

Evolution of Insulin Pumps & CGMs Toward An Artificial Pancreas



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View slides at www.diabetesnet.com/diabetes-resources/diabetes-presentations

Disclosure

- Book sales – all pump companies
 - Advisory Boards – Tandem Diabetes, Unomedical, Spring, Halozyme
 - Consultant – Bayer, Roche, BD, Abbott, Tandem Diabetes, Medingo, Spring
 - Speakers Bureau – Tandem Diabetes
 - Sub-Investigator – Glaxo Smith Kline, Animus, Sanofi-Aventis, Bayer, Bidel, Dexcom, Novo Nordisk
 - Pump Trainer – Accu-Chek, Animas, Medtronic, Omnipod
 - Web Advertising – Sanofi-Aventis, Sooil, Medtronic, Animas, Accu-Chek, Abbott, etc.
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What We'll Cover

- The Ideal Pump
 - Styling
 - Ease of Use
 - Safety
 - Glucose Outcomes & Clinical Oversight
 - Bolus Calculator
 - Pumps
 - Line and Patch Pumps Compared
 - Pressure and Wax Delivery Mechanisms
 - Closed Loop Components
-

The Ideal Pump

Components

- Accurate/precise dosing
 - Safer infusion sets
 - Smart phone control and connectivity
 - Fewer moving parts, Zero-step downloading
 - Clinical history accessible on device
-

The Ideal Pump Styling



- I-Phone, a la Steve Jobs
 - Color hi-res touch screen
 - Rounded corners
 - Individualized colors & cases
-

The Ideal Pump

Ease Of Use For Safety



- From 2007 through 2009, 17,000 of 375,000 people on pumps reported pump problems
 - 225 of 310 deaths unexplained, some due to programming errors
 - Failsafe pump operation is now a primary FDA focus
 - A recent pump FDA submission required 85,000 pages of user-interaction data
-

The Ideal Pump

Ease Of Use

- * ■ Foolproof operation to dose, load, prime, remotely operate, and download
- * ■ When interrupted, pump returns to same screen
 - Warning alert for any delay during major process, like giving a bolus, loading, or programming
- * ■ Organized – all basal and bolus settings on the same screen, helpful information clearly laid out
- * ■ Intuitive – minimal training required

* Underway

The Ideal Pump

Safety

- No device deaths, rare hospitalizations
- No infusion set failures, rare occlusions
- Precise dosing, no hidden insulin stacking, no over-delivery on airplane flights (1.0 to 1.4 u) ¹
- Monitor for hardware, software, & consistent dose errors
- Leak detection
- No easy to remove reservoirs (overdose risk)

Eliminate all unneeded sources for dose errors!

¹ BR King, et al: Diabetes Care September 2011 vol. 34 no. 9 1932-1933

The Ideal Pump

Safety – Pressure-MicroPulse Pump



Tandem t:slim

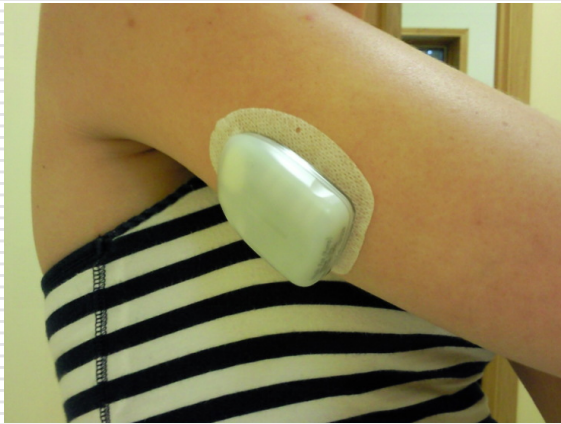
I-Phone style, color hi-res touch screen, easy to use

Thin 300 u reservoir

- Small solenoid generates pressure – isolated micro-delivery chamber delivers 0.001 to 0.03u per pulse
- All settings on one page
- No airplane/gravity problems
- Faster trumpet curve
- Clinical verification needed

Submitted for FDA and CE approval

The Ideal Pump Safe Infusion



Avg. BG for 396 pumps in 6 hr period before a set change was **200.8** compared to **170.8** mg/dl for same period 24 hrs later. ¹
(With over 6,400 BGs in each 6 hr time slot.)

Higher profile pods have higher risk of being knocked off, especially on active kids or teens, when an adult is toting a child, etc.



Low profile metal sets are safest for infants, children, & pregnancy with adhesive over site & line anchored with tape.

No loose, leaky, detached, occluded sets

¹ Unpublished data from Actual Pump Practices Study by Walsh, Roberts, Bailey

The Ideal Pump

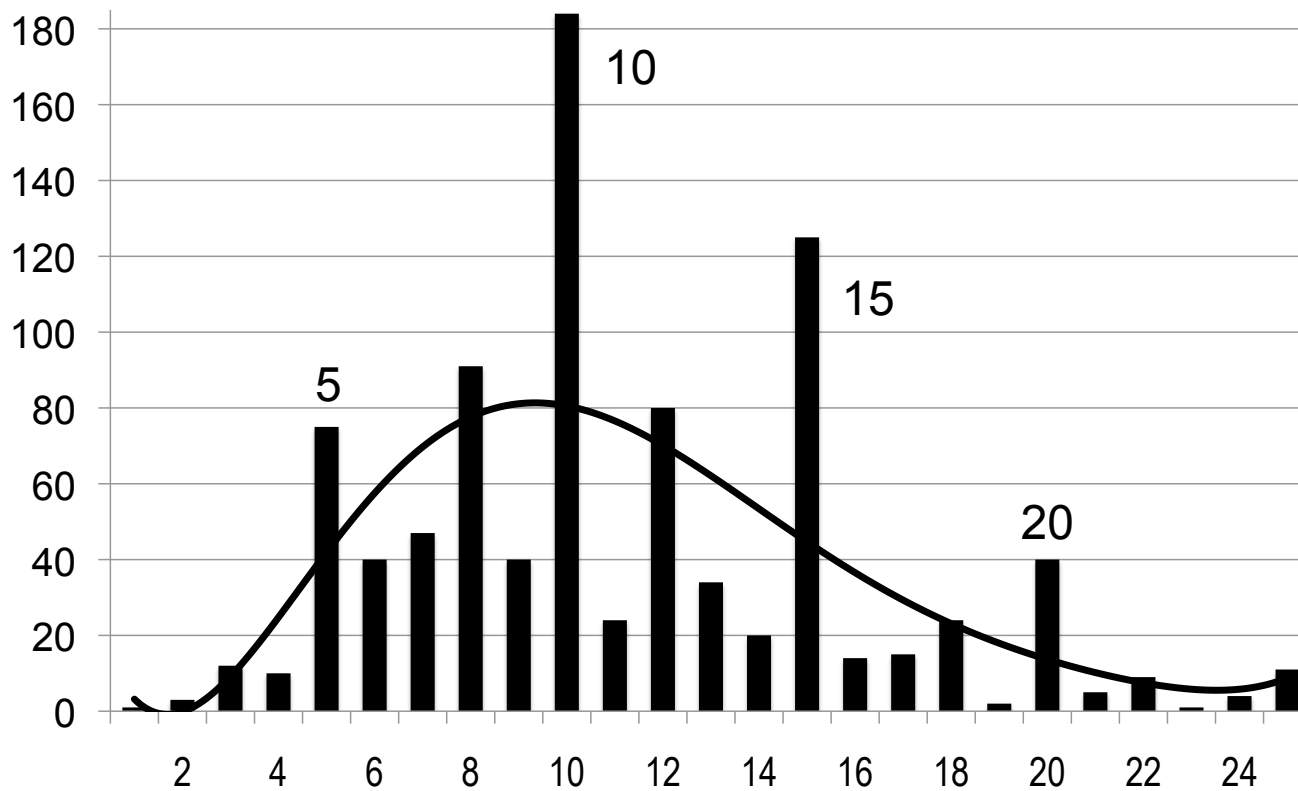
Show Glucose Outcomes

- Monitor basal and bolus errors → “What you’re doing is not working!”
 - Avg TDD vs Avg BG – the major BG controller
 - Estimate of impact on BG when a setting is changed
 - Basal/Carb Bolus Balance, Corr. bolus % of TDD
 - Avg BG, SD, number of tests
 - Frequency/time <50, <65, >140, >200, >300
-

The Ideal Pump

Use Formulas For Accurate Settings

9.1 Carb Factor Settings Found In 899 Pumps



APP Study:

CarbF settings found in 899 pumps during software upgrade in 2007

Note use of easy numbers for easy math: 5, 10, 15, 20

J Walsh, R Roberts, T Bailey:
J Diabetes Sci Technol, 4:
1174-1181, 2010

Settings do not match true need → **Use formulas for pump settings**

The Ideal Pump

Clinical Oversight

Make clinical information easily accessible in pump:

- An infusion set monitor P D
- Is the bolus calculator being used? P D
- Boluses per day P D
- Frequency and direction of bolus overrides P D
- Does carb intake per day match weight? P D
- Length of pump suspensions and stops P D
- Frequency of occlusions P D

P = device (pump, controller, smart phone) D = software download

The Ideal Pump

Bolus Calculator

- Standardized handling of bolus insulin on board (BOB) for maximum safety against insulin stacking

$$\mathbf{Bolus = Carb\ bolus + Corr\ bolus - BOB}$$

- BOB shown on home screen and each bolus screen
 - Realistic DIA times to minimize insulin stacking
 - Single correction target to ensure accurate correction boluses
-

The Ideal Pump

Standardized Handling Of BOB

Pump Bolus Recommendations Vary				
Glucose	Pump A	Pump B	Pump C	True Bolus Need
119 mg/dl	6u (+ 6u)	0u (0u)	6u (+ 6u)	0u
121 mg/dl	6u (+ 6u)	6u (+ 6u)	6u (+ 6u)	0u
240 mg/dl	10u (+ 6u)	6u (+ 2u)	6u (+ 2u)	4u
300 mg/dl	12u (+ 6u)	6u (0u)	6u (0u)	6u *

CarbF = 10 g, CorrF = 30 mg/dl, and correction target = 120 mg/dl. Two hours after dinner for 4 nights in a row, Joe eats a 60 gram dessert when he still has 6 units of BOB left from a 12 unit carb bolus he gave for his dinner meal. His glucoses on these four consecutive evenings were 119, 121, 240, and 300. On the first two evenings he played racquetball for 90 minutes after dinner before he ate his dessert and on the third he did not.

The Ideal Pump

A Short DIA = Hidden Insulin Stacking

After a 10 unit bolus, the estimated residual bolus activity at 3 hours is shown for each of these DIAs

	Estimated Bolus On Board For This DIA:			
For DIA setting =	3 hr	4.5 hr	5.0 hr	5.5 hr
Estimated BOB =	0 u	2.5 u	3.4 u	4.0 u

The Ideal Pump

Future Pump Features

- Show How A Setting Change Will Impact TDD & BG
- Temp Basal + Bolus Doses
- Super Bolus
- * ■ Meal Size Boluses
- Excess BOB Alert (bolusing without BG but ++BOB)
- * ■ Low BG Predictor Using Meter (HypoManager)
- * ■ Exercise Compensator
- Infusion Set Monitor – Leak Detector
- Automated Bolus and Basal Testing

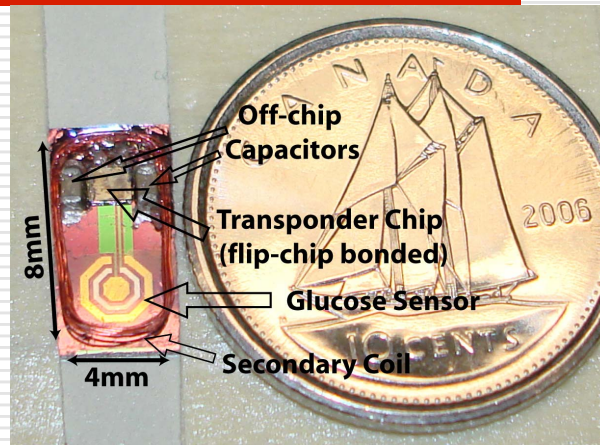
* Underway

The Ideal Pump

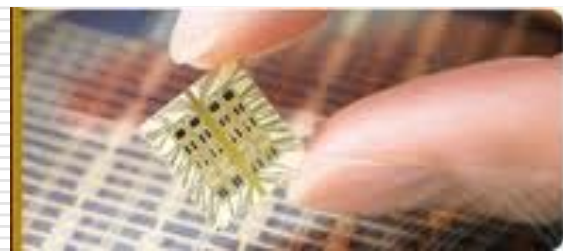
Closed Loop Pump/CGM

- Dual chamber pump – insulin and glucagon
 - Implanted, accurate, long-lasting CGM
 - External pump – fast insulin or Diaport
 - CGM with no lag time, at least +/- 15% accuracy, and less frequent but direct-from-meter calibration
 - Dual CGM sensors to reduce sensor error
 - Manual premeal bolus assist with auto-correction
-

Long-Lasting Implanted CGMs



- Few disposables
- Minor surgery
- Funded as rental



MicroCHIPS Illume



GlySens

CGM – Raman Spectroscopy



- First non-invasive monitor that may have reasonable accuracy
 - No calibration – set at factory
 - No consumables
 - Needs more battery power: 2 rechargeable external batteries
 - Continuous or intermittent use
-

CGM – Implanted Fluorescent



Molecules fluoresce & change color as glucose rises or falls

- Small size, low power, low cost, long life, great accuracy
- Dual fluorescent chambers for low and high BGs

From Y. J. Heo et al: Institute of Industrial Science at the University of Tokyo

Closed Loop Pathway

- * ■ Basal shutoff when low – current Veo pump
- * ■ Reduce basal for predicted low – 30 min lead
 - Reduce basal for predicted low and for BOB
- * ■ Manual partial bolus (or Afrezza) with auto correction
- * ■ Treat-to-a-Range – stop major lows and highs
- * ■ Full overnight closed loop
- * ■ Full 24 hr closed loop

* Underway

Early Closed Loops



Medtronic Veo

- 3 day sensor
- Low glucose suspend – basal off 2 hrs, on 1 hr, off 2



Animas Vibe

- 7-day Dexcom G4 sensor
- Closed loop studies underway with JDRF, Dexcom, BD, Afrezza

Vevo CE approved in Europe since 2009

Patch Versus Line Pumps

Line Pump

- Small infusion set size
= more site options
- Easy to detach for
showering, sports
- Variety of needle and
tubing lengths
- Infusion set can loosen,
leak, be knocked off

Patch Pump

- Worn on body
 - No external tubing in
some
 - Some require
controller to bolus
 - Patch can loosen,
leak, be knocked off
-

New Line Pumps



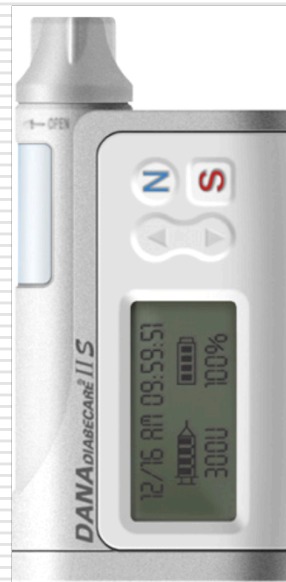
Tandem t:slim



CellNOVO



Asante Pearl



Dana Diabecare II-SG



D-Medical Spring

Pumps – Asante Pearl

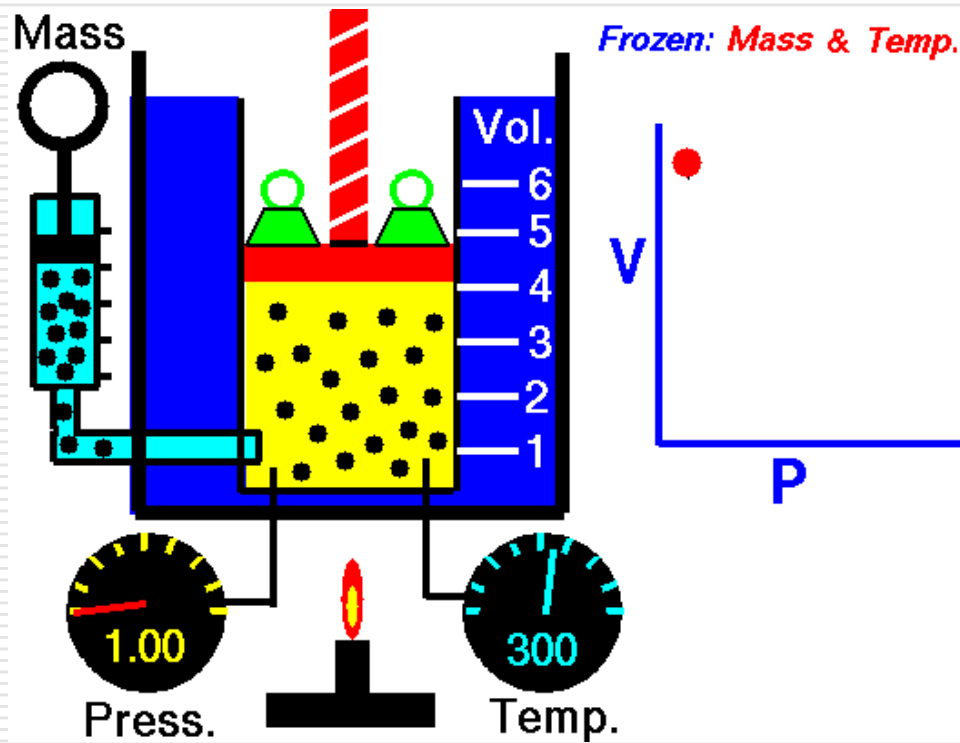


- Uses a prefilled pen cartridge
- Modular design
- 3.88" x 1.72" x 0.75"
- Luer lock infusion sets
- Alarms gradually get louder
- Built-in flashlight
- Pay as you go pricing

FDA and CE approved

The Ideal Pump

New Pressure Pumps



- Precise delivery – up to 1000ths of a unit
- Simpler “motor”, no gears, no stiction
- Less weight
- Thin 300 u reservoir
- No dose change from gravity or on airplanes
- Better trumpet curve

Boyle's Law: $pV = k$ or $\Delta V = k / \Delta p$

Pressure Pump – D-Medical Spring



- One moving part – a spring generates pressure for 300 unit reservoir – no motor, no gears
- Reusable hardware & screen
- Simple, low cost
- Small, very light
- Old school styling

Submitted for FDA and CE approval

Wax Motor – CellNovo Pump



- Small wax cube is heated to pump 0.05 u volumes of insulin
 - 10 u bolus = 200 pulse cycles – Slow boluses?
 - Performance in heat/cold?



- Data sent to internet or phone
- Connects to short infusion set
- 2 rechargeable pumps

CE approved in Europe

Remote Controls For Line/Patch Pumps



- Allows line pump to stay hidden
- BG meter and CGM readout
- Gives boluses
- Phone access
- Maintains dosing history



Some remotes must be present to bolus

Line Blurs Between Patch & Line Pumps

- Small line pumps can attach to skin like a patch
 - Remote lets line pumps hide
 - Patch pumps vary:
 - Autoinserted infusion set
 - Infusion set within a separate base
 - Infusion line to nearby infusion set
-

New Patch Pumps



Valeritas V-Go



Omnipod



Calibra



Roche/Medingo Solo



Debiotech Jewel

Also: Medtronic, Medsolve, Altea

Patch Pump – Roche Medingo Solo



- Precise dispensing screw
- Manual auto-inserter
- 200 units, 1 oz
- Bolus button on pump
- Color screen control
- Accurate bolus calculations



Submitted for CE approval

Patch Pump – Debiotech JewelPump



- Tiny micro-electro-mechanical (MEMs) silicon motor
- Nanotechnology motor can be mass produced
- Modular, light, 0.02 u delivery
- Current 400 u insulin bladder makes it large
- Cost ?

Submitted for CE approval

Patch Pump – Valeritas V-Go

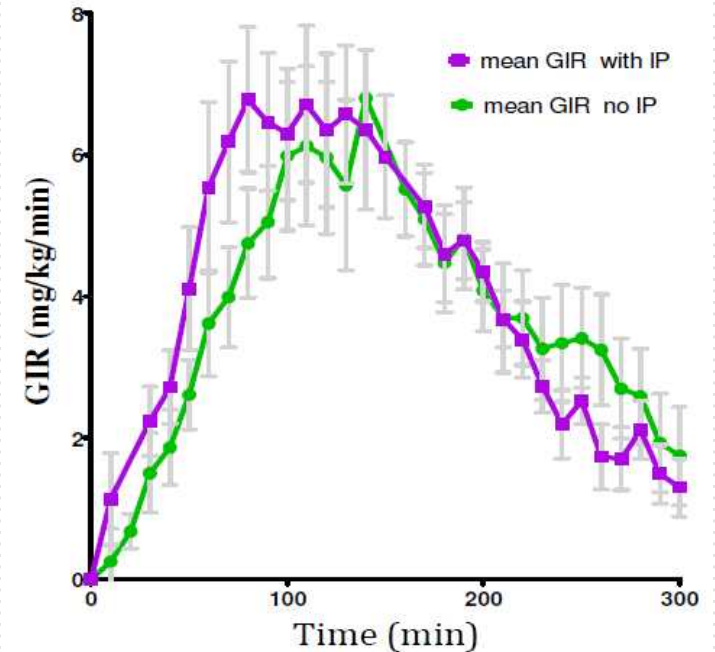


- Simple design for Type 2 & some Type 1 diabetes
- 1 u bolus button on pump
- No controller
- Preset basal rates
- No bolus calculator or BOB tracking

FDA approved

Ways To Speed Insulin Up

- Warm the infusion site
 - InsuPatch by InsuLine
- Faster insulins
 - Novo Nordisk
 - Bodel
- Speed up insulin absorption
 - Halozyme
- 1.5 mm intradermal microneedles
 - BD



Doggie Devices



Oh no !!!!

- 175,000 dogs in the U.S. have insulin-requiring Type 1 diabetes
 - Opportunity to develop inexpensive technologies, especially CGM
 - Later transfer to humans?
-