| Explain the roles of TGF-beta and VEGF in diabetes complications | • TGF-beta is a cytokine which inhibits ECM breakdown leading to basement membrane thickening  
• VEGF is a cytokine and survival factor. Too much increases vessel permeability, too little triggers apoptosis. It stimulates angiogenesis. |
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| Why are lots of free radicals produced in diabetes?  
What builds up? | • Lots of glucose is going through the TCA cycle so lots of electrons are passing along the chain on the inner mitochondrial membrane.  
• This generates a high membrane potential which inhibits a component of the chain, causing build-up of ubiquinone. This reduces O₂ to superoxide. |
| List four key substances involved in chronic diabetes complications | • 1. Advanced glycation end products (AGEs). Accumulations of glycated amino acids.  
• 2. Sorbitol. Produced from glucose, causes cell damage by an osmotic effect and generation of reactive oxygen species.  
• 3. TGF-beta. A cytokine which inhibits ECM breakdown causing basement membrane thickening  
• 4. VEGF. A cytokine and survival factor – too much causes vessel permeability and stimulates angiogenesis, too little triggers apoptosis. |
| Explain how vascular perturbations are involved in development of chronic diabetic complications  
3 things | • VEGF causes increased vessel permeability – they get “leaky”.  
• The basement membrane thickens (due to TGF-beta) and vasodilatation is inhibited – vessel calibre is reduced and autoregulation is lost.  
• Thinner vessels can cause platelet activation, increasing thrombosis risk. |
| Explain the mechanism of diabetic retinopathy  
2 main things | • 1. VEGF stimulates angiogenesis on the retina and makes the vessels leaky. Protein accumulates.  
• 2. TGF-beta thickens the basement membrane causing microaneurysm. Occlusions can also occur, causing ischaemic lesions. Ischaemia stimulates more angiogenesis, driving the retinopathy |
| What can be done to prevent/treat diabetic retinopathy? | • Tight control of blood glucose and BP reduces incidence and slows progression of retinopathy. |