

# News in Review

COMMENTARY AND PERSPECTIVE

## TRAUMA

### Toy Gun Eye Injury in Kids Is Up

**MIRRORING OTHER FINDINGS IN RE-**cent years, data from a French study suggest that the incidence of ocular trauma in children related to foam bullets and other types of projectiles from toy guns has risen over the past decade.<sup>1</sup>

**Methodology.** The researchers set out to examine the estimated annual incidence and severity of toy gun injuries seen at the Rothschild Foundation Hospital in Paris. They reviewed every case involving eye trauma related to use of nonpowder toy guns—including paintball guns, air guns, BB guns, airsoft guns, and foam bullet and dart blasters—treated at their eye emergency department between January 2010 and June 2022.

In all, 304 pediatric patients were seen during the study time frame, the majority (234) of whom self-reported as male, and the mean age was 16 years. The researchers reported 151 ocular injuries from foam projectiles, 110 from BB or airlift guns, 31 from paintball guns, and 12 from “unspecified” toy guns.

**Worrying trends.** The scientists said the data show a rise in the incidence of injuries from foam projectiles between 2014 and 2022. Meanwhile, during the same eight-year span, the mean age of pediatric patients injured by foam projectiles decreased from age 16 in 2014 to age 10 in 2022.

“We were surprised by the trend



**TREACHEROUS TOYS.** Eye injuries from foam projectiles can be serious.

showing that kids are being injured younger and younger. We even recorded a trauma in a one-month-old child,” said lead study author Alexandre Dentel, MD.

**The injuries.** He said that heading into this research, he and his colleagues underestimated the proportion of young people injured by foam “Nerf-type guns.” Foam projectile-related ocular trauma led to 51 intraocular hemorrhages, 45 corneal injuries, 22 iris injuries, 19 retinal injuries (including two retinal tears and one retinal detachment), 12 cases of ocular hypertension, three cataracts, and two open-globe injuries, the authors reported.

Dr. Dentel said that most cases of corneal abrasions “generally heal well within a few days” when treated with antibiotic eye drops. “For management, particular attention must be paid to intraocular pressure and examination of the central and peripheral retina—retinal lesions are quite frequent, such as Berlin’s edema [retinal swelling related to blunt trauma] and retinal breaks,” Dr. Dentel said. He noted that some of the more severe injuries involved chronic intraocular hypotony, includ-

ing some that “led to total blindness by phthisis bulbi.”

**A global problem.** While the study focused on one medical center in France, it reflects a growing concern among ophthalmologists in the United States and other countries over the widespread dangers posed by toy guns.<sup>2</sup>

Erin Shriver, MD, at the University of Iowa Hospitals and Clinics in Iowa City, who was not involved with the Paris research, said, “The term ‘toy guns’ gives one a sense that these guns are harmless when in fact they can cause significant ocular injuries and even result in permanent vision loss.”

She said there should be a national public awareness campaign on the risk of injuries from guns that shoot foam bullets, air soft guns (“soft” is a misnomer), and gel pellet guns.

“All children and adults should wear eye protection when using or when near others who are using nonpowder projectile weapons,” Dr. Shriver said, adding that parents should supervise children who are using toy weapons.

Dr. Dentel echoed those thoughts, saying that responsibility rests on the shoulders of toy manufacturers, too—

that they should supply protective goggles with each toy weapon and include images of children wearing goggles in their ads that promote toy guns.

—Brian Mastroianni

1 Dentel A et al. *JAMA Ophthalmol.* 2023;141(6):604-605.

2 Cohen S et al. *Eur J Pediatr.* 2023;182(3):1099-1103.

Relevant financial disclosures: Dr. Dentel—None. Dr. Shriver—None.

## GLAUCOMA

# Two Lipids Linked to Glaucoma Risk

**ANALYZING DATA FROM THOUSANDS** of study participants, researchers from Harvard and Icahn School of Medicine at Mount Sinai found that higher levels of two lipids, diglycerides and triglycerides, were associated with an increased risk of glaucoma. Specifically, they

report that lipid metabolism is associated with primary open-angle glaucoma (POAG)—and the association was greater in cases of paracentral visual loss.<sup>1</sup> Whether or not statins could help treat glaucoma remains unclear, said study author Louis M. Pasquale, MD, at Mount Sinai Health System.

“POAG, particularly in the subset [of people] with early paracentral loss, has a metabolic signature focused on lipid and mitochondrial metabolism,”

## RETINA

# Vitreous Biomarkers May Flag Early Alzheimer Disease

**EYE FLUIDS MAY ONE DAY HELP DIAGNOSE SOME BRAIN** diseases earlier, according to researchers at Boston University Medical Center and colleagues who report a correlation between certain vitreous biomarkers and neurodegenerative changes in postmortem brain tissue. The findings, they report, may one day help diagnose conditions like Alzheimer disease in the early stages.<sup>1</sup>

“While prior reports have shown that loss in the ganglion cell layer of the retina reflect dementia both pathologically and by imaging with OCT, this is the first study showing that biomarkers in eye fluid, specifically the vitreous, reflect brain pathology,” said study author Manju L. Subramanian, MD.

“Our findings provide further evidence to support the potential role of vitreous biomarkers in early diagnosis and prognostication of diseases like Alzheimer disease and chronic traumatic encephalopathy [CTE],” she said.

**Finding a correlation.** The researchers examined the postmortem brains and vitreous of 41 people who had Alzheimer disease (n=7), CTE (n=15), both Alzheimer disease and CTE (n=10), and no indication of neurodegenerative disease (n=9). Participants in the latter group, like all participants, had survived repetitive head injury (due to sports, military service, and physical violence, among other factors) but showed no signs of neurodegenerative disease, and served as the control.

The researchers measured levels of amyloid- $\beta$ , eotaxin-1, neurofilament light chain, phosphorylated tau, and total tau proteins—vitreous humor biomarkers previously correlated with impaired cognitive function.<sup>1,2,3</sup> The vitreous total tau was significantly higher in the only-Alzheimer group (p=0.08) and the only-CTE group (p=0.08) compared with the Alzheimer disease-CTE combined group and the control group.

**Surprise finding.** Vitreous neurofilament light chain

was not associated with confirmed neuropathological diagnosis, but it was associated with CTE. Specifically, it was linked with low stage CTE versus no CTE, as well as low stage CTE versus high stage CTE.

“While we hypothesized that proteins in the vitreous would be significantly altered in those with Alzheimer disease, we were surprised to find that neurofilament light chain is significantly associated with CTE, a neurological disorder seen in some professional athletes, military personnel, or anyone with a history of traumatic brain injury,” Dr. Subramanian said.

**Up next.** The researchers plan to investigate the aqueous as a potential reservoir for protein markers for Alzheimer disease. They also want to validate these biomarkers using more traditional Alzheimer disease diagnostic modes, such as MRI, PET scan, and cerebrospinal fluid in living patients.

**Working toward earlier diagnosis.** “Alzheimer disease pathological changes occur in the brain 10-20 years prior to the onset of symptoms, at which point it’s often too late for therapeutic drugs to have any meaningful effect. This is why finding a screening test for Alzheimer disease in the pre-symptom phase is so important,” Dr. Subramanian said.

Currently, Alzheimer disease and CTE can be confirmed only after a patient dies and an autopsy of the brain is performed, so the study findings could potentially shift diagnosis from postmortem analyses to using noninvasive diagnostic criteria revealed in certain biomarkers. “If eye biomarkers become the method of Alzheimer disease screening, then one may consider screening during a yearly eye exam or cataract surgery,” Dr. Subramanian said.

“The eye is certainly a window to our brain,” she added. “Our findings confirm this connection through the eye’s reflection of pathological changes in the brain for both Alzheimer disease and CTE.” —Miriam Karmel

1 Vig V et al. *J Alzheimers Dis.* 2023;93(3):1181-1193.

2 Wright LM et al. *J Alzheimers Dis.* 2019;68(4):1429-1438.

3 Subramanian ML et al. *Alzheimers Res Ther.* 2020;12(1):111.

Relevant financial disclosures: Dr. Subramanian—None.

said Dr. Pasquale, who hopes the findings shine a light on POAG pathogenesis and inform strategies that could help prevent glaucoma.

**Methodology.** In this nested case-control study to identify metabolites associated with POAG, the investigators analyzed blood sample data from more than 80,000 U.S. health professionals participating in the long-term Nurses' Health Studies and Health Professionals' Follow-Up Study. They identified individuals who went on to develop POAG during the course of the studies. In all, 599 cases of POAG were documented and compared to 599 matched controls who did not develop glaucoma.<sup>1</sup> Then, researchers examined data based on the metabolomic profiling of blood samples from all participants. The profiling used liquid chromatography tandem mass spectrometry to identify 369 metabolites associated with glaucoma. By comparing the metabolite profiles of individuals with POAG to those without the condition, the researchers aimed to identify potential biomarkers for glaucoma.

After adjusting for risk factors, they found that five individual lipids of the 369 metabolites demonstrated a nominal adverse association with POAG. Specifically, higher levels of diglycerides and triglycerides were associated with an increased risk of POAG (whereas higher levels of carnitines were associated with a reduced risk of POAG).

For comparison, they turned to data from the UK Biobank, in which 168 metabolites were measured using nuclear magnetic resonance spectroscopy in plasma samples from 2,238 prevalent glaucoma cases (a random subset of more than 100,000 participants) and 44,723 controls.

In all cohorts, "higher levels of diglycerides and triglycerides are adversely associated with glaucoma, suggesting that they play an important role in glaucoma pathogenesis," the authors wrote.



**DIGLYCERIDES AND TRIGLYCERIDES.** *Certain lipids may play an important role in glaucoma pathogenesis.*

"Achieving replication for our findings in the UK Biobank sets our work apart from other studies," Dr. Pasquale said.

**Surprising finding.** Researchers went one step further by stratifying POAG into cases with peripheral vision loss and those with paracentral vision loss. The metabolomic signature of dysregulated lipid metabolism and mitochondrial function was more profound in patients with early paracentral visual loss compared to those with peripheral vision loss.

"This was surprising because the sample size for this subset of POAG patients was small, and the number of retinal ganglion cells affected in early paracentral loss is considerably smaller compared to the overall number of retinal ganglion cells in the retina," Dr. Pasquale said.

**Treatment.** When asked about the possibility of using dyslipidemia-targeting treatments, such as statins, to lower the risk of glaucoma, Dr. Pasquale said, "The dyslipidemia we uncovered in this study is complex and is not necessarily corrected by statins, which are designed to lower LDL cholesterol."

He also said that which lipoproteins are carrying the lipids adversely associated with POAG remain to be determined.

**Study limitations.** The study population had a high percentage of White participants, so the findings may not be generalizable to other populations with

different race and ethnicity compositions, the authors wrote.

**Looking ahead.** "Our findings can help shed light on POAG pathogenesis and inform preventive strategies," said Dr. Pasquale. But, he said, many potentially unidentified metabolite associations with POAG are unexplored.

—Christos Evangelou, PhD

1 Zeleznik OA et al. *Nat Commun.* 2023;14(1):2860.

**Relevant financial disclosures:** Dr. Pasquale—National Eye Institute: S; Research to Prevent Blindness (NYC): S; The Glaucoma Foundation: S.

COMPREHENSIVE

## Air Pollution Can Take a Toll on Eyes

### THE DEVELOPMENT OF AUTOIMMUNE

eye diseases is typically attributed to genetic factors. But now, a comprehensive review of more than 30 studies by researchers from Anhui Medical University and Shanghai Jiao Tong University, in China, shows a correlation between environmental factors and autoimmune eye diseases, including uveitis, Graves ophthalmopathy, ocular allergic disease, glaucoma, and diabetic retinopathy. Of greatest concern is exposure to particulate matter and tobacco smoke, insufficient sun exposure, and high heat.<sup>1</sup>

**Particulate matter.** One key finding from the review is that "long-term exposure to fine and ultrafine particulate matter, such as PM<sub>2.5</sub> and PM<sub>0.1</sub>, from air pollution can activate inflammatory cells and reduce blood flow in the retina, exacerbating autoimmune eye diseases," said Tsai-Chu Yeh, MD, at Taipei Veterans General Hospital, who was not involved with the review but has published research on environmental factors and eye health.

**Excessive tobacco smoke.** Dr. Yeh noted that in vitro studies of cells from Graves ophthalmopathy patients found increased fibroblast proliferation in the presence of tobacco smoke. She said, "Environmental tobacco smoke exposure promotes fibroblast activity and affects the extracellular matrix."

**Heat and sunlight.** The review also found that a lack of vitamin D in the

eye due to insufficient sun exposure may contribute to autoimmune eye disease, said Dr. Yeh. In one of the studies reviewed, “the finding that the eye may have the ability to synthesize and utilize vitamin D3 locally when exposed to ultraviolet B radiation from sunlight is interesting,” she said. “This discovery challenges the traditional belief that the primary source of vitamin D is through dietary supplementation or synthesis in the skin.”

Dr. Yeh added that the study “highlights the therapeutic potential of an active form of vitamin D in attenuating the progression of autoimmune eye diseases by suppressing Th17 responses and inhibiting IL-17 production.”

**Heat.** Th17 cells come into play with exposure to high temperatures, as



**NEW YORK, NEW YORK.** In June 2023, the Statue of Liberty appears shrouded in smoke from the Canadian wildfires.

well. The authors wrote that heat stress contributes to the promotion of Th17 cells and activation of neutrophils, which can aggravate autoimmune eye disease.

**Clinical take-home.** People who are most at risk have preexisting autoimmune eye diseases and reside in areas

with high pollution levels or are exposed to indoor air pollutants, including environmental tobacco smoke, said Dr. Yeh. She suggested that clinicians educate patients about the potential impact of air pollution and meteorological factors on their eye health and emphasized “avoiding outdoor exposure during times of high pollution or extreme weather conditions.”

Dr. Yeh hopes the study findings encourage eye specialists to collaborate with

each other, other health care professionals, and public health authorities to advocate for improved air quality regulations and awareness campaigns.

—Patricia Weiser, PharmD

1 Cao F et al. *Environ Res.* 2023;231(Pt 1):116116.  
**Relevant financial disclosures:** Dr. Yeh—None

See the financial disclosure key, page 8. For full disclosures, including category descriptions, view this News in Review at [aao.org/eyenet](http://aao.org/eyenet).



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