# Anesthetizing the Diabetic Child: techniques, pitfalls, pumps and new insulins

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*A pediatric healthcare network*

# Disclosures

- No financial conflict of interest
- No discussion of off-label use of medication

# Clinical scenarios

- A 6 yo boy with DM presents for adenoidectomy; he is on Lantus 8 units at bedtime and Humalog before meals with a total of about 8 units given through the day. How do you handle his perioperative care?
- An 17 year old with DM comes for removal of wisdom teeth. He has an insulin pump and his blood sugar is 120. How should his insulin needs be managed?

# Possible choices

- Write orders for insulin and fluid administration
- Call endocrinology
- Ask parents
- Cancel case

# Historical management

- 2/3 the usual NPH dose on am of surgery
- Check blood glucose preop, intraop, postop
- Regular insulin administered subcutaneously
- Insulin dose based on sliding scale depending on blood glucose

# Problem with historical management

- These children aren't on NPH
- Parents hope you will maintain tight control

We're not in Kansas anymore, Toto….

# Background

- Revolution in diabetes management in past 5-10 years
  - Diabetes Control and Complications Trial: tighter control better (does this apply to children?)
  - New insulins
  - New technology: insulin pumps
- Do these changes in home diabetes management affect OR management of diabetic children?

# Objectives

- Epidemiology
- Physiology of insulin action and deficiency and surgical stress
- New insulins: pharmacokinetics
- Insulin pumps

# Objectives

- Perioperative insulin management for
  - brief ambulatory surgery
  - longer ambulatory and/or inpatient surgery
  - children with insulin pumps

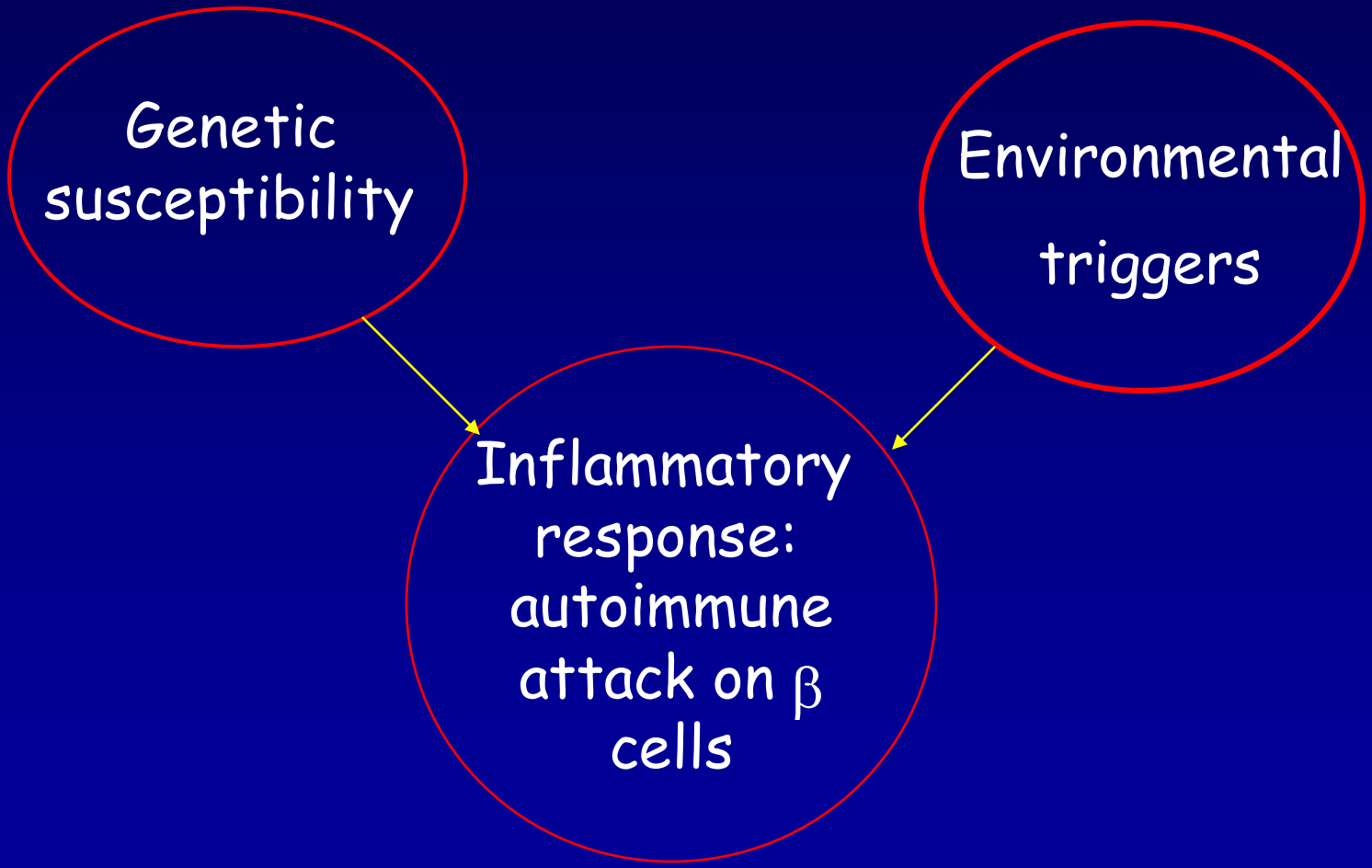
# Diabetes in children is a common problem in children

# Type 1 Diabetes Mellitus
## Epidemiology

- Children < 18 years old:

  1 / 500
- Peak age at onset: 10-12 yrs
- No family history in over 50%

# Pathogenesis: type 1 DM

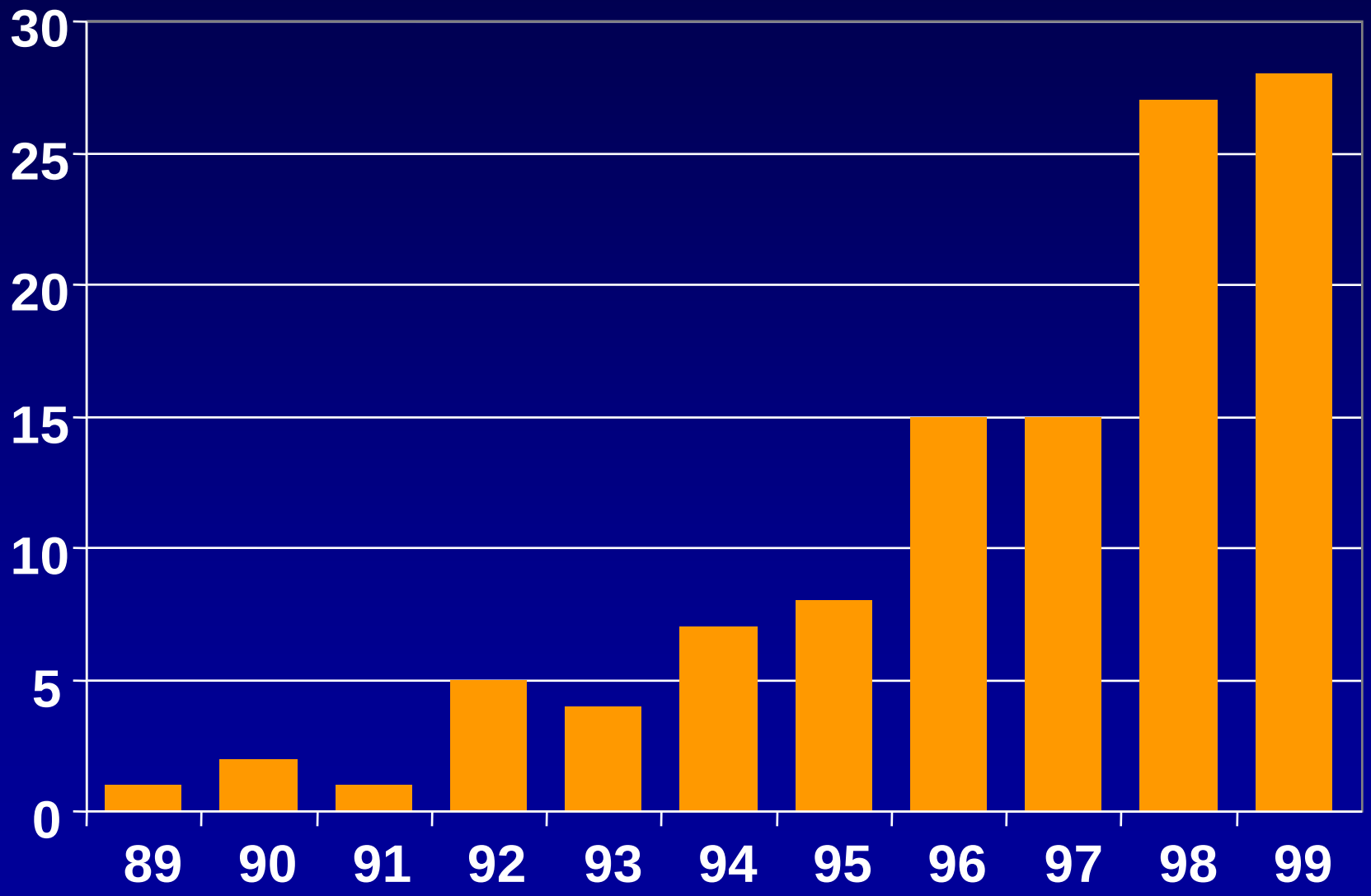


# High Risk Groups

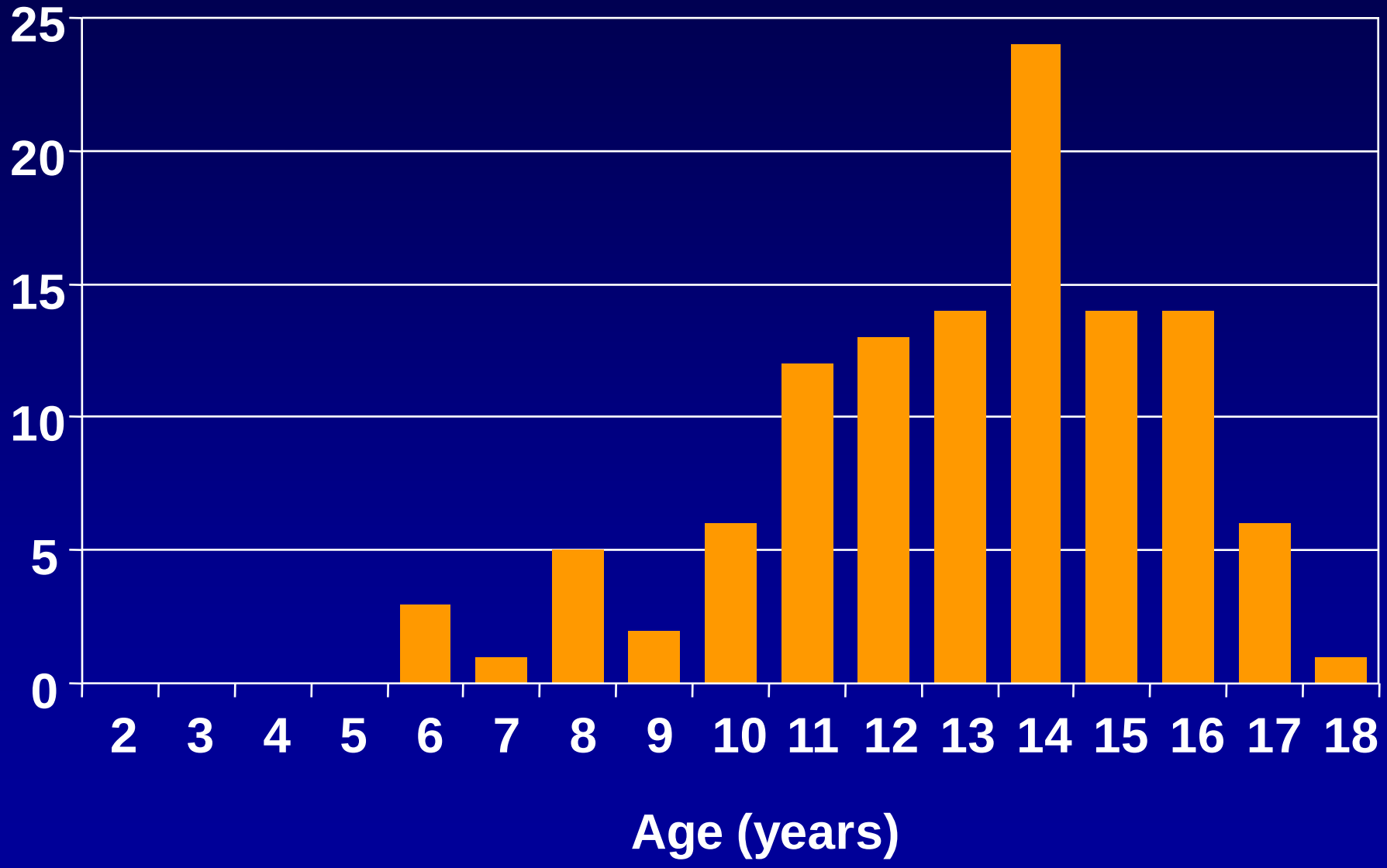
- FHx diabetes
- Trisomy 21
- Pancreatectomy
- Cystic fibrosis
- Steroid usage
- ALL (l-asparaginase)

# Type 2 Diabetes in Childhood: an increasing problem

# CHOP New Dx T2DM by Year



# CHOP New Dx T2DM by Age



# Type II Diabetes

- 1/3 of males and 39% of females born in 2000 will develop type II diabetes in their lifetime

# Physiologic effects of insulin deficiency

- Hormonal response
  - Increased glucagon, catecholamines, growth hormone, cortisol
- Metabolic response
  - Increased glycogenolysis, gluconeogenesis
  - Increased fat lipolysis → inc FFA, ketones
  - Inhibition of glucose utilization at cellular level except in brain, heart, red blood cells

# Metabolic effects of surgery/anesthesia

- Metabolic stress response
  - increased cortisol, catecholamines, glucagon, growth hormone,
  - inhibition of insulin secretion
  - insulin resistance
  - increased protein catabolism, gluconeogenesis, hyperglycemia
  - increased lipolysis

- In the presence of starvation (NPO), increase in glucose may be small, but lipolysis, protein catabolism, ketone production, and acidosis may occur
- Starvation + surgical stress can lead to hyperglycemia and accelerated development of ketoacidosis

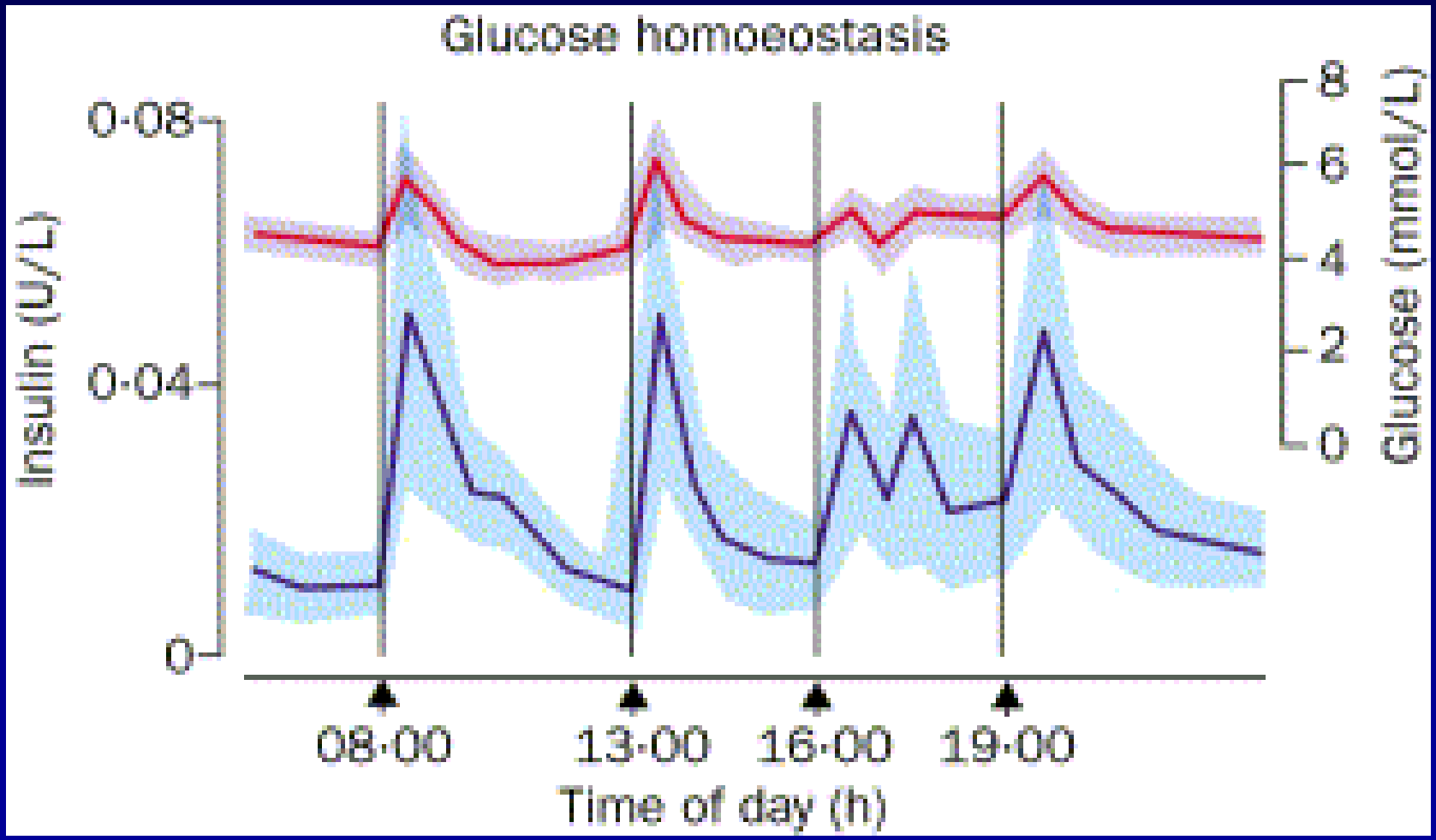
# Principles

- Minimize starvation
- Provide insulin in advance of surgery to minimize *cellular* starvation
- Monitor blood glucose and modulate with insulin/glucose administration
- Minimize stress response
  - Good analgesia
  - Epidural? No evidence in children

# Adverse effects of hyperglycemia

- Ketosis/hyperosmotic state/cerebral edema
- Increased incidence of postoperative infection
- Delayed wound healing
- Risk of neurologic injury
  - adult data: stroke patients, CPB in diabetic patients
  - pediatric data: CPB

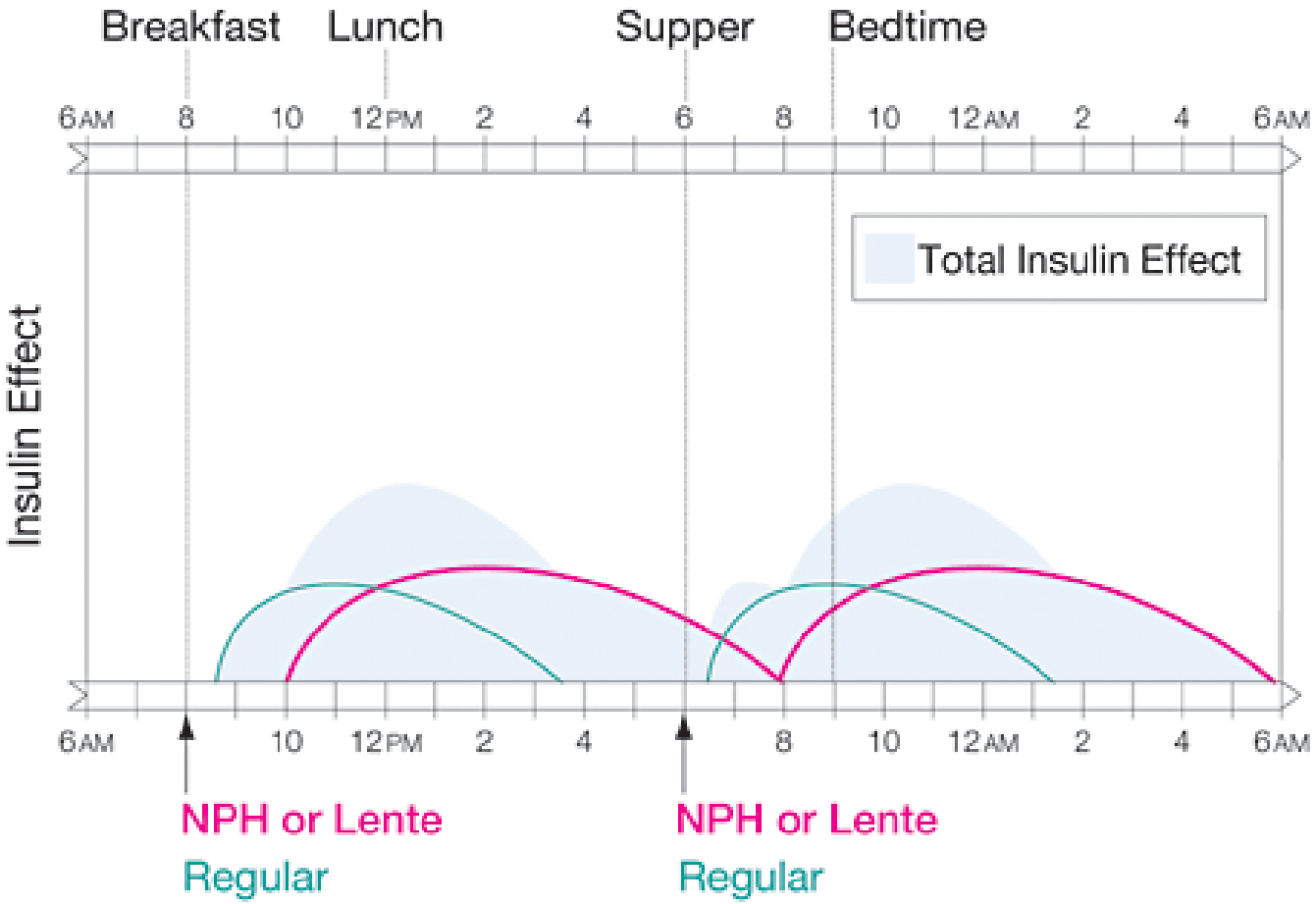
# Normal insulin secretion



# Historical Insulin Management of DM

- Infrequent doses of long acting insulin (NPH bid) combined with short acting insulin with meals (regular)
- Blood sugar testing 3-4 times a day

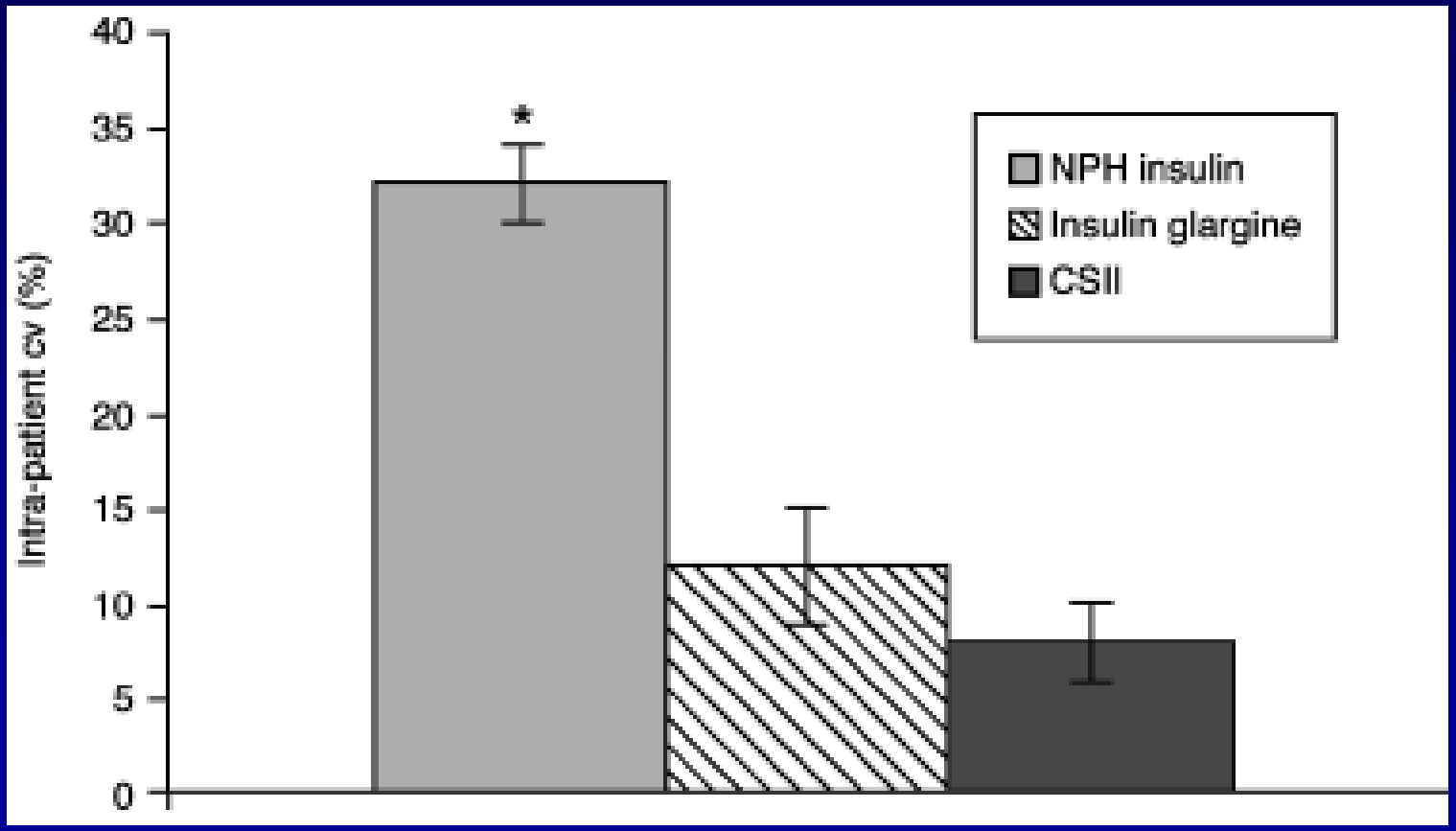
# Conventional diabetic management



# Problems with old regimen

- Poor matching of regular insulin onset with meals: delay required waiting 30 minutes to eat; difficult for children
- NPH variably absorbed, difficult to maintain in suspension: variable dose
- Inconsistent insulin levels; glucose response

# Subcutaneous absorption of older insulins is unpredictable



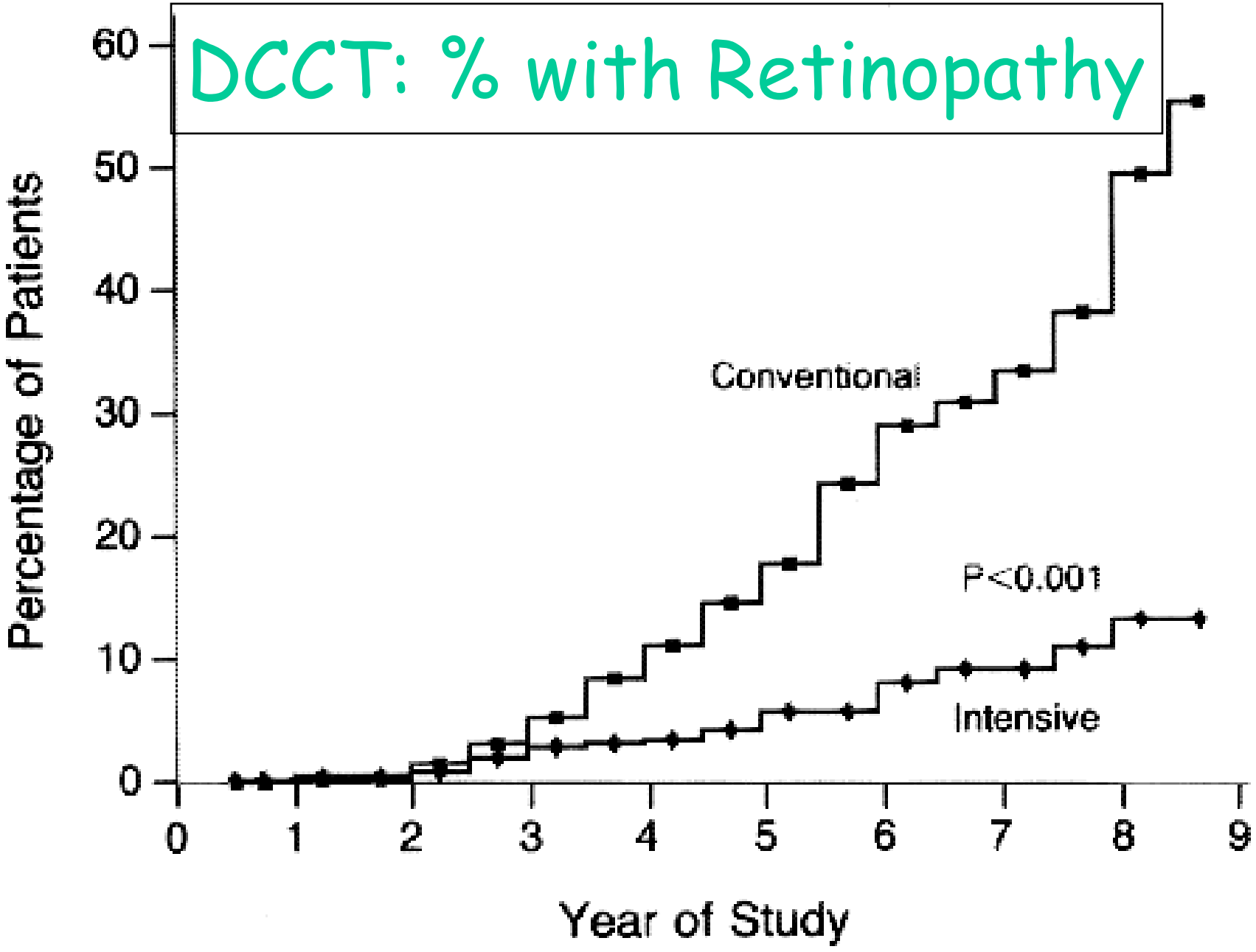
# Diabetes management has changed

- "Tighter" control
  - more frequent blood glucose testing
  - more frequent insulin administration
  - carbohydrate counting

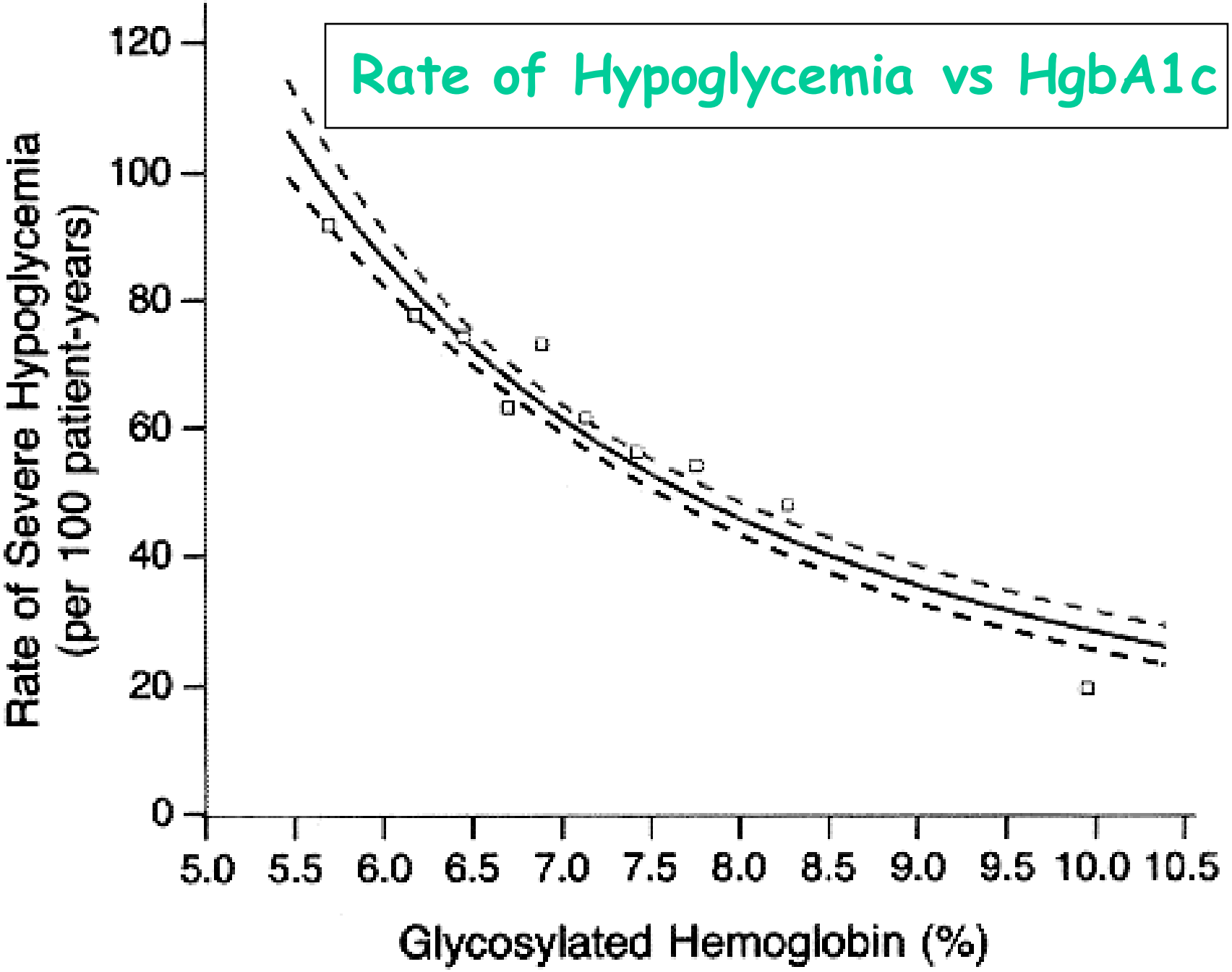
# Diabetes Control and Complications Trial (DCCT)

- Adults
- Better glycemic control
- More hypoglycemia but not severe
- Decreased development and progression of microvascular complications
- Recent caveats in older patients with established cardiovascular disease

# DCCT: % with Retinopathy



# Rate of Hypoglycemia vs HgbA1c




B

# Principles of new insulin Rx

- Continuous low basal level of insulin
  - Long acting insulin
  - Continuous subcutaneous infusion (insulin pump)
- Smaller more frequent doses of very short acting insulin to allow for flexibility in food choices and improved metabolic control (injection or insulin pump)

# Modern Insulin Management

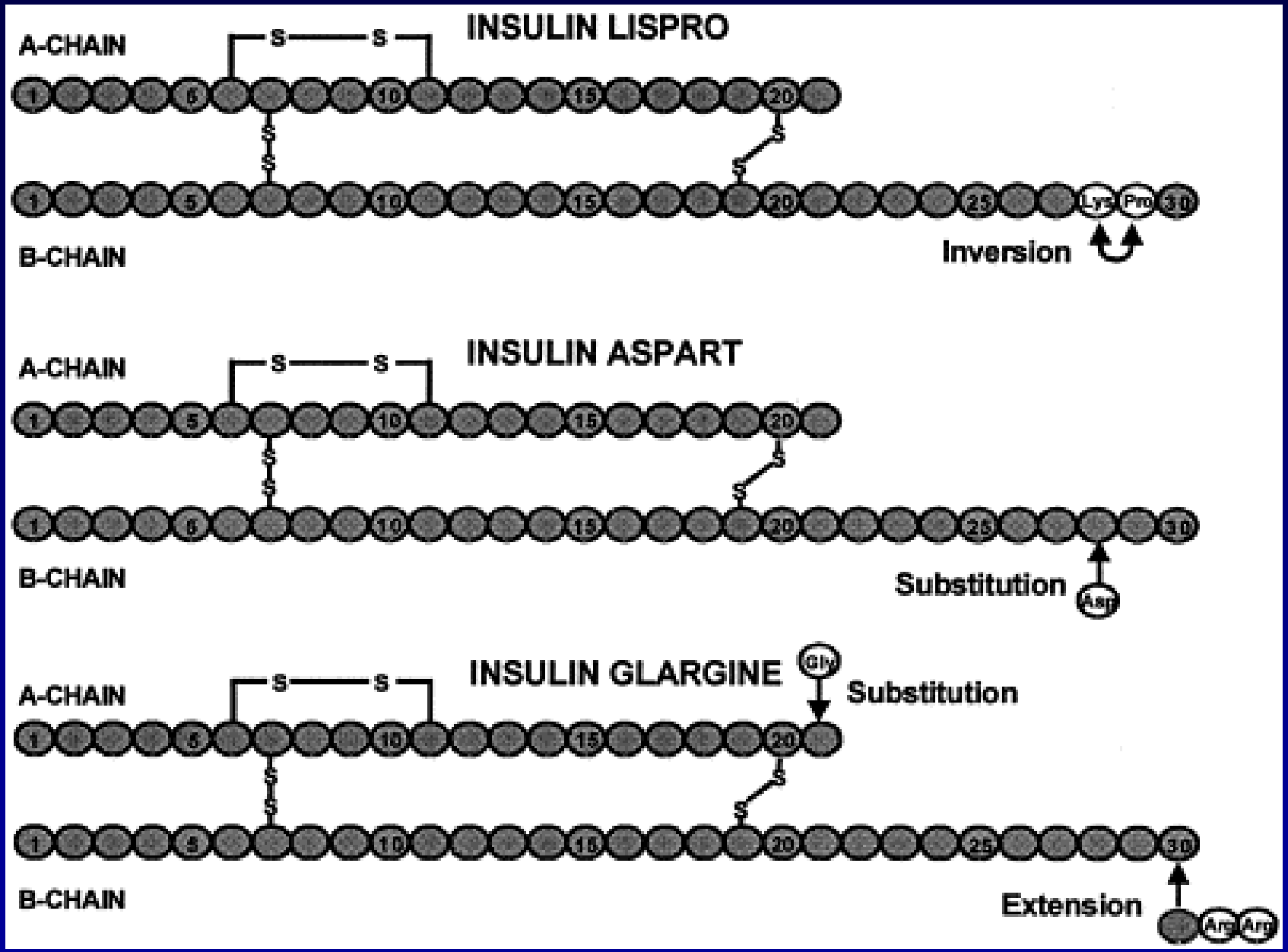
- Mimics physiologic insulin secretion
- Bolus short acting insulin with meals/ snacks/stress
- More frequent injections and glucose testing

# Sources of insulin: modern

- Recombinant DNA technology
  - duplicate the amino acid sequence of human insulin
- New ultra-short acting insulins
  - Lispro
  - Aspart
- New long acting insulin
  - Glargine: not in suspension/slow absorption: very flat and prolonged blood levels

# New insulins

- Short acting
  - Lispro = Humalog
  - Aspart = Novolog
- Long acting
  - Humulin CZI extended = Ultralente
  - Glargine = Lantus
    - Microprecipitate formation in subcutaneous tissue prolongs absorption


INSULIN LISPRO
A-CHAIN
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Pro
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B-CHAIN
Inversion
INSULIN ASPART
A-CHAIN
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B-CHAIN
Substitution
Asp
INSULIN GLARGINE
Gly
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S
1
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15
20
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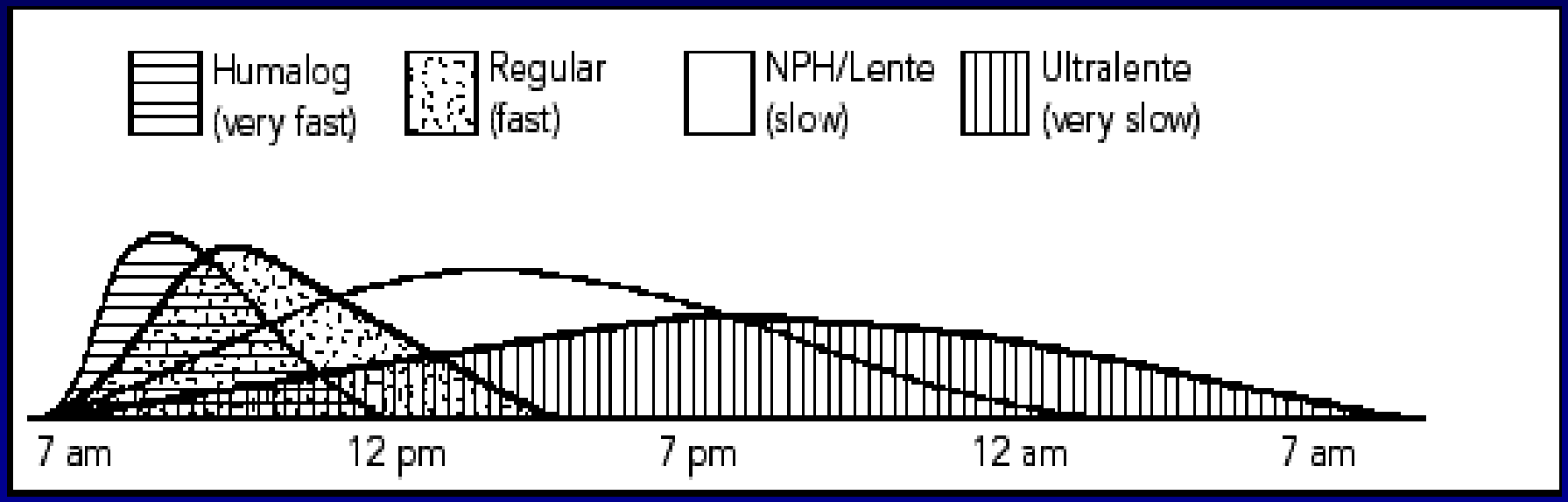
10
15
20
25
30
B-CHAIN
Extension
Arg
Arg

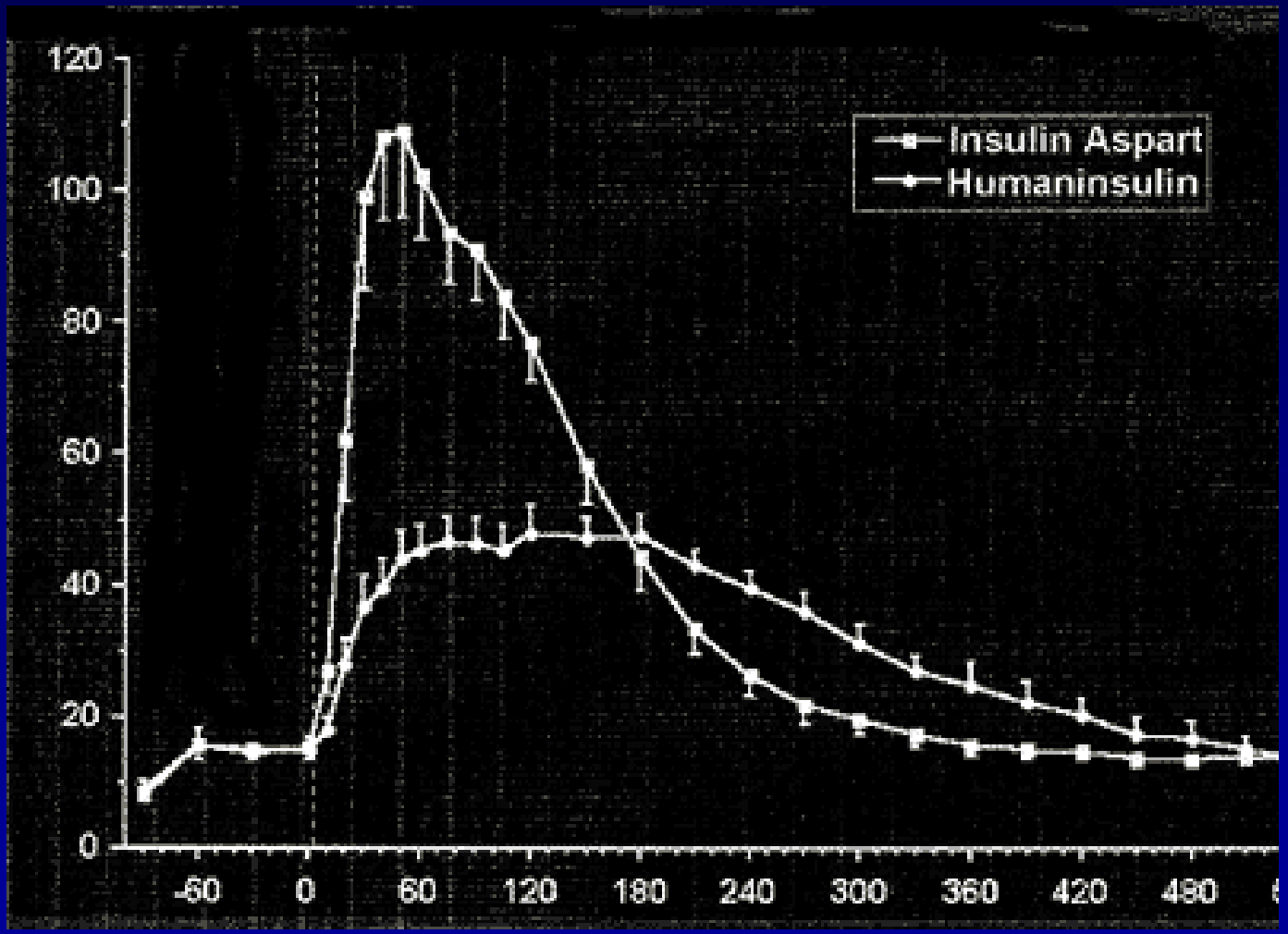
# Type 1 Diabetes Mellitus
## Insulin Therapy

| Type | Onset | Peak (hr) | Duration (hr) |
|---|---|---|---|
| Lispro / Novolog | 10 m | 1 | 3 |
| Regular | 30 m | 2-3 | 6 |
| NPH | 1-2 h | 5-6 | 8-12 |
| Lente | 1-2 h | 5-6 | 8-12 |
| Ultralente | 3-4 h | 12 | 12-24 |
| Lantus | 1-2 h | -- | 24 |

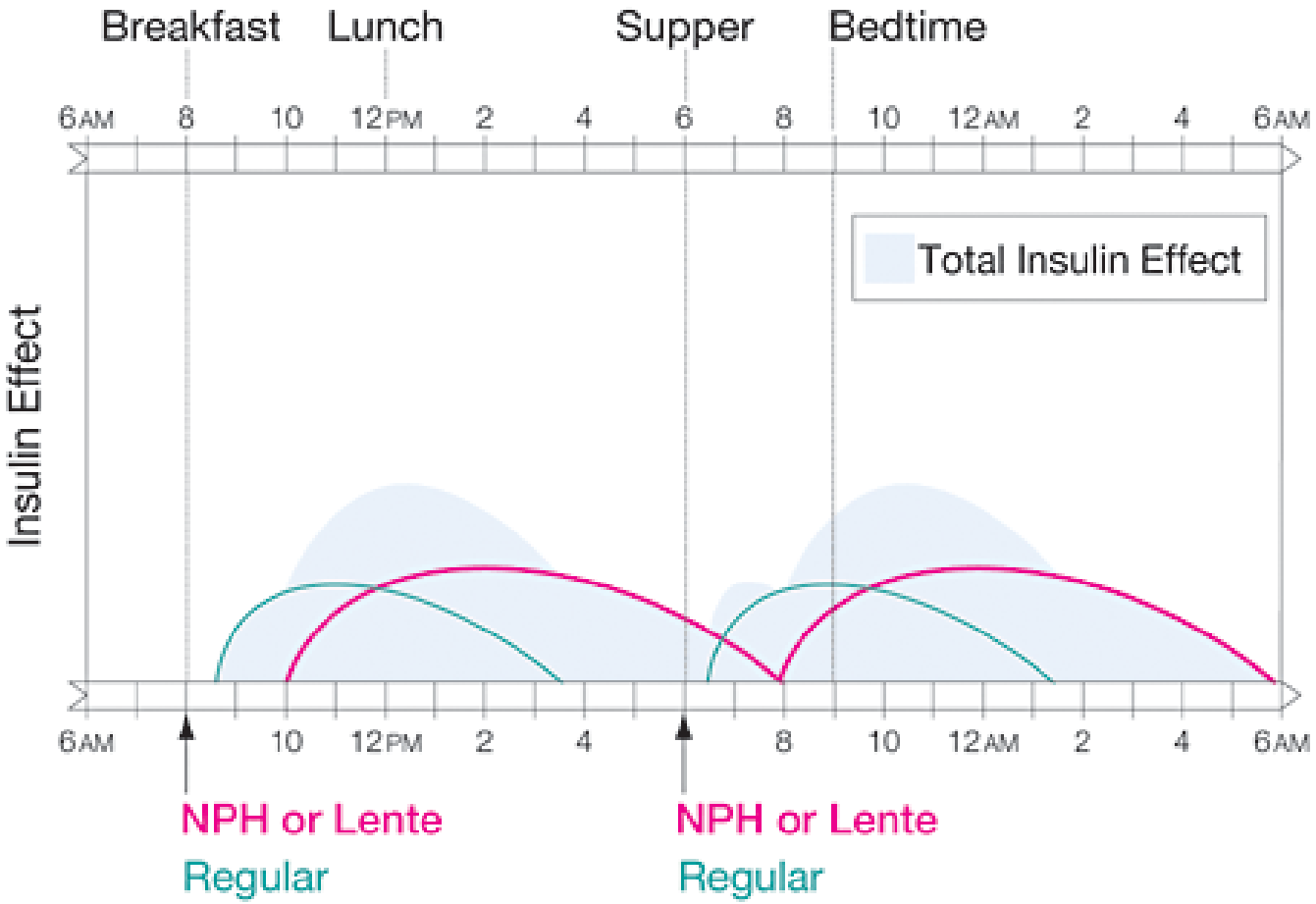
# Kinetics of old and new insulins



# Regular vs Aspart



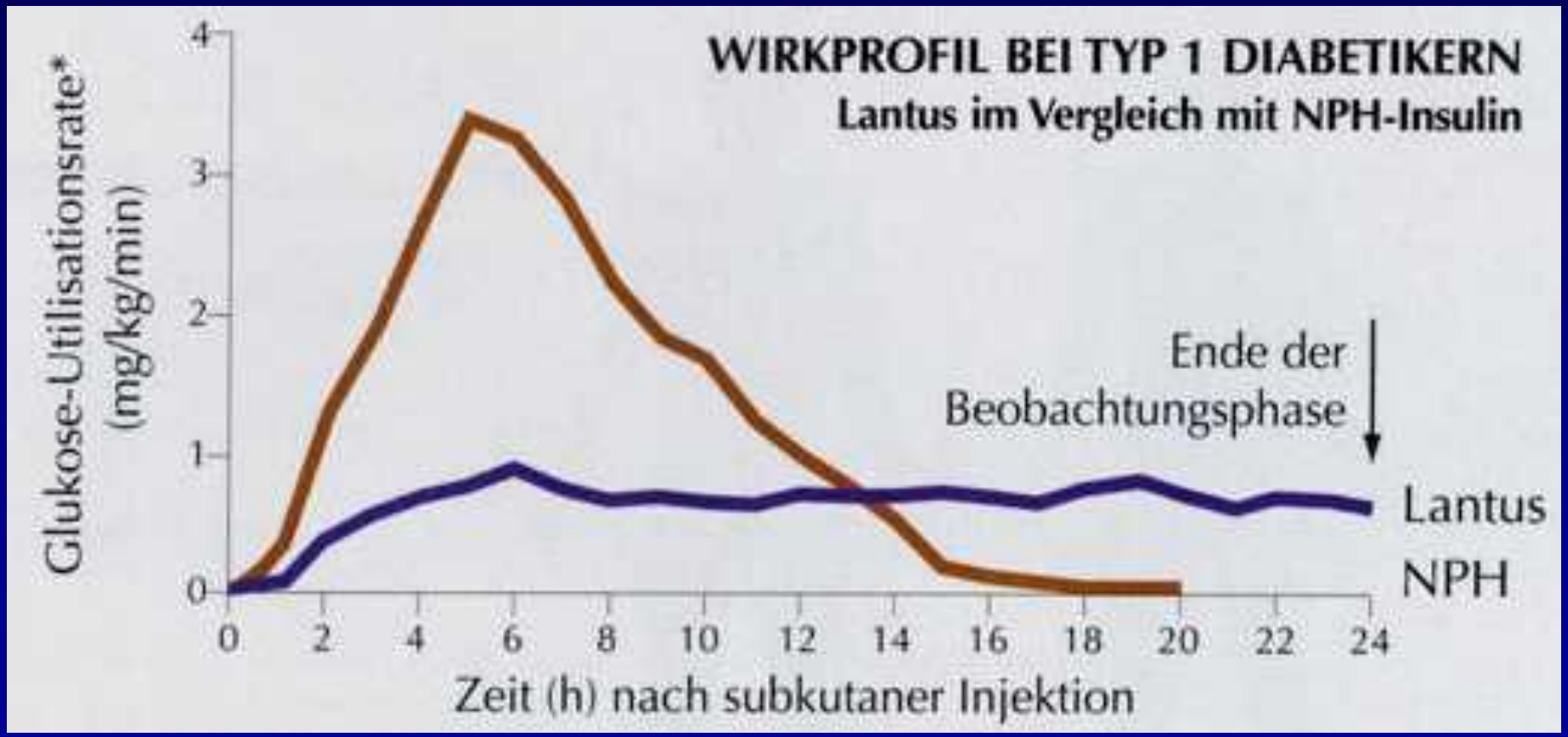
# Conventional diabetic management



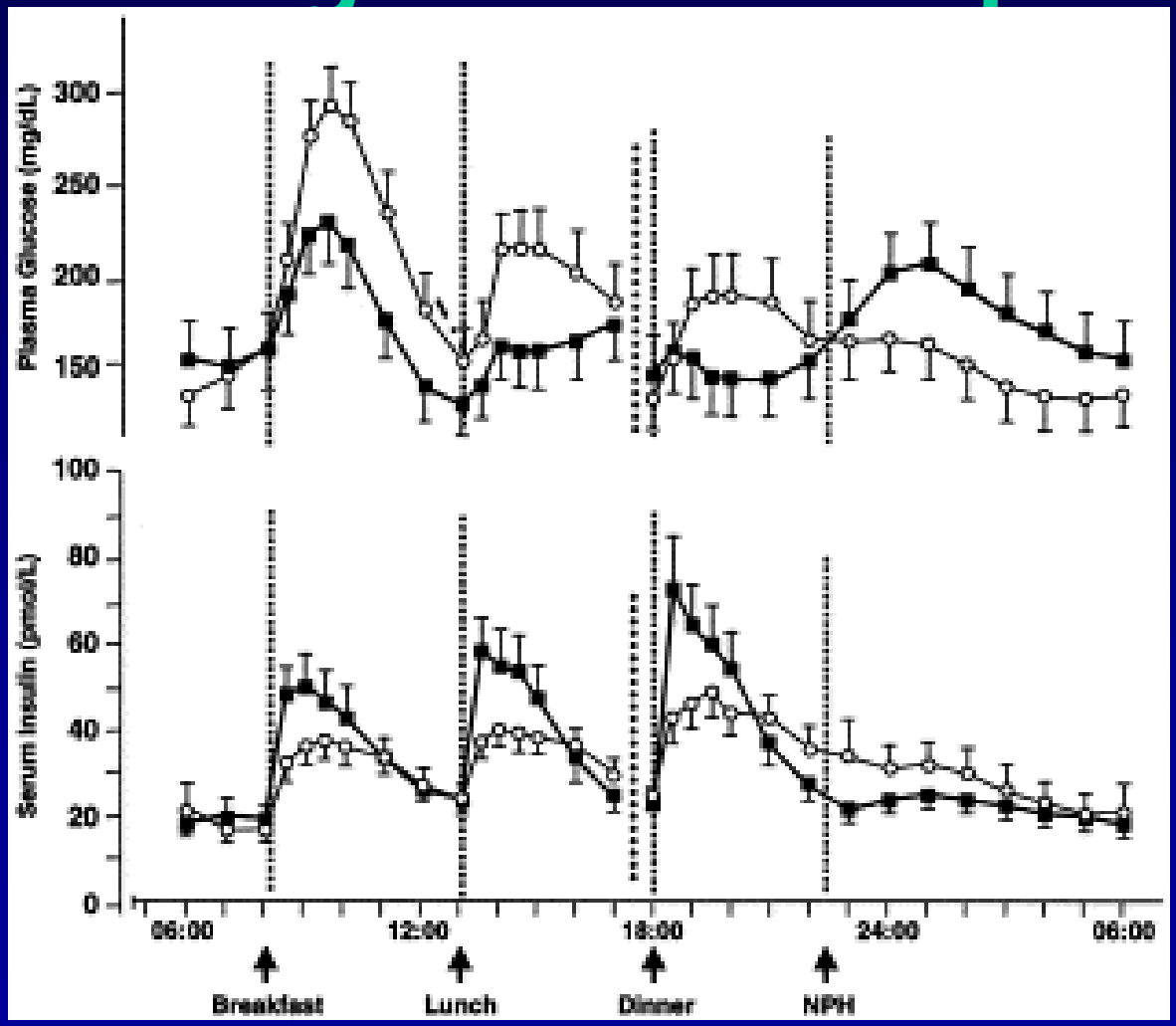
# New insulins provide more physiologic pattern

- Slow release low basal level insulin parallels basal pump infusion
  - Insulin glargine
- Ultra short acting insulin with meals/snacks parallels glucose load
  - Insulins aspart and lispro

# Lantus (glargine): peakless "basal" insulin



# Glucose/insulin: standard management vs lispro



# Glucometer

# First insulin pump

# New pump technology


h
m
prime
reset
clock
basal
S
data
units
bolus
temp
H-TRONplus
DISETRONIC

# Insulin pump use is growing

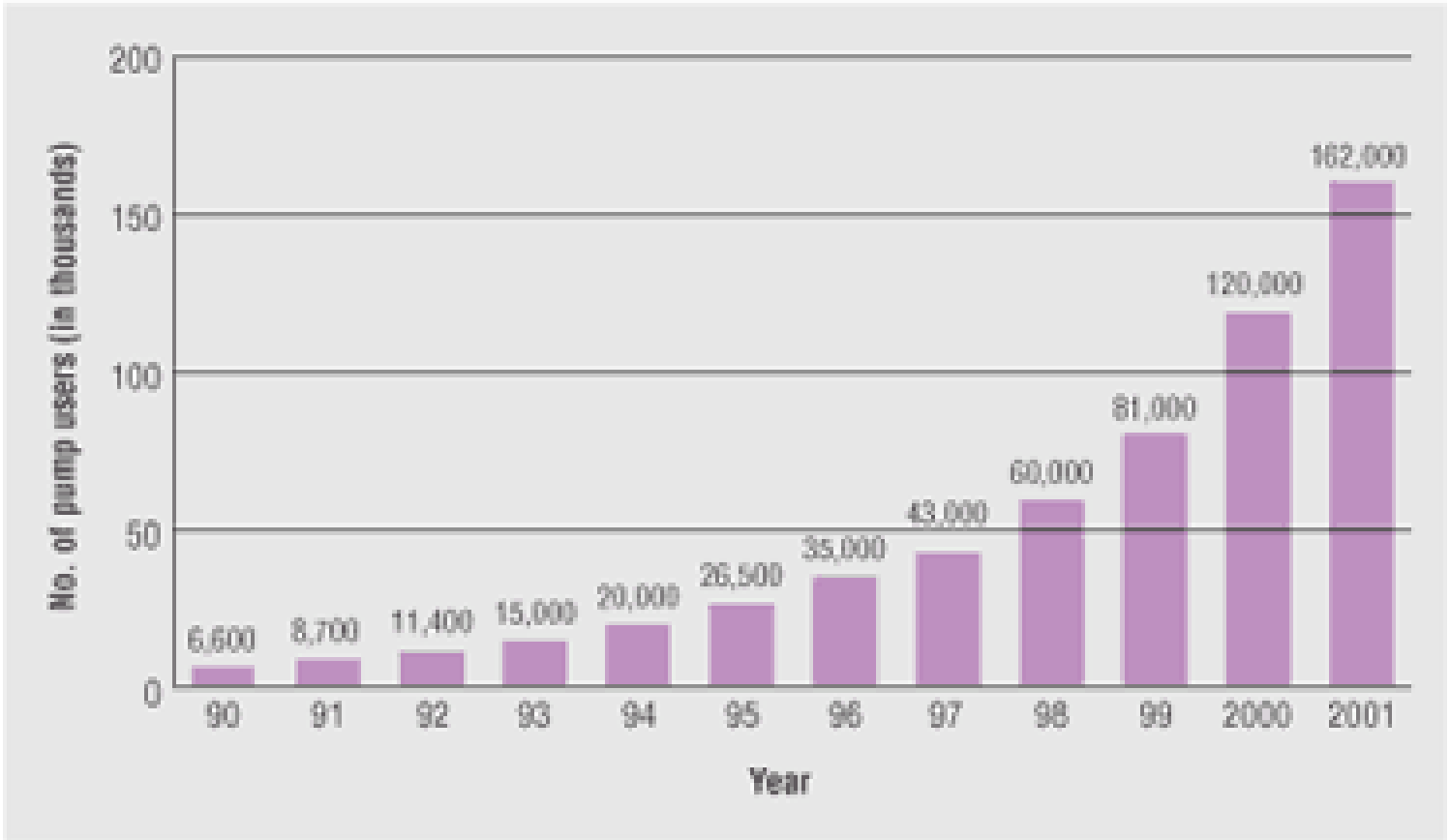
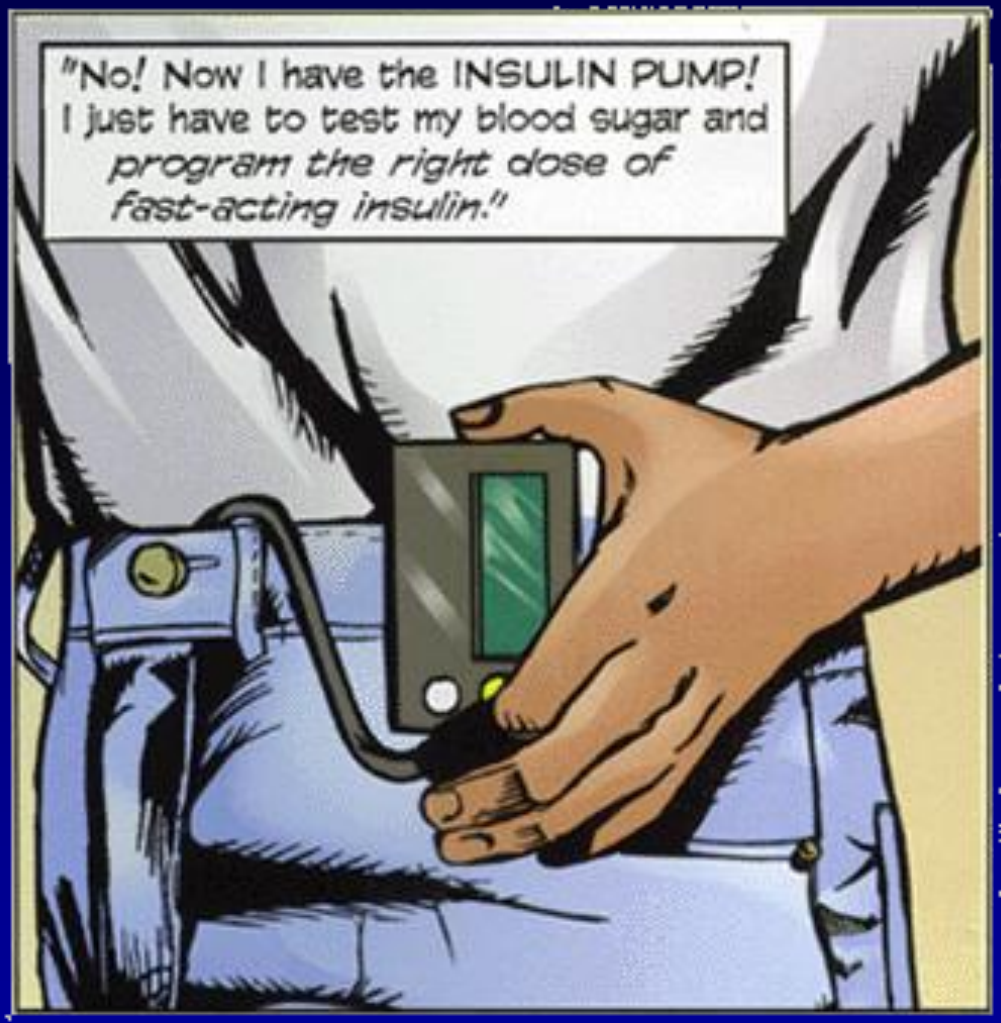
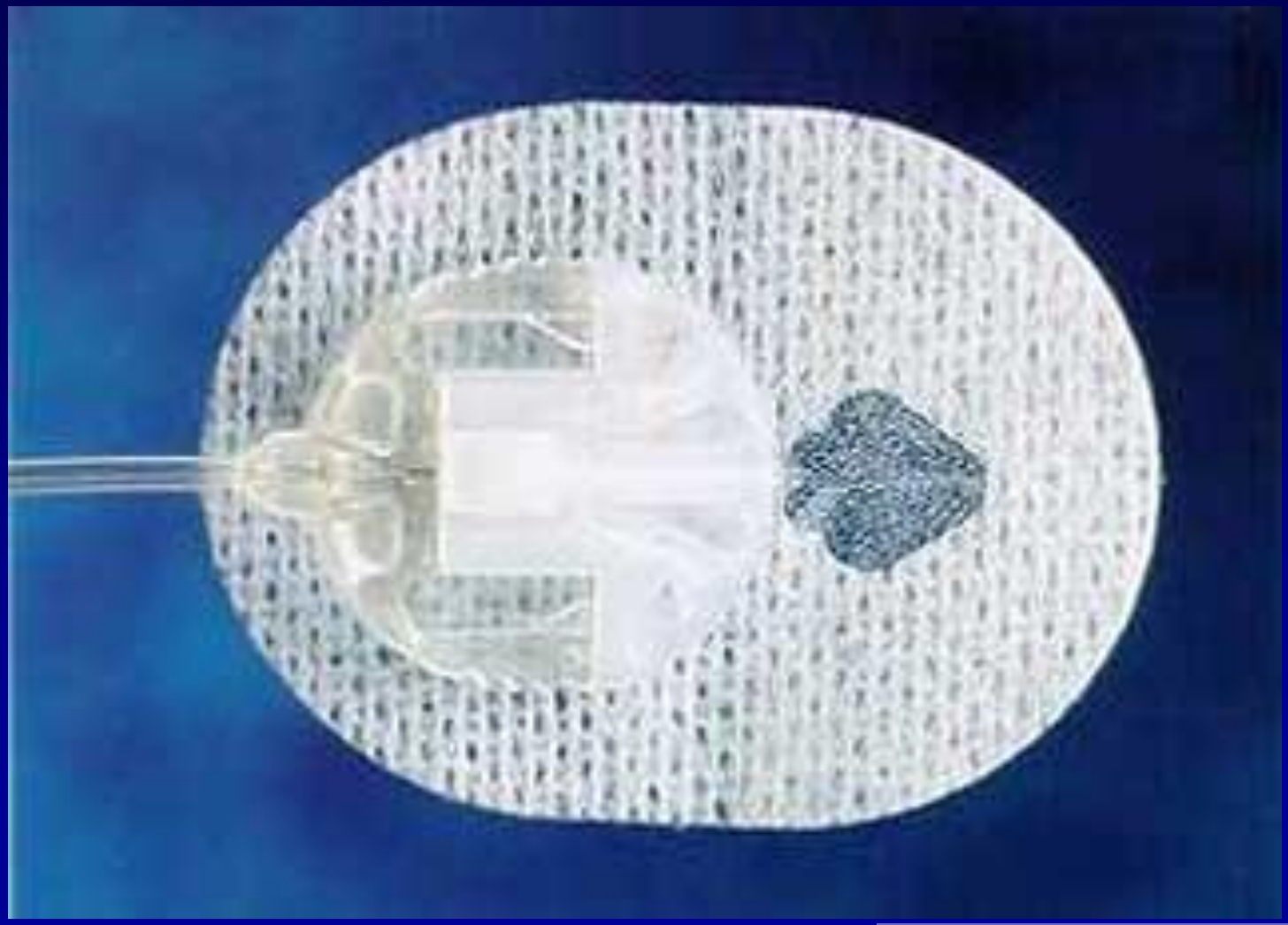



Figure 2. Number of patients using continuous subcutaneous insulin infusion pumps in United States by year. Total for 2001 is estimate.

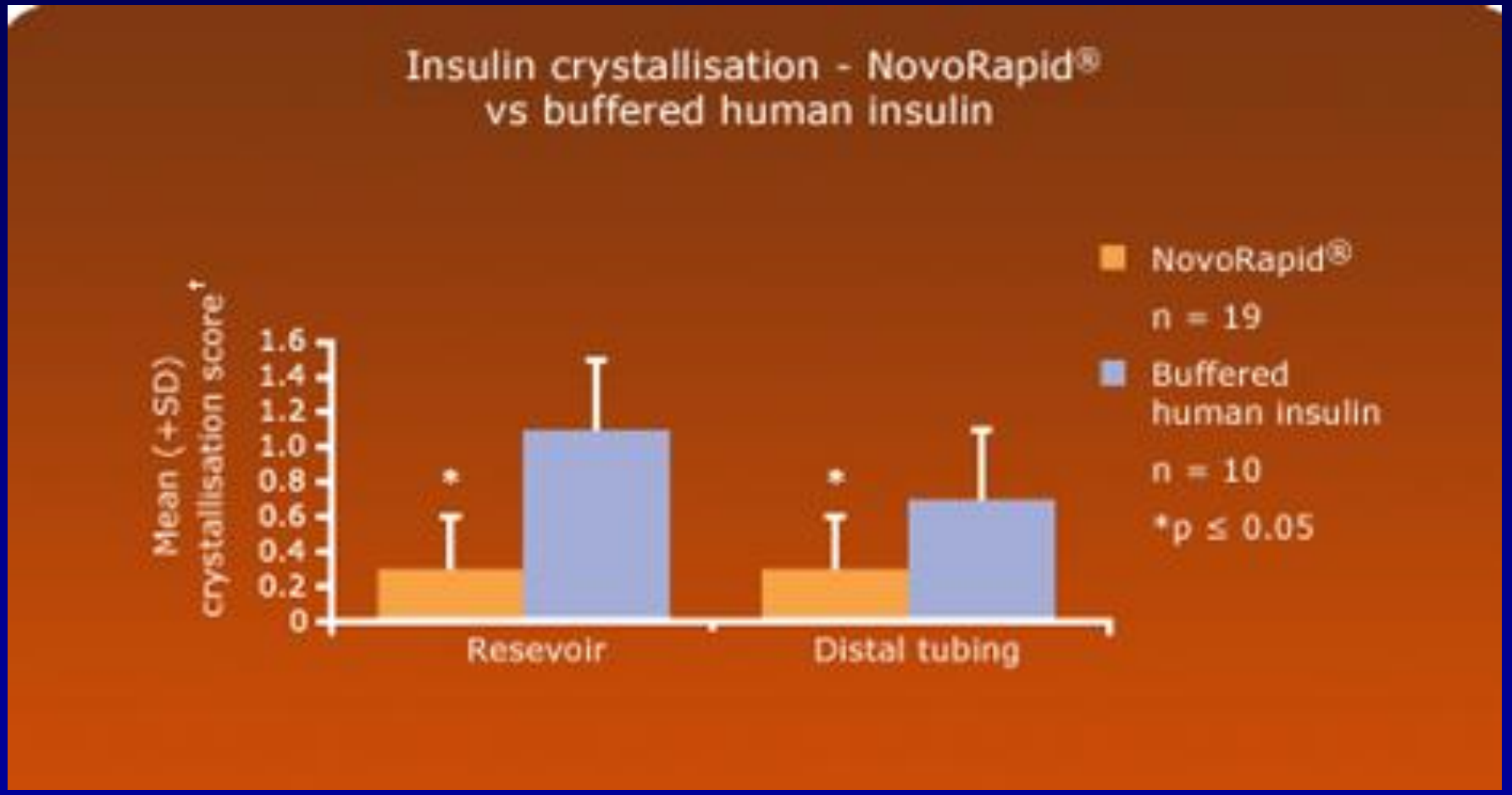

"No! Now I have the INSULIN PUMP! I just have to test my blood sugar and program the right dose of fast-acting insulin."


Detroit
21




ERROR CODES
ID 420.0323/V03/03.01
01 Empty Cartridge
02 Low Motor Battery (2)
03 Low Electronic Battery (3)
04 Occlusion
05 Bolus Limit Reached
06 Automatic Off
07 System Alarm
8x Technical Inspection Alert
09 Technical Inspection Due
10 Cartridge Low Warning
11 End of Temporary Basal Rate
DISETRONIC
1-800-688-4578
Read instruction manual before using.
Rx only

# Lispro/Aspart have minimal crystallization



# Insulin
# total daily dosage

| | |
|---|---|
| Honeymoon | 0.2-0.5 u/kg/day |
| After Honeymoon | 0.7-1.2 u/kg/day |

## Nutrition Facts

Serving Size 1 Box (25g)

| Amount/serving | |
|---|---|
| **Calories** | 90 |
| Fat Calories | 0 |
| | **%DV*** |
| **Total Fat** 0g | **0%** |
| Saturated Fat 0g | **0%** |
| **Cholesterol** 0mg | **0%** |
| **Sodium** 240mg | **10%** |
| **Total Carb.** 22g | **7%** |
| Fiber 0g | **0%** |
| Sugars 2g | |
| **Protein** 2g | |

| | | | |
|---|---|---|---|
| Vitamin A | 10% | Vitamin C | 15% |
| Calcium | 0% | Iron | 8% |
| Vitamin D | 10% | Thiamin | 25% |
| Riboflavin | 25% | Niacin | 25% |
| Vitamin $B_6$ | 20% | Folic Acid | 25% |
| Vitamin $B_{12}$ | 25% | Phosphorus | 2% |
| Magnesium | 2% | Zinc | 2% |
| Copper | 2% | | |

*Percent Daily Values (DV) are based on a 2,000 calorie diet.

# Carbohydrate Counting

| | |
|---|---|
| Breakfast | 45-60 g |
| AM snack | 15 |
| Lunch | 45-60 |
| PM snack | 15-30 |
| Dinner | 60-75 |
| BT snack | 15-30 |

# Perioperative Management

- Surgery
  - Short or long
  - Ambulatory or inpatient
- Home insulin program
  - Multiple daily injections or pump
  - Total daily dose
  - Insulin correction factor

# Insulin correction factor

- Decrease in glucose which will result from administration of 1 unit of insulin
- Rule of 1500 (regular) or 1800 (lispro)
- 1800/TDD = mg/dL drop in glucose/unit
- Example: TDD = 30 units
- 1800/30 = 60 mg/dL drop per unit lispro
- 1500/30 = 50 mg/dL drop per unit reg

# Preoperatively

- Consult with child's endocrinologist and parent
  - Dosing schedule
  - Tightness of control
  - Incidence of hypoglycemia
  - Dosing high BG (sliding scale)
- Parent will usually bring glucose meter, ketone strips

# Possible management strategies

- Intermittent subcutaneous short acting insulin (lispro or regular)
- Insulin infusion
- Continue patient's insulin pump?

# Continuous infusion vs Subcutaneous Insulin

LA Children's, 1989-1992, retrospective

Group 1: 9 inpatients

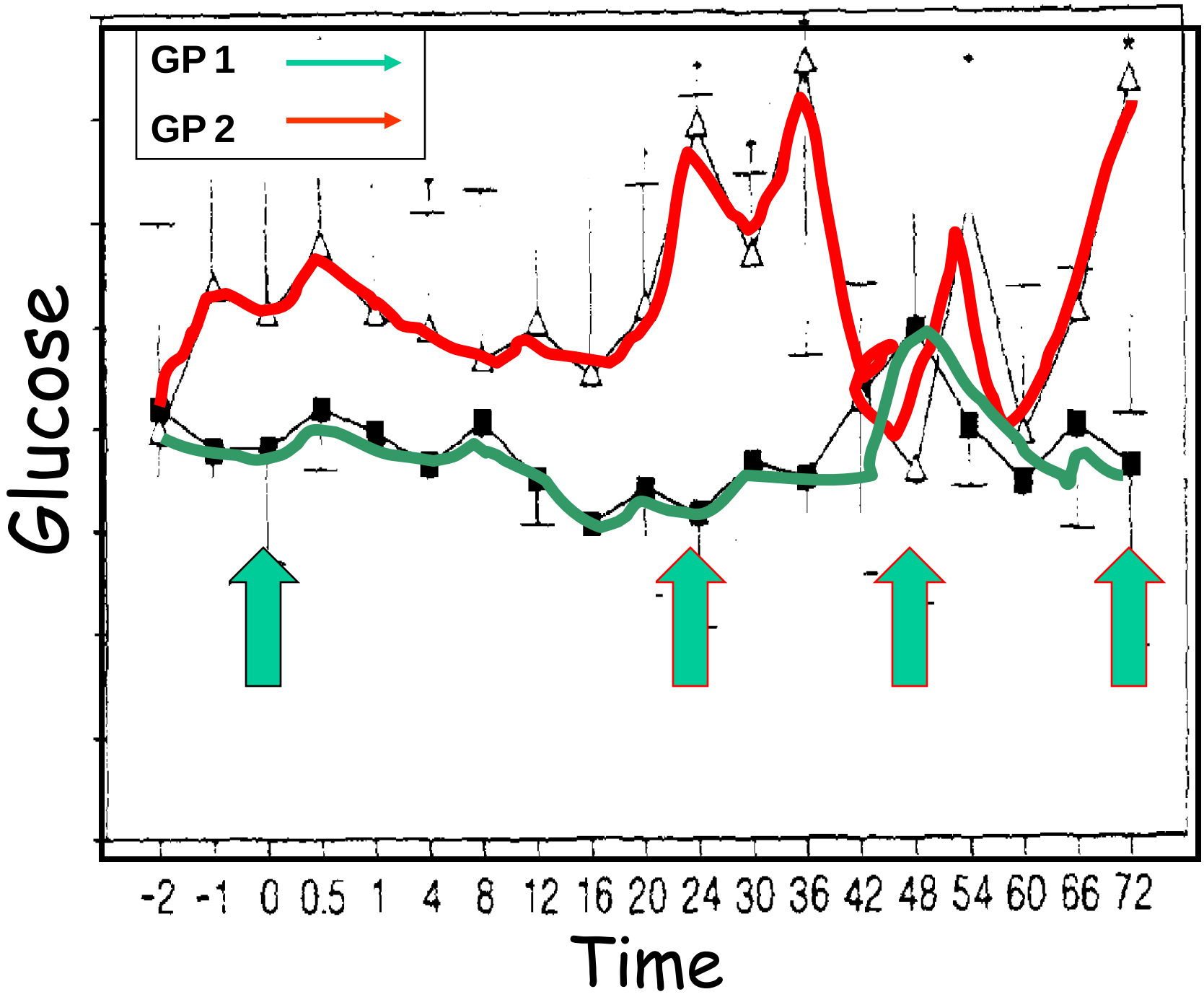
- infusion 0.06-0.1 u/kg/h
- start 2 h pre-surgery
- continue 2-3 days post-op
- BG goal 100-150 mg/dL

Kaufman, J Diab Compl 1996

# Continuous infusion vs Subcutaneous Insulin

Group 2: 10 inpatients

- 66% regular/75% NPH 2h pre-surgery
- insulin sq, 2-4 per day
- continued 2-3 days post-op
- BG goal 100 – 150 mg/dL


GP 1
GP 2
Glucose
-2 -1 0 0.5 1 4 8 12 16 20 24 30 36 42 48 54 60 66 72
Time

# Insulin management strategies

- Ambulatory surgery ≤ 60 min with minimal change in feeding postop
- No insulin infusion required
  - Reduce intermediate insulin (lantus or NPH) the night before by 10%
  - No am insulin at home
  - Check blood sugar and urine ketones on arrival
  - Consider cancellation if BG >300 and mod/large ketones

# Short ambulatory surgery

- If glucose > 250 administer short acting insulin subcu according to patient's correction factor
  - Avoid "stacking" doses
- During surgery administer saline or LR to replace deficit
- Check blood glucose q1 perioperatively
- If BG < 100, 2mL/kg D10 IV if during surgery or NPO
- Resume home insulin regimen when taking po
  - At regular meal time if possible

# Perioperative insulin strategies: ambulatory surgery in pump patients

- Follow normal fasting instructions
- Continue usual basal rates and correction boluses until arrival
- Measure BG on arrival
- If BG > 250 consider using humalog/ novolog per patients correction factor
- Disconnect pump and give to parent(s) on arrival

# Intraoperatively

- Check blood glucose q1 h
- Keep glucose between 100 – 200 mg/dL
- Dip all urine for ketones
  - No urinary catheter if not indicated for other reasons

# Perioperative insulin strategies: ambulatory surgery in pump patients

- Alternatively, may keep pump running at basal rate (many endocrinologist recommend increasing rate by 10% to deal with surgical stress response)
- Administer bolus per pump according to patients pump protocol
- Requires tutorial from parent
- Institutional policies re medical devices

# Caveats with use of pump

- Exposure of pump to heat can denature insulin and render ineffective
- Injection site is changed q 3 days, should be “new” site: old site can have erratic absorption
- No interference/risk with cautery
- Not safe in MRI

# Intraoperatively (ambulatory)

- Pump can be off for 1 hour without increase in BG
- With pump off > 2 hr, hyperglycemia and possible ketones will develop if insulin is not administered
- Check blood glucose q1h perioperatively
- Give subq humalog/novolg q2 h as above
- Aggressive nausea prophylaxis

# Perioperative insulin management: insulin infusion

- Long procedures with indefinite postoperative fasting periods
- If on Lantus, reduce PM dose by 10%
- Hold morning insulin
- Blood glucose on arrival
- Start D10(5) 0.45NS with 10 mEq/L KCl at maintenance
- Start insulin infusion

# Preparation of insulin infusion

- Syringe pump administration preferred
- Less surface area for insulin adsorption
- Concentration 0.02 – 0.5 unit/mL depending on size of patient

# Insulin infusion

| Blood glucose | Insulin infusion |
|---|---|
| Lantus night before | 0.02 U/kg/hr |
| 80 – 200 mg/dL | 0.02 U/kg/hr |
| 200 – 300 mg/dL | 0.03 U/kg/hr |
| 300 – 400 mg/dL | 0.04 U/kg/hr |
| > 400 mg/dL | 0.05 U/kg/hr |

# Insulin infusion

- Check blood glucose q1h during infusion
- Titrate infusion (chg 0.01 U/kg/hr to keep BG 100 – 200 mg/dL)
- Dip all urine for ketones
  - Urinary catheter for urine output/hydration

# Insulin infusion for pump patients

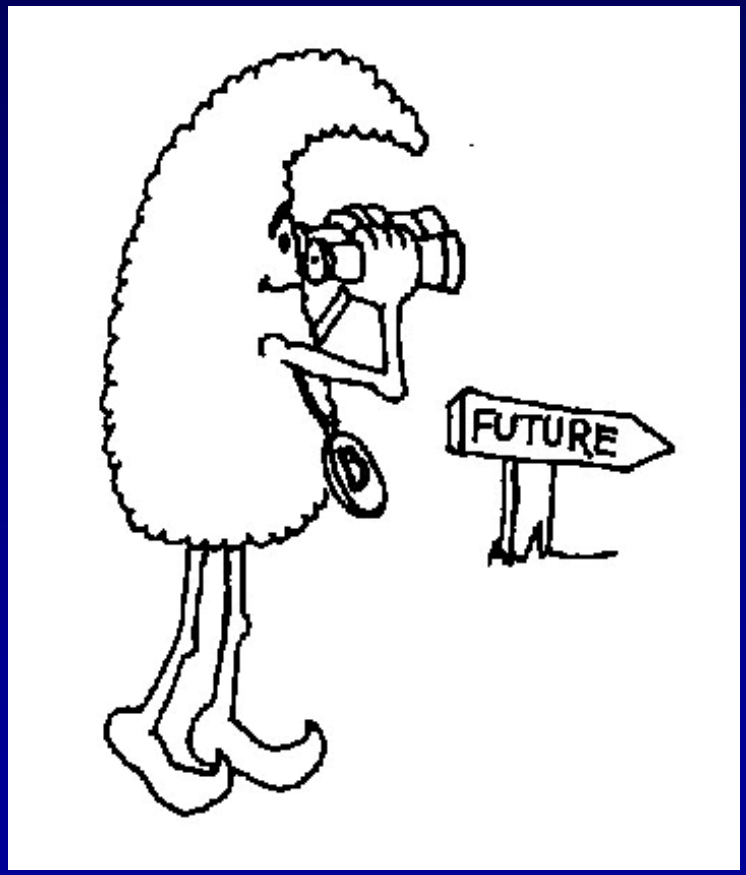
- Follow usual fasting instructions
- Continue usual basal/bolus rates until insulin infusion is started
- BG on arrival
- May treat with humalog/novolog until infusion started
- Infusion and D10/electrolytes as before

# Transition from insulin infusion back to regular treatment, pump

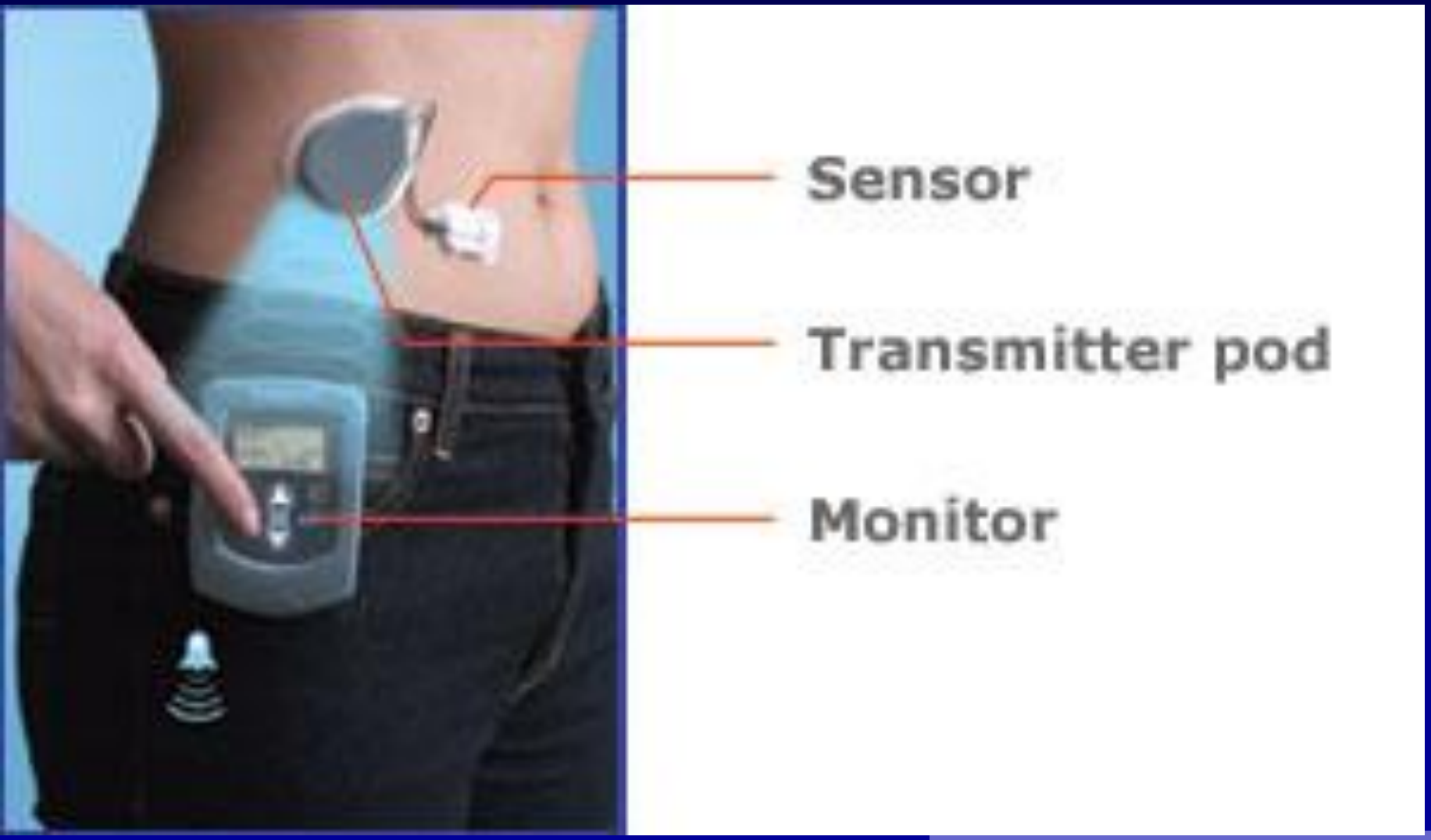
- Transition directly from insulin infusion to pump at usual rates
- May give total daily basal dose as Lantus (lasts 18-24 hr) OR
- Monitor blood glucose q2h for 4 hr
- Monitor before meals/snacks, 2am after first 4h
- Administer humalog for BG > 180 and before meals/snacks
- Resume usual basal pump rate 18-24 h after Lantus

# Postoperatively (ambulatory)

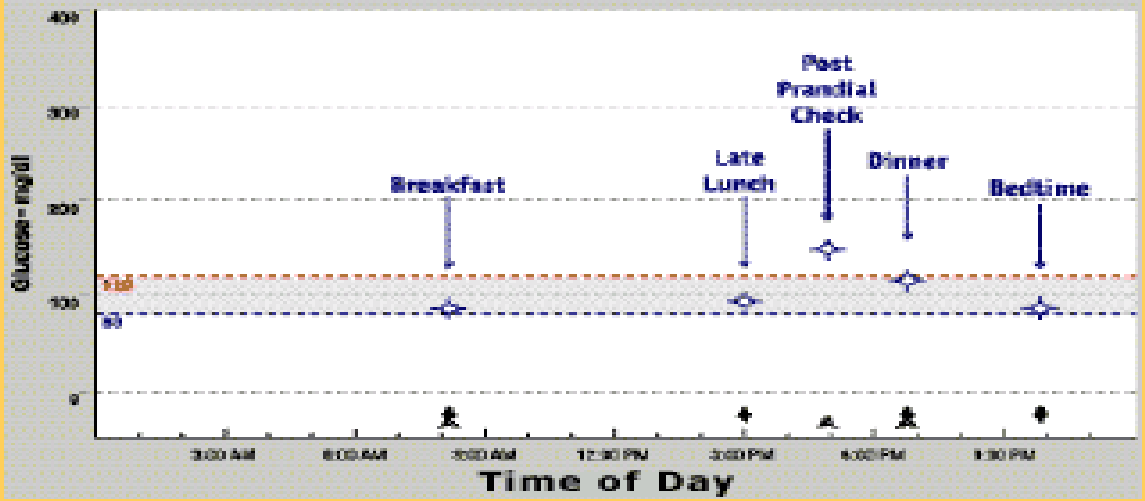
- Resume po intake per protocol
- If BG > 240, give humalog/novolog as above
- Dip all urine for ketones
- Parents may reconnect insulin pump at usual basal rates when ready for discharge


FUTURE

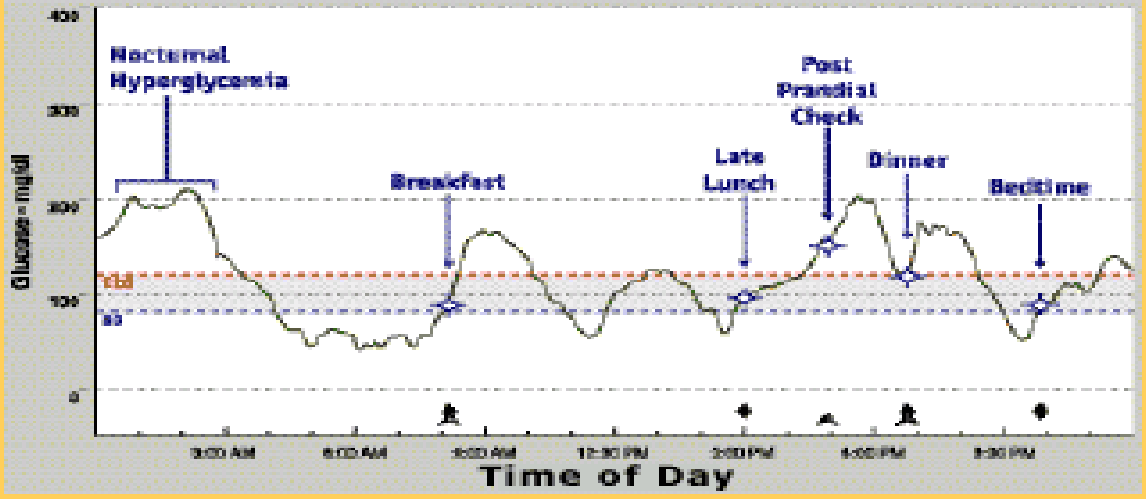

MEM
SET
ACT


Sensor
Transmitter pod
Monitor

## Point in time fingersticks



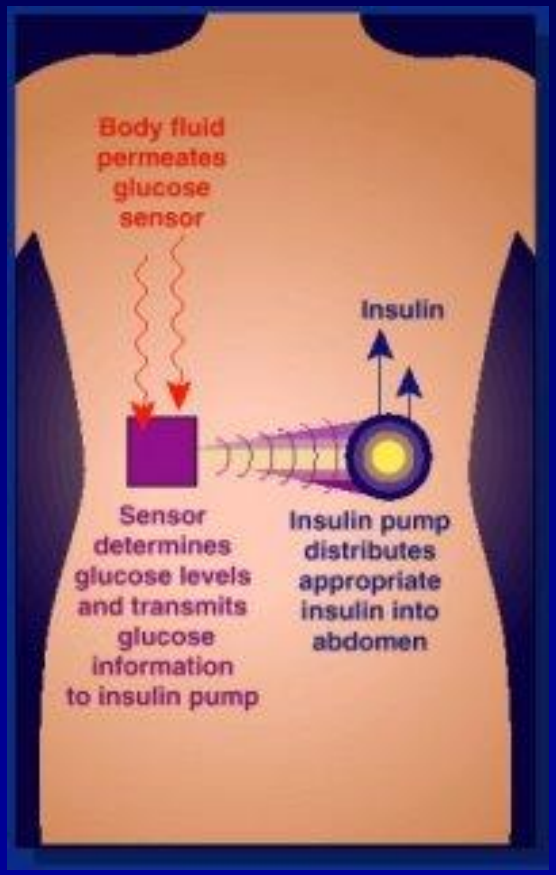

## CGMS System Gold data



- Closed loop continuous blood glucose/insulin infusion apparatus

Cleveland Clinic

# Closed loop system of the future?




- Totally implanted system??

# Some predictions for the future don't come true


SONY
Betamax
L-500

# Insulin Dry Aerosol Inhaler

# Further reading

- Syllabus text: protocols for pump use
- Rhodes et al, Perioperative management of pediatric surgical patients with diabetes mellitus, Anesth Analg 2005

# Summary

- Epidemiology
- Physiology of insulin action and deficiency and surgical stress
- New insulins: pharmacokinetics
- Insulin pumps
- Guidelines for perioperative insulin management

# Thank you for your attention

Questions?