

- ### Glucose Homeostasis
- Glycogen Synthesis (Excess Glucose)
 - Glycogenolysis – Hepatic, Muscle (8 hrs.)
 - Exercise, Starvation, Illness, Alcohol increase it
 - Gluconeogenesis – From precursors
 - Synthesis of glucose in liver and kidney
 - Muscle, Adipose tissue & kidney supply the fuel
 - Brain can use only glucose, has little glycogen
 - Can sustain only few minutes without glucose
 - Luckily brain doesn't need insulin for GLUT
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Golden Rule – Hypoglycemia

“Must be considered in any patient with mental confusion, altered consciousness or seizure”

It is probably the most common endocrine emergency and frequently occurs in patients receiving insulin treatment with tight control

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- ### Fasting State
- Short fast
 - Utilizes free glucose (15-20%)
 - Break down of glycogen (75%)
 - Overnight fast
 - Glycogen breakdown (75%)
 - Gluconeogenesis (25%)
 - Prolonged fast
 - Only 10 grams or less of liver glycogen remains.
 - Gluconeogenesis becomes sole source of glucose
 - Muscle protein is degraded for amino acids.
 - Lipolysis generates ketones for additional fuel.
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- ### Common Causes of Hypoglycemia
- DM medication - Insulin, OHA; Alcohol ingestion
 - Missed or delayed or inadequate meal
 - Unexpected or unusual physical activity
 - Errors in OHA or Insulin dose, schedule, route
 - Poorly designed Insulin regimen-Night ↓ Glucose
 - Variable Insulin absorption – lipohypertrophy
 - Gastro paresis due to autonomic neuropathy
 - Malabsorption, Endocrine disorders (Addison's)
 - Fictitious (self), Breast feeding by DM mother
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Rare Causes of Hypoglycemia

- Drugs: Quinine, Pentamidine, Salicylates, Sulfa
- Critical illness: Sepsis, Hepatic, Renal, Cardiac
- ↓ of Hormones: Cortisol, GH, Glucagon, Epinephr
- Tumours: Non β cell tumours, MEN 1 and 2
- Endogenous Hyper insulinism: Insulinoma, Ectopic Insulin, β cell disorders, Insulin Auto Ab.
- Disorders of children: Hyper insulinism, Enzyme↓
- Reactive (PP) Hypoglycemia: Alimentary, Other endogenous hyper insulinism, HFI, Galactosemia

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Signs of Hypoglycemia

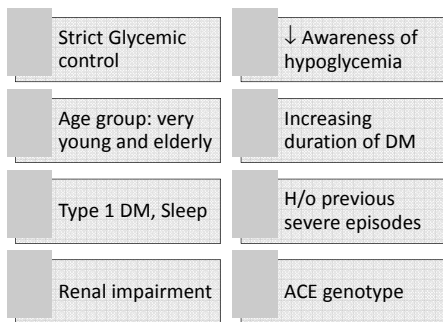
- Autonomic
Sweating, Pallor
Tachycardia, Increased SBP
- Neuroglycopenic
Focal Neurological deficits (FND), Ataxia, Seizures
- Others
Signs of underlying cause, H/o OHA, Insulin

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Risk Factors For Hypoglycemia

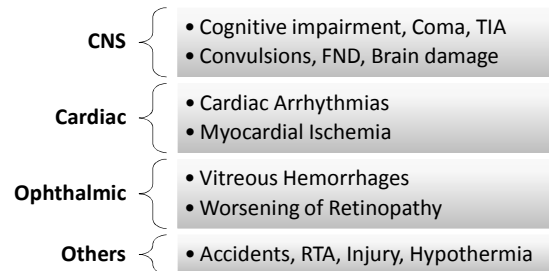


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Morbidity of Severe Hypoglycemia



Severe Hypoglycemia, if prolonged can be fatal

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Symptoms of Hypoglycemia

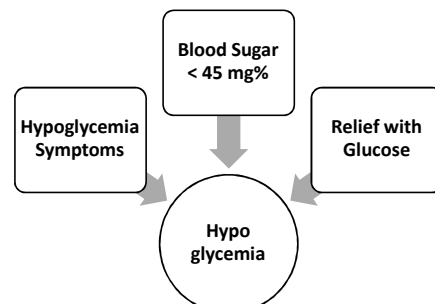
- Autonomic
Sweating, hunger, paresthesias (Ach)
Palpitation, Tremor, Anxiety (NE/E)
- Neuroglycopenic
Confusion, Drowsiness, Speech difficulty, Anger
Inability to concentrate, Incoordination, Irritability
Visual disturbances, Ataxia, Seizures, Unconscious
- Non-specific
Nausea, Headache, Tiredness

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Whipple's Triad (Criteria)



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Responses to ↓ Glucose levels

Response	Glycemic threshold	Physiological effects	Role in counter regulation
↓ Insulin	80 - 85 mg%	↑ R_a (↓ R_d)	Primary First Defense
↑ Glucagon	65 - 70 mg%	↑ R_a	Primary Second Defense
↑ Epinephrine	55 - 65 mg%	↑ R_a ↓ R_d	Critical Third Defense
↑ Cortisol, GH	50 - 55 mg%	↑ R_a ↓ R_d	Not Critical
↑ Food ingestion	50 - 55 mg%	↑ Exogenous Glucose	< 50mg% no cognitive change

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- ### Relative or Absolute Insulin Excess
- ↑ Dose of Insulin or OHA, Ill timed, wrong type
 - Overnight fast, Missed meal – ↓ Glucose input
 - Exercise – Insulin independent ↑ utilization
 - Increased insulin sensitivity – Good treatment
 - ↓ Endogenous production from glycogen - Alcohol
 - ↓ Insulin clearance as in renal failure
 - Increased utilization by tissues – Sepsis- cytokines
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- ### Know Our Brain !!
- Brain is the major glucose consumer
 - Consumes 120 to 150 g of glucose per day
 - Glucose is virtually the sole fuel for brain
 - Brain does not have any fuel stores like glycogen
 - Can't metabolize fatty acids as fuel
 - Requires oxygen always to burn its glucose
 - Can not live on anaerobic pathways
 - One of most fastidious and voracious of all organs
 - Oxygen and glucose supply can not be interrupted
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- ### Hypoglycemia Associated Autonomic Failure (HAAF)
- With relative or absolute insulin excess
 - Defective glucose counter regulation leading to compromised physiological defenses
 - Hypoglycemia unawareness – leading to compromised behavioral defenses
 - These have six fold ↑ in risk of hypoglycemia
 - HAAF patients are 25 times ↑ risk of sever hypo.
 - Every DM patient must be taught about hypo.
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- ### Hypoglycemia of Diabetes
- It's a fact of life -T1DM – 2 episodes/wk, 2-4% die
 - Recurrent morbidity in T1DM and T2DM
 - Sometimes fatal if prolonged and severe
 - Problems with hypoglycemia
 - Precludes tight glycemic control – its benefits
 - Recurrent episodes – HAAF (Autonomic failure)
 - Defective glucose counter regulation
 - Hypoglycemia unawareness
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- ### Reactive Hypoglycemia
- Postprandial (2-3 hrs. after meal) exclusively
 - Alimentary Hypoglycemia
 - Early hyper insulinism after food
 - ↑ in GLP-1, and its suppression of Glucagon
 - Autoantibodies to insulin – potentiate action
 - Frequent small feeds, Avoid simple sugars
 - High protein diet, Probably α-GIs (Acarbose)
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Fictitious Hypoglycemia

- Usually in a diabetic patient
- Sometimes in non diabetic persons also
- Surreptitious or malicious administration
- Insulin or OHA – Inadvertently or willfully
- DM patients, Doctors, HCW
- Suicidal attempts by Insulin use

Glucose Monitors are not accurate in low sugar ranges

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Treatment of Hypoglycemia

- Mild/Moderate Hypoglycemia
 - Check BG First
 - Treat with high Glycemic Index Food
 - Treat with proper quantity
 - Recheck in 15 Minutes
- Severe Hypoglycemia
 - Unconscious / Unresponsive
 - Seizure / Uncooperative
 - IV Glucose 25% or Glucagon

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Pseudo Hypoglycemia

- SMBG -Monitors inaccurate at low sugar levels
- Laboratory Errors
- Non use of fluoride
- Time delay in glucose testing after sampling
- Blood glucose instead of plasma glucose
- Metabolism by cells, RBC, WBC, Platelets
- Erythrocytosis, Leukocytosis, Thrombocytosis

Always draw a blood sample before giving glucose Rx.

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Certain Special issues

- Glucagon 1mg IM or SC
- But beware, it can take longer than IV glucose
- The condition of alcoholics, elderly and others with depleted glycogen stores will generally not improve with Glucagon as it acts by Glycogenolysis
- Octreotide for Rx of SU induced hypoglycemia
- Administered SQ with initial dose of 50 to 125 mcg.
- Only recommended after initial glucose Rx. is initiated
- Thiamine 100mg should be given along with glucose

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Hypoglycemia Prevention Strategies

- Aggressive HbA1c control/analogs
- Patient education/empowerment
- Consistent and frequent SMBG
- Adjusting Physical Activity /Food
- Individualized HbA1c goals
- Flexible regimens of insulin/OHA
- Correction of risk factors listed

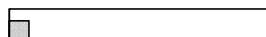
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Diabetes Drugs - Hypoglycemia

Hypoglycemic



- Insulin (Non Analog)
- SU - Glibenclamide
- Repaglinide, Mitiglinide

Non Hypoglycemic



- Metformin, Pioglitazone
- GLP-1, DDP-IV Inhibitor
- Acarbose, Voglibose

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