

# Worldwide Injection Technique Study: Injecting Practices

## Introduction

Despite increased attention in both the clinical arena and in published literature<sup>1 2 3 4 5</sup>, the role injection technique in optimizing the efficacy of insulin therapy is still not accorded the importance it deserves. Diabetes nurses and observant patients have long known that the technique of injection is critical to the successful use of insulin, but the medical community at large and most insulin-injecting patients remain woefully unaware of the hows and whys of proper technique. Recent years have seen increased emphasis on intensive insulin therapy and on the critical role of blood glucose measurements, but still too few patients understand that correct insulin injection technique is just as important to good glucose control as the type and dose of insulin delivered.

From February, 2014 until June, 2015 the Insulin Injection Technique Questionnaire (ITQ) survey was conducted among 13,264 patients in 425 centers from 42 countries. All patients had diabetes and had been injecting insulin for at least 6 months. We have already described the participant population in an earlier paper<sup>6</sup> and here propose to review the data related to injecting practice. The key parameters addressed hereafter relate to number of injections/day, choice of injection site, use and characteristics of skin folds (pinch-up), dwell time of needle under the skin, needle reuse and injecting through clothing. We also addressed the issue of injection safety and disposal of used sharps.

Injections and fingersticks administered to patients with diabetes in health care settings present a risk of blood exposure to the injector as well as to other worker in potential contact with sharps, which could lead to transmission of bloodborne pathogens. More than one million needle stick injuries are estimated to occur in the European Union each year. Statistics from other regions show similar rates. The everyday activities of health care workers in diabetes put them at risk of such injuries.

Serious infections with more than 30 potentially dangerous pathogens, including hepatitis B and C and HIV, can occur from injuries with contaminated needles and lancets. Though seroconversion is rare, injuries are not. Every one of these injuries can lead to expensive testing and prophylactic treatments, as well as months of mental anguish.

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<sup>1</sup> Strauss K. Insulin injection techniques: Report from the 1<sup>st</sup> International Insulin Injection Technique Workshop, Strasbourg, France—June 1997. *Pract Diab Int* 1998 ;15:16-20.

<sup>2</sup> Partanen TM, Rissanen A. Insulin injection practices, *Pract Diabetes Int* 2000;17:252-254.

<sup>3</sup> Strauss K, De Gols H, Hannet I, Partanen TM, Frid A. A pan-European epidemiologic study of insulin injection technique in patients with diabetes. *Pract Diab Int* 2002;19:71-76.

<sup>4</sup> American Diabetes Association Resource Guide 2003: Insulin Delivery. *Diabetes Forecast* 2003;56:59-76.

<sup>5</sup> American Diabetes Association Position Statements: Insulin Administration. *Diabetes Care* 2004;27:S106-S107.

<sup>6</sup> Worldwide Injection Technique Study: Population Surveyed 2015.

## Methods and Materials

Our previous paper<sup>7</sup> described the methods, materials, centers and patients who participated in the study.

## Results

### Number of Injections/Day

<u>INJECTIONS/ DAY</u>	<u>%</u>	<u>N</u>
1	16.0	1523
2	26.0	2480
3	13.0	1240
4	33.7	3213
5	7.7	735
6	2.1	197
7	.7	70
>7	.7	71
<b>Total</b>	100.0	9529

### Injection Sites and their Care and Maintenance

Figure 1 shows the recommended injection sites.<sup>8 9 10 11 12</sup>

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<sup>7</sup> Worldwide Injection Technique Study: Population Surveyed 2015.

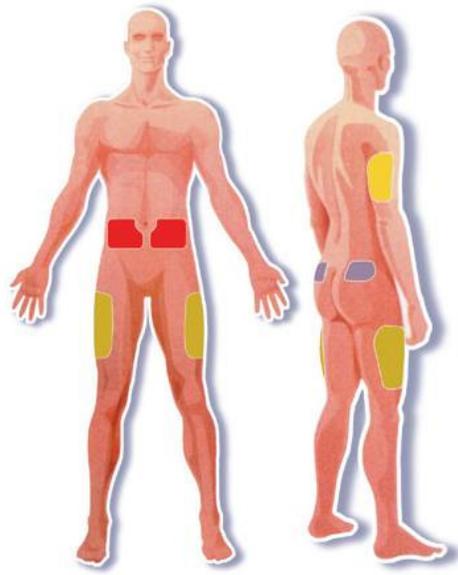
<sup>8</sup> Bantle JP, Neal L, Frankamp LM. Effects of the anatomical region used for insulin injections on glycaemia in type 1 diabetes subjects. *Diabetes Care* 1993;16:1592-1597.

<sup>9</sup> Frid A, Lindén B. Intraregional differences in the absorption of unmodified insulin from the abdominal wall. *Diabetic Medicine* 1992;9:236-239.

<sup>10</sup> Koivisto VA, Felig P. Alterations in insulin absorption and in blood glucose control associated with varying insulin injection sites in diabetic patients. *Annals of Internal Medicine* 1980;92:59-61.

<sup>11</sup> Annersten M, Willman A. Performing subcutaneous injections: a literature review. *Worldviews on Evidence-Based Nursing* 2005; 2:122-130.

<sup>12</sup> Vidal M, Colungo C, Jansà M. Actualización sobre técnicas y sistemas de administración de la insulina (I). [Update on insulin administration techniques and devices (I)]. *Av Diabetol* 2008;24:175-190.



The Abdomen was used by 90.9% of our patients, thigh by 43.0%, buttocks 13.8% and arm 31.9%. The percentages add to over 100 since many patients use more than one site. Table XX presents percentages for specific injecting zones or combinations of zones.

	Frequency	
	%	N
<b>Abdomen alone</b>	42.0	5365
<b>Thigh alone</b>	2.9	372
<b>Arm alone</b>	2.1	264
<b>Abdomen/Thigh</b>	16.6	2125
<b>Abdomen/Arm</b>	6.7	852
<b>Thigh/Arm</b>	2.8	358
<b>Abd/Thigh/Arm</b>	12.9	1648
<b>All 4</b>	7.8	996

### **Injecting Process**

Patients using pens were asked how long they leave the needle under the skin after the plunger has been completely pushed in.

**Table: Dwell Times after Pen Injection**

<b>Time</b>	<b>%</b>
< 5 sec	<b>18.6</b>
5 – 10 sec	<b>45.6</b>
> 10 sec	<b>31.9</b>
I'm not aware of how long	<b>3.9</b>

Patients were asked to perform a mock injection while the nurse observed the technique. One of the parameters checked was whether the patient lifted a skin fold and if so, was it lifted correctly and was it released appropriately. 63.7% of patients lifted a skin fold and 75.0% did it correctly. However less than half released the fold appropriately (option 3 in Table below).

**Table: Timing of release of Skin Fold**

<b>When released?</b>	<b>%</b>
Once the needle is in the skin	<b>18.5</b>
Once the insulin is totally injected	<b>33.5</b>
Once the insulin is injected and the needle is removed from the skin	<b>48.0</b>

## **Reuse of Injecting Devices**

About half of patients worldwide use their needle more than once. Pen users tend to reuse more than syringe users. There is huge variability across countries in this practice (data not shown).

**Table: Needle Reuse Data for Pen Needles and Syringes**

<b>Reuse Needle</b>	<b>% Pens</b>	<b>% Syringes</b>
Yes	<b>55.8</b>	<b>38.8</b>
No	<b>44.2</b>	<b>61.2</b>

There is also a huge amount of variability in terms of the times a needle is used. Most reuse is less than 5 times, but up to 30% of reusers use the needle 6 times or more.

**Table: Frequency of Reuse of Pen Needles**

Times	% Pens	% Syringes
2 times	30.7	35.4
3 to 5 times	39.7	44.0
6 to 10 times	16.0	11.4
More than 10 times	13.6	9.2

**Table: Reasons for Reuse**

Reasons	% Pens	% Syringes
Because I did not have another pen needle available	9.2	14.5
To save money	23.3	38.4
To prevent excess waste (environmental concern)	6.8	6.6
For convenience	41.2	26.1

The following groups tend to reuse more frequently than others: males, T2DM patients, adults (more than children or adolescents) and those taking multiple daily injections. Lipohypertrophy (LH) is more frequent in needle reusers but reuse is less powerful a factor than incorrect rotation, smaller injection areas and longer time on insulin in multi-variant analysis. Use of the 4 mm needle is associated with less needle reuse and less LH. Pain is also associated with needle reuse and seems to increase as a function of the number of times the needle is reused. Needle reuse seems to be lower with 32 G needles (of any length) for reasons which are not understood. Reuse is associated with unexplained hypoglycemia, glycemic variability, injecting through clothes, skipping injections, bleeding, hyperglycemia, incorrectly rotating sites, less frequent fingersticks and slightly higher HbA1c levels; although a causative relationship with any of these has not been established. Reuse is not associated with leakage from the skin or routine hypoglycemic reactions. Interestingly, reuse is less frequent when General Nurses, Diabetes Nurses or Diabetes Educator gave injection training than when Doctors,

Pharmacists or representatives of Industry did it. (Data not shown for above but all differences significant at  $p < 0.05$ ).

## Reconstituting Cloudy Insulins

Patients were asked if they used cloudy insulin (NPH, N or pre-mixed insulin) and if so, how many times to they roll or tip to reconstitute it before injecting. 65.5% use cloudy insulins.

**Table: Times vial or cartridge of cloudy insulin rolled or tipped**

Number rolls/tips	%
2	7.3
3	7.3
4	5.5
5	16.1
10	34.6
15	4.4
20	10.2

Patients were asked if they ever skipped injections and if so, how often and why. 44.7% said they skipped injections.

**Table: Frequency of Skipping Injections**

Frequency	%
Often (several times a week)	8.5
Sometimes (several times a month)	35.9
Almost never (several times a year)	55.6

The main reasons given for skipping injections were: I forgot (51.6%); I didn't eat (8.8%) and My glucose was too low (7.2%).

## Storage of Unused and Used Insulins

Patients were asked where they stored their insulin before opening it and 88.6% reported in the refrigerator. After opening it, 43.0% continued to store it in the fridge. Of these only 56.3% let it warm up to room temperature before injecting it. The 43.7% who injected it cold were at higher risk of having painful injections.

		Warm Up	
		Yes	No
Store Cold after Open	Yes	25.9%	26.7%
	No	30.7%	16.8%

## Disinfection and Injection through Clothing

Patients were asked if they disinfected the skin before injections and 56.8% said they did. (Of vial users, 28.8% reported disinfecting the vial cap before drawing up their insulin.) Only 8.0% of our patients injected through clothing.

## Needlestick Injuries

Patients were asked if there were any persons in the immediate surroundings who might accidentally get stuck with sharps and 14.7% said yes. They were then asked to identify these persons.

Who?	%
Children	<b>23.4</b>
Other family members (e.g. spouse)	<b>39.5</b>
Nurse or other professional	<b>4.6</b>
House keeper or rubbish collector	<b>8.2</b>

They were then asked if any sharps injuries had already occurred and 8.6% said yes. Finally they were asked whether any risk factors for those around them existed.

Why?	%
I don't use devices that prevent injuries to others (safety devices)	<b>22.9</b>
I don't have appropriate disposal containers for my used sharps	<b>35.5</b>
Used sharps are sometimes left in places where others might get stuck	<b>19.1</b>
I'm positive for hepatitis or another blood-borne illness	<b>3.7</b>

## Disposal of Used Sharps

Patients were asked how they dispose of their used sharps.

<b>Where Dispose?</b>	<b>%</b>
Into a container specially made for used sharps	<b>20.7</b>
Into a home container such as an empty bottle	<b>23.0</b>
Into the rubbish with the cap on	<b>48.1</b>
Into the rubbish without recapping	<b>6.9</b>
I clip off the needle and it stays in the clipper	<b>1.3</b>

Patients were then asked what the ‘final resting place’ was for their collection of used needles, i.e. where did they take the container once it was full.

<b>What do you do with the waste?</b>	<b>%</b>
Put it into the rubbish	<b>40.3</b>
Take it to a pharmacist	<b>12.8</b>
Take it to a doctor’s office	<b>6.3</b>
Take it to a laboratory	<b>0.4</b>
Take it to the hospital or clinic	<b>22.1</b>
Take it to a local deposit or collection service	<b>11.0</b>
None of the above	<b>7.1</b>

## **Discussion and Best Practice**

In the last two decade the practice of insulin injection been approached in a scientific fashion. Several studies have suggested that correct performance of injections may be as important to good glucose control as the type and dose of insulin delivered.<sup>13 14 15 16</sup>(67-70) In our evaluation of the results above we will also include a summary of best practice regarding the theme discussed.

### **Absorption by Site and IM Injections**

Absorption characteristics change depending on the type of insulin given. Abdominal site subcutaneous (SQ) injection of soluble rapid acting (‘regular’) insulin results in 29%

<sup>13</sup> Thow JC, Johnson AB, Fulcher G, Home PD. Different absorption of Isophane (NPH) insulin from subcutaneous and intra-muscular sites suggests a need to reassess recommended insulin injection technique. *Diabetic Medicine* 1990;7: 600-602.

<sup>14</sup> Thow JC, Home PD. Insulin injection technique: depth of injection is important. *BMJ* 1990; 301:3-4.

<sup>15</sup> Engstrom L. Technique of insulin injection: is it important? *Practical Diabetes* 1994;11: 39.

<sup>16</sup> Kolendorf K, Bojsen J, Deckert T. Clinical factors influencing the absorption of 125 I-NPH insulin in diabetic patients. *Horm Metabl Res* 1983;15:274-278.

lower post-prandial plasma glucose concentrations than thigh site injections.<sup>17 18</sup> This effect is due to faster absorption from the abdomen. Furthermore, the use of inappropriate sites and techniques may modify insulin absorption parameters leading to an uncoupling of maximum glucose load and peak insulin effect. This can lead to both unexpected hyperglycaemia as well as an increased risk of nocturnal hypoglycaemia.<sup>19 20 21 22 23 24 25</sup> Analogues can be given at any injection site with similar uptake and action (PK-PD), but human insulins (Regular, NPH) vary substantially – absorption being fastest from the abdomen and from the buttock, slowest.

Both human insulins and analogues have different absorption profiles when deposited into muscle. In 1988 Frid<sup>26</sup> showed that human soluble insulin were absorbed faster from muscle compared to fat tissue, especially when the muscles were exercised. Vaag<sup>27</sup> showed the same for NPH insulins in 1990. Thow<sup>28</sup> has shown that a significantly greater amount of infused glucose was required during a glucose clamp to maintain euglycemia after IM injection than after SC injection.

In contrast the rapid-acting insulin analogue lispro seems to have the same speed of absorption from fat tissue and resting muscle tissue.<sup>29</sup> There are no published studies for modern long-acting analogues but clinical experience and a case report<sup>30</sup> make it probable that long-acting analogues are absorbed faster from muscle compared to fat tissue.

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<sup>17</sup> Strauss K. Insulin injection techniques. *Practical Diabetes International* 1998;15:181-184.

<sup>18</sup> Bantle J, Neal L, Frankamp L. Effects of the anatomical region used for insulin injections on glycemia in Type I diabetes subjects. *Diabetes Care* 1993;16:1592-1597.

<sup>19</sup> Galloway J, Spradlin C, Nelson R, Wentworth S, Davidson J, Swarner J. Factors influencing the absorption, serum insulin concentration, and blood glucose responses after injections of regular insulin and various insulin mixtures. *Diabetes Care* 1981;4:366-376.

<sup>20</sup> Sindelka G, Heinemann L, Berger M, Frenck W, Chantelau E. Effect of insulin concentration, subcutaneous fat thickness and skin temperature on subcutaneous insulin absorption in healthy subjects. *Diabetologia* 1994;37:377-380.

<sup>21</sup> Henriksen JE, Djurhuus MS, Vaag A, Thye-Ronn P, Knudsen D, Hother-Nielsen O, Beck-Nielsen H. Impact of injection sites for soluble insulin on glycaemic control in Type 1 (insulin-dependent) diabetic patients treated with a multiple insulin injection regimen. *Diabetologia* 1993;36:752-758.

<sup>22</sup> Henriksen J, Vaag A, Ramsgaard Hansen I, Lauritzen M, Djurhuus M, Beck-Nielsen H. Absorption of NPH (Isophane) insulin in resting diabetic patients: evidence for subcutaneous injection in the thigh as the preferred site. *Diabetic Medicine* 1991;8: 453-457.

<sup>23</sup> Koivisto V, Felig P: Alterations in insulin absorption and in blood glucose control associated with varying insulin injection sites in diabetic patients. *Ann Intern Med* 1989;92:59-61.

<sup>24</sup> De Meijer PH, Lutterman JA, van Lier HJ, van't Laar A: The variability of the absorption of subcutaneously injected insulin: effect of injection technique and relation with brittleness. *Diabetic Medicine* 1990;7:499-505.

<sup>25</sup> Berger M, Cüppers HJ, Hegner H, Jörgens V, Berchtold P. Absorption Kinetics and Biologic Effects of Subcutaneously Injected Insulin Preparations. *Diabetes Care* 1982;2: 77-91.

<sup>26</sup> Frid Anders, Gunnarson R, Guntner P, Linde P. Effects of accidental intramuscular injection on insulin absorption in IDDM. *Diabetes Care* 11, 1988:41-45.

<sup>27</sup> Vaag A et al. Variation in absorption of NPH insulin due to Intramuscular injection. *Diabetes Care* Vol 13, No 1, Jan 1990, 74-76.

<sup>28</sup> Thow J, Johnson A, Fulcher G, Home P. Different absorption of Isophane (NPH) Insulin from subcutaneous and intramuscular sites suggests a need to reassess recommended insulin injection technique. *Diabetic Medicine*; 7: 3 April 1990, 600-602.

<sup>29</sup> Rave K et. al. Intramuscular versus subcutaneous injection of soluble and lispro insulins: Comparison of metabolic effects in healthy subjects. *Diabet Med* 1998;15:747-751.

<sup>30</sup> Karges B et. al. Early hypoglycemia after accidental intramuscular injection of insulin glargine. *Diabetic Medicine* 2005;22:1444-45.

Hence IM injections, especially into working muscle, can distort absorption of possibly all of the insulins and thus de-couple maximum glucose load from peak insulin activity. This can lead to poor glycemic control, including excessive glycemic variability. When this happens IM injections may lead to frequent and unexplained hypoglycemia according to a number of studies.<sup>31 32 33</sup>

Patients may be unaware that they are injecting IM. Thow<sup>34</sup> has shown that IM injections are no more uncomfortable than SC. It is likely that many patients have been unwittingly injecting IM for years without recognizing it – especially with the newer, thinner needles.

Hirsch<sup>35</sup> has recently shown that gender, BMI and body site are the most important factors impacting SC fat thickness. Women have approximately 5mm more fat than men for the same BMI. Hence, men are at much higher risk for IM injections than women (2-4X). The lower the BMI the higher the IM risk. Body site is also critical. Injections in the thigh (closely followed by arm) have 2 to 4-fold higher IM risk at any length needle than injections given in the abdomen. Thigh and abdomen are, of course, the most common sites patients use.

There is a general paucity of studies regarding insulin absorption from deep or superficial parts of subcutaneous fat tissue. However Frid<sup>36</sup> showed no difference in absorption of soluble human insulin from deep compared to superficial injection in patients with T1DM. A more recent study has also suggested that the depth of insulin injection (shallow versus deep SC tissue) does not affect the absorption or pharmacokinetics of insulin<sup>37</sup>.

## **GLP-1 agents**

Pending further studies, patients who inject GLP-1 agents should follow the recommendations already established for insulin injections with regards to needle length and site rotation.<sup>38</sup> GLP-1 agents may be given at any of the usual injection sites as the pharmacokinetics do not appear to be site-specific.<sup>39</sup>

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<sup>31</sup> Karges B et al. Early hypoglycaemia after accidental intramuscular injection of insulin glargine. *Diabetes Med* 2005 Oct; 22(10): 1444-5.

<sup>32</sup> Frid Anders, Gunnarson R, Guntner P, Linde P. Effects of accidental intramuscular injection on insulin absorption in IDDM. *Diabetes Care* 11, 1988:41-45.

<sup>33</sup> Spraul M, Chantelau E, Koumoulidou J, Berger M. Subcutaneous or nonsubcutaneous injection of insulin, *Diabetes Care* 1988; 11: 733-6.

<sup>34</sup> Thow J, Home P. Insulin Injection Technique: *BMJ* Vol 301; July 1990; 3-4.

<sup>35</sup> Hirsch L, Byron K, Gibney M. Intramuscular risk at insulin injection sites-measurement of the distance from skin to muscle and rationale for shorter-length needles for subcutaneous insulin therapy. *Diab Tech Ther* 2014;16(12):867-873.

<sup>36</sup> Frid et al., Intraregional Differences in the Absorption of Unmodified Insulin from the Abdominal Wall *Diabetic Medicine* 1992; 9: 236-239.

<sup>37</sup> de la Peña A, Ma X, Reddy S, Ovalle F, Bergenstal RM, Jackson JA. Application of PK/PD modeling and simulation to dosing regimen optimization of high-dose human regular U-500 insulin. *J Diabetes Sci Technol*. 2014, 8:821-9.

<sup>38</sup> . Byetta Pen User Manual. Eli Lilly and Company, 2007.

<sup>39</sup> Calara F, Taylor K, Han J, Zabala E, Carr EM, Wintle M, Fineman M. A randomized, open-label, crossover study examining the effect of injection site on bioavailability of exenatide (synthetic exendin-4). *Clin Ther* 2005;27:210-5.

## Proper use of Pens

After pushing the thumb button completely in, patients should count slowly to 10 before withdrawing the needle in order to get the full dose and prevent the leakage of medication.

<sup>40 41 42 43 44 45</sup> Counting past 10 may be necessary for higher doses. Counting only to 5 may be acceptable for lower doses. Patients may find the right time for themselves by trial and error, using leakage of insulin as a guide.

Pens and cartridges are for a single patient and should **never** be shared between patients due to the risk of biological material from one patient being drawn into the cartridge and then injected into another person. <sup>46 47</sup> Needles should be disposed of immediately after use instead of being left attached to the pen. This prevents the entry of air (or other contaminants) into the cartridge as well as the leakage of medication. Leakage of medication can affect dose accuracy. <sup>48 49 50 51 52</sup> Pen needles should be used only once.

<sup>53 54 55 56 57 58 59 60</sup>

## Proper use of Syringes

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<sup>40</sup> King L. Subcutaneous insulin injection technique. *Nurs Stand.* 2003;17:45-52.

<sup>41</sup> Ginsberg BH, Parkes JL, Sparacino C. The kinetics of insulin administration by insulin pens. *Horm Metab Research* 1994;26:584-587.

<sup>42</sup> Annersten M, Frid A. Insulin pens dribble from the tip of the needle after injection. *Pract Diab Int* 2000;17:109-111.

<sup>43</sup> Jamal R, Ross SA, Parkes JL, Pardo S, Ginsberg BH. Role of injection technique in use of insulin pens: prospective evaluation of a 31-gauge, 8mm insulin pen needle. *Endocr Pract* 1999;5:245-50.

<sup>44</sup> Rissler J, Jørgensen C, Rye Hansen M, Hansen NA. Evaluation of the injection force dynamics of a modified prefilled insulin pen. *Expert Opin Pharmacother* 2008;9:2217-22.

<sup>45</sup> Broadway CA. Prevention of insulin leakage after subcutaneous injection, *Diabetes Educator* 1991;17:90.

<sup>46</sup> Le Floch JP, Herbreteau C, Lange F, Perlemuter L. Biologic material in needles and cartridges after insulin injection with a pen in diabetic patients. *Diabetes Care* 1998;21:1502-1504.

<sup>47</sup> Bärtsch U, Comesse C, Wetekam B. Insulin pens for treatment of diabetes (article in German). *Ther Umsch* 2006;63:398-404.

<sup>48</sup> Annersten M, Frid A. Insulin pens dribble from the tip of the needle after injection. *Pract Diab Int* 2000;17:109-111.

<sup>49</sup> Byetta Pen User Manual. Eli Lilly and Company, 2007.

<sup>50</sup> Bärtsch U, Comesse C, Wetekam B. Insulin pens for treatment of diabetes (article in German). *Ther Umsch* 2006;63:398-404.

<sup>51</sup> Jamal R, Ross SA, Parkes JL, Pardo S, Ginsberg BH. Role of injection technique in use of insulin pens: prospective evaluation of a 31-gauge, 8mm insulin pen needle. *Endocr Pract* 1999;5:245-50.

<sup>52</sup> Chantelau E, Heinemann L, Ross D. Air Bubbles in insulin pens. *Lancet* 1989;334:387-388.

<sup>53</sup> Strauss K, De Gols H, Letondeur C, Matyjaszczyk M, Frid A. The second injection technique event (SITE), May 2000, Barcelona, Spain. *Pract Diab Int* 2002;19:17-21.

<sup>54</sup> Strauss K. Insulin injection techniques: Report from the 1<sup>st</sup> International Insulin Injection Technique Workshop, Strasbourg, France—June 1997. *Pract Diab Int* 1998 ;15:16-20.

<sup>55</sup> Danish Nurses Organization. Evidence-based Clinical Guidelines for Injection of Insulin for Adults with Diabetes Mellitus, 2<sup>nd</sup> edition, December 2006.

<sup>56</sup> Association for Diabetescare Professionals (EADV). Guideline: The Administration of Insulin with the Insulin Pen. September 2008.

<sup>57</sup> Chantelau E, Lee DM, Hemmann DM, Zipfel U, Echterhoff S. What makes insulin injections painful? *Brit Med J* 1991;303: 26-27.

<sup>58</sup> Schuler G, Pelz K, Kerp L. Is the reuse of needles for insulin injection systems associated with a higher risk of cutaneous complications? *Diab Res Clin Pract* 1992;16:209-212.

<sup>59</sup> Maljaars C. Scherpe studie naalden voor eenmalig gebruik [Sharp study needles for single use] *Diabetes and Levery* 2002;4:36-37.

<sup>60</sup> Torrance T. An unexpected hazard of insulin injection. *Pract Diab Int* 2002;19:63.

There are regions of the world where significant numbers of patients still use syringes as their primary injecting device. Even in countries where pens are used for most home injections, syringes are still often used in health care settings. In areas where U-40 insulin and U-100 are still on the market together (e.g. Asia, Africa) or where U-500 is used in addition to U-100 (e.g. UK and USA) careful attention must be paid to using the appropriate syringe for each concentration. There is no medical rationale for using syringes with detachable needles for insulin injection. Permanently-attached needle syringes offer better dose accuracy, smaller cannula diameters and reduced dead space, allowing the patient to mix insulins if needed. There are currently no syringes with a needle < 6mm in length, due to incompatibility with certain insulin vial stoppers.<sup>61</sup>

## Reconstituting Cloudy Insulins

German studies<sup>62 63 64 65 66</sup> have highlighted the previously unappreciated problem of inadequate suspension of cloudy insulins. Some longer-acting insulins contain a predetermined ratio of either crystalline insulin and solvent or crystalline insulin and rapid-acting soluble insulin. The crystalline elements must be resuspended prior to each injection, however patients may be unaware of how best to do this. Inadequate resuspension of NPH insulin before pen injection is common among patients treated with insulin. This leads to varying concentrations of NPH and unpredictable clinical responses to it.

Jehle<sup>67</sup> showed that NPH resuspension was only achieved after mixing (tipping or rolling) 20 times immediately before injection. Patients however find this procedure annoying. He found that fewer than 1 in 10 did it. Brown<sup>68</sup> found similar results and concluded that significant inappropriate dosing resulted from inadequate resuspension.

Kaiser<sup>69</sup> found that the amount of mixing needed to resuspend NPH varies according to manufacturer. Cartridges with the heaviest and highest number (3) of 'bullets' inside took less mixing. However cartridges have only 1 or 2 lighter glass 'bullets' inside and these take much more effort to resuspend. If resuspension is not done properly doses of NPH are well below what is anticipated by the patient. Kaiser found that all cartridges performed well when used according to the instructions for use, i.e. with 20× mixing.

## Insulin Storage

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<sup>61</sup> Caffrey RM. Diabetes under Control: Are all Syringes created equal? Am J Nursing 2003;103:46-49.

<sup>62</sup> King L. Subcutaneous insulin injection technique. Nurs Stand. 2003;17:45-52.

<sup>63</sup> Jehle PM, Micheler C, Jehle DR, Breitig D, Boehm BO. Inadequate suspension of neutral protamine Hagedorn (NPH) insulin in pens. Lancet 1999;354:1604-1607.

<sup>64</sup> Brown A, Steel JM, Duncan C, Duncun A, McBain AM. An assessment of the adequacy of suspension of insulin in pen injectors. Diab Med 2004;21:604-608.

<sup>65</sup> Nath C. Mixing insulin: shake, rattle or roll? Nursing 2002;32:10.

<sup>66</sup> Springs MH. Shake, rattle, or roll?... "Challenging traditional insulin injection practices" Am J Nursing 1999;99:14.

<sup>67</sup> Jehle PM, Micheler C, Jehle DR, Breitig D, Boehm BO. Inadequate suspension of neutral protamine Hagedorn (NPH) insulin in pens. Lancet. 1999;354(9190):1604-1607.

<sup>68</sup> Brown A, Steel JM, Duncan C, Duncun A, McBain AM. An assessment of the adequacy of suspension of insulin in pen injectors. Diabet Med. 2004;21(6):604-608.

<sup>69</sup> Kaiser P, Maxeiner S, Weise A, Nolden F, Borck A, Forst T, Pfützner A. Assessment of the mixing efficiency of neutral protamine Hagedorn cartridges. J Diabetes Sci Technol. 2010 May 1;4(3):652-7.

Most insulin storage data comes from the manufacturers, with few independent studies available. Store insulin in current use (pen, cartridge or vial) at room temperature (for a maximum of one month after initial use, and within expiry date). Store back up insulin bottles in an area of the refrigerator where freezing is unlikely to occur.<sup>70 71</sup> Unlike syringe users, the pen user cannot ‘see the insulin going in’ when injecting. Obstruction of flow with pens is rare but, when it happens, can have serious consequences: patients may think they got their dose when they didn’t. Therefore it is recommended to prime pens (observing at least a drop at the needle tip) before the injection to ensure there is unobstructed flow and to clear needle dead space. Once flow is verified, the desired dose should be dialed and the injection administered.<sup>72 73</sup>

## Dwell Times

Patients should be instructed to inject slowly and ensure that the plunger (syringe) or thumb button (pen) has been fully depressed.<sup>74</sup> When using a pen, they should wait another 10 seconds after dose delivery before removing the needle in order to avoid leakage/reflux; this ensures full delivery of the injected dose.<sup>75</sup>

## Skin Folds

Pinching up the skin is the one method that has been documented by computerized tomography (CT) scan and ultrasonography to increase the chance of subcutaneous injection. If one performs a pinch-up, it should be made with 2 fingers (thumb and index). The fold should be maintained throughout the injection, and 5-10 seconds afterwards, before removing the needle.<sup>76</sup>

Nevertheless, even a pinch-up may not protect children from intra-muscular injections if they use 8 mm needles (which are the shortest currently available in syringes). Polak<sup>77</sup> has shown however that a lifted skin fold does not always eliminate the risk of an IM injection, especially in younger thinner children and when using these longer needles. Intra-muscular injection occurred more frequently in boys and correlated with lower percentile of BMI and shorter distances from skin surface to muscle fascia, with or without a skin fold. A second study<sup>78</sup>, found that the use of 8mm needles in fifty thin to

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<sup>70</sup> Ahern J, Mazur ML. Site rotation. *Diabetes Forecast* 2001;54:66-68.

<sup>71</sup> Perriello G, Torlone E, Di Santo S, Fanelli C, De Feo P, Santusano F, Brunetti P, Bolli GB. Effect of storage temperature on pharmacokinetics and pharmacodynamics of insulin mixtures injected subcutaneously in subjects with type 1 (insulin-dependent) diabetes mellitus. *Diabetologia* 1988;31:811 -815.

<sup>72</sup> Bohannon NJ. Insulin delivery using pen devices. Simple-to-use tools may help young and old alike. *Postgraduate Medicine* 1999;106:57-58.

<sup>73</sup> Dejgaard A, Murmann C. Air bubbles in insulin pens. *The Lancet* 1989;334:871.

<sup>74</sup> Ginsberg BH, Parkes JL, Sparacino C. The kinetics of insulin administration by insulin pens. *Horm Metab Research* 1994;26:584-587.

<sup>75</sup> Annersten M, Frid A. Insulin pens dribble from the tip of the needle after injection. *Practical Diabetes International* 2000;17:109-111.

<sup>76</sup> Strauss K. Insulin injection techniques: Report from the 1<sup>st</sup> International Insulin Injection Technique Workshop, Strasbourg, France—June 1997. *Pract Diab Int* 1998 ;15:16-20.

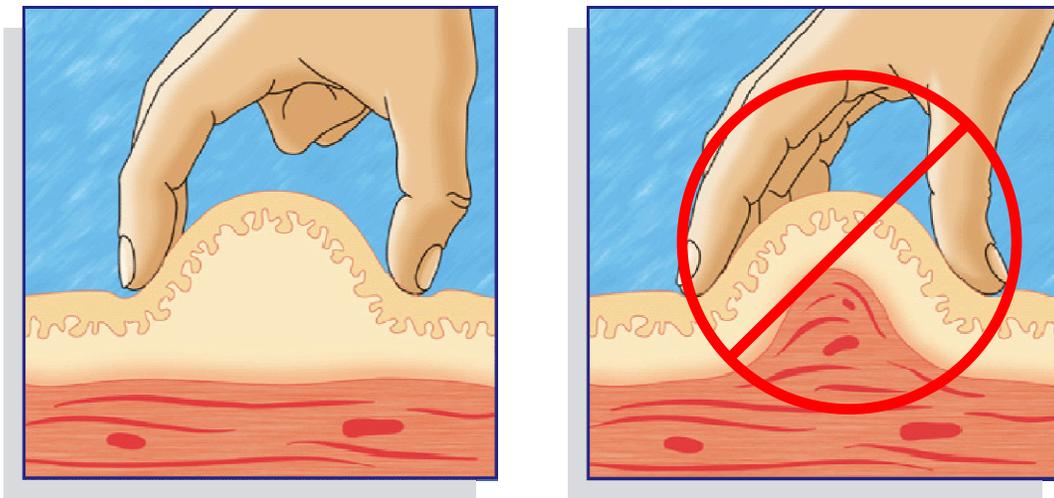
<sup>77</sup> Polak M, Beregszaszi M, Belarbi N, et al. Subcutaneous or intra-muscular injections of insulin in children: Are we injecting where we think we are? *Diabetes Care* 1996;19(12):1434-1436.

<sup>78</sup> Tubiana-Rufi N, Belarbi N, Du Pasquier-Fediaevsky L, Polak M, Licha-Munz G, Delcroix C, Hassan M, Czernichow P. Reduction of the risk of intra-muscular insulin injection with the 8 mm length needles in thin diabetic children. *Diabetologia* 1998;41:A 247.

normal children, all of whom used a pinch-up, significantly reduced but by no means eliminated the risk of intra-muscular injections. Thus needles even shorter than 8 mm must be used in children, which calls into question the use of syringes in this population.

The use of the 5mm needle in adults who do not use a pinch up should not be a matter of concern, unless the individual is very thin (e.g. BMI<18 kg/m<sup>2</sup>). In such cases a change to the gluteal region (where there are almost always abundant fat layers) as primary injection site, or a switch back to the 8mm needle using the pinch-up technique should be considered.

Skin folds are essential when the presumed distance from skin surface to the muscle is less than the length of the needle. Lifting a skin fold is an easy and effective means for ensuring SC injections. All patients should be taught the correct technique for lifting a skin fold from the onset of insulin therapy. A proper skin fold is made with the thumb and index finger (possibly with the addition of the middle finger). Lifting the skin by using the whole hand risks lifting muscle with the SC tissue and can lead to IM injections. The figure below shows correct (left) and incorrect (right) ways of performing the skin fold.<sup>79</sup>



The skin fold should not be squeezed so tightly that it causes skin blanching or pain. Lifting a skin fold in the abdomen and thigh is relatively easy (except in very obese tense abdomens), but it is more difficult to do in the buttocks (where it is rarely needed) and is virtually impossible (for patients who self-inject) to perform properly in the arm. The optimal sequence should be: 1) make skin fold; 2) inject insulin slowly; 3) leave the needle in the skin for 10 seconds (when injecting with a pen); 4) withdraw needle from the skin; 5) release skin fold; 6) dispose of used needle safely.

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<sup>79</sup> Strauss K. Insulin injection techniques. Practical Diabetes International 1998;15:181-184.

## Disinfection of Sites

Injections should be given in a clean site using clean hands.<sup>80</sup> The site should be disinfected when found to be unclean or if the patient is in a setting where infections can be easily spread (e.g. hospital or nursing home) Disinfection of the site is usually not required outside the hospital or nursing home setting.<sup>81 82 83 84 85</sup> If alcohol is used to clean the site, the skin must be allowed to dry completely before the injection is administered.<sup>86 87</sup>

## Safety Needles

The everyday work of healthcare workers (HCW) puts them at risk of serious infections with more than 30 potentially dangerous pathogens, including hepatitis B, hepatitis C and HIV, through injuries with contaminated needles. More than one million needle stick injuries are estimated to occur in the European Union each year.<sup>88</sup> Sharp devices used in hospital and other health care institutions represent a risk for the transmission of blood-borne pathogens to the user in the event of a needle stick injury (NSI) or muco-cutaneous blood exposure.<sup>89</sup> This risk can extend as well as to 'downstream' workers (cleaning personnel, rubbish removers, incinerators, as well as to the general public) if they receive an accidental NSI or muco-cutaneous blood exposure.<sup>90</sup> Studies have shown that the incidence of NSI among HCW giving injections to patients with diabetes (predominately insulin) is just as high, or higher, than workers in other departments or wards.<sup>91 92</sup> Studies have shown that patients with diabetes have sero-prevalence rates of blood-borne pathogens as high, or higher, than patients with other disease states.<sup>93 94 95</sup>

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<sup>80</sup> Gorman KC. Good hygiene versus alcohol swabs before insulin injections (Letter). *Diabetes Care* 1993;16:960-961.

<sup>81</sup> Association for Diabetescare Professionals (EADV). Guideline: The Administration of Insulin with the Insulin Pen. September 2008.

<sup>82</sup> Le Floch JP, Herbreteau C, Lange F, Perlemuter L. Biologic material in needles and cartridges after insulin injection with a pen in diabetic patients. *Diabetes Care* 1998;21:1502-1504.

<sup>83</sup> McCarthy JA, Covarrubias B, Sink P. Is the traditional alcohol wipe necessary before an insulin injection? Dogma disputed (Letter). *Diabetes Care* 1993;16:402.

<sup>84</sup> Schuler G, Pelz K, Kerp L. Is the reuse of needles for insulin injection systems associated with a higher risk of cutaneous complications? *Diab Res Clin Pract* 1992;16:209-212.

<sup>85</sup> Swahn Å. Erfarenheter av 94000 osterilt givna insulininjektioner (Experiences from 94000 insulin injections given without skin swab). *Sv Läkaresällskapets Handlingar Hygiea* 1982;92:160(30).

<sup>86</sup> McCarthy JA, Covarrubias B, Sink P. Is the traditional alcohol wipe necessary before an insulin injection? Dogma disputed (Letter). *Diabetes Care* 1993;16:402.

<sup>87</sup> Swahn Å. Erfarenheter av 94000 osterilt givna insulininjektioner (Experiences from 94000 insulin injections given without skin swab). *Sv Läkaresällskapets Handlingar Hygiea* 1982;92:160(30).

<sup>88</sup> EU Commission for Employment, Social Affairs and Inclusion, New legislation to reduce injuries for 3.5 million healthcare workers in Europe, 8<sup>th</sup> March 2010.

<sup>89</sup> Perry J, Parker G, Jagger J EPINet Report: 2004 Percutaneous Injury Rate. International Healthcare Worker Safety center, August 2007 (<http://healthsystem.virginia.edu/internet/safetycenter/>)

<sup>90</sup> Philippe Kiss, MD; Merc de Meester, MD; Lutgart Braeckman, MD, PhD; Needle stick Injuries in Nursing Homes: The Prominent Role of Insulin Pens, *Infect Control Hosp Epidemiol* 2008; 29:1192-1194

<sup>91</sup> Lee JM, Botteman MF, Nicklasson L, Cobden D, Pashos CL. Needle stick injury in acute care nurses caring for patients with diabetes mellitus: a retrospective study. *Curr Med Res Opin.* 2005;21(5):741-747.

<sup>92</sup> Costigliola V, Frid A, Letondeur C, Strauss K. Needlestick injuries in European nurses in diabetes. *Diabetes Metab.* 2012 Jan;38 Suppl 1:S9-14.

<sup>93</sup> Demir M, Serin E, Göktürk S, Ozturk NA, Kulaksizoglu S, Yılmaz U. The prevalence of occult hepatitis B virus infection in type 2 diabetes mellitus patients. *Eur J Gastroenterol Hepatol.* 2008 Jul;20(7):668-73.

<sup>94</sup> Simó R, Hernández C, Genescà J, Jardí R, Mesa J. High prevalence of hepatitis C virus infection in diabetic patients. *Diabetes Care.* 1996 Sep;19(9):998-1000.

Safety needles should be recommended whenever there is a risk of a contaminated needle stick injury (e.g. in hospital). Since most safety mechanisms will not protect against needle sticks through skin folds the use of shorter needles without a skin fold is recommended. If an IM injection is still a risk, using an angled approach (rather than a skin fold) is preferable.

Safety –engineered devices play a critical role in protecting injectors and downstream workers. Nurses and other health care workers at risk must receive appropriate education and training in how to minimize risk by following optimal injection techniques, using available safety devices, and wearing protective clothing (e.g., gloves).<sup>96</sup>

## **Disposal of injecting material**

Every country has its own regulations regarding the disposal of contaminated biologic waste. Of note in this study is the fact that more than half of used sharps go into the rubbish, with nearly 7% not even having the minimum protection of a cap. These ‘naked needles’ pose an imminent threat to anyone who comes near the rubbish, for example family members, house cleaners, rubbish collectors or those operating incinerators or frequenting dumps.

Options for discarding a used needle, in order of preference, are: 1) into a container especially made for used needles/syringes; 2) if not available, into another puncture-proof container such as a plastic bottle.

Options for final disposal of the container, in order of preference, are to take it: 1) to a Health Care facility (e.g. hospital); 2) to another Health Care provider (e.g. laboratory, pharmacist, doctor’s office). Under no circumstance should sharps material be disposed of into the public trash or rubbish system. All stakeholders (patients, HCPs, pharmacists, community officials and manufacturers) bear a responsibility (both professional and financial) for ensuring proper disposal of used sharps.

All HCPs and patients should be aware of local regulations. Legal and societal consequences of non-adherence should be reviewed.<sup>97</sup> (91) Proper disposal should be taught to patients from the beginning of injection therapy and reinforced throughout.<sup>98</sup> (92) Potential adverse events to the patients’ family (e.g. needlestick injuries to children) as well as to service providers (e.g. rubbish collectors and cleaners) should be explained. Where available, a needle clipping device should be used. It can be carried in the patient kit and used many times before discarding.

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<sup>95</sup> Mondy K, Overton ET, Grubb J, Tong S, Seyfried W, Powderly W, Yarasheski K. Metabolic syndrome in HIV-infected patients from an urban, midwestern US outpatient population. *Clin Infect Dis*. 2007 Mar 1;44(5):726-34. Epub 2007 Jan 22.

<sup>96</sup> Jagger J et al. The impact of U.S. policies to protect healthcare workers from bloodborne pathogens: The critical role of safety-engineered devices. *J Infect Pub Health* 2008;1:62-71.

<sup>97</sup> Workman RGN. Safe injection techniques. *Primary Health Care* 2000;10:43-50.

<sup>98</sup> Bain A, Graham A. How do patients dispose of syringes? *Practical Diabetes International* 1998;15:19-21.

We believe that our overall survey gives a detailed, up-to-date and representative view of injecting practice in the most commonly-used diabetic health care facilities in the world. We further believe that it lays the groundwork for new recommendations concerning best practices for patients, guides the care and education strategies for HCP and provides a road map for improving diabetes care to public health professionals and government officials worldwide. This paper will be followed by two others:

- **Worldwide Injection Technique Study: Injecting Complications**
- **Worldwide Injection Technique Study: Education and the Health Care Professional**

### **Duality of interest:**

Kenneth Strauss is employed by BD, a manufacturer of injecting devices.

### **Acknowledgments**

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