Management of Type 1 Diabetes (ISPAE module for Pediatricians 2023-24)

Dr. Zalak Upadhyay
Dr. Akanksha Parikh
Dr. Abraham Paulose
Dr. Rakesh Kumar
Dr. Aspi Irani

Outline

- Prevalence/Incidence
- Diagnosis
- Diabetic ketoacidosis (DKA) Management
- Ambulatory Management
  - ✓ Insulin
  - ✓ Monitoring
  - ✓ Medical Nutrition therapy
  - ✓ Exercise
  - ✓ Hypoglycemia and Sick day management
- Recent advances in management

Prevalence of T1D in children and adolescents in 2021

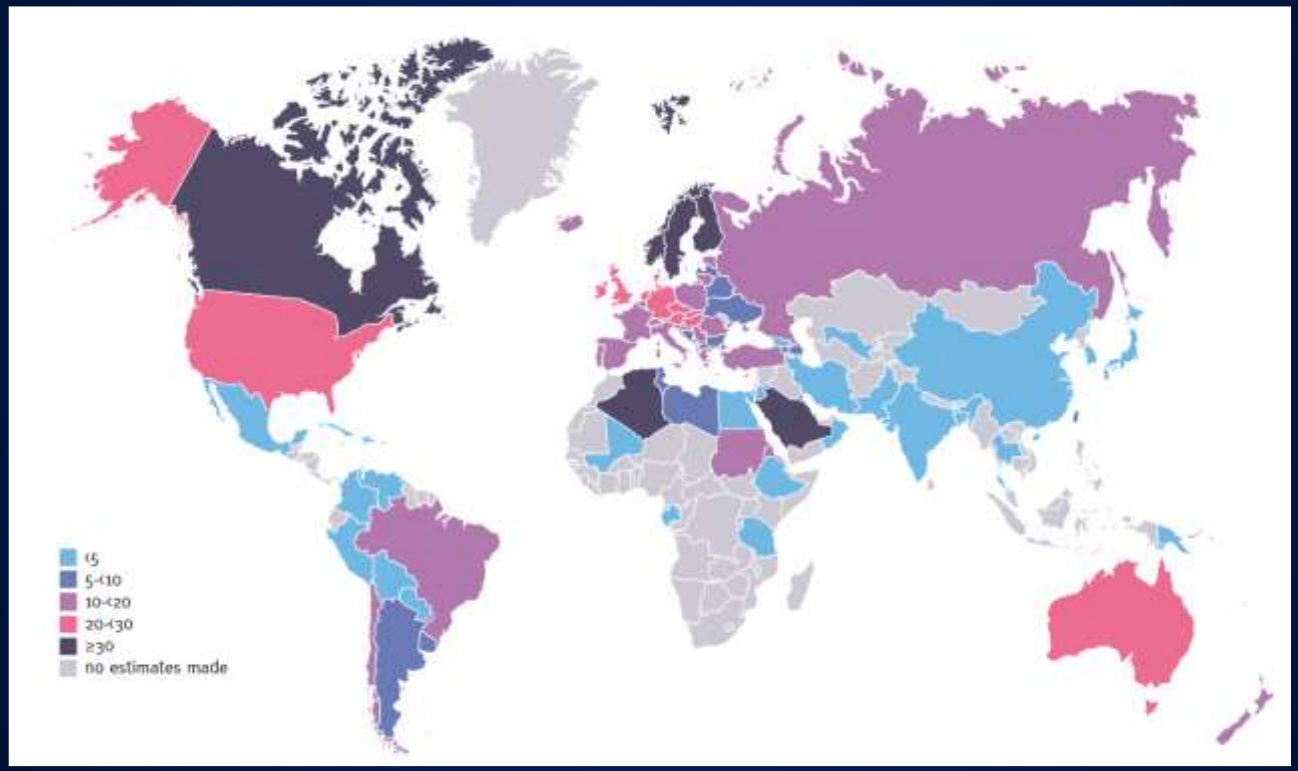
Type 1 diabetes in children an	
Number of prevalent (existing	651,700
Number of incident (new) case	108,300
Type 1 diabetes in children an	
Number of prevalent (existing	1,211,900
Number of incident (new) case	149,500

Rank	Country or territory	Number of children and adolescents with type 1 diabetes (0–19 years) in thousands
1	India	229.4
2	United States of America	157.9
3	Brazil	92.3
4	China	56.0
5	Algeria	50.8
6	Morocco[i]	43.3
7	Russian Federation	38.1
8	Germany	35.1
9	United Kingdom	31.6
10	Saudi Arabia	28.9

IDF Atlas, 2021

IDF Atlas, 2021

Global Incidence rates/lac/year (0-14 y)



IDF Atlas, 2021

Incidence of T1D in children and adolescents (0–19 y) in 2021

India- < 5 /lac population below 14 y

INDIA ON TOP!

Rank	Country or territory	Number of incident (new) cases (0–19 years) in thousands
1	India	24.0
2	United States of America	18.2
3	Brazil	8.9
4	Algeria	6.5
5	China	6.1
6	Morocco[i]	5.1
7	Russian Federation	4.0
8	Nigeria	3.8
9	Saudi Arabia	3.8
10	Germany	3.6

IDF Atlas, 2021

Diagnosis of Type 1 Diabetes

A, 9 years

- Presented with polyuria and secondary nocturnal enuresis past 2 weeks
- Mother also worried about recent weight loss and weakness, though appetite is good.
- Physical examination - unremarkable
- Consulted family doctor - prescribed a tonic, a de-worming medicine and started on antibiotic for presumed UTI

Case scenario continued…

- A few days later child developed abdominal pain with vomiting and breathlessness
- Went to ER and doctor on duty did random blood glucose and venous blood gas
- RBS was 250 mg/dL with pH 7.1, HCO_3^- 6 mEq/L

Presentation of new-onset T1D

OPD: (symptoms due to hyperglycemia)

- Polyuria
- Polydipsia
- Secondary nocturnal enuresis
- Polyphagia
- Weight loss/Fatigue
- Skin infections
- Oral or vaginal thrush- recurrent/ persistent
- Blurred vision
- Mood changes

Emergency Room: (presentation with ketoacidosis)

- Acute abdominal pain, vomiting
- Tachypnea/air hunger good air entry & no adventitious sounds
- Dehydration (accompanied with polyuria)
- Drowsiness
- *Consider DKA in DD of acute abdomen, tachypnea, altered sensorium*

Mayer-Davis EJ, Kahkoska AR, Jefferies C, Dabelea D, Balde N, Gong CX, Aschner P, Craig ME. ISPAD Clinical Practice Consensus Guidelines 2018: Definition, epidemiology, and classification of diabetes in children and adolescents. Pediatr Diabetes. 2018 Oct;19 Suppl 27(Suppl 27):7-19.

To confirm diabetes!!!

- Signs/symptoms of DM (polyuria, polydipsia, weight loss, polyphagia) with RBS > 200 mg/dL

OR

- Hemoglobin A1c ≥ 6.5 %

OR

- Fasting (> 8 hours) ≥ 126 mg/ dL

OR

- 2 hour plasma glucose level ≥ 200 mg/dL during oral glucose tolerance test (1.75 gm/ kg- max 75 gm glucose orally)

- Start treatment immediately, when suspected DKA, with RBS > 200 mg/ dL in clinic, with moderate to large ketones by ketone meter or urine ketodiastix.

Management of DKA

Definition of DKA and its severity

Child may present in DKA with abdominal pain, vomiting, deep sighing respiration, tachycardia, dehydration, confusion, drowsiness, loss of consciousness

Biochemical Criteria	Severity of DKA (based on VBG)
• BG > 200 mg/dL (usually)	• Mild: pH <7.3, HCO_3^- < 18 mmol/L
• Acidosis: pH < 7.3, HCO_3^- < 18 mmol/L	• Moderate: pH <7.2, HCO_3^- <10 mmol/L
• Ketonemia/Ketonuria	• Severe: pH < 7.1, HCO_3^- < 5 mmol/L

Initial management of DKA

- **Emergency assessment** by PALS & e**mergency measures:**
- Secure airway, provide O_2, insert NG tube if required
- Secure 2 peripheral IV catheters (avoid central line)
- Assess severity of dehydration (clinically unreliable)
- Assess level of consciousness (use GCS)
- Blood samples-VBG, blood glucose, beta-hydroxy butyrate, CBC, S. electrolytes, BUN, S. creatinine, S. calcium, S. phosphorus, urine analysis, ECG, cultures (when required)
- Start Rx before lab reports come in

Goals of therapy

- Restore circulation
- Correct dehydration & electrolyte imbalance
- Correct acidosis and reverse ketosis with insulin
- Restore BG gradually to near normal
- Monitor for complications of DKA and its treatment
- Identify and treat any precipitating event

Fluid management - 1st hour

- One or more boluses of 0.9% NS at 10-20 ml/ kg over 30 – 60 minutes to restore peripheral circulation
- If capillary refill time (CRT) prolonged- give over 15 minutes; repeat if needed
- If hypotension, thready pulse - give 20 ml/kg stat, then if needed, 2 more boluses @10 ml/kg. Consider use of inotropes

- **Insulin is never given in the 1st hour**

Fluid management - beyond 1st hour

- Give 0.9 % or 0.45% (both are equally effective*) NS **evenly** over 24-48 hours
- Fluid (ml/hr) = {2 (maintenance fluid) + deficit – bolus} ÷ 47 (or 35 or 23 i.e. total hours – hour of bolus)
- Calculate deficit as: 5-7% (moderate DKA); 7-10 % (severe DKA)
- **When RBS < 250** – add D5%
- **When RBS < 150** - add D10-12.5%

*Glaser NS, Ghetti S, Casper TC, Dean JM, Kuppermann N, Pediatric Emergency Care Applied Research Network (PECARN) DKA FLUID Study Group. Pediatric diabetic ketoacidosis, fluid therapy, and cerebral injury: the design of a factorial randomized controlled trial. Pediatric Diabetes. 2013 Sep;14(6):435-46.

Potassium, phosphorus, bicarbonate

- **Potassium-** start after 1st hour; if urine output (+) and S. K^+ < 5.5 mEq/L
  - Give @ 40 mmol/L
  - If S. K^+ < 3 mEq/L or ECG changes → K^+ drip in 1st hour @ 0.5mEq/kg with cardiac monitoring *and defer insulin till S. K^+ > 3 mEq/L*
- **Phosphorus –** Needed only if < 1 mEq/L with rhabdomyolysis, ileus, cardio-respiratory compromise, encephalopathy
- **Bicarbonate – contraindicated;** exceptions 1. life threatening hyperkalemia and 2. compromised cardiac function

Insulin Therapy

- Use only Regular insulin
- Start IV insulin infusion after 1 hr of fluid therapy, and provided S. K^+ > 3 mEq/L
- Give at **0.1 U/kg/hr** (can start with 0.05 U/kg/hr for toddlers, in mild DKA or if hypokalemia)
- **No insulin bolus** to be given
- Dilute 50 U of Regular insulin in 50 ml NS → 1U/ml; flush lines well
- Continue insulin infusion till **resolution of DKA** (pH>7.3, HCO_3 > 18 mEq/L, BOHB < 1mmol/L, or closure of anion gap)

Role of subcutaneous insulin in DKA

- In mild to moderate DKA when insulin infusion not possible
- *Not to be used if impaired peripheral circulation*
- Insulin analogs:- 0.15 U/kg every 2 hr (start 1 hour after fluid replacement); ↓ dose to 0.1 U/kg every 2 hr if BG ↓ by > 100 mg/dL per hour even after adding dextrose
- Regular insulin:- 0.13-0.17 U/kg/dose every 4 hr (0.8-1U/kg/day in divided doses). ↓/↑ dose by 10-20 % based on BG

Transition from IV to SC insulin in DKA

- When ketoacidosis is corrected, patient is ready to eat and meal is due
- Give rapid acting analog 15-30 min before or Regular insulin 1-2 hours before stopping iv infusion
- Basal dose can be given the night prior

Cerebral Edema

- Usually develops after starting Rx, rarely at presentation
- High index of suspicion-start Rx immediately if suspected
- Anticipate cerebral edema:
  - Younger age, new onset diabetes, longer duration of symptoms
  - Severe acidosis, ↑↑ BUN
  - Bicarbonate treatment/insulin administered in 1st hour
- Suspect when: new onset headache, recurrence of vomiting, Cushing triad, change in neurological status, focal neurological signs

Management of cerebral edema

- Initiate treatment at suspicion
- Decrease IV fluid rate by 1/3rd
- Elevate head end by 30 degrees
- Mannitol 0.5-1 g/kg over 10-15 min, repeat in 30 min to 2 hrs if no initial response
- 2.5-5 ml/kg of 3% NS over 10-15 min as alternative if no initial response to mannitol
- Intubate if impending respiratory failure
- **Cranial imaging only after initiating Rx (when child is stable)**

Ambulatory management of T1D

ISPAE

Comprehensive Management by a Pediatric Diabetes Team

Work up for a child with newly diagnosed DM

Routinely indicated:

Tests to look for associated autoimmune disorders, other comorbidities:-

- Total IgA, anti TTG IgA
- Anti thyroid antibodies
- TFT
- Lipid profile

Only if indicated:

Tests to confirm T1D/ exclude other causes of diabetes:

- C peptide with simultaneous blood glucose
- Antibody testing – GAD 65, IA-2,IAA, ZnT8
- Genetic work up (Neonatal/MODY)

All diabetes in children is not T1D!!

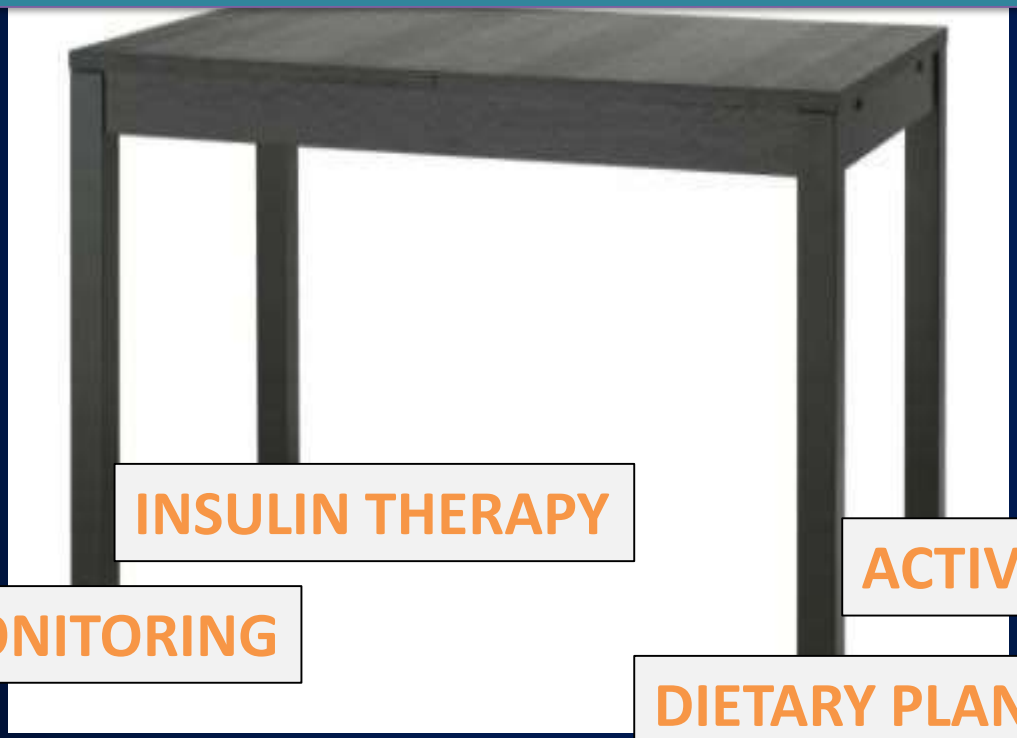
EXCEPTIONS

- < 6 months
- Overweight or obese adolescents with acanthosis with/without ketosis
- Strong (3 gen) family history of DM (MODY)
- Dysmorphisms
- Syndromic features

Medication – Insulin therapy

“4-legged table” approach

BLOOD GLUCOSE CONTROL



INSULIN THERAPY

MONITORING

ACTIVITY/EXERCISE PLAN

DIETARY PLAN

Accessories

- Technology
- CGM
- Insulin Pumps
- Support Groups
- Advocacy
- Social Support

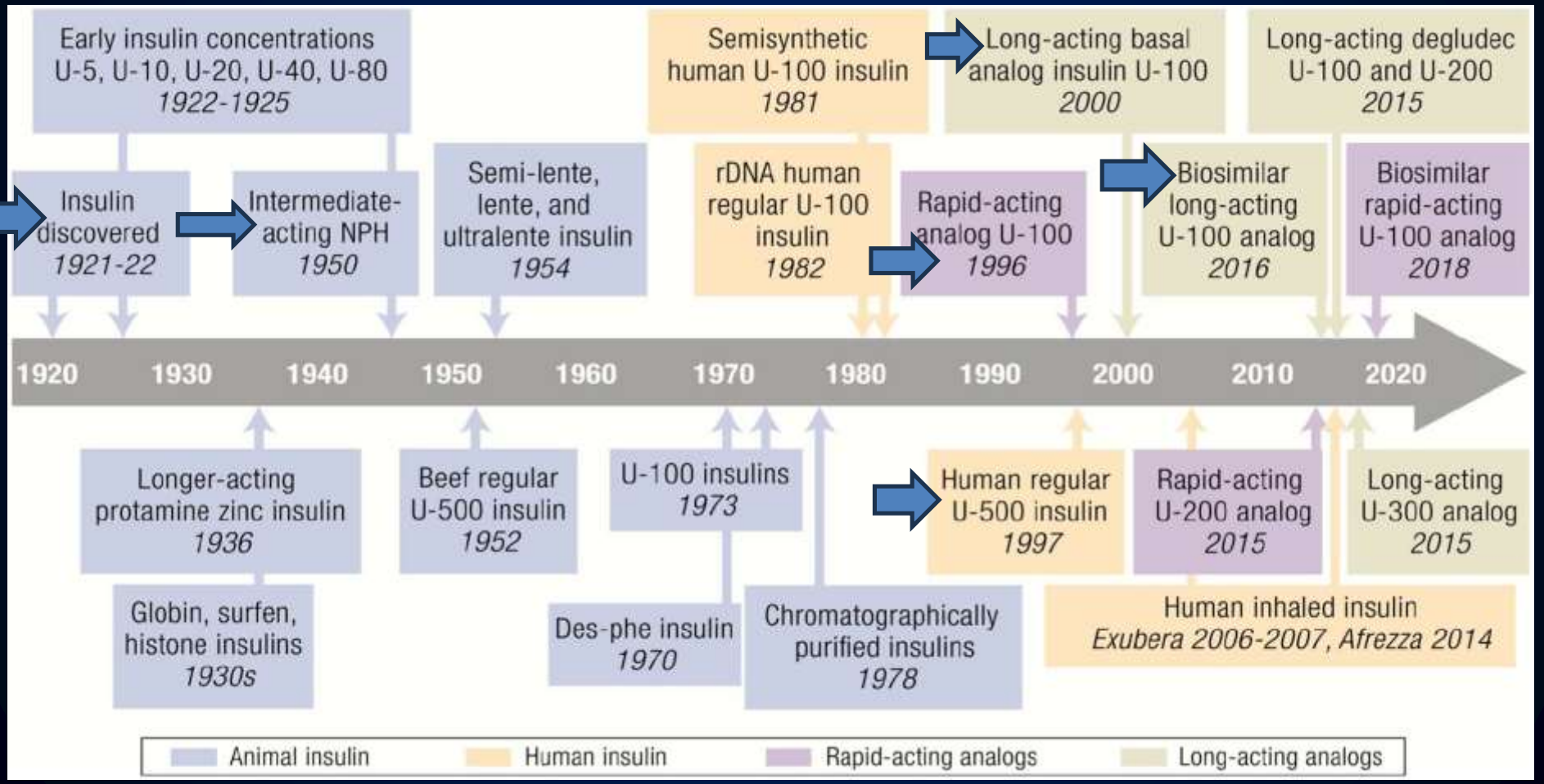
Diabetes self-management education (DSME) and Psychosocial support

Quiz

1. Who is in the picture ?
2. Name of the dog ?
3. When do we celebrate world diabetes day and why?

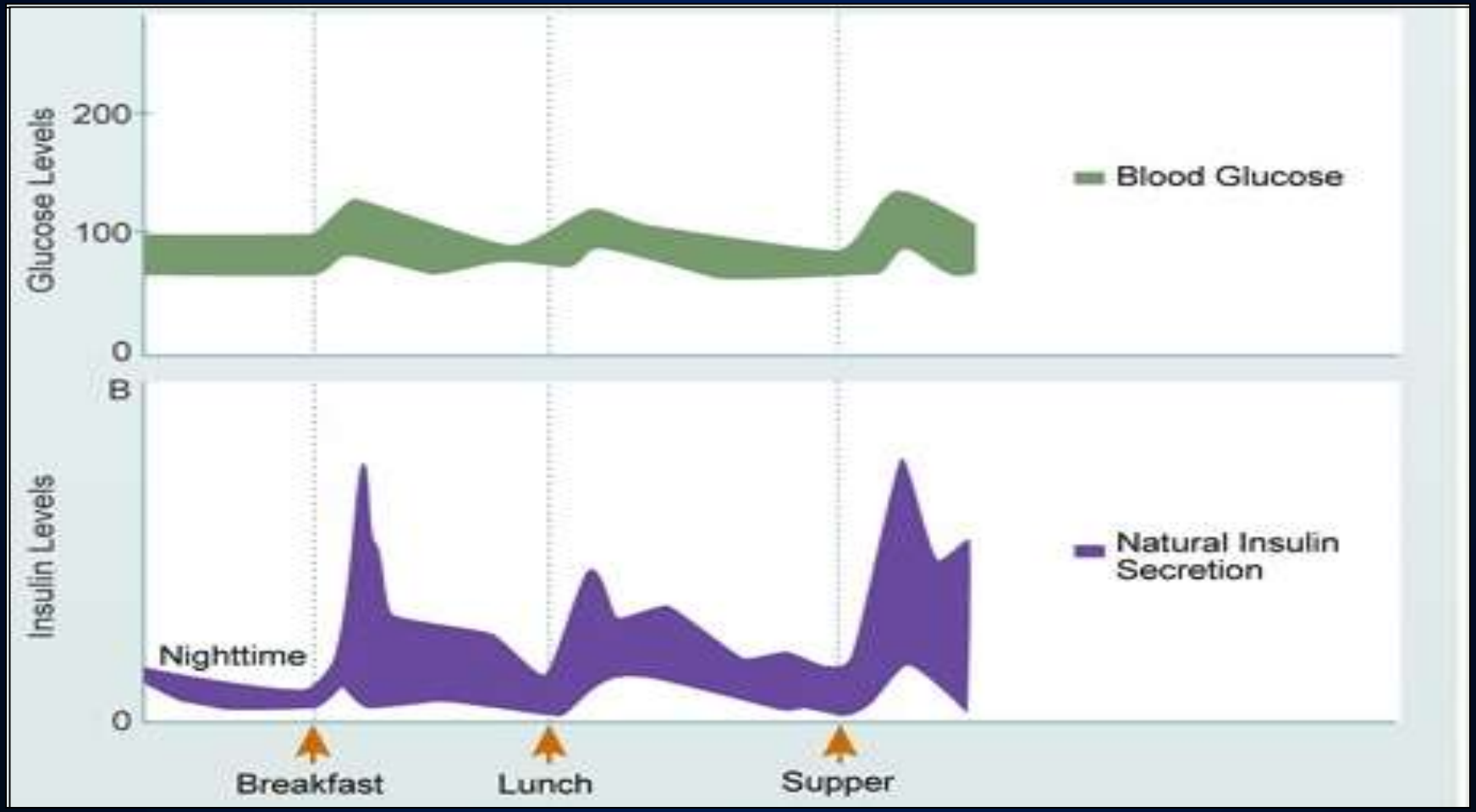
More than 100 years of insulin discovery

History of insulin discovery



Kishor Sharma J, Sharma D, Gupta A. A glorious past, dynamic present and a promising future: Insulin at 100. Journal of the Royal College of Physicians of Edinburgh. 2022;52(1):59-64.

Physiological basis of insulin therapy

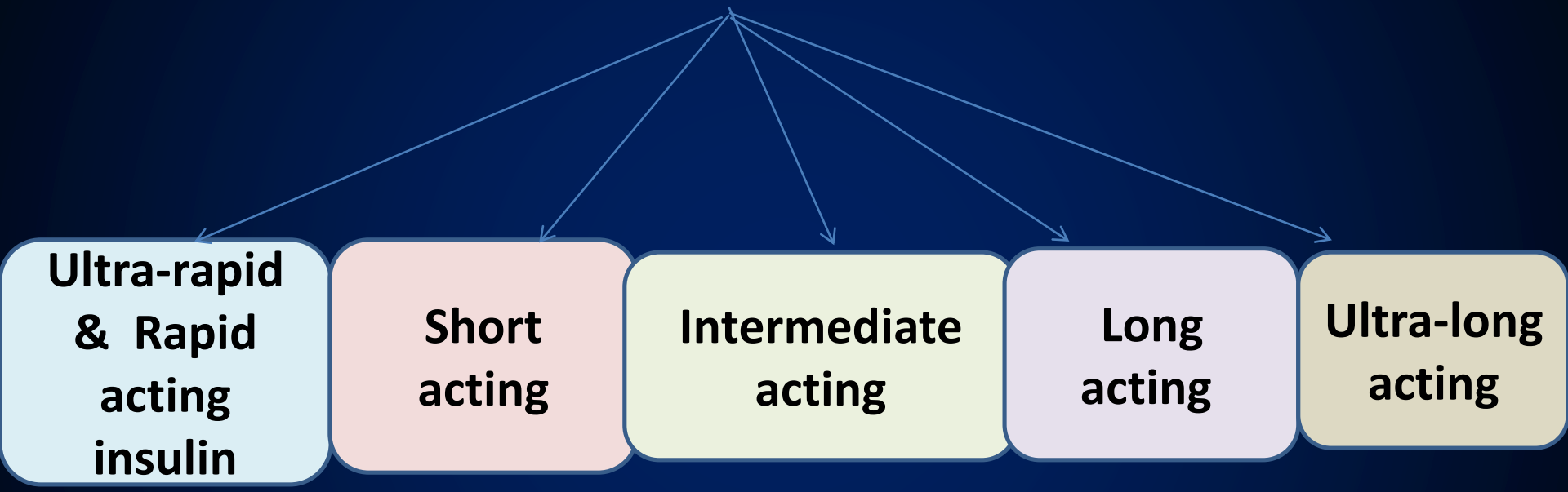


Normal physiology

A normal, healthy pancreas releases insulin:

- Continuously (between meals and overnight): to enable all cells to take up insulin; suppress hepatic glucose output; prevent ketogenesis: (BASAL insulin)
- Sharp rise prandially to promote glucose utilization and storage in liver/muscle: (BOLUS insulin)
- Pancreas releases insulin as per ambient blood glucose, and with very short half-life, thus maintains blood glucose within very narrow range of normal as rapid correction is possible
- The insulin released by pancreas, be it for basal action or as bolus, has same half life

Classification – based on their time-action profile

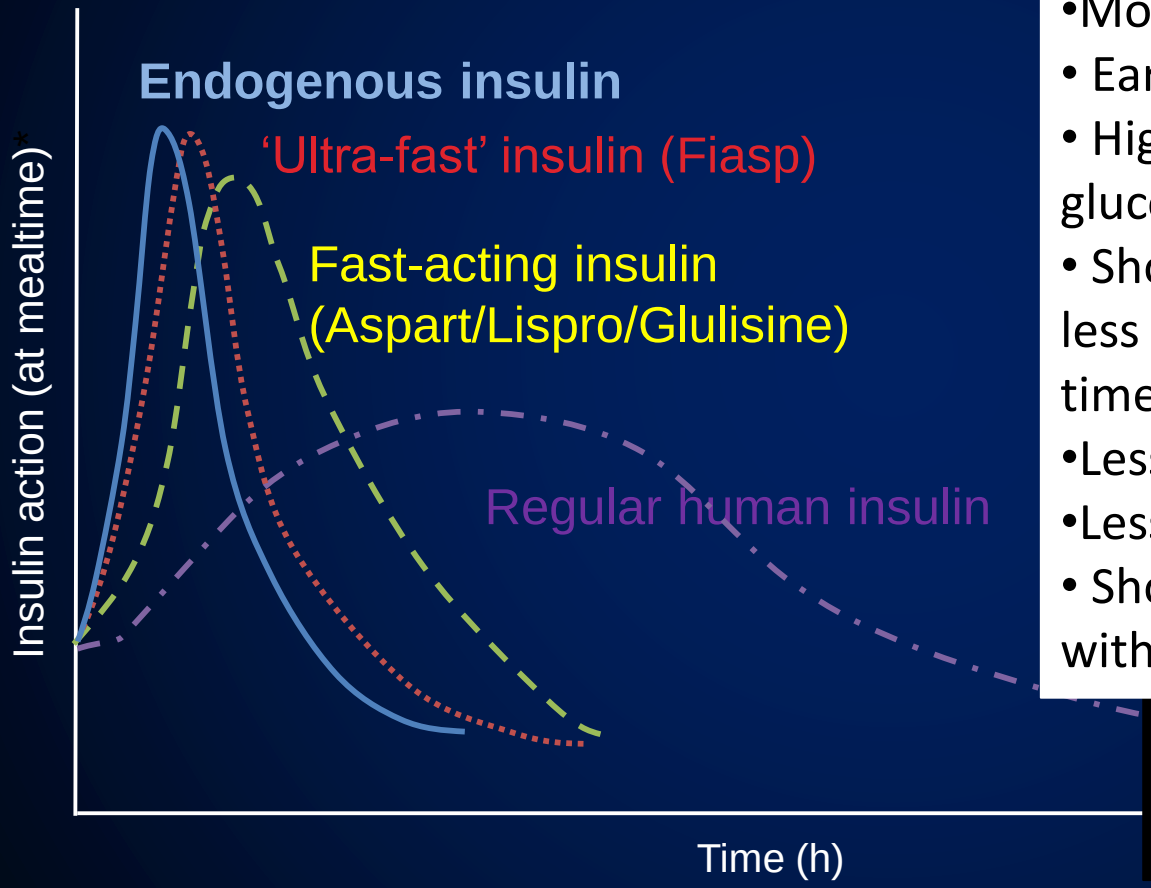


Premixed insulins
Not recommended

Insulin – Action Profile

Insulin Types	Onset of Action (h)	Peak of Action (h)	Duration of Action (h)
ULTRA RAPID ACTING – Fiasp, Lyumjev	0.1 - 0.2	1 - 3	3 – 5
RAPID ACTING – Aspart, Lispro, Glulisine	0.15 - 0.35	1 - 3	3 - 5
SHORT ACTING – Regular	0.5 - 1	2 - 4	5 – 8
INTERMEDIATE ACTING – NPH	2 - 4	4 - 12	12 - 24
LONG ACTING – Detemir Glargine U(100)	1-2 2-4	4 - 7 8 - 12	18 – up to 23 22 - 24
ULTRA LONG ACTING Degludec Glargine U(300)	0.5-1.5 2-6	Minimal peak Minimal peak	42 30 - 36

Fast-acting insulin analogs vs Regular insulin

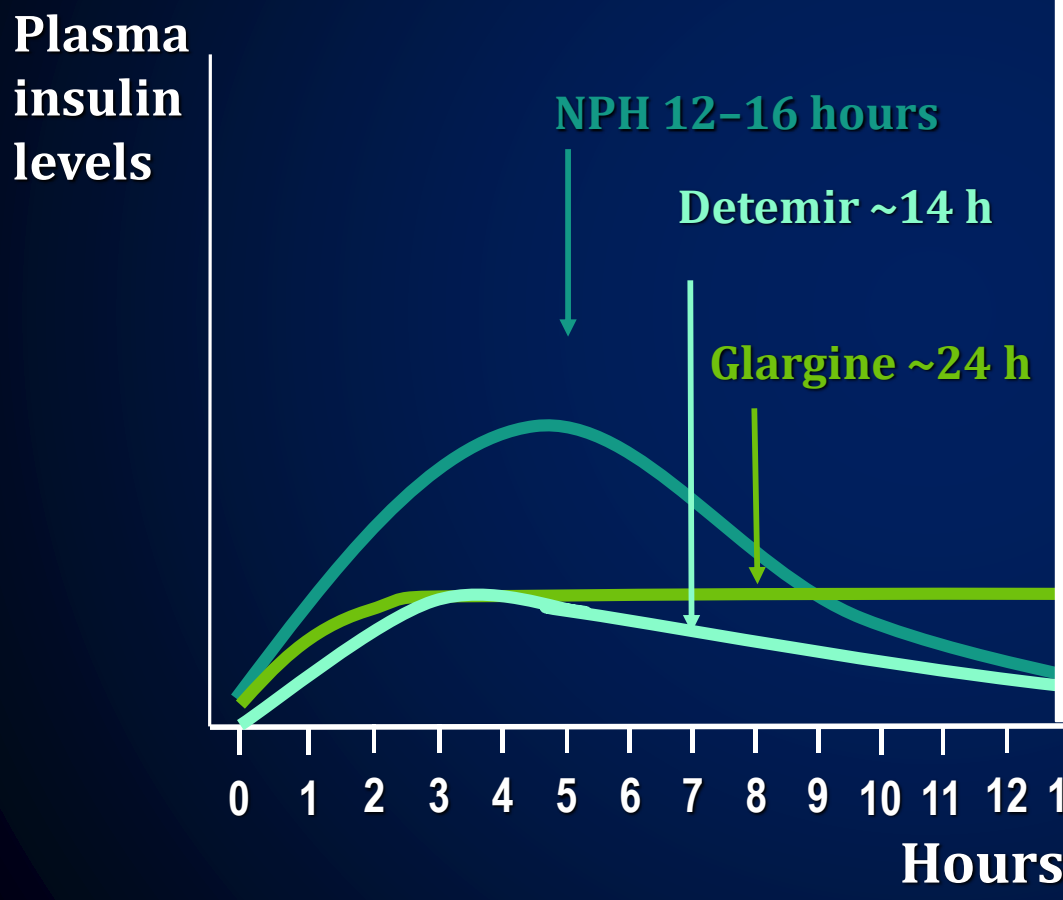


*Schematic representation

- More rapid onset of action
- Earlier peak (1 h)
- Higher peak giving better PP glucose control
- Shorter duration of action hence less hypo between meals & night time
- Less variability
- Less risk of nocturnal hypoglycemia
- Shorter waiting time – more so with Fiasp

Adapted from Home PD. Diabetes Obes Metab 2015;17:1011–20

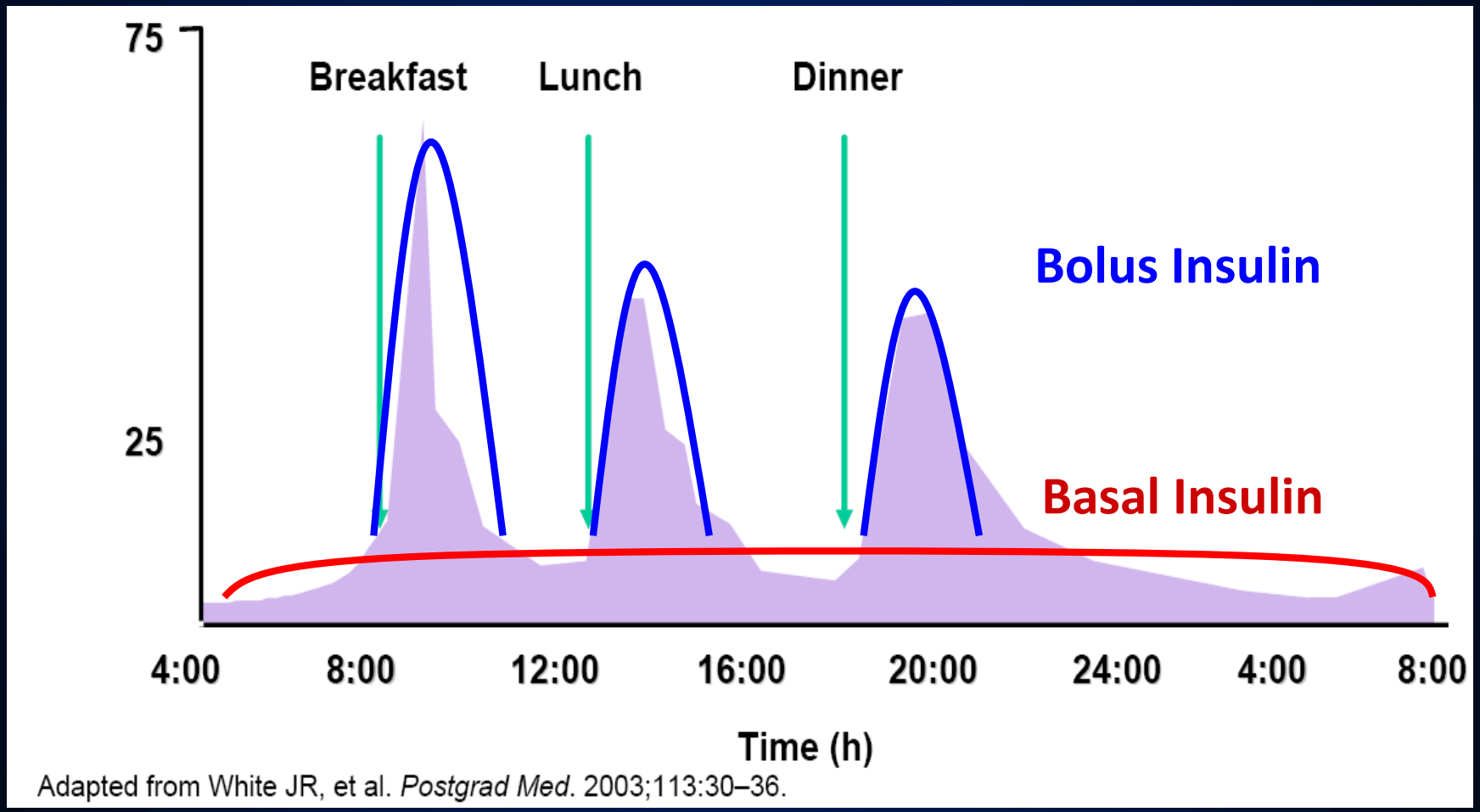
Action Profiles of NPH insulin vs. long-acting analogs



- Longer duration of action
- Less variability
- Absence of significant peak effect, hence less need for evening snack/ lower risk of nocturnal hypoglycemia
- Favorable effect on weight
- Glargine –usually given once a day in 80%
- NPH and Detemir – usually given 2 times a day
- NPH – used as a bolus in select situations

Burge MR, Schade DS. *Endocrinol Metab Clin North Am*. 1997;26:575-598; Barlocco D. *Curr Opin Invest Drugs.* 2003;4:1240-1244; Danne T et al. *Diabetes Care.* 2003;26:3087-3092

Ideal Insulin Replacement Strategy



Adapted from White JR, et al. *Postgrad Med*. 2003;113:30–36.

The basal/bolus Insulin concept

- **The ideal insulin replacement strategy**
- **Basal insulin (once/twice a day at fixed time)**
  - Suppresses glucose production between meals and overnight
  - 30-50% of daily needs
- **Bolus insulin (before meals)**
  - Limits hyperglycemia after meals

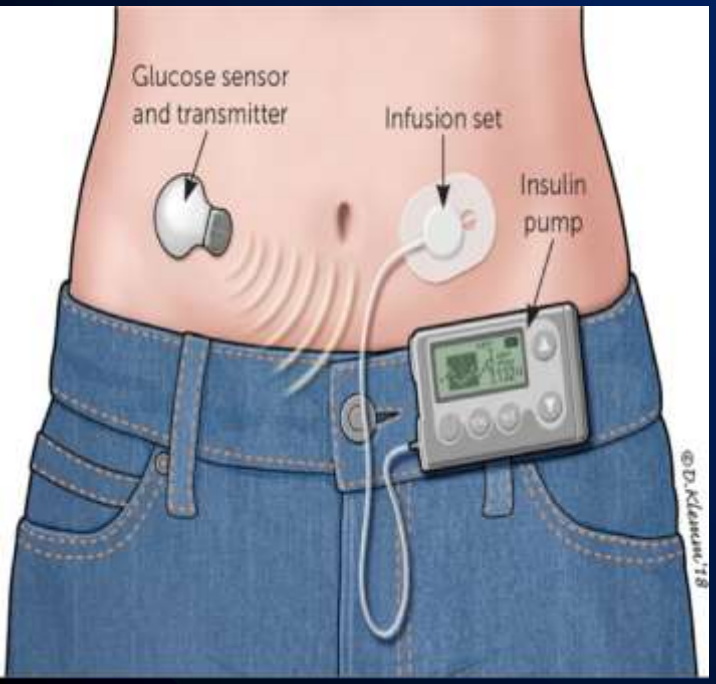
A classification of insulin regimens

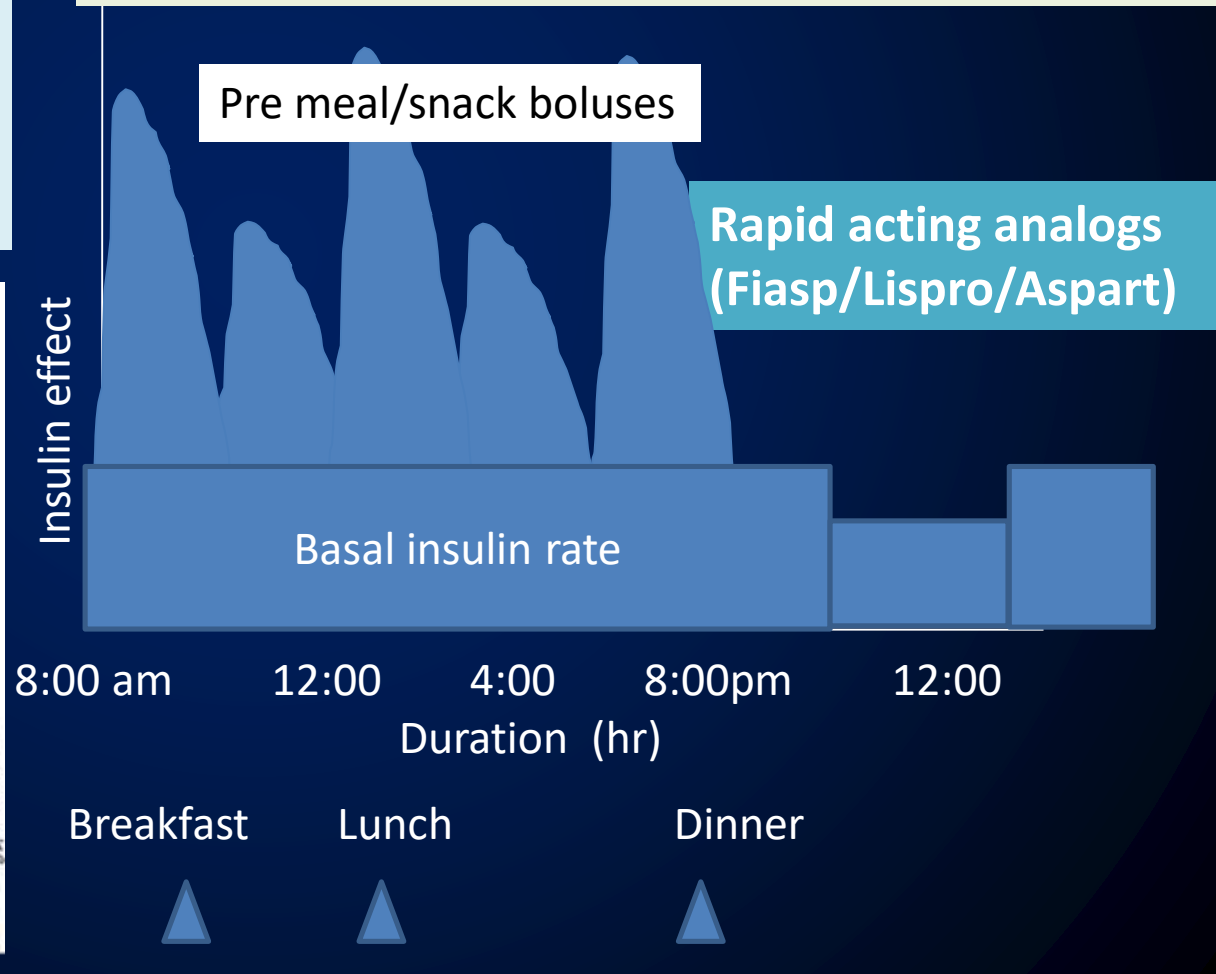
1) Basal bolus with CSII (continuous subcutaneous insulin infusion, using insulin pump)
2) Basal bolus with glargine or detemir plus a rapid acting insulin analog
3) Basal bolus using a combination of Regular insulin and analogs
4) Basal bolus using human insulins only; R 3 doses and 2 doses NPH
5) Two-dose regimen (also referred to as split-mix regimen using Regular insulin & NPH)

Basal bolus with CSII

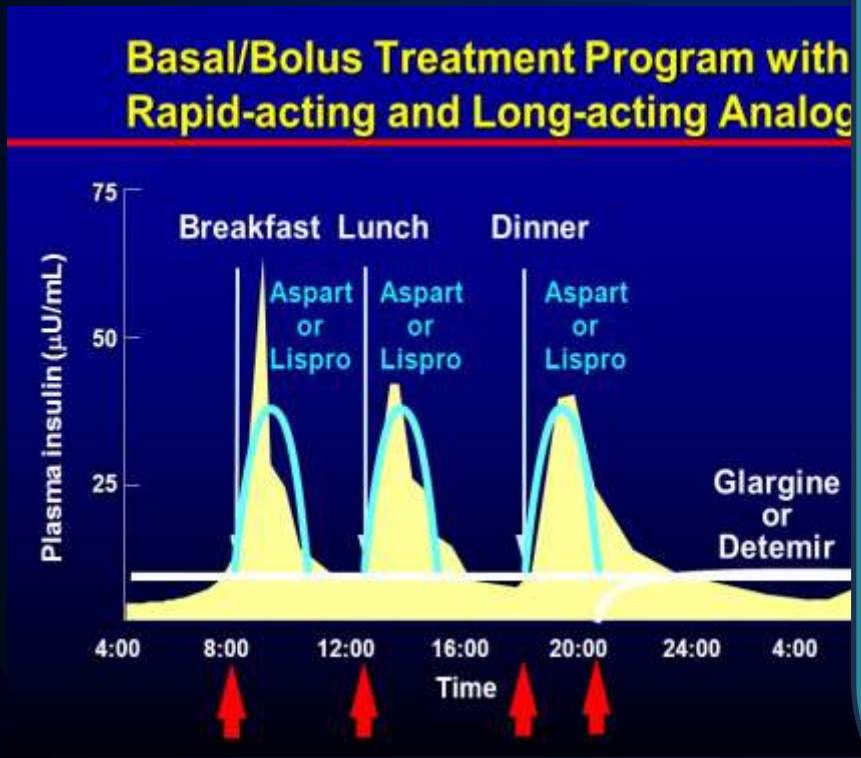
- Only rapid insulin as basal and bolus (more physiological)
- Multiple boluses possible (including snacks)
- Bolus calculators- different types of boluses to better match meal composition
- Basal rates can be varied over 24 hours
- Fractional doses can be given

- Can be integrated with CGM
- Automated basal rates (hybrid close loop)
- Alarms and guards against hypoglycemia





Basal bolus with analogs



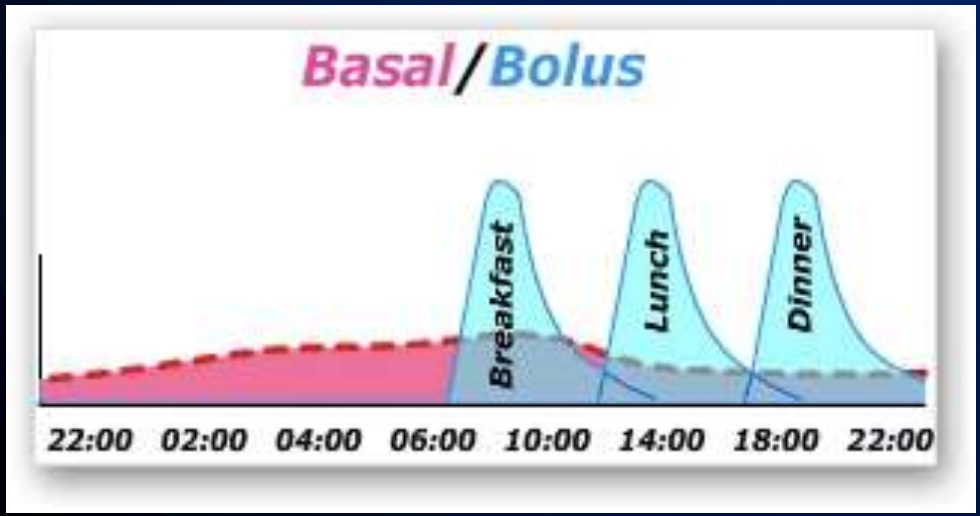
This "intensive insulin therapy" uses **basal analogs** (glargine/detemir, *or* degludec/glargine U300), ensuring less glycemic variability and less nocturnal hypo; with pre-meal/pre-snack **bolus analogs** (lispro/aspart/glulisine), ensuring better post-meal BG and lesser pre-meal hypo. *After CSII, it's the next best option for ideal insulin replacement.*

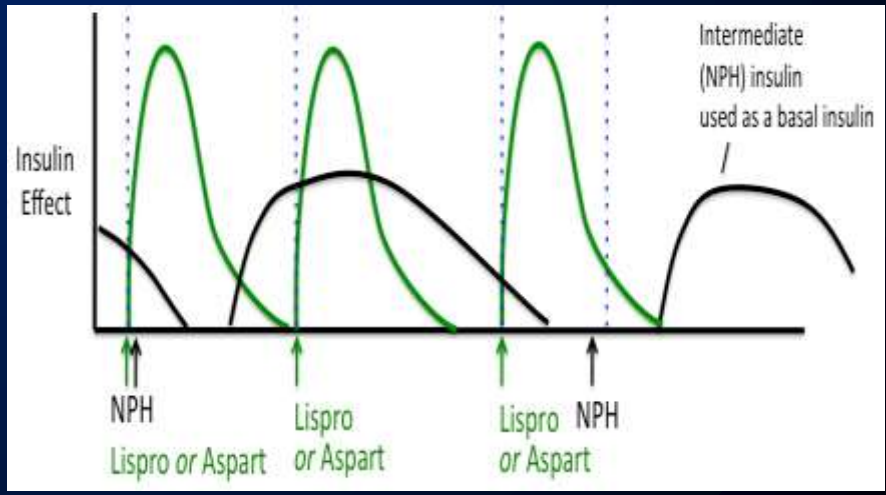
Basal bolus regimen: human insulin and analogs

To be used only when cost is a concern

When glargine is used as basal with regular insulin used as bolus. *Alert:* may lead to insulin stacking. Avoid repeated boluses.
Note: as regular insulin has long duration of action, requirement of basal inulin will be less.

When NPH is used as basal insulin; given twice daily (a compromise): significant day-to-day variability + peak effect-so higher chances of hypo and need for mandatory snack. Rapid acting analogs can be used for bolus insulin.

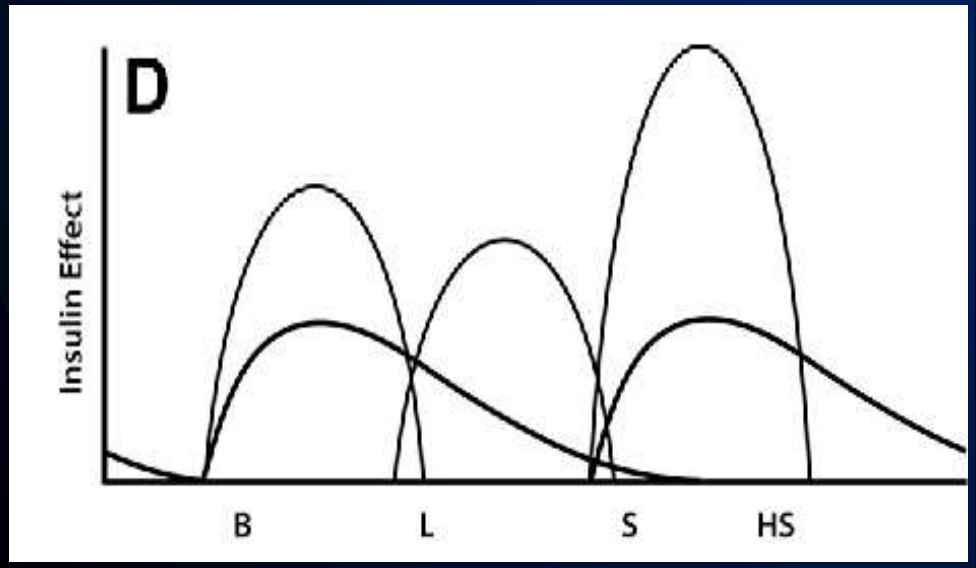


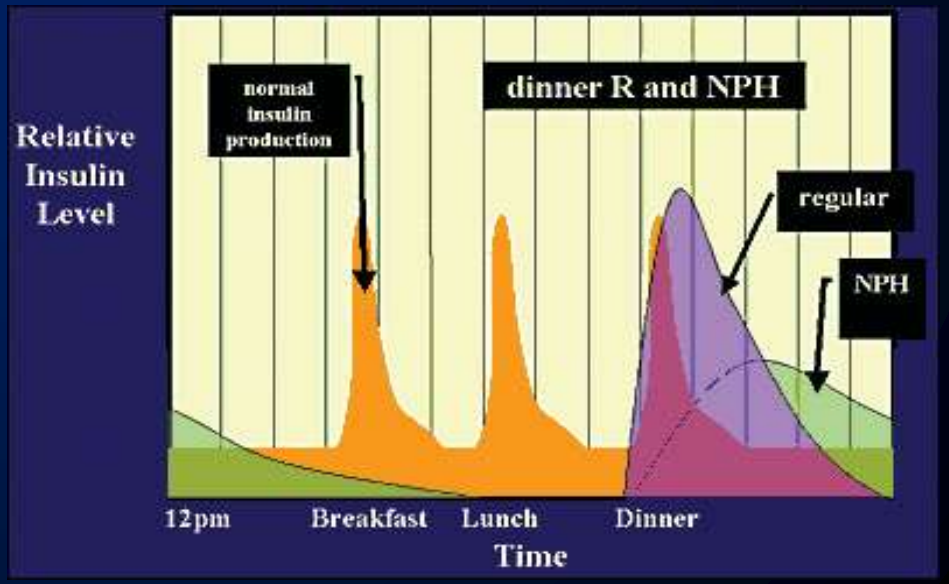


Basal bolus using human insulin

NPH is used as basal insulin twice daily, and Regular insulin as bolus;
May experience more hypos; Snacking needed at time of peak NPH action; lot of BG fluctuations expected

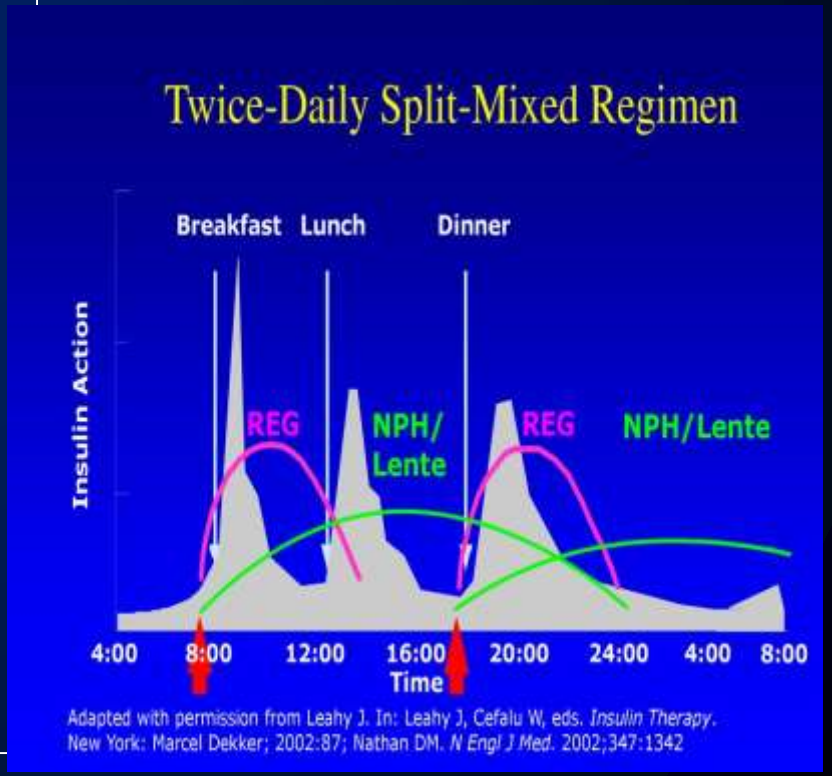
NPH used as basal insulin once daily & Regular insulin used as pre-meal bolus has long duration of action, with some basal effect





2 dose split-mixed regimen

- Only when afternoon/ evening injection is not possible (after exploring all possibilities)
- Combination of Regular + NPH mixed in single syringe pre-breakfast and pre-dinner. Peak of morning NPH insulin provides cover for lunch and evening snack
- Mismatch between food and insulin action profile: more hypos and hypers. Needs rigid schedule of meals and snacks.
- More harm because of high glycemic variability, though HbA1c may be “good”
- Hence not recommended in T1D



Calculation of dose

- **Weight** based calculation initially: later depends on BG levels, profile
- **Total** number of insulin units required in 24h (**bolus + basal**)
- Total daily dose (TDD) depends upon
  - Setting of diagnosis- presents in DKA or with osmotic symptoms
  - Partial remission phase/ honeymoon phase or total/permanent diabetes
  - Pubertal status of child
  - Illnesses, other factors

Step 1: Calculate TDD

- TDD = sum of all insulins administered in one day
- TDD = bolus + basal insulins

For e.g. TDD for a 7 year old girl on Inj. Aspart 3 - 4 – 3 and Inj. glargine 7 units:

TDD = 3 + 4 + 3 + 7 = 17 units

Calculation of TDD contd……

- TDD: depends upon clinical presentation: higher doses needed if glucotoxicity

  DKA at diagnosis: higher TDD (1 – 1.5 U/kg/day or more)

  No DKA at diagnosis: lower TDD (0. 7 – 1 U/kg/day)

  May go into partial remission phase / honeymoon stage after diagnosis – important to counsel patients that this is not a cure, as the dose requirement may be very low
- **Pre-pubertal children:** 0.7– 1.0 U/kg/day
- **Puberty:** up to 1 - 2 U/kg/day (A child weighing 40 kg may require

Correct dose: *Best glycemic control with minimal hypoglycemia and good growth*

Step 2: Split TDD into basal + bolus

- **Basal** Insulin: 30 - 40 % of TDD *if using regular insulin as bolus*

  30 - 50 % of TDD *if using rapid-acting insulin as bolus*

- **Bolus** insulin: 60% - 70% *as regular insulin* or 50 % - 70% *as rapid-acting*; divided between 3 – 4 pre-meal boluses

Fixed vs variable dose regimen

Fixed dose regimen – Insulin doses are fixed, and carb exchanges are used to keep carb content of meals constant from day to day. Can be considered less intensive.

Variable dose regimen – No set insulin dose; it is given based on pre meal glucose (consideri ng ISF) and intended carbohydrate intake (considering ICF). Considered a more intensive regimen.

The explanation and calculation of ISF/ ICF is covered in subsequent slides

Step 3 :- Dose titration
Bolus dose calculation

- Dose for the meal (ICR: Insulin to carb ratio) (+)
- Correction for high/low sugar (ISF: insulin sensitivity factor) (+/-)
- Anticipated activity (-)

Correction Factor (CF)

- CF or Insulin sensitivity factor (ISF)
- CF = mg/dl of blood glucose lowered by 1 unit of bolus insulin
- CF = 1800/TDD (Rapid acting insulin)

  1500/TDD (Regular insulin)

Cengiz E, Danne T, Ahmad T, Ayyavoo A, Beran D, Ehtisham S, Fairchild J, Jarosz-Chobot P, Ng SM, Paterson M, Codner E. ISPAD Clinical Practice Consensus Guidelines 2022: Insulin treatment in children and adolescents with diabetes. Pediatric Diabetes. 2022 Dec;23(8):1277-96.

Insulin-to-carb ratio (ICR)

- The number of carbohydrate grams covered by one unit of bolus insulin
- ICR = 500 ÷ TDD (Rapid acting insulin)
  450 ÷ TDD (Regular insulin)
- For very young children: 300 ÷ TDD rule may more appropriate

Smart CE, Annan F, Higgins LA, Jelleryd E, Lopez M, Acerini CL. ISPAD Clinical Practice Consensus Guidelines 2018: Nutritional management in children and adolescents with diabetes. Pediatr Diabetes. 2018 Oct;19 Suppl 27:136-154.

Correction doses

- Correction doses need to be administered pre and post meal if BG is high
- Set pre and post meal targets e.g. 100 mg/dL pre meal and 180 mg/dL post meal

- Correction dose = $\frac{\text{Observed BG} - \text{Target BG}}{\text{Correction factor}}$

Putting it all together

STEP 1: Calculate insulin dose for food

a) Count grams of carbohydrates in the food

b) Divide by the insulin-to-carb ratio

$$= \frac{\text{Total grams of carbohydrate to be eaten}}{\text{Insulin-to-carb ratio}}$$

Cengiz E, Danne T, Ahmad T, Ayyavoo A, Beran D, Ehtisham S, Fairchild J, Jarosz-Chobot P, Ng SM, Paterson M, Codner E. ISPAD Clinical Practice Consensus Guidelines 2022: Insulin treatment in children and adolescents with diabetes. Pediatric Diabetes. 2022 Dec;23(8):1277-96.

Putting it all together contd...

STEP 2:

If Premeal BG is high- calculate correction dose to normalise BG

STEP 3: Dose titration

Total dose: insulin needed for carbs + correction dose- anticipated activity

- Advise gap of 3 hrs between 2 boluses
- Bolus also depends on anticipated physical activity and active insulin in the body from previous dose
- Reduce bolus if physical activity within 2 hrs of bolus dose

Cengiz E, Danne T, Ahmad T, Ayyavoo A, Beran D, Ehtisham S, Fairchild J, Jarosz-Chobot P, Ng SM, Paterson M, Codner E. ISPAD Clinical Practice Consensus Guidelines 2022: Insulin treatment in children and adolescents with diabetes. Pediatric Diabetes. 2022 Dec;23(8):1277-96.

R, 8 years: practice activity

- On BBR with insulin aspart (22 U) and 14 U glargine
- Total Daily Dose: 36 U

- Pre-meal glucose: 280 mg/dL
- Target blood glucose: 100 mg/dL
- ICR: 1: 14

- Food intake CHO = 45 grams

- Insulin dose for carbs = 45/14 = 3.2 U

- Correction factor (rule of 1800) = 50 U (1800 ÷ 36)

- Correction dose:

280 - 100 = 180 ÷ 50 = 3.6 U

- Net bolus dose = insulin dose for carbs + correction dose = 3.2 U+ 3.6 U = 7 U

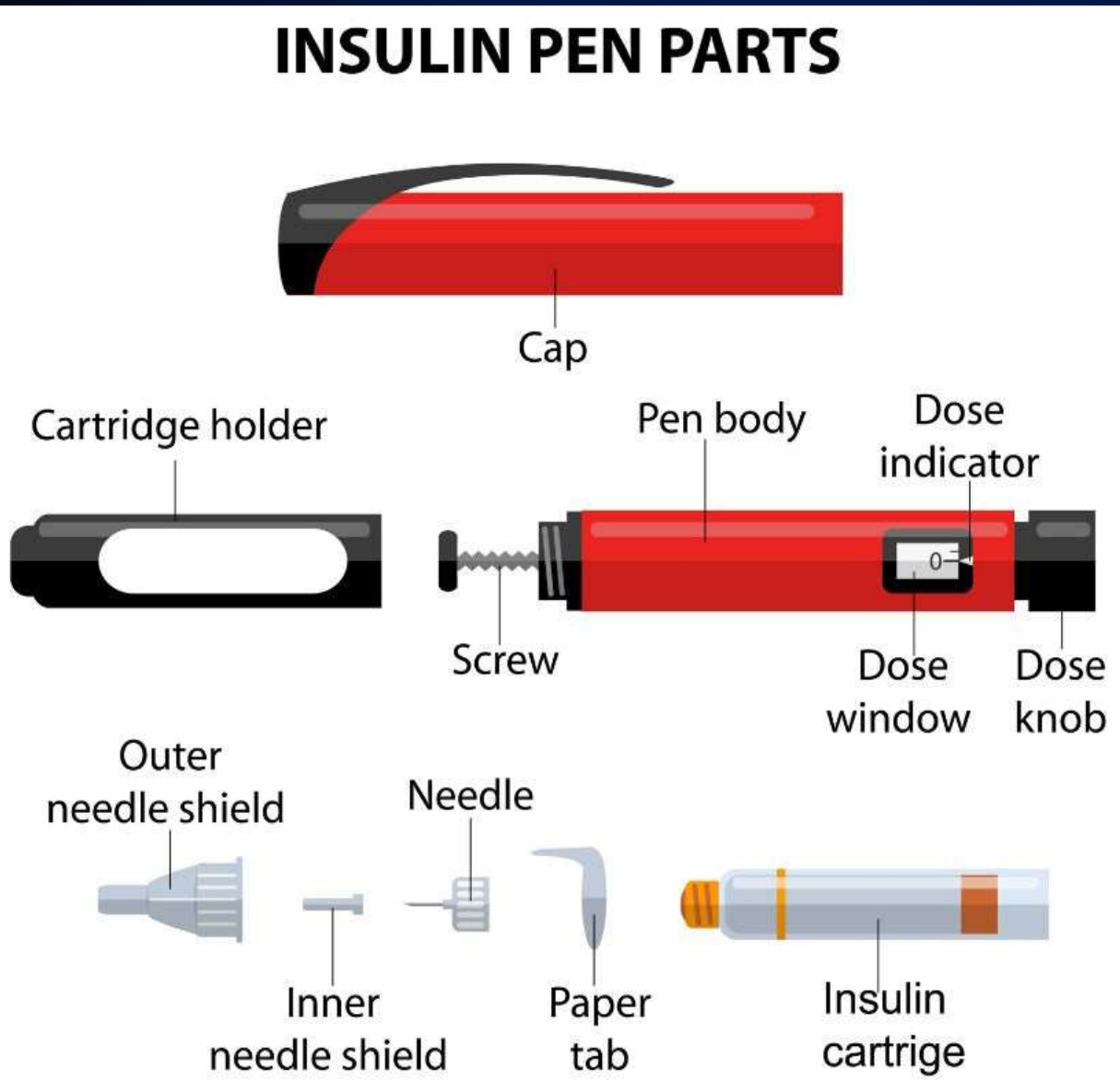
Practical aspects of insulin therapy

Matching IU/ml on vial with syringe

In India, different strengths of insulin and insulin syringes are available: 40 IU, 50 IU & 100 IU (50 IU syringe – 1 marking is 1 unit, whereas 100 IU syringe – 1 marking is 2 units)

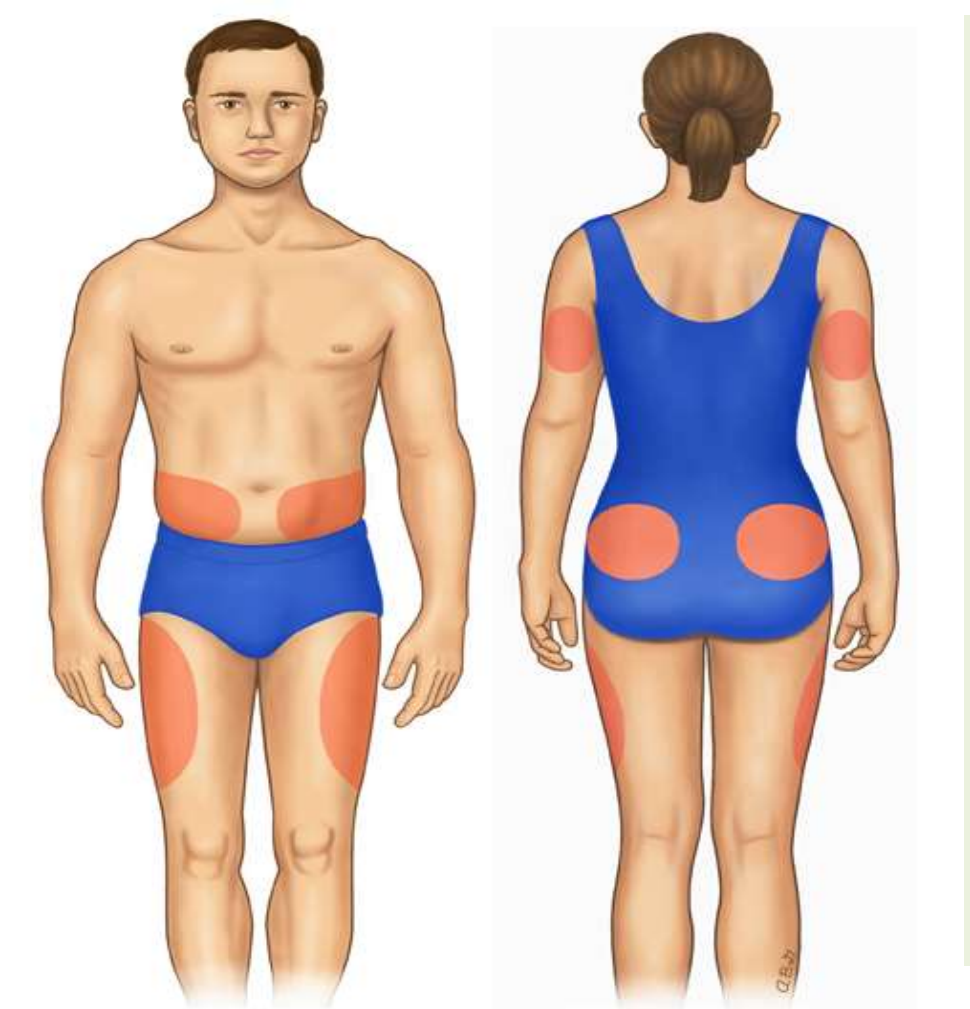
Always match the IU on syringe and bottle e.g. 40 IU syringe for 40 IU insulin vial

Insulin pens



- Pens - Disposable/ Reusable
- Needles can be 4mm, 5mm, 6mm or greater; 4mm- most appropriate.
- Pens - available with 0.5 (junior) and 1 unit markings

Insulin administration & storage



- Rotate sites every time
- Check for lipohypertrophy
- Buttocks/gluteal region can be used in toddlers
- Change the needle regularly (may use it 3-4 times)
- Priming (pushing out 1-2 units of insulin) is important after changing needle
- Discard the sharps appropriately

Insulin Storage

- Store unused insulin at 4-8 ºC in a refrigerator
- Earthenware pitcher (matka), cooling jars or zeer pot - if refrigeration unavailable
- Remove the insulin form refrigerator 15-20 minutes prior to administration – to make it less painful
- Insulin should never be frozen
- Direct sunlight or extreme heat damages insulin
- Discard insulins that have changed in appearance (clumping, frosting, precipitation ,discolouration)

Monitoring for Glycemic Control

Importance of monitoring glycemic control

- Why monitor BGs frequently?
  - Knowing current BG, trend & patterns of BG, & overall control
  - Detecting and correcting hypo/hyperglycemia
  - Observing impact of certain food types and exercise on BG
  - Checking adequacy of insulin dose for the amount of carbs consumed
  - Adjusting insulin doses during illness

Check BG → Record & Analyse → Take corrective action if required

Aim is to improve glycemic control and prevent acute and long - term complications

Tools for monitoring glycemic control

- Self-monitoring of blood glucose (SMBG) with glucometer
- Continuous Glucose Monitoring (CGM) with sensor device
- A1C
- Monitoring of blood or urinary ketones

DiMeglio LA, Acerini CL, Codner E, Craig ME, Hofer SE, Pillay K, Maahs DM. ISPAD Clinical Practice Consensus Guidelines 2018: Glycemic control targets and glucose monitoring for children, adolescents, and young adults with diabetes. Pediatr Diabetes. 2018 Oct;19 Suppl 27:105-114

Glucometer

Self-monitoring of blood glucose (SMBG) by glucometer: current BG value

Performing a capillary blood test

DiMeglio LA, Acerini CL, Codner E, Craig ME, Hofer SE, Pillay K, Maahs DM. ISPAD Clinical Practice Consensus Guidelines 2018: Glycemic control targets and glucose monitoring for children, adolescents, and young adults with diabetes. Pediatr Diabetes. 2018 Oct;19 Suppl 27:105-114.

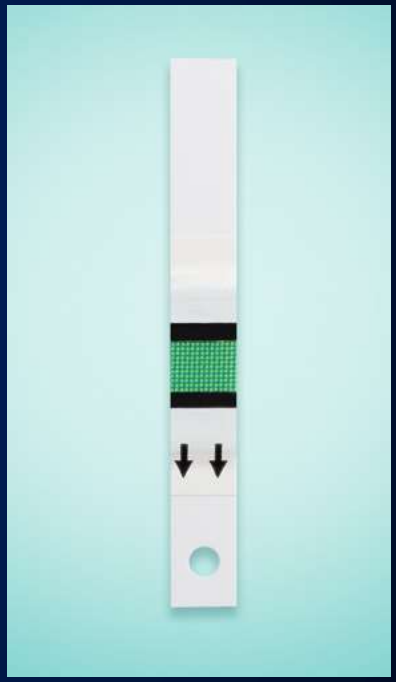
Tips to reduce finger prick pain

- Test on the side of the finger – not on the pulp!
- Warm the hands
- Adjust the lancet depth
- Rotate fingers regularly (neonates and infants - heel can also be used)
- Use a fresh lancet
- Get the best device for you
- Involve the kid!

DiMeglio LA, Acerini CL, Codner E, Craig ME, Hofer SE, Pillay K, Maahs DM. ISPAD Clinical Practice Consensus Guidelines 2018: Glycemic control targets and glucose monitoring for children, adolescents, and young adults with diabetes. Pediatr Diabetes. 2018 Oct;19 Suppl 27:105-114.

Glucose test strips: precautions

- Use a meter with matching strips
- Check expiry date
- Avoid strip exposure to high and low temperatures and humidity
- Hematocrit, drugs like paracetamol, vitamin C affects reading
- Safe disposal of strips after use



Tauschmann M, Forlenza G, Hood K, Cardona-Hernandez R, Giani E, Hendrieckx C, DeSalvo DJ, Laffel LM, Saboo B, Wheeler BJ, Laptev DN. ISPAD Clinical Practice Consensus Guidelines 2022: diabetes technologies: glucose monitoring. Pediatric Diabetes. 2022 Dec;23(8):1390-405.

How often should one test?

- Recommended testing: 6 to 10 times per day (minimum 4 times)
- Software to record and analyse BG values - improve patient understanding of diabetes management
- Futile to simply check BG without analysing and taking necessary action

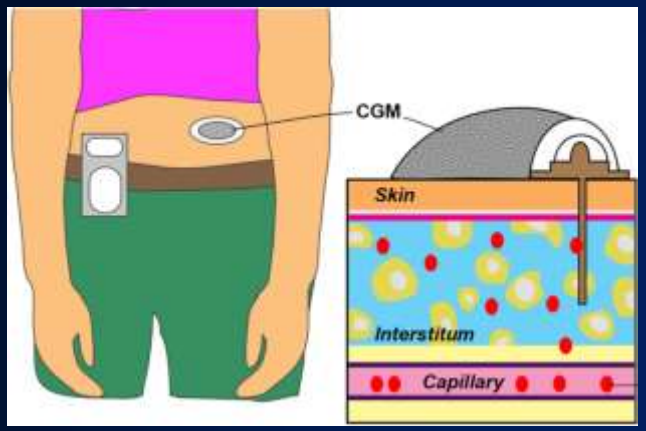
Tauschmann M, Forlenza G, Hood K, Cardona-Hernandez R, Giani E, Hendrieckx C, DeSalvo DJ, Laffel LM, Saboo B, Wheeler BJ, Laptev DN. ISPAD Clinical Practice Consensus Guidelines 2022: diabetes technologies: glucose monitoring. Pediatric Diabetes. 2022 Dec;23(8):1390-405.

When should we test?

- Before meals and 2 – 3 hours after meals
- At bedtime
- Test at midnight (2 am – 3 am) (once per week)
- If low blood glucose (hypo) or high BG is suspected
- 2-3 hourly during sick days
- Before, during (every 30 mins) and after vigorous exercise (including at 3 am on days of unaccustomed physical activity)

DiMeglio LA, Acerini CL, Codner E, Craig ME, Hofer SE, Pillay K, Maahs DM. ISPAD Clinical Practice Consensus Guidelines 2018: Glycemic control targets and glucose monitoring for children, adolescents, and young adults with diabetes. Pediatr Diabetes. 2018 Oct;19 Suppl 27:105-114

Continuous Glucose Monitoring System (CGMS)



- CGMS measures Interstitial glucose at periodic intervals
- It lags by 10 – 15 mins behind capillary blood glucose change
- It reveals current BG, trend of BG, 24 hour BG patterns including during school and sleep

Tauschmann M, Forlenza G, Hood K, Cardona-Hernandez R, Giani E, Hendrieckx C, DeSalvo DJ, Laffel LM, Saboo B, Wheeler BJ, Laptev DN. ISPAD Clinical Practice Consensus Guidelines 2022: diabetes technologies: glucose monitoring. Pediatric Diabetes. 2022 Dec;23(8):1390-405.

Indications of CGMS

- Use CGMS whenever possible, especially in preschool children*
- Particularly helpful in the following settings:**
  - Divergent HbA1c & BG level
  - Recurrent severe nocturnal hypoglycemia/hypoglycemia unawareness – hypoglycemia should be confirmed with simultaneous glucometer value
  - Marked unexplained glycemic excursions
  - Initiation and adjustment of insulin pump therapy

*Virmani A et al. ISPAD Clinical Practice Consensus Guidelines 2022: Management of the child, adolescent, and young adult with diabetes in limited resource settings. Pediatric Diabetes. 2022 Dec;23(8):1529-51.

**DiMeglio LA, Acerini CL, Codner E, Craig ME, Hofer SE, Pillay K, Maahs DM. ISPAD Clinical Practice Consensus Guidelines 2018: Glycemic control targets and glucose monitoring for children, adolescents, and young adults with diabetes. Pediatr Diabetes. 2018 Oct;19 Suppl 27:105-114.

Advantages of CGMS over self monitoring of blood glucose

- Improves TIR and A1C
- ↓ hypoglycemia & glycemic variability
- Predicts BG trends (↑ or ↓)
- Reveals BG patterns during sleep and school hours
- Data of real time CGMS can be shared with caregivers from a distance
- ↓ DKA events

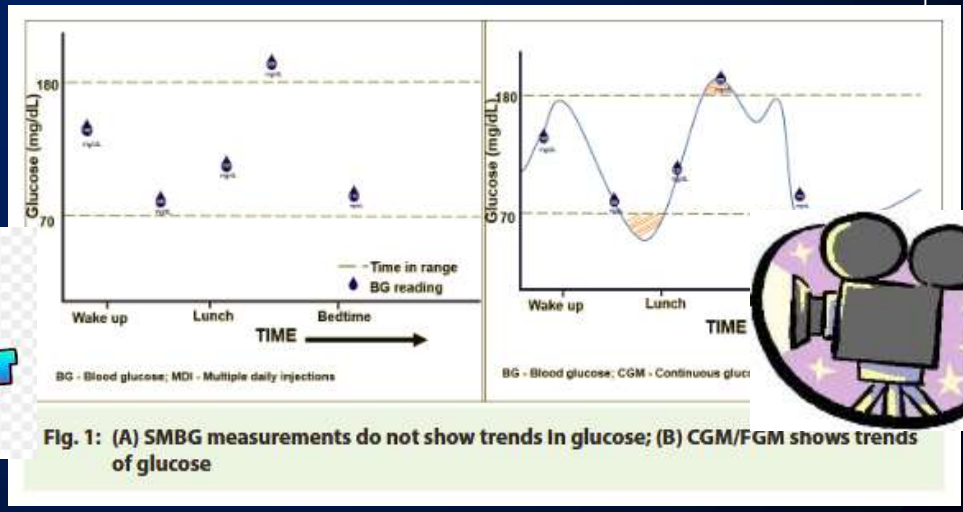


Fig. 1: (A) SMBG measurements do not show trends in glucose; (B) CGM/FGM shows trends of glucose

**Tauschmann M, Forlenza G, Hood K, Cardona-Hernandez R, Giani E, Hendrieckx C, DeSalvo DJ, Laffel LM, Saboo B, Wheeler BJ, Laptev DN. ISPAD Clinical Practice Consensus Guidelines 2022: diabetes technologies: glucose monitoring. Pediatric Diabetes. 2022 Dec;23(8):1390-405.

A1C

- A1C: Average BG control in last 2 to 3 months
- At least four A1Cs per year
- Influenced by more recent BG readings
- Can be falsely elevated in anemia
- Not reliable in thalassemia and other hemoglobinopathies

A1C	Estimated average BGL over last 8-12 weeks (mg/dL)
6%	126
6.5%	140
7%	154
7.5%	169
8%	183
8.5%	197
9%	212
9.5%	226
10%	240

American Diabetes Foundation

Monitoring of blood/urinary ketones

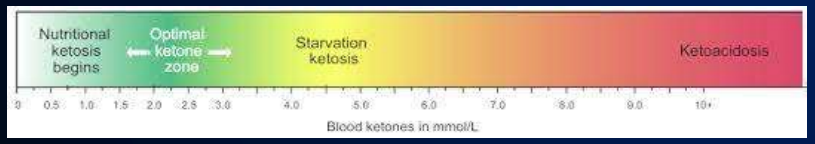
- Ketones - alternate source of energy from fat breakdown
- ↑ ketones: ↑ risk of DKA
- Blood ketones (Beta-hydroxy butyrate) > sensitive and specific than urinary ketones (acetoacetate and acetone)
- To be checked in:
  - Episodes of uncontrolled hyperglycemia
  - Intercurrent illness (sick days)
  - BG > 250 mg/dL before exercise

DiMeglio LA, Acerini CL, Codner E, Craig ME, Hofer SE, Pillay K, Maahs DM. ISPAD Clinical Practice Consensus Guidelines 2018: Glycemic control targets and glucose monitoring for children, adolescents, and young adults with diabetes. Pediatr Diabetes. 2018 Oct;19 Suppl 27:105-114.

Monitoring of blood/urinary ketones contd..

Blood ketone reading of

- <0.6 mmol/L: Normal
- 0.6- 1.5 mmol/L: Elevated
- 1.5- 3.0 mmol/L: High risk
- > 3.0 mmol/L: Ketoacidosis



Urinary ketone reading

- 5 mg/dL: 'Trace' ketones
- 15 mg/dL: 'Small' ketones
- 40 mg/dL: 'Moderate' ketones
- 80-160 mg/dL: 'Large' ketones

DiMeglio LA, Acerini CL, Codner E, Craig ME, Hofer SE, Pillay K, Maahs DM. ISPAD Clinical Practice Consensus Guidelines 2018: Glycemic control targets and glucose monitoring for children, adolescents, and young adults with diabetes. Pediatr Diabetes. 2018 Oct;19 Suppl 27:105-114.

Targets for glycemic control

Blood glucose targets

Setting	Target BG (mg/dL)
Pre-meal	70 – 144
Post-meal	< 180
Bedtime	90 - 180

de Bock M, Codner E, Craig ME, Huynh T, Maahs DM, Mahmud FH, Marcovecchio L, DiMeglio LA. ISPAD Clinical Practice Consensus Guidelines 2022: Glycemic targets and glucose monitoring for children, adolescents, and young people with diabetes

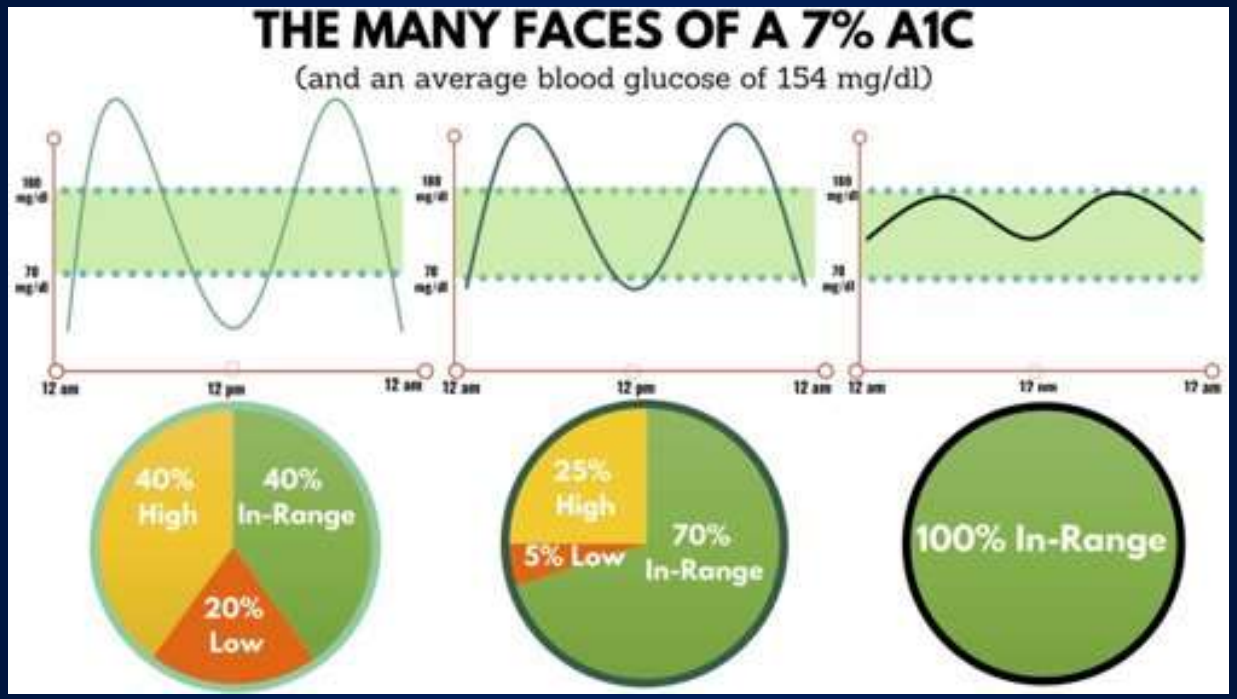
Target HbA1c

HbA1c	ISPAD	ADA	NICE
	< 7%	< 7.0%	≤ 6.5%

Target should be individualized with the goal of achieving a value as close to normal as possible, avoiding severe hypoglycemia, frequent mild to moderate hypoglycemia, and excessive burden for the child with diabetes and their family

de Bock M, Codner E, Craig ME, Huynh T, Maahs DM, Mahmud FH, Marcovecchio L, DiMeglio LA. ISPAD Clinical Practice Consensus Guidelines 2022: Glycemic targets and glucose monitoring for children, adolescents, and young people with diabetes

Limitations of HbA1c



- No information about acute glycemic excursions
- Does not identify intra & inter-day glucose variation.
- Not reliable in anemia, hemoglobinopathies, iron deficiency

It's time to move on….. to a new metric

HbA_{1C}

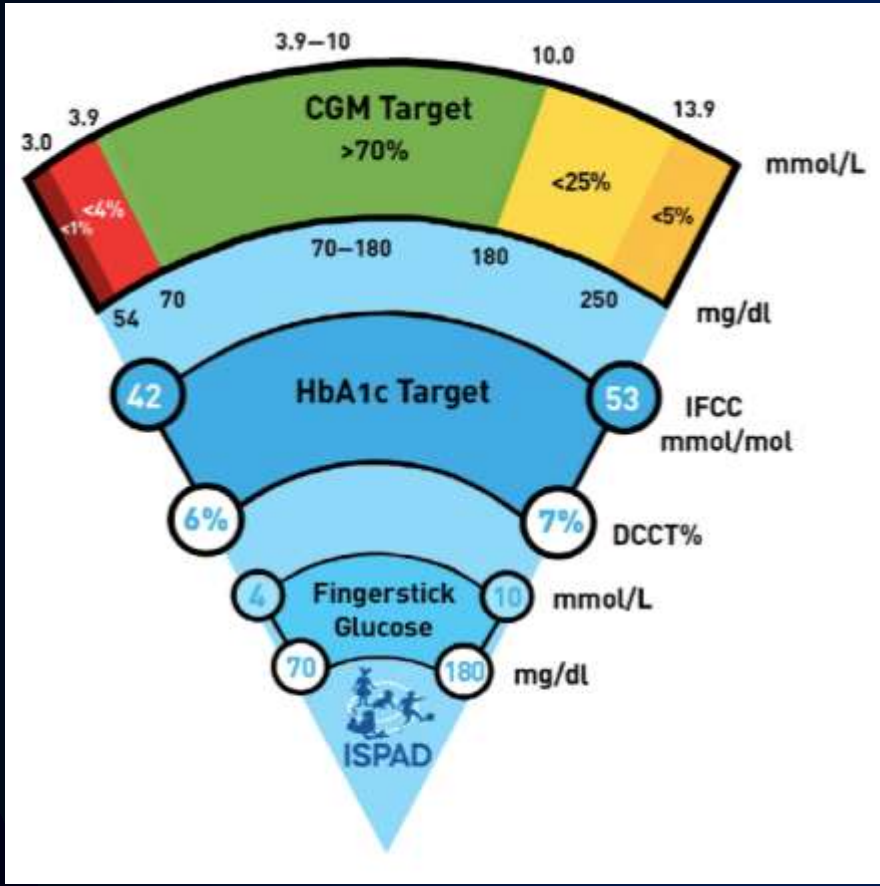
TIR

Time-in-range

"TIR goes beyond HbA_{1C} in representing blood glucose levels because it captures variation – the highs, lows, and in-range values that characterize life with diabetes".

TIR, time in range: diatribe https://diatribe.org/about-diatribe

Time in range (TIR)



de Bock M, Codner E, Craig ME, Huynh T, Maahs DM, Mahmud FH, Marcovecchio L, DiMeglio LA. ISPAD Clinical Practice Consensus Guidelines 2022: Glycemic targets and glucose monitoring for children, adolescents, and young people with diabetes

- TIR: time of the day spent in normal blood glucose range: 70 – 180 mg/dl

- TIR targets:

Blood glucose range (mg/dL)	Time of day (%)
70 – 180	>70
<70	<4
<54	<1
>180	<25
>250	<5
Glycemic variability	</= 36%

Recording and analysing BG

Maintaining a diabetes logbook

TIME	7.00 AM	12.30 PM	4 PM	7 PM	10 PM	3 AM
BG mg/dL	Pre: 150 Post: 180	140	180	160	140	110
Insulin	Lispro 10U	Lispro 7U		Lispro 6U	Lantus 20U	
Food Serving	3 Appam ½ Cup channa	1 Cup rice ½ Cup veg 1 Cup salad ½ Cup dal 1 Piece fish	1 Banana	3 Chapathi ½ Cup dal	1 Cup milk	
Carb (gm)	105 g	70 g	15 g	65 g	10 g	
Activity	Yoga ½ hour		Walking ½ hour			

- Note of special events affecting glycemic control (illness, parties, exercise…)
- Hypoglycemic episodes
- Episodes of ketonuria/ketonemia

Identifying BG patterns

	Pre BF	Post Bf	Pre Lunch	Post lunch	Pre dinner	Post dinner
2/06/23	240	186	140	118	230	90
3/06/23	190	200	170	110	197	74
4/06/23	214	120	98	245	289	69
5/06/23	91	148	134	190	110	91
6/06/23	234	189	90	117	265	64

High fasting BG
Action: Check 3 am BG

High Pre-dinner BG
Action: Ask regarding large evening snacks without insulin OR physical activity performed

Low post-dinner BG
Action: Reduce dinner bolus dose; advise complex carb snack if BG <90 mg/dL

Medical nutrition therapy

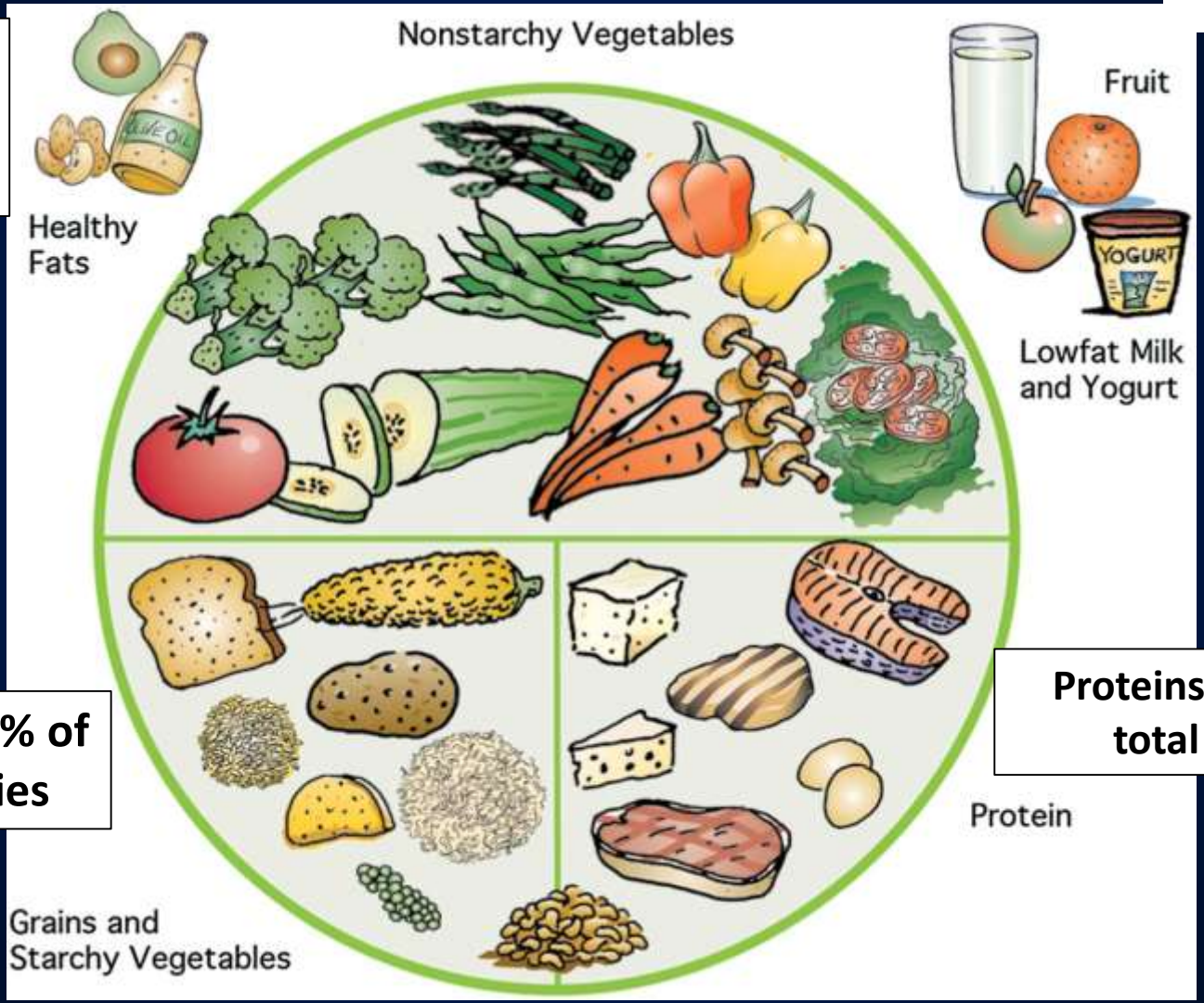
Meal planning: 5 key aspects

- Involve specialized dietician
- NO separate diabetic diet
- Healthy meal plan - Quantitatively for ideal wt, ht & BMI; qualitatively (healthy carbs, adequate protein and fibre and limited fats) for preventing macrovascular complications
- Matching insulin to carbs by advanced carb counting allows greater flexibility than fixed insulin doses for carb exchanges
- To prevent exercise induced and nocturnal hypo: Complex carbs before and after PA, Simple carbs during physical activity

Annan SF, Higgins LA, Jelleryd E, Hannon T, Rose S, Salis S, Baptista J, Chinchilla P, Marcovecchio ML. ISPAD Clinical Practice Consensus Guidelines 2022: Nutrition management in children and adolescents with diabetes. Pediatric diabetes. 2022 Dec;23(8):1297-321.

Healthy meal plan

Fats: <35% of total calories



Carbs: 40-50% of total calories

Proteins: 15-25% of total calories

Annan SF, Higgins LA, Jelleryd E, Hannon T, Rose S, Salis S, Baptista J, Chinchilla P, Marcovecchio ML. ISPAD Clinical Practice Consensus Guidelines 2022: Nutritional management in children and adolescents with diabetes. Pediatric diabetes. 2022 Dec;23(8):1297-321.

Exercise and diabetes

Exercise and diabetes

- Physical activity (PA) is part of routine diabetes care
- Impact on BG depends upon planned or unplanned/ moderate or intensive exercise/short or sustained/accustomed or not/active insulin in the body
- Target BG: 90 –250 mg/dL
- If BG >250 mg/dL → Check blood/urine ketones → if positive take corrective insulin and avoid exercise

Exercise and diabetes contd.....

- **Planned PA**:
  - ↓ meal bolus insulin (rapid analogue) by 25-50% if PA within 2 hrs
  - Usual dose if PA after 2 hrs of meal
- Check BG before, every 30 mins during, and after PA
- Test for early morning hypoglycemia (2 - 3 am) on days of unaccustomed exercise especially performed > 4 pm
- Do not inject insulin on exercising limb

Adolfsson P et al. ISPAD Clinical Practice Consensus Guidelines 2022: Exercise in children and adolescents with diabetes. Pediatric Diabetes. 2022 Dec;23(8):1341-72..

Hypoglycemia and Sick day management

Hypoglycemia

- BG <70 mg/dL – "alert value"

Autonomic	Neuroglycopenic
Trembling	Difficulty concentrating
Palpitations	Confusion
Anxiety	Weakness/lethargy
Sweating	Blurred vision
Hunger	Behavior change
Nausea	Dizziness

- Initial symptoms: identified by older children
- May go unrecognized by younger children
- Maybe absent in hypo unawareness

- Occur at lower BG levels
- Caregivers/onlookers should be able to identify and Rx symptoms
- ID tag: diagnosis, symptoms and Rx of hypo

Hypoglycemia management - "Rule of 15"

- Confirm if possible (blood glucose <70 mg/dL)
- Treat with " 15 g of fast sugar (0.3 g/kg in smaller kids)" (simple carbohydrate) e.g.: glucose tablets, 3 teaspoons sugar, 1 tablespoon honey, 150 ml juice
- AVOID chocolates/sweetmeats as fats and proteins delay absorption of sugar
- Retest in 15 minutes to ensure BG >70 mg/dL and retreat if needed
- Once BG >70 mg/dl eat 15 g of carb snack or regular meal

Abraham MB, Jones TW, Naranjo D, Karges B, Oduwole A, Tauschmann M, Maahs DM. ISPAD Clinical Practice Consensus Guidelines 2018: Assessment and management of hypoglycemia in children and adolescents with diabetes. Pediatr Diabetes.

Severe hypoglycemia management

- Injection of glucagon IM/SC as follows:

Age	Dose
< 10 years/ wt < 25 kg	0.5 mg
> 10 years/ wt > 25 kg	1 mg

- Thick paste of sugar smeared on dependent cheek pad can be life saving
- Hospital setting: bolus of 10% dextrose – 2 ml/kg (max 5ml/kg) followed by maintenance IV fluids till child can eat normally

Abraham MB, Karges B, Dovc K, Naranjo D, Arbelaez AM, Mbogo J, Javelikar G, Jones TW, Mahmud FH. ISPAD Clinical Practice Consensus Guidelines 2022: Assessment and management of hypoglycemia in children and adolescents with diabetes. Pediatr Diabetes. 2022;23(8):1322.

For every low/high BG: 3 Qs

	Questions to address	HIGH sugar (>180 mg/dl)	Low Sugar (<70 mg/dl)
1.	How to immediately **correct it**?	Extra Rapid - acting insulin (1 unit/50-100 mg extra sugar)	Glucon D (15-20 gm)
2	What is the **reason for it**?	Extra snacking, less previous bolus, unwell/sickness, stress	Missed/delayed meal, extra activity, high previous dose If recurrent: Hypothyroidism, Celiac, Addison's, CKD
3	How to **prevent it** next day?	Correct the reason found No reason- **increase previous** dose	Correct the reason found No reason- **decrease previous dose**

Sick day management: 4 Mantras

1. 2-3 hrly monitoring of BG and blood/urine ketones
2. NEVER stop insulin – extra insulin doses maybe needed as per BG and ketone levels
3. Hydration, hydration, hydration.
4. Treat underlying illness

Phelan H et al. Sick day management in children and adolescents with diabetes. Pediatric diabetes. 2022 Nov;23(7):912-25.

Additional insulin (hyperglycemia)

Blood glucose (mg/dl)	Urine/blood ketones	Extra correction bolus
< 180	Not tested	Continue routine doses
> 180	Negative	Give routine correction dose as required
> 180	Trace/small	Give 10% TDD extra insulin
> 180	Mod/Large	Give 20% TDD extra insulin

Basal insulin - ↑ by 20 to 30% in prolonged illness

↓ basal dose by 20% if GI illness

Ongoing diabetes care

Ongoing diabetes care

Every Visit (3 monthly):

- LOGBOOK
- Insulin dose & titration
- Hypoglycemia episodes
- Diet and exercise plan
- Growth & Puberty Assessment, BP
- Lipodystrophy
- Injection technique/Rotation/ SMBG technique
- Psychosocial stress and well-being
- HbA1c

LOGBOOK

- Yes/No
- Reliability of records – compare with glucometer readings
- SMBG trends?
- Titration of Insulin dose appropriate?
- Correction doses?
- SMBG records Vs HbA1c!
- Glucose variability?

DSME including revision of sick day and hypoglycemia management protocols as required or at least annually

Growth and diabetes

- **Poor growth in T1D:**
  - Hypothyroidism (stunting)
  - Hyperthyroidism (wasting)
  - Celiac disease
  - Uncontrolled diabetes (Mauriac syndrome)
  - Eating disorder

- **Excessive weight gain:**
  - Over-insulinization
  - Lifestyle related obesity
  - Recurrent hypos with overtreatment

Ongoing diabetes care contd..

Test	At or near diagnosis	On follow up
CBC	✓	Annually
Free T4, TSH	✓	Once in 2 yrs
Lipid profile	≥ 11 years of age	Once in 3 yrs Annually (if abnormal)
tTG-IgA, total IgA	✓	Every 2 to 5 yrs
Urine albumin/creat ratio	≥ 11 yrs of age or > 2- 5 years of diagnosis (whichever earlier)	Annually > 2 yrs if pubertal or else > 5 yrs of diagnosis
Fundus examination	≥ 11 yrs of age or > 2- 5 years of diagnosis (whichever earlier)	Every 2 – 3 yrs

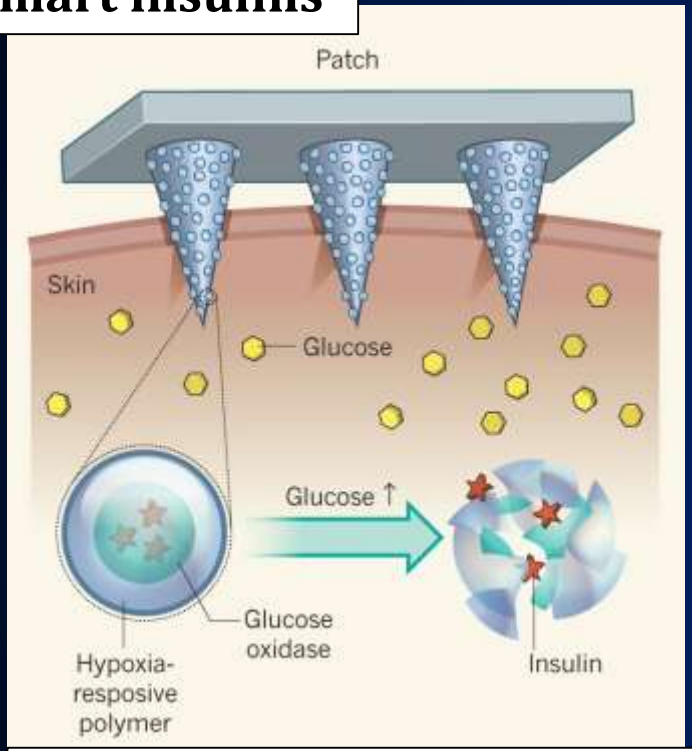
Special vaccines: pneumococcal and Influenza

Limbert C et al. ISPAD Clinical Practice Consensus Guidelines 2022: The delivery of ambulatory diabetes care to children and adolescents with diabetes. Pediatric Diabetes. 2022 Dec;23(8):1243-69

Recent Advances in T1D Management

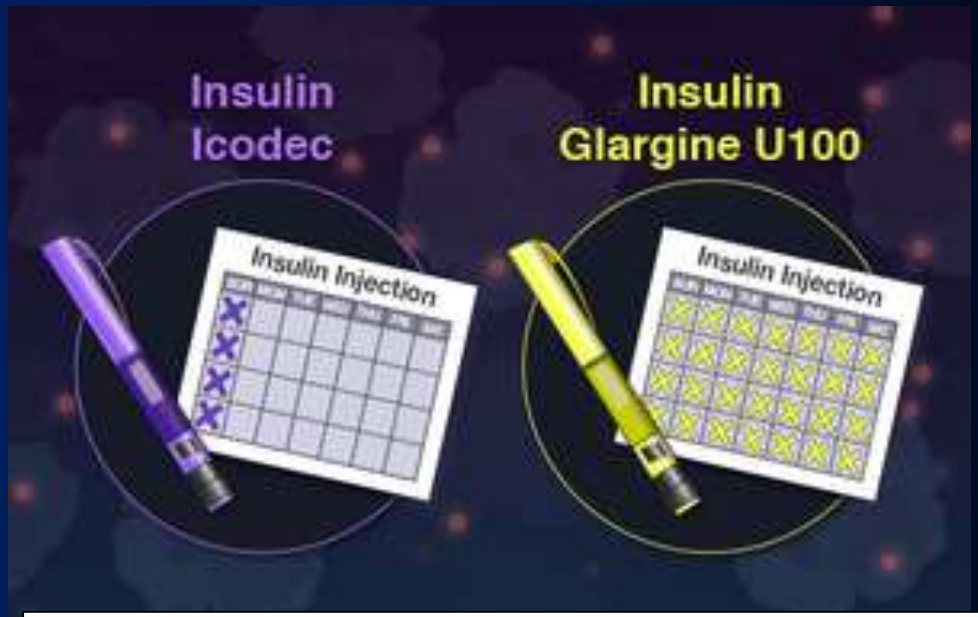
Newer methods for insulin delivery

Smart insulins



- Glucose responsive "smart" insulin systems release insulin α interstitial BG
- No need for external monitoring

Once weekly basal insulin - Icodec



- Reduces no. of injections required from 365 to 52
- Efficacy similar to daily degudec injections but higher rates of hypoglycemia

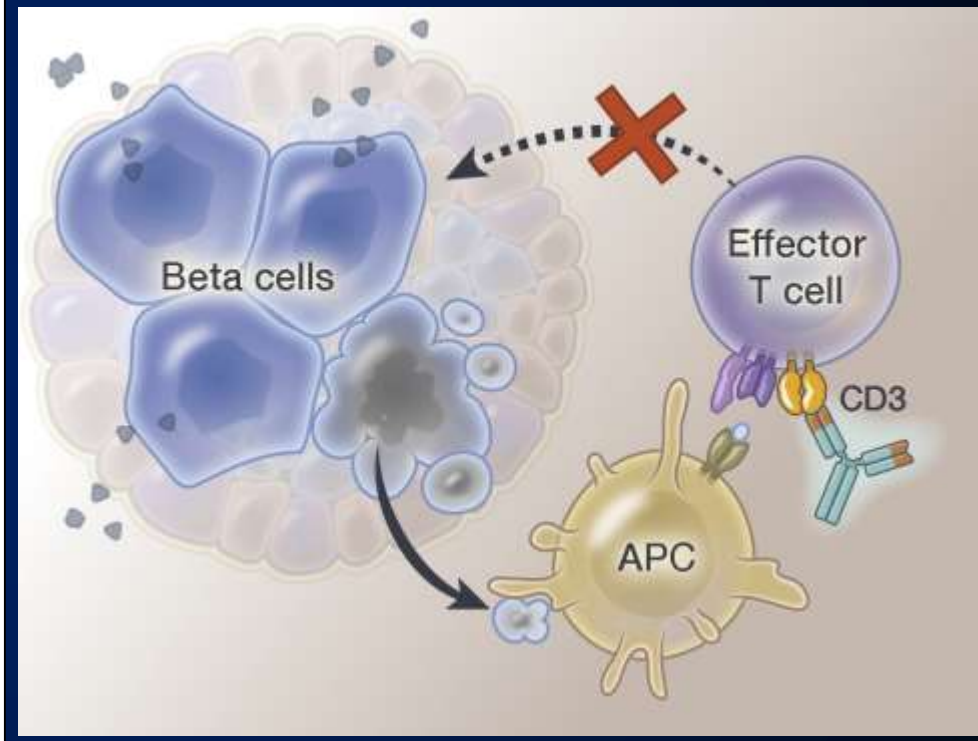
Prevention of clinical diabetes

- Delays onset of diabetes in individuals with autoimmunity and dysglycemia

  e.g. Tepelizumab (anti-CD3 antibody)

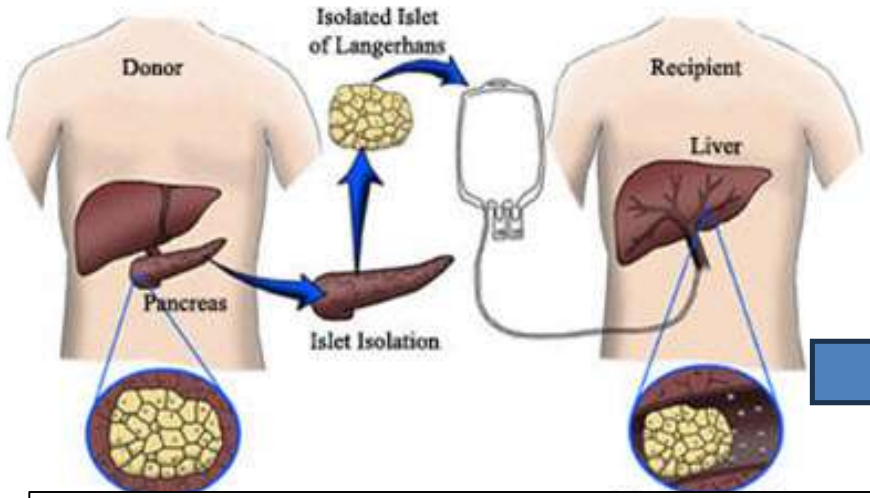
  - Single cycle of therapy delays onset of clinical diabetes by average 3 years
  - High cost, lymphopenia, rash
  - FDA approved > 8 yrs of age

Beta cell preservation: Immunotherapy



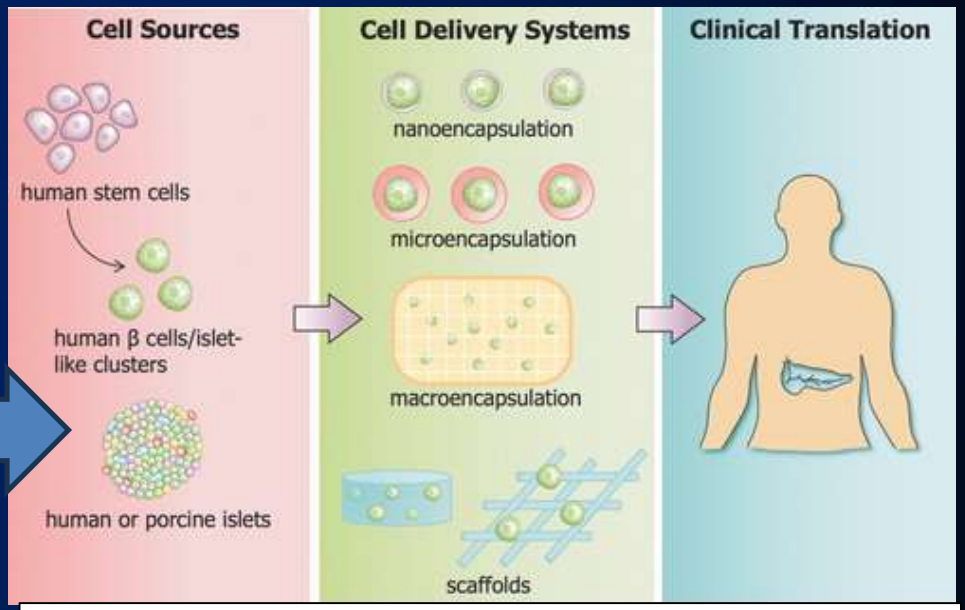
A step towards reversal of diabetes

β cell restoration: Islet cells/pancreatic transplant



- Restores beta and other pancreatic cells – ↓ insulin dependence and hypoglycemia
- ↓ donor availability
- Lifelong immunosuppression and tumor risk

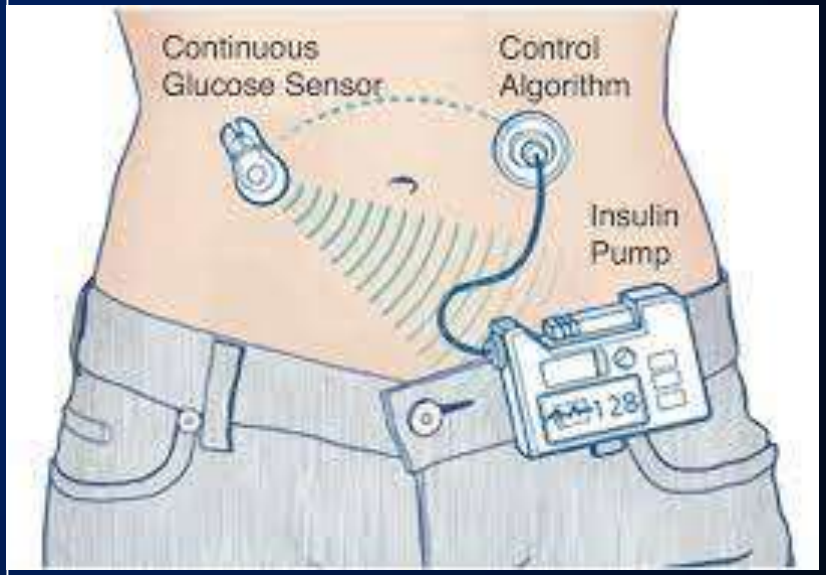
β cell regeneration: Stem cell transplant



- Embryonic/mesenchymal/pluripotent cells
- No donor dependence
- Can reverse autoimmunity
- Lifelong immunosuppression

Artificial pancreas – the future

- Artificial pancreas = closed loop system = CGMS + Algorithmic analysis + insulin pump
- Closed loop without need for manually entering carbs
- Closed loop with dual – insulin + glucagon infusions



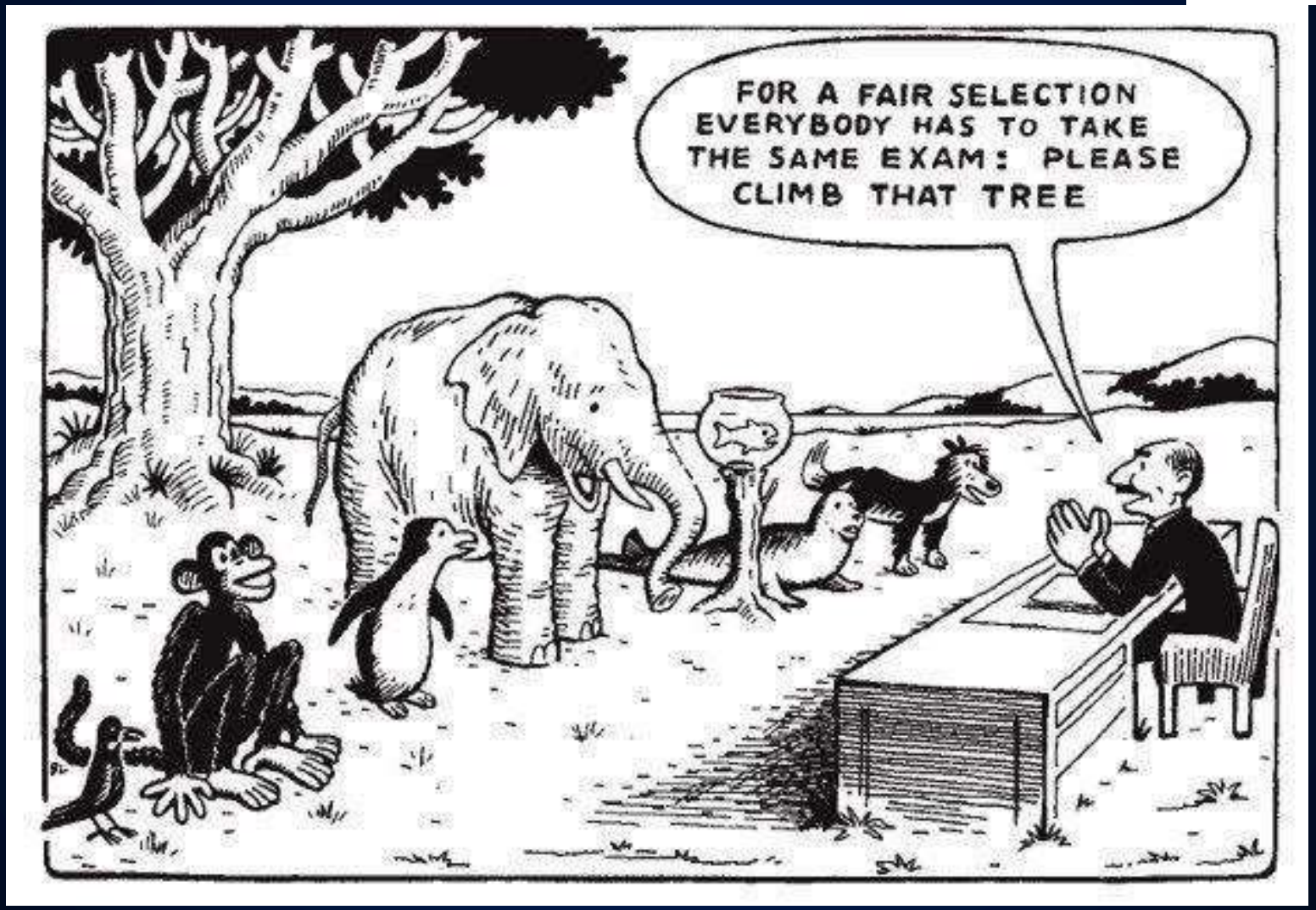
Summary

- Strong foundation of diabetes education + psychosocial support = optimal diabetes control and growth
- Intensive and dynamic insulin therapy
- CGMS and CSII wherever possible
- Monitor growth, puberty, complications & comorbidities
- Multidisciplinary individualized care

Summary contd…

- SMBG up to 6 to 10 times per day (at least 4) with proper record keeping
- Premeal 70-144 mg/dL; post-meal < 180 mg/dL; bedtime 90-180 mg/dL
- Every BG checked must be analysed & acted upon
- Target - HbA1c ≤ 7%; Time in Range > 70%
- Set individualized targets and goal

Thank you


FOR A FAIR SELECTION EVERYBODY HAS TO TAKE THE SAME EXAM: PLEASE CLIMB THAT TREE