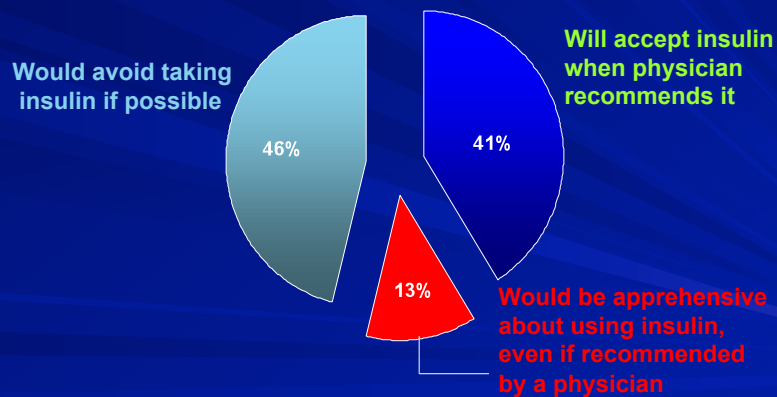# New Approaches For Injection Technique

Rita Saltiel-Berzin, RN, MPH, CDE, CHES

Worldwide Clinical Education Specialist

Are Patients Willing to Take Injections?
Feelings About Requiring Insulin in the Future

Up to 60% would not easily initiate insulin

Would avoid taking insulin if possible

Will accept insulin when physician recommends it

46%

41%

13%

Would be apprehensive about using insulin, even if recommended by a physician

Davidson J. *Diabet Med.* 2006;23(suppl. 4):163 (P457).

Patient Perceptions are Important

- Insulin Adherence among Type 2 Patients was 62-64%[1]
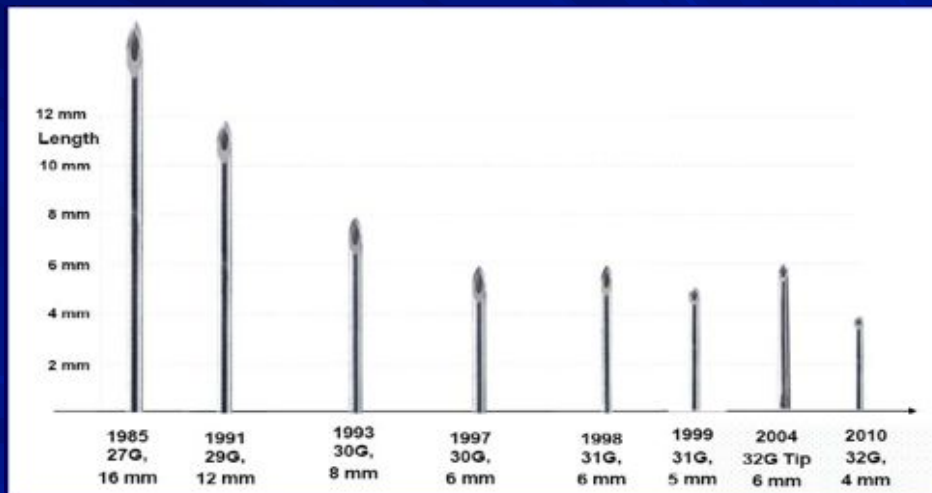 - An increased number of daily doses leads to a decline in adherence.[2]
- A third of patients who use insulin therapy say that they "dread" injections and it is the hardest part of managing their diabetes[3]

[1]Cramer, J.A. Diabetes Care, 2004
[2]Claxton, AJ. Clinical Therapeutics, 2001
[3]AADE: Injection Impact Report http://www.injectionimpact.com/

Changes in Needle Length Over the Years

| 1985 27G, 16 mm | 1991 29G, 12 mm | 1993 30G, 8 mm | 1997 30G, 6 mm | 1998 31G, 6 mm | 1999 31G, 5 mm | 2004 32G Tip 6 mm | 2010 32G, 4 mm |

From ATTD-Yearbook 2009/2010 NEW WAYS OF INSULIN DELIVERY, Prof. Dr. Lutz Heinemann Profil Institut für Stoffwechselforschung,Neuss, Germany

Glucose Variability Related to Insulin Uptake

■ Factors affecting insulin uptake:
  – The <u>type</u> of insulin
  – Insulin concentration
  – Body site: human insulin (not analogs)
  – SQ vs IM injection
  – Injection site : <u>warm</u>, <u>rubbed</u>, or <u>exercised</u>
  – Lipohypertrophy at injection site

■ What is injected is important, so is how insulin is injected
■ Injection Technique matters!

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Summary of Earlier Studies

■ Body site: "Human" insulin (Regular, NPH): Uptake – abdomen > arm ≈ thigh > buttock

■ Body site: Rapid and long-acting analogs: very <u>similar</u> time profiles across sites

■ Depth of injection:
  – Regular insulin absorbed at <u>similar</u> rates when injected deep or superficial SCT
  – Glycemic control unchanged in obese patients when insulin given with 6mm Vs 12.7mm needles, or when insulin given with 5mm Vs 8 mm needles

■ Both needle length and gauge affect patient pain and preference ratings
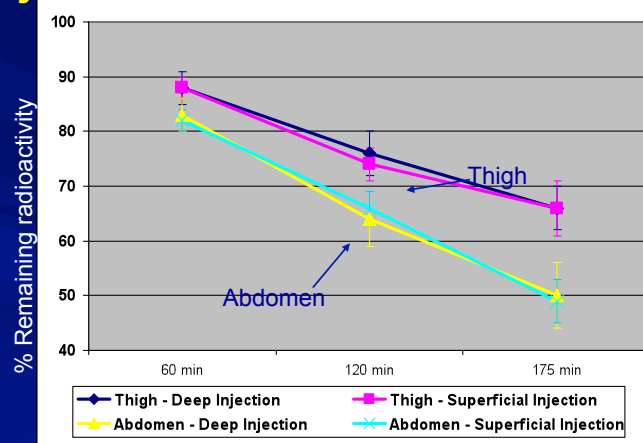
Insulin variability & site selection

Similar absorption of insulin ^{125}I-glargine after injection in arm, thigh and abdominal areas

Disappearance of radioactivity

abdomen

arm

thigh

p=N.S.
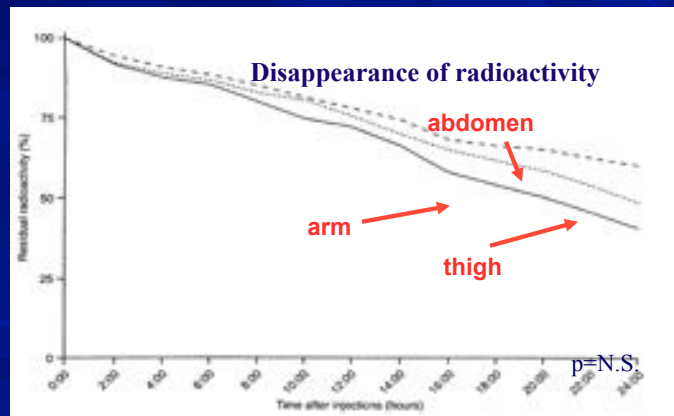
Owens et al, *Diabetes Care* 2000;23:813-19

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Injection Depth and Insulin Absorption

Thigh

Abdomen

No influence of the SC injection depth on the kinetics of insulin absorption was shown in the study

Frid et al., Intraregional Differences in the Absorption of Unmodified Insulin from the Abdominal Wall_*Diabetic Medicine* 1992;9;236-239

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Lipohypertrophy

- Associated with 3 Independent Risk Factors
  - Duration of insulin therapy
  - Lack of or poor injection Site Rotation
  - "Infrequent" changing of Needles

- Why is it a problem?
  - Decreases insulin absorption
  - May increase glucose variability

Blanco, et. al. Diab. Metab 2013 S1262-3636 (13)00121-3

Lipohypertrophy in a 70-year-old man. Axial CT image shows areas of lipohypertrophy within the subcutaneous fat of the anterior abdominal wall related to repeated insulin injections.

http://radiographics.rsna.org/content/31/7/2021/F39.expansion.html

Implications

- Injection technique, including body site, needle length, and insertion method (angle, ± pinch-up) and rotation all affect insulin delivery
  - Uptake varies by body site…. for some insulins, and by depth of injection
    - IM injection → accelerated, and more variable uptake Vs SC; may also increase pain
    - ID injection → accelerated uptake, shorter duration Vs SC; now under investigation
- Common belief is that obese patients "need" longer length needles to delivery medications SC
  - Deeper SC injections thought to increase insulin uptake

Skin and Subcutaneous Layer Thickness of Anatomical Sites Commonly Used for Subcutaneous Insulin Injections
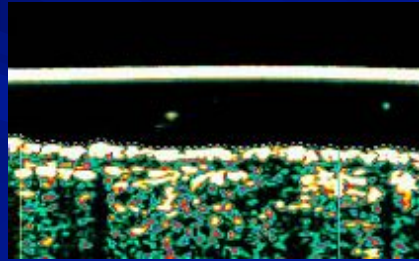
Gibney M, Arce C, Byron K, Hirsch L. *Curr Med Res Opin* 2010;26:1519-30

Demographics

Sample Size	Total	388
# With Observations	Skin Thickness / SQ Thickness	341 / 387
Gender	Male	55.2%
Race	White/Caucasian	156 (40.2%)
	Asian	98 (25.3%)
	Black / African American	62 (16.0%)
	Hispanic / Latino	55 (14.2%)
	Other	17 (4.4%)
Age Category	18 - 39	59 (15.2%)
	40 - 59	175 (45.1%)
	60 - 85	154 (39.7%)

- **Large sample size**
- **40% White/Caucasian, 14% Hispanic**
- **40% in 60-85 age group**

Demographics, cont'd

Diabetes Type	Type 2 / Type 1	280 (72.2%) / 108 (27.8%)
Insulin Use	Type 2/ Type 1	39.1% / 100%
BMI (kg/m^2)	Mean (SD)	29.88 (7.07)
	Min / Max	19.6 / 64.5
BMI Category	<25	114 (29.4%)
	25 – 29.9	110 (28.4%)
	≥30	164 (42.3%)

- **72% with Type 2 Diabetes**
- **More than 1/3 with type 2 inject insulin**
- **42% considered obese (BMI ≥30)**

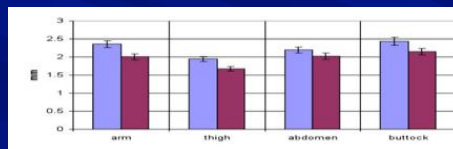## Distribution of Skin Thickness Values (in mm) by Body Site & BMI

- **Range of means from thinnest (thigh in BMI <25) to thickest (buttocks in BMI ≥30) is <u>less than 1 mm</u>**

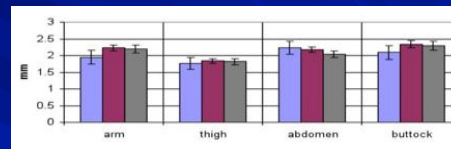- **Obese (BMI ≥30) had *slightly* higher skin thickness**
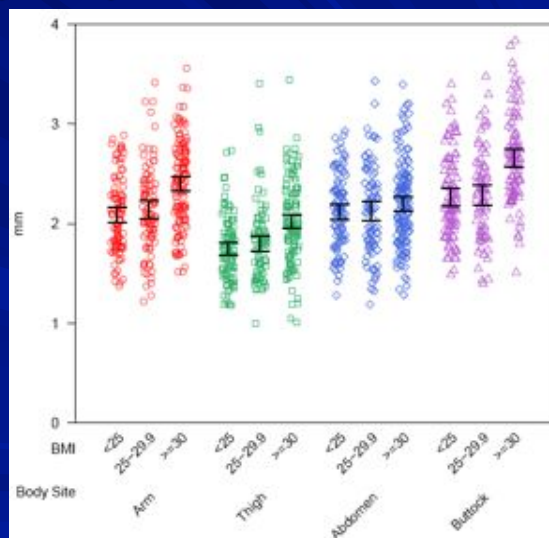
Skin Thickness in Adults

■ Average ~ 2-2.5 mm (range ~ 1.25-3.25 mm),
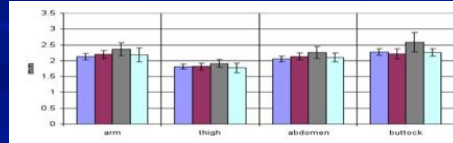 <u>regardless</u> of gender, age, ethnicity or BMI
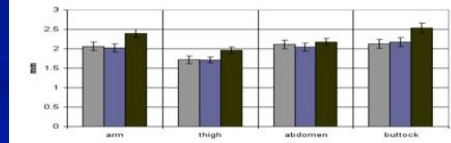
Gender

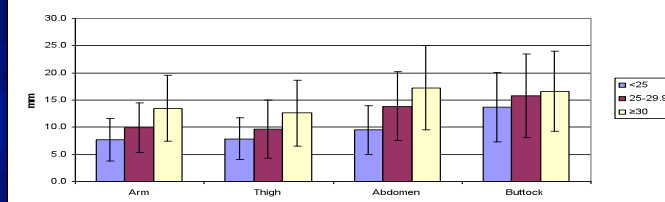**Age**

Ethnicity

BMI

Gibney M, et al. *Curr Med Res Opin* 2010;26:1519-30

SC Fat Thickness in Adults
• Much more variable

Subcutaneous Thickness by BMI - Mean and SD

BMI

Subcutaneous Thickness by Gender - Mean and SD
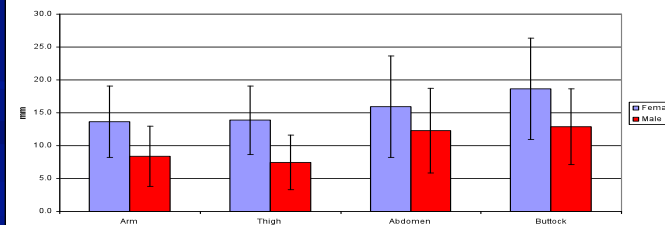
Gender

Gibney M, et al. *Curr Med Res Opin* 2010;26:1519-30

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MRI – Male 52 yrs, BMI 25.2, thigh

4 and 5 mm in SC tissue

6 mm at muscle fascia
8 mm in muscle
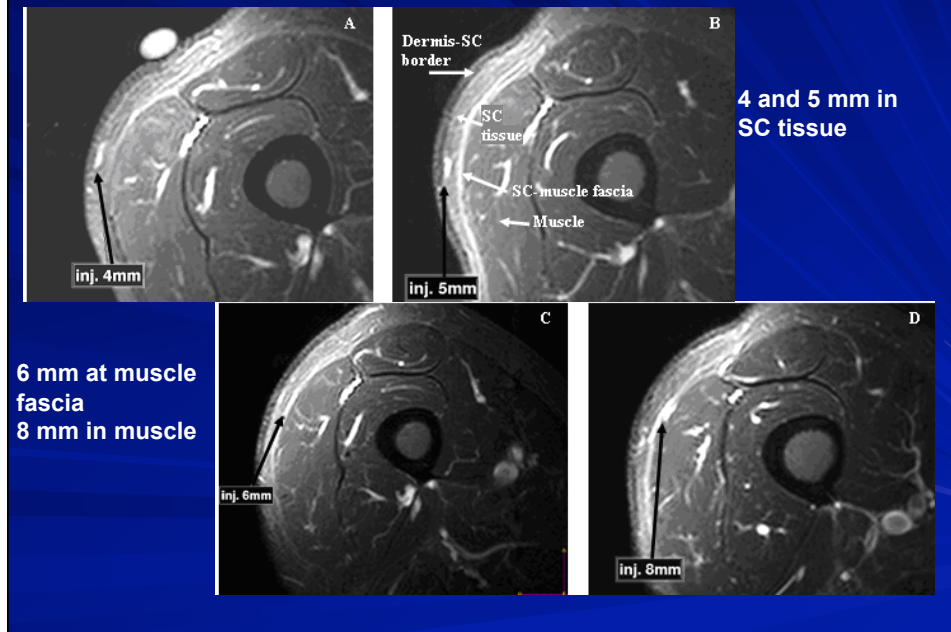
Estimates of Intra-Muscular Injection Risk From ST/SCT Data*

Pen Needle Length	IM
4 mm	0.4%
5 mm	1.8%
6 mm	5.7%
8 mm	15.3%
12.7 mm	45.0%

*Assume 90° insertion without pinch-up.
All injection sites combined (N = 1208)
No injections were given

Gibney M et al.
CMRO 2010;26:1519-30

Effect of IM / SC Injections (Regular Human Insulin) and Exercise
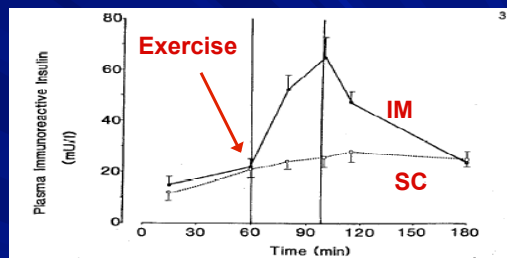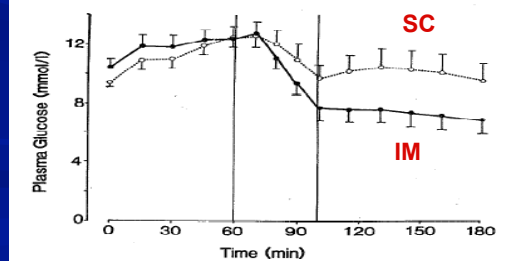
Diabetes Care 1990;13:473-7

Pediatrics: Skin Surface to Muscle Fascia (mm ±SD)

	2-6 yrs N = 31	7-13 yrs N = 49	14-17 yrs N = 21
ARM	4.89 ±1.47	6.02 ±1.86	6.31 ±1.94
THIGH	6.05 ±2.44	7.36 ±2.31	7.49 ±2.10
ABDOMEN	6.12 ±3.47	7.98 ±3.40	7.75 ±2.91
BUTTOCKS	6.53 ±2.26	8.73 ±3.18	8.12 ±2.81

Lo Presti D, et al. *Ped Diab* 2012

Calculated Incidence of IM Injections in Children of Different Age*

Needle Length	2-6 Years (248)	7-13 Years (392)	14-17 Years (168)
4 mm	20.2%	4.6%	2.4%
6 mm	66.5%	38.0%	34.5%
8 mm	83.9%	65.3%	66.1%
12.7 mm	97.2%	93.9%	96.4%

*All sites combined

Lo Presti et al. *Ped Diab* 2012

Recommendation for Needle Length, Pediatric

'Based on the mean values of skin + SC thickness in different pediatric age groups it seems preferable for all children to use the shortest needle possible. Currently this is the 4 mm pen needle.'

4mm
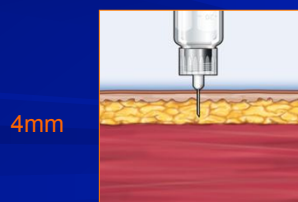
Safety, Efficacy and Patient Ratings of a new 4mm x 32G Pen Needle

Hirsch LJ, Gibney MA, Albanese J, et al. *Curr Med Res Opin* 2010;26:1531–41.

Evaluation of a New 4 mm x 32G Pen Needle

Subject Flow

Visit 1
205 Diabetics Consented

Visit 2
173 Randomized

→ **Baseline Fructosamine, Pain vs Usual Needle, Survey**

- Age 18 - 76 yrs (mean 53)
- BMI 20 to 49 kg/m2 (mean 31)
- 52% obese
- HbA1c 7.5 ± 1.0%
- T2 DM 63%

89 assigned to the **4mm/5mm group**

84 assigned to the **4mm/8mm group**

Period 1
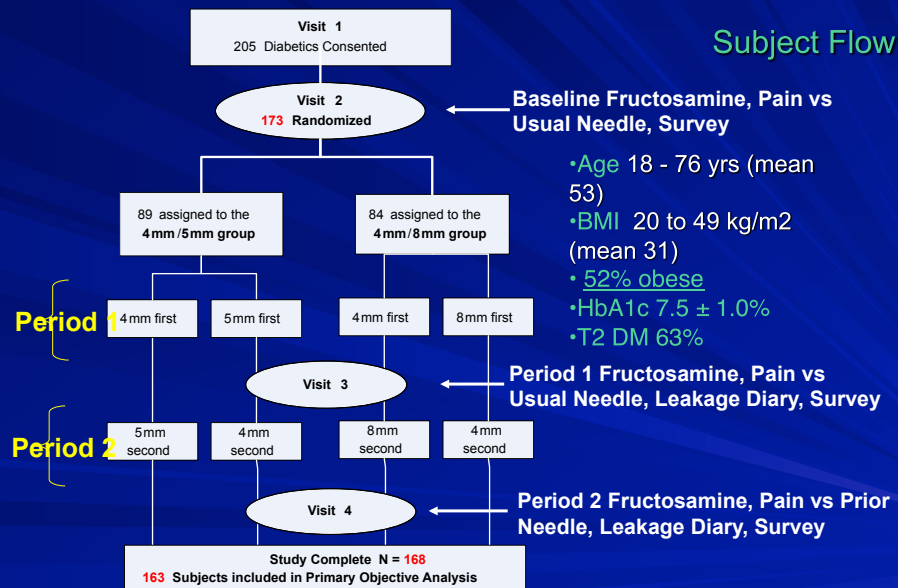4mm first | 5mm first | 4mm first | 8mm first

Visit 3 → **Period 1 Fructosamine, Pain vs Usual Needle, Leakage Diary, Survey**

Period 2
5mm second | 4mm second | 8mm second | 4mm second

Visit 4 → **Period 2 Fructosamine, Pain vs Prior Needle, Leakage Diary, Survey**

Study Complete N = 168
163 Subjects included in Primary Objective Analysis

Hirsch LJ, et al. *Curr Med Res Opin* 2010;26:1531–41.

Results Show that Use of 4mm Needle Results in Equivalent Glycemic Control

Mean Percent Absolute Difference in Fructosamine Values

Comparison	N	Absolute Difference	95% CI
4 mm vs 5 mm	83	4.93%	[3.84%, 6.01%]
4 mm vs 8 mm	80	5.45%	[4.53%, 6.37%]

Note: Analysis excludes one subject, #426, due to lab error

Leakage Was No More Frequent with 4mm Needle

Needle Length	# Subjects	# Subjects Reporting Leakage	%	Total # Events	
4 mm	164	72	44%	650	
5 mm	83	39	47%	481	838
8 mm	81	45	56%	357	

(B) Scale for reporting leakage by subjects

| 0	1µl	10µl	20µl	50µl
0	1+	2+	3+	4+
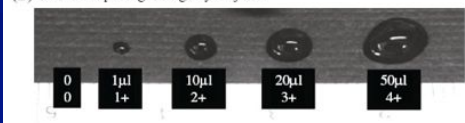
All three lengths have similar distribution of leakage droplet size

Most droplets for all lengths reported as ≤ 10µl (< 1 unit)

High rate of leakage reporting reflects training of subjects to report all such events

Fructosamine Differences Were Not Influenced by Subject BMI

– P > 0.7 for each PN comparison group

Scatterplot of Relative Difference vs BMI, by Needle Type
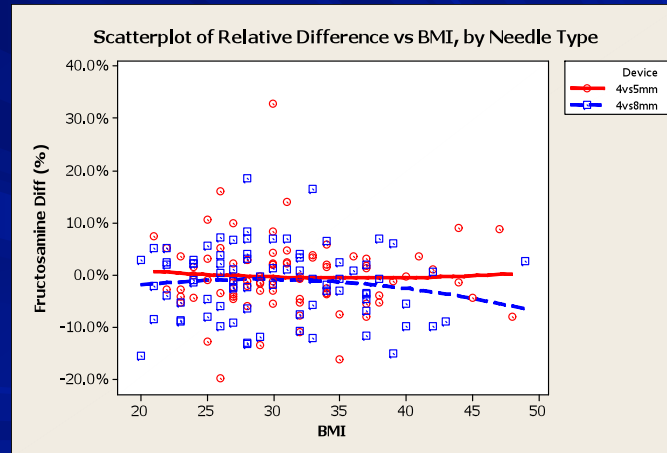
Relative Pain by VAS

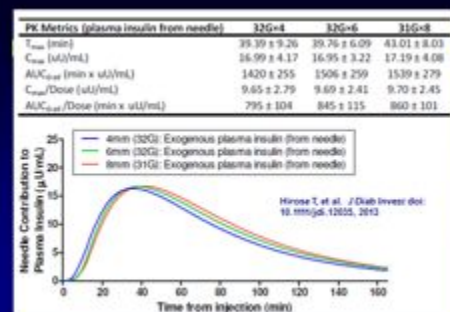| Group (N)	Mean Difference (mm)	SEM	95% CI Upper Bound (mm)	*P* value compared to 0
4mm/ 5mm (68)	-11.9	5.61	-2.6	0.019
4mm/ 8mm (69)	-23.3	4.24	-16.2	<0.001

Study Conclusions for 4mmx32G Needle vs 5mm and 8mm, 31G Needles

- Equivalent glycemic control
  - Across doses up to 40U, BMI
- Similar safety profile
- No increase in leakage from skin
- Favorable responses in Patient Surve[y]
  - Ease of Use, Pain, Overall Preference
- Ability to use one handed technique: simpler and ability to use hard to reach injection sites.

Pharmacokinetics Bioequivalence of 3 Needle Sizes

- 3 way randomized, crossover trial of 12 healthy Japanese Men
- Insulin Lispro injected in abdomen using 4mm, 6mm and 8mm needles.
- Pharmacokinetics bio-equivalence seen for all needle sizes

PK Metrics (plasma insulin from needle)	32G×4	32G×6	31G×8
T$_{max}$ (min)	39.39 ± 9.26	39.76 ± 6.09	43.01 ± 8.03
C$_{max}$ (uU/mL)	16.99 ± 4.17	16.95 ± 3.22	17.19 ± 4.08
AUC$_{0-of}$ (min × uU/mL)	1420 ± 255	1506 ± 259	1539 ± 279
C$_{max}$/Dose (uU/mL)	9.65 ± 2.79	9.69 ± 2.41	9.70 ± 2.45
AUC$_{0-of}$/Dose (min × uU/mL)	795 ± 104	845 ± 115	860 ± 101

Hirose, T., Ogihara, T, et. al. Asian Association for the Study of Diabetes, 2013

4mm in Obese – Prospective Study

■ Randomized, controlled open-label, 2-period crossover trial. Non-inferiority

- – 2 arms: 4 mm vs. 8 mm; 4 mm vs. 12.7 mm needles
- – HbA1c primary outcome (± 0.4%)
- – Pain, preference, skin leakage, etc. also assessed

■ 227 completed both periods

- – BMI ranged ~ 29 to 58 kg/m^2
- – Daily insulin doses < 10 to 350 units

■ Two abstracts presented at ADA June 2013

- – Results consistent with, and extend prior studies of pen needle performance

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Needle Tip Innovation…

Journal of Diabetes Science and Technology
Volume 6, Issue 2, March 2012
© Diabetes Technology Society

ORIGINAL ARTICLE

Impact of a Modified Needle Tip Geometry on Penetration Force as well as Acceptability, Preference, and Perceived Pain in Subjects with Diabetes

Laurence Hirsch, M.D., Michael Gibney, R.N., Julie Berube, Ph.D., John Manocchio, M.S.

~ 23% lower penetration force in bench testing, *in vitro*
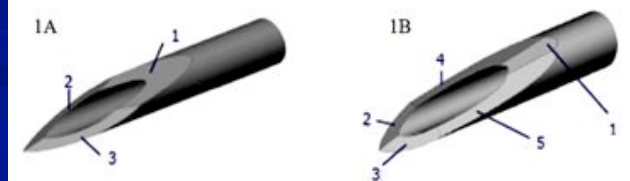
Research Related to *Teaching* Injection Technique

- Procedural vs. Declarative Knowledge
- Effect of Certainty on the Application of Knowledge
- Patient: Provider Communication
- Implications on Practice of Diabetes Educators

Procedural vs. Declarative Knowledge

- *Procedural Knowledge:* related to putting information into action.
  - Preparing and administering insulin
  - Treating hypoglycemia
  - Adjusting Insulin doses
- *Declarative Knowledge:* theoretical knowledge
  - Based on theory, rules and examples

Procedural vs. Declarative Knowledge

- Patient Knowledge as a whole *declines* over time, but procedural knowledge is remembered longer, especially if it becomes a routine activity.
- Education related to procedural knowledge has longer lasting effects than declarative knowledge.

Bruttomess, D. Diabetes Metabolism, 2006.

The Relationship between Certainty and Application of Knowledge

- Patients hesitate to use information that they are "uncertain" about or do not believe is correct.
- Patients use information that is incorrect, if they felt confident that it is correct
- Three years following a structured Diabetes Education Program
  - Overall knowledge decreased
  - Uncertain knowledge increased

Patient: Provider Communication

- Non-adherent patients felt their HCP did not properly explain the risks and benefits of insulin therapy.
- HCP's assess patient recall, comprehension of medication changes only 13% of the time.
- 40% of providers report discussing quality of life issues, but only 21% of patients remember this conversation.

Schillinger,D. Archives of Internal Medicine, 2003

Patient: Provider Communication

- Disconnect between HCP and Patient *Perceptions* regarding fears and difficulties with insulin injections.
  - 83% of HCP report discussions
  - 79% of patients report that their HCP *rarely or never* asks them about issues related to injections

Injection Impact Survey, AADE 2008

Effect of Education on Glycemic Control

- Peak effect of a structured diabetes program occurs at 4 months
- Effect remains significant, but declines until 12 month post-program[1]
- Duration of contact time was the *only* significant predictor of improved glycemic effect
  - 23.6 hours of contact time led to a 1% absolute decrease in A1C[2]

[1]Scain,SF et. Al., The Diabetes Educator, 2009
[2]Norris, S, et. Al., Diabetes Care, 2002

Implications of Research on Teaching Injection Technique

- **Injection** technique and knowledge should be assessed every 8 to 12 months
  - *Patients need to feel confident!* Incorrect information, believed to be true, requires an on-going educational effort to change.
  - Procedural information has a long lasting effect and requires *follow-up at each visit* to ensure proper application.
  - Assessing communication is essential.

Real World Examples

- Two Studies from Japan
- Takahasi, et. Al.
  - Reassessment of injection technique followed by an interactive tutorial
  - 4 months later, errors decreased by 58% and insulin dose declined significantly.

Effect of Re-education of Injection Technique Teaching: Japan

- Matsumura, et. Al.
  - Four months after reeducation, A1C levels improved from an average of 6.94% to 6.25%.
 - Decline in A1C varied according to quality of technique.

New Injection Recommendations: Pen Needle Lengths

- There has been a major shift towards shorter-length needles as studies proving their safety, efficacy and user preference have been published.
- 4, 5, and 6mm needles may be used by any adult patients, including obese ones.

Diabetes & Metabolism. 2010;36 (suppl.): S1-S29.   D. Hicks, et al. National Health Service, *The First UK Injection Recommendations*. London. October 2010.

AADE White Paper

Strategies for Insulin Injection Therapy in Diabetes Self-Management
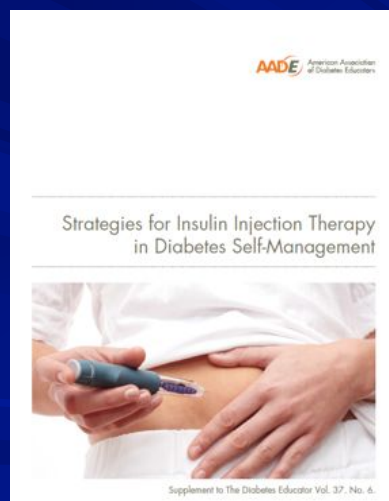
- Multidisciplinary expert panel proposed guidelines for insulin injection therapy.
- Purpose: To standardize education practice and help patients overcome obstacles to effective insulin injection therapy.

http://www.diabeteseducator.org/export/sites/aade/_resources/pdf/publications/AADE_MedEd_V2.pdf

AADE White Paper Summary

- "…4-5 mm pen needles enter the subcutaneous tissue with minimal risk of intramuscular injection and no additional leakage, even in obese patients."
- "Rotation of injection sites is critical to prevent lipohypertrophy…"
- "Children and Youth should use 4-6 mm needle."
- "Research shows that needle length should not be a concern in patients who are obese or overweight, with 4 to 5 mm pen needles comparable to longer needles in maintaining glycemic control, without adverse effects."

http://www.diabeteseducator.org/export/sites/aade/_resources/pdf/publications/AADE_MedEd_V2.pdf

Practical Tips

- Pens should be primed.

- Needles should be disposed of immediately after use.

- Patients should count slowly to 10 before withdrawing the needle.

- Shorter needles are safe and often better tolerated.

- Prescriptions should be specific; include needle gauge and size.

Davidson J. *Diabetes Metab.* 2010;36(suppl. 1)S2.
Frid A. *Diabetes Metab*. 2010;36(suppl. 1):S3-S18.

Tips for teaching insulin injection

Education/Counseling

- Assess patients belief system
- Correct misconceptions
- Reassess for knowledge, dosage, site and technique
- What to do if high or low blood glucose

REASSESS!!!

Technique

- Teach site selection and rotation
- Teach to change needles for each injection (especially pen needles)
- Teach re-suspension of mixed insulin
- Assess for lipohypertrophy
- Insulin storage

Translating the Research in Insulin Injection Technique: Implications for Practice

Purpose

Glucose variability leading to suboptimal glycemic control is common among people using injection therapies. Advanced technology and new studies have identified important issues related to injection technique: needle length and gauge, body mass index, skin and subcutaneous tissue thickness, adequate resuspension of cloudy insulins, leakage, choice of injection site and rotation, pinching a skinfold, and lipohypertrophy. All these issues can affect pain and bruising, insulin absorption, and blood glucose levels. The purpose of this article is to review current and past research regarding insulin injection therapy and to provide practical, translational information regarding injection technique, teaching/learning techniques specific to insulin administration, and implications for diabetes self-management education and support.

Conclusion

International injection recommendations for patients with diabetes have recently been published and have identified specific recommendations for health care professionals. This article provides an evidence-based translational and practical review of the research regarding injection technique and teaching/learning theory. Diabetes educators need to reevaluate how they provide instruction for the administration of insulin and other injectable medications. Research regarding skin and subcutaneous thickness reveals that shorter needles may be appropriate for the majority of patients regardless of body mass index. Periodic reassessment of injection technique, including suspension of cloudy insulins and

Rita Saltiel-Berzin, RN, MPH, CDE, CHES
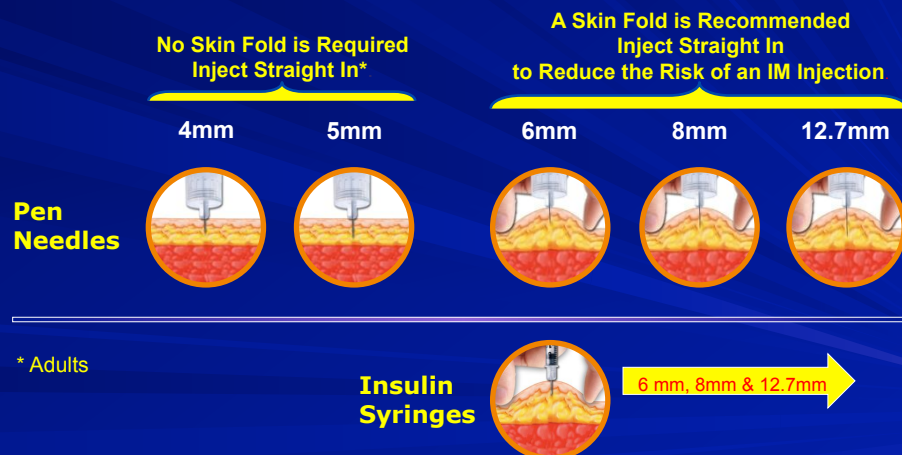Marjorie Cypress, PhD, C-ANP, CDE
Michael Gibney, RN, MA

From BD Medical–Diabetes Care, Department of Medical Affairs, Franklin Lakes, New Jersey (Ms Saltiel-Berzin and Mr Gibney), and ABQ Partners, Albuquerque, New Mexico (Dr Cypress).

DOI: 10.1177/0145721712455107

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Importance of Proper Injection Technique in Achieving Glycemic Control