

# News in Review

COMMENTARY AND PERSPECTIVE

## UVEITIS

### FDA Approves Insert for Chronic Posterior Uveitis

#### AN INTRAVITREAL INSERT THAT

slowly releases fluocinolone acetonide (FAi) to control inflammation associated with chronic, noninfectious posterior uveitis has been approved by the FDA. The novel drug delivery system was developed to break the treatment-quiescence-recurrence-treatment cycle that is a hallmark of the disease.

“For the first time, we’ll have an injectable delivery system that can be implanted in the clinic and can release the drug for up to three years,” said Glenn J. Jaffe, MD, at Duke University in Durham, North Carolina. Moreover, the implant will deliver “consistent dosing without the peaks and valleys [seen with] local corticosteroids,” he said. Dr. Jaffe is lead author of a report on the 12-month safety and efficacy results of a phase 3 FAi clinical trial.<sup>1</sup>

**A step forward.** FAi, which will be brought to market under the brand name Yutiq (EyePoint Pharmaceuticals), builds on the strengths of earlier implants. Ozurdex (Allergan), an injectable insert containing 0.7 mg dexamethasone, lasts about three months, whereas Yutiq lasts up to three years. Retisert (Bausch + Lomb) is a long-lasting fluocinolone acetonide implant, but it requires surgical implantation, whereas Yutiq can be implanted via an in-office procedure.



**BIRDSHOT.** This ultra-widefield image is of a 45-year-old patient with central retinal vein occlusion and birdshot chorioretinopathy (HLA-A29+).

**Study specifics.** Dr. Jaffe and his colleagues enrolled 129 people with recurrent noninfectious posterior uveitis. Subjects were randomly assigned to FAi (n = 87) or sham injection (n = 42). In the FAi group, 0.18 mg of the drug was delivered via the implant, which was injected through the pars plana into the vitreous cavity of the study eyes using a 25-gauge needle.

**Recurrences.** At 12 months, the FAi recurrence rate was significantly lower than that observed in the sham cohort (28% vs. 91%, respectively). The median time to first recurrence was 378 days in FAi eyes, compared to 70.5 days for sham eyes.

Recurrences were treated as needed. Through 12 months, 19% of the FAi group and 40% of the sham cohort had at least one adjunctive systemic treatment. Topical corticosteroid treatment was prescribed to 21% of FAi eyes and to 48% of sham eyes.

These findings confirmed what Dr. Jaffe had observed in 11 patients in an earlier study.<sup>2</sup> “What we saw was that the eyes remained quiet over a two-year period without recurrences. I was

frequently able to get patients off systemic medications and drops without additional injections,” he said.

**Additional findings.** Fewer FAi eyes lost 15 or more letters in best-corrected visual acuity (VA) than did sham eyes (14% vs. 31%, respectively). In addition, VA was preserved or improved more often with FAi.

With regard to intraocular pressure (IOP), FAi eyes were more likely to experience pressures greater or equal to 25 mm Hg or 30 mm Hg. More FAi eyes than sham eyes required IOP-lowering medication through 12 months, but the rate of surgical intervention was similar in the two cohorts.

Eyes treated with FAi were at greater risk of developing cataracts than were those in the sham cohort (33% vs. 12%, respectively). Of the 42 FAi eyes that were phakic at baseline, 14 (33%) required cataract surgery after 12 months.

**Assessing risks and benefits.** Although Dr. Jaffe did not downplay the cataract findings, he noted that cataracts are a known complication of uveitis treatment. “People on steroids

for a long enough period of time will eventually develop cataracts. I'd rather not have cataract, but if I can control the inflammation with an implant and keep patients seeing well, it's a worthwhile trade-off," he said.

As part of this assessment of risks and benefits, he referred to the implant's effect on recurrence rates, "which will help prevent secondary complications that can lead to vision loss."

—Miriam Karmel

1 Jaffe GJ et al. *Ophthalmology*. Published online Oct. 24, 2018.

2 Jaffe GJ et al. *Ophthalmology*. 2016;123(9):1940-1948.

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## DRUG SIDE EFFECTS

# Urology Rx Linked to Maculopathy

## RESEARCHERS AT EMORY UNIVERSITY

report a unique maculopathy associated with chronic exposure to pentosan polysulfate sodium (PPS), a drug approved by the FDA in 1996 to treat discomfort associated with interstitial cystitis (IC).<sup>1</sup>

**Previously unreported.** The previously unreported maculopathy is thought to primarily affect the retinal pigment epithelium (RPE). It may be mistaken for other well-known macular disorders such as pattern dystrophy or age-related macular degeneration (AMD).

"Hundreds, if not thousands, of patients diagnosed with pattern dystrophy and AMD since the drug's approval may actually have a preventable drug-associated maculopathy," said senior author Nieraj Jain, MD, at Emory Eye Center in Atlanta.

**Detective work.** After seeing a string of patients with similar pigmentary macular changes and a past history of IC, the researchers culled their clinic's electronic medical records for

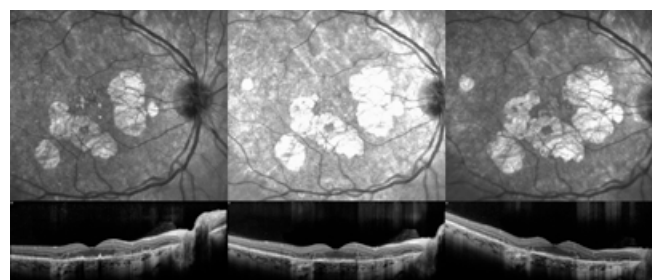
PPS. Within the prior two years, six patients had previously been identified by the authors for an unknown pigmentary maculopathy. "That makes it one of the more common conditions that we saw in our clinic of hereditary retinal diseases," Dr. Jain said. (Since study publication in November 2018, the number of affected patients has grown to 15.)

**Findings of note.** The new entity mimics hereditary pattern dystrophies, yet none of the patients had a family history of hereditary retinal degeneration, and none showed a pathogenic genetic mutation. Findings on fundus autofluorescence imaging were quite prominent, yet the fundus exam revealed only subtle paracentral hyperpigmentation at the level of the RPE, with surrounding pale yellow deposits.

Median exposure to PPS was 186 months; most patients reported trouble reading and experienced prolonged dark adaptation despite generally well-preserved visual acuity.

**Clinical implications.** "PPS-associated maculopathy has a permanent spot on our differential diagnosis for atypical pigmentary maculopathies," said lead author William Pearce, MD, at the Georgia Eye Institute in Savannah. "It is important that clinicians are aware of this association when evaluating patients with macular dystrophy or degeneration, as it could easily be overlooked due to the subtle findings."

**Looking ahead.** Dr. Jain stressed that causality must be confirmed. Nevertheless, he advises his affected patients to stop taking PPS. Should a cause and effect be determined, was there anything about the drug-approval process that could have prevented this? "Probably not, given that these patients were on the drug for years before manifesting visual symptoms," said Dr. Jain. "On the other hand, as pharmaceuticals become increasingly complex, we should rec-



**EVIDENCE.** These images, taken over a two-year period in one patient, demonstrate the progressive nature of the patchy RPE atrophy noted in more severe cases of PPS-associated maculopathy.

ognize the vital role that clinicians play in the postmarket surveillance of novel therapies." —Miriam Karmel

1 Pearce WA et al. *Ophthalmology*. 2018;125(11):1793-1802.

**Relevant financial disclosures**—Drs. Jain and Pearce: None.

## NEURO-OPHTHALMOLOGY

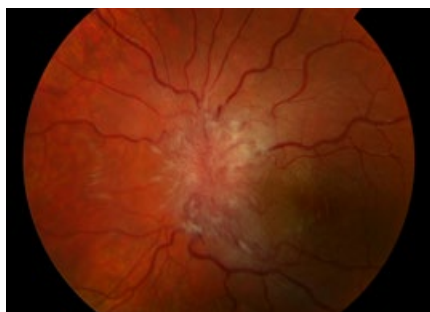
# Burden of IIH Rising

**BRITISH RESEARCHERS HAVE DOCUMENTED** a sharp uptick in the number of cases of idiopathic intracranial hypertension (IIH) in England—and a concomitant rise in the costs of treatment.<sup>1</sup>

From Jan. 1, 2002, to Dec. 31, 2016, the incidence of IIH rose by 108%, and the number of hospital visits soared by 442%, the researchers found. "The overwhelming increase in patients diagnosed with IIH, and the amount of hospital visits over the study period, was surprising," said Susan P. Mollan, MBChB, FRCOphth, at University Hospitals Birmingham in the United Kingdom.

**What sparked the study?** "We had been tasked by the Association of British Neurologists to set up a special interest group that was multiprofessional to write practical guidelines on the management of IIH.<sup>2</sup> But there was little data showing the demographic shifts and [documenting] how patients were accessing care," Dr. Mollan said.

**Findings.** Dr. Mollan and her colleagues extracted data on hospital activity in England. After applying exclusion criteria, they confirmed that 23,182 new cases of IIH were diagnosed from 2002-2016, with an incidence of 2.26



**PAPILLEDEMA.** Severe papilledema secondary to IIH in a young woman.

per 100,000 in 2002, rising to 4.69 per 100,000 in 2016. The overall incidence was higher in women (7.7 per 100,000) than in men (1.6 per 100,000).

**Treatment.** Hospital admissions rose from 1,315 per year in 2002 to

7,123 per year in 2016. More than half the study cohort had a single hospital episode and no additional hospital care in the year following diagnosis. However, 37.8% had repeat hospital activity. Most patients (91.6%) were managed medically; 7.6% had a shunt procedure; 0.68% underwent bariatric surgery; and 0.07% underwent optic nerve sheath fenestration.

**Costs.** The cost of IIH-related hospital care climbed from £9.2 million to £49.9 million during the study period—and the researchers estimated that, if this trend continues, the cost will total £462.7 million in 2030.

**More surprises.** The researchers uncovered two additional surprises: For the first time, IIH in adults was associ-

ated with poverty and adverse obstetric outcomes. More than half of cases occurred in socioeconomically deprived areas, and pregnant women with IIH were more likely to undergo cesarean sections compared to pregnant women in the general population.

**Wake-up call.** Overall, the results confirm that the newly developed guidelines<sup>2</sup> are needed, Dr. Mollan said. “Better strategies for these patients are required when they access emergency care.”  
—Jean Shaw

1 Mollan SP et al. *Eye*. Published online Oct. 24, 2018.

2 Mollan SP et al. *J Neurol Neurosurg Psychiatry*. 2018;89(10):1088-1100.

Relevant financial disclosures—Dr. Mollan: None.

## RETINA

# Mediterranean Diet Reduces Risk of Advanced AMD

## THE MEDITERRANEAN DIET HAS BEEN FOUND TO

lower the risk of cardiovascular disease and cognitive decline, but relatively few studies have examined its impact on age-related macular degeneration (AMD).

Now, a consortium of European researchers has found that the diet decreases an individual's risk of developing advanced AMD, particularly the dry form of the disease.<sup>1</sup> “We found that participants (55 years of age or older) who have a high adherence to the Mediterranean Diet have a 41% reduced risk of developing AMD,” said lead author Bénédicte M.J. Merle, PhD, at the Université de Bordeaux in Bordeaux, France.

**Rationale.** The Mediterranean Diet provides an abundance of omega-3 fatty acids, lutein, and zeaxanthin, all of which have been found to contribute to retinal health, Dr. Merle pointed out. “The Mediterranean Diet is replete in healthful nutrient-rich foods, such as plant foods and fish. It also limits the consumption of unhealthy foods, such as red and processed meats and savory and salty industrialized products. So, we wanted to assess if patients who adhere to this diet have a reduced risk of developing advanced AMD.”

In addition, she said, “We wanted to go further [than previous studies] by focusing on global nutrition rather than isolated nutrients.”

**Study specifics.** Researchers with the EYE-RISK project ([www.eyerisk.eu](http://www.eyerisk.eu)) investigated the associations between diet and incidence of advanced AMD in a large sample from two European population-based

prospective studies, the Alienor Study and the Rotterdam Study 1 (RS-1). Participants in the Alienor Study (n = 550) were 73 years of age or older, and those in RS-1 (n = 4,446) were 55 or older; all were free of advanced AMD at baseline.

**Dietary components.** The researchers evaluated participants' adherence to the full Mediterranean Diet, using a nine-component score that assessed consumption of plant foods (fruits, vegetables, legumes, and cereals), fish, meat, dairy products, alcohol, and the ratio of monounsaturated-to-saturated fatty acids.

**Outcomes.** All told, 155 of the 4,996 participants developed advanced AMD during a mean follow-up of 9.9 years in RS-1 (range, 0.6-21.7 years) and 4.1 years in Alienor (range, 2.5-5.0 years). Those who hewed more closely to the Mediterranean Diet were less likely to develop AMD, despite any regional variations. (For instance, those in RS-1 were more likely to consume dairy, while those in the Alienor Study were more likely to eat vegetables, cereals, and fish.) “Participants from the Alienor and the RS-1 studies had slightly different diets, but the association with AMD incidence was similar [between the two cohorts],” Dr. Merle said.

**The big picture.** Of note, none of the individual food categories was associated with AMD incidence, which highlights the need to assess overall dietary patterns rather than individual components, the researchers said. Additional studies are planned, Dr. Merle said.

—Jean Shaw

1 Merle BMJ et al, for the EYE-RISK Consortium. *Ophthalmology*. Published online Aug. 13, 2018.

Relevant financial disclosures—Dr. Merle: Bausch + Lomb: C; Laboratoires Théa: S.