



FIT Forum for **Injection Technique** Canada

Recommendations
for Best Practice in
Injection Technique
4th Edition 2020



Optimizing
injection technique
in diabetes

Preface

Our Objectives

- Identify the injection techniques currently being used by people with diabetes in Canada.
- Raise awareness of the impact that existing and emerging research regarding injection technique may have on health outcomes.
- Facilitate opportunities in which best practice regarding injection and infusion technique can be discussed, developed, implemented, and evaluated across Canada.

Preface

The Forum for Injection Technique (FIT) Canada provides evidence-based best practice recommendations for people with diabetes who are using injectable therapies. Originally developed in 2011, these recommendations have been disseminated broadly to ensure people with diabetes can achieve the best possible health outcomes, delivering the correct dose of medication to the correction injection site using proper technique. A new addition to the 4th edition of these recommendations is the area of infusion therapy. While much has been done and achieved, we are cognizant that gaps remain in injection/infusion technique knowledge. With the launch of this 4th edition, we will continue advocating for correct injection/infusion technique through dissemination initiatives which will include education for healthcare professionals and patients, patient support, and clinical research opportunities.

**The Canadian FIT Board –
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Introduction/Background

Broad dissemination of the results of an international survey¹ led to an increased awareness among healthcare professionals of the issues associated with improper injection technique. The Canadian Forum for Injection Technique (FIT) initiative was developed in response to these concerns.

Following the precedent set by the United Kingdom FIT initiative,⁽²⁾ as well as other international injection technique initiatives,⁽³⁻⁶⁾ the recommendations presented in the original document were designed to promote best practice in injection technique for healthcare professionals who are involved in diabetes care, and their patients.^(5, 6) They were also aimed at raising awareness of existing and emerging research regarding

injection technique. It was hoped that the implementation of these recommendations would have a direct impact on the health outcomes of people with diabetes who are using subcutaneous injection therapies. This document has been revised based on new evidence and continues to be distributed to all Canadian healthcare professionals who are involved in injection therapy for people with diabetes.

At the original meeting of Canadian diabetes education experts, many unmet educational needs regarding injection technique were discussed and the top 3 educational priorities identified were:

- 1 Techniques to avoid intramuscular injection
- 2 Steps to ensure healthy injection sites
- 3 Provision of clear and concise direction to healthcare professionals regarding proper injection technique

Utilizing these priorities as a framework, the original best practice document was developed by the Canadian FIT Board and reviewed by an expert committee of diabetes educators. Where evidence was unavailable, expert opinion guided the recommendation.

Following the publication of the initial FIT recommendations in October 2011, a Canadian injection practice survey was conducted.

(7) The data yielded new evidence regarding injection technique and —most importantly—new learnings regarding best practice.

This resulted in a revision to the document. Research regarding injection technique and the role of lipohypertrophy in glycemic variability has been increasing steadily since the launch of the international survey in 2009.

(1) In 2013 and 2014, two trials examined enhanced glycemic control through improved injection technique⁸ and conducted a cost analysis of improved injection technique.⁽⁹⁾ Of note, the rate of lipohypertrophy in both of these studies was significant. Grassi and colleagues reported the incidence of lipohypertrophy as follows: females, 48.1%; males, 51.9%.⁸ Blanco et al. observed a lipohypertrophy incidence of 64.4%.⁽⁹⁾ In 2016, a well-conducted study of people with type 1 diabetes demonstrated that the action and absorption of insulin was considerably more variable with a blunted action when

injections were administered into areas of lipohypertrophy, which led to deteriorations in postprandial glucose control.⁽¹⁰⁾

Most recently, another injection survey, in which 329 Canadian patients were enrolled, was published.⁽¹¹⁾ As a result, updated recommendations for patients and healthcare professionals have been published.⁽¹²⁾ The information acquired from these recommendations, as well as clinical experience since the publication of the 1st edition of the FIT Canada were incorporated into the 2nd and 3rd editions. In this most recent edition, new evidence regarding injection force and its possible sequelae have been incorporated. Infusion technique guidance has also been added in response to requests for information in this area.

Despite worldwide efforts in improving injection technique, the recent publications demonstrate that there is still inadequate knowledge of proper injection technique. There is compelling evidence to continue to assess injection and infusion techniques, examine patients for the presence of lipohypertrophy, and provide patient and healthcare professional education to ensure the prevention and timely management of lipohypertrophy. The development of FIT and the subsequent Canadian recommendations for injection and infusion techniques are supported by BD Canada and endorsed by Canadian pharmaceutical companies that manufacture insulins and glucagon-like peptide-1 (GLP-1) receptor agonists.

FIT CANADA

Endorsements

Since BD invented the first specialized insulin syringe in 1924, we have been committed, not only to furthering the innovation of insulin syringes and pen needles but also enhancing the insulin injection process through research and partnerships. One such partnership has been FIT Canada which provides invaluable injection technique (IIT) guidelines for Canadian Healthcare professionals and people living with diabetes by utilizing the latest IIT research and expert opinions. We at BD are proud of the continued partnership with FIT Canada (as well as FIT worldwide).



Brian K Pflug, PharmD, Global Medical Director US/Canada, Diabetes Care Medical Affairs

Utilizing the correct technique to administer injectable therapies for diabetes is critically important to help ensure patients benefit fully from their treatment. Eli Lilly Canada is dedicated to improving care for people with diabetes and welcomes this update to the FIT recommendations, to improve both healthcare profession and patient understanding of good injection technique. The comprehensive, evidence-based guidelines provided through FIT will play an important role in supporting improved diabetes care in Canada.



Joanne Lorraine MD FRCPC MEd, Medical Director, Diabetes Care, Eli Lilly Canada

For people with diabetes who take insulin or other injectable diabetes medications, providing tools to help guide the education of patients and health care professionals is essential. Being diagnosed with diabetes and managing a chronic disease can be overwhelming. At Novo Nordisk, we are committed to supporting healthcare professionals to deliver the highest quality of care for their patients, especially as the healthcare landscape continues to evolve. The FIT Canada best practice recommendations will support improved diabetes management and outcomes for Canadian patients.



Vicky Chan, Vice President, Clinical Development, Medical and Regulatory Affairs, Novo Nordisk Canada Inc

Sanofi Canada is committed to improving diabetes management through our integrated offering of treatments, medical devices, and services. We are proud to support the FIT Canada recommendations, whose goal is to promote best practice in diabetes injection technique. Proper injection technique is key to ensuring that patients receive the full benefit of injectable therapies. At Sanofi Canada, our focus is to simplify the management of complex disease for people with diabetes and their healthcare providers. We are working hard, in partnership with everyone committed to diabetes care to develop innovative solutions to help people with diabetes live as people, not as patients.



Sophia Kajla MD, Medical Head, General Medicines, sanofi-aventis Canada Inc

Contents

Objectives	3	6.0 Ensuring proper preparation and administration of insulin	17
Preface	3	6.1 Re-suspension of cloudy insulin	17
Introduction/Background	4	6.2 Leakage considerations	17
Endorsements	5	6.3 Effect of volume of injection on insulin action (kinetics)	18
1.0 Preparing for injection	8	6.4 Concentrated insulin: practical tips and special considerations	19
1.1 Psychological challenges of injections: Adults	8		
1.2 Injection site care	8	7.0 Injectable therapy – GLP-1 receptor agonist	20
2.0 The correct use of devices	9	7.1 Storage of GLP-1 receptor agonists	20
2.1 Use of syringes with an insulin vial	9	7.2 Practical tips and special considerations	21
2.2 Use of pen devices	10		
2.3 Use of pen needles	11	8.0 Injection area	22
2.4 Injections should be administered into subcutaneous tissue	13	8.1 Injection area selection	22
2.5 Tips for making injections more comfortable	13		
3.0 Disposal of injection materials	14	9.0 Lipodystrophy	23
4.0 Injectable therapy – Insulin	15	9.1 Definition of lipodystrophy	23
4.1 Temperature of insulin	15	9.2 Identification of lipohypertrophy	23
4.2 Storage of insulin	15	9.3 Factors contributing to the development of lipohypertrophy	24
5.0 Site-related factors that may affect insulin absorption	16	9.4 Effects of lipohypertrophy	25
5.1 Intramuscular injection	16	9.5 Assessment, prevention, and avoidance of lipohypertrophy	26
5.2 Injection site-related factors	16	9.6 Lipoatrophy	27

10.0	Site rotation	27	Figures	
10.1	Implementation	27	Fig. 1	Wash hands with soap and water
11.0	Bruising and bleeding	28	Fig. 2	Wipe the cartridge or vial with an alcohol swab
11.1	Recommendations	28	Fig. 3	Preparing an insulin syringe
12.0	Pregnancy	29	Fig. 4	Proper injection into a skin lift at a 90-degree angle
12.1	Recommendations	29	Fig. 5	Proper injection into a skin lift at a 45-degree angle
13.0	Older person	30	Fig. 6	Method for pushing in insulin pen injection dose knob completely
13.1	Special considerations	30	Fig. 7	How to perform a skin lift
14.0	Pediatrics	31	Fig. 8	Increased application force on the pen needle results in deeper injection
14.1	Thickness of subcutaneous fat	31	Fig. 9	Benefits of non-posted hub design pen needles
14.2	Injection sites	32	Fig. 10	Proper injection technique for subcutaneous absorption of insulin and GLP-1 receptor agonists
14.3	Needle anxiety and pain	32	Fig. 11	Proper way of disposing needles
14.4	Preparing children for injections	33	Fig. 12	Non-posted hub-based pen needle designs may reduce IM injections
14.5	Self-injection	33	Fig. 13	Method of mixing cloudy insulin
14.6	Insulin under- and overdosing	34	Fig. 14	Subcutaneous thickness in male and female adults
14.7	Adolescence	34	Fig. 15	Lipohypertrophic lesions
15.0	Insulin infusion	31	Fig. 16	The pinch characteristics of normal vs. lipohypertrophic tissue
15.1	Selecting an infusion set	35	Fig. 17	Proper palpation technique for detection of lipohypertrophy
15.2	Inserting an infusion set	36	Fig. 18	An example of lipoatrophy
15.3	Site selection and rotation	37	Fig. 19	Spacing injections within quadrants
15.4	Skin preparation	38	Fig. 20	Avoid indenting the skin when injecting
15.5	Insertion	39	Fig. 21	Recommended injection sites during the trimester of pregnancy
15.6	Troubleshooting	40	Fig. 22	Examples of insulin pumps
15.7	Recommendations for special considerations	41	Table	Examples of cannulae and insertion
15.8	Education	42		
16.0	Institutions	43		
16.1	Special considerations	43		
17.0	Best practice recommendations	44		
References		45		
Glossary		58		
References		45		
Glossary		50		

1.0

Preparing for Injection

1.1 Psychological challenges of injections: Adults

- 1 The healthcare professional should inform all people with type 2 diabetes early after diagnosis that they will likely require injectable therapy in the future to treat their diabetes. It is important to explain the natural progression of diabetes and that initiation of injection therapy at any point during the course of the disease should not be seen as personal failure.(13)
- 2 Few adults have true needle phobia (i.e. a fear of needles). However, many experience anxieties regarding injecting, particularly when embarking on an injectable therapy regimen. The healthcare professional should explore a patient's anxieties regarding the injection process and address any concerns or barriers to treatment, with the goal of working together to improve treatment adherence and quality of life.(14-16)

- 3 Both the short- and long-term advantages of achieving and maintaining target blood glucose levels should be emphasized to people with diabetes. Furthermore, it is important that healthcare professionals explain that finding the right combination of therapies which may include injectable therapy to achieve optimal glycemic targets is a primary treatment goal.(17, 18)



Figure 1. Wash hands with soap and water

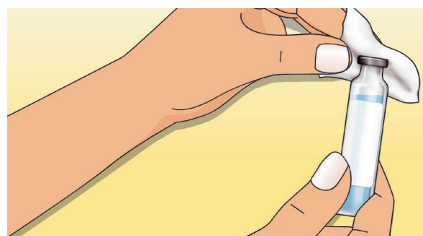


Figure 2. Wipe the cartridge or vial with an alcohol swab

1.2 Injection site care

- 1 Injections should be administered in a clean site on the body, using clean hands.(19)
- 2 If necessary, people should clean their hands and the injection site with soap and water (Fig. 1).(19)
- 3 Disinfection of the injection site is generally not required. However, alcohol swabs may be mandated for use prior to injections administered in a hospital or long-term care setting, or wherever nosocomial infections are more prevalent. If alcohol is used to clean the site, the skin must dry completely before the injection is administered.(20, 21) Cleaning the medication cartridge or vial with an alcohol swab is required (Fig. 2).(20)

2.0 The Correct Use Of Devices

2.1 Use of syringes with an insulin vial

- 1 Proper syringe selection is crucial. The decision regarding which syringe is appropriate should be based on the amount of insulin to be administered (volume: U-30, U-50, or U-100 syringes) and length of needle. Due to the need to pierce the insulin vial stopper, the shortest available needle length of an insulin syringe is currently 6-mm.

The use of a 6-mm needle is recommended with or without a skin lift, depending on assessment of the site and amount of subcutaneous tissue. Ensure a skin lift with an 8-mm needle.(22) The use of 12-mm or 12.7-mm needles is not recommended, due to an increased risk of intramuscular (IM) injection.

- 2 When preparing to draw up the insulin, the air equivalent to the dose should be drawn up first and injected into the vial, to facilitate easier withdrawal (Fig. 3).

- 3 If air bubbles are seen in the syringe, hold it with the needle pointed upwards, tap the barrel to bring them to the top, and then remove the bubbles by pushing the plunger to expel the air.

- 4 When using an 8-mm needle, injections should be administered into a skin lift at a 90-degree angle (Fig. 4). To prevent IM injection, lean individuals may need to inject into a skin lift at a 45-degree angle (Fig.5).(23-26)

This method may also be required with a 6-mm needle in particularly lean individuals.

- 5 When administering injections, the following steps should be taken if a skin lift is required (27, 28)
 - Insert the needle completely into the skin lift.
 - Depress the plunger completely
 - Remove the syringe at the same angle that it was inserted
 - Release the skin lift

- 6 Syringes should be used only once.(29-31)

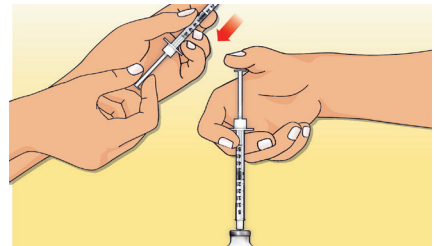


Figure 3. Preparing an insulin syringe

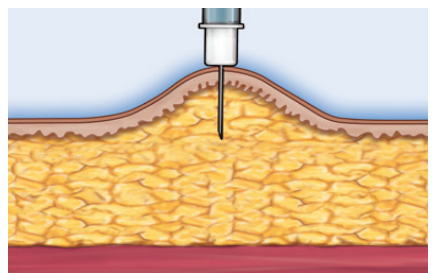


Figure 4. Proper injection into a skin lift at a 90-degree angle

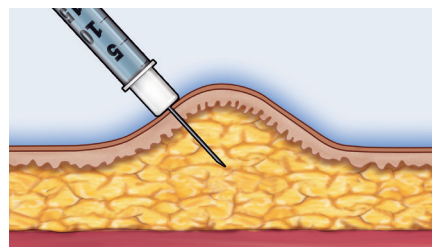


Figure 5. Proper injection into a skin lift at a 45-degree angle

2.0 The Correct Use Of Devices

2.2 Use of pen devices

When teaching patients proper pen use, healthcare professionals should consult the instruction manual for the specific device being used. Obstruction of insulin flow in a pen is rare but could lead to serious consequences. Understanding how to monitor movement of the rubber plunger within the pen is an important learning to ensure adequate insulin delivery.

- 1 Insulin pen devices should always be primed (with doses as per the manufacturer's instructions) with the needle pointing upwards; a flow of insulin should be observed at the needle tip before each injection. Once flow is verified, the desired dose should be dialed and the injection administered.(1, 32)
- 2 Pen devices and cartridges are for single-person use only and should never be shared, due to the risk of cross-contamination. (33, 34)
- 3 Pen needles should be used only once. Using a new needle each time may reduce the risk of needle breakage in the skin, clogging of the needle, complications (e.g. lipohypertrophy, abscess) and inaccurate dosing.(29-31, 35, 36)
- 4 The insulin injection dose knob should be depressed only when the pen needle is fully inserted. The injection dose knob should be pushed straight down from the top, not on an angle as this could lead to no dose being given. After pushing in the injection dose knob completely, the individual should count to 10 slowly (approximately 10 seconds, or as per the manufacturer's instructions) and maintain pressure on the injection dose knob before withdrawing the needle. These will ensure the full dose is delivered and prevent medication leakage (Fig. 6). Counting higher than 10 may be necessary for higher doses. (27, 28)
- 5 Pen devices with a dose window should be checked after each injection; the number 0 should be displayed when the desired dose has been injected. If a number other than 0 is showing, then the correct insulin dose has not been administered. In this event, replace the cartridge, attach a new pen needle, prime the pen (per the manufacturer's instructions) and administer the remainder of the dose.

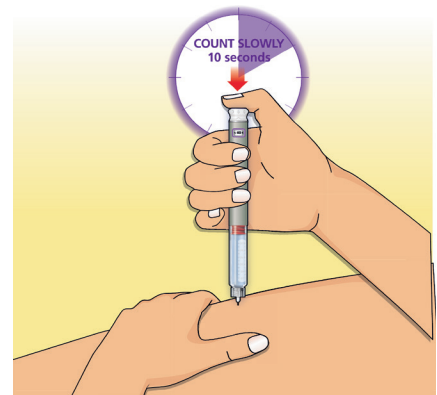


Figure 6. Method for pushing in insulin pen injection button completely

2.0 The Correct Use Of Devices

2.3 Use of pen needles

- 6 Needles should be safely disposed of immediately after use and should not remain attached to the pen. This prevents the entry of air or other contaminants into the cartridge or leakage of medication from the cartridge, both of which can affect subsequent dose accuracy. (27, 37)
- 7 Non-disposable pen devices should not be stored in the refrigerator, as the integrity of some parts (e.g. rubber) can be compromised by cold temperatures, which can in turn affect pen function.
- 8 Individuals should keep a spare syringe or a second pen at hand in case of breakage or malfunction. **A syringe should NEVER be used to remove insulin from a pen with concentrated insulin, as the scale on insulin syringes is made for U-100 insulin only. The use of current insulin syringes with concentrated insulin (U-200, U-300 or U-500) could result in an overdose.**
- 1 Choose the right needle:
 - A shorter needle should be used at the initiation of insulin therapy(26,38,39)
 - The needle gauge should be 30G, 31G or 32G (a higher gauge represents a smaller needle diameter)
 - 4-mm, 5-mm and 6-mm needles are suitable for all people with diabetes, regardless of body mass index (BMI). An 8-mm needle may be preferred by some patients
 - Currently available research data from across a wide range of BMIs (19 to 65 kg/m²) support the use of 4-mm pen needles to avoid the risk of IM injections(40)
 - 4-mm pen needles provide equivalent A1C control to 8-mm and 12-mm pen needles in people with obesity who are taking large doses of insulin(41)

2.0 The Correct Use Of Devices

2.3 Use of pen needles continued.

- 2 Injections with shorter needle lengths (i.e. 4-mm, 5-mm, 6-mm) should be administered in adults at a 90-degree angle to the skin surface.(23, 42)
 - A skin lift may be warranted to prevent an IM injection in a slim limb or abdomen, even when a shorter needle is used (Fig. 7)(23, 39)
 - A skin lift may not be required, particularly for patients who are using a 4-mm needle (22, 23, 43)
- 3 Injection at a 45-degree angle with a 6-mm needle may be required in extremely lean adults, if no skin lift is used.
- 4 When using 8-mm needles, injections should be administered into a skin lift at a 90-degree angle. Lean individuals should administer injections into a skin lift at a 45-degree angle to prevent possible IM injection.(23, 39)
- 5 The use of 12-mm needles is not recommended.(39)
- 6 Individuals should be trained to let the needle enter the skin gently. The skin should not dent under the pressure. An increased application force on the pen needle can lead to deeper injection of the insulin in the tissue. This may result in increased risk of IM injection, particularly in the arm and thigh regions in men with BMI <30 kg/m² (Fig. 8).(44)

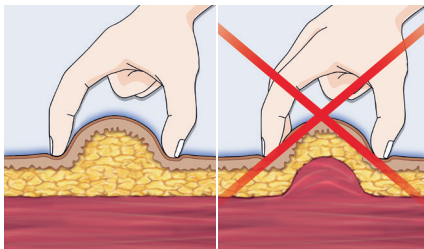


Figure 7. Correct (top) and incorrect (bottom) ways of performing a skin lift. To perform a skin lift correctly, lift the skin and subcutaneous tissue delicately between the thumb and index finger, leaving the muscle behind

- 7 Use of non-posted (contoured) pen needle designs may reduce the impact of unintended user pressure across a range of injection forces and subsequent inadvertent IM injections, compared to conventional posted-hub PN devices of equivalent lengths (Fig. 9).(44)

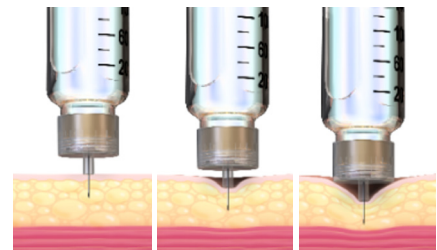


Fig. 8. Increased application force on the pen needle may result in deeper injection of the insulin in the tissue.(44)

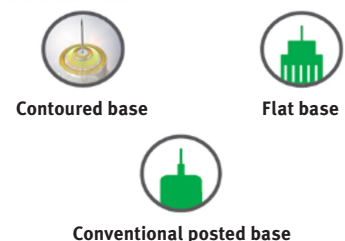


Fig. 9. Use of non-posted hub design pen needles may reduce the impact of unintended user applied injection force differences and subsequently inadvertent IM injections compared to posted-hub pen needle devices of equivalent lengths.(44)

2.0 The Correct Use Of Devices

2.4 Injections should be administered into subcutaneous tissue

- 1 To ensure proper injection technique (Fig. 10), individuals should consult with a healthcare professional who is trained in appropriate injection techniques. (6, 22)
- 2 When the needle is removed, check skin appearance for the following:
 - If the injection is administered correctly, the tissue beneath the skin (subcutaneous) appears normal (22)
 - A white area that appears when the needle is withdrawn may indicate that the insulin has not been injected deeply enough (intradermal injection)
 - Blood and/or bruising at the injection site may indicate that a minor capillary has been penetrated, with no resulting effect on absorption of the insulin. (6, 25, 45)

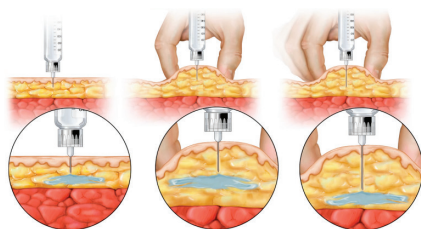


Fig. 10. Proper injection technique for subcutaneous absorption of insulin and GLP-1 receptor agonists: 4-mm pen needle with no skin lift (left); 8-mm pen needle with skin lift (right)

2.5 Tips for making injections more comfortable

- 1 Inspect and palpate the injection site prior to each injection. Any area with signs of lipodystrophy, edema, inflammation or infection should be avoided. (5, 46)
- 2 Avoid injecting into hair roots, scars, moles, stretch marks or other skin abnormalities.
- 3 Keep injectable therapies currently in use at room temperature. (47, 48)
- 4 Use a needle of shorter length and smaller diameter. (43)
- 5 Use a new needle for each injection. (35)
- 6 Insert the needle through the skin using a quick, smooth movement without excess force. (44, 49)
- 7 Inject medication slowly and evenly. Ensure that the plunger (syringe) or injection dose knob (pen) has been depressed fully. (49)

2.0 The Correct Use Of Devices

2.5 Tips for making injections more comfortable

- 7 If using alcohol swabs, inject only when the alcohol has dried fully.
- 8 Avoid injection through clothing, particularly in individuals who are using shorter needles, as there is an increased risk of intradermal injection and the site cannot be inspected.(50)
- 9 In some cases, the insulin dose should be distributed between 2 injections sites, as discomfort at the injection site may decrease at doses <50 units for insulins with 100 units/mL concentration.(51)
- 10 Higher-concentration basal and mealtime insulins are now available in Canada, which may permit higher doses to be administered in smaller volumes than was previously the case.
- 11 If needed, apply ice or analgesic cream to the site before administering an injection.
- 12 If needed, use such devices as Inject-Ease®, Insuflon® and i-port®.

3.0 Disposal of Injecting Materials

3.1 Disposal

- 1 All healthcare professionals, individuals with diabetes and caregivers should be aware of local regulations regarding sharps disposal and the consequences of inappropriate disposal (e.g. needle stick injuries to refuse workers). (52, 53)
- 2 Proper disposal technique should be demonstrated upon initiation of injection therapy and reinforced at subsequent healthcare visits (Fig. 11)
- 3 Where available, a needle-clipping device can be used.
- 4 Needles should never be resheathed.(54)



Fig. 11. All needles should be disposed of in an approved sharps container after use

4.0 Injectable Therapy – Insulin

4.1 Temperature of insulin

- 1 The temperature of insulin does not affect its pharmacokinetics or absorption, provided that it is stored at room or refrigeration temperature.(55)
- 2 Insulin administered at room temperature may reduce irritation, burning or pain, and facilitates the re-suspension of cloudy insulin.(48, 56-59)

4.2 Storage of insulin

- 1 Unopened insulin vials and cartridges should be stored at refrigeration temperature (2 to 8 oC).
- 2 As per specific product monographs, once insulin is opened for use, it should not be used past the recommended time (usually 28 days but could be up to 56 days), as per the manufacturer's recommendations.
- 3 Insulin should never be frozen or exposed to extreme heat (greater than 30 oC) for prolonged periods, as this will affect its potency and alter its action.
- 4 Keep the caps on insulin pens to protect the insulin from the light. Do not store insulin in direct sunlight.
- 5 Insulin should never be used past its product expiry date.

5.0 Site-Related Factors that may affect Insulin Absorption

5.1 Intramuscular injection

- 1 IM injection of all human insulin, and rapid- and long-acting analogues, should be avoided due to the risks of erratic blood glucose control and severe hypoglycemia.(60, 61)
- 2 Accidental IM injection into an arm, leg, or buttock prior to or during exercise may increase insulin absorption, and result in a faster action and more rapid decrease in blood glucose levels. (59, 62)
- 3 Excessive injection force can increase risk of IM injection.(44)
- 4 Use of non-posted pen needle designs may reduce inadvertent IM injections, compared to conventional posted-hub PN devices of equivalent lengths (Fig. 12).(44)

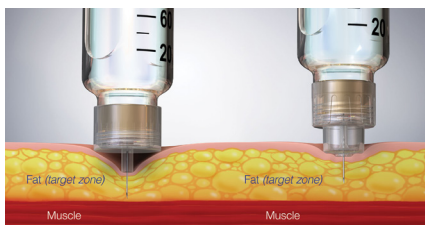


Fig. 12. Use of non-posted pen needle designs may reduce inadvertent IM injections

5.2 Injection site-related factors

- 1 Massaging the injection site immediately before or after an injection is not recommended, as it increases the absorption rate of insulin and results in an unpredictable time-action profile.(55, 63)
- 2 Avoid damaged skin (e.g. from surgical scars or lipodystrophy, as described in Section 9.0) when injecting insulin and GLP-1 receptor agonists.(5, 55)
- 3 Injecting into an area that has an increased skin temperature (e.g. after a sauna or hot bath) can increase the absorption rate of insulin.(64, 65)
- 4 Insulin is absorbed most consistently from the abdominal area.(66-72)
- 5 The upper arm and the lateral side of the thigh, not proximal to the knee, have moderate insulin absorption rates.(66, 69-72)
- 6 The slowest absorption of insulin occurs when it is injected in the buttock; thus, this may be the preferred injection site if slow absorption is desired.(66)
- 7 Rapid- and long-acting insulin analogues may be administered at any injection site, as absorption rates do not appear to be site-specific.(70, 73-77)
- 8 The abdomen is the preferred site for soluble human insulin (regular) since absorption of this insulin is fastest in this area. (66-68, 78-80)
- 9 Premixed regular/NPH insulin should be injected in the abdomen to increase the speed of absorption of this short-acting insulin, in order to cover postprandial glycemic excursions.(81)

6.0 Ensuring Proper Preparation and Administration of Insulin

6.1 Re-suspension of cloudy insulin

- 1 When using cloudy insulin (i.e. NPH and premixed insulin) the vial, cartridge or pen device should first be gently rolled 10 times, then tipped (not shaken) 10 times; finally, it should be inspected to ensure the suspension has a consistently milky white appearance (Fig. 13). (82-84)

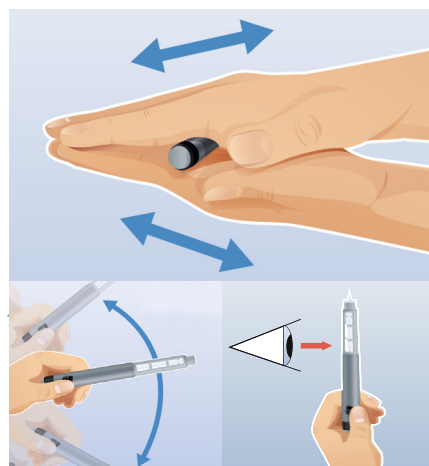


Fig. 13. Method of mixing cloudy insulin: roll 10 times, tip 10 times, then perform a visual check for milky white appearance

6.2 Leakage considerations

- 1 Larger doses of insulin are associated with more leakage and potentially more discomfort. (51, 85, 86)
- 2 In patients with obesity, there is no difference in glycemic control, safety, leakage rates and patient ratings between 4-mm, 5-mm, 8-mm and 12.7-mm pen needle lengths. (41, 43, 87-89) In one study, the amount and rate of leakage appeared to increase related to a coinciding increase in BMI. (87)
- 3 The volume of leakage is generally <0.1 IU (or $<1.0\%$ of total insulin, for most patients) and hence almost always clinically insignificant. (85, 90, 91)
- 4 One factor affecting leakage of insulin is not waiting for the full count after injection (10 seconds or as per manufacture recommendations) withdrawing the needle before the full dose is given or removing the needle before the full dose is given (the dose indicator not fully back to 0). These errors can lead to leakage which may occur from the site or needle tip post injection.

6.0

Ensuring Proper Preparation and Administration of Insulin

6.3 Effect of volume of injection on insulin action (kinetics)

- 1 The larger the dose, the more delayed the action of NPH and short-acting (regular) human insulins. The clinical evidence regarding these human insulin formulations suggests a longer, flatter action profile with doses >50 units, which may compromise glycemic control. When injecting >50 units of short-acting (regular) or intermediate-acting (NPH) insulin per dose, it may be prudent to split the dose into 2 separate injections depending on the desired clinical outcome. (55, 65, 86, 92, 93)
- 2 The time-action profile of insulin analogues including first generation long-acting (insulin detemir and insulin glargine) and rapid acting insulin is not affected by the volume of injection. The decision to use 2 injection sites may be a function of the device (i.e. a maximum single dose of 60 - 80 units) or discomfort with injection volume, rather than a requirement to achieve a better pharmacokinetic profile.
- 3 Insulin therapy should be individualized and in accordance with the needs of the individual patient; any changes made to the dose or regimen should be done under medical supervision, and close monitoring is recommended.
- 4 Second generation long acting basal insulins (insulin glargine U-300 [TOUJEO](94) and insulin degludec U-100, U-200 [TRESIBA] (95) provide improved steady-state pharmacokinetic and pharmacodynamic profiles, with no pronounced peak and a longer duration of action than first generation long acting basal insulins®. Splitting these insulins into more than 1 injection would be a function of exceeding the maximum dose delivery of the device. There are currently no data to support dividing a large dose into a twice-daily regimen.

7.0 Injectable Therapy – GLP-1 Receptor Agonists

6.4 Concentrated insulin: practical tips and special considerations

- 1 Concentrated insulin delivers the same dose with less volume. This concept requires further study to ascertain if there will be more, less, or no difference in rates of lipodystrophy.
- 2 Concentrated insulin is available in a pre-filled pen device specifically designed for this type of insulin. The dosing window shows the number of units that will be delivered in a smaller volume.
- 3 There is no calculation required when switching or starting these insulins: 1 unit on the pen = 1 unit of insulin. It is delivered in less diluent.
- 4 Concentrated insulins are not available in vials; therefore, it is imperative that there is NO pen-to-syringe transfer, to avoid dosing errors. It is also important that none of the concentrated insulins be removed from the prefilled pen device for use in a syringe, pump, or other delivery device, to avoid potential overdose or hypoglycemia.

The injection technique for GLP-1 receptor agonists is similar to insulin. However, there are a few practical differences. While lipohypertrophy is largely associated with insulin therapy (e.g. incorrect site rotation, reuse of needles), insulin as a growth factor also contributes significantly to the development of lipohypertrophy. It is therefore not surprising that the available evidence indicate that GLP-1 receptor agonist injections do not lead to lipohypertrophy. It is, however, still important to rotate injection sites with these agents. The results of ongoing trials will provide further information.

While no studies have been published regarding the effect of injecting a GLP-1 receptor agonist into an area of lipohypertrophy, it may be hypothesized that, like insulin, erratic medication absorption may occur. Considering the time-action profile of current GLP-1 receptor agonists, the clinical implications of these absorption distortions would have less impact than with insulin. Still, patients should be advised to avoid injecting GLP-1 receptor agonists into lipohypertrophic areas.

7.0 Injectable Therapy – GLP-1 Receptor Agonists

7.1 Storage of GLP-1 receptor agonists

- 1 GLP-1 receptor agonists should be stored per the manufacturer's recommendations in a refrigerator (2 to 8 oC). They should not be stored directly adjacent to a refrigerator cooling element.
- 2 GLP-1 receptor agonists should not be frozen. If freezing occurs accidentally, the medication should be discarded.
- 3 For multi-dosing, reusable pen devices, once removed from the refrigerator and the initial dose has been given, the products can be stored for 30 to 56 days at room temperature (no higher than 30 oC) according to the manufacturer's recommendations or in a refrigerator (2 to 8 oC).
- 4 Single-use devices can be stored for approximately 14 days at room temperature (no higher than 30 oC) as per the manufacturer's recommendations.

7.2 Practical tips and special considerations

GLP-1 receptor agonists are absorbed equally from each of the usual injection sites (i.e. abdomen, arm and thigh). (96-98)

- 1 Regular priming of reusable devices with each injection is not required for GLP-1 receptor agonists. Due to the design of these pen devices, priming or flow check (Ozempic and Victoza), or "Activation" (Adlyxine), is required only once, prior to administration of the first dose. (97, 99-101)
- 2 Trulicity™ is a once weekly GLP-1 receptor agonist that is available in a ready-to-use (no reconstitution required) single dose/single use pen, with a hidden, pre-attached needle. The needle, which extends and retracts automatically, is 29-G, with a 5-mm injection depth. Both doses —0.75 mg and 1.5 mg —are delivered in a 0.5 mL injection volume. No priming is required for Trulicity™. (102)
- 3 Bydureon® is a GLP-1 receptor agonist that utilizes biodegradable microsphere technology for controlled extended release. Bydureon® is supplied in a dual chamber pen injector. The front chamber contains the 2-mg once-weekly dose of exenatide powder, while the rear chamber contains sufficient diluent to re-suspend the exenatide with microspheres (total volume: 0.65 mL). Reconstitution is required. A 23-G (7-mm) needle is used to deliver Bydureon® subcutaneously. Administration with a 7-mm needle should follow the same technique as with an 8-mm needle. No priming is required for Bydureon®. (99)

8.0 Injection Area

8.1 Injection area selection

A plethora of research, using various imaging techniques, has demonstrated that, regardless of age, BMI, gender or race, skin thickness (epidermis and dermis) is relatively consistent. It ranges from 1.25- to 3.25-mm at its extremes, but averages around 2.0-mm.(22, 103-109)

The thickness of subcutaneous tissue has a much wider variance, and is related to gender, body site and BMI. The subcutaneous layer increases proportionally with an increase in BMI (Fig. 14).(22, 71, 105, 110-112)

Best practice indicates that rates of unexplained hypoglycemia and increased glycemic variability are lower when the abdomen is used exclusively as an injection site.

To avoid IM injection, and in consideration of safety and ease in self-injection, the abdomen, thighs, and buttocks are the recommended self-injection areas for adults. Men have a higher risk of IM injection at all injections sites with the highest risk being in the thigh followed by the arm, abdomen and buttock. (44) The risk of an IM injection is inversely proportional to BMI for both genders, and is influenced by the force used in the injection.

Needle depth accuracy is affected by needle design, needle type and force responsible for injection depth.(44)

- 1 The buttocks are noted to have the thickest subcutaneous layer of these areas.(4, 105, 107-109)
- 2 The areas of injection are defined as:
 - –Abdomen boundaries: 1-cm above symphysis, 1-cm below lowest rib, 2- to 3-cm away from umbilicus and laterally at the flanks

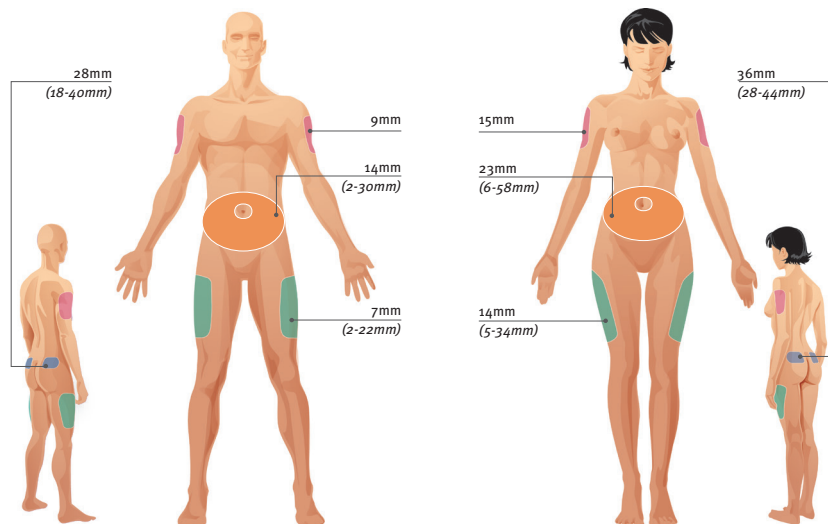


Fig. 14. Subcutaneous thickness in male and female adults. Mean values and ranges (in parentheses) are from a series of studies using ultrasound(4)

8.0 Injection Area

8.1 Injection area selection continued.

- Thighs: upper third anterior lateral aspect of both thighs
 - Buttocks: posterior lateral aspect of both upper buttocks and flanks
- 3 The abdomen offers the most consistent absorption of regular and NPH insulin.(5)
 - 1 The arm is not a preferred area for self-injection, due to difficulty accessing the correct zone, difficulty in handling the delivery device to achieve the necessary 90-degree angle and the lessened thickness of subcutaneous fat, which could create a greater potential for IM injection.(4, 5, 105, 112-114)

9.0 Lipodystrophy

9.1 Definition of lipodystrophy

Lipodystrophy is a disorder of the adipose tissue that is frequently related to insulin injections. It is the most common complication of subcutaneous injections and includes lipoatrophy as well as lipohypertrophy.(115, 116)

9.2 Identification of lipohypertrophy

Lipohypertrophy is the most common lipodystrophy found at injection sites.(117, 118)

Lipohypertrophic areas can develop under the skin where the same injection or infusion site is used repeatedly. Described as thickened or rubbery lesions (Fig. 15),(2, 6) lipohypertrophic areas may vary in size and shape; some are visually apparent, while others may require palpation for detection. Recent research suggests that some areas of lipohypertrophy may be detected only via ultrasound.(10, 117, 119-121)



Fig. 15. Lipohypertrophic lesions

9.0 Lipodystrophy

9.3 Factors contributing to the development of lipohypertrophy

When palpated with the fingertips, lipohypertrophic areas may feel dense and hard.(99, 117, 122-124) These lesions can also be identified by pinching the skin: while healthy skin can be pinched together tightly, lipohypertrophic lesions cannot (Fig. 16).

- 1 Unlike other injectable agents (e.g. GLP-1 receptor agonists, heparin) insulin is a growth factor that contributes to the enlargement of adipocytes and swelling of the fat tissue when injected repeatedly into a small subcutaneous area. This anabolic activity of insulin is a significant contributor to the development of lipohypertrophy. (116, 117, 119, 121, 125)
- 2 Although the exact causes have not been substantiated, factors known to be associated with increased areas of lipohypertrophy include: longer duration of insulin use;(126) more frequent injections; higher dosage of insulin; the use of non-purified insulin (prior to the use of human insulin and insulin analogues); repeated injection or infusion into a small area (i.e. smaller than the size of a postage stamp); reuse of needles; and failure to inspect injection or infusion sites on a regular basis. (8, 9, 57, 118, 120, 125-129)



Fig. 16. The pinch characteristics of normal (left) vs. lipohypertrophic (right) tissue(124)

9.0 Lipodystrophy

9.4 Effects of lipohypertrophy

The effects of injecting or infusing insulin into a lipohypertrophic site have been documented as a decrease in the rate of insulin absorption as well as a variable rate of absorption thereby resulting in variable glycemic response, increased rates of unexpected hypoglycemia and increased A1C. (10, 117, 120, 121) Studies have also shown that when insulin is injected into lipohypertrophic sites, larger daily doses of insulin are required to achieve glycemic targets resulting in increased cost for the insulin user. (9, 117, 120, 121) There is also the potential for the development of disfiguring anatomical lesions. (8, 9, 125, 128)

It has been noted that patients repeatedly choose lipohypertrophic sites for injections or infusions, as these areas have limited nerve innervations and result in relatively painless injections. (36, 131, 132)

Recent international trials have found that the prevalence of lipohypertrophy ranges from 49% to 64% or higher among study participants. (121)

The strongest correlating factor in all studies was the lack of injection site rotation. (8-10, 125)

A previous international survey found that 28% of participants could not remember ever having their injection sites checked by a healthcare professional. This clearly indicates the need for a heightened level of awareness among both healthcare professional and patients to check injection sites daily and rotate sites as necessary to reduce the risk of lipohypertrophy. (8, 12, 116, 120, 121, 125, 133)

Due to the potential for the thickness of the subcutaneous fat layer to vary, even within the same anatomical area (e.g. the abdomen), (108) the use of a 4-mm needle minimizes the potential for IM injection and allows patients to use a larger area for injection, i.e. a postcard-sized area vs. a postage stamp-sized area.

9.0 Lipodystrophy

9.5 Assessment, prevention, and avoidance of lipohypertrophy

- 1 Structured education in regard to injection techniques and lipohypertrophy has resulted in A1C improvements, less glycemic variability and fewer episodes of unexplained hypoglycemia.(116, 117, 120, 121, 130, 134) Education regarding lipohypertrophy should be included during all insulin initiations and reinforced during all discussions with insulin-using patients.(8, 117, 121, 135-138)
- 2 Injection or infusion sites should be inspected and palpated by a healthcare professional at each visit:
 - The inspection should be performed while the patient is in a standing(124) or supine position
 - Adequate lighting should be ensured
 - The injection area should be palpated in a circular, sweeping motion using the fingertips
 - Assessment may be enhanced with the use of examination gel or lotion
- 3 Patients should be taught how to manually inspect and palpate their injection sites to detect lipohypertrophy (Fig. 15).(139)
- 4 To prevent lipohypertrophy and maintain consistent medication absorption resulting in fewer episodes of unexplained hypoglycemia,(116, 117, 121) patients should rotate their injections within an anatomical area, use larger injection zones and use a new needle with each injection (Fig. 17).(5, 6, 9, 32, 117, 121, 131, 133,)
- 5 Patients should be instructed never to use lipohypertrophic sites when injecting medication. (117, 121, 136-138)
- 6 In order to reduce the risk of hypoglycemia when changing from a lipohypertrophic injection site to a healthy site, patients should be cautioned to reduce their insulin dose initially and monitor their blood glucose levels more frequently.(8, 117, 121, 134)
- 7 Recent research has shown that by avoiding injections into lipohypertrophic sites over a 3- to 6-month period, these lesions may decrease by up to 50% in diameter or in some instances resolve completely. (121, 130, 134)



Fig. 17. Proper palpation technique for detection of lipohypertrophy

9.0 Lipodystrophy

9.6 Lipoatrophy

Lipoatrophy, although relatively rare, has been seen more frequently with the use of animal insulins. It is described as a depression of the skin, frequently deep but varying in size, located in an area of repeated insulin injections (Fig. 18).

The cause is attributed to an immunological reaction to the injected insulin resulting in damage and disappearance of the fat layer under the dermis.⁽¹¹⁶⁾ It is more commonly seen in women with type 1 diabetes who experience other autoimmune disorders.⁽¹¹⁵⁾ By switching to recombinant human insulin/ insulin analogs and choosing new injections sites, lipoatrophy is usually/ can be averted.^(115, 116, 140)



Fig. 18. An example of lipoatrophy

10.0 Site Rotation

10.1 Implementation

Site rotation is essential to avoid lipohypertrophy and to facilitate consistent medication absorption, thereby contributing to a decrease in glycemic variability and unexplained hypoglycemia.(8, 9, 12, 57, 123, 125-127, 141, 142)

- 1 To prevent lipohypertrophy and maintain consistent medication absorption, patients should be assisted in the development of a personalized, structured rotation regimen for injection and insertion sites.(79, 117, 121, 143)
- 2 For insulin injections, structured rotation is recommended in the same anatomical area (e.g. abdomen, thigh) at the same time of day, with injections administered at least 1- to 2-cm apart (i.e. the width of 1 finger) across the entire area (Fig.19).(9, 71, 79, 144)

- 3 A recent study of colored pen needle caps accompanied by education information within the packaging demonstrated a statistically significant improvement in injection site rotation.(145)
- 4 The abdomen remains the preferred injection/infusion area; however, patient preference remains an important consideration.(33) Care should be taken to avoid injecting or inserting within 2- to 3-cm of the umbilicus.
- 5 Injection or insertion site rotation should be discussed with, and demonstrated by, patients at every visit.(4, 133, 143) This should be documented in the patient's chart.(8)

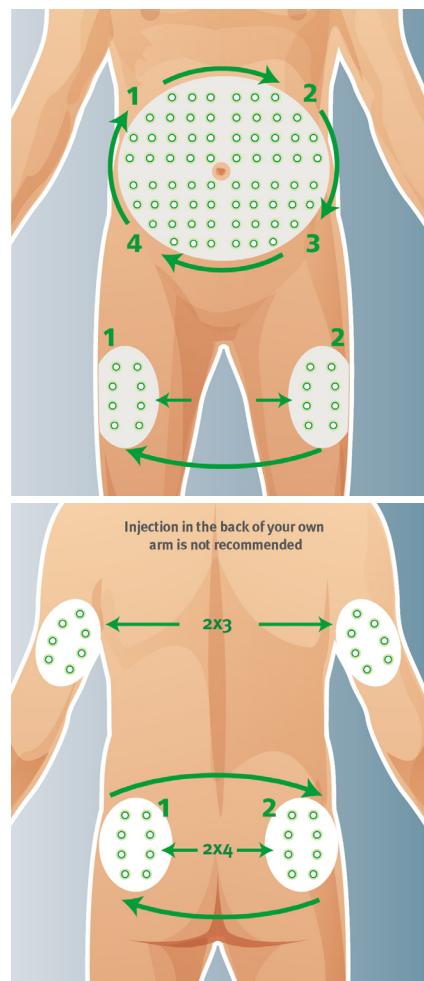


Fig. 19. Injections within any quadrant should be spaced at least 1- to 2-cm from each other. Sample structured rotation plan for abdomen and thighs: divide the injection area into quadrants or zones then use 1 zone per week and move clockwise

11.0 Bruising and Bleeding

11.1 Recommendations

Local bruising and/or bleeding may occur occasionally at an injection site and is more common in patients who are taking antiplatelet therapy. Bruising and bleeding do not impede medication absorption and does not appear to be associated with choice of injection site. Using a thinner gauge pen needle (33-G and 34-G) has been shown to contribute to less bruising.⁽¹⁴⁶⁾ Also, switching to a shorter, thinner needle may have positive psychological implications for adherence.^(12, 128, 147, 148) The primary contributor to bruising and bleeding at the injection site is erroneous injection technique including excessive force.^(6, 26, 45, 107, 115, 117, 121, 134)

- 1 Patients should be reassured that occasional bruising or bleeding at an injection site will not affect medication efficacy. (12, 43, 137)
- 2 Avoid indenting the skin when injecting. Increased force with an injection can lead to an increase in bruising and a greater potential for an IM injection.^(44, 121) Place the needle into the skin, while maintaining visibility of the needle hub (Fig. 20).^(12, 137, 148)
- 3 To decrease the potential for bruising or bleeding, injections sites should be rotated, massaging the skin at the injection site should be avoided and the use of thinner shorter needles should be encouraged. (115, 149)
- 4 Frequent bruising or bleeding at an injection site warrants a review of injection technique. (115, 116, 121, 134)

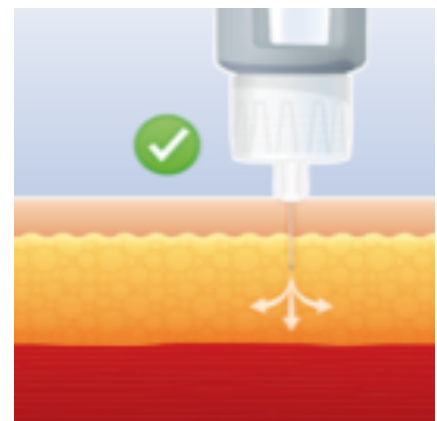


Fig. 20. Avoid indenting the skin when injecting

12.0 Pregnancy

12.1 Recommendations

Due to the paucity of evidence regarding insulin injection technique during pregnancy, the following recommendations are based upon available research and clinical experience.(26, 45) During pregnancy, questions often arise from women regarding why, where and how insulin should be administered. The initial concerns of the mother regarding the effect of insulin injections or infusion on the fetus must be explored, to facilitate medication adherence. Ease of use and safety issues (e.g. hypoglycemia) should also be discussed.(150)

- 1 Education regarding insulin use during pregnancy is essential for all pregestational women and women with gestational diabetes who require insulin. This education should include discussion of the psychological adjustment to insulin use, changes to insulin requirements during pregnancy, appropriate injection sites and site rotation, and prevention of hypoglycemia.
- 2 The abdomen is the preferred area of injection for pregnant women.(151, 152)
- 3 The thigh may be used as an alternate injection area.(107)
- 4 Shorter needles (4 mm or 5 mm) should be used, to decrease the potential for IM injection.(12, 103-105)
- 5 Injections within 2- to 3-cm of the umbilicus,(102, 104) or areas on the abdomen where the skin is taut, should be avoided.
- 6 During the third trimester of pregnancy, when the skin is taut over the central abdomen, the lateral sides of the abdomen are the recommended areas for injection (Fig. 21).



Fig. 21. Recommended injection sites during the third trimester of pregnancy

13.0 Older person

13.1 Special considerations

Education and treatment approaches for the older population are challenged by both physical and psychological issues. These include epidermal thinning and dermal atrophy with a decrease in skin integrity, reduction in subcutaneous fat, and a loss of muscle mass and strength.¹⁵³ Changes in cognition can be exhibited by memory loss and further exacerbated by a decrease in hearing and sight. Impaired counterregulatory hormones reduce the recognition of hypoglycemia, creating a greater potential for falls and fractures.¹⁵⁴ The approach to older patients must be highly individualized, while integrating all aspects of their lives (e. physical, social and spiritual realms).⁽¹⁵⁵⁻¹⁵⁷⁾

Assessing cognitive and functional abilities affected by aging is a primary concern when evaluating safety in injection technique in the older population.⁽¹⁵⁷⁾

- 1 Individualized assessment should be done using standardized tests for cognitive and functional abilities.^(157, 158) The clock drawing test is recommended as an assessment tool to determine cognitive function.¹⁵⁹ Depression screening should be mandatory.^(107, 157, 158, 160)
- 2 A structured diabetes management and injection technique plan should be written, based upon a comprehensive physical and psychological assessment.^(107, 155, 158) Simplified insulin regimens with the use of basal insulins are preferred for safety in the older person.⁽¹⁶¹⁾
- 3 Insulin pen use is recommended versus vial and syringe. Disposable prefilled pens, memory pens and pens with assistive devices have added safety features recommended for use by the older person.^(32, 157, 162) Technology assisted injection devices are helpful for adherence and tracking purposes resulting in safer insulin use for the older person.^(163, 164)
- 4 Education of family members and friends is encouraged for support and safety. Encourage family members to be involved on a daily basis.^(155, 165) Telephone follow-up with this group is recommended.^(155, 165, 166)

14.0 Pediatrics

14.1 Thickness of subcutaneous fat

- 5 The recommended area for self-injection for the older patients is the abdomen. The use of an insulin pen device with a 4-mm pen needle is encouraged, to avoid the need for a skin lift. Healthcare professionals may recommend the outer aspect of the arm as an alternate site for caregivers who are responsible for injecting and have been trained in injection technique. Safety engineered devices are recommended for third-party caregivers, where there is a risk of disease transmission.(12, 71, 107, 153)
 - 6 All training regarding injection therapy should include a return demonstration.(139, 158)
- Many children and adolescents are emaciated at the time of diabetes diagnosis. As well, children aged 2 to 6 years, those who are slim and very lean teenage boys have minimal subcutaneous fat tissue. All these factors render the administration of insulin into subcutaneous fatty tissue very challenging. Appropriate injection techniques are key to achieving optimal blood glucose control.
- 1 The healthcare professional should conduct an individualized assessment to determine the amount of subcutaneous fat thickness at each injection site. This assessment will guide the choice of needle length and administration technique. (167) Professionals should inspect injection sites and provide targeted, individualized instruction on a regular basis. (168)
 - 2 Insulin pens are the injection devices of choice due to their shorter needle lengths (4 mm, 5 mm or 6 mm);169 4-mm needles are the safest needle length currently available.(106)
 - A 4-mm needle can be inserted at a 90-degree angle without a skin lift in adolescents and children >6 years of age; children aged 2 to 6 years require a skin lift in order to avoid IM injection.(24, 106)
 - If a child or adolescent is lean, 5-mm and 6-mm needles require a 45-degree angle injection with a skin lift(90, 170)
 - 3 If a young child cannot remain immobile during the injection procedure – as is required with pen use – a syringe with a 6-mm needle may be used. In order to avoid an IM injection, it is critical to inject into a site with sufficient adipose mass, perform a skin lift and angle the injection.(169, 170)

14.0 Pediatrics

14.2 Injection sites

Small children have less surface area at injection sites. As well, since many children and adolescents do not adhere to an adequate site rotation plan, lipohypertrophy is a common occurrence. Barriers to the use of multiple sites include fear that a new site will be painful to inject into and comfort with an existing routine.(171, 172)

- 4 The healthcare professional should educate parents, children, and adolescents regarding the need for injection site rotation. Indeed, parents must reinforce the consequences of injecting into “favourite spots.”

- 5 Injection site rotation, both inter-site and intra site, must be performed diligently. Injections should be moved from one injection to the next within a site by approximately 1-cm (a finger width) in a predetermined pattern to avoid repeat injections at the same location.

- 6 For children and adolescents who self-inject, supervision may be required to ensure adequate site rotation.

14.3 Needle anxiety and pain

Needle anxiety is common in children and adolescents, as well as their parents; younger children report greater fear and pain. Parents’ attitudes are important for their child’s acceptance of injections.(173-175)

- 1 The healthcare professional should ask patients about needle fear and pain, as many do not report it voluntarily.(2)
- 2 At diagnosis of diabetes, the healthcare professional should consider intervention strategies for the child’s parents, as follows:
 - Inform them that displayed distress and negative attitudes can influence their child’s cooperation with the administration of insulin
 - Have parents experience the injection regimen by performing a saline injection with a syringe or pen needle attached to an empty insulin pen.

14.0 Pediatrics

14.4 Preparing children for injections

3 Younger children may be helped by:(167)

- Distraction therapy (provided it does not involve trickery), e.g. injecting while watching a favourite television show, blowing bubbles, or looking for hidden objects in picture books
- Play therapy, e.g. injecting a favourite stuffed toy

4 Older children and adolescents experiencing needle anxiety may be helped by cognitive behavioural therapy, if available, including:(167)

- Relaxation training
- Guided imagery
- Graded exposure
- Active behavioural rehearsal
- Modeling and reinforcement
- Incentive scheduling

Anticipatory fear is often worse than the actual experience of injection. Parents who are well-prepared beforehand will transmit less anxiety to a child. In fact, the presence of a calm and reassuring parent is the most effective support for a distressed child.(33, 34)

14.5 Self-injection

The age at which children can self-inject is related to developmental maturity rather than chronological age. Most children →10 years of age can either administer their own injections or help with them.(176)

If self-injecting, young children should do so under supervision, and share the responsibility with their parents.(167, 176)

14.0

Pediatrics

14.6 Insulin under- and overdosing

Intentional under- and overdosing of insulin is common in children and adolescents, and can lead to severe hypoglycemia or diabetic ketoacidosis.(177-180)

- 1 If insulin dose manipulation is suspected or confirmed, the healthcare professional should instruct parents to be more involved in insulin administration.(181)
- 2 If omission or overdosing remains an issue, parents should be instructed to assume the responsibility of injecting insulin.
- 3 Supervision of injections by parents or caregivers should include checking the dose prior to injection and ensuring the injection has penetrated the skin.

14.7 Adolescence

Adolescence is defined as puberty through 18-years of age. During this stage of life, insulin resistance is more common, and higher doses of insulin are often required to achieve near-normal glucose control. Studies have demonstrated that insulin levels are higher during puberty than they are during adulthood or the years preceding puberty.(182)

Although the majority of adolescents with type 1 diabetes adapt well to the difficult challenges of puberty, it must be recognized that their healthcare and emotional needs are distinctly different from those of younger children or older adults. Adolescence involves training to become an independent adult and may result in failures and mistakes, as well as successes. Many adolescents have a greater tendency to skip insulin, due to peer pressure, rebellion, pain, depression, or diabetes burnout. As well, some adolescents associate insulin with weight gain, and therefore choose to skip insulin doses.(182)

15.0 Insulin infusion

15.1 Selecting an infusion set

An insulin pump is a small computerized device programmed to mimic the human pancreas (Fig.22). It delivers small continuous doses of insulin for basal needs and variable amounts of bolus insulin, as needed, for food or corrections. Insulin is delivered into the subcutaneous space by either an infusion set with a cannula and tubing, or a cannula within a pod that attaches directly onto the skin. Insulin infusion sets are available in a variety of lengths, diameters, connector material and designs to meet individual needs and preferences.



Fig. 22. Examples of insulin pumps

An insulin infusion set consists of a cannula (composed of steel or Teflon) that is inserted into the subcutaneous tissue, and tubing that is attached to the pump's insulin reservoir. A patch pump does not have tubing but consists of a cannula inserted into the skin that connects directly to a pod.(3, 6, 7)

When selecting an appropriate infusion set, the following factors should be considered:

- Cannula length
- Cannula composition (steel or Teflon)
- Patient or caregiver preference
- Patient's ability to self-insert the device
- Patient's lifestyle and physical activity level

- 1 Cannula
Choosing the appropriate cannula length is dependent on the thickness of the patient's subcutaneous tissue and the preference of the insertion angle preference.(3) (Table 1)
 - The criteria for choosing the cannula length is similar to choosing an insulin pen needle length.(8) Skin thickness studies suggest that shorter cannulae may reduce the risk of IM insertion(22)
 - The angle of insertion is dependent on the type of infusion set used: steel cannulae require a straight insertion, whereas Teflon cannulae can be inserted straight or at an angle (20 to 45 degrees, depending on the patient)

Composition	Length	Angle of insertion
Steel	6 mm, 8 mm, 10 mm	Straight
Teflon	6 mm, 9 mm, 13 mm, 17 mm	Straight or angled
Pod/patch pumps	Automatic insertion of 50 degrees to a depth of 6.5 mm	

Table: Examples of cannulae and insertion

15.0

Insulin infusion

15.2 Inserting an infusion set

- A review of known patient sensitivities is important when considering the choice of cannula. Those with sensitivity to Teflon should use a steel cannula. In some patients, the risk of local inflammatory reaction is reduced with steel cannulae, due to better biocompatibility.(183)

- 2 choosing tubing length, it is important to consider placement of the infusion set, and where the pump will be worn on the user's body. The tubing should be long enough to allow the user to interact easily with the pump to avoid tugging on the infusion line, which can be transferred to the cannula under the skin. Lateral movement of the cannula induced by body movement or inadequate tubing length may lead to kinking or bending of a Teflon cannula or detachment of a steel cannula. (184)

An infusion set may be inserted manually or with an automatic insertion device (which can be either reusable or disposable). The automatic insertion device and technique used are dependent on the type of set and the amount of subcutaneous tissue at the insertion site. An automatic insertion device is recommended for a flexible Teflon cannula to reduce the risk of kinking. (185, 186)

Automatic insertion devices should be considered for patients with:

- Needle phobia
- Dexterity limitations
- Low vision
- Difficulty inserting into hard-to-reach areas
- Low confidence with manual insertion

All patients should be instructed to perform manual insertion of an insulin infusion set if an automatic insertion device is unavailable.

Insertion of a steel cannula offers more reliable infusion as it is done manually; thus, the risk of kinking is eliminated, and the rate of insertion failure is reduced, compared with the use of Teflon cannulae and insertion devices.

15.0 Insulin infusion

15.3 Site selection and rotation

Selecting a site should be individualized. Many patients prefer to insert the insulin infusion set in the abdomen or upper outer thigh at the beginning of pump therapy, as these sites are easily visible.

The same criteria for choosing insulin injection sites should apply to choosing insulin infusion set site selection. Proper infusion site selection minimizes the risk of insertion site reactions, lipodystrophy, and scar tissue formation, and promotes better insulin absorption.

- 1 The principles of insulin injection site rotation should also be applied to the rotation of insulin infusion sites.
- 2 All components of the infusion set i.e. insulin, reservoir and tubing should be changed every 2- to 3-days (as per manufacturers' recommendations), or sooner if glycemic control deteriorates.

- 3 A 2015 study by Pfützner and colleagues regarding the tolerability of 2-day vs. 4-day use of insulin infusion sets found higher rates of catheter- and treatment-related adverse events in the latter group.¹⁸⁷ Moreover, extending insulin infusion set use beyond 2- to 3- days is known to increase the risk of skin irritation (e.g. itching, bruising, and general discomfort) and occlusion^(188, 189) and therefore is not recommended.

- 4 Patch pumps can be placed in the same sites as infusion sets and may be appropriate for patients who have difficulty accessing harder-to-reach areas. Consideration should be given to proximity to skinfolds, where the patch may detach when users are in a bending or sleeping position or are performing regular daily activities.

- 5 Insulin infusion set changes prior to bedtime should be avoided, as users will not be awake to assess that the set is infusing properly.

15.0

Insulin infusion

15.4 Skin preparation

- 1 Skin hygiene education is a priority during insulin pump training and should be re-emphasized at regular intervals. The risk of local bacterial infection is higher with insulin pump therapy than with subcutaneous injections, as the infusion set remains in place for 2- to 3- days. During this time, the area can become hot and humid, which provides an ideal condition for bacterial growth. To aid in the prevention of skin infections, it is important that patients clean the infusion site prior to insertion of the insulin infusion set.(186)
 - 2 The risk of infection and skin irritation from adhesive materials can be reduced with the use of antiseptic agents and protection of the site with a layer of protective material (e.g. bio-occlusive barrier, spray or cream).(186) The material should be applied around - but not directly on - the area of skin where the cannula is inserted, to prevent occlusion.
- Insertion through a barrier (such as a clear adhesive dressing) remains controversial, as the small amount of dressing inserted with the cannula may increase the risk of occlusion; as such, this practice is not recommended.
- 3 To reduce the risk of infection, irritation or occlusion at the infusion site, patients should be advised to inspect infusion sites daily. If any signs or symptoms of infection are present, patients should change the infusion set or patch pump. Signs and symptoms of infection include pain, swelling, itching, redness, warmth, drainage (clear, cloudy, white, yellow, or bloody), unpleasant odour, and unexplained hyperglycemia.
 - 4 Application of lotions or other cosmetic skin products at the infusion site should be avoided, as they can cause further skin irritation.(186)
 - 5 Products such as a transparent adhesive dressing may be used to improve adhesion. Patients who use protective barrier products may find their application helpful both prior to insertion and during removal of the insulin infusion set.
 - 6 Frequent infusion set and cartridge changes may be required for patients who are prone to site irritation or infection, or those who require large volumes of insulin.

15.0 Insulin infusion

15.5 Insertion

- 1 Patients should be advised to wash their hands thoroughly with soap and water before inserting the infusion set, and clean the infusion site with an antiseptic solution or soap and water.(123)
- 2 Patients should allow skin to air dry prior to inserting the infusion set or applying the patch pump.
- 3 Insulin infusion sets must be inserted through healthy subcutaneous tissue.
- 4 Avoid underlying muscle, as well as areas of skin irritation, lipohypertrophy or lipoatrophy
- 5 When inserting a Teflon infusion set manually, a rapid, smooth motion should be performed to reduce the risk of kinking.
- 6 There is presently a paucity of evidence regarding the stability of the infusion cannula of a patch pump and how well it adheres to the skin. Considerations regarding variability include the height and weight of the patch.(184)
- 7 Angled insulin infusion sets are most commonly used without the infusion line being anchored with tape, so any tug or movement of the infusion line is not directly transferred to its Teflon cannula under the skin. To reduce redness, irritation, leakage and localized bumps at the point of insertion (known colloquially as ‘pump bumps’) from this movement, the tubing on an angled insulin infusion set can be anchored to the body with tape.
- 8 When priming the tubing of the pump, patients should ensure that the cannula is disconnected from the set to avoid an unintentional insulin bolus, which increases the risk of hypoglycemia.
- 9 Pain and discomfort at the insertion site may result from poor insertion technique, potential infection, the type of cannula material used, skin-related issues or site location.

15.0 Insulin infusion

15.6 Troubleshooting

1 *Unexplained Hyperglycemia*

Sudden onset of unexplained hyperglycemia, particularly if accompanied by nausea or vomiting, should prompt blood and urine ketone assessment, administration of insulin via an alternate source (e.g. insulin pen or syringe),(189, 190) followed by an assessment of the infusion set, tubing and insulin reservoir and changing if required.

Possible causes of unexplained hyperglycemia include leakage, air bubbles, blockage, or occlusion at the infusion site, missed bolus, incorrect time of infusion, empty reservoir, dislodged infusion site or ignored alarms.

Insulin pumps infuse rapid-acting insulin only, therefore diabetic ketoacidosis (DKA) can develop quickly (i.e. within hours) after insulin infusion is interrupted. Patients and their caregivers should be made aware of the risks and symptoms of DKA and know how to act accordingly.

2 *Silent Occlusion*

Silent occlusion is defined as an interruption in insulin flow that does not trigger a pump alarm, and therefore remains unknown to the user. Silent occlusions are thought to occur before full occlusions do and are believed to be a cause of unexplained hyperglycemia.(190, 191)

Factors that increase the risk of occlusion include(186):

- Poor insertion technique
- Incorrect infusion set selection
- Incorrect angle of insertion
- Improper placement of the cannula
- Cannula inserted into or adjacent to muscle fascia
- Degradation of cannula or cartridge
- Crystallization of insulin
- Blockages resulting from blood or tissue-derived proteins (e.g. thrombin)
- Bubble formation is a potential source of occlusion, and the presence of bubbles can be concerning to both professionals and patients. Removing bubbles from the reservoir should be a key aspect of insulin preparation at insulin infusion set and site changes.(192)

3 *Lipohypertrophy*

Lipohypertrophy is thought to be the most common complication associated with the use of insulin infusion sets. Studies in adults and children estimate a prevalence of 26% to 42% in those who use an insulin pump.(190, 193) A recent study of adults with type 1 diabetes and lipohypertrophy demonstrated that lipohypertrophy was present in 34% of insulin pump users.(194)

In the presence of repeated and persistent unexplained hyperglycemia, patients should be counselled to perform self-monitoring of blood glucose more frequently and a review of their insertion habits should be completed at the next opportunity.

15.0 Insulin infusion

15.7 Recommendations for special considerations

1 *Pediatrics*

When choosing an appropriate insulin infusion set and infusion site for infants and children, consider the amount of subcutaneous tissue available in the buttocks and abdomen.

Infants have a higher BMI and more subcutaneous tissue than preschool children (i.e. those between 2 and 6 years of age). School-aged children slowly gain subcutaneous tissue until they reach puberty.^(192, 195, 196) Hence, using the buttocks for infusion sets may be a more suitable infusion site than the abdomen in preschool children. Indeed, a recent study reported significantly lower glycemic variability with this method of insulin infusion vs. infusion in the abdomen.⁽¹⁹⁷⁾

2 *Pregnancy*

In the first trimester of pregnancy, a woman's normal infusion set, and infusion sites are often adequate to maintain blood glucose control. In the second and third trimesters, as the abdominal tissue stretches, it may be necessary to move the infusion site to the lateral sides of the abdomen and adjust the angle of insertion.⁽¹⁹⁸⁾

Infusion sets may need to be changed from a 90-degree straight Teflon set to an angled Teflon or straight stainless-steel set if kinking occurs or unexplained hyperglycemia develops. The angle of insertion may need to be adjusted, to ensure that the set is secure and infusing into healthy tissue.

During pregnancy, the use of stainless-steel insulin infusion sets is advised, as they reduce the risk of hyperglycemia due to kinking.

3 *Physical Activity*

Active people who are at risk of infusion set dislodgement may consider a longer angled infusion set for increased security.⁽¹⁸⁶⁾

If cannula kinking occurs in patients who have high muscle mass and low body fat, a steel cannula may be considered.^(191, 199-201)

The infusion set should be stabilized securely to reduce the risk of movement, dislodgement, and patient discomfort.

15.0

Insulin infusion

15.8 Education

- 1 Education and training of infusion sets, and sites should be assessed routinely.
- 2 Encourage various insulin infusion sets to determine the most appropriate device for their need.
- 3 Ongoing education for new technologies, insulin, infusion sets and devices.
- 4 Education of site assessment and reinforce routine self-assessment.

16.0 Institutions

16.1 Special considerations

The safety of patients and healthcare professionals in medical institutions and long-term care facilities is a primary consideration regarding injection technique.

Needle stick injuries are a frequent, yet largely preventable, occurrence among healthcare professionals.

Consideration must be given to the safe disposal of all injection and infusion devices to prevent injury to healthcare workers.

Cross-contamination among patients is also preventable with appropriate use and disposal of injection or infusion devices. Institutions are encouraged to develop a 'safety culture' through staff education and increased awareness of best practice.

- 1 Safety engineered devices (i.e. syringes or pen needles) should be used by healthcare professionals for all injections in an institutional setting, thereby eliminating the need to recap needles.(6, 54, 59)
- 2 Injectable delivery systems should be for individual use only. (6, 34)
- 3 Injection sites should be clean and free of infection, edema, bruising or lipohypertrophy.(20, 32, 45)
- 4 Alcohol swabs may be used to clean the injection site (note, however, that this does not disinfect the site); the skin should be thoroughly dry before injecting.(20, 30, 32, 46)
- 5 To avoid IM injection, the use of a shorter, safety- engineered pen needle (5-mm) or an angled injection(22, 103-105) (syringe only) is preferred over a skin lift, to reduce the risk of a needle stick injury.
- 6 Prior to injecting, all healthcare professionals should have a clear line of sight to the disposal unit they will be using.
- 7 All institutions should have clear policies and procedures that ensure a 'no blame' approach to the reporting of needle stick injuries.(202)
- 8 All institutions should have an established education program in injection technique to ensure best practice.(154)

CLINICAL TIP

"One pen, one patient!"

17.0

Best practice recommendations

17.0 Best practice recommendations

- 1 Prepare patients regarding the need for injection therapy, provide proper education and ensure regular assessment of injection sites and techniques.
- 2 To reduce risk of lipohypertrophy, reinforce rotation of injection sites within all zones of an anatomical area and discourage needle re-use.
- 3 Healthcare professionals and patients alike should be taught how to inspect and palpate injection sites, and how to prevent lipohypertrophy.
- 4 Use of non-posted (contoured) pen needle designs may reduce the impact of unintended user pressure across a range of injection forces and subsequent inadvertent IM injections, compared to conventional posted-hub PN devices of equivalent lengths.(44)
- 5 The abdomen is the preferred injection area, for consistency of absorption and for ease of self-injection. Instructions should be provided for caregivers for alternate site specifically the arm for a third-party injection.
- 6 Glycemic variability and poor glycemic control may be related to injection techniques, including use of excessive injection force.
- 7 If lipohypertrophy is identified, increased glucose monitoring, potential reduction of insulin dose and careful assessment are required when utilizing healthy sites.
- 8 The injection technique for GLP-1 receptor agonists is similar to insulin with a few practical differences. Patients should avoid injecting GLP-1 receptor agonists into areas of lipohypertrophy.
- 9 With respect to special populations:
 - The lateral sides of the abdomen are the preferred injection sites for pregnant women
 - Safety is a primary consideration in the elderly population; as such, cognitive and functional abilities should be assessed
 - Young children who self-inject, and older children and adolescents who are suspected of insulin under- or overdosing, should be closely supervised by a parent
- 10 Education about the functionality of insulin pumps is the most important education. Failure to understand pump mechanics could have serious consequences

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Glossary

A1C (glycated hemoglobin): A test that measures the average level of blood glucose over the past 2 to 3 months. According to the Diabetes Canada, the target A1C for most people with diabetes is 7.0%.

Blood glucose: The concentration of glucose in the blood, which is represented in millimoles per litre (mmol/L) of blood.

Blood glucose targets: The blood glucose level range recommended by a diabetes healthcare professional for successful diabetes management. According to Diabetes Canada, blood glucose targets for people with diabetes are as follows:

- Fasting blood glucose: 4.0 to 7.0 mmol/L
- 2-hour postprandial blood glucose: 5.0 to 10.0 mmol/L (5.0 to 8.0 mmol/L in those whose A1C remains above 7.0%)

Diabetes: A metabolic disorder characterized by the presence of hyperglycemia due to defective insulin secretion, defective insulin action, or both.

Glycemic variability: The degree to which a person's blood glucose fluctuates between high and low levels.

Hyperglycemia: The presence of excessively high levels of glucose in the blood, which occurs when the body does not have enough insulin or cannot use the insulin it does have to turn glucose into energy. Chronic hyperglycemia in diabetes is associated with microvascular complications (i.e. retinopathy, nephropathy, neuropathy) and macrovascular complications (i.e. hypertension, acute coronary syndrome, stroke, heart failure).

Hypoglycemia: An abnormally low concentration of glucose in the circulating blood. Hypoglycemia is defined as a blood glucose level ≤ 4.0 mmol/L

Injection area (anatomical area):

Appropriate Injection areas are as follows: abdomen, thighs, buttocks, back of arm.

Injection site: The point of insertion or injection of medication.

Injection site rotation: A system to ensure that people do not inject medication into the same site each time they administer an injection. Rotating injection sites is crucial for people who administer injectable medications, to prevent lipohypertrophy and to facilitate consistent medication absorption.

Injection zone: The injection area divided into quadrants (abdomen) or halves (thighs).

Insulin: A hormone produced in the pancreas that regulates the amount of sugar in the blood by stimulating cells ■ especially liver and muscle cells ■ to absorb and metabolize glucose. Insulin also stimulates the conversion of blood glucose into glycogen and fat, which are the body's chief sources of stored carbohydrates.

Insulin analogues: A tailored form of insulin in which certain amino acids in the insulin molecule have been modified. The analogue acts in the same way as insulin, but with some beneficial differences for people with diabetes.

Insulin pen: A pen-sized injection device that is used to inject insulin and is composed of an insulin cartridge (either integrated or bought separately) and a dial to measure the dose.

Lipoatrophy: The loss of subcutaneous fat from one area of the body.

Lipodystrophy: A medical condition characterized by abnormal or degenerative conditions of the body's adipose tissue.

Lipohypertrophy: An accumulation of subcutaneous fat tissue at a site where insulin has been injected continuously.

Needle: A hollow, pointed instrument used to deliver injectable medications into the body. A needle can be used with an insulin syringe to deliver medication from a vial. A pen needle consists of a hollow needle which is embedded in a plastic hub and attaches to the end of an injection pen.

Skin lift: A manoeuvre used when injecting insulin or other injectable medications to ensure optimal medication uptake. To perform a skin lift correctly, an individual should lift the skin and subcutaneous tissue delicately between the thumb and index finger, leaving the muscle behind.



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