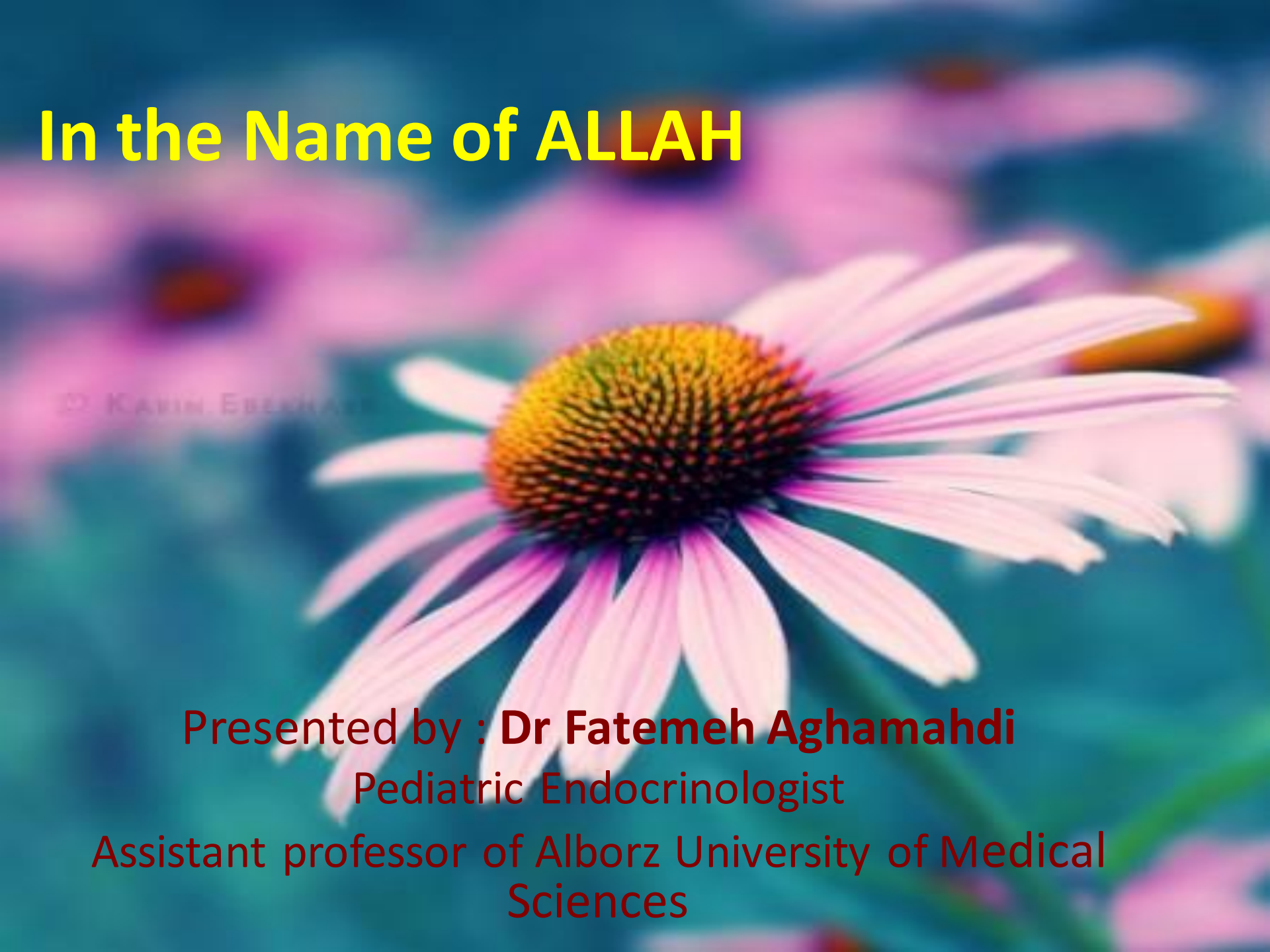
In the Name of ALLAH



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What we will talk in this lecture:

- DKA Complications
  - Common Complications
  - Serious Complications
- Insulin Therapy after DKA
  - Insulin Types
  - Insulin Dosage

References:

- NATIONAL CLINICAL GUIDELINE Management of Paediatric Diabetic Ketoacidosis
- European Society for Paediatric Endocrinology (ESPE)[3]
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Common Complications

- Inadequate rehydration
- Hypoglycemia
- Hypokalemia

Serious Complications

- **Cerebral Edema**
- Pulmonary Edema
- CNS Hemorrhage or Thrombosis
- Cardiac Arrhythmias
- Pancreatitis
- Renal Failure

Cerebral edema due to DKA is almost exclusively a pediatric condition

Cerebral Edema

- CE occurs in 0.3%- 1% of all episodes of DKA
- Initial 24 hours of treatment
- Younger children (< 4 yrs)
- Delayed diagnosis
- Greater dehydration and acidosis, lower pCO2
- Insulin given before fluids

Etiology of CE

- ***Vasogenic*** - excessive accumulation of water and solutes in the interstitial space, due to dysfunction of the blood-brain barrier
- ***Cytotoxic*** - excessive accumulation of water and solutes in the intracellular space, due to dysfunction of cell-volume regulatory mechanisms
- **Both** forms may co-exist

Clinical Factors Associated with *Cerebral Edema*

- Prolonged Illness
- Severe acidosis - low PA CO_2
- Severe dehydration
- Bicarbonate therapy
- Persistent hyponatremia
- Excessive fluid admistration
- Insulin given before fluids

Cerebral Edema, Signs and Symptoms

- Headache and slowing of heart rate
- Change in neurological status
- incontinence or specific neurological signs
- Rising BP, decreased O2 saturations
- Late signs such as seizures, papilloedema and respiratory arrest are associated with a very poor prognosis

Management

- ✓ Contact ***Consultant*** Paediatrician/Endocrinologist and Anaesthetist immediately
- ✓ Exclude ***hypoglycaemia*** as a cause of neurological deterioration
- ✓ ***Mannitol*** (0.5g – 1g/kg over 10-15mins) or ***Hypertonic Sodium Chloride*** (2.5mL -5 mL/kg of Sodium Chloride 3%w/v solution)
- ✓ ***Reduce maintenance fluid infusion rate*** by one third and also recalculate rehydration to deliver over 72 hours (instead of 48 hours)

Management:

- ✓ Nurse at ***45 degree*** angle
- ✓ ***Transfer to PICU/ICU*** (if not there already)
- ✓ Consider ***imaging*** and Neurosurgical consult
- ✓ Consider either - ***Mannitol infusion*** - 0.25g/kg/hr or Mannitol 20%- 1g/kg every 6 hours


NovoRapid®
FlexPen®
Apidra SoloStar
Lantus SoloStar
100 Units/ml - 100 Unità/ml
Solution injectable en stylo prérempli
Solution for injection in a pre-filled pen
KwikPen
100 U/mL
injection
Insulin glargine
SC use
NovoMix® 30
FlexPen®
Levemir®
FlexPen®

Types of Insulin

TABLE 1 Types of insulin preparations and suggested action profiles for s.c. administration

Insulin type	Onset of action (h)	Peak of action (h)	Duration of action (h)
Ultra-rapid acting analog (faster aspart)[a,c]	0.1-0.2	1-3	3-5
Rapid-acting analogs (aspart, glulisine, and lispro)	0.15-0.35	1-3	3-5
Regular/soluble (short acting)	0.5-1	2-4	5-8
NPH*	2-4	4-12	12-24[a]
Basal long-acting analogs			
Glargine[b]	2-4	8-12	22-24[a]
Detemir	1-2	4-7	20-24[a]
Glargine U300*+*	2-6	Minimal peak	30-36
Degludec[c]	0.5-1.5	Minimal peak	>42

Methods of Insulin Therapy

- Glucose and meal-adjusted injection regimens
- Less-intensive regimens
- Fixed insulin dose regimens
- Pump therapy
- Sensor-augmented therapies

DISTRIBUTION OF INSULIN DOSE

- During the partial remission phase, the total daily insulin dose is often <0.5 IU/kg/day.
- After partial remission phase

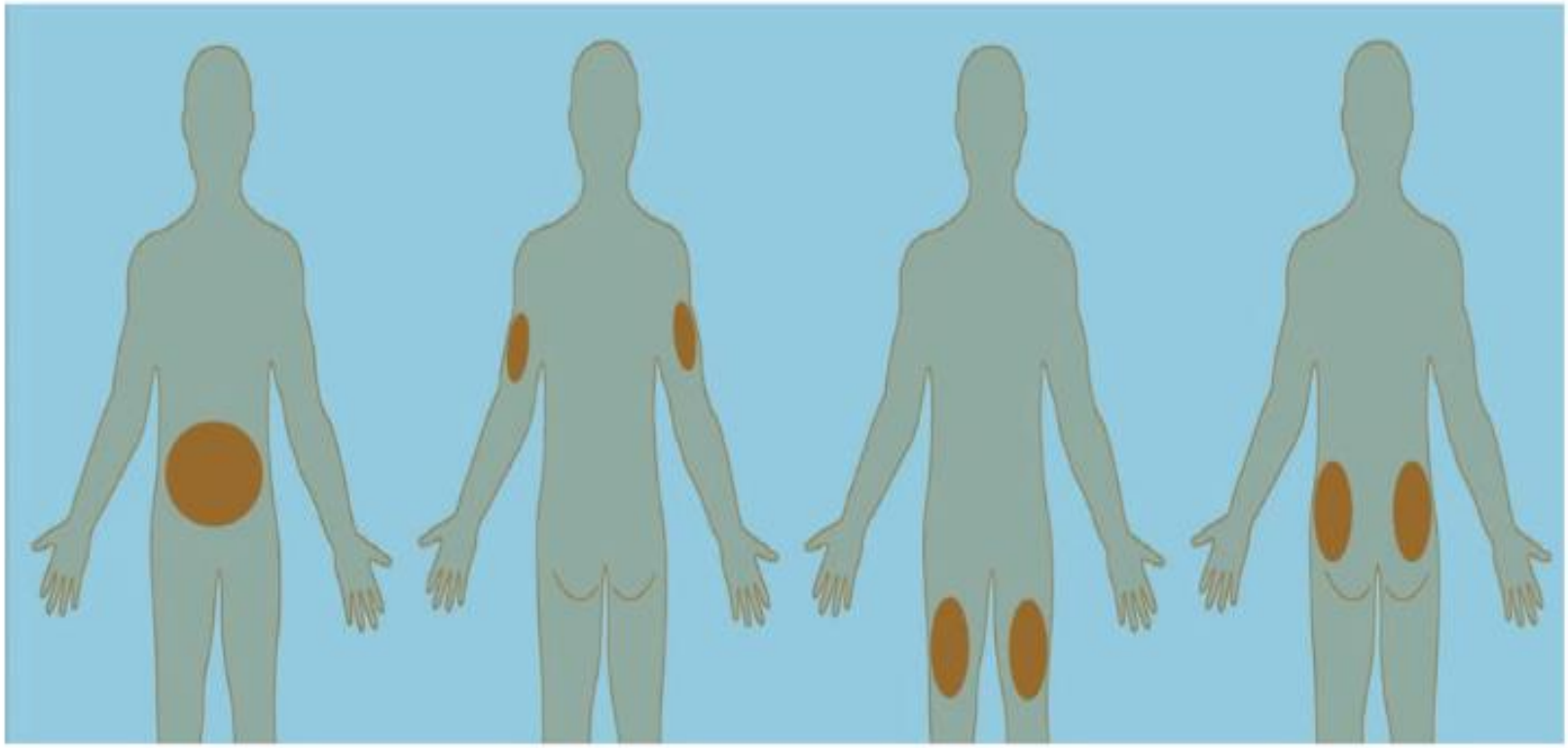
  ✓ Prepubertal children usually require 0.7 to 1.0 IU/kg/day.

  ✓ During puberty, requirements may rise substantially above 1 and even up to 2 U/kg/day.

❖ In children on basal-bolus regimens, the basal insulin may represent between 30% (typical for regular insulin) and 50% (typical for rapid-acting insulin) of total daily insulin.

Injection sites and speed of absorption

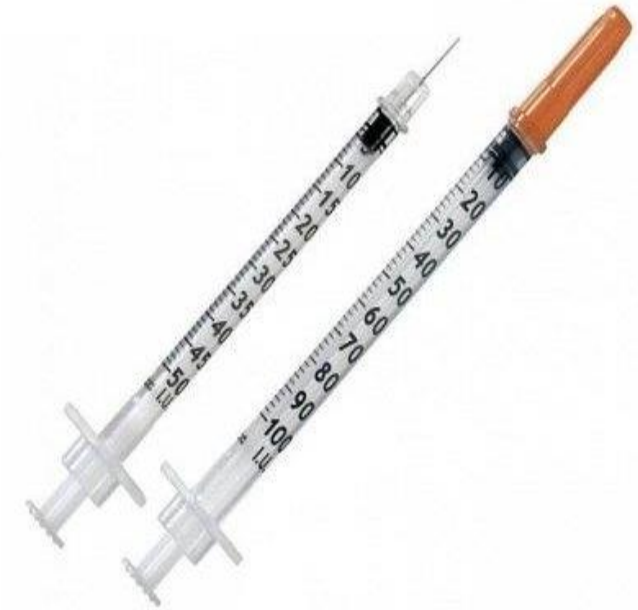
Abdomen	Lateral aspect of arm	Front of thigh/lateral thigh	Lateral upper quadrant of the buttocks
~15 min	~ 20 min	~30 min	~30 min
quick	*intermediate*	*slow*	*slow*

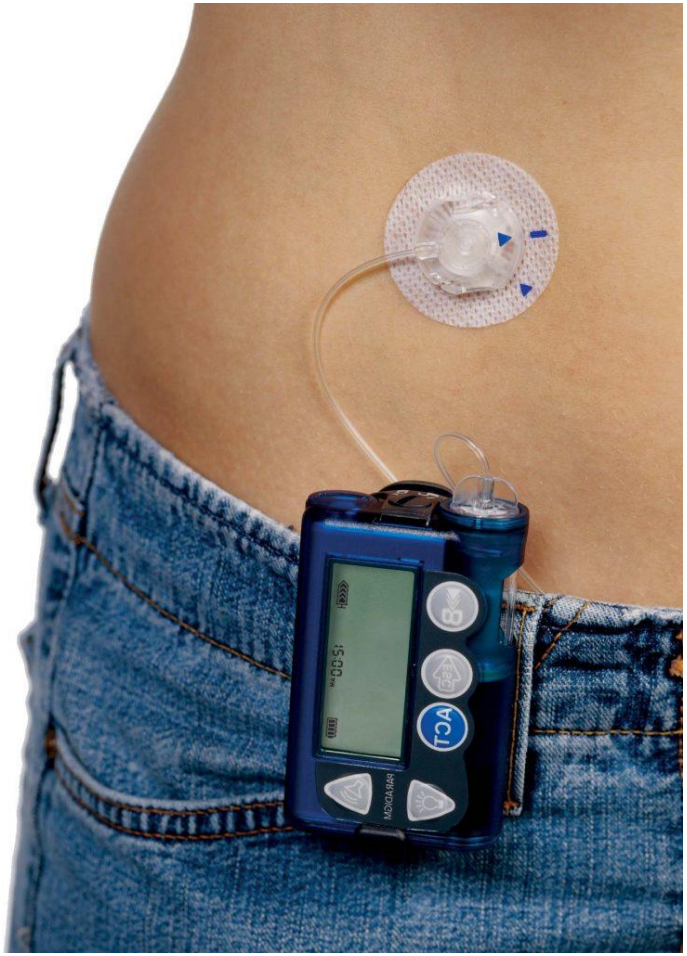


Schematic representation of injection sites and relative timing of insulin absorption. For details see Reference [100]

Devices for insulin delivery

- Insulin syringes
- Pen injector devices
- Subcutaneous indwelling catheters
- Automatic injection devices
- Jet injectors
- Continuous subcutaneous insulin infusion
- Sensor-augmented pump therapy and “closed loop”





Blood sugar levels in mg/dl	Level	Symptoms	A1C test results
400-800	Very high	Stomachache, difficulty breathing	
200-400	High	Low energy	
80-200	Goal, under 5 years	Fine!	< 8.5%
70-180	Goal, 5 to 11 years	Fine!	< 8.0%
70-150	Goal, 12 years and up	Fine!	<7.5%
70-120	Normal	Fine!	

TABLE 1 Glycemia and blood glucose target recommendations

Target HbA1c	HbA1c <53 mmol/mol (<7.0%) • This target must be individualized with the goal of achieving a value as close to normal as possible while avoiding severe hypoglycemia, frequent mild to moderate hypoglycemia, and excessive stress/burden for the child with diabetes and their family. • Factors that must be considered when setting an individualized target include, but are not limited to: ◦ Access to technology, including pumps and CGM ◦ Ability to articulate symptoms of hypoglycemia and hyperglycemia ◦ History of severe hypoglycemia/hypoglycemic unawareness ◦ History of compliance with therapy ◦ Whether child is a high or low glycator ◦ Whether child has continued endogenous insulin production (eg, in the new onset or "honeymoon" period of diabetes)			
Necessary elements for successful glycemic management	• HbA1c measurements at least quarterly • Glucose monitoring using CGM or self-monitored BG measurements up to 6 to 10 times per day • Regular review of glucose values with therapy adjustments as necessary			
Glycemic targets		**NICE goal A1c** ≤48 mmol/mol (≤6.5%)[49]	**ISPAD goal A1c** <53 mmol/mol (<7%)	**ADA goal A1c** <58 mmol/mol (<7.5%)[50]
	Premeal	4.0-7.0 mmol/L (70-126 mg/dL)	4.0-7.0 mmol/L (70-130 mg/dL)	5.0-7.2 mmoL/L (90-130 mg/dL)
	Postmeal	5.0-9.0 mmol/L (90-162 mg/dL)	5.0-10.0 mmol/L (90-180 mg/dL)	
	Prebed	4.0-7.0 mmol/L (70-126 mg/dL)	4.4-7.8 mmol/L (80-140 mg/dL)	5.0-8.3 mmol/L (90-150 mg/dL)

Abbreviations: ADA, American Diabetes Association; BG, blood glucose; CGM, continuous glucose monitoring; HbA1c, hemoglobin A1c; ISPAD, International Society for Pediatric and Adolescent Diabetes; NICE, National Institute for Health and Care Excellence.

Insulin Therapy – Key Message

- ✓ Insulin is the **mainstay** of medical management
- ✓ The choice of insulin regimen depends on many factors:
  - Age
  - Weight
  - Stage of puberty
  - Duration and phase of diabetes
  - State of injection sites
  - Nutritional intake and distribution
  - Exercise patterns
  - Daily routine
  - Results of blood glucose monitoring and glycated hemoglobin
  - Intercurrent illness
  - Family lifestyle
  - Socioeconomic factors
  - Family, patient, and physician preferences

Insulin Therapy – Key Message

- ✓ Insulin treatment must be started as soon as possible after diagnosis (usually within 6 hours if ketonuria is present) to prevent metabolic decompensation and diabetic ketoacidosis

- ✓ Insulin therapy must be individualized for each patient in order to
  achieve optimal metabolic contro

Thanks for your attention