TO TAN OR NOT TO TAN, THAT IS THE QUESTION

a place of mind
THE UNIVERSITY OF BRITISH COLUMBIA
Faculty of Medicine

University of Victoria

let's talk science

DISCLOSURES

- We are medical students
- This session is not intended to give you a diagnosis or replace going to see a health care professional
- Physics will be discussed

WHAT YOU WILL LEARN

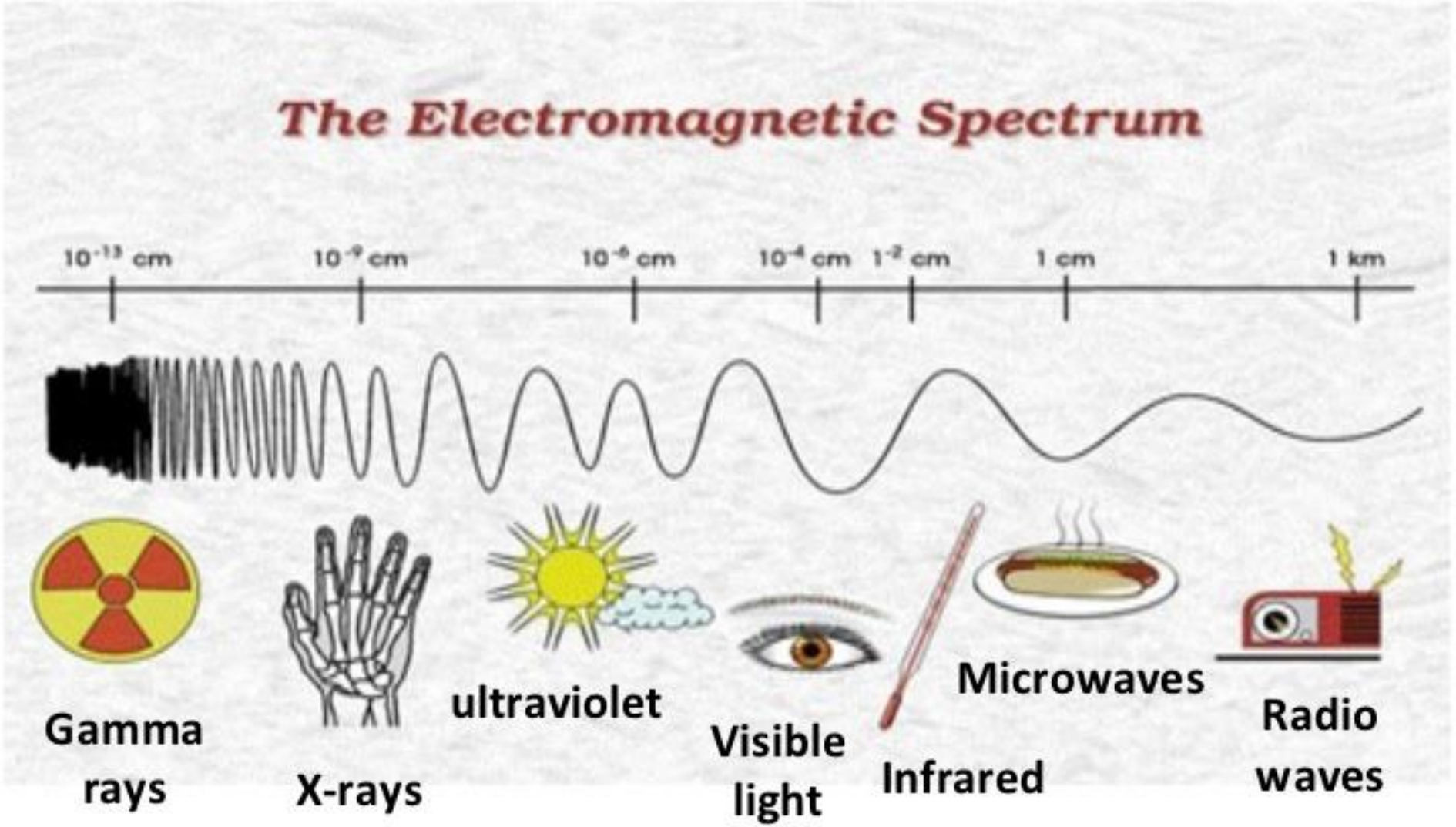
- The risks of too much sun exposure
- How sunscreen works
- What strength sunscreen to use and when to apply
- The risks of using sunscreen
- The benefits of tanning
- Vitamin D

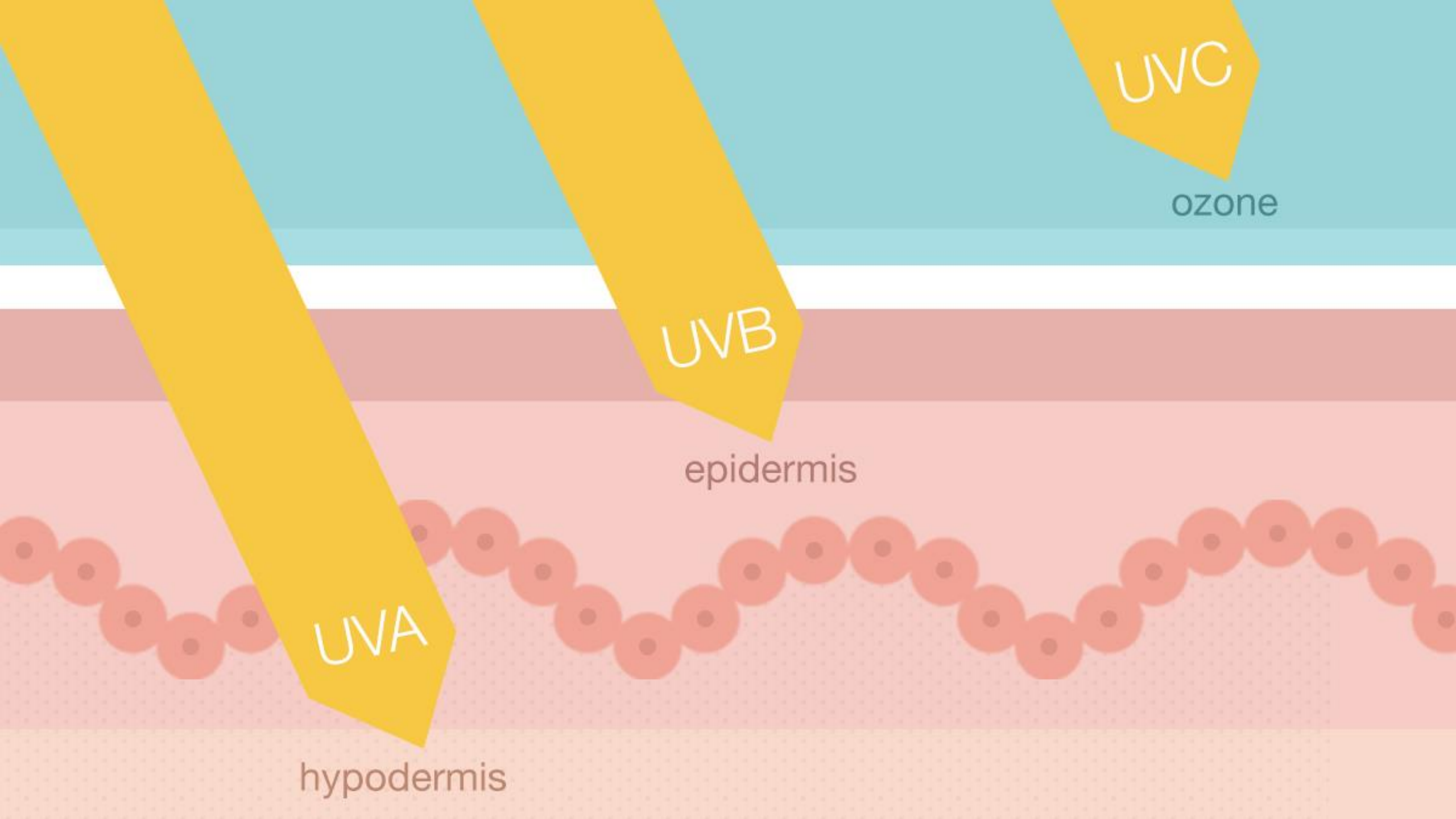
WHAT ARE THE RISKS OF TOO MUCH SUN EXPOSURE?

SUN FUN FACTS

- It's big!
- It's far away!
- It's old!

The Electromagnetic Spectrum




UVC
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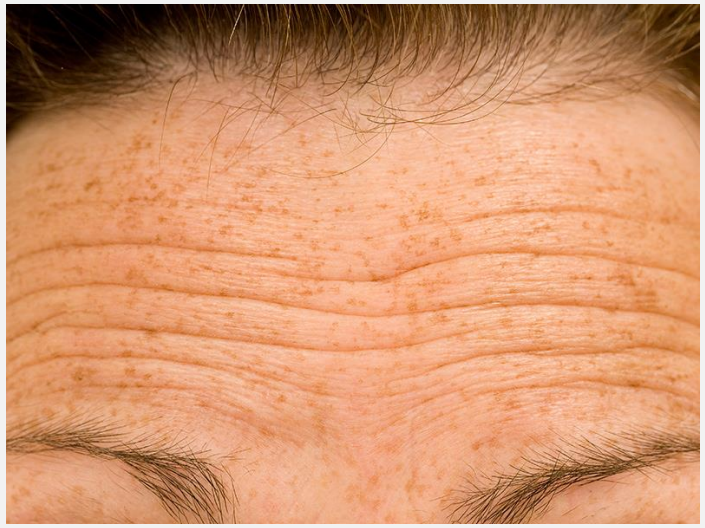
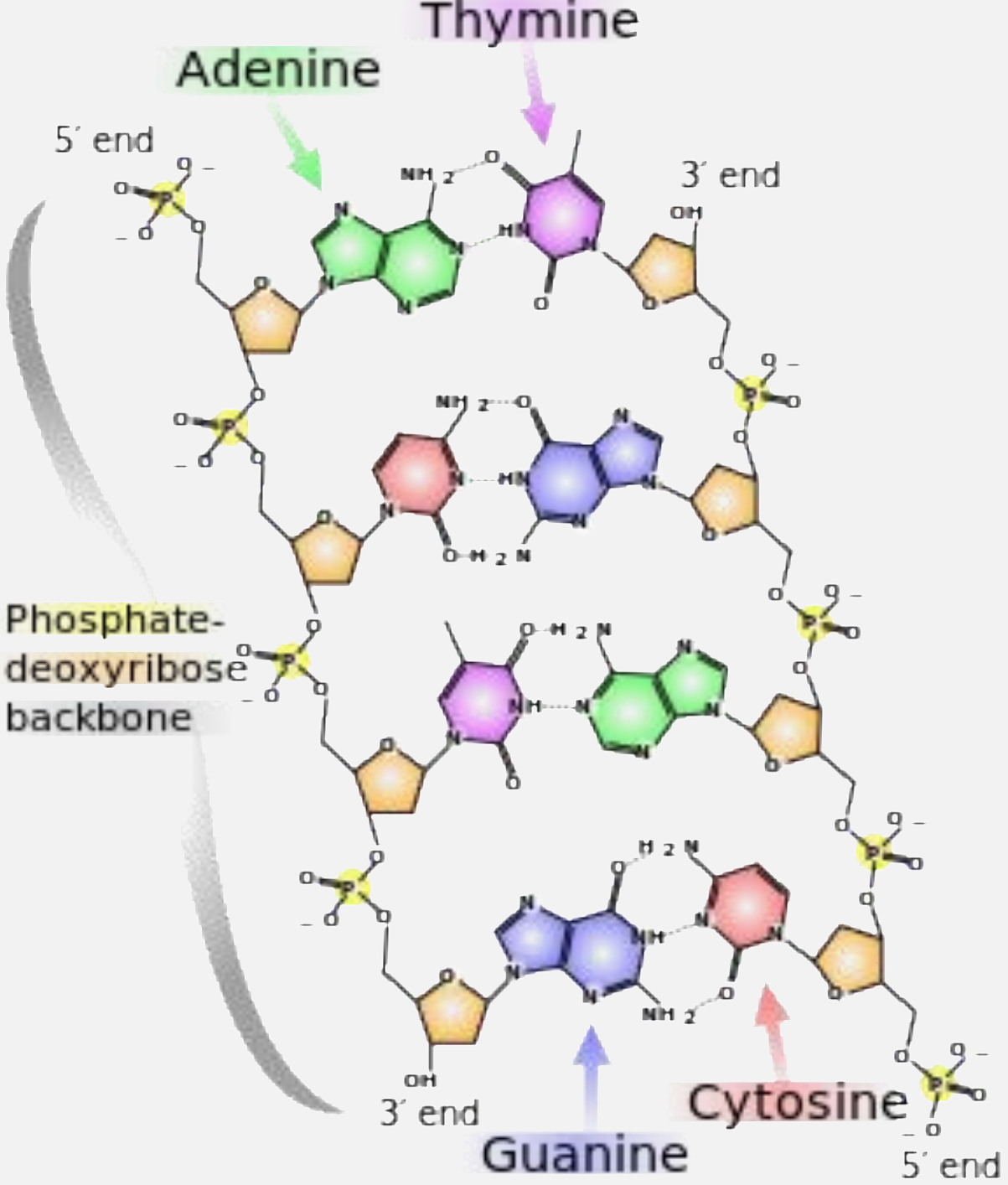
UVB
epidermis
UVA
hypodermis




Cancer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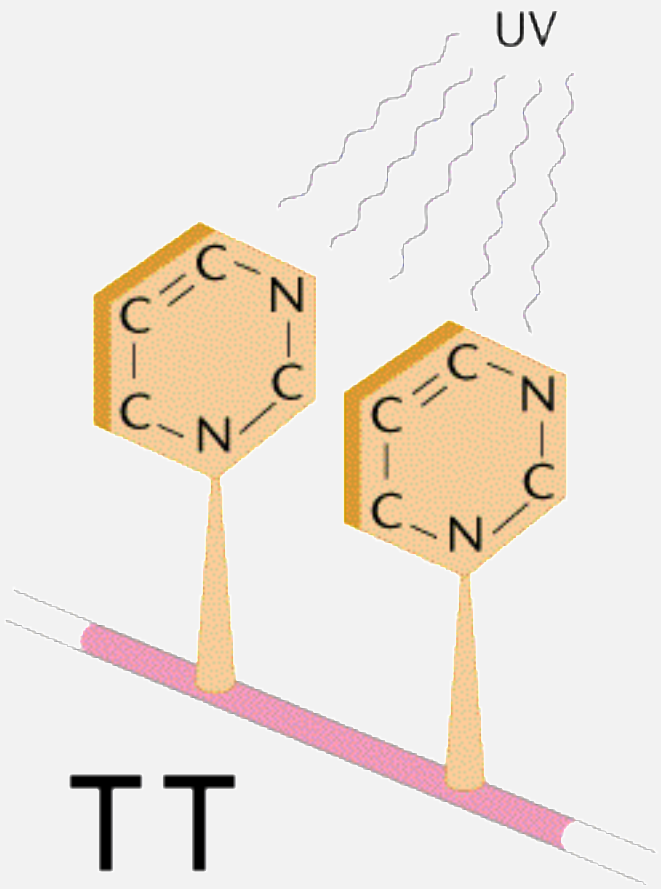
Adenine
5′ end
3′ end
Phosphate-
deoxyribose
backbone
3′ end
Cytosine
Guanine
5′ end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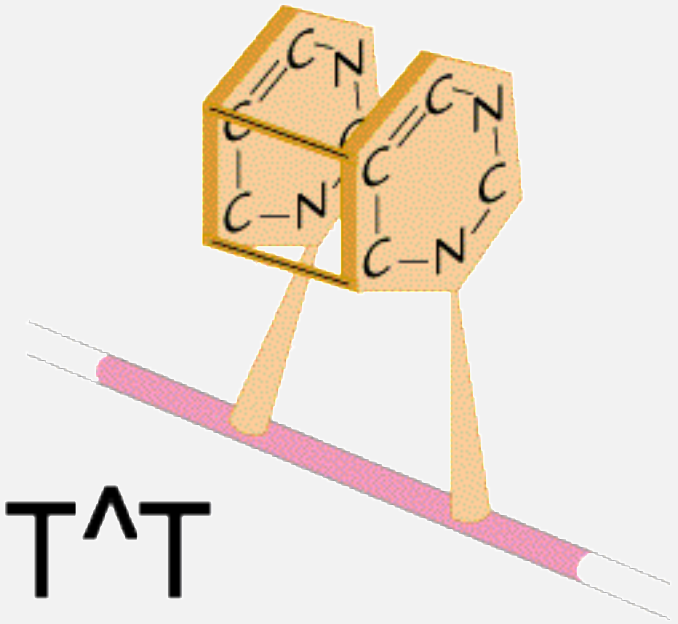
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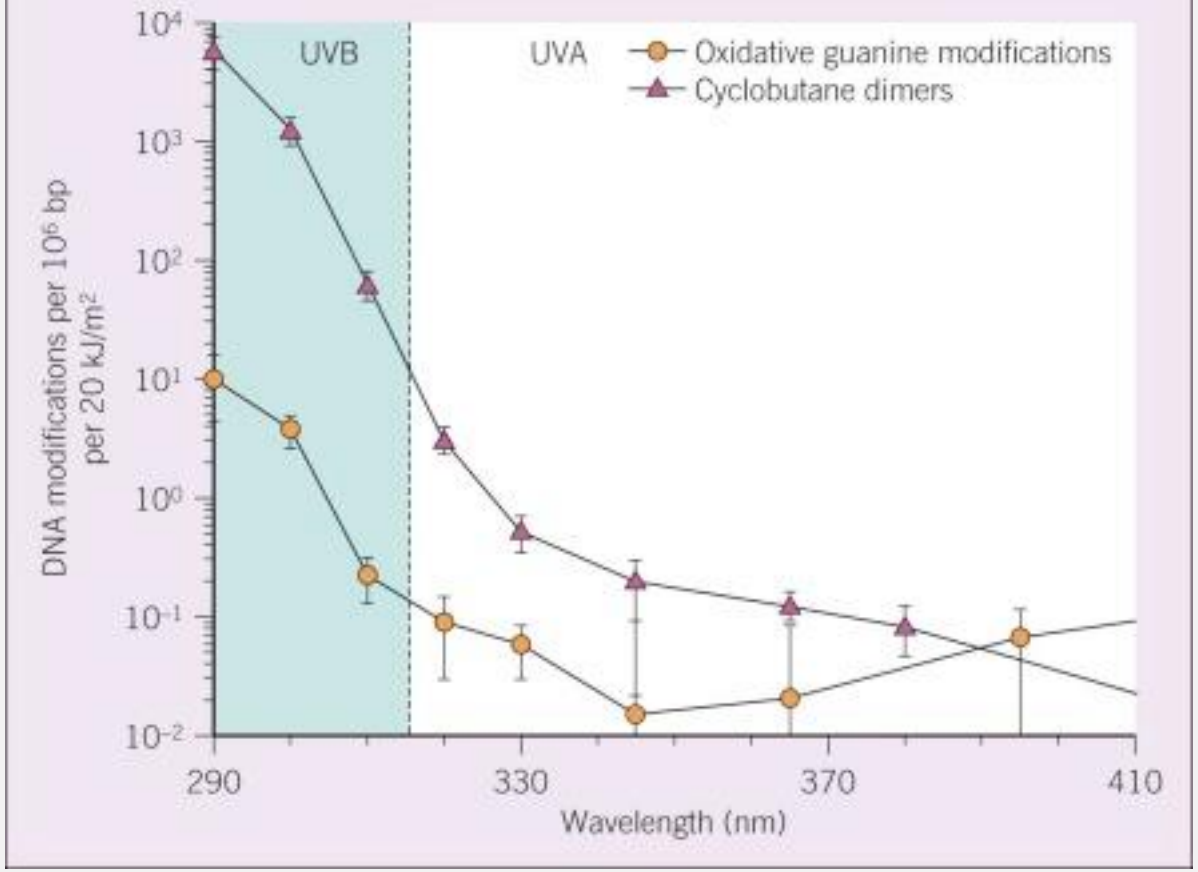
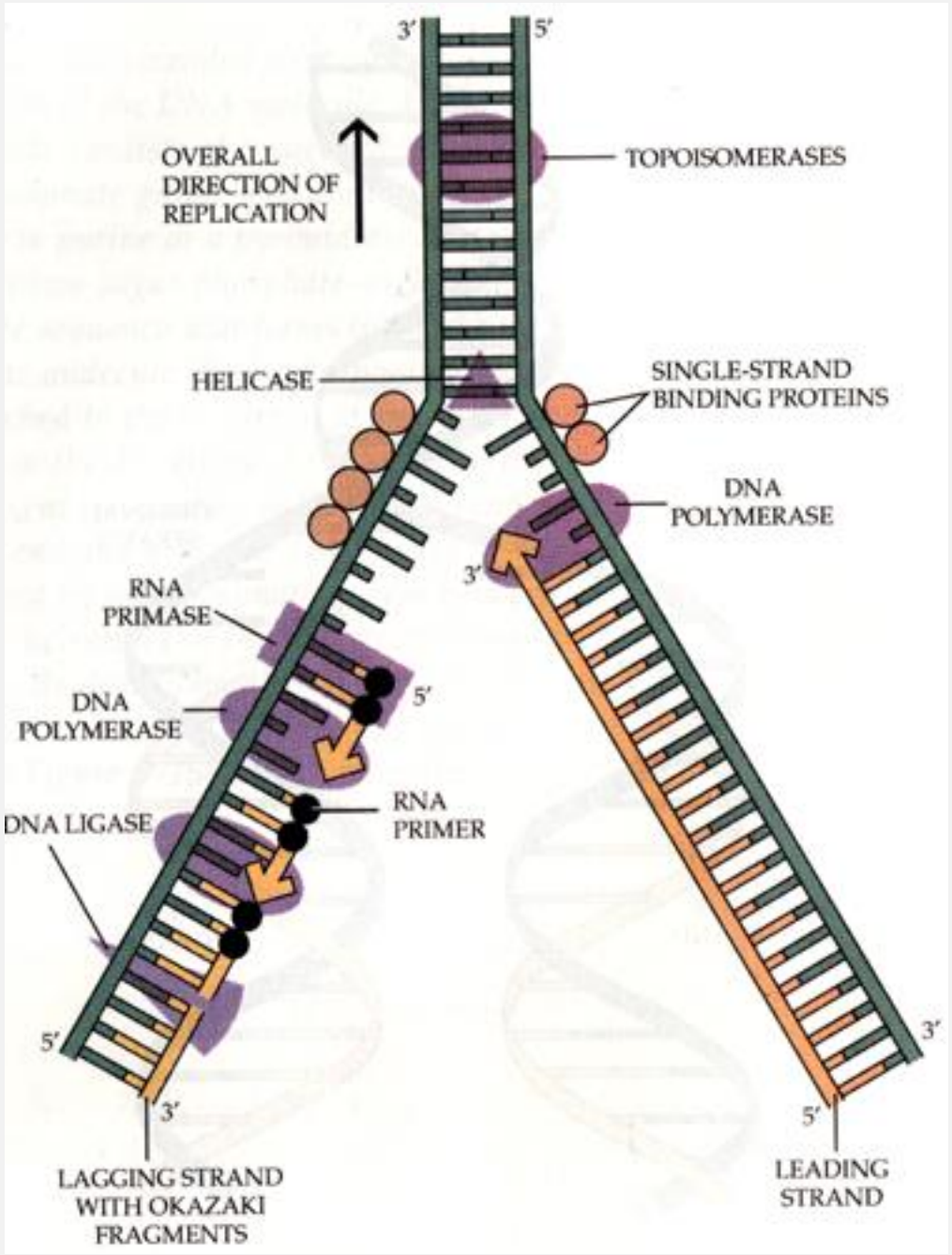
ACTION SPECTRUM FOR INDUCTION OF CYCLOBUTANE DIMERS AND OXIDATIVE GUANINE MODIFICATIONS



WHAT HAPPENS NEXT?

- Repair (DNA excision repair or photo reactivation)
- Cell dies
- Cell divides and a mutation is introduced


3′
5′
OVERALL DIRECTION OF REPLICATION
TOPOISOMERASES
HELICASE
SINGLE-STRAND BINDING PROTEINS
DNA POLYMERASE
3′
RNA PRIMASE
DNA POLYMERASE
5′
RNA PRIMER
DNA LIGASE
5′
3′
3′
5′
LAGGING STRAND WITH OKAZAKI FRAGMENTS
LEADING STRAND

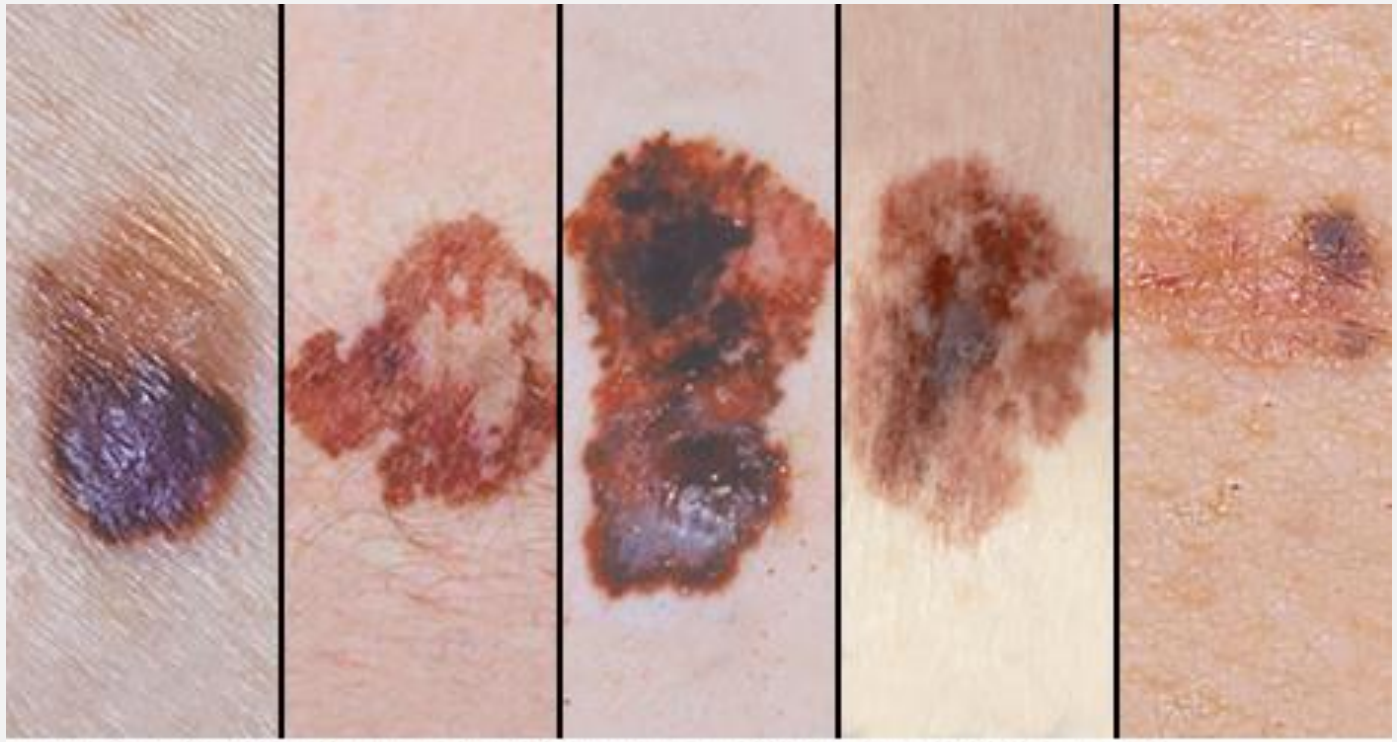
STATISTICS

- 1 in 57 lifetime risk of developing melanoma for men and 1 in 74 for women
- The rate of melanoma cancer is on the rise
- Survival rate 98% if detected early, drops to 65% if late detection
- 40-50% of people who life to 65 will have squamous cell carcinoma or basal cell carcinoma at least once

SQUAMOUS CELL CARCINOMA

BASAL CELL CARCINOMA

MELANOMA



WHAT TO WATCH FOR

- Asymmetry
- Border irregularity
- Color changes
- Diameter greater than 1/4 inch (about 6 millimeters)
- Evolving


MAYBE NEXT TIME YOU'LL TRY A LITTLE SUNSCREEN...
I guess you could say he's bacon in the sun
ifunny.co

A TALE OF TWO METHODS

- Physical barrier
  - e.g. zinc oxide, titanium oxide
  - near perfect, UVA & UVB
- Chemical barrier
  - filter and absorb UV radiation
  - chemically convert UV to heat
  - vary in ability to absorb UVB, UVA, or both

SPF = SUN PROTECTION FACTOR

1/15 or 93%

150 min

1/30 or 96.7%

300 min

1/50 or 98%

500 min

LIMITATIONS OF SPF

- Doesn't take into account how long chemicals remain active
- Only applies to UVB
  - measures visible damage to skin
- Doesn't measure free radical damage

Table 1

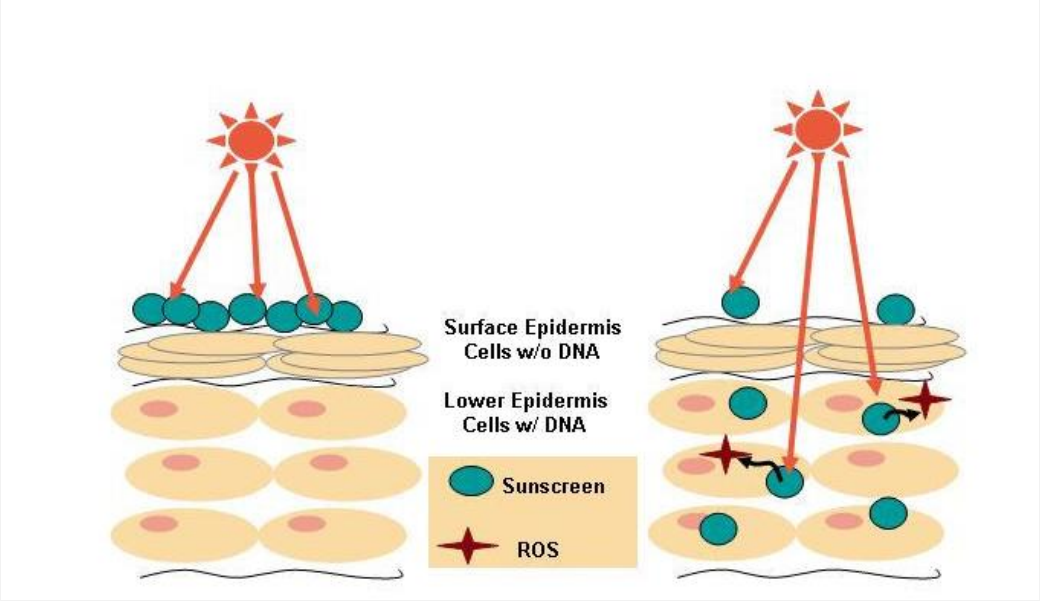
FDA-Approved Active Sunscreen Product Ingredients and Their Effects on UV Radiation

	Ingredient	UVA	UVB
Inorganic Agents	Titanium dioxide	I, II	X
	Zinc oxide	I, II	X
Organic Agents	p-aminobenzoic acid (PABA)		X
	Padimate-O		X
	Cinoxate		X
	Octinoxate		X
	Homosalate		X
	Octisalate		X
	Trolamine salicylate		X
	Oxybenzone	II	X
	Sulisobenzone	II	X
	Dioxybenzone	II	X
	Meradimate	II	
	Avobenzone	I	
	Octocrylene	II	X
	Ecamsule	I, II	X
	Ensulizole		X

I: protects against 340–400-nm UVA radiation; II: protects against 320–340-nm UVA radiation; X: protects against UVB radiation.

Source: References 1, 6, 11, 13.

FREE RADICALS, SUNSCREEN, AND YOU



CHEMICALS, CHEMICALS, CHEMICALS…

- Environmental Working Group (EWG)
  - retinyl palmitate (vitamin A)
  - oxybenzone
  - octinoxate
  - homosalate
  - octisalate
  - octocrylene
  - titanium dioxide
  - zinc oxide
  - avobenzone

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	Octinoxate		X
	Homosalate		X
	Octisalate		X
	Trolamine salicylate		X
	Oxybenzone	II	X
	Sulisobenzone	II	X
	Dioxybenzone	II	X
	Meradimate	II	
	Avobenzone	I	
	Octocrylene	II	X
	Ecamsule	I, II	X
	Ensulizole		X

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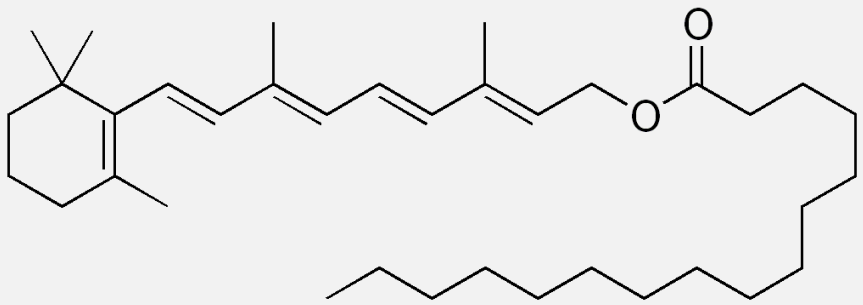
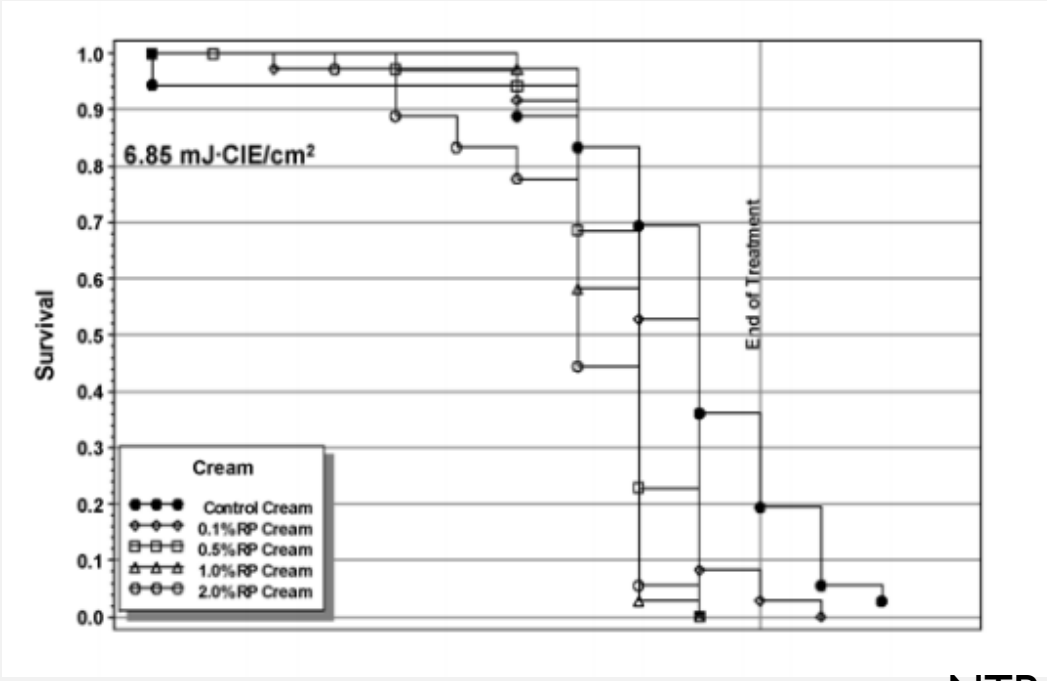
Source: References 1, 6, 11, 13.

RETINYL PALMITATE (VITAMIN A)

- Common component of skin creams to "slow the aging process"
- Cancer causing?
  - National Toxicology Program, 2009



RETINYL PALMITATE (VITAMIN A)

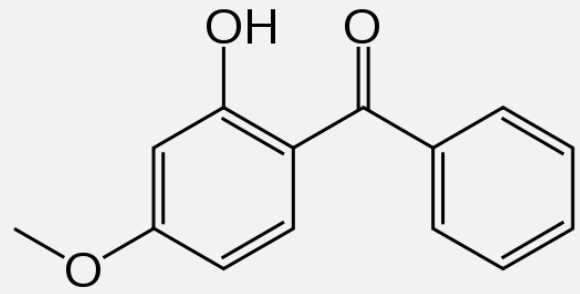


NTP, 2009

RETINYL PALMITATE (VITAMIN A)

- Confounding variables
  - study performed in mice
  - UV exposure to skin cream vs. sunscreen

OXYBENZONE



- absorbs light and photostabilizes
- common in many sunscreens, hair products, & cosmetics
- the most common allergen in sunscreen
- 2008 study showed that 96.8% of oxybenzone sunscreen users had oxybenzone or its metabolites in their urine
- EWG: concerned that it might disrupt endocrine system

CHEMICALS, CHEMICALS, CHEMICALS…

- American Cancer Society statement on Cosmetics:

> "It's important to have a sense of the difference between the hazard an ingredient may pose and the risk a person faces from being exposed to it. Scientists use the term hazard to describe the potential of a chemical to cause unwanted health effects. Risk is used to describe the chances of an unwanted health effect in a person from normal use of the ingredient. A substance may be deemed to be potentially hazardous for some reason, but it may pose very little risk to people during normal use."

SUNSCREEN VS. CANCER

- What are the risks for developing skin cancer?
  - too much exposure to UV radiation
  - pale skin
  - exposure to large amounts of coal, paraffin, arsenic, or certain oils
  - family history
  - multiple/unusual moles
  - severe sunburns in the past
  - weakened immune system
  - older age

ACS, 2016

SUNSCREEN VS. CANCER

- What are the risks for developing skin cancer?
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  - older age

ACS, 2016

SUNSCREEN VS. CANCER

- 2010 Case Control Study
  - looked at individuals diagnosed with Melanoma between 2004 and 2007
  - included 1,167 cases vs. 1,101 controls

Lazovich, D et al. (2010) Indoor Tanning and Risk of Melanoma: A Case-Control Study in a Highly Exposed Population

Table 3. The association between indoor tanning history with melanoma risk (Skin Health Study)

Indoor tanning	Cases	Controls	Age- and gender-adjusted OR (95% CI)	Multivariate adjusted OR* (95% CI)
	n (%)	*n* (%)		
Never used	433 (37.1)	538 (48.9)	1.00	1.00
Ever used	734 (62.9)	563 (51.1)	1.81 (1.51-2.21)	1.74 (1.42-2.14)
Frequency of use (h)				
1-9	322 (27.6)	289 (26.2)	1.58 (1.28-1.96)	1.46 (1.15-1.85)
10-19	74 (6.3)	66 (6.0)	1.62 (1.12-2.34)	1.81 (1.21-2.70)
20-49	129 (11.1)	90 (8.2)	2.10 (1.53-2.88)	2.18 (1.54-3.08)
50+	200 (17.1)	95 (8.6)	3.27 (2.42-4.41)	3.18 (2.28-4.43)
P trend			<0.0001	<0.0001
Frequency of use, sessions				
≤10	149 (12.8)	141 (12.8)	1.47 (1.12-1.93)	1.34 (1.00-1.81)
11-24	130 (11.1)	100 (9.1)	1.84 (1.36-2.48)	1.80 (1.30-2.49)
25-100	173 (14.8)	147 (13.4)	1.71 (1.30-2.23)	1.68 (1.25-2.26)
>100	275 (23.6)	154 (14.0)	2.71 (2.08-3.51)	2.72 (2.04-3.63)
P trend			0.0005	0.0002
Age at initiation (y)				
<18	209 (17.9)	161 (14.6)	2.18 (1.62-2.94)	1.85 (1.33-2.57)
18-24	175 (15.0)	125 (11.4)	2.14 (1.60-2.85)	1.91 (1.39-2.62)
25-34	150 (12.9)	143 (13.0)	1.43 (1.09-1,87)	1.46 (1.09-1.97)
35+	199 (17.1)	134 (12.1)	1.79 (1.38-2.33)	1.83 (1.37-2.43)
P trend			0.37	0.68
Duration of use (y)				
1	123 (10.5)	110 (10.0)	1.52 (1.13-2.03)	1.47 (1.06-2.02)
2-5	236 (20.2)	194 (17.6)	1.74 (1.36-2.21)	1.64 (1.26-2.15)
6-9	124 (10.6)	95 (8.6)	1.93 (1.41-2.64)	1.85 (1.31-2.61)
10+	245 (21.0)	146 (13.3)	2.47 (1.90-3.21)	2.45 (1.83-3.28)
P trend			0.0036	0.006

SUNSCREEN VS. CANCER

- The Complications
  - long time from exposure to cancer
  - UVA & UVB
  - application & dose
  - false sense of security
  - free radical generation
  - changing formulations
  - protective effects of the sun

LICENSE TO TAN?

- General consensus is that the goal is to limit/reduce sun exposure
- Specifically UV exposure
  - Shade seeking
  - Clothing
  - Wearing sunscreen when exposure is inevitable

THE SUN AND US

- Almost every ancient civilization worshipped a god of the sun
  - Apollo: Greek Sun God
  - Amaterasu: Japanese Sun Godess
  - Mithras: Iranian/Persian Sun God
  - Ra: Egyptian Sun God
  - Sol: Norse Sun Godess

SHOULD I BECOME A VAMPIRE?

- 90% of women believe tanned skin to be more attractive
- Subjective association with high energy and increased self confidence
- May correlate to reduced risk of different types of cancer
- UVR exposure may be inversely proportional to incidence of autoimmune disorders
- UVR exposure modulates the immune system
  - Immunosuppressive effects
  - Decreased melatonin secretion
- Decreased turnover of serotonin

O'Leary, R., Diehl, J., and Levins, P. (2014). Update on tannin: More risks, fewer benefits. Journal of the American Academy of Dermatology. 70(3)
Robyn M. Lucas, Anne-Louise Ponsonby, Considering the potential benefits as well as adverse effects of sun exposure: Can all the potential benefits be provided by oral vitamin D supplementation?, Progress in Biophysics and Molecular Biology, Volume 92, Issue 1, September 2006, Pages 140-149, ISSN 0079-6107, http://dx.doi.org/10.1016/j.pbiomolbio.2006.02.019. (http://www.sciencedirect.com/science/article/pii/S0079610706000058)

NATURAL PROTECTION

- Constitutive pigmentation vs. Facultative pigmentation
- Melanocytes produce brown-black eumelanin and red-yellow pheomelanin
- Eumelanin provides more effective photoprotection
- Melanin settles above nucleus of keritnocytes increasing pigmentation and preventing DNA damage
- UV induced damage triggers pro-opiomelanocortin transcription in keratinocytes leading to alpha MSH, ACTH, and Beta endorphin
- Facultative pigmentation induced by repeat UVR provides estimated SPF-2

O'Leary, R., Diehl, J., and Levins, P. (2014). Update on tannin: More risks, fewer benefits. Journal of the American Academy of Dermatology. 70(3)

VITAMIN D AND THE SUN

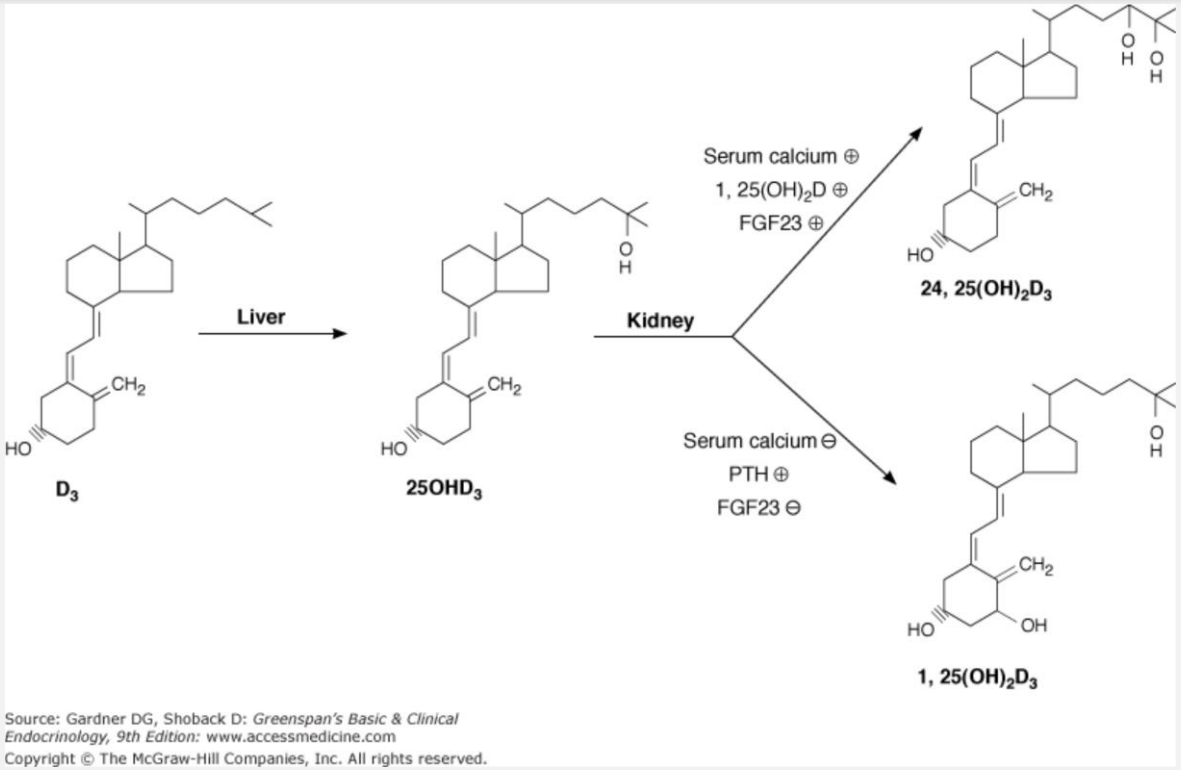
- Hess and Unger observed seasonal incidence of rickets parallel with season variations in sunlight
- McCollum et al in 1922 discover heating, oxidized cod liver oil cures rickets in rats
- In 1925 Hess isolates sitosterol from cottonseed oil and notes that it is antirachitic once activated by UV radiation
- Hess hypothesizes that cholesterol in skin is activated by UV radiation
- 1980 Holick elucidates exact sequence of steps leading to cutaneous photoproduction of cholecalciferol

Kochevar I.E., Taylor C.R., Krutmann J (2012). Chapter 90. Fundamentals of Cutaneous Photobiology and Photoimmunology. In Goldsmith L.A., Katz S.I., Gilchrest B.A., Paller A.S., Leffell D.J., Wolff K (Eds), *Fitzpatrick's Dermatology in General Medicine, 8e.* Retrieved April 04, 2016 from http://accessmedicine.mhmedical.com.ezproxy.library.ubc.ca/content.aspx?bookid=392&Sectionid=41138799.

VITAMIN D BASICS

- What it is
  - Two secosteroids: D2(ergocalciferol) and D3(Cholecalciferol)
  - Metabolized in liver to biologically active 25(OH)D(Calcifediol)
  - Metabolized in kidney to biologically active 1,25(OH)2D (Calcitrol)

From: Chapter 8. Metabolic Bone Disease
Greenspan's Basic & Clinical Endocrinology, 9e, 2011



Legend:

The metabolism of vitamin D. The liver converts vitamin D to 25(OH)D. The kidney converts 25(OH)D to 1,25(OH)2D and 24,25(OH)2D. Control of metabolism is exerted primarily at the level of the kidney where low serum phosphate, low serum calcium, and high parathyroid hormone (PTH) levels favor production of 1,25(OH)2D whereas FGF23; high serum calcium and phosphate, and 1,25(OH)2D inhibit 1,25(OH)2D production while increasing 24,25(OH)2D production. Plus (+) and minus (−) signs denote the stimulatory and inhibitory enzymatic reactions, respectively, driving the metabolic steps indicated.

Greenspan's Basic & Clinical Endocrinology, 9e > Chapter 8. Metabolic Bone Disease

Print

Table 8–3 Vitamin D and Its Metabolites.

Name	Abbreviation	Generic Name	Serum Concentration[a]
Vitamin D Vitamin D_3 Vitamin D_2	D D_3 D_2	Calciferol Cholecalciferol Ergocalciferol	1.6 ± 0.4 ng/mL
25-Hydroxyvitamin D	25(OH)D	Calcifediol	26.5 ± 5.3 ng/mL
1,25-Dihydroxyvitamin D	$1,25(OH)_2D$	Calcitriol	34.1 ± 0.4 pg/mL
24,25-Dihydroxyvitamin D	$24,25(OH)_2D$		1.3 ± 0.4 ng/mL
25,26-Dihydroxyvitamin D	$25,26(OH)_2D$		0.5 ± 0.1 ng/mL

[a] Values differ somewhat from laboratory to laboratory depending on the methodology used, sunlight exposure, and dietary intake of vitamin D in the population study. Children tend to have higher $1,25(OH)_2D$ levels than do adults.

Data from Lambert PW et al. In: Bikle D, ed. *Assay of Calcium Regulating Hormones*. Springer; 1983.

VITAMIN D BASICS

- What it does
  - Regulation of calcium and phosphate homeostasis
  - Primarily acts on receptors that act as transcription factors
  - Intestinal calcium transport
  - Stimulates bone resorption
  - Renal reabsorption of calcium
  - Enables innate immune system and suppresses adaptive immune system
  - Modulation of myocardial contractility and vascular tone
- What happens when you don't have it
  - Children with growing bones rickets
  - Osteomalacia in adults

VITAMIN D BASICS

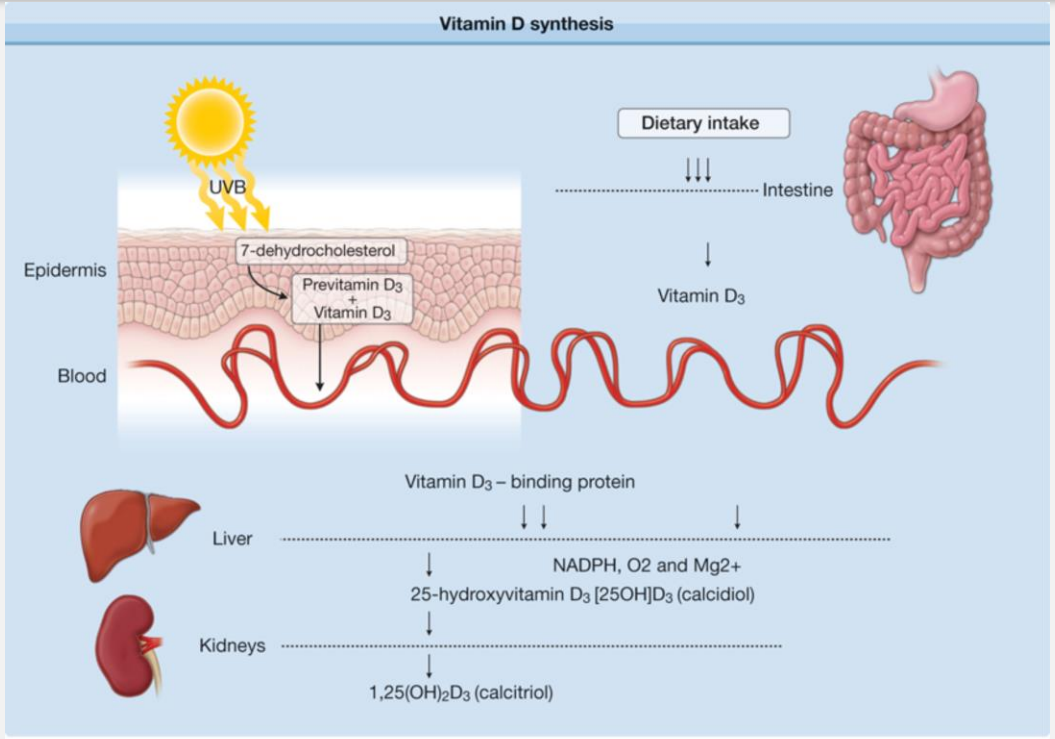
- How much you need
  - Canadian guidelines 800-2000 IU daily
  - Upper limit of intake is 4000 IU daily
  - Toxic at levels greater than 200 ngl/mL
  - Below 25 nmol/l is considered deficient according to stats can
  - Optimal is above 50 nmol/l although some evidence suggests 75 nmol/l

Guideline for Vitamin D Testing and Supplementation in Adults. Adapted from: Ontario Health Technology Assessment Series 2010 and the BC Vitamin D testing protocoll 2010

VITAMIN D BASICS

- How you get it
  - Dietary intake
    - Fortified Milk, orange juice, yogurt, cheese
    - Fish oils, fish livers, and eggs
  - Cutaneous synthesis
    - Vitamin D3 is formed in the skin from 7-dehydrocholesterol
    - Cleavage of B ring requires UVB light to form previtamin D3
    - Thermal isomerization to vitamin D3, lumisterol and tachysterol

From: Chapter 90. Fundamentals of Cutaneous Photobiology and Photoimmunology
Fitzpatrick's Dermatology in General Medicine, 8e, 2012



Legend:

Vitamin D synthesis: Vitamin D is synthesized in the epidermis in response to UVB and is also absorbed from the intestine. It is then transported on a binding protein to the liver, where it undergoes 25-hydroxylation. This metabolite calcidiol is the major circulating form of Vitamin D. The final step occurs mainly in the proximal tubules of the kidneys, where it is acted upon by 25(OH)D-1-α-hydroxylase, an enzyme whose activity is increased by parathyroid hormone and low PO42−. This l-α-hydroxylation is also believed to occur peripherally such as in the skin, where Vitamin D promotes differentiation.

CANADIAN STATS

- 68% of Canadians had blood concentration over 50 nmol/L
- 40% below cut-off in winter
- 25% below cut-off in the winter

Canadian Health Measures Survey (CHMS) August 2009-November 2011

http://www.statcan.gc.ca/pub/82-624-x/2013001/article/11727-eng.htm


Solution=Sun?

LOW VITAMIN D STATUS DESPITE ABUNDANT SUN EXPOSURE

- 93 adults, mean age 24 yr., BMI 23.6 kg/m^2,recruited from University and A'ala Park Board Shop
- Mean sun exposure 28.9 hr/wk (self reported)
- 51% had low vitamin D status defined as serum 25-(OH)D less than 30 ng/ml(75nmol/l)
- Similar results found in a study in Queensland Australia by Kimlin et al.
- Similar results found in study in Chile by Gonzalez et al.

Michael Kimlin, Simone Harrison, Madeleine Nowak, Michael Moore, Alison Brodie, Carolyn Lang, Does a high UV environment ensure adequate Vitamin D status?, Journal of Photochemistry and Photobiology B: Biology, Volume 89, Issues 2–3, 14 December 2007, Pages 139-147, ISSN 1011-1344, http://dx.doi.org/10.1016/j.jphotobiol.2007.09.008. (http://www.sciencedirect.com/science/article/pii/S1011134407001376)

Binkley, et al. (2013). Low Vitamin D Status Despite Abundant Sun exposure. Journal of Clinical Endocrinology and Metabolism. http://dx.doi.org.ezproxy.library.ubc.ca/10.1210/jc.2006-2250

Gonzalez, G. et al. (2007) Highprevalence of vitamin D deficiency in Chilean Healthy Ostmenopausal women with normal sun exposure: additional evidence for a worldwide concer. Menopause. 14(3). DOI: 10.1097/GME.0b013e31802c54c0

DO I GO OUTSIDE OR NOT?

- All things in moderation