



Fisiopatologia das Principais Doenças Crônicas relacionadas à idade

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Aterosclerose

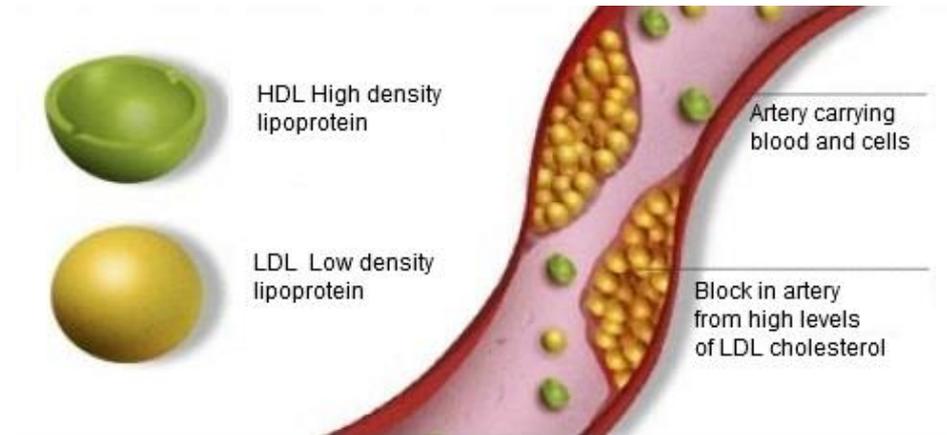
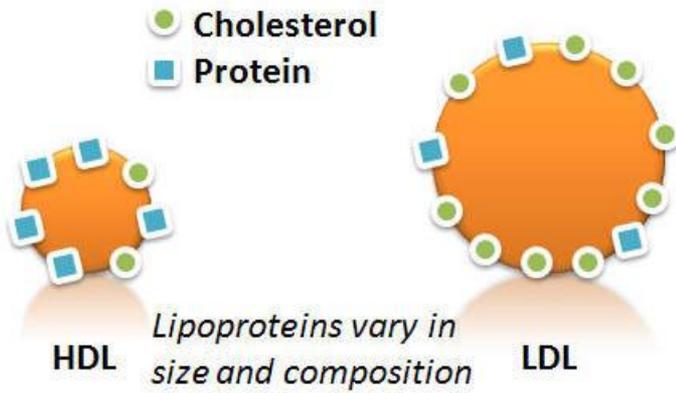
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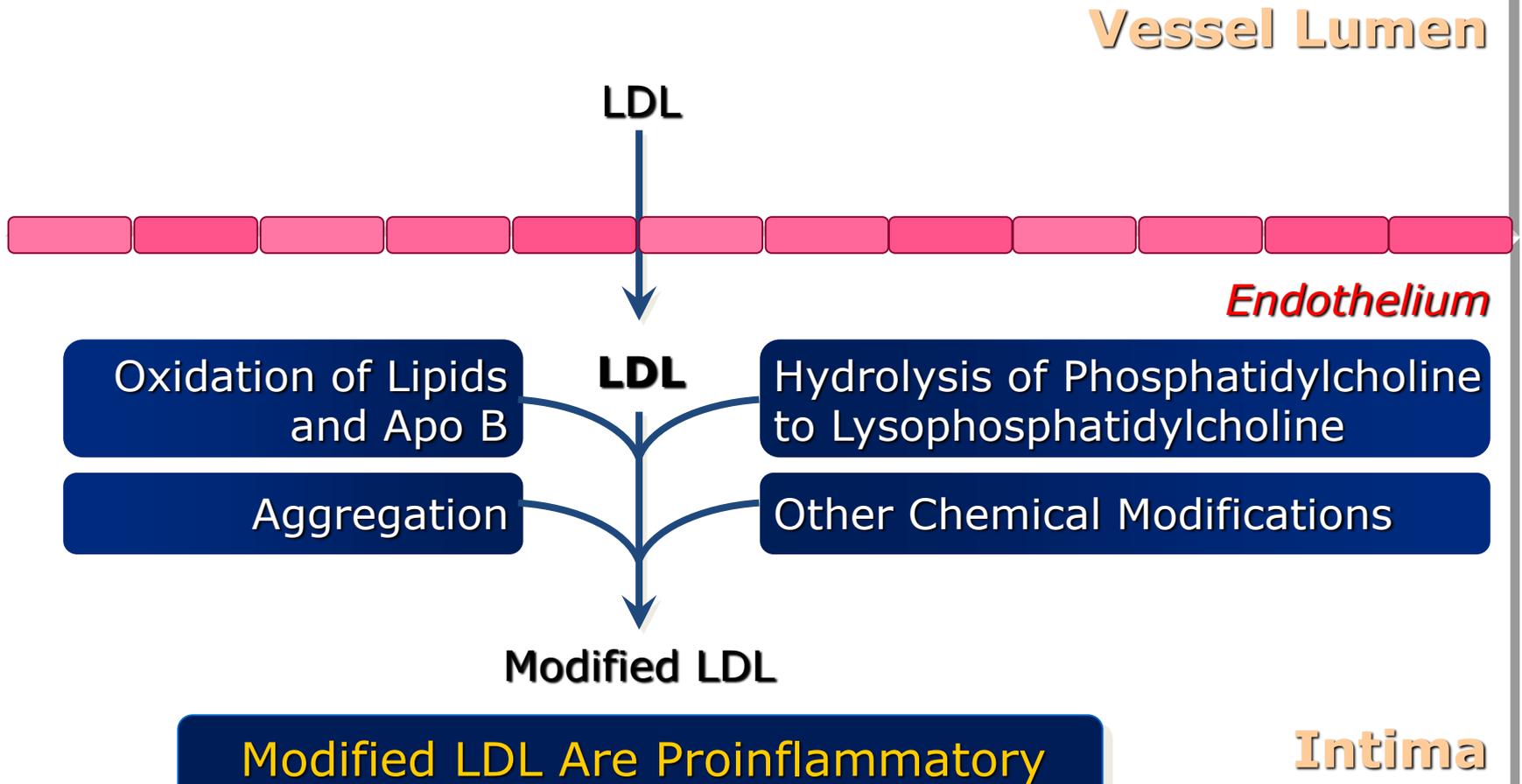
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Lipoproteins

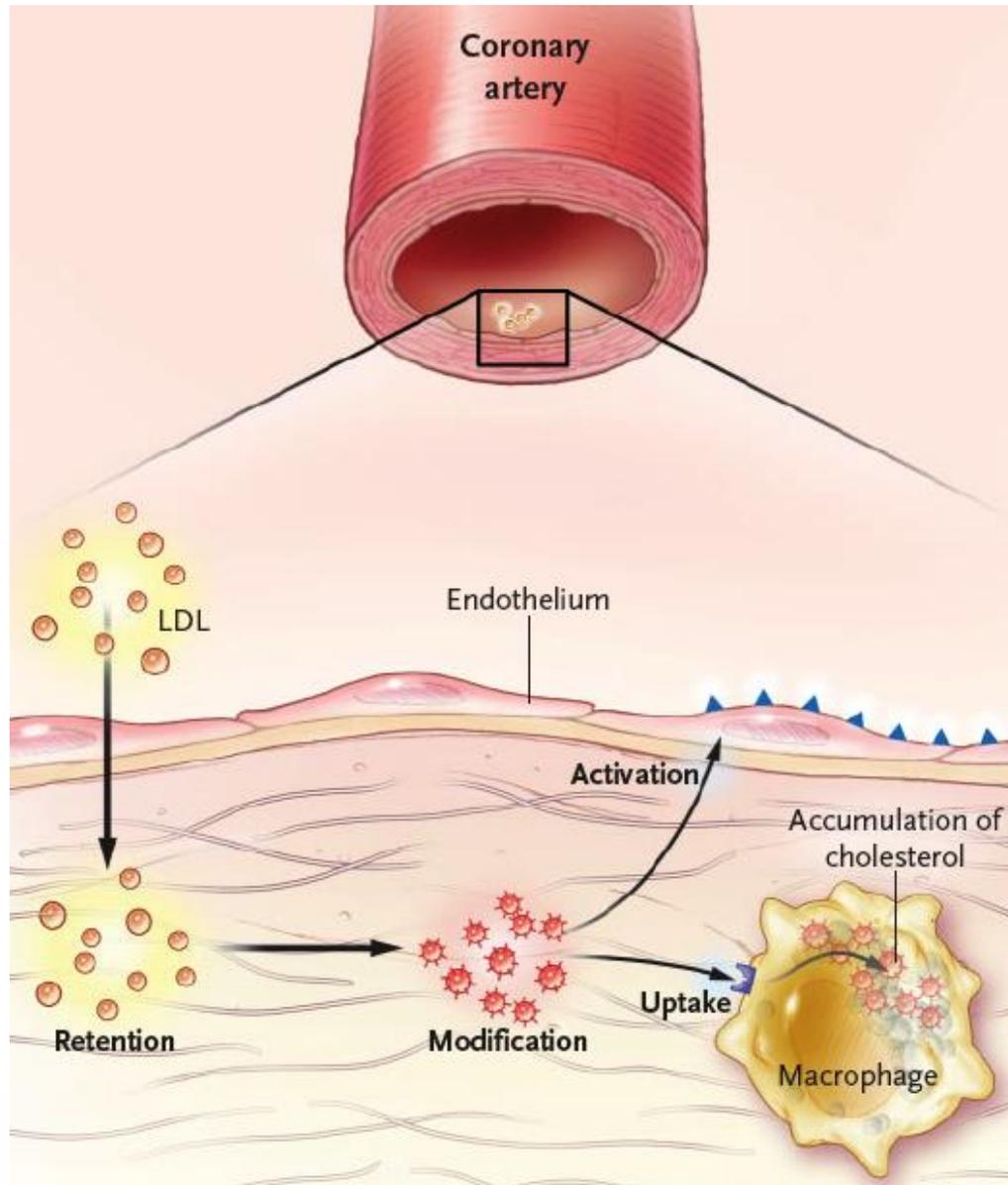


LDL na Inflamação

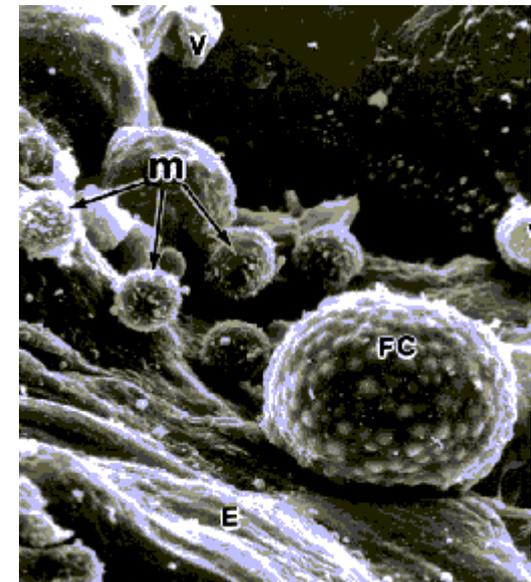
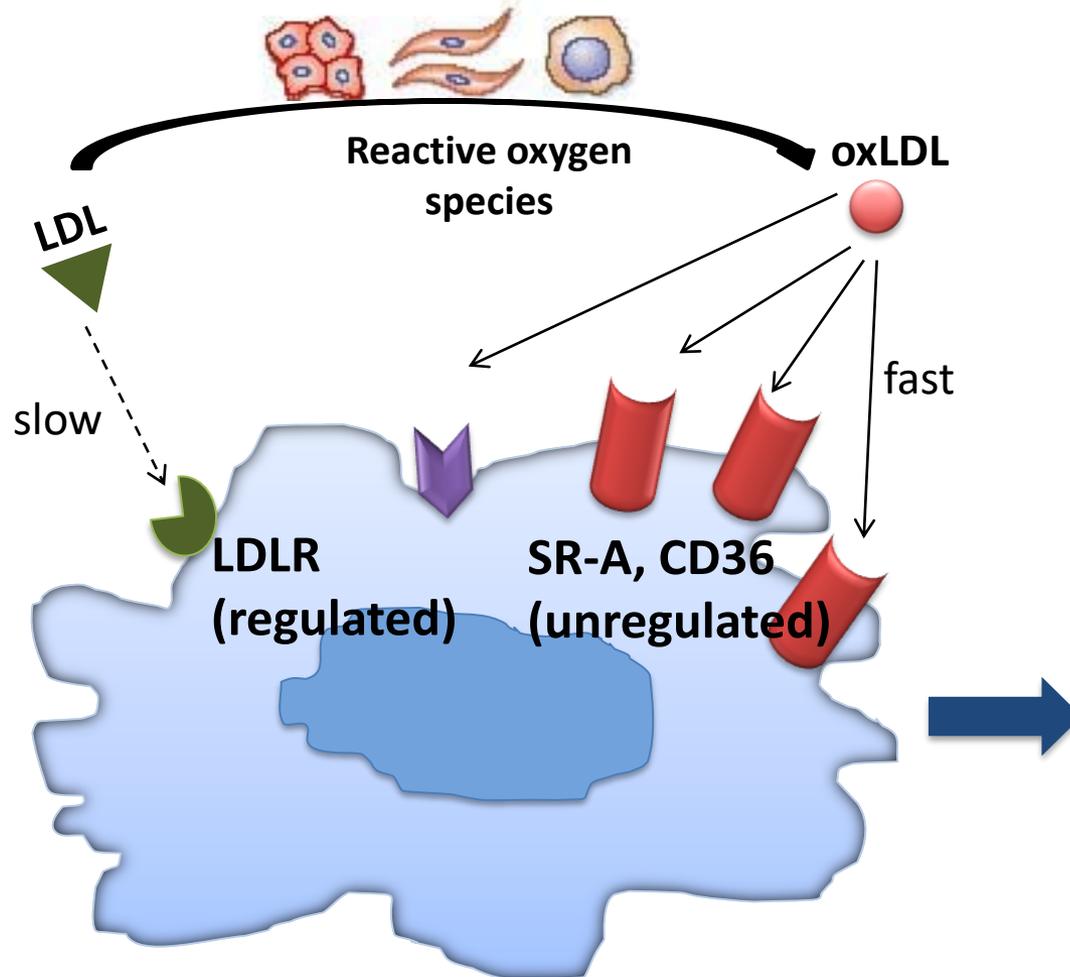
LDL Readily Enter the Artery Wall Where They May Be Modified



Lesão precoce: Lipoproteínas modificadas e as células espumosas

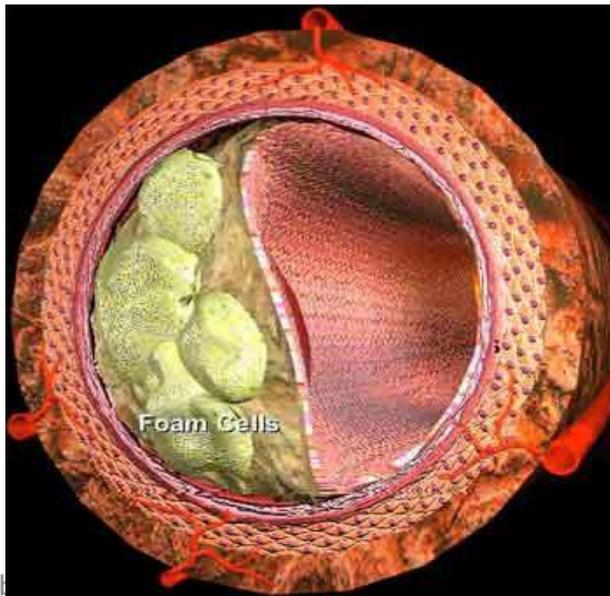
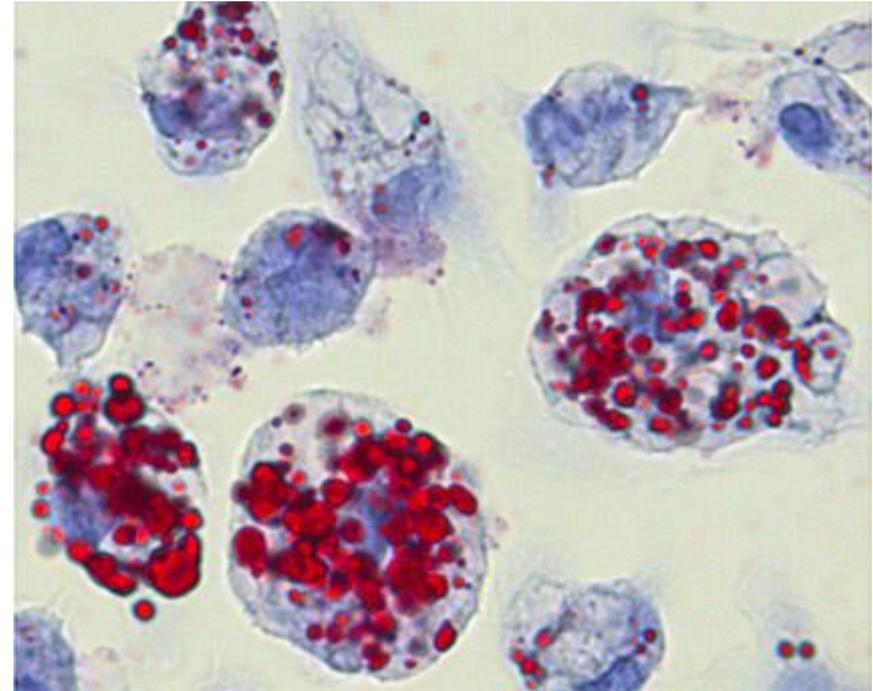
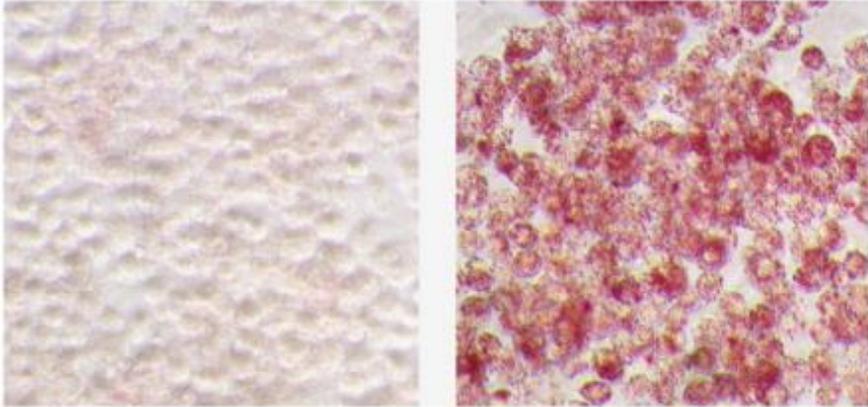


Captação de oxLDL pelos macrófagos



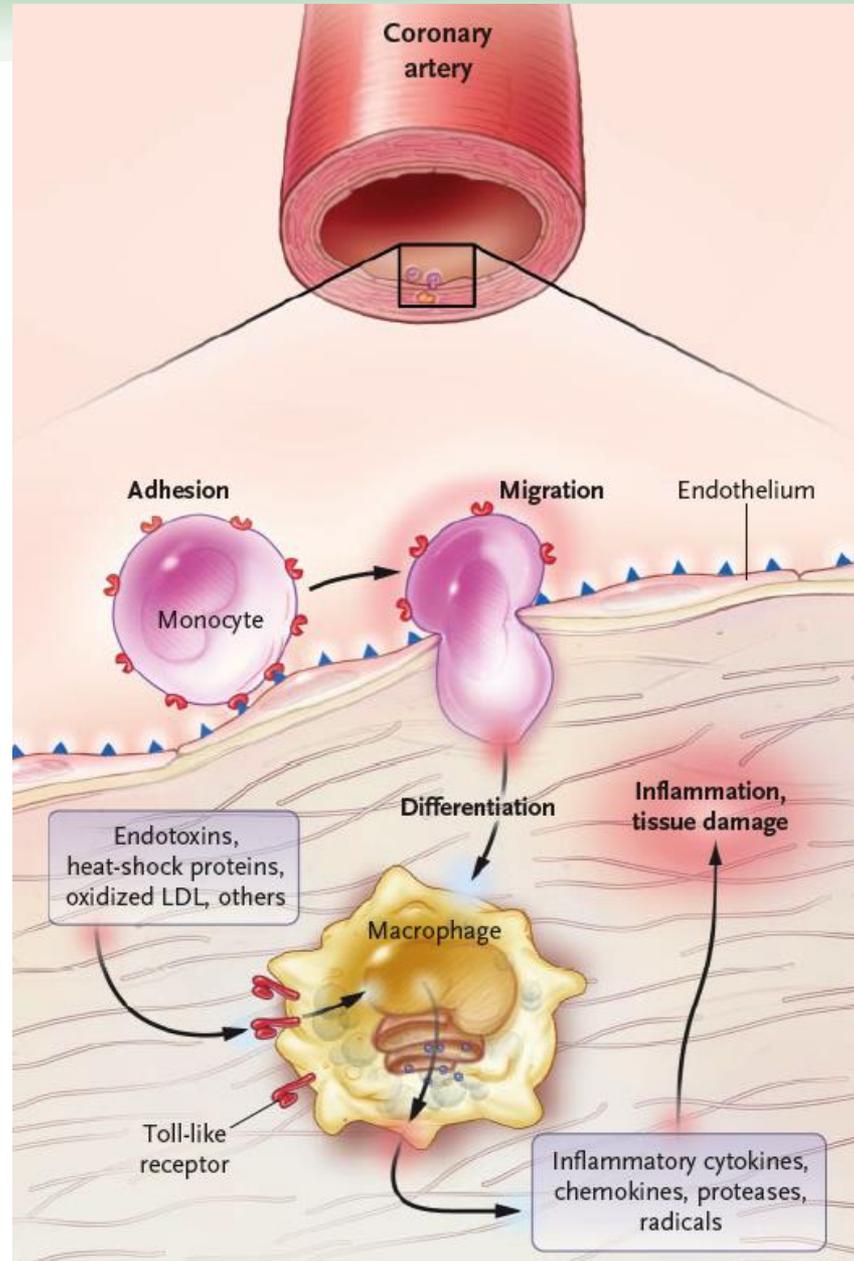
foam cells

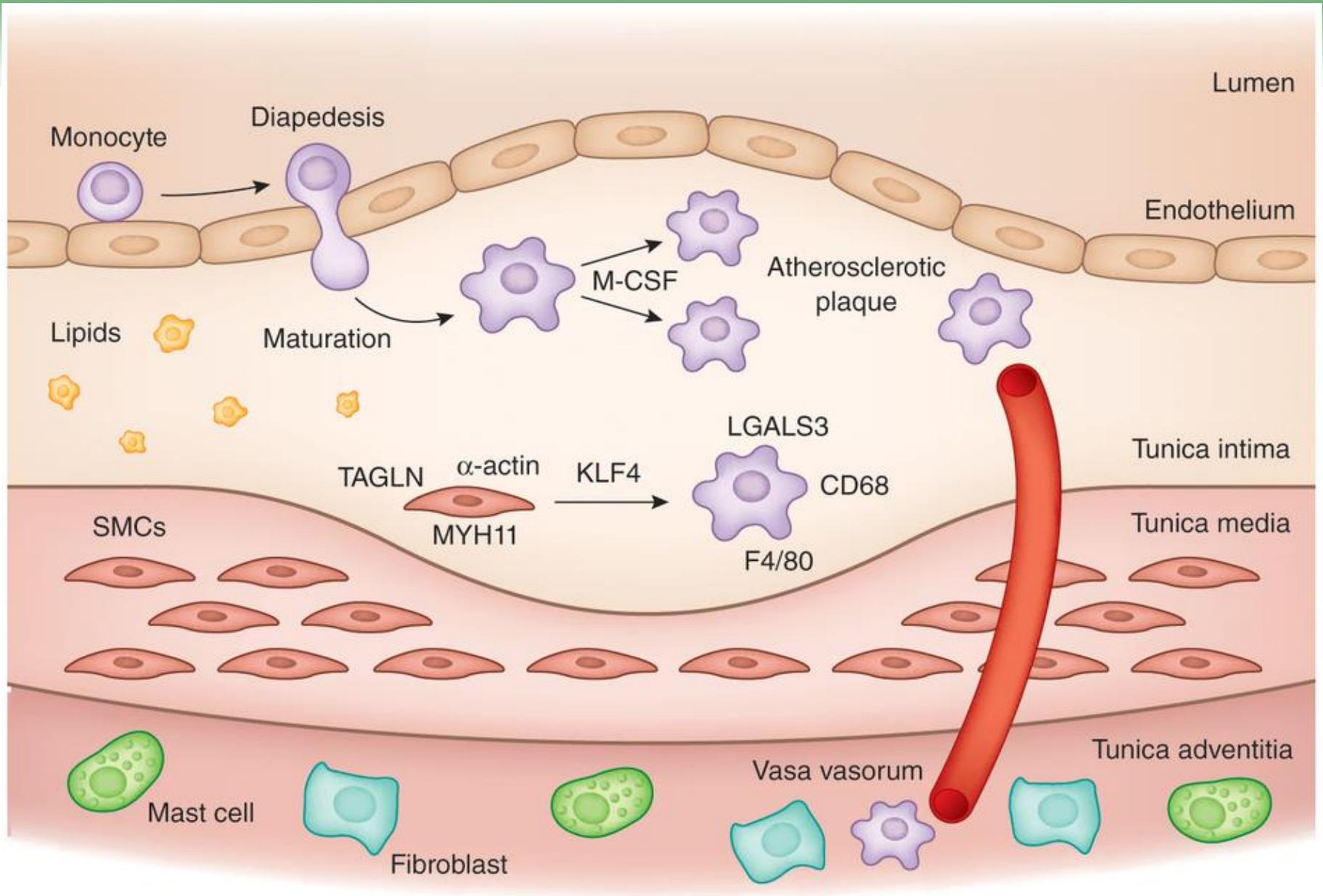
Foam Cells



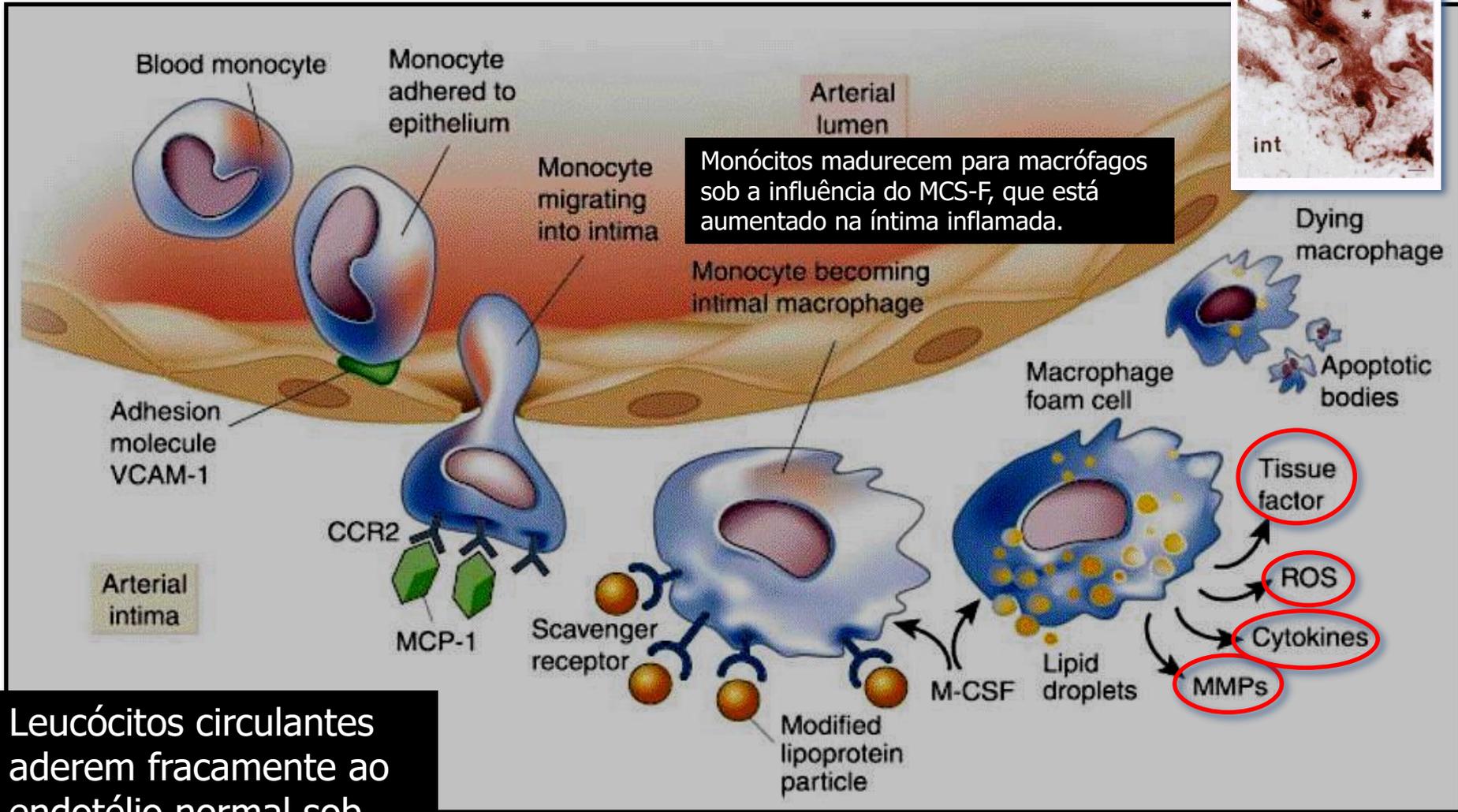
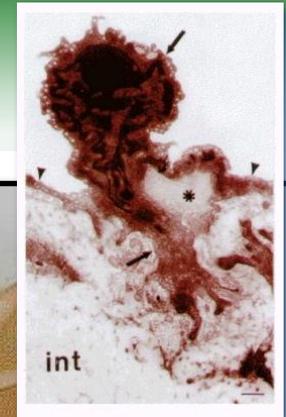
Foam cells are unable to metabolize and efflux the cholesterol that they have accumulated. As a result, they die which exacerbates the inflammatory conditions in and around the atherosclerotic lesion.

Macrófagos como mediadores iniciais



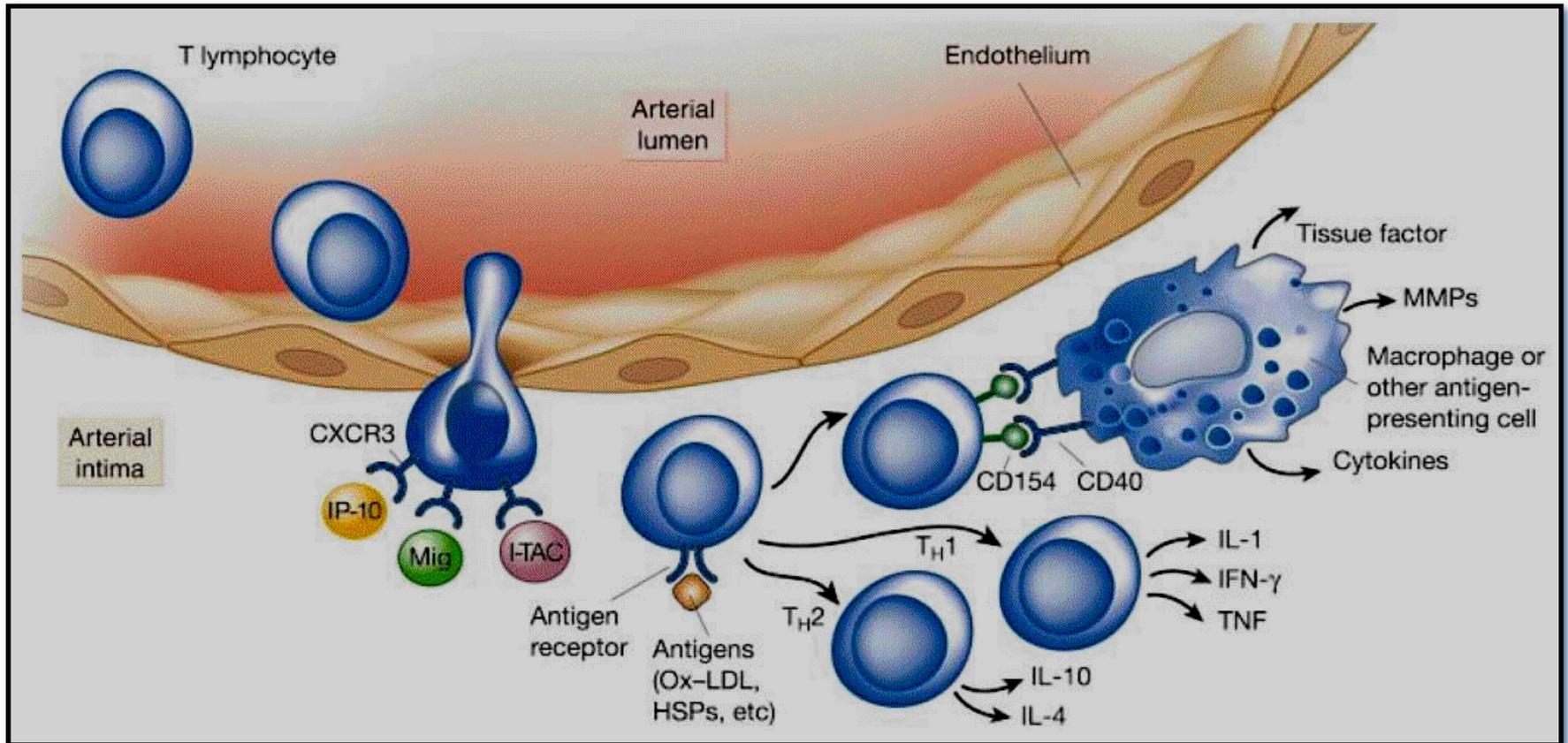


Aterogênese e inflamação: papel do monócito / macrófago

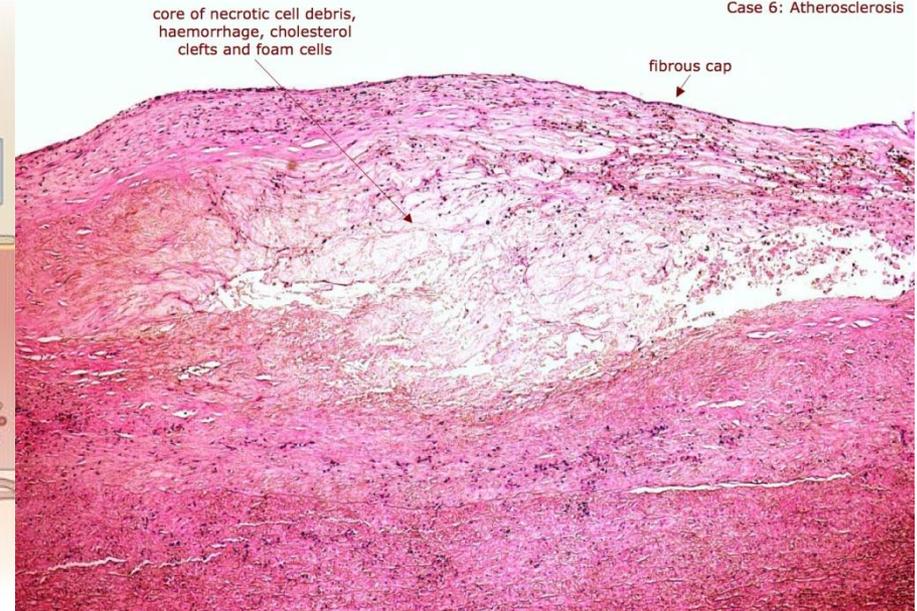
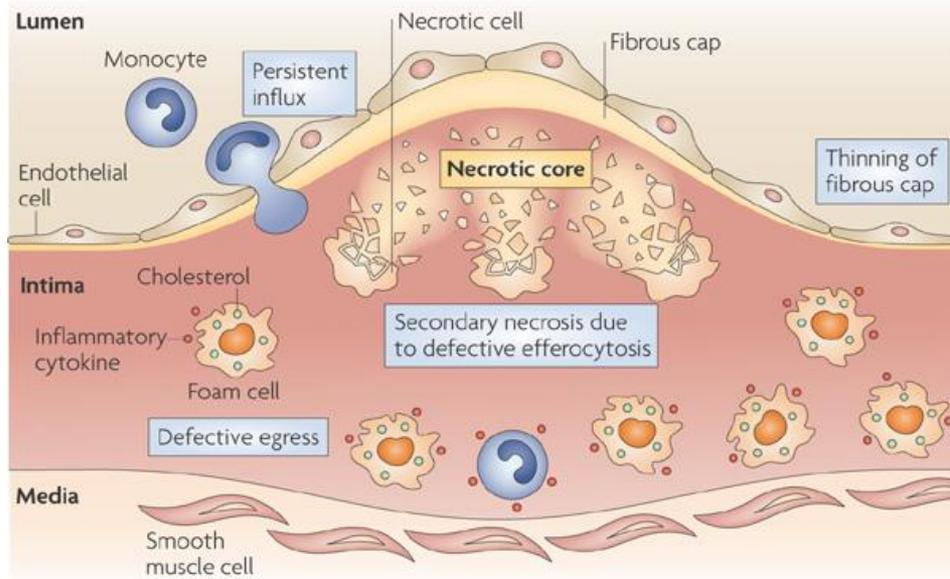


Leucócitos circulantes aderem fracamente ao endotélio normal sob condições normais.

Aterogênese e inflamação: papel do linfócito T

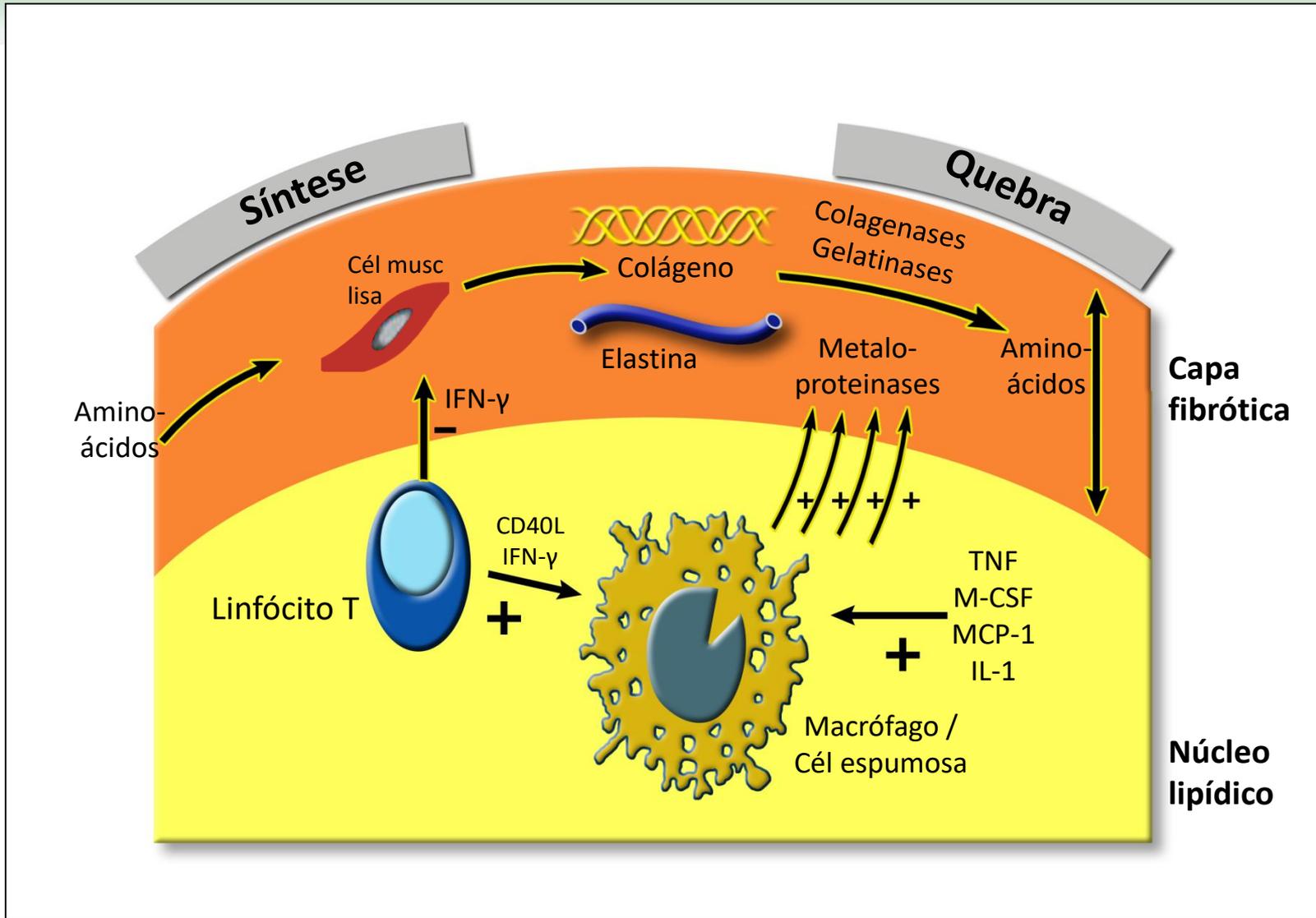


Placa aterosclerótica

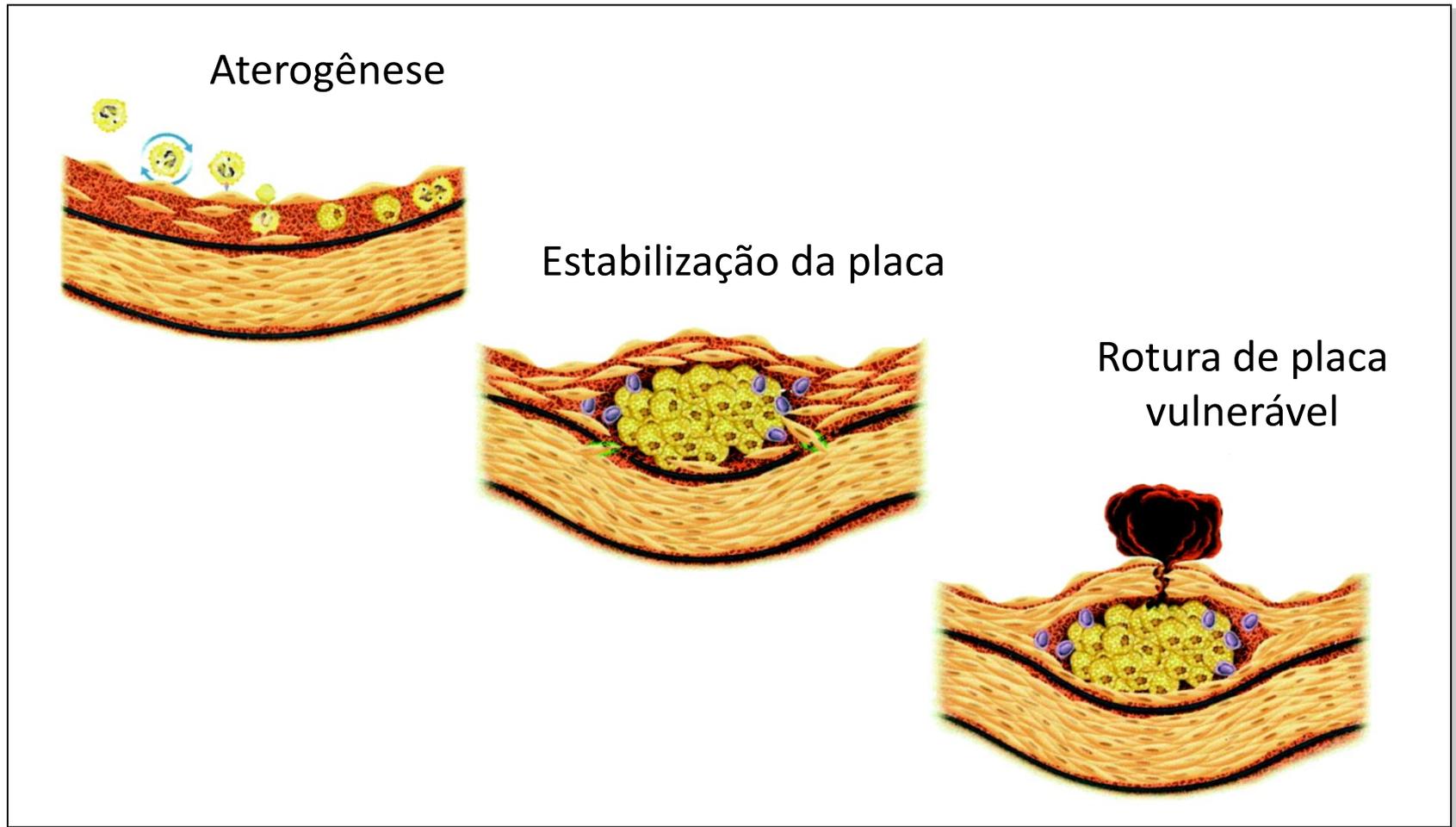


Nature Reviews | Immunology

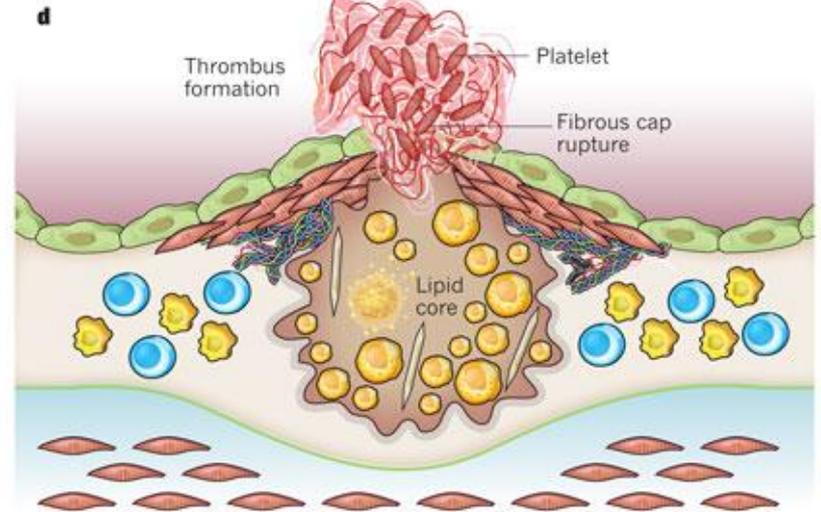
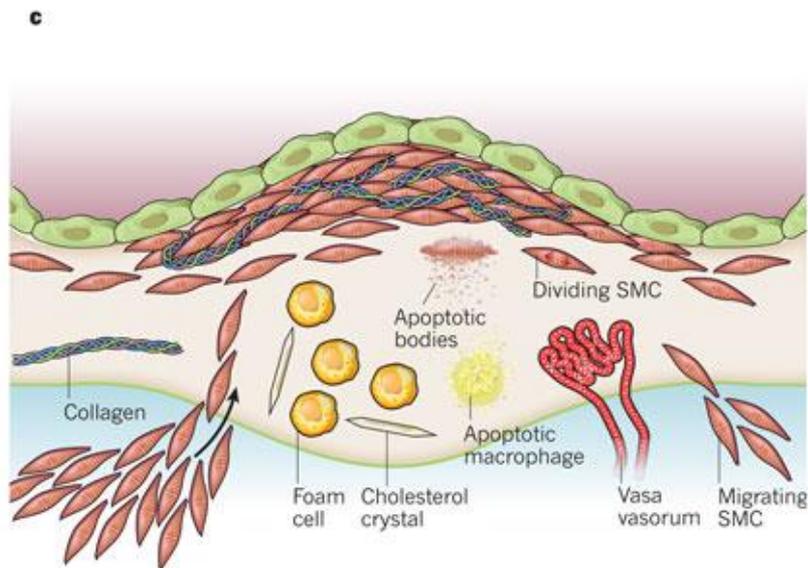
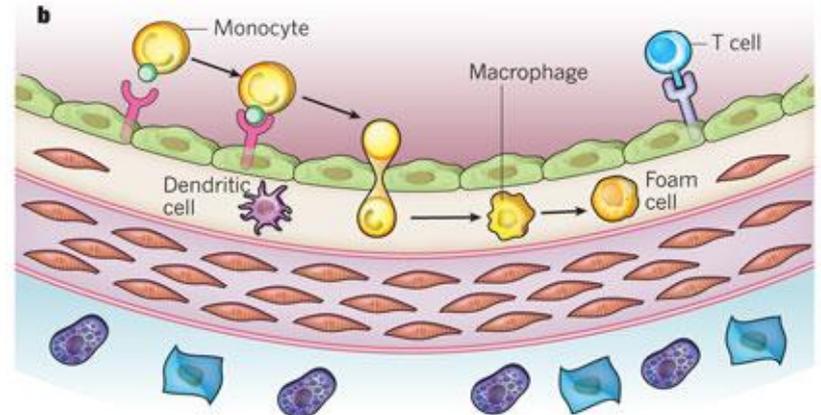
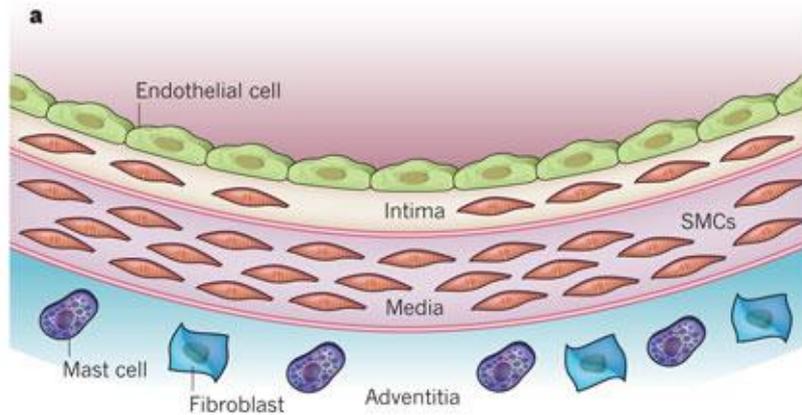
Instabilização da placa e inflamação

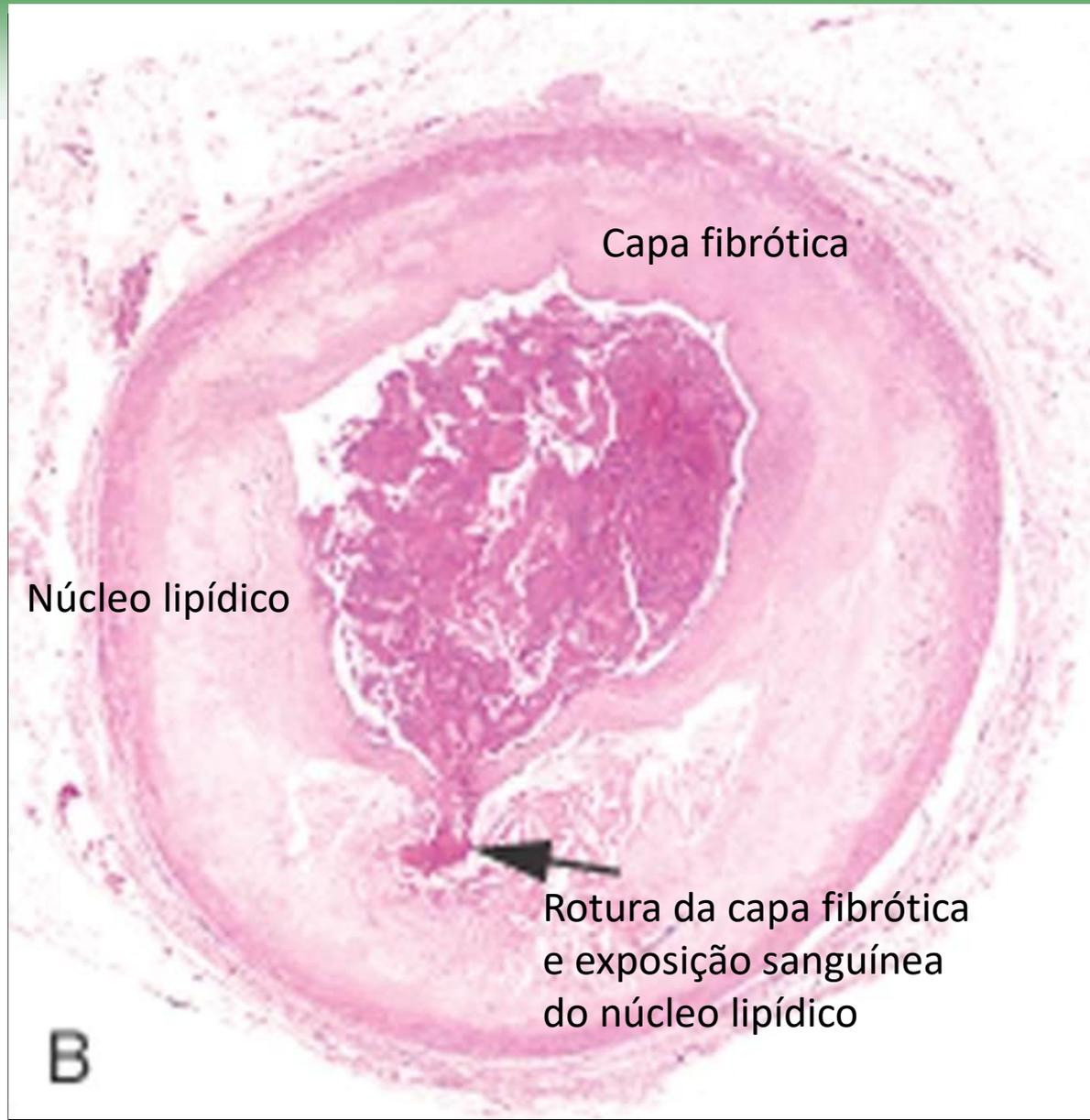


Inflamação: participa em todas as fases da aterosclerose

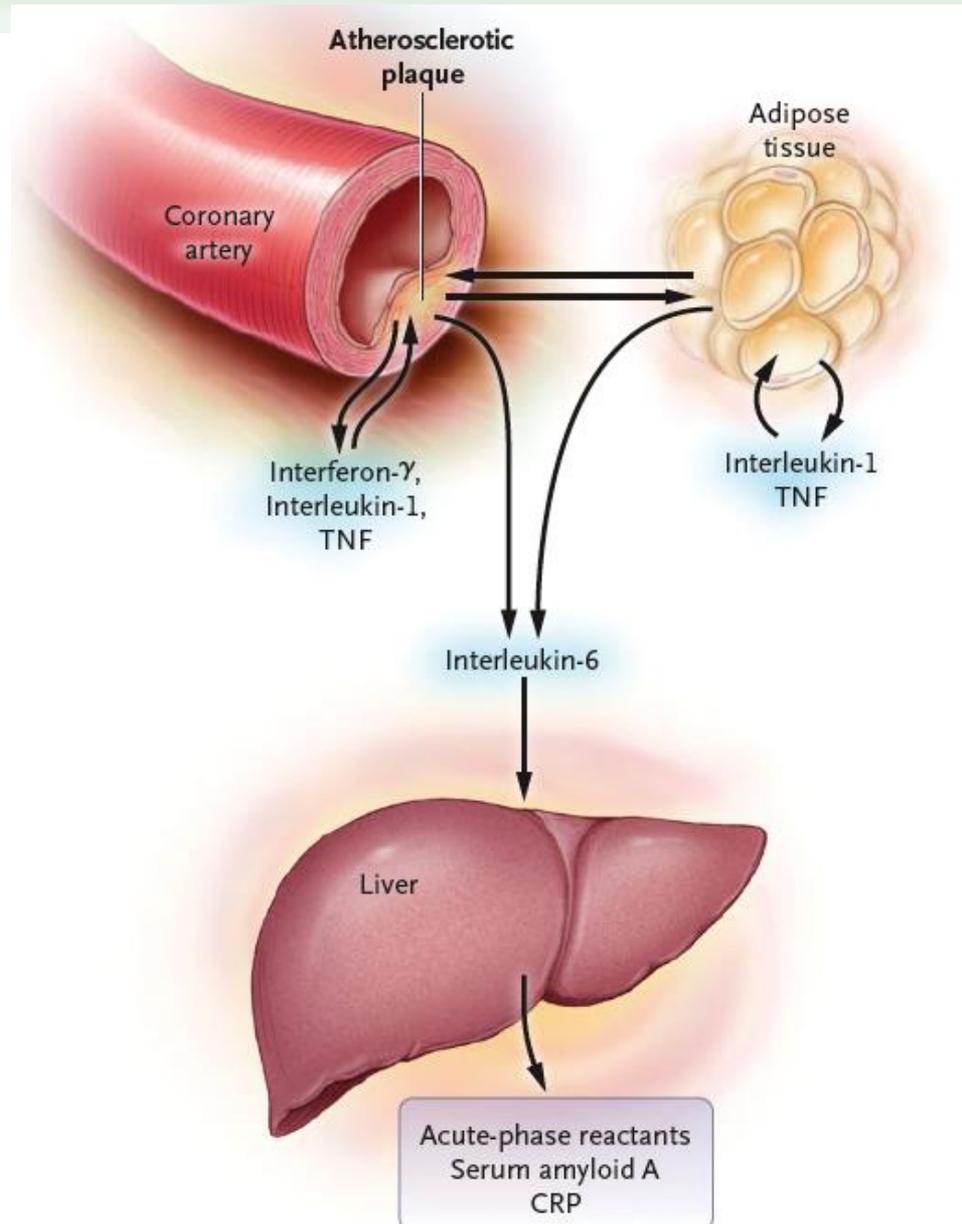


Trombose (Ruptura da Placa)

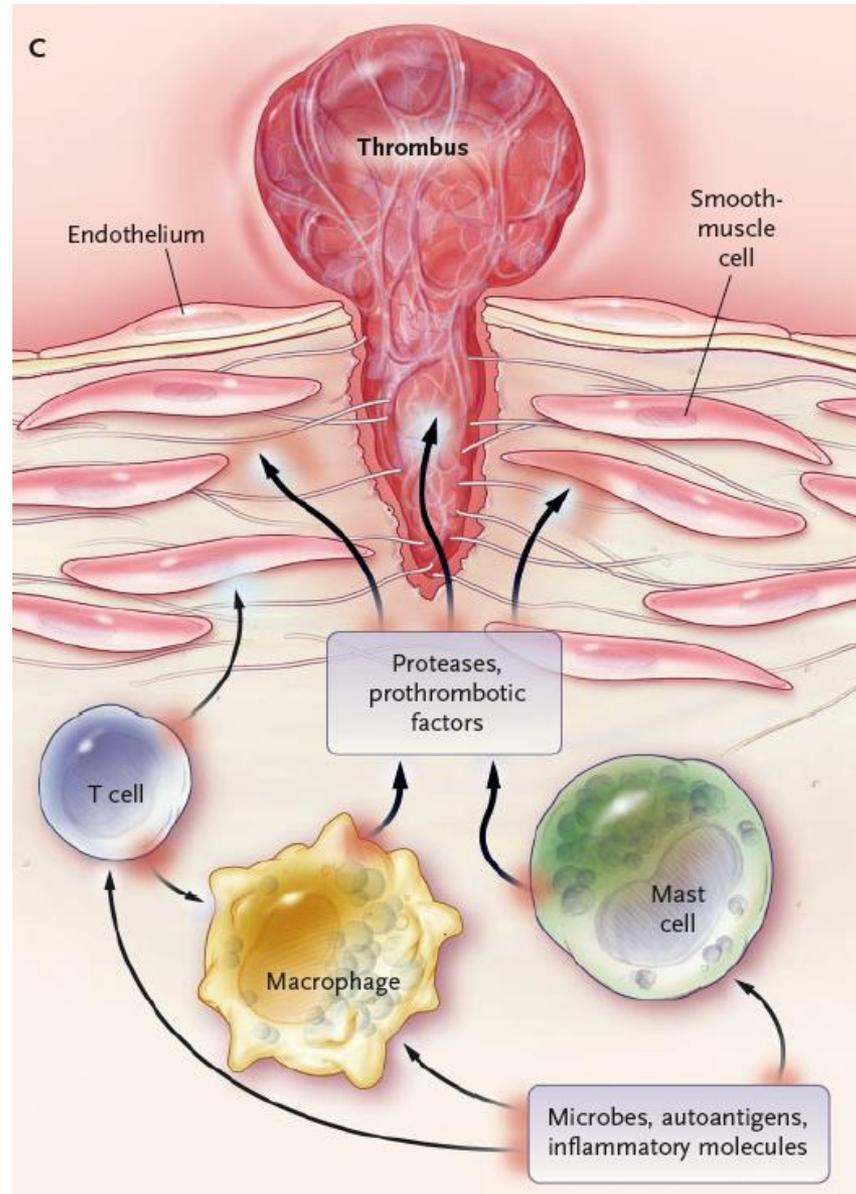




Inflamação sistêmica na aterosclerose



Células envolvidas na aterosclerose





Diabetes

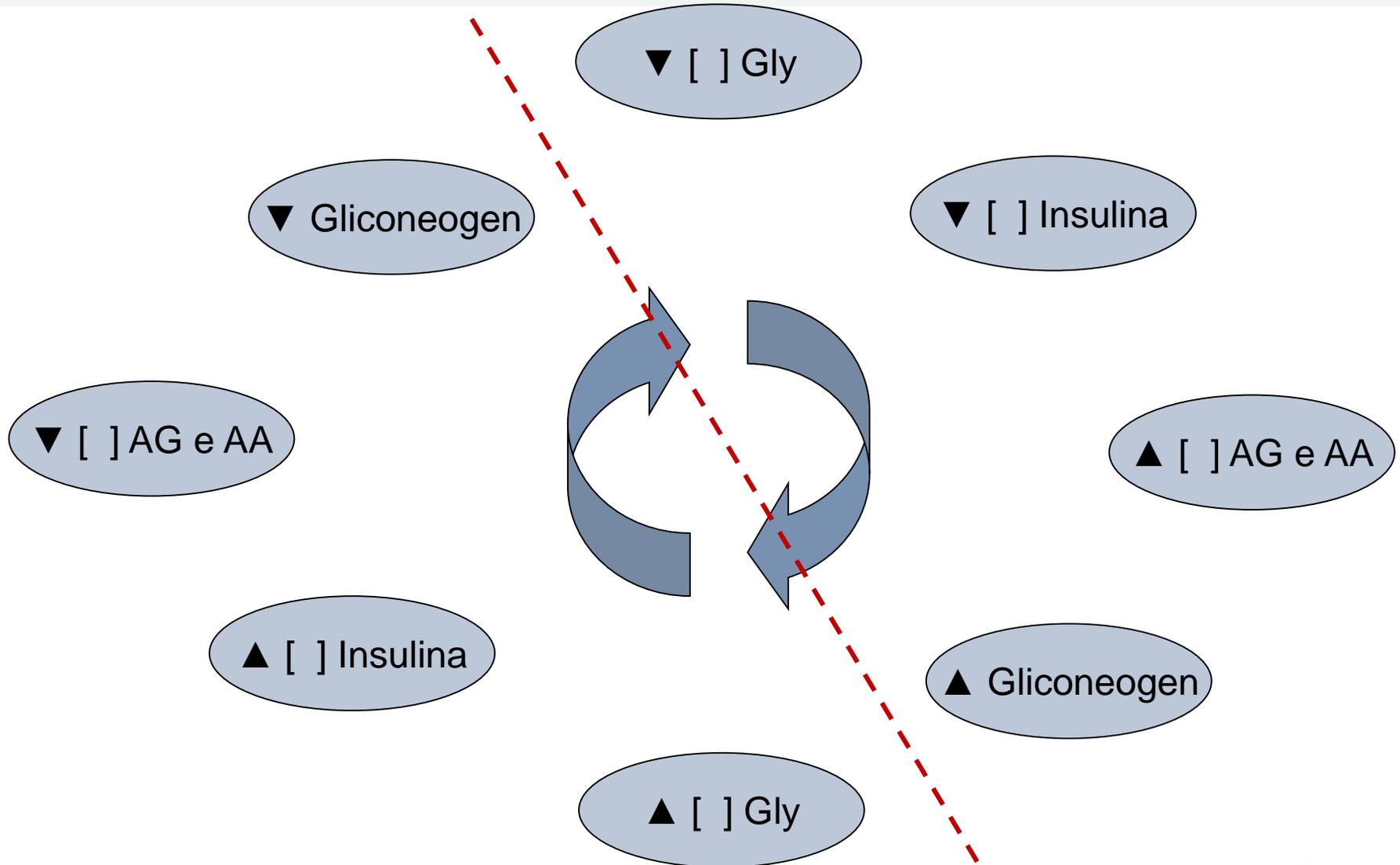
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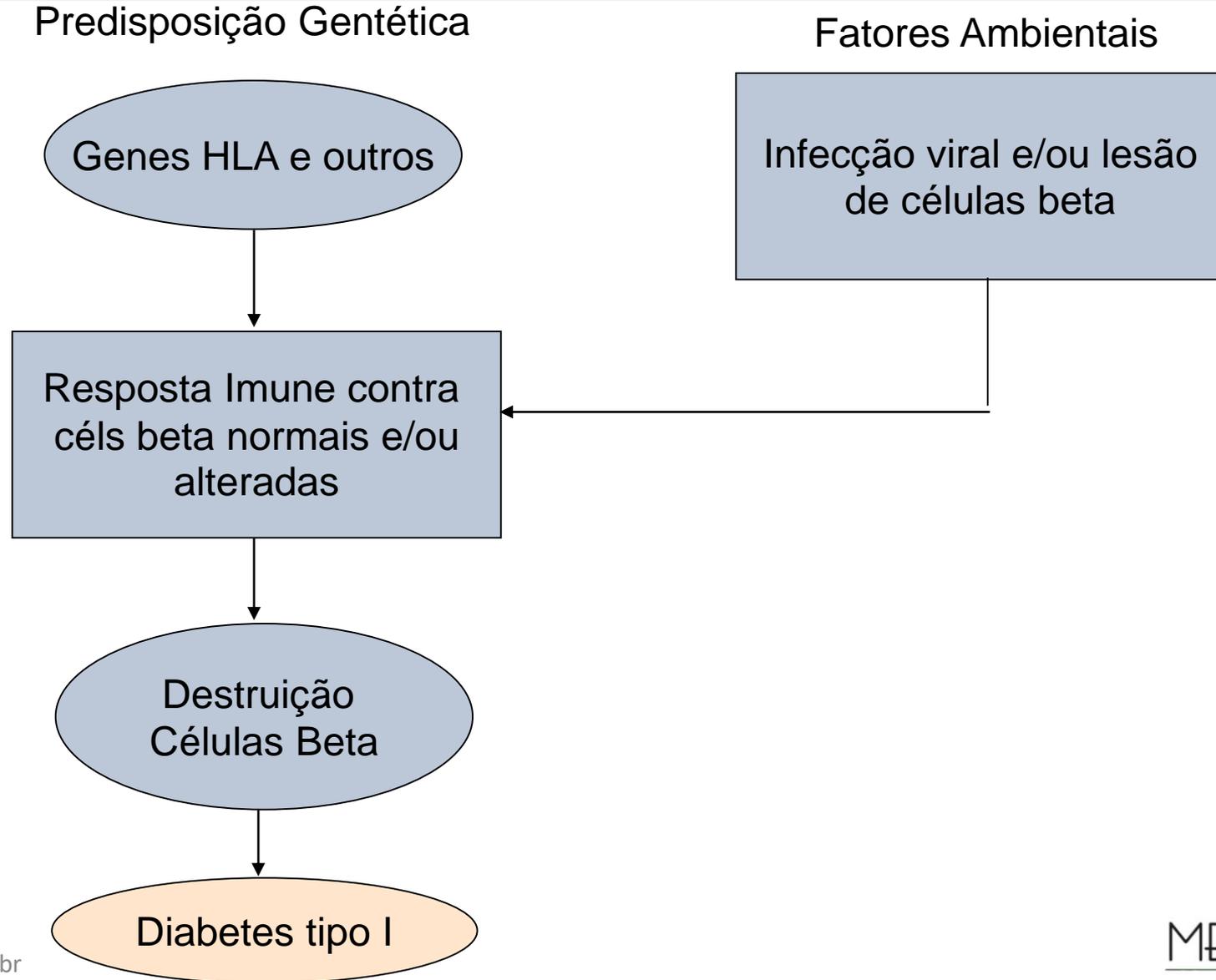


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Insulina



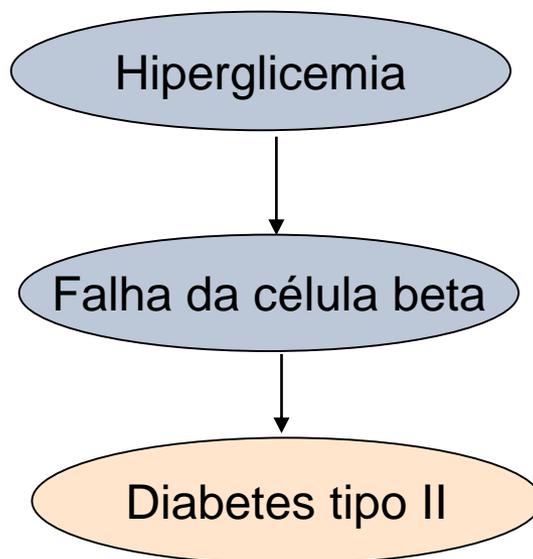
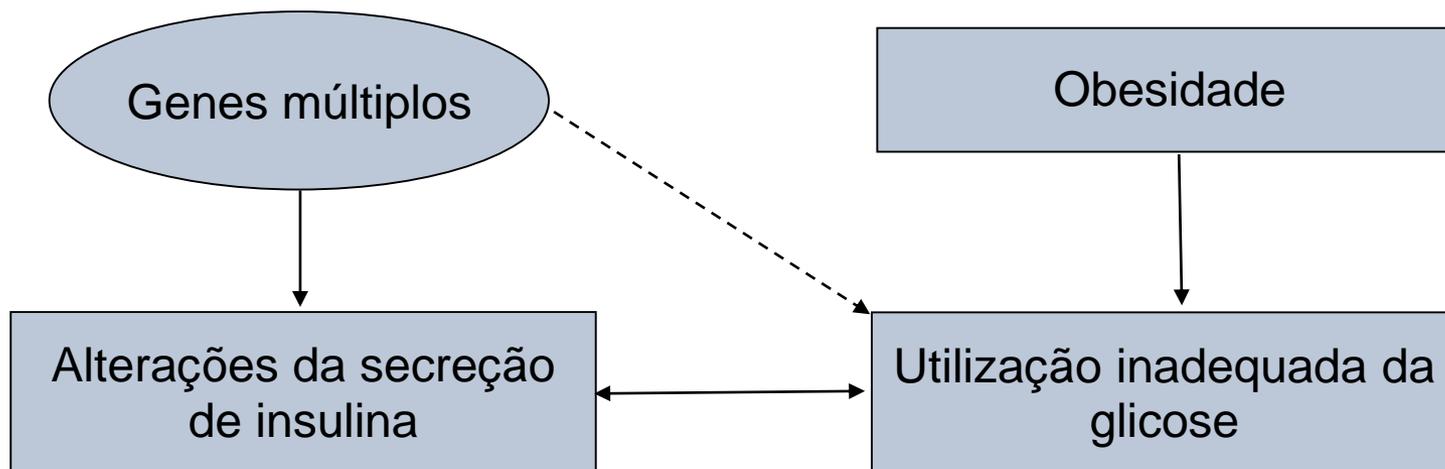
Fisiopatologia do DM Tipo I



Fisiopatologia do DM Tipo II

Predisposição Gentética

Fatores Ambientais



Fisiopatologia do DM Tipo II

↘ Alteração receptor

↘ Alteração sinalização

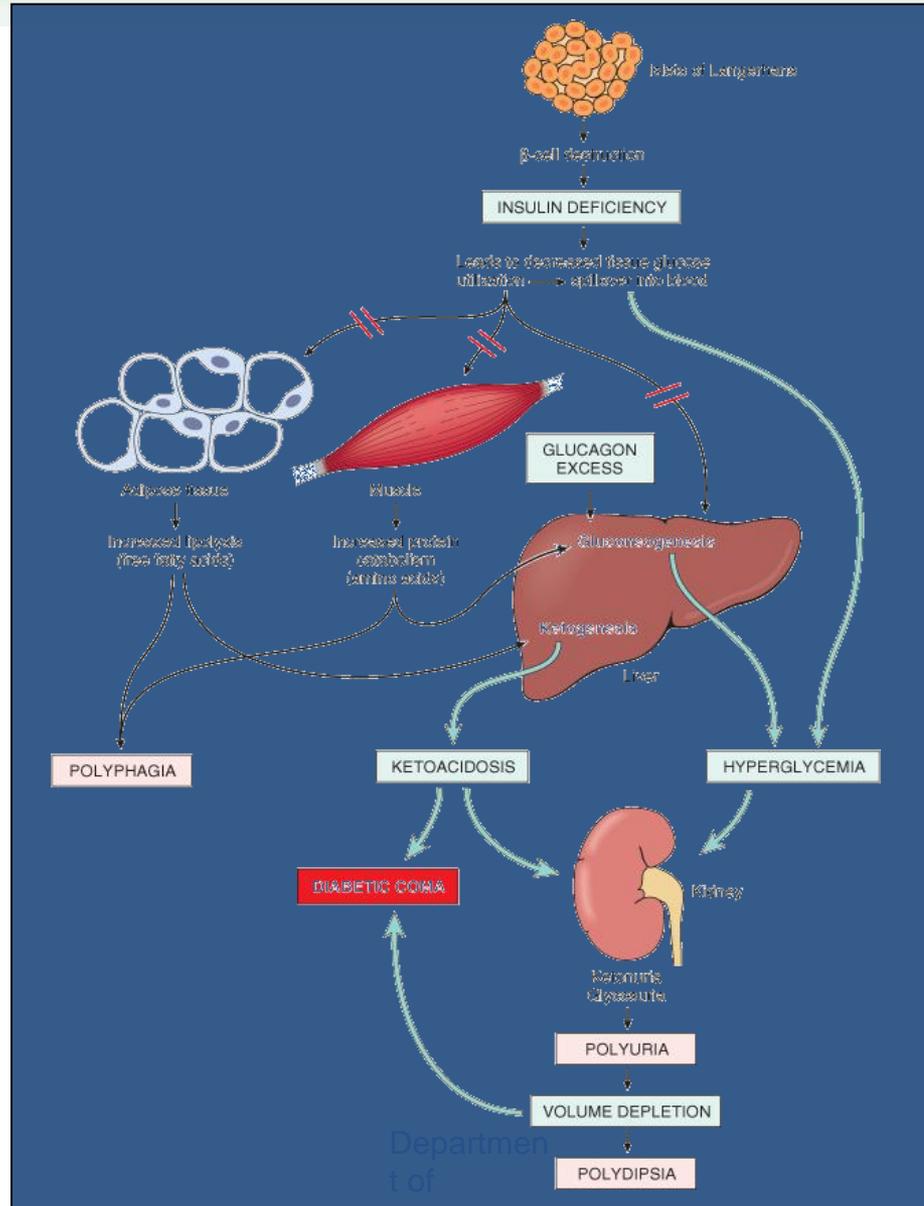
↘ Produtos do metabolismo lipídico

↘ Obesidade

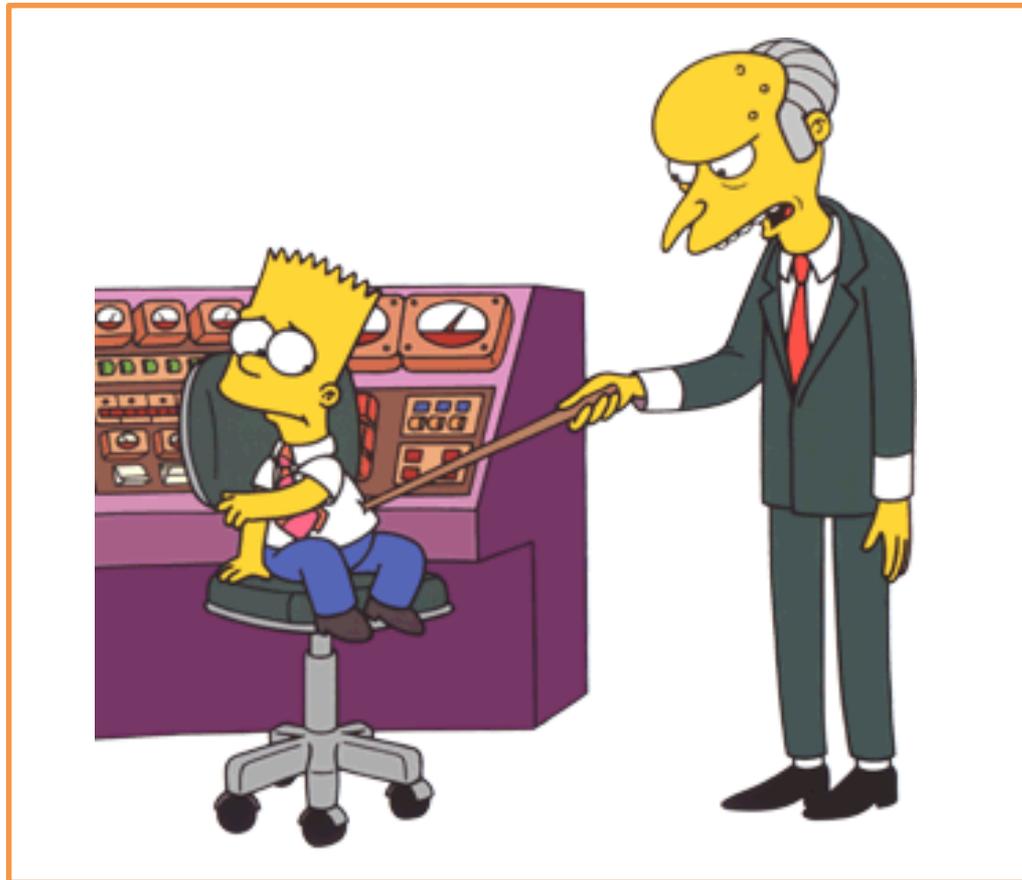
↘ Diminuição adiponectina (que diminui resistência periférica)

↘ Citocinas inflamatórias

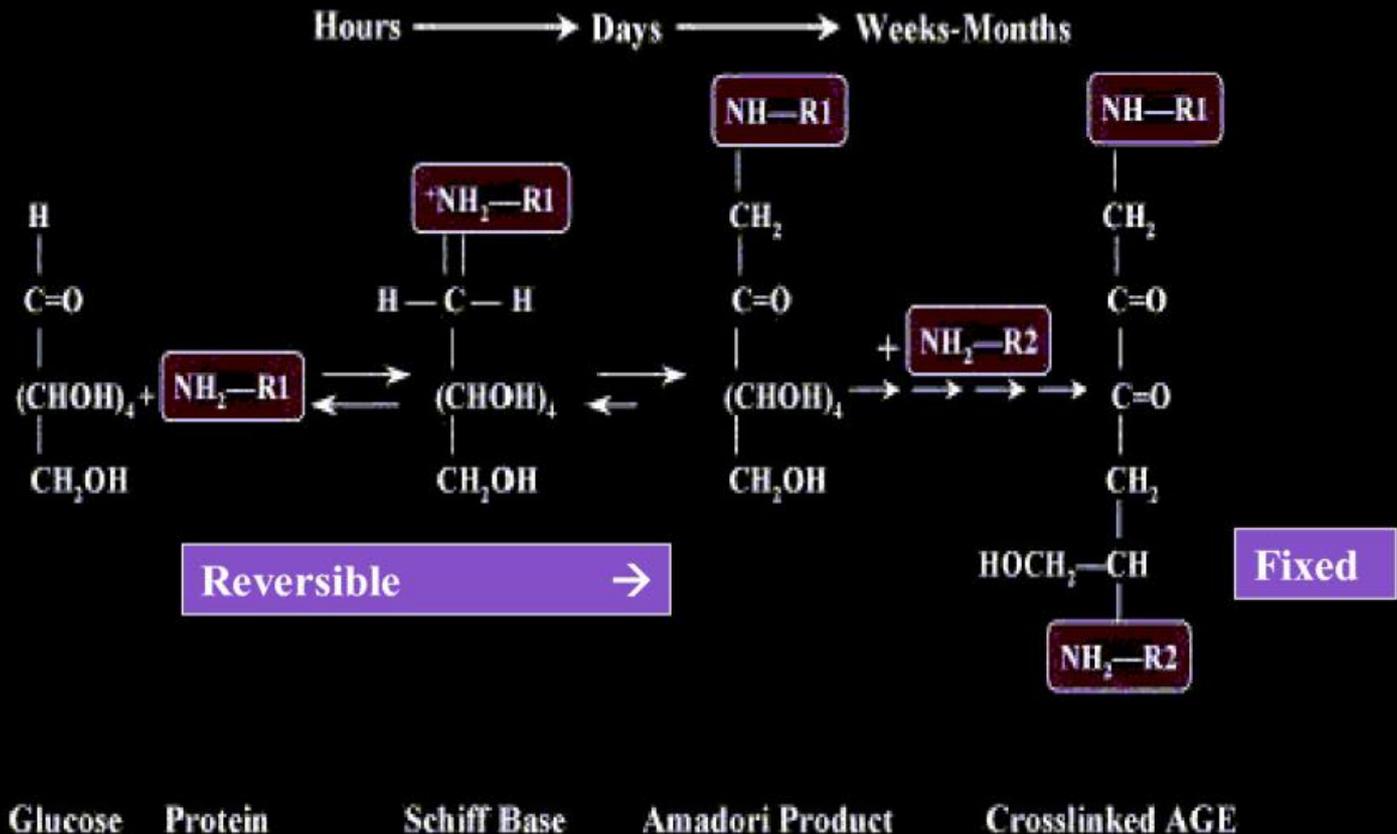
Insulina



Patogênese das Complicações Crônicas



Advanced Glycated End Products

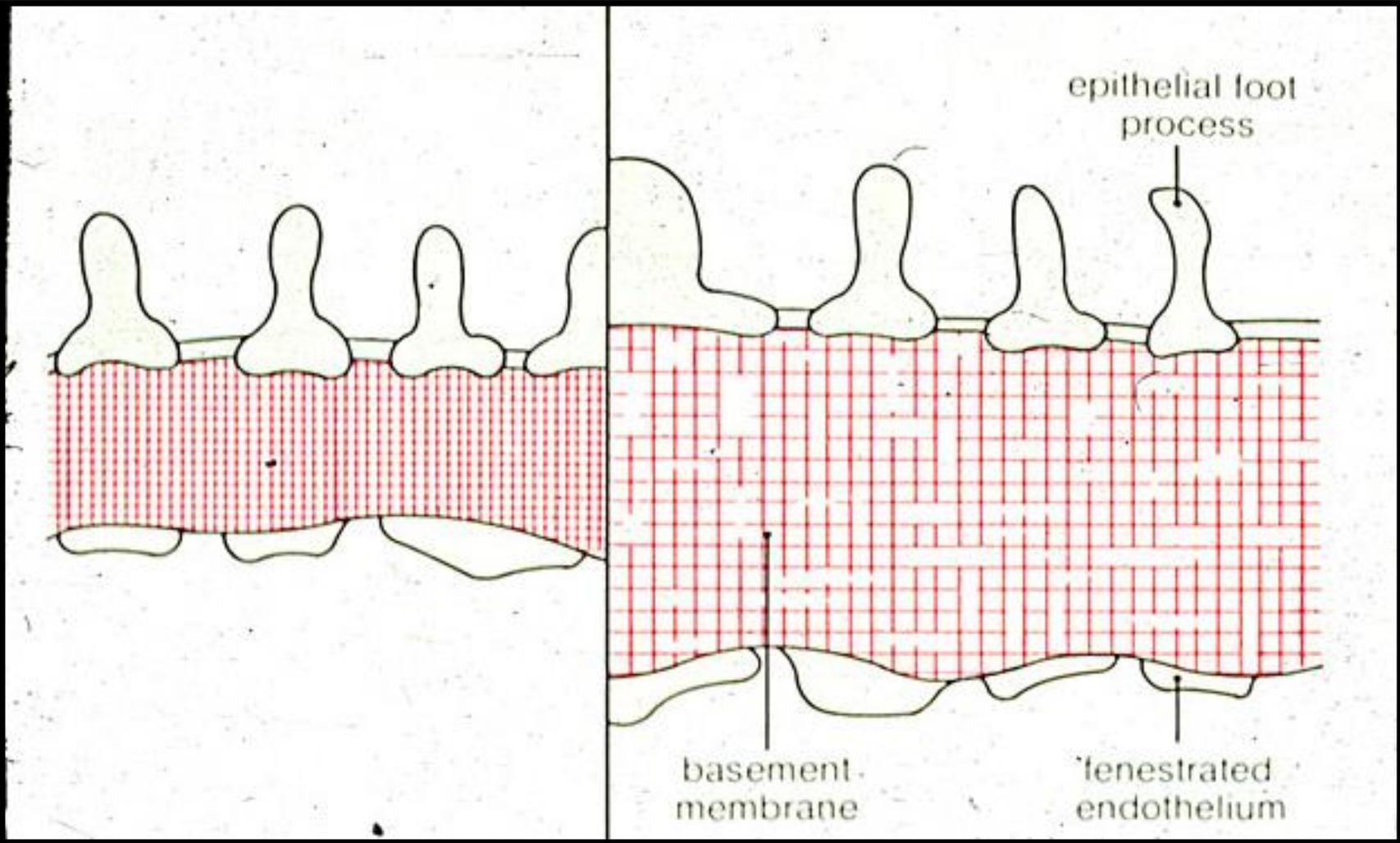


Copyright 2002, Aronson and Rayfield; licensee BioMed Central Ltd.
 Cardiovasc Diabet. 2002; 1(1):1 Formation of Advanced Glycation Products [82].

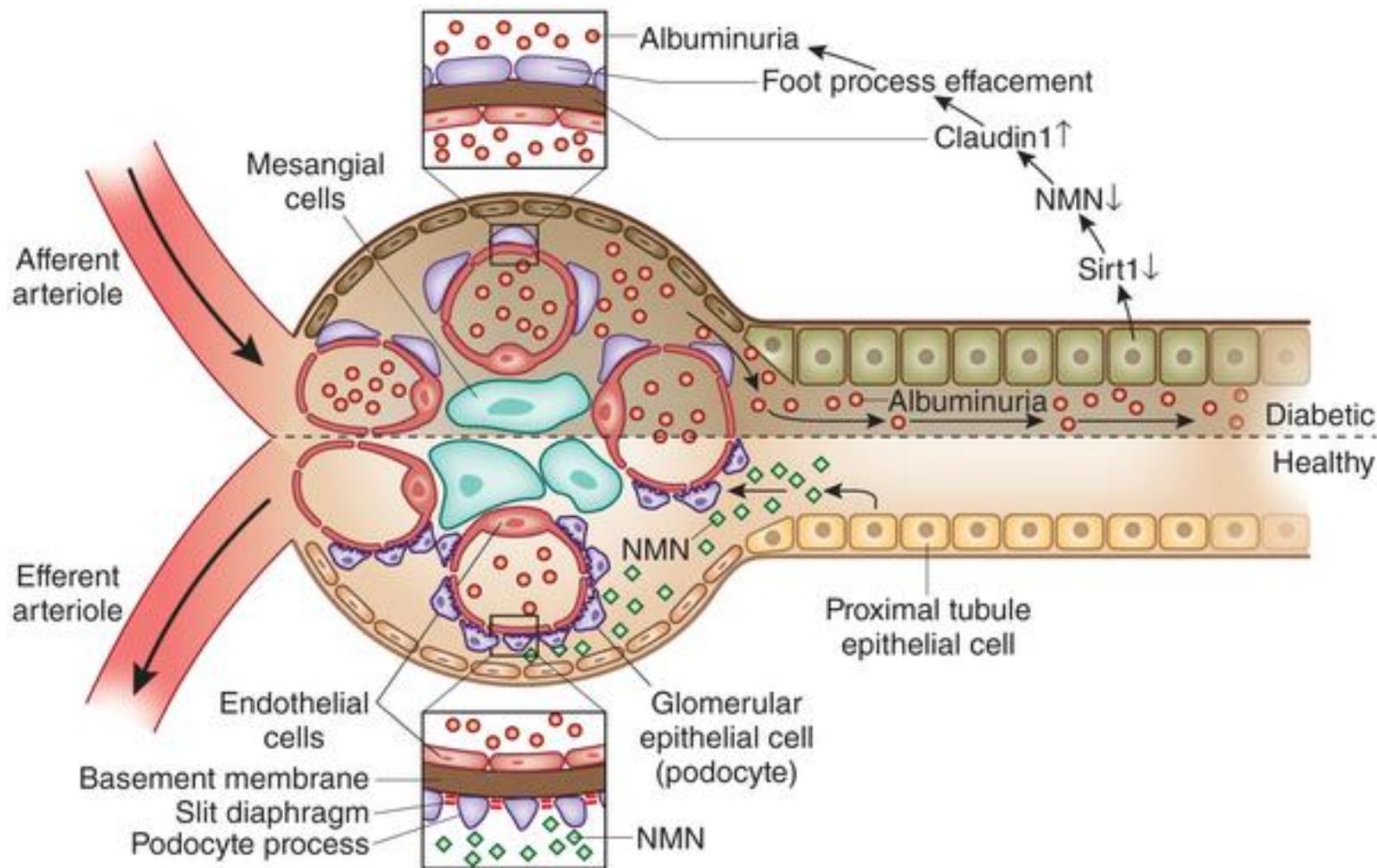
Advanced Glycated End Products

- **Ligação a polipeptídios – colágeno**
- **Ligação a proteínas não glicosiladas (LDL, Ig, Complemento)**
- **Resistência à digestão protéica**
- **Induz à oxidação lipídica**
- **Inativação do Óxido Nítrico**
- **Ligação aos ácidos nucleicos**

Advanced Glycated End Products



Advanced Glycated End Products

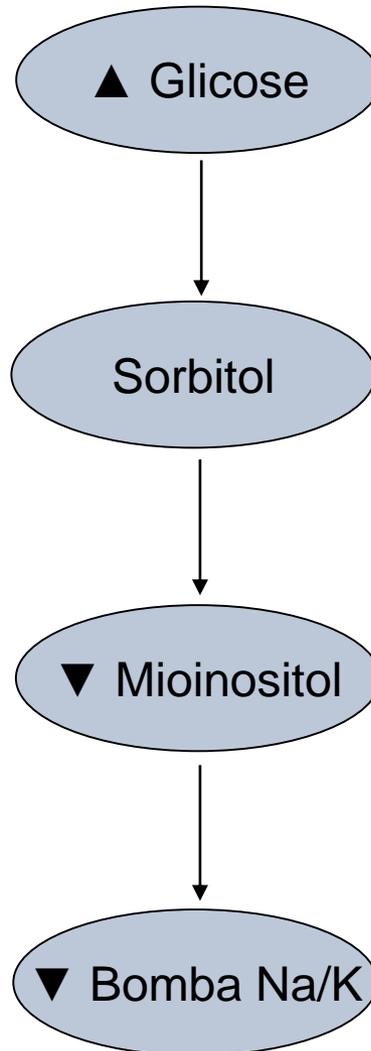


Nihalani D, Susztak N, Sirt1–Claudin-1 crosstalk regulates renal function, Nature Medicine 2013

Advanced Glycated End Products

- **Ligação dos AGEs aos receptores de monócitos e células mesenquimais:**
 - * **Migração dos monócitos**
 - * **Secreção de citocinas e fatores de crescimento**
 - * **Aumento da permeabilidade vascular**
 - * **Aumento da atividade pró-coagulante**
 - * **Aumento da proliferação celular**
 - * **Aumento da produção de matriz extracelular**

Glicose e Na/K ATPase



Alterações Morfológicas

- **Pâncreas**
- **Artérias (aterosclerose)**
- **Membrana Basal dos pequenos vasos (microangiopatia)**
- **Rins (Nefropatia)**
- **Retina (Retinopatia)**
- **Nervos (Neuropatia)**

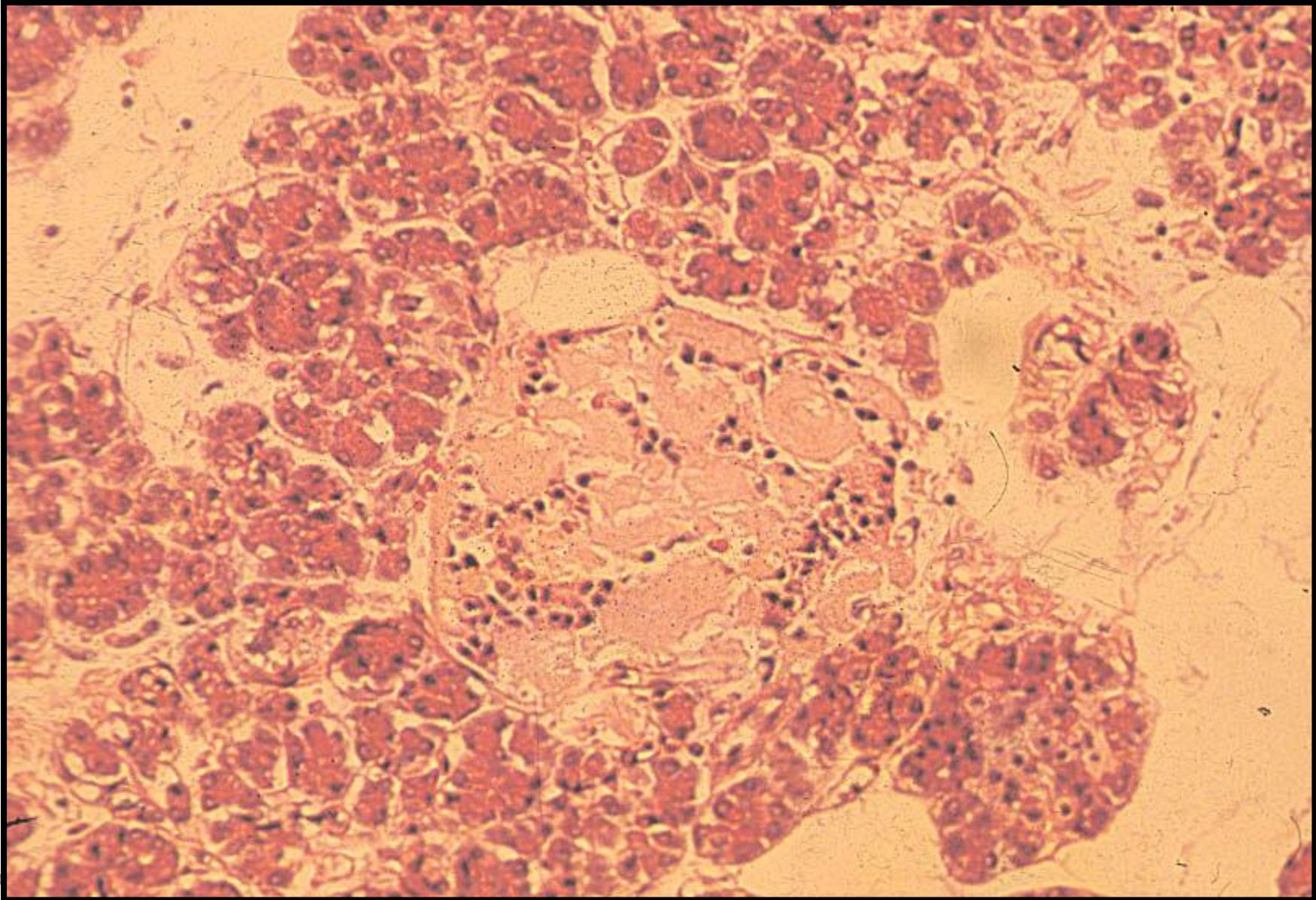
Pâncreas

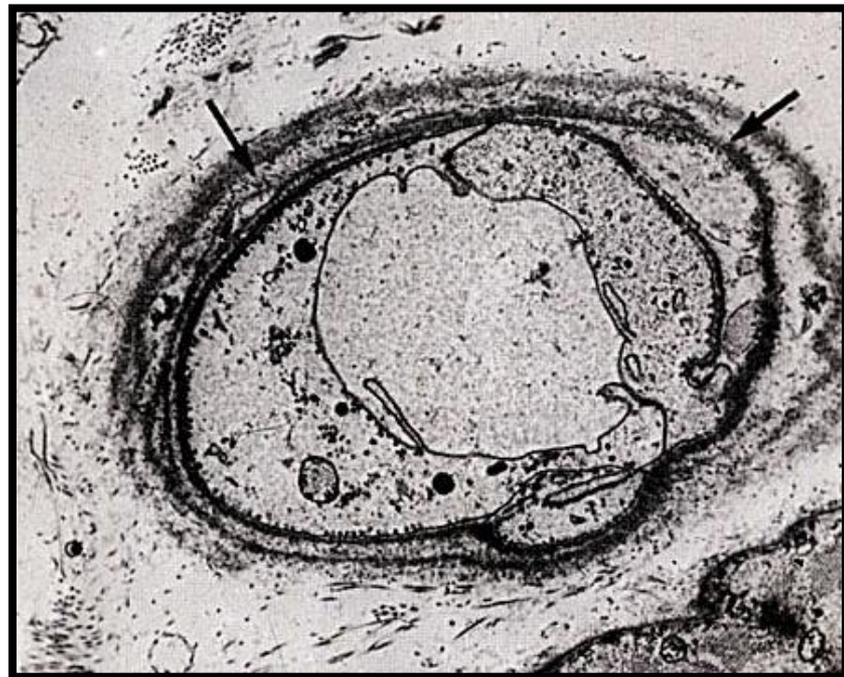
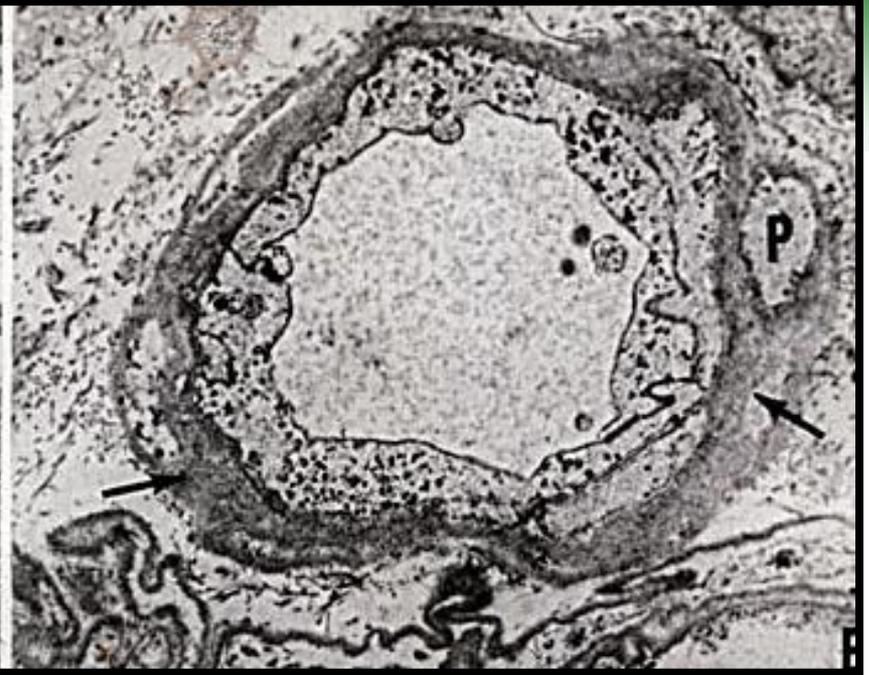
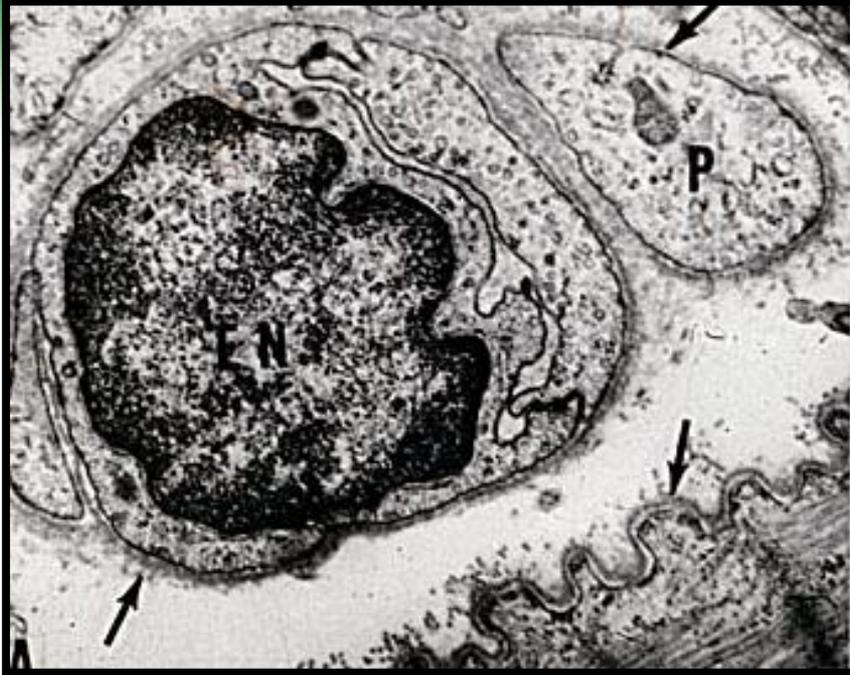
- **Lesão células B – Insulinite (Tipo I)**
- **Alterações de MB – Deposição de amilina (Tipo II)**

Pâncreas



Pâncreas





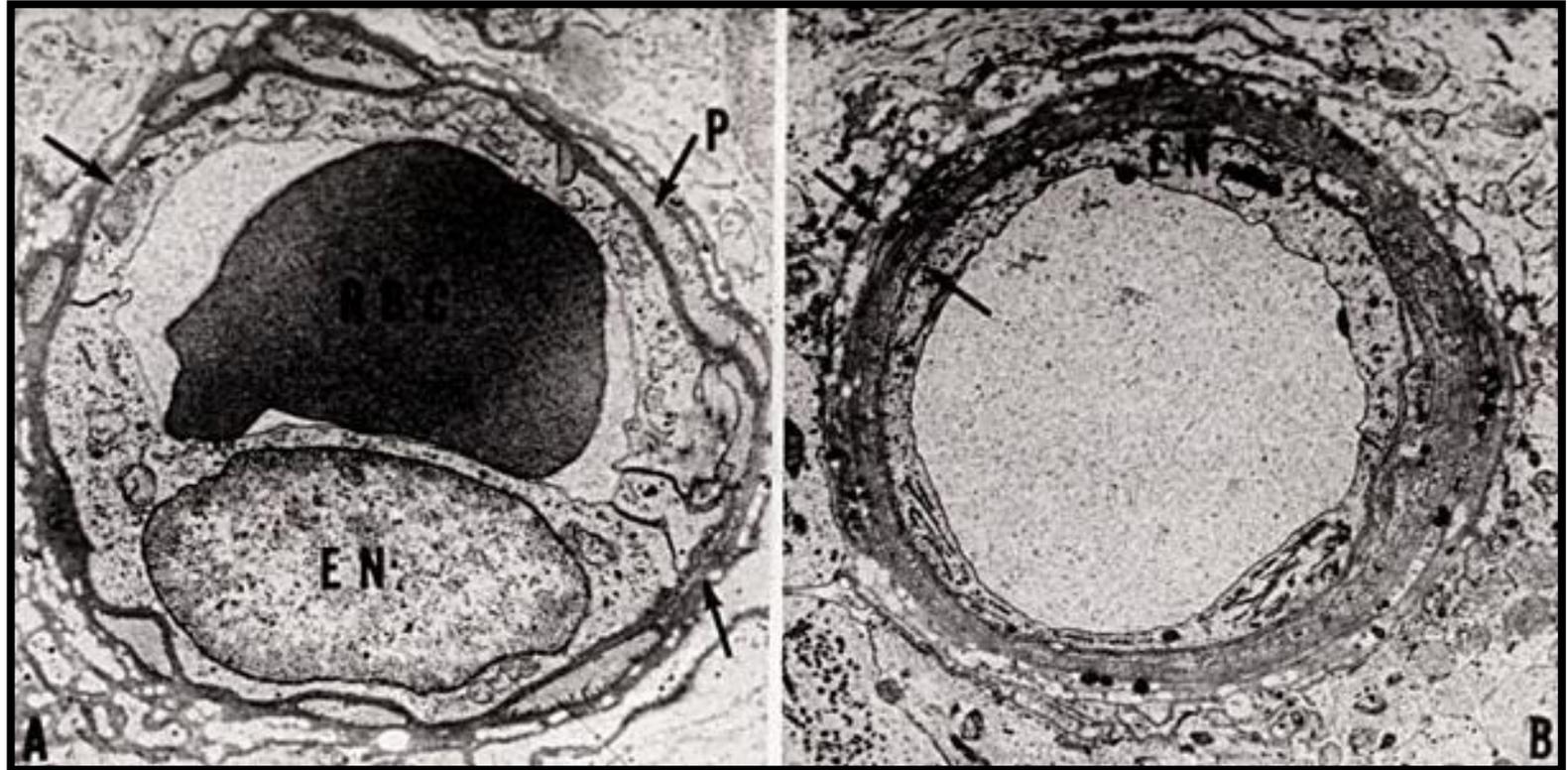
Alterações Oculares

- **Aumento Permeabilidade de vasos retinianos – hemorragia – descolamento de retina / glaucoma**
- **Fragilidade de vasos - microaneurismas**

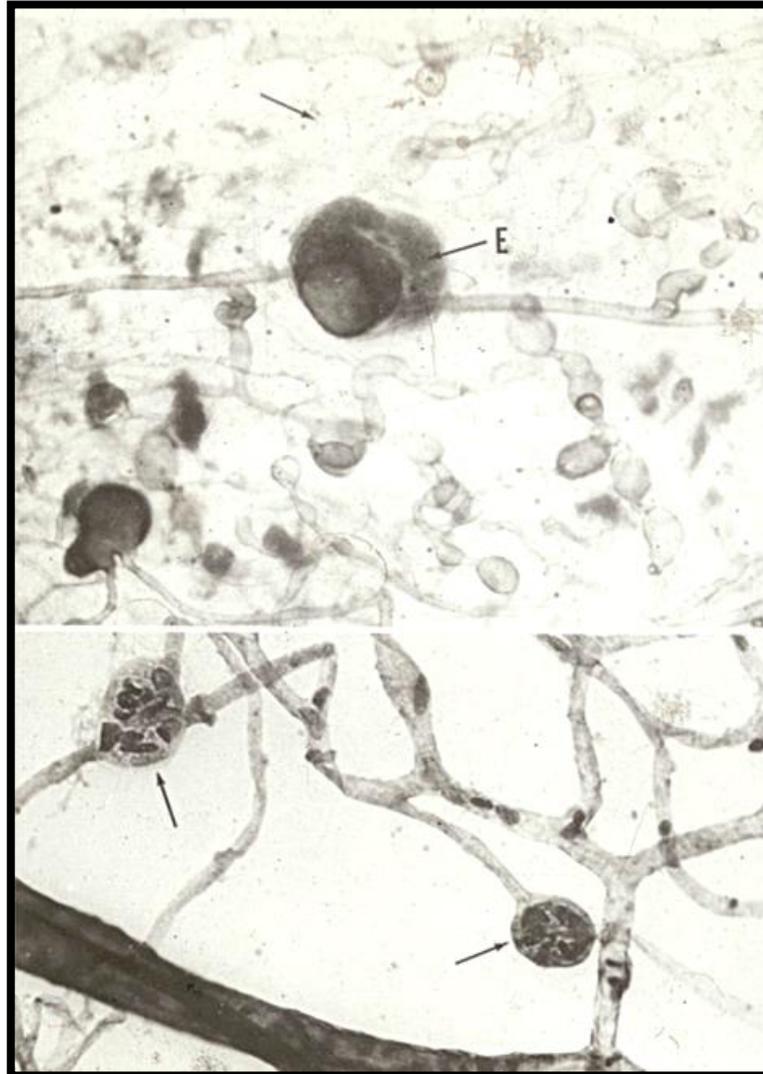
Alterações Oculares

- **1º - Retinopatia**
 - **microaneurismas**
 - **exsudatos e hemorragias**
 - **retinite proliferante**
- **2º - Cataratas**
- **3º - Alterações da íris**
- **4º - Alterações da refração e acomodação**
- **5º - Neurite óptica com atrofia de papila**

Alterações Oculares



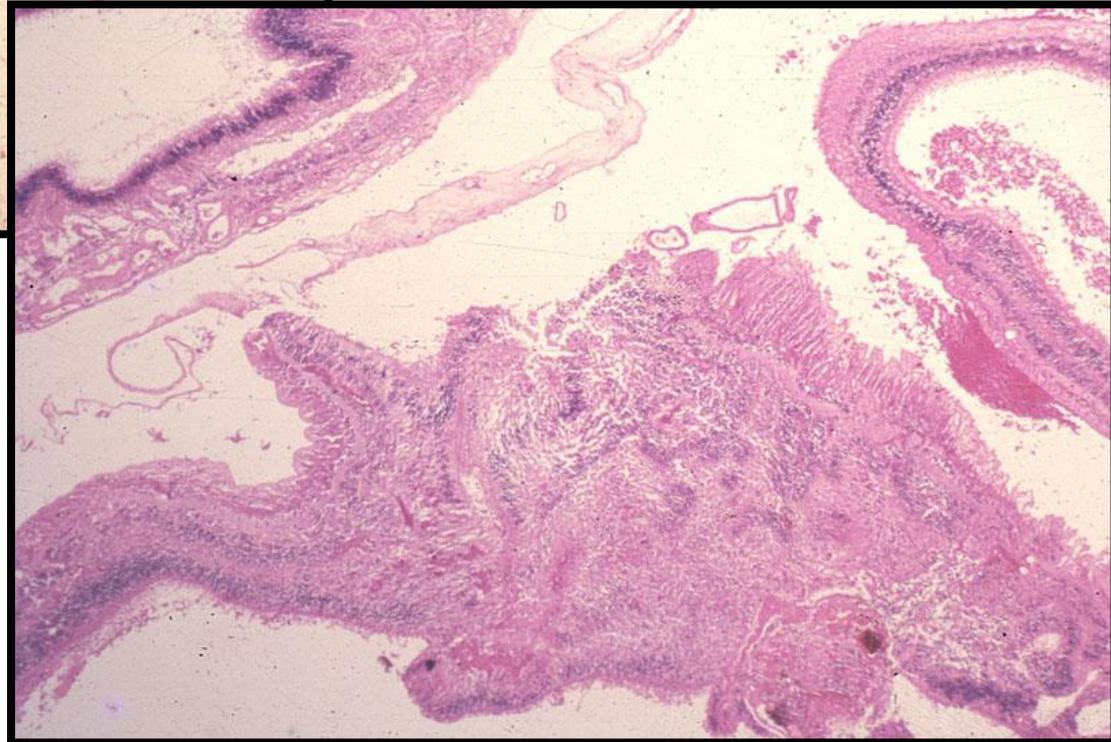
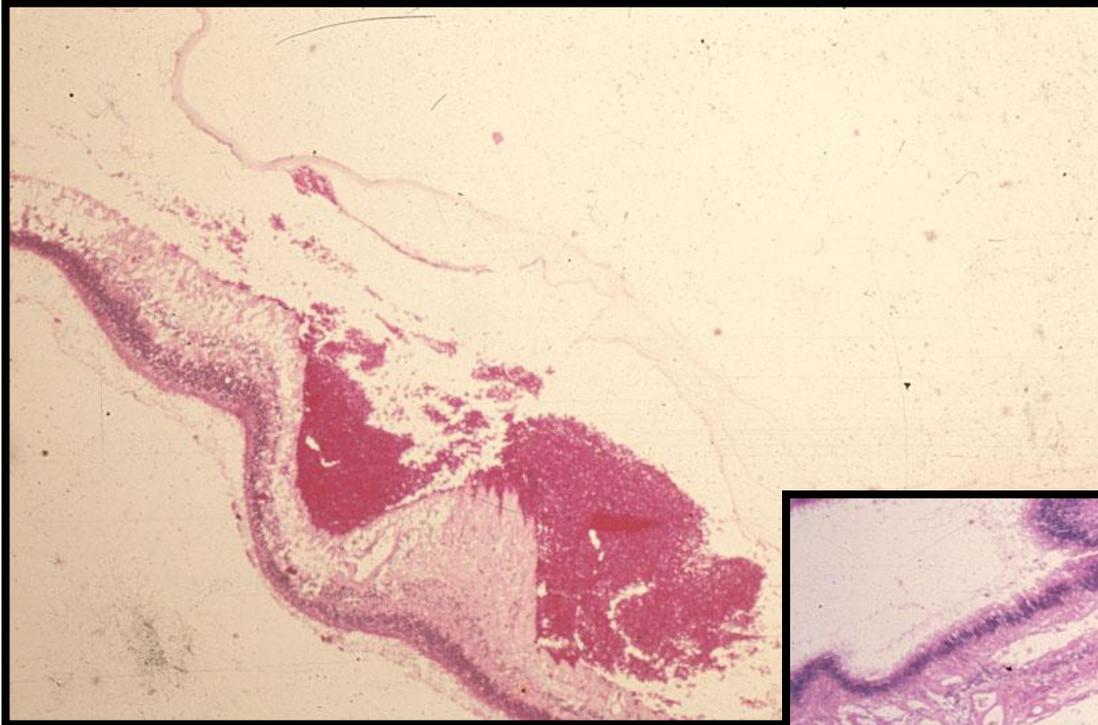
Alterações Oculares



Alterações Oculares



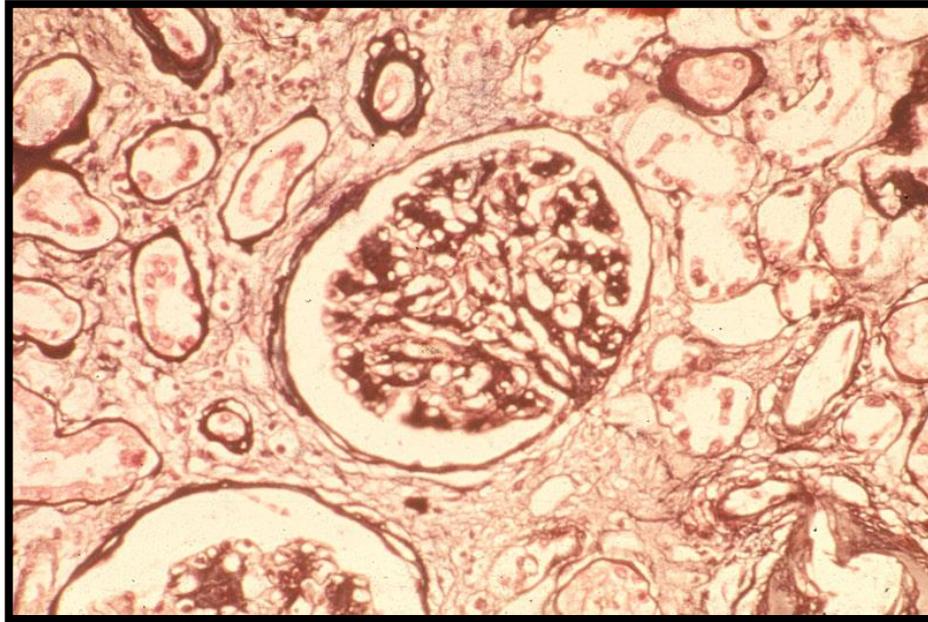
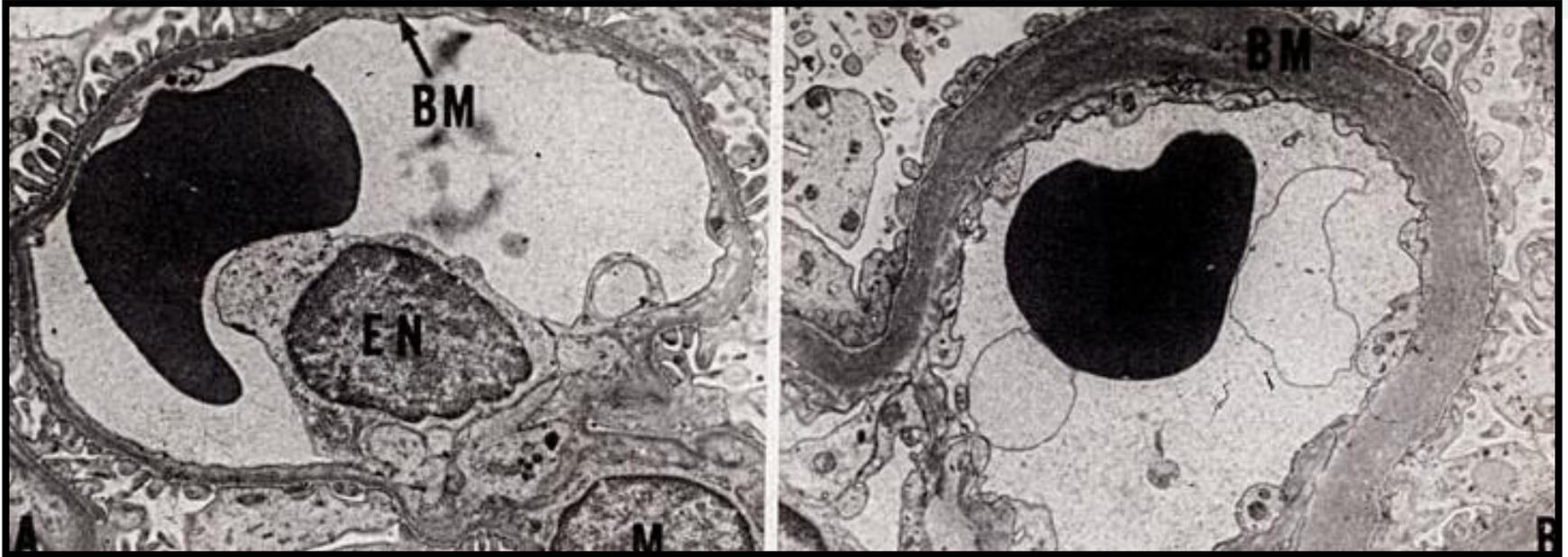
Alterações Oculares



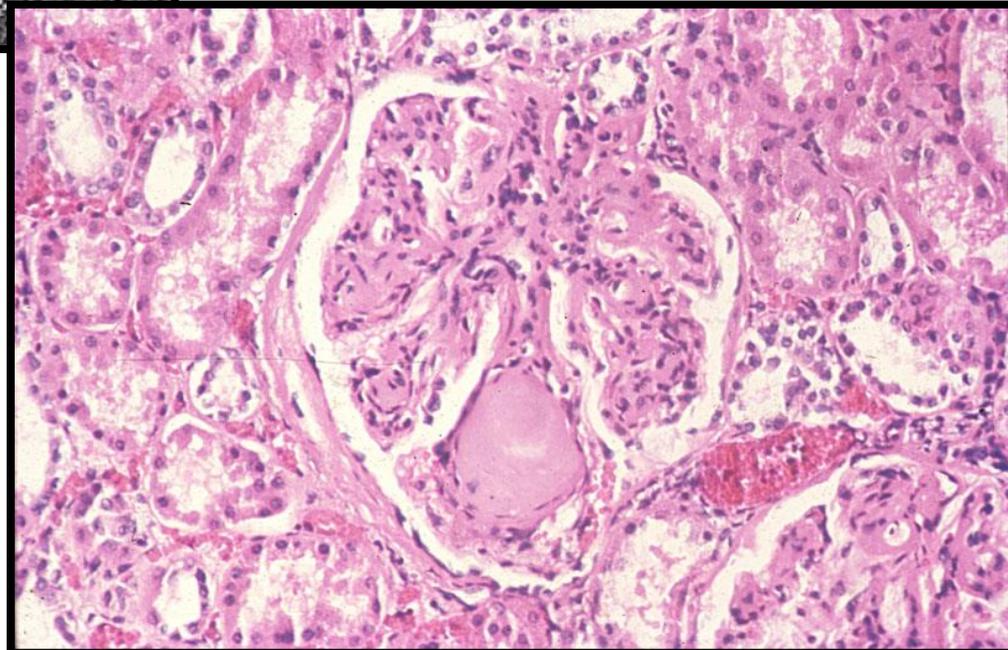
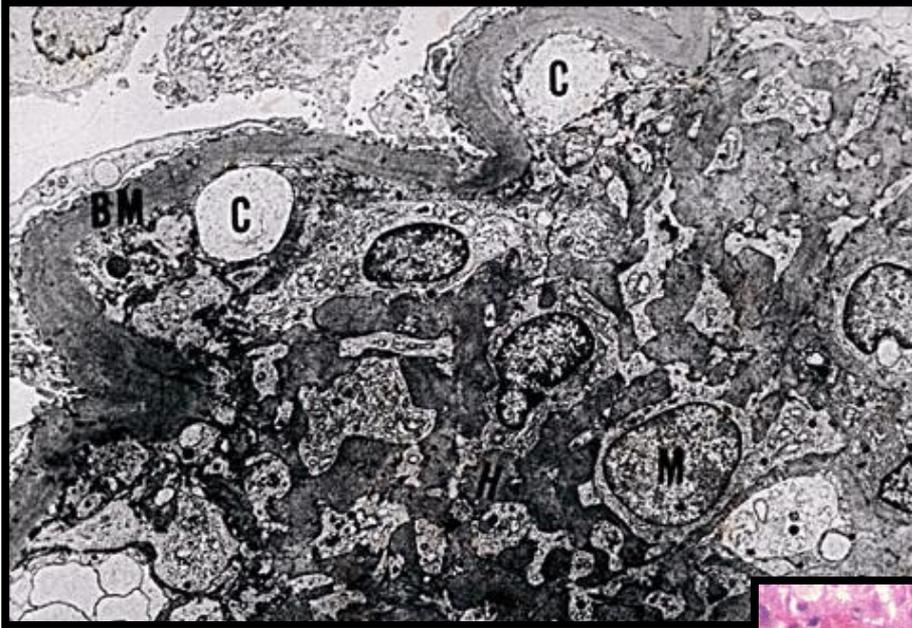
Nefropatia Diabética

- **Aumento permeabilidade da MB – microalbuminúria / esclerose glomerular**
- **Hialinização arteriolar – hipertensão arterial**
- **Predisposição a infecções - pielonefrite**

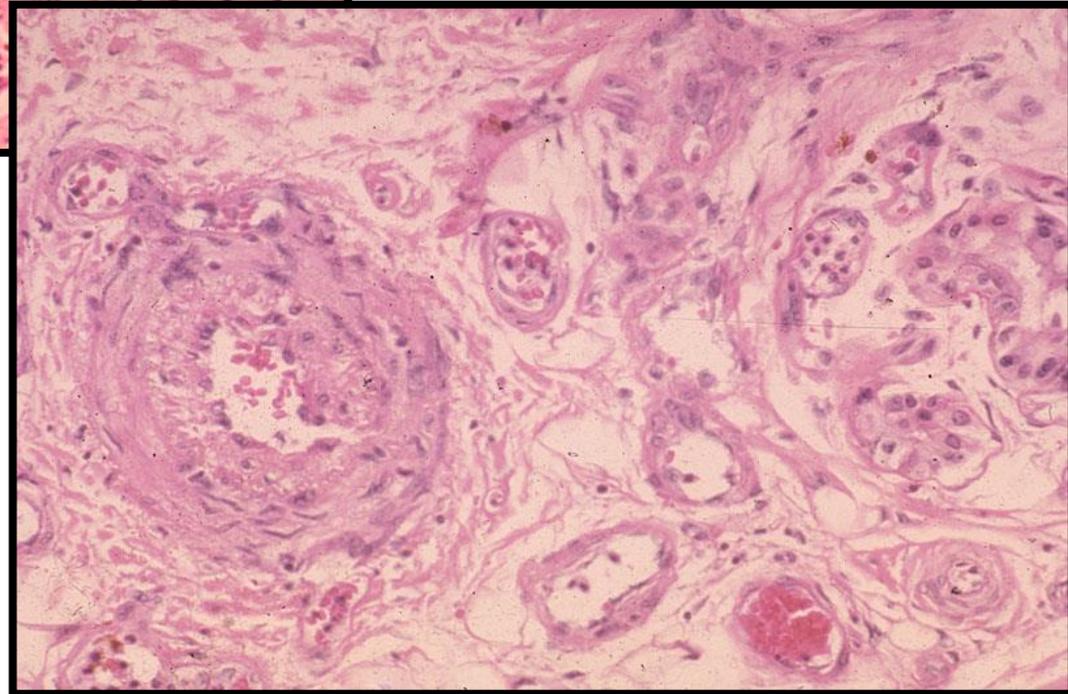
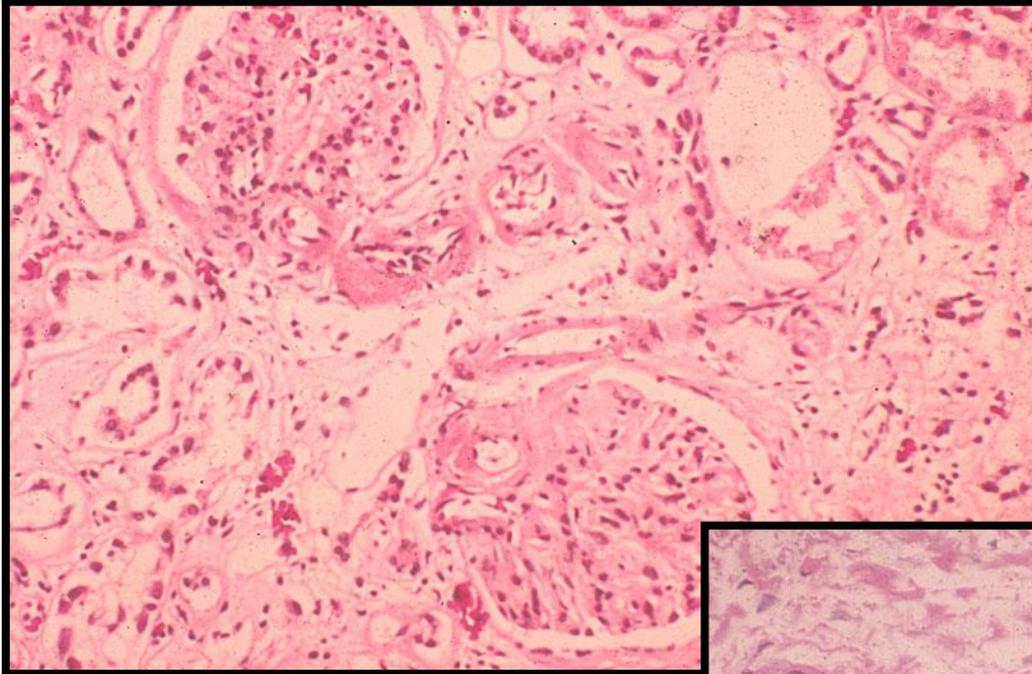
Nefropatia Diabética



Nefropatia Diabética



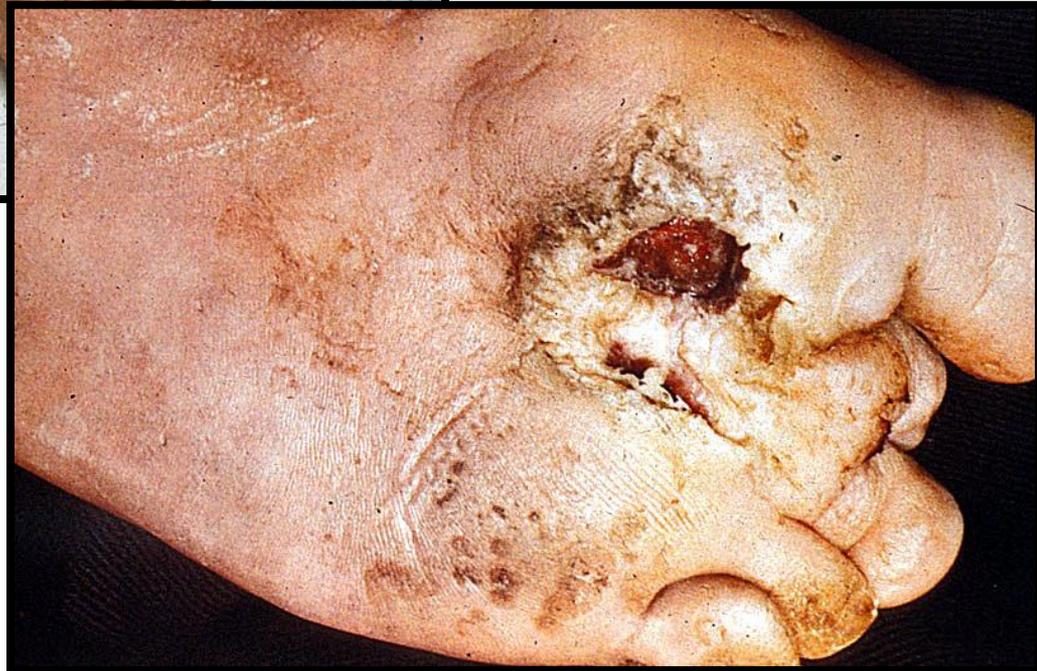
Nefropatia Diabética



Pé Diabético

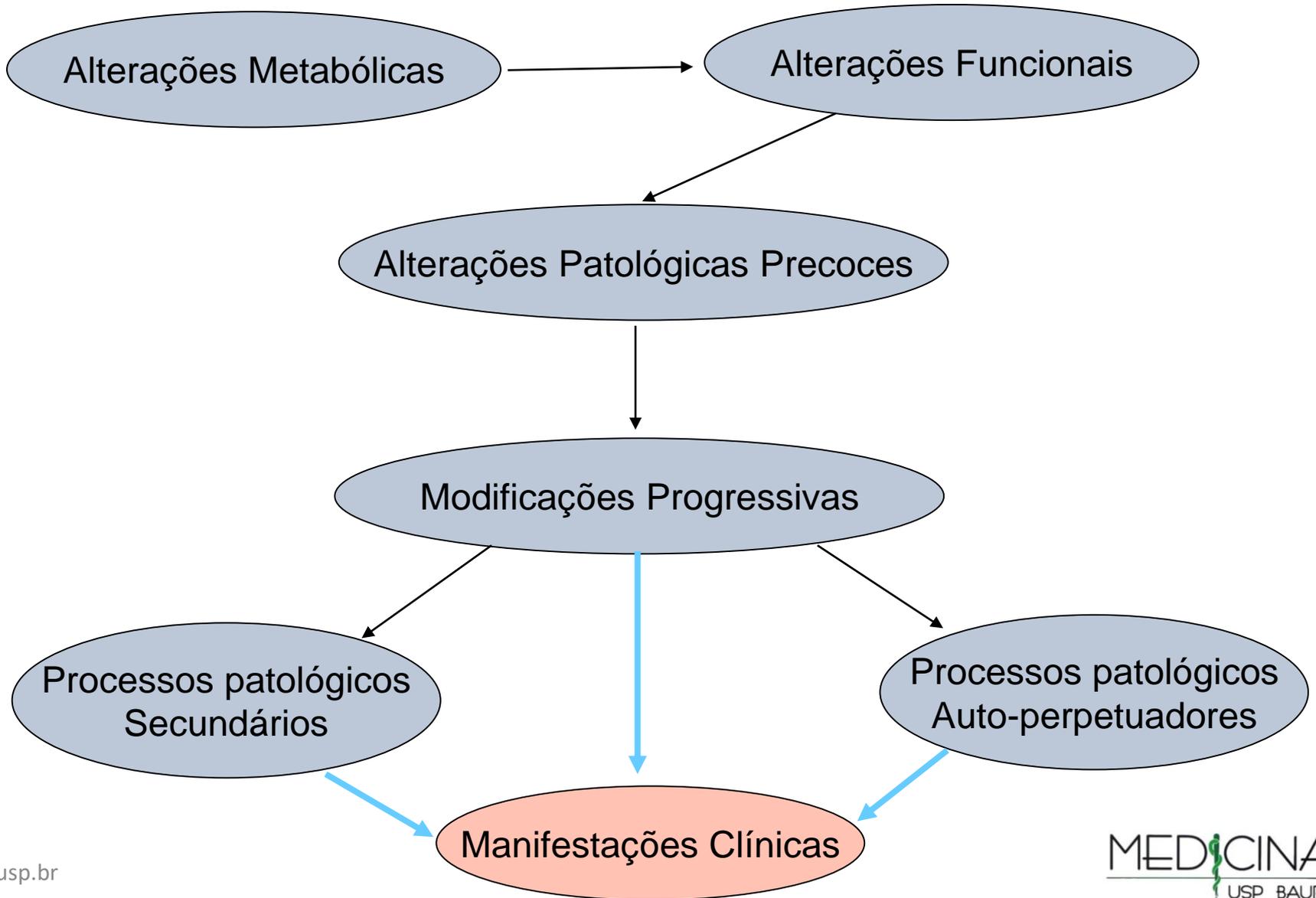
- **Aterosclerose periférica – isquemia**
- **Alteração vascular dos nervos periféricos + alterações de bomba - neuropatia**
- **Alterações do sistema de coagulação e recorrência das lesões**

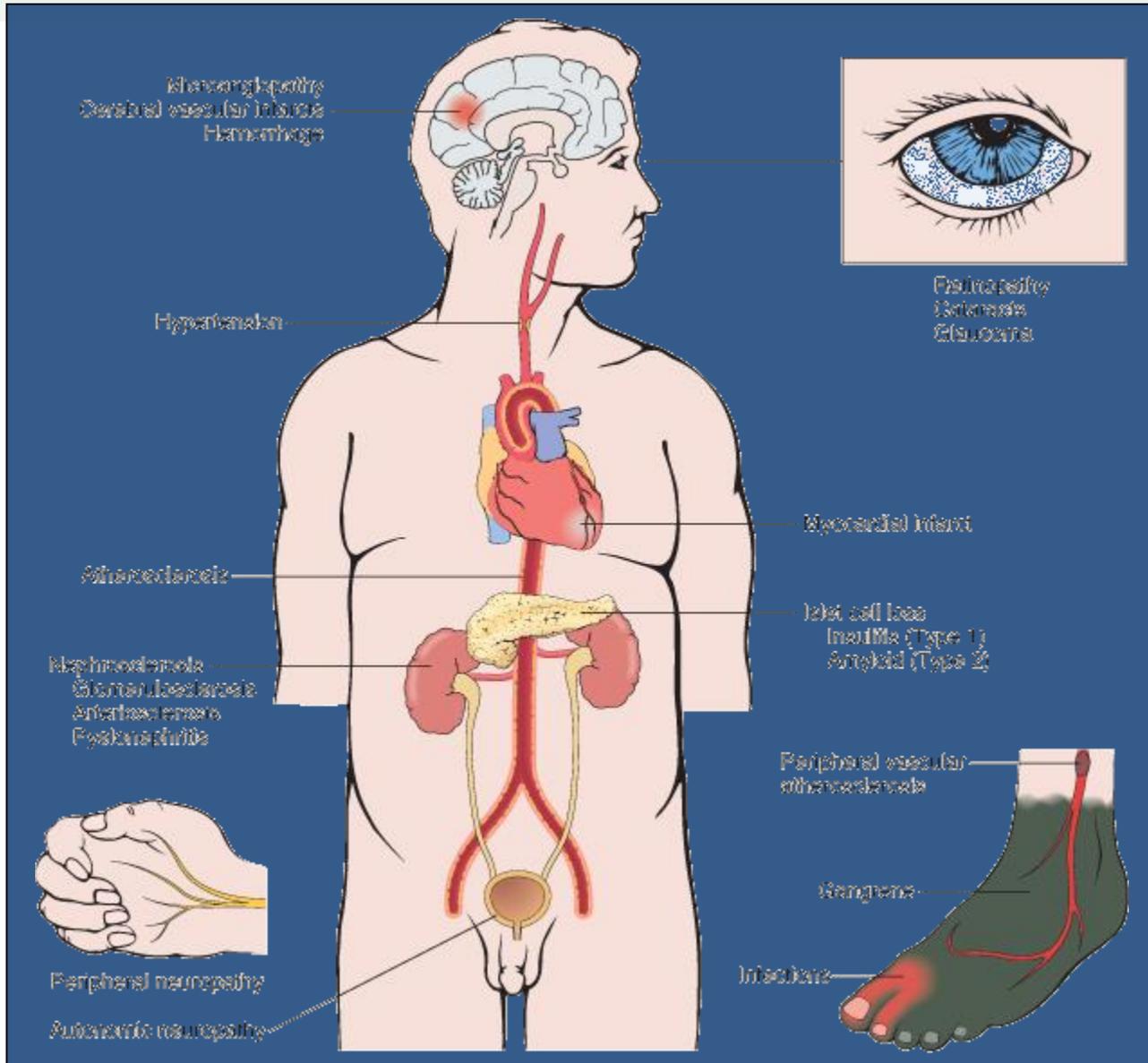
Pé Diabético



Pé Diabético







Macroangiopathy
Cerebral vascular infarct
Hemorrhage



Proliferative
retinopathy
Glaucoma

Hypertension

Myocardial infarct

Atherosclerosis

Islet cell loss
Insulinoma (Type 1)
Amyloid (Type 2)

Nephropathy
Glomerulosclerosis
Arteriosclerosis
Fibrosis

Peripheral vascular
atherosclerosis



Peripheral neuropathy
Autonomic neuropathy

Gangrene

Infections



