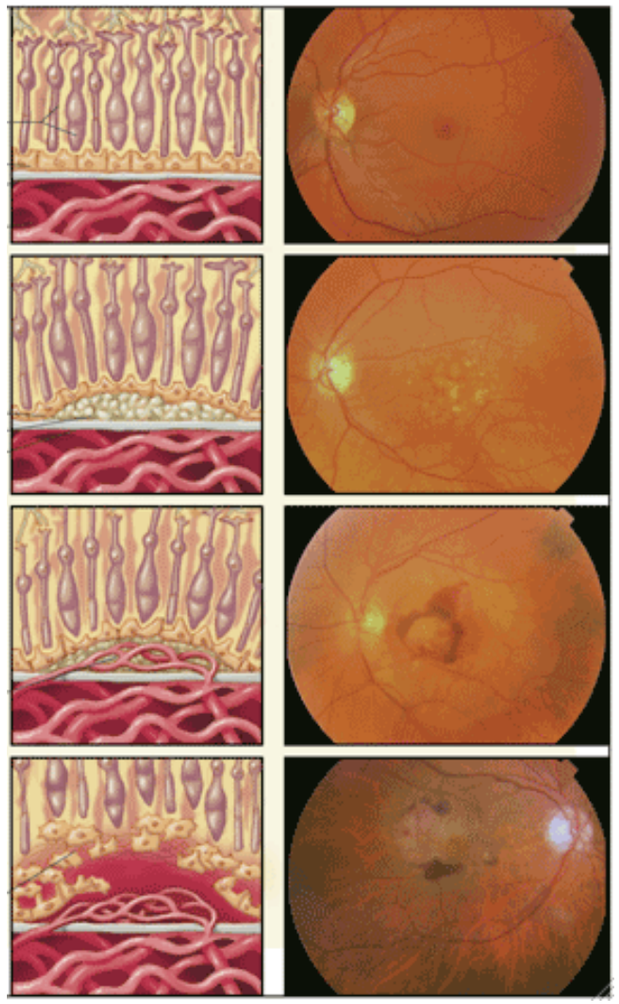
TREATMENT IN AMD



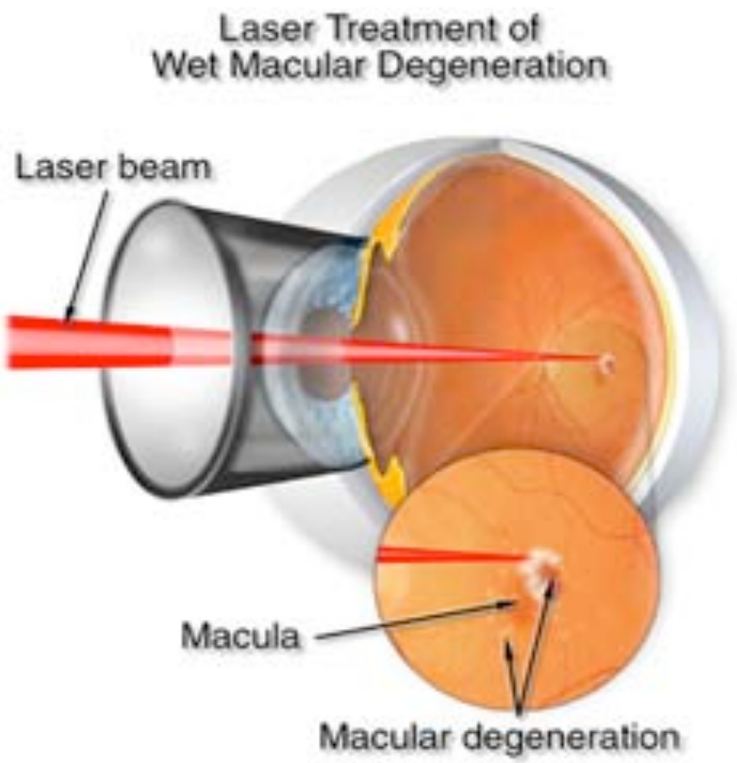
พญ. ปฐมา ภูรยานนทชัย

Treatment modalities

1. Laser photocoagulation
2. Photodynamic therapy (PDT)
3. Anti-vascular endothelial growth factor (Anti-VEGF)
4. Surgery
5. Medication

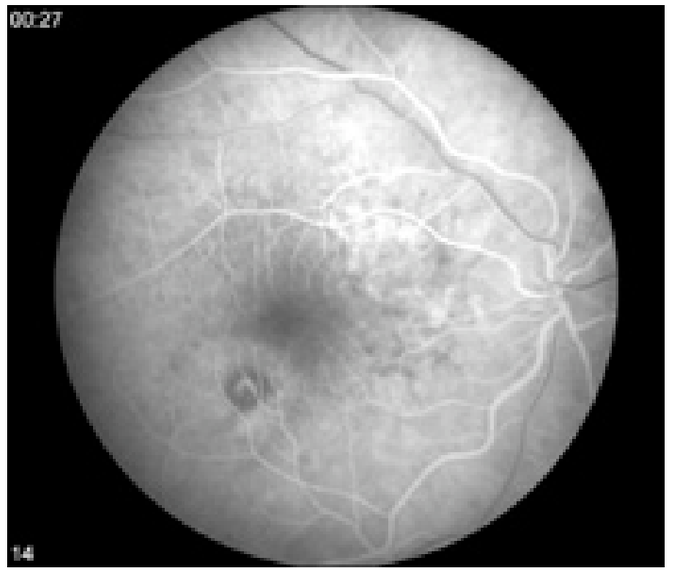
Laser photocoagulation

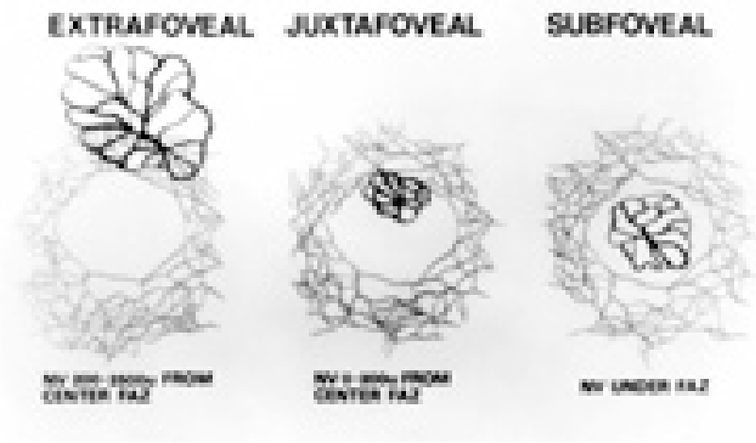
- 1982: Argon laser photocoagulation for AMD by the Macular Photocoagulation Study (MPS) group
- 1991: Subfoveal CNVM lesion



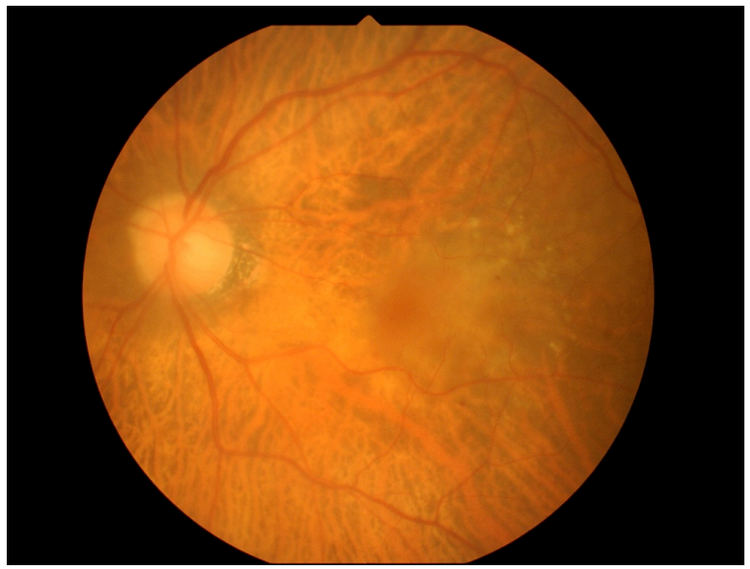
MPS protocol

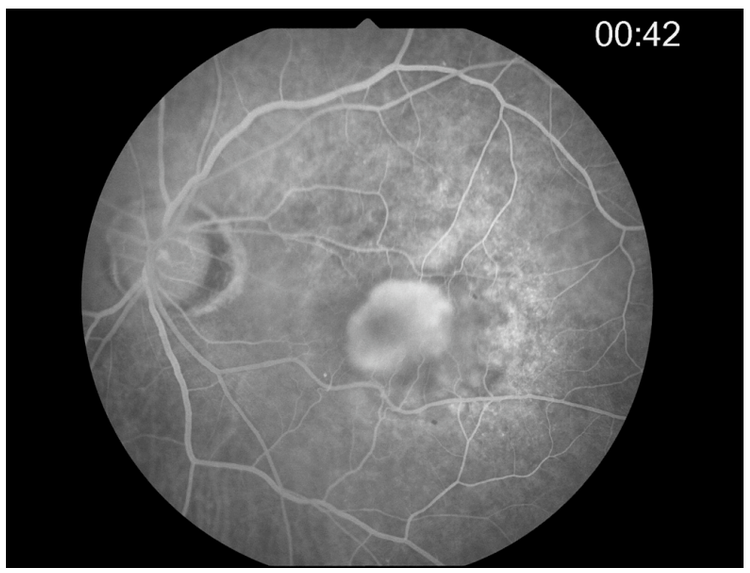
- ***FFA***: 72-96 hrs prior to treatment
- ***CNV***: well-demarcated lesion border, not greater than 2 DA in size
  - Extrafoveal CNV
  - Juxtafoveal CNV
  - Subfoveal CNV





Laser application





Laser photocoagulation

- ***Advantages***
  - Argon green laser photocoagulation
  - Simple method
  - Lowest cost of treatment

- ***Disadvantages***
  - Central scotoma esp. in subfoveal CNVM
  - Subfoveal recurrence may be as high as 50%

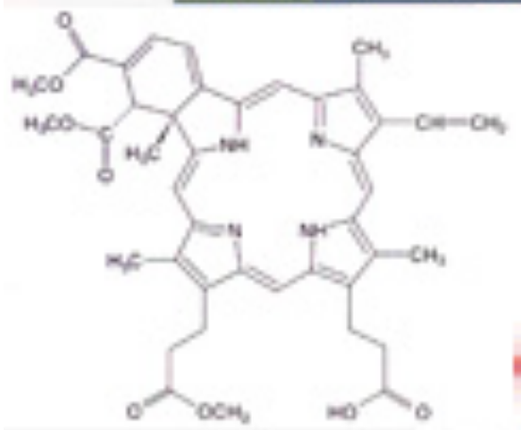
Photodynamic therapy (PDT)

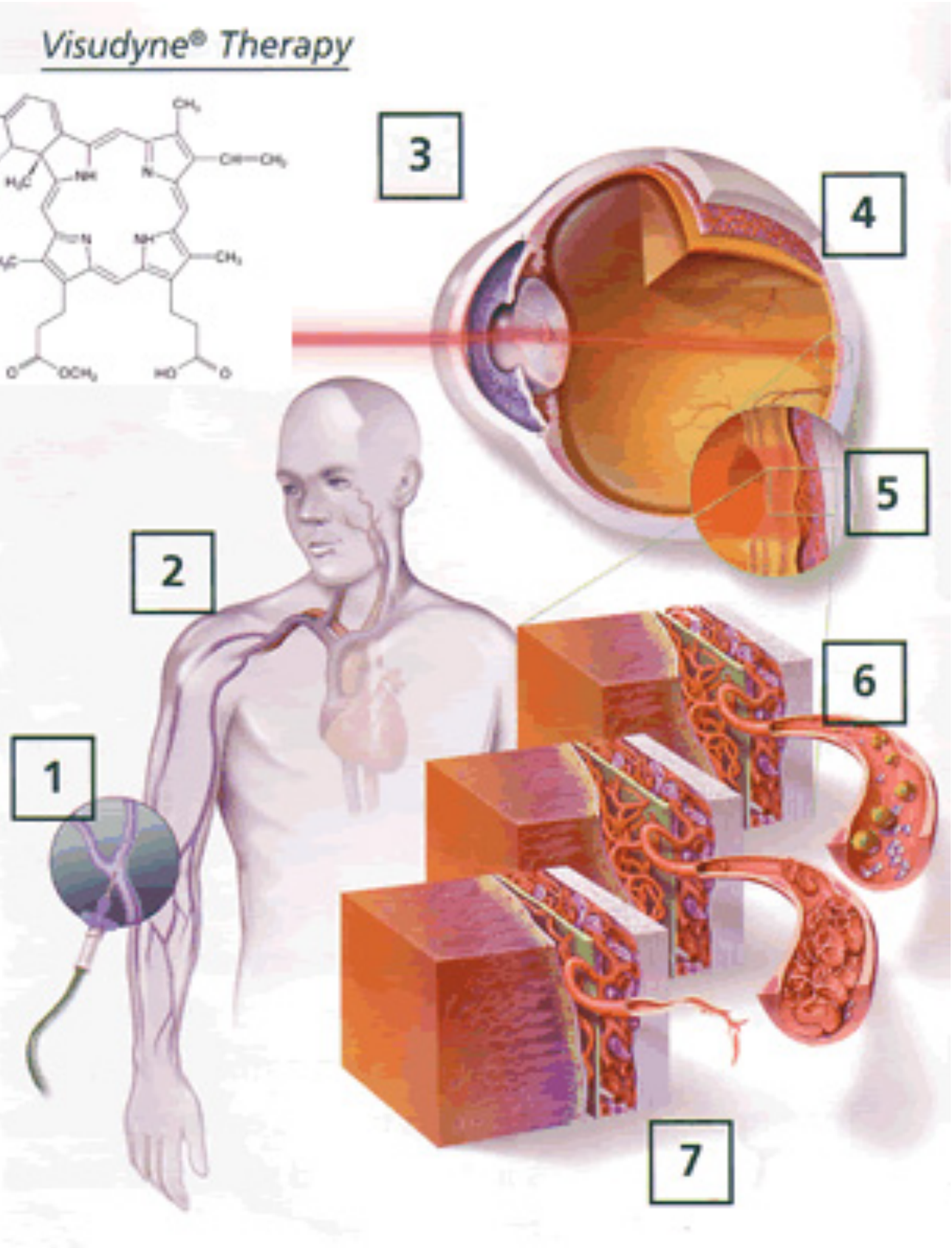
- Observed in 1900: Micro-organisms exposed to light in the presence of a dye were killed
- Method: Light-sensitive compound (photosensitizer) transforms light energy into chemical energy (*singlet oxygen*) to disrupt target cells and tissues
- Photosensitization consists of 2 steps;
  - Intravenous injection of photosensitizer
  - Subsequent light irradiation at a specific wavelength

Verteporfin (Visudyne®)

- Benzoporphyrin derivative monoacid ring A
- 2nd-generation, lipophilic, photosensitizing agent derived from porphyrin
- Binds with plasma LDL which is selectively taken up by neovascular endothelium
- Absorption peak at 689 nm.
- Plasma half-life of 5-6 hrs with rapid clearance from body (90% excreted in feces)

Visudyne® Therapy





Treatment regimen

- Greatest linear diameter (GLD) measured from FFA finding
- Spot size = GLD + 1000 microns
- Wt and Ht for BSA calculation
- Drug dose = 6 mg/m^2
- Verteporfin infusion over 10 min.
- Infrared diode laser application (689 nm, 600 mW/cm^2, 50 J/cm^2) for 83 s.
- Avoid exposure to bright light for 48 hrs.
- FFA follow-up q 3 months

TAP investigation

- Treatment of Age-related Macular Degeneration with Photodynamic Therapy
- Component of classic lesion
- Lesion size not greater than 5400 microns in diameter
- 61% of treated eyes, compared to 46% of eyes assigned to placebo, lost less than 3 lines of vision at 1 yr.
- Treated eyes more often had improvement of one or more lines of VA than placebo (16% vs. 7%).

TAP investigation

- Subgroup analyses of lesion with predominantly classic component found that 67% of treated eyes lost less than three lines of vision at one year, compared to only 39% of untreated eyes.

VIP trial

- Verteporfin In Photodynamic Therapy Study Group
- Classic lesion not eligible to TAP and occult lesion
- 54% of treated patients compared with 67% of placebo-treated patients lost at least 3 lines of vision in 2 yrs.
- Subgroup analyses suggested that the treatment benefit was greater for patients with either smaller lesions (4 disc areas or less) or lower levels of visual acuity (letter score < 65, VA = 20/50 or worse) at baseline.

Precaution for PDT

- Photosensitive for 48 hrs
- Considered carefully in pt with hepatic impairment or biliary obstruction
- Extravasation ➳ cold compress
- Reported side effects:
  - Hemodynamic instability if bolus injected
  - Lower back pain
  - Extensive choroidal ischemia

Angiogenesis in AMD

Angiogenesis

- *Angiogenesis-stimulating growth factors*
  - Angiogenin
  - Fibroblast growth factor
  - Platelet-derived growth factor
  - Vascular endothelial growth factor
  - Transforming growth factor
  - Interleukin-8

- *Angiogenesis inhibitors*
  - Angioarrestin
  - Angiostatin
  - Heparinase
  - Interferon alpha, beta, gamma
  - Plasminogen activator inhibitor
  - Interleukin-12

VEGF antagonist

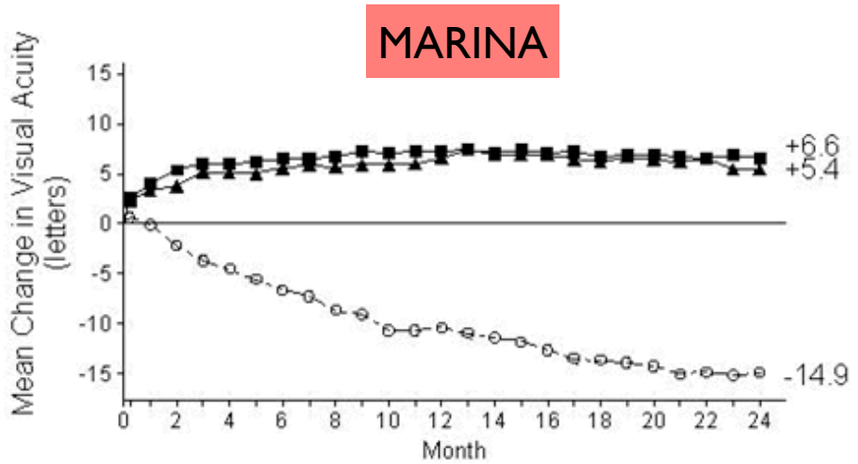
- Anti-VEGF : Bevacizumab

  Ranibizumab

- VEGF trap
- VEGF aptamer : Pegaptanib

Ranibizumab (Lucentis®)

MARINA



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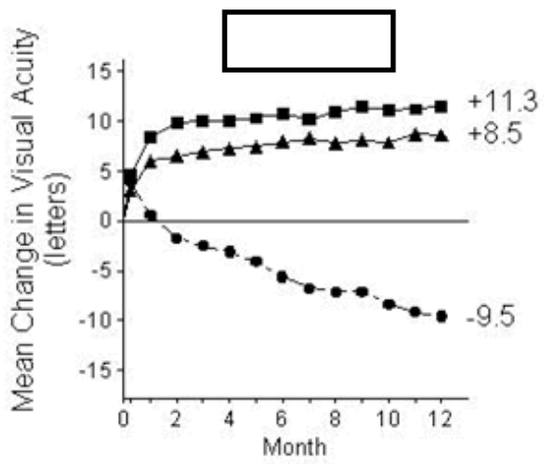
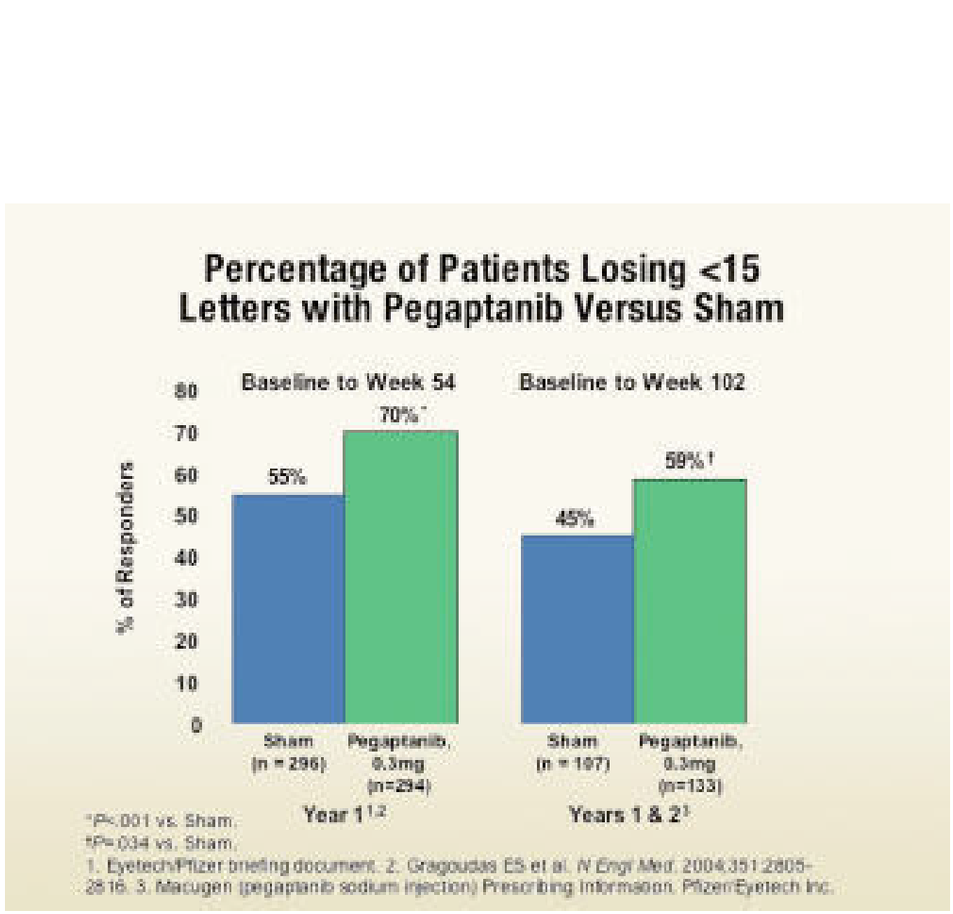
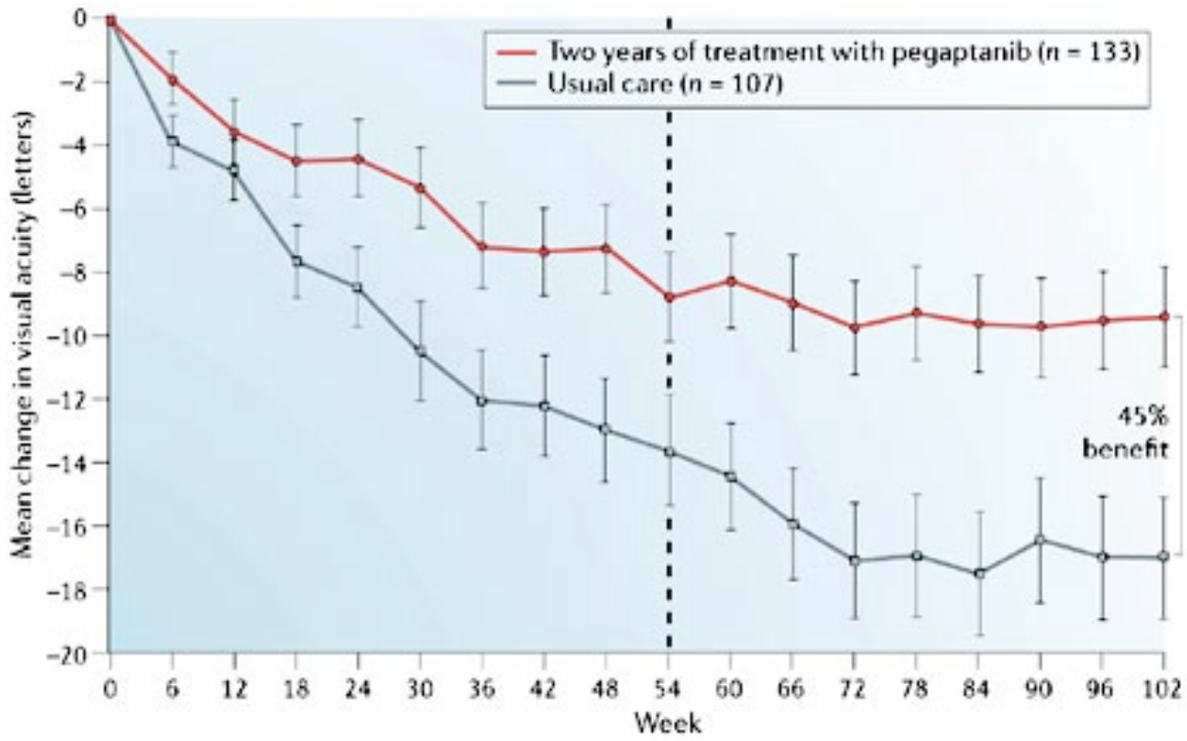


Study 1:
- LUCENTIS 0.5 mg (n=240)
- LUCENTIS 0.3 mg (n=238)
- Sham (n=238)

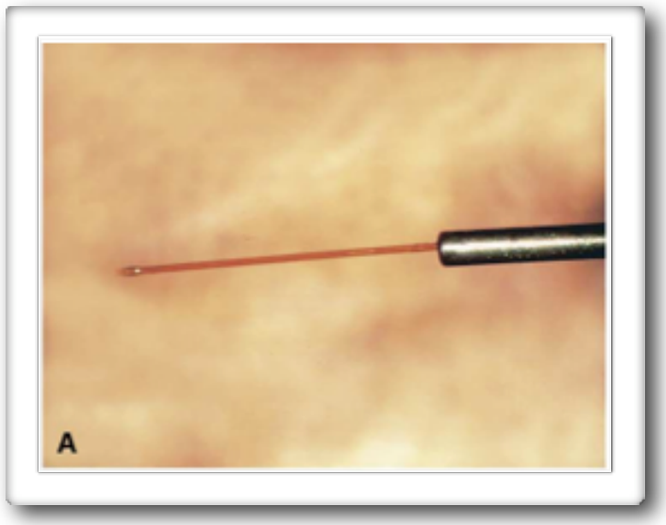
Study 2:
- LUCENTIS 0.5 mg (n=139)
- LUCENTIS 0.3 mg (n=140)
- Verteporfin PDT (n=143)

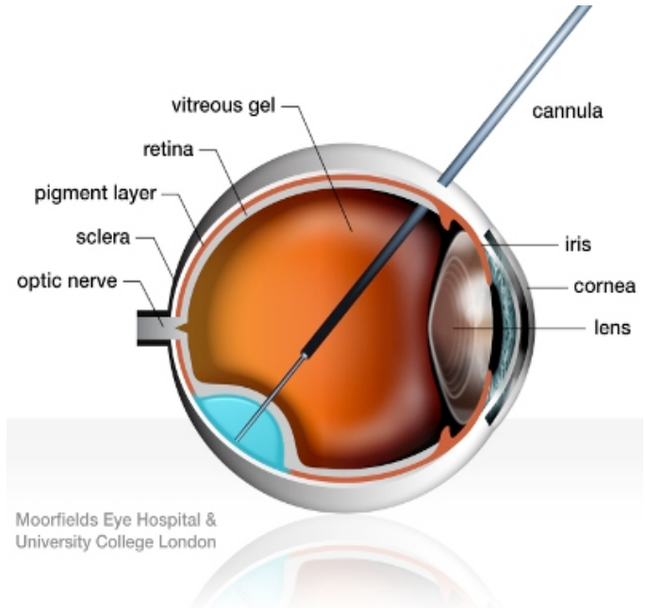
Pegaptanib (Macugen®)

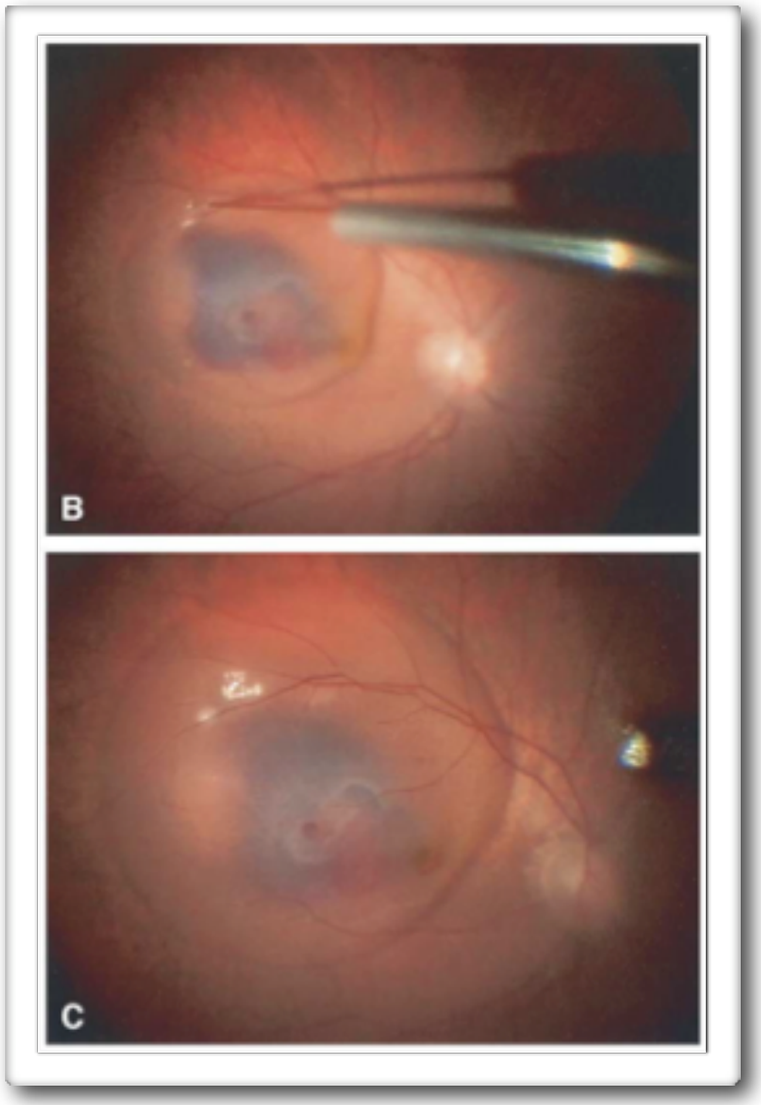


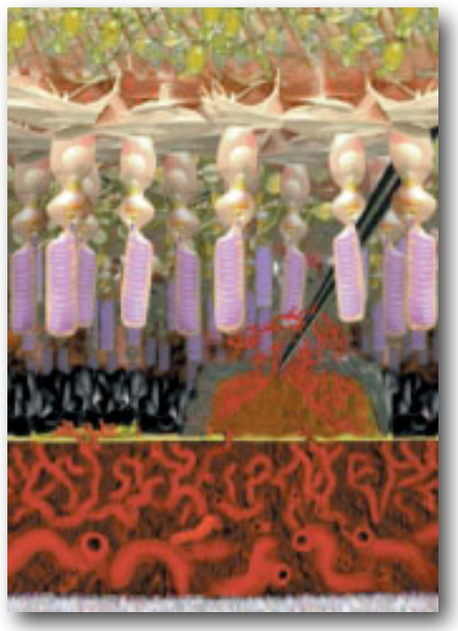


Submacular surgery

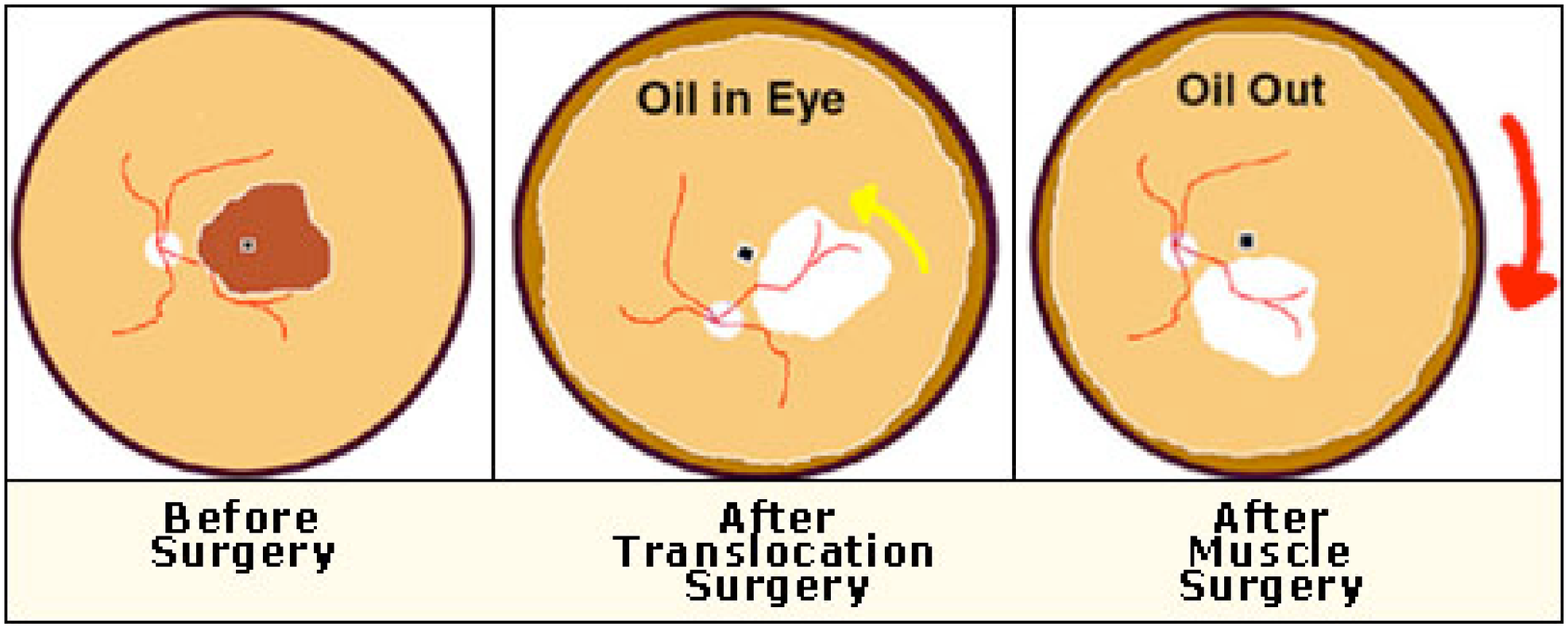








Macular translocation



Surgical outcomes

- Guarded post-op visual results
- Limited advantage to patients with large lesion and very poor pre-op vision
- Requires experienced vitreoretinal surgeon
- Needs multiple surgeries (macular translocation)

AMD risk factors

- Aging**
- ***Smoking***** (3-5 folds higher)
- Family history
- AMD gene: complement factor-H
- ***Exposure of sunlight*** esp. blue light

Medical treatment & Life modification

- Quit smoking !!
- Sunglasses
- Multivitamin + antioxidant + Lutein + Zeaxanthin
- Food with nuts and fish

AREDS

- Age-Related Eye Disease Study (AREDS)
- Evaluated the benefit of zinc and antioxidants in retarding cataract and AMD progression.
- Four categories of patients in AMD study:
  - *Category 1* = *no drusen or a few small (<63 μm) drusen.*
  - *Category 2* = *several small drusen or a few medium-sized drusen in one or both eyes.*
  - *Category 3* = *many medium-sized drusen or one or more large (≥125 μm) drusen in one or both eyes*
  - *Category 4* = *advanced AMD in one eye or vision loss due to AMD in one eye*

AREDS recommendation

- The reduction in risk for advanced AMD for those taking the nutritional supplement (high-dose vitamins and zinc) was 25%.

  ★ 500 mg. of vitamin C

  ★ 400 IU of vitamin E

  ★ 15 mg. of beta-carotene (often labeled as equivalent to 25,000 IU of vitamin A)**

  ★ 80 mg. of zinc as zinc oxide

  ★ 2 mg. of copper as cupric oxide

AREDS
Age-Related Eye Disease Study
National Eye Institute
NATIONAL INSTITUTES OF HEALTH

On-going researches in PSU eye clinic (2008)

- 2-yr results of PDT in Songklanagarind Hospital
- Combined PDT+Ranibizumab (Lucentis®) in AMD
- Electrophysiologic change in AMD treated by Ranibizumab (Lucentis®)