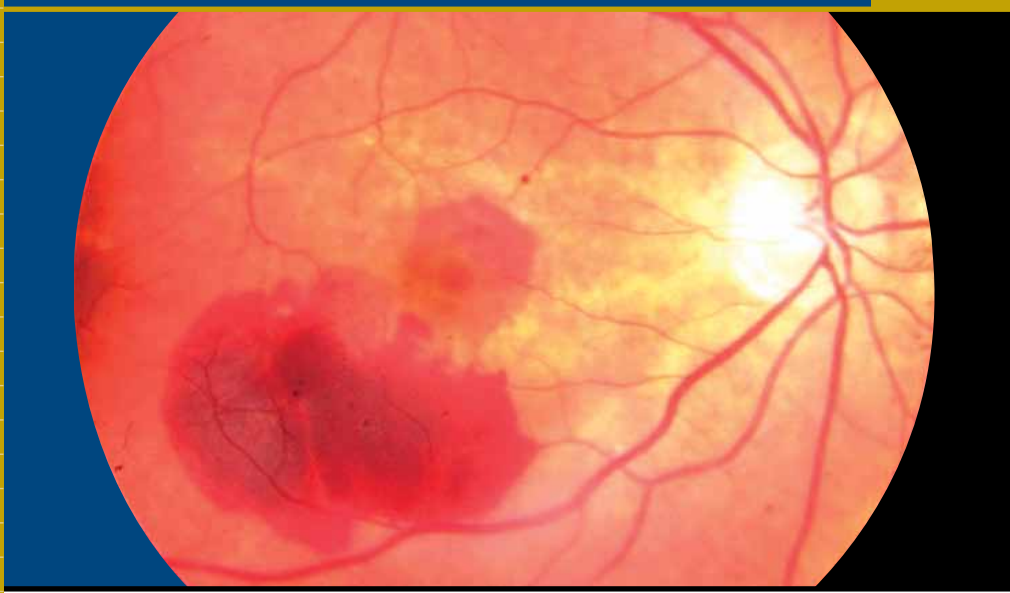
the LIGHT PIPE

Fall 2011



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THE NEWSLETTER OF

GEORGIA RETINA

CATT Trial Review

The Comparison of AMD Treatment Trial (CATT) research group recently released its results, confirming information leaked to the media that bevacizumab (Avastin) and ranabizumab (Lucentis) differ little in preserving visual acuity over one year of treatment in exudative age related macular degeneration (AMD).

Patients receiving monthly injections of bevacizumab gained 8.0 letters of visual acuity after one year, compared with 8.5 letters for ranabizumab according to the study. The two drugs did not differ significantly in this regard. However, there were some differences favoring ranabizumab (Lucentis).

The study actually looked at four treatment groups-bevacizumab or ranabizumab, given either monthly or "as needed" (PRN) on a single masked basis. There were about 300 patients in each arm.

Patients in the PRN groups received injections only when retinal imaging suggested signs of activity. The mean number of doses given was 6.9 and 7.7 for the bevacizumab and ranabizumab groups, respectively.

In comparison to the fixed monthly dosing groups, the as needed groups did slightly poorer on visual outcome with slightly more difference between the groups in favor of ranabizumab, but the difference was not statistically significant.

There were some other differences between the drugs and dosing groups favoring ranabizumab. The most significant was total foveal thickness. Total foveal thickness shrank more, relative to baseline, in the two ranabizumab groups compared with the two bevacizumab groups. A similar trend was

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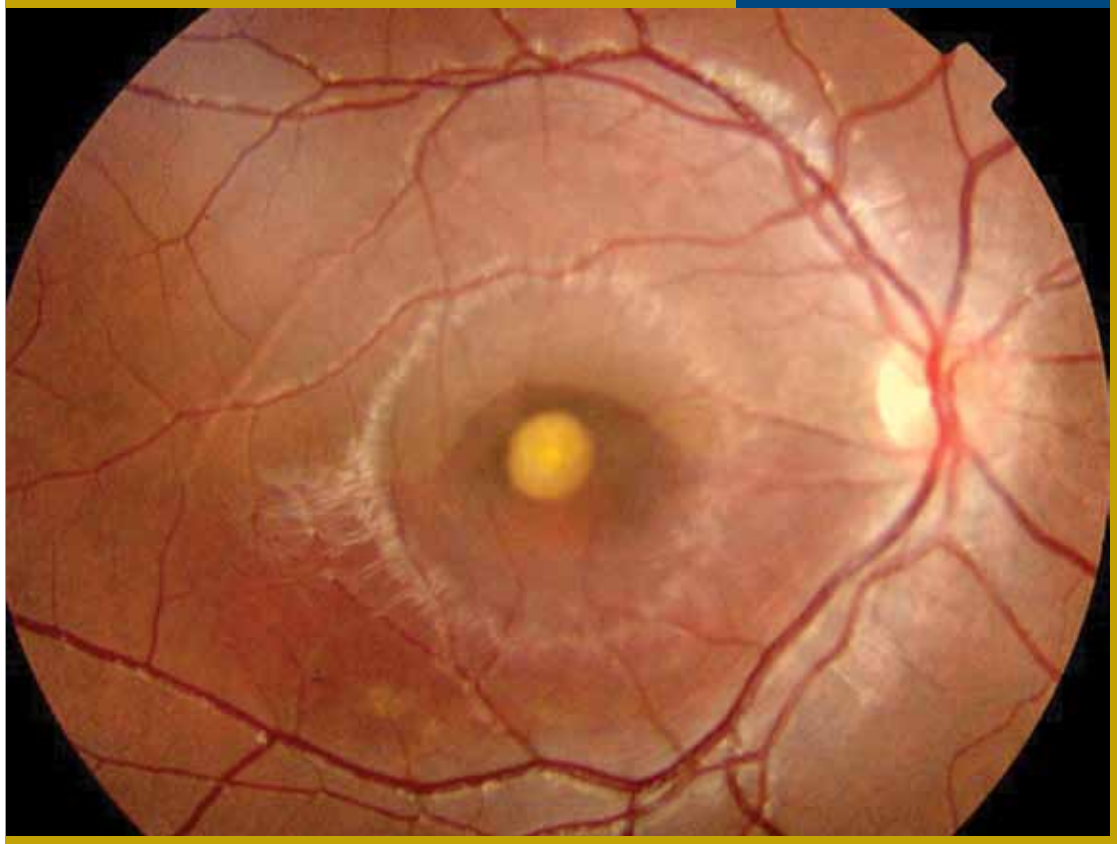

What's your diagnosis?

A 15-year-old African American male presented to a local optometrist when he complained of decreased vision in the right eye. He has no past ocular history and his past medical history is noncontributory. He has two brothers with optic nerve head drusen. The visual acuity was 20/400 OD and 20/20 OS with normal pressures and no afferent pupillary defect. The anterior segment was unremarkable, the fundi are below:

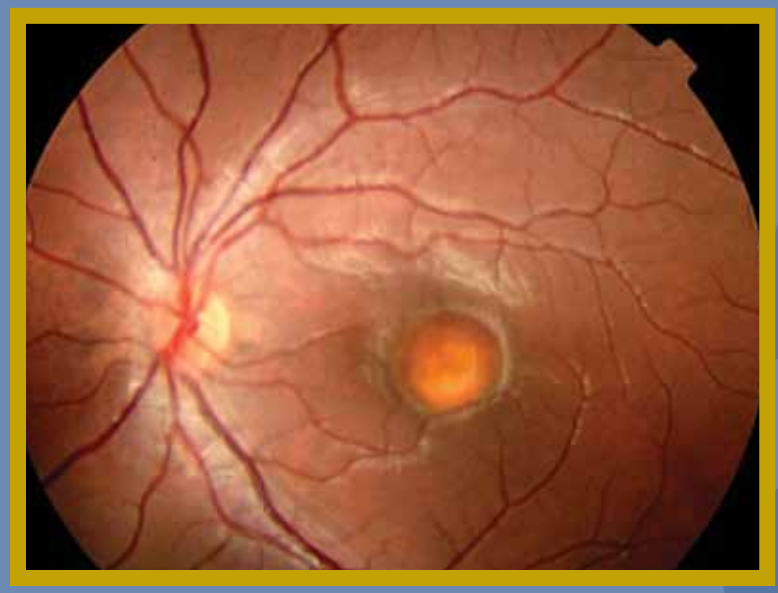

Photo Quiz Answer on page 10

Macula Risk®

A Prognostic Genetic Test for AMD Progression.

Age related macular degeneration is the leading cause of legal blindness in the U.S. for people over the age of 50. The incidence of AMD grows from 1 in 10 people over the age of 60 to more than 1 in 4 people over the age of 75. Most people do not know they have AMD until they start to lose central vision in one eye. Vision loss can happen quickly and without warning; with current treatment it may be arrested and in some cases improved. Therefore, early detection and treatment of AMD is critical for the prevention of blindness.

As we know, frequent monitoring is recommended for those 'at risk'. However, the traditional approach of regular clinical monitoring of patients with early and intermediate dry AMD can be suboptimal, as significant asymptomatic progression may occur between appointments in high-risk individuals. The greatest clinical challenge in AMD is early detection of conversion to wet AMD.

Recent advances in understanding both the highly heritable nature of AMD and the contribution of different genetic variants to risk, combined with the availability of genetic testing, are changing the traditional approach to patient monitoring. Genetics is becoming a strong predictor of the risk of progression of AMD to advanced disease. Genetic testing is a powerful tool that can help the primary eye care professional and the retina specialist move toward the goal of early detection. Such testing may identify individuals in need of heightened monitoring, but should not be to downgrade the level of concern.

Since 2006, genetic studies have identified at least 10 validated genetic risk markers for advanced AMD. These are:

- Complement pathway components, such as complement factor H (CFH) and complement component 3 (C3) involved in amplification of inflammatory signals.

Genetics is becoming a strong predictor of the risk of progression of AMD to advanced disease. Genetic testing is a powerful tool that can help the primary eye care professional and the retina specialist move toward the goal of early detection.

- A gene on chromosome 10, age-related maculopathy susceptibility 2 (ARMS2) and a mitochondrial enzyme, nicotinamide adenine dinucleotide dehydrogenase subunit 2 (ND2), involved in oxidative phosphorylation; retinal oxidative stress may contribute to retinal damage in AMD.
- A tissue inhibitor of matrix metalloproteinase (TIMP3) involved in degradation of extracellular matrix and associated with neovascularization.

The two most important risk markers are CRH and ARMS2.

The doctors at Georgia Retina are now offering to their 'at risk' patients the Macula Risk® genetic test, a prognostic DNA test intended for patients who have a diagnosis of early or intermediate AMD. Macula Risk® identifies those most likely to progress to advanced AMD with vision loss. Macula Risk® is reimbursed by most insurance providers including Medicare. The Macula Risk® test must be ordered by a doctor (ophthalmologists and optometrists) and the patient must have a diagnosis code (ICD-9) for AMD in order to obtain reimbursement. If the patient has no signs of AMD or they have no valid insurance then they will need to pay the laboratory via a check or credit card. We do not recommend testing without an eye examination and a correct diagnosis of early or intermediate AMD. Some patients with positive family histories may elect to self-pay for the Macula Risk® test. The patient sample is a cheek swab taken in our office. Macula Risk® allows us to stratify patients for appropriate monitoring as recommended by the AAO Preferred Practice Patterns.

In addition, people who are at increased risk may benefit from:

- An increased frequency of eye examinations by the eye care professional
- Disease education and 'at-home' Amsler Grid testing
- Preventative eye vitamin therapy
- Lifestyle changes, e.g., smoking cessation, diet modifications
- Early diagnosis and treatment of 'wet' AMD with effective therapies
- Other disease management elements as determined by their doctor

If you have a patient you think might benefit from the Macula Risk® test, please feel free to speak with one of the Georgia Retina doctors to find out more information.

Physician Spotlight

Georgia Retina Physicians Make Atlanta "Top Docs" List

Two of Georgia Retina's physicians, Dr. Scott Lampert and Dr. Michael Jacobson, were recently named Top Doctors by *Atlanta Magazine,* and were featured in their July 2011 Top Doctors issue. In addition, Dr. Jay Stallman appeared on Castle Connolly's Top Doctors list for Atlanta. Castle Connolly Medical, Ltd. is America's most trusted source for identifying top doctors and is used by *Atlanta Magazine* to generate its Top Doctors list. We are very proud of Drs. Lampert, Jacobson and Stallman and thank all of those who helped support their nominations.

DR. MICHAEL JACOBSON

DR. SCOTT LAMPERT

DR. JAY STALLMAN

REMINDER: Please check your fax machine!

Georgia Retina is moving forward toward electronic medical records. In preparation for our move into the realm of EMR and in order to ultimately be green and save some trees, you will now be receiving your correspondence from us via fax. It is important for you to know this for two reasons. Firstly, you may be looking through your snail mail to hear back from us about a patient you are concerned about, when in reality, it is actually sitting on your fax machine. Secondly, we believe that we have almost all the fax numbers of the doctors who refer to us; however, if your fax number changes, please make sure to contact us immediately. Perhaps in the distant future, instead of sending our correspondence via fax, we will be able to send it with email; but as you know, at this time, email would be a violation of the HIPPA requirements because its level of security cannot be assured. Please do not hesitate to call one of our offices if you have any questions in this regard or if you are having trouble receiving these faxes

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seen with retinal thickness plus subfoveal fluid but the difference was not as significant. Interestingly, these differences did not seem to translate into differences in visual acuity.

Findings of fluid on optical coherence tomography (OCT) were significantly more common with bevacizumab on both dosing regimens compared with ranabizumab, with the monthly dosing providing better control than the as-needed schedule.

Also, dye leakage on angiography was significantly more common with bevacizumab as needed versus ranabizumab as needed. However, there was no meaningful difference in this measure between drugs given on the fixed monthly schedule.

As one would expect with a cost difference per injection of about $1950, the most significant difference between the two drugs and treatment groups was cost. The cost of providing bevacizumab delivered on a monthly basis was $595. Ranabizumab was provided at a yearly cost of $23,400. The cost of the drugs given on an as-needed regimen was $385 and $13,800, respectively.

The suggestion overall is that bevacizumab does not appear to be inferior to ranabizumab in the treatment of exudative AMD although there are some differences that favor ranabizumab. We are yet to see if this study does much to alter current treatment habits and trends.

Recent publicity from a *New York Times* article discussing several severe cases of endophthalmitis occurring after bevacizumab injections has raised some fear among patients. The lack of FDA approval for intraocular injection of bevacizumab may also be a deterrent for some patients and doctors to use the drug exclusively.

Furthermore, expansion of the indications for ranabizumab has increased its use and the use of bevacizumab for those same indications. Whether the results of the CATT trial will be similarly replicated for other retinal diseases such as vein occlusion and diabetic macular edema is yet to be seen. Georgia Retina will be participating in the upcoming CRAVE study, a head-to-head trial of these two anti-VEGF agents for macular edema secondary to retinal vascular occlusion. The Diabetic Retinopathy Clinical Research Network (DRCRnet) will likely be moving forward with a similar trial for diabetic macular edema. For now, it is to be expected that both drugs will continue to be used, as they are both extremely effective. Ultimately, cost may prove to be the overwhelming driving factor.

American Society of Retina Specialists Review

The annual meeting of the American Society of Retina Specialists was held in Boston in late August. Here are some highlights of the presented research:

- The most effective treatment paradigm for both proliferative diabetic retinopathy and diabetic macular edema seems to be combination therapy: photocoagulation, intravitreal pharmacotherapy, and surgical intervention on an individualized basis. There is mounting evidence that anti-VEGF medications are more preferable than corticosteroids as first-line pharmacotherapy.
- An additional intravitreal treatment for neovascular AMD is on the horizon. VEGF Trap-Eye was shown to be well tolerated, with a favorable safety profile. Compared to Lucentis at monthly dosing, this new medication appears to have non-inferior efficacy at every-2-month. It is expected to become available within a year.
- The use of genetic testing among AMD patients to categorize risk of developing advanced stages of disease may lead to individualized management strategies and follow up intervals. A commercially available genetic test is Macula Risk.
- Indocyanine green angiography may help develop management strategies for anti-VEGF resistant choroidal neovascularization. Adjunctive treatments for resistant cases include thermal laser to feeder vessels, photodynamic therapy, and intravitreal corticosteroids.
- Small case studies of systemic pharmacotherapy for central serous retinopathy were presented. Rifampin, an anti-mycobacterial agent, and low-dose methotrexate, an immune modulator show some evidence of success. These agents may be helpful in those cases that do not resolve spontaneously or by photocoagulation.

Retinal detachment:

- There were several presentations regarding retinal detachment repair techniques. The take-home messages are that scleral buckling *still* rivals vitrectomy in successful reattachment percentages.

The most effective treatment paradigm for both proliferative diabetic retinopathy and diabetic macular edema seems to be combination therapy: photocoagulation, intravitreal pharmacotherapy, and surgical intervention on an individualized basis.

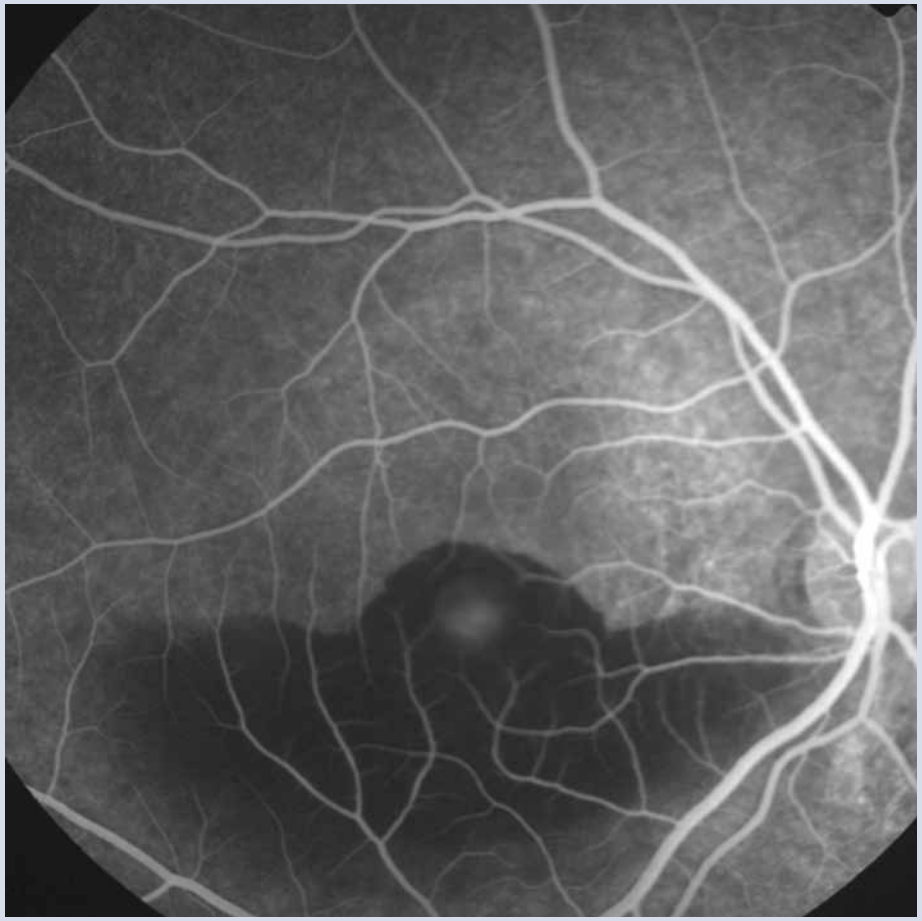
- Sutureless, small incision, transconjuctival vitrectomy (25 and 23 gauge) has comparable success in RD repair as larger incision, sutured 20 gauge surgery.
- A trend towards a shorter duration of face down positioning following macular hole surgery was evident, with some studies exhibiting good success with minimal to no positioning.
- There were several studies and much discussion regarding the development of antibiotic resistance in the setting of repeated topical antibiotic use. Current studies and evolving practice patterns suggest that the use of povidone-iodine at the time of injection without post-injection antibiotics is increasing as a method of preventing endophthalmitis.

PHOTO QUIZ ANSWER:

This is a case of Best Vitelliform Macular Dystrophy complicated by a choroidal neovascular membrane in the right eye with associated subretinal. The hemorrhage is best visuallized on fluorescein angiography.

Diagnosis

Best disease was first characterized in 1883 by Franz Best. It is an autosomal dominant macular dystrophy with variable penetrance and no systemic associations. Traditionally, Best Disease was diagnosed by clinical appearance in combination with an abnormally low Arden ratio on electroculogram in the presence of a normal full-field ERG (electroretinogram). A normal Arden ratio is >1.5. This patient had an Arden ratio of 1.04 OD and 1.02 OS. The EOG is also abnormal in phenotypically normal carriers. Genetic testing is now the gold standard for diagnosis. The VMD2 gene is found on the long arm of chromosome 11 and testing is available commercially.

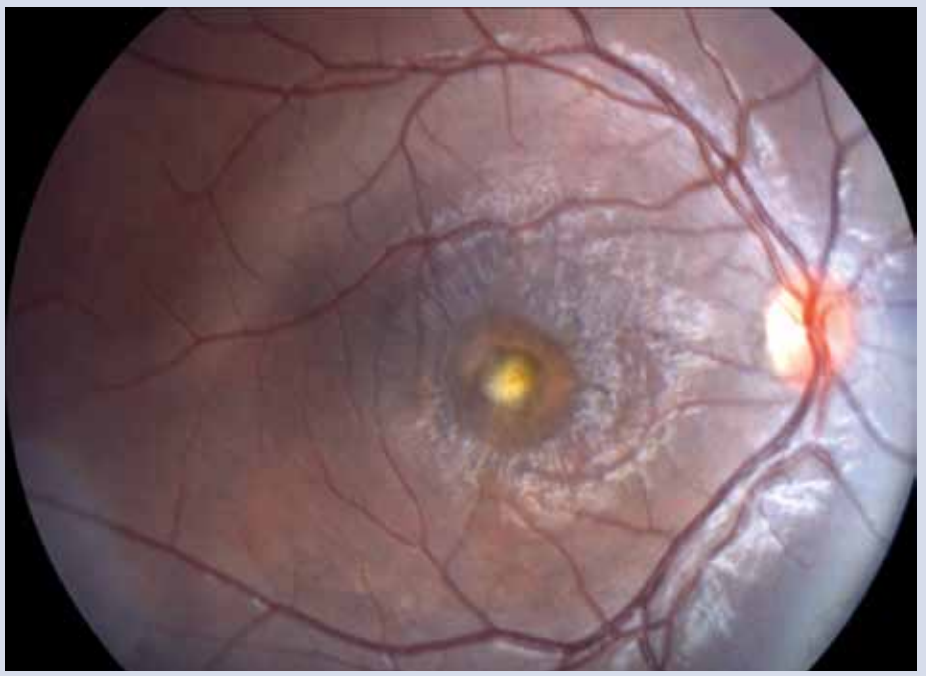


The disease typically progresses through four stages, beginning with a mild disturbance of the retinal pigment epithelium and progressing through the “yolk” stage and “pseudohypopyon” stages. The vision is often well maintained at the 20/40 or better level until late stages are reached. The late stages of the disease may display varying degrees of atrophy, fibrosis, or choroidal neovascularization.

While there is no treatment for Best Disease, various methods have been employed to treat choroidal neovascular membranes associated with the condition. These include focal laser therapy, photodynamic therapy, and anti-VEGF agents.

Treatment

Due to his age and the amount of hemorrhage present, this patient was observed for several weeks in the hope that as the hemorrhage cleared, the vision would improve. After lengthy discussion with the patient and his parents, and in the absence of any improvement after six weeks, photodynamic therapy was applied to the area of neovascularization in the right eye. The treatment was well tolerated, the hemorrhage cleared, and the vision improved. At six months post-PDT, the vision had improved to 20/40 OD.



Participating Insurance Plans:

- Aetna U.S. Healthcare
- BCBS of Georgia
- Beech Street
- Blue Choice
- CCN PPO
- Choice Care Network
- Cigna
- Coventry Healthcare
- Evolutions Healthcare System
- First Health
- Great-West
- Humana
- Medicaid
  - Peach State Medicaid
  - Wellcare Medicaid
  - Amerigroup Medicaid
- Medical Resource Network
- Medicare
- Medicare Railroad
- Multiplan PPO
- National Preferred Provider Network
- Novanet
- Private HealthCare Systems
- Southcare PPO
- TriCare PPO, HMO
- State Health
- United Healthcare
- USA Managed Care Organization
- WellCare Medicare HMO

Other plans are pending; please call to check specific participation.

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