Question 53

32 year old woman who has type 1 diabetes mellitus for 12 years is found to have mild background retinopathy. Her blood pressure is 120/80 mmHg and her HbA1C is 7.6% (3.8 – 6.0).

Which one of the following is most likely to retard the progression of the retinopathy?

A. Aspirin  
B. Laser photocoagulation  
C. Reduction in blood pressure  
D. Improvement of glycaemic control  
E. ACE inhibitor therapy

Answer: D

Diabetic retinopathy:
- major cause of morbidity in both Type 1 and 2 DM  
- commonest cause of blindness in middle age people  
- majority are asymptomatic till advanced (might be too late)  
- often transient worsening of symptoms during 1st year of intense insulin therapy (lower blood glucose -> decreased plasma volume -> marginal vessels at risk) and pregnancy  
- strong association between retinopathy and nephropathy independent of glycaemic control, duration of diabetes (?) common pathogenesis  
  - albuminuria (ur albumin excretion > 200 microg/min) is a predictor for retinopathy in hispanics but not whites  
  - presence of retinopathy is a predictor of excess mortality risk (by IHD and stroke) but this is not significant once corrected for nephropathy

Primary cause is chronic hyperglycaemia (as per DCCT)

Main mechanisms:
1) Impaired auto-regulation of retinal blood flow  
   - retinal blood flow usually constant but autoregulation impaired in hyperglycaemia  
   - leading to increased shear stress

2) Accumulation of sorbitol in retinal cells  
   - unclear mechanism  
   - glucose in cells usually metabolized to sorbitol (via aldose reductase) then to fructose  
   - increase intracellular osmolality and decreased myoinositol  
   - also contribute to cataracts as swollen lens fibres rupture

3) Accumulation of advanced glycosylated end products (AGE) in extracellular fluid  
   - via Amadori pathway  
   - accumulated AGES crosslink with collagen  
   - contribute to cataracts

4) Retinal micro-thrombosis

5) Raised vasoactive substances

6) Genetics/ Ethnic group  
   - more common in blacks and Hispanics  
   - ? polymorphism in platelet glycoprotein receptors

Diabetic changes in the eye
1) Non-proliferative
Year 2002 Paper two: Questions supplied by Jo

- hard exudates (leakage of proteinaceous and lipid rich material)
- soft exudates (infarcted retina distal to occlusion)
- haemorrhages (dot in inner layers, blot superficially)
- microaneurysms
- thickened basement membrane (as in nephropathy)

2) **Proliferative**
   - related to vessel changes secondary to ischaemia
   - new vessel formation
     - initially new and fragile -> burst and bleed
     - mature vessels are fibrous -> contract -> distort retina -> retinal detachment
     - may form in anterior chamber and block aqueous flow -> **glaucoma**

3) **Cranial nerve palsies**
   - usually CN3 *pupil sparing* palsy (compressive lesions pick off external para-sympathetic fibres first)
   - other CN palsies may be related to CVA or rhino-cerebral mucormycosis

4) **Cataracts**
   - AGE products in lens

A. In the ETDRS in the 1990s
   - Aspirin (up to 650mg/day) not shown to have any effect on progression of retinopathy, visual loss or to increase risk of bleeding in eye (8 year follow up)

B. Photocoagulation is the main treatment but question is whether it retards progression
   - ETDRS also showed no difference in visual loss whether treated early or late
   - Early pan-retinal coagulation decreased visual acuity and peripheral vision, thus not recommended
   - Early focal coagulation recommended in macular oedema
   - Some observational studies show regression of retinopathy but this is mostly related to good glycaemic control

C. **BP reduction**
   - Decreases diabetic retinopathy just as it does hypertensive retinopathy
   - Not the most crucial factor
   - Diastolic BP seems to be better predictor of outcome

D. Glycaemic control most effective at primary prevention; highly effective in secondary prevention in mild to moderate cases; little to no effect in severe retinopathy (even in euglycaemic patients post pancreatic transplant)

E. **ACEi** may decrease retinopathy independent of BP control
   - mechanism unclear (likely not due to ACE action, but to sulphonyl side group that retards new vessel formation as in captopril and rat corneas)
   - study with lisinopril in normotensive T1DM showed 10% reduction in progression, but only when there’s little or no nephropathy (lancet 1997 Jan 3;351(9095):28-31)