Lessons Learned From the Field: Treating Diabetes in School

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No disclosures
## Objectives

<table>
<thead>
<tr>
<th>Assessing and Treating Hypoglycemia</th>
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<tr>
<td>Assessing and Evaluating Insulin Pump Site Infections</td>
</tr>
<tr>
<td>Assessing and Treating Unexplained Hyperglycemia</td>
</tr>
</tbody>
</table>

## Patients/Parents/School RN’s Need to Know

| Seasonal variation in the risk of severe hypoglycemia. |
| 24 hour risk of hypoglycemia after exercise due to “Triple Jeopardy.” |
| Complex carbohydrate, protein and fat intake may reduce the occurrence of nocturnal hypoglycemia. |
| Early recognition of symptoms & treatment with rapid-acting glucose are important to prevent mild from progressing to moderate and later to severe hypoglycemia. |
Steps to Prevent and Treat Severe Hypoglycemia

1. Identify early symptoms at rest and when active

2. Check BG to verify symptoms

3. Carry rapid acting carbohydrate 24/7 and treat with 5-10 (under 6 yo), 10-15 (6-13 yo) or 15-20 (>13 yo) grams

4. Re-check BG in 15 minutes & determine need to re-treat

5. Share symptoms with friends and adults.

Foods Commonly Used to Treat Hypoglycemia

<table>
<thead>
<tr>
<th>Food</th>
<th>Kcals</th>
<th>Total sugars</th>
<th>GI</th>
<th>Galactose</th>
<th>Glucose</th>
<th>Fructose</th>
<th>Sucrose</th>
</tr>
</thead>
<tbody>
<tr>
<td>OJ 120 mL</td>
<td>52</td>
<td>10.15</td>
<td>46 L</td>
<td>0</td>
<td>2.53</td>
<td>2.51</td>
<td>5.1</td>
</tr>
<tr>
<td>AJ 120 mL</td>
<td>58</td>
<td>12.18</td>
<td>39 L</td>
<td>0.02</td>
<td>3.10</td>
<td>6.94</td>
<td>2.11</td>
</tr>
<tr>
<td>Dex4™ 4 GT</td>
<td>64</td>
<td>16</td>
<td>100 H</td>
<td>0</td>
<td>16</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Cola 120 mL</td>
<td>45</td>
<td>13</td>
<td>63 M</td>
<td>0</td>
<td>4.91</td>
<td>5.4</td>
<td>2.58</td>
</tr>
<tr>
<td>Milk 240 mL*</td>
<td>146</td>
<td>12.83</td>
<td>34 L</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Honey 1T</td>
<td>64</td>
<td>17.4</td>
<td>55 M</td>
<td>0.66</td>
<td>7.57</td>
<td>8.67</td>
<td>0.19</td>
</tr>
<tr>
<td>Sugar 1T</td>
<td>48</td>
<td>12.49</td>
<td>61 M</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>12.49</td>
</tr>
</tbody>
</table>

*Lactose 12.83g, fat 7.93 g

Data from Nutrition Data System for Research Software NDS-R version 2006; Nutrition Coordinating Center U of Minnesota, Minneapolis
Glucose Responses to Commonly Used Treatments for Hypoglycemia

Brodows et al. *JAMA* 1984;252:3378  Steady state serum insulin ~50 uU/mL

<table>
<thead>
<tr>
<th>Dose</th>
<th>Route of Administration</th>
<th>Time of Onset of Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mg</td>
<td>IV</td>
<td>1 minute</td>
</tr>
<tr>
<td>1 mg</td>
<td>IM</td>
<td>13 minutes</td>
</tr>
<tr>
<td>1 mg</td>
<td>SC</td>
<td>20 minutes</td>
</tr>
</tbody>
</table>

Glucagon
Pharmacokinetics & Bioavailability of Injected Glucagon: Differences Between IM, SC and IV Administration

Muhlhause et al. Diabetes Care DC 8:398:39--42, 1985

I = insulin
G = glucagon
- - - IV dosing of G
. . . . IM dosing of G
--- SC dosing of G
* Significant differences between IM and SC dosing

12 yo Boy w Pump “No Delivery” Alarm During 1100 Pre-lunch Bolus

School RN notifies mother and discusses that balance of dose should be administered as Humalog via injection.

Intended dose was 3 units but 30 units given.

Student reported “my arm hurts” after receiving the injection.

Mother brought back-up insulin pump to school and changed pumps. At 1130 his BG was 156 mg/dl and he went to a slightly later lunch.

Student returned to school RN after lunch stating “my arm hurts” and student went home.
12 yo Boy w Pump Malfunction During 1100 Pre-lunch Bolus

At home at ~1330, BG = 56 mg/dl and he mentioned to his mother, "she used a 'really big needle' . . . full to the top." Student’s mother called his school RN and she recounted that she had injected 30 rather than 3 units.

Parent and patient went to OSH ER and patient was fine after receiving IV glucose.

Plasma Blood Glucose and A1c Goals for T1D Patients by Age-group

<table>
<thead>
<tr>
<th>Values by Age (years)</th>
<th>Pre-meal BG (mg/dl)</th>
<th>Bedtime/ Overnight BG (mg/dl)</th>
<th>HbA1c (%)</th>
<th>Rationale</th>
</tr>
</thead>
</table>
| Pre-school 0-6        | 100-180             | 110-200                       | <8.5      | 1. Vulnerability to hypoglycemia  
2. More insulin sensitive  
3. Unpredictable dietary intake and physical activity  
A lower goal, i.e., <8.0%, is reasonable if it can be achieved without excessive hypoglycemia |
| School age 6–12       | 90-180              | 100–180                       | <8        | Vulnerability to hypoglycemia  
A lower goal, i.e., <7.5%, is reasonable if it can be achieved without excessive hypoglycemia |
| Adolescents           | 90-130              | 90–150                        | <7.5      | A lower goal, i.e., <7.0%, is reasonable if it can be achieved without excessive hypoglycemia |
| Young Adults          |                     |                               | <7.0      | }
Effect of Continuous Glucose Monitoring on Hypoglycemia in T1D
Time Spent Below 63 mg/dL by Month

Assessing Unexplained Hyperglycemia

Check serum (or urine) ketones

Check the insulin delivery system
Skin → Cannula → Tubing → Reservoir → Pump → Patient
Assessing Unexplained Hyperglycemia: Skin → Cannula → Tubing → Reservoir → Pump → Patient

Cutaneous Complications:
Is skin red, swollen, irritated, tender?
Is there a purulent discharge?
Is atrophy or hypertrophy present?
Is cannula in skin? Is cannula bent?
Cannula lengths vary from 3 mm (Mio) to 17 mm (Silhouette)
When did you last change infusion set?

aspart (NovoLog®) retains stability & bacteriostatic effect 6 – 7 d vs.
lispro (Humalog®) for 48 h

Two studies reporting infusion site infections (staph epi, staph aureus and/or enterococi appearing as cellulitis w/o purulent drainage) in adults (n = 161 and n = 40) w/ established T1D using beef pork Regular insulin. Infection defined as ≥ 1 mm erythema or inflammation.

29% of patients had an infection if cleansed site w soap & H2O then alcohol (one infection per 27 pt-mo); 54% had more than one site infection.

40% if prepped site w antiseptic then alcohol vs. 70% of patients had an infection if cleansed site only w alcohol.

TSS has been reported in patients using CSII
### Assessing Unexplained Hyperglycemia:

**Skin → Tubing → Reservoir → Pump → Patient**

MRSA and insulin pump site infections

**Aim:** To investigate colonization of s.c. insulin pump catheters by skin flora & determine correlation between S. aureus carrier state & its presence on the skin and catheter.

141 catheters from 94 children with T1DM using CSII were cultured:
- 34 examinations (24.1%) in 30 children (31.9%) were +;
- coagulase negative staph were isolated (30): mainly Staph epi; MRSA was detected in 7 examinations in 6 children.

S. aureus carrier state was proven in 31.9% of all examined patients, more often in children with a + catheter culture (41.4%), all were MRSA -.

No correlation between S. aureus carrier state and catheter colonization.

Statistically significant correlations between:
- coagulase negative staphylococci presence, including the MRSA strains, on the skin and on the catheter surface (p< 0.0001);
- HbA1c and bacterial catheter colonization (p = 0.0335) were observed.

Microorganisms found on the skin are the most frequent cause of the subcutaneous catheter infection.

### Infusion Set Issues

**Skin → Tubing → Reservoir → Pump → Patient**

- When irritation, tenderness, erythema, streaking, purulent discharge or infection occur, i.e., “When in doubt, take it out!”
- Rotate sites, i.e., 1-2 inches apart, to avoid regions of hypertrophy or atrophy, every 2 days
- Never change site at bedtime unless plan to check BG q 2-3 h post - set change
Assessing Unexplained Hyperglycemia: Skin → Tubing → Reservoir → Pump → Patient

Cutaneous Complications

Study design: cross-sectional in pediatric patients
50 consecutive patients with T1D using CSII for >6 months:
- 26 female; age 13.3 ± 3.5 years;
- CSII duration 2.8 ± 1.7 years; HbA1c 7.7% ± 1.1%.

Results
Scarring: 94% scars <3 mm diameter,
Erythema not associated with nodules: 66%,
Subcutaneous nodules: 62%,
Lipo-hypertrophy: 42%.

Predictors
BMI z-score (r = -0.3, p = .039), i.e., slimmer subjects and subjects using perpendicular infusion sets (p = 0.03) were less likely to have skin concerns;
No correlation with HbA1c, insulin brand or site.
< 5% of patients and parents considered stopping CSII because of skin concerns.

Infusion Site Preparation

Prep the skin with an antiseptic, i.e., Betadine, IV prep, or Hibiclens, StaphAseptic to reduce common skin bacteria; isopropyl alcohol swabs do not reduce the bacteria count.
Don't breathe on the reservoir or infusion set cannula before insertion.

Apply a sterile dressing before inserting cannula:
IV 3000 by Smith and Nephew or Bio-Occlusive dressing by J + J.
# Recommended Antibiotics

<table>
<thead>
<tr>
<th>Topical:</th>
<th>Bactroban (mupirocin) or Altabax (retapamulin)</th>
</tr>
</thead>
<tbody>
<tr>
<td>p. o.:</td>
<td>Dicloxacillin, Keflex</td>
</tr>
<tr>
<td>I.V.:</td>
<td>Cephalosporin</td>
</tr>
</tbody>
</table>

## Infusion Set Information

<table>
<thead>
<tr>
<th>Infusion Set Information</th>
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</table>
16 yo competitive female student-athlete presents with Chief Complaint: “It hurts where I insert my pump site.”

<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
</tr>
</thead>
<tbody>
<tr>
<td>When did you first notice this?</td>
<td></td>
</tr>
<tr>
<td>How has skin changed over past 24 + hours?</td>
<td></td>
</tr>
<tr>
<td>What have you done to treat it thus far?</td>
<td></td>
</tr>
<tr>
<td>When did you last change infusion set?</td>
<td></td>
</tr>
<tr>
<td>How often do you change infusion sets?</td>
<td></td>
</tr>
<tr>
<td>How do you prep your skin before inserting set?</td>
<td></td>
</tr>
</tbody>
</table>

Parents’ History:

- Thursday: soccer practice and game: BG’s good;
- Friday: felt nauseous but – ketones and friends had viral gastro;
- Saturday: soccer practice; site started to hurt; emailed MQ: see PCP or ER physician
- Sunday: saw PCP: not lanced, started Keflex and warm compresses;
- Monday: not as active as usual, pus extruding with warm compresses; in evening: febrile sent to ER
- Tuesday early a.m.: eventually to ER and site lanced, wick placed x 2, pus cultured + staph epi, started IV Ceftrixone and p.o. Bactrim
| **Unexplained Hyperglycemia**  
**Differential diagnosis of inadequate insulin delivery:** |
<table>
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<tbody>
<tr>
<td>BG &gt; 250 mg/dl for more than 2-3 h without &quot;known&quot; association with food, exercise, insulin omission, illness or stress</td>
</tr>
<tr>
<td>• Forgotten/missed injections or boluses</td>
</tr>
<tr>
<td>• Inaccurate bolus calculation</td>
</tr>
<tr>
<td>• Pre-menstrual insulin resistance</td>
</tr>
<tr>
<td>• Illness</td>
</tr>
<tr>
<td>• Emotional stress</td>
</tr>
<tr>
<td>• Interrupted patient-set-tubing-reservoir-pump connection</td>
</tr>
<tr>
<td>• Over-treatment of hypoglycemia</td>
</tr>
</tbody>
</table>
Comparison of Human Regular to lispro after CSII Interruption and in Tx of Acutely Decompensated IDDM

- 18 patients w T1D (age 30 ± 11 y; duration 15.5 y; HbA1c 7.7 ± 1.1%) bx w CSII (9 w human Regular and 9 w lispro)

- CSII interruption: basal infusion was stopped at 0300 and plasma insulin, glucose and β-OHB were measured q 15-60 min for 6 h after interruption of CSII; R patients TDD = 0.6 u/kg/d and bolus/basal = 1.0 and lispro patients TDD = 0.7 u/kg/d and bolus/basal = 0.8. To be eligible for CSII interruption, BG 60-150 mg/dl during h prior to pump interruption.

- Insulin Replacement: plasma insulin, glucose and β-OHB were measured q 15 min for 2 h after a single abdominal injection of either human R or lispro to correct the hyperglycemia and ketosis that developed during the ketosis phase of the study. To be eligible for insulin replacement, BG > 250 mg/dl or moderate ketonuria.

![Graphs showing changes in plasma insulin, glucose, and β-OHB concentrations after cessation of basal insulin infusion (time 0) in patients treated with lispro or regular human insulin.](image)
Treating Unexplained Hyperglycemia
BG > 250 mg/dl

+ If negative urine ketones or β-OHB < 0.5 mmol/l, use correction factor via pump or syringe.

+ If β-OHB 0.5 -1.0 mmol/l, give correction by syringe as 10%* of average TDD, or 0.1 u/kg* x 1, change infusion set and be certain basal rates are accurate. Within 2 h, β-OHB should normalize.

+ If β-OHB ≥1.0 mmol/l, give correction by syringe as 15-20%* of average TDD, or 0.15-0.2 u/kg* x 1, change infusion set and be certain basal rates are accurate. Within 3 h, β-OHB should normalize.
‘... the diabetic is running
in crowded traffic when
in the midst of an infection . . .”

Elliott P. Joslin, 1922

SDR # 1 for pump and basal bolus patients:
NEVER omit or reduce your basal insulin
during illness

Ketonemia in patients with T1D who use an insulin
pump is an impending medical emergency because
there is no subcutaneous depot of intermediate- or
long-acting insulin and DKA can develop within 4-6

At the first sign of infection or if nausea or vomiting
occur, immediately check serum (or urine) ketones.
<table>
<thead>
<tr>
<th>SDR # 2 for pump patients: When ketones present or BG &gt; 400 mg/dl, always give “booster” dose by syringe.</th>
</tr>
</thead>
<tbody>
<tr>
<td>+ When calculating “booster” dose, ask patient to review TDD’s in pump and take the recent week’s average TDD.</td>
</tr>
<tr>
<td>+ Average TDD should be approximately double the patient’s basal insulin dose (review from pump).</td>
</tr>
<tr>
<td>+ Booster ~ 0.2 units rapid-acting insulin /kg/dose</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SDR # 2 for pump and basal bolus patients: When ketones are present, give booster dose by syringe.</th>
</tr>
</thead>
<tbody>
<tr>
<td>+ Booster doses, to correct ketonemia, are identical to those for patients receiving s.c. insulin. However, studies of CSII interruption were performed in healthy patients with T1D and do not account for increased counter-regulatory hormones present during infection. Pickup JC et al. Diabetologia 22: 175-9, 1982. Kozantowski G et al. Diabetologia 24: 314-8, 1983.</td>
</tr>
<tr>
<td>+ Booster doses can also be delivered as 0.2 u/kg/dose* with same consideration that studies were done in healthy adult patients who had CSII interruption. Atlia et al. D Care 21: 817-21, 1998.</td>
</tr>
</tbody>
</table>
### SDR # 2b for pump patients:
increase basal rate by 25 - 50% for 2 - 4 h

Increase basal rate by 25 to 50% for 2 - 4 hours immediately post booster dose.

If ketones now negative but BG’s remain above target range, further increase basal rate to 50% above baseline for 4 hours, and continue to monitor BG’s q 2 to 4 h until illness has resolved.

### SDR # 3 for pump patients:
After giving booster injection by syringe, change infusion set immediately.

Ask which infusion set and the length of cannula on infusion set patient is using.
<table>
<thead>
<tr>
<th>SDR #4 for pump patients:</th>
</tr>
</thead>
<tbody>
<tr>
<td>do not disconnect or suspend the pump or lower the basal rate if you are unable to eat</td>
</tr>
</tbody>
</table>

+ Increase BG monitoring to q 1-2 h to detect impending hypoglycemia due to diminished carbohydrate intake or evolving hyperglycemia or ketonemia due to infection.

+ If impending hypoglycemia, consider s.c. mini-glucagon dosing, i.e., 1 u on insulin syringe per y.o.l. or 0.01 mg/y.o.l. or 0.003 mg/kg/dose.

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| Diabetes Ketone Correction Plan |
FDA Adverse Event Reports for Insulin Pumps in Adolescents, Age 12 to 21 years, 01/01/96 - 12/31/05

Parameter \( n \) (%)
Total \((n=1594\) reports)
- Males 637 (40.0)
- Females 934 (58.6)
- Unknown 23 (1.4)

Types of events \((n=1594\) reports)
- Injuries 1038 (65.1)
- Malfunctions 528 (33.1)
- Other events 15 (0.9)
- Deaths 13 (0.8)

102 (6.4%) Insulin Pump Reports Indicating Adolescent Issues That May Have Contributed to the Adverse Event

Males 42: Females 59; mean age 15.8 y; 82% hospitalized

“Adolescent issues”
- Education 47
- Non-compliance 19
- Sports and other activities 12
- Risk-taking including 2 suicide attempts
6.4% Insulin Pump Reports Indicating Adolescent Issues That May Have Contributed to the Adverse Event

Cope et al. 121: e1133. (2008)

Food and Drug Administration Adverse Event Reports for Insulin Pumps in Children Ages 1–12 years, 1/1/96 - 12/31/09

On Arrival to School:
10 yo Boy Presents with N & V

- At 0731 father emailed BCH diabetes team and mentioned student “spilling ketones” but dad sent him to school.
- At 0830 BG 457 mg/dL; school RN did not check ketones but phoned his father who brought student home.
- At 0930 father documented large urine ketones and gave 4 units of Humalog.
- At 1300, BG = 297 mg/dL and blood ketone = 3.8 mmol/l and patient complaining his legs hurt and father noted he was limping and vomiting;
- At 1455 BG=229 and blood ketone = 4.1 mmol/l; father limited his intake because of high BG levels and student said he was not hungry. Sent to local ER then transferred to BCH.

On Arrival to School:
10 yo Boy Presents with N & V

While in OSH ER, the father reports via e/m the student is “pretty good” at giving his own injection of Lantus at dinner.

Date of discharge: saw MQ in clinic: patient denies that he thinks the Lantus “stings” but says it “hurts” when he pushes the Lantus all the way in so sometimes he does not push the Lantus in.
### Additional History

Patient had been admitted for treatment of DKA 6 days earlier;
Discharged home without seeing Social Worker to decipher etiology of inadequate insulin delivery.
I attempted to see him on the day of this d/c while in Waltham clinic but not discharged until next day.

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### Thank You for Taking Care of Our Diabetes Patients and Their Families

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