Solar Ultraviolet Radiation Dosimetry and Epidemiology

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DCEG Radiation Epidemiology and Dosimetry Course 2019





www.dceg.cancer.gov/RadEpiCourse

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



U.S. Surgeon General's Call to Action to Prevent Skin Cancer (2014)

UV radiation exposure assessment

ELECTROMAGNETIC SPECTRUM



Solar radiation spectrum



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





Nimbus-7 TOMS Version 8 Local Noon Erythemal UV Irradiance on May 06, 1990





) 300 360 420> rradiance (mW/m²) Flight Center

Total Ozone Mapping Spectrometer



Ozone Processing Team - NASA/GSFC Code 613.3



Nimbus -7 Satellite (1978-1993)

- Satellite circled Earth once a day near noontime
- Validated by ground-based measurements
- 10 latitude by 10 longitude global grid
- Several wavelengths available

Satellite-based ambient UVR

Nimbus—7 TOMS Version 8 Local Noon Erythemal UV Irradiance on May 06, 1990



NASA



http://toms.gsfc.nasa.gov/n7toms/nim7toms_v8.html

- Earth-sun distance
- Time of year
- Latitude

Goddard Space Flight Center

- Column ozone
- Cloud optical thickness



Satellite-based erythemal exposure model

The Erythemal Exposure is defined by the integral

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

where

 $d_{\rm es} = {\rm Earth}$ -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).

 $t_{\rm sr}, t_{\rm ss} =$ Time of sunrise, time of sunset.

C =Cloud attenuation factor.

 $\tau_{\rm cl} = {\rm Cloud}$ 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.

 $\Omega = \text{Total column ozone.}$

http://macuv.gsfc.nasa.gov/doc/erynotes.pdf

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 (reddening) 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



Muen and Damato. Eye, 2007.

Cataract



Ultraviolet radiation and incidence of cataracts in a nationwide US cohort

Arash Delavar^a, D. Michal Freedman^a, Raquel Velazquez-Kronen^a, Mark P. Little^a, Cari M. Kitahara^a, Bruce H. Alexander^b, Martha S. Linet^a, and Elizabeth K. Cahoon ^{D^a}

- 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.

Delavar et al., 2018



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

^aCancer Facts and Figures 2017, ACS; ^bRogers *et al.*, 2015; ^cMohan and Chang, 2014; ^dKaria 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)



- Sunscreen active ingredients zinc oxide and titanium dioxide recomended, 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

Effect of Sunscreen Application Under Maximal Use Conditions on Plasma Concentration of Sunscreen Active Ingredients A Randomized Clinical Trial

Murali K. Matta, PhD; Robbert Zusterzeel, MD, PhD, MPH; Nageswara R. Pilli, PhD; Vikram Patel, PhD; Donna A. Volpe, PhD; Jeffry Florian, PhD; Luke Oh, PhD; Edward Bashaw, PharmD; Issam Zineh, PharmD, MPH; Carlos Sanabria, MD; Sarah Kemp, RN; Anthony Godfrey, PharmD; Steven Adah, PhD; Sergio Coelho, PhD; Jian Wang, PhD; Lesley-Anne Furlong, MD; Charles Ganley, MD; Theresa Michele, MD; David G. Strauss, MD, PhD

- 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







Erythema

Skin cancer

Photosensitizing agents

Examples

Sunscreens

Cosmetics

Antibiotics

Retinoids

NSAIDs

Diuretics

Estrogens

Basal cell

carcinoma



Erythema

Motrin

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



Early age at menarche increases melanoma risk, NIH-AARP



Donley, BJC, 2019

Ambient UVR, <u>age at menarche</u>, and melanoma risk, NIH-AARP



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



Ambient ultraviolet radiation level (minimum erythemal dose units/day)

UVR and reduced cancer risks



IJC International Journal of Cancer

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

Shih-Wen Lin^{1,2}, 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



UVR and reduced lymphoma risks in the U.S.

Int J Cancer. 2015 March 1; 136(5): E432-E441. doi:10.1002/ijc.29237.

Relationship between ambient ultraviolet radiation and non-Hodgkin lymphoma subtypes: a U.S. population-based study of racial and ethnic groups

Elizabeth K. Cahoon¹, Ruth M. Pfeiffer², David C. Wheeler³, Juan Arhancet⁴, Shih-Wen Lin⁵, Bruce H. Alexander⁶, Martha S. Linet¹, and D. Michal Freedman¹

 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



Relationship between ambient ultraviolet radiation and Hodgkin lymphoma subtypes in the United States

Emily M Bowen¹, Ruth M Pfeiffer¹, Martha S Linet¹, Wayne T Liu¹, Dennis D Weisenburger², D Michal Freedman¹ and Elizabeth K Cahoon^{*,1}

 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

What is a notable biological response to exposure to UVA?

- A. Sunburn
- B. Aging
- C. Vitamin D production
- D. None of the above

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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

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

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