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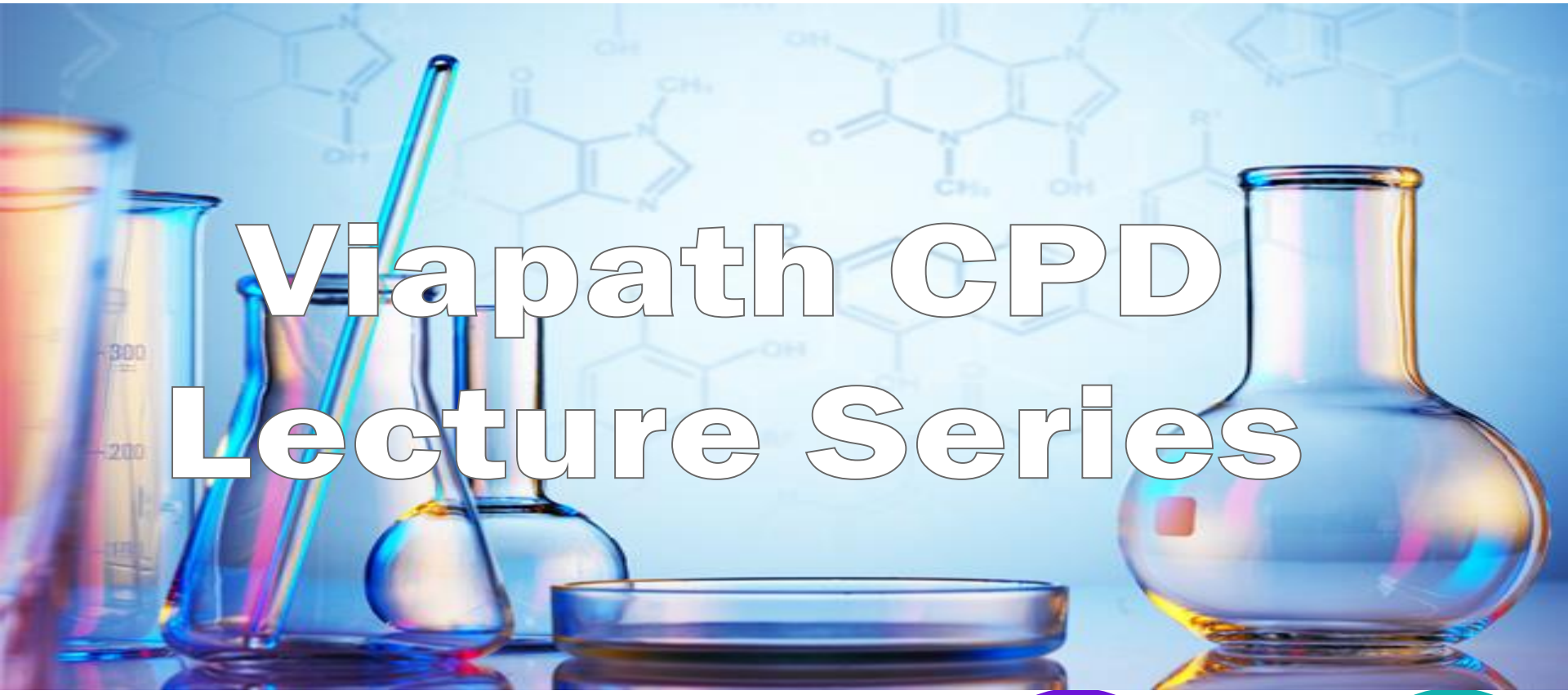
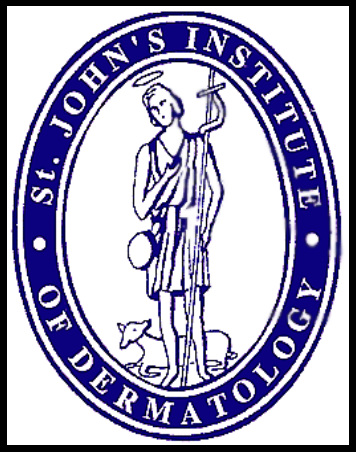
Future Leaders in Innovation est 2013



Viapath CPD Lecture Series

Wednesday 30th January 2019
18:00 to 19:00

‘Dying for a tan’:- evidence for photocarcinogenesis



G.E.Orchard PhD, CSci, MSc, FIBMS, CMS

Viapath Analytics, Histopathology Department, St.John’s Institute of Dermatology, St. Thomas’ Hospital, London

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Cancer Research UK 2014

Statistics

- 15,429 cases malignant melanoma
- 132,000 new cases of non- melanoma
- 2,459 deaths malignant melanoma
- 1/54 people will be diagnosed with malignant melanoma
- Over last decade melanoma incidence increased by (45%)

Skin cancer 'will treble in 30 years'

BY SARAH GETTY

SKIN cancer cases will treble in the next 30 years unless people change their sunbathing habits, experts warned yesterday.

Children could be three times more likely than their grandparents to develop malignant melanoma as the sun-worshipping culture shows no signs of abating, campaigners said.

Even if people do take notice of sun safety campaigns, rates will still double in 30 years because of the amount of Sun exposure people have had already.

The warnings came as Cancer Research UK launched its SunSmart campaign to encourage people to take precautions to protect themselves against the Sun's harmful rays.

Prof Brian Diffey, from Newcastle General Hospital, said: 'It may be 20 or 30 years before we can see the benefits of these campaigns.'

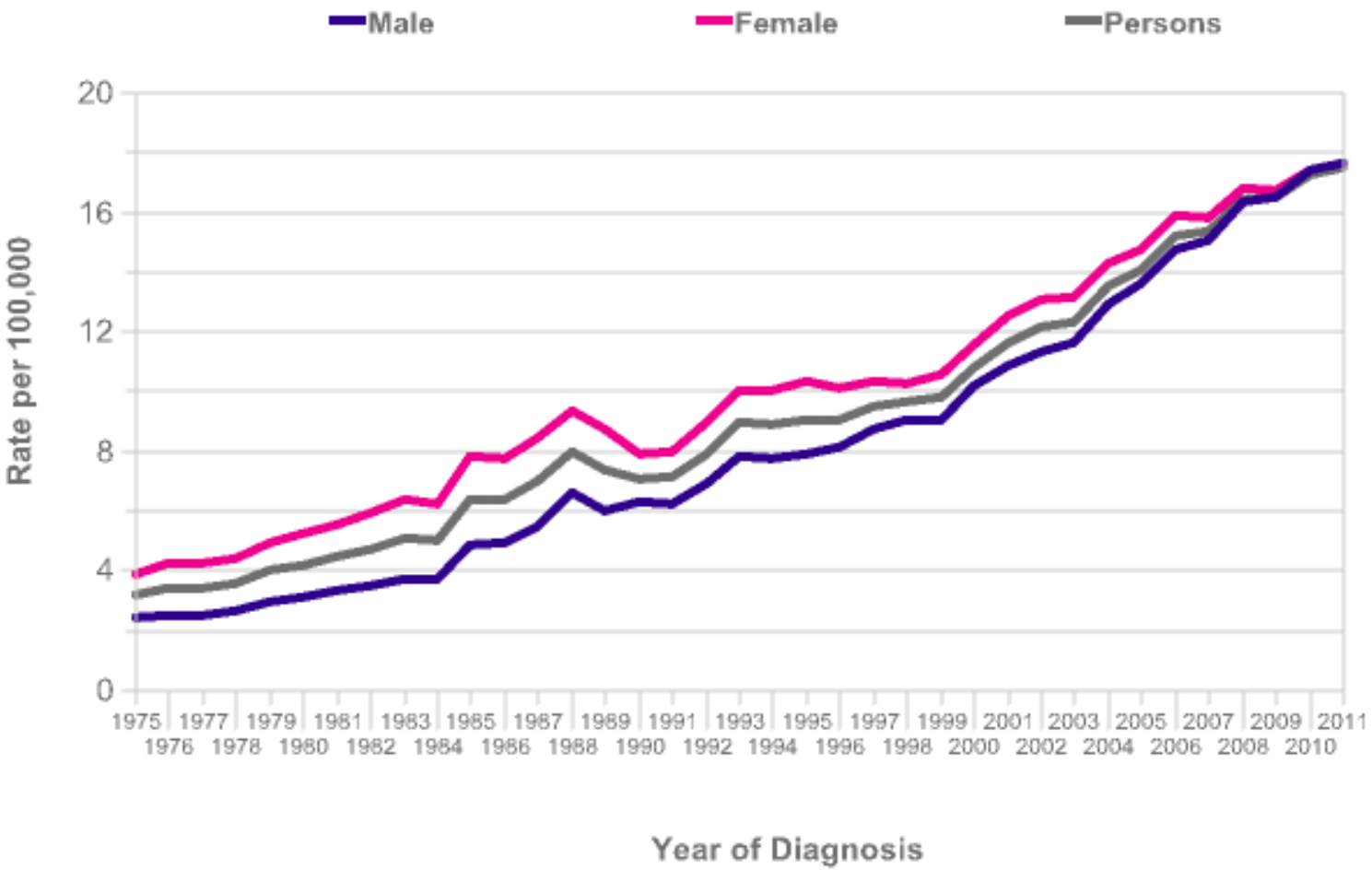
There are more than 7,300 cases of malignant melanoma – the deadliest form of skin cancer – diagnosed in Britain each year, with 1,700 deaths annually. Rates of malignant melanoma are rising faster than any other type of cancer.

Prof Diffey said an increase in overseas holidays and global warming were major contributors to rising rates of skin cancer. Increased use of sunbeds was still only a minor contributory factor, he added.

'It is vital that people monitor their moles and skin blemishes and report any changes in them,' he said.

IT'S not just your joints that stiffen with age ... it's your skin, too, scientists have found. And the discovery could lead to new ways to tackle ageing. It has always been thought that changes in the dermis, the deepest layer of skin, caused wrinkles. But researchers in New York found other cells closer to the surface also stiffen with age. Now, they are testing new skin creams on laboratory mice, New Scientist reports.

Malignant melanoma UK incident trend



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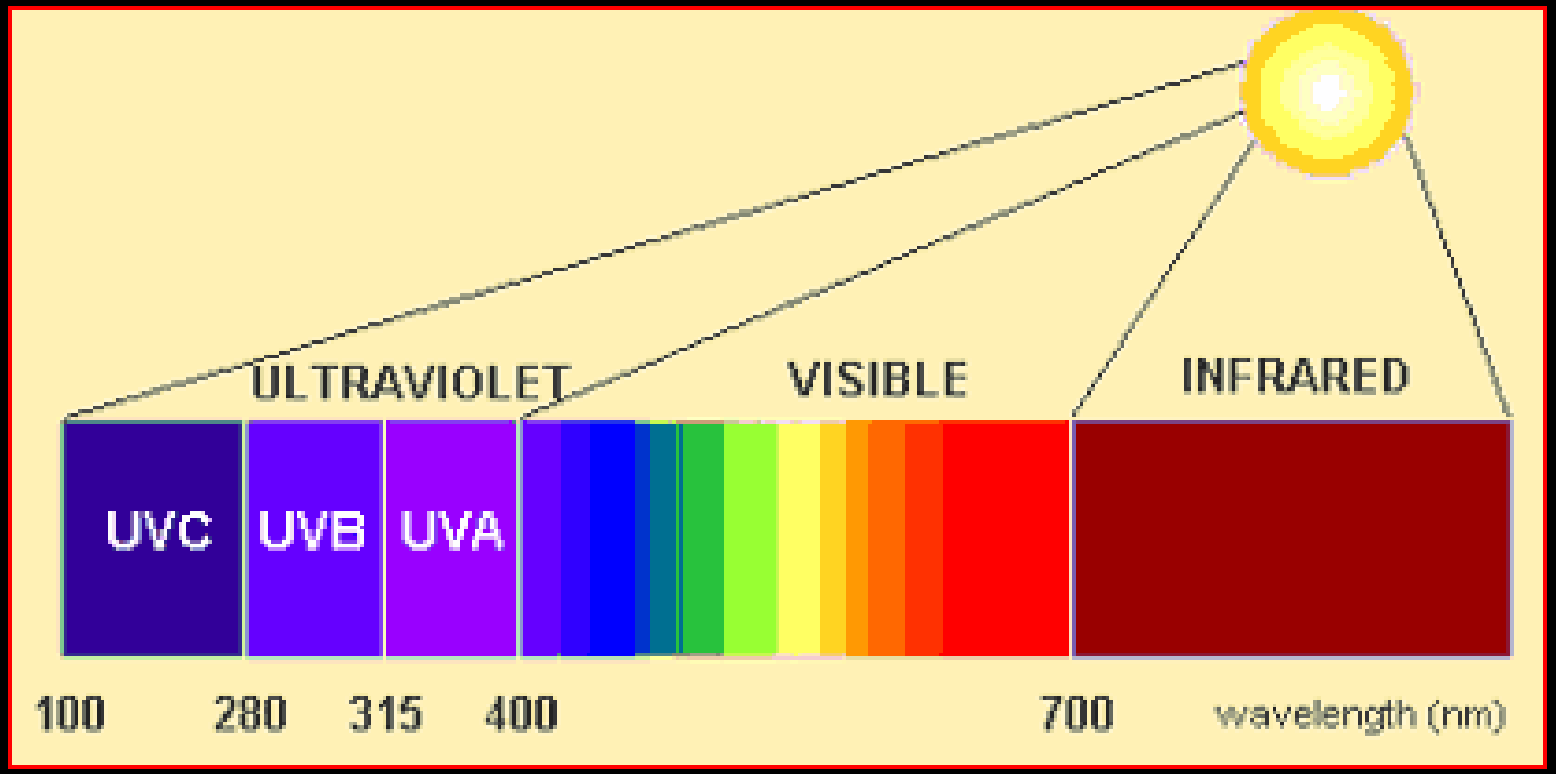
Solar Radiation (UVR 5%)



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Benefits of vitamin D

Vitamin D and skin cancer

Burns EM, Elmets CA, Yusuf. N.

Photochem Photobiol 2015 91(3): 766.

Findings

- Vitamin D important in Cellular proliferation, differentiation and apoptosis, immune regulation, hormone secretion and skeletal health
- Also has beneficial signalling affects in several cancer types including skin cancer?
- Vitamin D production stimulated by UVB
- How much UVB is needed to enhance the benefits but diminish detrimental affects?

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St. Thomas' Hospital (1936)
Sunlight benefits for the treatment of TB

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Sunburn

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Master Ross Orchard

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St. John's Histopathology staff:- Skin types from around the world

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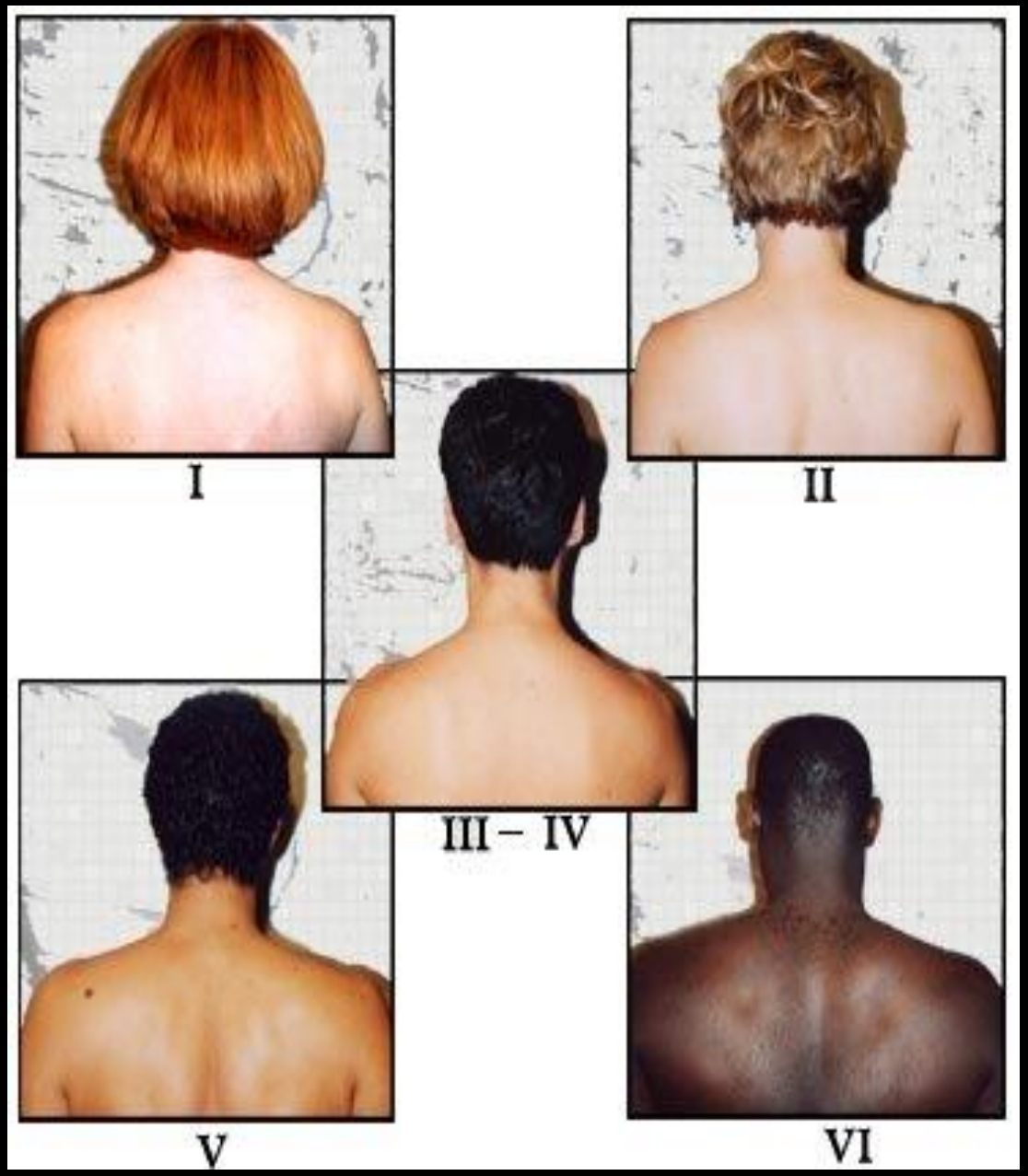
Tanning Ability

LOW

HIGH



Sunburn & Skin Cancer Risk

HIGH

LOW

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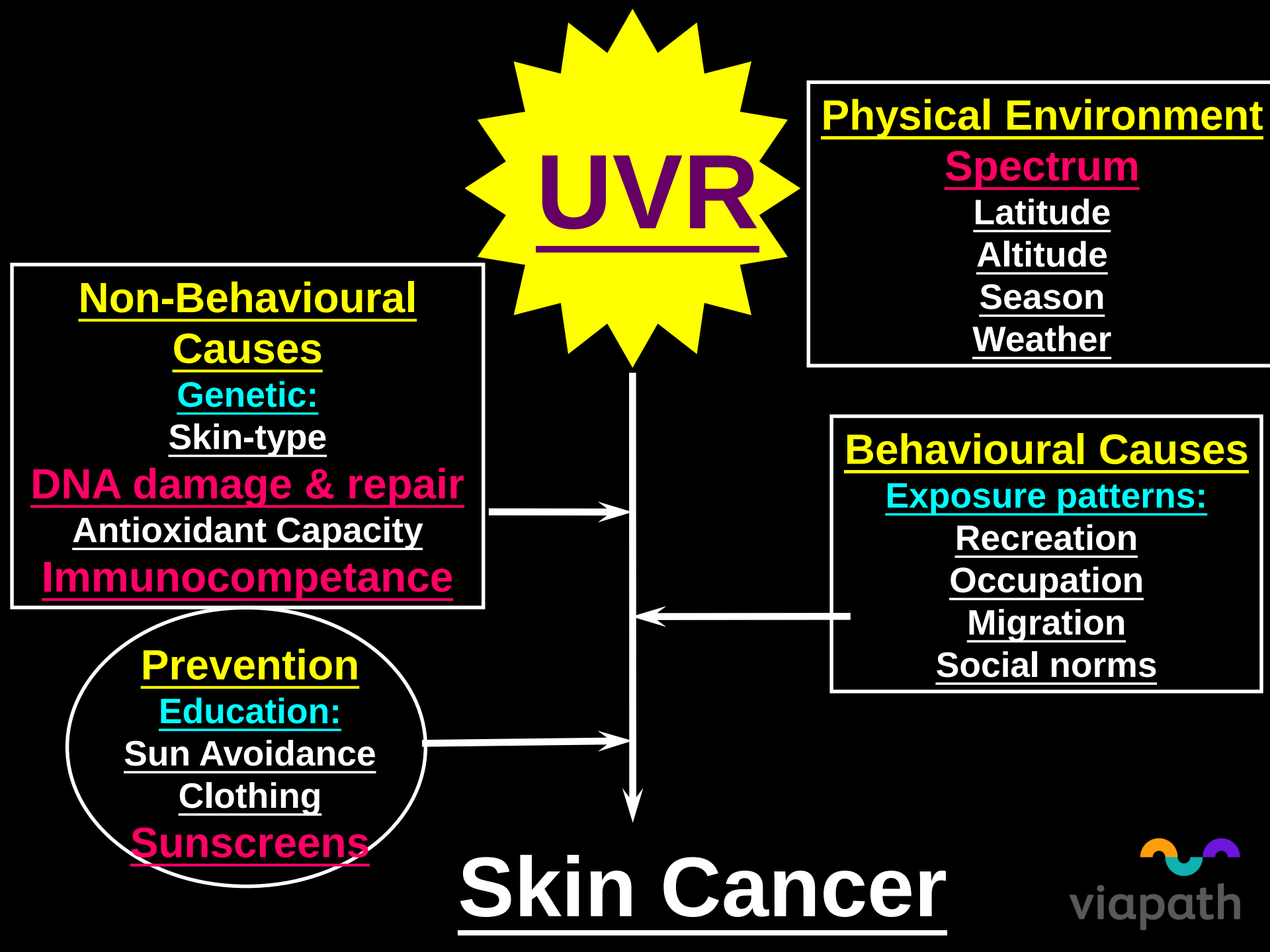
UVR
Physical Environment
Spectrum
Latitude
Altitude
Season
Weather
Non-Behavioural Causes
Genetic:
Skin-type
DNA damage & repair
Antioxidant Capacity
Immunocompetance
Behavioural Causes
Exposure patterns:
Recreation
Occupation
Migration
Social norms
Prevention
Education:
Sun Avoidance
Clothing
Sunscreens
Skin Cancer
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Harmful Effects of Solar UVR

- Acute inflammation (sunburn/erythema)
- DNA and oxidative damage
- Mutation (e.g. p53)
- Immunosuppression
- Skin cancer
- Photoageing
- Photodermatoses

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The harmful effects of ultra violet light on skin

* Impairs immunological balance
* Increases keratinocyte proliferation
* Increase expression of oncoproteins ex P53
* Increases keratinocyte DNA damage ex increased expression of thymine dimers
* Elicites increased solar elastosis
* Dehydrates dermal matrix

UVR DNA Damage

Multiple types DNA damage

- Single stranded breaks
- Purine photoproducts
- DNA- protein cross- links
- (6-4) photoproducts
- PYRIMIDINE DIMERS

UVR is both a tumour initiator creating mutations and tumour promoter producing biochemical effects

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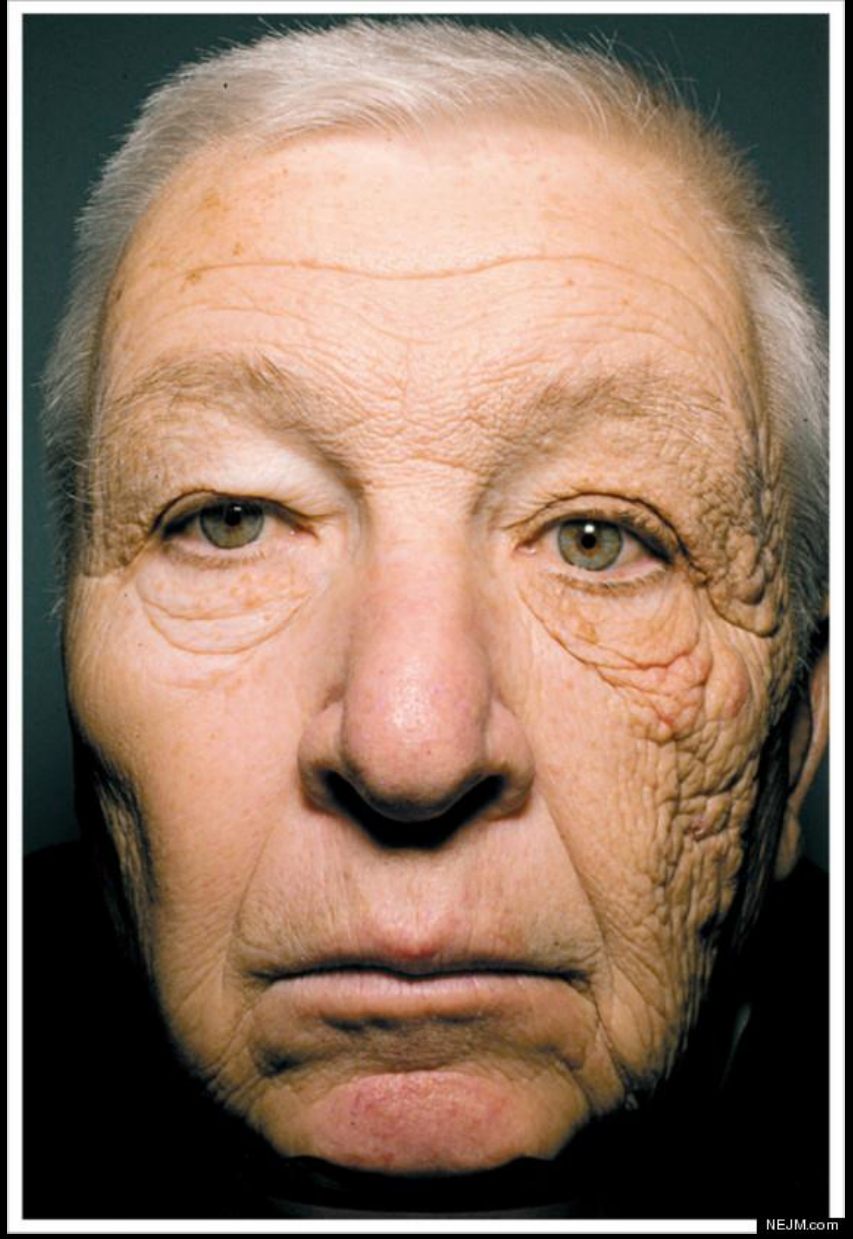

69 yr old truck driver from Canada-UVA induced Unilateral dermatoheliosis

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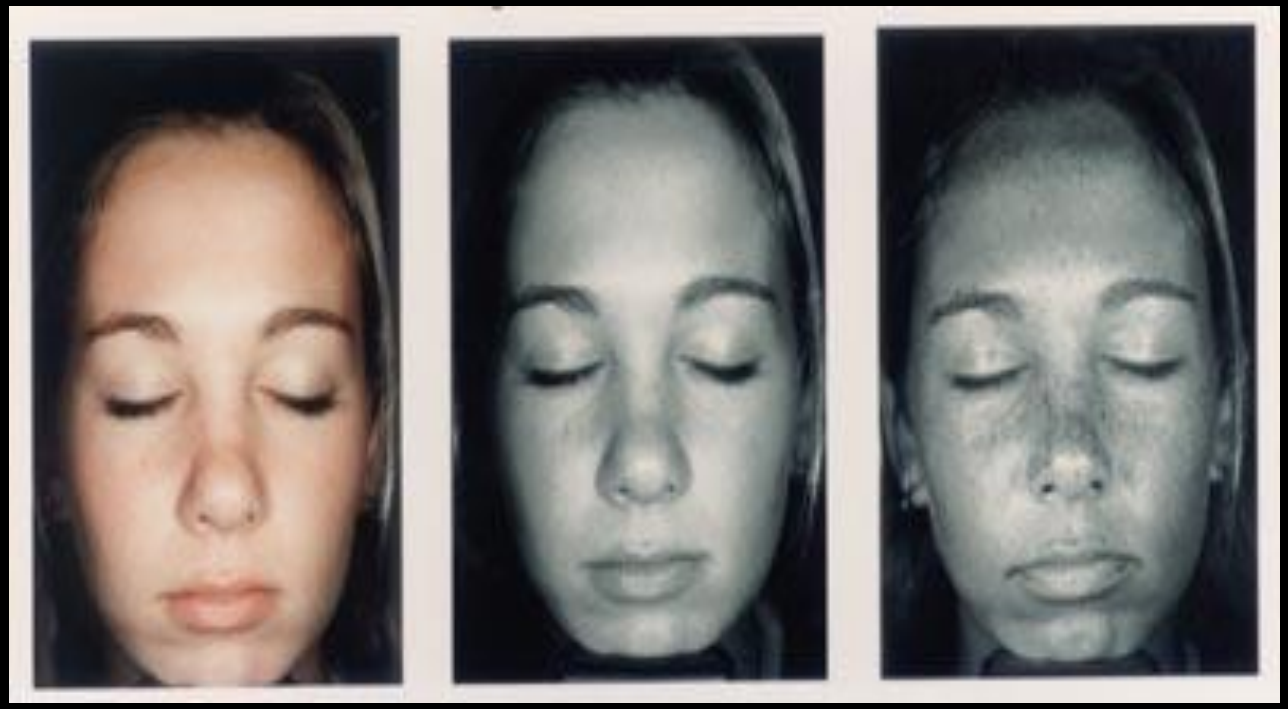
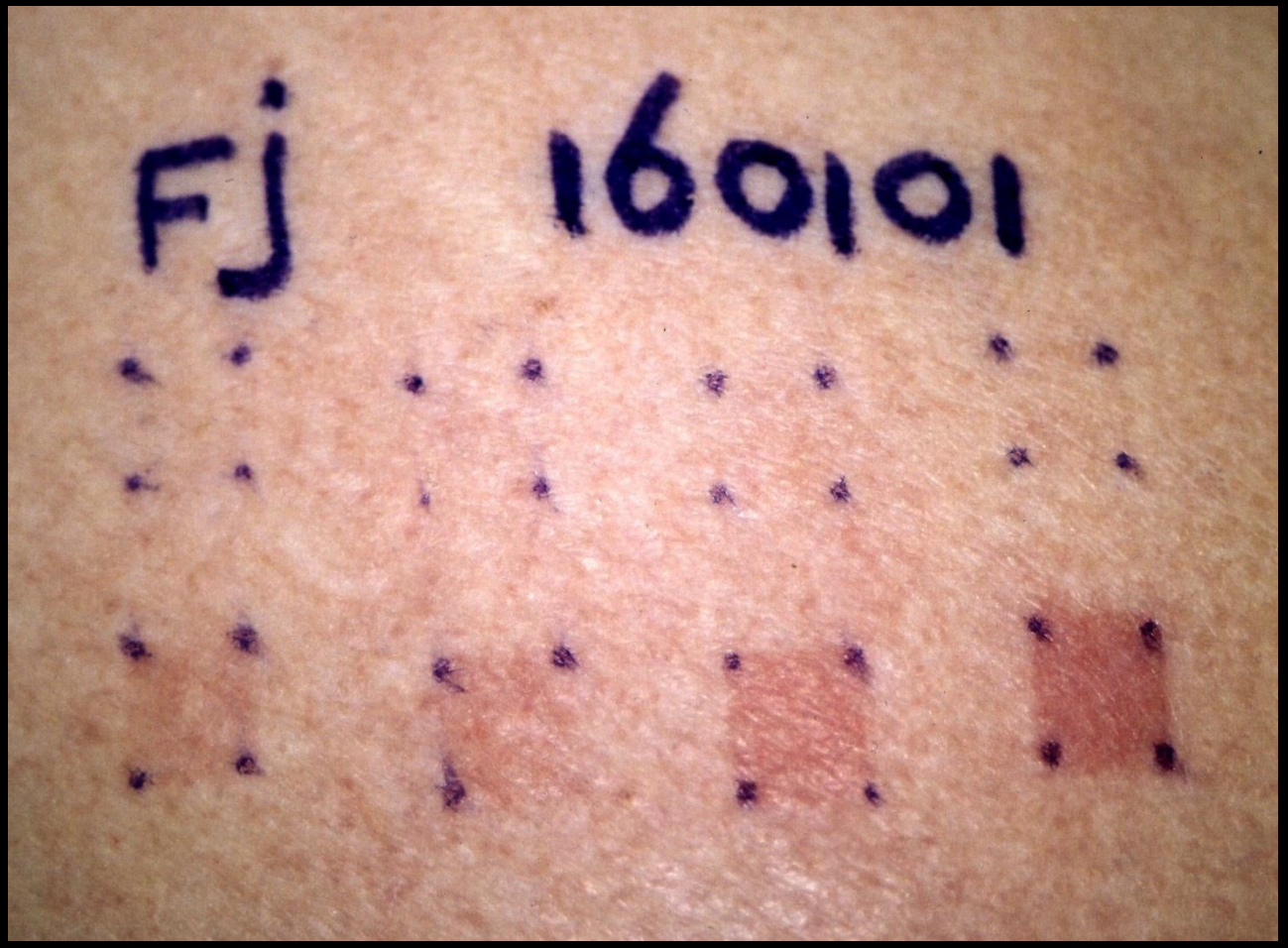
4 Years

17 Years



64 Years

Minimal Erythema Dose (MED) Assessment



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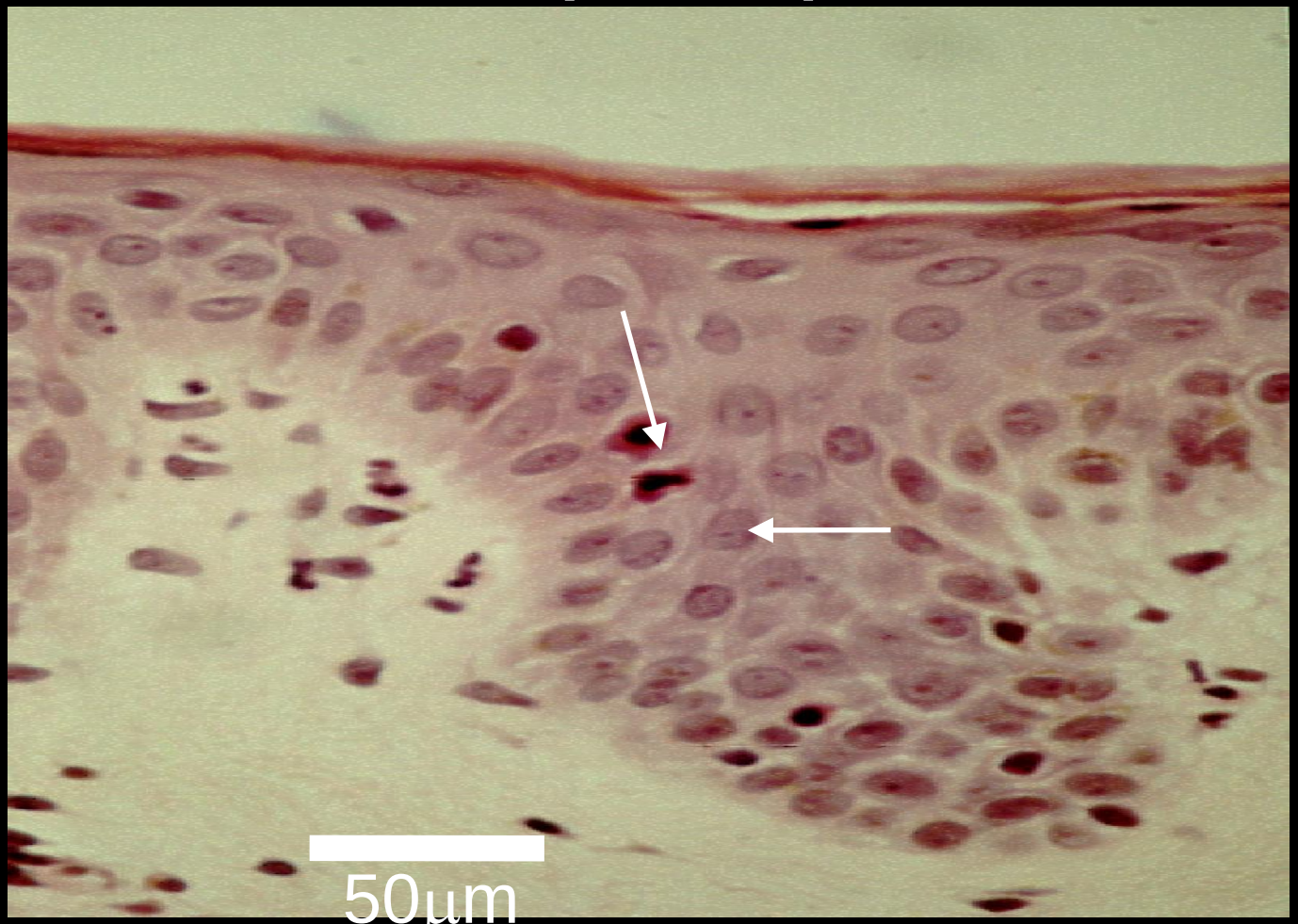
Apoptosis - Sunburn Cell (SBC)



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Immunocytochemistry in the evaluation of photodamaged skin

- P53
- bcl2
- CD1a
- Ki-67 (MIB-1)
- Thymine dimer

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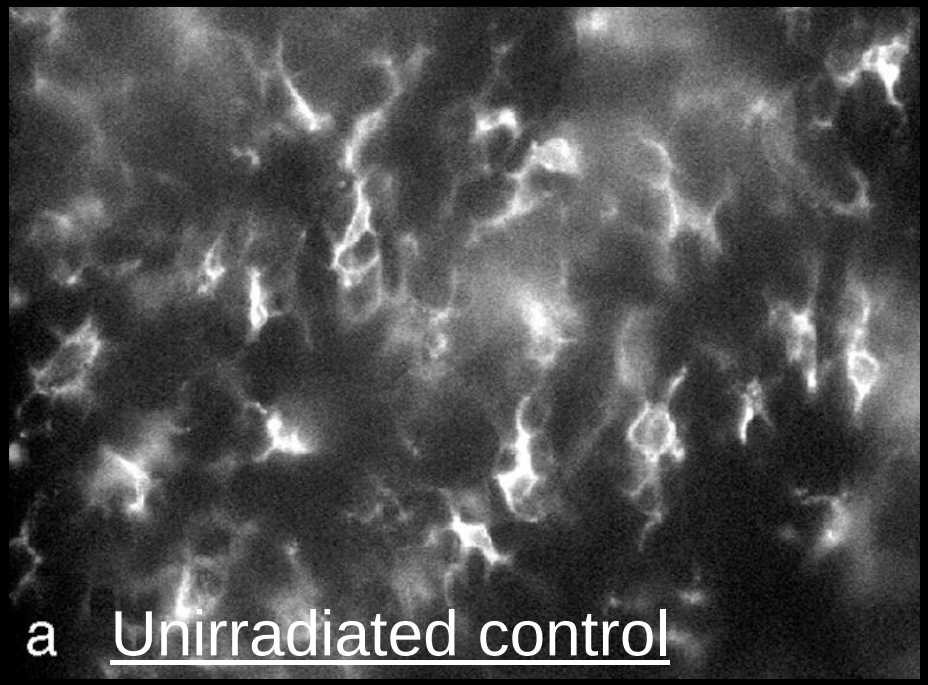
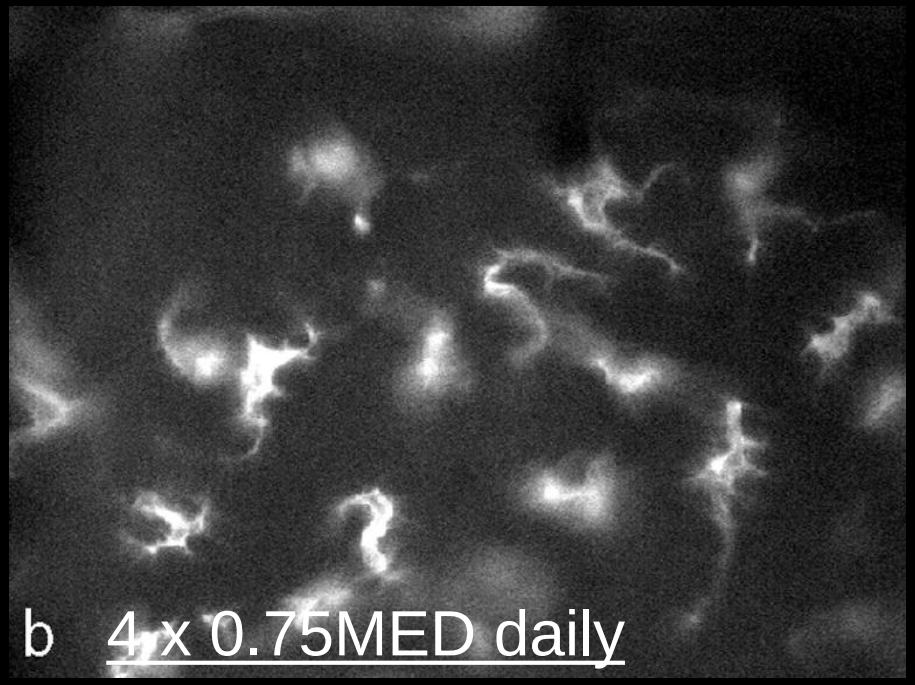
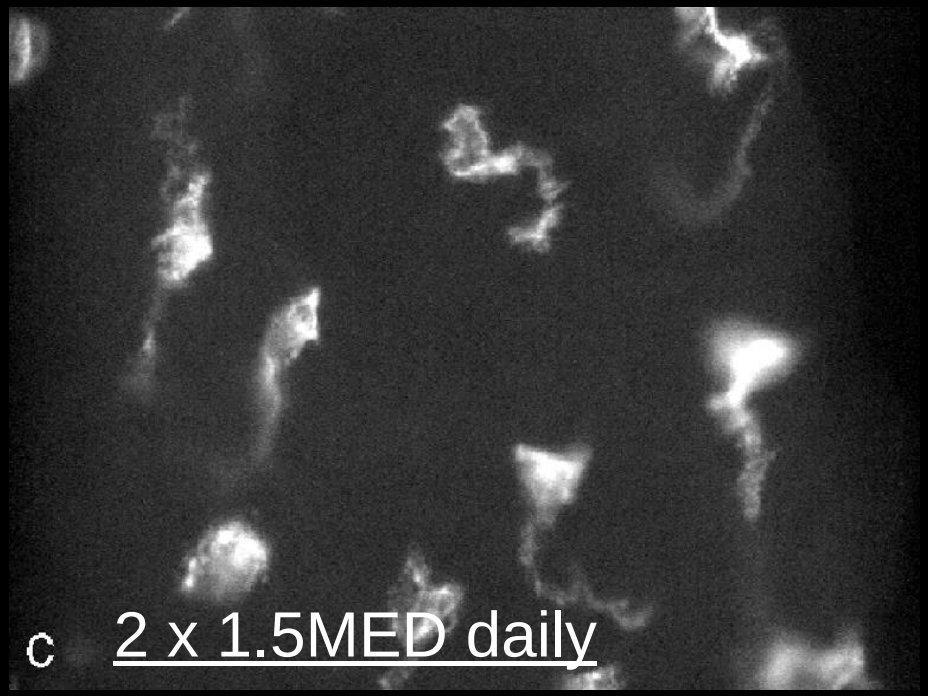
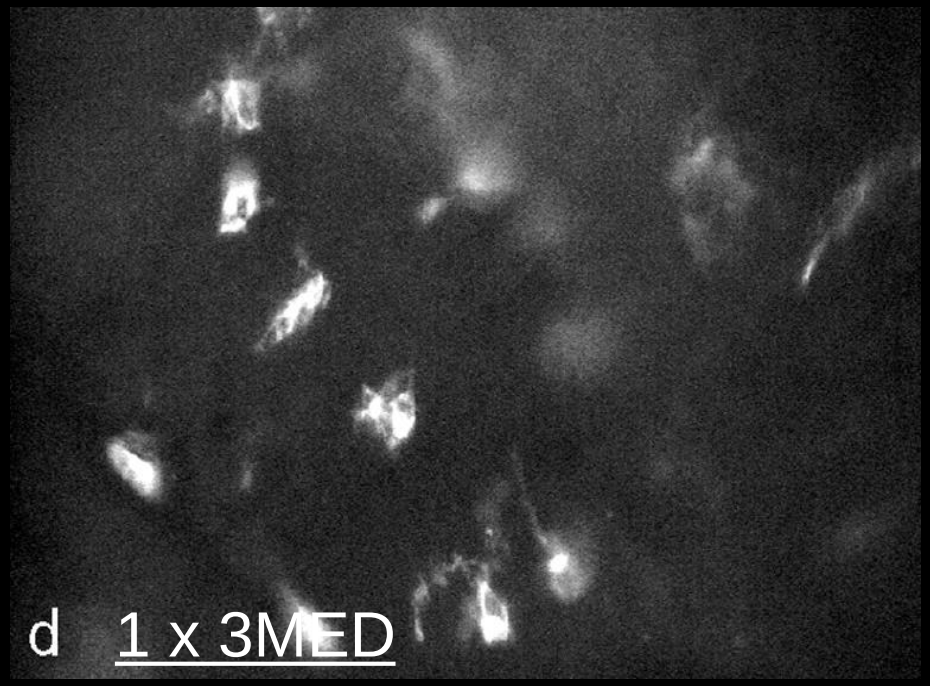
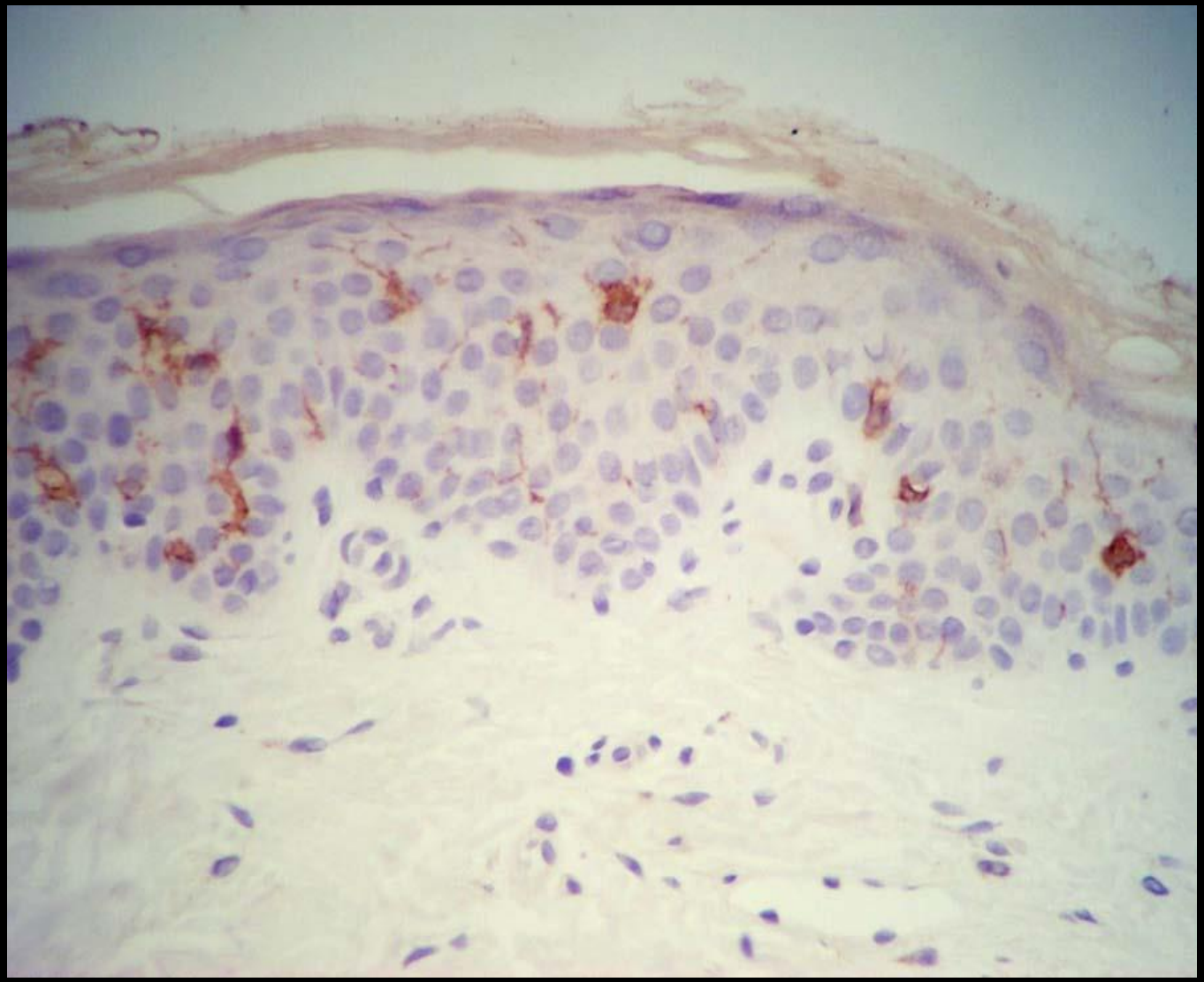

a Unirradiated control


b 4 x 0.75MED daily


c 2 x 1.5MED daily


d 1 x 3MED

CD1a labelling in normal non sun exposed skin



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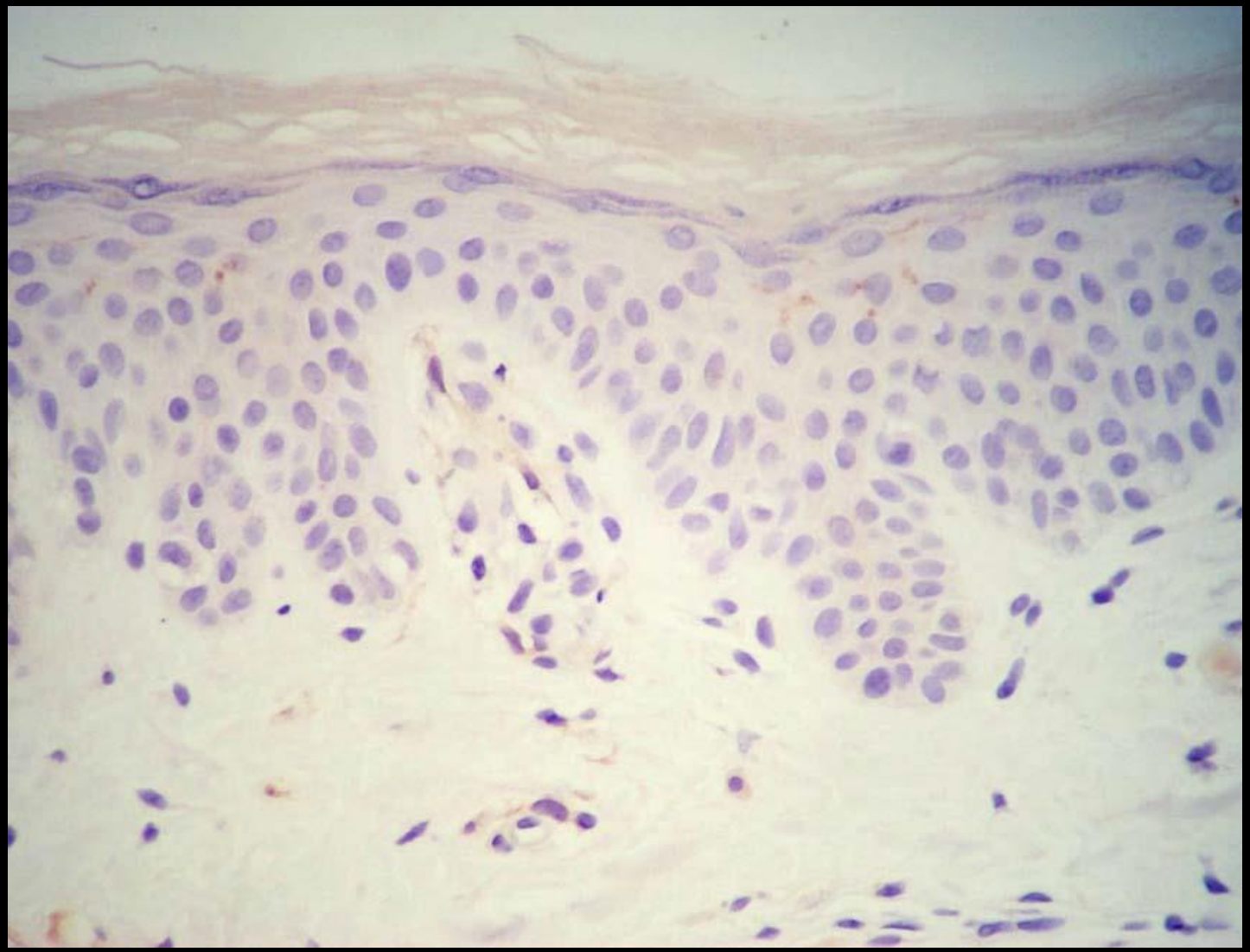
CD1a labelling following 1 x MED



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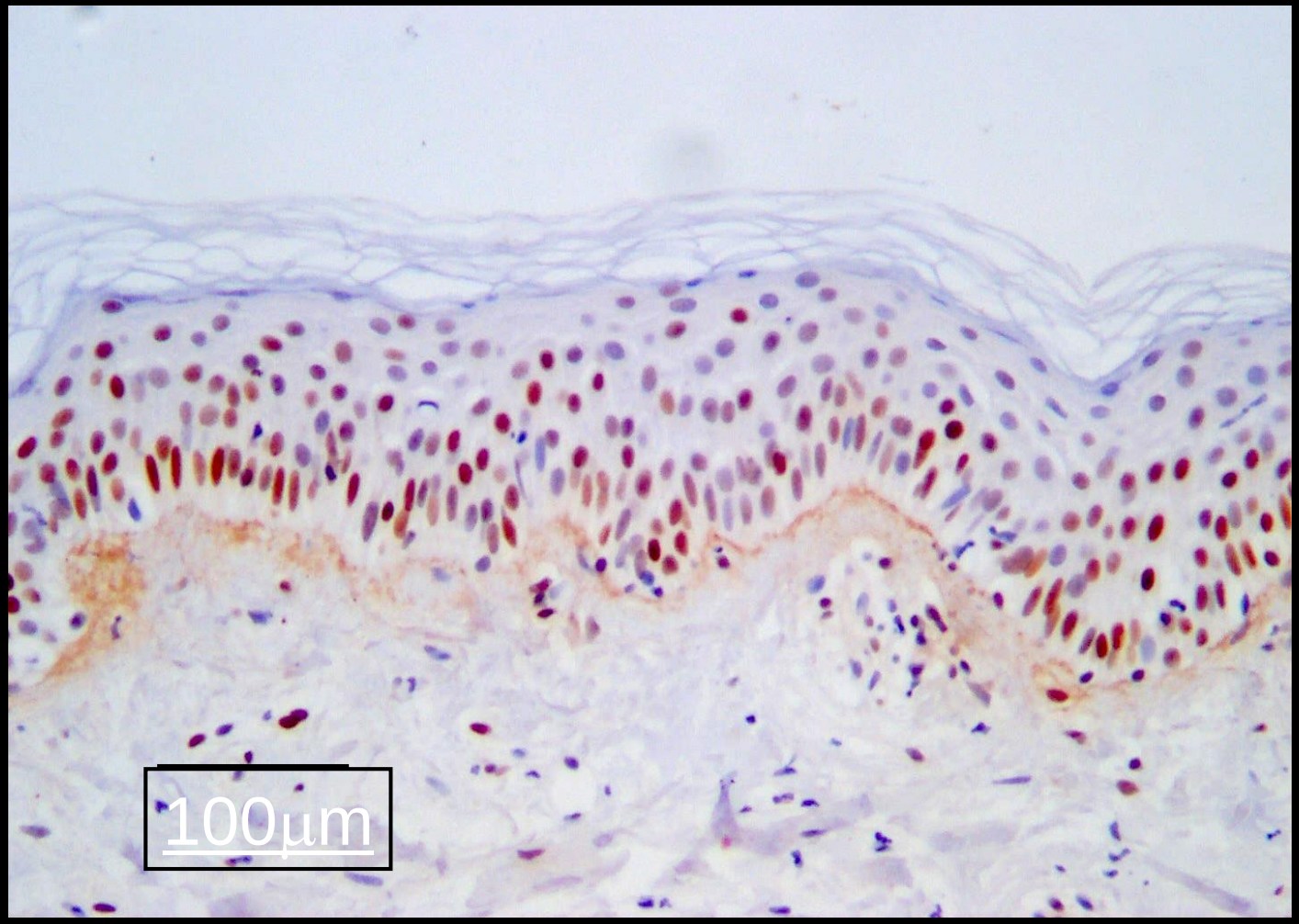
Induction of p53 by SSR



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p53

- Readily induced by UVR in the epidermis
- Transcription factor
- Guardian of the genone
  - cell cycle arrest to allow for DNA repair
  - apoptotic pathway if repair not viable

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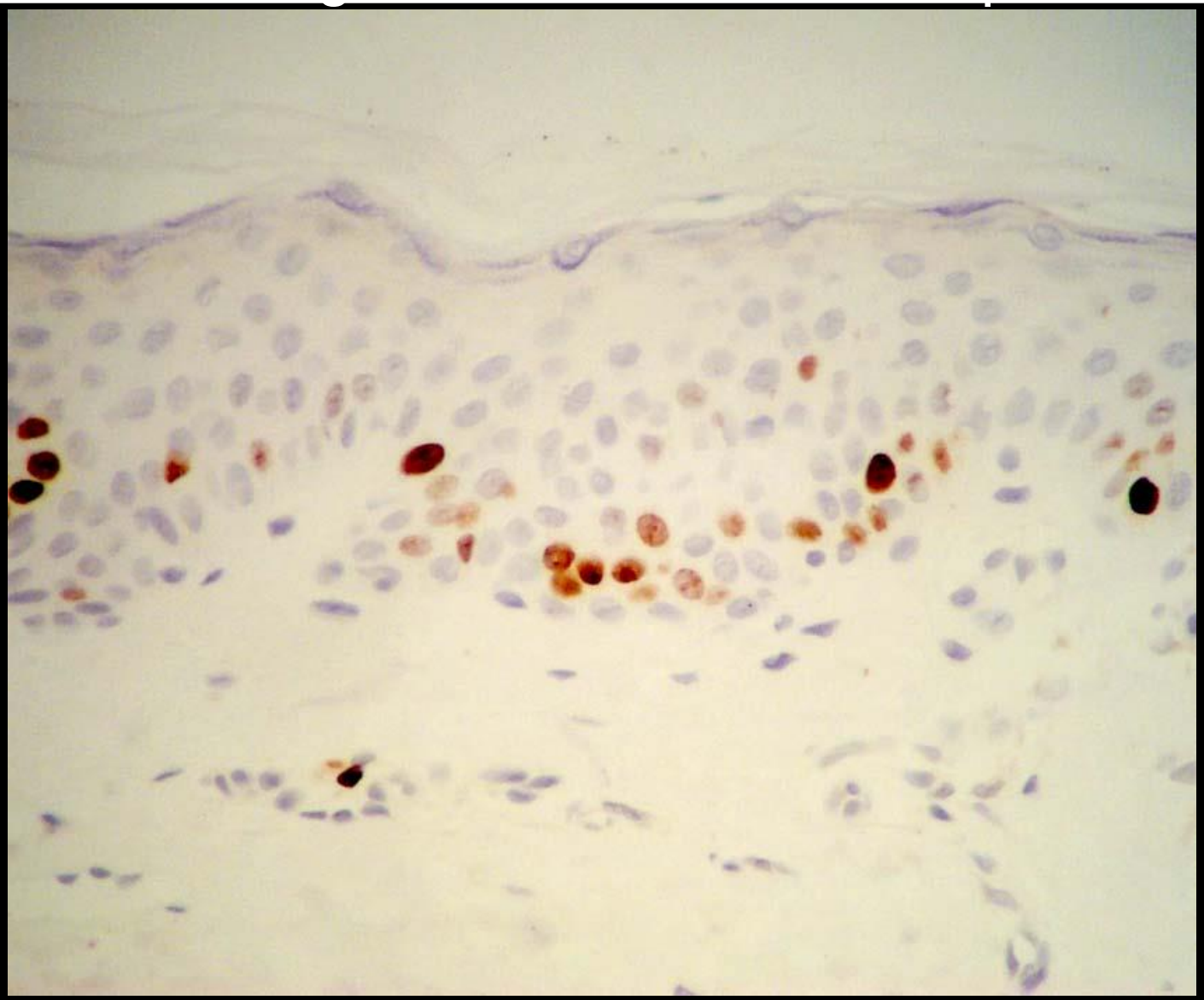
Ki67 labelling in normal non sun exposed skin



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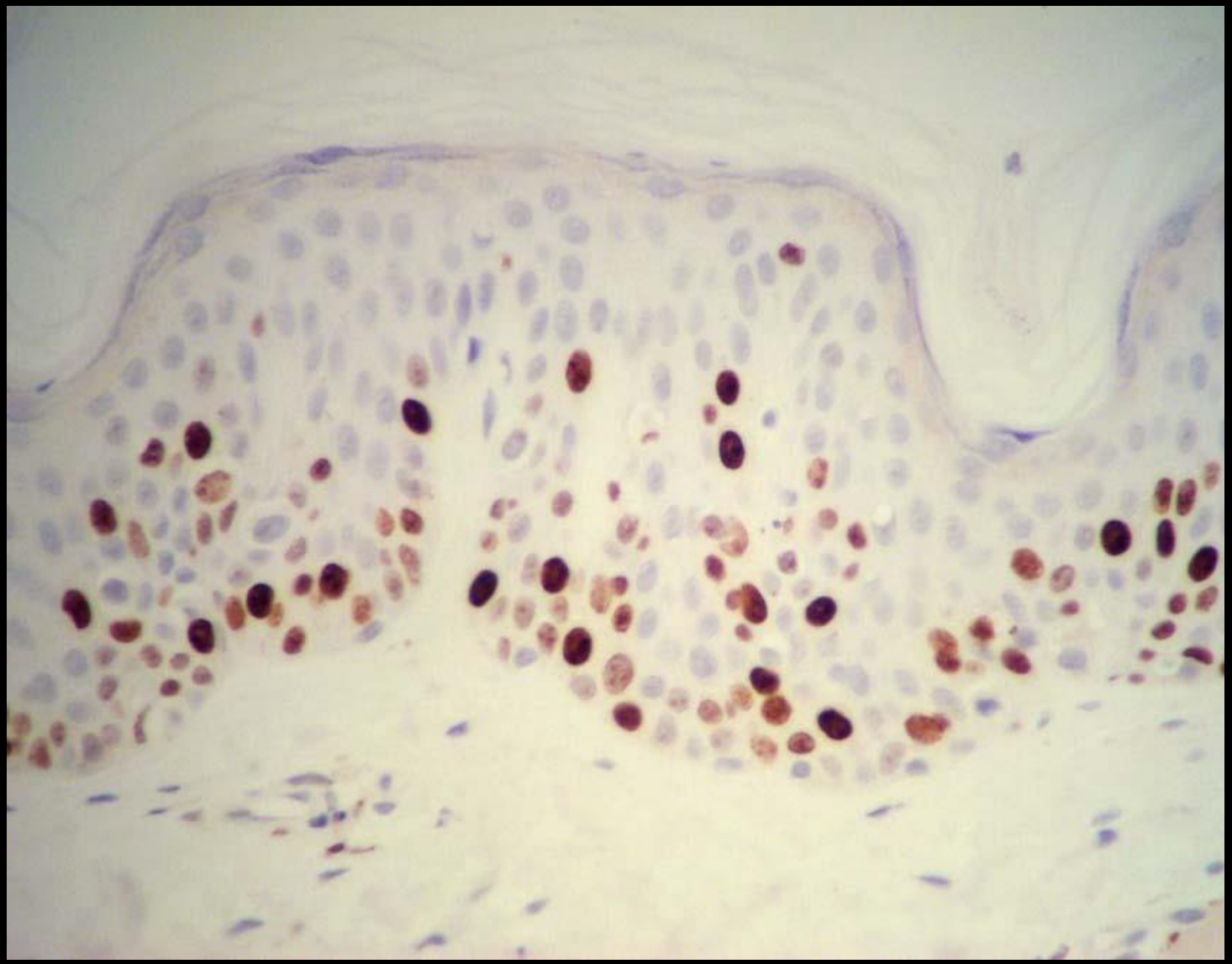
Ki67 labelling following 1xMED exposure



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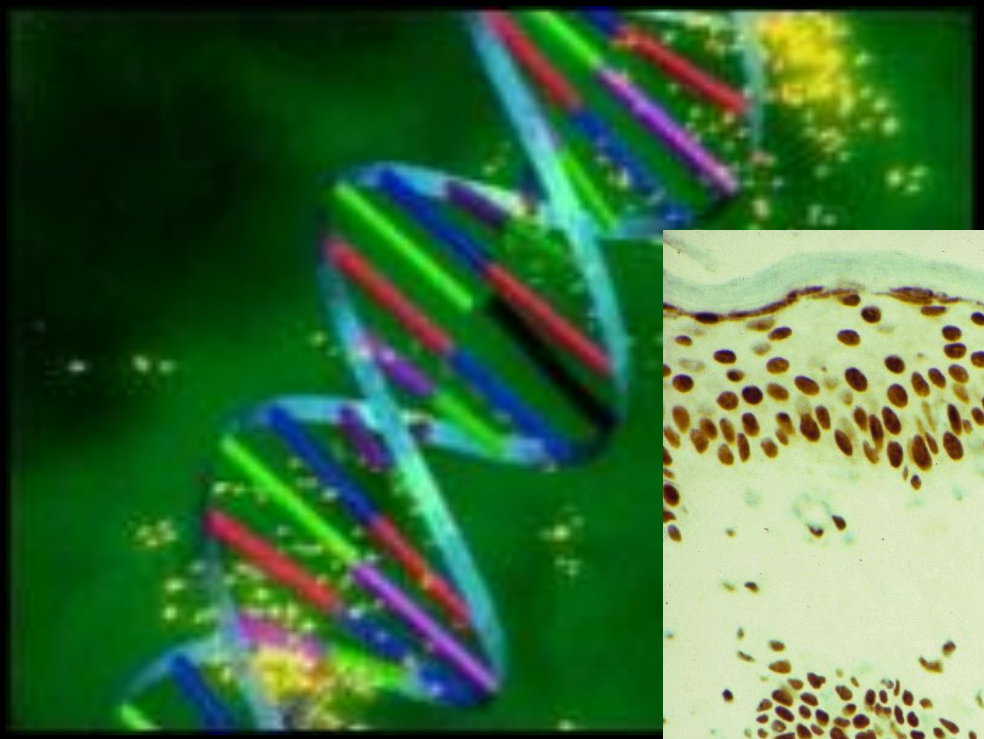
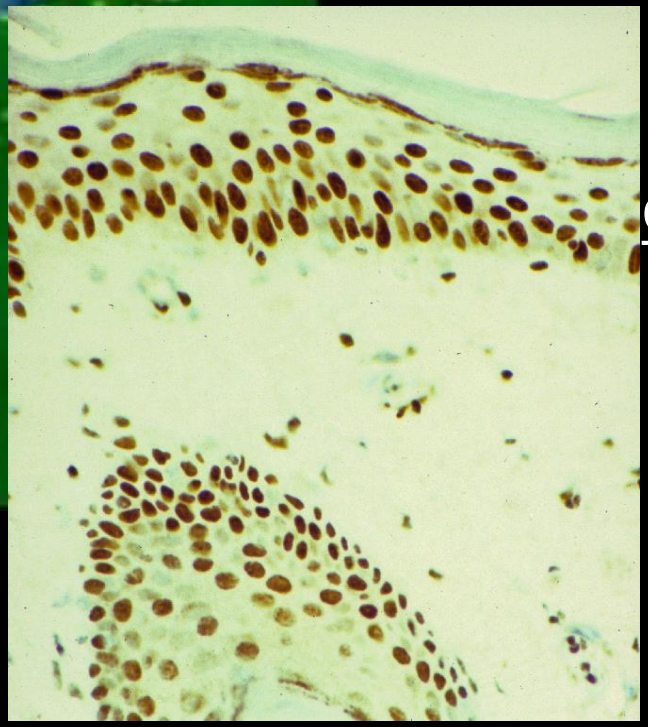
UVB-Induced DNA Damage



→ Mutation of Skin cells



epidermis

dermis

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Skin cancer and sunburn episodes

Long-term ultraviolet flux, other potential risk factors, and skin cancer risk: a cohort study

Wu.S, Han.j, Laden. F, Qureshi. A.A

Cancer Epidermiology Biomarkers and Prevention 2014: 23(6); 1080-9.

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Key Findings

- Cohort of 108.916 US woman (1989-2009) Nurses' health study II
- Incidence of BCC, SCC and MM over time course
- For MM participants with > 5 blistering sunburns between ages of 15-20 years old results in a 80% increase in chances developing MM, 68% increase in chances of developing BCC or SCC.

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Sunbeds and skin cancer

Tanning salons and skin cancer

Dore JF, Chignol MC

Photochem Photobiol Sci. 2012 11(1): 30-7

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Findings

- Across USA and Europe 40-50% teenagers 15-18yrs have used indoor tanning (highest in Scandinavia and Minnesota)
- Epidemiological studies show exposure to sunbeds increases risk of both melanoma and non melanoma skin cancers
- Increased risk with long term usage (accumulative exposure
- Associated risk of sunbed use in melanoma patients younger than 30 may be as high as 43-76%
- Sun bed usage in adolescents should be strongly discouraged

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Cheerleaders USA
'Dying for a tan':-
evidence for photocarcinogenesis

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Woman shares shocking skin cancer selfie to warn about dangers of tanning

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sunbed fact #1
Using a sunbed once a month or more could increase the risk of skin cancer by 50%
THE LOOK
TO DIE FOR?
BIN THE BEDS

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LIKE TANNING?

SKIN CANCER IS HOT

76,250 cases of melanoma will be diagnosed in the US this year.

skincancer.org

Cocktails are not always what they seem

- Citrus fruit, like oranges and grapefruit, contain chemicals called furocoumarins that could increase your risk for melanoma.
- Research, at Warren Alpert Medical School of Brown University. Analysed the fruit-eating habits of 100,000 Americans and revealed that those who consumed the most oranges and grapefruits — and their juices — had a 36 percent higher chance of melanoma compared to folks who never indulged.
- These fruits, and their juices, were not linked to any other types of cancer. Apparently — and other studies have shown this — citrus furocoumarins make the skin more sensitive to the UV radiation contained in sunlight. Of the citrus fruits, grapefruit showed the highest association with melanoma risk.

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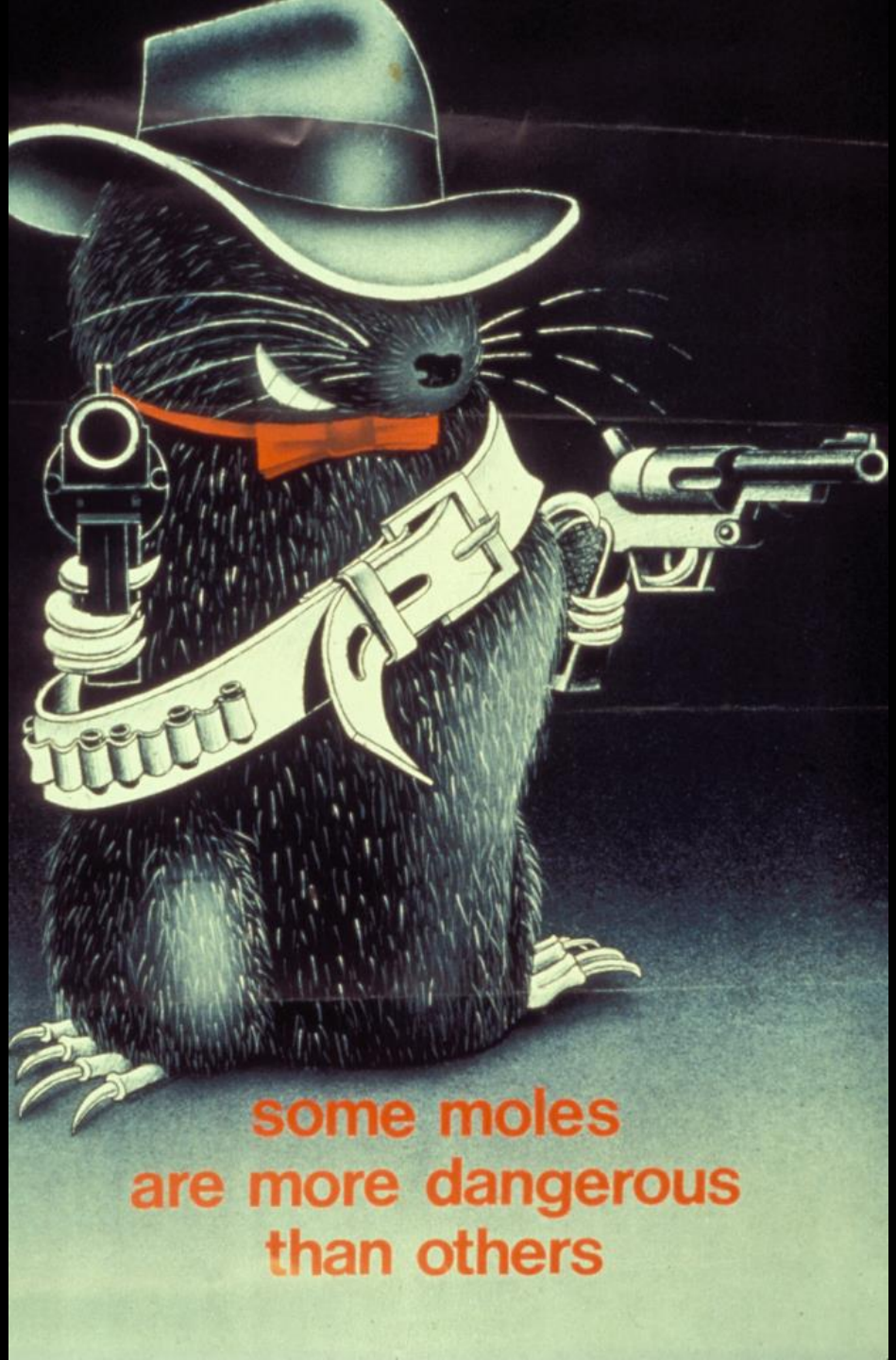
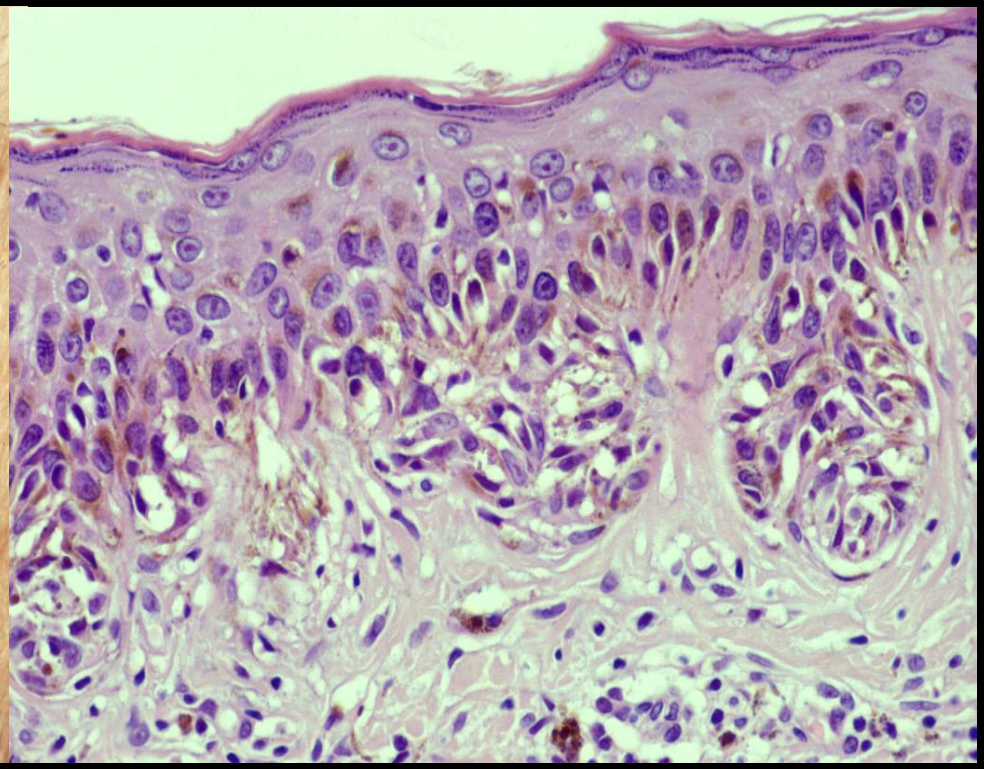


Lentigo maligna



-Commonly affects elderly
-Accounts for 15% of all melanomas
-Histologically characterized by in-situ epidermal component plus spindle cell/ epithelioid cells in the dermis.

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Radial & Vertical Growth Phase Clark et al

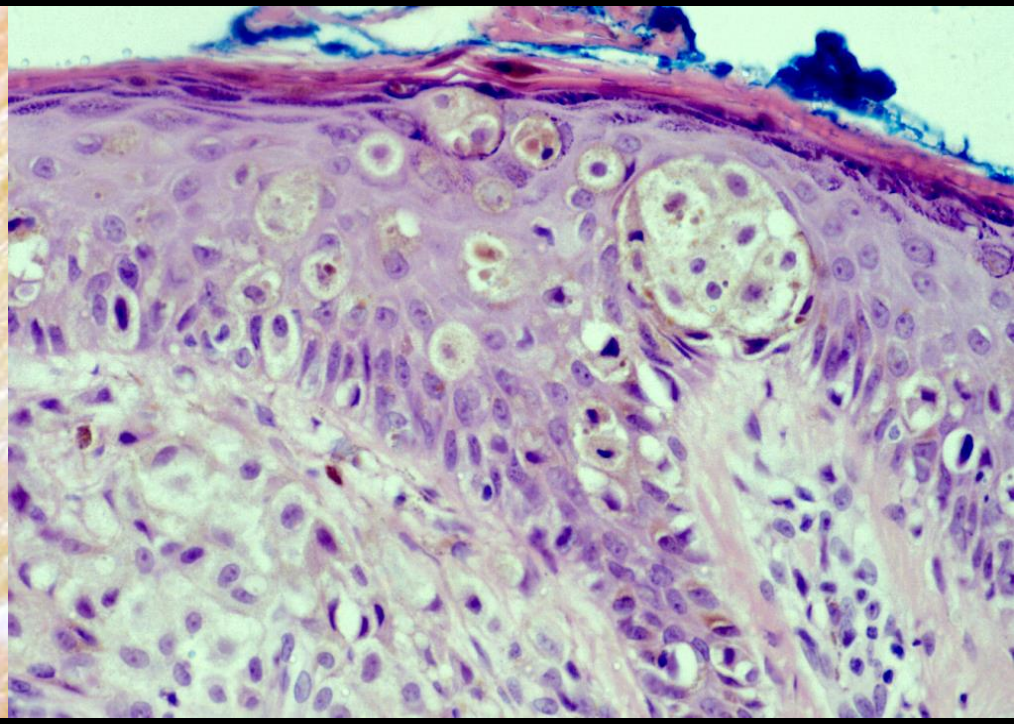
Radial

* Progressive centrifugal spread of a flat pigmented area.
* Epidermal and papillary dermal proliferation of atypical melanocytes
* Precedes development of vertical growth phase.

Vertical

* Large aggregates of tumour cells extending to the reticular dermis.

Superficial Spreading Malignant Melanoma



-Most common form of MM
-Accounts for 50-75% of MM
-Epidermal nests of atypical melanocytes (pagetoid/ “buckshot”)
-Biphasic growth pattern- Radial followed by vertical growth phase

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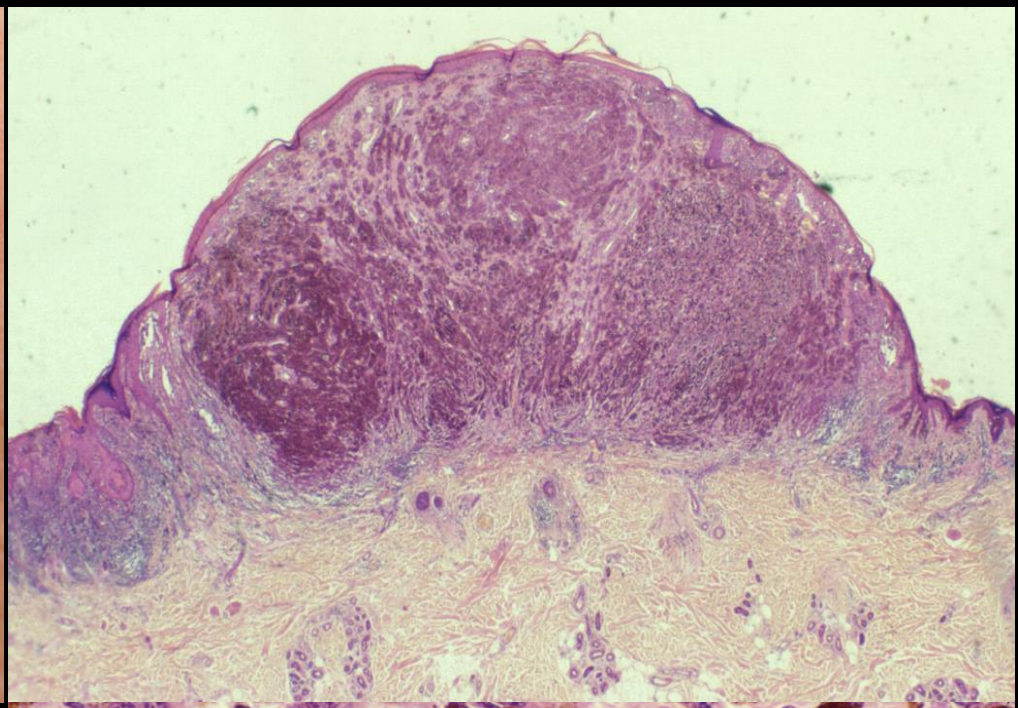
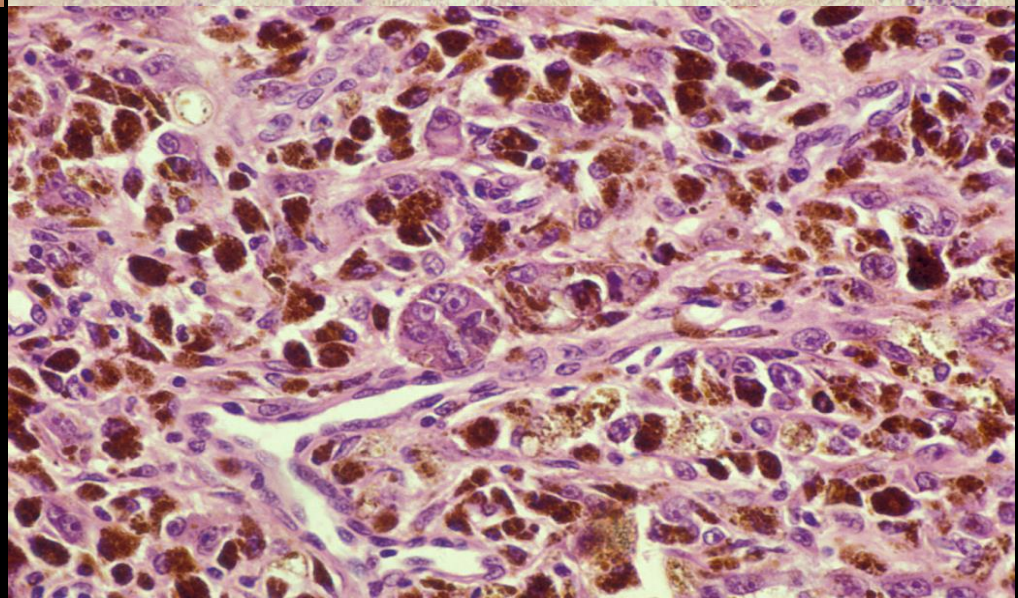
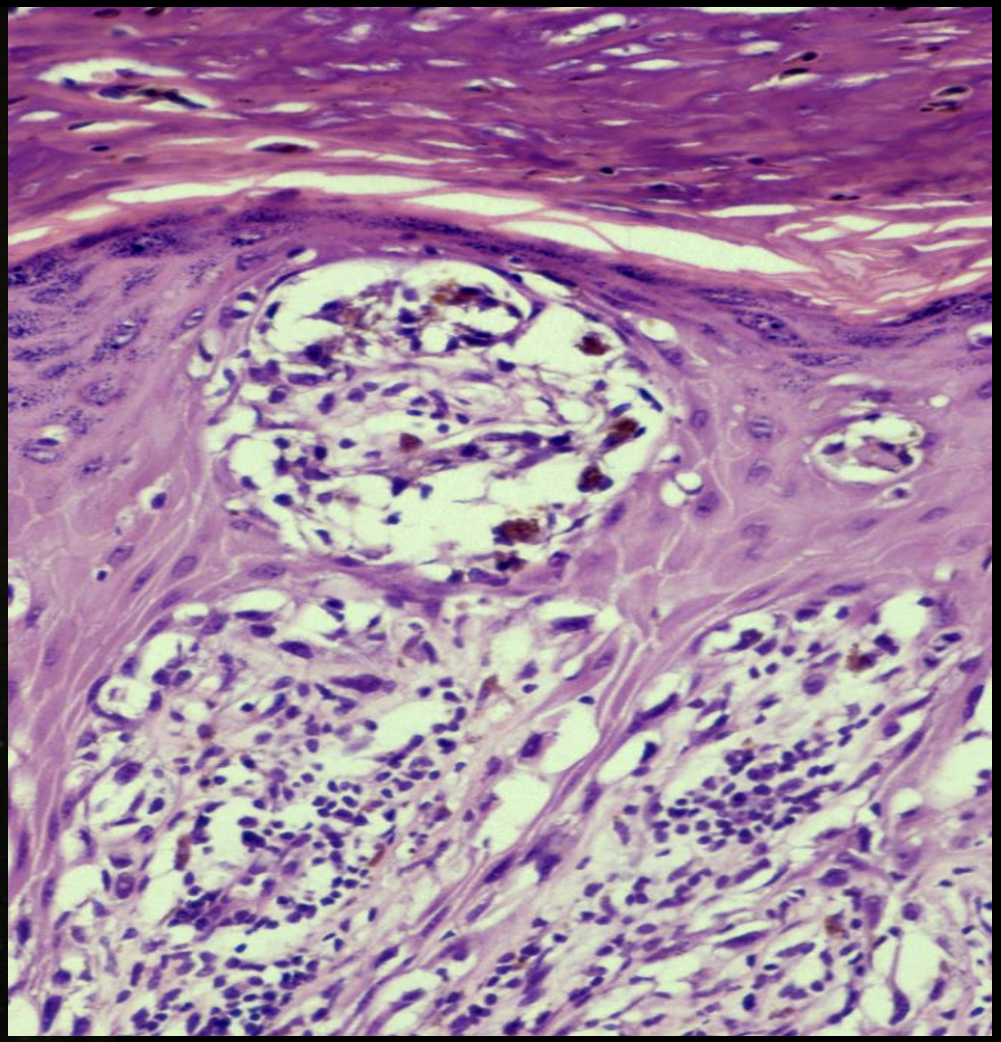
Nodular melanoma





Occurs commonly in young adults (15%)
No adjacent intra-epidermal component of atypical melanocytes
No radial growth phase
Dermal component composed of oval/ round epithelioid cells

Acral lentiginous



Occurs palms/soles, nail beds, mucus membranes
Accounts for 5-10% of MM (dark skin)
Histologically characterised by a lentigenous pattern of atypical melanocytes with invasive dermal component, consisting of spindle or epithelioid cells.

Too Much Sun!

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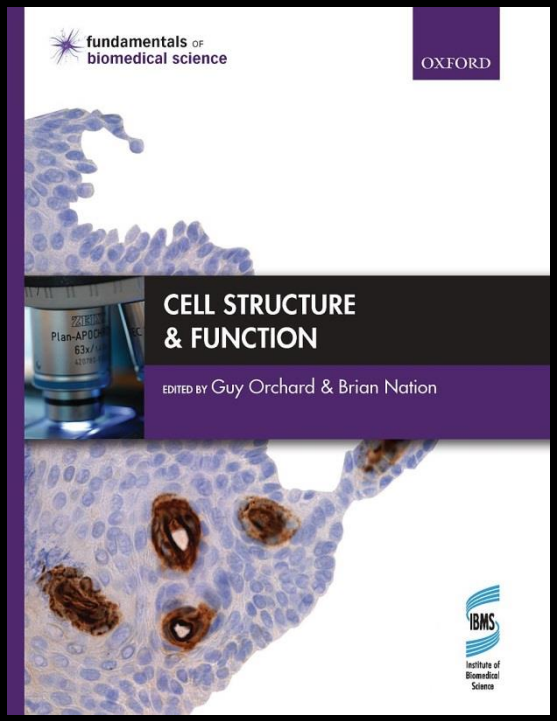
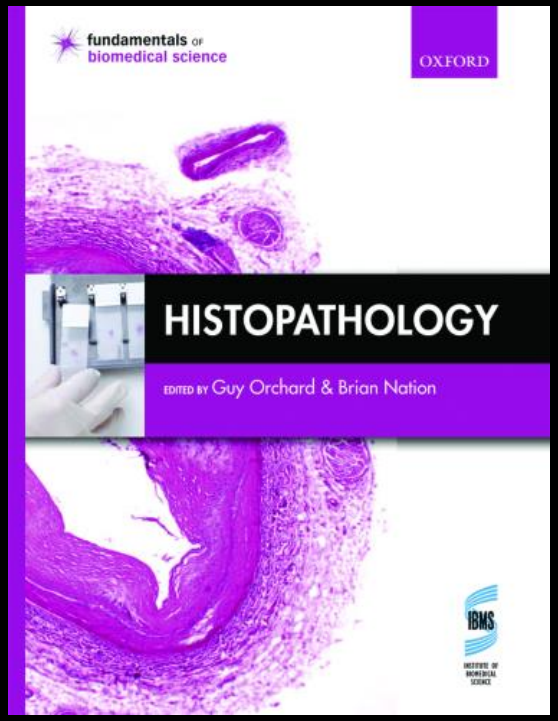
Cancer Research UK

'No tan is a safe tan'- (unless it comes out of a bottle)

Oxford University Press





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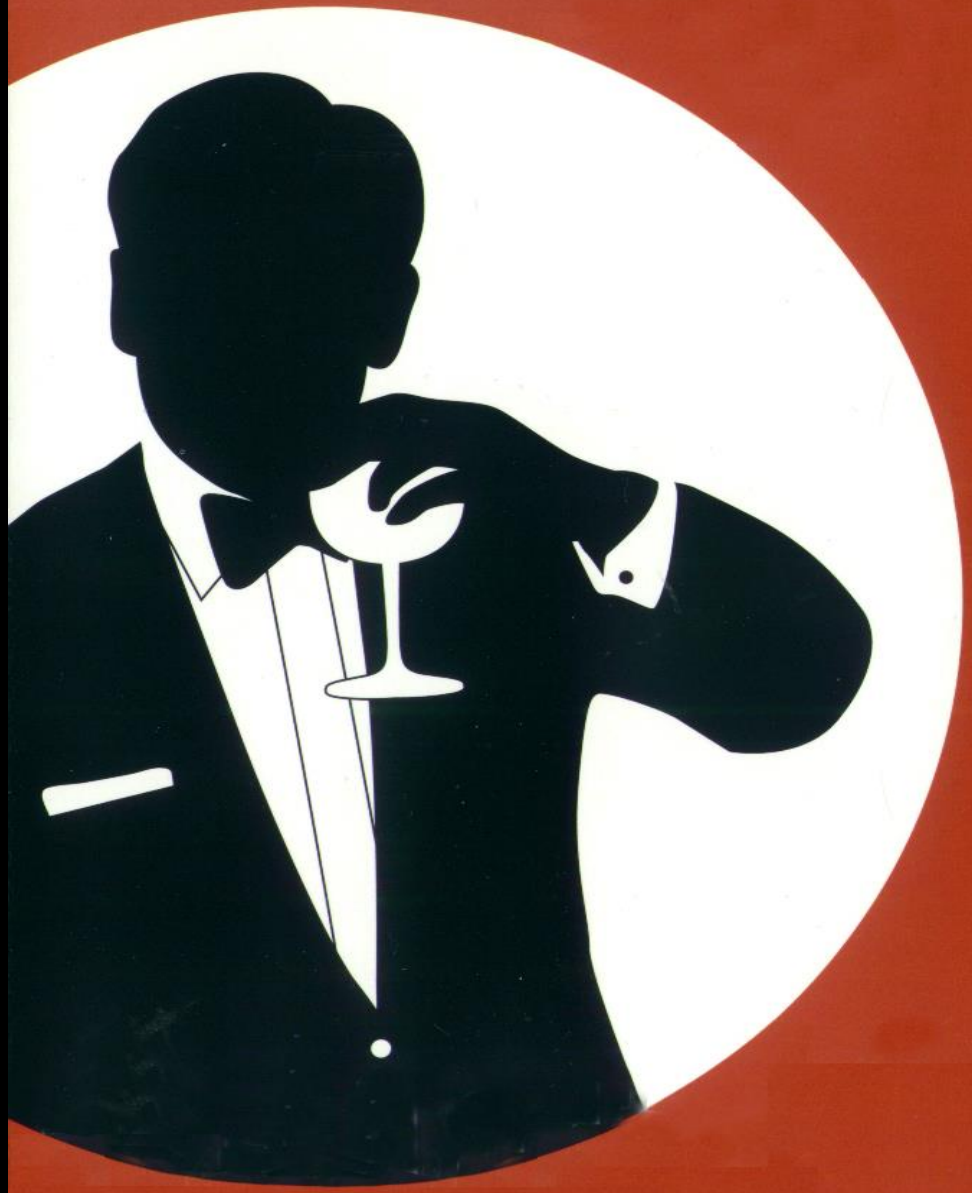

Thank you for your attention!

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