ECHO Diabetes Correction Insulin & Sick Day Insulin

Carol Greenlee MD March 7, 2024

Pre-Question - which two options are correct?

- Correction Insulin therapy
 - A. Is intended to lower blood glucose level to the desired target range
 - B. Can safely be administered every 15 minutes until blood glucose is at target
 - C. Requires therapy with an insulin pump
 - D. Can be used with or without mealtime insulin
 - A & B
 - A & C
 - A & D
 - B & C
 - B & D
 - C & D

Insulins

2)

Basal Insulin:

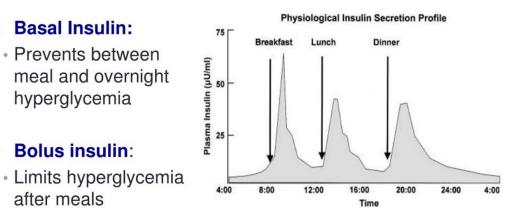
hyperglycemia

Bolus insulin:

after meals

- Dosing to try to replace /mimic the natural secretion of insulin
 - **Basal insulin** is designed to *suppress* hepatic glucose production and improve basal (fasting) hyperglycemia
 - Bolus (mealtime, prandial) Insulin –as rapid-acting insulin - limits hyperglycemia after meals(covers food carbs) – should hold(not give) if NPO or not eating
 - **Correction Insulin** *extra* rapid-acting insulin given for high blood glucose to decrease BG levels to target range - based on patient's "sensitivity or correction factor" - can be used to:
 - Add more insulin to a mealtime bolus to correct for a high premeal blood glucose
 - Used alone to correct a high blood glucose outside of mealtime or if NPO or illness

Definitions



Adding Rapid-acting Insulin – Meal Coverage (prandial) vs Correction Insulin

Bolus (mealtime, prandial) Insulin ("Carbohydrate Coverage")

- as rapid-acting insulin limits hyperglycemia after meals(covers food carbs)
- should hold if NPO or not eating [based on ingested carbs not time of day or BG level]

Correction Insulin ("High Blood Sugar Correction Dose") = *extra rapid-acting insulin given for high blood glucose* to decrease BG levels to *target range* [based on blood glucose level]

- The dose of "correction insulin" is the amount of insulin needed to lower the BG from its current level to the *target level* over the *time of insulin action*
 - depends on how sensitive the patient is to insulin (sensitivity factor or correction factor)
- You want to correct a high BG to a target level BG (not to zero)
 - Current BG Target BG = the *amount BG needs to come down to get to target*
 - E.g., 230-100 = 130 mg/dl BG needs to come down 130 mg/dl not 230 mg/dl

Next need a Correction Factor or Sensitivity Factor to determine Correction Dose of insulin

Calculating the Correction Dose

Correction dose of Insulin = CF

Correction Factor (CF) or Sensitivity Factor (SF)

The CF = the mg/dl drop in BG caused by 1 unit of insulin (depends on sensitivity to insulin - weight, age, renal function, etc.)

The right correction dose will return the BG to within 30 mg/dl of the target blood glucose about **3-4 hours** after the dose is injected (RA insulin analog)

Calculating a Correction Factor(CF)/Sensitivity Factor(SF)

For patient new to insulin/sick day insulin calculate by using **3000/weight in Kg**

or - If patient already treated with insulin can Use 1700/TDD* e.g., patient weighs 100 kg **3000/100kg=30** 1u should reduce BG by 30 points

If impaired renal function/older age – will need "weaker" correction dose by using larger CF (SF) number (e.g., 50 – 1u lowers BG 50 points vs 30 points) This gives **less insulin** as the correction dose of insulin

With severe IR/infection, may need to go to "stronger" correction dose by using smaller CF (SF) number (e.g., 20 - 1u lowers BG 20 points vs 30 points) This gives **more insulin** as the correction dose of insulin

Quick "cheat sheet" for Correction Factor(CF)/Sensitivity Factor(SF)

CF based on patient weight

- <60 lb. = 100
- 60—80 lb. = 75
- 81—100 lb. = 60
- 101—120 lb. = 50
- 121—140 lb. = 45
- 141—170 lb. = 40
- 171-200 lb. = 30
- 201—230 lb. = 25
- 231—270 lb. = 20
- >270 lb. = 15

Correction Insulin

- Correction insulin doses can be used to:
 - add more insulin to a mealtime bolus to *correct* for a high premeal blood glucose
 - used alone to *correct* a high blood glucose outside of mealtime or if NPO or with illness
 - Can be used with basal-bolus insulin therapy
 - Can be added to oral therapy and/or basal insulin

Adding Correction Insulin to Prandial (rapid-acting) Insulin for Meal Coverage

- Add insulin to a mealtime bolus to correct for a high premeal blood glucose –
- Case example: the patient is on a fixed carb diet of 50 grams/meal & has an ICR of 1:10 → will take 5u Rapid Acting insulin for meal coverage dose
 - Can estimate Correction Factor as 3x ICR or 1700 Rule (1800 Rule for Regular Insulin)
 - Adjust based on response [some studies suggest 1700 Rule underestimates bolus needs*]
- They have a **Correction Factor of ~30** (1 unit lowers the BG 30 points)
 - If their premeal target is 80-140 range (target BG 110) and if their premeal BG is above target range (e.g.,200) they can *add correction insulin to their premeal dose* to help *reduce the high BG as well as cover the carbs.*
 - The patient can use the *Correction Formula* to calculate the dose of correction insulin: [Current BG – Target BG/CF = Correction dose]
 - For this patient that would be $[200 110 = 90] \rightarrow [90/30 = 3u] \rightarrow$
 - they would add the 3u correction dose to the 5u meal dose for 8u total dose before the meal

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- Case example: the patient is on a fixed carb diet of 50 grams/meal & has an ICR of 1:10
 → takes 5u Rapid Acting insulin for meal coverage dose
- They have a **Correction Factor of ~30** (1 unit lowers the BG 30 points)
 - If their premeal target is 80-140 range (target BG 110) and if their premeal BG is above target (e.g.,200) they can *add correction insulin to their premeal dose* to help *reduce the high BG as well as cover the carbs.*
 - Many patients are not comfortable with math, especially division you might provide a *Correction Scale* for them to use (less precise but still helpful):
 - 5u if BG 80-140 (only needs meal coverage since premeal BG is in target range for this patient)
 - 6u (5u+1u) if 141-170 (adding 1 unit for BG 30 points above target range to the meal insulin coverage dose)
 - 7u(5+2u) if 171-200, etc. (adding 2 units for 60 points above target range) see cheat sheet

Be sure to practice with them and have them demonstrate ("show me") back how to use

Correction Scales for different Correction Factors – general

- CF 50: for BG 141-190 add 1u; 191-240 2u; 241-290 3u; 291-340 4u; 341-390 5u; 391-440 6u; 441-490 7u, etc.
- **CF 40:** for BG 141-180 add 1u; 181-220 2u; 221-260 3u, 261-300 4u, 301-340 5u, 341-380 6u, 381-420 7u, 421-460 8u, 461-500 9u, etc.
- **CF 30:** for BG 141-170 add 1u; 171-200 2u; 201-230 3u; 231-260 4u; 261-290 5u; 291-320 6u; 321-350 7u; 351-380 8u; 381-410 9u, etc.
- **CF 25:** for BG 141-165 add 1u; 166-185 2u; 186-210 3u; 211-235 4u; 236-260 5u; 261-285 6u; 286-305 7u; 306-330 8u; 331-355 9u, etc.
- CF 20: for BG 141-160 1u; 161-180 2u; 181-200 3u; 201-220 4u, etc. OR
 - BG 141-180 add 2u; 181-220 4u; 221-260 6u, 261-300 8u, 301 -340 10u, 341-380 12u, 381-420 14u, 421-460 18u, 461-500 18u, etc.

Example for Using Correction Insulin for Illness

- During illness aim for blood glucose in **110-180 range (target ~140)**
 - Therefore, you might use target BG of 140 for 110-180 range
 - If high risk of low BG aim for 140-180 range (target BG 160)
- Example of Correction dose calculation for CF 30
 - [current BG-target BG/CF] e.g., Current BG is 350 and target is ~140
 - 350-140/30 = 210/30 = 7u correction dose of rapid acting insulin to bring BG down 210 points
 - If this does not bring glucose down to target range you can strengthen the CF to increase the correction dose: 210/25 = 8u; 210/20 = 10.5u; 210/15 = 14u
 - Can give patient a **correction scale**: e.g., for BG 180-210 1u; BG 211-240 2u; BG 241-270 3u, 271-300 4u, BG 301-330 5u, etc.
 - See cheat sheet to copy and paste for different CF values

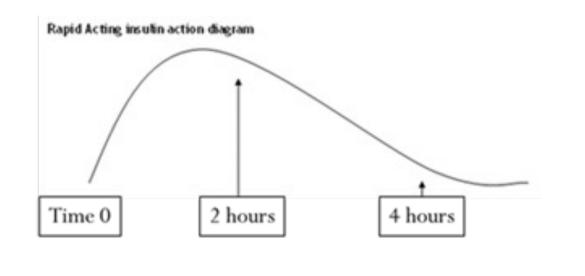
Correction Scales for different Correction Factors for Illness

- **CF 50:** for BG 181-230 give 1u; 231-280 2u; 281-330 3u; 331-380 4u; 381-410 5u; 411-460 6u; 461-510 7u, etc.
- **CF 40:** for BG 181-220 give 1u; 221-260 2u; 261-300 3u, 301-340 4u, 341-380 5u, 381-420 6u, 421-460 7u, 461-500 8u, 501-540 9u, etc.
- **CF 30:** for BG 181-210 give 1u; 211-240 2u; 241-270 3u; 271-300 4u; 301-330 5u; 331-360 6u; 361-390 7u; 391-420 8u; 421-450 9u, etc.
- **CF 25:** for BG 176-200 give 1u; 201-225 2u; 226-250 3u; 251-275 4u; 276-300 5u; 301-325 6u; 326-350 7u; 351-375 8u; 376-400 9u, etc.
- CF 20: for BG 181-200 1u; 201-220 2u; 221-240 3u; 241-260 4u, etc. OR
 - BG 181-220 give 2u; 221-260 4u; 261-300 6u, 301-340 8u, 341-380 10u, 381-420 12u, 421-460 14u, 461-500 18u, 501-540 18u, etc.

Guide for Using Correction Insulin

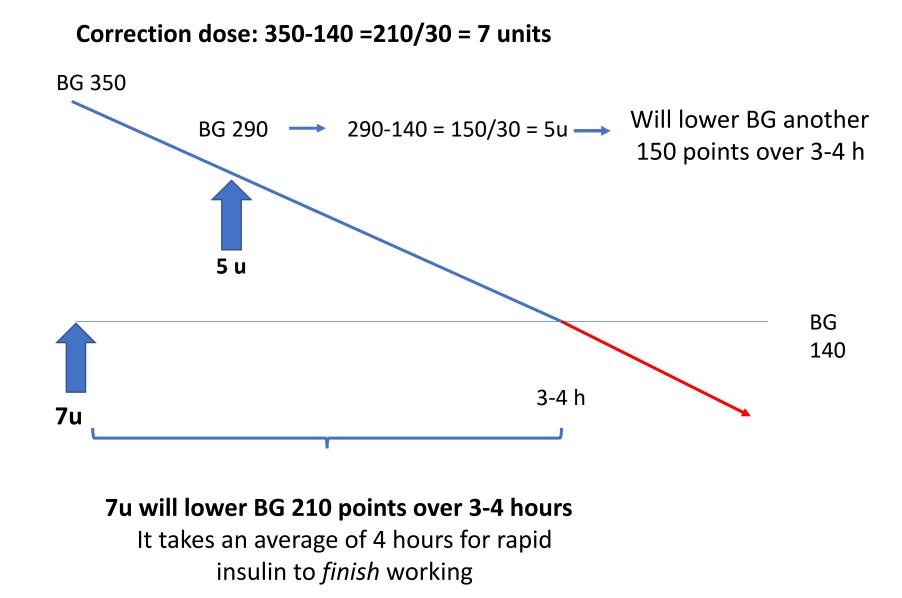
Only give (dose) Correction Insulin

- every 3-4 hours for analog insulin -
- every 4-6 hours for Regular insulin -
- otherwise end up "stacking" insulin and risk of low BG
 - Explain it takes Fast Insulin 3-4 hours to finish working



Can give Meal insulin every time you eat since this is covering ingested carbs – but Correction insulin should usually only be given every 3-4 hours

"Stacking" Correction Doses



What BG level to start adding correction insulin

- Practical approach:
 - If SF is 40 or less, can start at any BG >140
 - 145-100/40 = 45/40 = 1 unit
 - 145-100/30 = 40/30 = 1.5 unit can round
 - If BG 278-100 = 178/30 = 5.
 - 145-100/20 = 45/20 = 2.0 units
 - If SF is >40 more practical to start correcting at BG > [CF+100]
 - e.g., if CF 70 recommend start adding correction insulin at BG >170
 - 171 100/70 = 71/70 = 1 unit
 - vs 141-100/70 = 41/70= .56 units (can do with pump but not injections)
 - For illness can start correcting at BG >180 (200 -250) depending on situation

"Sick-day Insulin" - Glucocorticoid Induced Hyperglycemia

- The mechanisms by which corticosteroids cause hyperglycemia include both *increased insulin resistance*:
 - increased hepatic gluconeogenesis
 - increases in central and visceral adiposity
 - greater lipolysis in peripheral fat stores and
 - a rise in glucagon
 - impaired endogenous GLP1 activity

• and *impairment of insulin synthesis*:

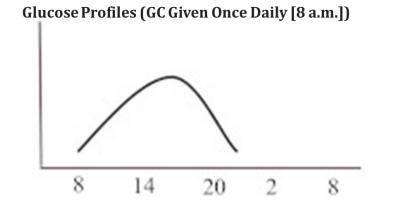
- direct effects on Beta cells to inhibit insulin production and secretion
 - Inflammation & injury of Beta cells
- a reduction in the incretin effect
- "Despite being common, glucocorticoid-induced diabetes and hyperglycaemia remains a neglected clinical issue and action is needed to generate more evidence to underpin clinical guidance." https://onlinelibrary.wiley.com/doi/full/10.1111/dme.14843

Variable Individual Glycemic Response to Glucocorticoids(GCs)

- GCs may be administered by various regimes and in variable doses and may cause hyperglycemia when administered at supraphysiological doses by any route (topical, oral, inhaled, intramuscular, intravenous, or intra-articular)
- Difficult to provide guidelines on dosing insulin for GC therapy
 - "the GC induced additional *insulin requirements* to achieve reasonable glycaemic control varied considerably and independently from previous insulin dose (30–100% increase) which makes recommendations for adjustments challenging"
 - Factors that influence glycemic response:
 - Individual GC receptor sensitivity, ability to inactivate or activate GCs
 - Profile of the GC medication/ variations in systemic absorption(e.g., inflamed joints)
 - Effect of illness/stress on glucose metabolism & GC metabolism
 - Comorbidities and other medications (e.g., renal function, BMI, protease inhibitors, age)
 - Most suggest that the glucose lowering agents of choice should match daily glucose profiles
 - the mechanism of action of GL agent should fit to the corresponding GC agent.

GCs in the outpatient population

- A single or short course of an oral GC (e.g., prednisolone) in the morning may be the *commonest mode* of administration.
 - In susceptible patients, this will often result in a rise in blood glucose by late morning that continues into the evening (~4 to 8 hours following the administration of oral GCs)
 - Overnight the blood glucose generally falls back, often to baseline levels the next morning.
 - Fasting blood glucose measurements can underestimate glucocorticoid-induced hyperglycemia and diabetes, particularly in intermediate-acting treatments that are administered in single morning doses.
 - Glucocorticoids cause predominantly postprandial hyperglycemia
 - **Postprandial glycemia after lunch** offers the greatest diagnostic sensitivity.

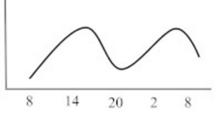


Insulin is usually the treatment of choice because of its efficacy and safety. Insulin provides:

- an immediate onset of action
- an unlimited hypoglycemic power
- can be easily titrated

Insulin therapies

- Morning administration of basal human insulin (Humulin or Novolin N) may closely fit the glucose excursion induced by a single dose of oral steroid in the morning.
 - E.g., 10 units of basal human (NPH) insulin with a daily dose increase of between 10% and 20%, titrated to the blood glucose level
 - dose increments of up to 40% have been shown to be required in some individuals
 - ADA [with] "once-or twice-daily steroids, administration of NPH is standard approach (because NPH action peaks at 4-6h after administration it is best to give it concomitantly with steroids) – [NPH can be] administered in addition to daily basal-bolus insulin or in addition to oral anti-diabetic medications"



Estimation of the Initial Dose of Insulin in Glucocorticoid- Induced Hyperglycemia, According to the Type and Dose of Glucocorticoids

Prednisone dose, mg/day	Dexamethasone dose, mg/day	Insulin NPH, glargine/detemir dose, IU/kg/day
≥40	≥8	0.4
30	6	0.3
20	4	0.2
10	2	0.1

Can use **weight-based** dosing – various starting doses:

- starting with 0.4 IU/kg of NPH insulin
- starting with 0.3 IU/kg of NPH insulin
- starting with 0.2-0.3 IU/kg NPH insulin

Others suggest

- recommended initiating **10 units of basal human insulin (NPH)**
- with a daily dose increase of 10% to 20%
- however, some individuals may require up to 40% dose increments

Another option – increase TDD of insulin

- very little evidence available consider a cautious increase in total daily insulin dose (TDD) according to prednisolone (or prednisolone equivalent [PE]) dose:
 - PE of 20 mg \rightarrow 10% increase in TDD
 - PE of 40 mg \rightarrow 20% increase in TDD
 - PE of 60 mg \rightarrow 30% increase in TDD
- Basal analogue insulin may be appropriate if hyperglycemia is present throughout the day and into the evening (especially for long-acting glucocorticoids such as dexamethasone & multidose or continuous glucocorticoid use)
 - Care should be taken to identify and protect against nocturnal and early morning hypoglycemia if insulin glargine, insulin detemir or insulin degludec are used in this context.

A variety of suggestions for tapering insulin dose as taper glucocorticoid dose

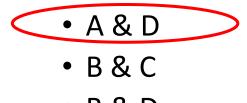
- "In a pragmatic approach, insulin dose can be adjusted by half the percentage of the GC dose change.
 - For example, when GCs are increased or tapered by 50%, insulin dose is suggested to be increased or reduced by 25%, respectively."
- "the dose of NPH insulin could be decreased by 0.1 unit per kg for every 10 mg reduction in the prednisone dose."
- "a weekly 5 mg reduction of prednisolone from 20 mg may require a 20–25% reduction in insulin dose"
- "If steroid dose **reduced**, consider dose reduction of insulin by 25–50%
 - If steroid dose *ceased*, consider reduction to pre steroid treatment"
- "This glucose increase was sustained the day after GC therapy was discontinued, indicating a longer lasting hyperglycaemic effect despite the use of an intermediateacting GC agent"
- *"hyperglycemia may not resolve with steroid discontinuation"*
 - Ongoing increased insulin requirements
 - Persistent diabetes after steroid induced diabetes

Summary – Key Points

- Correction insulin utilizes Regular or RAA insulin to reduce elevated BGs to target range
 - based on the patient's individual Sensitivity Factor & Target range
 - can be added to mealtime insulin or used between meals and/or when patient NPO or ill
 - can be used as "sick day insulin" added to non-insulin meds &/or basal insulin
 - need to avoid "stacking" doses of correction insulin
 - allow 3-4 hours between correction doses for RAA insulin & 4-6 h for Regular Insulin
- Glucocorticoids by any route can cause variable glycemic response in PWD
 - Most common outpatient GC treatment is once or twice daily oral Prednisone/Prednisolone
 - NPH insulin dosed at same time as the GC is usually preferred
 - dose can be based on GC dose & weight or started with 10u & titrated up/down by 10-40%
 - can be dosed "on top of" baseline meds, including basal or basal/bolus insulin
 - May also need correction insulin with meal boluses
 - Continue baseline meds unless poor dietary intake
 - Taper of Insulin dose is usually needed as GC dose is tapered various suggestions
 - Glycemia may not return to baseline after GC stopped

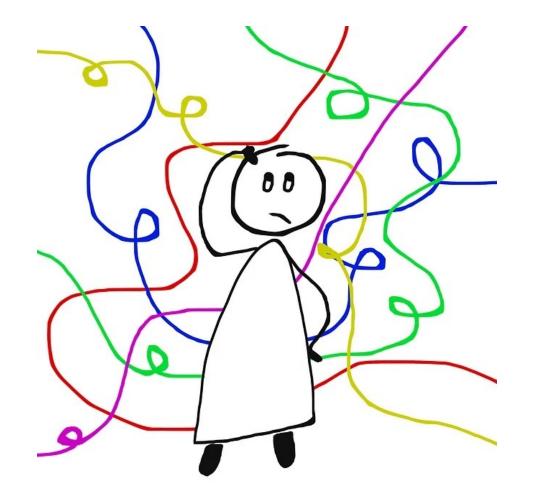
Post-Question - which two options are correct?

- Correction Insulin therapy
 - A. Is intended to lower blood glucose level to the desired target range
 - B. Can safely be administered every 15 minutes until blood glucose is at target
 - C. Requires therapy with an insulin pump
 - D. Can be used with or without mealtime insulin
 - A & B
 - A & C



- B & D
- C & D

Questions, Comments, Clarifications, etc.



Glucocorticoid-induced hyperglycemia

- <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8157052/#:~:text=In%20a%20pragma</u> <u>tic%20approach%2C%20insulin,reduced%20by%2025%25%2C%20respectively</u>.
- <u>https://www.waterloowellingtondiabetes.ca/userContent/documents/Professional-Resources/Steroid%20Induced%20DM%20HCP%20Guide_Final_Feb2023.pdf</u>
- <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8157052/</u>
- https://journals.sagepub.com/doi/10.1177/2633559X211056902
- <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9142341/</u> <u>https://www.diabetes.org.uk/resources-s3/2017-</u> 09/JBDS%20management%20of%20hyperglycaemia%20and%20steriod%20therapy_ 0.pdf
- <u>https://www.health.qld.gov.au/__data/assets/pdf_file/0018/1175211/g-steroid-induced-hyperglycaemia.pdf</u>

Glucocorticoid-induced hyperglycemia

- <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9545315/</u>
- <u>https://www.nature.com/articles/s41574-022-00683-6</u>
- <u>https://www.tandfonline.com/doi/full/10.2147/DMSO.S330253</u>
 - The dose of insulin should be based on the dose of GC. If the dose of prednisolone (or its equivalent dose of GC) is 10, 20, 30, or 40 mg, then the dose of NPH or basal insulin should be 0.1, 0.2, 0.3, 0.4 U/kg per day, respectively.

https://www.tandfonline.com/doi/full/10.2147/DMSO.S330253

- Patients with pre-existing diabetes who are already on oral or injectable therapy can continue the same as long as they are clinically stable and eating adequately. However, depending on the degree of hyperglycemia, modification of doses may be required.
 - Metformin, dipeptidyl peptidase-4 (DPP-4) inhibitors, sodium/glucose cotransporter-2 (SGLT2) inhibitors, pioglitazone, Glucagon-like peptide 1 receptor agonist (GLP1Ra), and existing insulin regimens should be continued. The dose of sulfonylurea can be increased if needed.
- The expert group also agreed that existing or current therapy should be continued in such patients.
- The committee recommended initiating 10 units of basal human insulin with a daily dose increase of 10% to 20% to blood glucose level; however, some individuals may require up to 40% dose increments, as shown in some studies

Alternative options <u>https://www.mdpi.com/2077-0383/10/10/2154</u>

- If short acting GCs are used, then an increase of rapid-acting insulin at the time point of GC intake might be sufficient. A correctional rapid-acting insulin dose can be administered in case of persistent hyperglycaemia after 3–4 h when the rapid-acting insulin action has tapered off
- Adjustments of insulin therapy when intermediate-acting steroids (e.g., prednisolone) are used:
 - Approach A: An increased dose of rapid-acting insulin at the time of intermediate-acting prednisolone administration might be appropriate aiming to achieve glucose control at noon.
 - Approach B: In case of pre-existing therapy with intermediate-acting basal-insulins (NPH insulin or insulin detemir) that are usually injected twice daily, a dose increases at the time point of GC intake (usually in the morning) is recommended.
 - Approach C: In patients previously using (ultra-)long acting basal-insulins (insulin glargine U100/U300 or insulin degludec), approach A might be sufficient; in case of an expected long-term GC treatment, these patients might benefit most from a switch to intermediate-acting basal insulins (NPH insulin, insulin detemir. In such case, the basal insulin should be injected twice daily with a proportionally higher dose at the time point when the GC agent is administered.
- Adjustments of insulin therapy when long-acting steroids (e.g., dexamethasone) are used:
 - Long-acting GCs will trigger continuous and long-lasting hyperglycaemia over 24 h, thus it might be suitable to adjust the total daily basal-insulin dose according to the GC dose as outlined above.
- ** tapering steroids (reduce steroid by 50%, reduce insulin by 25% prolonged GC effect)

Titrating & tapering Insulin with GCs

- In those identified as experiencing steroid-induced hyperglycemia (whether new onset or pre-existing DM), BGs need to be monitored more frequently as courses of GC treatment begin to assess a patient's response and the degree of added pharmacology that is required to optimize BGs. Timely dose increases of up to 20%/day are not uncommon as a treatment cycle begins.
- As tapering or discontinuation of GCs occur, concomitant reduction in in BG lowering medications must occur to avoid hypoglycemia.
- There is no standard algorithm that encompasses the art & science of this process. It depends upon individual responses to the titration schedule, type and dose of steroid, and extent of the duration of steroid
- Patients on agents that can cause hypoglycemia should be counselled to check their BG more frequently than usual during tapering periods for 1-3 days after a reduction in GC dose, (as it can take this much time for the glycemic effect of GCs to diminish), to be able to make appropriate adjustments to diabetes medications.
- Some patients **will not return to baseline pharmacologic medication doses** and may require higher doses to maintain normal BGs than they did prior to GC treatment.