The emerging associations of SARS-CoV-2 morbidity and mortality with complement dysfunction are intriguing. They might be a basis for management decisions and possible treatment avenues. However, macular degeneration is a complex disease and should not be considered a straightforward marker of complement dysfunction, especially as patients with macular degeneration have other evident risk factors that can be attributed to increased susceptibility to this pandemic. Research into ways to modulate the complement cascade should nonetheless be encouraged, as this could hopefully be found to be beneficial to patients with macular degeneration, and perhaps eventually to patients infected with SARS-CoV-2 as well.

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Sauer et al. 2018), we centred a standard ETDRS grid at the macula and averaged lifetimes over the inner and outer circle of the grid. Significance of lifetime differences was tested by Mann–Whitney U-test, changes over time by Wilcoxon test (SSP 27.0, IBM, Armonk, NV, U.S.A.).

A general prolongation of lifetimes over the follow-up period was found. An example is given in Fig 1A–F. On average over all subjects, the lifetimes increased nonsignificantly in the first follow-up by 12.0 ± 42.6 ps (inner ETDRS ring, SSC), 8.6 ± 32.9 ps (outer ring, SSC), 7.2 ± 26.3 ps (inner ring, LSC), and 8.6 ± 22.9 ps (outer ring, LSC). For the second follow-up, the increases were significant: 15.8 ± 30.3 ps, (p = 0.025, inner ring, SSC), 12.2 ± 26.8 ps (p = 0.05, outer ring, SSC), 14.7 ± 19.7 ps (p = 0.005, inner ring, LSC), and 17.6 ± 19.0 ps (p = 0.001, outer ring, LSC). The lifetime increases per year were by the factor 1.36–2.26 (1. Follow-up) and 1.15 to 1.86 (2. Follow-up) higher than that reported for normal ageing (Sauer et al. 2020). The baseline lifetimes were higher for eyes which developed GA than for those which did not: 383 ± 91 ps versus 278 ± 63 ps (inner ring, SSC, p = 0.006), 356 ± 98 ps versus 273 ± 55 ps (outer ring, SSC, p = 0.013), 393 ± 36 ps versus 328 ± 27 ps (inner ring, LSC, p = 0.001), and 279 ± 43 ps versus 328 ± 42 ps (outer ring, LSC, p = 0.017). Figure 1G shows the lifetime change from baseline to the second follow-up per individual for the inner ring, LSC. Lifetime increase was

Fluorescence lifetimes increase over time in age-related macular degeneration

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Editor,

Quantitative fundus autofluorescence FAF measurements revealed a decline of FAF intensity with age in AMD patients (Reiter et al. 2019). Fluorescence lifetime imaging ophthalmoscopy (FLIO) showed longer FAF lifetimes for AMD eyes than for age-matched controls (Dysli et al. 2017) and a annular lifetime pattern was described (Sauer et al. 2018). Here, we investigated changes of lifetimes in AMD during longitudinal follow-up of up to 75 months. Fifty-seven patients with initially early or moderate AMD were investigated with FLIO (Schweitzer et al. 2007) in a short-wavelength spectral channel (SSC: 500–560 nm) and in a long-wavelength channel (LSC: 560–720 nm). Patients were excluded when they developed cataracta proveta or underwent cataract extraction during follow-up. Finally, we report on 28 eyes of 26 patients (mean age at baseline: 72.0 ± 8.0 years) who had a first follow-up between 13 and 36 months (mean: 25.7 ± 6.2 months, 19 eyes) and/or a second one between 37 and 74 months (mean: 50.9 ± 6.4 months, 21 eyes, 13 eyes had both follow-ups). Seven eyes, which developed geographic atrophy (GA), were excluded from the follow-up, but their baseline values were compared to that of the 28 eyes without transition into GA. GA lifetimes were calculated from the fluorescence decays per pixel by a three-exponential fit. As prolonged lifetimes were reported in an annular pattern (Sauer et al. 2018), we centred a standard ETDRS grid at the macula and averaged lifetimes over the inner and outer circle of the grid. Significance of lifetime differences was tested by Mann–Whitney U-test, changes over time by Wilcoxon test (SSP 27.0, IBM, Armonk, NV, U.S.A.).

A general prolongation of lifetimes over the follow-up period was found. An example is given in Fig 1A–F. On average over all subjects, the lifetimes increased nonsignificantly in the first follow-up by 12.0 ± 42.6 ps (inner ETDRS ring, SSC), 8.6 ± 32.9 ps (outer ring, SSC), 7.2 ± 26.3 ps (inner ring, LSC), and 8.6 ± 22.9 ps (outer ring, LSC). For the second follow-up, the increases were significant: 15.8 ± 30.3 ps, (p = 0.025, inner ring, SSC), 12.2 ± 26.8 ps (p = 0.05, outer ring, SSC), 14.7 ± 19.7 ps (p = 0.005, inner ring, LSC), and 17.6 ± 19.0 ps (p = 0.001, outer ring, LSC). The lifetime increases per year were by the factor 1.36–2.26 (1. Follow-up) and 1.15 to 1.86 (2. Follow-up) higher than that reported for normal ageing (Sauer et al. 2020). The baseline lifetimes were higher for eyes which developed GA than for those which did not: 383 ± 91 ps versus 278 ± 63 ps (inner ring, SSC, p = 0.006), 356 ± 98 ps versus 273 ± 55 ps (outer ring, SSC, p = 0.013), 393 ± 36 ps versus 328 ± 27 ps (inner ring, LSC, p = 0.001), and 279 ± 43 ps versus 328 ± 42 ps (outer ring, LSC, p = 0.017). Figure 1G shows the lifetime change from baseline to the second follow-up per individual for the inner ring, LSC. Lifetime increase was
found for almost all subjects. Decreasing lifetimes were associated with a transition to neovascular AMD in one eye (blue arrowhead) and massive subretinal drusenoid deposits in two eyes (green arrowheads).

As fluorescence lifetimes are the average time, fluorescent molecules remain in an excited state after short laser pulse excitation, this measure is characteristic for the molecule and its embedding matrix. Thus, prolongation of FAF lifetimes indicates a pathologic change in molecular fluorophore composition in the course of AMD and might be a precursor of GA. That way, FLIO can give additional diagnostic information on molecular alterations in the natural history of AMD.

Fig. 1. (A, B) FAF intensity (LSC) images of a patient at baseline (A) and follow-up of 55 months (B). (C–F) FAF lifetime images at baseline and follow-up (C, D: SSC, E, F: LSC). Lifetimes are colour-coded as shown in the scale bar (SSC: 150–400 ps, LSC: 200–400 ps), the longer lifetimes in the follow-up appear in blue colour in the paramacular area. G: Change of FAF lifetimes for all patients from baseline to the 37–74 months follow-up interval in LCS for the inner ring of the ETDRS grid. Arrowheads indicate subjects who, against the general trend, showed decreasing lifetimes.

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Optic disc drusen diagnosed by optical coherence tomography in a 3-year-old child

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Optic disc drusen (ODD) are present in approximately 2% of the general population (Chang & Pineles 2016; Malmqvist et al. 2020). However, detecting them can be a challenge, especially in children.

In our clinic, a 3-year-old boy was evaluated for suspected bilateral optic disc oedema. The general medical history was unremarkable. Best-corrected visual acuity was 0.8 and 0.5 monocularly, and 0.8 binocularly. Apart from refractive esotropia, the pupils, visual fields, motility and anterior segments were normal. Dilated ophthalmoscopy and fundus photography (Fig. 1A) showed bilateral optic disc protrusion with slightly blurred margins. Enhanced depth imaging optical coherence tomography (EDI-OCT) (Fig. 1B) revealed bilateral ODD, distinguished as prelaminar, hyporeflective structures with a hyperreflective margin. There were no signs of associated ocular or systemic disorders.

The usefulness of OCT in diagnosing ODD has recently been emphasized (Costello et al. 2018; Malmqvist et al. 2018a). In children, ODD are often located too deep and not enough calcified to make them detectable using conventional methods such as autofluorescence or ultrasound (Chang & Pineles 2016; Malmqvist et al. 2018b). Our report is the first OCT-based demonstration of ODD in a patient as young as 3 years of age. Hence, it expands the potential utility of this non-invasive diagnostic tool in the work-up of mild-to-moderate optic disc oedema in well-cooperating paediatric patients. In the appropriate clinical setting, it may reduce the need for more extensive and invasive examinations such as cerebral scan and lumbar puncture.

Compared to ultrasound or autofluorescence, EDI-OCT, when appropriately analysed, has the additional advantage of providing enough resolution to allow the examiner to quantify and eventually measure the volume of the ODD. Although currently mainly used for research purposes, it is conceivable that such quantitative ODD information in the near future may prove useful when prognosticating the risk of ODD-associated complications such as ischaemic optic neuropathy.

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