Special Cases and Considerations

Dr. Dragana Lovre

December 1, 2022

Classification of Diabetes

1. Type 1 diabetes
   - Due to autoimmune b-cell destruction, usually leading to absolute insulin deficiency

2. Type 2 diabetes
   - Due to a progressive loss of b-cell insulin secretion frequently on the background of insulin resistance

3. Gestational diabetes mellitus (GDM)
   - Diabetes diagnosed in the second or third trimester of pregnancy that was not clearly overt diabetes prior to gestation

4. Specific types of diabetes due to other causes
   - Monogenic diabetes syndromes (such as neonatal diabetes and maturity-onset diabetes of the young [MODY])
   - Diseases of the exocrine pancreas (such as cystic fibrosis), or
   - Drug- or chemical-induced diabetes (such as with glucocorticoid use, in the treatment of HIV/AIDS, or after organ transplantation)

Recent FDA approved drugs

SGLT2 Inhibitors

BRAND NAME	OTHER NAME
Farxiga	dapagliflozin
Invokana	canagliflozin
Jardiance	empagliflozin
Steglatro	ertugliflozin

GLP-1 receptor agonists

BRAND NAME	OTHER NAME
Adlyxin	lixisenatide
Bydureon	exenatide
Byetta	exenatide
Ozempic	semaglutide
Tanzeum	albiglutide
Trulicity	dulaglutide
Victoza	liraglutide

AACE T2D Management Algorithm

PROFILES OF ANTIDIABETIC MEDICATIONS

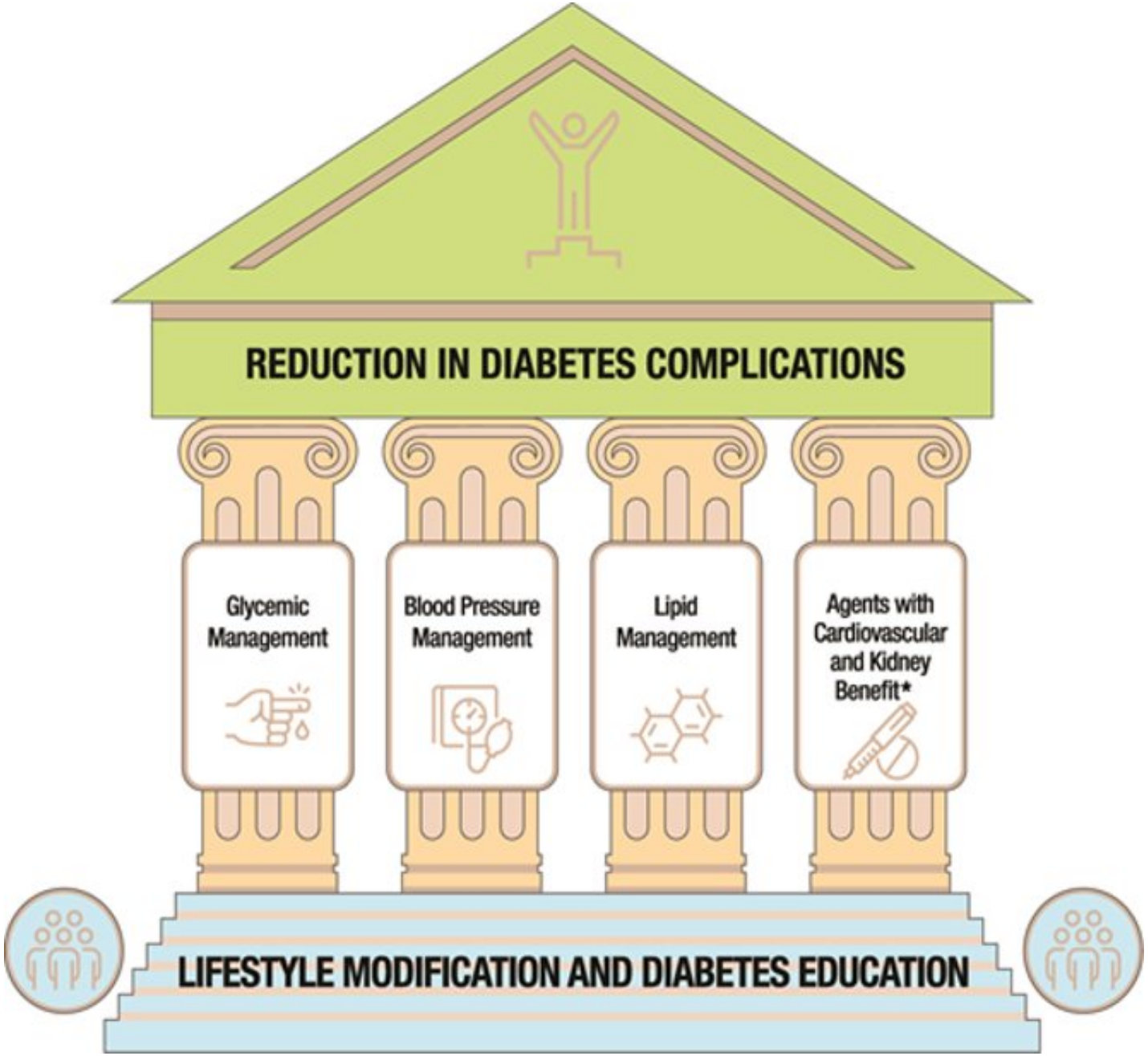
	MET	GLP1-RA	SGLT2i	DPP4i	AGi	TZD (moderate dose)	SU / GLN	COLSVL	BCR-QR	INSULIN	PRAML
HYPO	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Moderate/Severe / Mild	Neutral	Neutral	Moderate to Severe	Neutral
WEIGHT	Slight Loss	Loss	Loss	Neutral	Neutral	Gain	Gain	Neutral	Neutral	Gain	Loss
RENAL / GU	Contra-indicated if eGFR <30 mL/min/1.73 m²	Exenatide Not Indicated CrCl <30; Possible Benefit of Liraglutide	Not Indicated for eGFR <45 mL/min/1.73 m²; Genital Mycotic Infections; Possible CKD Benefit	Dose Adjustment Necessary (Except Linagliptin); Effective in Reducing Albuminuria	Neutral	Neutral	More Hypo Risk	Neutral	Neutral	More Hypo Risk	Neutral
GI Sx	Moderate	Moderate	Neutral	Neutral	Moderate	Neutral	Neutral	Mild	Moderate	Neutral	Moderate
CHF	Neutral	See #1	See #2	See #3	Neutral	Moderate	Neutral	Neutral	Neutral	CHF Risk	Neutral
CARDIAC ASCVD						May Reduce Stroke Risk	Possible ASCVD Risk	Benefit	Safe	Neutral	
BONE	Neutral	Neutral	Neutral	Neutral	Neutral	Moderate Fracture Risk	Neutral	Neutral	Neutral	Neutral	Neutral
KETOACIDOSIS	Neutral	Neutral	DKA Can Occur in Various Stress Settings	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral

- Few adverse events or possible benefits
- Use with caution
- Likelihood of adverse effects

1. Liraglutide—FDA approved for prevention of MACE events.
2. Empagliflozin—FDA approved to reduce CV mortality. Canagliflozin—FDA approved to reduce MACE events.
3. Possible increased hospitalizations for heart failure with alogliptin and saxagliptin.

DOI 10.4158/CS-2018-0535

WELL-AHEAD



https://diatribe.org/your-guide-2022-changes-ada-standards-care#glucose

Case 1

- 45 y/o AAF PMH of Morbid Obesity, T2DM (on insulin), HTN and HLD c/o “lumps and bumps at insulin injections site that do not go away anymore despite me rotating my injections”
- Has been on insulin (basal/bolus) 5 times per day for >15 years. Pt was diagnosed with “bad” gestational diabetes required insulin and since has been on insulin.
- Her insulin dose continued to increase to current dose of
  - Insulin lispro 65 units with each meal (3x per day)
  - Insulin glargine 100 units BID

History cont'd

- A1C 10.6% (8 months ago)
- Managed mostly by PCP, never seen by Endocrinologist
- Pt recently started exercising and was started on Liraglutide, which she is tolerating well. Pt has lost about 30 lbs in last six months.
- SMBG
  - FBG 180-230
  - Rest numbers vary, mostly >200
- A1C now 8.8%
- She continues to struggle with her weight and diet.

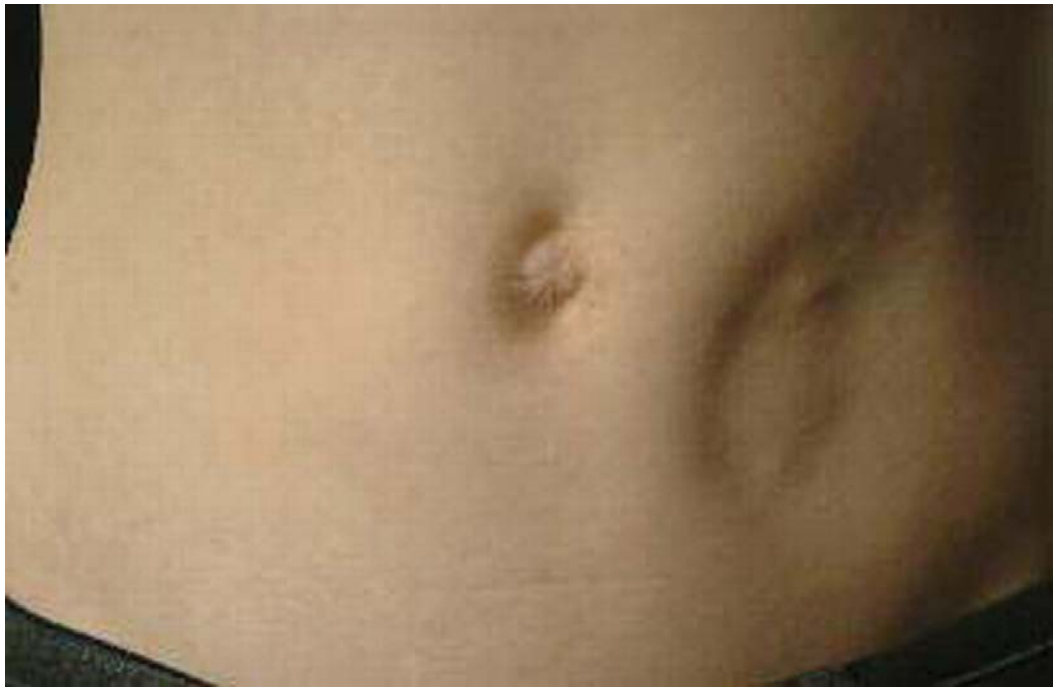
History cont’d

- PMH: Obesity, HTN, HLD, T2DM , Neuropathy, and Retinopathy
- MEDs: Lisinopril, Pravastatin, Metformin, Liraglutide, and insulin as above mentioned

Positive Physical Exam findings

- VS: WNL, BMI 45.7
- Neck: acanthosis nigricans
- Abdomen: multiple localized areas of lipodystrophy LLQ and LUQ
- Foot exam significant for decreased sensation in BLE

Lipodystrophy

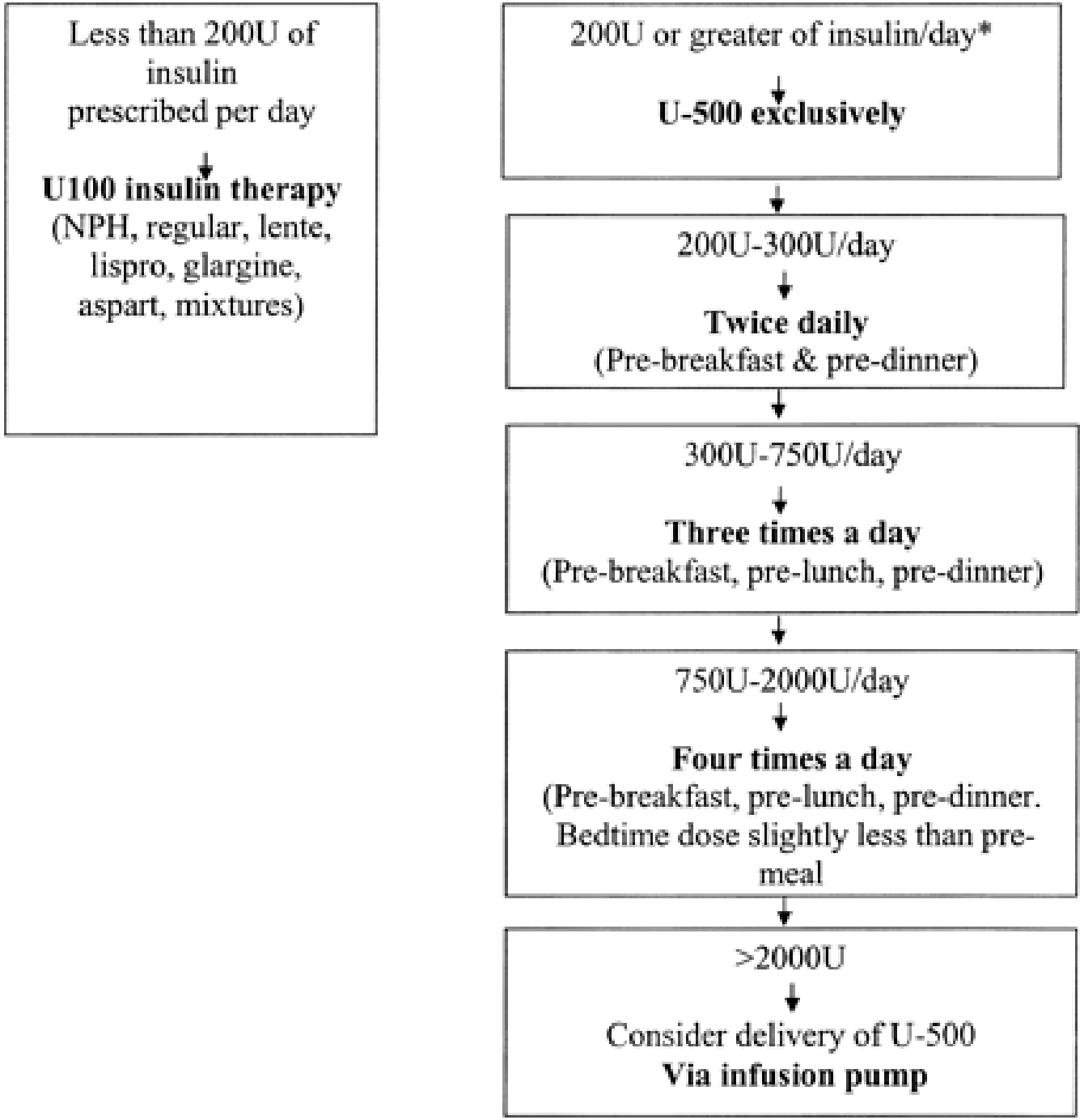


Key points about the case

- Very high doses of insulin TDD 395 units
- Lipodystrophy
- High BMI
- Decrease sensation in BLE

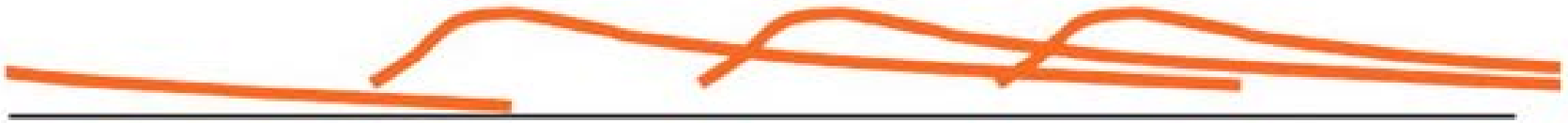
Causes

- Extreme insulin-resistance syndromes
- Type A IR syndromes (inherited) insulin-receptor mutations
- Rabson-Mendenhall syndrome, Donohue syndrome (aka Leprechaunism)
- Type B IR syndrome with auto antibodies against the insulin receptor
- the HAIR-AN (hyperandrogenism, insulin resistance, and acanthosis nigricans) syndrome
- The lipodystrophic states
- Type 2 diabetes mellitus
- Obesity, infection, glucocorticoid excess, and pregnancy



How does it work? U-500 insulin starts working the first hour after it is injected and lasts up to 12 hours.

Example: This is a typical dose schedule for U-500 insulin.



Midnight	6:00 AM	Noon	6:00 PM	Midnight
Dose at each meal (unit markings on an insulin syringe)	22 ▲	20 ▲	24 ▲	

Your glucose goals: Fasting and before meals_____ 2 hours after meals _____ A1C _____

Check your blood glucose: Bring your logbook and meter to every visit. Times to check are marked below with ↓.

Eat and take your U-500 insulin at regular times. Your doses are listed below. Mealtimes are marked with ▲.

U-500R initiation

↓

HbA1c >10% → Increase TDD by 10%

HbA1c 8–10% → Maintain same TDD

HbA1c <8% → Decrease TDD by 10–20%

↓

TDD 150–300 units	Twice daily injections (60/40) Three daily injections (40/30/30, 45/35/20, 40/40/20, or 33/33/33)
TDD 300–600 units	Three daily injections (as above) Four daily injections (30/30/30/10) CSII (50% as basal infusion and 50% as bolus)
TDD >600 units	Four daily injections (25/25/25/25 or 30/30/30/10) CSII

Take home points on this case

- Recognizing patients with extreme forms of insulin resistance
- Recognizing the role of insulin U-500 therapy for patients with extremel insulin resistance

Case 2 - Presented to me by the endo fellow

- 71 y/o CM PMH of Obesity, T2DM (on insulin), HTN, HLD and CKD-2 seen for follow up visit in Endocrine clinic
- Has been on insulin (basal/bolus) 5 times per day for 5 years.
- Was initially on Metformin but did not tolerate (GI Side effects).
- Tried SU and due to hypoglycemia it was stopped few years ago.

History cont'd

- SMBG
  - FBG 150-180
  - Occ. Random BG in the low 200s
- A1C now 7.8%
  - Goal is 7-7.5%, pt lives alone and works a lot on the fields alone and does not have scheduled meals
- Not willing to change his diet and unable to change his schedule

History cont’d

- MEDs: Lisinopril, Atorvastatin, and insulin glargine 25 units Qhs and lispro 5 units with meals
- Positive Physical Exam findings
  - VS: WNL, BMI 33
  - Neck: acanthosis nigricans
  - Foot exam significant for decreased sensation in BLE

Key points about the case

- Fairly low doses of insulin – likely due to high physical activity
- CKD-2, would benefit from SGLT-2 inhibitors (no absolute contraindications)
- High risk for CVD would benefit from GLP-1 RA
- Due to his lifestyle would benefit from agents with less risk for hypoglycemia

Case 3

- 74 y/o HF well known to me (5 yrs.) PMH of mild T2DM for 6 yrs (only on Metformin after careful dietary changes), thyroid cancer and HLD seen for follow up visit in Endocrine clinic
- A1c has been in 6% range mostly and a few times in low 7% range for many years
- Patient lost to follow up for a few years mostly due to COVID
- On my schedule as an urgent referral due to A1c of 12%.

History cont’d

- SMBG
  - FBG 180-250
  - Random BG as high as 400s
  - Patient was recently started on insulin glargine 10 units BID and lispro 3-5 units with meals with large glucose excursions and frequent hypoglycemia.
  - Patient also c/o just not feeling well, some mild nausea and loosing weight from 130s lbs. to now 109lb over the last year without trying

History cont’d

- MEDs: Atorvastatin, and insulin glargine 10 units BID and lispro 3-5 units with meals
- Positive Physical Exam findings
  - VS: WNL, BMI 17
  - Appears ill as compared to few years ago

Key points about the case

- Sudden extreme change in A1c without an obvious cause (no change in diet, no steroids or any other change in health or medications)
- Unintentional Weight loss of more than 20 lbs.
- When you know your patient well and something is “off” it should trigger a detailed history and ROS and more vs less approach

Questions?