



Inpatient Diabetes/Hyperglycemia

May 5, 2023

Nazanene H. Esfandiari, MD

Professor

MEND Service Chief

Co-Director, Hospital Intensive Insulin Program

Co-Director, Endocrine Sequence, Scientific Trunk, U of Michigan Medical School

Metabolism, Endocrinology, & Diabetes (MEND)



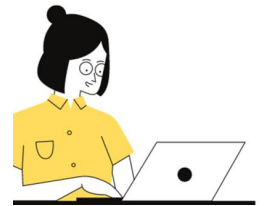
Nothing to Disclose

Objectives

- Impact of hyperglycemia in the inpatient setting
- Target glucose in the hospital
- Management of different cases in the hospital
 - Stress hyperglycemia
 - Type 1 diabetes and the use of technology
 - Type 2 diabetes
 - Steroid-Induced hyperglycemia
 - Cystic Fibrosis Related Diabetes (CFRD)
 - Tube feeding and TPN/PPN use
 - ESRD
- SGLT2 inhibitors and GLP 1 analogues in the hospital
- Discharge instructions

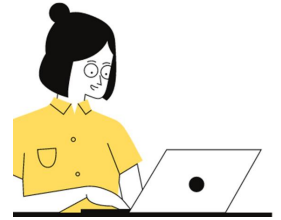


Case 1



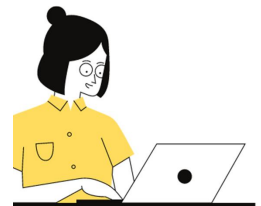
- A 70-year-old woman with type 2 diabetes, HTN and dyslipidemia, is admitted with COVID infection with respiratory symptoms. Prednisone 40 mg daily is started in the morning and her glucose rose to high 300-low 400 mg/dl. She takes glargine 40 units SQ daily, meal lispro 10 units and lispro moderate sliding scale. In addition, she takes lisinopril 20 mg daily and atorvastatin 40 mg daily. Her glucoses before admission were between 100 and 160 mg/dl.
- On physical exam, BP: 130/70 mmHg, HR: 64/min, and BMI of 30 kg/m². She appeared in mild respiratory distress with rhonchi bilaterally. No leg edema and heart exam was unremarkable.
- Labs: A1C: 7.0%, WBC: 9.8 (4-10), Creatinine: 1.2 mg/dl with eGFR of 50. Fasting glucose is 120 mg/dl but the rest of the day she is in high 300-low 400 mg/dL.

Case 1



- Which of the following regimen is the best treatment option in the management of her diabetes in the context of COVID infection?
 - A. Increase glargine dose
 - B. Change lispro to Fiasp (insulin aspart)
 - C. Increase lispro moderate sliding scale to high dose sliding scale
 - D. Add NPH in the morning to glargine and lispro
 - E. Add metformin 500 mg twice daily to glargine and lispro

Case 2



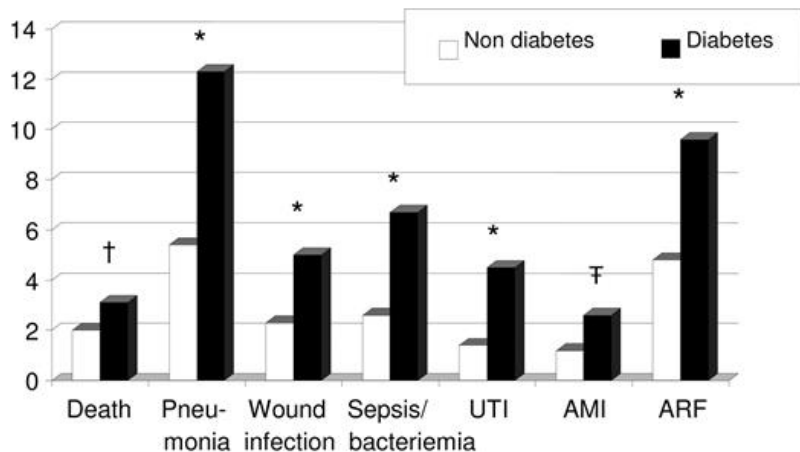
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He has fever and his blood glucoses are running around 250-300 mg/dl.

In addition to starting IV antibiotics, what is the best treatment option for his diabetes?

- A. Start glargine 17 units SQ daily and lispro 6 units with each meal
- B. Start glargine 30 units SQ daily and lispro 10 units with each meal
- C. Start regular insulin per sliding scale
- D. Add sitagliptin to metformin

Thirty Day Mortality and Inhospital Complications in diabetic and non-diabetic subjects Undergoing Non-Cardiac Surgery

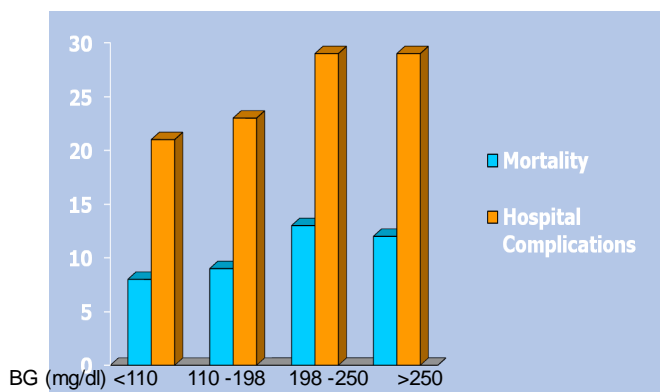


3,184 noncardiac surgery patients
Emory University Hospital January 2007-June 2007

A Frisch & Umpierrez et al. Diabetes Care, May 2010

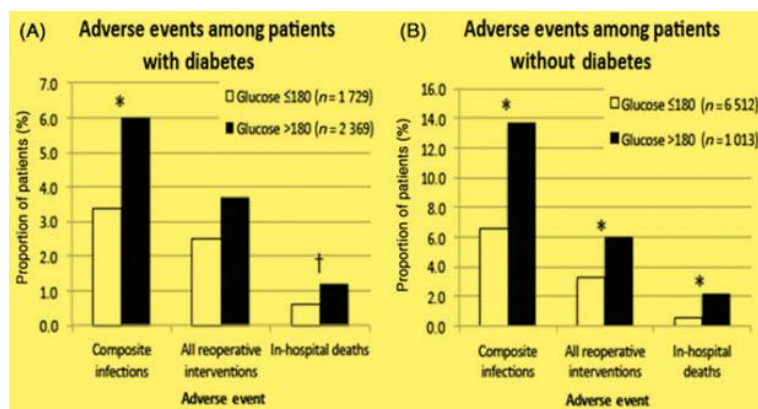
Hospital Hyperglycemia and Outcomes – non ICU

Day of Admission BG and Pneumonia Outcomes



2,471 patients with Community Acquired Pneumonia : $p < 0.05$ vs BG < 198 mg/dl

Perioperative BG and Outcomes



Outcomes stratified by perioperative hyperglycemia (>180 mg/dL at any point on the day of surgery, postoperative day 1 or 2) for diabetic patients (A) and nondiabetic patients (B). * $P < 0.01$; † $P < 0.05$.

ADA 2023: DIABETES CARE IN HOSPITAL

Perform an A1c test on all patients with diabetes or hyperglycemia (BG >140 mg/dl) if not performed in the prior 3 months



Insulin should be administered using validated written or computerized protocols that allows for predefined adjustments in the insulin dosage based on BG



Glycemic Targets

- Insulin Therapy should be initiated in persistent hyperglycemia ≥ 180 mg/dl.
- Target BG in ICU: 140-180 mg/dl
- Target BG in non-ICU: 140-180 mg/dl
- Expert Consensus and ES BG targets in non-ICU: 100-180 mg/dl

Glucose lowering treatment in hospital

- Basal or basal plus bolus correction insulin regimen is the preferred treatment for non-ICU patients with poor oral intake or NPO.
- Basal, prandial and correction bolus for non-ICU patients with good nutritional intake.

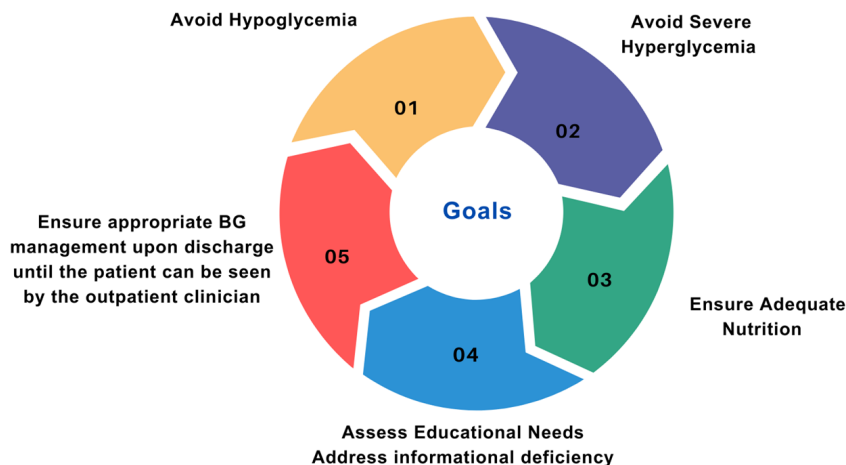


Transition of Care

Structured discharge plan tailored to the individuals

Diabetes Care 2023;46(Supplement_1):S267–S278

Goals in The Inpatient Setting



Hypoglycemia

Hypoglycemia alert- BG < 70 mg/dl but ≥54 mg/dl(level 1)

Significant hypoglycemia - BG < 54 mg/dl (level 2)

Severe hypoglycemia –a severe event characterized by altered mental and/or physical functioning that requires assistance from another person for recovery (level 3)

Diabetes Care 2019;42(Supplement_1):S61–S70

Nutrition and monitoring

- Carb consistent diet
- Monitor capillary glucose level before each meal, bedtime and 3 am
- Give meal insulin close to the meal or as soon as the meal is consumed



Oral and Non-Insulin Agents in the Hospital

Sulfonylureas - Hypoglycemia

Metformin - CI with decreased renal perfusion, use of iodinated contrast dye

Thiazolidinediones - Edema and CHF

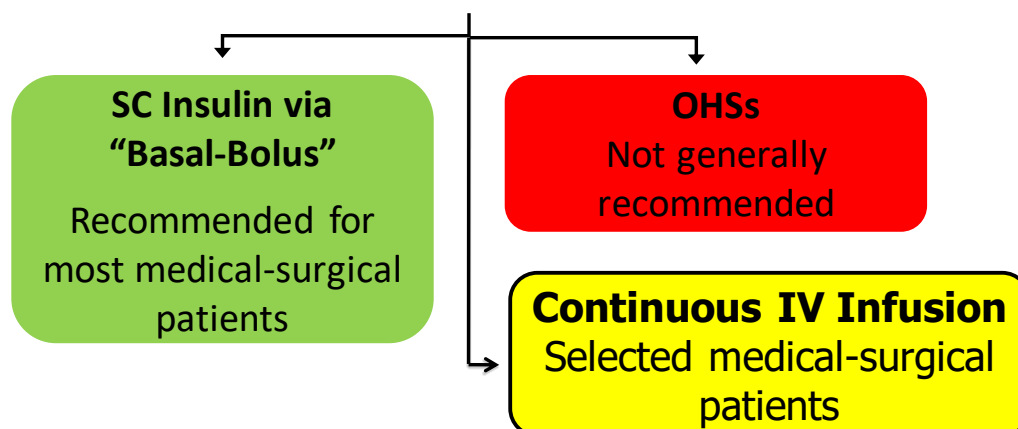
GLP1-RA - Nausea

SGLT-2 inhibitors - Controversial. Use for heart failure with caveats

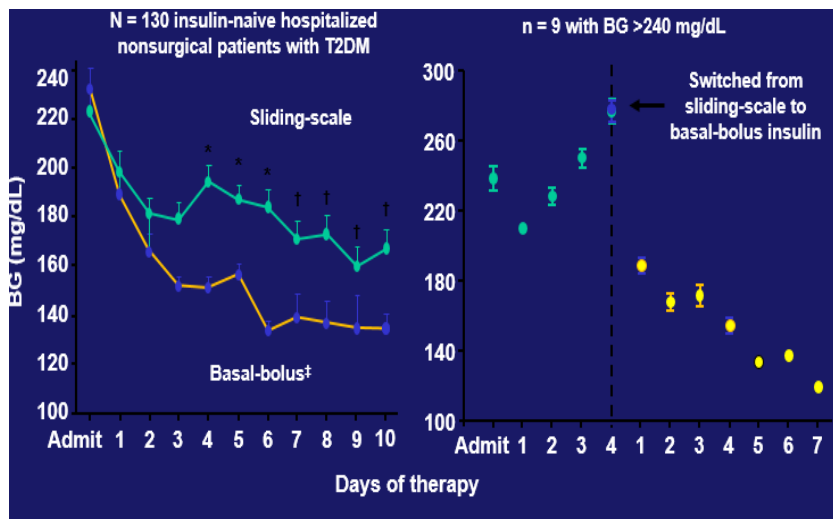
DPP4 inhibitors - Use is evaluated in several studies. Safety and efficacy data with Sitagliptin, but FDA warns saxagliptin, and alogliptin in patients with heart failure. Linagliptin can be used in CKD and ESRD.

Pharmacologic Therapy of Inpatient Hyperglycemia

Antihyperglycemic Therapy



Does Basal Bolus Improve BG?

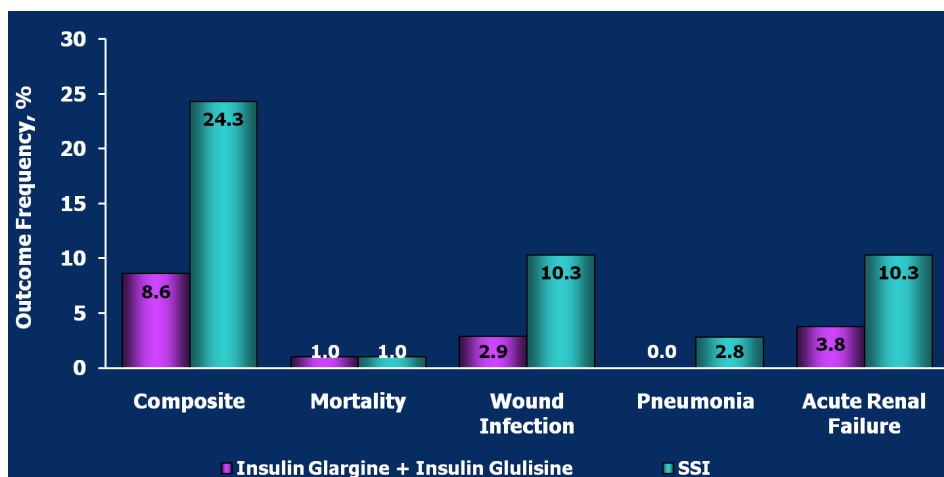


- RABBIT – BB trial
- RABBIT-2 - Surgery Trial
 - Does improved control translate to Improved outcomes?

Umpierrez G, Diabetes Care Feb 2011, 34 (2) 256-261 RAnomized Study of Basal Bolus Insulin Therapy in the Inpatient Management of Patients With Type 2 Diabetes

Does Basal Bolus Impact Postoperative Complications?

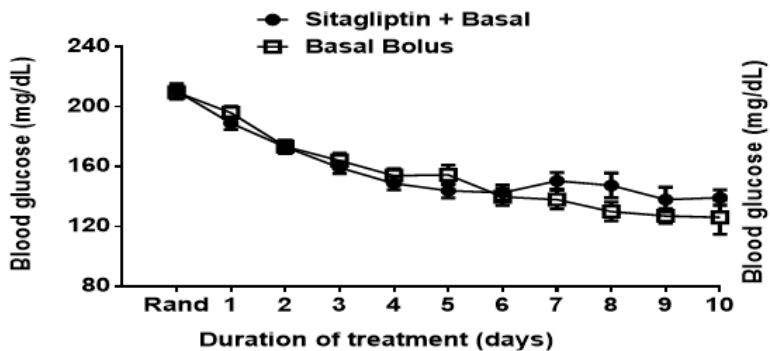
RABBIT-2 Surgery Composite Complications



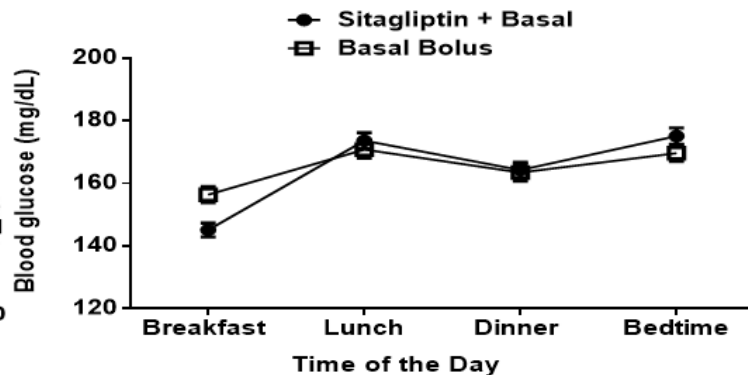
Umpierrez G, Diabetes Care Feb 2011, 34 (2) 256-261 RAnomized Study of Basal Bolus Insulin Therapy in the Inpatient Management of Patients With Type 2 Diabetes

Sita-Hospital Trial – Mean daily BG

Mean Daily BG (mg/dl)



Mean BG AC & HS (mg/dl)



Data are mean \pm SE

138 patients/each group

Pasquel, Gianchandani, et al. Lancet Diabetes Endocrinol. 2017;5(2):125-133



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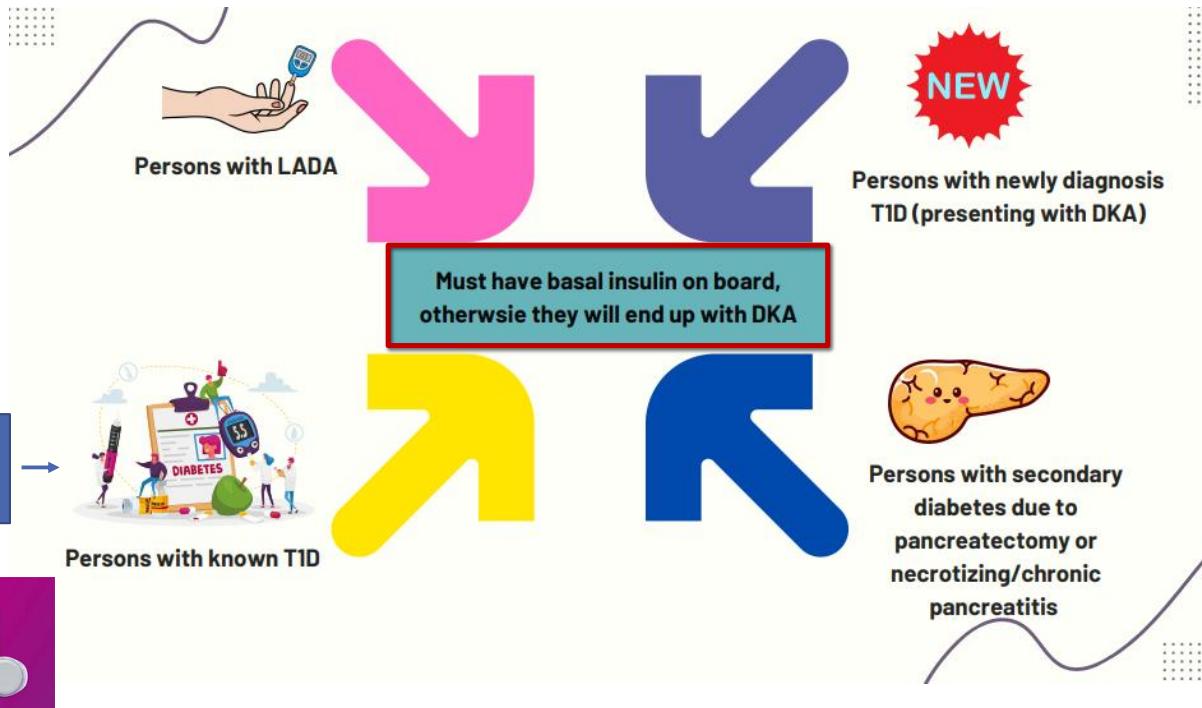
Hyperglycemia

Glucose > 140
A1C < 6.5%
No hx of diabetes
BG normalizes after illness

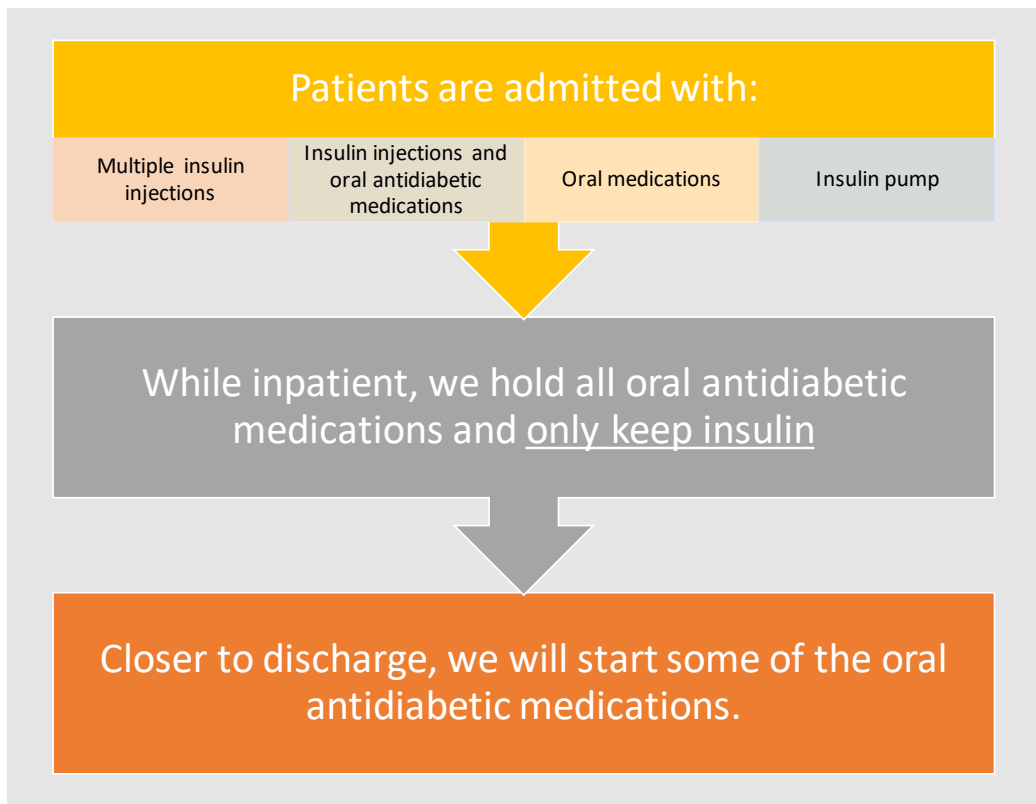
22-46% of non-critically ill hospitalized patients

Dhatariya et al. Endotext 2020

Type 1 Diabetes in the Hospital



Type 2 Diabetes



Steroid-Induced Hyperglycemia

Definition: abnormally elevated blood glucose level associated with the use of glucocorticoids

Dexamethasone versus methylprednisolone versus prednisone

Relative Glucocorticoid Potencies And Duration of Action

Table 1
Preparations of Glucocorticosteroids

PREPARATION	GLUCOCORTICOID POTENCY	MINERALOCORTICOID EFFECT	HALF-LIFE
Cortisone	1.0	++	4–6 h
Prednisone	4.0	+	6–12 h
Methylprednisolone	4.8	+/-	6–12 h
Dexamethasone	20.0	0	1–2 d

One Suggested Approach - Hyperglycemia with Glucocorticoid Therapy

Prednisone equivalent (mg/day)	NPH (units/kg/day)*
> 40	0.4
30	0.3
20	0.2
10	0.1

Administered in AM with prednisone *in addition* to current insulin regimen
NPH 0.1 units/kg for every 10 mg of prednisone, up to 40 mg of prednisone,
doses >40mg, use 0.4 units/kg.

Glargine may be preferred if dexamethasone used or Prednisone given bid

NPH for Glucocorticoid induced Hyperglycemia

Low Dose Glucocorticoid dose		High Dose Glucocorticoid dose	
10-39 mg Prednisone/ Prednisolone <u>or</u> 40-159 mg Hydrocortisone <u>or</u> 8-31 mg Methylprednisolone <u>or</u> 1.5-5.9 mg Dexamethasone/ 24 hours		≥ 40 mg Prednisone/ Prednisolone <u>or</u> ≥ 160 mg Hydrocortisone <u>or</u> ≥ 32 mg Methylprednisolone <u>or</u> ≥ 6 mg Dexamethasone /24 hours	
↓	↓	↓	↓
No DM	Type 2 DM	No DM	Type 2 DM
5 units NPH per glucocorticoid dose*	10 units NPH per glucocorticoid dose*	10 units NPH per glucocorticoid dose*	20 units NPH per glucocorticoid dose*
<p>*Full dose NPH given at the same time as glucocorticoid administration <i>except</i>:</p> <ul style="list-style-type: none"> Methylprednisolone/ hydrocortisone dosed every 4-6 hours or dexamethasone- NPH given three times per day at 0800, 1600, and 2200. 2200 dose reduced 25%. If patient is NPO, start dose at 50% 			

Figure 3. NPH Treatment for Experimental Group- Initial Starting Dose
Abbreviations: DM = Diabetes Mellitus; NPH = Neutral Protamine Hagedorn

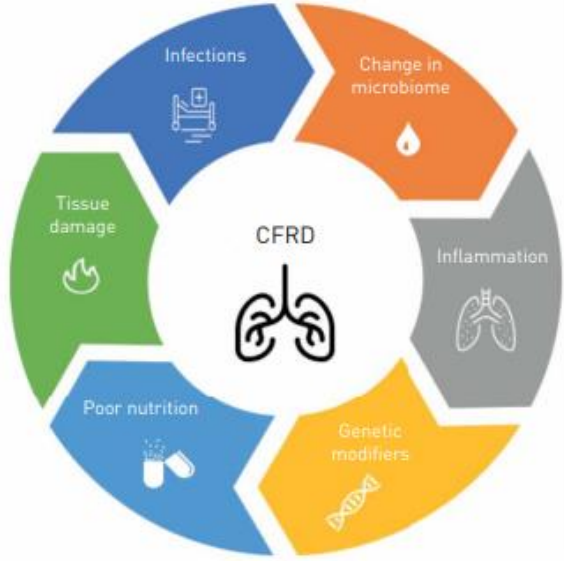
Grommesh t al. Endocr Pract.2016 Feb;22(2):180-9.

Cystic Fibrosis Related Diabetes

Diagnosis: 2-hr OGTT

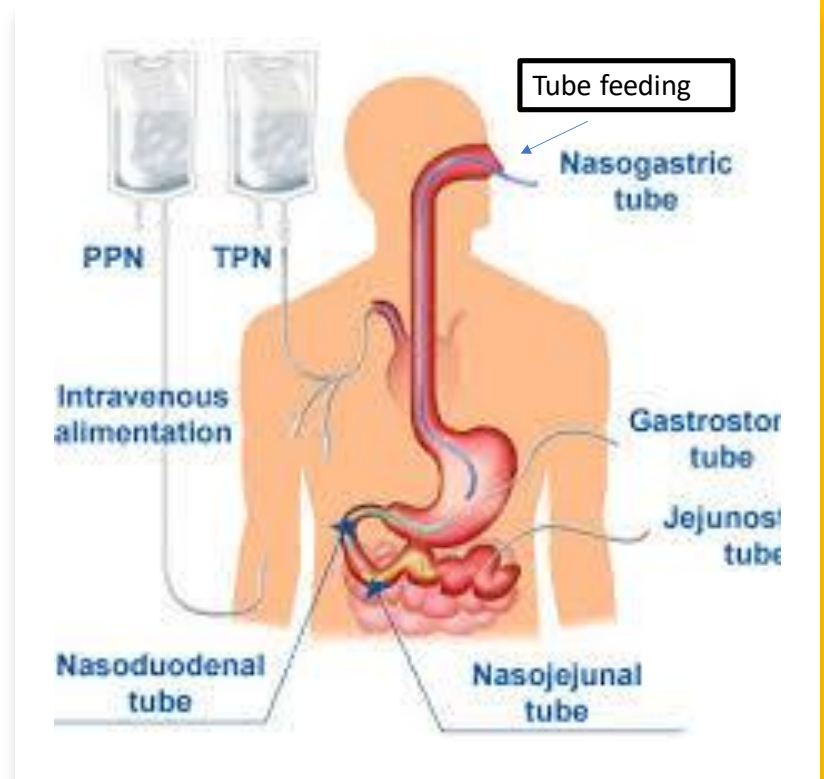
Early stage: Postprandial hyperglycemia
 Late stage: increased fasting glucose

Treatment: insulin



Parenteral Nutrition

- We can add regular insulin to TPN
 - If on insulin drip, give 80% of dose received by insulin drip
 - If on sliding scale while receiving TPN, add all insulin received by sliding scale and give 80% of total dose in the TPN
- You can always prescribe regular insulin moderate sliding scale in addition of insulin added to the TPN



Tube feeding

Moderate Sliding Scale with Regular insulin SQ every 6 hours

Start Regular Insulin based on 1 unit for every 10 gr of carbs plus sliding scale

For nocturnal tube feed (12hr), Regular Insulin SQ every 6 hours x 2 or one dose of NPH SQ

Name	Gm-carb/Volume-ml/Can
Fibersource	40/250 160/1000ml
Nepro	37.9/250 151.6/1000ml
Nutren 1.5	44/250 168/1000ml
Nutren1.0	34/250 128/1000ml
Nutren 2.0	54/250 196/1000ml
Novasource renal	43.5/237 183/1000ml
Osmolite 1.2	37.5 /237 157.5/1000ml
Peptamen 1.0	32/250 128/1000ml
Peptamen1.5	47/250 184/1000ml
Replete	28/250 112/1000ml
Renal low protein formula	49/250 196/1000ml
Renal Formula	43.5/237 183/1000ml
Jevity 1.5	51.1/237 215.7/1000ml
Jevity 1.0	36.5/237 154/1000ml
Renal Low protein no electrolyte formula	290.4/1000ml
Vivonex	61.7/300?

BG Goal – ESRD on dialysis

- Patients with CRI and ESRD can experience significant episodes hypoglycemia
 - Exogenous insulin is metabolized solely by kidney which is slower in RI
 - Kidney does not produce glucose
- Hospitalized patients with diabetes on hemodialysis
 - TDD of insulin > 0.23 units/kg/day

➤ Relation to HD

- Early am hypoglycemia - 37% episodes

➤ What can we change?

- **Have higher BG goals ≈ around 180 mg/dl**
- **Use low dose sliding scales – threshold of 200 mg/dl**
- Trial linagliptin + scale in T2D if insulin dose is low
- LA insulin given in am for ESRD patient

Table 2. Comparison of Glucometrics and Insulin Doses in Those With and Without Hypoglycemia.

Variable	Overall (n = 150)	Hypoglycemia (n = 76)	No hypoglycemia (n = 74)	P value
HbA1C % (n = 91)	7.33 ± 1.82	7.76 ± 2.2	6.87 ± 1.16	.017
Lowest BG, mg/dl	73.0 ± 30.2	50.9 ± 12.2	95.8 ± 25.9	<.0001
Highest BG, mg/dl	313.8 ± 97.8	328.8 ± 106.8	298.4 ± 85.5	.057
Average pre-HD glucose, mg/dl	176.9 ± 56.6	173.0 ± 62.2	180.8 ± 50.2	.399
Standard deviation of pre-HD glucose	47.8 ± 29.1	51.5 ± 31.1	43.9 ± 26.6	.111
Average post-HD glucose, mg/dl	167.3 ± 47.8	161.0 ± 50.8	173.7 ± 44.0	.102
Standard deviation of post-HD glucose	48.8 ± 29.5	55.0 ± 47.9	42.4 ± 36.2	.009
Clinically significant hypoglycemia (BG < 54 mg/dl)	42 (28%)	42 (55.3%)	0	<.001
Severe hypoglycemia (BG < 40 mg/dl)	16 (10.7%)	16 (21.1%)	0	<.001
Total insulin, units	25.3 ± 22.9	28.8 ± 24.3	21.6 ± 20.9	.054
Total insulin by weight, units/kg	0.288 ± 0.234	0.344 ± 0.247	0.231 ± 0.206	.003
Basal insulin, units	15.1 ± 15.7	17.2 ± 15.2	12.9 ± 16.1	.097
Basal insulin by weight, units/kg	0.168 ± 0.161	0.198 ± 0.156	0.136 ± 0.162	.019
Basal: total insulin	0.568 ± 0.342	0.604 ± 0.302	0.531 ± 0.377	.196

SGLT2 Inhibitors in the Hospital

➤ Beware of euglycemic DKA

- **Euglycemic DKA definition:**
 - arterial pH <7.3
 - serum bicarbonate <18 mEq/L
 - ketonemia while presenting blood glucose < 250 mg/d
- Risk of dehydration, volume contraction, and genitourinary tract infections
- Wait for stabilization of patient's condition
- Do not use in active infections or acute illness
- Do not use in ESRD
- Need to stop drugs app 3-4 days before a procedure
- Start in patients with type 2 diabetes and CHF when patient is stable clinically and close to discharge

↓

Dapagliflozin 10 mg daily (eGFR \geq 25)
Empagliflozin 10 mg daily (eGFR \geq 20)
Canagliflozin 100 mg daily (eGFR \geq 30)

1. Joint British Diabetes Societies for Patient Care. The Management of Diabetic Ketoacidosis in Adults (March 2023 version)
2. Neal, Bruce, et al. "Canagliflozin and cardiovascular and renal events in type 2 diabetes." *New England Journal of Medicine* 377.7 (2017): 644-657.
3. Empagliflozin in Patients with Chronic Kidney Disease. The EMPA-KIDNEY Collaborative Group. January 12, 2023 *N Engl J Med* 2023; 388:117-127
4. Dapagliflozin in Patients with Chronic Kidney Disease. Hidde J.L. Heerspink, Ph.D., Bergur V. Stefánsson, M.D. et al. *N Engl J Med* Oct 2020

GLP1 Analogues in The Hospital

- GLP 1 analogues can cause nausea
- Many patients in the hospital have nausea
- Not enough data to start in the in-patient setting
- GLP-1 analogues are expensive and often not on hospital formularies; their use in the hospital setting is therefore uncommon.

Discharge Algorithms

Consider to discontinue based on clinical scenarios

- Sulfonylurea (CKD, elderly, HF)
- DDP4i (no saxagliptin and alogliptin in HF)
- Thiazolidinediones (HF, weight, elderly)

Pre-admission regimen

NIA or diet control

If **A1c <8%** and no red flags:

- May continue home regimen (only if appropriate)

If **A1c 8-9%** or red flag present:

- Consider increasing NIA dose or adding another (max 3).

-If NIAs maxed, consider glargine 0.1 units/kg, or 40% of hospital dose.

If **A1c >9%**

- Start insulin on discharge. Basal insulin at 70% of hospital dose.

Basal Insulin

If **A1c <8%** and no red flags:

- Continue/restart home regimen

If **A1c 8-9%** or red flag present:

- Consider increasing basal insulin if fasting BG allows. Or if fasting BG at goal consider adding mealtime insulin.

If **A1c >9%**:

- Consider adding mealtime insulin

Basal-Bolus Insulin

If **A1c <8%** and no red flags:

- Continue/restart home regimen

If **A1c >8%** or red flag present:

- Intensify insulin regimen. A 10-20% increase in TDD is good place to start with further adjustments as outpatient.
- Aim to increase basal-bolus insulin to achieve or maintain a 50:50 ratio of basal and bolus insulin

RED FLAGS for preadmission regimens

- Home NIA cannot be restarted due to new CI
- Requiring >20 units/day insulin in hospital if previously not on insulin
- Requiring >20% more insulin in the hospital than at home

Consider replacing with these agents based on clinical scenarios

- SGLT-2i
- DDP-4i (sitagliptin, linagliptin)
- GLP 1 analogues

Summary

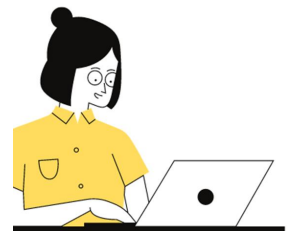
- Target glucose 140-180 in ICU and non-ICU setting (most of the time)
- Insulin infusion is the preferred method in the ICU setting
- Basal and bolus are the preferred method in the non-ICU setting
- Evidence of DPP4 inhibitors use, alone or in combination with basal insulin, is safe in the inpatient setting
- In patients with type 1 diabetes, do NOT stop basal insulin even if patients are NPO
- Use NPH for steroid use except for Dexamethasone (Lantus)
- Remember the risk of euglycemic DKA with SGLT2 inhibitors use
- Hold SGLT2 inhibitors 3-4 days prior to procedure.

Case 1



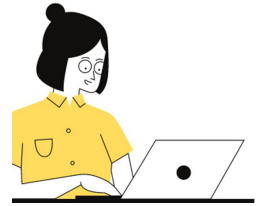
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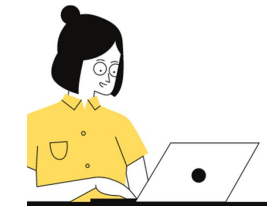
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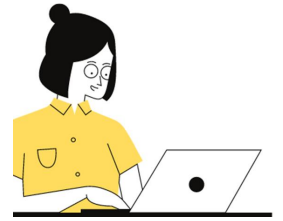


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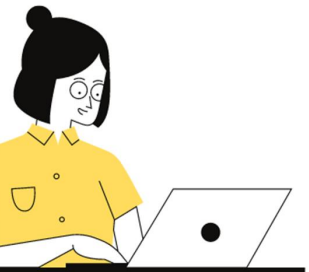
Case 2

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Case 2

- Starting TD dose = TDD= $0.5 \text{ units} \times 67 \text{ kg} = 34 \text{ units}$
- Basal (glargine) = $50\% \text{ TDD} = 34/2 = 17 \text{ units}$
- Meal (aspart/lispro) = $50\% \text{ of TDD} = 17 \text{ units}$ [Divide with B, L, D = 6 units with each meal]

Thank You!

