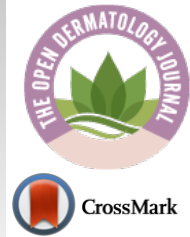




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REVIEW ARTICLE

Pesticides and Pollutants associated with Rising Cases of Melanoma

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Abstract:

UV radiation is a well-researched cause of malignant melanoma, however more than the sun may be to blame for today's increased rates of the deadliest form of skin cancer. Pesticides and industrial pollutants are an overlooked yet major causative factor that is still being exposed to ecosystems. This article identifies documented cases of the chemical causes of melanoma stemming from a study that articulates these dangers in the year 2000. It concludes with a message that a clear risk between chemicals and melanoma exists and calls to action the need for mediation.

Keywords: Melanoma, Pesticides, Pollution, Carcinogens, Industry, Screening.

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1. INTRODUCTION

Melanoma, the most serious form of dermal cancer, impacts over 1 million Americans to date and is increasing in incidence [1]. It often develops from an existing nevus but can appear suddenly on any part of the body. Melanoma is often seen in sun-exposed areas of the face but can also appear in sun-deficient areas such as the soles of the feet. The simple "ABCDE" rule can be applied in diagnosing melanoma which encompasses asymmetrical lesion, irregular border, color differences, diameter of more than 6 millimeters, and evolving changes over periods of time. Full diagnosis requires a biopsy and imaging to investigate a multitude of risks ranging from local invasion to fatal metastasis. Fortunately, when melanoma is detected at an early stage, it is considered highly treatable through the use of surgical excision, radiation, and immunotherapy [2]. Early detection and an understanding of melanoma risk factors are key to reducing melanoma morbidity and mortality.

Current screening recommendations to aid in early detection by the American Academy of Dermatology (AAD) include regular skin examinations for all, but especially those that fall into high risk categories such as high sun exposure and fair complexion [3]. Despite being a lethal and relatively common cancer, risk factors other than ultraviolet radiation (UVR) have hardly been explored. Without diminishing the importance of UVR and sun exposure as a primary cause of

skin damage and malignancy, we would like to further investigate the noteworthiness of lesser-known environmental factors on melanoma including known chemicals and pesticides.

2. BACKGROUND

As rates of melanoma have increased over the past years, so have the rate of global warming and ozone depletion. Ozone depleting substances (ODS) including chlorofluorocarbons (CFC), freons, carbon tetrachloride, and methylchloroform are manmade pollutants made by engines and the destruction of several different polymers. They were unregulated until their ozone-depleting properties were discovered and the substances were banned by the Montreal Protocol on Substances that Deplete the Ozone Layer in 1989 [4]. Destruction of the ozone layer is widely known as being responsible for increased global temperatures, but it specifically results in higher amounts of UVB radiation reaching the ground [5]. Levels of UVB radiation are highly correlated with latitude, however UVA radiation is not [5]. Interesting enough, studies show that 92% of all melanomas are actually caused by UVA-induced indirect damage, not UVB [6, 7]. If true, then why are melanoma rates rapidly increasing despite a higher amount of only UVB reaching the skin of humans? This leads one to postulate that non-solar factors must somehow fit into melanoma's causation. The lack of UVA radiation despite ozone depletion and increasing UVB rays points to other factors, in addition to sunlight, being responsible for the aforementioned increase in melanoma rates.

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3. PESTICIDES & POLLUTANTS: A MISSING PIECE?

Pesticides have been recognized as generally carcinogenic substances for several decades [8]. As pesticides act on the nervous system and melanocytes derive from neural crest cells of the early neural tube, the theory that pesticides penetrate the melanocyte and promote dysplasia is feasible. A 2000 study in the *Journal of the American Academy of Dermatology* suggested pesticides as a non-solar cause of melanoma [9]. This study cited the existence of over 1000 different types of pesticides and posed the idea that pesticides could be partially responsible for increasing rates of melanoma. In 2022, over 17,000 pesticide products were on the market [10]. An early instance of possible pesticide-induced melanoma was banana plantation workers in Costa Rica [11]. High exposure to dibromochloropropane insecticide to the banana workers resulted in a standard incidence rate for melanoma well over the 95% confidence interval [11].

The Los Angeles County Cancer Surveillance Program identified a group of organic chemists with exceptionally high rates of melanoma. Interviews were conducted and it was determined that the impacted chemicals were working with organic substances used in pesticides, leading the program to call for additional studies on chemical causes of melanoma [12]. Similarly, results appeared consistent with an association between melanoma and dioxin-spraying soldiers during the Vietnam War when compared to those who also served in the Vietnam War but did not spray pesticides [13]. Farmers are another category with exceptionally high pesticide exposure and several studies exist to examine the effects. While deriving for percent cropland in each county to determine high, medium, and low agriculture activity areas, it was determined that high and medium activity areas had statistically significant risk estimates and higher rates of melanoma than lower activity areas [14]. This study also examined the risk of UVR exposure by stratifying for latitude, so we held it to high importance. Most of the high activity areas are in northern states with little expected UVR exposure compared to other states, hence it seems unlikely that sun exposure and UVR would have a significant effect on risk of melanoma [14]. Therefore, perhaps the risk in farmer populations again lies in pesticide exposure. This is demonstrated yet again in licensed pesticide applicators on farms. Dennis *et al.* examined 50 dose-response relationships between agricultural pesticides and cutaneous melanoma incidence in a cohort of licensed pesticide dispensing professionals on farms while controlling for known risk factors of melanoma [15]. The study found similar findings to others mentioned in this article that increased melanoma rates were seen with those who dispensed, handled, and were exposed to pesticides [15].

Like pesticides, many pollutants are already recognized as generally carcinogenic substances. However, several flawed studies originally dismissed the idea of various pollutants causing melanoma, most notably pollutants such as benzenes and petroleum hydrocarbons from the refining industry [16]. These early studies were often produced by the polluting industries in question and included implicit bias as they were funded by the industries themselves [16]. A 2005 review article disputed earlier claims from industry scientists and found

significant association between melanoma and exposure to petroleum hydrocarbons, polycyclic aromatic hydrocarbons (PAHs), polychlorinated biphenyls (PCBs), benzene, aromatic hydrocarbons, and heavy oils in the refining industry, forging the way for workplace improvements and cancer prevention [16]. A more recent study examined firefighter's significant exposure to PAHs in smoke [17]. As PAHs were determined to be a risk factor in a 2005 study, further firefighter studies explored these pollutants and noted an excess of melanoma and many other cancers in over 16,000 Nordic firefighters [18]. It was nearly impossible for firefighters to avoid PAH exposure as PAH particles were found on the firefighter's skin underneath layers of gear and PPE [17]. Similarly, the Province of Taranto in Southern Italy was investigated by the SENTIERI project (Studio Epidemiologico Nazionale dei Territori e degli Insediamenti Esposti a Rischio da Inquinamento - Epidemiological Study of Residents in Italian Contaminated Sites) due to a nearby steel plant illegally releasing toxic pollutant (including benzene and PCBs as referenced in the 2005 study) fumes and dust into the air [19]. It was found that the rate of cutaneous melanoma in males was doubled in comparison to males found in other regions of southern Italy who were not exposed to the steel plant pollution [19]. The increased risk of melanoma due to steel plant pollutants was new information, as previous studies only examined risks of respiratory tumors and mesotheliomas.

CONCLUSION

In this review, we found common pesticides and pollutants with multiple examples of melanoma-causing factors. A clear risk exists. Upon comparison to early research that initially discovered these connections, much more data has been published and further mechanisms have been explained. However, even the most recent articles still conclude that further research is needed to complete the association between melanoma and non-solar risk factors. This review is in congruence with that same message but hopes to instill the point that the time has come to finalize the research. Beginning interventions to decrease environmental exposures to harmful pesticides and pollutants such as regulation of pesticide quantity, requiring use of advanced personal protective equipment, and using renewable energy sources in factories, is necessary and must be completed in a timely manner. Additional peer-reviewed research would ideally lead to the commercial banning of the carcinogenic substances in question. Damage to ecosystems and humans has already been done, and more will proceed without rapid mediation.

LIST OF ABBREVIATIONS

ODS	=	Ozone Depleting Substances
CFC	=	Chlorofluorocarbons
UVR	=	Ultraviolet Radiation
PAH	=	Polycyclic Aromatic Hydrocarbons
PCB	=	Polychlorinated Biphenyls

CONSENT FOR PUBLICATION

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CONFLICT OF INTEREST

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