

Wet Age Related Macular Degeneration services in Epsom and St Helier

Mr. M. Usman Saeed,
 MBBS, FRCS, FRCOphth
 Consultant Ophthalmologist
 Clinical lead for AMD, Uveitis and Surrey Diabetic retinal screening
 Clinical Audit lead for Ophthalmology
 Complex cataract surgeon

www.londoneyedoctors.co.uk

- Annual incidence of wet AMD = 25,000
- Prevalence of 243,000
- likely to rise to 300,000 by 2025
- Wet AMD comprises 10% of advanced AMD cases

www.londoneyedoctors.co.uk

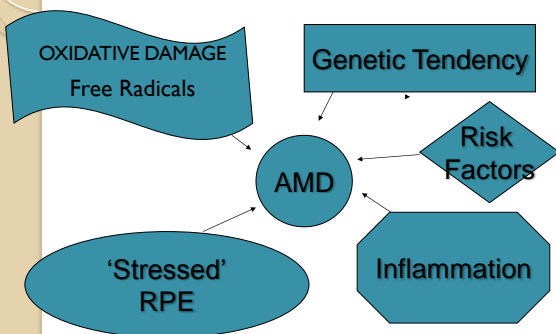


www.londoneyedoctors.co.uk

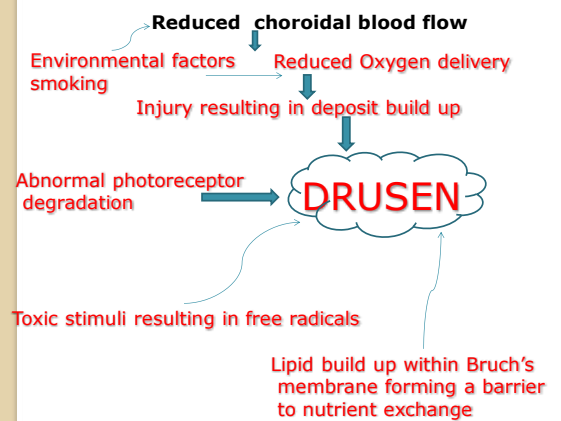
WHY DO WE GET AMD ?

www.londoneyedoctors.co.uk

Ageing Retina



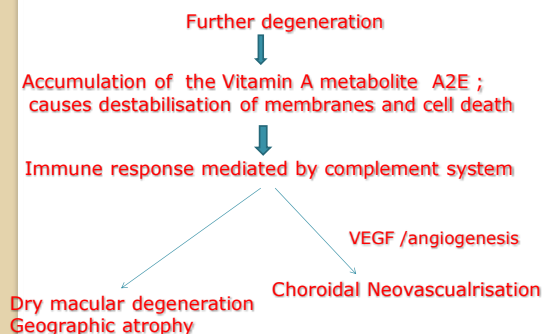
www.londoneyedoctors.co.uk



www.londoneyedoctors.co.uk

- Drusen seen in normal ageing retina
- Area occupied by drusen and subsequent pigmentary changes directly correlates with progression to vision loss from geographic atrophy and choroidal neovascularisation
- AMD strongly age related and smoking is the most consistent and modifiable significant risk factor.

www.londoneyedoctors.co.uk



www.londoneyedoctors.co.uk

Risk Factors...

- Age
- Cigarette Smoking
- Early Menopause
- Hypertension (high blood pressure) and/or cardiovascular disease
- A diet high in certain vegetable fats, especially those found in snack foods like potato chips
- Prolonged sun exposure
- Heredity
- Race

www.londoneyedoctors.co.uk

Risk Factors...

- **Age** - a person's age is by far the largest risk factor for AMD. It is estimated that 25% of the population between 65 and 74 have AMD. Above age 75, 33% have AMD.
- **Cigarette Smoking** - Cigarette smoking has been implicated as a great risk factor for AMD. Two separate studies found that current and former smokers, when compared with people who never smoked, had as much as **twice** the risk of developing AMD.
 - In former smokers of one pack or more a day, the risk of developing AMD remained elevated even after having quit for more than 15 years.

<http://www.blindness.org/disease/riskfactors.asp?type=2>

www.londoneyedoctors.co.uk

Risk Factors...

- ▶ **Estrogen and Early Menopause** - ? link between estrogen production and the onset of AMD in women.
- ▶ Higher incidence of AMD in women
- ▶ women who experience earlier onset of menopause may be at greater risk of developing the disease.
- ▶ **Elevated Blood Pressure**
- ▶ Patients with wet AMD were more than 4 times as likely to have moderate to severe hypertension than those without macular degeneration.

<http://www.blindness.org/disease/riskfactors.asp?type=2>

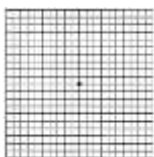
www.londoneyedoctors.co.uk

Risk Factors...

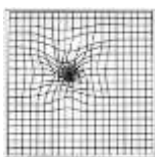
- ▶ **Dietary Fat Intake** –
- ▶ high intake of monounsaturated, polyunsaturated and vegetable fats is associated with a twofold-increased risk of developing Wet AMD.
- ▶ two or more servings of fish per week showed a lower risk of developing macular degeneration.
- ▶ **Sun Exposure** –
- ▶ UV light exposure can damage cells through a process called oxidative stress. Some researchers have theorized that UV light exposure may damage the macula and lead to AMD.

www.londoneyedoctors.co.uk

The AMSLER GRID...



Normal Vision



Macular Degeneration

Self Monitoring : Amsler Grid is not a substitute for an ophthalmic review. It allows patients to check their eyesight regularly for possible symptoms of macular degeneration.

www.londoneyedoctors.co.uk

Macular degeneration subtypes

- ▶ **Dry macular degeneration**
- ▶ 90%
- ▶ Slow progressive
- ▶ Mild to moderate visual loss, occasionally severe
- ▶ **Wet macular degeneration**
- ▶ 10%
- ▶ Rapidly progressive
- ▶ Severe visual loss

www.londoneyedoctors.co.uk

Dry macular degeneration

Diagnosis and treatment

www.londoneyedoctors.co.uk

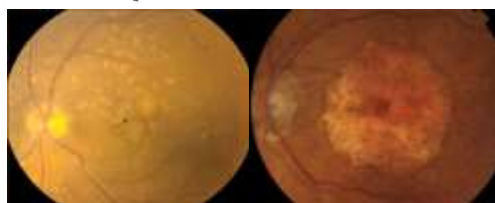
Dry macula degeneration

- 'Wear and tear'
- Varying degrees of atrophy
 - A few areas of pigmentation
 - A few drusen
 - Confluent drusen
 - Geographic atrophy
- Reduction in visual acuity
- Distortion
- Loss of central vision

www.londoneyedoctors.co.uk

Refer if:

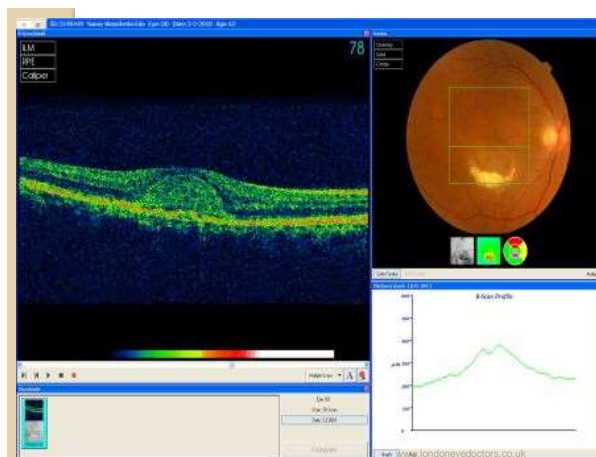
- Need for LVA
- Need to register for CVI
- Reason to suspect conversion to wet



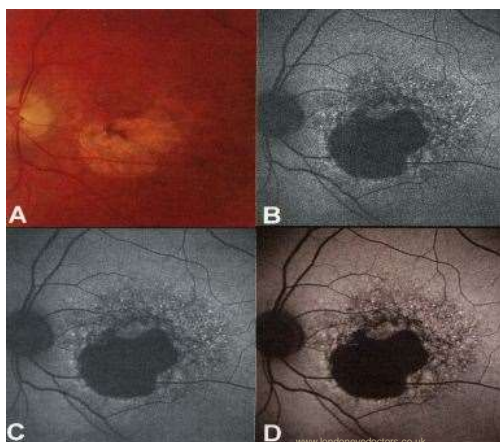
High risk soft confluent drusen

Geographical Atrophy

www.londoneyedoctors.co.uk



www.londoneyedoctors.co.uk



Treatment for Dry macular degeneration

- Up to date spectacles
- Low vision aids (magnifying glasses , angle poise lamps, better lighting)
- Stopping smoking
- Nutritional supplements
- Aids to improve reading (Kindle ,kobo, ipad, big screen TV)
- Registration as partial sight, visual impaired , severely sight impaired

www.londoneyedoctors.co.uk

Role of Nutritional supplements

- ▶ Category 1: few drusen
- ▶ Category 2: small drusen
- ▶ Category 3: multiple large drusen or GA not involving centre of macula
- ▶ Category 4: advanced AMD or reduced VA
- ▶ Results:
 - zinc alone, antioxidants alone, zinc plus antioxidants **significantly reduced risk of developing advanced AMD in category 3 and 4 patients.**

www.londoneyedoctors.co.uk

www.londoneyedoctors.co.uk

Zinc plus antioxidants

- Reduced risk of advanced AMD 25%
- Reduced risk for moderate vision loss 19%

www.londoneyedoctors.co.uk

AREDS recommendations

- Extensive drusen ,one large drusen,non central geographic atrophy in one or both eyes
- Or advanced AMD, or vision loss in one eye
- And without contraindications such as smoking
 - Should consider taking a supplement of antioxidants plus zinc such as those used in this study.

www.londoneyedoctors.co.uk

Which ones ?

- Preservision :
 - Original formula in AREDS I
 - Preservision original
 - Preservision lutein (for smokers)
 - Preservision complete (early AMD)
- ICAPS
- Nutroftotal (Lutein,Zeaxanthin,Omega 3,Reservatrol)
- Macushield (Lutein and Mesozeoxanthin)

www.londoneyedoctors.co.uk

Wet macular degeneration

- Transformation from dry AMD due to development of choroidal / subretinal neovascularisation.
- Increased distortion
- Loss of vision
- Elevation of macula
- Haemorrhage

www.londoneyedoctors.co.uk

Wet macular degeneration

Diagnosis and treatments

www.londoneyedoctors.co.uk

Wet AMD

- Happens because of choroidal neovascularisation followed by breaks in Bruch's' membrane with subsequent intra-retinal and sub-retinal bleeding
- Fibrosis and scarring

www.londoneyedoctors.co.uk



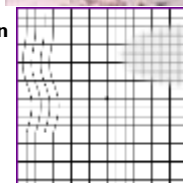
www.londoneyedoctors.co.uk

High priority

Caucasian
Smoker / Ex smoker
Increasing age above 50 years

Recent drop in visual function

Self Reported Distortion



www.londoneyedoctors.co.uk

History of wet AMD in the other eye

Soft / Confluent Drusens

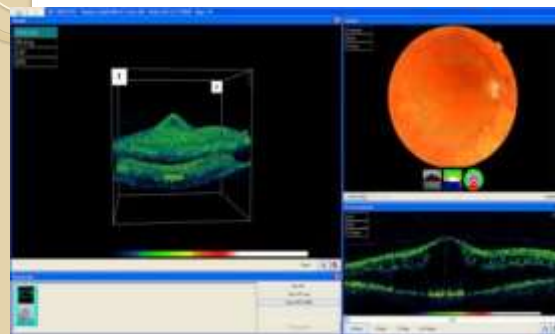
Bleed, Exudate, Grey elevation

Management

- Early diagnosis
- Fast track referral to local macula service
 - Logmar VA
 - OCT, FFA , ICG
 - Decision to discharge, monitor or treat.

www.londoneyedoctors.co.uk

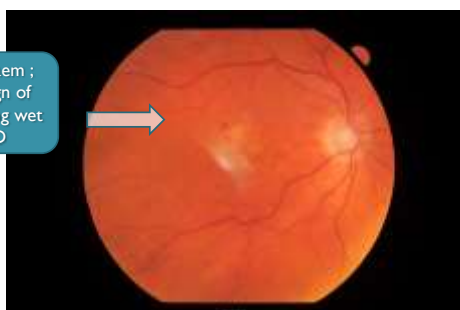
Wet AMD 3D OCT



www.londoneyedoctors.co.uk

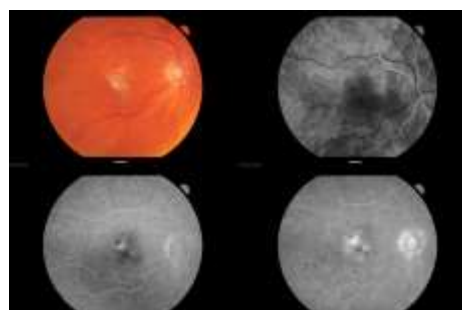
AMD Retinal photo

Small haem ;
early sign of
developing wet
AMD

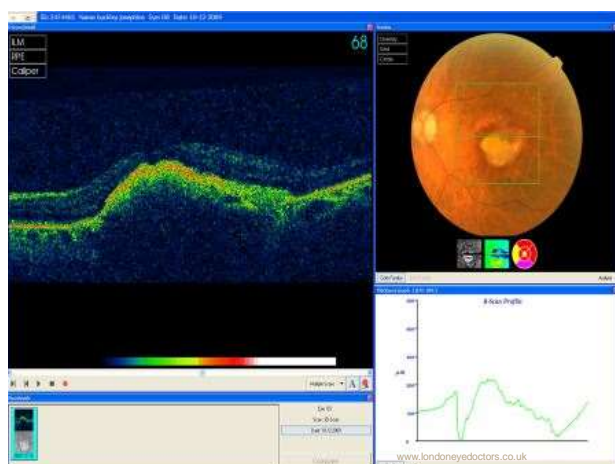


www.londoneyedoctors.co.uk

Wet AMD on FFA

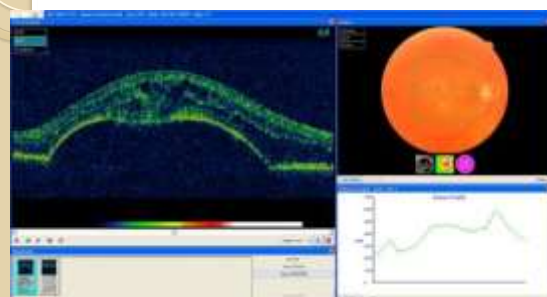


www.londoneyedoctors.co.uk



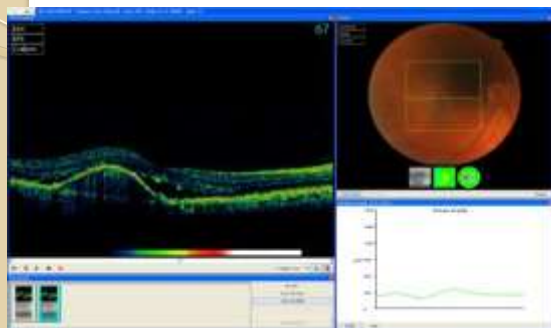
www.londoneyedoctors.co.uk

Pigment Epithelial Detachment with intra retinal fluid



www.londoneyedoctors.co.uk

PED with subretinal fluid



www.londoneyedoctors.co.uk

Treatments used for wet AMD

- Intravitreal Lucentis injections
- Intravitreal Avastin injections (not licensed)
- Photodynamic therapy (dye & Cold laser)
- Epi-retinal brachytherapy (early stages . Good results)
- Conventional Argon Laser (Hot laser)
- External beam radiotherapy (?)
- Trans-pupillary thermotherapy (bad results)

www.londoneyedoctors.co.uk

Treatment

- Eylea (Aflibercept)
- Lucentis (Ranibizumab)
- Avastin (Bevacizumab) ... not on NHS
 - Course of three monthly injections
 - Monthly monitoring
 - Observation or treat

www.londoneyedoctors.co.uk

Current Treatments for Wet AMD...

- **Lucentis™ (ranibizumab)** — The FDA approved Lucentis in June 2006 for the treatment of wet AMD.
 - Lucentis (ranibizumab) is a humanized anti-VEGF antibody fragment that inhibits VEGF activity by competitively binding with VEGF.
 - VEGF = Vascular Endothelial Growth Factor is an important protein involved in the initiation of neovascular growth.
 - So by inhibiting VEGF, Lucentis prevents further growth of unwanted blood vessels on macula.
 - A two-year study showed that **95 percent** of people with wet AMD who received monthly injections of Lucentis experienced no significant loss in visual acuity. Genentech also reported moderate visual **improvement** in 24.8 percent of participants treated with a 0.3 mg dose of Lucentis and 33.8 percent of participants treated with a 0.5 mg dose.



http://www.blindness.org/disease/treatment_detail.asp?type=2&id=6

<http://en.wikipedia.org/wiki/VEGF>

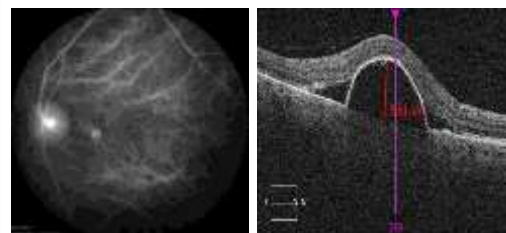
www.londoneyedoctors.co.uk

- VEGF binds to VEGF receptors initiating a signalling cascade that results in endothelial cell activation and angiogenesis
- Lucentis is a monoclonal antibody
- Anti VEGF
 - Inhibits choroidal neovascularisation
 - Reduction in retinal thickness – less leakage and bleeding
 - Doesn't eliminate fibrosis

www.londoneyedoctors.co.uk

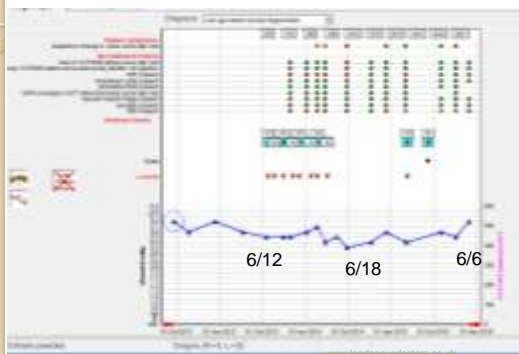
Specific types of Wet AMD

IPCV



www.londoneyedoctors.co.uk

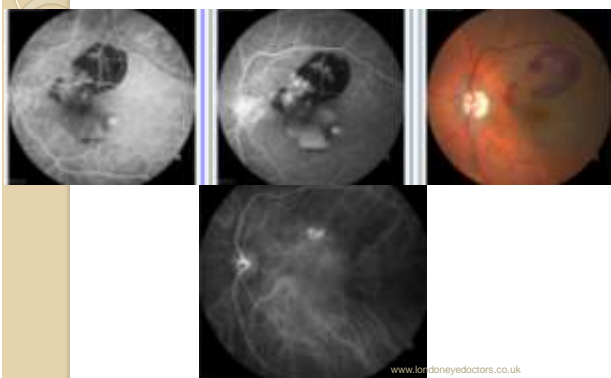
Summary of treatments



Preparation for intravitreal injection



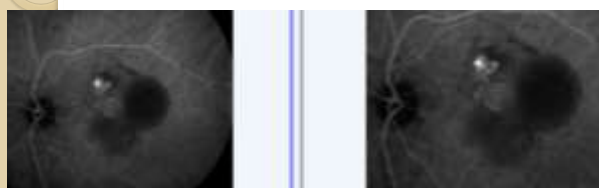
Wet AMD IPCV



Vision and treatment

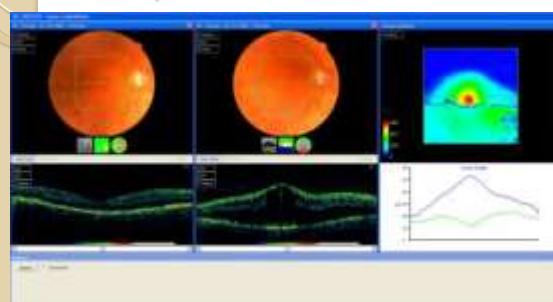


Better imaging



PDT funding ; not granted – case for a PDT service

Need for continuing retreatment in some patients



Generally



- 80% stabilise with treatment
- Up to 30% show an improvement in visual acuity
- Long term follow up required
 - Significant commitment for patient and demands on the NHS

www.londoneyedoctors.co.uk

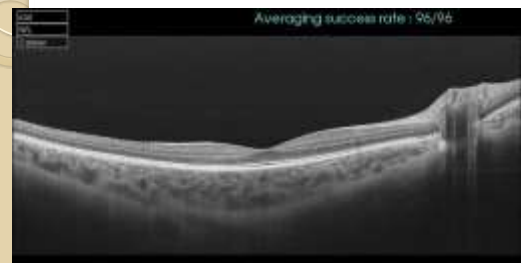
Newer developments

Development of better OCTs
Swept source OCTs
SLO OCTs



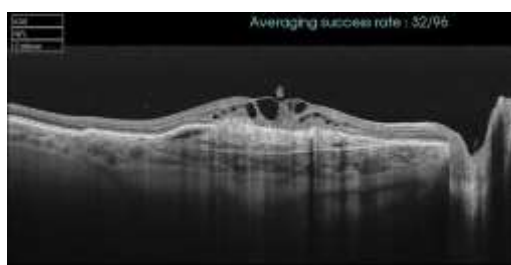
www.londoneyedoctors.co.uk

Normal OCT



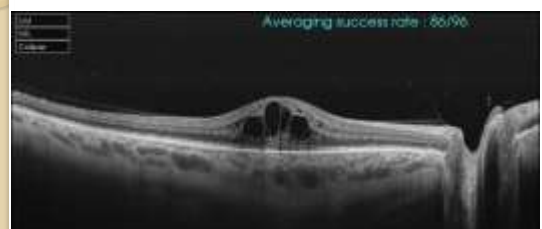
www.londoneyedoctors.co.uk

AMD with scarring + fluid



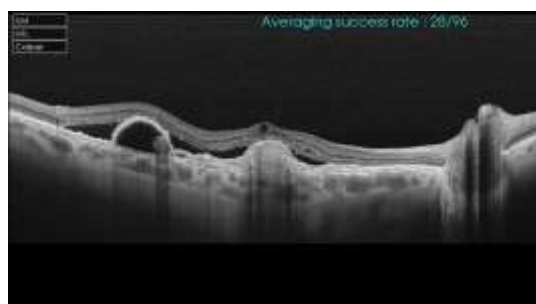
www.londoneyedoctors.co.uk

Post operative CMO



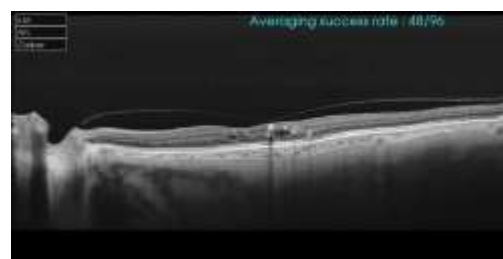
www.londoneyedoctors.co.uk

Multifocal wet AMD + scarring ; still active



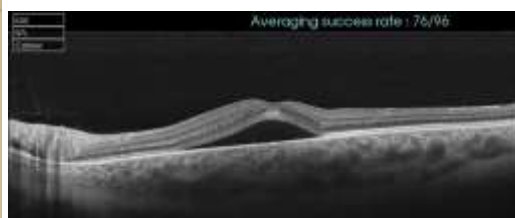
www.londoneyedoctors.co.uk

Diabetic maculopathy; Vitreous attached



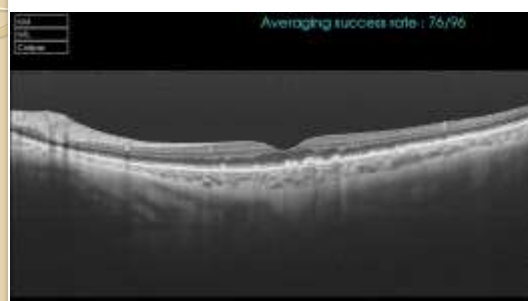
www.londoneyedoctors.co.uk

CSR; self limited



www.londoneyedoctors.co.uk

Dry AMD; drusen



www.londoneyedoctors.co.uk

Photodynamic therapy

- 2004-2009
- Usually classic CNVM or predominantly classic CNVM could be treated
- Visual acuity drop immediately after treatment was quite common
- Long term results were better than sham treatment
- Gradually fallen out of favour . Still Used in IPCV variant of wet AMD

www.londoneyedoctors.co.uk

PDT for Wet AMD

- **Visudyne® (verteporfin) and Photodynamic Therapy (PDT)** verteporfin, which is a light-activated .Verteporfin has no effect on its own, but in the presence of light and oxygen, it reacts with oxygen to produce a cell-killing (cytotoxic) effect.
- Visudyne is injected intravenously. When the drug reaches the eye, a low-intensity laser is directed to the region of blood vessel growth, activating the drug, which destroys the unhealthy vessels.
- Still useful in IPCV variant of wet AMD



www.londoneyedoctors.co.uk

Argon laser treatment

- In some cases, if diagnosed early, laser treatment laser beams destroy extra-foveal leaky blood vessels that form close to the macula.
- High risk of recurrence
- High risk of visual loss
- For laser surgery to be effective, it is critical that wet macular degeneration be diagnosed before extensive vision loss occurs. Therefore, individuals should consult with an eye doctor at the first sign of blurred or distorted central vision.

www.londoneyedoctors.co.uk

SURGICAL TREATMENTS FOR AMD

www.londoneyedoctors.co.uk

Macular translocation

- Done by maverick VR surgeons ; David Wong in UK/Hong Kong, Klaus Eckhardt in Germany, Gibran Khurshid in USA
- The retina is detached , 360 retinotomy, rotated and then reattached by extensive retinal surgery.
- Then surgery to remove silicon oil
- Then surgery to rotate extra-ocular muscles
- Done in **Only eyes** with “very poor vision”

www.londoneyedoctors.co.uk

Radiotherapy

- ▶ **Epiretinal Brachytherapy:**
- ▶ PPV then radiotherapy
 - low dose radiation of macular using special applicator in conjunction with Lucentis – prelim results show only 2 injections needed
 - long term radiation effects to be assessed

www.londoneyedoctors.co.uk

- MERLOT trial
- CABERNET trial

- **NO superiority over conventional treatments !**

www.londoneyedoctors.co.uk

Intraocular lenses and telescopes for AMD



www.londoneyedoctors.co.uk

NICE guidance on telescopic systems

1 Guidance

- 1.1 Evidence on the efficacy of implantation of miniature lens systems for advanced age-related macular degeneration (AMD) shows that the procedure can improve both vision and quality of life in the short term. Short-term safety data are available for limited numbers of patients. There is currently insufficient long-term evidence on both efficacy and safety. Therefore this procedure should only be used with special arrangements for clinical governance, consent and audit or research.

www.londoneyedoctors.co.uk

IOL Vip (telescopic systems)

- 2 lenses:- eyepiece/ objective
- Deviation of image away from diseased macula
- Requires ability of healthy retina to recognise image
- Ideal for small scars
- May need training pre op / post op

www.londoneyedoctors.co.uk

Who may benefit

- Can be useful in wet and dry AMD
- Small area of scarring
- Careful patient selection
- Close central vision versus peripheral vision
- Expensive IOL system
- May be available on a closely audited basis

www.londoneyedoctors.co.uk

FUTURE TREATMENTS FOR AMD

www.londoneyedoctors.co.uk

Future treatments

- New drugs under development

Lampalizumab - Recruiting

Lampalizumab (or with Placebo) is a drug that is injected into the eye. In earlier Phase II trials, it was shown to reduce the area of the geographic atrophy by 23%. A Phase III clinical trial is now underway for individuals with geographic atrophy from dry AMD. Several research sites are actively recruiting new study patients with AMD. For more information, visit www.lampalizumab.com.

- Injections for dry AMD

- Stem cell treatment

www.londoneyedoctors.co.uk

Future directions

Lacisate For Dry AMD - Recruiting

The clinical trial, Prospective Randomised for Dry-eye Age-related Macular Degeneration (PRO-RAND) is a multicenter double-masked Phase III study of individuals with dry eye and macular degeneration who use a high-dose dry eye therapy (Lacisate). The study will determine whether specific receptors of Prokineticin-2 (Lacisate) can reduce eye viscosity, reduce tear evaporation and improve tear film stability.

Individuals will be assigned randomly to two groups: one will be using Lacisate for dry AMD as usual and one receiving placebo. Lacisate is a drug that is injected into the eye. The study will determine whether the use of Lacisate can reduce the progression of dry AMD in all participants. The trial centers are in London and South Coast.

MacroCLEAR Eymdrops - Recruiting

This is a Phase III, double masked, single center study. A single eye of 60 individuals with mild to moderate dry Age-Related Macular Degeneration (AMD) will be randomly assigned to receive either 1% MG-101 or a placebo over 2 years. The study design will assess the efficacy, safety, and tolerability of MG-101 for these patients.

Bone Marrow CD34 Stem Cells - Recruiting

In this Phase I clinical trial, participants will be treated with intravitreal injection of CD34+ stem cells isolated from bone marrow. The patient receives stem cells derived from his own bone marrow. This study will determine whether there are any major safety and feasibility concerns. Patients will be followed for 6 months after treatment, including eye examinations and imaging. Macular degeneration is one of the retinal diseases being studied with this method.

www.londoneyedoctors.co.uk

Retinal Implants

- RP and AMD: preservation of ganglion cells and retinal neurons (outer retinal degeneration)
- Biomimetic devices
- Mimic the biological function of the damaged retina by using a microelectrical stimulus to create pixel based vision

www.londoneyedoctors.co.uk

Our results at St Helier Hospital and Epsom (previously Sutton Hospital)



www.londoneyedoctors.co.uk

www.londoneyedoctors.co.uk

AMD team

- Mr Usman Saeed Consultant and AMD lead
- Dana Church AMD coordinator
- Katherine Brown AMD –DMO coordinator
- Sharon Sullivan
- Debbie Mouslou

www.londoneyedoctors.co.uk

<https://www.epsom-sthelier.nhs.uk/ophthalmology>

www.londoneyedoctors.co.uk