

# Don't let cigarettes SMOKE out your patient's vision

Cigarette or tobacco smoking is a well-known preventable cause of disease, disability and premature death. It is a major risk factor for the leading causes of death such as cancer, heart disease and stroke. In addition to these grave diseases, cigarette smoking has also been associated with a number of ocular conditions, particularly cataract and age-related macular degeneration (AMD).

Cigarette smoke contains as many as 4,000 active compounds. Most of them are toxic either on acute or long-term exposure. These include nicotine, tar, nitrosamines, polycyclic aromatic hydrocarbons, hydrogen cyanide, formaldehyde, carbon monoxide and heavy metals such as cadmium, aluminum, lead and mercury. These toxic substances can affect the ocular tissues mainly through ischaemic or oxidative mechanisms.

The list of eye disorders associated with cigarette smoking continues to grow. Of these, smoking directly accelerates cataract and AMD, the leading causes of severe visual loss and blindness. Other less common ocular disorders, such as retinal ischaemia, amaurosis fugax, anterior ischaemic optic neuropathy, oculomotor cranial nerve palsies, tobacco-alcohol amblyopia and Graves ophthalmopathy are also significantly related to this harmful habit.<sup>1</sup> In addition, cigarette smoke commonly causes ocular surface irritation due to conjunctival inflammation and this may also be seen in non-smokers with passive exposure.

Cataract is a major cause of blindness especially in the developing world. Cigarette smoking is associated with a modestly increased risk of nuclear sclerotic type of cataract (Figure 1).<sup>2</sup> Smokers have up to two times higher risk of developing cataract compared to non-smokers.<sup>1,2</sup>



Figure 1: Cigarette smoking increases the risk of nuclear sclerotic cataract.

Moreover, there is a dose-response relationship for smoking intensity. There is a significant correlation with the pack-years (calculated as the number of packs smoked per day multiplied by the number of years of smoking) smoked.<sup>1</sup> Smoking also has a detrimental effect on the development of cataract in type II diabetic patients.<sup>1</sup>

Cataract formation is probably induced by the effect of smoking on the oxidant-antioxidant status of the lens. Smoking also promotes the accumulation of heavy metals such as cadmium in the crystalline lens, which increases precipitation of copper and lead. Some of this smoking-related damage to the lens may be reversible. Although smoking cessation is associated with a reduced risk of cataract over time, a longer duration is needed with a higher smoking intensity to achieve the same benefit. Considering the magnitude and seriousness of the cataract problem worldwide, an important preventive measure is to motivate smokers to quit smoking and to discourage non-smokers from picking up the habit.

AMD, the other major ocular disease associated with smoking, is the leading cause of severe vision loss amongst the elderly in developed countries.<sup>13,4</sup> Most cases of AMD are irreversible and largely untreatable despite recent advances in treatment options. Current United States Food and Drug Administration (FDA) approved therapeutic developments for AMD such as photodynamic therapy (PDT) and anti-vascular endothelial growth factor (anti-VEGF) agents at best attempt to stabilise the disease or slow its progression. These treatment options are also costly. As there is no curative treatment for AMD, the identification and modification of AMD risk factors have the potential for greater public health impact on the morbidity from AMD than the few treatment modalities at hand.

Of the established risk factors for AMD, age is the most important but clearly non-modifiable. Other non-modifiable risk factors include ethnicity and heredity. Environmental risk factors include cigarette smoking and nutritional factors.<sup>5</sup> Of these, smoking has most consistently been associated with an increased risk of AMD. Dietary antioxidant and micronutrient supplementation has been shown to be effective in reducing the progression of at least certain subgroups of the disease by the Age Related Eye Disease Study (AREDS) conducted in the United States.<sup>6</sup>

The results of six large population-based studies from North America, Europe and Australia suggest that smoking significantly increases the risk of AMD.<sup>7-12</sup> Smokers have at least two to four times higher risk of developing AMD compared to non-smokers.<sup>8</sup> Smoking constitutes an independent and avoidable risk factor for AMD in both sexes. A

strong association has been found between smoking and the advanced exudative stages of the disease (wet AMD). This risk is higher in males compared to females (Figure 2). A pooled analysis of three major epidemiological studies (Beaver Dam Eye Study [USA], Rotterdam Study [Netherlands] and Blue Mountains Eye Study [Australia]) has shown a greater than four-fold increased risk of wet AMD, the more severe form of the disease, in current smokers compared to never-smokers.<sup>4</sup>

A dose-response effect is evident as the risk increases with an increase in the number of pack-years smoked. A recent study from the United Kingdom has further confirmed the strong association between pack-years smoked and the risk of wet AMD as well as geographic atrophy, the most severe form of dry AMD (Figure 3).<sup>13</sup> The risk of AMD is also increased in non-smokers with passive exposure to cigarette smoke.<sup>15</sup>

Smoking increases the risk of developing AMD by reducing choroidal blood flow and promoting ischaemia and micro-infarctions, all of which increase the susceptibility of the macula to degenerative changes. In addition, smoking is thought to increase oxidative stress and lipid peroxidation of retinal tissues by reducing the plasma concentrations of the antioxidants. Smokers have been found to have reduced macular pigment optical density with a reduction in the levels of the protective carotenoids lutein and zeaxanthin in the macular retina.

Very importantly, there is evidence that ex-smokers have a lower risk of developing AMD compared to current smokers, suggesting at least a partial reversal of the effect.<sup>5</sup> Although ex-smokers have an increased risk of developing AMD compared to never-smokers, this risk is considerably lower than current smokers. With time, the risk of developing AMD for ex-smokers approaches the risk for never-smokers. However, any healing from damage due to cigarette smoking occurs at a very modest pace, and the importance of never starting to smoke or quitting the habit early needs to be emphasised. As AMD is frequently not amenable to treatment, reducing the risk of the disease is an important reason to avoid or quit smoking.

Despite the strong evidence, there is a general lack of awareness about the risk of developing AMD from smoking among both the general public and healthcare professionals. In a recent survey in the United Kingdom, the awareness of the risk of blindness from smoking amongst hospital patients was found to be only 9.5% compared with other better known smoking-related diseases such as lung cancer (92.2%) and heart disease (87.5%).<sup>14</sup> Interestingly, about half the smokers in this study were willing to quit smoking if they developed early signs of blinding eye diseases.

Besides the poor awareness of blindness as a smoking related condition, the awareness of AMD itself is also low. A survey conducted by AMD Alliance International involving more than 15,000 people in 14 countries showed that the awareness levels, at their highest, were only 20 to 30% in the United States, Canada, and Australia, while elsewhere, particularly in Europe, South Africa, Hong Kong, and Japan, levels were much lower.<sup>15</sup> Even among those few who were aware of AMD, only 32% could identify smoking as a risk factor for the disease.<sup>15</sup> The low awareness of

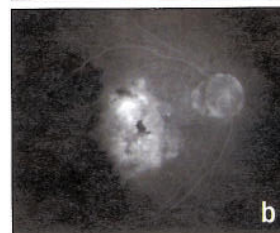
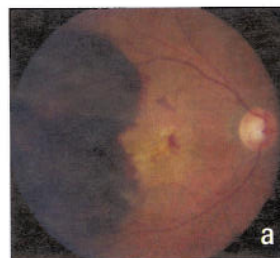


Figure 2: (a) Wet age-related macular degeneration showing choroidal neovascularisation and subretinal haemorrhage. (b) Fluorescein angiography of the same eye shows fluorescein leakage from the choroidal neovascularisation

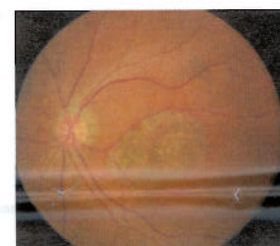


Figure 3: The risk of geographic atrophy, the most severe form of dry age-related macular degeneration, is increased with cigarette smoking

AMD and its risk factors in Asian countries has prompted the AMD Alliance International, a coalition of 55 member organisations from 21 countries and the largest global non-profit body dedicated to raising the awareness of AMD, to open its Asia Pacific office in Singapore later this year.

Advice from health professionals can be instrumental in motivating smokers to quit smoking. Many people fear blindness more than they fear other illnesses. Efforts directed towards augmenting the campaign against cigarette smoking by adding the increased risk of blindness to the better-known arguments against smoking may increase its effectiveness. The growing research implicating smoking in AMD has already prompted efforts in some countries such as Australia to urge their governments to warn smokers of this little appreciated risk. Doctors and other healthcare professionals on their part should actively ask their patients for a history of smoking and highlight the less well-known risks to them.

In conclusion, there is convincing evidence that cigarette smoking is a risk factor for potentially blinding eye conditions such as cataract and AMD. Although the strongest risk is for current smokers, smoking cessation gradually reduces this risk, suggesting possible benefits of targeted anti-smoking campaigns. Raising the awareness of smoking-related blindness among healthcare professionals and the general public could potentially help to motivate smokers to quit smoking and to discourage non-smokers from starting this harmful habit.

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