

Glycemic Control

Insulin In The Hospital Setting

Glycemic Control

- The Evidence For Insulin's Benefit
- The Mechanism of Insulin's Benefit
- The Achievement of Insulin's Benefit
- A Few Cases...

Glycemic Control In The Hospital

Major Prospective Studies

- | | |
|-------------------------------|---|
| ↳ DIGAMI Post MI
BMJ, 1997 | ↳ 28% Decreased All Cause Mortality |
| ↳ Leuven 1 SICU
NEJM, 2001 | ↳ 34% Decreased In Hospital Mortality + Reduced Morbidity |
| ↳ Leuven 2 MICU
NEJM, 2006 | ↳ 16% Decrease In Hospital Mortality* + Reduced Morbidity |
- * MICU Stay > 3 Days

Glycemic Control In The Hospital

Major Prospective Studies

- ↳ Portland **Post CABG** ~45% Decrease Mortality
J Thoracic CV Surg 2003
- ↳ Lazar **Post CABG** Major Morbidity Reduction^{*}
Circulation, 2004
- ↳ Krinsley **ICU** 29% Decrease Mortality
Mayo Clin Proc, 2004

* Pacing, A, Fib, Infection, Days On Vent, In ICU, In Hospital

Characteristics Of Negative Trials

- Lack Of Glycemic Separation
- Underpowered

Insulin In The Hospital Setting

The days of casual
glycemic control for
critically ill patients
should be over!

So, Reducing Glucose Is Good!!

But how low should we go...

Glycemic Control In The Hospital

Major Prospective Studies

- ↳ **DIGAMI Post MI**
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- ↳ **Leuven 2 MICU**
NEJM, 2006 ↳ 16% Decrease In Hospital Mortality* + Reduced Morbidity

* MICU Stay > 3 Days

AACE Position Statement 12/16/03: Hospital Glycemic Goals

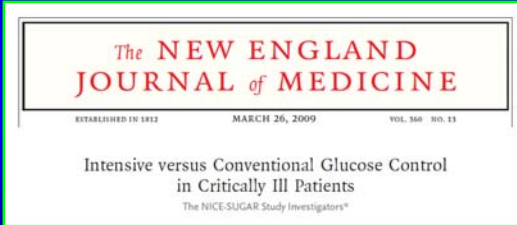
Intensive Care Units: 110 mg/dL

Non-Critical Care Units:

Pre-Prandial 110 mg/dL

Max. Glucose 180 mg/dL

NICE-SUGAR
Normoglycemia in Intensive Care Evaluation-Survival Using Glucose Algorithm Regulation



The NICE-SUGAR Study Investigators. *NEJM* 360: 1283-1297, 2009

NICE-SUGAR
Normoglycemia in Intensive Care Evaluation-Survival Using Glucose Algorithm Regulation

- 6104 Patients From ICUs of 42 Hospitals in Australia, New Zealand, and North America
- **Conventional**
 - Insulin Given For Glucose > 180 mg/dl and Stopped For Glucose < 144 mg/dl
- **Intensive**
 - Glucose Target: 81 – 108 mg/dl

The NICE-SUGAR Study Investigators. *NEJM* 360: 1283-1297, 2009

NICE-SUGAR
Normoglycemia in Intensive Care Evaluation-Survival Using Glucose Algorithm Regulation

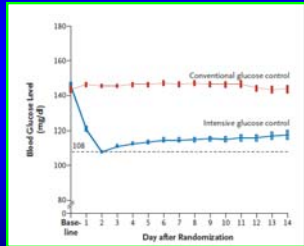
Primary Outcome
Death from Any Cause Within 90 Days After Randomization

90% Power To Detect Absolute Mortality Difference of 3.8% Assuming Baseline Mortality of 30%

The NICE-SUGAR Study Investigators. *NEJM* 360: 1283-1297, 2009

NICE-SUGAR

Normoglycemia in Intensive Care Evaluation-Survival Using Glucose Algorithm Regulation



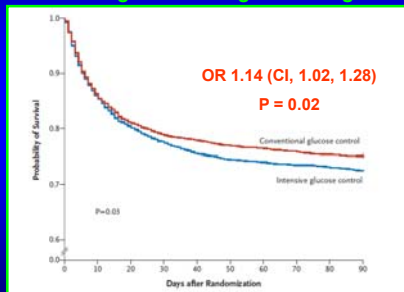
144 ± 23 mg/dl

115 ± 18 mg/dl

The NICE-SUGAR Study Investigators. *NEJM* 360: 1283-1297, 2009

NICE-SUGAR

Normoglycemia in Intensive Care Evaluation-Survival Using Glucose Algorithm Regulation



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NICE-SUGAR

Normoglycemia in Intensive Care Evaluation-Survival Using Glucose Algorithm Regulation

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Hypoglycemia and Risk of Death
in Critically Ill Patients

The NICE-SUGAR Study Investigators*

The NICE-SUGAR Study Investigators. *NEJM* 367: 1108-1118, 2012

NICE-SUGAR

Normoglycemia in Intensive Care Evaluation-Survival Using Glucose Algorithm Regulation

Hypoglycemia	HR For Mortality
None	
Moderate (41-70 mg/dl)	1.41 (1.21, 1.62, $p < 0.001$)
Severe (≤ 40 mg/dl)	2.10 (1.59, 2.77, $p < 0.001$)
Hypoglycemia: no insulin	3.84 (2.37, 6.23, $p < 0.001$)

The NICE-SUGAR Study Investigators. *NEJM* 367: 1108-1118, 2012

Insulin In The Hospital Setting

The days of casual
glycemic control for
critically ill patients
should be over!

AACE Position Statement 12/16/03: Hospital Glycemic Goals

~~Intensive Care Units: 110 mg/dL~~

~~Non-Critical Care Units:~~

~~Pre-Prandial 110 mg/dL~~

~~Max. Glucose 180 mg/dL~~

**ADA/AACE Consensus Statement on
Inpatient Glycemic Control
2009**

- **Critically Sick Patients**
 - Threshold to Start Insulin Therapy No Greater Than 180 mg%
 - On Therapy Goal Is 140-180 mg%
- **Non Critically Sick Patients***
 - Pre-Meal < 140 mg%
 - Random < 180 mg%

Moghissi, E et al *Endocrine Practice* May/June, 2009
*Reaffirmed by the Endocrine Society, 2012

Take Home Points

- There is considerable evidence that good glycemic control is beneficial to critically ill patients.
- Hypoglycemia must be avoided.

Glycemic Control

- The Evidence For Insulin's Benefit
- The Mechanism of Insulin's Benefit
- The Achievement of Insulin's Benefit
- A Few Cases...

Beneficial Effects Of Insulin In The Critical Care Setting

- Hyperglycemia Is Bad
- Since Insulin Reduces Glucose, It Is Good...
- *But Beyond Glucose...*

Insulin

In The Critical Care Setting

Vasodilates
Acts As Metabolic Modulator
Enhances Cell Survival
Restrains Platelets
Promotes Fibrinolysis
Enhances Granulocyte Function
Is A Potent Anti-Inflammatory Agent

Take Home Points

- There is considerable evidence that good glycemic control is beneficial to critically ill patients.
- Hypoglycemia must be avoided.
- Beneficial effects may be mediated in part by properties of the insulin molecule itself.

Glycemic Control

- The Evidence For Insulin's Benefit
- The Mechanism of Insulin's Benefit
- The Achievement of Insulin's Benefit
- A Few Cases...

IV Insulin Infusion Protocols

IV Insulin Protocol Based On Insulin Sensitivity

Algorithm 1		Algorithm 2		Algorithm 3		Algorithm 4	
BG	Units/hr	BG	Units/hr	BG	Units/hr	BG	Units/hr
< 80 = Hypoglycemia							
<80	Off	<80	Off	<80	Off	<80	Off
80-109	0.2	80-109	0.5	80-109	1	80-109	1.5
110-119	0.5	110-119	1	110-119	2	110-119	3
120-149	1	120-149	1.5	120-149	3	120-149	5
150-179	1.5	150-179	2	150-179	5	150-179	7
180-209	2	180-209	3	180-209	6	180-209	9
210-239	2	210-239	4	210-239	7	210-239	12
240-269	3	240-269	5	240-269	8	240-269	16
270-299	3	270-299	6	270-299	10	270-299	20
300-329	4	300-329	7	300-329	12	300-329	24
330-359	4	330-359	8	330-359	14	>330	28
>360	6	>360	12	>360	16		


IV Insulin Protocol Based On Insulin Sensitivity

Algorithm 1	Algorithm 2	Algorithm 3	Algorithm 4	Algorithm 5	Algorithm 6
BG units/h	BG units/h	BG units/h	BG units/h	BG units/h	BG units/h
< 70 0.05	< 70 0.05	< 70 0.05	< 70 0.05	< 70 0.05	< 70 0.05
70-74 0.1	70-74 0.1	70-74 0.1	70-74 0.1	70-74 0.1	70-74 0.1
75-79 0.1	75-79 0.1	75-79 0.2	75-79 0.2	75-79 0.2	75-79 0.2
80-84 0.2	80-84 0.2	80-84 0.3	80-84 0.3	80-84 0.3	80-84 0.3
85-89 0.3	85-89 0.4	85-89 0.4	85-89 0.5	85-89 0.6	85-89 0.6
90-94 0.4	90-94 0.6	90-94 0.7	90-94 0.8	90-94 1.0	90-94 1.2
95-99 0.5	95-99 0.8	95-99 1.1	95-99 1.4	95-99 1.9	95-99 2.3
100-104 0.7	100-104 1.0	100-104 1.3	100-104 1.8	100-104 2.4	100-104 3.0
105-109 1.0	105-109 1.3	105-109 1.8	105-109 2.4	105-109 3.3	105-109 4.0
110-114 1.2	110-114 1.6	110-114 2.1	110-114 2.8	110-114 3.8	110-114 4.5
115-119 1.5	115-119 2.0	115-119 2.6	115-119 3.4	115-119 4.5	115-119 5.2
120-124 1.7	120-124 2.3	120-124 3.0	120-124 3.9	120-124 5.1	120-124 5.9
125-129 2.0	125-129 2.6	125-129 3.4	125-129 4.4	125-129 5.7	125-129 6.5
130-134 2.3	130-134 3.0	130-134 3.9	130-134 5.0	130-134 6.3	130-134 7.1
135-139 2.6	135-139 3.4	135-139 4.4	135-139 5.6	135-139 7.0	135-139 7.8
140-144 3.0	140-144 3.9	140-144 4.9	140-144 6.1	140-144 7.5	140-144 8.3
145-149 3.3	145-149 4.2	145-149 5.2	145-149 6.4	145-149 7.8	145-149 8.6
150-154 3.6	150-154 4.5	150-154 5.5	150-154 6.7	150-154 8.1	150-154 8.9
155-159 4.0	155-159 4.9	155-159 5.9	155-159 7.1	155-159 8.5	155-159 9.3
160-164 4.3	160-164 5.2	160-164 6.2	160-164 7.4	160-164 8.8	160-164 9.6
165-169 4.6	165-169 5.5	165-169 6.5	165-169 7.7	165-169 9.1	165-169 9.9
170-174 5.0	170-174 5.9	170-174 6.9	170-174 8.1	170-174 9.5	170-174 10.3
175-179 5.3	175-179 6.2	175-179 7.2	175-179 8.4	175-179 9.8	175-179 10.6
180-184 5.6	180-184 6.5	180-184 7.5	180-184 8.7	180-184 10.1	180-184 10.9
185-189 6.0	185-189 6.9	185-189 7.9	185-189 9.1	185-189 10.5	185-189 11.3
190-194 6.3	190-194 7.2	190-194 8.2	190-194 9.4	190-194 10.8	190-194 11.6
195-199 6.6	195-199 7.5	195-199 8.5	195-199 9.7	195-199 11.1	195-199 11.9
200-204 7.0	200-204 7.9	200-204 8.9	200-204 10.1	200-204 11.5	200-204 12.3
205-209 7.3	205-209 8.2	205-209 9.2	205-209 10.4	205-209 11.8	205-209 12.6
210-214 7.6	210-214 8.5	210-214 9.5	210-214 10.7	210-214 12.1	210-214 12.9
215-219 8.0	215-219 8.9	215-219 9.9	215-219 11.0	215-219 12.4	215-219 13.2
220-224 8.3	220-224 9.2	220-224 10.2	220-224 11.3	220-224 12.7	220-224 13.5
225-229 8.6	225-229 9.5	225-229 10.5	225-229 11.6	225-229 13.0	225-229 13.8
230-234 9.0	230-234 9.9	230-234 10.9	230-234 12.0	230-234 13.3	230-234 14.1
235-239 9.3	235-239 10.2	235-239 11.2	235-239 12.3	235-239 13.6	235-239 14.4
240-244 9.6	240-244 10.5	240-244 11.5	240-244 12.6	240-244 13.9	240-244 14.7
245-249 10.0	245-249 10.9	245-249 11.9	245-249 13.0	245-249 14.2	245-249 15.0
250-254 10.3	250-254 11.2	250-254 12.2	250-254 13.3	250-254 14.5	250-254 15.3
255-259 10.6	255-259 11.5	255-259 12.5	255-259 13.6	255-259 14.8	255-259 15.6
260-264 11.0	260-264 11.9	260-264 12.9	260-264 14.0	260-264 15.1	260-264 15.9
265-269 11.3	265-269 12.2	265-269 13.2	265-269 14.3	265-269 15.4	265-269 16.2
270-274 11.6	270-274 12.5	270-274 13.5	270-274 14.6	270-274 15.7	270-274 16.5
275-279 12.0	275-279 12.9	275-279 13.9	275-279 15.0	275-279 16.0	275-279 16.8
280-284 12.3	280-284 13.2	280-284 14.2	280-284 15.3	280-284 16.3	280-284 17.1
285-289 12.6	285-289 13.5	285-289 14.5	285-289 15.6	285-289 16.6	285-289 17.4
290-294 13.0	290-294 13.9	290-294 14.9	290-294 16.0	290-294 16.9	290-294 17.7
295-299 13.3	295-299 14.2	295-299 15.2	295-299 16.3	295-299 17.2	295-299 18.0
300-304 13.6	300-304 14.5	300-304 15.5	300-304 16.6	300-304 17.5	300-304 18.3
305-309 14.0	305-309 14.9	305-309 15.9	305-309 17.0	305-309 17.8	305-309 18.6
310-314 14.3	310-314 15.2	310-314 16.2	310-314 17.3	310-314 18.1	310-314 18.9
315-319 14.6	315-319 15.5	315-319 16.5	315-319 17.6	315-319 18.4	315-319 19.2
320-324 15.0	320-324 15.9	320-324 16.9	320-324 18.0	320-324 18.7	320-324 19.5
325-329 15.3	325-329 16.2	325-329 17.2	325-329 18.3	325-329 19.0	325-329 19.8
330-334 15.6	330-334 16.5	330-334 17.5	330-334 18.6	330-334 19.3	330-334 20.1
335-339 16.0	335-339 16.9	335-339 17.9	335-339 19.0	335-339 19.6	335-339 20.4
340-344 16.3	340-344 17.2	340-344 18.2	340-344 19.3	340-344 19.9	340-344 20.7
345-349 16.6	345-349 17.5	345-349 18.5	345-349 19.6	345-349 20.2	345-349 21.0
350-354 17.0	350-354 17.9	350-354 18.9	350-354 20.0	350-354 20.5	350-354 21.3
355-359 17.3	355-359 18.2	355-359 19.2	355-359 20.3	355-359 20.8	355-359 21.6
360-364 17.6	360-364 18.5	360-364 19.5	360-364 20.6	360-364 21.1	360-364 21.9
365-369 18.0	365-369 18.9	365-369 19.9	365-369 21.0	365-369 21.4	365-369 22.2
370-374 18.3	370-374 19.2	370-374 20.2	370-374 21.3	370-374 21.7	370-374 22.5
375-379 18.6	375-379 19.5	375-379 20.5	375-379 21.6	375-379 22.0	375-379 22.8
380-384 19.0	380-384 19.9	380-384 20.9	380-384 22.0	380-384 22.3	380-384 23.1
385-389 19.3	385-389 20.2	385-389 21.2	385-389 22.3	385-389 22.6	385-389 23.4
390-394 19.6	390-394 20.5	390-394 21.5	390-394 22.6	390-394 22.9	390-394 23.7
395-399 20.0	395-399 20.9	395-399 21.9	395-399 23.0	395-399 23.3	395-399 24.1
400-404 20.3	400-404 21.2	400-404 22.2	400-404 23.3	400-404 23.6	400-404 24.4
405-409 20.6	405-409 21.5	405-409 22.5	405-409 23.6	405-409 23.9	405-409 24.7
410-414 21.0	410-414 21.9	410-414 22.9	410-414 24.0	410-414 24.3	410-414 25.1
415-419 21.3	415-419 22.2	415-419 23.2	415-419 24.3	415-419 24.6	415-419 25.4
420-424 21.6	420-424 22.5	420-424 23.5	420-424 24.6	420-424 24.9	420-424 25.7
425-429 22.0	425-429 22.9	425-429 23.9	425-429 25.0	425-429 25.3	425-429 26.1
430-434 22.3	430-434 23.2	430-434 24.2	430-434 25.3	430-434 25.6	430-434 26.4
435-439 22.6	435-439 23.5	435-439 24.5	435-439 25.6	435-439 25.9	435-439 26.7
440-444 23.0	440-444 23.9	440-444 24.9	440-444 26.0	440-444 26.3	440-444 27.1
445-449 23.3	445-449 24.2	445-449 25.2	445-449 26.3	445-449 26.6	445-449 27.4
450-454 23.6	450-454 24.5	450-454 25.5	450-454 26.6	450-454 26.9	450-454 27.7
455-459 24.0	455-459 24.9	455-459 25.9	455-459 27.0	455-459 27.3	455-459 28.1
460-464 24.3	460-464 25.2	460-464 26.2	460-464 27.3	460-464 27.6	460-464 28.4
465-469 24.6	465-469 25.5	465-469 26.5	465-469 27.6	465-469 27.9	465-469 28.7
470-474 25.0	470-474 25.9	470-474 26.9	470-474 28.0	470-474 28.3	470-474 29.1
475-479 25.3	475-479 26.2	475-479 27.2	475-479 28.3	475-479 28.6	475-479 29.4
480-484 25.6	480-484 26.5	480-484 27.5	480-484 28.6	480-484 28.9	480-484 29.7
485-489 26.0	485-489 26.9	485-489 27.9	485-489 29.0	485-489 29.3	485-489 30.1
490-494 26.3	490-494 27.2	490-494 28.2	490-494 29.3	490-494 29.6	490-494 30.4
495-499 26.6	495-499 27.5	495-499 28.5	495-499 29.6	495-499 29.9	495-499 30.7
500-504 27.0	495-499 27.9	495-499 28.9	495-499 30.0	495-499 30.3	495-499 31.1
505-509 27.3	505-509 28.2	505-509 29.2	505-509 30.3	505-509 30.6	505-509 31.4
510-514 27.6	505-509 28.5	505-509 29.5	505-509 30.6	505-509 30.9	505-509 31.7
515-519 28.0	510-514 28.9	510-514 29.9	510-514 31.0	510-514 31.3	510-514 32.1
520-524 28.3	515-519 29.2	515-519 30.2	515-519 31.3	515-519 31.6	515-519 32.4
525-529 28.6	520-524 29.5	520-524 30.5	520-524 31.6	520-524 31.9	520-524 32.7
530-534 29.0	525-529 29.9	525-529 30.9	525-529 32.0	525-529 32.3	525-529 33.1
535-539 29.3	530-534 30.2	530-534 31.2	530-534 32.3	530-534 32.6	530-534 33.4
540-544 29.6	535-539 30.5	535-539 31.5	535-539 32.6	535-539 32.9	535-539 33.7
545-549 30.0	540-544 30.9	540-544 31.9	540-544 33.0	540-544 33.3	540-544 34.1
550-554 30.3	545-549 31.2	545-549 32.2	545-549 33.3	545-549 33.6	545-549 34.4
555-559 30.6	550-554 31.5	550-554 32.5	550-554 33.6	550-554 33.9	550-554 34.7
560-564 31.0	555-559 31.9	555-559 32.9	555-559 34.0	555-559 34.3	555-559 35.1
565-569 31.3	560-564 32.2	560-564 33.2	560-564 34.3	560-564 34.6	560-564 35.4
570-574 31.6	565-569 32.5	565-569 33.5	565-569 34.6	565-569 34.9	565-569 35.7
575-579 32.0	570-574 32.9	570-574 33.9	570-574 35.0	570-574 35.3	570-574 36.1
580-584 32.3	575-579 33.2	575-579 34.2	575-579 35.3	575-579 35.6	575-579 36.4
585-589 32.6	580-584 33.5	580-584 34.5	580-584 35.6	580-584 35.9	580-584 36.7
590-594 33.0	585-589 33.9	585-589 34.9	585-589 36.0	585-589 36.3	585-589 37.1
595-599 33.3	590-594 34.2	590-594 35.2	590-594 36.3	590-594 36.6	590-594 37.4
600-604 33.6	595-599 34.5	595-599 35.5	595-599 36.6	595-599 36.9	595-599 37.7
605-609 34.0	600-604 34.9	600-604 35.9	600-604 37.0	600-604 37.3	600-604 38.1
610-614 34.3	605-609 35.2	605-609 36.2	605-609 37.3	605-609 37.6	605-609 38.4
615-619 34.6	610-614 35.5	610-614 36.5	610-614 37.6	610-614 37.9	610-614 38.7
620-624 35.0	615-619 35.9	615-619 36.9	615-619 38.0	615-619 38.3	615-619 39.1
625-629 35.3	620-624 36.2	620-624 37.2	620-624 38.3	620-624 38.6	620-624 39.4
630-634 35.6	625-629 36.5	625-629 37.5	625-629 38.6	625-629 38.9	625-629 39.7
635-639 36.0	630-634 36.9	630-634 37.9	630-634 39.0	630-634 39.3	630-634 40.1
640-644 36.3	635				

The Initial Algorithm		→	The Next Algorithm	
< 120	Off		< 120	Off
120-149	1.0		120-149	1.5
150-179	1.5		150-179	2.0
180-209	2.0		180-209	3.0
210-239	2.0		210-239	4.0
240-269	3.0	→	240-269	5.0
270-299	3.0		270-299	6.0
300-329	4.0		300-329	7.0
Etc.			Etc.	


Computer-based Insulin Infusion Protocols

Glucommander
Practical Alternative to IV Insulin Protocols



FDA CLEARS MD SCIENTIFIC'S TIGHT GLUCOSE CONTROL SOFTWARE
EndoTool™ Glucose Management System Calculates Intravenous Insulin Dosing

85763
CH-20021 (MAR/17/05)
Page 1 of 1


Clarian Health Partners
Methodist | IU | Riley

Clarian GlucoStabilizer Insulin Infusion Program

Recommended IV Fluids To Prevent Hypoglycemia, Hypokalemia & Ketosis:

- ✓ Glucose: 5-10 gms/hour
- ✓ Potassium: 20 meq/L
- ✓ The Primary Service Should Choose the Type and the Rate of the Fluid Depending on the Underlying Disease

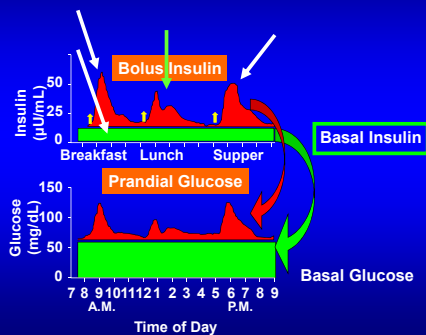
Take Home Points

- Intensive care patients, not eating or not eating very much, should be treated with continuous intravenous insulin.

Life After The Drip....

*Transition From IV to SQ Insulin
In The Adult Patient*

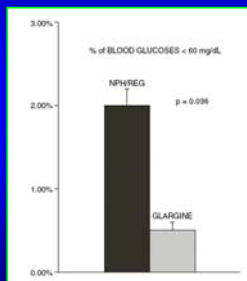
Basal - Bolus



Currently Available Basal Insulins

- Neutral Protamine Hagedorn (1946)
- Insulin Glargine (2001)
- Insulin Detemir (2006)

NPH/Reg Vs. Glargine Insulin After Cardiovascular Surgery



Yeldandi, R et al *Diabetes Technology & Therapeutics* 8: 609-616, 2006

Transition to SQ: An Approach

To Transition A Patient From An IV Insulin Infusion To SQ Insulin

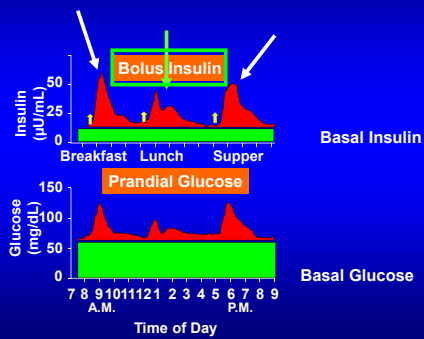
Multiply Last Drip Dose By 20, And Give This Amount As Glargine

Turn The IV Drip Off 2 Hours Later

Example: Last Drip Dose Is 1.0 Unit/Hour;
Give $1.0 \times 20 = 20$ Units Of Glargine SQ;
Discontinue Drip Two Hours Later

This Is Basal Insulin

Basal - Bolus



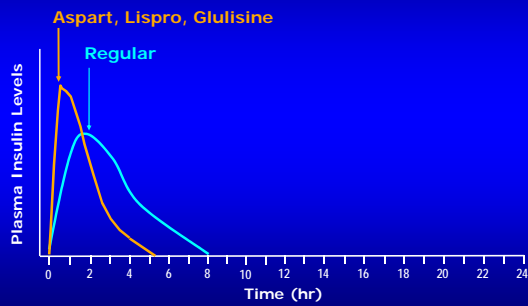
Transition From IV to SQ Insulin In The Adult Patient

- **Basal Insulin**
- **Bolus Insulin**
- **Prandial Insulin**
- **Correction Factor Insulin**

Currently Available Bolus Insulins

- Regular (1921)
- Insulin Lispro (1996)
- Insulin Aspart (2000)
- Insulin Glulisine (2006)

Insulin Profiles



First, The Prandial Dose...

When Patient Is Able To Eat,

✓ Add Rapid Acting Insulin For
Mealtime Coverage

✓ **Rule Of Thumb**

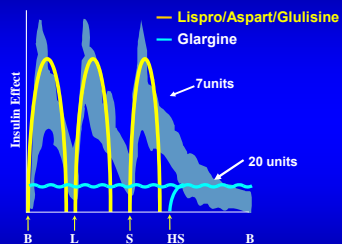
50% Basal

50% Prandial, Divided Over 3 Meals

Example: Patient Is On 20 Units
Glargine Daily; Give 7 Units With
Each Meal Of Lispro (Humalog) Or
Aspart (Novolog) Or Glulisine
(Apidra)

This Is Prandial Insulin

Basal-Bolus Insulin Therapy: Glargine at HS and Mealtime Insulin Lispro, Aspart, Or Glulisine



Transition From IV to SQ Insulin In The Adult Patient

- Basal Insulin
- Bolus Insulin

Correction Factor Insulin

Correction Factor Dose, Added To Prandial Dose

Low Dose
Total Insulin Dose <40 units/day

Premeal BG	Additional Insulin
120-170	1 unit
171-220	2 units
221-270	3 units
271-320	4 units
>320	5 units

Medium Dose
Total Insulin Dose 40-80 units/day

Premeal BG	Additional Insulin
120-170	1 units
171-220	3 units
221-270	5 units
271-320	7 units
>320	9 units

High Dose
Total Insulin Dose >80 units/day

Premeal BG	Additional Insulin
120-170	3 units
171-220	5 units
221-270	7 units
271-320	9 units
>320	11 units

**What About Patients
Admitted With
Hyperglycemia On The
Floor?**

Sliding Scale

~~**Episodic Bolus Insulin**~~

~~**WITHOUT**~~

~~**Basal Insulin**~~

Basal Bolus Versus SSI

Randomized Study Of Basal-Bolus Insulin Therapy In The Inpatient Management Of Patients With Type 2 Diabetes
The RABBIT 2 Trial

- 130 Type 2 Diabetic Patients Admitted to General Medicine Services
- Managed By Internal Medicine Residents Who Received A Copy Of Assigned Treatment Protocol
- Basal-Bolus Regime With Glargine And Glulisine Compared To SSI

Umplierrez, G. et al Diabetes Care 30: 2181-2186, 2007

Basal Bolus Versus SSI

Randomized Study Of Basal-Bolus Insulin Therapy In The Inpatient Management Of Patients With Type 2 Diabetes
The RABBIT 2 Trial

The graph displays blood glucose levels over a 10-day period. The Basal Bolus group (open circles) starts at approximately 230 mg/dL and decreases to about 165 mg/dL by day 10. The SSI group (filled circles) starts at approximately 230 mg/dL and decreases to about 135 mg/dL by day 10. Error bars are shown for each data point.

Days of Therapy	Basal Bolus (mg/dL)	SSI (mg/dL)
Admit	230	230
1	200	190
2	185	165
3	180	155
4	195	155
5	185	155
6	180	135
7	175	140
8	175	135
9	165	135
10	165	135

Umplierrez, G. et al Diabetes Care 30: 2181-2186, 2007

Basal Bolus Versus SSI

Randomized Study Of Basal-Bolus Insulin Therapy In The Inpatient Management Of Patients With Type 2 Diabetes
The RABBIT 2 Trial

- Glucose Difference Between Groups 27 mg% ($p < 0.01$)

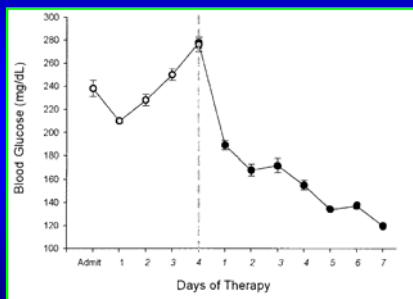
Percentage of Patients at Target (< 140 mg/dL)	
Basal - Bolus	Sliding Scale Insulin
66%	38%

- No Difference In Hypoglycemia ($<0.5\%$)

Umponree, G. et al Diabetes Care 30: 2181-2186, 2007

Basal Bolus Versus SSI

Randomized Study Of Basal-Bolus Insulin Therapy In The Inpatient Management Of Patients With Type 2 Diabetes
The RABBIT 2 Trial



Umponree, G. et al Diabetes Care 30: 2181-2186, 2007

Basal Bolus Versus SSI

The RABBIT 2 Surgery Study

- 211 Type 2 Diabetic Surgical Patients on Surgical Wards, NOT ICU
- Age 58 ± 11 Years
- Admission Glucose 190 ± 92 mg/dl
- HbA1c 7.7 ± 2.2 %
- Basal-Bolus Regime With Glargine And Glulisine Compared To SSI

Umponree, G. et al Diabetes Care 34: 256-261, 2011

Basal Bolus Versus SSI

The RABBIT 2 Surgery Study

	SSI	Basal Bolus	p
Glucose	176 ± 44	157 ± 32	< 0.001
Hypoglycemia	4.7%*	23%	< 0.001

* % of patients, but no difference in severe hypoglycemia (< 40 mg/dl)

Umplierrez, G. et al Diabetes Care 34: 256-261, 2011

Basal Bolus Versus SSI

The RABBIT 2 Surgery Study

	SSI	Basal Bolus	p
Glucose	176 ± 44	157 ± 32	< 0.001
Hypoglycemia	4.7%*	23%	< 0.001
Composite AE	24.3%	8.6%	= 0.003

* % of patients, but no difference in severe hypoglycemia (< 40 mg/dl)

Umplierrez, G. et al Diabetes Care 34: 256-261, 2011

Basal Bolus Versus SSI

The RABBIT 2 Surgery Study

Table 2—Composite hospital complications and outcomes composite hospital complications

	All	SSI	Basal-bolus insulin	P value
Wound infections	14	11	3	0.050
Pneumonia	3	3	0	0.247
Acute respiratory failure	6	5	1	0.213
Acute renal failure	15	11	4	0.106
Bacteremia	3	2	1	0.999
Number of patients with complications	35	26	9	0.003
Mortality	2	1	1	NS
Postsurgery ICU admission (%)	16	19.6	12.5	NS
Length of stay (days)				
ICU	2.51 ± 1.90	3.19 ± 2.14	1.23 ± 0.60	0.003
Hospital	6.8 ± 8.9	6.3 ± 5.6	7.23 ± 11.39	NS

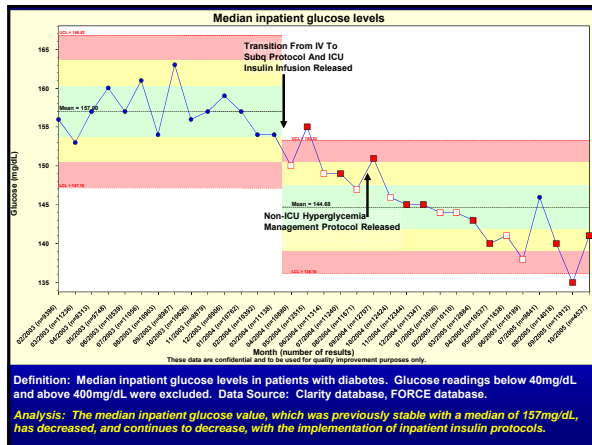
Umplierrez, G. et al Diabetes Care 34: 256-261, 2011

Starting Basal-Bolus From Scratch

Calculate Starting Total Daily Dose (TDD)

- ✓ Previous Total Daily Insulin Units Used or
- ✓ 0.4 units/kg (Type 1 DM)
- ✓ 0.6 units/kg (New Onset Or Lean Type 2)
- ✓ 0.8 units/kg (Type 2 DM)

This Is Very Conservative and Actual Needs May Turn Out to Be Substantially More



Take Home Points

- Intensive care patients, not eating or not eating very much, should be treated with continuous intravenous insulin.
- When patients begin to eat, either in ICU or on wards, they should be transitioned to a basal bolus insulin regime.

A Word About Oral Agents....

Therapy of Type 2 Diabetes Mellitus: Hospital Use of Oral Agents

Secretagogues	Illness Decreases Endogenous Insulin
α Glucosidase Inhibitors	Not for Acute Illness With Variable Intake
Metformin	Hold for Acute Illness If Renal, Cardiac, or Liver Function Unstable, or Surgery, or Radiocontrast
Glitazone(s)	Can Give or Not

Take Home Points

- In selective, non critically ill patients, oral glycemic agents can be considered.

Have A Discharge Plan

Can A Patient Go Back To Oral Agents At Discharge?

- If Pre-Admission Control Acceptable, YES!!!
- Admission HbA1C Helpful
- If Pre-Admission Control Not Acceptable, Medication Adjustment Needed

Glycemic Control

- The Evidence For Insulin's Benefit
- The Mechanism of Insulin's Benefit
- The Achievement of Insulin's Benefit
- A Few Cases...

Floor Patient

- 65 y/o male with DM2, hyperlipidemia, HTN, and DJD
- Admitted to General Medicine with chest pain
- Metformin 1000mg BID and glipizide 5mg BID; HbA1c 6.4% 2 weeks ago
- Glucose on floor arrival 275 mg/dl
- Admit orders
 - ✓ Serial troponins
 - ✓ Possible adenosine myoview

Floor Patient

- 65 y/o male
- DM2, hyperlipidemia, HTN, and DJD
- Metformin 1000mg BID and glipizide 5mg BID
- HbA1c 6.4%
- Glucose 275 mg/dl
- Admit orders
 - ✓ Serial troponins
 - ✓ Possible adenosine myoview

What should be started to control glucose?

- Metformin only
- Glipizide only
- Metformin and glipizide
- Glargine and log
- Insulin and metformin
- Insulin and glipizide

Floor Patient

- 65 y/o male (75kg)
- DM2, hyperlipidemia, HTN, and DJD
- Metformin 1000mg BID and glipizide 5mg BID
- HbA1c 6.4%
- Glucose 275 mg/dl
- Admit orders
 - ✓ Serial troponins
 - ✓ Possible adenosine myoview
- Start glargine and log

What would be the insulin doses?

- 75 kg patient
- $75 \times 0.8 = 60$ units insulin total
- $60 / 2 = 30$ units
- 30 units basal (glargine)
- 30 units prandial (log) -- 10 units after each meal
- Medium dose correction factor

Floor Patient

- 65 y/o male (75kg)
- DM2, hyperlipidemia, HTN, and DJD
- Metformin 1000mg BID and glipizide 5mg BID
- HbA1c 6.4%
- Glucose 275 mg/dl

Patient NPO after midnight for adenosine myoview

How should insulin orders be changed once he is NPO?

- Stop all of the insulin
- Hold the prandial log only, continue glargine and correction scale
- Hold the glargine only, continue log and correction scale

Floor Patient

- 65 y/o male (75kg)
- DM2, hyperlipidemia, HTN, and DJD
- Metformin 1000mg BID and glipizide 5mg BID
- HbA1c 6.4%
- Glucose 275 mg/dl

Patient NPO after midnight for adenosine myoview

Reversible defect on myoview led to stent

With which diabetes medication(s) should the patient be sent home?

- Glargine and log
- Metformin 1000mg BID and glipizide 5mg BID
- Insulin pump

ICU Patient

- 65 y/o female with DM2, HTN, & hyperlipidemia
- Admitted to the MICU with sepsis
- Metformin 1000mg BID, glipizide 10mg BID q day
- HbA1c 8% 3 months ago
- Glucose on MICU arrival 230 mg/dl
- *What therapy should be started for glucose control?*
 - Continue metformin and glipizide
 - Start glargine and log
 - Start an insulin drip

ICU Patient

- 65 y/o female with DM2, HTN, & hyperlipidemia
- Admitted to the MICU with sepsis
- Glucose on MICU arrival 230 mg/dl
- Insulin drip started

What diabetes lab should be ordered?

- a) Urine microalbumin
- b) Hemoglobin A1c
- c) Nothing

ICU Patient

- 65 y/o female with DM2, HTN, & hyperlipidemia
- Admitted to the MICU with sepsis
- Glucose on MICU arrival 230 mg/dl
- Insulin drip started
- Clear liquids started

How should new diet be covered?

- a) Adjust the insulin drip
- b) Continue the drip, start SC log with carbohydrate counting
- c) Continue the drip, restart glipizide

ICU Patient

- 65 y/o female with DM2, HTN, & hyperlipidemia
- Admitted to the MICU with sepsis
- Glucose on MICU arrival 230 mg/dl
- Insulin drip started
- Clear liquids started
- Transferring to Gen Med

What about insulin orders?

- a) Continue the insulin drip
- b) Stop the drip, start sliding scale log
- c) Stop drip, start glargine/log

ICU Patient

- 65 y/o female with DM2, HTN, & hyperlipidemia
- Admitted to the ICU with sepsis
- Glucose on MICU arrival 230 mg/dL
- Insulin drip started
- Clear liquids started
- Transferring to Gen Med

What are the insulin doses, assuming last drip dose was 1.5 units/hour?

Glargine (1.5 units x 20 = 30 units)
Log (30 units / 3 = 10 units)
10 units after each meal
Medium dose correction factor

ICU Patient

- 65 y/o female with DM2, HTN, & hyperlipidemia
- Admitted to the ICU with sepsis
- Glucose on MICU arrival 230 mg/dL
- Insulin drip started
- Clear liquids started
- Transferring to Gen Med

What happens to the insulin drip?

Discontinue the insulin drip 2 hours after glargine injected

Former ICU, Now Floor, Patient

- 65 y/o female with DM2 and sepsis
- Glargine 30 units daily and log 10 units TID
- Medium dose correction factor
- Daily insulin dose adjustments
 - Take the previous day's correction factor insulin dose
 - Add to today's insulin dose

ADA/AACE Consensus Statement on Inpatient Glycemic Control 2009

- **Critically Sick Patients**
 - Threshold to Start Insulin Therapy No Greater Than 180 mg%
 - On Therapy Goal Is 140-180 mg%
- **Non Critically Sick Patients***
 - Pre-Meal < 140 mg%
 - Random < 180 mg%

Moghissi, E et al Endocrine Practice May/June, 2009
*Reaffirmed by the Endocrine Society, 2012

Correction Factor Dose, Added To Prandial Dose

Low Dose Total Insulin Dose <40 units/day

Premeal BG	Additional Insulin
120-170	1 unit
171-220	2 units
221-270	3 units
271-320	4 units
>320	5 units

Medium Dose Total Insulin Dose 40-80 units/day

Premeal BG	Additional Insulin
120-170	1 units
171-220	3 units
221-270	5 units
271-320	7 units
>320	9 units

High Dose Total Insulin Dose >80 units/day

Premeal BG	Additional Insulin
120-170	3 units
171-220	5 units
221-270	7 units
271-320	9 units
>320	11 units

Former ICU, Now Floor, Patient

- 65 y/o female with DM2 and sepsis
- Glargine 30 units daily and log 10 units TID
- Medium dose correction factor
- Yesterday's Glucose values:
 - Fasting 175 mg/dl 3 units
 - Pre-lunch 190 mg/dl 3 units
 - Pre-dinner 225 mg/dl 5 units
 - HS 190 mg/dl
- 11 units of correction factor (CF) aspart given

Former ICU, Now Floor, Patient

How would you adjust today's insulin dose?

Since all readings are above target, you could add $\sim\frac{1}{2}$ of CF to glargine and the remainder divided equally with each meal.

Former ICU, Now Floor, Patient

- 65 y/o female with DM2 and sepsis
- Glargine 30 units daily and log 10 units TID
- Medium dose correction factor

Former ICU, Now Floor, Patient

- 65 y/o female with DM2 and sepsis
- Glargine 35 units daily and log 12 units TID
- Medium dose correction factor
- Yesterday's Glucose values:
 - Fasting 120 mg/dl 1 unit
 - Pre-lunch 150 mg/dl 1 unit
 - Pre-dinner 150 mg/dl 1 unit
 - HS 180 mg/dl
- 3 units of correction factor (CF) aspart given

Former ICU, Now Floor, Patient

How would you adjust today's insulin dose?

Fasting glucose is at target, but the rest of the day is above target. So, you could add the 1/3 of the entire CF with each meal

Former ICU, Now Floor, Patient

- 65 y/o female with DM2 and sepsis
- Glargine 35 units daily and log 12 units TID
- Medium dose correction factor

Former ICU, Now Floor, Patient

- 65 y/o female with DM2 and sepsis
- Glargine 35 units daily and log 13 units TID
- Medium dose correction factor
- Yesterday's Glucose values:
 - Fasting 115 mg/dl
 - Pre-lunch 118 mg/dl
 - Pre-dinner 119 mg/dl
 - HS 170 mg/dl
- No correction factor (CF) aspart given

Former ICU, Now Floor, Patient

- Patient going home!!
- On Glargine and aspart
- HbA1c 9%

How should her diabetes medication(s) be adjusted?

- a) Discontinue insulin and restart oral medications
- b) Reintroduce metformin to insulin
- c) Continue insulin only

Special Situations

- Patients Receiving Corticosteroids
- Patients Receiving Tube Feeds
- Patients With Renal Failure

Patient on Glucocorticoids

Glucocorticoid Effects on Glucose Metabolism

- Increased hepatic gluconeogenesis increases fasting glucose
- Inhibition of glucose uptake especially in adipose tissue increases post-prandial glucose
- Predominant effect is post-prandial, so glucose rises during the day

Take Home Points

- In selective, non critically ill patients, oral glyemic agents can be considered.
- In glucocorticoid treated patients, consider giving more than 50% as bolus.
- Consider NPH instead of glargine in patients on shorter acting glucocorticoids.

Special Situations

- Patients Receiving Corticosteroids
- Patients Receiving Tube Feeds
- Patients With Renal Failure

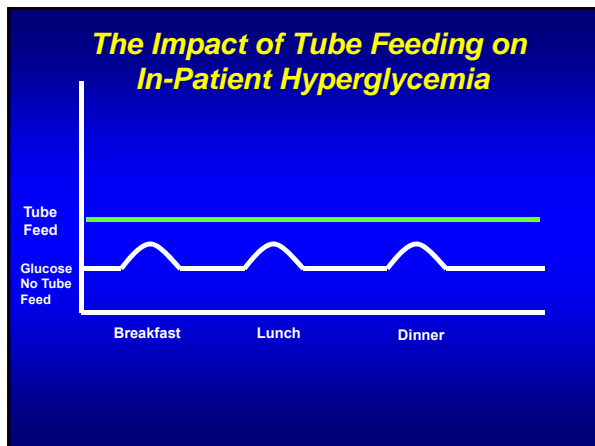
The Impact of Tube Feed on In-Patient Hyperglycemia

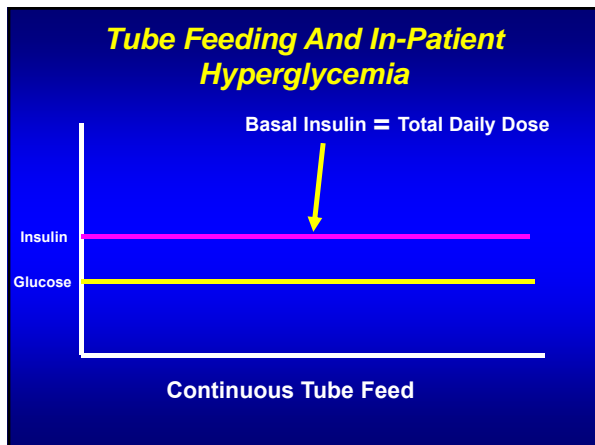
Continuous And Persistent Carbohydrate Absorption



Continuous And Persistent Hyperglycemia

The Basal/Bolus Rule Is Different.....





- ### Patients on Continuous Tube Feed
- Check Blood Glucose Every 6 Hours
 - Give Correction Factor Rapid Acting Insulin Based On Algorithms

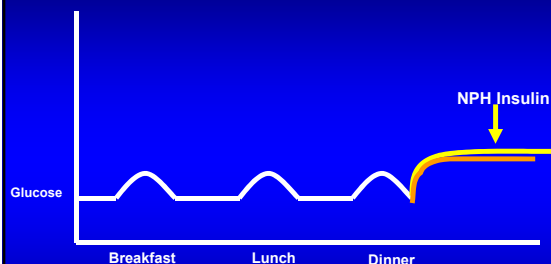
Patients on Continuous Tube Feed

- **Decrease Total Dose**
 - 10% If Glucose Level < 120 mg/dl
 - 20% Glucose Level < 80 mg/dl
- **Increase Total Dose**
 - By Adding The Total Dose Of Correction Factor Insulin The Previous Day

BEWARE of HYPOGLYCEMIA

- High Risk Of Hypoglycemia If Tube Feed Temporarily Stopped
- Immediately Initiate IV Fluids To Provide The Amount Of Glucose That Was In The Tube Feeding

Tube Feed at Bedtime



Patient on Continuous Tube Feeding

- 71 year old male with type 2 diabetes recovering from massive CVA leaving him unable to swallow
- His outpatient glycemic regime consisted of oral agents only, no insulin
- He is receiving continuous tube feeding
- He weighs 180 lbs (82 kg)

How would you begin to develop his insulin regime?

Starting Basal-Bolus From Scratch

Calculate Starting Total Daily Dose (TDD)

- ✓ Previous Total Daily Insulin Units Used or
- ✓ 0.4 units/kg (Type 1 DM)
- ✓ 0.6 units/kg (New Onset Or Lean Type 2)
- ✓ 0.8 units/kg (Type 2 DM)

Starting Basal-Bolus From Scratch

Calculate Starting Total Daily Dose (TDD)

- ✓ Previous Total Daily Insulin Units Used or
- ✓ 0.5 units/kg (Type 1 DM)
- ✓ 0.8 units/kg (New Onset Or Lean Type 2)
- ✓ 1.0 units/kg (Type 2 DM)

Patient on Continuous Tube Feeding

- Weight based total daily dose of insulin would be 1.0 units/kg X 82 kg = 82 units
- So, give 82 units glargine as basal
- There is no bolus
- There is, however, correction factor; high dose correction factor

Correction Factor Dose, Added To Prandial Dose

Low Dose Total Insulin Dose <40 units/day

Premeal BG	Additional Insulin
120-170	1 unit
171-220	2 units
221-270	3 units
271-320	4 units
>320	5 units

Medium Dose Total Insulin Dose 40-80 units/day

Premeal BG	Additional Insulin
120-170	1 units
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>320	9 units

High Dose Total Insulin Dose >80 units/day

Premeal BG	Additional Insulin
120-170	3 units
171-220	5 units
221-270	7 units
271-320	9 units
>320	11 units

Patient on Continuous Tube Feeding

- Patient on 82 units glargine
- Yesterday's Sugars **CF Aspart**
 - 6 AM 210 mg/dl 5 units
 - Noon 280 mg/dl 9 units
 - 6 PM 290 mg/dl 9 units
 - Midnight 310 mg/dl 9 units
- 32 units correction factor aspart

How would you adjust today's insulin dose?

Patient on Continuous Tube Feeding

- Patient on 114 units glargine (may split)
- Yesterday's Sugars CF Aspart
 - 6 AM 180 mg/dl 5 units
 - Noon 250 mg/dl 7 units
 - 6 PM 270 mg/dl 7 units
 - Midnight 280 mg/dl 9 units
- 28 units correction factor aspart

How would you adjust today's insulin dose?

Patient on Continuous Tube Feeding

- Patient on 142 units glargine (may split)
- Yesterday's Sugars CF Aspart
 - 6 AM 135 mg/dl 3 units
 - Noon 155 mg/dl 3 units
 - 6 PM 160 mg/dl 3 units
 - Midnight 170 mg/dl 3 units
- 12 units correction factor aspart

How would you adjust today's insulin dose?

Patient on Continuous Tube Feeding

- Patient on 154 units glargine (may split)
- Yesterday's Sugars CF Aspart
 - 6 AM 110 mg/dl 0 units
 - Noon 115 mg/dl 0 units
 - 6 PM 119 mg/dl 0 units
 - Midnight 119 mg/dl 0 units
- 0 units correction factor aspart

How would you adjust today's insulin dose?

Take Home Points

- In tube fed patients, give basal and correction factor. There is no bolus *per se*.

Special Situations

- Patients Receiving Corticosteroids
- Patients Receiving Tube Feeds
- Patients With Renal Failure

The Impact Of Renal Failure On In-Patient Hyperglycemia

- ✓ Decreased Insulin Clearance
- ✓ Decreased Gluconeogenesis
- ✓ *Both Increase The Risk Of Hypoglycemia*

Reduce Dose For Renal Insufficiency

GFR cc/min	Total Insulin Dose
>30	No Change
15-29	Reduce to 70%
<15 or Dialysis	Reduce to 50%

Take Home Points

- In tube fed patients, give basal and correction factor. There is no bolus *per se*.
- Remember to consider e GFR in those with impaired kidney function.

Special Situations

- Patients Receiving Corticosteroids
- Patients Receiving Tube Feeds
- Patients With Renal Failure

Take Home Points

- There is considerable evidence that good glycemic control is beneficial to critically ill patients.
- Hypoglycemia must be avoided.
- Beneficial effects may be mediated in part by properties of the insulin molecule itself.

Take Home Points

- Intensive care patients, not eating or not eating very much, should be treated with continuous intravenous insulin.
- When patients begin to eat, either in ICU or on wards, they should be transitioned to a basal bolus insulin regime.

Take Home Points

- In selective, non critically ill patients, oral glyemic agents can be considered.
- In glucocorticoid treated patients, consider giving more than 50% as bolus.
- Consider NPH instead of glargine in patients on shorter acting glucocorticoids.

Take Home Points

- In tube fed patients, give basal and correction factor. There is no bolus *per se*.
- Remember to consider e GFR in those with impaired kidney function.

Glycemic Control

- The Evidence For Insulin's Benefit
- The Mechanism of Insulin's Benefit
- The Achievement of Insulin's Benefit
- A Few Cases...
