

POPPER MACULOPATHY: LONG-TERM FOLLOW-UP AND CASE SERIES

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Purpose: To report a case series of popper maculopathy.

Methods: Clinical history, examination findings, retinal imaging, and progress of the disease are described.

Results: Four male patients with a mean age of 37 years (range 25–48) and different duration of popper use (ranging from first time user to chronic user) presented with central scotomata, phosphenes, or photophobia. Optical coherence tomography in all cases demonstrated subfoveal disruption of the ellipsoid zone. Three cases also showed hyperreflectivity of the ellipsoid zone, and one case had a foveal detachment. Chronic user of poppers was associated with more severe macular changes. One patient had a 3-year follow-up and demonstrated complete resolution of signs on retinal imaging after ceasing popper use.

Conclusion: Popper maculopathy may show complete resolution of signs on long-term follow-up, even after chronic popper ingestion.

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“Poppers” is the colloquial term, which refers to glass vials containing volatile alkyl nitrite compounds, which “pop” when they are broken for human consumption.¹ They have been in use for decades in the homosexual community, as well as at electronic dance festivals, for their euphoric, aphrodi-

siac, and myorelaxant properties.^{2,3} Poppers are illegal; however, they can still be purchased if they are marketed as alternative products, which include room deodorizers or video head cleaners.² Their use has been associated with a maculopathy that may cause bilateral vision loss, scotomata, photophobia, and central phosphenes.^{2,4–6} Bilateral yellow dots are seen at the foveae, corresponding to outer retinal changes at the fovea on optical coherence tomography (OCT).⁷ This retrospective case series describes four patients with popper maculopathy (Table 1).

Case 1

A 39-year-old myopic man presented with a 3-day history of bilateral blurred central vision the morning after he ingested poppers in combination with sildenafil. Other than chronic use of poppers, he had no other significant medical history. Best-corrected visual acuities were 6/9 in the right eye and 6/18 in the left eye improving with pinhole to 6/9. Fundoscopy revealed bilateral yellow foveal dots (Figure 1A). Optical coherence tomography (CIRRUS 5000 HD-OCT; Carl Zeiss Meditec AG, Jena, Germany) demonstrated focal hyperreflectivity and irregularity of the ellipsoid zone at the fovea (Figure 1B). Fundus autofluorescence (Zeiss VISUCAM 500; Carl Zeiss Meditec AG) was normal (Figure 1C). The patient was advised to avoid popper and sildenafil usage.

At 1-month follow-up, vision had improved to 6/6 in the right eye and 6/7.5 in the left eye, with OCT revealing near complete restoration of the photoreceptors in the left eye. At 3-year

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Table 1. Demographic and Clinical Data of all Patients

Patient	1	2	3	4
Age (years)	39	48	34	25
Sex	Male	Male	Male	Male
Presenting symptoms	Central scotoma	Central scotoma	Central scotoma	Photophobia
Duration of follow-up (months)	39	3	0	0.5
VA on initial presentation (OD, OS)	6/9, 6/18	6/12, 6/12	6/6, 6/5	6/6, 6/6
VA on last follow-up (OD, OS)	6/4.8, 6/4.8	6/15, 6/12	N/A	6/6, 6/6
OCT changes on initial presentation	Foveal hyperreflectivity/irregularity of the EL	Subfoveal hyporeflectivity	Foveal hyperreflectivity/irregularity of the EL	Foveal hyperreflectivity of the EL
OCT changes on last follow-up	Normal	Subfoveal hyporeflectivity	N/A	Foveal hyperreflectivity of the EL

EL, ellipsoid layer.

follow-up, visual acuity improved to 6/4.8 in the right eye and 6/4.8 in the left eye. Fundus examination (Figure 1D) and OCT (Figure 1E) were normal, and the patient was asymptomatic.

Case 2

A 48-year-old man presented with gradual worsening of distance vision and bilateral scotomata more than a few months. His medical history included HIV positive with a stable viral load, not requiring any treatment, and ocular history of LASIK surgery. Best-corrected visual acuity was 6/12 in both eyes. Slit-lamp examination revealed an apparently normal right macula but small yellow circular lesion at the left the macula (Figure 2A). Fluorescein angiography (Zeiss VISUCAM 500) was normal (Figure 2B). On enhanced-depth imaging OCT (CIRRUS 5000 HD-OCT), subfoveal hyporeflectivities were seen at both foveae (Figure 2C). Three months after his initial presentation, his best-corrected vision worsened to 6/15 in the right eye, whereas the left eye remained at 6/12. He did not experience improvement in symptoms, and his OCT revealed no change. After further questioning, he admitted to chronic and regular continued use of poppers, which he initially denied. Unfortunately, he was lost to follow-up.

Case 3

A 34-year-old man was referred by his general practitioner with a 3-day history of central visual distortion after a rare episode of poppers ingestion. He had been prescribed Finasteride for hair loss but was otherwise healthy with no ocular history and an infrequent use of poppers. On examination, his corrected visual acuity was 6/6 in the right eye and 6/5 in the left eye. Yellow dots were noted at both maculae, and OCT (CIRRUS 5000 HD-OCT) showed subtle hyperreflectivity and irregularity of the ellipsoid line at the fovea. The patient was lost to follow-up.

Case 4

A 25-year-old man presented with a 2-day history of photopsia associated with blurry vision after inhaling poppers for the first time. He had no other significant medical or ocular history. On examination, his best-corrected visual acuity was 6/6 in both eyes,

and the funduscopy revealed bilateral focal yellow dots. On OCT (Heidelberg Spectralis HRA+OCT; Heidelberg Engineering Inc, Heidelberg, Germany), there were bilateral focal foveal hyperreflectivities in the ellipsoid line, and microperimetry (MAIA; CenterVue, Padova, Italy) showed decreased foveal sensibility in both eyes. Fundus autofluorescence was normal (Zeiss VISUCAM 500). The patient was advised to avoid using poppers. At follow-up, 2 weeks later, his vision remained unchanged with similar findings on OCT and microperimetry. The patient failed to present for his 3-month examination but reported spontaneous resolution of his symptoms.

Discussion

Poppers have been used for several decades as a recreational drug, but the first report of popper-induced maculopathy was only documented by Pece et al in 2004.³ Since then, there has been an increase in the number of reported cases, with just over 50 patients described.⁴ Explanations for this increase include a change in the compound from isobutyl nitrite to isopropyl nitrite in 2007, increased usage of the drug, stronger dosages, better detection with spectral domain OCT, and greater awareness by the ophthalmic community.^{2,5-7} The use of poppers is believed to be high, with reported lifetime usage ranging from 5% to 6% of French teenagers⁷ to 10% of the 16-year- to 59-year-old U.K. population² to 29.5% in a 2002 Global Drug Survey⁴ to 60% of Australia's male homosexual community.¹ This highlights the importance of a focused drug history and vigilance of the disease, particularly in patients with bilateral vision loss who are homosexual male or attend dance festivals. Diagnosis can be complicated by patient denial of popper use, which is not uncommon¹ and was seen in Case 2. The incidence of maculopathy with popper use may be higher than

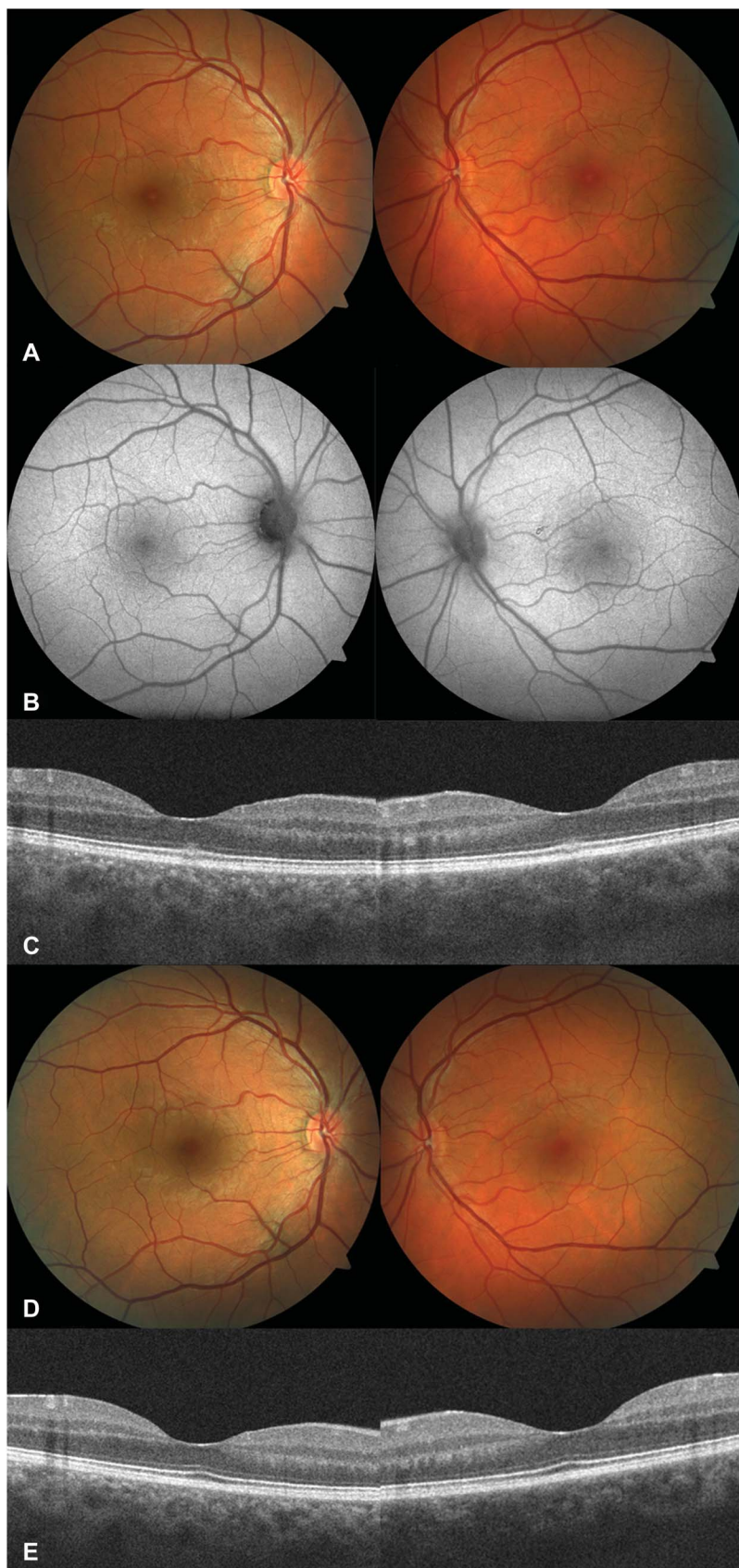
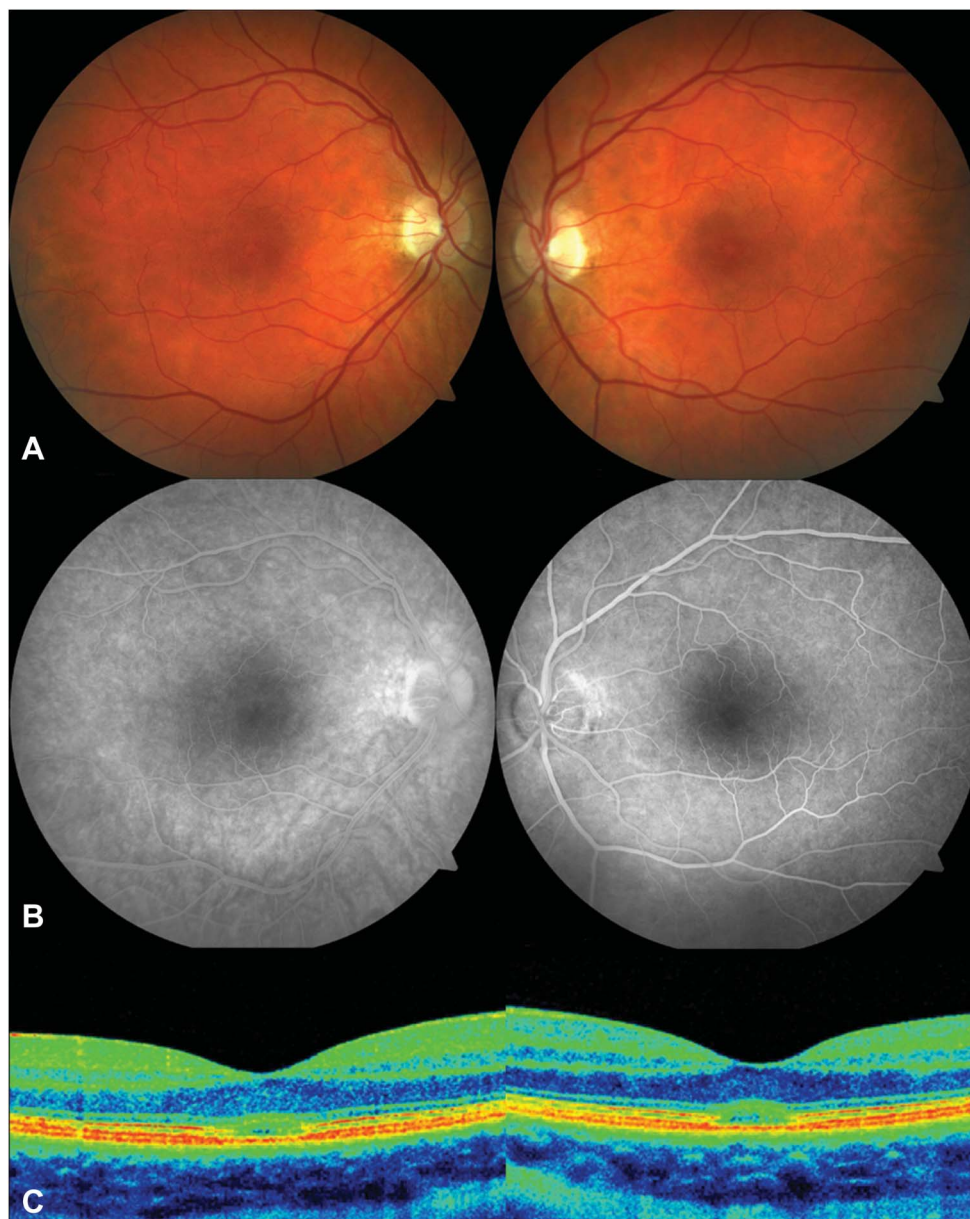


Fig. 1. Color fundus photographs demonstrating yellow dots at the fovea (A). Fundus autofluorescence is normal (B). OCT demonstrates subtle hyperreflectivity and irregularity of the ellipsoid line at the fovea (C). Three years later, foveal appearance is normal on color fundus photography (D) and OCT (E).

Fig. 2. Color fundus photographs demonstrate a small circular yellow spot at the left fovea with an apparently normal right macula (A). Fluorescein angiography is normal (B). Enhanced-depth imaging OCT demonstrates subtle subfoveal hyporeflectivities in both eyes (C).



previously realized because 12.2% of users responded that they believed that their vision might or had been affected in the 2002 Global Drug Survey,⁴ and 20 of 36 (56%) patients taking poppers were found to have maculopathy in a study by Schulze-Döbold et al.⁸

Our cases highlight several features of popper maculopathy. First, the OCT appearance may include hyperreflectivity of the ellipsoid zone (Cases 1, 3, and 4) or a subfoveal hyporeflectivity (Case 2) despite normal fundus autofluorescence (Cases 1 and 4) and fluorescein angiography (Case 2). This suggests a direct effect on the outer retina, rather than involvement of the retinal pigment epithelium or retinal circulation. The pathophysiology of popper maculopathy remains unknown, although it may relate

to toxic effects of nitric oxide on the photoreceptors mediated through activation of guanylate cyclase.^{1,7} Second, the OCT appearance in all cases and decreased foveal sensitivity on microperimetry in Case 4 suggest that the pathology in popper maculopathy does not extend extrafoveally, an observation that has been previously confirmed by adaptive optics.⁷ Third, a dose response suggested by others⁴ is confirmed by the fact that in our patients those with chronic popper use (Cases 1 and 2) had more severe macular changes than those taking it infrequently (Case 3) or for the first time (Case 4). Fourth, Case 2 demonstrates that popper maculopathy may resolve spontaneously after cessation of the drug, even after chronic use. This improvement after chronic use has been described

previously⁹ but may be the exception rather than the norm because some cases have failed to show improvement after cessation of poppers.^{2,4,5} Finally, Case 2 has a 3-year follow-up, the longest we are aware of reported in a patient with popper maculopathy (the next longest being 30 weeks⁹). During this time, there does not seem to have been ongoing macular degeneration. Most cases of popper maculopathy describe follow-up of only a few months. Long-term follow-up is especially difficult, given that these patients are often noncompliant and fail to represent when their symptoms resolve after cessation of the drug.

Because of their underreported use and subtle fundus signs, popper maculopathy can easily be missed.⁴ Vigilance for this disease together with an understanding of its natural history and imaging characteristics will assist the clinician in the diagnosis and management of such patients.

Key words: alkyl nitrite, isopropyl nitrite, maculopathy, poppers.

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