

Understanding and Treating Diabetes in the Post-Transplant Patient

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Goals of This Lecture:

- Let's learn something new!
- Get excited about treating Diabetes!



Diabetes in the Transplant Patient

- Risk Factors, Screening, Diagnosis
- Inpatient Management
- Outpatient Management

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Risk Factors

- Meds:
Chemotherapeutic agents,
Immunosuppressants
- Nutrition: TPN, TF
- Infection
- Stress
- Age >40-45
- Obesity
- AA, Hispanic Races
- Family History
- Hepatitis C, CMV
- Polycystic Kidney Ds
- Certain Genetic Mutations

Rates of Occurrence

- Diabetes occurs post-transplant at
 - Kidney Transplant: 10-74%
 - Heart Transplant: 11-38%
 - Liver Transplant: 7-30%
 - Lung Transplant: 32%

Screening

Outpatient Monitoring:

- Monitor blood sugar **prior** to transplant, typically fasting qam. Alert provider to BG >126 mg/dL.
- Monitor blood sugar **post** transplant with FBS weekly X4, recheck in 3 months, 6 months and annually thereafter if no abnormality presents

Inpatient Initiation of Monitoring:

- Check blood sugar ACHS and begin treatment with BG >140 mg/dL.

Diagnosis

Diagnosis	Test
Prediabetes: Impaired Fasting Glucose	Fasting plasma glucose of 100-125 mg/dL No clear A1c criteria for Prediabetes, although >5.7% has been suggested
Prediabetes: Impaired Glucose Tolerance	75-g OGTT 2 hr plasma glucose of 140-199 mg/dL Fasting plasma glucose \geq 126 mg/dL
Diabetes	Fasting plasma glucose \geq 126 mg/dL OR random plasma glucose \geq 200 mg/dL with symptoms OR 75-g OGTT 2 hr plasma glucose \geq 200 mg/dL OR A1c >6.5%

*A diagnosis of diabetes must be confirmed on a subsequent day, by measurement of FPG, 2-h PG, or random plasma glucose (if symptoms are present).

Post-Transplant DM Diagnosis

- October, 2013 → 2nd International Consensus Panel enacted key changes:
 - Change terminology from New Onset Diabetes After Transplant (NODAT) to Post-Transplant DM (PTDM)
 - Recommend evaluation/diagnosis outpatient, stable, and on long-term maintenance immunosuppression doses
 - HbA1c can be used to diagnose DM if elevated (>6.5%) but should not be used alone as a screen for PTDM (particularly in 1st year)
- Unclear full significance of timing of DM diagnosis (1 vs. 5 vs. 20 years post-transplant)

Post-Transplant Diabetes Mellitus

- Insulin resistant phenotype
- Usually requires some insulin, at least short-term
- May be possible to taper to oral agents or monitor with lifestyle modifications alone
- Adjustments in regimen may be necessary at any time based on steroids and other factors

Types of Diabetes

- Pre-Existing Type 1 or Type 2
- Post-Transplant DM

Pre-Existing Diabetes

- Type 1:
 - Steroids increase insulin requirement and dose. Consider starting with double prandial and ss coverage if pt is well controlled at baseline.
- Type 2:
 - Cannot use all oral agents. Mostly consider SFU for postprandial hyperglycemia.
 - Usually requires insulin, at least short-term.
- Both: Insulin and/or oral agent dose will increase from ESRD to having a working kidney



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Diabetes in the Transplant Patient

- Risk Factors, Screening, Diagnosis
- Inpatient Management:
 - Goals and Factors to Consider
 - Weight-Based Dosing
 - Transitioning from Drip to SQ
 - Making Adjustments to Your Regimen
 - When to involve Endocrine
- Outpatient Management

Guidelines From Professional Organizations on the Management of Glucose Levels in the ICU

Year	Organization	Patient Population	Treatment Threshold	Target Glucose Level	Definition of Hypoglycemia	Updated since NICE-SUGAR Trial, 2009
2009	AACE and ADA	ICU patients	180	140-180	<70	Yes
2009	Surviving Sepsis Campaign	ICU patients	180	150	Not stated	Yes
2009	Institute for Healthcare Improvement	ICU patients	180	<180	<40	Yes
2008	American Heart Association	ICU patients w/ ACS	180	90-140	Not stated	No

Goals

- Goal: BG 140-180 mg/dL
- Treatment should be started initially with insulin
- Several studies have assessed the benefit of tight control in hospitalized patients, but findings are not consistently positive.
- Tighter control (such as 80-110 mg/dL) increases risk of hypoglycemia.
- Know when to adjust your target BG or A1c.

Factors to Consider

- **Medications** (pressors and glucocorticoids) and severity of illness impact insulin secretion and insulin resistance.
- **Food intake** can be unpredictable
- **Tests and procedures** interrupt meals and medication dosing
- **Prior history** of DM and type if pre-existing as well as degree of prior control (A1c)
- **Nutritional status** (NPO, enteral, parenteral)

PRODUCT (Chemical Name)	mg/ml	Dosage	POTENCY (When compared w/ Hydrocorti- sone mg to mg)	Hydro- cortisone Equivalency	Route of Admin.	Type	Contains Benzyl Alcohol
Solu-Cortef® (Hydrocortisone Sodium Succinate)	50	See insert	1	50	IM or IV	Rapid Acting Short Duration	NO
Aristospan® (Triamcinolone Hexacetonide)	20	0.25-2 ml	5	100	IA & Soft Tissue	Long Acting	YES
Celestone Soluspan® (Betamethasone Sodium Phosphate & Betamethasone Acetate)	3+3	0.25-2 ml	25	150	IM, IA, IL & Soft Tissue	Both Rapid & Long Acting	NO
Kenalog®-40 (Triamcinolone Acetonide)	40	0.25-2 ml	5	200	IM, IA, IL & Soft Tissue	Long Acting	YES
Depo-Medrol®-40 (Methylprednisolone Acetate)	40	0.25-2 ml	5	200	IM, IA & Soft Tissue	Long Acting	SDV-NO MDV-YES
Depo-Medrol®-80 (Methylprednisolone Acetate)	80	0.25-2 ml	5	400	IM, IA & Soft Tissue	Long Acting	SDV-NO MDV-YES
Dexamethasone Sodium Phosphate	4	See insert	25	100	IM, IV, IA, IL & Soft Tissue	Rapid Acting Short Duration	YES
Dexamethasone Sodium Phosphate PF	10	See insert	25	250	IM or IV	Rapid Acting Short Duration	NO
Solu-Medrol® (Methylprednisolone Sodium Succinate)	40	See insert	5	200	IM or IV	Rapid Acting Short Duration	NO

Steroid Potency

- Consider strength of steroid when adjusting insulin.
- All steroids are not the same!

Weight-Based Dosing

- Stop all orals and non-insulin injectables
- Calculated starting Total Daily Dose (TDD)
 - 0.2-0.3 unit/kg if ≥ 70 yo or GFR < 30 ml/min
 - 0.4 unit/kg if BG 140-200 untreated
 - 0.5-0.6 unit/kg if BG 201-400 untreated
- Divide TDD:
 - 50% as basal
 - 50% as nutritional (equally divided)

Sliding Scale

- If patient able and expected to eat: usual
- If patient not able to eat: sensitive Q6H
- If fasting and pre-meal BG persistently >140 without hypoglycemia: resistant
- **Alternatively** you may use **5% of the TDD** per 50 pts

BG (mg/dl)	Insulin-sensitive	Usual	Insulin-resistant
>141–180	2	4	6
181–220	4	6	8
221–260	6	8	10
261–300	8	10	12
301–350	10	12	14
351–400	12	14	16
>400	14	16	18

Example #1

- Grumpy Dwarf is a 40 yo M who presents following DDKT, now stable on POD 1.
- Home regimen is Linagliptin (Tradjenta) 5 mg qday, Glucotrol (Glipizide) 5 mg BID. Pt states compliance. A1c is 9.0%.
- No additional pressors, IV dextrose.
- Wt is 100 kg.
- Taking Methylprednisolone 500 mg today x1 dose with scheduled taper.



Example #1 Cont.

- Weight: $100 \text{ kg} \times 0.5 \text{ un/kg} = 50 \text{ un TDD}$
- Basal Dose: 25 un basal daily. Give first dose at least 2 hours prior to stopping drip.
- Bolus Dose: 8 un rapid or short acting insulin with meals (weight-based). Given high dose steroid, may consider starting at double → 16 un meal coverage.
 - May want to hold this order until pt is eating at least 50% of meal trays consistently.
- Sliding Scale: Standard dosing requirements with no complicating factors: 2 or 3 un/50 > 150 ACHS. May choose to double for 5/50 > 160 ACHS due to steroids.
- ACHS BG checks
- Diabetic Diet as tolerated.

Insulin Drip

- **IV insulin infusion** is ideal (IV insulin half-life=5-9 min.) following standard, validated protocol for at least first 24 hrs.
- **BG monitoring q1-2h** is imperative to avoiding hypoglycemia while on drip. Check more frequently with change in IV meds or nutrition.
- As status improves, **transition to subcutaneous** insulin based on most recent IV insulin infusion rate while pt is fasting. Use rates that have maintained euglycemia only.
- Be sure to **overlap IV and subcutaneous long-acting insulin** by at least 2 hrs to avoid rebound hyperglycemia after stopping insulin drip.
- Type 2 DM with <2un/h IV insulin requirement may do well on a **non-intensive subcutaneous regimen** or scheduled insulin. Can try sliding scale only at first.

Transitioning from Drip to SQ Insulin

- Patients without a history of DM
 - If <1 unit/hour: may not require scheduled insulin
 - Treat with scheduled insulin to determine if scheduled insulin is required
- All patients with T1DM and most with T2DM
 - Require SQ long- and short-acting insulin
 - Give basal insulin 1-2 hours before discontinuation of IV insulin
- Some T2DM pts may only require mealtime + ss. Others may only require ss.

Transitioning from Drip to SQ Insulin

- Extrapolate insulin requirement over preceding 6 to 8 hours to a 24-hour period
- Various approaches:
 - Surgical patients not eating:
 - 60-80% of the TDD as basal demonstrated to be safe and effective in surgical patients (Clement 2004, Schmeltz 2006)
 - Medical patients:
 - 75-80% of TDD divided between basal and bolus (Schmeltz 2006, Yeldandi 2006, Bode 2004)



Example #2:

- Goofy Dwarf is a 50 yo F who presents following liver transplant, now POD 6.
- Euglycemia is maintained with insulin drip with rates of 2.5 un/hr on average.
- No complicating factors such as pressors or IV dextrose.
- Diet: Clear liquids. PO intake is poor.
- No current steroids.
- Wt: 100 kg

BG in mg/dL	Drip Rate in un/hr
90	1.5
110	2.5
100	2.0
140	3.0
150	3.5
120	2.5
200	5.0

Example #2 Cont:

- Take average drip rate of 2.5 un/hr and multiply by 24 hrs.
 - $2.5 \times 24 = 60$
- Reduce by 20%.
 - $60 \times 0.8 = 50$
- Use this dose to calculate TDD.
 - 50 un TDD
 - 25 un for basal coverage
 - 25 un for bolus coverage (8 un with meals)
 - Moderate insulin requirements ss: 2 or 3/50 > 150 ACHS

Impact of Nutrition

- No Food Intake:
 - Give continuous insulin infusion via IV (insulin drip)
 - Alternatively give basal insulin + sliding scale
- Continuous Enteral Feeding: Basal insulin + TF coverage + sliding scale correction q4-6h.
 - *If feeding interrupted, give IV glucose to prevent hypoglycemia.*
- Total Parenteral Nutrition: Add regular insulin to IV bag and titrate dose in increments of 5-10un/liter.
- Reassess insulin requirement with any change in nutritional status.

Confounding Variables

- Changes in caloric or carbohydrate intake
- Change in clinical status or medications (corticosteroids, vasopressors)
- Make adjustments based on daily BG patterns
- Poor coordination of BG testing and administration of insulin with meals
- Errors during patient transfer
- Renal or liver insufficiency

Adjusting Goal Targets

- Consider elevating goal target in the following situations:
 - Elderly >60 yo
 - ESRD, liver disease, partial or total pancreatectomy
 - CAD, CVA
 - Reduced hypoglycemic awareness
 - Recurrent hypoglycemia
- Watch for IV fluids with Dextrose, vasopressors, edema, snacking which can falsely increase your daily dosing.
- Be more aggressive with insulin dosing when pt has elevated TDD or BMI >35 kg/m².

When to Involve Endocrine

- U500 insulin or High Dose Requirements
- Low Dose Requirements
- Erratic Inpatient or Outpatient Control
- Insulin Pump
- Anytime!



Watch Out!



- **Common Med Errors with Insulin:**
 - Insulin to Carb mismatch: Providing meal or TF insulin without meal/TF
 - Holding SS or Long-acting insulin for NPO
 - Using meal coverage when pt isn't eating to bring down a high BG
 - “Pt refused” when it seems like too much or too little.
 - Poor communication between teams and nurses
 - Overtreating Hypoglycemia. Remember Rule of 15.

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Diabetes in the Transplant Patient

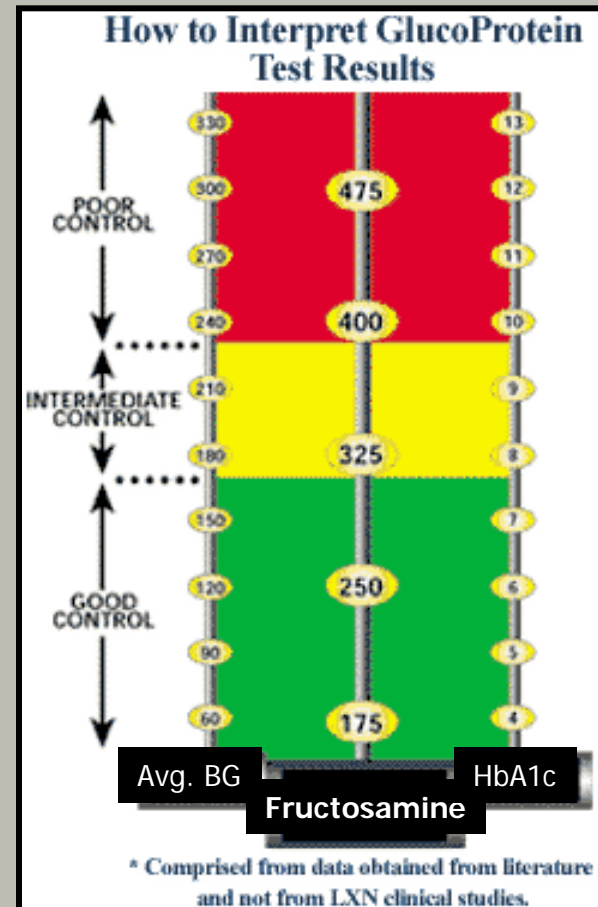
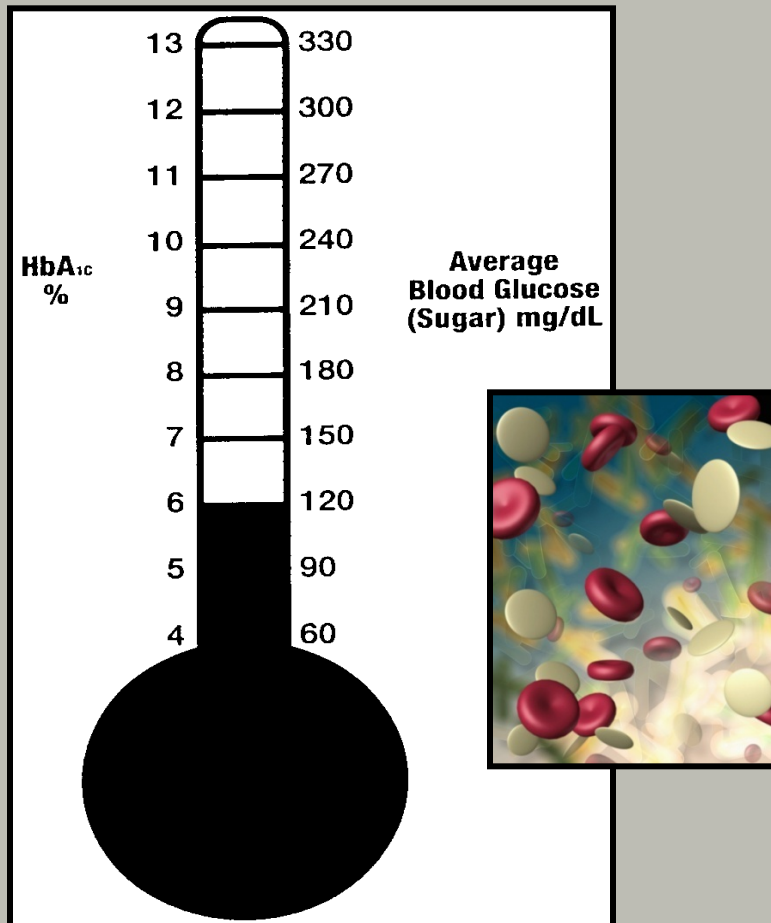
- Risk Factors, Screening, Diagnosis
- Inpatient Management
- Outpatient Management:
 - Assessment
 - Lifestyle Modification
 - Oral Agents
 - Non-Insulin SQ Agents
 - Insulin
 - Hypoglycemia

ADA Goals of Care

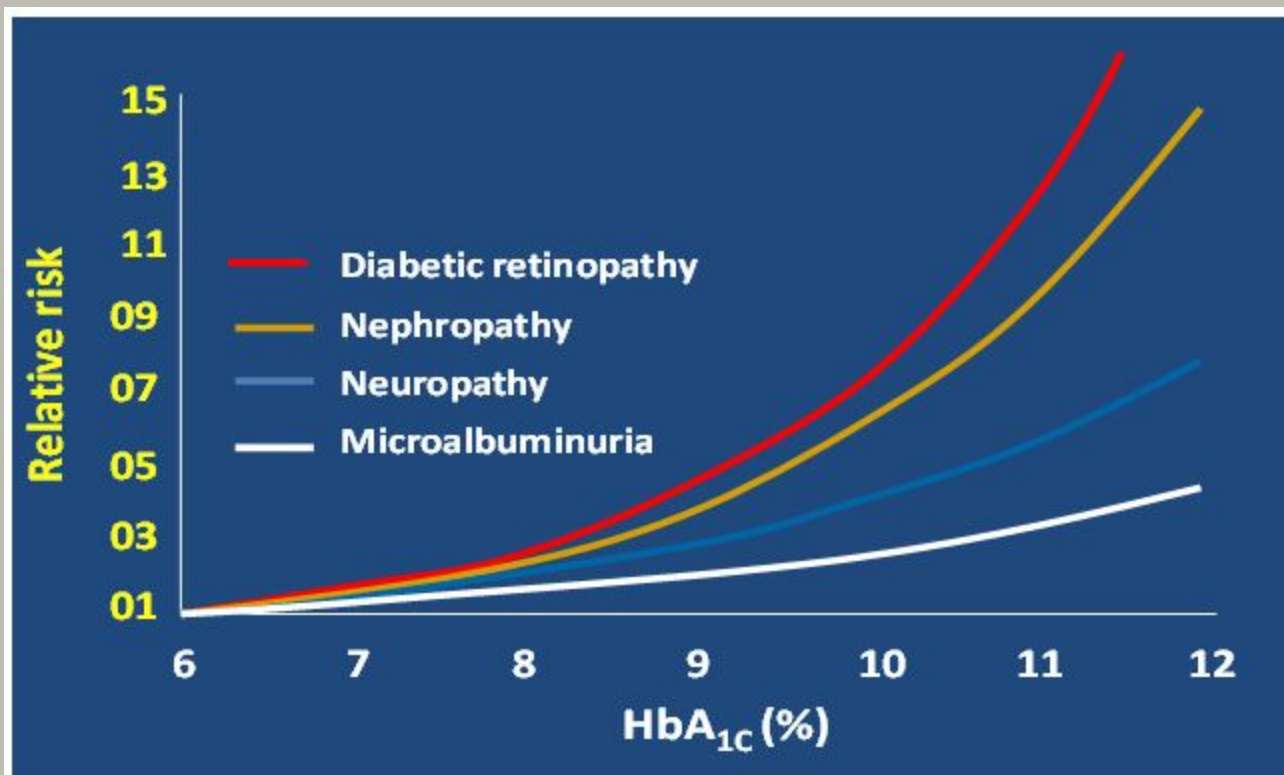
	Normal	Goal
HbA1c	4-6%	<7% *
Pre-prandial Blood Sugar	70-100 mg/dl	90-130 mg/dl (70-120)
Post-prandial Blood sugar	<140 mg/dl	<180 mg/dl (<160)

ADA
Recommendation:
Check A1c at least 2
x/yr if in target and
stable; q 3 months if
therapy has changed
or not meeting goals.
Diabetes Care 29:S4-
S42, 2006

Assessment of Glycemic Control



A1c and Risk of Complications



The relative risk is exponential!

Blood Glucose Monitoring

- Provides vital data for clinical decision making
- Provides patient with accountability and feedback about his/her behavior
- Advise patient about:
 - Appropriate meter
 - When to test
 - How to record results
 - How to interpret and respond to results
 - Insurance/financial issues, prescription required for reimbursement



Record Keeping

Vanderbilt Diabetes Program Blood Glucose Record

Patient Name: [REDACTED] Patient Phone Number: () _____ or Email Address: _____

Week of: 7.6.1

Deliver this Fax to: Kathleen Wolff at Fax Number: 343-4953

Blood Sugar Test Results

Day/Date	Breakfast			Lunch			Dinner			Bedtime		Notes
	Before	After		Before	After		Before	After		Before		
	131	200										
	116			121	193							
	76						99	201				
	95									164		
	123	197										
	82			125	203		116	189				
Average Blood Sugar												

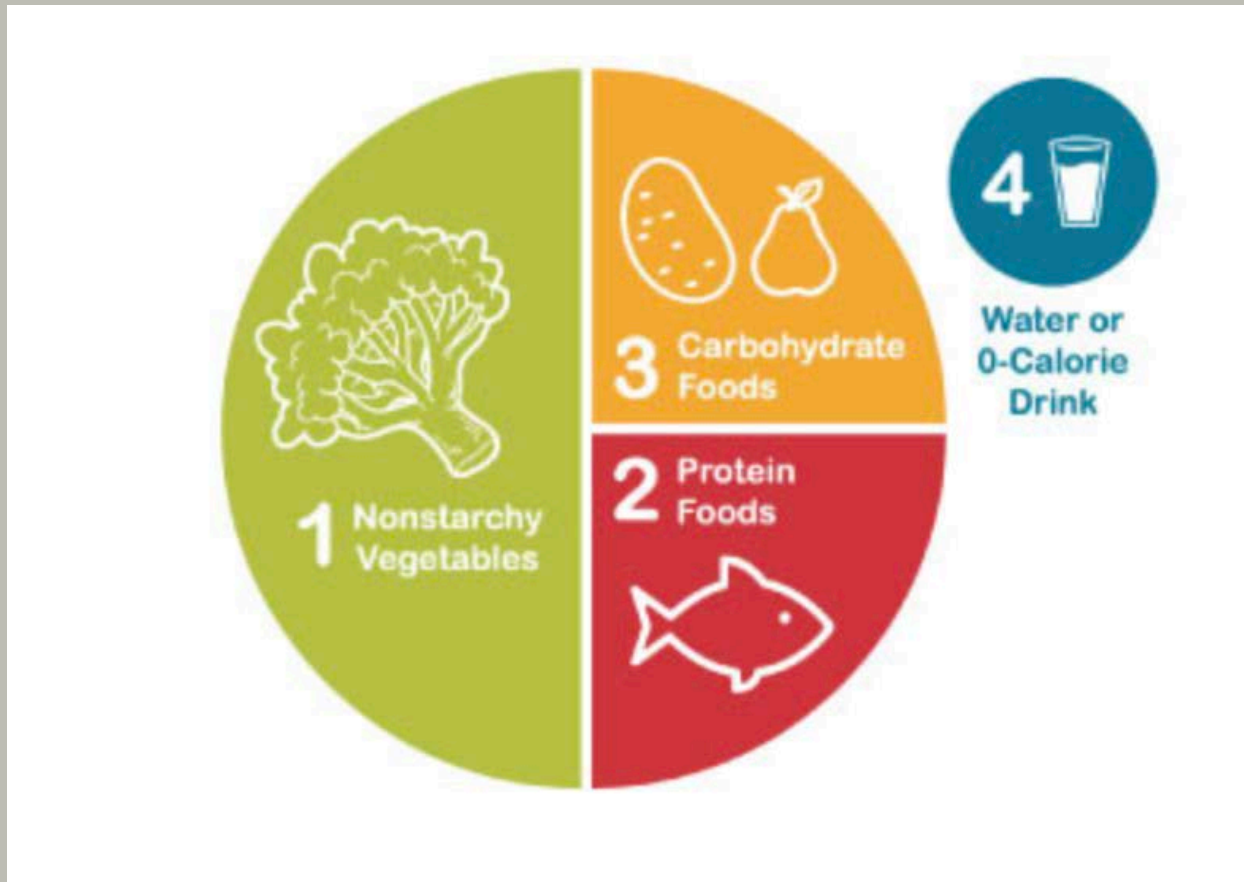
*Notes: Record Illness, Low Blood Sugar, Exercise, Large Meal, Emotional Stress, etc...

Target pre-meal BS 70-120

Target post meal BS <160

Target HbA1c 6-6.5%

Diet: The Plate Method



Examples!



[Avocado Toast with Turkey Bacon and Tomato](#)

Avocado toast is a quick and easy breakfast that includes whole grains and healthy fats. Add a slice of turkey bacon and some sliced tomato for some more protein and veggies. For a more filling breakfast, add a ½ cup of nonfat Greek yogurt and a handful of fresh blueberries (or other seasonal fruit)

Lean protein: turkey bacon, Greek yogurt
Nonstarchy vegetables: Tomato, avocado
Carbohydrate foods: whole-wheat bread, blueberries



[Apple Pie Yogurt Parfait](#)

Enjoy the flavors of the all-American dessert, apple pie, in a healthy, balanced breakfast parfait. These are great for making ahead—just store the granola separately and add just before eating so it stays crunchy.

Lean Protein: Greek Yogurt
Carbohydrate foods: granola, apple



This perfect weeknight meal features [Lemon Chicken with Rosemary and Garlic](#). Fill half your plate with a double serving of [Collard Greens with Yellow Squash](#) and complete your plate with half of a roasted sweet potato topped with a little bit of butter.

Lean Protein: Chicken
Nonstarchy Vegetables: Collards, yellow squash
Carbohydrate foods: sweet potato



We gave classic meatloaf a healthy makeover with this [Southwest-Style Turkey Meatloaf](#). Pair with simple [Mashed Red Potatoes](#) and a [Green Salad with Orange, Avocado, and Onion](#).

Lean Protein: ground turkey
Nonstarchy Vegetables: salad greens, onion
Carbohydrate foods: potatoes, oranges



This meal is perfect for lunch or dinner and works great for meal prepping. [Easy Beef Chili](#) is paired with a sweet and savory [Kale Apple Slaw](#). Top the chili with a dollop of Greek yogurt and [Almost Smooth Salsa](#).

Lean Protein: lean ground beef, beans
Nonstarchy Vegetables: kale, tomatoes, onion, salsa
Carbohydrate foods: apple; beans; yogurt



Here is a light, vegetarian meal, perfect for dinner or lunch. Veggie-packed [Slow-Cooker Ratatouille](#) gets a protein boost by adding white beans. Complete the plate with a simple [Side Greek Salad with Red Wine Vinaigrette](#).

Lean Protein: beans
Nonstarchy Vegetables: lettuce, tomato, onion, eggplant, cabbage, bell pepper
Carbohydrate foods: beans

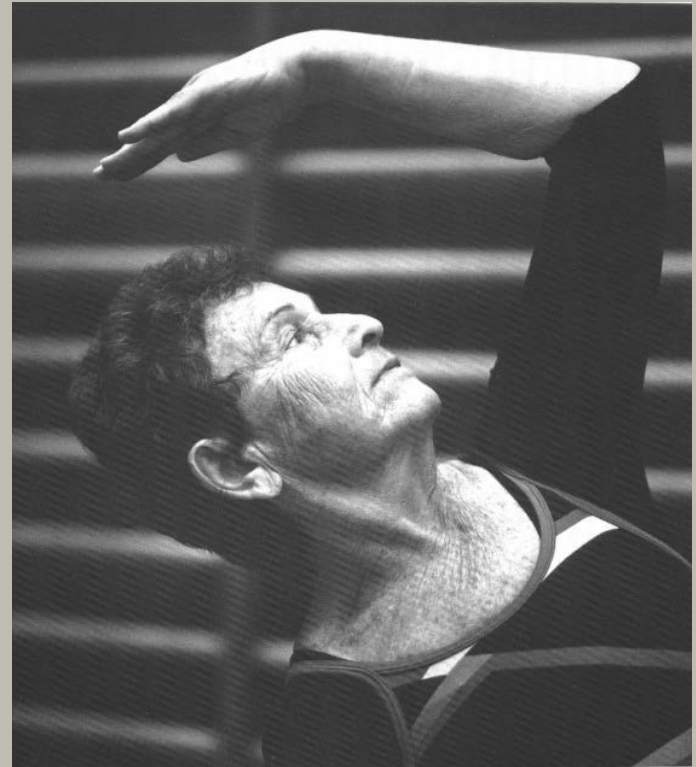
Resources

- App and Websites
 - My Fitness Pal
 - Calorie King (Also available in a book)
 - Live Strong
 - Spark People (Look for Meal Plan, Grocery List)



Physical Activity

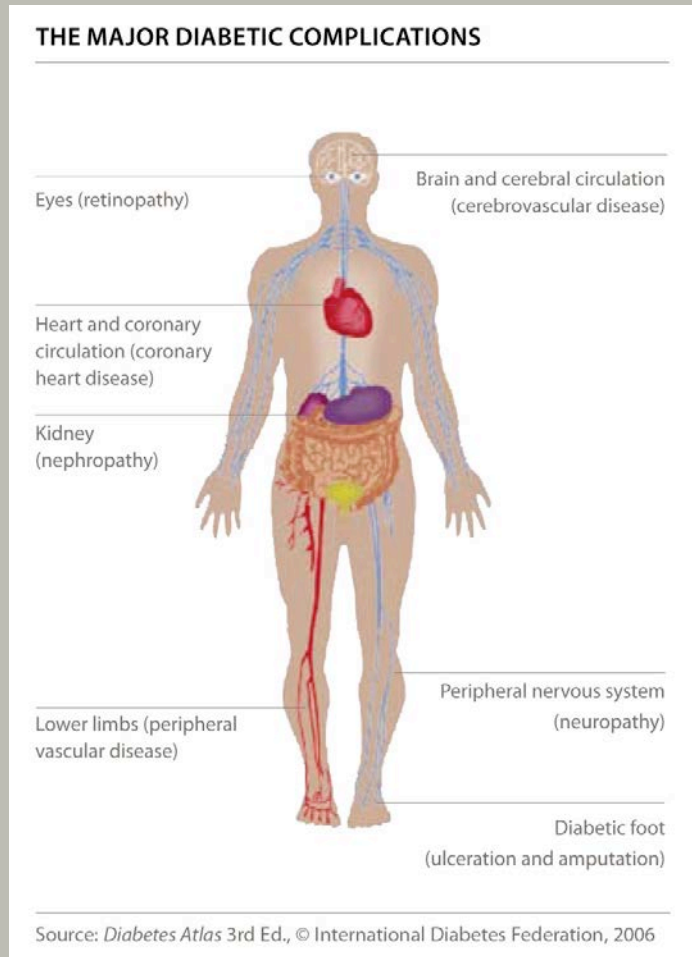
- Set small, reasonable goals: **Something is better than nothing!**
- Aim for **30 minutes** of moderate-to-vigorous intensity aerobic exercise **at least 5 days a week** or a total of **150 minutes per week**.





Chronic Effects of Diabetes

- Macrovascular
- Microvascular
- Consider short-term risks in the post-op setting



Oral Diabetes Meds

Drug Class	Action	Names
Insulin Secretagogues	Increase Glucose Secretion	Sulfonylureas: Glipizide, Glyburide, Glimepiride (Amaryl®) Meglitinides: Nateglinide (Starlix®) Repaglinide (Prandin®)
Biguanides	Increase insulin sensitivity, decrease hepatic glucose output	Metformin (Glucophage®)
AlphaglucoSIDase Inhibitors (AGI's)	Inhibit absorption of glucose from the gut	Acarbose (Precose®) Miglitol (Glyset®)
Thiazolidindiones (TZD's)	Increase insulin sensitivity	Rosiglitazone (Actos®) Pioglitazone (Avandia®)
DPP-4 Inhibitors	Increase insulin secretion, decrease glucagon secretion	Sitagliptin (Januvia®) Saxagliptin (Onglyza®)
SGLT2 Inhibitors *NEW CLASS!*	Increase glucose reabsorption in kidney	Canagliflozin (Invokana®) Dapagliflozin (Farxiga®) Empagliflozin (Jardiance®)
Bile Acid Resins	Cholesterol-lowering med that also reduces BG by binding bile acids in the digestive tract	Colesevelam (Welchol®)

Non-Insulin Injectables

Drug Class	Action	Names
GLP-1 Receptor Agonists	stimulate insulin production while suppressing the liver's glucose output, slows gastric emptying	<ul style="list-style-type: none"> - Albiglutide (Tanzeum) weekly - Dulaglutide (Trulicity) daily - Exenatide (Byetta) twice daily - Exenatide Extended Release (Bydureon) weekly - Liraglutide (Victoza) daily
Amylin Analogue	slows food from moving too quickly through the stomach and helps keep after-meal glucose levels from going too high, also reduces glucose production from liver.	Pramlintide (Symlin)



Table 1. Hypoglycemic Agents for Treating Type 2 Diabetes Mellitus

Medication	Average A1C reduction	Potential adverse effects	Precautions/contraindications
Alpha-glucosidase inhibitors Acarbose (Precose) Miglitol (Glyset)	0.5% to 0.8%	Flatulence, diarrhea, abdominal bloating	Avoid when creatinine clearance < 25 mL per minute per 1.73 m ² (0.42 mL per second per m ²) Most effective when given with a starchy, high-fiber diet Reverse hypoglycemia with glucose, not sucrose
Biguanides Metformin	1.0% to 1.3%	Nausea, diarrhea, abdominal bloating Extended-release preparations have fewer gastrointestinal adverse effects	Estimated GFR 30 to 44 mL per minute per 1.73 m ² : review use of metformin Estimated GFR < 30 mL per minute per 1.73 m ² : discontinue use Discontinue during acute illness or procedure that could predispose patient to lactic acidosis
Dipeptidyl-peptidase-4 inhibitors Alogliptin (Nesina)* Linagliptin (Tradjenta)* Saxagliptin (Onglyza)* Sitagliptin (Januvia)*	0.5% to 0.9%	Headache, pancreatitis (rare)	Linagliptin does not require dosage adjustment in renal insufficiency Saxagliptin dosage adjustment required when administered with concomitant CYP3A4 inhibitors
Glucagon-like peptide-1 receptor agonists Albiglutide (Tanzeum)* Dulaglutide (Trulicity)* Exenatide (Byetta, Bydureon)* Liraglutide (Victoza)*	0.8% to 2.0%	Nausea, vomiting, sense of fullness Weight loss of 1 to 4 kg (2.2 to 8.8 lb) is likely Pancreatitis (rare)	Exenatide is not recommended if creatinine clearance < 30 mL per minute per 1.73 m ² (0.50 mL per second per m ²) Boxed warning for personal or family history of medullary thyroid carcinoma; patients with multiple endocrine neoplasia type 2
Meglitinides Nateglinide (Starlix)* Repaglinide (Prandin)	0.5% to 1.0%	Hypoglycemia	Metabolized primarily by the liver (CYP3A4 and CYP2C9)
Sodium-glucose cotransporter 2 inhibitors Canagliflozin (Invokana)* Dapagliflozin (Farxiga)* Empagliflozin (Jardiance)*	0.5% to 0.9%	Increased urinary tract and genital infections, increased low-density lipoprotein cholesterol level Weight loss of 0.7 to 3.5 kg (1.5 to 7.7 lb) is typical	Dosage adjustment required in renal insufficiency
Sulfonylureas Glimepiride (Amaryl) Glipizide (Glucotrol) Glyburide	0.4% to 1.2%	Hypoglycemia, weight gain	Dosage adjustment required in renal insufficiency Administer with meals
Thiazolidinediones Pioglitazone (Actos) Rosiglitazone (Avandia)	0.5% to 1.4%	Weight gain, edema	Contraindicated in patients with New York Heart Association class III or IV congestive heart failure Decrease concomitant insulin dose at initiation

GFR = glomerular filtration rate.

*—Drug available only as brand name in the United States.

Information from references 1 and 9.

Considerations for Transplant Pts

Table 4. Non-Insulin Diabetes Treatments: Potential Considerations for Use in the Solid Organ Transplant Patient

Agent	Safety or Efficacy Studies in Transplant Patients	Potential Considerations in Organ Transplant Patient
Metformin	Effective in stable KTX patients but contraindicated for many other TX groups, including during acute hospitalizations (177, 214)	Should not be used during acute hospitalization, with ↓ GFR, ↑ LFTs, CHF, or active, significant infection; and should be held for planned iv contrast procedure
Sulfonylureas	Efficacy is not well documented in transplant patients. Did not alter cyclosporine pharmacokinetics in a small study of KTX recipients with PTDM (215–218)	Increased risk of more frequent and more prolonged hypoglycemia with ↓ GFR
Repaglinide	Effective and safe with no interaction with CNIs in a small study of KTX recipients with PTDM (180)	Less risk of hypoglycemia with ↓ GFR than sulfonylureas
Thiazolidinediones (eg, pioglitazone)	Effective and safe in small studies of KTX recipients (177, 180, 183, 219, 220)	Known risk for weight gain, edema, heart failure, and reduced bone mass, contraindicated with known elevated liver function tests with the exception for known fatty liver disease including after liver transplant; contraindicated with known heart failure; unknown impact on risk for heart failure risk after transplant

More Considerations

Table 4. Non-Insulin Diabetes Treatments: Potential Considerations for Use in the Solid Organ Transplant Patient

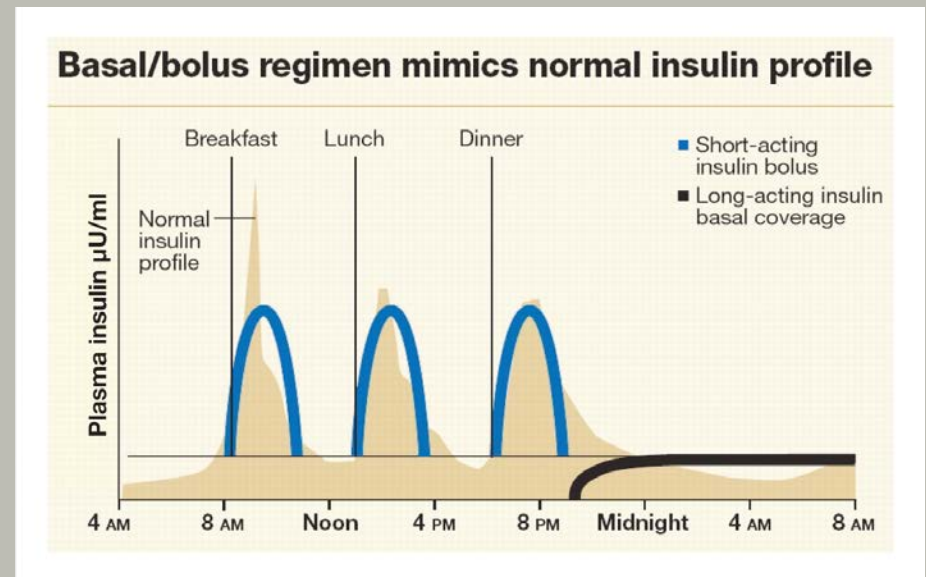
Agent	Safety or Efficacy Studies in Transplant Patients	Potential Considerations in Organ Transplant Patient
α -Glucosidase inhibitors	No studies of safety or efficacy to date in organ transplant populations	Avoid with \downarrow GFR; unlikely to be an effective single agent
GLP-1 agonists (exenatide, liraglutide, lixisenatide)	Liraglutide did not affect tacrolimus concentration in a very small study of KTX recipients (185)	Decreases bowel motility, which may impact absorption of immune suppression agents and has not yet been studied; should not use if GFR < 40 ml/min
DPP-4 inhibitors (sitagliptin, vildagliptin, saxagliptin, linagliptin, alogliptin)	Retrospective and small random controlled trials of KTX recipients show safety of several DPP-4 inhibitors (8, 181–184)	Reduce dose of all but linagliptin with \downarrow GFR
SGLT-2 inhibitors (dapagliflozin, canagliflozin, empagliflozin)	Known to increase risk of genitourinary infections in those with previous history, which is a concern in immunocompromised transplant patients, known to cause volume dehydration and hypotension, which may also be a concern in these patients as well as recent reports of diabetic ketoacidosis raise concerns of safety for most transplant populations (186, 187)	Avoid until safety studies are performed

Insulin

- Maintenance Insulin (Basal) – NPH, Levemir, Lantus, Toujeo, Tresiba, Basaglar
 - 50% of daily needs
 - Suppresses glucose production while fasting
- Prandial and SS Coverage (Bolus)
 - Limits hyperglycemia after meals
 - Immediate risk and sharp peak at 1-2 hrs
 - 10-20% of total daily insulin requirement at each meal

Normal Endogenous Insulin Secretion

- Guidelines just a starting point.
- When correction is required before most meals, \uparrow basal
- When BG remains consistently elevated at one time point, \uparrow preceding bolus
- Fasting BG also a good measure of basal insulin dose but be wary of the bedtime snack!



Insulin Duration of Action: Rapid-Acting

Type of Insulin (Trade Names)	Supplier	Appearance	Begins Working	Peak Activity	All gone
RAPID ACTING					
Afrezza (Regular insulin)	MannKind	Inhaled	12 minutes	30–45 minutes	2 hours
Lyumjev® (insulin lispro)	Eli Lilly	Clear	15–17 minutes	57 minutes	4.6–7.3 hours
Fiasp® (insulin aspart)	Novo Nordisk	Clear	16–20 minutes	90–120 minutes	5–6 hours
NovoLog® / NovoRapid® (insulin aspart)	Novo Nordisk	Clear	15–20 minutes	60–180 minutes	3–5 hours
Apidra® (insulin glulisine)	Sanofi	Clear	15–20 minutes	60–120 minutes	4–5 hours
Humalog® (insulin lispro)	Eli Lilly	Clear	20–45 minutes	60–120 minutes	4–5 hours
Admelog® (insulin lispro)	Sanofi	Clear	20–45 minutes	45–150 minutes	3.5–4.75 hours



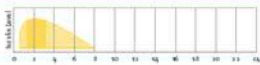
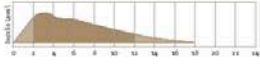
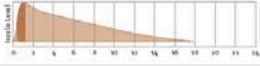
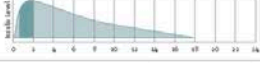

Insulin Duration of Action: Long-Acting

Type of Insulin (Trade Names)	Supplier	Appearance	Begins Working	Peak Activity	All gone
LONG ACTING					
LANTUS® (insulin glargine U-100)	Sanofi	Clear	4–6 hours	No pronounced peak	Up to 24 hours (depends on injected dose)
Toujeo® (insulin glargine U-300)	Sanofi	Clear	4–6 hours	No pronounced peak	Up to 24 hours (depends on injected dose)
Basaglar® (insulin glargine U-100)	Eli Lilly	Clear	4–6 hours	No pronounced peak	Up to 24 hours (depends on injected dose)
SEMGLEE™ (insulin glargine U100)	Viatrix	Clear	4–6 hours	No pronounced peak	Up to 24 hours (depends on injected dose)
Levemir® (insulin detemir)	Novo Nordisk	Clear	1–2 hours	2 - 12 hours (mild, varies by dose)	Up to 24 hours (depends on injected dose)
Tresiba (insulin degludec U-100 or U-200)	Novo Nordisk	Clear	1–2 hours	About 12 hours	42+ hours

Short-Acting, Intermediate, and Mixed Insulin Options

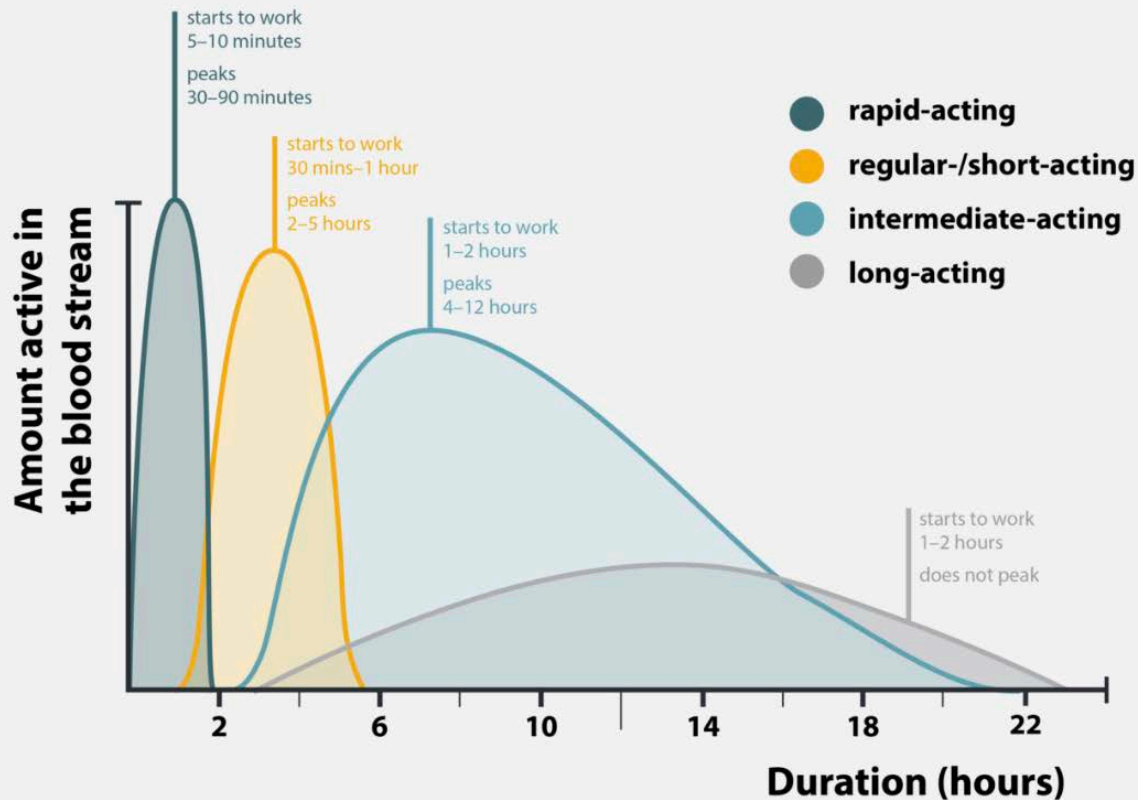
Type of Insulin (Trade Names)	Supplier	Appearance	Begins Working	Peak Activity	All gone
SHORT ACTING					
Regular (Humulin, Actrapid, Velosulin®)	Eli Lilly and Novo Nordisk	Clear	30 minutes	2–4 hours	5–8 hours
INTERMEDIATE ACTING					
NPH (Insulatard®)	Eli Lilly and Novo Nordisk	Cloudy	2–4 hours	6–8 hours	12–15 hours
Human Regular U-500	Eli Lilly	Clear	30 minutes	5–6 hours	18–20 hours
PRE-MIXED (ACTION VARIES)					
NPH/Regular 70/30 or 50/50 are common mixes	Eli Lilly and Novo Nordisk	Cloudy	30 minutes	Varies	18–24 hours
NPL/Humalog 75/25 and 50/50	Eli Lilly	Cloudy	10–15 minutes	Varies	12–15 hours
NovoLog Mix 70/30	Novo Nordisk	Cloudy	10–15 minutes	Varies	10–12 hours

TYPES OF INSULIN

Product	Name	Type of Insulin	Presentation	Schematic Action Profile*	
Basal					
Lantus®	Insulin Glargine	Long-acting	10ml Vial 3ml Cartridge 3ml SoloSTAR®		SANOFI
Humulin® NPH	Isophane (NPH)	Intermediate-acting	10ml Vial 3ml Cartridges		LILLY
Protaphane®	Isophane (NPH)	Intermediate-acting	10ml Vial 3ml Penfill®		Novo Nordisk
Rapid Acting					
Apidra®	Insulin Glulisine	Rapid-acting	10ml Vial 3ml Cartridge 3ml SoloSTAR®		SANOFI
Humalog®	Insulin Lispro	Rapid-acting	10ml Vial 3ml Cartridge		LILLY
NovoRapid®	Insulin Aspart	Rapid-acting	10ml Vial 3ml Penfill® 3ml FlexPen®		Novo Nordisk
Short Acting					
Actrapid®	Insulin Neutral	Short-acting	10ml Vial 3ml Penfill®		Novo Nordisk
Premix					
Humulin® 30/70	30% Insulin Neutral / 70% Isophane (NPH)	Premixed Insulin	10ml Vial 3ml Cartridge		LILLY
Humalog® Mix 25®	25% Insulin Lispro / 75% Insulin Lispro Protamine Suspension	Premixed Insulin Lispro	3ml Cartridge		LILLY
Humalog® Mix 50®	50% Insulin Lispro / 50% Insulin Lispro Protamine Suspension	Premixed Insulin Lispro	3ml Cartridge		LILLY
PenMix® 30 & Mixtard® 30	30% Insulin Neutral / 70% Isophane (NPH)	Premixed Insulin	10ml Vial 3ml Penfill®		Novo Nordisk
NovoMix® 30	30% Insulin Aspart / 70% Insulin Aspart Protamine	Premixed Insulin Aspart	3ml FlexPen®		Novo Nordisk

Insulin Duration Of Action

Types of Insulin



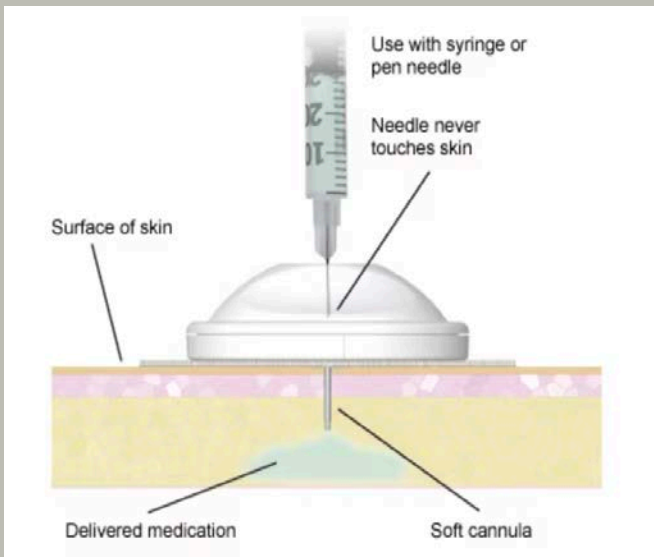
Inhaled Insulin

- Inhaled insulin begins working within 12 to 15 minutes, peaks by 30 minutes, and is out of your system in 180 minutes.
- Types: Technosphere insulin-inhalation system (Afrezza® Human Insulin)
 - Rapid acting human insulin
 - Take prior to your meals
 - Each puff is approximately 4 un, 8 un, or 12 un. Depending on dose prescribed.
 - Similar dosing, although slightly more effective than SQ insulin.



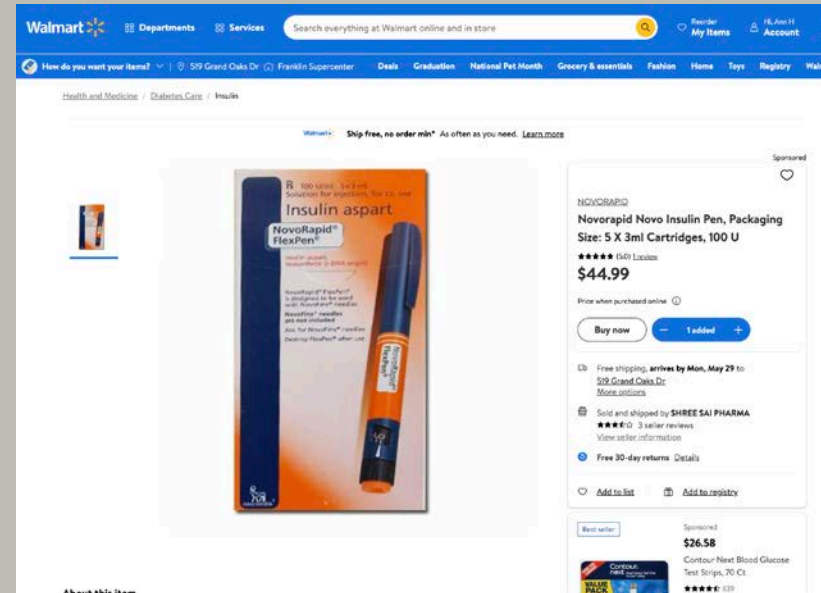
Afraid of Needles?

- I-Port: reduces pain and anxiety with injections by using the same site every day, instead of multiple areas
- Uses a Built-in Inserter device, which leaves a flexible cannula under the skin
- Change site every 3 days
- Used with both pens and syringes (must be 5 mm and greater)



Affordability

- Wal-Mart's Brand: Reli-On – NPH, Regular, or 70/30 insulins \$25 per vial. No Rx needed.
- As of July, 2021: Analog: Wal-Mart analog insulin vials (\$72.88) and FlexPen[®] (\$85.88). Reli-On Novolog. Also available at Sam's.



Cost Of Diabetes Medications

- Cost Effective Insulin Regimens
 - Over-the-counter insulin
 - Glucometer, Strips
- May also consider use of SFU if appropriate.
 - Other generic, low-cost oral agents include Metformin, TZD (Actos), etc although these may not typically be correct for the post-transplant setting.

Pre-Mixed Insulins

- Protamine + Short or Rapid-Acting Insulin
 - Novolin 70/30[®] = 70% NPH+30% Regular
 - Humulin 70/30[®], Humulin 50/50[®]
 - Humalog 75/25[®] = 75% NPL+25% Lispro
 - Novolog 70/30[®] = 70% NPH + 30% Aspart
- Time to Peak: 4-8 hours
- Duration: 17-25 hours
- Clinical Use: Elderly, cognitive or psych. impairment, multiple co-morbid illnesses, low cost, poor compliance
- Can access over-the-counter *without a prescription*
- Cost: \$25 at Wal-Mart

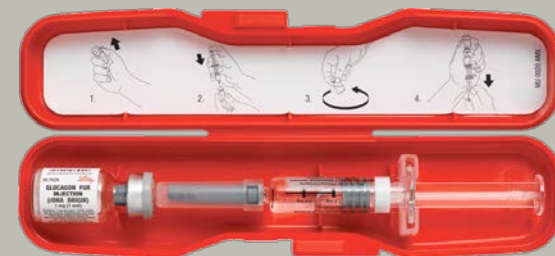
Continuous Glucose Monitoring Sensor

- Measures interstitial fluid
- Gives trends
- Alerts
- Highly Accurate
- Medtronic, Dexcom
Freestyle Libre



Hypoglycemia

- Below 70: **Rule of 15**
- Causes
- Severe Hypoglycemia
- Hypoglycemia Unawareness

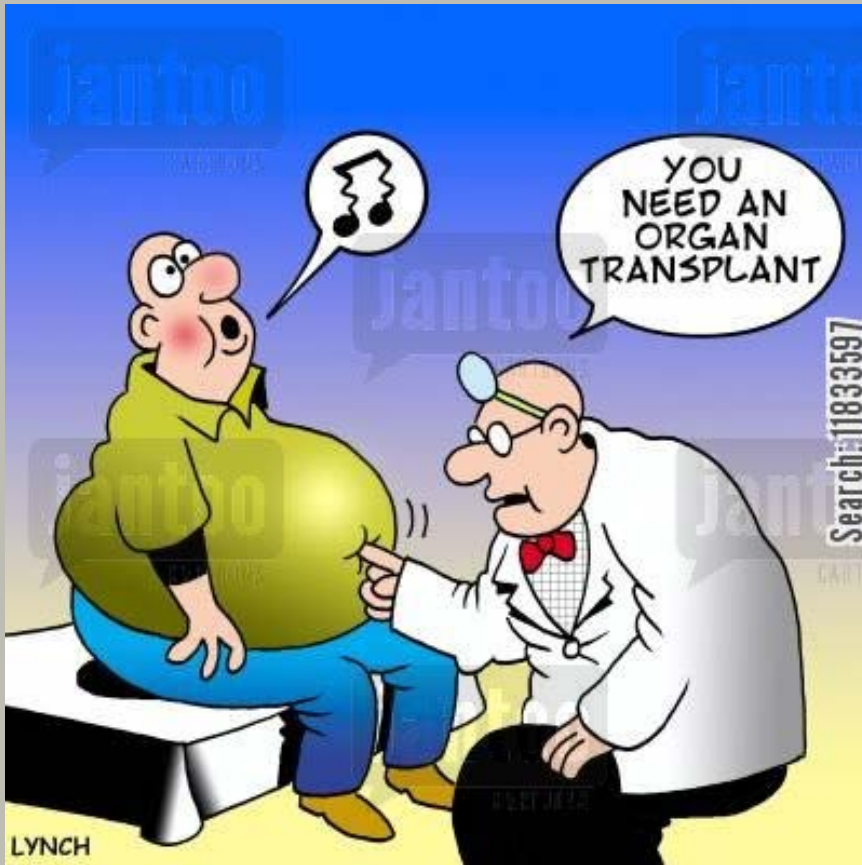


Take Home Points

- Approach med compliance, diet, and exercise in a non-judgmental way.
- Start with Weight-Based Dosing if you need a starting place.
- Educate, educate, educate!

Test/Exam	Frequency
Wgt.	Each visit
Blood Pressure	Each visit
HbA1c	Every 3 months
Dilated eye exam	Yearly if no DR
Lipid Panel	Yearly if low risk
Foot exam	Yearly if low risk
Microalbumin	Yearly

Roll With The Punches and Enjoy The Challenge of Caring For People With Diabetes!





Thank You!

Ann Hackett, APRN-BC, MSN, CDE