Diabetes complications

Objectives:

- **not given**

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Resources: 435 team + Davidson + kumar + Recall questions step up to medicine.

- Editing file
- Feedback

Introduction

A leading cause of morbidity & mortality, they are divided into acute and chronic:

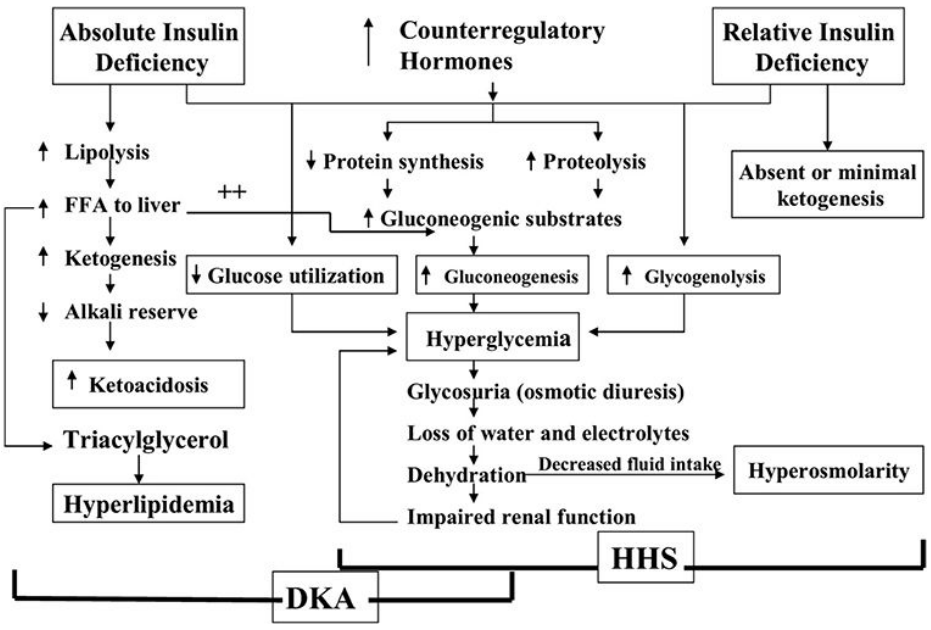
ACUTE	CHRONIC
Diabetic ketoacidosis (type1)	Microvascular complications
Hyperosmolar hyperglycemic syndrome (type 2)	Macrovascular complications + non-vascular effect

★ Epidemiology:

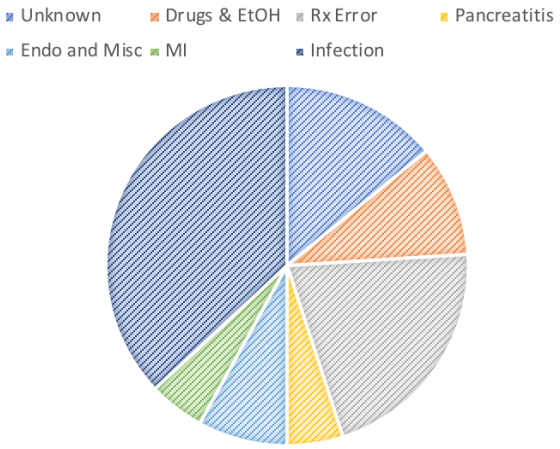
- Diabetes is the leading cause for:
  I. Blindness
  II. Renal failure
  III. Non traumatic lower extremity amputation
- The presence of DM complication tremendously increases medical care cost 10X Vs pt without complications
- Usually present after long period of hyperglycaemia
- Can be delayed/prevented with early DM detection and control
- Diabetic ketoacidosis (DKA) and the hyperosmolar hyperglycemic state (HHS) are the **two most** serious acute metabolic complications of diabetes.
- DKA is responsible for more than 500,000 hospital days per year at an estimated annual due to medical expense and indirect cost of 2.4 billion USD.
- 35 % increase in the number of cases between 1996 to 2006.
- **DKA is the most common cause of death in children and adolescents with type 1 diabetes** and accounts for 50% of all deaths in diabetic patients younger than 24 years of age.

Pathogenesis of DKA and HHS

When there is no insulin (type 1) and the body needs energy, the body will use fat (lipolysis) > lead to prodution of ketones > DKA



Precipitating causes of DKA in 106 cases:



Omission of Insulin as a Cause of DKA[1]

- **Most commonly**, patients omit insulin when they have a **gastroenteritis** or other causes of vomiting. **(INFECTION)**.
    - [No food = No insulin] > WRONG
- Insulin Pump failure. more and more these days.[2]
- Acting out.
- Young women with eating disorders often reduce their insulin dose to help them keep their weight down.
    - Intercurrent illness can precipitate DKA when insulin therapy is marginal.

Clinical Presentation (of Acute DM complications)

Hyperglycemic Hyperosmolar State[3]	Diabetic Ketoacidosis
History: more serious ○ More insidious development than DKA (weeks vs hours\days). ○ Greater osmolality and mental status changes than DKA. ○ **Dehydration** presenting with a shock-like state.	**History:** ○ Thirst ○ Polyuria ○ Abdominal pain ○ **Nausea and or vomiting** ○ Profound weakness

[1] مثل المريض ينسى يأخذ الأنسولين

[2] b/c most of DM1 pt use insulin pump wich releases short acting insulin. when the pump fails for any reason they will have DKA .

[3] They have enough insulin to not produce ketones but not enough to supply the organs with glucose.

Patient Profile: I. older. II. With comorbidities. III. History of type 2 diabetes, Which may have been unrecognized. Usually in HHS glucose level in the blood >600 (hyperosmolar) so they present with severe dehydration. If we compare DKA and HHS in terms of osmolarity, HHS is much more hyperosmolar.	**Physical Exam:** ○ Kussmaul respirations ○ Fruity breath ○ Relative hypothermia . ○ Tachycardia ○ Supine hypotension, orthostatic drop of blood pressure ○ Dry mucous membranes ○ Poor skin turgor in DKA glucose level >250 + high anion gap + increase blood and urine ketones + low K that's why we give a patient with DKA potassium before insulin

	DKA			HHS
	Mild (plasma glucose >250 mg/dl)	Moderate (plasma glucose >250 mg/dl)	Severe (plasma glucose >250 mg/dl)	Plasma glucose >600 mg/dl
Arterial pH	7.25–7.30	7.00 to <7.24	<7.00	>7.30
Serum bicarbonate (mEq/l)	15–18	10 to <15	<10	>18
Urine ketone*	Positive	Positive	Positive	Small
Serum ketone*	Positive	Positive	Positive	Small
Effective serum osmolality†	Variable	Variable	Variable	>320 mOsm/kg
Anion gap‡	>10	>12	>12	Variable
Mental status	Alert	Alert/drowsy	Stupor/coma	Stupor/coma

*Nitroprusside reaction method. †Effective serum osmolality: 2[measured Na^+ (mEq/l)] + glucose (mg/dl)/18. ‡Anion gap: $(Na^+) - [(Cl^- + HCO_3^-$ (mEq/l)].

★ Diagnostic Criteria for DKA and HHS

Diabetic Ketoacidosis (DKA)

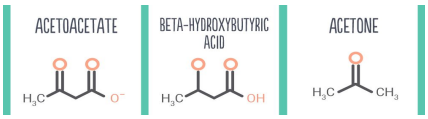
Lab findings:
- Variable hyperglycemia
- Increased blood and urine ketones
- Low bicarbonate
- High anion gap
- Low arterial pH (metabolic acidosis) the most IMP.
- Low PCO2 (respiratory compensation)

Potassium Balance in DKA:
- Potassium is dominantly intracellular.
- Urinary losses occur during evolution of DKA (due to glycosuria).
- Total body **potassium stores are greatly reduced in any patient with DKA**.
- Potassium moves from inside the cell to the extracellular space (plasma):
  - ➢ During insulin deficiency.
  - ➢ In presence of high blood glucose
  - ➢ As cells buffer hydrogen ions Acidosis.

Blood levels of potassium prior to treatment are usually high but may drop precipitously during therapy.

Ketone bodies in DKA:
- unless β-Hydroxybutyric (β-OH) is specifically ordered, the ketone bodies are estimated by the nitroprusside reaction in the lab, which measures only acetones and acetoacetate (AcAc). Nowadays, B ketones can be estimated.
- Acetone is not an acid.

Unlike the HHS :
there are no/very minimal amounts of ketone bodies, since the pt already has enough insulin to shut down the ketone body formation.



★ Treatment Of DKA:

- **Successful treatment of DKA requires:**
  - Correction of dehydration, hyperglycemia, and electrolyte imbalance
  - Identification of comorbid precipitating events
  - Frequent patient monitoring

Managing DKA

Click here for DKA and HHS management in details (they were in the Doctor's slides)

To make it simple (enough for you):

Treatment is mainly FLUIDS for the dehydration.

Amount of Fluid:

1-2 liters as a bolus then give them as a continuous rate.

Type of Fluid: Normal Saline.

Potassium:

- If the K is high (>4.2) we go with the treatment (insulin) but we check the serum K within 1-2 hours.
- If the K is low (< 3.3) we give K before giving insulin[4].
- If the K level is in between, we give both potassium and insulin at the same time.

Insulin:

we give insulin 0.1U/kg bolus then 0.1U/Kg effusion

When the blood sugar reaches 200, we **have to add D5**. we don't want to rapidly lower the blood sugar to less than that. we hold it there at 200 and slowly bring it down to an acceptable range.

When to Transition From IV Insulin Infusion to SC Insulin[5]:

- **BG[6] < 200 mg/dL and 2 of the following:**
  - HCO3 ≥ 18 mEq/L.
  - Venous pH > 7.3
  - Anion gap ≤ 12 mEq/L.
  - Good oral intake.

★ Summary:

DKA and HHS are life-threatening emergencies!

- **Management involves:** YOU DON'T HAVE TO GO DEEPER INTO DETAIL
  - ✓ Attention to precipitating cause
  - ✓ Fluid and electrolyte management (Potassium).
  - ✓ Insulin therapy.
  - ✓ Patient monitoring
  - ✓ Prevention of metabolic complications during recovery
  - ✓ Transition to long-term therapy
- **Patient education and discharge planning should aim at prevention of recurrence.**

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[4] (عشان ما ينزل البوتاسيوم أكثر)

[5] They have to be out of DKA for us to switch to subcutaneous insulin. the BG must be <200 AND pt is not acidotic with no anion gap (high anion gap means the pt will not eat, if he's not eating we shouldn't give SC.

[6] Blood Glucose

DM Complication Pathology (chronic)

★ Vascular complication

- **Microvascular (DM specific):**
  - Retinopathy
  - Nephropathy
  - Neuropathy

- Early blood sugar control can lead to a ↓ in microvascular complications.

- **Macrovascular** (Similar to those in non-DM but occur at greater frequency in DM individuals) . other risk factors may play a bigger role.
  - Coronary heart disease
  - Peripheral vascular disease
  - Cerebrovascular disease

★ Non-vascular complication[7].

- **Gastroparesis**
- **Infections**
- **Skin Changes**
- **Hearing loss**
- **Others:**
  - Relationship to hyperglycaemia is not certain.
  - Might be associated with DM rather than complicating DM
  - e.g Depression, OSA, Fatty liver, Hip fracture, Osteoporosis, cognitive impairment, low testosterone in men.

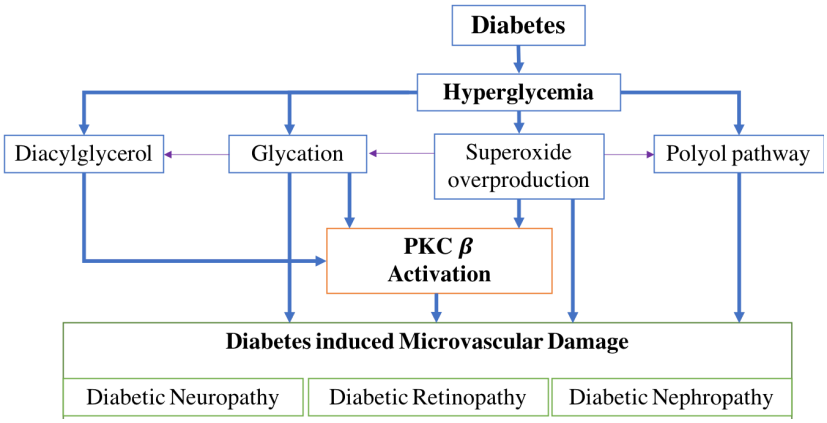
Pathology of hyperglycemic vascular complications:

- **Increased protein glycation:**
  - Free radical generation
  - Endothelial damage
- **Increased postprandial hyperlipidemia.**
- **Activation of protein kinase Cβ (PKCβ).**
- **Activation of D-Dimers and prothrombin fragments oxidative stress, glucose autoxidation:**
  - LDL oxidation
  - Impaired NO-dependent vasodilation
  - Coagulation activation
  - Increased leukocyte adhesion
  - Increased endothelial permeability

[7] Diabetes affect every single cell in the body.

اللي ابيكم تعرفونه انه فيه اكثر من pathway :

1- Protein glycation
2- ↑ free radical generation formation.
3- Activation of protein kinase C
4- ↑ d-dimers



.endothelium inflammation of the blood vessels + hypercoagulable state كلها تؤدي إلى
which cause DM complication in addition to another DM risk factors: HTN, dyslipidemia , smoking….
- We still don't know the exact mechanism of each pathway yet.

1. Retinopathy:

- **Non-proliferative**: usually appears late in the first decade of the disease or early second decade[8]. Characterized by retinal vascular microaneurysms, blot hemorrhage, and cotton wool spots.
- **Proliferative:** hypoxemia → neovascularization leading to **vitreous hemorrhage**, fibrosis, and retinal detachment.
- Macular edema[9]: can occur in non proliferative or proliferative stage.

Treatment:

- Prevention (most effective treatment)
- Glycemic and BP control will slow the progression
- Laser Photocoagulation → he benefits off of it: it prevents neovascularization > prevents retinal bleeding.
- Ocular injection (Anti-VEGF[10] therapy for macular edema)
- Screening: Yearly dilated eye exam[11].

2. Nephropathy:

- Microalbuminuria. (Proteinuria up to 300)
- Macroalbuminuria.
- Other important risk factors e.g. HTN and race.

Treatment:

- Prevention is the most effective therapy.
- Aim is to slow / reverse process.
- DM control.
- BP control.
- Administration of ACEI or ARBs.

Screening: Albumin creatinine ratio in spot urine. yearly.

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[8] If DM is uncontrolled
[9] Occurs if you're in the proliferative or nonproliferative.
[10] Vascular Endothelial Growth Factor.
[11] In DM1: after 5 year of diagnosis of DM then yearly. DM2: at the time of diagnosis then yearly

3. Neuropathy: Neuropathy is the most common chronic complication in DM.

- **Polyneuropathy.** (Stocking-glove neuropathy, develop from distal to proximal and usually bilateral)
  - Most common form is distal symmetric polyneuropathy.
  - Remember, up to 50% have no symptoms.
  - Signs, sensory loss, loss of ankle deep reflex[12].
  - Axonal degeneration, irreversible damage that is related to DM.
- **Mononeuropathy**
  - Dysfunction of cranial or peripheral nerve.
  - less common than the polyneuropathy
  - e.g. 3rd cranial nerve. (Imp to know this, eyes look down and out)
- **Autonomic neuropathy may be involved**
- **Cardiovascular system (resting achy, orthostatic hypotension, sudden death)**
- **G.I. (gastroparesis, alternating constipation and diarrhea)**
- **G.U. (bladder emptying abnormalities)**

Treatment:

- Prevention is the best treatment
- Tight glycemic control. (gradual treatment)
- Treat other risk factors (dyslipidemia, HTN, smoking)
- B12 / folate supplementation if deficient
- For symptoms (pregabalin, amitriptyline)
- Precaution (foot ware, for inspection…)

Screening:

- Monofilament examination.
- Ask patient about symptoms.

4. Cardiovascular effects in DM: Important risk factor for ischemic heart disease.

- Direct causation is not established.
- Occurs in higher frequency in uncontrolled DM.
- Other risk factors are important in the pathogenesis.

Treatment:

- Aggressive cardiovascular risk modification. (control BP, Dyslipidemia. Stop smoking and change sedentary lifestyle)
- Early glycemic control

Screening:

- Based on symptoms and signs
- Not recommended in asymptomatic individuals.

5. Lower extremity complication:

- **Interaction of several pathogenic factors:**
  - Neuropathy (interfere with normal protective mechanism[13])
  - Abnormal foot biomechanics (Hammer toe, charcot foot) leading to abnormal weight bearing.
  - Autonomic neuropathy (anhidrosis promoting dry skin and fissure formation)
  - PAD and poor wound healing (impaired resolution of minor breaks in skin)

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[12] ممكن المريض يشتكي من حرارة في أسفل قدمه

[13] يعني انت اذا مشيت حافي ممكن تدعس على شيء حاد وتسب رجلك على طول, هم لا ممكن يدعس عليها ويمشي

- **Risk factors for foot ulcer or amputation:** the most imp risk factors is previous ulcers and amputation.
  - Male sex
  - Duration of DM > 10 years
  - Peripheral neuropathy
  - Abnormal structure of the foot
  - PAD
  - Smoking
  - Hx of previous ulcer or amputation
  - Visual impairment
  - Poor glycemic control

Treatment:

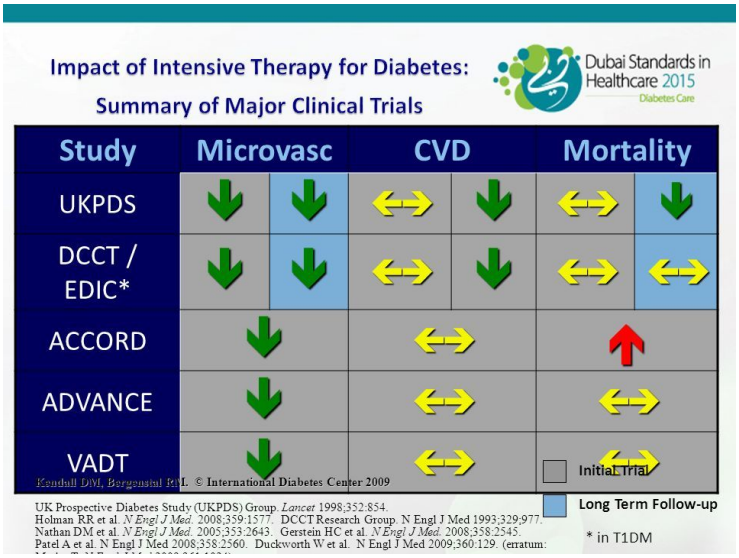
- Prevention.
- Identification of high risk individuals.
- Education.
- Institution of measures to prevent ulceration.
- Attention to other risk factors for vascular disease.
- For developed ulcer, multidisciplinary team.

Extra:

The DCCT & Kumamoto Study

Demonstrated the power of control.

- 70-76% less retinopathy
- 50% less nephropathy
- 60% less Neuropathy



Summary

A. ACUTE complications:

1. **Diabetic ketoacidosis** (type1)
2. **Hyperosmolar hyperglycemic syndrome** (type2)

   management:
   - Attention to precipitating cause.
   - Fluid and electrolyte management.
   - Insulin therapy.
   - If the pt has low k level give him k first then insulin.
   - Patient monitoring.
   - Prevention of metabolic complications during recovery.
   - Transition to long-term therapy.
3. **Hypoglycemia.** a common side effect of insulin use.

B. CHRONIC complications:

Vascular complications:

- Microvascular
  1. Retinopathy:
     *Non-proliferative, proliferative, macular edema.
     treatment: Prevention, Glycemic and BP control will slow the progression, Laser Photocoagulation, Ocular injection.
     Screening: every year.
  2. Nephropathy: Important risk factor is HTN.
     *Microalbuminuria, Macroalbuminuria.
     treatment: Prevention, ACEI/ARB.
     Screening: Albumin creatinine ratio in spot urine.
  3. Neuropathy: the most common complication in DM.
     *Polyneuropathy (Most common form), mononeuropathy, Autonomic.
     treatment: Prevention, Treat other risk factors (dyslipidemia, HTN, smoking), B12 / folate supplementation if deficient,
     For symptoms (pregabalin, amitriptyline),
     Precaution (foot wear, for inspection…).
     Screening: Monofilament examination. Ask patient about symptoms.
- Macrovascular:
  4. Cardiovascular:
     Treatment: Aggressive cardiovascular risk modification-Early glycemic control
     Screening: Based on symptoms and signs
  5. Lower extremity:
     Risk factors for foot ulcer or amputation: the most imp risk factors is a previous ulcer/s and amputation.

Non-vascular complications:

Gastroparesis, Infections, Skin Changes, Hearing loss.

Questions

1. What is the most common microvascular complication of DM ?

A. Retinopathy

B. Neuropathy

C. Nephropathy

2. The most common cause of DKA is?

A. Omit insulin when they have infection

B. Eating disorder

C. insulin pump failure

3. Patient known to have DM2 came to your clinic with very high blood Glucose level >600, you need to correct and drop his glucose very fast.

A. true

B. false

4. Patient known to have DM1 came to you with high blood glucose, DKA and the lab result shows low potassium level.

A. give him K before insulin

B. give him insulin before K

C. Patient observation

5. Most common side effect of insulin use is:

A. Headache

B. Sweating

c. Hypoglycemia

Answers:

1.B/ 2.A / 3.B/ 4.A/ 5.C