# Macular degeneration: peculiar sunlight exposure in an agricultural worker

Enrico Oddone<sup>1,2</sup>, Giuseppe Taino<sup>3</sup>, Silvia Vita<sup>4</sup>, Monica Schimd<sup>4</sup>, Francesco Frigerio<sup>2</sup>, Marcello Imbriani<sup>1,2</sup>

<sup>1</sup> Department of Public Health, Experimental and Forensic Medicine, Occupational Medicine Unit "Salvatore Maugeri", University of Pavia, Pavia, Italy

<sup>2</sup> Department of Occupational Medicine, Toxicology and Environmental Risks, IRCCS "Salvatore Maugeri" Foundation, Pavia, Italy

<sup>3</sup> Department of Occupational Medicine, Toxicology and Environmental Risks, Hospital Occupational Medicine Unit (UOOML), IRCCS "Salvatore Maugeri" Foundation, Pavia, Italy

<sup>4</sup> Ophthalmologic Rehabilitation Unit, IRCCS "Salvatore Maugeri" Foundation, Pavia, Italy

**KEY WORDS:** Age-related macular degeneration; sunlight exposure; blue light; agriculture; occupational exposure; personal protective equipment

**PAROLE CHIAVE:** Degenerazione maculare; esposizione alla luce solare; luce blu; agricoltura; esposizione occupazionale; dispositivi di protezione individuale

# SUMMARY

**Background:** Occupational exposure to sunlight, in particular to blue light (wavelength of 380-550 nm), is a risk factor for several pathologies, including chronic retinal photochemical damage and, more specifically, age-related macular degeneration (AMD). Moreover, in addition to the effect of blue light, there is evidence about the role of near ultraviolet light (UV-A) as a risk factor for AMD since, given the wavelength, a precise "turning point" between effect and no effect is not definable. **Methods and results:** This work reports the case of a woman employed in the agricultural sector from 15 to 25 years of age, with no significant occupational exposure to other risk factors for AMD, who later developed this pathology. The case is of particular interest given that she worked as a "mondina", a task involving the transplanting of young rice seedlings into water-flooded fields and manual weed control. This practice, although replaced by the introduction of pesticides, entailed the exposure to sunlight reflection on the water surface in addition to direct exposure to natural light. **Conclusion:** This brief case-report points out that occupational exposure to the short wavelength component of visible light and UV-A deserve further attention regarding preventive measures and the adoption of adequate personal protective equipment, in particular in productive sectors involving lengthy eye exposure to solar radiation and to the reflectance of surrounding surfaces. Furthermore, the cases of AMD and cataract should receive a complete and accurate occupational anamnesis for a more proper recognition of the possible role of ccupational solar radiation exposure in the induction of the disease.

# RIASSUNTO

«Degenerazione maculare: report di un caso insorto in una agricoltrice con un'inusuale esposizione a luce solare». Introduzione: L'esposizione occupazionale a luce solare, ed in particolare a luce blu (lunghezza d'onda 380-550

Pervenuto il 10.1.2019 - Revisione pervenuta il 26.3.2019 - Accettato il 3.5.2019

Corrispondenza: Enrico Oddone, Department of Public Health, Experimental and Forensic Medicine, Occupational Medicine Unit "Salvatore Maugeri", University of Pavia, Pavia, Via Severino Boezio 24, 27100 Pavia, Italy - Tel. 390382592807 - Fax: +390382592839 - E-mail: enrico.oddone@unipv.it

Authors' contributions: All the Authors have substantially contributed in the conception and the drafting of the work. The final version was approved by all the Authors.

nm) rappresenta un fattore di rischio per molte patologie, compreso il danno fotocromatico cronico della retina e, più nello specifico, la degenerazione maculare (DM). Inoltre, non è da sottovalutare un potenziale rischio da esposizione alla luce ultravioletta prossima allo spettro del visibile nello sviluppo della DM, anche perché non è possibile discriminare, considerando la lunghezza d'onda, in modo preciso la soglia di non-effetto. Metodi e risultati: Questo lavora riporta il caso di una donna occupata nell'agricoltura dai 15 ai 25 anni (senza altre esposizioni occupazionali a fattori di rischio per DM) che successivamente ha sviluppato questa patologia. Il caso è di particolare interesse dato che la lavoratrice ha svolto la mansione di "mondina", consistente nel trapianto in risaia delle pianticelle di riso e nella disinfestazione manuale delle colture dalle erbe infestanti. Questa occupazione, oggi scomparsa con l'introduzione dei pesticidi, ha comportato l'esposizione sia a luce solare diretta, sia a quella riflessa dalla superficie dell'acqua. Conclusioni: Questo breve case-report indica che l'esposizione occupazionale alle lunghezze d'onda più corte dello spettro della luce visibile e a UV-A merita grande attenzione al fine di attuare le idonee misure di prevenzione e di fornire i corretti dispositivi di protezione individuale, soprattutto in settori produttivi che espongano l'occhio a intensa luce solare diretta o riflessa dalle superfici attorno al lavoratore. Inoltre, i pazienti che ricevono una diagnosi di cataratta o DM dovrebbero essere sottoposti ad una attenta anamnesi occupazionale

#### INTRODUCTION

Sunlight is currently viewed as a suspected risk factor for age-related macular degeneration (AMD), in particular for those patients who have had prolonged exposures during their working life (16). Moreover, given that the limit between near ultraviolet (UV-A) and visible light (380 or 400 nm) is somewhat questionable, we shall also consider UV-A in addition to visible "blue-light" as risk factors for AMD (9). Beginning in the '90s, several studies have pointed out interesting results, ranging from a slight, non-significant increase in risk to two or even four-fold increased risk, as reported by a recent meta-analysis underlining a pooled odds ratio (OR) of AMD (OR 1.38, 95% CI 1.09-1.74) for people exposed to sunlight (18). Solar radiation could thus be considered a risk factor for chronic retinal photochemical damage and, most likely, for age-related macular degeneration (AMD) (9). These observations are of particular interest for occupational medicine due to the wide variety of occupations entailing frequent sunlight exposure: farmers, gardeners, fishermen, watermen, mountain guides are all examples of occupations in which such a risk cannot be disregarded, although the circumstances of exposure could be very different from one task to another. A more comprehensive list of the main occupational activities subject to high sunlight exposure are reported in Boniol et al. (2) and Modenese et al. (10). Furthermore, cataracts can also be related to sunlight exposure and, in addition to previous

cataract surgery, thus included among AMD risk factors (8).

In addition, some indoor exposures involving blue-light were observed to be related to AMD. In particular, occupational welders using welding arcs showed increased risk of macular degeneration (6, 22, 25), and exposure to blue-light among medical personnel in dentistry (13) or dermatology (23) is causing increasing concern.

The aim of this report is to highlight the case of a woman formerly employed in agriculture (a task involving frequent sunlight exposure) who later developed AMD, and to depict the risk related also to short but intense sunlight exposures without the use of any personal protective equipment.

#### **CASE DESCRIPTION**

A bilateral dry AMD was diagnosed in 2008 in a 75-year-old woman currently suffering from hypertension, hyperthyroidism and rheumatoid arthritis, under treatment with ramipril, methimazole and lorazepam. She had had a surgical intervention at the age of 62 for breast cancer, and in 2006 she had undergone cataract surgery on both eyes. No family history for AMD, diabetes, hypertension and autoimmune diseases was detected. She did not report any use of chloroquine or similar compounds in the past, while a smoking habit was reported from about 30 to 50 years of age (10 cigarettes per day). No detailed information was available regarding her diet or antioxidant assumptions. During the most recent Optical Coherent Tomography (OCT) in May 2016, several drusenoid detachments of the retinal pigment epithelium (PED) were observed in the right eye along with the confluence of drusen in the left eye.

Starting in 1948, at the age of 15, she worked as a farmer for about 8 years, and during the following 2 years she was employed as a "mondina". This was a specific task involving the transplantating of young rice plants into water-flooded fields and the manual removal of weeds. In fact, the Italian term "mondina", or its synonym "mondariso", originates from the verb "mondare", i.e. to clean. Nowadays, this occupation has disappeared in Western countries, replaced by pesticides, although it was a common female occupation during the 19th century and the first half of the 20th, mostly in the northwest plains of Northern Italy. The only personal protective equipment provided to these female workers was a brimmed hat useful in protecting the head from the sun, though probably not in protecting the eyes from the sun's reflection on the water. No measurements of eye exposure in this activity are available, although it must be emphasised that the high exposure from long working hours, including the central hours of the day, generally in the late springearly summer months (with the highest level of solar radiation), the absence of shade in the surrounding area, and the working position (feet in the water, bust bent forward, standing and directly looking at the water), all resulted in high exposure to sunlight. Such an uncomfortable task became a social issue that inspired the 1951 Oscar-nominated film "Riso amaro" (Bitter Rice).

After this first employment period, she worked for 3 years as a labourer in a chemical plant for the production of synthetic textiles (rayon fibres), with no detectable exposure to occupational risk factors for AMD. She then stopped working for any industry, being fully committed to home life and family care.

## DISCUSSION

Despite its protective action in some pathologies, sunlight exposure is a well-known risk factor for a number of acute and chronic diseases (7). Some evidence suggests a putative causal role of sunlight exposure in the onset of AMD (16, 18). Exposure causes retinal damage and is considered to be responsible for frameworks of AMD. Experimental data is available showing retinal damage induced by blue light (1, 11). Cataracts and previous cataract surgery can also be related to sunlight exposure (9).

Although the pathogenic mechanism of AMD is not completely understood, it seems clear that bluelight exposure can induce oxidative stress in the retina (1, 16): animal experiments reveal that some retinal chromophores, like A2E, can induce phototoxic damage when oxidized by blue-light (24). Moreover, it was observed that blue-light photoreactivity of melanosomes intensifies with aging (11), representing, along with the aerobic photoreactivity of retinal pigment epithelium lipofuscin (14), other potential sources of reactive oxygen species, thereby contributing to cellular dysfunction. It is interesting to note that similar considerations are also valid for UV-A (2, 9).

Several epidemiologic studies suggest an association between sunlight exposure and the development of AMD. Some of these studies show a remarkable and significant increase in risks (4, 12, 21), while a recent meta-analysis indicates a pooled risk estimation of about 1.38 (95% CI 1.09-1.74) (18). It should be noted that two of these studies were carried out on the population of islands located in the Adriatic sea (Croatia) (12, 21), where a large part of the residents work as fishermen or agriculturists, according to the authors' definition (21). These results are consistent with previous ones, underlining increased risks for watermen exposed to blue-light (20). Despite the difference between fishermen or watermen and "mondine", the occupational tasks of all these categories are associated with exposure to sunlight reflection on the water surface in addition to direct natural light exposure. Even if exposure data are lacking, due in part to the fact this task is out-of-date in developed countries, in our opinion the exposure was possibly even higher in "mondine", for the above-mentioned reasons: long working hours in the middle of the day, in late spring, bent forward with the face close to the water, looking directly into the water, in bright sunshine with no shade, probably no sunglasses, etc.

Moreover, exposure to sunlight during the teenage years and the thirties was found to be related to early AMD (3, 5, 16). In addition, it was observed that in young subjects the proportion of UV-A capable of reaching the retina is higher than in adults (17). Although our case had no early onset, it is interesting to note that she had an early exposure beginning at 15 and ending at 25 years of age, with the last two years accounting for the most intense exposure to sunlight.

No data is currently available on the latency of work-related AMD, but our case experienced a remarkably long latency of approximately 60 years since her first exposure.

Finally, it is worth observing that our worker also suffered from cataracts, undergoing surgery for this pathology. The association in the same person of two different diseases (AMD and cataracts) having a common risk factor (UV exposure) supports the hypothesis of a possible association.

Despite the rarity of this exposure, the outdatedness of the task, and the current lack of data firmly supporting the relationship between sunlight exposure and AMD, this case has the advantage of highlighting how sunlight exposure could exert its damaging effect on the retina also for short durations of exposure because of the potential relevance of reflected radiation, and with a considerable latency period. According to evidence in the literature, blue-light is probably the most dangerous part of the visible light regarding macular degeneration (1, 11). This consideration demands careful attention also regarding those exposures to artificial light which have the same wavelength as blue-light, especially for the purpose of assessing risks in all occupational settings in which workers use blue light-emitting devices.

In Italy, the chronic degenerative diseases of the retina (such us AMD) are not listed in the occupational disease tables included in both the Ministerial Decree of April 9, 2008, and the Ministerial Decree of April 11, 2009. However, based on a solid demonstration of causality with exposure to sunlight, they have been included in the item "Other diseases caused by occupational exposure to UV including solar radiation (ICD-10 to be specified)" present in the tables of occupational diseases in the Ministerial Decree of April 9, 2008 (19). Moreover, due to the possible relationship between solar light exposure and the onset of AMD, all the cases diagnosed with AMD and cataracts should receive a complete and accurate occupational anamnesis.

We are aware that our case holds several other risk factors for AMD, such as hypertension and smoking habits, along with a complicated clinical history. However, we think that this case could suggest an interaction between environmental/occupational risk factors and personal behavior, pointing out the need to pay particular attention to the additional occupational risk burden in such an important productive sector like agriculture.

## CONCLUSIONS

We think that this brief case-report could highlight that occupational exposure to sunlight (especially to the short wavelength component of its spectrum, such as blue light) and to near UV-A deserve further attention for the purpose of adopting appropriate preventive measures and using adequate personal protective equipment, in order to prevent the onset of chronic retinal photochemical damage, and possibly AMD. Moreover, this work could contribute to stress the need for an adequate occupational anamnesis in all AMD (and cataract) cases, for ethical reasons, both at the individual level for a possible recognition of the disease as work related, and at a more general level for an appropriate evaluation of the real burden of occupational AMD and cataract.

No potential conflict of interest relevant to this article was reported by the authors

### REFERENCES

- 1. Algvere PV, Marshall J, Seregard S: Age-related maculopathy and the impact of blue light hazard. Acta Ophthalmol Scand 2006; 84: 4-15
- Boniol M, Koechlin A, Boniol M, et al: Occupational UV exposure in french outdoor workers. J Occup Environ Med 2015; 57: 315-320
- Cruickshanks KJ, Klein R, Klein BE: Sunlight and agerelated macular degeneration. The Beaver Dam Eye Study. Arch Ophthalmol 1993; 111: 514-518

- Hirakawa M, Tanaka M, Tanaka Y, et al: Age-related maculopathy and sunlight exposure evaluated by objective measurement. Br J Ophthalmol 2008; 92: 630-634
- 5. Klein BE, Howard KP, Iyengar SK, et al: Sunlight exposure, pigmentation, and incident age-related macular degeneration. Invest Ophthalmol Vis Sci 2014; 55: 5855-5861
- 6. Li Q, Zhang X: [The Influence of risk factors on visual performance in of phototoxic maculopathy in occupational welders]. Zhonghua lao dong wei sheng zhi ye bing za zhi (Chinese journal of industrial hygiene and occupational diseases) 2014; 32: 759-761. Chinese
- Lucas R: Solar ultraviolet radiation: Assessing the environmental burden of disease at national and local levels. Prüss-Ustün A and Perkins van Deventer E, eds. Geneva, World Health Organization. 2010 (Environmental Burden of Disease Series, No. 17)
- Modenese A, Gobba FM: Cataract frequency and subtypes involved in workers assessed for their solar radiation exposure: a systematic review. Acta Ophthalmol 2018; 96: 779-788
- 9. Modenese A, Gobba FM: Macular degeneration and occupational risk factors: a systematic review. Int Arch Occup Environ Health 2019; 92: 1-11
- Modenese A, Korpinen L, Gobba FM: Solar radiation exposure and aoutdoor work: an underestimated risk. Int Int J Environ Res Public Health 2018; 15. pii: E2063
- Pang J, Seko Y, Tokoro T, et al: Observation of ultrastructural changes in cultured retinal pigment epithelium following exposure to blue light. Graefes Arch Clin Exp Ophthalmol 1998; 236: 696-701
- Plestina-Borjan I, Klinger-Lasic M: Long-term exposure to solar ultraviolet radiation as a risk factor for age-related macular degeneration. Coll Antropol 2007; 31(Suppl 1): 33-38
- Price RB, Labrie D, Bruzell EM, et al: The Dental Curing Light: A Potential Health Risk. J Occup Environ Hyg 2016; 13: 639-646
- 14. Rozanowska M, Korytowski W, Rozanowski B, et al: Photoreactivity of aged human RPE melanosomes: a

comparison with lipofuscin. Invest Ophthalmol Vis Sci 2002; 43: 2088-2096

- 15. Rozanowska M, Pawlak A, Rozanowski B, et al: Agerelated changes in the photoreactivity of retinal lipofuscin granules: role of chloroform-insoluble components. Invest Ophthalmol Vis Sci 2004; 45: 1052-1060
- Schick T, Ersoy L, Lechanteur YT, et al: History of sunlight exposure is a risk factor for age-related macular degeneration. Retina 2016; 36: 787-790
- 17. Sliney DH: How light reaches the eye and its components. Int J Toxicol 2002; 21: 501-509
- 18. Sui GY, Liu GC, Liu GY, et al: Is sunlight exposure a risk factor for age-related macular degeneration? A systematic review and meta-analysis. Br J Ophthalmol 2013; 97: 389-394
- Taino G, Paraluppi P, Giorgi M, et al: Occupational diseases caused by artificial optical radiation (AOR). Med Lav 2013; 104: 3-23
- Taylor HR, West S, Munoz B, et al: The long-term effects of visible light on the eye. Arch Ophthalmol 1992; 110: 99-104
- Vojniković B, Njirić S, Coklo M, Spanjol J: Ultraviolet sun radiation and incidence of age-related macular degeneration on Croatian Island Rab. Coll Antropol 2007; 31(Suppl 1): 43-44
- 22. Vukicevic M, Heriot W: Phototoxic maculopathy associated with arc welding: clinical findings and associated functional vision impairment. Clin Experiment Ophthalmol 2008; 36: 695-697
- Walker DP, Vollmer-Snarr HR, Eberting CL: Ocular hazards of blue-light therapy in dermatology. J Am Acad Dermatol 2012; 66: 130-135
- 24. Wielgus AR, Collier RJ, Martin E, et al: Blue light induced A2E oxidation in rat eyes--experimental animal model of dry AMD. Photochem Photobiol Sci 2010; 9: 1505-1512
- 25. Yang X, Shao D, Ding X, et al: Chronic phototoxic maculopathy caused by welding arc in occupational welders. Can J Ophthalmol 2012; 47: 45-50