SGLT-2 Inhibitors: Fast Facts for Louisiana Providers

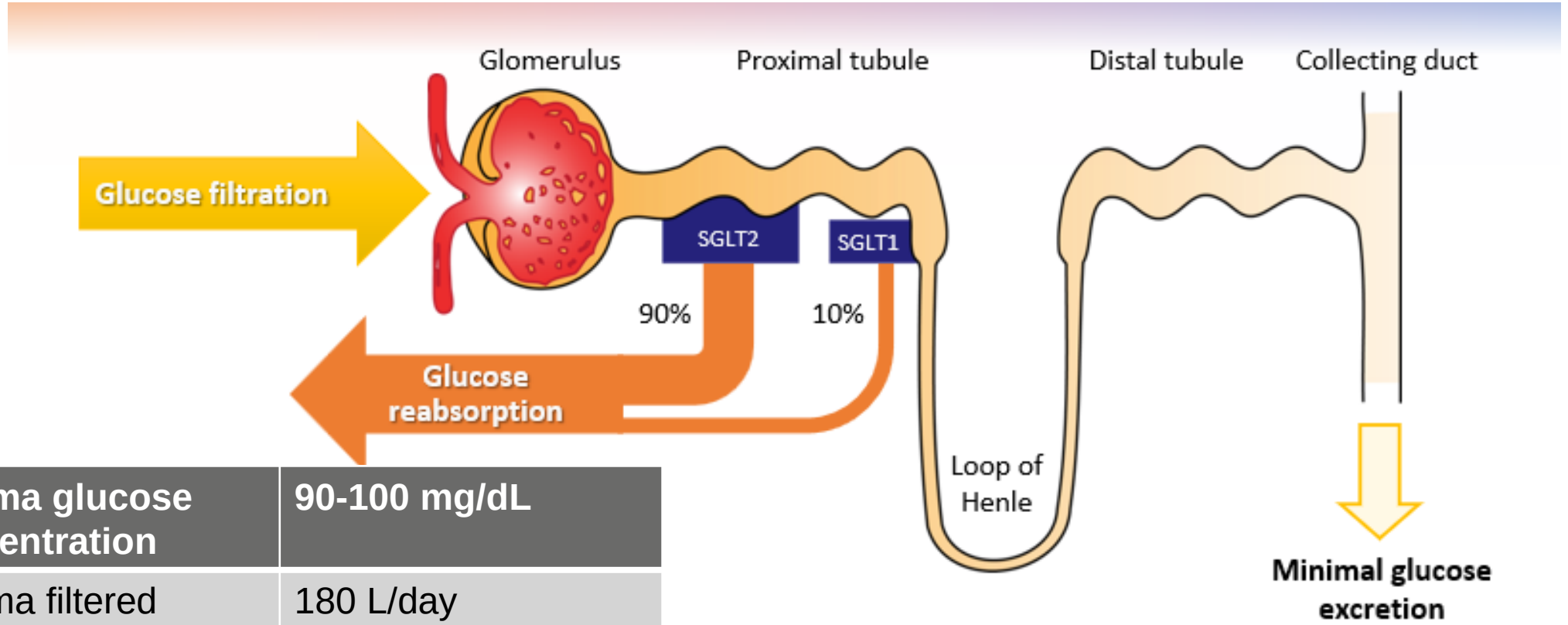
Arianna Mohiuddin, MD
Tulane University School of Medicine
October 20, 2022

What are SGLT-2 Inhibitors?

- **SGLT-2 (sodium glucose cotransporter-2) inhibitors are medications that ↓ blood glucose by ↑ urinary glucose excretion.**
- **SGLT-2 is found in the proximal tubule and causes resorption of around 90% of the filtered glucose load.**
- **Because of this mechanism of action, SGLT-2 inhibitors do not cause hypoglycemia by themselves.**
- **They causes a modest reduction in blood pressure and weight.**
- **In those with cardiac or renal comorbidities, SGLT-2 inhibitors have demonstrated benefit for cardiac and renal outcomes.**

Clar C, Gill JA, Court R, Waughn N. *Systematic review of SGLT2 receptor inhibitors in dual or triple therapy in type 2 diabetes*. BMJ Open 2012; 2

Renal glucose handling in the nephron of a healthy individual

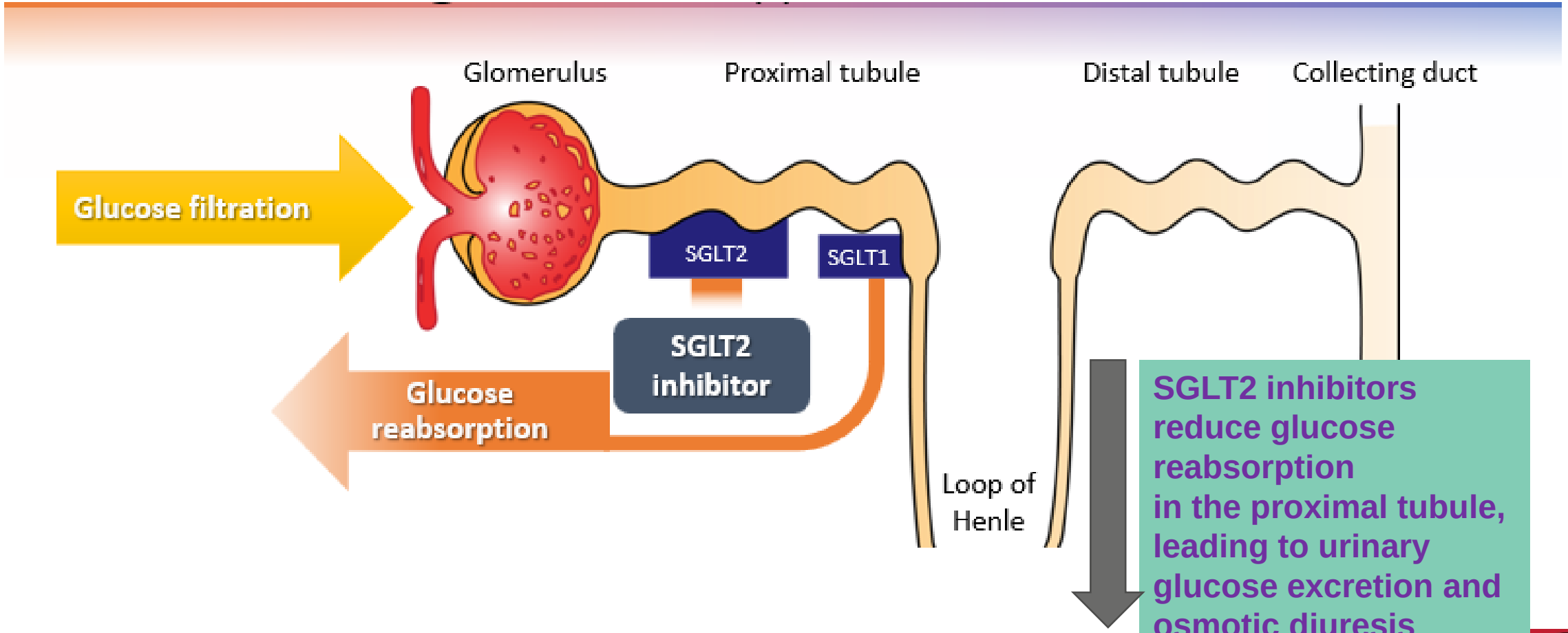


Plasma glucose concentration	90-100 mg/dL
Plasma filtered	180 L/day
Glucose filtered	160-180 g/day
Glucose excretion	Minimal

SGLT: sodium–glucose co-transporter.

Figure adapted from: Bailey CJ. *Trends Pharmacol Sci.* 2011;32:63–71.

How do SGLT-2 Inhibitors Work?



SGLT2 inhibitors reduce glucose reabsorption in the proximal tubule, leading to urinary glucose excretion and osmotic diuresis

SGLT: sodium–glucose co-transporter.

Figure adapted from: Bailey CJ. *Trends Pharmacol Sci.* 2011;32:63–71.

What have the clinical trials shown? Rule of 3's

- EMPA-REG OUTCOME (Canaglifozin)
- CANVAS (canaglifozin)
- DECLARE-TIMI (dapaglifozin)

- These trials demonstrated that SGLT-2 inhibitors exert **cardioprotective** and **renal protective effects** independent of their effects on blood glucose.

Association of SGLT2 Inhibitors With Cardiovascular and Kidney Outcomes in Patients With Type 2 DiabetesA Meta-analysis
Darren K. McGuire, MD, MHSc[1]; Weichung J. Shih, PhD[2,3]; Francesco Cosentino, MD, PhD[4]; et al

The three most commonly prescribed SGLT-2 Inhibitors

	Empagliflozin	Dapagliflozin	Canagliflozin
Therapeutic dose (mg/day) Starting dose	10–25 10	5–10 10	100–300 100
Administration	QD With or without food	QD With or without food	QD Before first meal
Peak plasma concentration (hours post-dose)	1.5	Within 2	1–2
Absorption (mean oral bioavailability)	≥ 60%	~ 78%	~ 65%
Metabolism	← Primarily glucuronidation - no active metabolite →		
Elimination (half-life, hours)	Hepatic:renal 43:57 [12.4]	Hepatic:renal 22:78 [12.9]	Hepatic:renal 67:33 [13.1]*
Selectivity over SGLT1	1:5000	> 1:1400	> 1:160[1]
Glucose excretion with higher dose (g/day)	78	~ 70	119

Data from http://www.ema.europa.eu. Sha et al. Diab Obes Metab 2015;17:188–97.

WELL-AHEAD

Project ECHO

Contraindications and Precautions for SGLT-2 Inhibitors

- SGLT-2 Inhibitors should not be used in the following patient population:
  a. Type 1 diabetes mellitus
  b. Type 2 diabetes mellitus and eGFR <45 (ertuglifozin, dapaglifozin) or eGFR <30 (empaglifozin, canaglifozin)
  c. Prior DKA– includes euglycemic DKA
- **Avoid SGLT-2 inhibitor use in the following patient populations:** those with frequent UTI's, history of genital mycotic infections, low bone mineral density, those at high fall/fracture risk, hx of foot ulcerations, or DKA risk factors.

Adapted from: Real-Life Prescribing of SGLT2 Inhibitors: How to Handle the Other Medications, Including Glucose-Lowering Drugs and Diuretics
David Lam and Aisha Shaikh
Kidney360 April 2021, 2 (4) 742-746; DOI: https://doi.org/10.34067/KID.0000412021

Monitoring and Side Effects

- **Volume status** and **renal function – prior to use.**
- Check risk of **genital mycotic infections** and **foot ulceration**.
- Risk of
  - vulvovaginal candidiasis
  - Hypotension with AKI
  - UTI’s
  - Fractures
  - Fournier's gangrene (necrotizing fasciitis of the perineum)
  - LE amputations

Adapted from: Real-Life Prescribing of SGLT2 Inhibitors: How to Handle the Other Medications, Including Glucose-Lowering Drugs and Diuretics
David Lam and Aisha Shaikh
Kidney360 April 2021, 2 (4) 742-746; DOI: https://doi.org/10.34067/KID.0000412021

WELL-AHEAD

Project ECHO

Real Life Prescribing of SGLT-2 Inhibitors: Patient Information: 1/2

- **Increase in Urine Output**
- **Blood Glucose**
- **Follow the 'Sick Day Rule' of when to hold the medication.**
- Stop the **medication 3 to 4 days before a scheduled surgery** that requires patients to to be NPO
- Avoid very low carb or **keto diets** as it may increase the risk of DKA.

Adapted from: Real-Life Prescribing of SGLT2 Inhibitors: How to Handle the Other Medications, Including Glucose-Lowering Drugs and Diuretics
David Lam and Aisha Shaikh
Kidney360 April 2021, 2 (4) 742-746; DOI: https://doi.org/10.34067/KID.0000412021

Real Life Prescribing of SGLT-2 Inhibitors: Patient Information: 2/2

- **Lower extremity wounds/ulcers**
- **Dysuria**
- **Redness or itching in the genital area, or foul-smelling vaginal or penile discharge**

Adapted from: Real-Life Prescribing of SGLT2 Inhibitors: How to Handle the Other Medications, Including Glucose-Lowering Drugs and Diuretics
David Lam and Aisha Shaikh
Kidney360 April 2021, 2 (4) 742-746; DOI: https://doi.org/10.34067/KID.0000412021