Chronic complications of diabetes mellitus

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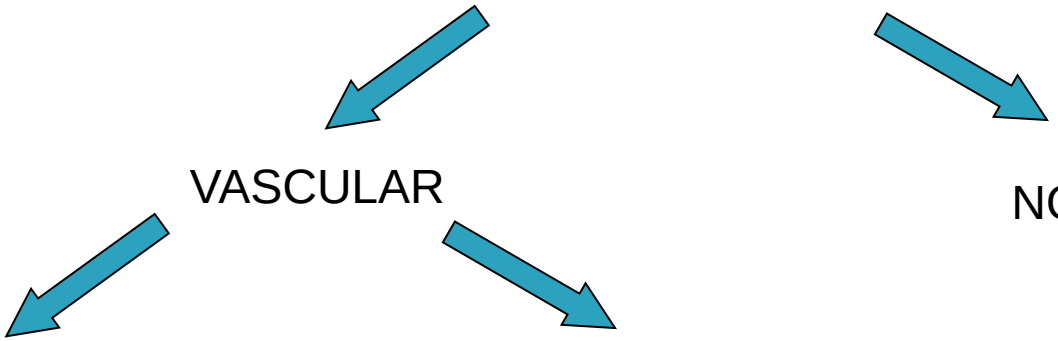
UNIWERSYTET MEDYCZNY W ŁODZI

Chronic complication of DM– responsible for the majority of morbidity and mortality in diabetic patients



MICROVASCULAR

1. RETINOPATHY
2. NEUROPATHY
3. NEPHROPATHY

MACROVASCULAR

1. CORONARY ARTERY DIS.
2. PERIPHERAL ARTERIAL DIS.
3. CEREBROVACULAR DIS.

NONVASCULAR

1. GASTROINTESTINAL
2. GENITOURINARY
3. DERMATOLOGIC
4. INFECTIOUS
5. CATARACTS
6. GLAUCOMA
7. PERIODONTAL DIS.

- The longer duration of hyperglycemia – the higher risk of chronic complications (second decade of DM).
- Type 2 DM – chronic complications at the moment of diagnosis !!!
- Reduction of hyperglycemia, proper control of DM prevents or delays microvascular complications, decreases risk of cardiovascular events.
- Genetic susceptibility of developing particular complications !!!

MECHANISM OF COMPLICATION

1. Increased intracellular glucose → formation of **advanced glycosylation end products** (AGEs) via nonenzymatic glycosylation of intra- and extracellular proteins.

AGEs:

* accelerate atherosclerosis
* promote glomerular dysfunction
* reduce NO synthesis
* induce endothelial dysfuncion

MECHANISM OF COMPLICATION

2. Hyperglycemia increases glucose metabolism via **sorbitol pathway.**

   Excess of glucose is converted to sorbitol by the aldose reductase

   Increased sorbitol leads to:

   * higher cellular osmolality
   * generation of ROS
   * cellular dysfunction

MECHANISM OF COMPLICATION

3. Hyperglycemia increases formation of diacylglycerol activating protein kinase c (PKC); PKC alters transcription of genes for fibronectin, type IV collagen, extracellular matrix proteins in endothelium and neurons.

4. Hyperglycemia increases flux through hexosamine pathway which promotes the glycosylation of proteins like endothelial NO synthase.

Ophthalmologic complications of DM

DM is a leading cause of blindness between the ages 20 and 74; blindness is a result of progressive retinopathy and macular edema.

DIABETIC RETINOPATHY

NONPROLIFERATIVE
After 1st decade of DM

Vascular microaneursm
Blot hemorrhages
Cotton wool spots

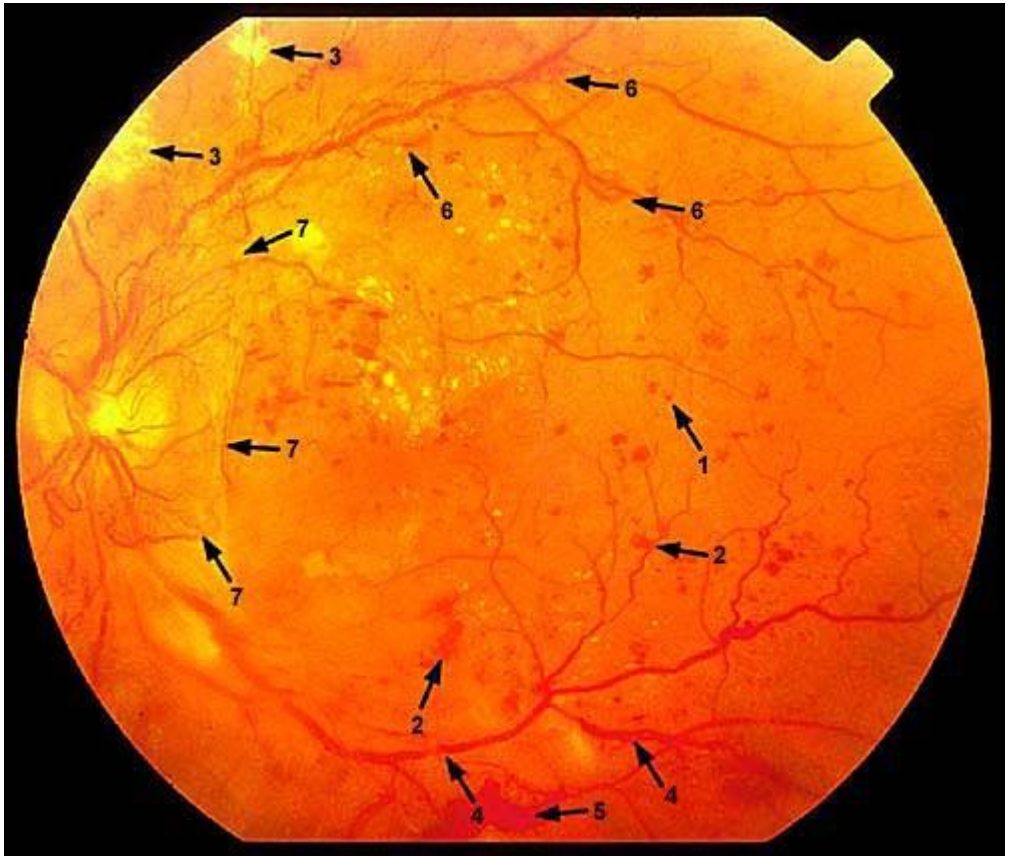
Increased vascular permeability
Abnormal retinal microvasculature
Retinal ischemia

PROLIFERATIVE

Neovascularisation – response to retinal hypoxia

Vitreous hemorrhage
Fibrosis
Retinal detachement

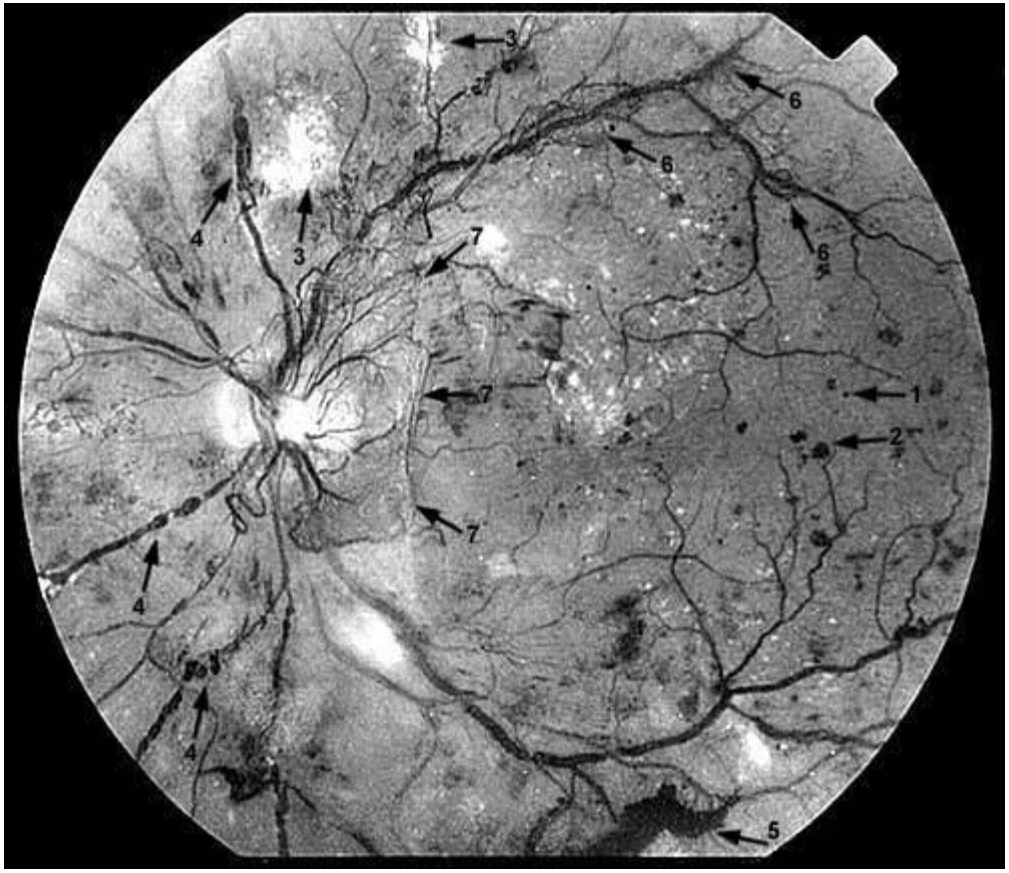
Proliferative diabetic nephropathy advanced in both eyes, with neovascularisation within the optic nerve disc



Left eye:
1 – microaneurism,
2 – ecchymoses,
3 – hard exudation,
4 – abnormalities of the veins,
5 – preretinal hemorrhage,
6 – focus of neovascularisation,
7 – neovascular coat
on the optic nerve disc

Patient 50 years old, male, T2DM diagnosed 8 months before; treated with insulin, hypertension – not treated,

Macular edema - can occur even when noproliferative retinopathy is present; 25% risk of visual loss over the next 3 years;
Fluorescein angiography detects macular edema.



Fluorescein angiography of the left eye (black-and-white picture, before giving contrast):

Left eye:
1 – microaneurism,
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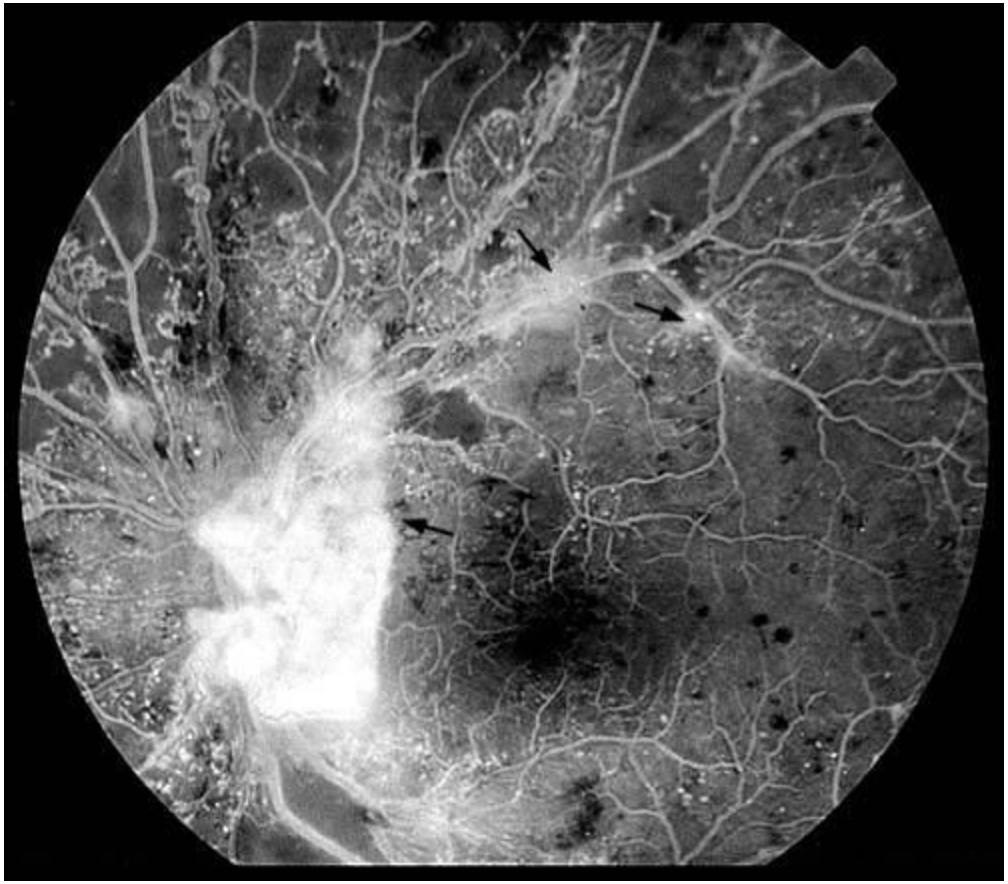
Arterio-venous phase after giving contrast.
The arrows point to substantial leakage within the optic nerve disc and other regions.



Treatment of diabetic retinopathy

- PREVENTION!!!
  - intensive glycemic ad blood pressure control
  - regular eye examinations
  - Prophylactic laser photocoagulation
    (panretinal- proliferative DR; focal – macular edema)

Diabetic nephropathy – leading cause of ESRD

CHRONIC HYPERGLYCEMIA

HYPERFILTRATION AND INCREASED GLOMERULAR CAPILLARY PRESSUSE → First years after the onset of DM INCREASE OF GFR

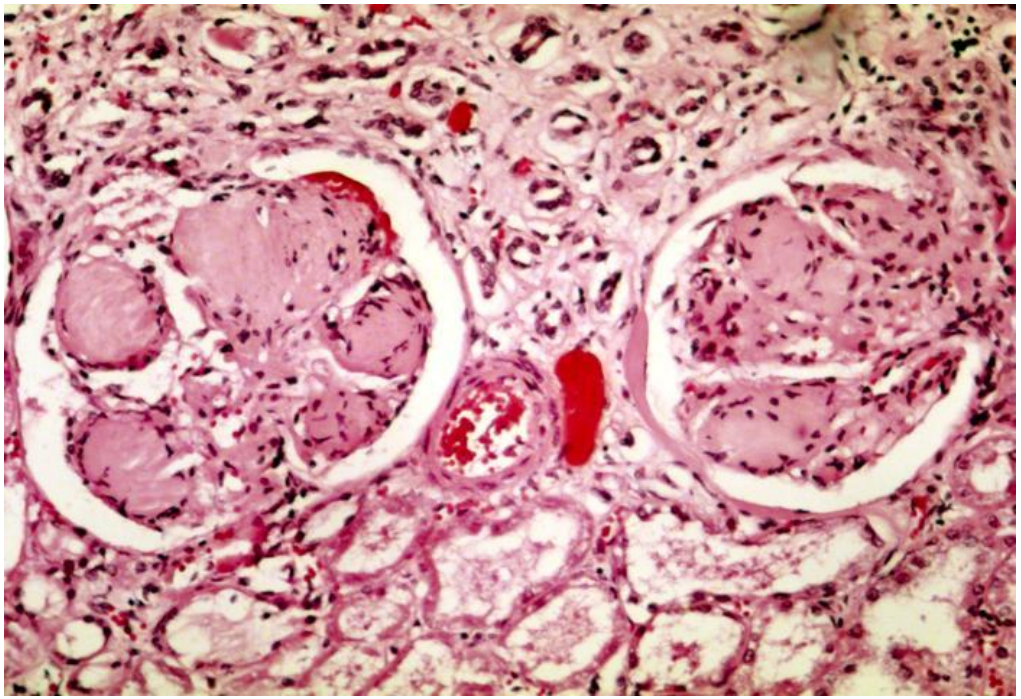
STRUCTURAL CHANGES IN THE GLOMERULUS:
- increased extracellular matrix
- basement membrane thickening
- mesangial expansion
- fibrosis

→ After 5-10 years:
MICROALBUMINURIA
30 – 300 mg / mg creatinine
in a spot collection
GFR returns to normal

After 10 years (in 50% of microalb.):
MACROALBUMINURIA >300 mg/d
Decline in GFR

ESRD

Diabetic nephropathy:
Glomerulosclerosis, damage of podocytes, proliferation of mesangium, glazing of glomeruli, fibrosis of interstitium.



Prevention of diabetic nephropathy

1. Proper control of glycemia
2. Strict blood pressure control (< 130/80 mmHg)
3. Administartion of **ACE inhibitors** or **ARBs**
4. Treatment of dyslipidemia
2. Monitoring albuminuria and creatinine level (eGFR) annually –
   in DM 1 > 5 years,
   in DM 2 at the moment of diagnosis;
   when eGFR < 60 ml/min/1.74m ^{2}→ nephrology consulatation

Test for microalbuminuria positive → exclude other reasons and repeat within 3–6 months → 2 of 3 test positive: treatment

DIABETIC NEUROPATHY

(in 50% of individuals with long-standing DM 1 and 2)

POLINEUROPATHY

Distal symmetric polyneuroapthy

Distal sensory loss (begins in feet, spreads approximately)

*Hyperesthesia
*Numbness
*Tingling, burning
*Pain – in lower extremities, at rest, worsens at night

MONONEUROPATHY

Dysfunction of isolated cranial (III, IV, VI, VII) or peripheral nerves

AUTONOMIC NEUROPATHY

1. Cardiovascular
* tachycardia
•orthostatic hypotension
• sudden death

2. Gastrointestinal
•gastroparesis
• diarrhea/constipation

3. Genitourinary
•bladder-emptying abnormalities
*sexual dysfunction

4. Sympathetic nervous system dysfunction
*hyperhydrosis/anhydrosis
*hypoglycemia unawareness

Examination of the superficial esthesia with monofilament

Lower extremity complications

DM is a leading cause of nontraumatic lower extremity amputation; result of interaction of several factors:

Peripheral sensory and motor neuropathy

Repeated trauma of foot without the knowledge

* abnormal foot muscle mechanism
* structural changes

Autonomic neuropathy

Altered superficial blood flow in the foot

Anhydrosis

* drying of the skin
* fissure formation

Peripheral arterial disease

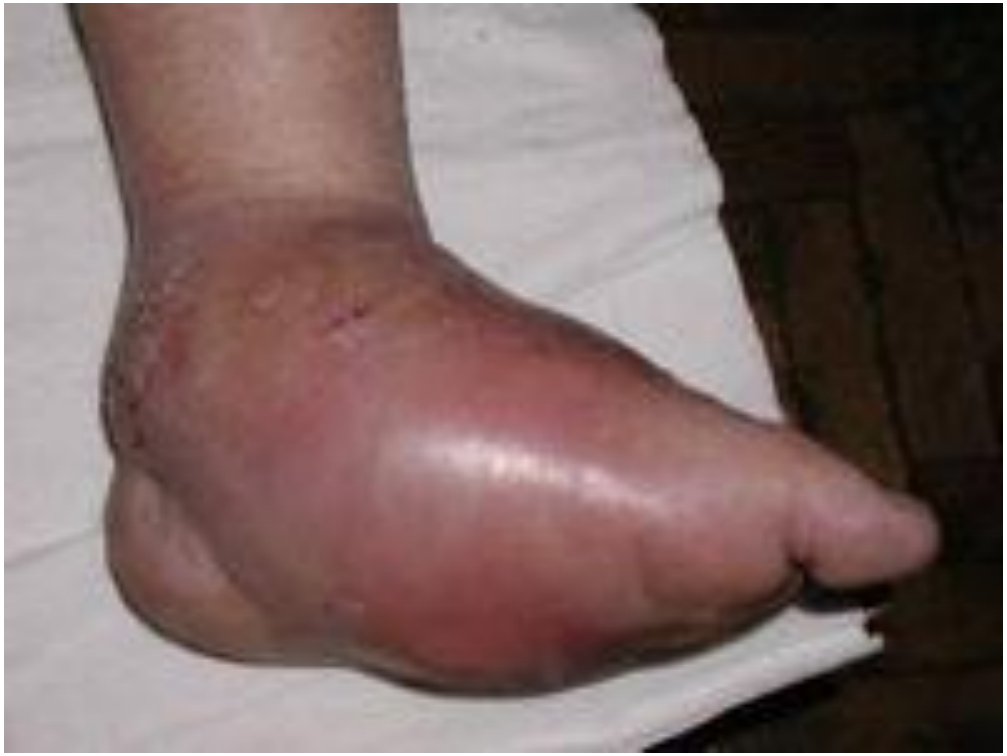
Chronic ischemia

* poor wound healing

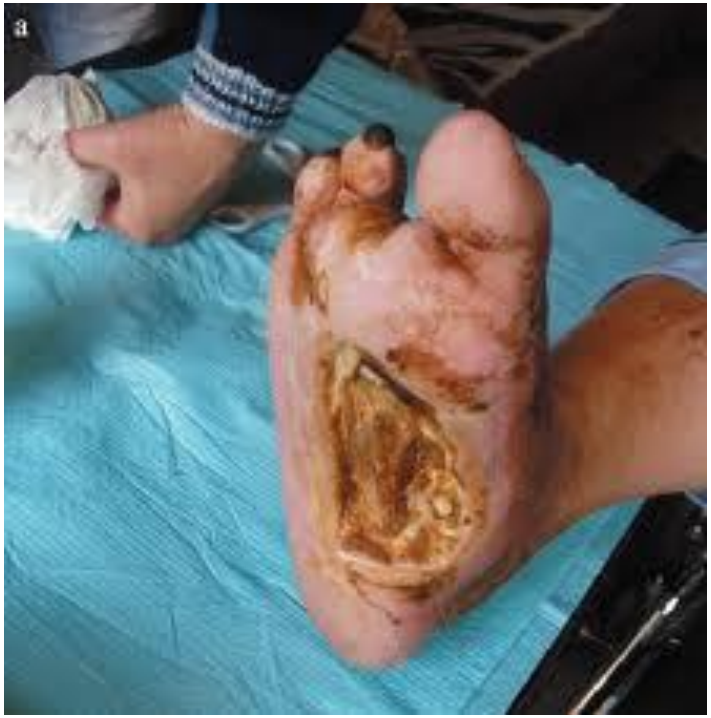
* infections

FOOT ULCERS

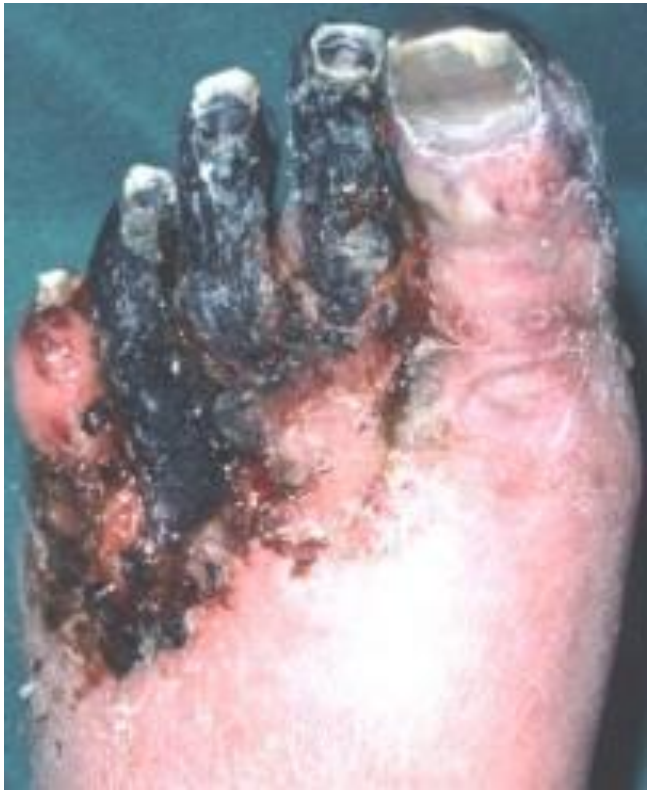
Deformation of diabetic foot – Charcot's joint
Instability and hypermobility which is a result of peripheral nerve damage.



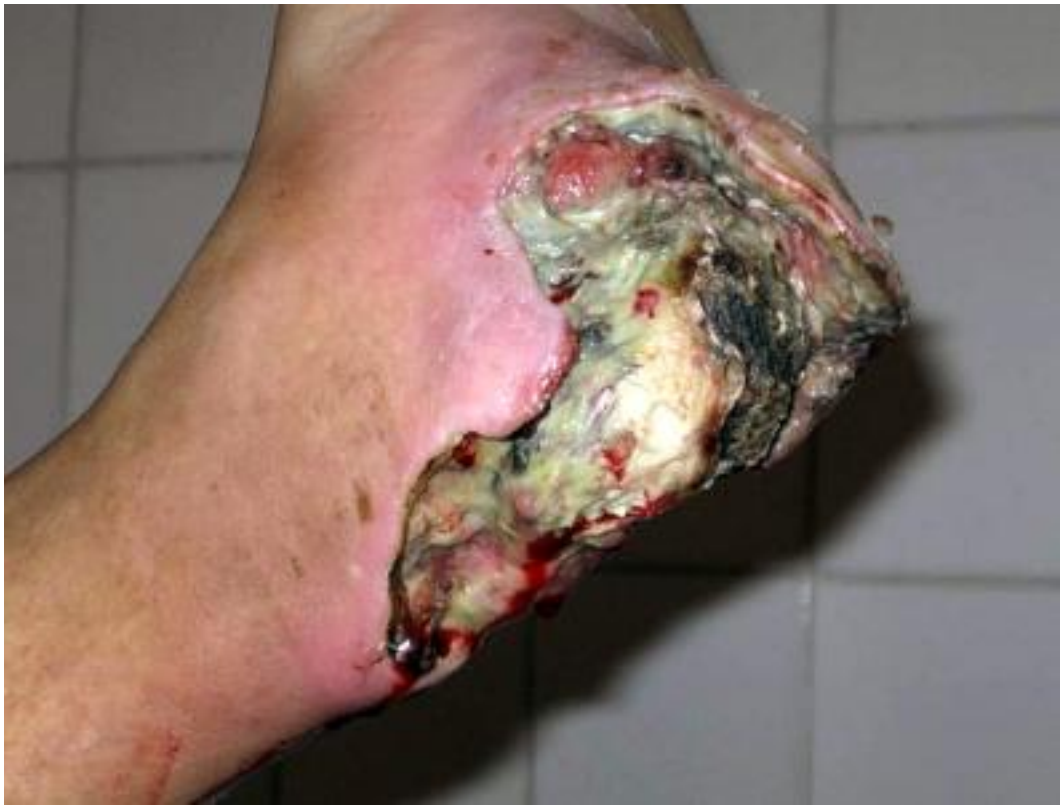
Deep ulceration in diabetic foot



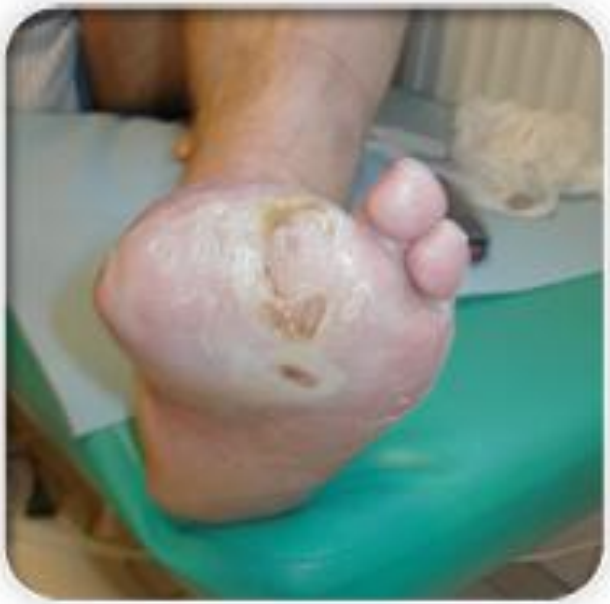
Necrotic diabetic foot



Necrotic and infected diabetic foot, damaged Achilles tendon



Amputations of digits in diabetic foot



CARDIOVASCULAR COMPLICATIONS

DM increases risk for:

- Peripheral arterial disease
- Chronic heart failure
- Coronary artery disease (*silent ischemia*)
- Myocardial infarction
- Sudden death
- Cerebrovasular disease

Prevention: control of glycemia, blood pressure, hyperlipidemia (nutritional therapy, physical activity), smoking cessation