Solar Ultraviolet Radiation Dosimetry and Epidemiology

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Overview

- Background on UV radiation (UVR)
- UVR exposure assessment
- Health risks
- Health benefits
- Summary
Background on UV radiation
Public health importance

- Prevention (identify susceptible populations)
- Consumer products
- Medical radiation guidelines
- Insights into carcinogenesis
Annual economic burden of skin cancer in the United States

- Treatment: $8.1 billion (Guy et al., 2015)
  - $4.8 billion for keratinocyte carcinomas (basal and squamous cell skin cancer)
  - $3.3 billion for melanoma
UV radiation exposure assessment
95% of UVA: 315-400 nm
5% of UVB: 280-315 nm
Individual measures of UVR

- Susceptibility (light skin/hair/eye pigmentation)
- Self-reported time outdoors
- Outdoor/indoor occupation
- Tanning bed use
- Lack of sunscreen use/protective clothing
- Sunburns
Environmental measures of UVR

- Proximity to the Equator
- Ambient UVR
  - Ground-based
  - Satellite-based
Satellite circled Earth once a day near noontime

Validated by ground-based measurements

10 latitude by 10 longitude global grid

Several wavelengths available

Nimbus -7 Satellite (1978-1993)
Satellite-based ambient UVR

- Earth-sun distance
- Time of year
- Latitude
- Column ozone
- Cloud optical thickness

http://toms.gsfc.nasa.gov/n7toms/nim7toms_v8.html
Satellite-based erythemal exposure model

The Erythemal Exposure is defined by the integral

\[
\text{Exp.} = \frac{1}{d_{es}^2} \int_{280\text{nm}}^{400\text{nm}} d\lambda \ S(\lambda)W(\lambda) \int_{t_{sr}}^{t_{ss}} dt \ C(\lambda, \vartheta, \tau_{cl})F(\lambda, \vartheta, \Omega)
\]

where

\(d_{es} = \) Earth-Sun distance, in A.U.

\(S = \) Solar irradiance incident on the top of the atmosphere at 1 A.U.

\(W = \) Biological action spectrum for erythemal damage (see below).

\(t_{sr}, t_{ss} = \) Time of sunrise, time of sunset.

\(C = \) Cloud attenuation factor.

\(\tau_{cl} = \) Cloud optical thickness.

\(\vartheta = \) Solar zenith angle (function of time, \(t\)).

\(F = \) Spectral irradiance at the surface under clear skies, normalized to unit solar spectral irradiance at the top of the atmosphere.

\(\Omega = \) Total column ozone.

UV radiation spectrum

UVA: 320-400 nm
95% reaches Earth’s surface

UVB: 290-320 nm
5% reaches Earth’s surface

UVC: 100-290 nm
0% reaches Earth’s surface
Skin erythema (reddenning) response to various UVR wavelengths

Figure 7. The CIE reference erythema action spectrum (McKinlay and Diffey 1987).
Characteristics of UVB

- Penetrates only surface layer of skin
- Causes sunburn
- Direct DNA damage (C>T)
- Skin adaptation
- Vitamin D production
Characteristics of UVA

- Deeper skin penetration
- Causes skin aging
- Skin does not adapt
- Indirect DNA damage
- Breaks down vitamin D bound to VDR
- Sunscreens, window glass, tanning beds increase relative UVA exposure
UV radiation

The bad news
Risks of UVR exposure to the eye

- Uveal melanoma
  - Risk factors include white race, light eye color, fair skin
  - Evidence for UVR inconsistent

- Cataracts
  - Causes blindness in 16 million people annually
  - WHO estimates 20% of cataracts caused by UVR


Uveal melanoma

Cataract
9399 cases of cataract and 3826 cases of cataract surgery among 44,891 eligible participants.

History of blistering sunburns and ambient UVR (quintile 5 vs. 1) was associated with an increased risk of cataract (HR = 1.08; 95% CI: 1.01–1.16) and cataract surgery (HR = 1.16; 95% CI: 1.05–1.29).

Self-reported time outdoors or previous keratinocyte carcinoma diagnosis was not associated with either both cataract or cataract surgery.
Skin cancer in the United States is increasing

New cases, deaths of melanoma

- **Melanoma**
  - 80,000 annual cases\(^a\)
  - 10,000 deaths\(^a\)

- **Basal cell carcinoma**
  - 4 million annual cases\(^b\)
  - 3,000 deaths\(^c\)

- **Squamous cell carcinoma**
  - 1 million annual cases\(^b\)
  - 5,000 deaths\(^d\)

\(^a\)Cancer Facts and Figures 2017, ACS; \(^b\)Rogers et al., 2015; \(^c\)Mohan and Chang, 2014; \(^d\)Karia et al., 2013.
Skin cancer prevention focused on reducing UVR exposure

- Health promotion and educational interventions to improve personal sun protection through use of clothing, hats, sunscreen, staying in shade, and avoiding exposure

- Legislation involving artificial tanning increased from 2 (2003) to 11 (2011) (Pawlak et al., 2012)
  - Brazil banned tanning salons in 2009
  - Australia banned tanning salons in 2015
  - United States: patchwork of legislation across counties and states focused on minors (<18 years old)
FDA Proposes Sunscreen Regulation Changes

February 2019

- Sunscreen active ingredients zinc oxide and titanium dioxide recommended, but not aminobenzoic acid (PABA) and trolamine salicylate not approved
- Dosage forms: sprays, oils, lotions, creams, gels, butters, pastes, ointments, and sticks recommended, but more information needed on powders
- New proposed sun protection factor (SPF) and broad spectrum requirements
- New labeling requirements

https://www.fda.gov/media/124654/download
Objective: To determine whether the active ingredients (avobenzone, oxybenzone, octocrylene, and ecamsule) of 4 commercially available sunscreens are absorbed into systemic circulation.

Findings: application of 4 commercially available sunscreens under maximal use conditions resulted in plasma concentrations that exceeded the threshold established by the FDA.
Where is the research headed?
Modifiers of UVR-related skin cancer risks

Well-known
- Skin/hair/eye pigmentation
- Family history of melanoma

New research directions
- Immune deficiency (e.g., HIV, transplant recipients)
- Infectious agents (e.g., HPV infection)
- Photosensitizing agents (e.g., short and long term medications)
Importance of research on photosensitizing agents

- Public health initiatives
  - Add warning labels on medications
  - Recommend skin cancer screening for some populations

- Clinical practice
  - Stress sun protection at the time of prescribing a medication
  - Consider alternative medications during summer months
Photosensitizing agents

Examples
- Sunscreens
- Cosmetics
- Antibiotics
- Retinoids
- NSAIDs
- Diuretics
- Estrogens

Photosensitizing agents + Sunlight → Erythema → Skin cancer
Photosensitizing agents

Examples
- Sunscreens
- Cosmetics
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Photosensitizing agents + sunlight → Erythema

Basal cell carcinoma

Skin cancer
Photosensitizing agents and basal cell carcinoma in U.S. radiologic technologists

Rationale

- USRT is nationwide, prospective cohort of indoor workers
- One of few cohorts to ascertain basal cell carcinoma

Findings

- *BCC not associated* with NSAIDs (Cahoon et al., *IJC*, 2012)
- *BCC risk* ↑ with diuretic use (McDonald, .., Cahoon, *CEBP*, 2014)
- *BCC risk* ↑ with late age at menopause, use of MHT (Cahoon et al., *JCO*, 2015)
Reproductive factors, hormone use, and melanoma, NIH-AARP

Rationale

- Melanoma diagnosed during pregnancy and estrogen receptors found in melanoma lesions
- Prior epidemiological studies inconsistent (mainly case-control), conducted in locations with little variation or low levels of UVR
- AARP is large (N women=167,503; n melanoma cases=1,061), prospective, population-based study with substantial variation in ambient UV and comprehensive measures of hormone exposure
Estrogen levels from puberty to menopause

- **Puberty**
- **Menstruation**
- **Pregnancy**
- **Menopause**

Relative estrogen levels vs Age

https://www.mayomedicallaboratories.com/test-catalog/Clinical+and+Interpretive/81816
Early age at menarche increases melanoma risk, NIH-AARP

HR (≤10 vs >15 yrs)=1.25
P_{trend}=0.04

Importance of early-life exposures

Donley, BJC, 2019
Ambient UVR, age at menarche, and melanoma risk, NIH-AARP

Age at menarche (p-interaction=0.02, df=2)

- ≤10 years (p-trend=0.02)
- 11-14 years (p-trend=0.009)
- ≥15 years (p-trend=0.12)

UVR dose-response highest among women who experienced early age at menarche

Donley, BJC, 2019
Drug-induced photocarcinogenesis: challenges

- Confounding by indication
- Surveillance bias
- Cancer registries often do not ascertain or confirm non-melanoma skin cancers
- Measuring UV radiation exposure
- Clarifying biological mechanisms (examining photosensitivity reactions)
UV Radiation

The good news
Benefits of UV Radiation

- Vitamin D production promotes healthy bones and muscles
- UVR treatment
- Reduced risk of autoimmune conditions
- Reduced risk of some cancers
Beneficial effects of UVR treatment

Rickets
- softening of bones in children

Lupus vulgaris
- tuberculosis of the skin
- UVB lamp that was so successful in curing the disease it won Neils Finzen the Nobel prize in 1903

Vitiligo
- autoimmune disease causing patchy loss of skin pigmentation due to destruction of melanocytes

Psoriasis
- autoimmune disease of skin causing sores and scaling of the skin
- 2-3% of the population
UV radiation and reduced risk of some autoimmune diseases

- Type 1 diabetes
- Rheumatoid arthritis
- Multiple sclerosis
UVR during first trimester and risk of multiple sclerosis

Staples. BMJ, 2010
UVR and reduced cancer risks

Prospective study of ultraviolet radiation exposure and risk of cancer in the United States

Shih-Wen Lin1,2, David C. Wheeler3, Yikyung Park2, Elizabeth K. Cahoon2, Albert R. Hollenbeck4, D. Michal Freedman2 and Christian C. Abnet2

Key findings: Reduced risks for colon, female breast, NHL, HL, prostate, lung, kidney, and bladder cancer
Reduced risks of B-cell lymphomas including the most common subtypes of NHL, CLL/SLL, follicular lymphoma, and diffuse large B-cell lymphoma with ↑ UVR

Reduced risk of all HL subtypes with increasing ambient UVR
Summary

- Risks include skin cancers, eye disease, and systemic immune suppression
- Benefits include treatment, vitamin D production, potentially reduced risks of some autoimmune diseases and cancers
- Future research aimed at refining our understanding and quantifying risks and benefits to guide public health policies
Quiz Question 1

What is a notable biological response to exposure to UVA?

A. Sunburn
B. Aging
C. Vitamin D production
D. None of the above
Quiz Question 1

What is a notable biological response to exposure to UVA?

A. Sunburn
B. Aging
C. Vitamin D production
D. None of the above
Quiz Question 2

What is a notable biological response to exposure to UVB?

A. Sunburn
B. Vitamin D production
C. Direct DNA damage
D. All of the above
Quiz Question 2

What is a notable biological response to exposure to UVB?

A. Sunburn
B. Vitamin D production
C. Direct DNA damage
D. All of the above
U.S. Department of Health & Human Services
National Institutes of Health | National Cancer Institute
dceg.cancer.gov/

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