

Essentials of Diagnosis, Treatment and Prevention of Major Endocrine Diseases: Diabetes Mellitus – 2/2017

LECTURE IN INTERNAL MEDICINE FOR IV COURSE STUDENTS

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Clinical Investigation

Complications: 1

- The major long-term complications relate to damage to blood vessels with the risk of "macrovascular" diseases development (coronary artery disease, stroke, peripheral vascular disease)

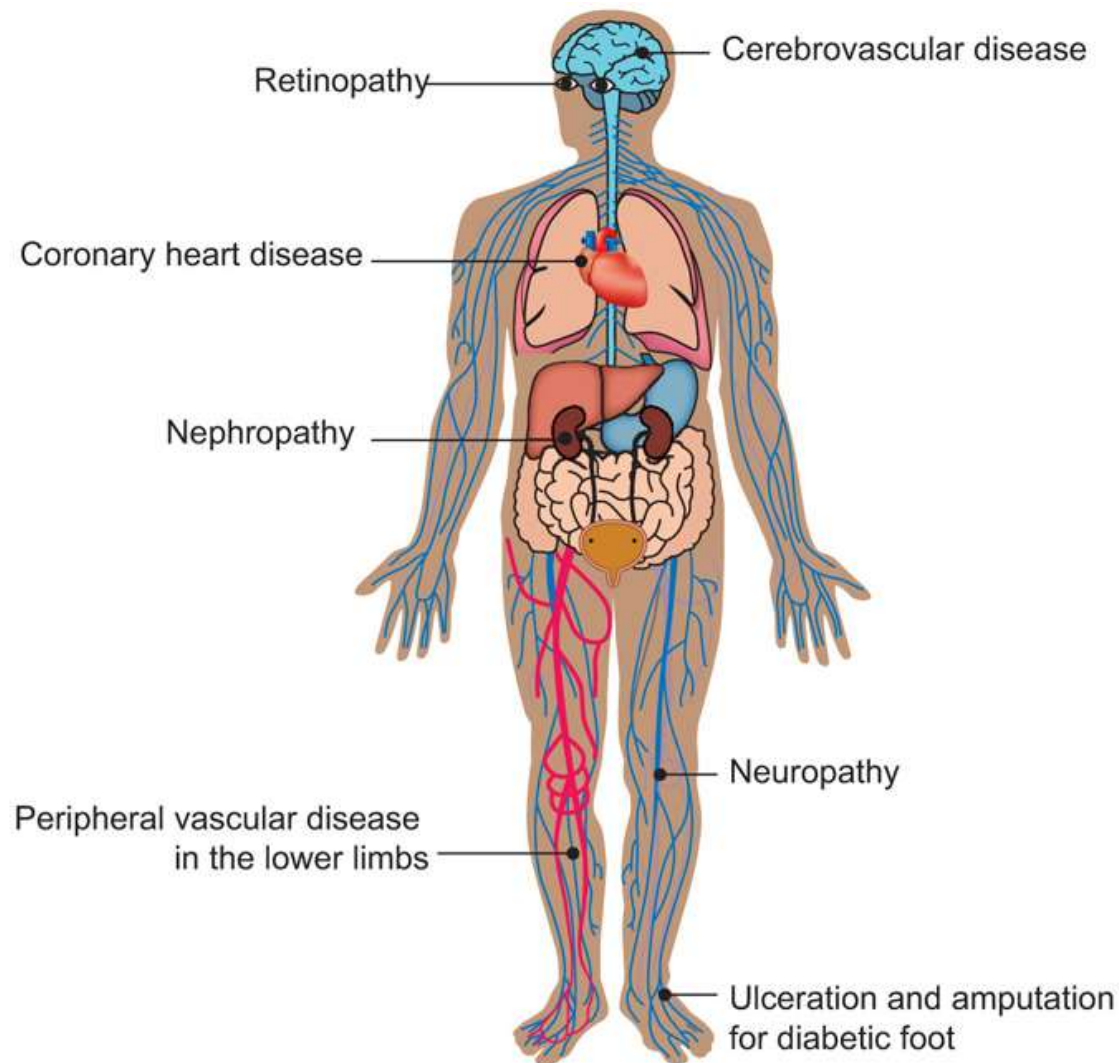
Clinical Investigation

Complications: 2

- The primary complications of diabetes due to damage in small blood vessels include damage to the eyes, kidneys, and nerves (diabetic retinopathy that result in gradual vision loss and blindness, diabetic nephropathy that leads to chronic kidney disease, diabetic neuropathy, diabetes-related foot problems (diabetic foot ulcers, occasionally requiring amputation), proximal diabetic neuropathy that causes painful muscle wasting and weakness, cognitive deficit

Clinical Investigation

Complications: 3



TEST - 1

R.R. is a 62 year-old man who was initially seen because of gangrene of the foot and shortness of breath. He had been told that he had a mild case of diabetes 4-5 years ago. He has seen physicians intermittently, and is unaware of what his glucose regulation has been. He denies polydipsia or polyuria. About 6 months ago, he injured his right foot, and it has failed to heal. One year ago, he was admitted to a coronary care unit for shortness of breath. A myocardial infarction was said to have been ruled out. He stopped smoking 15 years ago. Current medications were 5 mg glyburide twice a day.

TEST - 2

Physical examination showed weight of 170 pounds, height 5'9", and blood pressure 180/105 mmHg. He had bilateral engorged jugular veins and inspiratory moist rales. Dorsalis pedis and posterior tibial pulses were absent bilaterally. The right foot was erythematous, and several toes had areas of dry gangrene (2nd toe, lateral aspects of big toe, 5th toe), no tenderness and no pus. Sensation in the right foot was diminished. Laboratory data were plasma glucose 237 mg/dl, total serum cholesterol 266 mg/dl (desirable: <200 mg/dl), high-density lipoprotein (HDL) cholesterol 29 mg/dl (desirable: >35 mg/dl), triglycerides 285 mg/dl (desirable: <200 mg/dl), and HbA1c 8.9% (normal <6.2%).

TEST - 3

The patient was educated, taught self-monitoring of blood glucose, instructed in diet, given treatment for his congestive heart failure, which controlled his dyspnea, and had his glyburide increased to 10 mg in the morning and 5 mg at night. Two years ago, he had a femoral-popliteal bypass and removal of two toes. Repeat blood studies showed only a modest improvement in glycemic control (plasma glucose levels 180-210 mg/dl). Fasting triglycerides were 240 mg/dl, HDL cholesterol was 33 mg/dl, and total cholesterol was 286 mg/dl.

TEST - 4

Questions

1. What are the chronic complications of diabetes in this case?2. Why was a serious complication such as gangrene preceded by minimal symptoms of diabetes?
2. Identify the cardiovascular and microvascular risk factors in the history, physical examination, and laboratory data in this patient.
3. What are the management objectives from what you know about the clinical conditions of this patient?

Clinical Investigation

Complications: Peripheral Neuropathy 1

- Numbness or reduced ability to feel pain or temperature changes
- A tingling or burning sensation
- Sharp pains or cramps
- Increased sensitivity to touch — for some people, even the weight of a bed sheet can be agonizing

Clinical Investigation

Complications: Peripheral Neuropathy 2

- Muscle weakness
- Loss of reflexes, especially in the ankle
- Loss of balance and coordination
- Serious foot problems, such as ulcers, infections, deformities, and bone and joint pain

Clinical Investigation

Complications: Autonomic Neuropathy 1

- A lack of awareness that blood sugar levels are low (hypoglycemia unawareness)
- Bladder problems (urinary tract infections, urinary retention or incontinence)
- Constipation and/or uncontrolled diarrhea
- Slow stomach emptying (gastroparesis), leading to nausea, vomiting, bloating and loss of appetite
- Difficulty swallowing
- Erectile dysfunction in men

Clinical Investigation

Complications: Autonomic Neuropathy 1

- Vaginal dryness and other sexual difficulties in women
- Increased or decreased sweating
- Inability of your body to adjust blood pressure and heart rate, leading to sharp drops in blood pressure after sitting or standing that may cause you to faint or feel lightheaded
- Problems regulating body temperature
- Changes in the way eyes adjust from light to dark
- Increased heart rate at rest

Clinical Investigation

Complications: Radiculoplexus Neuropathy 1

- Radiculoplexus neuropathy (diabetic amyotrophy, femoral neuropathy, proximal neuropathy) affects nerves in the thighs, hips, buttocks or legs more common in older adults with type 2 DM
- Symptoms are usually on one side of the body, though in some cases symptoms may spread to the other side

Clinical Investigation

Complications: Radiculoplexus Neuropathy 2

- Most people improve at least partially over time, though symptoms may worsen before they get better
- This condition is often marked by:
- Sudden, severe pain in hip and thigh or buttock
- Eventual weak and atrophied thigh muscles
- Difficulty rising from a sitting position
- Abdominal swelling, if the abdomen is affected
- Weight loss

Clinical Investigation

Complications: Mononeuropathy 1

- Mononeuropathy (focal neuropathy) involves damage to a specific nerve and it's most common in older adults
- Mononeuropathy can cause severe pain, it usually doesn't cause any long-term problems

Clinical Investigation

Complications: Mononeuropathy 2

- Signs and symptoms depend on which nerve is involved and may include: difficulty focusing eyes, double vision or aching behind one eye; paralysis on one side of the face (Bell's palsy); pain in a shin or foot; pain in a lower back or pelvis; pain in the front of a thigh, pain in the chest or abdomen

Clinical Investigation

Complications: Mononeuropathy 3

- Sometimes mononeuropathy occurs when a nerve is compressed, e.g. carpal tunnel syndrome (numbness or tingling in fingers or hand, especially in thumb, index finger, middle finger and ring finger, etc.).

Clinical Investigation

Complications: Diabetic Foot Ulcers 1



- Diabetic foot ulcers occur in 15% of people with DM and precedes 84% of all diabetes-related lower-leg amputations

Clinical Investigation

Complications: Diabetic Foot Ulcers 2



- Risk factors are diabetic neuropathy, peripheral vascular disease, cigarette smoking, poor glycemic control, previous foot ulcerations or amputations, diabetic nephropathy, and ischemia of small and large blood vessels

Clinical Investigation

Complications: Diabetic Foot Ulcers 3



- Diabetic foot lesions are responsible for more hospitalizations than any other complication of diabetes

Diagnosis

World Health Organization (WHO) Criteria Methods and criteria for diagnosing diabetes

- Diabetes symptoms (e.g. polyuria, polydipsia and unexplained weight loss for Type 1) plus:
 - a random venous plasma glucose concentration ≥ 11.1 mmol/l or
 - a fasting plasma glucose concentration ≥ 7.0 mmol/l (whole blood ≥ 6.1 mmol/l) or
 - two hour plasma glucose concentration ≥ 11.1 mmol/l two hours after 75g anhydrous glucose in an oral glucose tolerance test (OGTT).
- With no symptoms diagnosis should not be based on a single glucose determination but requires confirmatory plasma venous determination.

Diagnosis

World Health Organization (WHO) Criteria

Gestational diabetes

The criteria for diagnosing gestational diabetes is different. Gestational diabetes should be diagnosed if the woman has either:

- a fasting plasma glucose level of 5.6mmol/l or above or
- a 2-hour plasma glucose level of 7.8mmol/l or above.

Diagnosis

World Health Organization (WHO) Criteria

Glycated Hemoglobin A1c (HbA1c) testing to diagnose diabetes

- An HbA1c of 48mmol/mol (6.5%) is recommended as the cut off point for diagnosing diabetes
- In patients without symptoms of diabetes the laboratory venous HbA1c should be repeated, and if the second sample is <48mmol/mol (6.5%) the person should be treated as at high risk of diabetes and the test should be repeated in 6 months or sooner if symptoms develop

Diagnosis

Glycated hemoglobin (Hb A1C) test

- Glycated hemoglobin (Hb A1C) test indicates average blood sugar level for the past two to three months
- Glycated hemoglobin (Hb A1C) test measures the percentage of blood sugar attached to hemoglobin, the oxygen-carrying protein in red blood cells
- The higher blood sugar levels, the more hemoglobin patient will have with sugar attached
- An Hb A1C level of 6.5 percent or higher on two separate tests indicates that patient have diabetes

Diagnosis

World Health Organization (WHO) Criteria

Condition	2 hour glucose	Fasting glucose	Hb A1C	
	mmol/l(mg/dl)	mmol/l(mg/dl)	mmol/mol	DCCT %
Normal	<7.8 (<140)	<6.1 (<110)	<42	<6.0
Impaired fasting glycaemia	<7.8 (<140)	≥6.1(≥110) & <7.0(<126)	42-46	6.0–6.4
Impaired glucose tolerance	≥7.8 (≥140)	<7.0 (<126)	42-46	6.0–6.4
Diabetes mellitus	≥11.1 (≥200)	≥7.0 (≥126)	≥48	≥6.5

Management

Organization of DM Care: 1

- All people with DM should be receiving continuing preventative care through education and medical interventions
- All people with DM need annual surveillance to detect early on the development of late tissue damage, and where this is detected access to protocols and resources for its management

Management

Organization of DM Care: 2

- All people with DM should have continuing access to DM team, for help in management and social difficulties arising from DM
- All people with DM have a role in the development and organization of the service of which they are a part

Management

Organization of DM Care: 3

- All DM management teams should have an active policy of quality improvement
- Appropriate special care should be offered to those with special needs, including pregnant women.

Management

Diet and Activity: 1

- All patients on insulin should have a comprehensive diet plan, created with the help of a professional dietitian, that includes the following:
 - A daily caloric intake prescription
 - Recommendations for amounts of dietary carbohydrate, fat, and protein

Management

Diet and Activity: 2

- Instructions on how to divide calories between meals and snacks
- Exercise is also an important aspect of diabetes management. Patients should be encouraged to exercise regularly

Management

Self-Monitoring in Glycemic Control: 1

- Benefits of tight glycemic control include not only continued reductions in the rates of DM complications but also in overall mortality
- Optimal DM control requires frequent self-monitoring of blood glucose levels, which allows rational adjustments in hypoglycemic medications

Management

Self-Monitoring in Glycemic Control: 2

- All patients should learn how to self-monitor and record their blood glucose levels with home analyzers and adjust their hypoglycemic medications doses accordingly
- Real-time continuous monitoring of glucose—using continuous glucose monitors (CGMs)—can help patients improve glycemic control

Management

Continuous Glucose Monitors (CGMs)



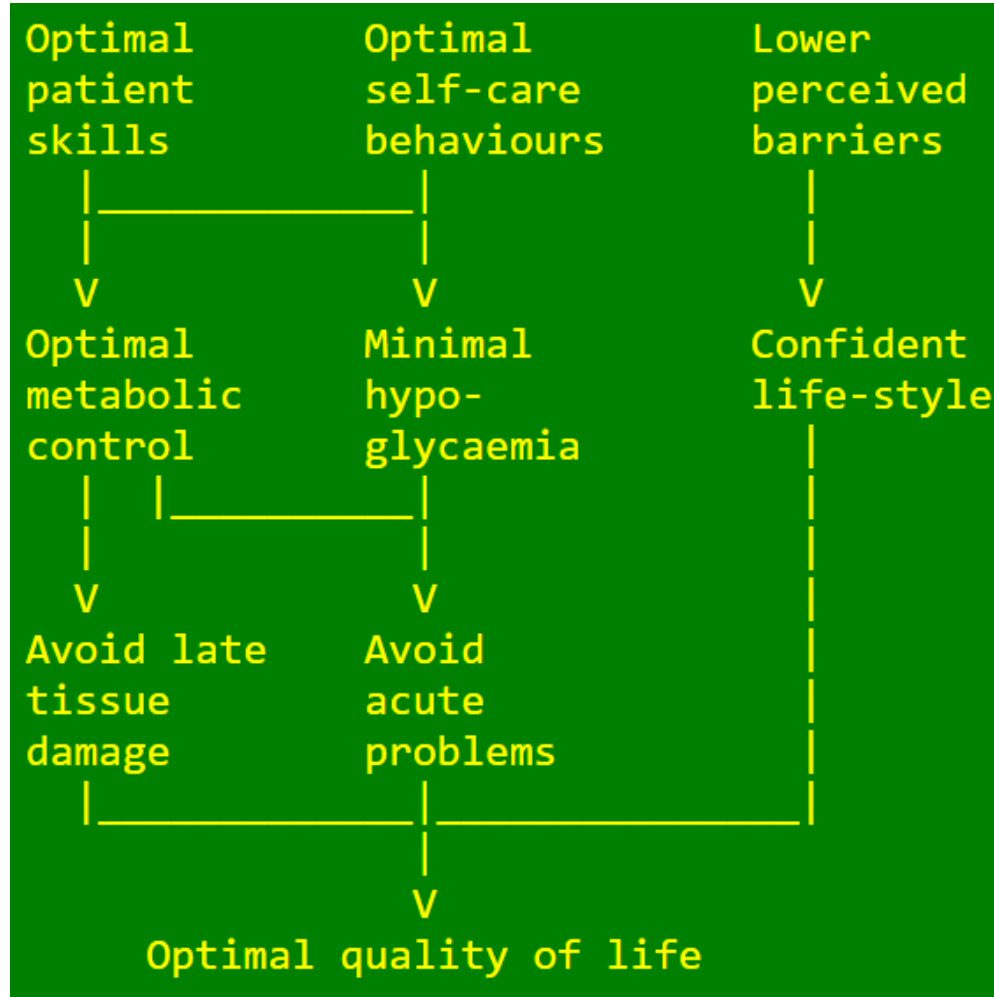
Continuous glucose monitors (CGMs) contain subcutaneous sensors that measure interstitial glucose levels every 1-5 minutes, providing alarms when glucose levels are too high or too low or are rapidly rising or falling

Management Glucose Meters



Management

Objectives of DM Management



Management

Insulin: Therapy 1

- Patients with type 1 DM require lifelong insulin therapy
- Most require 2 or more injections of insulin daily, with doses adjusted on the basis of self-monitoring of blood glucose levels
- Insulin replacement is accomplished by giving a basal insulin and a preprandial (premeal) insulin

Management

Insulin: Therapy 2

- The basal insulin is either long-acting (glargine or detemir) or intermediate-acting (NPH)
- The preprandial insulin is either rapid-acting (lispro, aspart, insulin inhaled, or glulisine) or short-acting (regular)

Management

Insulin: Types 1

The commonly used types of insulin in DM patients are:

- fast-acting which begin to work within 5 to 15 minutes and are active for 3 to 4 hours
- short-acting which begins working within 30 minutes and is active about 5 to 8 hours

Management

Insulin: Types 2

The commonly used types of insulin in DM patients are:

- intermediate-acting, includes NPH insulin which begins working in 1 to 3 hours and is active 16 to 24 hours; long acting, which begins working within 1 to 2 hours and continue to be active, without major peaks or dips, for about 24 hours, although this varies in many individuals

Management

Insulin: Types 3

The commonly used types of insulin in DM patients are:

- ultra-long acting, which begins working within 30–90 minutes, and continues to be active for greater than 24 hours
- combination insulin products, which include a combinations of either fast-acting or short-acting insulin with a longer acting insulin

Management

Insulin: Methods of Administration 1

- Insulin is usually taken as subcutaneous injections by single-use syringes with needles, an insulin pump, by repeated-use insulin pens with needles, or by use an injection port in conjunction with syringes
- Administration schedules often attempt to mimic the physiologic secretion of insulin by the pancreas

Management

Insulin: Methods of Administration 2

- Insulin pumps are a reasonable solution for some, and advantages are better control over background or 'basal' insulin dosage, bolus doses calculated to fractions of a unit, and calculators in the pump that may help with determining 'bolus' infusion dosages
- Insulin pumps may be like 'electrical injectors' attached to a temporarily implanted catheter or cannula.

Management

Insulin: Insulin Pump



Management

Insulin: Dosage and Timing 1

- One international unit of insulin (1 IU) is defined as the "biological equivalent" of 34.7 μg pure crystalline insulin
- The unit of measurement used in insulin therapy is not part of the International System of Units (abbreviated SI) which is the modern form of the metric system

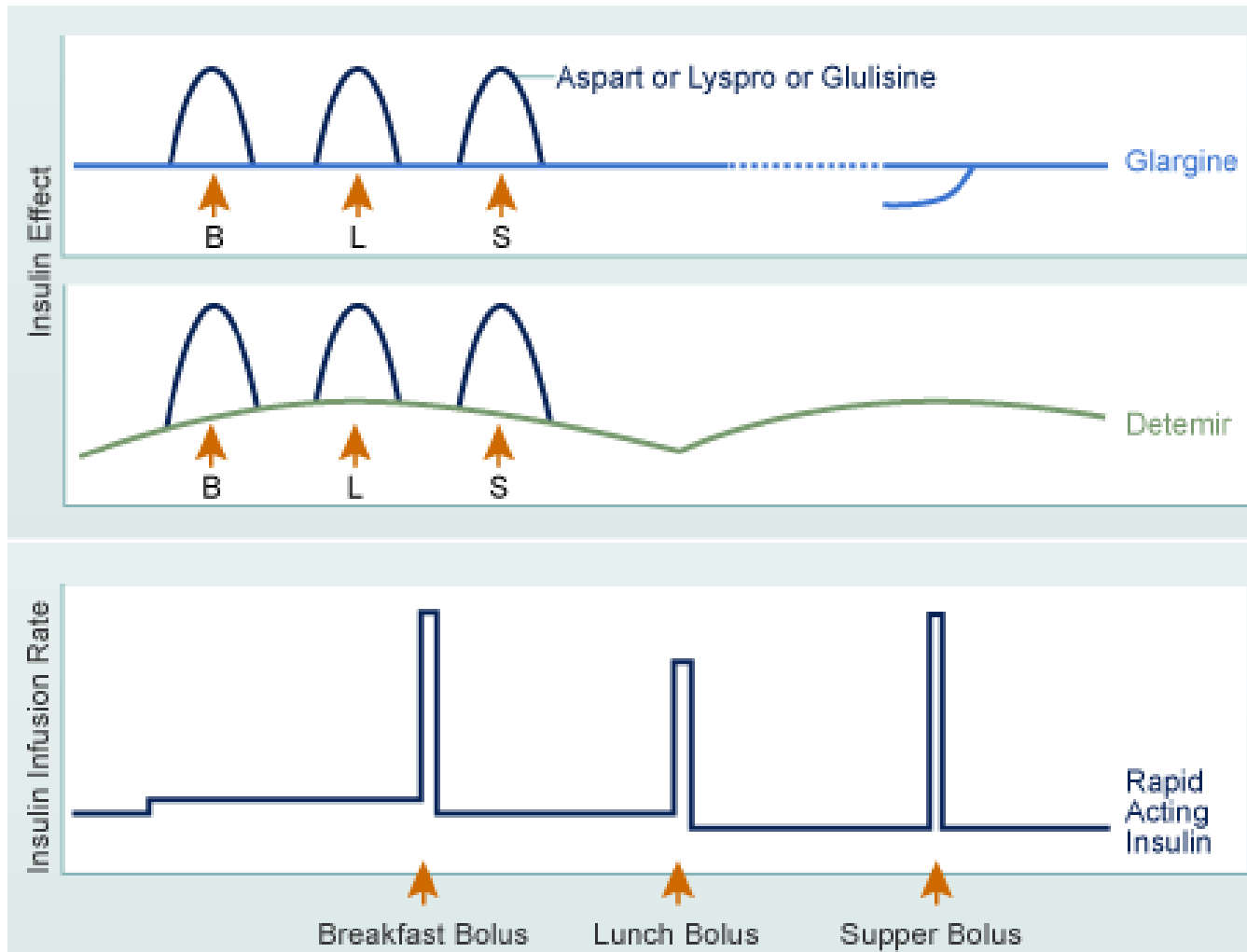
Management

Insulin: Dosage and Timing 2

- Instead the pharmacological international unit (IU) is defined by the WHO Expert Committee on Biological Standardization

Management

Insulin: Multiple Daily Injections



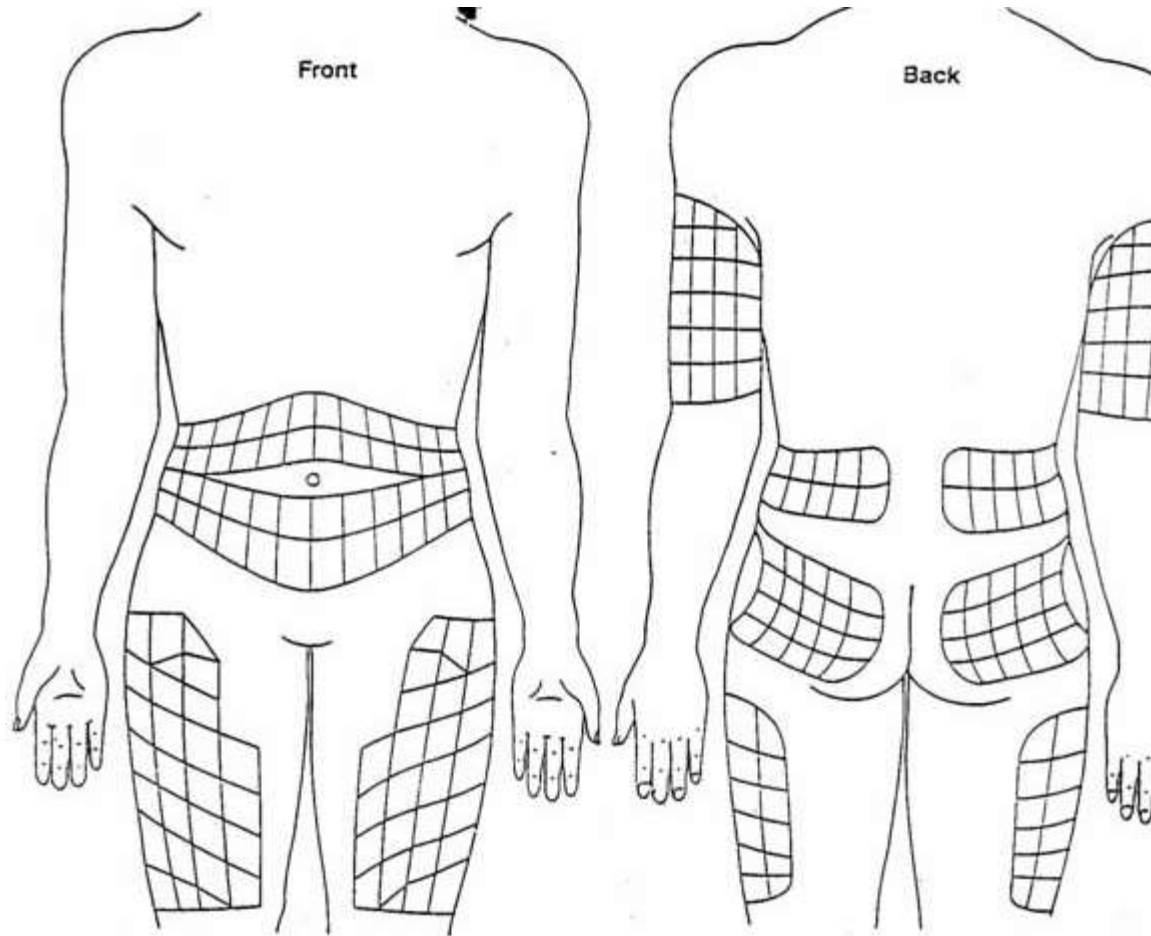
Management

(Insulin: Sample regimen using insulin NPH and regular insulin

		before breakfast	before lunch	before dinner	at bedtime
NPH dose		12 units		6 units	
regular insulin dose if fingerstick glucose is (mg/dl) [mmol/L]:					
70-100	[3.9-5.5]	4 units		4 units	
101-150	[5.6-8.3]	5 units		5 units	
151-200	[8.4-11.1]	6 units		6 units	
201-250	[11.2-13.9]	7 units		7 units	
251-300	[14.0-16.7]	8 units	1 unit	8 units	1 unit
>300	[>16.7]	9 units	2 units	9 units	2 units

Management

Insulin Administration



TEST - 1

A 19-year old marine was brought to the infirmary after passing out during basic training. He had repeatedly complained of severe weakness, dizziness, and sleepiness during the preceding 4 weeks of boot camp. In a previous episode 3 weeks earlier, he had drowsiness and generalized tiredness, and was brought to the infirmary, where after IV administration of saline, he was returned to duty with the diagnosis of dehydration. Upon questioning, he reported unquenchable thirst, and the repeated need to urinate. Although he ate all of his rations as well as whatever he could get from his fellow trainees, he had lost 19 pounds. (Baseline body weight was 150 pounds, height 5'8"). On the last day, he complained of vague abdominal pain, which was worse on the morning of admission. He had vomited once. During examination, he was oriented but tachypneic. He appeared pale, dehydrated with dry mucous membranes, and poor skin turgor.

TEST - 2

His respiratory rate was 36/minute with deep, laborious breathing; his heart rate was 138/minute regular, and his blood pressure was 90/60. His chest was clear, heart tones were normal. There was an ill-defined generalized abdominal tenderness, which was otherwise soft to palpation and showed no rebound. There was a generalized muscular hypotonia; his deep tendon reflexes were present but very weak. Laboratory, on admission, showed glucose of 560 mg/dl, sodium 154, potassium 6.5, pH 7.25, bicarbonate 10 mM/liter, chloride 90, BUN (blood urea nitrogen) 38 mg/dl, creatinine 2.5 mg/dl. (Normal values: glucose, 70-114 mg/dl; Na = 136-146; K, 3.5-5.3; Cl, 98-108; CO², 20-32 [all in mM/l]; BUN, 7-22mg/dl; creatinine, 0.7-1.5 mg/dl). A urine sample was 4+ for glucose and had "large" acetone. HbA1c was 14% (n=4-6.2%). Serum acetone was 4+ undiluted, and still positive at the 4th dilution. Beta-Hydroxybutyrate level was 20 millimols/liter (normal=0.0-0.3 mM/l).

TEST - 3

He was treated with insulin and saline I.V. By the 4th hour of treatment, potassium chloride was added to the IV at a rate of 15 mEq/hour. Sixteen hours later, he was active, alert, well hydrated and cheerful, indicating he felt extremely well. He requested that his IV be discontinued. His physician decided to switch his insulin to subcutaneous injections and to start a liquid diet. He was later put on a diabetes maintenance diet and treated with one injection of Human Lente insulin in the morning. Although his blood sugars the next morning were 100-140 mg/dl, he had frequent episodes of hypoglycemia during the day, and his HbA1c was 9%. Eventually, he was put on 3 injections of regular insulin/day, and a bedtime intermediate duration (Lente) insulin.

TEST - 4

Questions

- Why did the patient improve after being given IV saline in his first admission?
- Why was dyspnea his presenting symptom?
- He was hyperkalemic on admission, and yet, why was potassium later added to the IV infusion?
- What is the possible reason why a single injection of insulin in the morning failed to control his diabetes without causing hypoglycemia?

Management

Treatment of Type 2 DM: 1

- Individualized glycemic targets and glucose-lowering therapies
- Diet, exercise, and education as the foundation of the treatment program
- Use of metformin as the optimal first-line drug unless contraindicated
- After metformin, the use of 1 or 2 additional oral or injectable agents, with a goal of minimizing adverse effects if possible

Management

Treatment of Type 2 DM: 2

- Ultimately, insulin therapy alone or with other agents if needed to maintain blood glucose control
- Where possible, all treatment decisions should involve the patient, with a focus on patient preferences, needs, and values
- A major focus on comprehensive cardiovascular risk reduction

Management

Oral Antihyperglycemic Drugs: Biguanides

- Biguanides decrease hepatic glucose production, decrease gastrointestinal glucose absorption, and increase target cell insulin sensitivity
- Example: Metformin
- Contraindications: Metabolic acidosis with or without coma, abnormal creatinine clearance from any cause including diabetic ketoacidosis, shock, acute myocardial infarction, septicemia, renal disease (serum creatinine level ≥ 1.5 mg/dL in males or ≥ 1.4 mg/dL in females), lactation, radiologic contrast study within 48 hours

Management

Oral Antihyperglycemic Drugs: Sulfonylureas

- Sulfonylureas increase beta-cell insulin secretion, decrease hepatic glucose output, and increase insulin receptor sensitivity at peripheral target tissues
- Examples: Glyburide, glipizide, glimepiride, tolazamide, tolbutamide
- Contraindications: Sulfa allergy, type 1 DM, diabetic ketoacidosis, concomitant use with bosentan

TEST - 1

P.A. is a 52-year old man who presented with a 2-week history of polyuria, polydipsia, polyphagia, weight loss, fatigue, and blurred vision. A random glucose test performed 1 day before presentation was 352 mg/dl. The patient denied any symptoms of numbness, tingling in hands or feet, dysuria, chest pain, cough or fevers. He had no prior history of diabetes and no family history of diabetes.

Admission non-fasting serum glucose 248 mg/dl (N=<180 mg/dl), HbA1c 9.6% (N=4-6.1%). Electrolytes, BUN and creatinine were normal. Physical examination revealed weight of 180 pounds, height 5'5.5" (IBW 140-145). The rest of the examination was unremarkable, i.e., no signs of retinopathy or neuropathy.

TEST - 2

The patient was taught self-monitoring of blood glucose and begun on 5 mg glyburide once a day. He was instructed in diet (1800 cal ADA). Blood glucose levels ranged from 80 to 120 mg/dl within 2 weeks of starting glyburide, his symptoms disappeared and weight remained constant.

During the next two months, blood glucose levels decreased to 80 mg/dl, and glyburide was stopped. Patient did not return until one year later; fasting serum glucose was 190 mg/dl, and HbA1c 8%. He again had polyuria and nocturia. Weight was unchanged from time of presentation. The physician put him on 5 mg/day of glyburide. His blood sugar one month later remained at 180 mg/day. At this point, his physician decided to put him on insulin alone, 20 units/day at bedtime. Two weeks later, his fasting plasma glucose was 120 mg/dl.

TEST - 3

Questions

1. What are the mechanisms of blurred vision which was part of his initial symptoms?
2. Are there correlations between his abnormal blood chemistries and his other symptoms?
3. Why did an 1,800 calorie a day diet fail to lower his body weight?
4. Was insulin treatment at this time the only possible option?

TEST

A 52-year-old man with recently diagnosed type 2 diabetes mellitus comes to the physician for a follow-up examination. Physical examination shows no abnormalities. Laboratory studies show an increased hemoglobin A1c despite patient compliance with diet and exercise recommendations. Treatment with a sulfonylurea is started. Which of the following is most likely to occur in this patient?

(A) Decreased entry of glucose into the muscle cells (B) Decreased production of glucose from the liver (C) Decreased secretion of insulin from the pancreas (D) Decreased speed of carbohydrate absorption from *the* intestines (E) Increased entry of glucose into the muscle cells (F) Increased production of glucose from the liver (G) Increased secretion of insulin from the pancreas (H) Increased speed of carbohydrate absorption from the intestines

Management

Oral Antihyperglycemic Drugs: Thiazolidinediones

- Thiazolidinediones increase insulin receptor sensitivity and influence the production of gene products involved in lipid and glucose metabolism; their mechanism of action depends on the presence of insulin for activity
- Examples: Pioglitazone, rosiglitazone
- Contraindications: Hypersensitivity to product or components, established NYHA class III/IV heart failure

Management

Oral Antihyperglycemic Drugs: Alpha-Glucosidase Inhibitors

- Inhibit the upper gastrointestinal enzymes that convert dietary starch and other complex carbohydrates into simple sugars, which can be absorbed
- Examples: Acarbose (Precose) & Miglitol (Glycet)
- Contraindications: Diabetic ketoacidosis; cirrhosis; inflammatory bowel disease, colonic ulceration, partial intestinal obstruction,

Management

Peptide analogs

- Injectable Incretin mimetics as insulin secretagogues: glucagon-like peptide-1 (GLP-1) analog and gastric inhibitory peptide (glucose-dependent insulintropic peptide, GIP) analog
- Injectable Amylin analogues that slow gastric emptying and suppress glucagon have all the incretins actions except stimulation of insulin secretion
- Glycosurics (SGLT-2 inhibitors) block the re-uptake of glucose in the renal tubules, promoting loss of glucose in the urine

Management

Treatment of Gestational DM: 1

- Diet: avoid single large meals and foods with a large percentage of simple carbohydrates
- Insulin: the goal of insulin therapy during pregnancy is to achieve glucose profiles similar to those of nondiabetic pregnant women
- Glyburide and metformin: trials have shown these 2 drugs to be effective, and no evidence of harm to the fetus has been found

Management

Treatment of Gestational DM: 2

- Management of the neonate: the employment of frequent blood glucose checks and early oral feeding (ideally from the breast) when possible, with infusion of intravenous glucose if oral measures prove insufficient.

Management Surgery

- A pancreas transplant is occasionally considered for people with type 1 DM who have severe complications of their disease, including end stage kidney disease requiring kidney transplantation
- Weight loss surgery in those with obesity and type 2 DM is often an effective measure
- Many are able to maintain normal blood sugar levels with little or no medications following surgery and long-term mortality is decreased

Prognosis

- The general statistical prognosis is that 15% of sufferers of type 1 DM will die before the age of 40, sensible blood sugar control and a healthy diet can lead to a long life for sufferers
- Contracting type 2 DM in 40's means five to 10 years off average life expectancy; however, as with the above, this is a vast improvement on recent years
- As Heart Disease is the leading cause of death in Type 2 DM sufferers, keeping to a regime that minimises the risk is very much recommended

Prophylaxis 1

- There is no known preventive measure for type 1 DM
- Type 2 DM can often be prevented or delayed by maintaining a normal body weight, engaging in physical exercise, and consuming a healthful diet
- Higher levels of physical activity reduce the risk of diabetes by 28%

Prophylaxis 2

- Dietary changes known to be effective in helping to prevent diabetes include maintaining a diet rich in whole grains and fiber, and choosing good fats, such as the polyunsaturated fats found in nuts, vegetable oils, and fish
- The relationship between type 2 DM and the main modifiable risk factors (excess weight, unhealthy diet, physical inactivity and tobacco use) is similar in all regions of the world

Abbreviations

BUN - blood urea nitrogen test

CGMs - continuous glucose monitors

DKA - diabetic ketoacidosis

DM - diabetes mellitus

GDM - Gestational diabetes mellitus

GIP - glucose-dependent
insulinotropic polypeptide

GLP-1 - the postprandial glucagonlike
peptide-1

HbA1c - Glycated Hemoglobin A1c

HLA - human leukocyte antigen

HONK - hyperosmolar nonketotic
state

IGT - impaired glucose tolerance

IFG - impaired fasting glucose

IU - international unit of insulin

NYHA - New York Heart Association

OGTT - oral glucose tolerance test

SGLT-2 - Sodium-glucose co-
transporter 2

SNPs - single-nucleotide
polymorphisms

WHO - World Health Organization

Diagnostic and treatment guidelines

- [IDF Clinical Practice Guidelines](#)
- [Type 2 diabetes in adults: management](#)
- [Diabetes in pregnancy: management from preconception to the postnatal period](#)
- [Guidelines on diabetes, pre-diabetes, and cardiovascular diseases](#)
- [Managing older people with type 2 diabetes: global guidelines\(external link\)](#)