

Insulin therapy

clinical cases

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Case 1

- A 41 years old man with history of diabetes is presented to our clinic for follow up. He has been on oral agent for 4 years. He reports unintentional 10 kg weight loss in 4 month. His family history is remarkable for diabetes in his mother and MTC in his aunt.
- His blood pressure is 130/80. His weight is 60 kg and height is 170 cm (BMI: 20.8 kg/m²). Physical examinations other than loss of protective sensation on lower limbs are unremarkable.
- Drug history and laboratory data are as followed :

Case 1

- DH: tab metformin 1 gr BD/ tab gliclazide 60mg BD/ tab atorvastatin 40 mg QD
- Laboratory data :

Variable	Value	reference
FBS	210 mg/dl	80-130
Hb1AC	9.5 %	<7%
BUN	18 mg/dl	5-20
Cr.	1.7 mg/dl	0.6-1.2
GFR	40 ml/min	>90

Case 1 (cont.)

- What is the best option for the patient?
 1. Adding Empagliflozin to patient's medications
 2. Withdraw metformin and adding basal insulin to Gliclazide
 3. Withdraw Metformin and Gliclazide and starting basal insulin
 4. Reduce metformin to 500mg q12 hrs, withdraw Gliclazide and adding basal insulin

- The early introduction of insulin should be considered if :
 - There is evidence of ongoing catabolism (weight loss)
 - Symptoms of hyperglycemia are present
 - When A1C levels ($>10\%$) or blood glucose levels ($>300\text{mg/dl}$) are very high.

If injectable therapy is needed to reduce A1C¹

Consider GLP-1 RA or GIP/GLP-1 RA in most individuals prior to insulin²

INITIATION: Initiate appropriate starting dose for agent selected (varies within class)

TITRATION: Titrate to maintenance dose (varies within class)

If above A1C target

Add basal insulin³

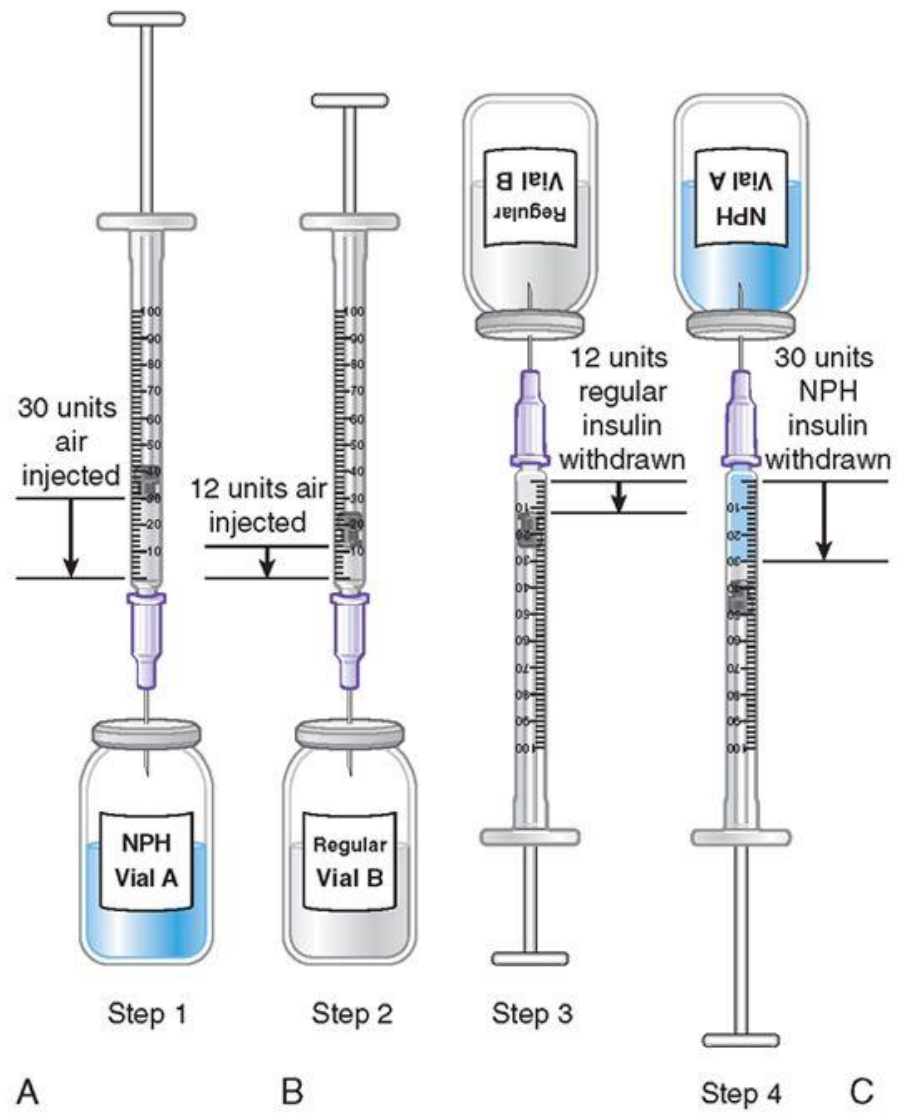
Choice of basal insulin should be based on person-specific considerations, including cost. Refer to Table 9.4 for insulin cost information. Consider prescription of glucagon for emergent hypoglycemia.

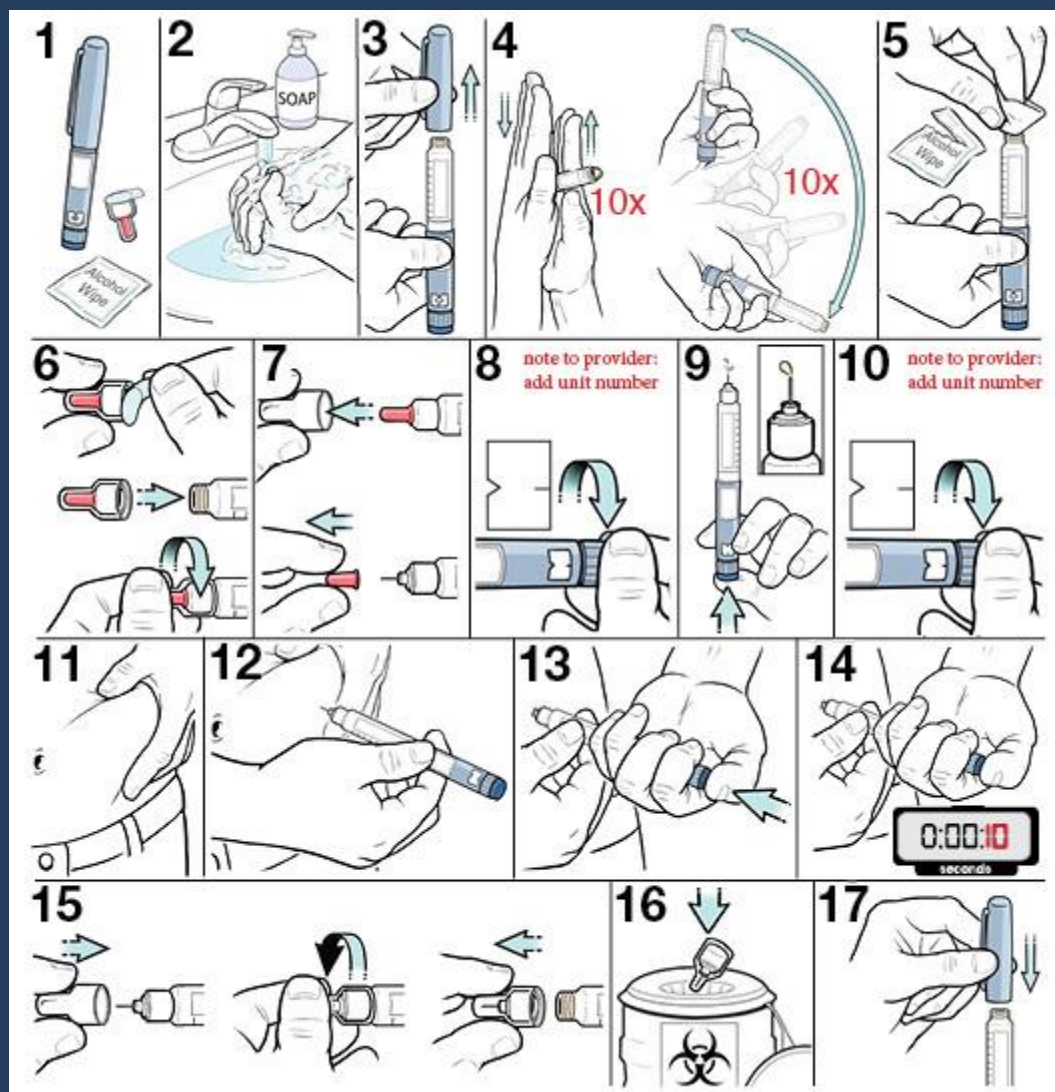
Add basal analog or bedtime NPH insulin⁴

INITIATION: Start 10 units per day OR 0.1–0.2 units/kg per day

TITRATION:

- Set FPG target (see Section 6, “Glycemic Targets”)
- Choose evidence-based titration algorithm, e.g., increase 2 units every 3 days to reach FPG target without hypoglycemia
- For hypoglycemia determine cause, if no clear reason lower dose by 10–20%





Case 1 (cont.)

- After 1mo. of insulin therapy the patient comes to clinic for follow up. He reports weight gain of 2 kg (wt: 62 kg) and improve in his overall well being. No history of hypoglycemia is reported. He uses 34 unit Glargine every night. He reports occasional hypoglycemia. His HbA1C is 8.9%. His SMBG is as followed :

Fasting	2hpp	BS pre-dinner	BS bedtime
150	210	140	110
110	180	170	140
96	195	153	124
182	230	180	136

Case 1 (cont.)

- What is the best next step?

Table 6.3—Summary of glycemic recommendations for many nonpregnant adults with diabetes

A1C	<7.0% (53 mmol/mol)*#
Preprandial capillary plasma glucose	80–130 mg/dL* (4.4–7.2 mmol/L)
Peak postprandial capillary plasma glucose†	<180 mg/dL* (10.0 mmol/L)

- Goals should be individualized based on:
 - duration of diabetes
 - age/life expectancy
 - comorbid conditions
 - known CVD or advanced microvascular complications
 - hypoglycemia unawareness
 - individual patient considerations

If injectable therapy is needed to reduce A1C¹

Consider GLP-1 RA or GIP/GLP-1 RA in most individuals prior to insulin²

INITIATION: Initiate appropriate starting dose for agent selected (varies within class)

TITRATION: Titrate to maintenance dose (varies within class)

If already on GLP-1 RA or dual GIP and GLP-1 RA or if these are not appropriate OR insulin is preferred

If above A1C target

Add basal insulin³

Choice of basal insulin should be based on person-specific considerations, including cost. Refer to Table 9.4 for insulin cost information. Consider prescription of glucagon for emergent hypoglycemia.

Add basal analog or bedtime NPH insulin⁴

INITIATION: Start 10 units per day OR 0.1–0.2 units/kg per day

TITRATION:

- Set FPG target (see Section 6, “Glycemic Targets”)
- Choose evidence-based titration algorithm, e.g., increase 2 units every 3 days to reach FPG target without hypoglycemia
- For hypoglycemia determine cause, if no clear reason lower dose by 10–20%

Assess adequacy of basal insulin dose

Consider clinical signals to evaluate for overbasalization and need to consider adjunctive therapies (e.g., basal dose more than ~0.5 units/kg/day, elevated bedtime–morning and/or post–preprandial differential, hypoglycemia [aware or unaware], high variability)



- Clinical signals that may prompt evaluation of overbasalization include:
 - basal dose more than 0.5 units/kg/day
 - high bedtime– morning or post-preprandial glucose differential
 - hypoglycemia (aware or unaware)
 - high glycemic variability

- If above A1C target and not already on a GLP-1 RA or dual GIP and GLP-1 RA, consider these classes, either in free combination or fixed-ratio combination, with insulin.
- If A1C remains above target:

Add prandial insulin⁵

Usually one dose with the largest meal or meal with greatest PPG excursion; prandial insulin can be dosed individually or mixed with NPH as appropriate

INITIATION:

- 4 units per day or 10% of basal insulin dose
- If A1C <8% (64 mmol/mol) consider lowering the basal dose by 4 units per day or 10% of basal dose

TITRATION:

- Increase dose by 1–2 units or 10–15% twice weekly
- For hypoglycemia determine cause, if no clear reason lower corresponding dose by 10–20%

If on bedtime NPH, consider converting to twice-daily NPH regimen

Conversion based on individual needs and current glycemic control. The following is one possible approach:

INITIATION:

- Total dose = 80% of current bedtime NPH dose
- 2/3 given in the morning
- 1/3 given at bedtime

TITRATION:

- Titrate based on individualized needs

If above A1C target

If above A1C target

Stepwise additional injections of prandial insulin (i.e., two, then three additional injections)

Proceed to full basal-bolus regimen (i.e., basal insulin and prandial insulin with each meal)

Consider self-mixed/split insulin regimen

Can adjust NPH and short/rapid-acting insulins separately

INITIATION:

- Total NPH dose = 80% of current NPH dose
- 2/3 given before breakfast
- 1/3 given before dinner
- Add 4 units of short/rapid-acting insulin to each injection or 10% of reduced NPH dose

TITRATION:

- Titrate each component of the regimen based on individualized needs

Consider twice-daily premixed insulin regimen

INITIATION:

- Usually unit per unit at the same total insulin dose, but may require adjustment to individual needs

TITRATION:

- Titrate based on individualized needs

Case 2

- A 37 years old man with history of diabetes for 6 years and poor compliance presented with FBS 350 and HbA1C 11%. You have started conventional insulin and doses have been adjusted.
- After 1mo. patient comes to clinic for follow up. He reports overnight hypoglycemia four times in this period. He is now on 20 unit NPH with 6 unit Reg. before breakfast and 20 unit NPH with 12 unit Reg. before dinner. His SMBG is as followed :

Fasting	2hpp	BS predinner	BS bedtime	BS 3 am
130	270	140	110	58
240	310	170	140	
96	200	153	124	43
300	390	180	136	

- What would you do for his hypoglycemia?
 1. Withdraw insulin regular before dinner
 2. Withdraw insulin NPH before dinner
 3. Recommend to inject insulin NPH at bedtime
 4. Reduce insulin NPH before breakfast

regimen

Twice-daily "split-mixed": N+R



Timing

Pre-breakfast: 40% N + 15% R
Pre-dinner: 30% N + 15% R



Adjusting
doses

Morning N: based on pre-dinner BGM.
Morning R: based on pre-lunch BGM.
Evening R: based on bedtime BGM.
Evening N: based on fasting BGM.

Advantages :

1. Least number of injection
2. Insulins can be mixed in one syringe.
3. Least (N+R) expensive insulins vs analogs.
4. Eliminates need for doses during the day.

Disadvantages :

1. Risk of hypoglycemia in afternoon or middle of night from N.
2. Fixed mealtimes and meal content.
3. Coverage of post-lunch glucose often suboptimal.
4. Difficult to reach targets without hypoglycemia.

regimen

Three injections daily: N+R



Timing

Pre-breakfast: 40% N+15%R
Pre-dinner: 15% R
Bedtime: 30% N



Adjusting
doses

Morning N: based on pre-dinner BGM.
Morning R: based on pre-lunch BGM.
Pre-dinner R: based on bedtime BGM.
Evening N: based on fasting BGM.

Advantages :

1. Morning insulins can be mixed in one syringe.
2. May be appropriate for those who cannot take injection in middle of day.
3. Morning N covers lunch to some extent.

Disadvantages :

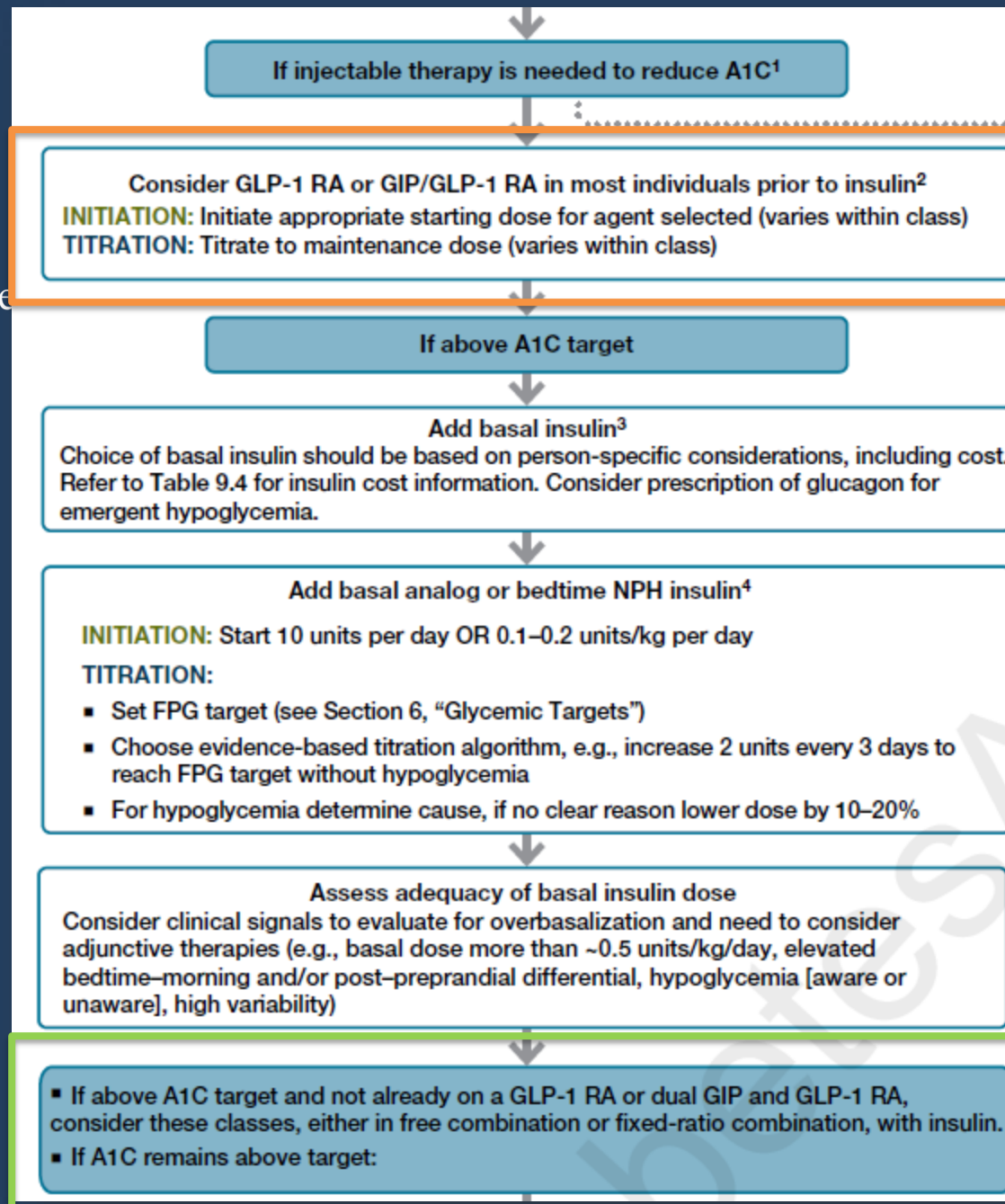
1. Requires relatively consistent mealtimes and carbohydrate intake.
2. Coverage of post-lunch glucose often suboptimal.
3. R must be injected at least 30 min before meal for better effect.

Case 3

- A 64 year old woman with history of diabetes is presented to our clinic with history of diabetes. She is on 1 gr metformin BID. She has history of retinopathy and neuropathy and history of PCI 2 years ago. Her laboratory results are as followed:

Variable	Value	Reference
FBS	210 mg/dl	80-130
2hpp	290 mg/dl	<180
HbA1C	9.5 %	<7%
BUN	13 mg/dl	5-20
Cr.	2.5 mg/dl	0.6-1.2
GFR	24 ml/min	>90

- What is the



- Liraglutide :
0.6 mg/d → 1.2 mg/d → 1.8 mg/d



Case 3

- A 52-year old woman with type 2 diabetes had been treated with insulin for 16 years. She reported episodes of hypoglycemia since 2 years ago which became worse. Recently she has had blood glucose even less than 55 mg/dl without any symptoms.
- She is taking 16 units of NPH in mornings, 10 units of NPH at bedtime and 6 units of regular insulin before meals which she always injected them in abdomen prior each meals. She has no history of weight loss or weakness.
- Physical examination was remarkable for loss of vibration and pinprick sensation. Blood pressure and peripheral pulses are good. No sign of foot ulcers.

- She had regular same diet for 8 years after visiting a nutritionist.
- Her SMBG for 2 consecutive days is as followed:

Fasting	2 hpp	BS before dinner	BS bedtime	BS 2am
200	210	45	240	50
69	187	163	160	120

- Laboratory examination shows :

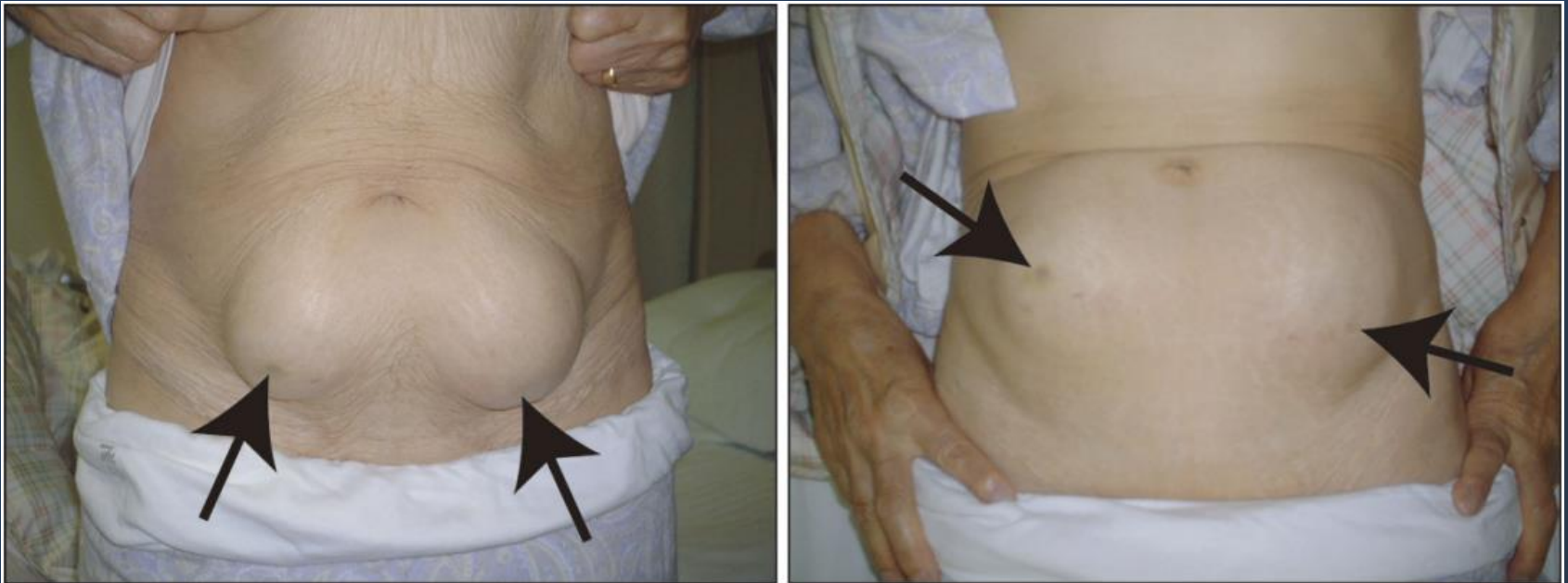
lab	value	reference
FBS	180 mg/dl	80-130
HbA1C	8.5 %	<7%
BUN	22 mg/dl	5-20
Cr.	1.2 mg/dl	0.6-1.2
AST	22 mg/dl	U/l
ALT	14 mg/dl	U/l
TSH	2.5 mIU/l	0.4-4

- What could be the cause of hypoglycemia?
 - Poor adherence to therapy
 - insulin–meal interval non-concordance
 - Hypothyroidism
 - Malabsorption
 - Lipohypertrophy at injection site
 - Primary adrenal insufficiency
 - Pancreatic insulinoma

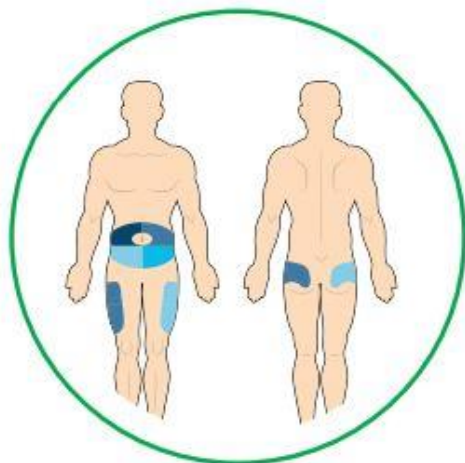
- Repeated insulin injections at the same site lead to lipogenesis by virtue of the hormone's anabolic action, manifested as tissue hypertrophy.
- Using the same needle for multiple injections leads to tissue trauma, which is also a contributory factor.
- By virtue of their faster absorption, the rapid-acting analogs may minimize the tissue exposure to insulin. Hence, they are associated with a lower prevalence of lipohypertrophy compared with regular insulin.



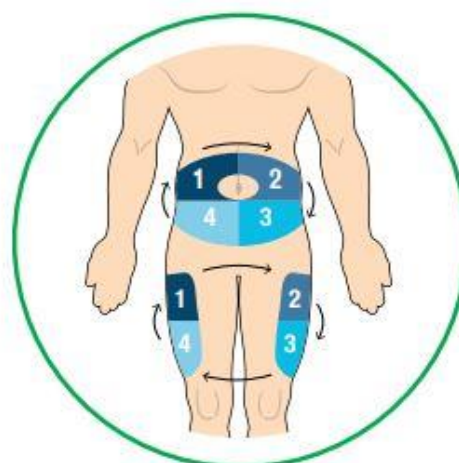
Sharma D. A case of regression of insulin lipohypertrophy with correct injection technique. Journal of Diabetology. 2022 Apr 1;13(2):184.



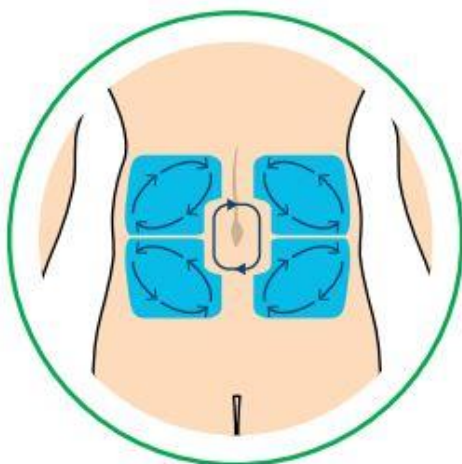
Fujikura J, Fujimoto M, Yasue S, Noguchi M, Masuzaki H, Hosoda K, Tachibana T, Sugihara H, Nakao K. Insulin-induced lipohypertrophy: report of a case with histopathology. *Endocrine journal*. 2005;52(5):623-8.



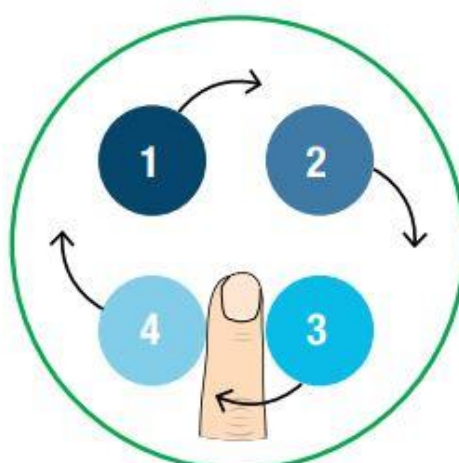
1. Choose an area.



2. Divide that area into four quadrants.



**3. Select a site within a quadrant to start injecting.
Use one quadrant per week.**



**4. Inject one finger-width
away from your last
injection.**

Case 4

- There is a 56 years old man admitted in hospital. Insulin is started for him and after adjusting dose, you are planning to discharge him. He is concern about hypoglycemia and what he should do if it happens. What would you advise?

Step 1:

Take 15 grams of fast-acting carbs such as:



Step 2:



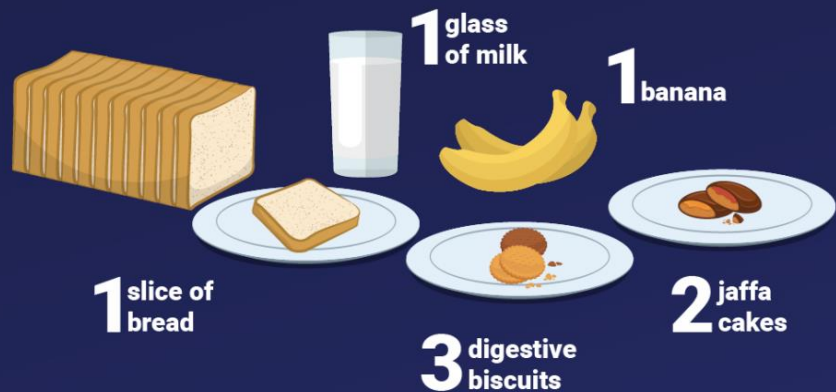
15 min

Wait
test

If BS is still below
go to step 3

Step 3:

Take 15 grams of slow-acting carbs, such as:



Case 5

- A 87 years old woman with history of diabetes, HTN, heart failure (EF:30%) and rheumatoid arthritis, presented to the clinic for glycemic control. She uses insulin glargine 26 unit at nights and insulin aspart 8 units before meals. She reports occasional hypoglycemia but due to deformities she is not able to measure her blood glucose. Her laboratory results are as followed:

Lab	Value	Referenca
FBS	180 mg/dl	80-130
HbA1C	7.8%	<7%
BUN	14 mg/dl	5-20
Cr.	1.1 mg/dl	0.6-1.2
GFR	92 ml/min	>90

- What is the best option for her?
 1. Withdraw insulins and order metformin, gliclazide and pioglitazone
 2. Withdraw insulin aspart, order metformin and adjust glargine
 3. Adjust insulin doses based on FBS and patient reports of hypoglycemia
 4. Admit the patient and adjust insulin doses

Simplification of Complex Insulin Therapy

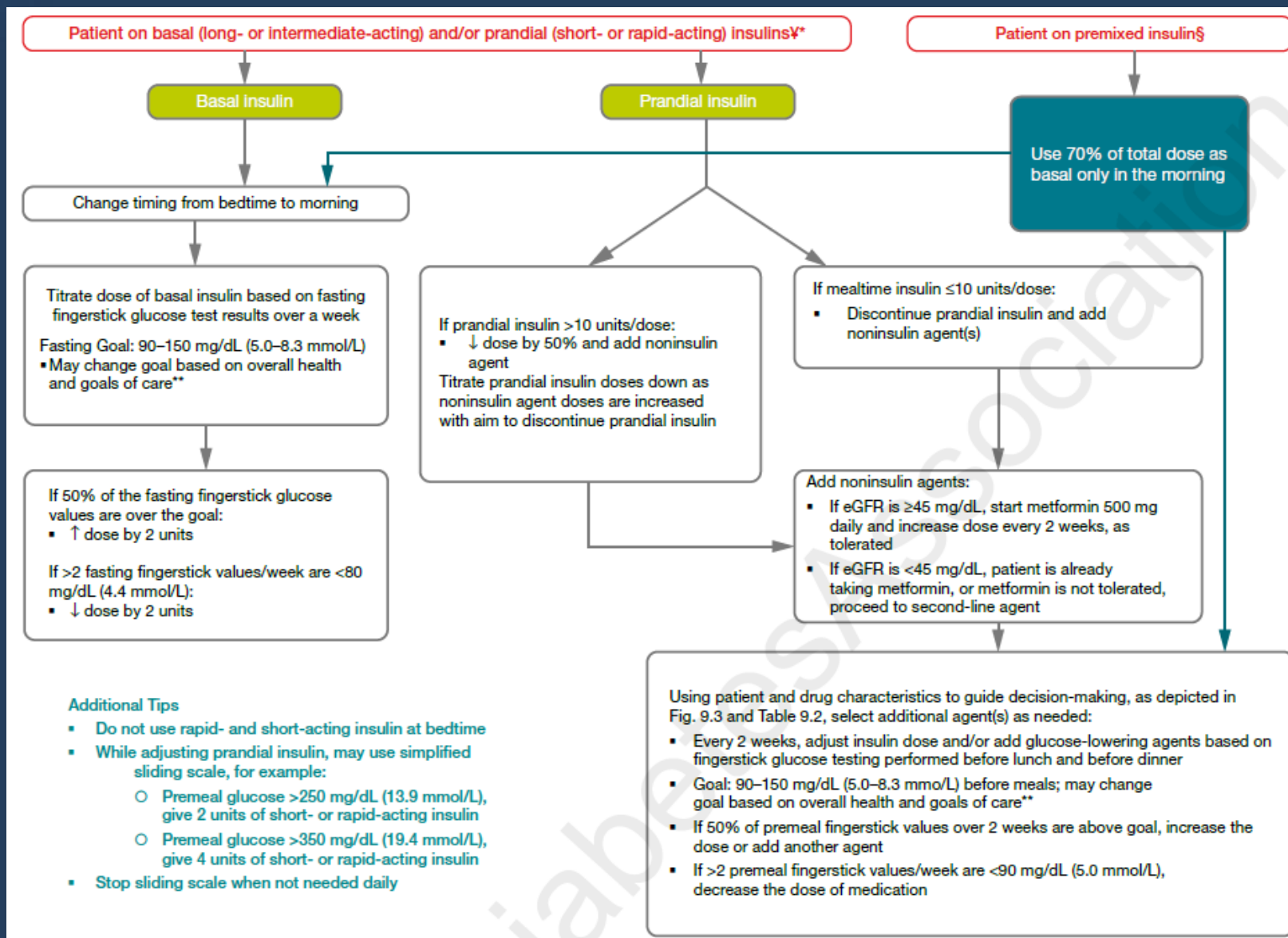


Table 13.1—Framework for considering treatment goals for glycemia, blood pressure, and dyslipidemia in older adults with diabetes

Patient characteristics/ health status	Rationale	Reasonable A1C goal‡	Fasting or preprandial glucose	Bedtime glucose	Blood pressure	Lipids
Healthy (few coexisting chronic illnesses, intact cognitive and functional status)	Longer remaining life expectancy	<7.0–7.5% (53–58 mmol/mol)	80–130 mg/dL (4.4–7.2 mmol/L)	80–180 mg/dL (4.4–10.0 mmol/L)	<130/80 mmHg	Statin, unless contraindicated or not tolerated
Complex/intermediate (multiple coexisting chronic illnesses* or two or more instrumental ADL impairments or mild-to-moderate cognitive impairment)	Intermediate remaining life expectancy, high treatment burden, hypoglycemia vulnerability, fall risk	<8.0% (64 mmol/mol)	90–150 mg/dL (5.0–8.3 mmol/L)	100–180 mg/dL (5.6–10.0 mmol/L)	<130/80 mmHg	Statin, unless contraindicated or not tolerated
Very complex/poor health (LTC or end-stage chronic illnesses** or moderate-to-severe cognitive impairment or two or more ADL impairments)	Limited remaining life expectancy makes benefit uncertain	Avoid reliance on A1C; glucose control decisions should be based on avoiding hypoglycemia and symptomatic hyperglycemia	100–180 mg/dL (5.6–10.0 mmol/L)	110–200 mg/dL (6.1–11.1 mmol/L)	<140/90 mmHg	Consider likelihood of benefit with statin