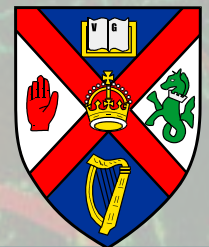
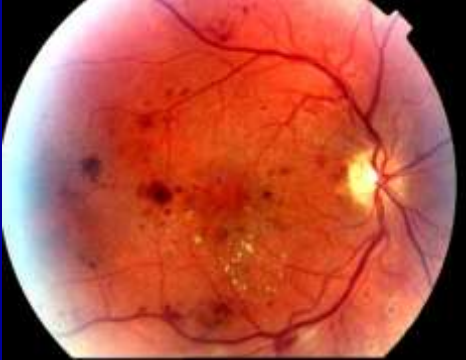


# Vascular Changes in Diabetic Retinopathy

*Alan Stitt  
Centre for Vision & Vascular Science  
Queen's University Belfast*

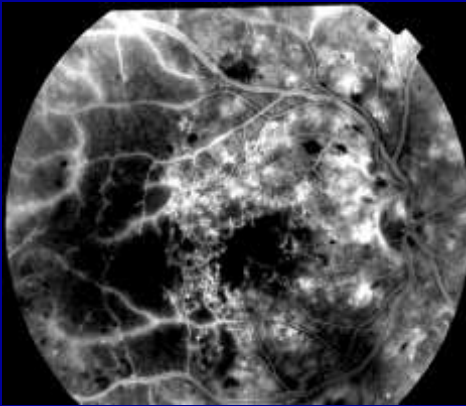


# Talk structure



Characteristics of the retinal microvasculature

How this microvasculature and the neuroglial network is altered in diabetes

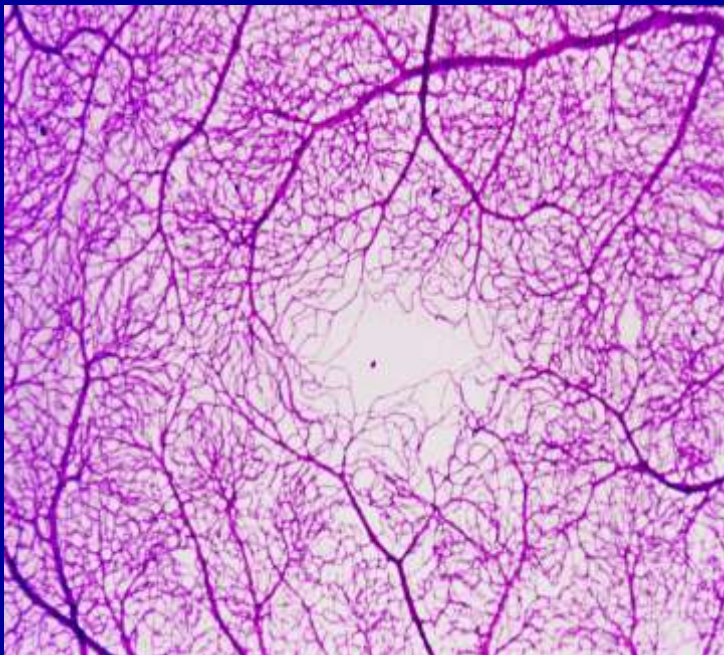


Pathogenic mechanisms

Understanding pathogenesis can lead to better treatments

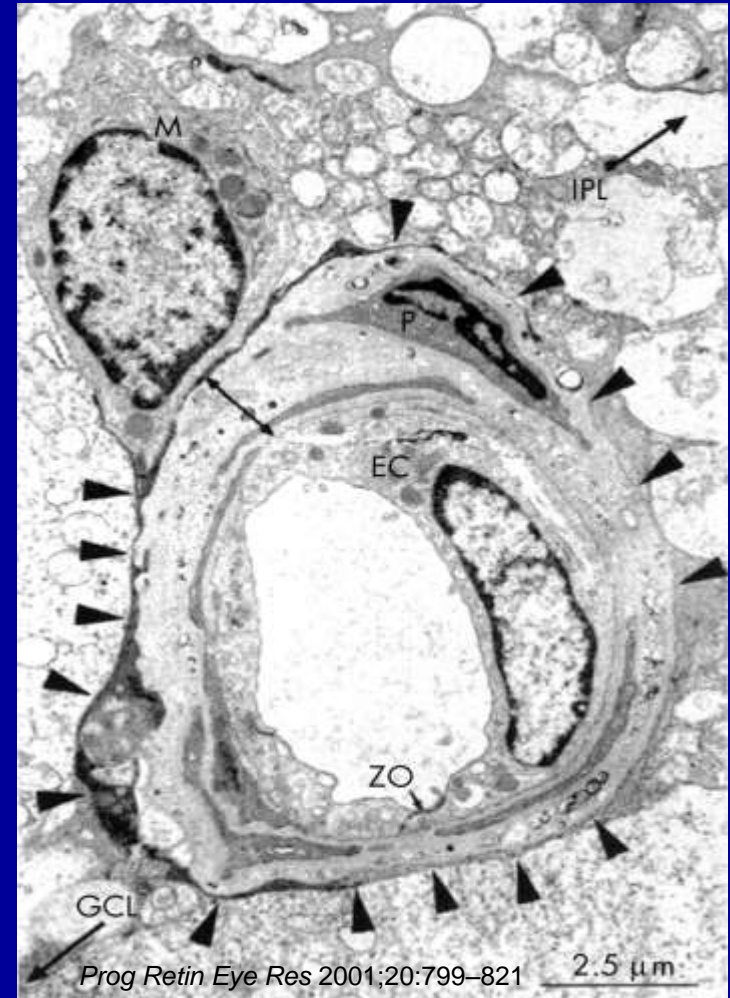
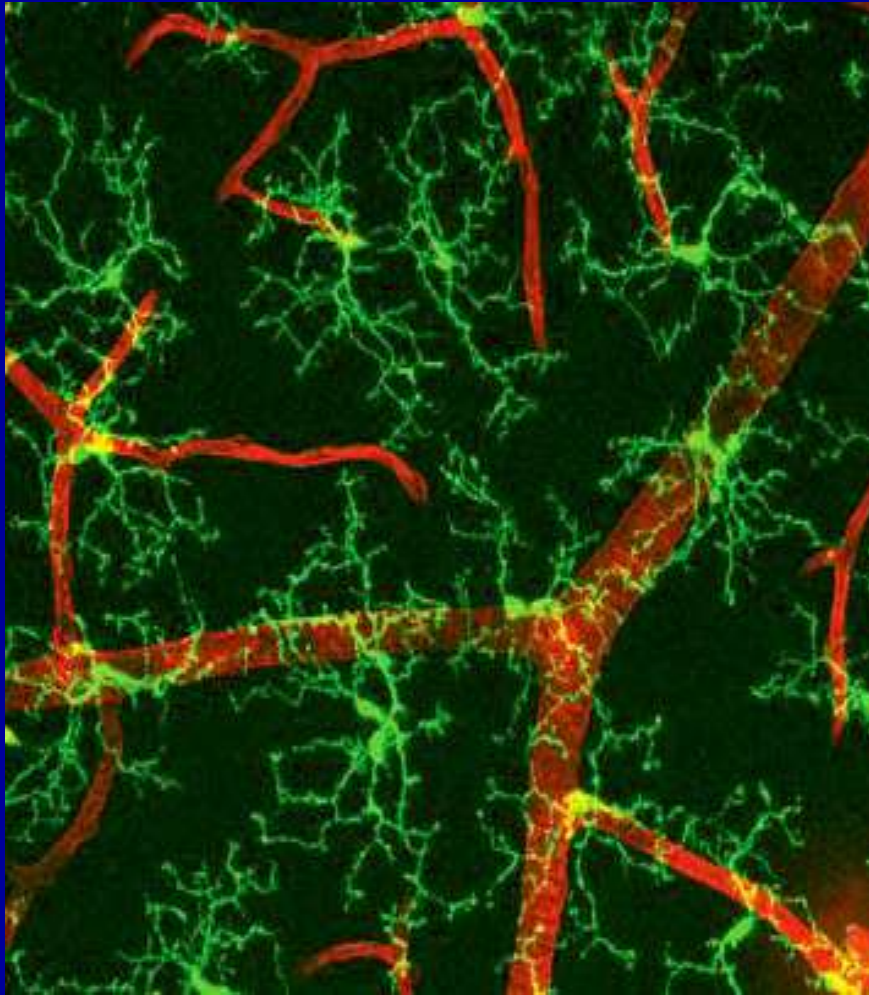
Type 2 Diabetic  
9 years duration

# **Unique nature of the retinal vasculature**

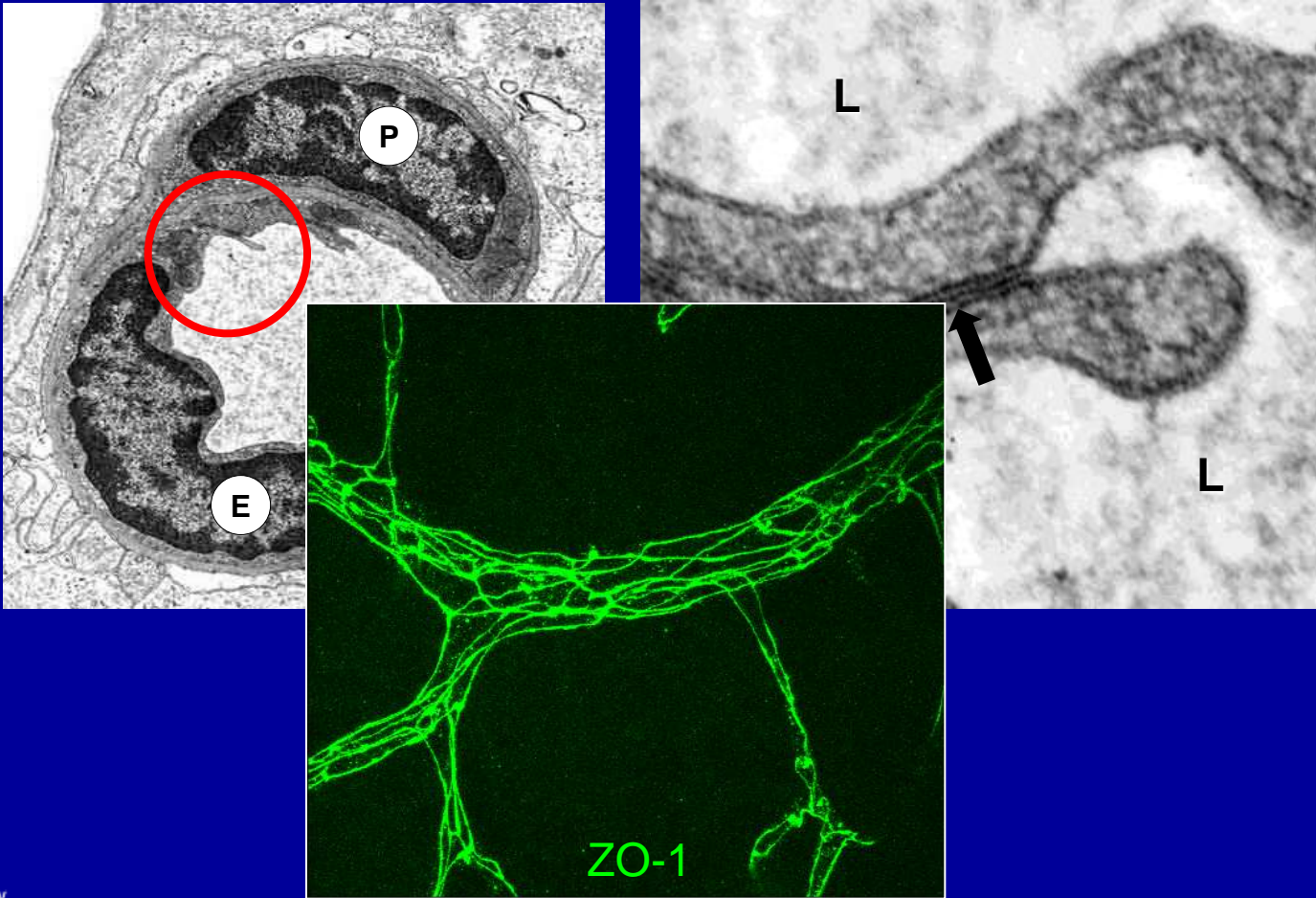


- *Highly specialised end-artery system*
- *Autoregulation of blood flow in response to metabolic needs of neural retina*
- *Multi-cell capillary unit*
- *Inner retina blood barrier (analogous to Blood brain barrier)*

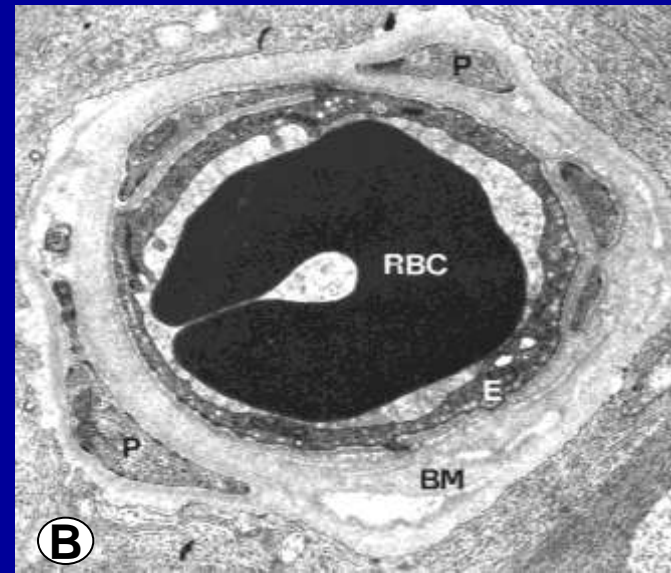
# Retinal blood vessels do not occur in isolation



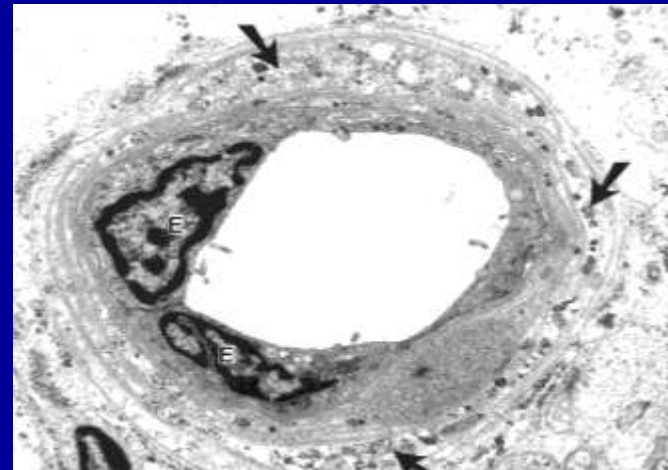
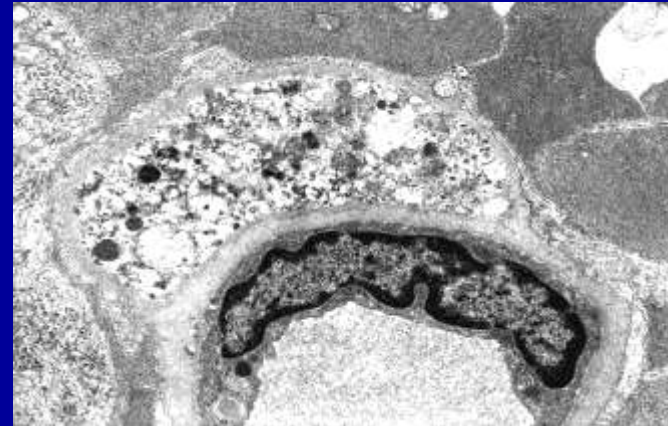
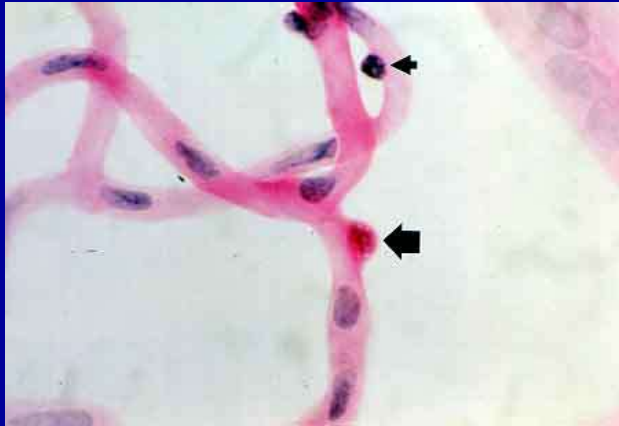
# Retinal Capillary Structure

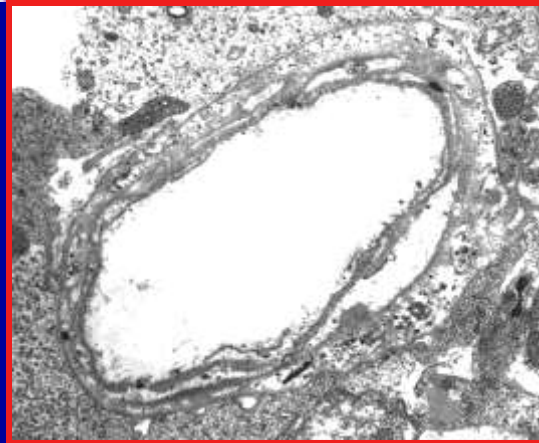
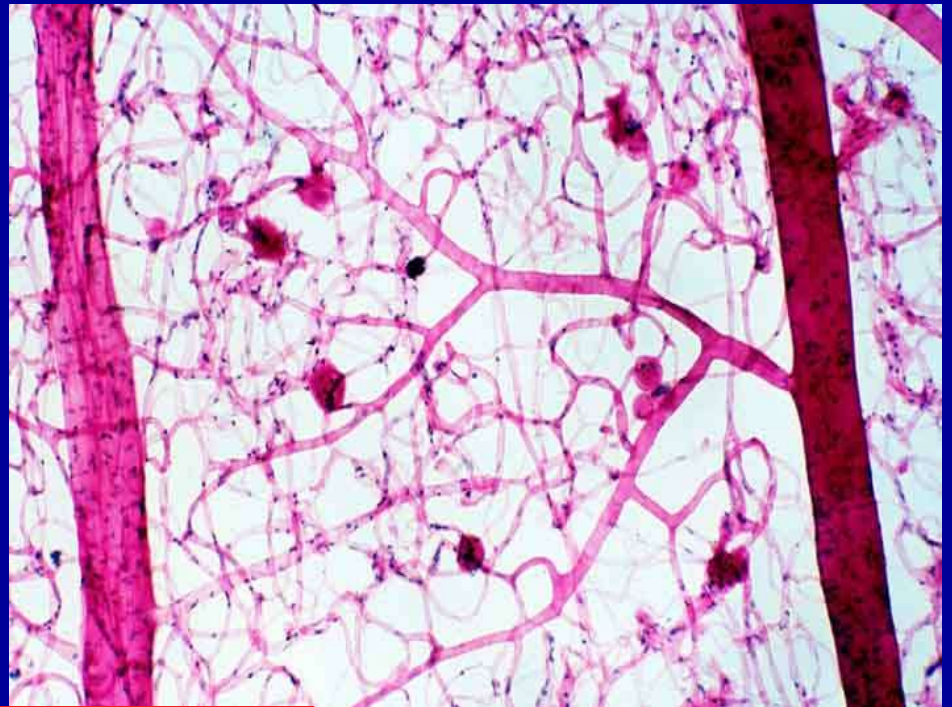
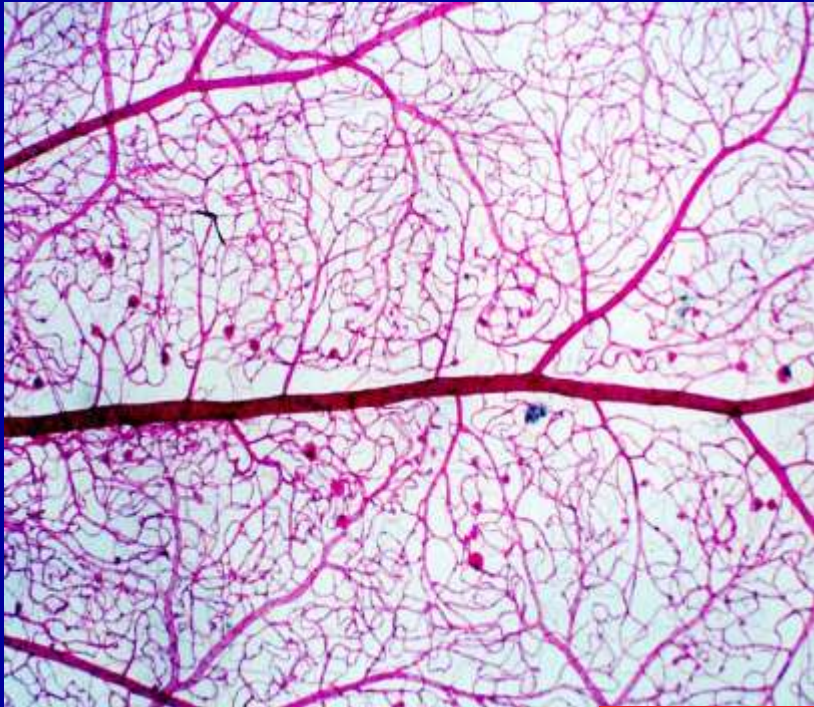


# Capillary pathology in human diabetic retinopathy: BM thickening



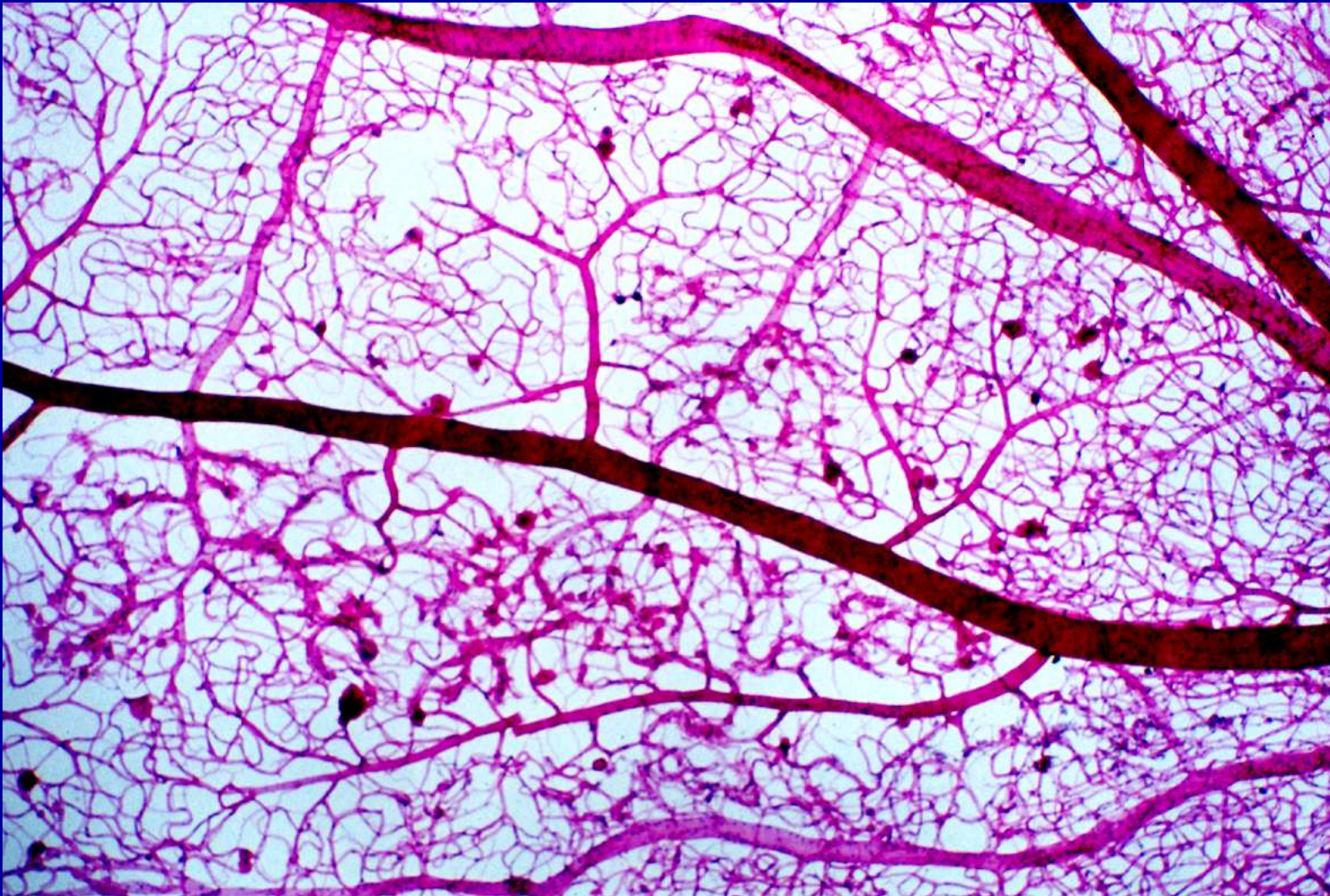
# Progression of microvascular pathology in diabetic retinopathy

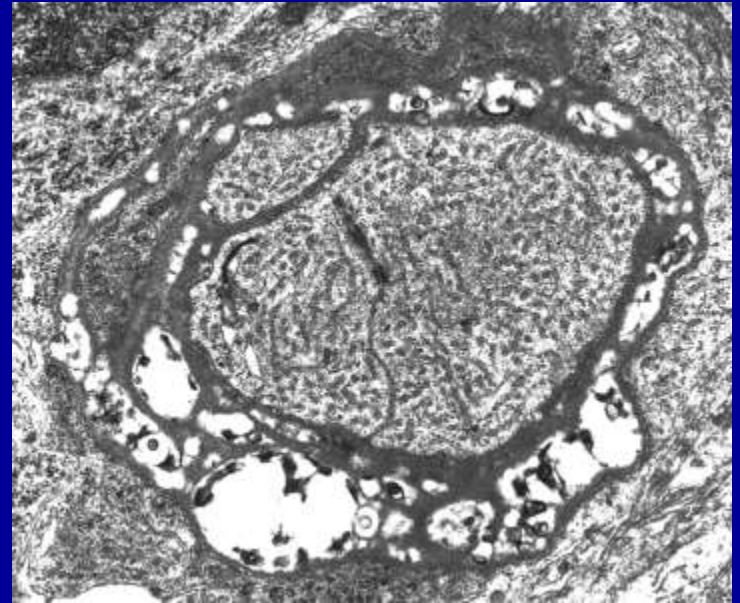
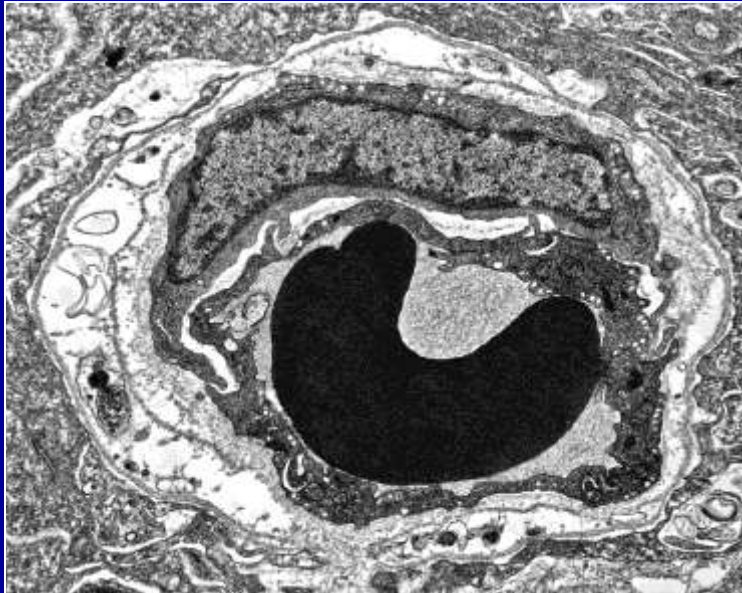
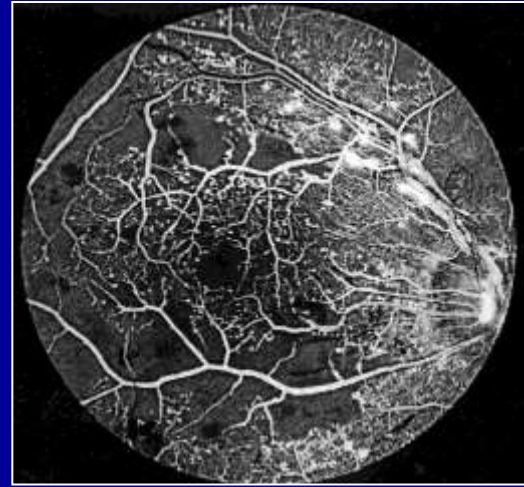
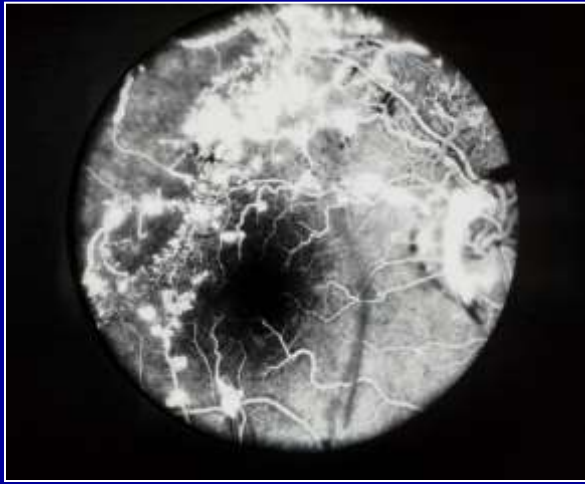






# Vascular remodelling – not reperfusion in diabetic retina:

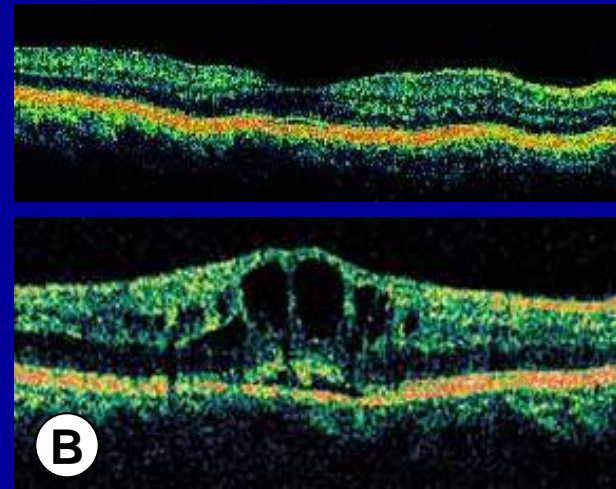




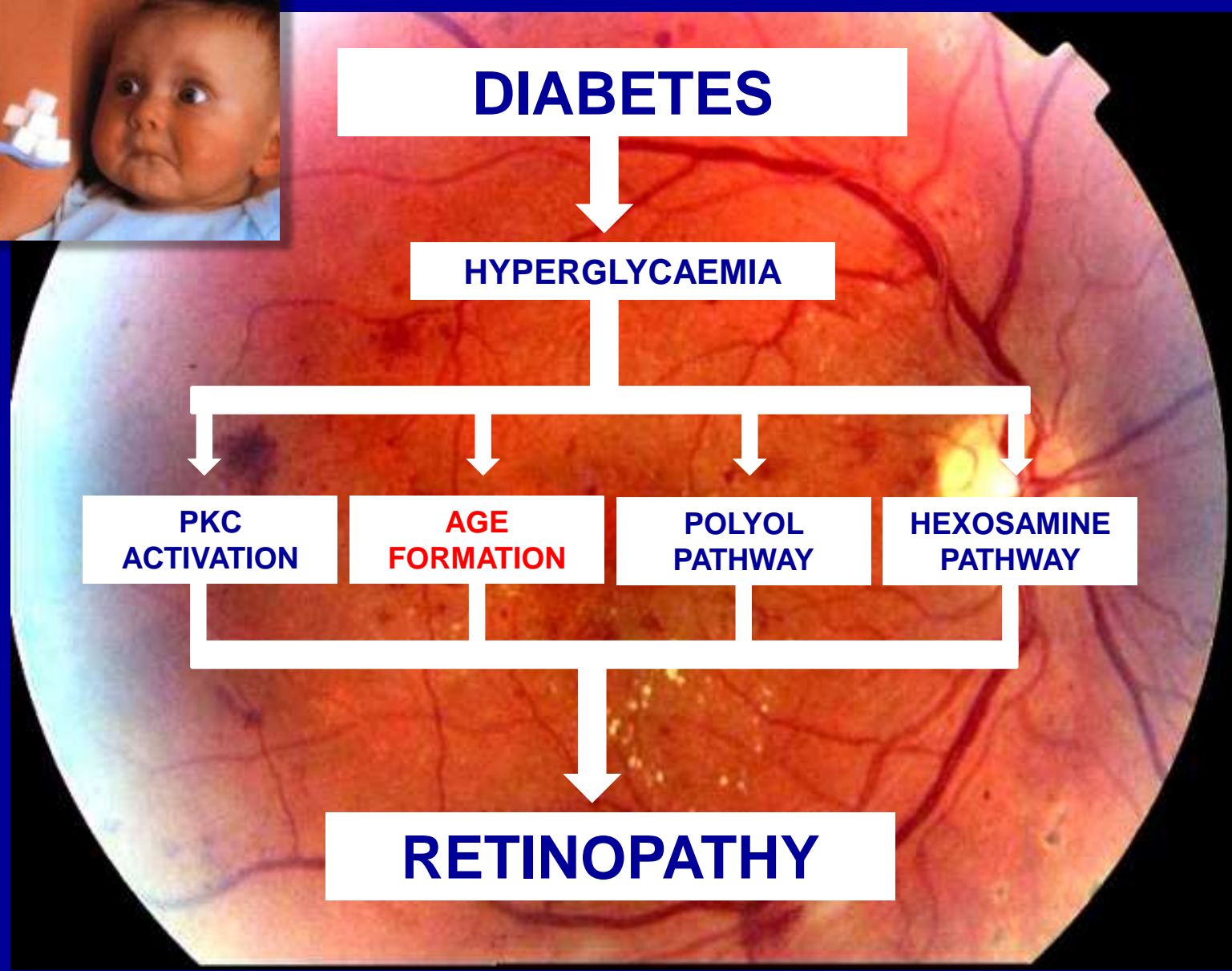
BRVO

DR

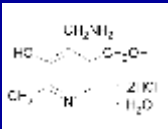
# Sight-threatening stages – only after extensive vasodegeneration



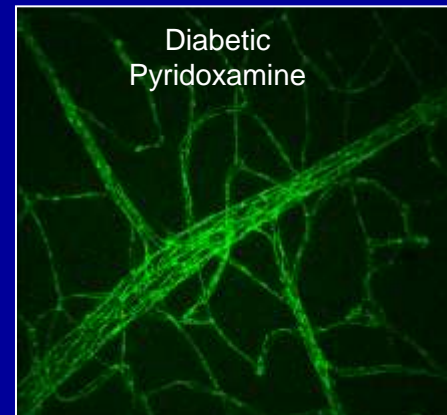
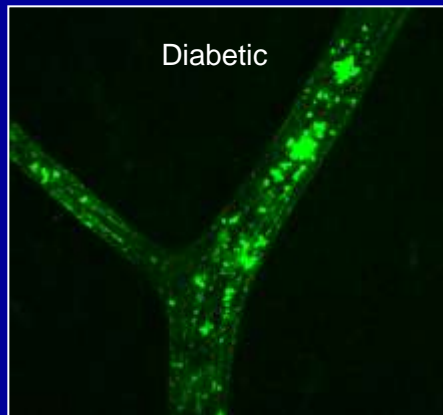
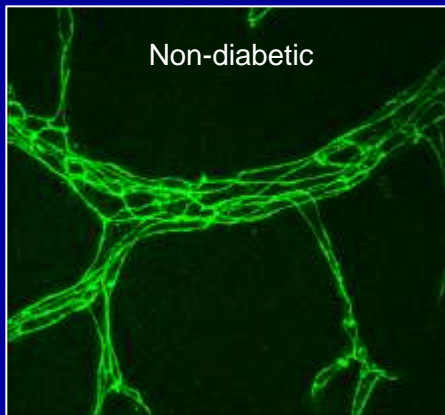
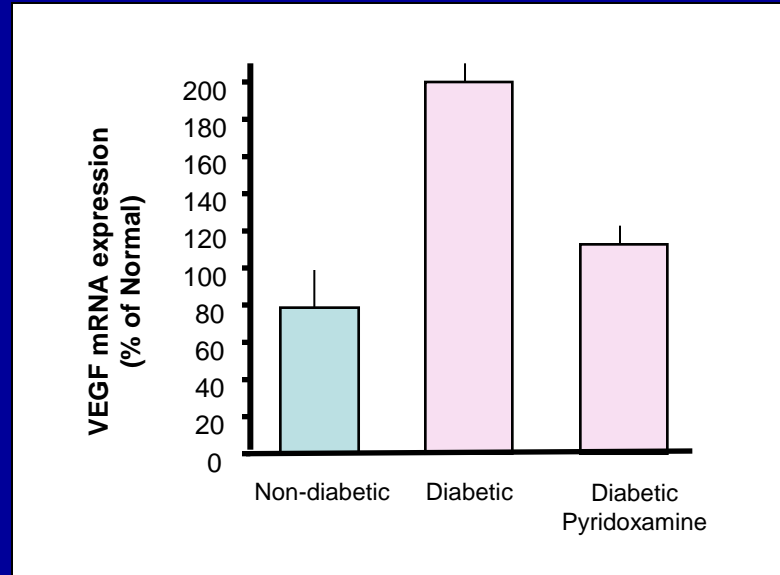
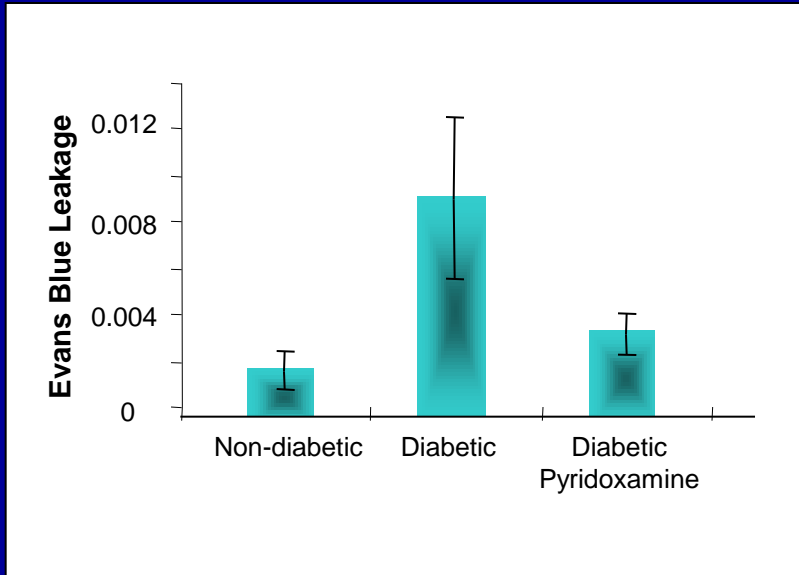
What causes vasogeneration?



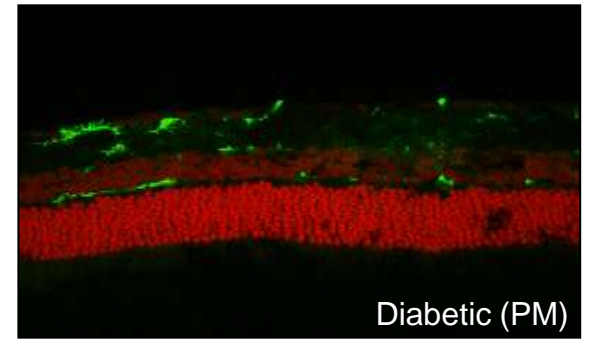
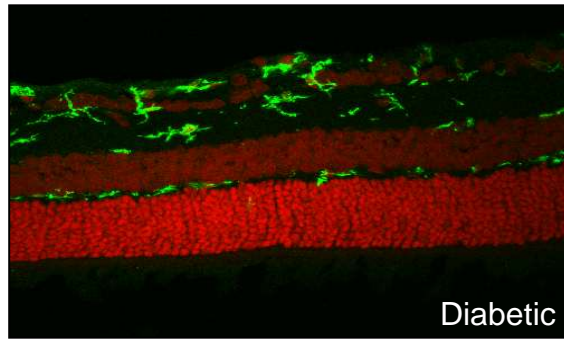
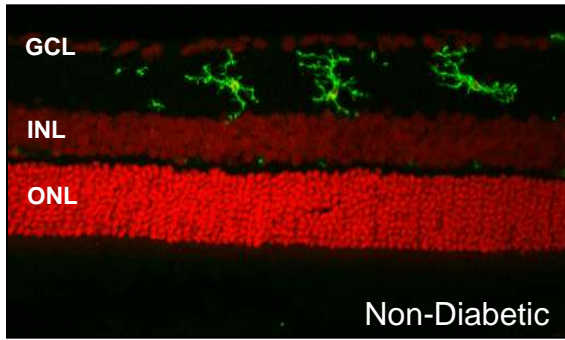




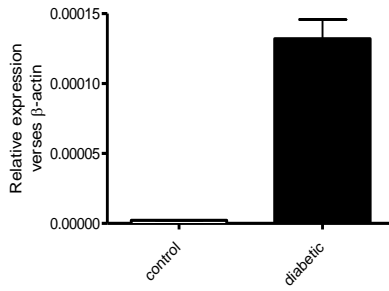
# AGE-inhibition prevents blood retinal barrier breakdown



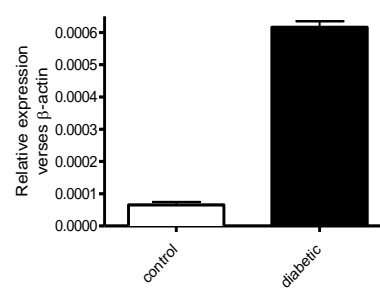
# AGE INHIBITION PREVENTS MICROGLIAL ACTIVATION IN DIABETIC RETINA



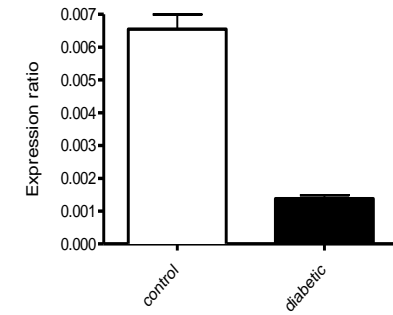
IL-1beta



TNF-alpha

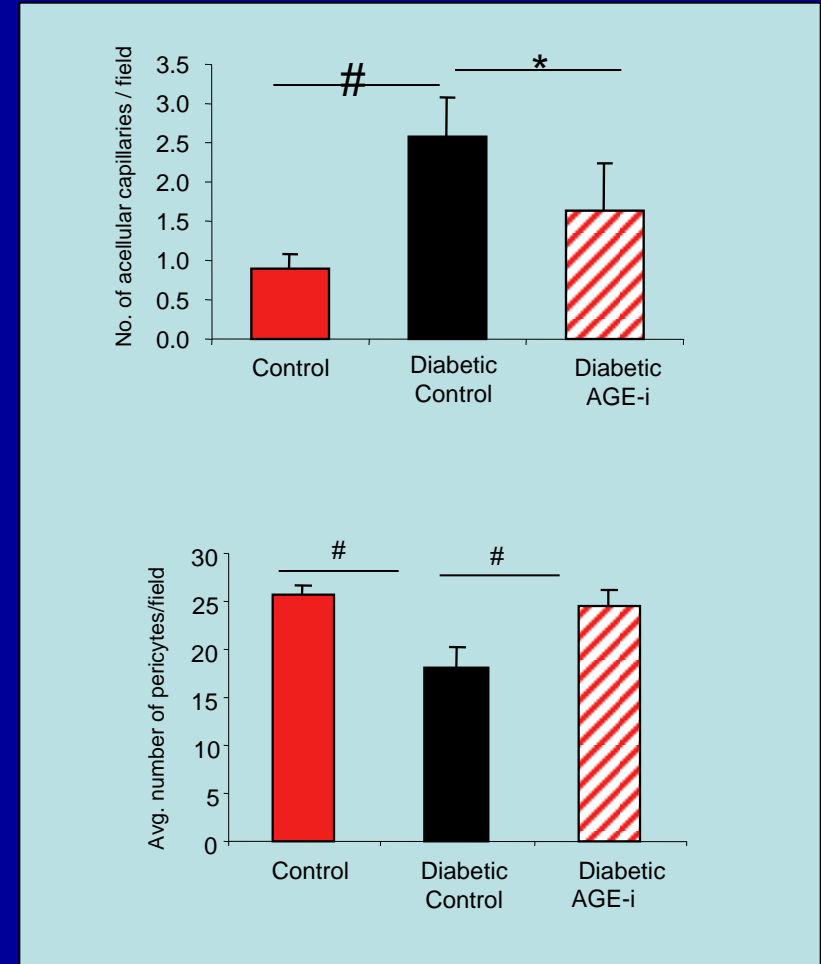
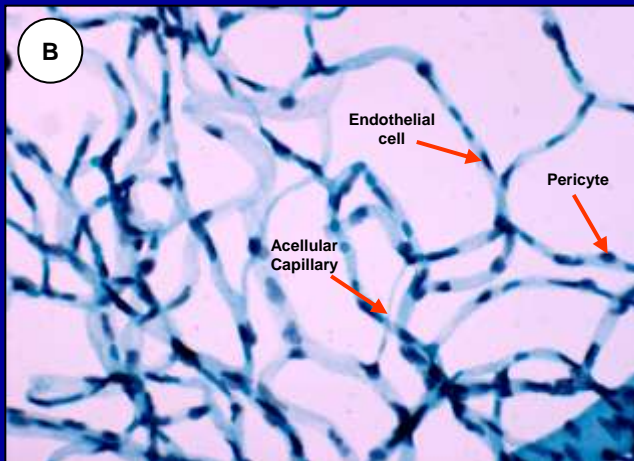
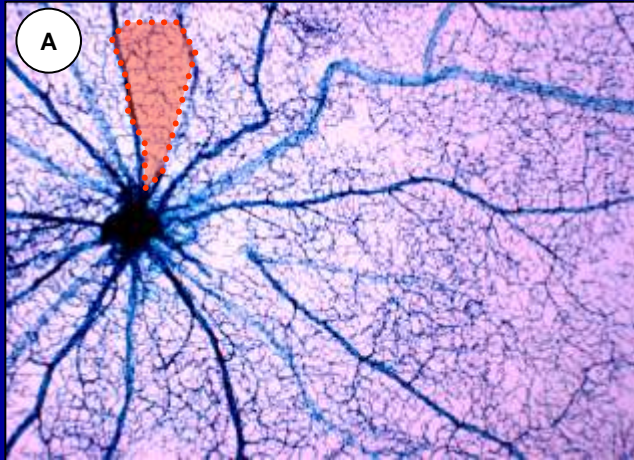


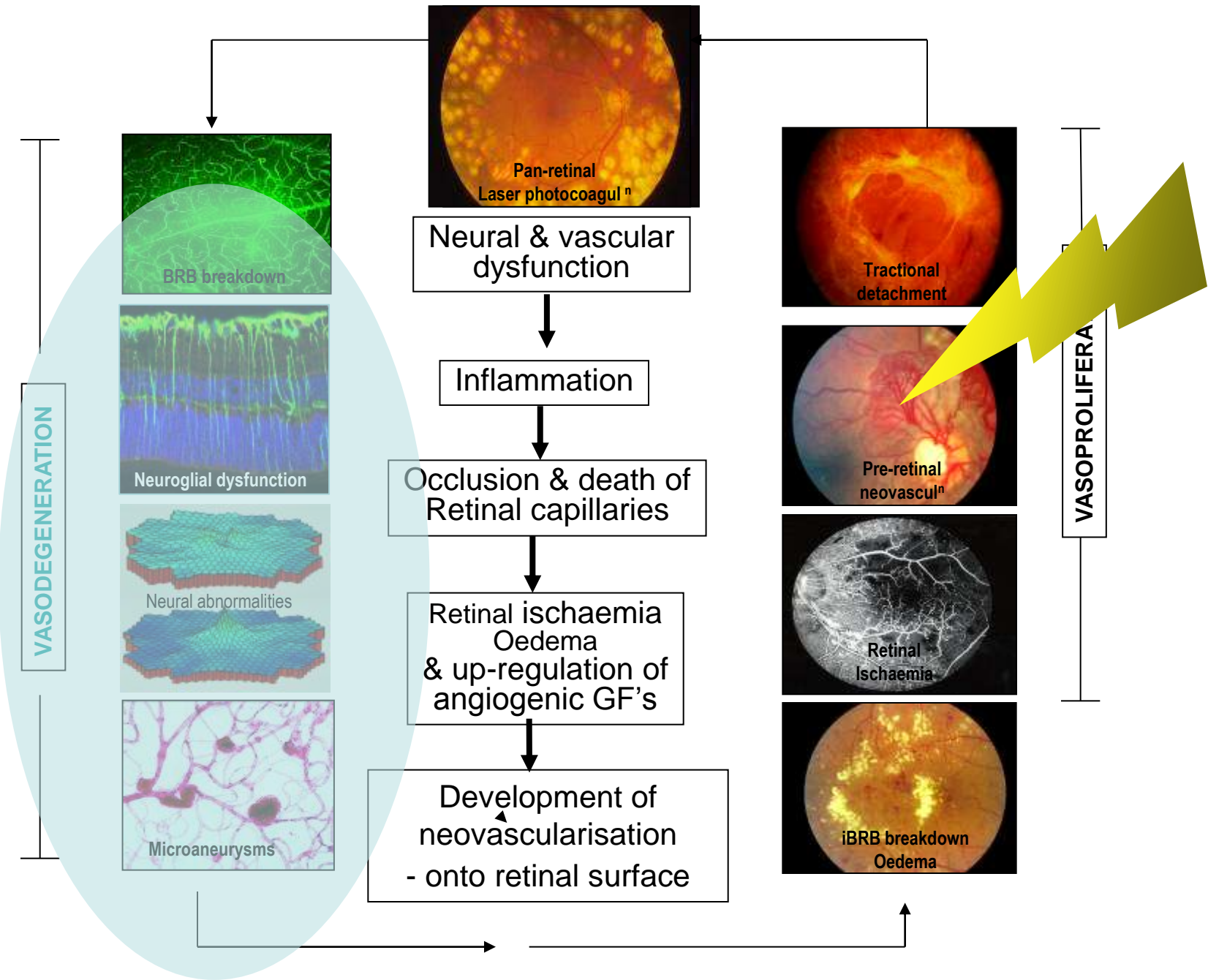
IL-10





# AGE-inhibition prevents acellular capillary formation



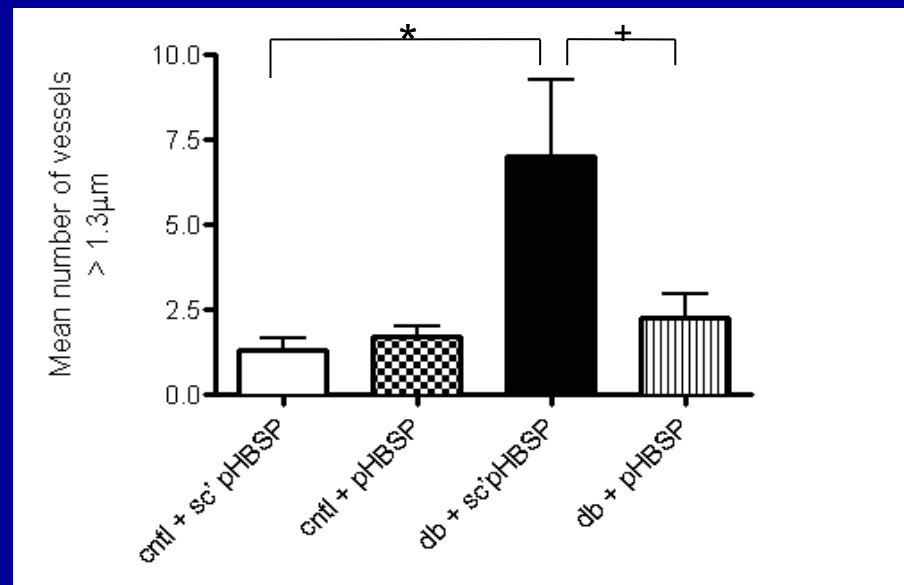
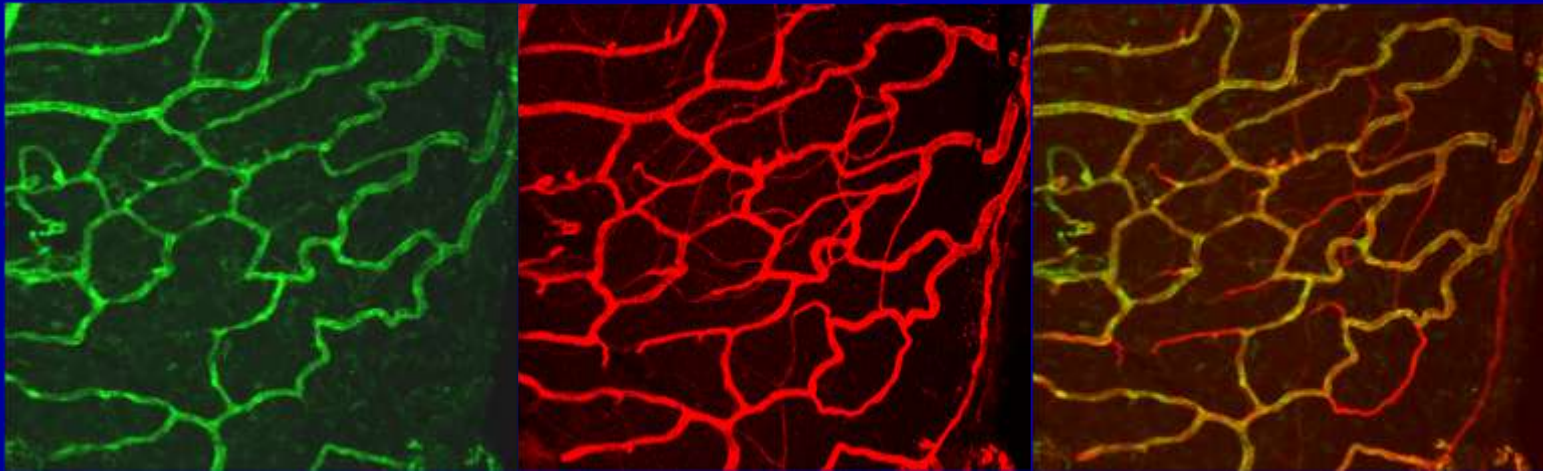




- Tissue protective / anti-inflammatory in brain injury (stroke) models
- Non-erythropoietic
- 11 amino acid peptide – crosses blood brain (& retinal) barrier



# An EPO analogue protects against capillary degeneration

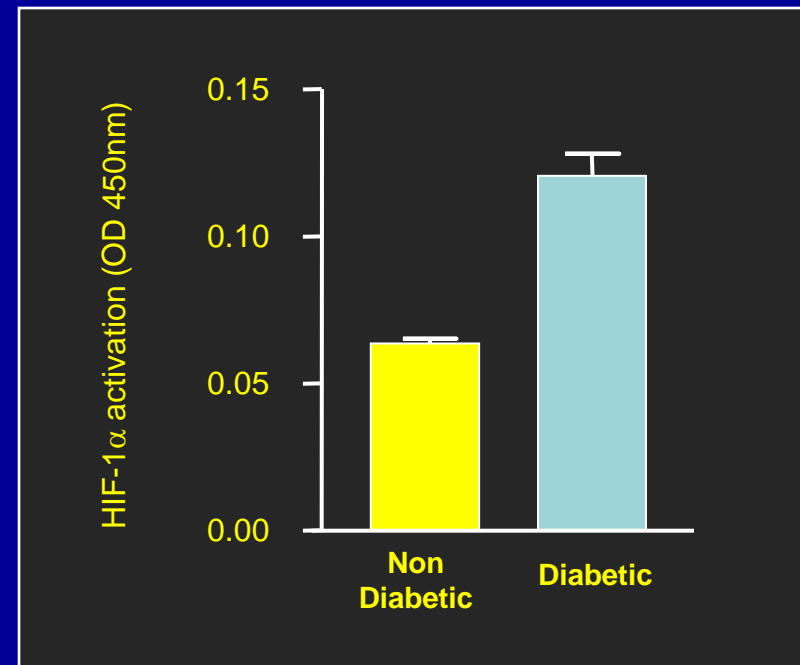
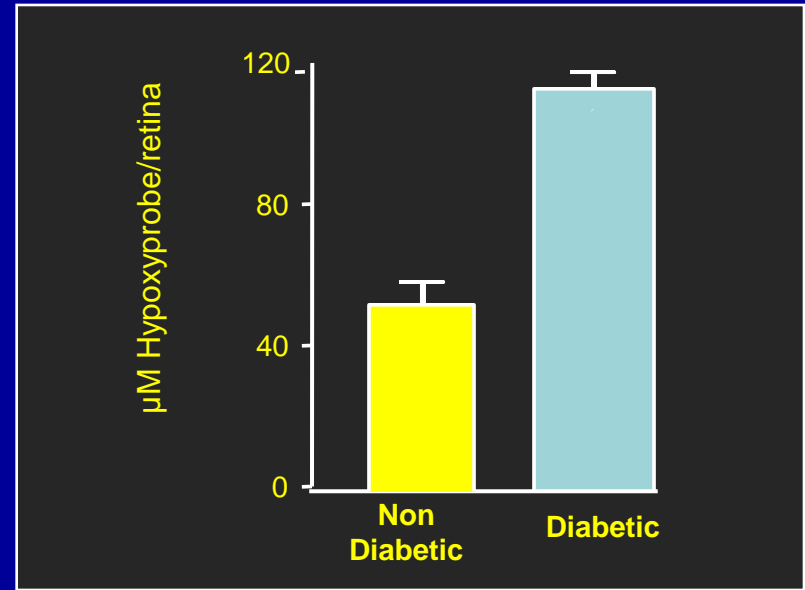
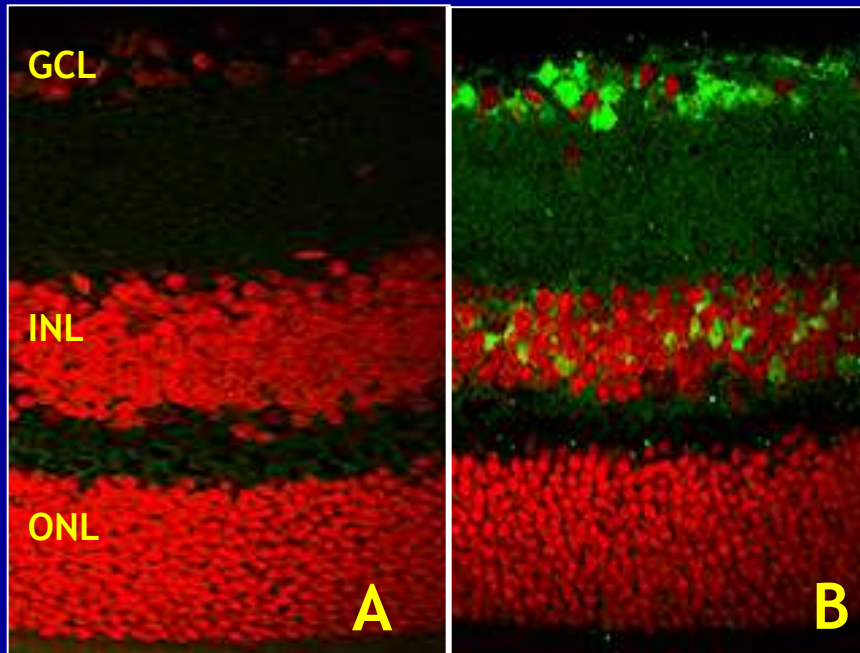


# Summary

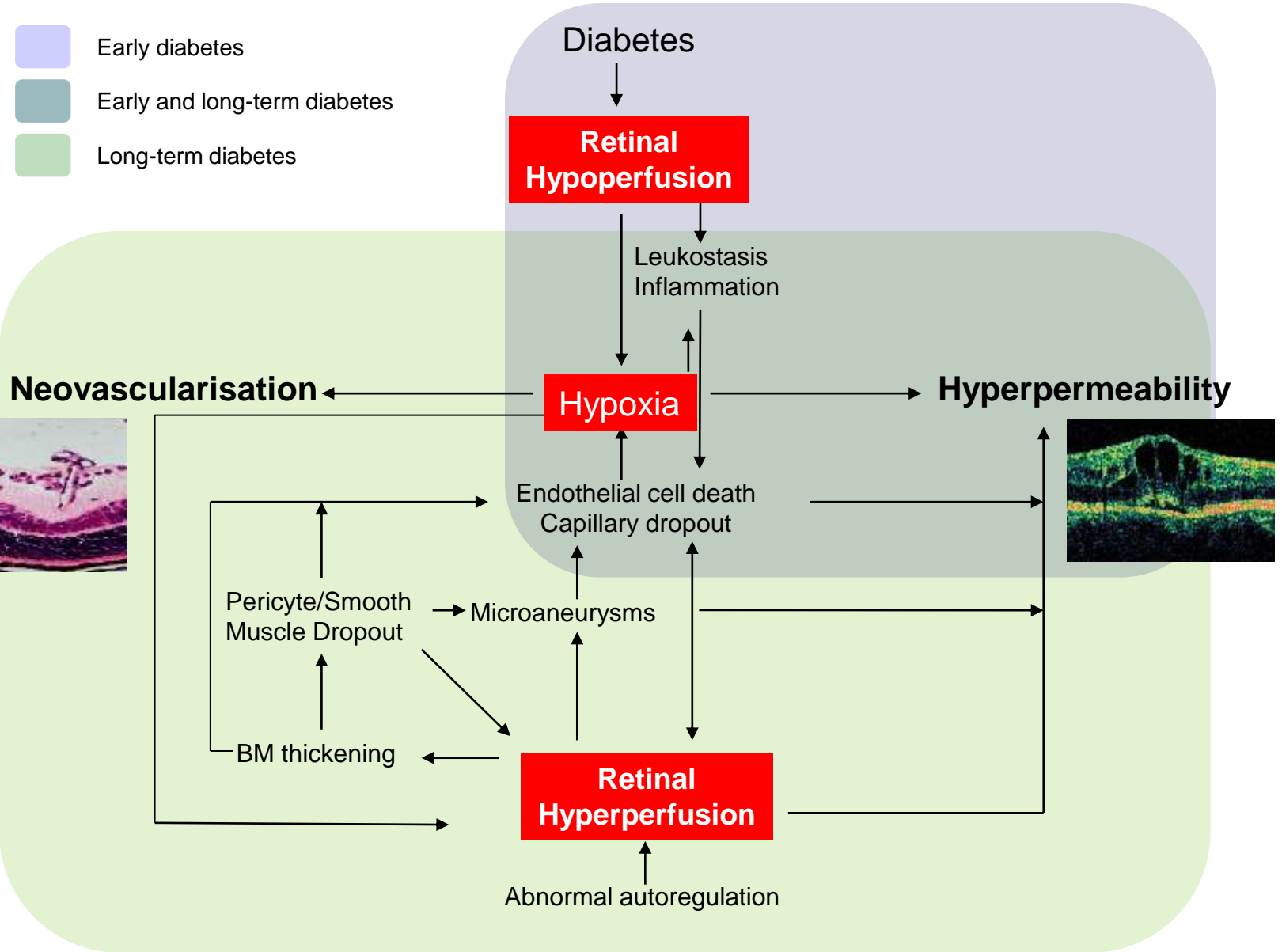
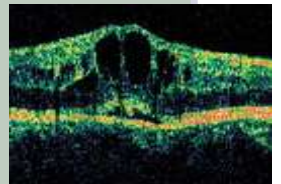
- Diabetes is a vasodegenerative disease
- Diabetes impacts on all cells of the retina – not just the vasculature.
- Inflammation is now recognised as a key component of early-stage degenerative diabetic retinopathy
- Pathogenesis is complex and multi-factorial. Intervention could prevent progression to sight-threatening stages.

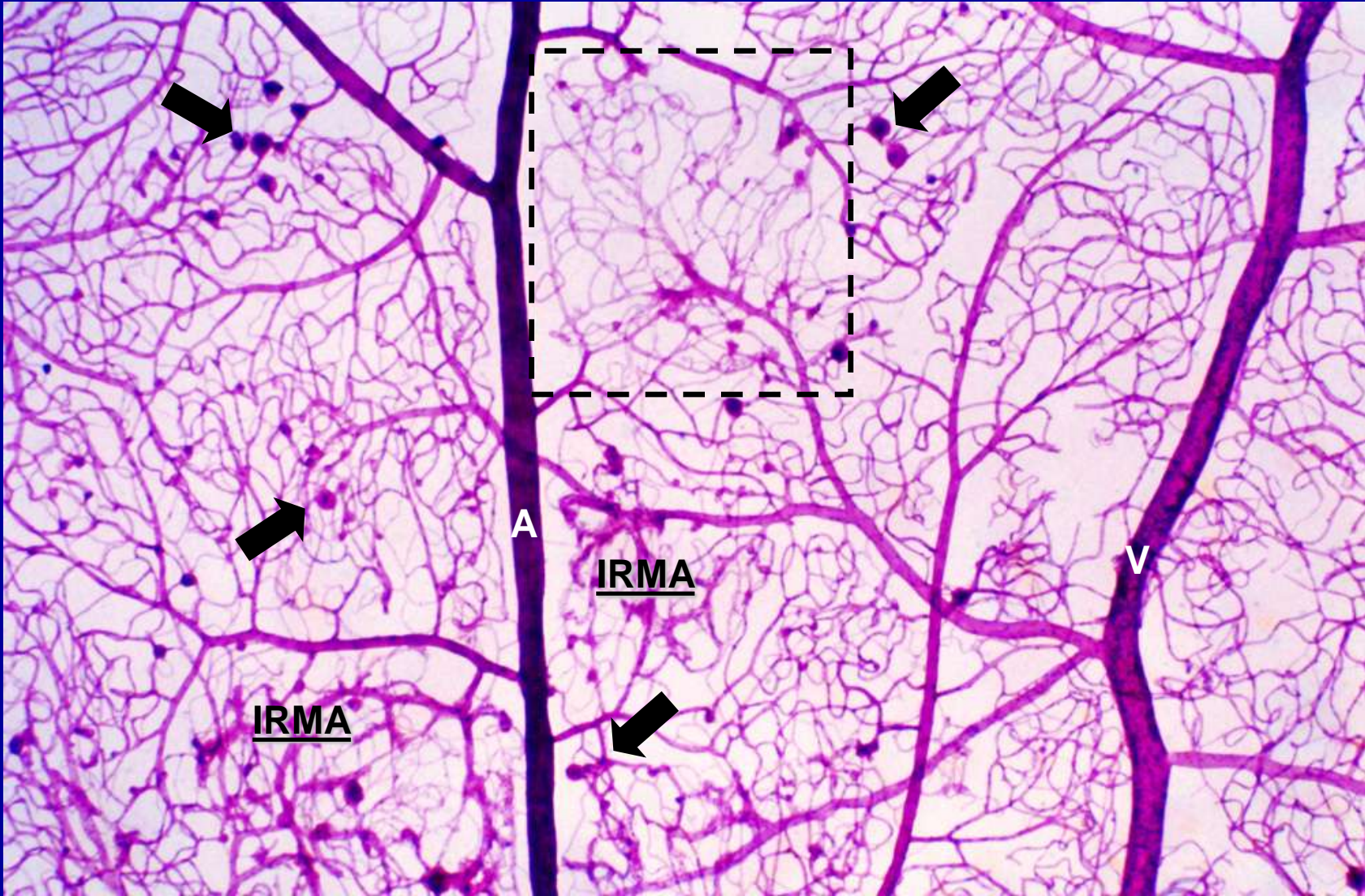
## Hypoxia is increased in early diabetes

- ❖ Pimonidazole hydrochloride (2-nitroimidazole)
- ❖ Activated in cells at  $pO_2 < 10\text{mmHg}$



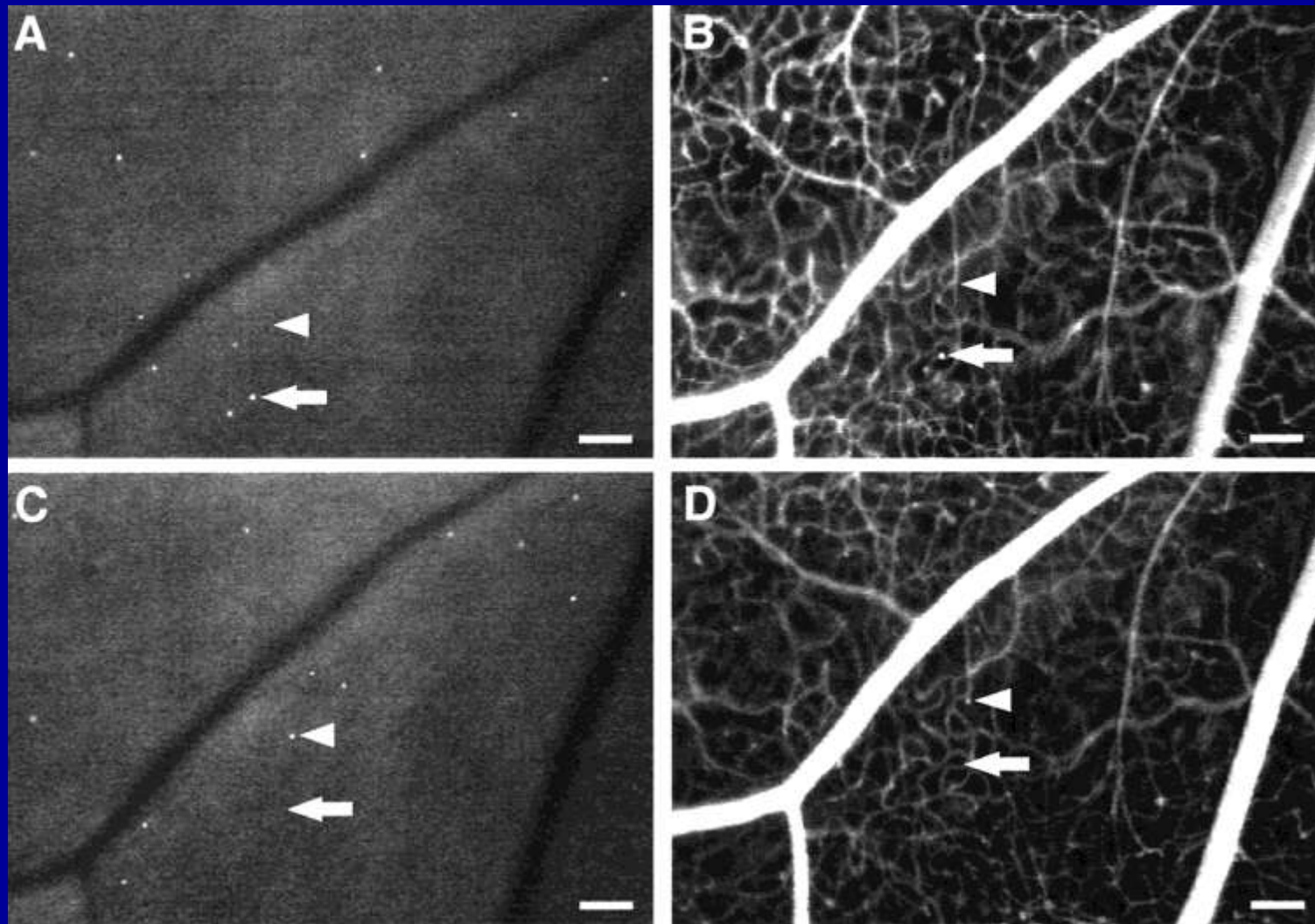
- Early diabetes
- Early and long-term diabetes
- Long-term diabetes

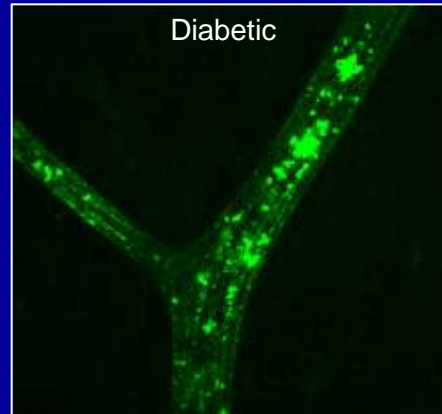
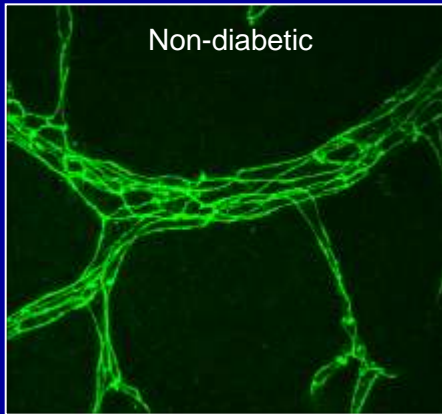
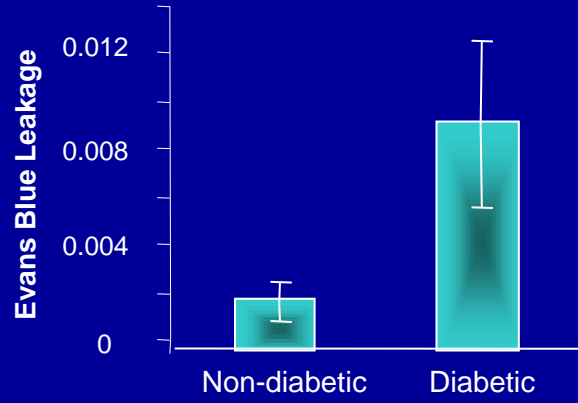
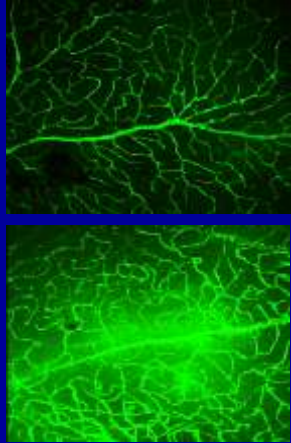




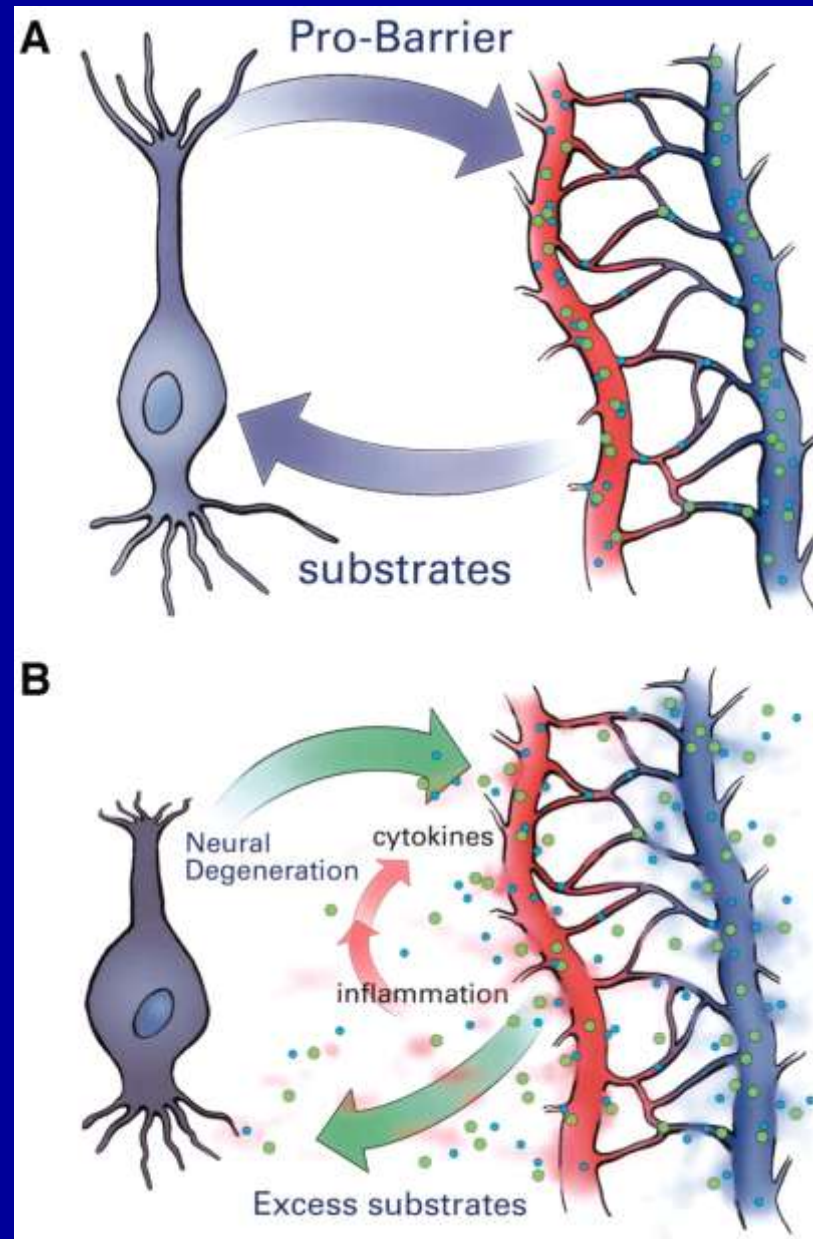


Static leukocytes are in flux, block capillary flow, and transmigrate.



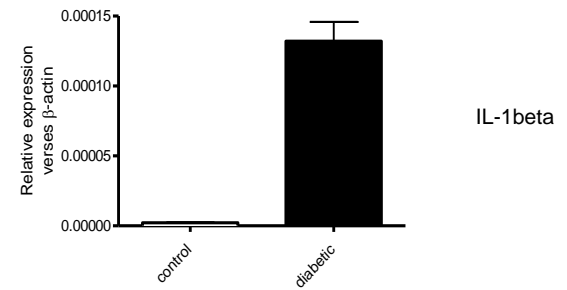
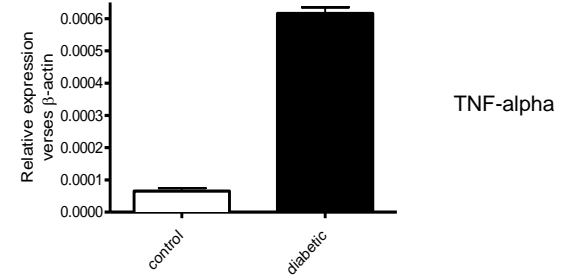
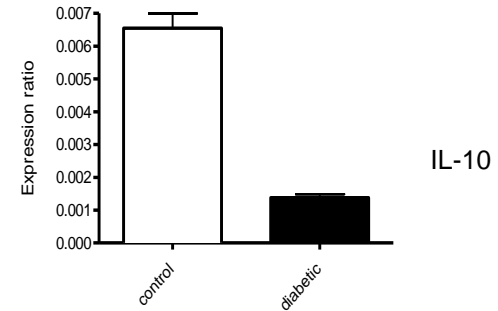
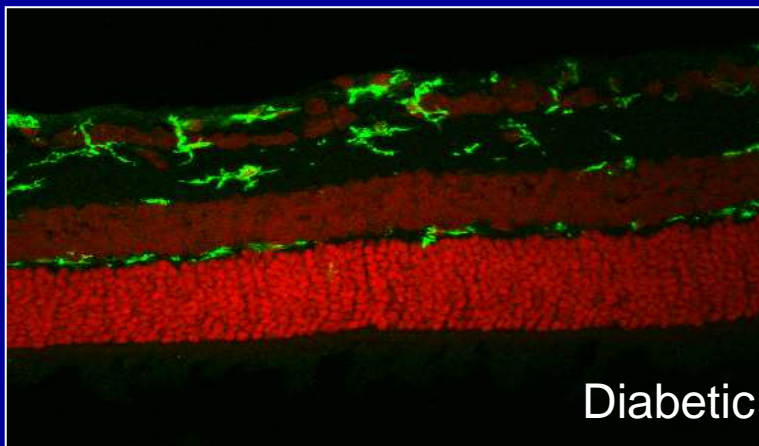
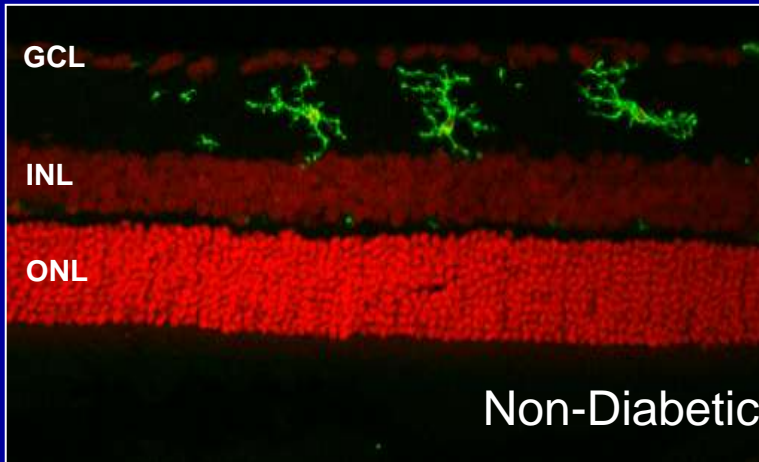
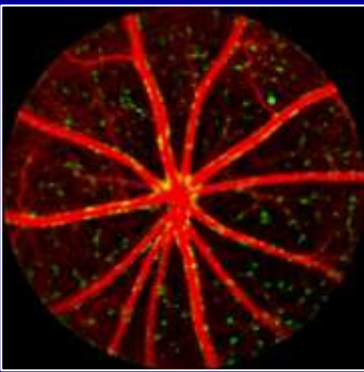


# Glial – vascular abnormalities in early diabetes

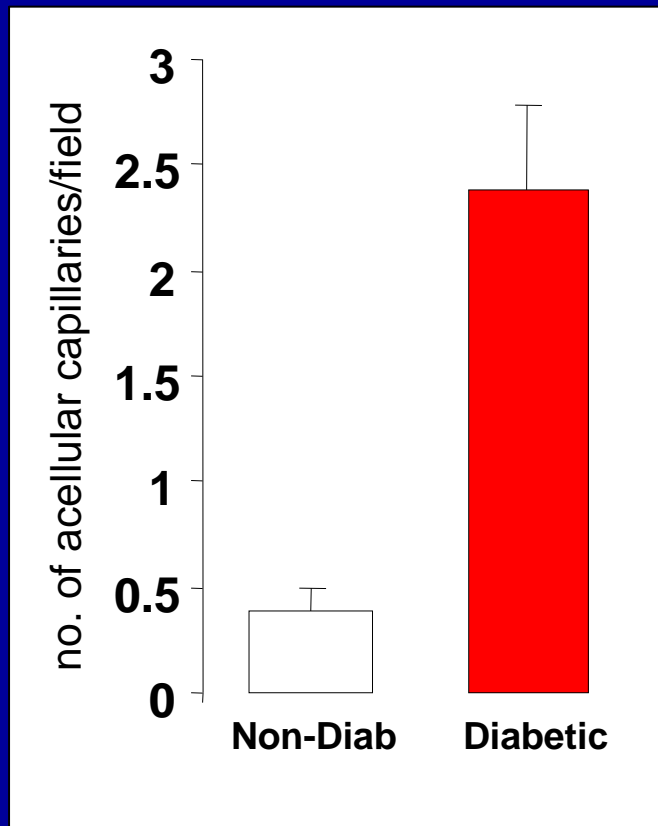
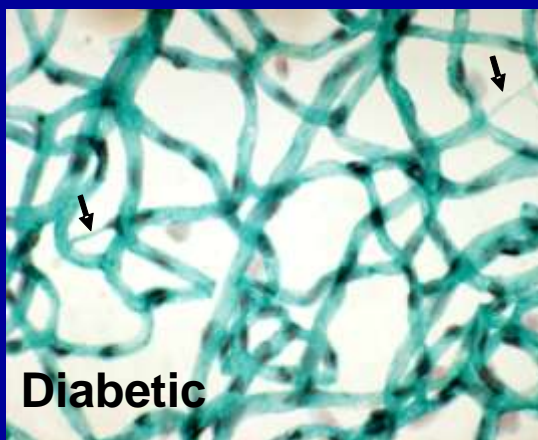
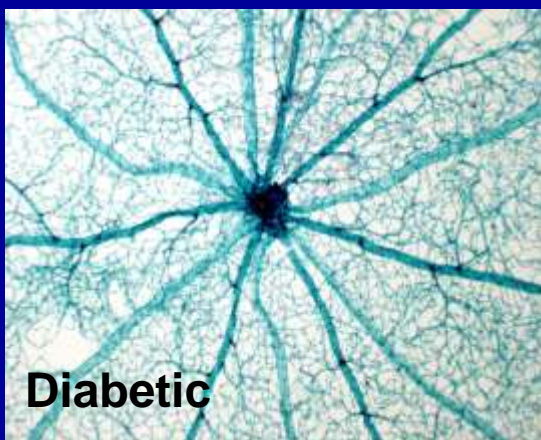
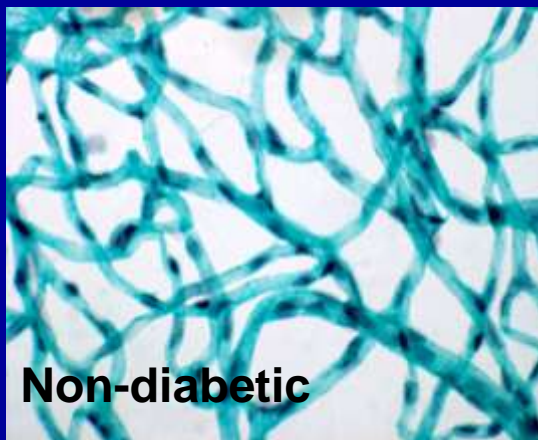
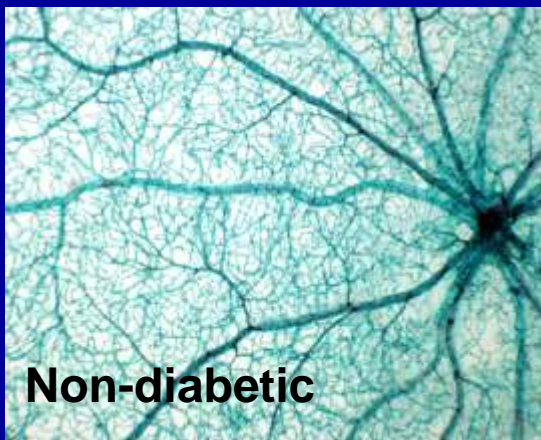


*Antonetti et al.*  
*Diabetes* 2006 55(9) 2401-2411

# Pro-inflammatory processes in diabetic retina



# Diabetic rodents show the early stages of retinopathy



# Neural and glial abnormalities in early diabetes

