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Vitrectomy as an Aerosol-Generating Procedure in the Time of COVID-19

The VAPOR Study

The coronavirus disease 2019 (COVID-19) pandemic has highlighted the risk to patients and healthcare staff of viral transmissions arising from aerosol-generating procedures (AGPs). As severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) ribonucleic acid can be isolated from human conjunctiva and tears, aerosol generation during surgery may carry risk of viral transmission.

Studies have suggested that high-speed instruments such as bone or dental drills may generate aerosols. It is unclear what other surgical procedures are AGPs. Vitrectomy for retinal detachment repair is one of the most frequently performed emergency ophthalmic surgery procedures. The American Society of Retina Specialists and Royal College of Ophthalmologists both have classified vitrectomy surgery as an AGP based on the fact that high-speed vitrectomy cutters are used. Recent studies using plastic models and cadaveric corneoscleral tissue have not detected significant aerosols. However, debate is ongoing about the potential of vitrectomy to be aerosol or droplet generating during surgery in humans.

In this study, we investigated the potential for aerosolization during vitrectomy surgery in both in vivo and ex vivo conditions. The study adhered to the tenets of the Declaration of Helsinki and was approved by the local human research ethics committee at the Royal Victorian Eye and Ear Hospital. As per the ethics committee participant informed consent was not required. Aerosol generation was assessed in 3 sets of experiments. First, vitrectomies (n = 3) in cadaveric sheep eyes were performed in a perspex box closed system (Fig S1, available at www.ophthalmologyretina.org). Five milliliters of 10% fluorescein was diluted into a 500-ml bottle of balanced salt solution-infusion fluid. Three 23-gauge valved ports (Alcon, Inc. Fort Worth, TX) were sited into the sheep eye at the limbus of the instability of ports at the pars plana in a sheep’s eye. The vitrectomy cutter (Alcon Accurus, Alcon Inc. Fort Worth, TX) was inserted and turned on (cut rate, 2500 cuts/minute) for 10 minutes. Fluid–air exchange and air–gas exchange (using a vent) were performed. The perspex box was removed for analysis of any fluorescein droplet deposition using photographs captured with an iPhone 8 (Apple, Inc. Cupertino, CA) and cobalt blue filter in a 3-dimensional—printed custom housing unit (Supplemental Fig 1D). Second, a particle counter (3016-IAQ; Lighthouse, Fremont, CA) was used to quantify the number of aerosolized particles of specific sizes (0.3 μm, 0.5 μm, 1.0 μm, 2.5 μm, 5.0 μm, and 10 μm) within the Perspex box during sheep eye vitrectomy. Particle counting also was performed during open-air vitrectomy, with the cutter tip submerged and turned on in a balanced salt solution-filled 40-mm gallipot. Third, the same particle counter was used to measure aerosolized particles during standard vitrectomy surgery in 18 patients (25-gauge Alcon Constellation valved vitrectomy system with a cut rate of 5000 cuts/minute). The counter was positioned above the drape 30 cm from the operated eye at a level plane on a tray between the primary and assisting surgeons. Surgery was performed under regional anesthesia, and patients wore a Hudson facemask with low-flow oxygen (<2 l/minute). Particle recordings were obtained at standardized time points: before draping, after draping, during vitrectomy, during fluid–air exchange, during gas–air exchange, after port removal, and after drape removal. The ocular surface was coated with HPMC-PAA gel (Alcon, Inc. Fort Worth, TX) mixed with balanced salt solution. An empty operating room was used as a negative control; a water spray mist at 30 cm and loud talking into the particle counter served as positive controls. Calibration was performed before each surgery. Mean paired comparison and repeated-measures analyses of variance were performed as appropriate.

No fluorescein-stained droplets were detectable on the inside of the perspex box after the sheep eye vitrectomy. Similarly, no significant change was found in mean particle counts before or during sheep eye vitrectomy: 64.5 ± 20.5 particles/m³ versus 47.3 ± 23.6 particles/m³ (P = 0.46) for the smallest 0.3-μm particles and 2.5 ± 0.7 particles/m³ versus 1.67 ± 1.5 particles/m³ (P = 0.47) for the largest 10-μm particles, respectively (Supplemental Fig 2, available at www.ophthalmologyretina.org). However, when the cutter was operated externally (open-air system), the particle levels increased, particularly for the smallest particle of 0.3 μm (141.3 ± 111.5 particles/m³ vs. 61.0 ± 25.1 particles/m³; P = 0.06) and 1.0 μm (20.0 ± 12.5 particles/m³ vs. 61.0 ± 24.1 particles/m³; P = 0.06), although this did not reach statistical significance.

Particle counts during routine human vitrectomy surgeries were lower than predraping levels for all particle sizes (P < 0.05 for all particle sizes except for the 10-μm particles), and repeated measurements during the surgeries did not differ significantly with time or specific intraoperative manoeuvres (Fig 1). Mean concentrations of the largest particles (10 μm), which have been suggested potentially to be infective respiratory droplets, were 24.1 ± 8.4 particles/m³ after draping and 14.4 ± 7.1 particles/m³ during vitrectomy (P < 0.0001). Interestingly, an increase in particle concentration was noted from the end of the procedure to after drape removal (P < 0.05 for all particle sizes). At all stages during surgery, concentrations of all particles were lower than the levels recorded for the positive controls of spray mist or talking into the counter.

To our knowledge, this is the first study to quantify aerosols and droplets levels generated during human vitrectomy surgery in real-world conditions. The results of all 3 experiments are consistent with previous ex vivo vitrectomy and phacoemulsification studies demonstratinig that although the vitrectomy cutter is a high-speed device, surgery using valved ports is unlikely to generate significant aerosolization. However, when used in open-air conditions inside a gallipot, a vitrectomy cutter may cause a slight increase in particle concentration.

Interestingly, particle measurements obtained before draping, particularly the largest particle sizes, were significantly higher than in an empty operating room (negative control) and during all stages of surgery (P = 0.02 for 10-μm particles; Fig 1). We hypothesize that this may be the result of the movement of personnel in the operating room before each surgery, which seems to increase particle dispersion. Additionally, the use of a nonocclusive oxygen mask by the patient may be a source of aerosol generation before draping and after drape removal.

The results of this study demonstrate that the vitrectomy component of vitrectomy surgery, when performed under regional
anesthesia with valved ports, does not increase aerosol or droplet counts significantly around the surgical field. However, careful removal of the surgical drape is advised because removal seems to increase particle dispersion. It is possible that suctioning underneath the drape, or the use of a surgical mask for the patient and avoidance of an oxygen mask, could reduce the accumulation of respiratory particles under the drape and their dispersion at the time of drape removal. We did not test whether nonvalved port use is associated with aerosolization, although findings from open-air use of the cutter indicate that some particle generation may take place. In addition, because we did not examine the transmissibility of SARS-CoV-2 from aerosolized ocular fluids or test aerosol generation under general anesthesia, definitive conclusions regarding the safety of vitrectomy surgery cannot be made. However, on the basis of the evidence presented herein, we consider the risk to be very low.

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No animal subjects were included in this study.

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Abbreviations and Acronyms:
AGP = aerosol-generating procedure; COVID-19 = coronavirus disease 2019; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

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Familial amyloidosis is an inherited disorder that involves amyloid deposition in various tissues and organs. The most common mutation is in transthyretin (TTR) protein, which carries thyroxine and vitamin A. Transthyretin is synthesized mainly in the liver, but also in the retinal pigment epithelium and choroid plexus. Patients with amyloidosis TTR (ATTR) most frequently have neurological and cardiac involvement. However, ocular involvement can be the presenting manifestation. This is a case report of a patient diagnosed with ATTR with ocular involvement and a characteristic OCT pattern. This is the second documented case reported of ocular amyloidosis and this OCT pattern. 

This study was approved by the Moorfields Eye Hospital institutional review board. The protocol adhered to the tenets of the Declaration of Helsinki, and informed consent from the patient was obtained. A 69-year-old White British man sought treatment at the uveitis clinic at Moorfields Eye Hospital in March 2017 with significant bilateral visual deterioration. The patient had a history of bilateral vitritis since 2010 and previous bilateral vitrectomies. Patients with amyloidosis TTR (ATTR) most frequently have neurological and cardiac involvement. However, ocular involvement can be the presenting manifestation. This is a case report of a patient diagnosed with ATTR with ocular involvement and a characteristic OCT pattern. This is the second documented case reported of ocular amyloidosis and this OCT pattern. 

At presentation, his best-corrected visual acuity, tested with a logarithm of the minimum angle of resolution chart, was 0.60 bilaterally, and the intraocular pressure was within normal limits. Anterior segment examination showed bilateral mild anterior chamber activity, but no abnormalities were seen in the conjunctiva, cornea, iris, pupil, or trabecular meshwork. Dilated funduscopy in the right eye revealed 2 inactive paravascular scars that had been noted previously, vitreous opacities, and blot hemorrhages in the retinal periphery. The left eye harbored an epiretinal membrane and vitreous strands. Fundus fluorescein angiography in the right eye showed vascular staining and blocking defects corresponding to retinal hemorrhages. Bilaterally, peripheral hypofluorescence, resulting from capillary nonperfusion, was present. OCT in the right eye showed subtle thickening of the internal limiting membrane (ILM) with 2 paravascular scars. However, in the left eye, retinal surface deposits with a needle-shaped pattern extending from the ILM to the vitreous were present (Fig 1).

Because he experienced recurrence of the vitritis, we performed another right-eye vitreous biopsy that showed eosinophil amorphous material, consistent with amyloid (Congo red staining and green birefringence), but no evidence of lymphoma or malignancy. Subsequently, we referred the patient to the National Amyloidosis Centre, where he was diagnosed with ATTR associated with the V30MTR variant (late-onset) with cardiac involvement and small-fiber neuropathy.

Three months later, best-corrected visual acuity was 0.47 bilaterally and OCT of the left eye revealed slight progression of the previous findings. In January 2019, the patient was referred again because he had increased floaters in his left eye. On examination, no active inflammation was found, but persistent left eye vitreous strands were found, accounting for his visual symptoms. A further vitrectomy in the left eye was undertaken for visual improvement, and this was achieved. OCT of the right eye showed persistent mild ILM thickening, and OCT of the left eye showed persistent retinal surface depositions, as shown in Figures 2 and 3 (available at www.ophthalmologyretina.org).

Familial amyloidosis was described first by Andrade1 in 1952 in a group of patients with the ATTR changing valine at amino acid 30 to methionine (Val30Met) mutation. The amyloidogenic mutated proteins identified are TTR, apolipoprotein A-I, and gelsolin. The ATTR Val30Met is the most common mutation in the TTR gene and accounts for the substitution of methionine for valine at position 30 of protein ATTR.2

The most prevalent ocular manifestation in ATTR is the presence of vitreous amyloid deposits causing visual deterioration. The vitreous involvement usually is bilateral, but asymmetric.6 Vitrectomy may improve the visual acuity, but the amyloid deposits may recur. Other ocular features are abnormal conjunctival vessels, neuroretrochoriitis, deposits on the pupillary border and lens, glaucoma, and retinal vein occlusion.

Our patient demonstrated bilateral vitreous opacities and retinal ischemia, but no glaucoma and no conjunctival, corneal, or pupillary involvement. Bilaterally, the vitreous opacities regressed after the first vitrectomy, but recurred after some years, and the patient underwent a further vitrectomy, which gave the diagnosis

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**Characteristic Needle-Shaped Pattern Seen on OCT in a Patient with Ocular Amyloidosis**

Familial amyloidosis is a genetic disorder that affects the proteins in the body, leading to the formation of abnormal protein deposits called amyloid. These deposits can cause damage to various tissues and organs, including the eye. In this case, the patient had bilateral vitreous opacities and retinal surface depositions, as shown in Figures 2 and 3 (available at www.ophthalmologyretina.org).

At presentation, his best-corrected visual acuity, tested with a logarithm of the minimum angle of resolution chart, was 0.60 bilaterally, and the intraocular pressure was within normal limits. Anterior segment examination showed bilateral mild anterior chamber activity, but no abnormalities were seen in the conjunctiva, cornea, iris, pupil, or trabecular meshwork. Dilated funduscopy in the right eye revealed 2 inactive paravascular scars that had been noted previously, vitreous opacities, and blot hemorrhages in the retinal periphery. The left eye harbored an epiretinal membrane and vitreous strands. Fundus fluorescein angiography in the right eye showed vascular staining and blocking defects corresponding to retinal hemorrhages. Bilaterally, peripheral hypofluorescence, resulting from capillary nonperfusion, was present. OCT in the right eye showed subtle thickening of the internal limiting membrane (ILM) with 2 paravascular scars. However, in the left eye, retinal surface deposits with a needle-shaped pattern extending from the ILM to the vitreous were present (Fig 1).

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