



**An Inconvenient Truth:
The Challenges of Treating Macular Disease**

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September 21, 2013

- No financial disclosures

Disclaimer: The views and opinions expressed in this presentation are purely for educational purposes and are not meant as a political statement. I mean it. Seriously.

Also, I would like to thank Google and the many nefarious websites where some of these images were obtained.



"It ain't what you DON'T KNOW that gets you into trouble.
It's what YOU KNOW FOR SURE that just ain't so."
Mark Twain

Leading up to this point...

- Anti-VEGF = standard of care in treating neovascular AMD
- Excellent results when compared to previous treatments
- Inconvenient truths of using anti-VEGF agents?



Serious adverse events (SAE)

- Local:
 - Endophthalmitis (sterile or infectious)
 - Lens changes
 - Retinal tear, vitreous hemorrhage
- Systemic: heart attack, stroke, death



Inconvenient Truth #1

- We cause ocular hypertension and glaucoma



Glaucoma and anti-VEGF

- Repeated IOP spikes
- Damage to the TM (hydrostatic, toxic?)
- Deposits of contaminants from improper packaging/shipping of Avastin



Glaucoma and anti-VEGF

- More injections (>25) → more likely to develop OHT

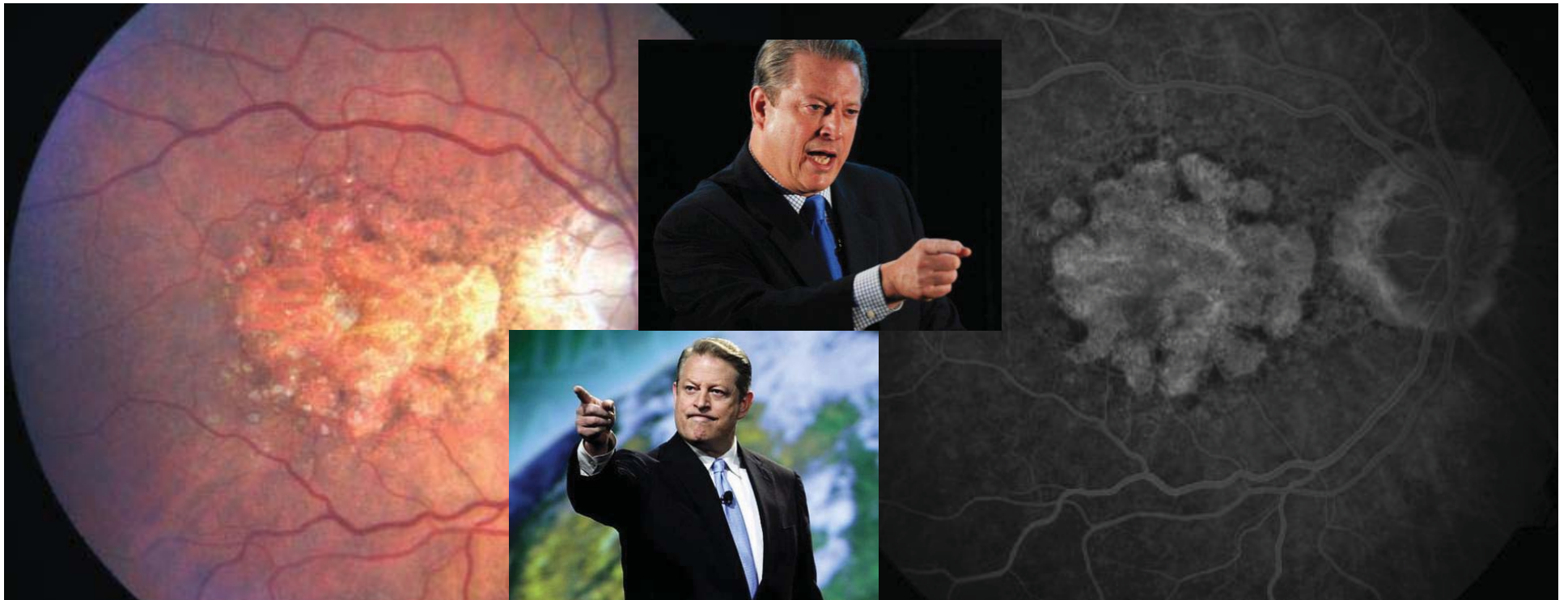
Inconvenient Truth #2

- We make geographic atrophy worse



Inconvenient Truth #2

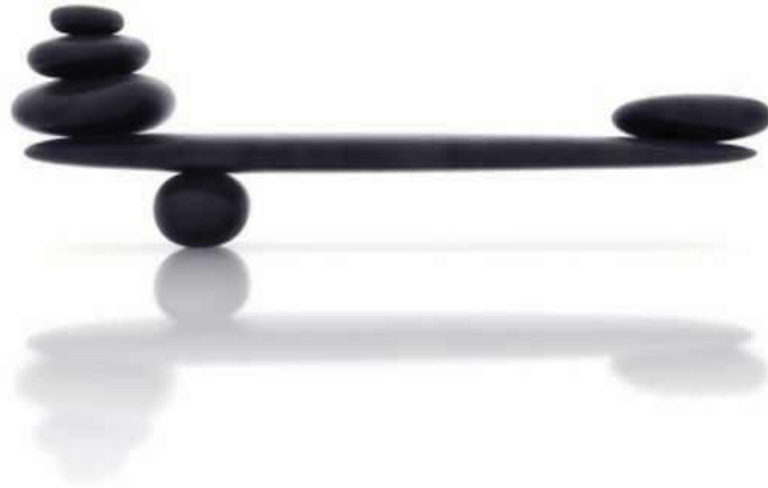
- We make geographic atrophy worse



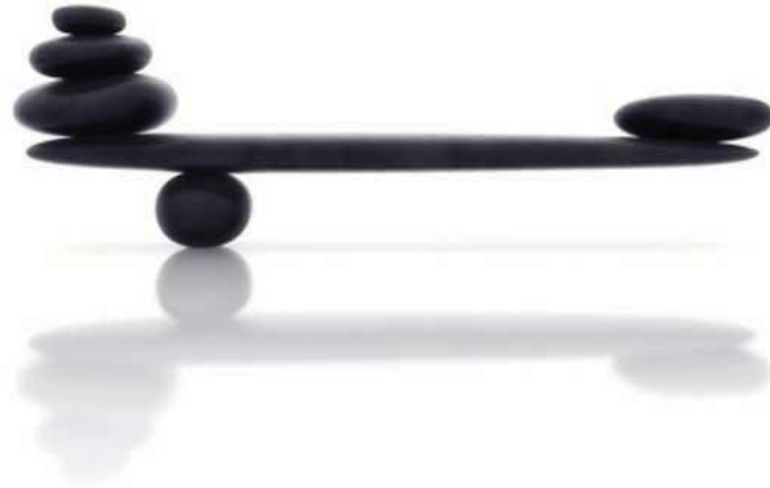
Geographic atrophy (GA) and anti-VEGF

- CATT and IVAN studies: more progression of GA in patients treated continuously (monthly) versus discontinuously (prn)
 - But (slightly) better visual acuity outcomes in the monthly treated groups in both studies
 - Only through two years
 - “small” sample size
 - Meta analysis?

The Constant Balance



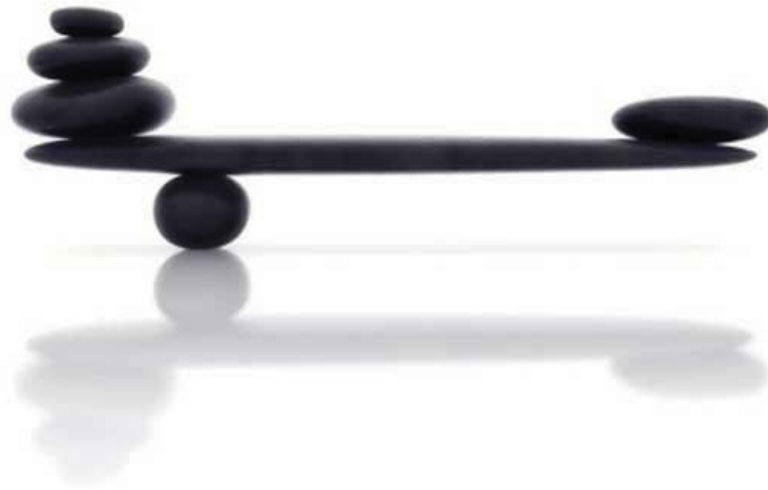
The Constant Balance



Risks

Benefits

The Constant Balance



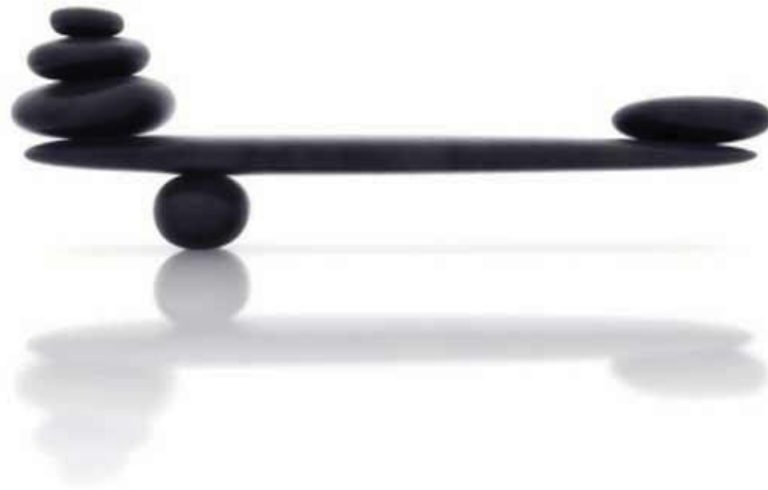
Risks

- Minor: %
- SAE: %

Benefits

- Improved/stabilized vision

The Constant Balance



Risks

- Minor: %
- SAE: %

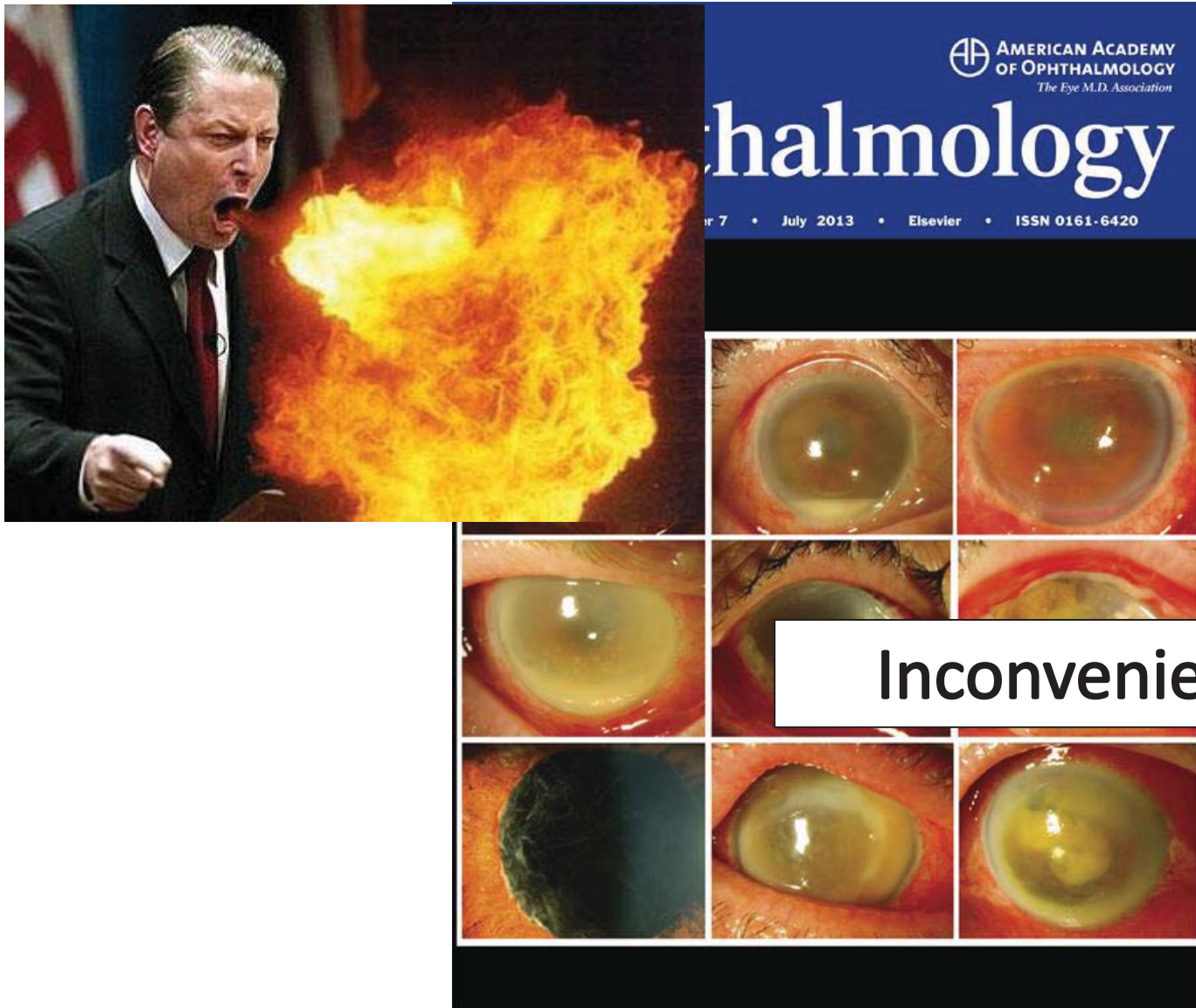
Benefits

- Improved/stabilized vision

Avastin did what???



Avastin did what???



The New York Times

August 2011

Avastin Injections Are Reported to Cause Blindness

By ANDREW POLLACK

Published: August 30, 2011

At least 16 people in two states have gotten severe eye infections, and some have been blinded, from injections of the drug [Avastin](#), according to health authorities and to lawyers representing the patients.

 Enlarge This Image



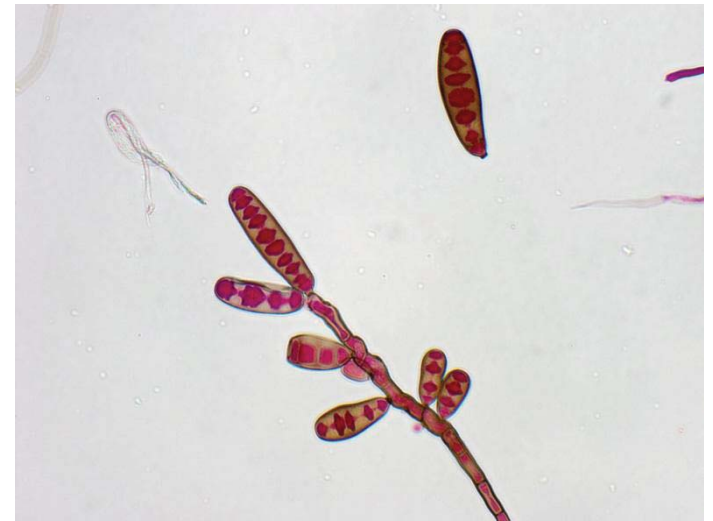
The incidents, in Florida and Tennessee, demonstrate the risks associated with the money-saving practice of injecting Avastin into the eye to treat the wet form of age-related [macular degeneration](#), a common cause of severe vision loss in the elderly.

Avastin, sold by [Genentech](#), is approved to treat [cancer](#), not eye disease. But many retina specialists use Avastin off label because it costs only about \$50 an injection, compared with \$2,000 for Lucentis, another Genentech drug that has the same mode of action and is approved as an eye treatment.



October 2012

- New England Compounding Center (NECC)
 - Outbreak of fungal meningitis from spinal injections (contaminated methylprednisolone)
 - 75 facilities, 23 states, 720 patient infected
 - 48 deaths
 - Increased scrutiny of compounding pharmacies
 - Regulation???
 - Ability to keep Avastin in the office???





SEARCH

- Home
- Food
- Drugs
- Medical Devices
- Radiation-Emitting Products
- Vaccines, Blood & Biologics
- Animal & Veterinary
- Cosmetics
- Tobacco Products

Safety

- Home
- Safety
- Recalls, Market Withdrawals, & Safety Alerts



Recall -- Firm Press Release

FDA posts press releases and other notices of recalls and market withdrawals from the firms involved as a service to consumers, the media, and other interested parties. FDA does not endorse either the product or the company.

Avella Specialty Pharmacy Issues Voluntary Nationwide Recall of Two Medications Due to Concerns of Sterility Assurance at Testing Vendor



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Safety

- Home
- Safety
- MedWatch The FDA Safety Information and Adverse Event Reporting Program
- Safety Information

MedWatch The FDA Safety Information and Adverse Event Reporting Program

Avastin Unit Dose Syringes by Clinical Specialties: Recall - Potential For Serious Eye Infection



- Home
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- Vaccines, Blood & Biologics
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- Cosmetics
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Drugs

- Home
- Drugs
- Drug Safety and Availability

Drug Safety and Availability

Drug Alerts and Statements

Importing Prescription Drugs

FDA Alerts Health Care Professionals of Infection Risk from Repackaged Avastin Intravitreal Injections

The U.S. Food and Drug Administration (FDA) is alerting health care professionals that repackaged intravitreal injections of Avastin (bevacizumab) have caused a cluster of serious eye infections in the Miami, Florida area.

PERSPECTIVE

Avastin Doesn't Blind People, People Blind People

SERAFIN GONZALEZ, PHILIP J. ROSENFELD, MICHAEL W. STEWART, JENNIFER BROWN, AND
STEVEN P. MURPHY



Can we get away with less injections over time (and thus less risk)?

- Not really (inconvenient truth # 4)
- CATT (and IVAN?)- decrease in visual acuity in year 2 when switched to prn dosing
- CATT, IVAN, GEFAL, and MANTA meta analysis:
 - Lucentis slightly "safer" than Avastin
 - Outcomes?

Long-term outcomes of anti-VEGF SEVEN-UP study

ANCHOR
and
MARINA

Years 1,2



HORIZON

Year 4



SEVEN-UP

Year 7

When compared to ANCHOR or
MARINA baseline:

- 43% of eyes were stable or improved
- 12% improved by 15 letters or more
- 34% declined by 15 or more letters



What's next?

- MAHALO: Phase 2 study



Summary

- Anti-VEGF agents work well for neovascular AMD
- They are not perfect
- The future of Avastin???
- The future of compounding pharmacies???
- The future of Al Gore???

Thank you

References

- Scary websites to acknowledge: lonelyconservative.com (Gore breathing fire); www.therichest.com (pointing Gore); www.dailybill.com (thumbs up Gore); twitchy.com (Michael Moore photo)
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