Diabetes Mellitus

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QUMS

26/8/91

Diabetes Mellitus

- 1500 BC Egypt:
  - Ebers Papyrus describes a disorder with frequent urination and weight loss
- "Diabetes" is Greek for "siphon"
- "Mellitus" is Latin for "sweet"

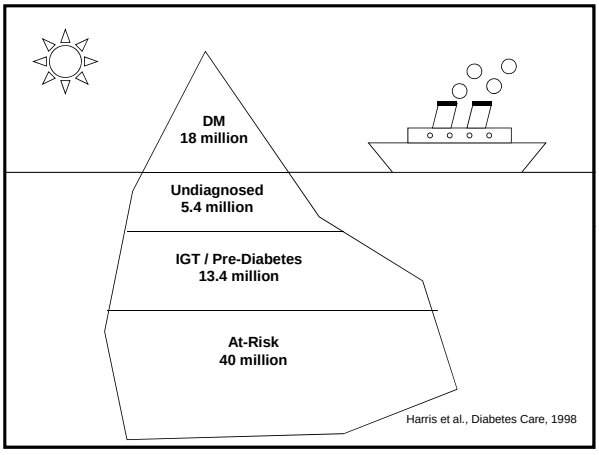
DIABETES MELLITUS

- Diabetes mellitus comprises a group of common **metabolic disorders** that share the phenotype of hyperglycemia.
- Several distinct types of DM exist and are caused by a ***complex interaction of***
- ***genetics***
- ***environmental factors***
- ***life-style choices.***

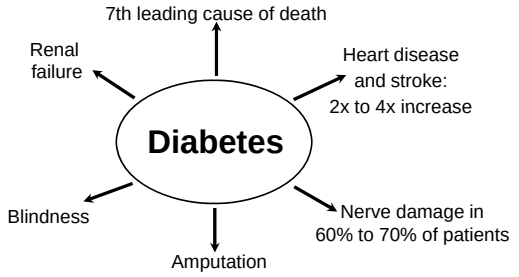
DIABETES MELLITUS

The metabolic dysregulation associated with DM causes

- **Secondary Pathophysiologic changes in multiple organ systems**
- Impose a tremendous burden on the
  1-individual with diabetes
  2- the health care system.

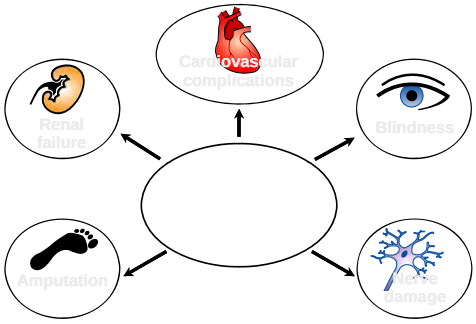


Diabetes Mellitus in the US: Health Impact



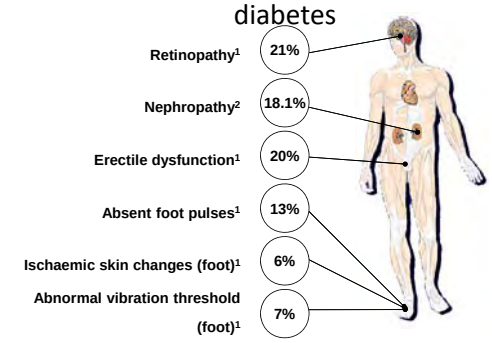
Diabetes Statistics. March 1999. NIDDK publication NIH 99-3892.
Harris MI et al. *Diabetes Care*. 1993;16:1446–1452.

Complications of Diabetes



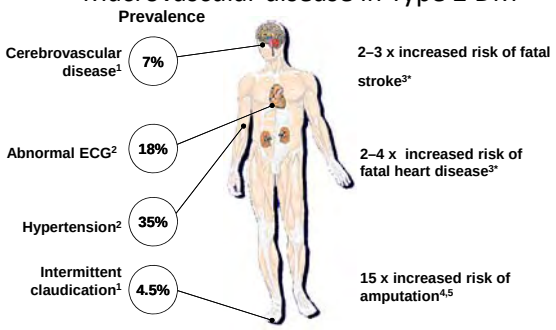
http://www.cdc.gov/diabetes/pubs/factsheet.htm#contents. Accessed 2/10/04.

Microvascular disease at diagnosis of diabetes



1. UKPDS 6. Diabetes Res 1990; 13: 1–11.
2. The Hypertension in Diabetes Group. J Hypertens 1993; 11: 309–17.

Macrovascular disease in Type 2 DM



*compared with general population

1. Wingard DL *et al.* Diabetes Care 1993; 16: 1022-25.
2. UKPDS 6. Diabetes Res 1990; 13: 1–11. 3. Balkau B *et al.* Lancet 1997; 350: 1680. 4. King's Fund. Counting the Cost. BDA, 1996.
5. Most RS, Sinnock P. Diabetes Care 1983. 6: 67-91.

Prevalence of Diabetes and Impaired Fasting Glucose in the Adult Population of Iran

National Survey of Risk Factors for Non-Communicable Diseases of Iran

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OBJECTIVE — Despite concerns regarding a diabetes epidemic in the Middle East, internationally published data on national estimates of prevalent type 2 diabetes in Iran do not exist. With this article, we document a dramatically high prevalence of diabetes in Iran.

RESEARCH DESIGN AND METHODS — Our data are based on the results of the first Survey of Risk Factors of Non-Communicable Diseases of Iran, 2005. In this national cross-sectional survey, 70,981 Iranian citizens aged 25–64 years were recruited.

RESULTS — 7.7% of adults aged 25–64 years, or 2 million adults, have diabetes, among whom one-half are undiagnosed. An additional 16.8%, or 4.4 million, of Iranian adults have impaired fasting glucose.

CONCLUSIONS — The high prevalence of diabetes in working-age adults is an ominous sign for this developing nation. As the relatively young Iranian population ages in the future and urbanization continues or accelerates, the prevalence of diabetes will likely escalate.

Diabetes Care 31:96–98, 2008

Third national surveillance of risk factors of non-communicable diseases (SuRFNCD-2007) in Iran: methods and results on prevalence of diabetes, hypertension, obesity, central obesity, and dyslipidemia

BMC Public Health 2009, **9**:167 doi:10.1186/1471-2458-9-167

Methods: The results of this study are extracted from the third national Surveillance of Risk Factors of Non-Communicable Diseases (SuRFNCD-2007), conducted in 2007. A total of 5,287 Iranian citizens, aged 15-64 years, were included in this survey. Interviewer-administered questionnaires were applied to collect the data of participants including the demographics, diet, physical activity, smoking, history of hypertension, and history of diabetes. Anthropometric characteristics were measured and serum biochemistry profiles were determined on venous blood samples. Diabetes (fasting plasma glucose ≥ 126 mg/dl),

Results: The prevalence of diabetes, hypertension, obesity, and central obesity was 8.7 % (95%CI=7.4-10.2%), 26.6 % (95%CI=24.4-28.9%), 22.3% (95%CI=20.2-24.5%), and 53.6% (95%CI=50.4-56.8%), respectively. The prevalence of hypertriglyceridemia and hypercholesterolemia was 36.4% (95%CI=34.1-38.9%) and 42.9% (95%CI=40.4-45.4%), respectively. All of the mentioned prevalence rates were higher among females (except hypertriglyceridemia) and urban residents.

The economic costs of diabetes: a population-based study in Tehran, Iran

A. Esteghamati · O. Khalilzadeh · M. Anvari · A. Meysamie · M. Abbasi · M. Forouzanfar · F. Alaeddini

Diabetologia
DOI 10.1007/s00125-009-1398-4

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Results Total annual direct costs of diabetic and control participants were $152.3±14.5 and $52.0±5.8, respectively, which is indicative of 2.92 times higher costs in diabetic patients. The most expensive components of direct costs were medications and devices, and hospitalisation in diabetic patients (28.7% and 28.6%, respectively). Total indirect costs were $39.6±2.4 and $16.7±1.1 in diabetic and non-diabetic individuals. The aggregate annual direct costs of diabetes were estimated to be $112.424±10.732 million and $590.676±65.985 million in Tehran and Iran, respectively. Diabetes complications contributed 53% of the aggregate excess direct costs of diabetes.
Conclusions/interpretation Diabetes is an expensive medical problem in Iran and planning of national programmes for its control and prevention is necessary.

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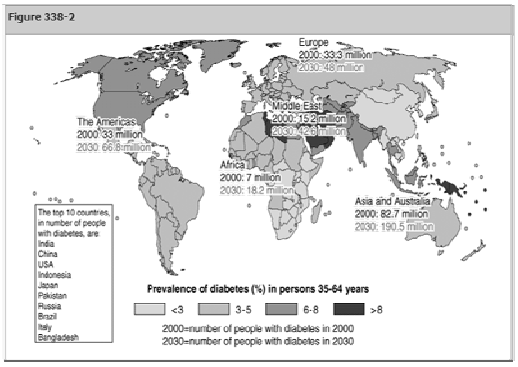
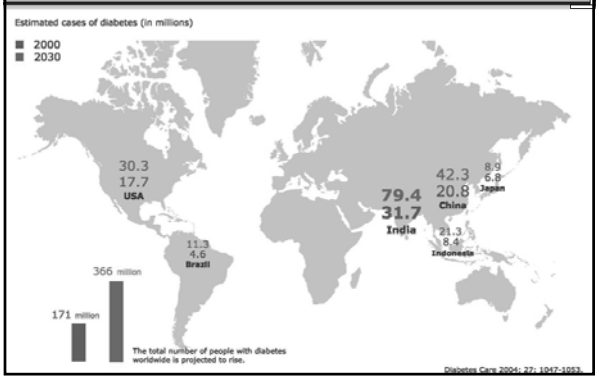


Global prevalence of diabetes.
Estimated cases of diabetes (in millions)



STANDARDS OF MEDICAL CARE IN DIABETES—2011

I. CLASSIFICATION AND DIAGNOSIS OF DIABETES

Classification of Diabetes

- Type 1 diabetes
  - β-cell destruction
- Type 2 diabetes
  - Progressive insulin secretory defect
- Other specific types of diabetes
  - Genetic defects in β-cell function, insulin action
  - Diseases of the exocrine pancreas
  - Drug- or chemical-induced
- Gestational diabetes mellitus

ADA. I. Classification and Diagnosis. *Diabetes Care* 2011;34(suppl 1):S12.

Criteria for the Diagnosis of Diabetes

A1C ≥6.5%

OR

Fasting plasma glucose (FPG) ≥126 mg/dl (7.0 mmol/l)

OR

Two-hour plasma glucose ≥200 mg/dl (11.1 mmol/l) during an OGTT

OR

A random plasma glucose ≥200 mg/dl (11.1 mmol/l)

ADA. I. Classification and Diagnosis. *Diabetes Care* 2011;34(suppl 1):S13. Table 2.

Criteria for the Diagnosis of Diabetes

A1C ≥6.5%

The test should be performed in a laboratory using an NGSP-certified method standardized to the DCCT assay*

*In the absence of unequivocal hyperglycemia, result should be confirmed by repeat testing.

ADA. I. Classification and Diagnosis. *Diabetes Care* 2011;34(suppl 1):S13. Table 2.

Criteria for the Diagnosis of Diabetes

Fasting plasma glucose (FPG) ≥126 mg/dl (7.0 mmol/l)

Fasting: no caloric intake for at least 8 h*

*In the absence of unequivocal hyperglycemia, result should be confirmed by repeat testing.

ADA. I. Classification and Diagnosis. *Diabetes Care* 2011;34(suppl 1):S13. Table 2.

Criteria for the Diagnosis of Diabetes

Two-hour plasma glucose ≥200 mg/dl (11.1 mmol/l) during an OGTT

The test should be performed as described by the World Health Organization, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water*

*n the absence of unequivocal hyperglycemia, result should be confirmed by repeat testing.

ADA. I. Classification and Diagnosis. *Diabetes Care* 2011;34(suppl 1):S13. Table 2.

Criteria for the Diagnosis of Diabetes

In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200 mg/dl (11.1 mmol/l)

ADA. I. Classification and Diagnosis. *Diabetes Care* 2011;34(suppl 1):S13. Table 2.

Prediabetes: IFG, IGT, Increased A1C

Categories of increased risk for diabetes (Prediabetes)*

FPG 100-125 mg/dl (5.6-6.9 mmol/l): IFG

or

2-h plasma glucose in the 75-g OGTT 140-199 mg/dl (7.8-11.0 mmol/l): IGT

or

A1C 5.7-6.4%

*For all three tests, risk is continuous, extending below the lower limit of a range and becoming disproportionately greater at higher ends of the range.

ADA. I. Classification and Diagnosis. *Diabetes Care* 2011;34(suppl 1):S13. Table 3.

II. TESTING FOR DIABETES IN ASYMPTOMATIC PATIENTS

Recommendations: Testing for Diabetes in Asymptomatic Patients

- Consider testing overweight/obese adults with one or more additional risk factors
  - In those without risk factors, begin testing at age 45 years (B)
- If tests are normal
  - Repeat testing at least at 3-year intervals (E)
- Use A1C, FPG, or 2-h 75-g OGTT (B)
- In those with increased risk for future diabetes
  - Identify and, if appropriate, treat other CVD risk factors (B)

ADA. II. Testing in Asymptomatic Patients. *Diabetes Care* 2011;34(suppl 1):S13-S14.

Criteria for Testing for Diabetes in Asymptomatic Adult Individuals (1)

1. Testing should be considered in all adults who are overweight (BMI ≥25 kg/m^2*) and have additional risk factors:

- Physical inactivity
- First-degree relative with diabetes
- High-risk race/ethnicity (e.g., African American, Latino, Native American, Asian American, Pacific Islander)
- Women who delivered a baby weighing >9 lb or were diagnosed with GDM
- Hypertension (≥140/90 mmHg or on therapy for hypertension)
- HDL cholesterol level <35 mg/dl (0.90 mmol/l) and/or a triglyceride level >250 mg/dl (2.82 mmol/l)
- Women with polycystic ovarian syndrome (PCOS)
- A1C ≥5.7%, IGT, or IFG on previous testing
- Other clinical conditions associated with insulin resistance (e.g., severe obesity, acanthosis nigricans)
- History of CVD

*At-risk BMI may be lower in some ethnic groups.

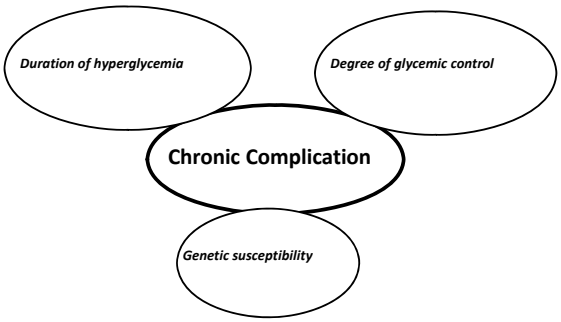
ADA. Testing in Asymptomatic Patients. *Diabetes Care* 2011;34(suppl 1):S14. Table 4.

Criteria for Testing for Diabetes in Asymptomatic Adult Individuals (2)

2. In the absence of criteria (risk factors on previous slide), testing for diabetes should begin at age 45 years

3. If results are normal, testing should be repeated at least at 3-year intervals, with consideration of more frequent testing depending on initial results and risk status

ADA. Testing in Asymptomatic Patients. *Diabetes Care* 2011;34(suppl 1):S14. Table 4.



Major determinants of chronic complication

Glycemic Control and Complications

- The DCCT demonstrated that improvement of glycemic control reduced:
- nonproliferative and proliferative retinopathy (47% reduction)
- microalbuminuria (39% reduction)
- clinical nephropathy (54% reduction)
- neuropathy (60% reduction).

- Improved glycemic control also slowed the progression of early diabetic complications.

Mechanisms of Hyperglycemia Induced Tissue Damage

1. *Formation of advanced glycation end products*
2. *Aldose reductase activity/redox changes*
3. *Diacylglycerol- protein kinase C activation*
4. Hexosamine pathway
5. *stress oxidative pathway , formation of (ROS)*

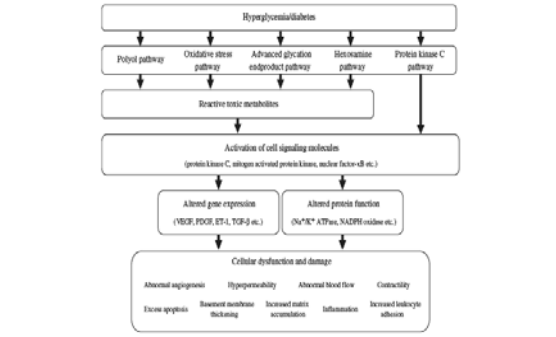


Figure 1 | Mechanisms by which hyperglycemia induced diabetic vascular complications. ET-1, endothelin-1; NADPH, nicotinamide adenine dinucleotide phosphate; PDGF, platelet-derived growth factor; TGF-β, transforming growth factor-β; VEGF, vascular endothelial growth factor.

Vascular complication

Microvascular

1- **Eye disease**

- Retinopathy(nonproliferative /proliferative)
- Macular edema

2- **Neuropathy**

- Sensory and motor(mono/ polyneuropathy)
- Autonomic

3- Nephropathy

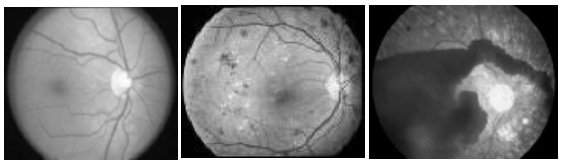
Macrovascular

- Coronary artery disease
- Peripheral arterial disease
- Cerebrovascular disease

Retinopathy

- Damage to blood vessels in and around the retina. It could occur with varying degrees of severity.

Normal ----------→ Small hemorrhages ----------→ Large hemorrhage



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Renal Complications

- First years after the onset of DM

1. Glomerular hyperperfusion (RBF High)
2. GFR increase
3. Renal hypertrophy (size enlarged)

During the first 5 years of DM

1. Thickening of glomerular basement membrane
2. Glomerular hypertrophy
3. Mesangial volume expansion occur as GFR returns to normal.

Renal Complications

- After 5–10 years of type 1 DM, ~40% of individuals begin to excrete small amounts of albumin in urine.

Microalbuminuria is defined as:

- 30–300 mg/d in a 24-h collection
- 30–300 mg/mg creatinine in a spot collection (preferred method).

Renal Complications

- Although the appearance of microalbuminuria in type 1 DM is an important risk factor for progression to overt proteinuria (>300 mg/d)
- Only ~50% of individuals progress to macroalbuminuria over the next 10 years.

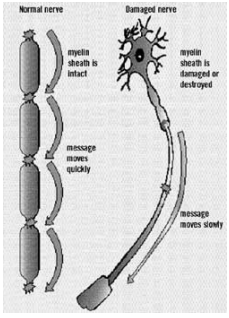
Renal Complications

- Once macroalbuminuria is present, there is a steady decline in GFR
- ~50% of individuals reach ESRD in 7–10 years

Once macroalbuminuria develops

- blood pressure rises slightly
- pathologic changes are likely irreversible.

Damage to the Nerves



http://www.mtsinai.on.ca/EBFFRC/MS/default.htm

- Numbness and tingling in feet and night leg cramps may result from nerve damage due to prolonged high glucose levels that cause changes in the nerves and "neuron starvation" from lack of cellular glucose.
- Nerve damage can also lead to a loss of the ability to feel pain in the feet, leading to undue pressure››calluses›› ulceration. (Neuropathy)

Neuropathy

- Diabetic neuropathy occurs in ~50% of individuals with long-standing type 1 and type 2 DM.

It may manifest as

1. Polyneuropathy
2. Mononeuropathy
3. Autonomic neuropathy.

- As with other complications of DM, the development of neuropathy correlates with
- Duration of diabetes
- Glycemic control
- Additional risk factors are BMI (greater BMI, greater risk of neuropathy)
- Smoking

Other COMPLICATIONS

- Gastrointestinal (gastroparesis, diarrhea)
- Genitourinary (uropathy/sexual dysfunction)
- Dermatologic
- Infectious
- Cataracts
- Glaucoma
- Periodontal disease

Gl and GU Dysfunction

- Long-standing type 1 and 2 DM may affect the motility and function of gastrointestinal (GI) and genitourinary systems.

The most prominent GI symptoms are :

- Delayed gastric emptying (gastroparesis)
- Altered small- and large-bowel motility (constipation or diarrhea).

GU Dysfunction

- Diabetic autonomic neuropathy may lead to genitourinary dysfunction including :
- cystopathy
- erectile dysfunction
- female sexual dysfunction
- reduced sexual desire
- dyspareunia
- reduced vaginal lubrication

Cardiovascular Morbidity and Mortality

- Cardiovascular disease is increased in individuals with type 1 or type 2 DM.
- The Framingham Heart Study revealed a marked increase in PAD, CHF, CAD, MI, and sudden death (risk increase from one- to fivefold) in DM.

Cardiovascular Morbidity and Mortality

Risk factors for macrovascular disease in diabetic individuals include :

- Dyslipidemia
- Hypertension
- Obesity
- Reduced physical activity
- Cigarette smoking

Cardiovascular Morbidity and Mortality

- Additional risk factors more prevalent in the diabetic population include:
- Microalbuminuria
- Macroalbuminuria
- Elevation of serum creatinine
- Abnormal platelet function

Dyslipidemia

The most common pattern of dyslipidemia is:

- Hypertriglyceridemia
- Reduced HDL c
- DM itself does not increase levels of LDL
- But small dense LDL particles found in type 2 DM are more atherogenic because they are more easily glycated and susceptible to oxidation.

Dyslipidemia

- Based on the guidelines by ADA and AHA, priorities in the treatment of hyperlipidemia are:
  1) Lower the LDL c
  2) Raise the HDL c
  3) Decrease TG
- A treatment strategy depends on the pattern of lipoprotein abnormalities

Hypertension

- A blood pressure goal of <125/75 is suggested for individuals with macroalbuminuria, hypertension, and diabetes.

Lower Extremity Complications

- DM is the leading cause of nontraumatic lower extremity amputation in the US.
- Foot ulcers and infections are also a major source of morbidity in individuals with DM

Lower Extremity Complications

- The reasons for the increased incidence of these disorders in DM involve the interaction of several pathogenic factors:

1. neuropathy
2. abnormal foot biomechanics
3. PAD
4. poor wound healing.

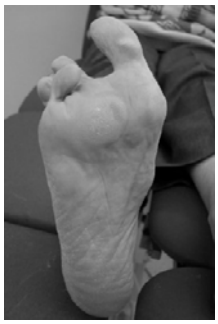
Lower Extremity Complications

- The peripheral sensory neuropathy interferes with normal protective mechanisms
- Allows the patient to sustain major or repeated minor trauma to the foot, often without knowledge of the injury.

Diabetic Neuropathy

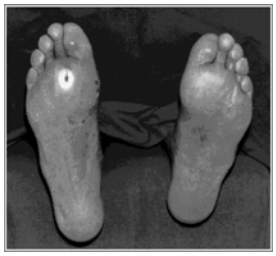
Patients with neuropathy lose their sensation of pain. As a result, they exert a lot of pressure at one spot under the foot when they walk, building up a callus at that site without causing discomfort.

The pressure becomes so high that eventually it causes breakdown of tissues and ulceration.

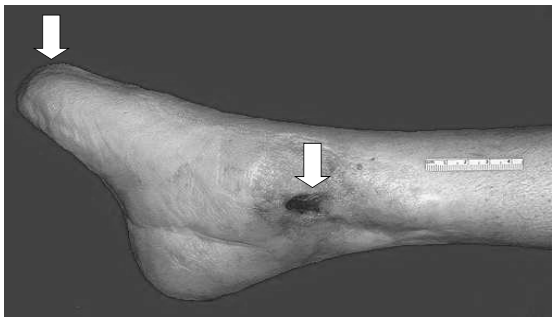


Foot ulcer

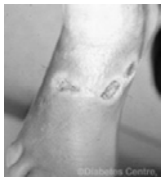
- A foot ulcer in a diabetic patient, most probably due to nerve damage. Note the callus (hard skin) around the ulcer, indicating that the foot was subjected to excess pressure.

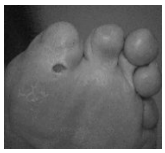


Diabetic Gangrene



A TYPICAL NEUROPATHIC ULCER IS…



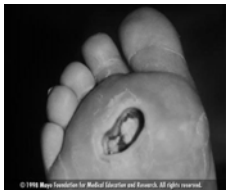


1) PAINLESS

2) SURROUNDED BY CALLUS

3) ASSOCIATED WITH GOOD FOOT PULSES (BECAUSE THE CIRCULATION IS NORMAL)

4) AT THE BOTTOM OF THE FOOT & TIPS OF TOES



w.diabetes.usyd.edu.au/foot/Neurop1.html www.thefootclinic.ca/services_diabetic.php

IV. PREVENTION/DELAY OF TYPE 2 DIABETES

Recommendations: Prevention/Delay of Type 2 Diabetes

- Refer patients with IGT (A), IFG (E), or A1C 5.7-6.4% (E) to support program
  - Weight loss 7% of body weight
  - At least 150 min/week moderate activity
- Follow-up counseling important (B); third-party payors should cover (E)
- Consider metformin if multiple risk factors, especially if hyperglycemia (e.g., A1C>6%) progresses despite lifestyle interventions (B)
- In those with prediabetes, monitor for development of diabetes annually (E)

ADA. IV. Prevention/Delay of Type 2 Diabetes. *Diabetes Care* 2011;34(suppl 1):S16.

V. DIABETES CARE

Diabetes Care: Initial Evaluation

- A complete medical evaluation should be performed to
  - Classify the diabetes
  - Detect presence of diabetes complications
  - Review previous treatment, glycemic control in patients with established diabetes
  - Assist in formulating a management plan
  - Provide a basis for continuing care
- Perform laboratory tests necessary to evaluate each patient's medical condition

ADA. V. Diabetes Care. *Diabetes Care* 2011;34(suppl 1):S16.

Components of the Comprehensive Diabetes Evaluation (6)

Laboratory evaluation

- A1C, if results not available within past 2–3 months
- If not performed/available within past year
  - Fasting lipid profile, including total, LDL- and HDL-cholesterol and triglycerides
  - Liver function tests
  - Test for urine albumin excretion with spot urine albumin/creatinine ratio
  - Serum creatinine and calculated GFR
  - TSH in type 1 diabetes, dyslipidemia, or women >50 years of age

ADA. V. Diabetes Care. *Diabetes Care* 2011;34(suppl 1):S17. Table 8.

Components of the Comprehensive Diabetes Evaluation (7)

Referrals

- Annual dilated eye exam
- Family planning for women of reproductive age
- Registered dietitian for MNT
- Diabetes self-management education
- Dental examination
- Mental health professional, if needed

ADA. V. Diabetes Care. *Diabetes Care* 2011;34(suppl 1):S17. Table 8.

Recommendations: Glucose Monitoring

- Self-monitoring of blood glucose should be carried out 3+ times daily for patients using multiple insulin injections or insulin pump therapy (A)
- For patients using less frequent insulin injections, noninsulin therapy, or medical nutrition therapy alone
  - SMBG may be useful as a guide to success of therapy (E)
  - However, several recent trials have called into question clinical utility, cost-effectiveness, of routine SMBG in non–insulin-treated patients

ADA. V. Diabetes Care. *Diabetes Care* 2011;34(suppl 1):S17.

Recommendations: A1C

- Perform A1C test at least twice yearly in patients meeting treatment goals (and have stable glycemic control) (E)
- Perform A1C test quarterly in patients whose therapy has changed or who are not meeting glycemic goals (E)
- Use of point-of-care testing for A1C allows for timely decisions on therapy changes, when needed (E)

ADA. V. Diabetes Care. *Diabetes Care* 2011;34(suppl 1):S18.

Correlation of A1C with Estimated Average Glucose (eAG)

	Mean plasma glucose	
A1C (%)	mg/dl	mmol/l
6	126	7.0
7	154	8.6
8	183	10.2
9	212	11.8
10	240	13.4
11	269	14.9
12	298	16.5

These estimates are based on ADAG data of ~2,700 glucose measurements over 3 months per A1C measurement in 507 adults with type 1, type 2, and no diabetes. The correlation between A1C and average glucose was 0.92. A calculator for converting A1C results into estimated average glucose (eAG), in either mg/dl or mmol/l, is available at http://professional.diabetes.org/GlucoseCalculator.aspx.

ADA. V. Diabetes Care. *Diabetes Care* 2011;34(suppl 1):S18. Table 9.

Recommendations: Glycemic Goals in Adults (1)

- Lowering A1C to below or around 7%
  - Shown to reduce microvascular and neuropathic complications of diabetes
  - If implemented soon after diagnosis of diabetes, associated with long-term reduction in macrovascular disease
- Therefore, a reasonable A1C goal for many non-pregnant adults is <7% (B)

ADA. V. Diabetes Care. *Diabetes Care* 2011;34(suppl 1):S19.

Glycemic Recommendations for Non-Pregnant Adults with Diabetes (1)

A1C	<7.0%*
Preprandial capillary plasma glucose	70–130 mg/dl* (3.9–7.2 mol/l)
Peak postprandial capillary plasma glucose†	<180 mg/dl* (<10.0 mmol/l)

*Postprandial glucose measurements should be made 1–2 h after the beginning of the meal, generally peak levels in patients with diabetes.

ADA. V. Diabetes Care. *Diabetes Care* 2011;34(suppl 1):S21. Table 10.

Recommendations: Immunization

- Provide an influenza vaccine annually to all diabetic patients (C)
- Administer pneumococcal polysaccharide vaccine to all diabetic patients ≥2 years
- One-time revaccination recommended for those >64 years previously immunized at <65 years if administered >5 years ago
- Other indications for repeat vaccination: nephrotic syndrome, chronic renal disease, immunocompromised states (C)

ADA. V. Diabetes Care. *Diabetes Care* 2011;34(suppl 1):S27.