

Defining the Ideal Injection Techniques When Using 5-mm Needles in Children and Adults

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OBJECTIVE — We aimed to establish the ideal injection techniques using 5-mm needles to reliably inject insulin into the subcutaneous fat in both children and adults and to quantify the associated pain and leakage of the test medium.

RESEARCH DESIGN AND METHODS — A total of 259 subjects (122 children/adolescents and 137 adults) were injected with sterile air corresponding to 20 IU insulin (200 μ l) with 32-G 5-mm needles at 90° or 45°, in the abdomen and thigh, and with or without a pinched skin fold. Injection depth was assessed via ultrasonography. Subjects rated pain on a visual analog scale. Test medium injections into the abdomen and thigh (0.2–0.6 ml) were also administered to assess injection leakage.

RESULTS — Among children, 5.5% of injections were intramuscular (IM) and 0.5% were intradermal, while in adults, the incidence was 1.3 and 0.6%, respectively. The frequency of IM injections was greater in boys and negligible among adult women. Subcutaneous fat thickness was the primary predictor of the likelihood of IM injections ($P < 0.001$). A third of all patients reported experiencing no pain during insulin injection, with children/adolescents experiencing considerably more discomfort than adults. Some leakage of medium was observed, but was unrelated to injection volume and was generally minimal.

CONCLUSIONS — 5-mm needles are reliably inserted into subcutaneous fat in both adults and children. These needles were associated with reduced pain and minimal leakage. We recommend an angled injection with a pinched skin fold for children, while in adults, the technique should be left to patient preference.

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Although there are many new technologies assisting in diabetes care, multiple daily injections remain the mainstay of therapy where insulin is required. Such injections aim to reliably deposit insulin into subcutaneous fat while minimizing inadvertent intramuscular (IM) injections (1). Intramuscular injections of regular, NPH, and glargine insulin have been associated with variability in glycemic control and an increased risk of

severe hypoglycemia (2–6). Although no studies have systematically evaluated the frequency of IM injections among diabetic patients, these appear to be relatively common (6,7).

The risk of IM insulin deposition is associated with a number of factors including younger age, male sex, lower BMI, injection technique (angle of insertion and a lifted or pinched skin fold), and needle length (5,8–11). Furthermore, the

thinner a person's skin or subcutaneous fat layer, the greater the chances of an accidental IM injection (5). Little information is known about skin thickness, although it appears to vary with age, obesity, and puberty (1).

Not surprisingly, needle length has been shown to be an important variable determining site of insulin deposition (5,12). However, although decreasing the length of the insulin needle reduces the incidence of IM injections, the use of 5-mm needles may result in insulin being administered too superficially in the dermal layer (13,14). The consequence of intradermal insulin deposition is largely unknown, but may lead to increased immune response, injection pain, and insulin leakage (14).

Despite this, there have been few studies examining injection technique. Perpendicular insertion of 6-, 8- and 12.7-mm needles has been associated with frequent IM injections in children and adolescents with rates of 42, 38, and 86%, respectively (1,5,8). By using an angled insertion of 6-mm needles, the risk of IM injections was markedly reduced (1). More recently, 4-mm needles inserted vertically were shown to be safe and effective in the majority of lean children and adults (12). However, no evidence-based recommendations exist for 5-mm needles, which are being used with increasing frequency. Although there are some data on children with other needle lengths (1,5,8), little information is available on adults, and it remains unclear how suitable shorter needles are for this group, especially for the obese.

Our primary aim was to establish the ideal injection techniques required to reliably inject insulin into the subcutaneous fat in both children and adults using 5-mm needles. We also aimed to assess the level of discomfort associated with each technique and quantify the respective amounts of backflow or leakage of test medium to the skin surface.

RESEARCH DESIGN AND METHODS

Otherwise healthy children and adolescents with type 1 diabetes aged 5–19 years were recruited

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Table 1—Demographics of the studied population

	Children		Adolescents		Adults	
	Girls	Boys	Girls	Boys	Women	Men
n	17 (44)	22 (56)	39 (47)	44 (53)	78 (57)	59 (43)
Age (years)	8.6 ± 1.2	8.6 ± 1.3	14.1 ± 2.7	14.0 ± 2.0	45.4 ± 13.9	44.3 ± 13.9
BMI	—	—	—	—	28.5 ± 7.0	27.3 ± 5.2
BMI SDS	0.79 ± 1.16	0.52 ± 1.02	1.0 ± 1.1	1.1 ± 1.0	—	—
BMI >85% or >27 kg/m ² *	5 (29)	6 (27)	15 (38)	23 (53)	40 (51)	26 (44)
BMI >95% or >30 kg/m ² *	3 (18)	3 (14)	8 (20)	14 (33)	32 (41)	13 (22)†
Abdominal skin thickness (mm)	1.5 ± 0.3	1.5 ± 0.4	2.0 ± 0.4	2.1 ± 0.7	2.0 ± 0.5	2.1 ± 0.4
Abdominal subcutaneous fat (mm)	8.9 ± 5.0	7.6 ± 4.1	15.5 ± 9.4	10.9 ± 6.2‡	21.9 ± 11.2	16.9 ± 9.1‡
Thigh skin thickness (mm)	1.3 ± 0.5	1.3 ± 0.3	1.7 ± 0.4	1.7 ± 0.4	1.7 ± 0.6	1.9 ± 0.4†
Thigh subcutaneous fat (mm)	11.0 ± 6.7	7.4 ± 3.7†	14.0 ± 7.3	8.1 ± 3.1§	18.1 ± 9.5	9.3 ± 3.9§

Data are n (%) or means ± SD. *BMI >85% and >95% centiles apply to children, whereas BMI >27 kg/m² and >30 kg/m² refer to adults. †P < 0.05, ‡P < 0.01, §P < 0.001 for between-sex comparisons.

from the diabetes clinics at Starship Children's Hospital, Auckland, New Zealand. Adults with type 1 and type 2 diabetes aged between 20 and 85 years were also recruited. Exclusion criteria included moderate-to-severe lipohypertrophy, other medical conditions such as celiac disease or autoimmune thyroid disease, associated syndromes (e.g., Down's syndrome), and other secondary causes of diabetes (e.g., cystic fibrosis). Lipohypertrophy was assessed clinically, and, in those subjects who demonstrated mild lipohypertrophy, no injections were made into areas where any adipose thickening was noted. Young subjects had weight and height measured and pubertal status recorded by a pediatric endocrinologist (P.L.H. or T.E.P.).

All subjects were injected with sterile air corresponding to 20 IU insulin (200 μ l) with NovoFine 32-G 5-mm needles (Novo Nordisk, Copenhagen, Denmark) using NovoPen 4 pens (Novo Nordisk). Eight injections were administered either perpendicularly or at 45°, in the abdomen and thigh, and with or without a pinched skin fold. Immediately after each injection, an assessment of the depth was made by a radiologist (J.M.P.) via ultrasonography using a Phillips IU-22 ultrasound machine and a 17.0-MHz linear array transducer (1). The ultrasound site of the injected air was assessed as intradermal, subcutaneous fat, or IM. In addition, after each injection, subjects were asked to rate the injection pain on a facial and visual analog scale (15), with pain response measured in millimeters.

Subjects were also injected with test medium (insulin-free diluent) using FlexPen (Novo Nordisk A/S). Injection volumes of 200, 400, and 600 μ l were tested

(equivalent to 20, 40, and 60 units of insulin). Using known unit doses of the diluents, milligram doses were converted to units (slope: 0.1 mg = 10 μ l; $r = 0.98$). Four injections were made using either a perpendicular or angled insertion and with a pinched skin fold into either the abdomen or lateral thigh. All injections were given by two experienced diabetes nurse specialists while the patient was supine, and the needle was withdrawn after a slow count to six. After 20–30 s, the area was gently wiped with tissue paper and weighed using scientific scales (accurate to 10 μ g).

Ethical approval was received from the Auckland Ethics Committee, and informed written consent was obtained from all parents and older subjects. In younger subjects, oral consent was also obtained.

General linear regression models were used to compare the demographic characteristics of the subjects between sex, using age as a covariate. Generalized linear mixed models were used to investigate the associations between the outcomes from the injections and the site (thigh or abdomen), angle (45° or 90°), and pinching (unpinched or pinched). The person was treated as a random effect to allow for the correlations between measurements on the same subject. Factors including age, sex, BMI standard deviation score (BMI SDS), skin thickness, subcutaneous fat thickness, and pubertal status (for children) were included in the models where appropriate. A logit link was used for binary outcomes namely: IM injection (yes/no), leakage (yes/no), and pain (yes/no). The level of pain was only investigated within the group who had pain. Percentages and means are pre-

sented to give an estimate of effect magnitude.

RESULTS— There were 259 subjects included in this study, including 122 children/adolescents and 137 adults (Table 1). The detailed demographic data are shown in Table 1. Skin thickness varied minimally with sex and age, although thigh skin thickness in adult males was 10% greater than in females ($P < 0.05$, Table 1). The mean BMI steadily increased with age in both males and females, and consequently the same pattern was observed for subcutaneous fat. Abdominal subcutaneous fat thickness was not significantly different between prepubertal boys and girls, but it was 42% ($P < 0.01$) and 30% ($P < 0.01$) greater in female than in male adolescents and adults, respectively. This sex difference was particularly pronounced in thigh subcutaneous fat, which was thicker in females than males by 49% before puberty ($P < 0.05$), 73% in adolescence ($P < 0.001$), and 95% in adulthood ($P < 0.001$) (Table 1).

A total of 2,072 injections were administered: 976 to children/adolescents and 1,096 to adults (Table 2). Among children, relatively few injections were inserted outside subcutaneous fat irrespective of the site and technique used for administration, with 54 IM (5.5%) and 5 intradermal (0.5%) injections recorded. The incidence of IM injections among adults was even lower, and 14 IM (1.3%) and 7 intradermal (0.6%) administrations were recorded (Table 2).

Note that there were no adverse side effects associated with the injections administered to the subject. In particular, no bleeding or bruising was observed.

Table 2—Frequency of intradermal, subcutaneous fat, and IM injections in children (n = 976) and adults (n = 1,096) according to the various injection techniques

Technique	Children/adolescents			Adults		
	Intradermal	Subcutaneous fat	IM	Intradermal	Subcutaneous fat	IM
Unpinched						
Abdominal						
45°	0	113 (92.6)	9 (7.4)	1 (1)	135 (98.5)	1 (0.7)
Vertical	1 (1)	111 (91.0)	10 (8.2)	1 (1)	134 (97.8)	2 (1.5)
Thigh						
45°	1 (1)	119 (97.5)	2 (1.6)	0	136 (99.3)	1 (0.7)
Vertical	0	110 (90.2)	12 (9.8)	0	131 (95.6)	6 (4.4)
Pinched						
Abdominal						
45°	1 (1)	111 (91.0)	10 (8.2)	1 (1)	136 (99.3)	0
Vertical	1 (1)	115 (94.3)	6 (4.9)	2 (1)	135 (98.5)	0
Thigh						
45°	0	119 (97.5)	3 (2.5)	2 (1)	134 (97.8)	1 (0.7)
Vertical	1 (1)	119 (97.5)	2 (1.6)	0	134 (97.8)	3 (2.2)
Total	5 (0.5)	917 (94.0)	54 (5.5)	7 (0.6)	1,075 (98.1)	14 (1.3)

Data are n (%).

Intramuscular injections

There was a significant association between age and the likelihood of an IM injection ($P < 0.01$), which was much less frequent among adults (Table 2). Despite the relatively small number of IM injections, analyses showed clear sex differences in the incidence of IM injections among children and adolescents (Table 3). In prepubertal boys, site made no difference, but angled and pinched injection appeared to reduce IM incidence (Table 3). Among girls, no IM deposition was recorded when the skin was pinched or the injection was applied to the thigh. Among adolescents, injection technique did not affect the frequency of IM administration, and no IM injections were recorded during thigh injections in females.

Such sex differences were more marked among adults, and the incidence of IM injections among women was negligible. In the abdomen, pinched angled injections are also likely to decrease the likelihood of an IM injection occurring (Table 3). Subcutaneous fat thickness was the primary predictor of the likelihood of IM injections ($P < 0.001$) and likely accounted for the sex differences (Table 1).

Pain

Approximately one-third of all patients reported experiencing no pain during insulin injection (32% children and 31% adults). The angle or site of injection had no bearing on whether the subject experienced pain or not. Among subjects who experienced pain, children/adolescents

experienced considerably more discomfort than adults (20.9 ± 0.8 vs. 14.1 ± 0.7 mm, respectively; $P < 0.001$). In addition, abdominal injections were less painful than those applied to the thigh (16.2 ± 0.6 vs. 18.8 ± 0.6 mm, respectively; $P < 0.001$).

Leakage

Injections in adults were more likely to lead to leakage than those given to younger subjects (70% with detectable leakage among adults vs. 56% among children/adolescents, $P < 0.01$). The volume of medium given (200, 400, or 600 μ l) did not affect the likelihood of leakage occurring ($P = 0.41$). However, leakage was more likely to occur with vertical injections (65% for vertical and 59% for an-

Table 3—Frequency of IM injections according to sex and pubertal status

	Children		Adolescents		Adults	
	Girls	Boys	Girls	Boys	Females	Males
Total injections	136	176	312	352	624	472
IM injections	5 (3.6)	16 (9.1)	8 (2.6)	25 (7.1)	1 (0.2)	13 (2.8)
Site						
Abdomen	5 (7.4)	8 (9.1)	8 (5.1)	14 (8.0)	1 (0.3)	2 (0.8)
Thigh	0	8 (9.1)	0	11 (6.3)	0	11 (4.7)
Angle						
45°	2 (2.9)	5 (5.6)	5 (3.2)	12 (6.8)	0	3 (1.3)
Vertical	3 (4.4)	11 (12.5)	3 (1.9)	13 (7.4)	1 (0.3)	10 (4.2)
Technique						
Unpinched	5 (7.4)	10 (11.4)	4 (2.6)	14 (8.0)	1 (0.3)	9 (3.8)
Pinched	0	6 (6.8)	4 (2.6)	11 (6.3)	0	4 (1.7)

Data are N or n (%).

Table 4—Amount of leakage associated with injections of insulin medium

Injection technique	Injection volume (μ l)		
	200	400	600
Abdominal			
Angled	2 \pm 3	2 \pm 6	2 \pm 3
Vertical	2 \pm 3	1 \pm 7	3 \pm 5
Thigh			
Angled	4 \pm 8	3 \pm 7	5 \pm 7
Vertical	7 \pm 12	11 \pm 18	6 \pm 11

Data are means \pm SD. 10 μ l is an equivalent volume to 1 unit of insulin. All injections were applied with pinched skin.

gled, $P < 0.001$) and with thigh injections (66% to thigh and 58% to abdomen, $P < 0.001$). Nonetheless, the amount of leakage recorded in each case was generally minimal, amounting to the equivalent of a fraction of a unit (Table 4).

CONCLUSIONS— This study demonstrated that 32-G 5-mm needles can be reliably inserted into subcutaneous fat, are relatively pain free, and are associated with minimal leakage from the injection site. Previous studies using 6-, 8-, and 12.7-mm needles have demonstrated that injection technique is important in determining injection depth (1,5,8). These data indicated that, in children, 8-mm needles have an unacceptable rate of IM injections. Even 6-mm needles had a high rate of IM injections when inserted vertically, although none were reported with an angled insertion (1). It was thus recommended that 6-mm needles should be inserted at an angle in children and should be preferred to 8-mm needles in leaner children at higher risk of IM injections.

The current investigation examined several different paradigms involving needle insertion with 5-mm needles. Although all paradigms used resulted in the majority of injections correctly sited in subcutaneous fat, it is of concern that some techniques led to 10% of insulin injections being intramuscular in young subjects. There was an expected reduction in IM injections using a pinched skin fold and angled insertion in prepubertal children, and this combination appears to result in the most reliable insertion into subcutaneous fat in children and lean adults. In adolescents and adults (especially women), unless they are particularly thin, any of the injection paradigms used would be acceptable and the tech-

nique should be based on patient preference.

Discomfort and pain were remarkably low in this study. We observed no significant difference in pain perception between 45° and 90° injections, which is consistent with previous findings (16). Needle pain is directly related to needle diameter, and the study needle used is one of the thinnest commercially available. While not directly comparable, a previous study using the same methodology resulted in significantly higher pain scores for both 31-G 6-mm and 30-G 8-mm needles insertion, and it was our experience that the 32-G 5-mm needles were somewhat less painful (1). It is worth noting that among individuals who experience discomfort, children had higher scores than adults. Needle aversion and phobia appear to be common in children with diabetes (17), and pain associated with daily injections is said to be important in discouraging patients to adhere to treatment (18). Thus, less painful injections would probably help with the acceptance and tolerability of insulin therapy, potentially leading to increased treatment compliance.

Possible concerns regarding smaller needles include greater insulin leakage or back flow. This issue was assessed in a previous study of lean children and adults using 4-mm needles, and such problems were not observed. In our study and in doses up to 0.6 ml (equivalent to 60 units insulin), we similarly demonstrated minimal leakage. Although greater in the thigh and with perpendicular needle insertion, leakage (when present) was usually very small. All injections were administered while the patient was supine and, although unlikely, it is nonetheless possible that more leakage would have occurred in a sitting position or with a flexed leg.

In summary, we have demonstrated in both adults and children that 5-mm needles can reliably be inserted into subcutaneous fat. In children, our findings indicate that an angled approach with a pinched skin fold should be used. In adults, the technique should be left to patient preference. The reduced incidence of pain observed with the use of these needles in comparison to previous studies may improve compliance issues, especially in children, although this will require further study. Finally, there is evidence that no substantial back flow or leakage occurs from using shorter needles in doses up to 60 units.

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