**Glucose Homeostasis**

- α-cells release Glucagon stimulate glycogen breakdown and gluconeogenesis
- β-cells release insulin stimulate glucose uptake by peripheral tissues

**Definition of Hypoglycemia**

- Mild – Bl Glucose < 60 mg%
  - Adrenergic Symptoms
- Moderate – B G < 50 mg%
  - Cognitive Symptoms
- Severe – B G < 40 mg% ??
  - Unconsciousness

**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

**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.

**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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**Dr R V S Sarma MD FIMSA**
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

Risk Factors For Hypoglycemia

- Strict Glycemic control
- Awareness of hypoglycemia
- Age group: very young and elderly
- Increasing duration of DM
- Type 1 DM, Sleep
- H/o previous severe episodes
- Renal impairment
- ACE genotype

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

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

Morbidity of Severe Hypoglycemia

- CNS
  - Cognitive impairment, Coma, TIA
  - Convulsions, FND, Brain damage
- Cardiac
  - Cardiac Arrhythmias
  - Myocardial Ischemia
- Ophthalmic
  - Vitreous Hemorrhages
  - Worsening of Retinopathy
- Others
  - Accidents, RTA, Injury, Hypothermia

Whipple’s Triad (Criteria)

- Blood Sugar < 45 mg%
- Relief with Glucose
**Hypoglycemia**

### Responses to ↓ Glucose levels

<table>
<thead>
<tr>
<th>Response</th>
<th>Glycemic threshold</th>
<th>Physiological effects</th>
<th>Role in counter regulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>↓ Insulin</td>
<td>80 - 85 mg%</td>
<td>↑ R₃ (↓ R₂)</td>
<td>Primary First Defense</td>
</tr>
<tr>
<td>↑ Glucagon</td>
<td>65 - 70 mg%</td>
<td>↑ R₃</td>
<td>Primary Second Defense</td>
</tr>
<tr>
<td>↑ Epinephrine</td>
<td>55 - 65 mg%</td>
<td>↑ R₃, ↓ R₄</td>
<td>Critical Third Defense</td>
</tr>
<tr>
<td>↑ Cortisol, GH</td>
<td>50 - 55 mg%</td>
<td>↑ R₃, ↓ R₄</td>
<td>Not Critical</td>
</tr>
<tr>
<td>↑ Food ingestion</td>
<td>50 - 55 mg%</td>
<td>↑ Exogenous Glucose</td>
<td>&lt; 50 mg% no cognitive change</td>
</tr>
</tbody>
</table>

### 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

### 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

### 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.

### 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

### 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)
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

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 / Uncoooperative
  - IV Glucose 25% or Glucagon

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.

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

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

Diabetes Drugs - Hypoglycemia

<table>
<thead>
<tr>
<th>Hypoglycemic</th>
<th>Non Hypoglycemic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin (Non Analog)</td>
<td>Metformin, Pioglitazone</td>
</tr>
<tr>
<td>SU - Glibenclamide</td>
<td>GLP-1, DDP-IV Inhibitor</td>
</tr>
<tr>
<td>Repaglinide, Mitiglinide</td>
<td>Acarbose, Voglibose</td>
</tr>
</tbody>
</table>