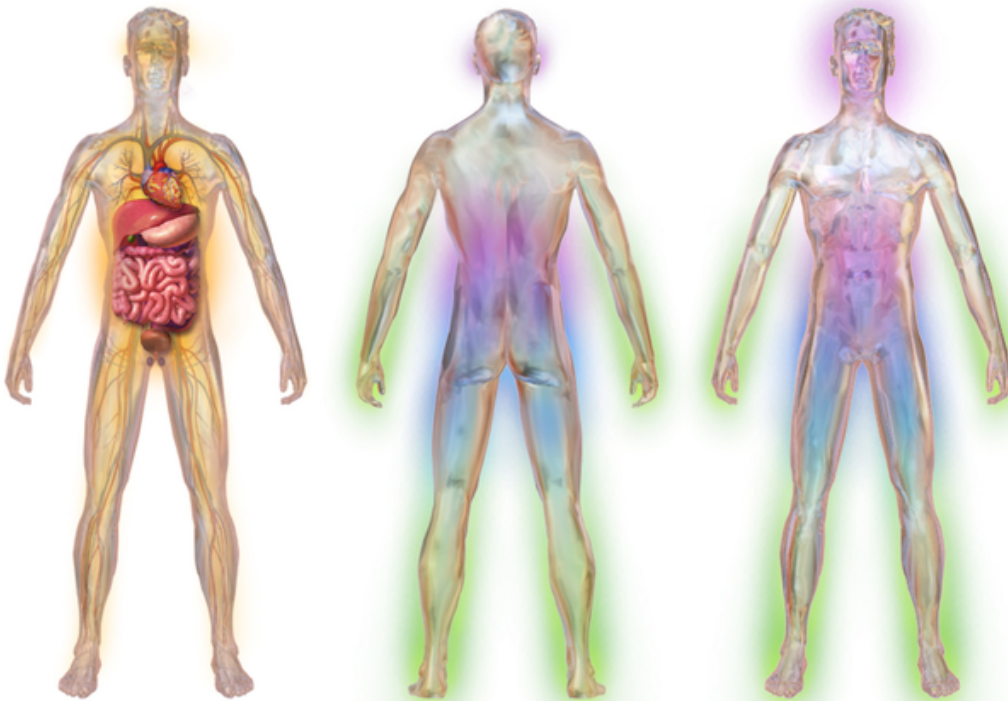


Diabetes Complications: Diabetic Retinopathy, Nephropathy and Neuropathy

[See online here](#)

Patients with long-term high blood sugar concentration can expect serious consequences that cut across all systems of the body. Accurate knowledge of complications that may arise from diabetes is important not only for examination purposes as physicians may inadvertently contribute to these complications. Amputations, blindness, kidney damage, and cardiovascular disease due to diabetes can be avoided with evidence-based management.



Introduction

Long-term **diabetes mellitus** causes damage to small and large **blood vessels**, resulting in microvascular and macrovascular complications, respectively, which result in increased mortality rates. Strict glycemic control is crucial to the prevention of these complications, especially microvascular complications such as retinopathy, nephropathy, and neuropathy. Therefore, early diagnosis and early treatment measures to ensure euglycemia are crucial for increasing the length and quality of life of diabetic patients.

Risk of Long-term Complications

Complications	Relative risk
Myocardial infarction	Men: 3.7 Women: 5.9
Cardiovascular death	Diagnosis before the age of 30: 9.1 Diagnose after the age of 30: 2.3
Apoplexy	2-4
Blindness	5.2
Renal failure in men	12.7
Lower-extremity amputations	22.2-45
Foot ulcers	Frequently

Macroangiopathy

Hyperglycemia increases the risk of **atherosclerosis**, which leads to the stiffness and narrowing of vessel walls. Although non-diabetics experience arteriosclerosis, diabetes increases this risk multiple times. This is caused by the vascular endothelium dysfunction, which is potentiated by hyperglycemia.

Firstly, the dysfunction is caused by glycated LDL. These molecules penetrate the tunica intima and activate oxidative and inflammatory processes there, resulting in the typical **plaques** noted in the endothelium. Secondly, lipolysis is not inhibited by a lack of insulin. The resulting atherosclerosis and vessel narrowing present in a variety of conditions, such as:

- Peripheral arterial occlusive disease, intermittent claudication
- [Coronary heart disease](#), myocardial infarction
- Carotid stenosis (cerebrovascular sclerosis)
- Transient ischemic attack, stroke

Myocardial infarction is particularly dangerous for diabetics as it is often painless and unnoticed by patients because of the concurrent diabetic neuropathy. **Sixty percent of all diabetics die from cardiovascular disease.**

Reducing cardiovascular risk factors and blood glucose monitoring are essential in diabetic patients. Factors such as obesity, lack of exercise, smoking, and alcohol consumption contribute to the development of macroangiopathy and should be eliminated. [Hypertension](#) and hyperlipidemia are other risk factors that need to be appropriately managed. The administration of anticoagulants is also useful to prevent the formation of thrombi.

Microangiopathy

As previously mentioned, diabetes mellitus affects the small vessels (microangiopathy) and large vessels (macroangiopathy). Hyperglycemia results in the non-enzymatic glycosylation of proteins. These advanced glycosylated end-products are accumulated in structural proteins and connective tissue within the capillary basement membranes and renal glomeruli. The result is vessel occlusion, ischemia, hypoxia, and reduced glomerular filtration rate (GFR).

Microangiopathy is often symptomatically linked to the eye, [kidney](#), and nerves, but it

can also affect other areas of the body.

Diabetic Retinopathy



Image: 'Diabetic Retinopathy' License: [Public Domain](#)

Diabetic retinopathy is divided into non-proliferative retinopathy and proliferative retinopathy.

Non-proliferative retinopathy, also called **background retinopathy**, is the earliest stage of retinal involvement in diabetic patients. It is characterized by microaneurysms, dot hemorrhages, exudates, and retinal edema.

Proliferative retinopathy presents with the formation of new blood vessels. Due to hypoxia, which is the consequence of hyperglycemia, growth factors are increasingly formed and new blood vessels appear (neovascularization). In this case, vascular endothelial growth factor (VEGF) plays a decisive role; VEGF is detectable in [blood](#) and can be inhibited by drugs.

The new blood vessels can grow even in the vitreous humor. However, these blood vessels are very unstable and may cause **bleeding** in the eye. If the newly formed blood vessels do not lead to any vision problems, or only slight impairment is noticed, then the non-proliferative retinopathy is addressed. If increased bleeding into the vitreous humor and the new blood vessels cause problems, it is called proliferative retinopathy. The consequences range from blurred vision to retinal detachment, glaucoma, and blindness.

Diabetic macular edema is defined as retinal thickening within the center of the macula, due to plasma leakages. It can occur at any stage of diabetic retinopathy.

Note: Diabetes is the leading cause of acquired blindness in developed countries.

Treatment of diabetic retinopathy

Diabetic retinopathy is primarily treated by **laser therapy**. It should be performed as soon as neovascularization or vitreous hemorrhage occurs. **Intravitreal corticosteroids** (dexamethasone, triamcinolone, and fluocinolone) positively affect diabetic macular edema.

Angiogenesis inhibitors such as pegaptanib and bevacizumab directly block vessel growth-promoting substances (VEGF) in the eye that lead to swelling of the central retina. In many cases, they are repeatedly injected in the eye every few weeks.

Diabetic Nephropathy

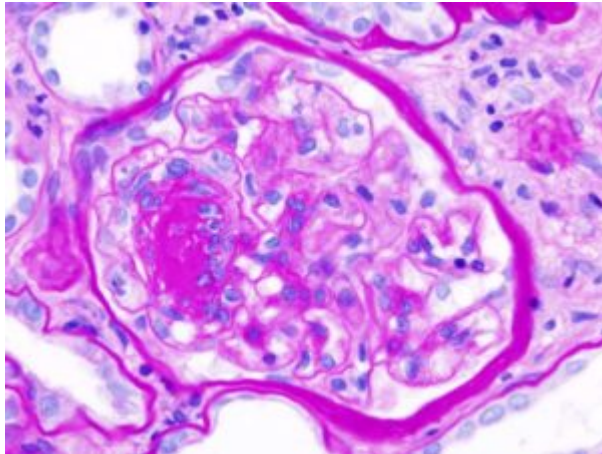


Image: 'Histopathological image of diabetic glomerulosclerosis with nephrotic syndrome' by KGH. License: [CC BY-SA 3.0](https://creativecommons.org/licenses/by-sa/3.0/)

Diabetic nephropathy is divided into 5 progressive stages that are asymptomatic at the initial stages, being partially reversible. However, they eventually lead to irreversible damage. Depending on the stage, different symptoms may be observed; therefore, corresponding therapeutic measures are necessary. **Euglycemia** and **normotension** are the primary **treatment goals** in all the stages.

Stage 1: High glomerular filtration

This stage is reversible, asymptomatic, and characterized by increased GFR. The hyperglycemia leads to enlarged kidneys and increased filtration capacity.

Stage 2: Normal albuminuria stage

This stage is reversible, asymptomatic, and characterized by normal albumin excretion in urine (< 30 mg/24 h). It usually begins after several years of diabetes. The basement membrane of the glomeruli is considerably thickened and the mesangial matrix is increased, leading to restricted filtration performance.

Stage 3: Early-stage diabetic nephropathy

This stage is characterized by **microalbuminuria** (30 - 300 mg/24 h) and **hypertension**. Diffuse glomerular changes can be seen and the glomeruli become more permeable to proteins. These symptoms usually occur only after 5-15 years of diabetes. They are a sign of the beginning of **renal failure**. The treatment of this stage with **angiotensin-converting enzyme inhibitors (ACEIs) is recommended** to protect the kidneys, lower protein excretion, and normalize blood pressure.

Stage 4: Clinical diabetic nephropathy

This is characterized by the excretion of large amounts of albumin (> 500 mg/24 h) and often occurs after 10-25 years of diabetes. Renal hypoperfusion, hypertension, and reduced filtration performance is also seen. In addition to ACE inhibitors, diuretics, calcium channel blockers, and beta-blockers may be used during this stage. Although the GFR continues to decline in this stage, the serum creatinine level may be normal.

Stage 5: Renal failure

This is an irreversible stage. Filtration performance is notably reduced, and pathological

creatinine values are detectable in the blood. Since the renal failure is irreversible, only dialysis and renal transplantation remain as therapeutic measures.

Diabetic Neuropathy

Persistent chronic hyperglycemia leads to neuropathy. The neurons are affected due to ischemia and insufficient oxygen supply because of angiopathy. Both **peripheral** and **autonomic nerves** may be affected.

The earliest symptoms of diabetic neuropathy often present **as tingling, pain, and numbness** in the extremities. These symptoms are **warning signs** and should not be ignored. If not properly managed, the peripheral nerve fibers are progressively damaged in a glove-and-stocking distribution, resulting in **reduced or complete loss of pain perception**. Injuries will remain unnoticed by the patient and can spread unhindered. A **diabetic foot** is an especially dangerous complication that can lead to the amputation of the limb.

Diabetics should obtain insured medical foot care for the prevention of diabetic foot syndrome. In addition, attention should be paid to suitable footwear. Diabetic patients should check their feet daily for any injuries, abrasions, or scratches. In the case of very painful neuropathies, **tricyclic antidepressants**, such as amitriptyline, may be of benefit. Furthermore, **gabapentin** and **pregabalin** are effective against neuropathic pain.



[Image](#): 'Three classes of chronic wound on a diabetic patient's foot' by Openi. License: [CC BY 3.0](#)

If the autonomic nerves are damaged, it may have multiple effects on the body. Thus, diabetics may experience the following:

- Erectile dysfunction
- Dizziness, syncope (fainting)
- Diabetic gastroparesis, [diarrhea](#), constipation
- Diabetic cystopathy with frequent infections
- Circulatory disorders of the skin
- Heartburn, difficulty swallowing (dysphagia), gastroparesis
- Related cancers

Other Complications

Apart from typical long-term consequences, diabetes also causes other complications that are less well-known. These include stiff shoulder (**frozen shoulder**) or finger/hand changes (**cheiropathy**). Diabetic neuropathic osteoarthropathy, also called **neuropathic arthropathy**, is a disease that leads to



Image: 'Charcot foot in diabetes in the X-ray a. p. and weird. Destructions with (sub)luxations are most pronounced around the Lisfranc line. At the lateral edge of the foot one can also recognize air inclusions as an indication of a deep infection fistula to the skin.' By Hellerhoff. License: [CC BY-SA 3.0](https://creativecommons.org/licenses/by-sa/3.0/) A neuropathic arthropathy in x-ray

a non-infectious, inflammatory destruction of the bones and joints. It represents a special form of diabetic foot ulcers.

In [diabetes mellitus type 1](#), there is increased prevalence of other autoimmune disorders such as **Hashimoto's thyroiditis**, **Addison's disease**, **vitiligo**, and **pernicious anemia**.

References

- Bright, C., Habel, M., & Concept Media, inc. (2004). *Neuropathy, nephropathy, and retinopathy*. Irvine, CA: Concept Media.
- Holt, R. I., & Wiley InterScience (Online service). (2010). *Textbook of diabetes*. Chichester, West Sussex: Wiley-Blackwell.
- Shaw, K. M., & Cummings, M. H. (2006). *Diabetes: Chronic Complications*. Hoboken: John Wiley & Sons, Ltd.
- Watkins, P. J. (2003). *ABC of diabetes*. London: BMJ Pub. Group.

Legal Note: Unless otherwise stated, all rights reserved by Lecturio GmbH. For further legal regulations see our [legal information page](#).