We would like to acknowledge that we are gathered today on the traditional territories of the Musqueam, Squamish and Tsleil-Waututh peoples.

Source: www.johomaps.com/na/Canada/bc/Vancouver/firstnations/firstnations.html

Conflict of interest

- I declare that I have no conflict of interests.

Dermotoxins/sensitizers in the workplace

Karen Bartlett, PhD

Professor Emeritus, School of Population and Public Health

Occupational and Environmental Health Division

Karen.bartlett@ubc.ca

Learning objectives

- Discover dermotoxic and sensitizing agents
- Understand how dermotoxic and sensitizing agents exert their effects on the skin
- Explore the relationship between sensitizers of the skin and the respiratory system
- Identify common dermotoxins
- Outline strategies to improve skin health

Eight pounds and two square meters!

- **Skin notation**: Danger of cutaneous absorption contributing to total exposure

- **Skin irritation**: Physical injury of skin due to corrosive, pH extremes or other mechanisms that damage the skin barrier
  - Irritant contact dermatitis

- **DSEN/ S(D)** notation: Sensitization resulting from exposure to chemical.
  - Allergic contact dermatitis

Eight pounds and two square meters!

- **Skin notation**: Danger of cutaneous absorption contributing to total exposure

225

- **Skin irritation**: Physical injury of skin due to corrosive, pH extremes or other mechanisms that damage the skin barrier
  - Irritant contact dermatitis

76

- **DSEN/ S(D)** notation: Sensitization resulting from exposure to chemical.
  - Allergic contact dermatitis

51

Case study: nuisance or sensitizer?

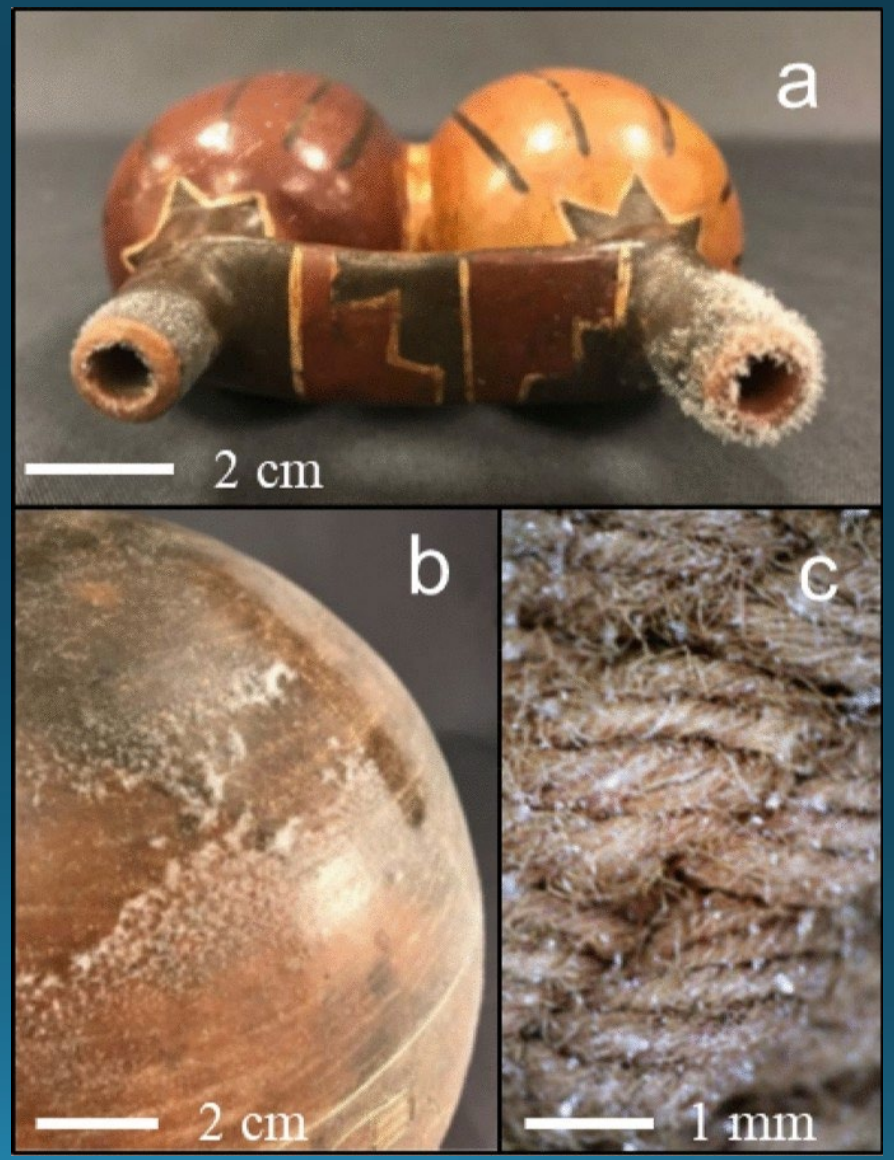
- Original question regarded formation of visible crystals of 2,2,6,6-tetramethyl-4-piperidionol (TMP-ol) on artifacts displayed at the Smithsonian and Rijksmuseum museums.

Case study: nuisance or sensitizer?

- Original question regarded formation of visible crystals of 2,2,6,6-tetramethyl-4-piperidionol (TMP-ol) on artifacts displayed at the Smithsonian and Rijksmuseum museums.
- Crystals were the result of a chemical reaction between organic acids in the artifacts and volatile TMP-ol in the adhesive of the display case.

Case study: nuisance or sensitizer?

- Original question regarded formation of visible crystals of 2,2,6,6-tetramethyl-4-piperidionol (TMP-ol) on artifacts displayed at the Smithsonian and Rijksmuseum museums.
- Crystals were the result of a chemical reaction between organic acids in the artifacts and volatile TMP-ol in the adhesive of the display case.



https://heritagesciencejournal.springeropen.com/articles/10.1186/s40494-020-00454-4

Case study: TMP-ol crystals

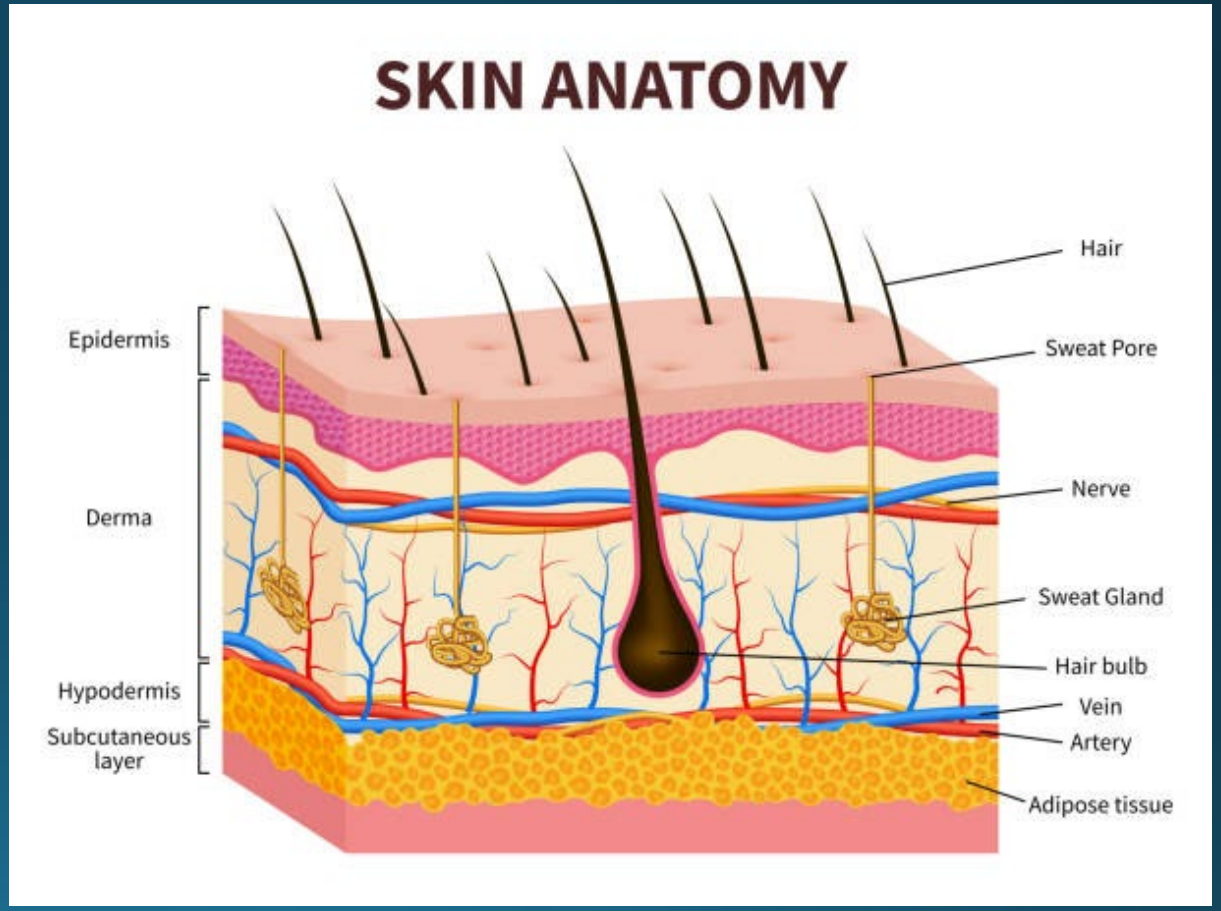
At risk for sensitization:

- Employees/ curators
- Visiting scholars/anthropologists/archeologists

- **Owners of the artifacts!**

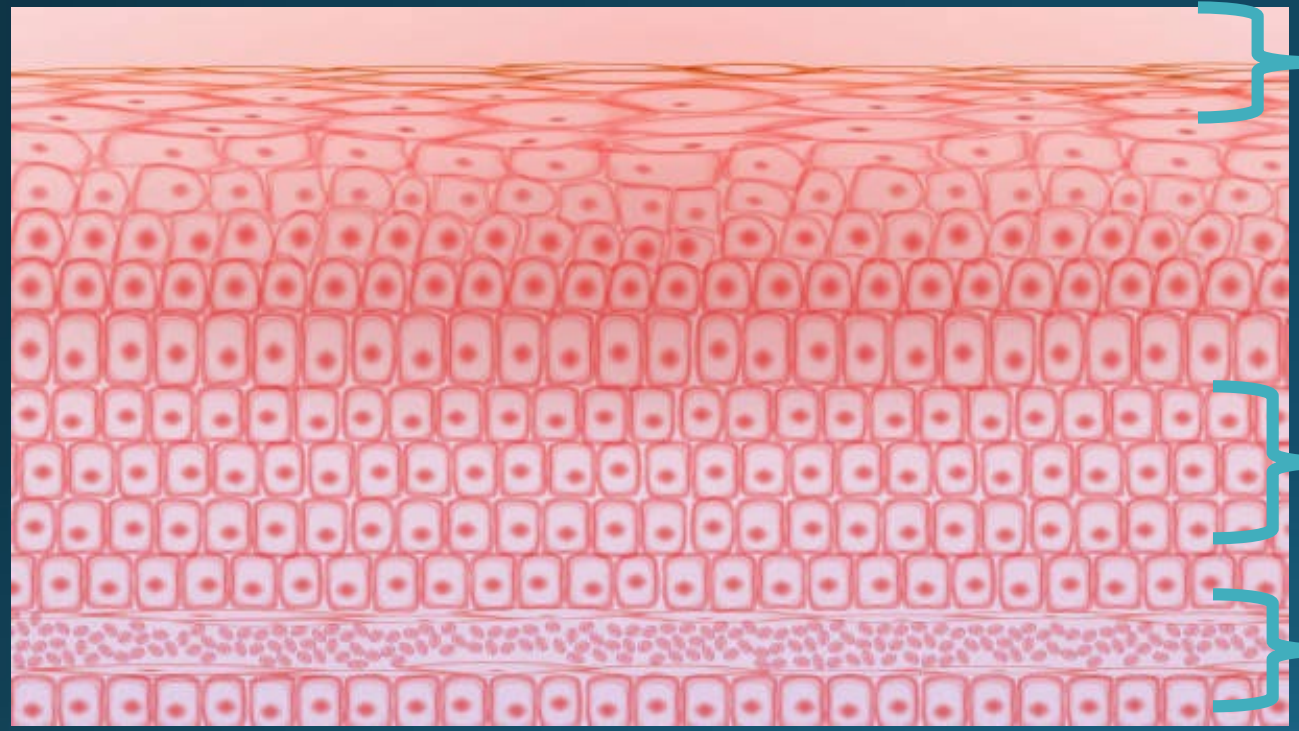
Integrated skin barrier

- Skin thickness varies with body parts
  - Thickest skin = palms of hands, heels of feet (4 mm)
  - Thinnest skin = eyelids, genitalia (0.5 mm)
- Skin barrier properties do not vary by amount of melanin or by sex.



https://www.thedermspecs.com/blog/skin-anatomy-101/

Living and non-living; water & lipids

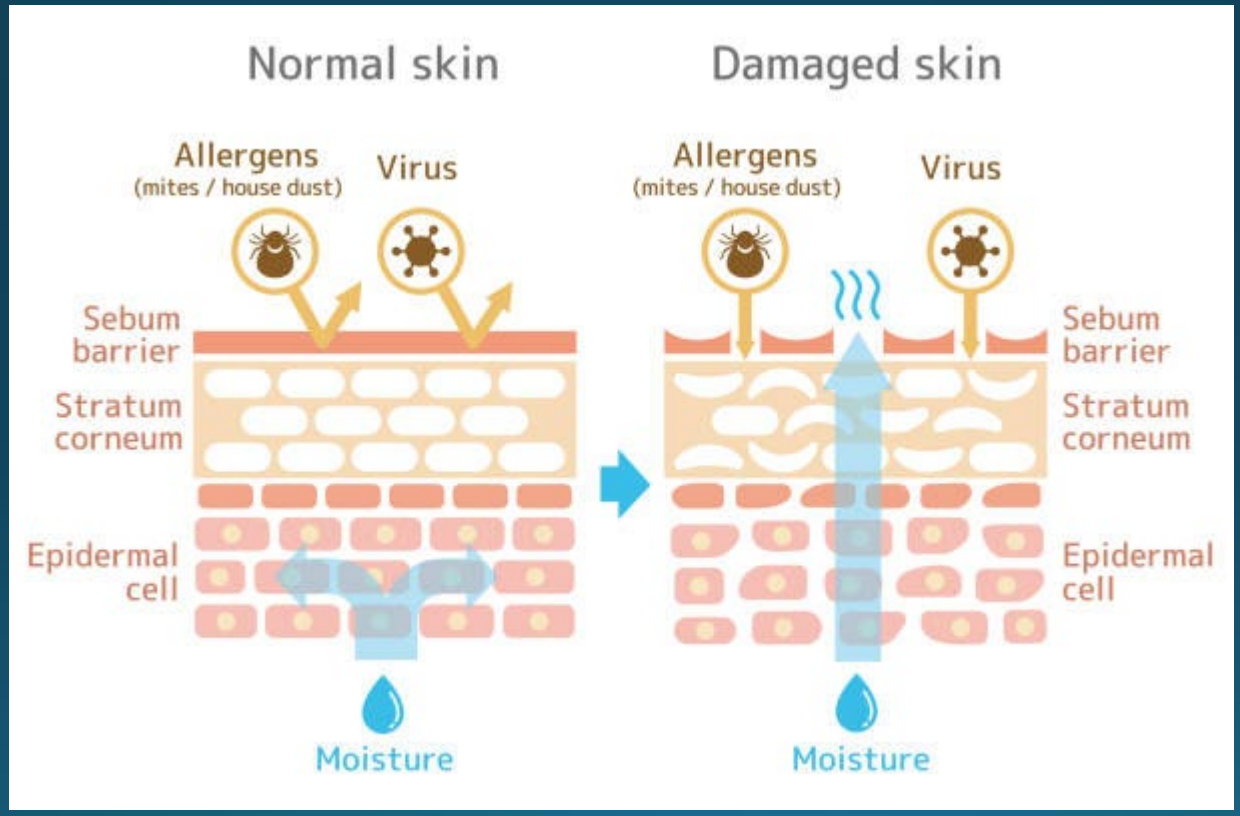


- Topmost layer = stratum corneum composed of corneocytes (cross-linked fibrous keratin proteins) Water and lipid channels into:
- Epidermis – primarily aqueous environment
- Dermis – blood vessels, glands, hair follicles: new cells formed here and migrate, becoming corneocytes in about 14 – 28 days

https://www.thedermspecs.com/blog/skin-anatomy-101/

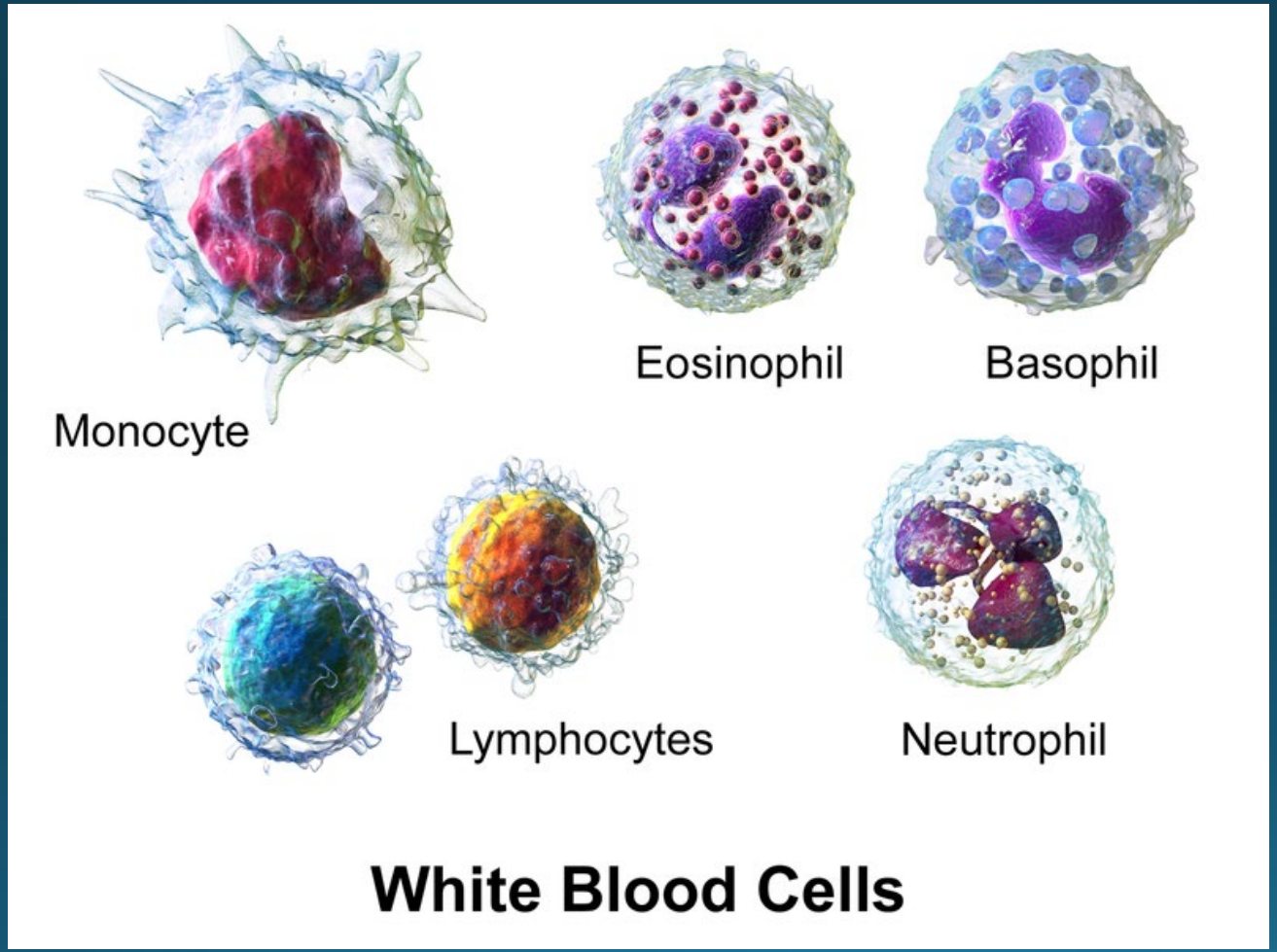
Damaged skin:

- ➡ increased permeation
- ➡ allergic and irritant contact dermatitis



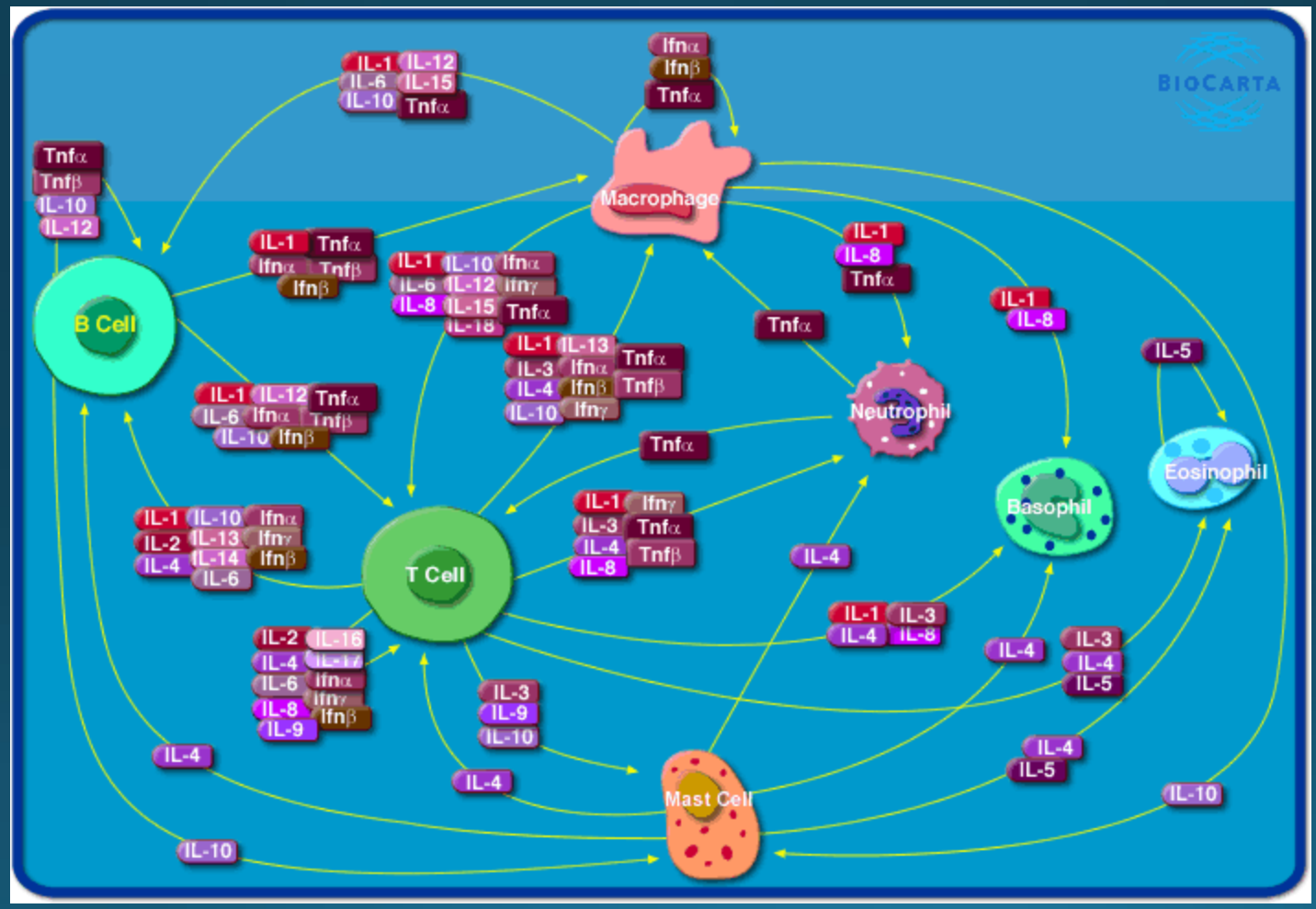
https://www.thedermspecs.com/blog/skin-anatomy-101/

Quick refresher: Cells of the innate immune system



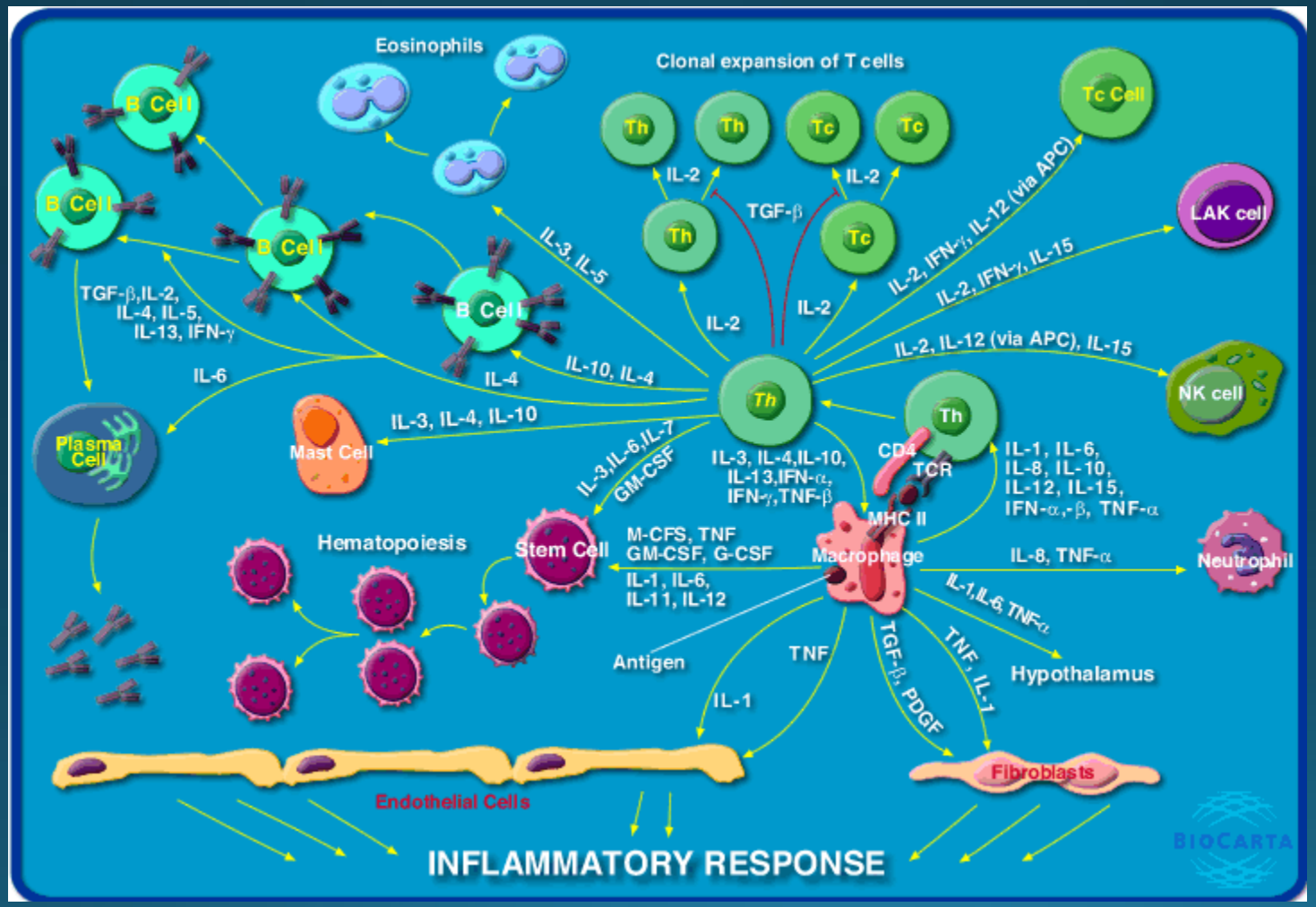
http://en.wikipedia.org/wiki/File:Blausen_0909_WhiteBloodCells.png

Quick refresher: Innate immune system - cytokines



http://www.biocarta.com/pathfiles/m_cytokinepathway.asp

Quick refresher: Innate immune system – inflammatory response



http://www.biocarta.com/pathfiles/h_inflampathway.asp

Worker presents with symptoms (could be either atopic or irritant)

https://dermnetnz.org/topics/irritant-contact-dermatitis

Crossing the skin barrier

- **Molecular diffusion**
  - Small molecules < 500 MW
  - Larger molecules can penetrate through sebaceous glands & hair follicles

Crossing the skin barrier

- Molecular diffusion
  - Small molecules < 500 MW
  - Larger molecules can penetrate through sebaceous glands & hair follicles
- **Physically or chemically damaged skin**

Crossing the skin barrier

- Molecular diffusion
  - Small molecules < 500 MW
  - Larger molecules can penetrate through sebaceous glands & hair follicles
- Physically or chemically damaged skin
- **Particles**
  - Small particles (< 7 µm) can end up in hair follicles
  - < 3 µm can cross intact stratum corneum & hair follicles
  - Solids dissolve in sweat or lipids

Crossing the skin barrier

- Molecular diffusion
  - Small molecules < 500 MW
  - Larger molecules can penetrate through sebaceous glands & hair follicles
- Physically or chemically damaged skin
- Particles
  - Small particles (< 7 µm) can end up in hair follicles
  - < 3 µm can cross intact stratum corneum & hair follicles
  - Solids dissolve in sweat or lipids
- **Systemic absorption**

Crossing the skin barrier

- Molecular diffusion
  - Small molecules < 500 MW
  - Larger molecules can penetrate through sebaceous glands & hair follicles
- Physically or chemically damaged skin
- Particles
  - Small particles (< 7 µm) can end up in hair follicles
  - < 3 µm can cross intact stratum corneum & hair follicles
  - Solids dissolve in sweat or lipids
- Systemic absorption
- **Skin to respiratory sensitization** (Arrandale et al. 2012; Am J Ind Hyg 55:353-360)
  - Isocyanates, metal salts, formaldehyde, glutaraldehyde – allergens processed in skin may induce more respiratory sensitization than by respiratory route alone.

Systemic absorption of chemicals

Systemic absorption of chemicals

- Hairdressers' concentration significantly increased compared to office workers
- Post shift urine sample
  - Phthalates
  - VOC metabolites
    - Acrolein, 1,3-butadiene, xylene
  - Parabens (methyl-, ethyl-, propyl)
  - 2-naphthol
  - 3-[(2-ethylhexyl)oxy]propane1,2-diol

e.g. Newmeyer, et al. *J Exposure Sci & Environ Epi* 2023; Louis, et al. *Environ Internat* 2021; Kolena et al. *Appl Sci* 2019

Common sensitizers by occupation

Occupation	Sensitizers
Office work	Fungi, dust mites (↑RH%); allergens from cats, dogs, mice, cockroaches, etc.
Construction workers	Isocyanates, chromates, epoxy and phenolic resins, wood, formaldehyde, solder
Dental technicians	Rubber, epoxy and acrylic monomer, amine catalysts, glutaraldehyde, anesthetics
Farmers, florists, gardeners	Plants, woods, fungicides, insecticides
Food handlers, cooks, bakers	Flour additives, vegetables, spices, garlic, rubber, benzoyl peroxide
Hairdressers, beauticians	Paraphenylenediamine (hair dye), ammonium persulphate (bleach), glycerylmonothioglycolate (permanents) surfactants (shampoos), nickel, perfume, essential oils, preservatives in cosmetics
Medical personnel	Rubber, colophony, formaldehyde, glutaraldehyde, disinfectants, antibiotics
Metal workers, mechanics	Nickel, cobalt, chrome, biocides in cutting oils, hydrazine and colophony in flux
Printers and photographers	Nickel, cobalt, chrome, rubber, paraphenylene diamine and azo dyes, developers
Textile workers	Formaldehyde, azo- and anthraquinone dyes, rubber, biocides

Common Respiratory sensitizers

- Hexahydrophthalic anhydride
- Maleic anhydride
- Methyltetrahydrophthalic anhydride
- Phthalic anhydride
- Trimellitic anhydride
- Chloramine T
- Cyanuric chloride
- Ethylene diamine
- Glutaraldehyde
- Diphenylmethane-4-4'-diisocyanate
- Toluene diisocyanate
- Hexamethylene diisocyanate
- Ammonium tetrachloroplatinite II

Risk assessments: skin condition

- **Abrasions & cuts**

Risk assessments: skin condition

- Abrasions & cuts
- **UV light (sunlight) initially increases permeability, but prolonged UV irradiation decreases permeability!**

Risk assessments: skin condition

- Abrasions & cuts
- UV light (sunlight) initially increases permeability, but prolonged UV irradiation decreases permeability!
- **Cold damage inhibits repair of barrier**

Risk assessments: skin condition

- Abrasions & cuts
- UV light (sunlight) initially increases permeability, but prolonged UV irradiation decreases permeability!
- Cold damage inhibits repair of barrier
- **Cytotoxic damage to Langerhans cells, keratinocytes**

Risk assessments: skin condition

- Abrasions & cuts
- UV light (sunlight) initially increases permeability, but prolonged UV irradiation decreases permeability!
- Cold damage inhibits repair of barrier
- Cytotoxic damage to Langerhans cells, keratinocytes
- **Organic solvents or surfactants (surface as well as intercellular) – lipids can be removed or disorganized**

Risk assessments: skin condition

- Abrasions & cuts
- UV light (sunlight) initially increases permeability, but prolonged UV irradiation decreases permeability!
- Cold damage inhibits repair of barrier
- Cytotoxic damage to Langerhans cells, keratinocytes
- Organic solvents or surfactants (surface as well as intercellular) – lipids can be removed or disorganized
- **Occlusion <u>increases</u> permeation through the skin**
  - **Prohibits evapouration of chemical**
  - **Rapid skin hydration and increased temperature increase permeation**
  - **Stratus corneum normally contains 5 – 15% water: hyper hydration**

Risk assessments skin condition

- **Increased temperature increases permeability (occlusion)**

Risk assessments skin condition

- Increased temperature increases permeability (occlusion)
- **Increasing relative humidity increases permeability**

Risk assessments skin condition

- Increased temperature increases permeability (occlusion)
- Increasing relative humidity increases permeability
- **Highly volatile chemicals will evapourate before percutaneous absorption occurs**

Risk assessments skin condition

- Increased temperature increases permeability (occlusion)
- Increasing relative humidity increases permeability
- Highly volatile chemicals will evapourate before percutaneous absorption occurs
- **Decontamination prevents:**
  - **Percutaneous absorption and dermatitis**
  - **Transfer of contaminates to mouth**
  - **Transfer of toxic chemicals to other sensitive areas of the body**

Controls: Chemical Protective Clothing

- **American Society for Testing and Materials (ASTM) standardization of CPC – also NFPA, ISO, CEN**

Controls: Chemical Protective Clothing

- American Society for Testing and Materials (ASTM) standardization of CPC – also NFPA, ISO, CEN
- **Most CPC are made of polymer chains that (on a molecular level) move against each other = flexibility**

Controls: Chemical Protective Clothing

- American Society for Testing and Materials (ASTM) standardization of CPC – also NFPA, ISO, CEN
- Most CPC are made of polymer chains that (on a molecular level) move against each other = flexibility
- **Degradation**
  - **Exposure to chemical results in change in physical properties (tear resistance, etc.)**

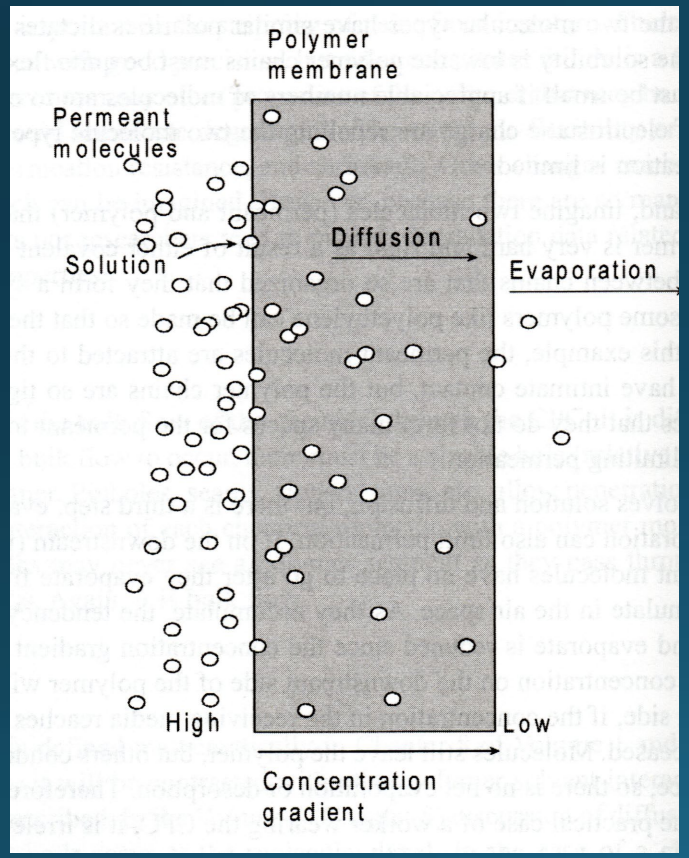
Controls: Chemical Protective Clothing

- American Society for Testing and Materials (ASTM) standardization of CPC – also NFPA, ISO, CEN
- Most CPC are made of polymer chains that (on a molecular level) move against each other = flexibility
- Degradation
  - Exposure to chemical results in change in physical properties (tear resistance, etc.)
- **Penetration**
  - **Bulk flow of chemical through pinholes, seams, etc.**

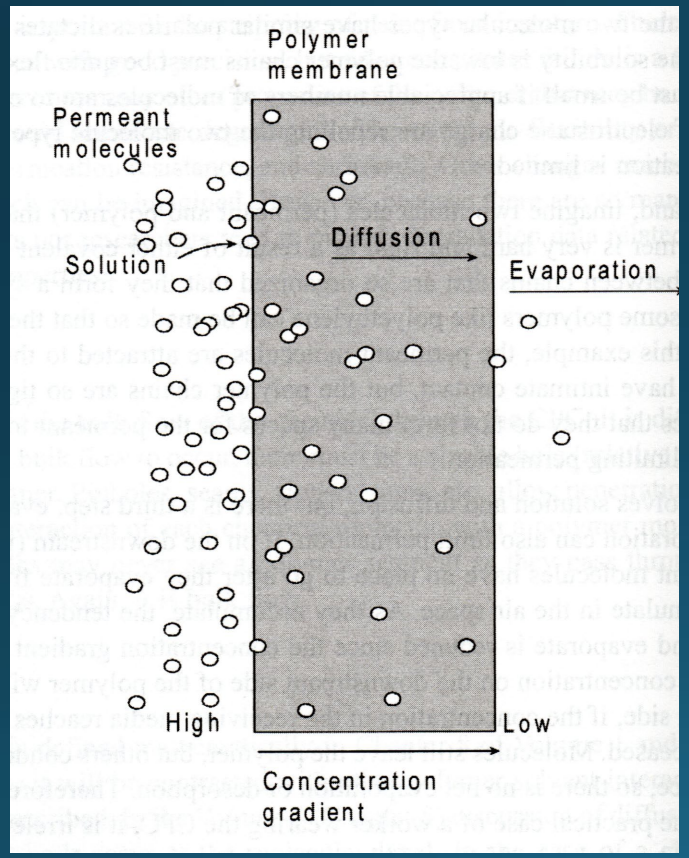
Controls: Chemical Protective Clothing

- American Society for Testing and Materials (ASTM) standardization of CPC – also NFPA, ISO, CEN
- Most CPC are made of polymer chains that (on a molecular level) move against each other = flexibility
- Degradation
  - Exposure to chemical results in change in physical properties (tear resistance, etc.)
- Penetration
  - Bulk flow of chemical through pinholes, seams, etc.
- **Permeation**
  - **Chemical moves through the polymer chains**

Diffusion across glove polymer



Diffusion across glove polymer



Irritant contact dermatitis

OSHA glove selection chart (*examples*)

Chemical	Neoprene	Latex rubber	Butyl	Nitrile
Acetone	G	VG	VG	P
Ammonium hydroxide	VG	VG	VG	VG
Benzene	F	F	F	P
Carbon disulfide	F	F	F	F
Diesel fuel	G	P	P	VG
Epoxy resins, dry	VG	VG	VG	VG
Formaldehyde	VG	VG	VG	VG
Gasoline (unleaded)	G	P	F	VG
Ketones	G	VG	VG	P
Styrene	P	P	P	F
Toluene	F	P	P	F
Toluene diisocyanate	F	G	G	F

http://www.osha.gov/Publications/osha3151.pdf

OSHA glove selection chart (*examples*)

Chemical	Neoprene*	Latex rubber*	Butyl	Nitrile*
Acetone	G (2.4 - > 60)	VG (1.2 - > 180)	VG	P (4.2 – 18)
Ammonium hydroxide	VG (> 240)	VG (< 60)	VG (> 480)	VG (> 240)
Benzene	F (1.2 – 18.6)	F (0.6 – 10.8)	F (<60)	P (4.2 – 36)
Carbon disulfide	F	F	F	F
Diesel fuel	G (> 60)	P (< 60)	P (< 60)	VG (> 240)
Epoxy resins, dry	VG	VG	VG	VG
Formaldehyde	VG (> 60)	VG (< 60)	VG (> 480)	VG (> 480)
Gasoline (unleaded)	G (< 60)	P (< 60)	F (< 60)	VG (> 480)
Nitric Acid	G (< 60)	F	F (> 60)	F (< 60)
Styrene	P	P	P	F
Toluene	F (1.2 – 31.2)	P (0.6 – 40.8)	P (< 60)	F (7.8 - 72)
Toluene diisocyanate	F	G	G	F

http://www.osha.gov/Publications/osha3151.pdf

* (time to breakthrough, minutes)

ChemRest Butyl II 875/875R product insert

EN ISO 374-1:2016/Type A

ABCIKLMNPST

		Permeation EN 16523-1:2015	Degradation % EN 374-4:2013
A	Methanol	Level 6	–2.6%
B	Acetone	Level 5	–1.7%
C	Acetonitrile	Level 6	0.7%
I	Ethyl acetate	Level 2	30.2%
K	Sodium hydroxide 40%	Level 6	–72.8%
L	Sulphuric acid 96%	Level 5	–11.0%
M	Nitric acid 65%	Level 6	–46.7%
N	Acetic acid 99%	Level 6	–52.2%
P	Hydrogen peroxide 30%	Level 6	–38.3%
S	Hydrofluoric acid 40%	Level 6	N/A
T	Formaldehyde 37%	Level 6	–82.8%

Level 1 > 10 min
Level 2 > 30 min
Level 3 > 60 min
Level 4 > 120 min
Level 5 > 240 min
Level 6 > 480 min

- Notes from product insert:
  - Gloves had a minimum shelf life of 5 years.
  - This information does not reflect the actual duration of protection in the workplace and the differentiation between mixtures and pure chemicals.
  - It is recommended to check that the gloves are suitable for the intended use because the conditions at the workplace may differ from the type test depending on temperature, abrasion and degradation.
  - When used, protective gloves may provide less resistance to the dangerous chemical due to changes in physical properties.

Decontamination of Chemical Protective Clothing

- Can CPC be decontaminated and reused?
  - Chemical is still inside the matrix – it will off gas over time
- Donning and doffing sequence

Donning	Doffing
1) wash hands	1) remove gloves
2) put on gown	2) remove gown
3) put on mask/respirator	3) wash hands
4) put on eye protection	4) remove eye protection
5) put on gloves	5) remove mask/respirator
	6) wash hands

Conclusions & take home message

- Once sensitized, the immune system will always react.
- Dermal exposure can result in respiratory sensitization as well.
- Dermal PPE is **not** a one-size-fits-all solution.
- A risk assessment is required as well as training and education.
- Sensitization can be avoided with due care and attention.