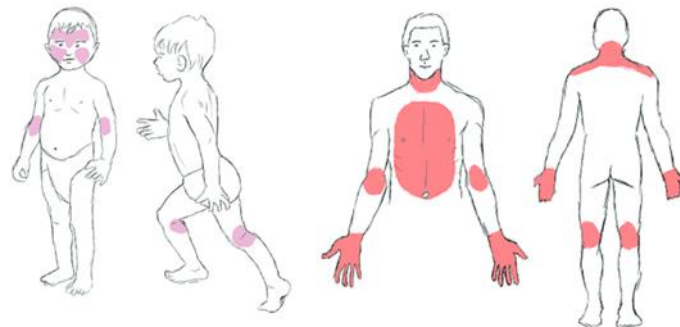
Physician's Global Assessment (PGA)

Dermatitis (eczema)

- skin inflammation- swelling, rash, dryness, itchiness, redness
- cause unknown
- genetics, environment, immunal dysregulation
- treatment: moisturizing creams, corticosteroids, irritant/allergen avoidance
- **atopic dermatitis** is the most common type, common in childhood
- **allergic contact dermatitis, irritant contact dermatitis, seborrheic dermatitis, stasis dermatitis**



Atopic dermatitis



Areas affected by atopic dermatitis

Assessment of dermatitis

Eczema Area and Severity Index (EASI)

- preferred tool in clinical trials
- four symptoms- erythema, edema/papulation, excoriation and lichenification (0- 3 scale)
- % involved area by body region (0- 6 scale)
- (add up symptom scores per body part) x (body part area score) x multiplication factor
- add individual body part scores
- single final EASI score (0-72)

Area of Involvement:

% involvement	0	1-9%	10 - 29%	30 - 49%	50 - 69%	70 - 89%	90 - 100%
Region score	0	1	2	3	4	5	6

Severity of Signs:

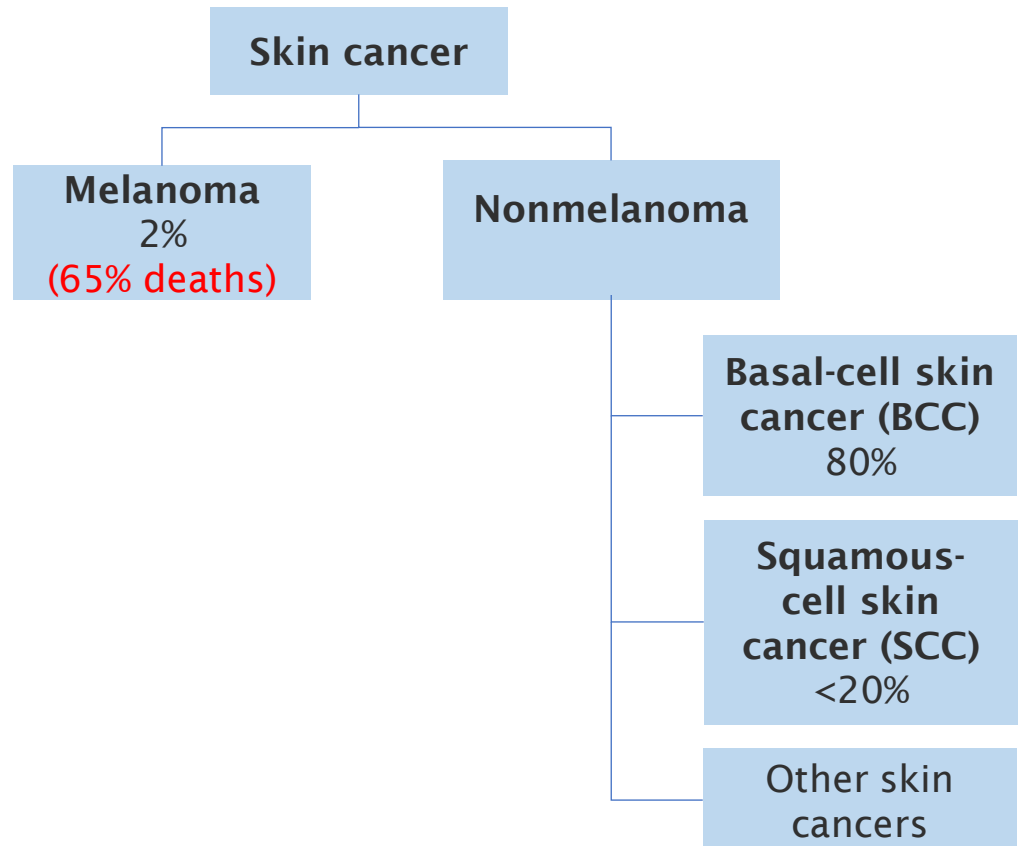
0	None
1	Mild
2	Moderate
3	Severe

Scoring table:

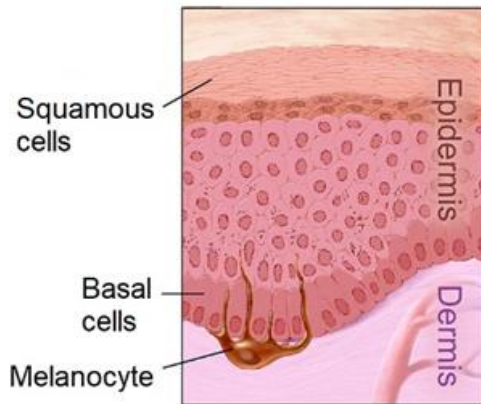
Body region	Erythema	Edema/ papulation	Excoriation	Lichenification	Area score	Multiplier	Score
Head/neck	(+)	+	+)	x	x 0.1	
Trunk	(+)	+	+)	x	x 0.3	
Upper extremities	(+)	+	+)	x	x 0.2	
Lower extremities	(+)	+	+)	x	x 0.4	
The final EASI score is the sum of the 4 region scores							_____ (0-72)

Skin cancer

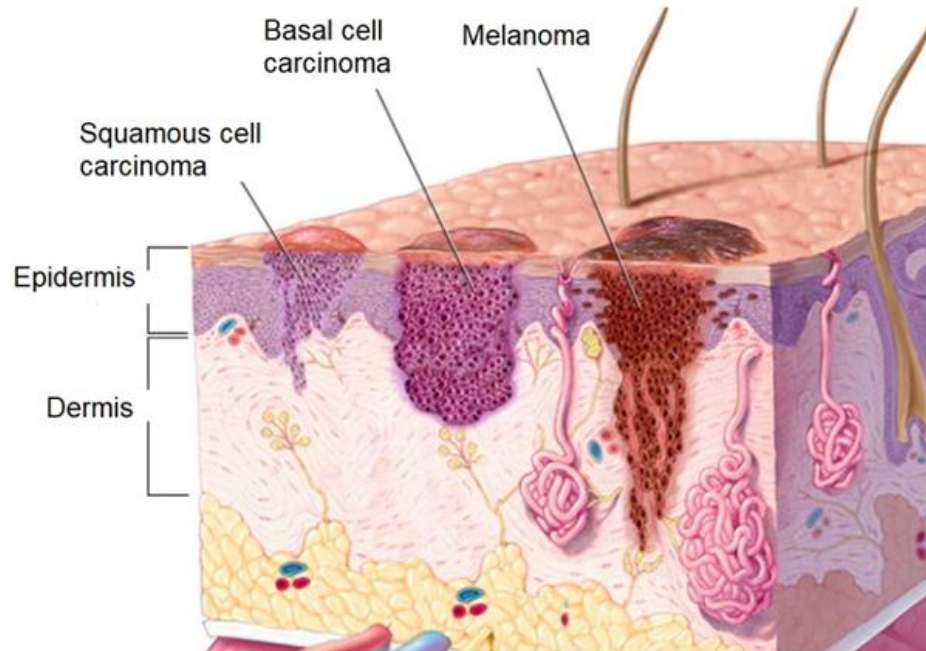
- most common type of cancer worldwide
- develops mainly on areas of skin exposed to sun
- rapidly rising incidence



Skin cancer



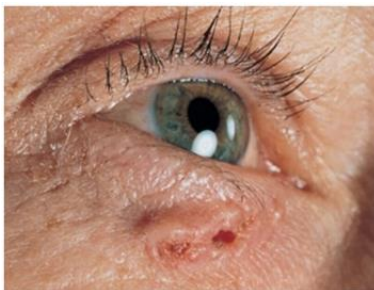
Cells producing main types of skin cancer



Main types of skin cancer

Skin cancer

- **Basal cell carcinoma**
most common and least deadly form
metastasis is rare
- **Squamous cell carcinoma**
metastasizes more often than BCC
good prognosis if removed early
- **Melanoma**
pale skin and chronic sun exposure
metastatic melanoma: brain, liver, bones, lymph nodes and abdomen
treatment: surgical removal; immunotherapy, targeted drug therapy, chemotherapy, radiation.



Basal cell carcinoma

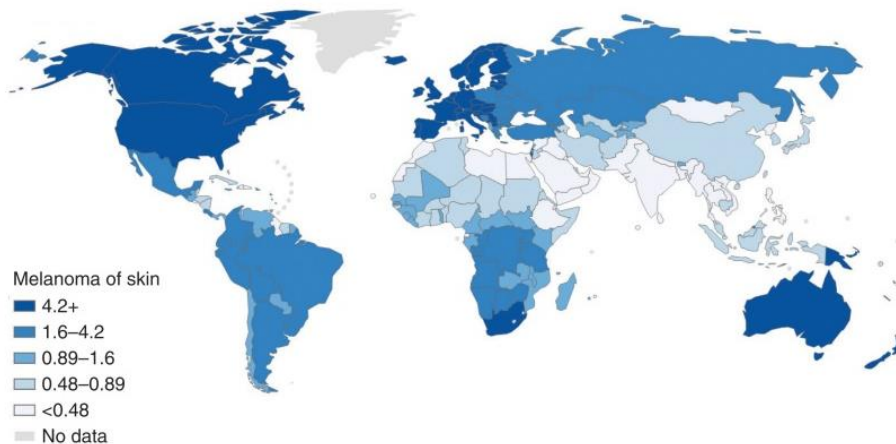


Squamous cell carcinoma



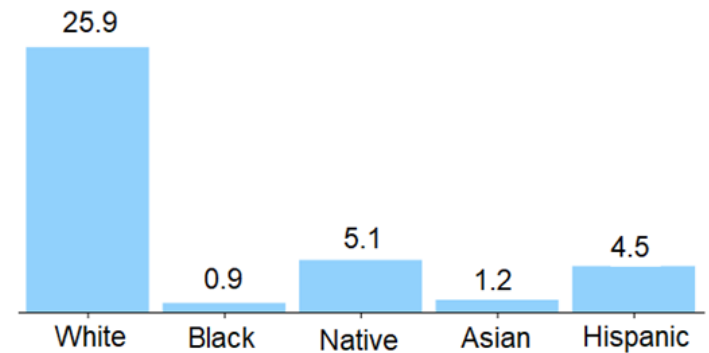
Melanoma

Incidence of melanoma



Melanoma incidence by geography

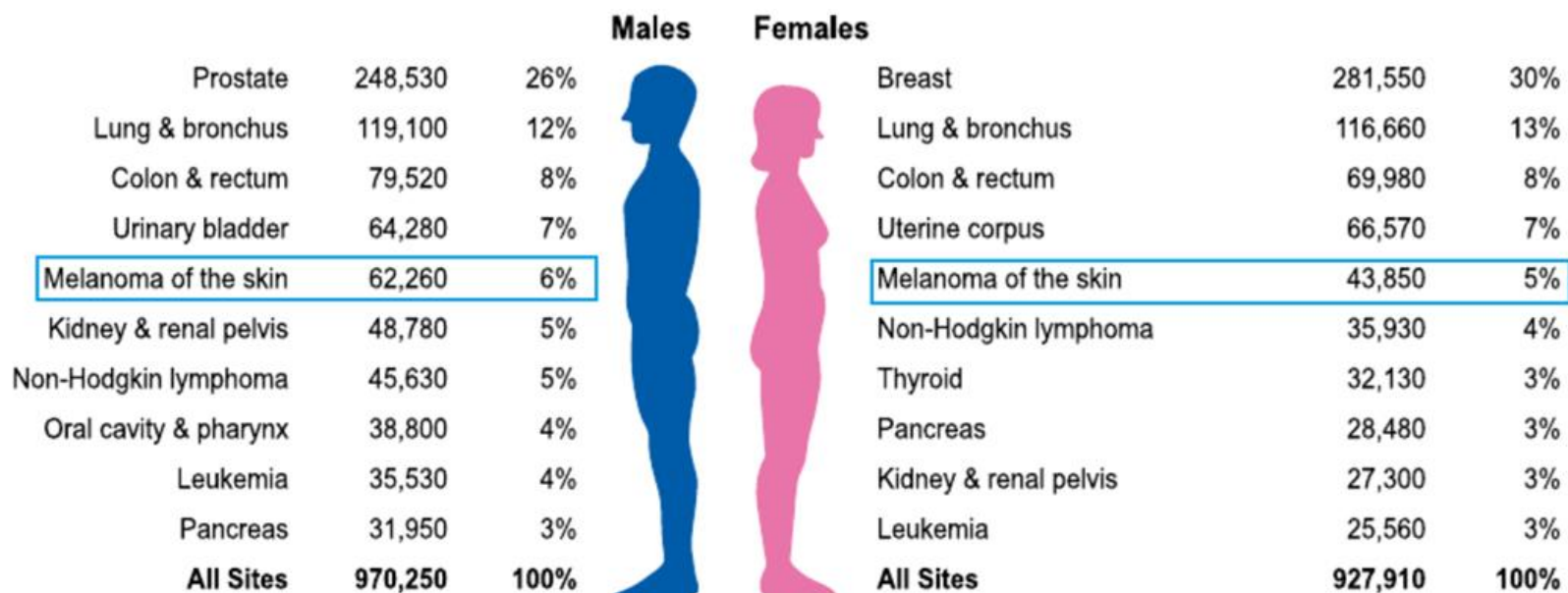
<https://www.ncbi.nlm.nih.gov/books/NBK481862/>



Melanoma rate in the US per 100,000 people by race, CDC.

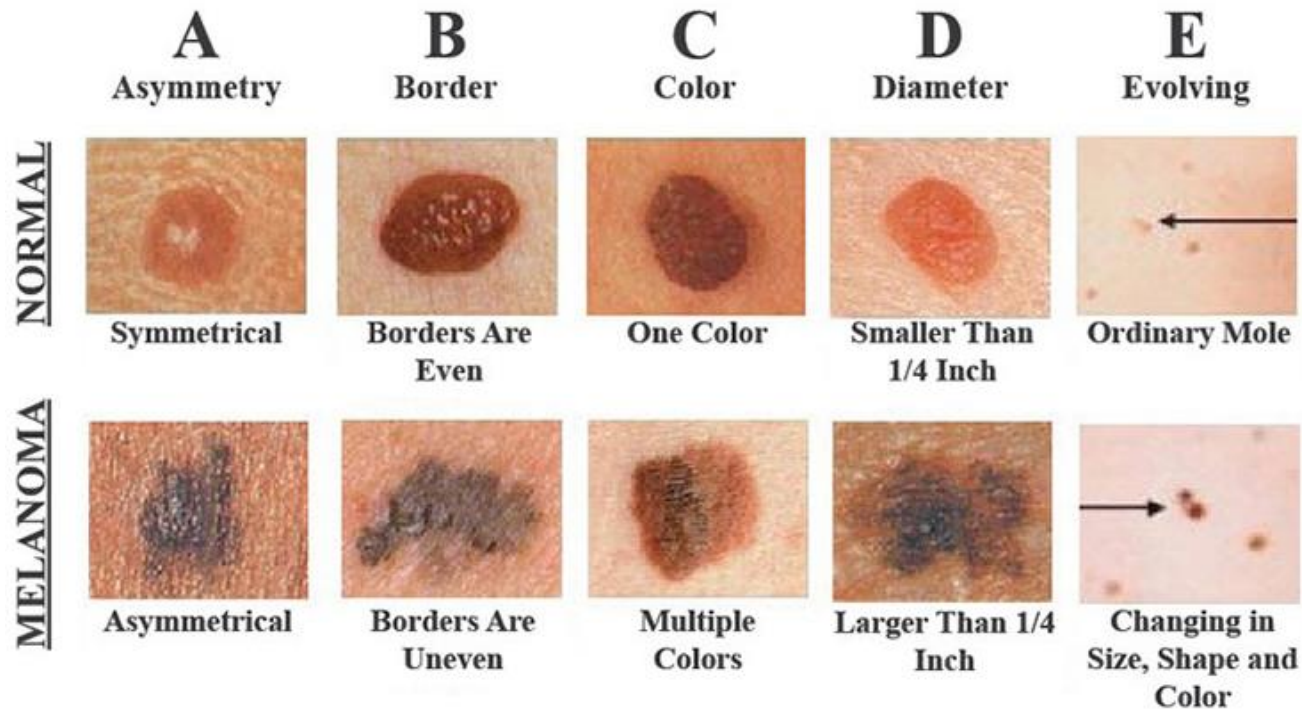
<https://gis.cdc.gov/Cancer/USCS/DataViz.html>

Melanoma



*Estimated numbers of cases for melanoma and other most common cancers for 2021
(American Cancer Society) <https://doi.org/10.3322/caac.21654>*

Assessment of melanoma



The ABCDE acronym for melanoma symptoms

Assessment of melanoma

TNM staging system (AJCC system): classification the spread of tumor

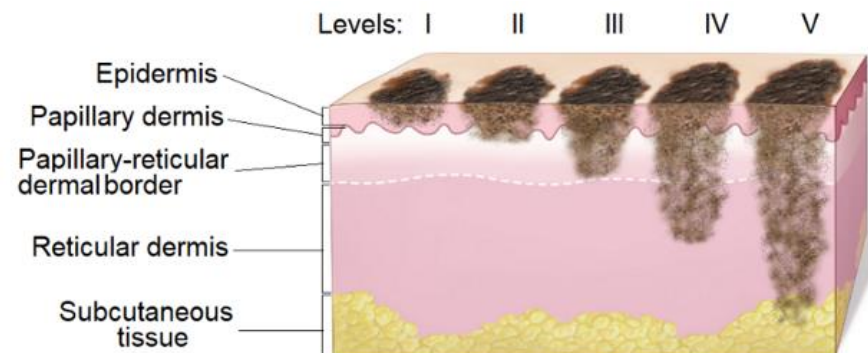
T (tumor)- size of the primary tumor (thickness) and invasion of nearby tissue

N (node)- spread to nearby lymph nodes

M (metastasis)- distant spread

Example: T4b N1 M1b

Level 1	Melanoma confined to the epidermis
Level 2	Invasion into papillary dermis
Level 3	Invasion to the border of papillary and reticular dermis
Level 4	Invasion into the reticular dermis
Level 5	Invasion into the subcutaneous fat



Clark's level

Assessment of melanoma

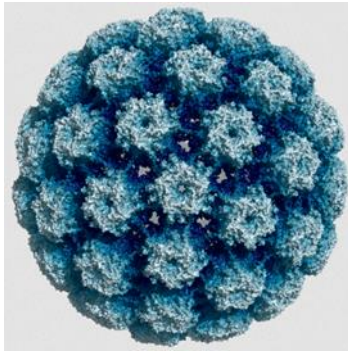
*AJCC 8th edition M category
(distant metastasis) criteria.
LDH is lactate dehydrogenase.*

M Category	Anatomic Site	LDH Level
M0	No evidence of distant metastasis	Not applicable
M1	Evidence of distant metastasis	
M1a	Distant metastasis to skin, soft tissue including muscles, and/or nonregional lymph node	Not recorded or unspecified
M1a(0)		Not elevated
M1a(1)		Elevated
M1b	Distant metastasis to lung with or without M1a sites of disease	Not recorded or unspecified
M1b(0)		Not elevated
M1b(1)		Elevated
M1c	Distant metastasis to non-CNS visceral sites with or without M1a or M1b sites of disease	Not recorded or unspecified
M1c(0)		Not elevated
M1c(1)		Elevated
M1d	Distant metastasis to CNS with or without M1a, M1b, or M1c sites of disease	Not recorded or unspecified
M1d(0)		Not elevated
M1d(1)		Elevated

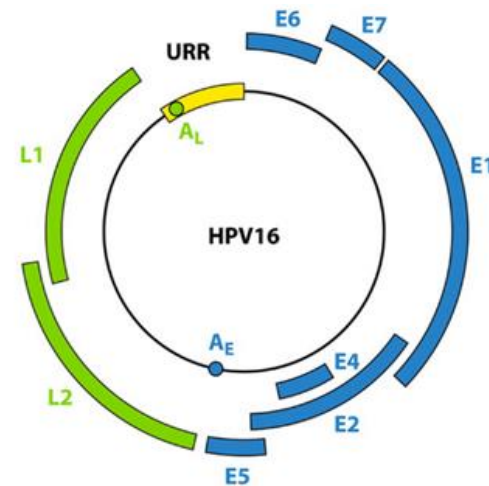
Doi:
 10.1080/14737140.2018.1489246

Conditions associated with human papillomavirus

- > 200 HPV genotypes
- spread through skin-to-skin contact
- HPV 16 and 18- most important high-risk cancer causing types
- infects basal epithelial cells, via surface skin wounds
- causes warts and lesions which may lead to cancer

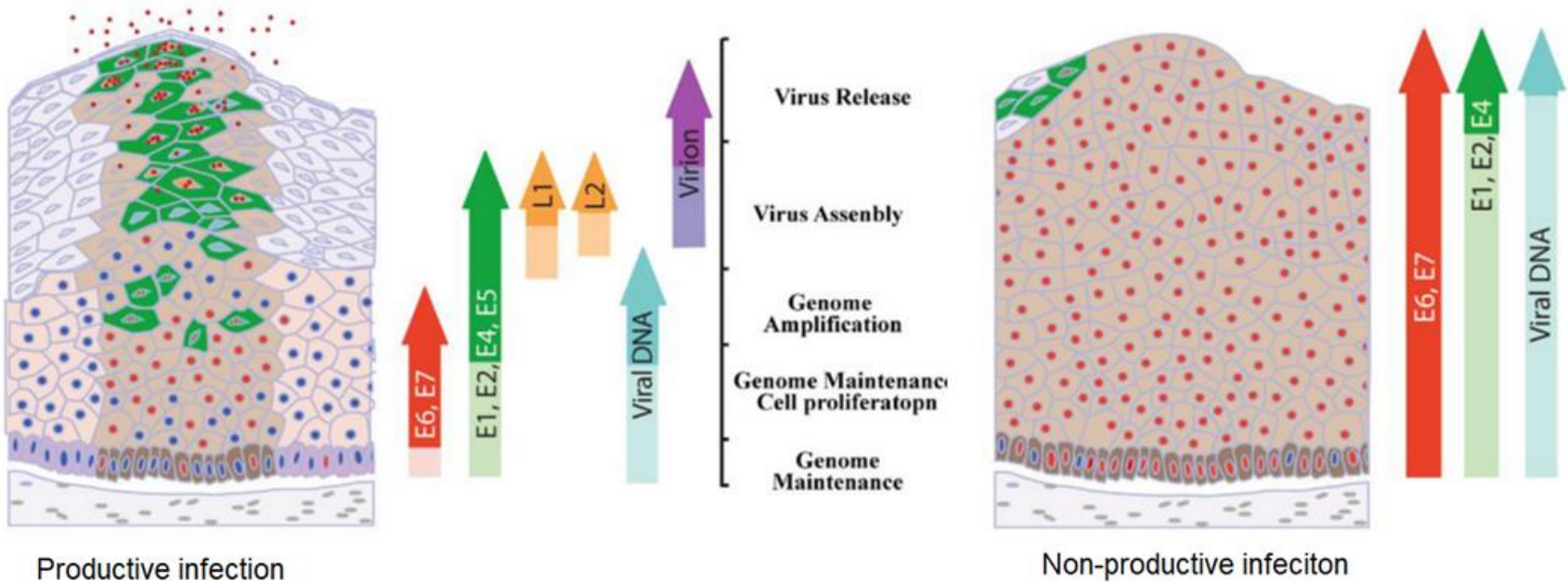


HPV16 capsid



HPV16 genome organization

HPV life cycle



Expression of HPV genes in a productive vs. non-productive infection

- benign lesions
- hypertrophy of all layers of the dermis, resulting in thickening, folding and hyperkeratosis
- usually disappear spontaneously
- treatment: surgery, cryotherapy, drugs, acid, and laser

1) nongenital warts

common warts (most often hands)
flat warts (backs of hands and legs)
plantar warts (soles of feet)

2) genital warts

most common sexually transmitted infection, usually asymptomatic



common warts, flat warts on the face, and plantar warts

Assessment of warts

- frequency of complete clearance of warts at follow-up
- frequency of reduction in number and/or size of warts
- duration of the response.
- effect of treatment on a single wart per patient in a large patient group; two warts in a single patient receiving alternative treatments
- digital photography
- Physician's Global Assessment; Patient's Global Assessment

Cervical and other cancers

- persistent infection with the oncogenic or high-risk types may cause cancer
- **cervical cancer** is by far the most common HPV-related cancer
- second most common cause of cancer-related deaths in women worldwide
- 70% of cervical cancers caused by HPV 16 and 18 (3 vaccines)
- also anal, penile, vaginal, vulval, and oropharyngeal cancers

Our excellence is your success



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