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DIABETES MELLITUS

Part 2:
COMPLICATIONS

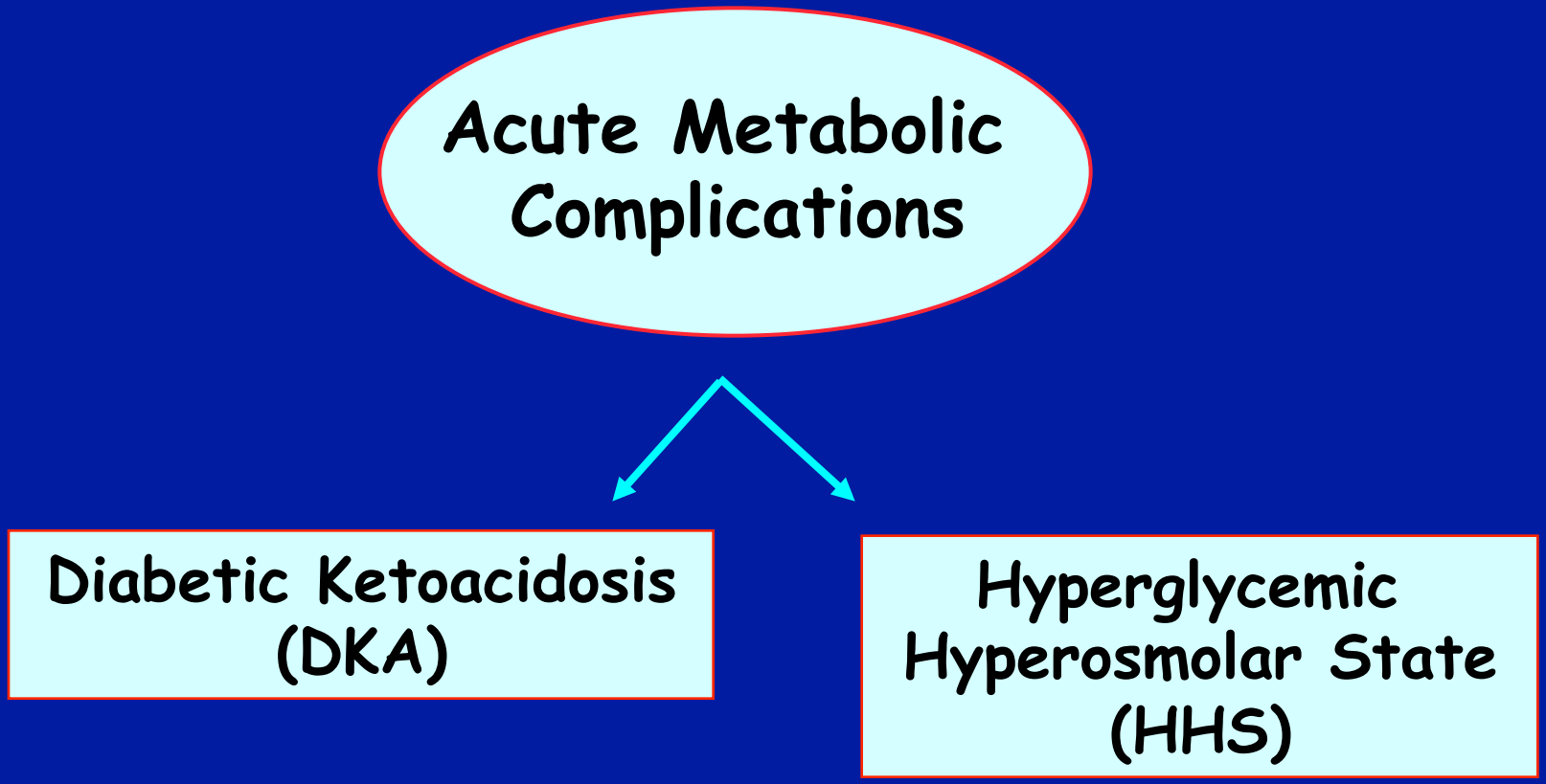
M2 - Endocrine Sequence

A. Kumagai

Winter 2009

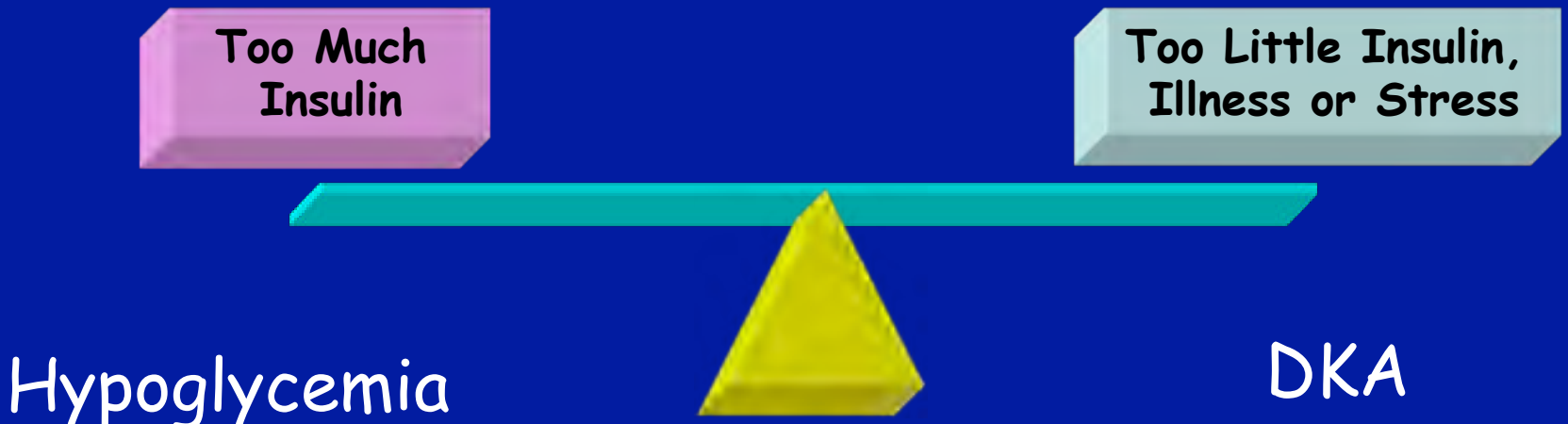
University of Michigan
Medical School

DIABETES MELLITUS



DIABETIC KETOACIDOSIS (DKA)

Definition: A life-threatening state that results from a relative or absolute deficiency of insulin



DIABETIC KETOACIDOSIS (DKA)

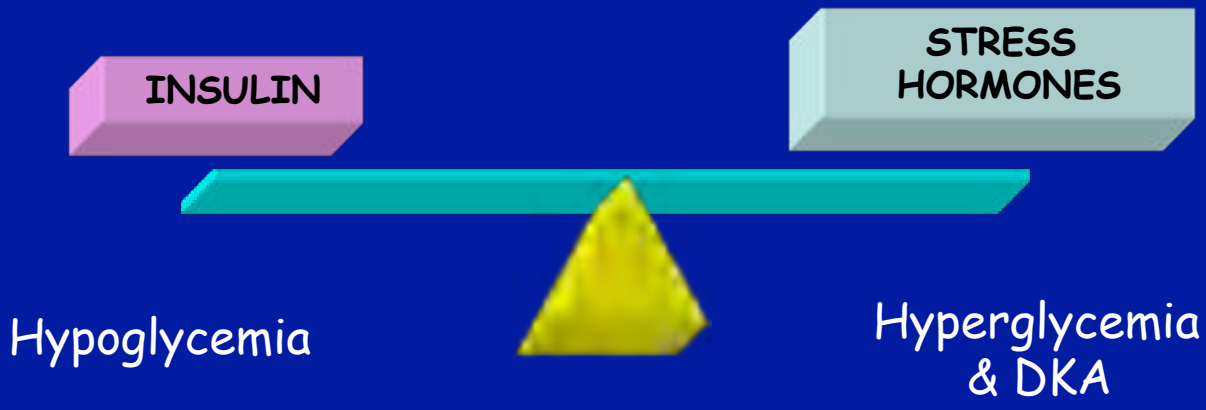
Definition: A life-threatening state that results from a relative or absolute deficiency of insulin.

- Usually occurs in individuals with Type 1 diabetes.
- Insulin levels are very low.
- High levels of "stress hormones": epinephrine, norepinephrine, growth hormone and cortisol.

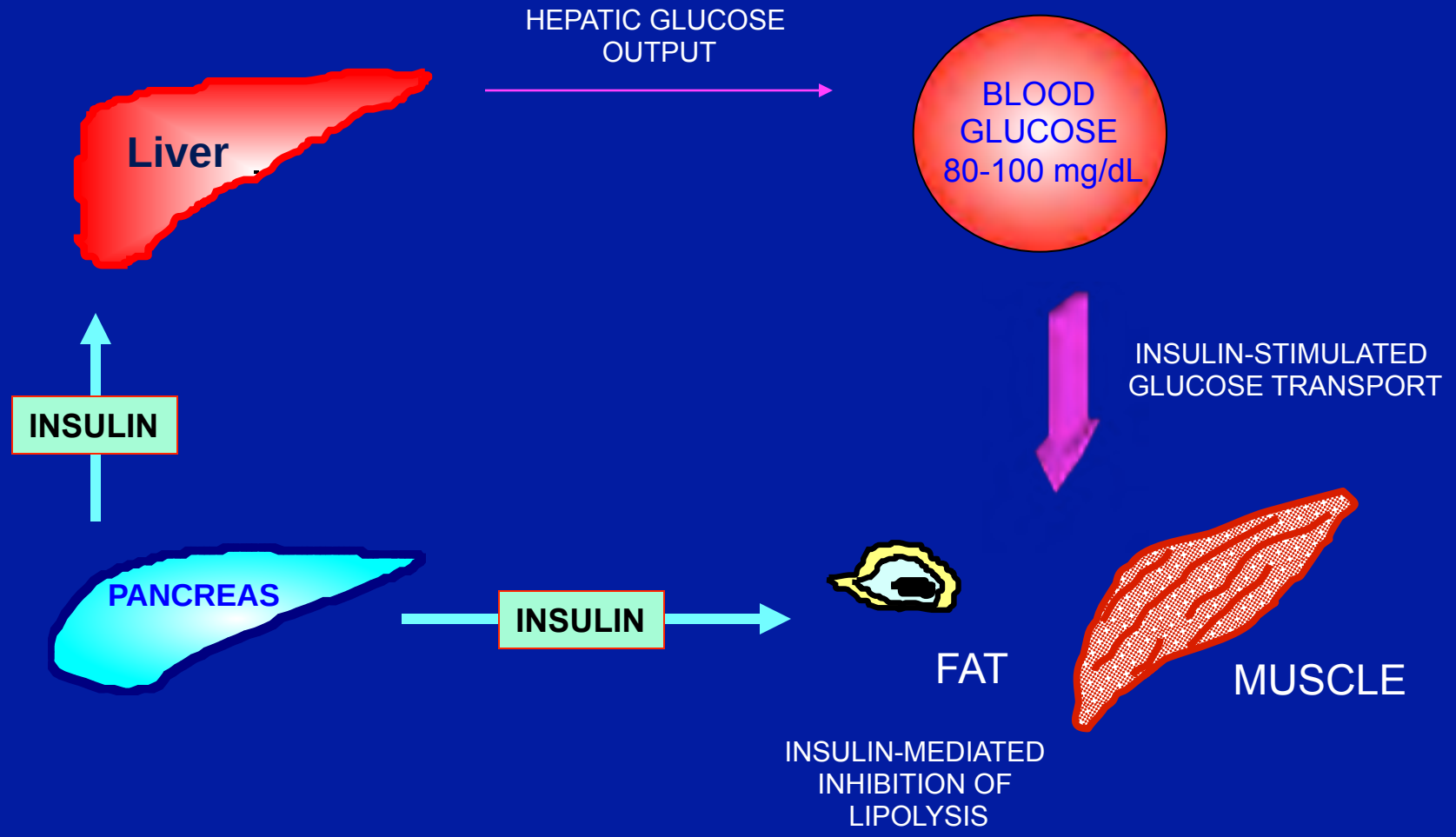
DIABETIC KETOACIDOSIS (DKA)

PRECIPITATING FACTORS (VERY IMPORTANT):

- Insufficient or no insulin.
- Physical stress: dehydration, trauma.
- Surgery, infections, heart attacks, etc.



Diabetic Ketoacidosis: Pathophysiology



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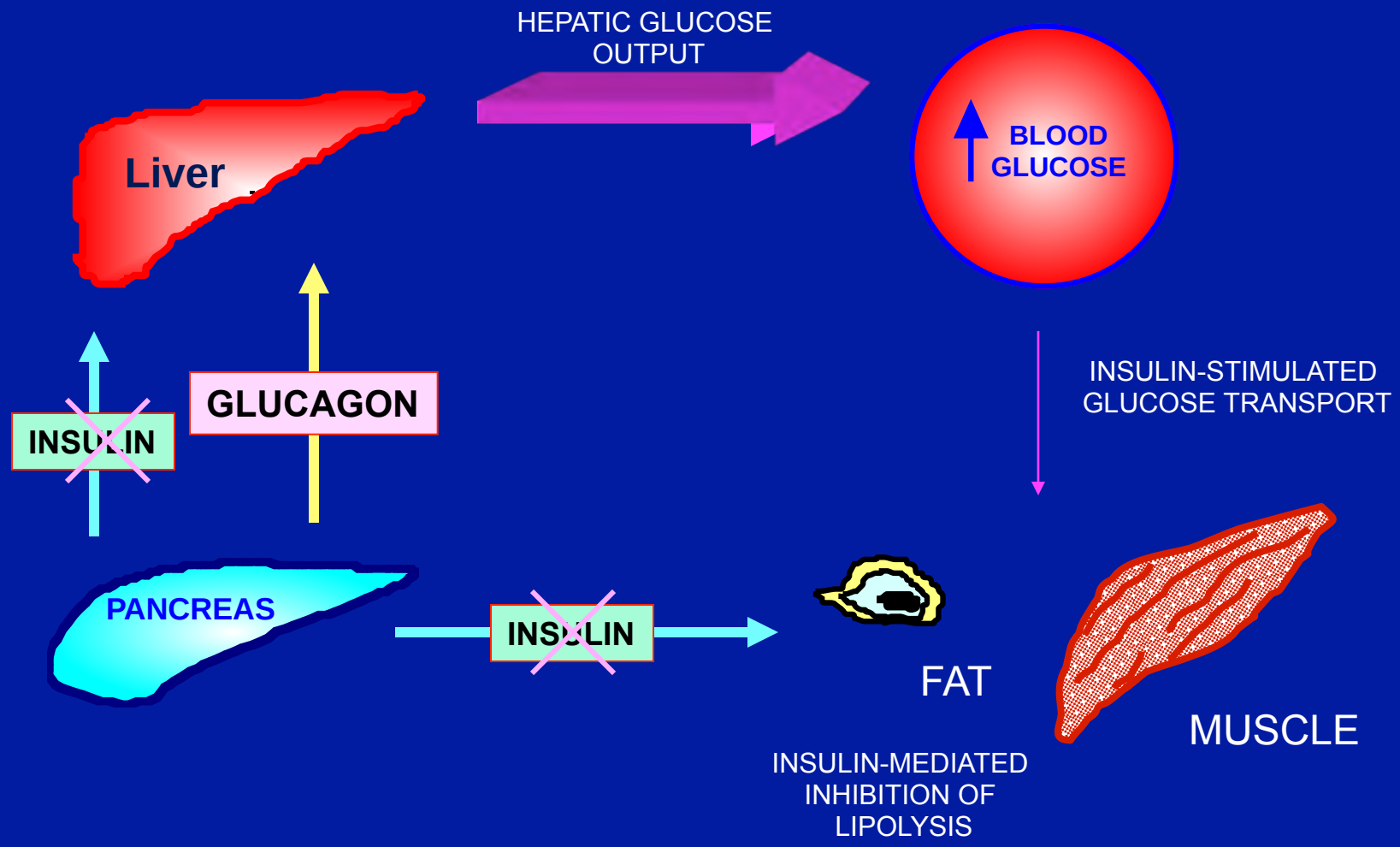
Diabetic Ketoacidosis: Pathophysiology



Meanwhile, in the adipocyte…

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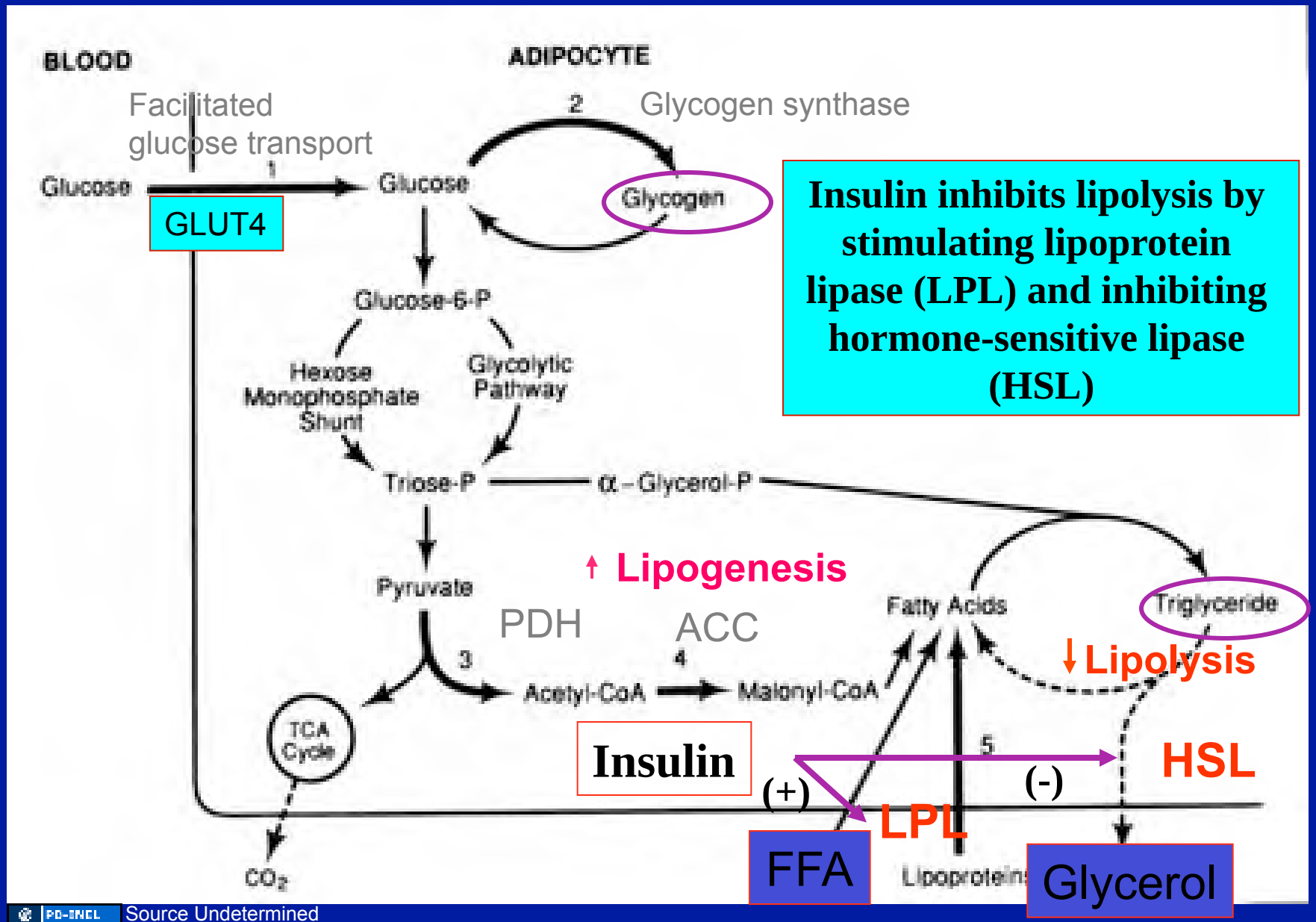
Insulin-regulated carbohydrate metabolism: adipocyte



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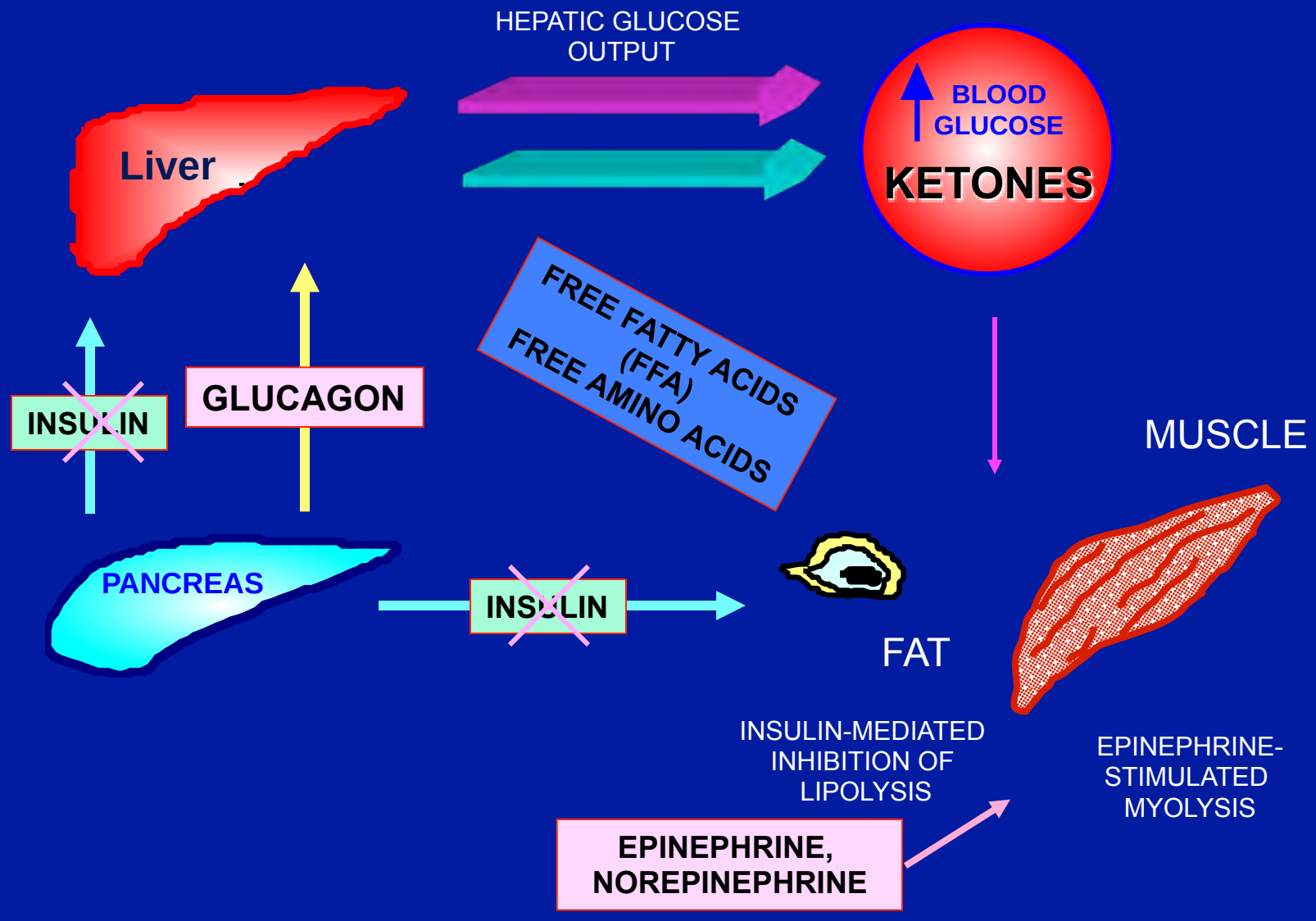
Diabetic Ketoacidosis: Pathophysiology



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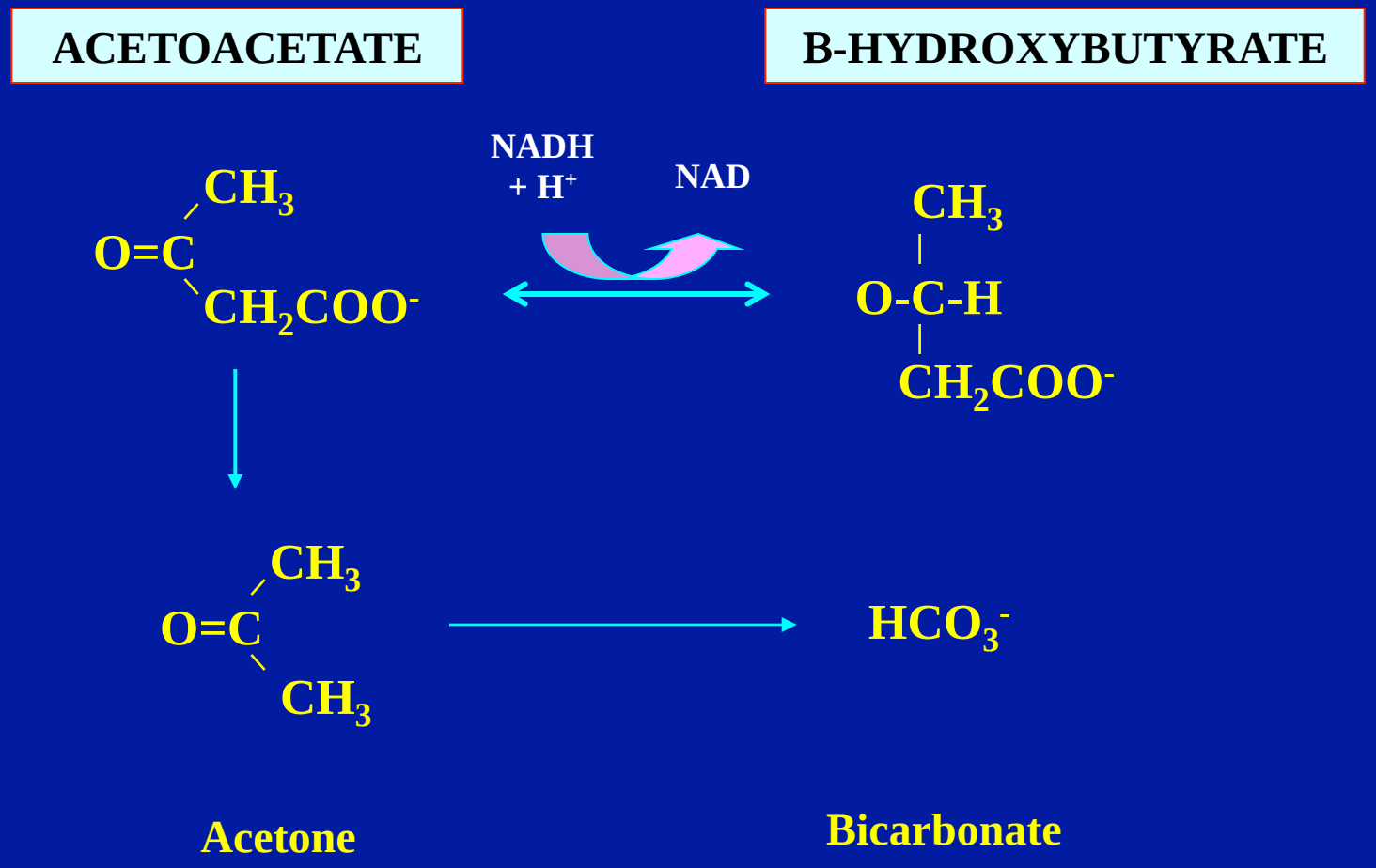
Diabetic Ketoacidosis: Ketoacids



Diabetic Ketoacidosis: Signs & Symptoms

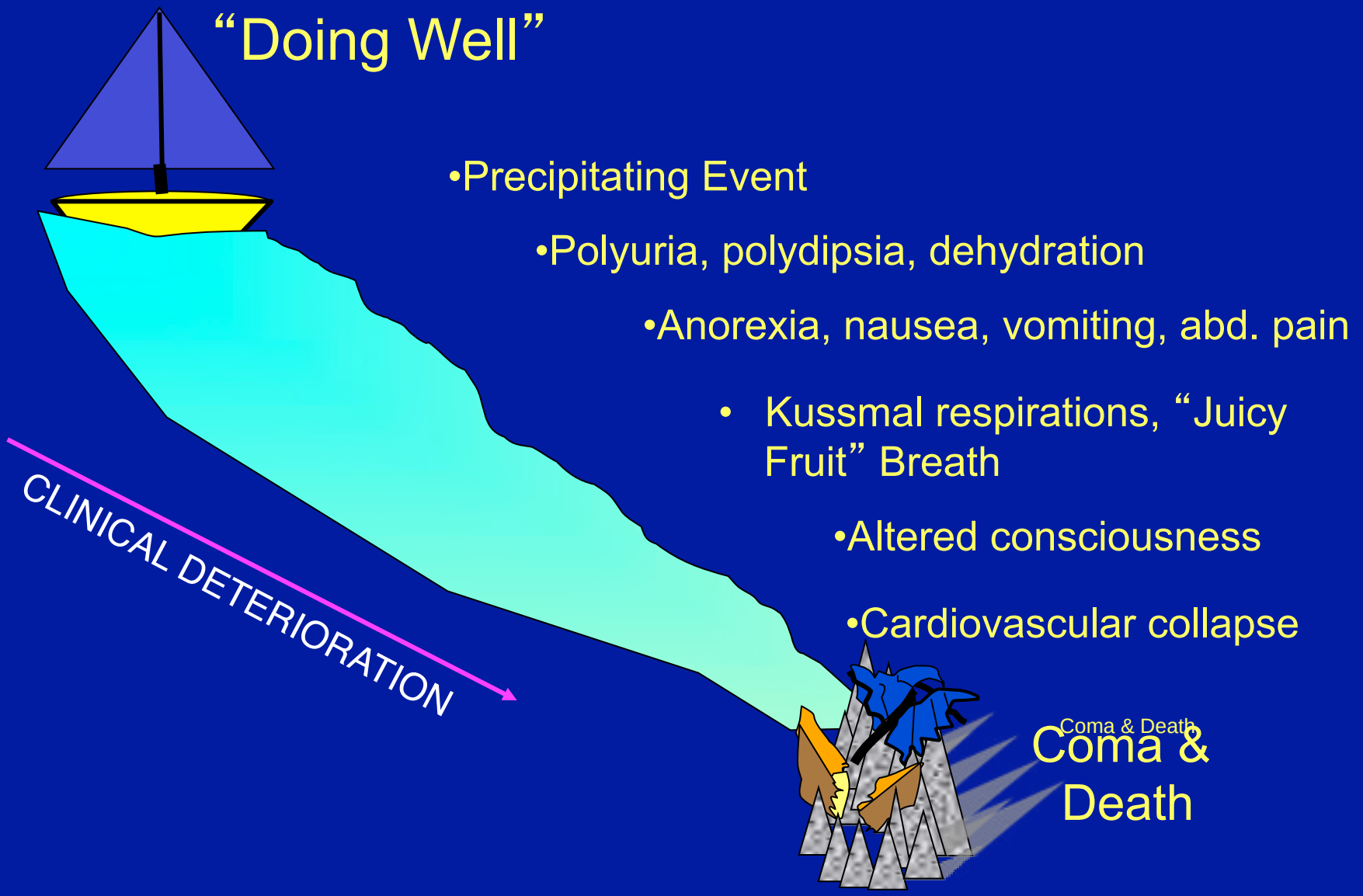
HYPERGLYCEMIA

- Polyuria and polydipsia
- Severe volume depletion
- Electrolyte depletion
- Eventual: renal hypoperfusion, prerenal azotemia, hypotension and shock

KETONES

- Acidosis
- Compensatory resp. alkalosis
- Hypotension
- Shock

Diabetic Ketoacidosis: Clinical Course (Worst Case Scenario)



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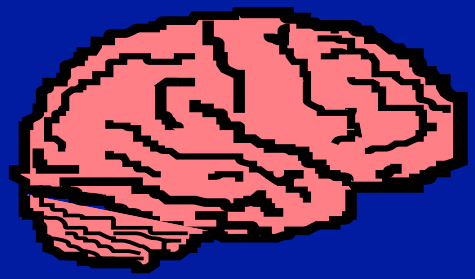
Diabetic Ketoacidosis: Effects on Mental Status

Factors leading to impairment of CNS function:



BRAIN

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Diabetic Ketoacidosis: Effects on Mental Status

Factors leading to impairment of CNS function:

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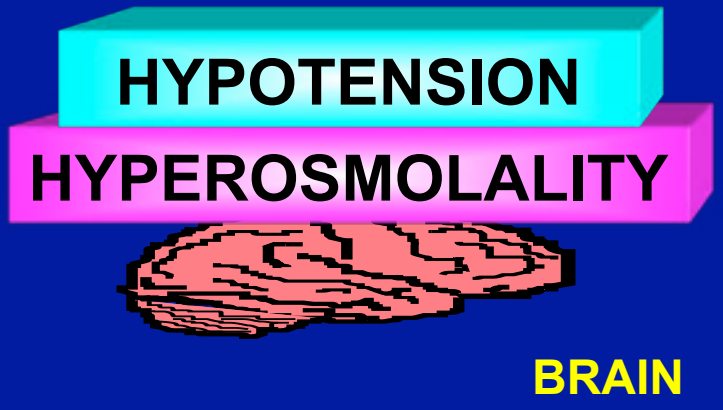
Diabetic Ketoacidosis: Effects on Mental Status

Factors leading to impairment of CNS function:



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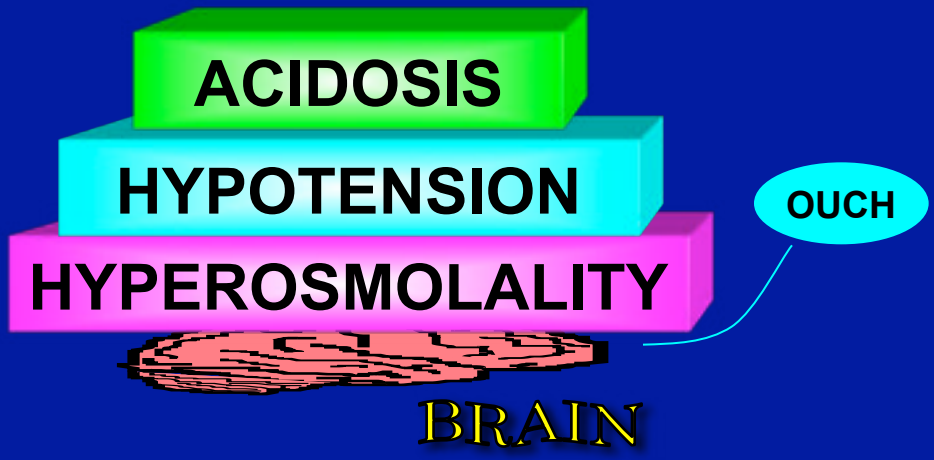
Diabetic Ketoacidosis: Effects on Mental Status

Factors leading to impairment of CNS function:



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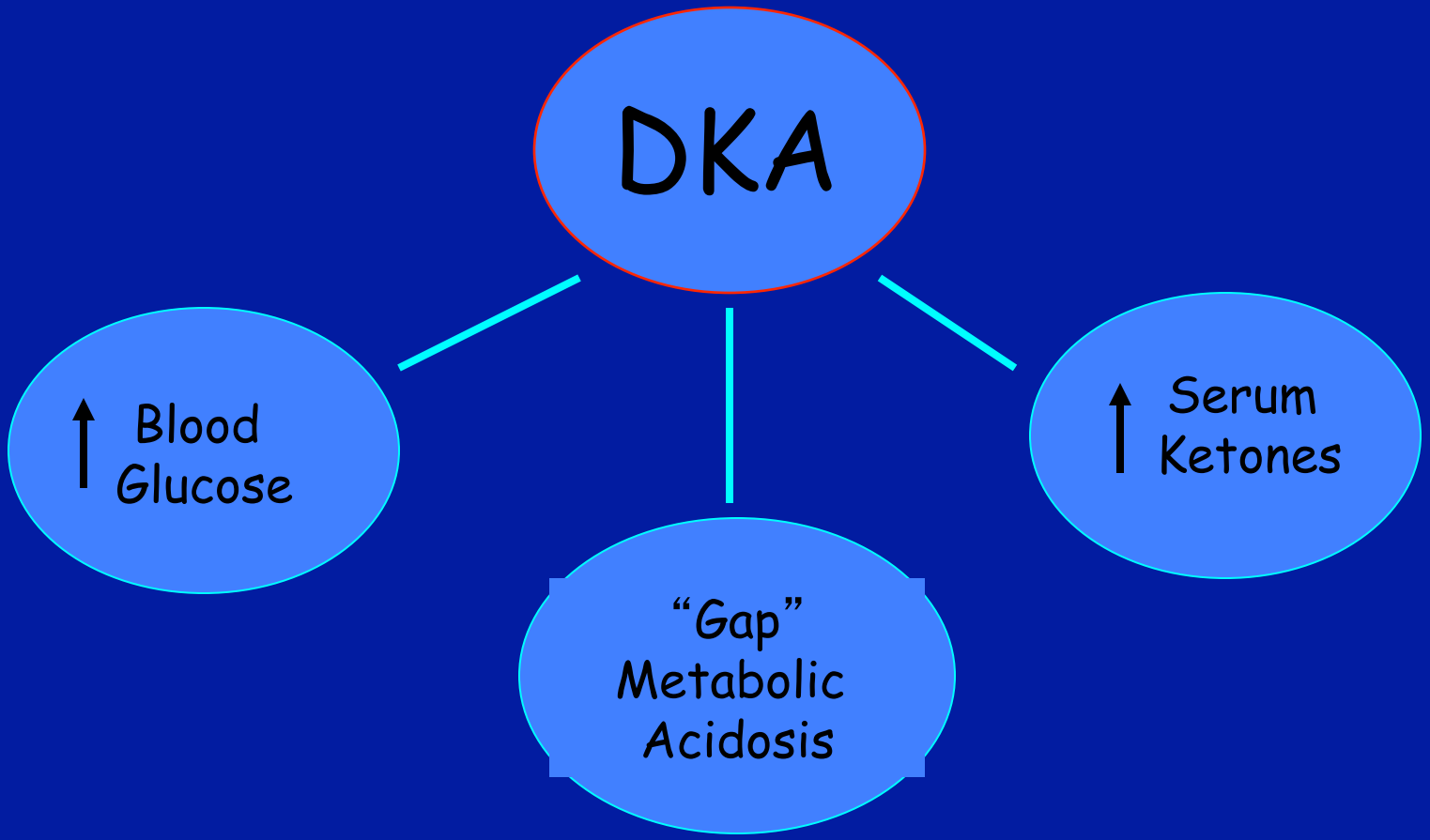
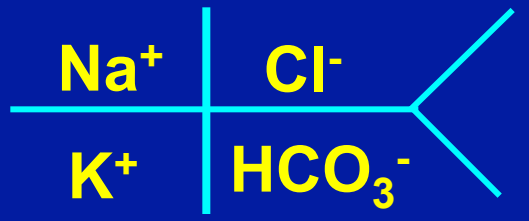
Diabetic Ketoacidosis: Diagnosis

The Diagnostic Triad of DKA:



Diabetic Ketoacidosis: Diagnosis

The "Anion Gap" represents the presence of unmeasured anions.



Anion Gap = Na^+ - (Cl^- + HCO_3^-)

(Normal = 12)

Organic acids, such as acetoacetate and β-hydroxybutyrate, decrease the HCO_3^- (which is a biologic buffer) and aren't measured in the gap. Therefore, the gap increases.

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Diagnosis of Diabetic Ketoacidosis

Signs and symptoms of DKA may be accompanied by those of the underlying precipitating disorder; HOWEVER,

DKA *per se* DOES NOT CAUSE FEVER.

Therefore, if a fever is present, assume there is an infection until proven otherwise!!

Diabetic Ketoacidosis: Treatment

1. Intravenous insulin.

2. IV Fluids: Initially rapid because of severe volume depletion - loss of 7-10 L of total body water.

3. Electrolyte replacement: esp. Na, K, Mg, and PO_4.

4. Carbohydrate replacement (5-10% dextrose) once serum glucose is below 250 mg/dL

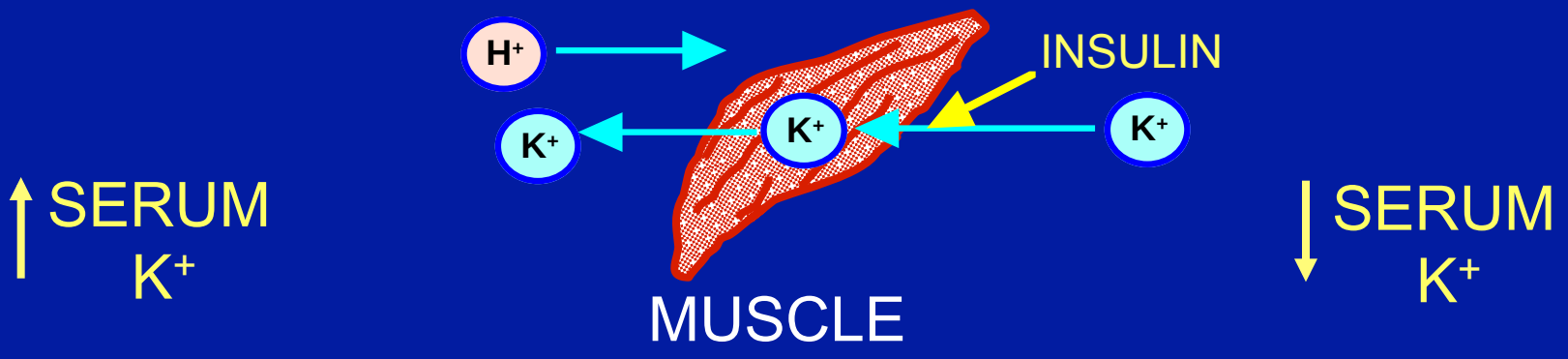
5. Administration of bicarbonate for acidosis is NOT recommended.

6. Diagnose and treat PRECIPITATING EVENT!

Treatment of Diabetic Ketoacidosis:
Don't Let an Elevated K^+ Fool You!

Bottom Line: "As soon as you see pee, give K^+!

ACIDOSIS **INSULIN Rx**



During acidosis, H^+ shifts into cells to be buffered by intracellular buffers. K^+ shifts out of cells in exchange.

Consequently, serum K^+ is usually elevated DESPITE total body K^+ depletion.

Treatment with insulin causes K^+ to shift back into cells, and serum K^+ may drop like a rock during therapy.

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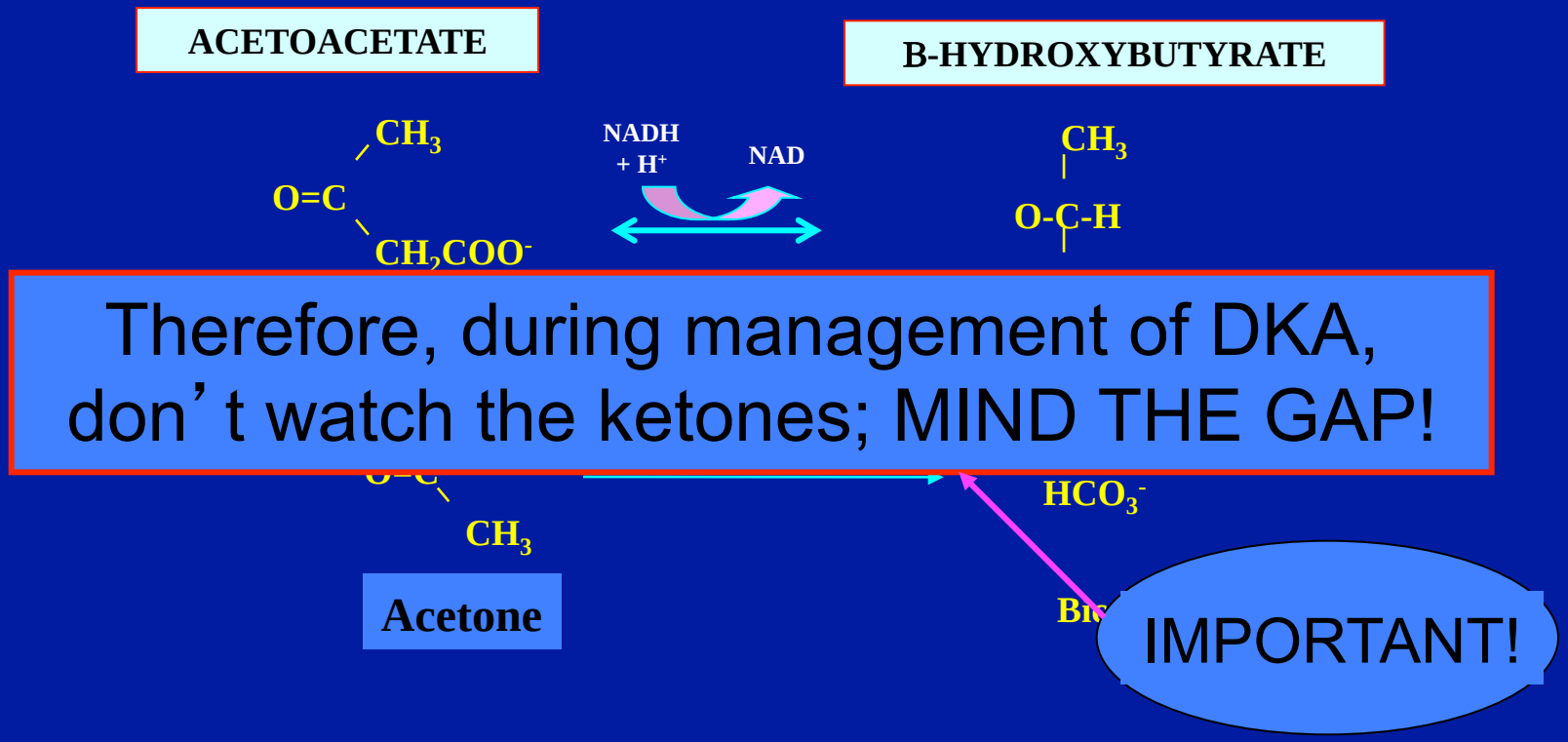
Treatment of Diabetic Ketoacidosis: "Mind the Gap"



Acetone is produced during the normal regeneration of bicarbonate and is detected by most serum ketone assays. Therefore, the serum ketones normally increase during recovery from DKA.

Treatment of Diabetic Ketoacidosis:

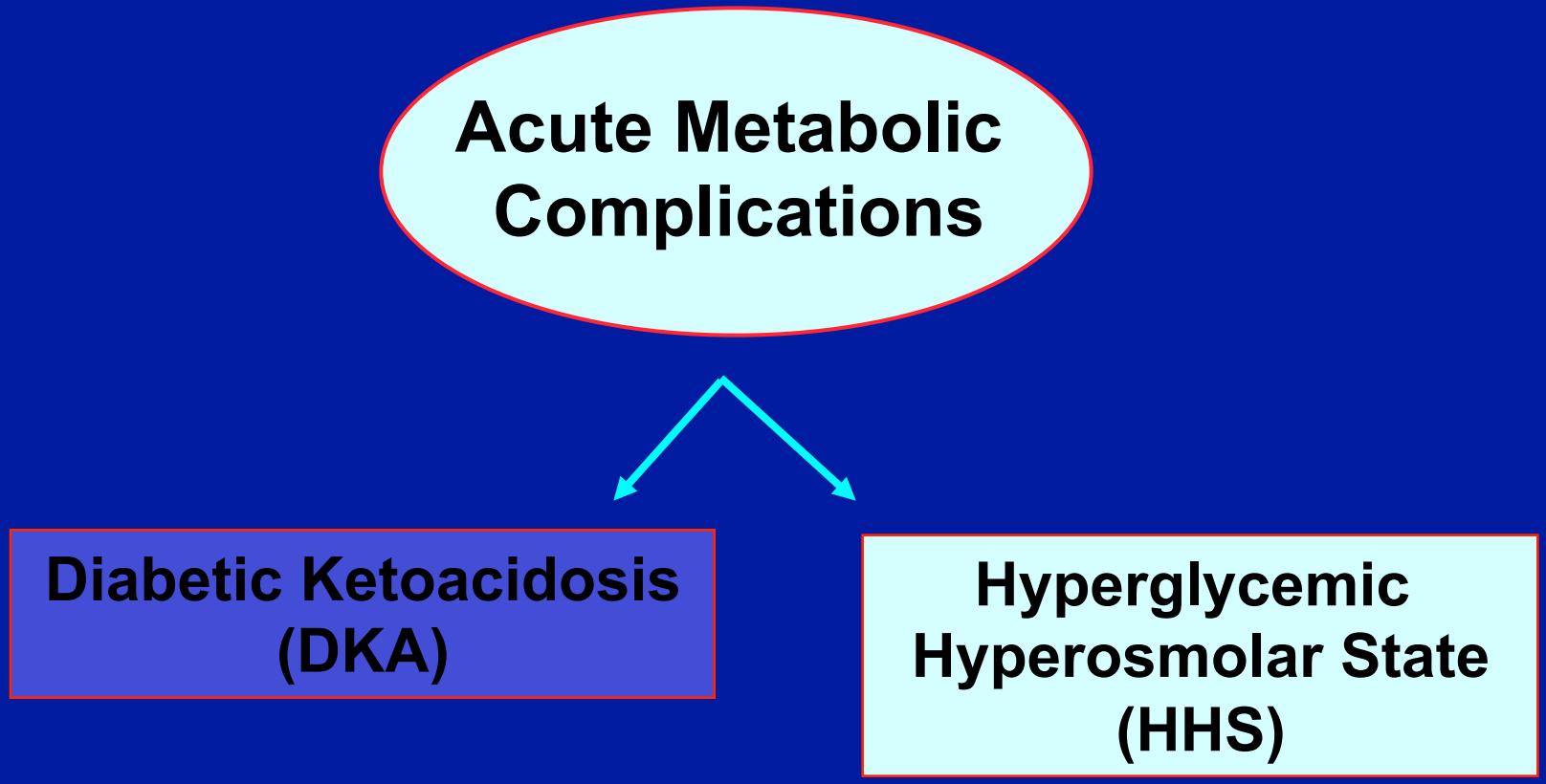
BY-SA NC Márcio Cabral de Moura (Flickr)

Treatment of Diabetic Ketoacidosis

Finally,

Diagnose and treat the underlying precipitating event!

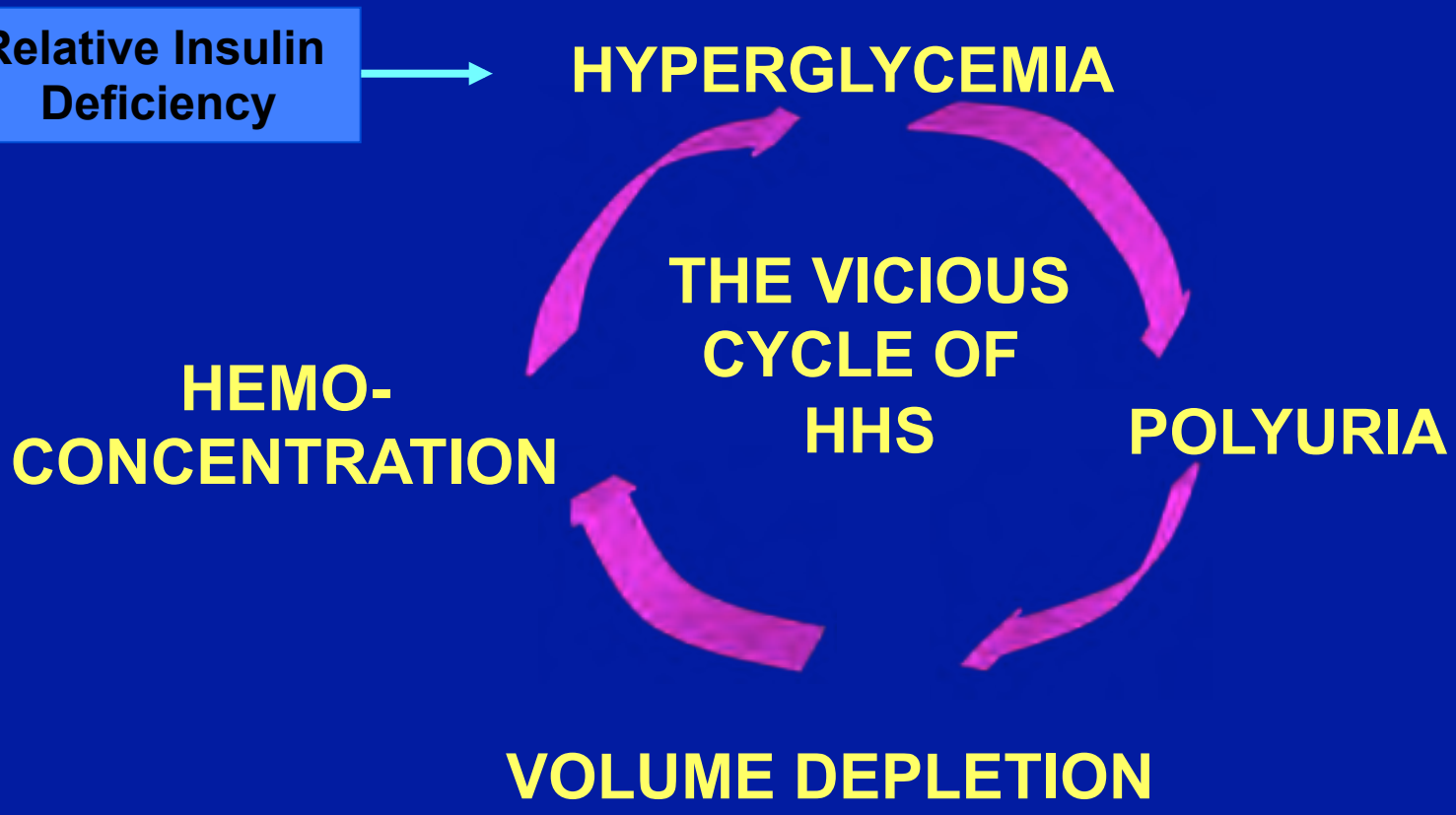
DIABETES MELLITUS



Hyperglycemic Hyperosmolar State

- Life-threatening metabolic disorder of extreme hyperglycemia without ketosis.
- Typically seen in elderly with type 2 diabetes, some 30% of whom are previously not diagnosed with diabetes.
- Common precipitating events: myocardial infarction, stroke, sepsis.
- Potentially deadly: mortality may exceed 40%.

Hyperglycemic Hyperosmolar State
Pathogenesis



Hyperglycemic Hyperosmolar State
Clinical Aspects

Increasing volume depletion and hemo-concentration may result in:

- Hyperviscosity and increased risk of thrombosis
- Disturbed mentation and obtundation
- Neurologic signs
  - Focal signs, e.g., sensory or motor deficits or focal seizures
  - Motor abnormalities, e.g., flacidity, depressed reflexes, tremor or fasciculations.

Ultimately, without treatment, coma and death

Hyperglycemic Hyperosmolar State Treatment

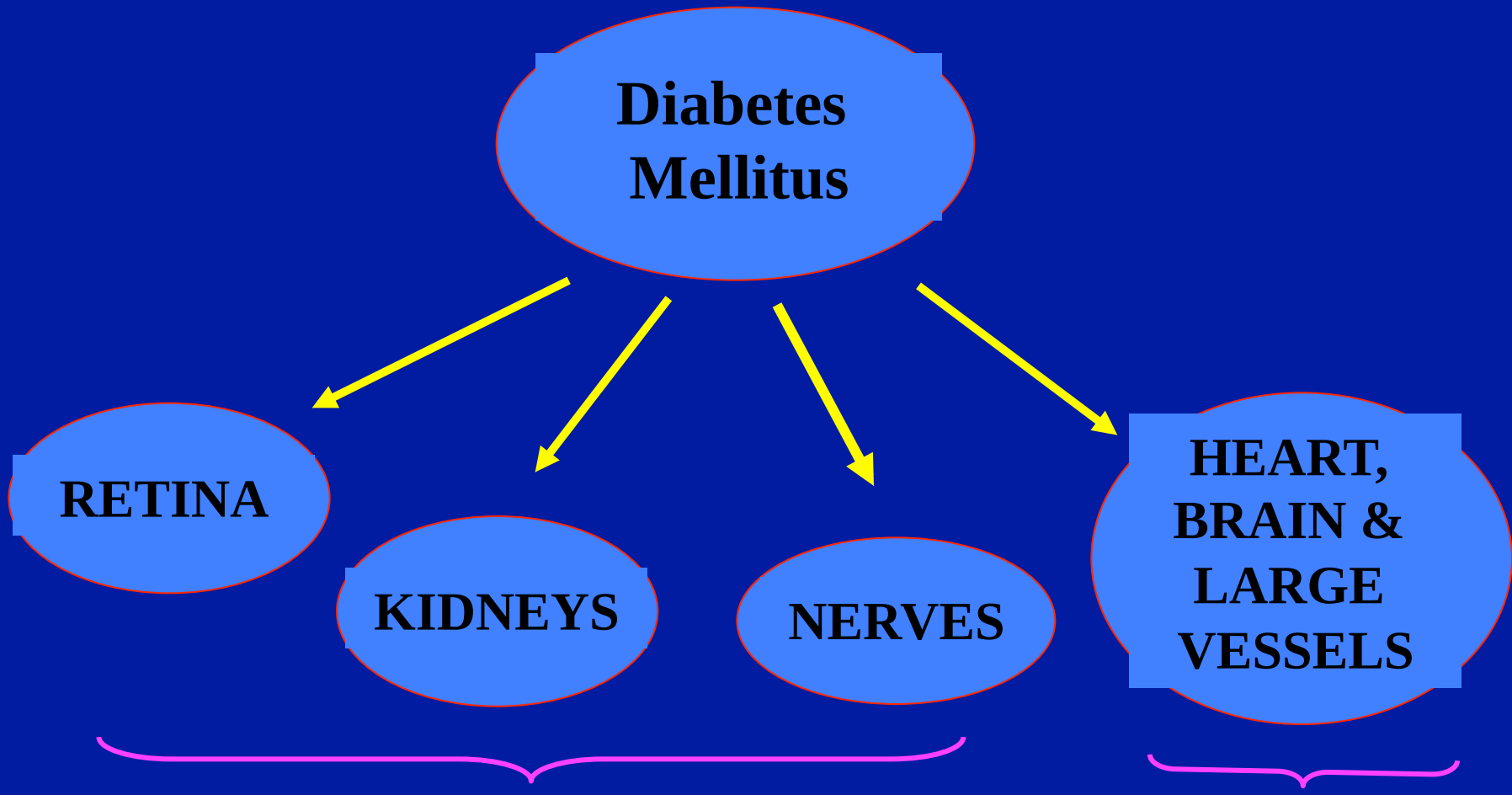
Similar to the treatment of DKA:

- Volume correction with normal saline.
- Replacement of electrolytes.
- IV insulin.
- Diagnosis and treatment of underlying cause.

Diabetes Mellitus

Chronic Complications

Diabetes Mellitus: Chronic Complications



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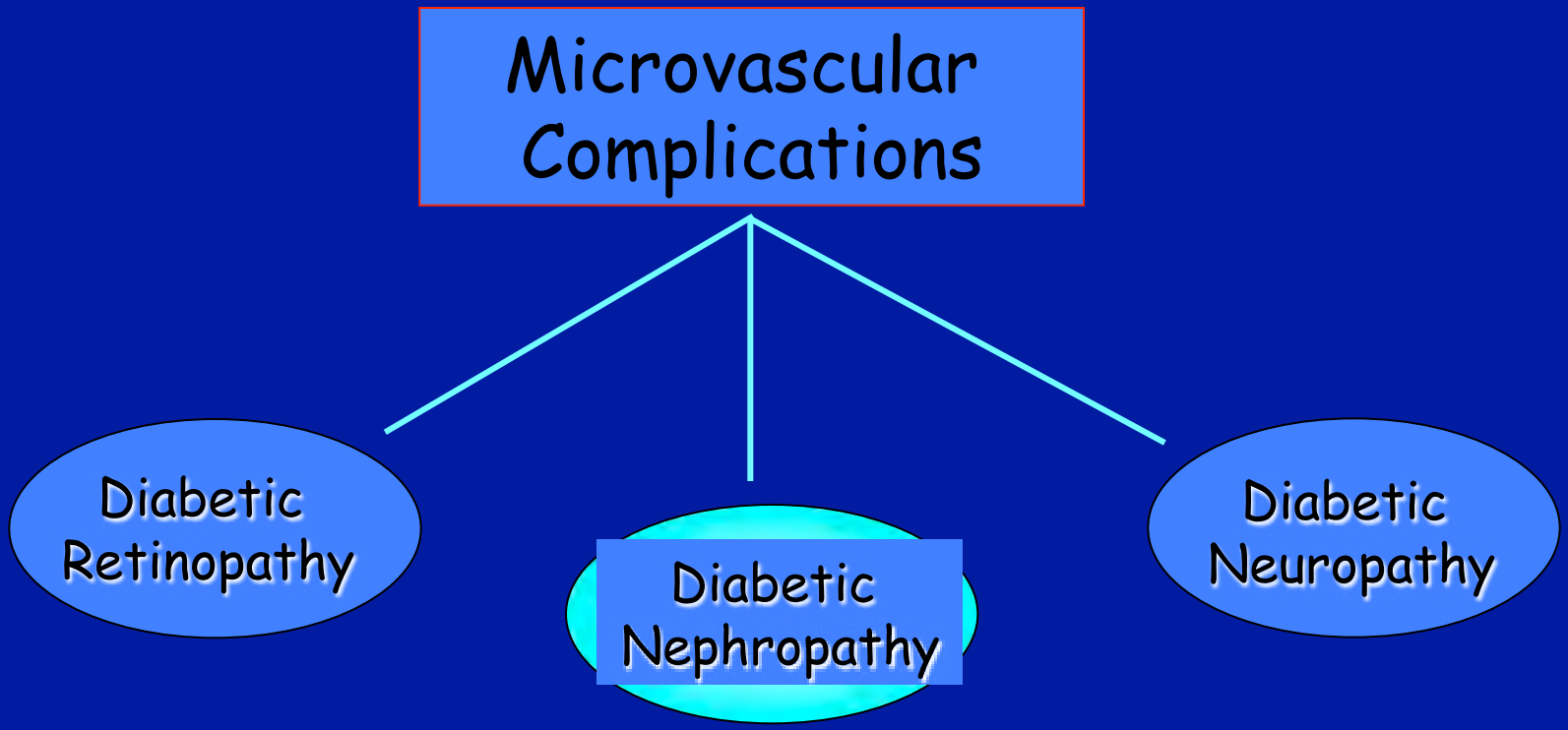
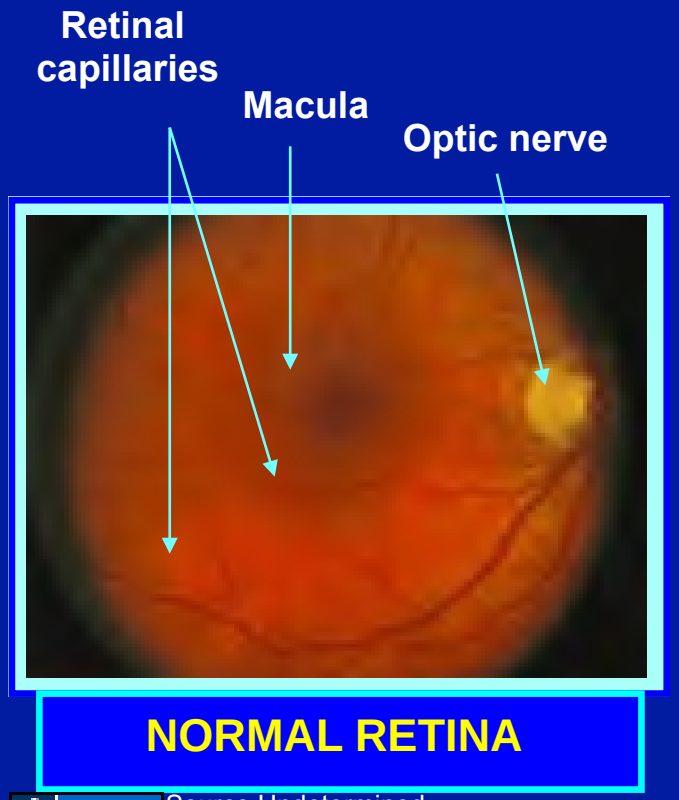
Diabetes: Chronic Complications



Diabetic Retinopathy

Retinal Fundus Photographs



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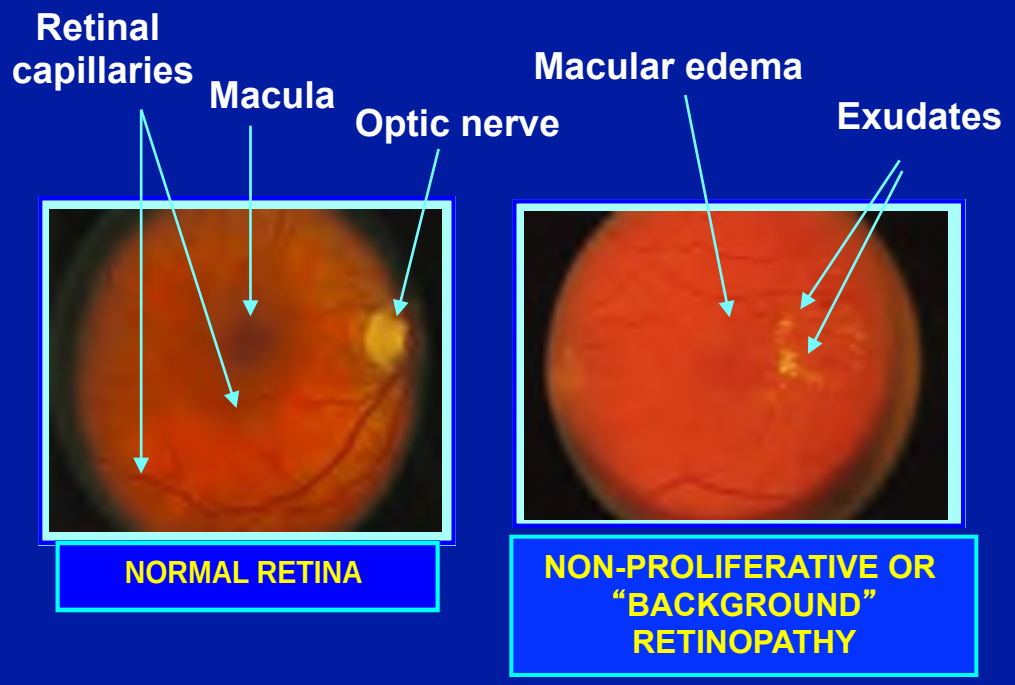
Diabetic Retinopathy

Retinal Fundus Photographs



Disease Progression

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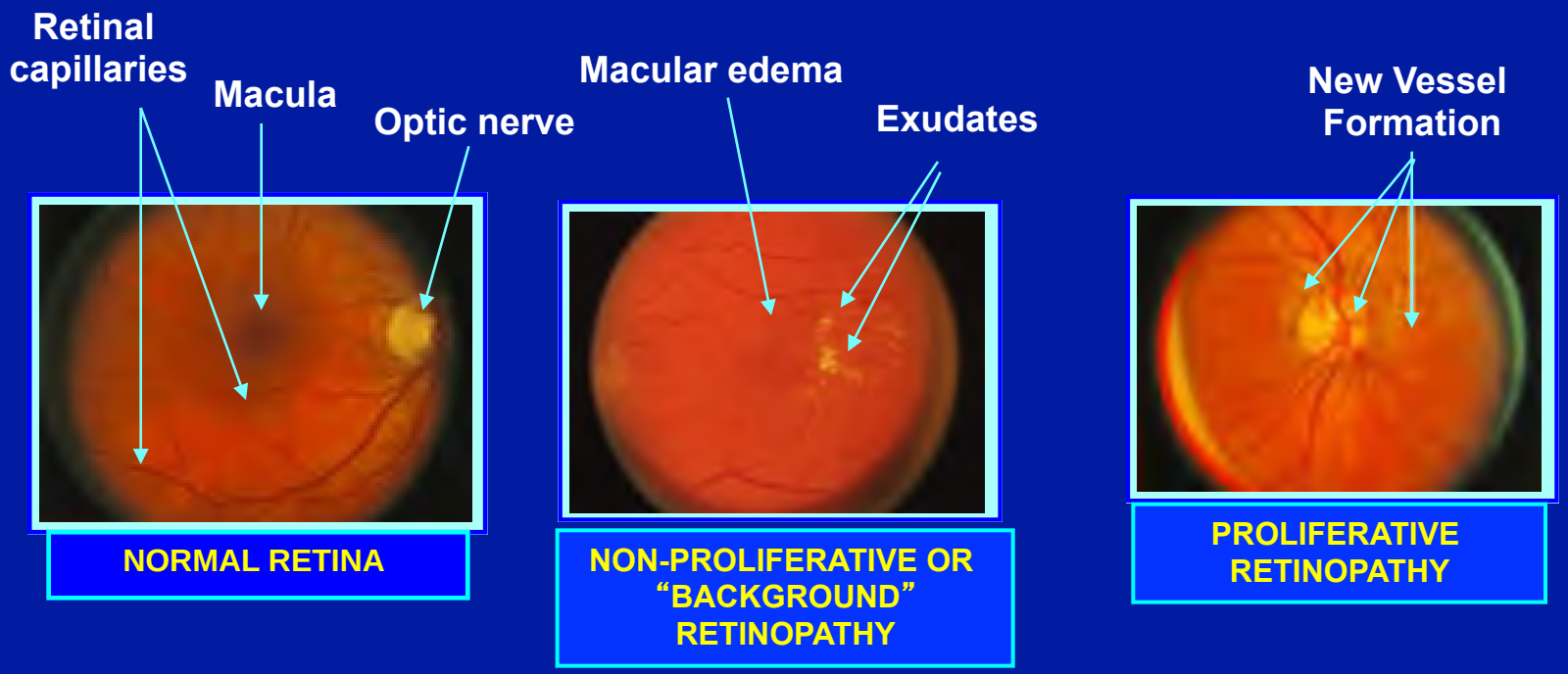
Diabetic Retinopathy

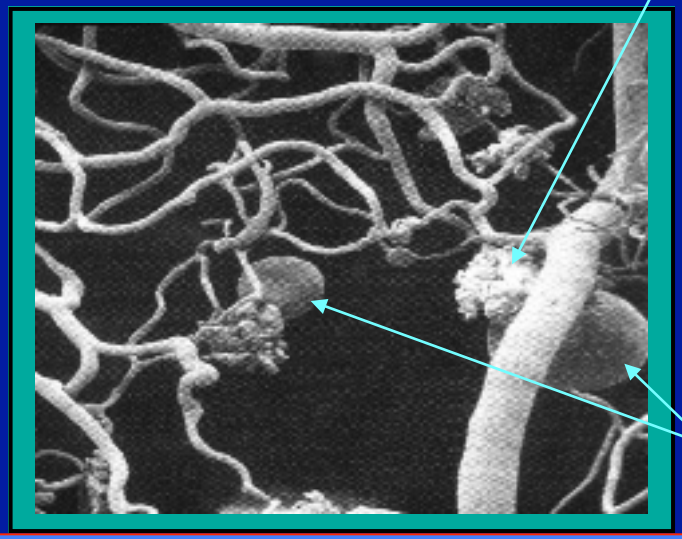
Retinal Fundus Photographs



Disease Progression

PD-INCL Source Undetermined (All Images)

Diabetic Retinopathy



EM Photograph of Plastic Cast of Retinal Capillaries from Diabetic Retina

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Exudates

- leakage of plasma proteins into neuroretina.

Microaneurysms

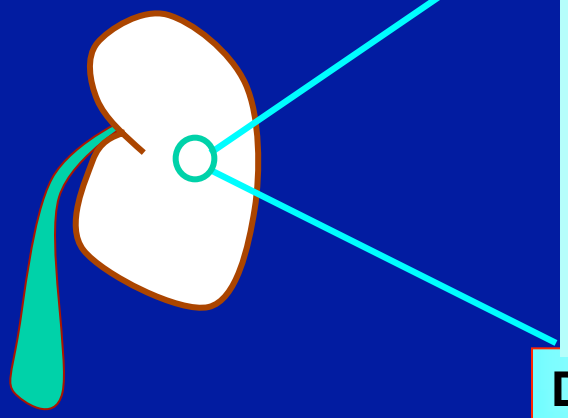
Later stages of retinopathy involve death of endothelial cells and capillary “drop out,” progressive ischemia and proliferative neovascular changes.

Diabetic Retinopathy

Remember:

Diabetic retinopathy is the leading cause of new adult blindness in the United States.

Diabetic Nephropathy



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Diabetic glomerulosclerosis

PD-INCL Source Undetermined

Diabetic glomerulosclerosis is characterized by bas
membrane thickening and mesangial cell proliferation.

This is EXTREMELY important!

Diabetic nephropathy may be diagnosed in its earliest--and potentially, reversible--stages by detection of extremely small amounts of albumin in the urine, so-called “microalbuminuria.”

Diabetic Nephropathy

Remember:

Diabetic nephropathy is the leading cause of renal failure requiring dialysis in the United States.

DIABETIC NEUROPATHY:
Peripheral Sensory Neuropathy

Diabetic "Charcot Feet"

Diabetic Foot Ulcer

PD-ENCL Source Undetermined

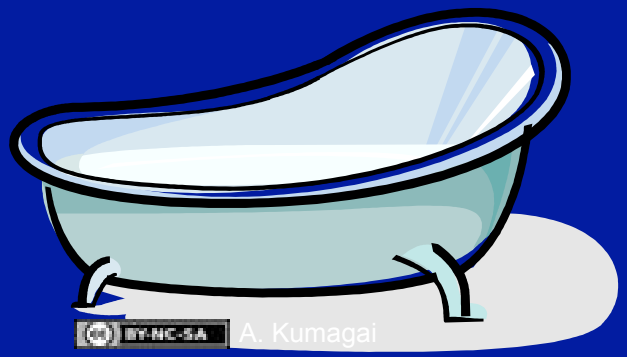
Symmetrical neuropathy is the most common:

- Primarily involving the distal extremities with "stocking-glove" distribution.
- Sensory: decreased vibration, temperature, proprioception.
- Initially may present with painful paresthesias: "burning" or "pins-and-needles" sensation. Eventually leads to complete loss of sensation.
- Predisposed to skin breakdown, ulcer formation and unrecognized trauma.

DIABETIC NEUROPATHY:
Peripheral Sensory Neuropathy

Of bottlecaps and bathtubs …

oparrish (Flickr)



DIABETIC NEUROPATHY:
Autonomic Neuropathy

- Gastroparesis
- Constipation or Diarrhea

- Chronic edema
- Postural hypotension

- Cardiac arrhythmias
- Sudden Death

- ERECTILE DYSFUNCTION
- Urinary retention

Abnormal sweating and increased callus formation

Diabetic Neuropathy

Remember:

Diabetes is the leading cause of non-traumatic lower extremity amputations in the United States.

DIABETIC COMPLICATIONS

MACROVASCULAR COMPLICATIONS

Gangrene is 14 times more common in people with diabetes than those without.

Coronary Heart Disease:

- **Twice as common in people with diabetes.**
- **Occurs at an earlier age and places women with men.**
- **For MI's: individuals with diabetes have a hig… mortality rate and lower 5-year survival rate.**
- **MI's often occur WITHOUT CHEST PAIN.**

This is EXTREMELY important!

Risk of death from stroke is approximately 3 times greater for people with diabetes than for those without.

DIABETIC COMPLICATIONS:
Diabetes and Pregnancy

1. Problems for the Mother:
   - Insulin Requirements increase and metabolic control often worsens during pregnancy.
   - Diabetic retinopathy and possibly nephropathy may worsen.

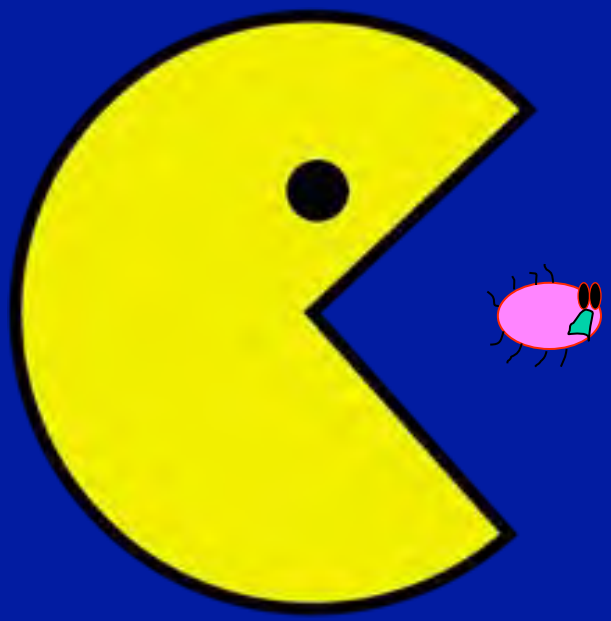
2. Problems for the Baby:
   - Infant mortality is higher in babies from diabetic mothers.
   - Congenital malformations are more frequent.
   - Respiratory distress syndrome (RDS) is more common.

DIABETIC COMPLICATIONS:
Diabetes and Pregnancy

High blood sugars in pregnancy can lead to…

BIG BABIES

Hyperglycemia lowers resistance to infection and interferes with wound healing.



At BGs of >250 mg/dL, WBC motility and opsinization of bacteria are significantly impaired.

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DIABETIC COMPLICATIONS

- Complications from influenza are more common in individuals with diabetes.
- Infections with tuberculosis and pneumococcal pneumonia are common.
- Yeast infections are common among diabetes women.
- Wound healing is delayed in poorly controlled diabetes.

Diabetic Complications

"Diabetes is a dreadful affliction, the melting down of flesh and limbs into urine…Life is short, unpleasant and painful...

-- Areteus of Capadocia, 2nd C. A.D.

What can we do???

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