Evidence-based clinical guidelines for injection of insulin for adults with diabetes mellitus
Evidence-based clinical guidelines for injection of insulin for adults with diabetes mellitus, 2nd edition

Authors:
Birtha Hansen, cand. cur., clinical nursing specialist, Århus University Hospital
Grete Kirketerp, SD, MPM, stud.cur., ward sister, Odense University Hospital
Gitte Ehlers, diabetes nurse, Hospital Vestsjælland, Kalundborg Hospital
Elisabeth Nordentoft, clinical nursing specialist, Hospital Vestsjælland, Slagelse
Grethe Hansen, diabetes nurse, Steno Diabetes Centre, Gentofte

Edited by: Danish Nurses Organization Layout: Danish Nurses Organization

Printed by: Danish Nurses Organization, 2007
Translation: Alfa & Omega A/S, Aarhus

ISBN 87-7266-303-0 Graphics Unit 07-21

Copyright © Dansk Sygeplejeråd 2007 (Danish Nurses Organization)

December 2006

All rights reserved.

Photographic, mechanical or other form of reproduction or duplication is only permitted if the source is quoted.
## Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foreword</td>
<td>5</td>
</tr>
<tr>
<td>Introduction</td>
<td>6</td>
</tr>
<tr>
<td>Method</td>
<td>11</td>
</tr>
<tr>
<td>Incidence of diabetes mellitus</td>
<td>14</td>
</tr>
<tr>
<td>Treatment of diabetes mellitus</td>
<td>15</td>
</tr>
<tr>
<td>Structure and function of the skin</td>
<td>17</td>
</tr>
<tr>
<td>Insulin treatment and types of insulin</td>
<td>19</td>
</tr>
<tr>
<td>Injection sites</td>
<td>22</td>
</tr>
<tr>
<td> Factors that affect absorption of insulin from subcutaneous adipose tissue</td>
<td>22</td>
</tr>
<tr>
<td> Intramuscular injection and rapid-acting insulin</td>
<td>23</td>
</tr>
<tr>
<td> Intramuscular injection and intermediate-acting insulin</td>
<td>24</td>
</tr>
<tr>
<td> Risk of intramuscular injection</td>
<td>24</td>
</tr>
<tr>
<td> Consequences of intracutaneous injection</td>
<td>26</td>
</tr>
<tr>
<td>Adherence</td>
<td>27</td>
</tr>
<tr>
<td> People with diabetes who have needle phobia</td>
<td>28</td>
</tr>
<tr>
<td> Devices for dealing with needle phobia</td>
<td>28</td>
</tr>
<tr>
<td>The insulin injection process</td>
<td>30</td>
</tr>
<tr>
<td> Which areas can be used for insulin injection</td>
<td>30</td>
</tr>
<tr>
<td> The optimum injection site for premixed insulin</td>
<td>33</td>
</tr>
<tr>
<td> Rotation of injection sites within the same anatomical area to prevent lipohypertrophy</td>
<td>34</td>
</tr>
<tr>
<td> Injection in lifted skin fold</td>
<td>36</td>
</tr>
<tr>
<td> Injection without a skin fold</td>
<td>37</td>
</tr>
<tr>
<td> Injection without a skin fold in the hip</td>
<td>38</td>
</tr>
<tr>
<td> Injection without a skin fold in the abdomen</td>
<td>38</td>
</tr>
<tr>
<td> Injection angle</td>
<td>39</td>
</tr>
<tr>
<td>Choosing needle length</td>
<td>40</td>
</tr>
<tr>
<td>Swabbing skin prior to injection</td>
<td>46</td>
</tr>
<tr>
<td>Re-use of insulin needles for pen systems</td>
<td>48</td>
</tr>
</tbody>
</table>
Disposal of needles and insulin pens  50
Risk of infection  51
General guidelines for insulin injection in adults  52
Bibliography  54
Appendices  62
Foreword

Every day millions of people are required to inject themselves with insulin, while elsewhere in the primary and secondary healthcare sectors, nurses administer injections to patients.

Studies have shown that use of correct injection technique is of great importance in being able to control diabetes and is thus also important for the individual’s health, quality of life and any late diabetic complications.

However, some years ago the Danish Diabetes Nurses’ Society confirmed in a study involving diabetic outpatient clinics/diabetes schools that standards and clinical guidelines for injection techniques varied considerably from place to place and were not evidence-based.

Therefore the authors of this publication decided to prepare a set of clinical guidelines for the best possible injection technique for administering insulin, founded on evidence-based material.

The first edition of the publication was published in 2002. The text of the second edition has been revised to a minor extent and the bibliography has been updated from 2002 to 2005. The clinical guidelines have been revised to reflect new information within this area.

This updated version represents – in line with the Danish Nurses’ Organization’s “National Strategy for Nursing Research” – up-to-date nursing knowledge.

I hope that it will be used in clinical practice and that it will contribute to promoting good health and preventing ill health.

Connie Kruckow
President
Introduction

Every day millions of people with diabetes mellitus have to inject themselves with insulin, and it is essential that they do it correctly. It has been shown to be the case that many people with diabetes inadvertently inject themselves in muscle, because there is less subcutaneous adipose tissue at the usual injection sites than they supposed, and if the wrong needle length is chosen the injection will be intramuscular (Frid & Lindén, 1992III, C). One consequence of this is fluctuating and unpredictable blood glucose levels, resulting in poorly-regulated diabetes, which can lead to reduced quality of life and, in the longer term, late diabetic complications.

In recent years needles have become shorter and shorter. Thus, it is essential that health care professionals know how to select the correct needle length for each individual patient. For many people with diabetes, having to start insulin treatment can be more traumatic than the actual diagnosis of diabetes. A survey asking people how they found having to start insulin treatment produced the following results:

- 45.8% of respondents said they were very worried about needles and were bothered by them when they started insulin treatment.
- 37.5% of respondents were quite worried and bothered by needles (Diglas et al. 1999IIa, B).
- 10% of 7-15 year-olds said they actually had a needle phobia that could affect adherence and lead to poor metabolic control (Hanås 1998IV, D).

It is therefore extremely important that health care professionals be aware of these facts and recommend aids and techniques to reduce the pain and discomfort suffered, so that good glycaemic control can be maintained and health preserved. As well as being extremely important for the individual concerned, it also makes sense from an economic viewpoint, as the treatment of late diabetic complications is extremely costly.

In spite of instruction in correct injection technique, we as diabetes nurses experience several problems in relation to this, e.g. lipohypertrophy, which is defined as a visible or noticeable thickening of the subcutaneous adipose tissue at injection sites. This is supported by a Finnish study, in which
65% of participants had skin complications for example thickening of the skin,
23% of participants used an area the size of a postage stamp to distribute their injections,
15% of participants had never had their injection sites checked by a professional (Partanen & Rissanen, 2000III, C).

Based on the aforementioned study, a number of questions can be posed. For example:

- Could it be possible that professionals have insufficient knowledge in carrying out insulin injections properly?
- How should the correct needle length be chosen?
- Is there perhaps insufficient knowledge of the fact that injection sites should be checked for lipohypertrophy?

Lipohypertrophy has serious consequences with regard to the life situation of the individual, as it affects physical, psychological and social health due to fluctuating blood glucose levels. Lipohypertrophy also results in poor metabolic control, with a risk of developing late diabetic complications in the form of blindness, renal failure and amputations.

As stated above, there are numerous problems relating to correct injection of insulin, and therefore good clinical practice concerning injection technique is very important.

Problems in connection with insulin injection
In practice it has proved to be the case that some people with diabetes inject insulin in the same small area time after time, which can result in lipohypertrophy. Lipohypertrophy can alter and delay the uptake of insulin from the injection site, thereby causing unstable blood glucose levels and leading to poor metabolic control (Young et al 1984III, C; Kølendorf et al. 1983III, C). In a Spanish study involving 150 people with diabetes, 52% of the participants had lipohypertrophy and of these 41% had unstable blood glucose levels and poor diabetes regulation (Saez-de Ibarra & Gallego 1998III, C). This is supported by a Finnish study (Partanen & Rissanen 2000III, C), involving 100 people with type 1 diabetes. By investigating injection sites it was found that 65% of patients had skin complications in the form of thickening of the skin (46%), lipohypertrophy (29%) as well as a rash (8%) and lipoatrophy (1%). 23% stated that they used
an area the size of a postage stamp over which to distribute their injections, and only 30% of respondents distributed their injections systematically. 15% had never had their injection sites checked by a professional. It also proved to be the case that those who had the worst metabolic control, with HbA1C over 8.6%, also had the most skin complications and used a small injection area. They also never had their injection sites checked. 15% never injected in a lifted skin fold, and in half of the cases, the injection angle was 90 degrees, even though most patients used a 12.7 mm needle, which gives rise to a greater risk of injecting into muscle (Frid & Lindén, 1986). There is reason to suppose that people with diabetes in Denmark have the same problems at their injection sites as described above. At the Steno Diabetes Centre in Gentofte, it was discovered that 55% of patients who received standard instruction on injection technique had lipohypertrophy. However, only 20% had lipohypertrophy when they received more intensive instruction on injection technique and had their insulin sites checked on each visit. The insulin dose was also divided into two injections when administering more than 40 units of insulin (Nielsen et al. 1998).

Experiences from the authors’ daily clinical practice supports the above, as there are often problems of varying degrees with lipohypertrophy at injection sites.

The Danish Diabetes Nurses’ Society carried out a survey among the diabetes nurses who teach at diabetes outpatient clinics/diabetes schools regarding guidelines and standards for instruction in injection technique.

The aim of the survey was to investigate whether the standards/guidelines for instruction in injection technique for adults with diabetes in Denmark are evidence-based. The guidelines and standards reported were reviewed by the authors.

It proved to be the case that the advice and guidance that was given varied from place to place and was not written from the perspective of evidence-based knowledge. The conclusion was that where there was no source or reference for the standards/guidelines, these were not founded on evidence-based knowledge. No report was published (Hansen et al. 1998-1999).
The work group
No evidence-based clinical guidelines have been developed in Denmark for injection of insulin. Neither are there any descriptions of indicators of quality (County of Aarhus, 1999, Danish National Board of Health, 1996).

Against this background, a work group was set up within the Danish Diabetes Nurses’ Society in 1999. This work group consists of the following nurses: Birtha Hansen, Århus University Hospital; Grete Kirketerp, Odense University Hospital; Gitte Ehlers, Hospital Vestsjælland, Kalundborg Hospital; Elisabeth Nordentoft, Hospital Vestsjælland, Slagelse Hospital and Grethe Hansen, Steno Diabetes Centre in Gentofte. All have worked for many years in the field of care and treatment of people with diabetes and have attended relevant courses, in-service training and refresher courses, as well as national and international conferences.

The Danish Diabetes Nurses’ Society has given the group financial support by covering all travel expenses. Financial support was provided for writing these guidelines by the Danish Diabetic Association and pharmaceutical firms Becton Dickinson, Novo Nordisk A/S and Sanofi Aventis. Research consultant Marianne Nord Hansen, the DNO, provided guidance for the group in connection with the drawing up of the clinical guidelines.

Aim
The aim of the clinical guidelines is that health care professionals with a background in evidence-based knowledge can perform and provide information of the correct insulin injection technique for adults with diabetes mellitus.

Target group
The target group for these Clinical Guidelines is: Health care professionals in primary and secondary health care. The Clinical Guidelines are thus aimed, for example, at: GPs, practice nurses, primary care nurses, social and health care assistants and hospital nurses.

People with diabetes and their relatives, who may take over injection of insulin in the event of illness, may also find these guidelines useful.

It is expected that the Clinical Guidelines for insulin will be used at all relevant training institutions: nursing schools, social and health care colleges, etc. They can also be included in teaching material in various contexts in both primary and secondary health care.
Scope
The mission of the work group was to develop clinical guidelines for injection of insulin for adults with diabetes (over 18 years of age). Adults were chosen because there are other problems relating to children and thus other literature needs to be selected. The development of clinical guidelines for children is another project. Other problems relating to living with a chronic disease such as diabetes are not dealt with here. These include: problems relating to adherence, inadequate social support and networks, psychological problems with failure to fully accept the disease, insufficient personal resources, learning disabilities.

As correct injection of insulin and evaluation of the quality of this is a basic requirement for achieving good metabolic regulation, the problem is limited to:

- How is correct injection of insulin performed in adults, when based on evidence-based knowledge?
- What indicators can measure quality and to what degree is the evidence-based standard fulfilled?
Method

The method used for illustrating the problem was to treat it as a literature review study with systematic information retrieval. The following search terms were used: insulin, insulin injection and insulin absorption. A search was performed using AND/OR and the English words: insulin, insulin injection and insulin absorption. Both qualitative and quantitative studies were included.

Information retrieval

For information retrieval the group was assisted by the librarians at the Danish Nursing College at Århus University and the Medical Research Library at Odense University Hospital. Literature from the period 1985-2001 was searched for (see page 12 for updating), and articles were also included that are older but are judged to be relevant to illustrate the problem. Literature was searched for in the databases MEDLINE, CINAHL, SPRILINE, the Danish Article Database, the Danish Diabetic Association’s journal for diabetes treatment “Tidsskrift for diabetesbehandling”, various patient information leaflets from the pharmaceutical industry, and nursing textbooks. A total of 247 abstracts came to light and all were read by two people. All abstracts other than those in Danish, Norwegian, Swedish or English were rejected. Abstracts dealing with children were rejected unless the problem was deemed to be relevant in an adult context. Abstracts that did not describe the problem or were deemed irrelevant were rejected. Articles from all the databases listed above were included. The majority of them are descriptive studies or overviews. The rest of the articles are clinically controlled studies, 10 in all, plus one meta-analysis. Most of the articles were published in international medical journals with the exception of a small number of articles from the Danish Article Database. To ensure reproducibility, various individuals in the work group have searched for literature independently of one another using the search terms listed above. The level of evidence and its strength were assessed by all members of the group together to ensure reproducibility. Reproducibility is also ensured by two people from the work group having critically assessed the selected literature independently of one another, following which the result was set out before the entire group for critical assessment. A special tool was used for this systematic and critical assessment of the literature. Each article was assessed first by two group members, after which the whole work group assessed the article together, based on the chart. This is a form of checklist, against which quantitative and qualitative
For the 2006 update, literature was sought from the period 2001-2005. In the update the same search terms and criteria were used as in the first edition, in the knowledge that this included animal experiments. Searches were performed in the following databases: Medline, CINAHL, Embase, Cochrane and the Danish Article Database, as well as articles and patient information leaflets from the pharmaceutical industry. The following search terms were used: insulin, insulin injection and insulin absorption. A search was performed using AND/OR and the English words: insulin, insulin injection and insulin absorption. A total of 121 abstracts came to light. These were read by two people. All abstracts other than those in Danish, Norwegian, Swedish or English were rejected. Abstracts dealing with children were rejected, as were abstracts that did not describe the problem in question. In all, 17 articles were read, and of these, two were found to be valid and reliable on the basis of the aforementioned assessment chart. These articles were read by all members of the group.

Of these two articles, one is a clinically-controlled study and the other a descriptive study.

For the 2006 update, literature was sought from the period 2001-2005. In the update the same search terms and criteria were used as in the first edition, in the knowledge that this included animal experiments. Searches were performed in the following databases: Medline, CINAHL, Embase, Cochrane and the Danish Article Database, as well as articles and patient information leaflets from the pharmaceutical industry. The following search terms were used: insulin, insulin injection and insulin absorption. A search was performed using AND/OR and the English words: insulin, insulin injection and insulin absorption. A total of 121 abstracts came to light. These were read by two people. All abstracts other than those in Danish, Norwegian, Swedish or English were rejected. Abstracts dealing with children were rejected, as were abstracts that did not describe the problem in question. In all, 17 articles were read, and of these, two were found to be valid and reliable on the basis of the aforementioned assessment chart. These articles were read by all members of the group.

Of these two articles, one is a clinically-controlled study and the other a descriptive study.

The literature used
The majority of the literature used concerns adults with diabetes. However, articles concerning children were also used, as some of these were assessed as being of significance for adults. For assessment of the level of evidence and its strength, the chart from: “Dansk Medicinsk Selskab. Sekretariat for Reference-programmer” was used. Guidance for preparing reference programmes
26.11.2000. The level of evidence and its strength were assessed by all members of the group together to ensure reproducibility (appendix 2).

It has been decided to state both evidence graduation and strength each time a source is named. Ordinarily, the strength of the evidence will only be named in the overall recommendations, but this has been decided against. As the general recommendations will also be used by both patients and relatives, the strength of evidence has been left out of the recommendations.

Hearing
In connection with development of the clinical guidelines, two hearings were held. The purpose of these was to develop guidelines that were as valid as possible, and to promote their implementation. At the Danish Diabetes Nurses’ Society’s national conference held in October 2001, a pilot consultation took place, in which six diabetes nurses read and commented on the report. The open national hearing took place in March 2002, to which representatives from professional associations were invited: diabetes nurses, practice nurses and primary care nurses, representatives of the Danish Endocrine Society and the Organization of General Practitioners, and user representatives from the Danish Diabetic Association.

Updating and publication
The Danish Diabetes Nurses’ Society is responsible for updating the clinical guidelines every three years.

In 2006 the work group undertook a minor revision of the text and updating of the literature from 2002-2005.

Articles have been published in Klinisk Sygepleje, Praktisk Lægegerning, Diabetesbladet, Dit lægemagasin and one article in a textbook, Diabetes (Munksgaard 2006). In addition, the clinical guidelines have been presented at the international conference of diabetes nurses (FEND) in 2002 in Budapest and published in Practical Diabetes International November Vol. 19. No. 9 Supplement 2002.
Incidence of diabetes mellitus

Diabetes mellitus is a disease experiencing explosive growth. It is estimated that 300,000 people have diabetes in Denmark. Of these, 20,000-25,000 people have type 1 diabetes (insulin-dependent diabetes), while around 275,000 people have type 2 diabetes (non-insulin-dependent diabetes). It is also estimated that around 150,000 people have as-yet undiagnosed type 2 diabetes. Around 80,000 people with type 2 diabetes are undergoing insulin treatment. Each year between 6,000 and 8,000 new cases of type 2 diabetes are diagnosed. Increasing life expectancy means that increasing numbers of people are developing type 2 diabetes as a result of unhealthy lifestyles, with a diet too high in fat, not enough exercise and obesity resulting from these things. There is a growing tendency for young people (even children) to develop type 2 diabetes. In addition to this, people with type 1 diabetes are living longer, so overall there will be more and more people, including elderly people, with diabetes (Beck-Nielsen et al. 2000a, A, Danish Diabetic Association 1998IV, D).
Treatment of diabetes mellitus

Treatment of diabetes involves permanent lifestyle changes. Treatment includes:

- a diabetic diet
- exercise
- teaching people with diabetes how to care for themselves better
- possibly treatment with tablets and/or insulin

People with diabetes have to make daily choices between different treatment options, and they are themselves responsible for maintaining good metabolic control by adjusting the various elements of their treatment. Learning to live with a chronic disease like diabetes is a lifelong and demanding process. It has been demonstrated that good metabolic control significantly reduces the incidence of late diabetic complications in both type 1 and type 2 diabetes (DCCT 1993lb, A; UKPDS 1998lb, A).

It can be difficult to achieve and then maintain good metabolic control on a daily basis, because there are many factors that play a part. Intensive insulin treatment requires, in addition to the actual insulin treatment, frequent blood glucose measurements and comprehensive patient education. Treatment with multiple insulin injections (3-5 daily injections) provides greater flexibility in everyday life and in the diabetes treatment, but also imposes greater demands with regard to blood glucose measurements and self-care (DCCT, 1993lb, A).

A number of devices have been developed to help with insulin injections, for example, various insulin pens and types of needle. The devices require new skills, both for the individual with diabetes and for health care professionals in both primary and secondary health care. Therefore, new devices must be introduced in consideration of current clinical guidelines.

Information and education is a cornerstone in the treatment of diabetes, together with a diabetic diet, exercise and medical treatment (DCCT 1993lb, A; Genev 1992III, C). The objective for instruction in injection technique is:

- to teach people with diabetes correct injection technique, including how to choose the right injection areas and how to take care of these areas.
A secondary objective is:
• to overcome any anxiety concerning injections. Guidance is provided on how the insulin acts, correct use and storage of insulin, and how to dispose of it in a safe manner together with the other devices.
Structure and function of the skin

In order to inject insulin correctly it is necessary to understand the structure of the skin and also the subcutaneous adipose tissue into which the insulin is to be injected. The skin has a number of functions, of which the most important is protection against external influences, as well as being a sensory and deposit organ that is vital for heat regulation. The skin protects the body/organism against penetration by bacteria, and is also involved in heat regulation. Heat is regulated through changes in the blood flow to the skin. The skin is composed of three layers:

1) epidermis
2) dermis
3) subcutis.

Figure 1. Structure of the skin
(Arne W. Jensen in Nielsen O, Springborg A. Ind under huden. Anatomi og Fysiologi.)
An understanding of the skin’s structure is essential to be able to perform insulin injections correctly.

The epidermis consists of multilayered squamous epithelium. The uppermost layer of cells is continually being shed as it wears away and is replaced by new cells formed from cylinder cells, which lie below in the dermis. This process takes about four weeks (Nielsen and Springborg, 2002). The epidermis varies in thickness in different parts of the body – it is thickest where there is most wear, and it also depends on gender and age. In general men have thicker skin than women, and younger people have thicker skin than older people. Women over 70 have significantly thinner skin. The skin is of medium thickness over the upper abdomen and thicker over the gluteal region. On average skin thickness varies between 1 mm and 2 mm (Lasagni & Seidenari 1995III, C). One study has shown that skin thickness at three standard injection sites in adults with diabetes varied from 1.4 to 4.1 mm in men and from 1.1 to 3.6 mm in women (Pemberton & Holman 1989III, C).

The dermis is composed of dense connective tissue, which contains collagen and elastic fibrils, which in connection with normal water content give the skin its characteristic elasticity and tension. The dermis is where most of the nerve end organs relating to pressure, touch and pain sensations are to be found. The multilayered squamous epithelium of the epidermis penetrates the dermis where there are hair follicles.

The subcutis is composed of loose connective tissue that contains numerous fat cells and is the most important fat and water depot of the body. The lowest layer of subcutis lies on top of the muscle fascia, which surrounds the muscle (Nielsen and Springborg 2002). There is enormous individual variation in the thickness of the subcutaneous layer. There is considerable variation between different anatomical points of the body. Similarly, various factors have an impact on the thickness of subcutaneous adipose tissue in each individual, e.g. body mass index (BMI), gender and age (Lawton, 2000).
Insulin treatment and types of insulin

People with type 1 diabetes produce little or no insulin of their own and are therefore completely dependent on daily insulin injections. People with type 2 diabetes usually do not need insulin at the start of their treatment, but 50% will eventually require insulin as the disease progresses, and beta-cell function declines. The aim of insulin treatment is:

- to control the acute effect of diabetes, which is to say, prevent hyperglycaemia
- to prevent the risk of developing late diabetic complications through optimal regulation of diabetes.

Figure 2. Breakdown of insulin in the organism.
The absorption rate of insulin varies from person to person. There is also considerable variation in uptake rate between injection sites and injection times in individuals. The aim of insulin treatment is constant glycaemic control in order to maintain day-to-day protection and prevent the development of late diabetic complications. It is therefore important to minimize factors that interfere with this control (Kolendorf et al. 1983III, C). To achieve optimal glycaemic control it is important to have an understanding of how insulin is absorbed. Insulin solutions that are injected consist of a hexamer (six insulin molecules bound together). The hexamer’s physiological role is to continue the formation and storage of insulin granulates in the pancreatic beta-cells. The molecule is broken down into a dimer (two insulin molecules bound together), which is again broken down into a monomer (one insulin molecule) so it can be taken up into the bloodstream. The rate at which it is broken down into monomer form determines the rate of insulin uptake in the body (Figure 2).

Insulin used to be produced from extracts from bovine and porcine pancreatic tissue. Today, the majority is produced using DNA recombination technology that uses modified yeast or bacteria to produce human insulin. This technique has led to the development of a variation on biosynthetic insulin analogues that permits a more physiological approach to insulin treatment. These biosynthetic insulin analogues consist of monomer or dimer insulin molecules, resulting in faster uptake from the injection sites. In addition, insulin analogues have been produced with an increased half-life, providing a longer-lasting effect with a more straight effect profile (Lawton, 2000).

The following types of insulin are now available:

An extra-rapid-acting insulin analogue (e.g. NovoRapid, Humalog, Apidra)
- Extra-rapid-acting insulin analogue is injected immediately before a meal and takes effect after approximately 15 minutes, with maximum effect after 1-3 hours. The effect ceases after 3-5 hours. This is taken up faster and has a shorter duration of action than the soluble human rapid-acting insulin.

- Rapid-acting insulin or soluble insulin (e.g. Actrapid, Insuman Rapid) Rapid-acting insulin is injected approximately 30 minutes before a meal. It takes maximum effect within 1-3 hours and has a duration of action lasting 6-8 hours.
- Intermediate-acting (e.g. Insulatard, Humulin NPH, Insuman Basal)
  Intermediate-acting insulin has a duration of action lasting 24 hours, with
  maximum effect after 4-12 hours. Intermediate-acting insulin in a pen is
  mixed by moving the pen's glass sphere back and forth until the solution
  is a uniform milky-white colour, which is to say at least 10 times forward
  and 10 times back (Jehle et al. 1999b, A).

- Premixed insulin consists of extra-rapid-acting or rapid-acting insulin,
  which is produced in different concentrations (e.g. NovoMix 30, Humalog
  Mix 25, Insuman Komb 25, Mixtard 30). Premixed insulin must be turned
  at least 10 times forward and 10 times back until the solution is a uniform
  milky white (Jehle et al. 1999b, A). NovoMix 30 must also be rolled in a
  horizontal position the first time it is used.

- Slow-acting insulin analogue (Levemir, Lantus). Slow-acting insulin
  analogues have a longer duration of action, with a more straight profile.
  The effect sets in 60 minutes after the injection and lasts for up to 24
  hours. This clear slow-acting insulin should not be agitated before use.
Injection sites

The optimum site for injecting insulin is the subcutaneous adipose tissue. Intramuscular injection of insulin should be avoided, as this makes it difficult to maintain good glycaemic control. This was the conclusion of an international workshop on insulin injection technique (Strauss 1998IV, D). Subcutaneous injection of insulin means that the insulin is absorbed in the systemic blood system rather than the portal blood system, where naturally-produced insulin is taken up. The subcutaneous adipose tissue prolongs the insulin absorption rate, which means that insulin injection times must be carefully planned, taking into account food, exercise and insulin type.

Factors that affect the absorption of insulin from subcutaneous adipose tissue

One of the main problems that arise during insulin treatment is that blood glucose concentrations often vary unpredictably throughout the day. The cause of this variation can be partly explained by the fact that the day-to-day variation in absorption of intermediate-acting insulin in each individual patient is an average of 25% (19-104%), and the variation quotient for absorption of intermediate-acting insulin among patients is approximately 50% (Lauritzen et al. 1979IIa, B). In fact, up to 35% variation in absorption has been demonstrated in the individual patient (Binder et al. 1984V,D).

- **The type of insulin** is of crucial significance for absorption. A larger volume and a higher concentration of insulin delays insulin uptake. Human insulin is taken up faster than porcine and bovine insulin (Houtzagers 1989IV, D). It has been proven that there is no variation in the rate of insulin uptake, even if the insulin is in the top or bottom layer of subcutaneous adipose tissue (De Meijer 1990IIa, B; Frid & Lindén1992III, C). In practice the dose is divided in the event of 40-50 IU insulin. A Danish study supports this (Nielsen et al 1998Ib, A). It is therefore recommended that the insulin dose be divided in the event of doses over 40 IU.

- **Factors relating to the patient:** Exercise, e.g. training of muscles that are close to the insulin depots, increases absorption and can increase the risk of hypoglycaemia. Exercising a muscle can increase blood flow up to
7 times compared with before the exercise starts, and this has a dramatic effect on insulin uptake (Strauss et al. 1999 IV, D). Massaging the injection site increases the absorption rate. Higher temperatures increase the absorption rate, e.g. a sauna or a hot bath. Low ambient temperatures reduce the absorption rate. Smoking gives rise to slower insulin uptake (Hildebrandt & Madsbad 1989 IV, D; Houtzagers 1989 IV, D).

- **Injection technique** is important. Choice of the right needle length ensures that the insulin is placed in the subcutaneous adipose tissue in order to provide more uniform insulin uptake. If the insulin is accidentally placed in muscle this can result in major variations in uptake. The speed of the injection itself is of no significance, although this can vary from under 3 seconds up to 30 seconds (Houtzagers 1989 IV, D; Hildebrandt & Madsbad 1989 IV, D).

- **Injection area** is of great significance. Insulin uptake rates vary from anatomical area to anatomical area in the subcutaneous adipose tissue, e.g. the absorption of insulin is fastest from the abdomen and slowest from the thigh and hip, and faster from the upper arm than from the thigh or hip. Therefore it is not appropriate for the patient to switch injection area from day to day (Houtzagers 1989 IV, D).

- **The thickness** of the subcutaneous adipose tissue varies a great deal from person to person, and from injection site to injection site. Even within the same area, e.g. the thigh, the thickness of the subcutaneous adipose tissue varies a great deal (Houtzagers 1989 IV, D; Frid & Lindén 1992 III, C).

- **Extra-rapid-acting insulin** analogues have a lower uptake variation than intermediate-acting insulin (Lawton 2000 IV, D).

**Intramuscular Injection and Rapid-Acting Insulin**

If insulin is unintentionally injected intramuscularly, this causes glycaemic control to become unstable and to vary. Variations in uptake rate provide unwanted fluctuations in metabolic control. A study by Frid et al. (1988 III, C) found that the uptake of rapid-acting insulin was at least 50% faster from muscle than from the subcutis on the thigh. In contrast, on the abdomen there was no significant difference in uptake rates between subcutaneous and intramuscular injection. In order to minimize day-to-day variations in insulin uptake, it is therefore recommended that rapid-acting insulin always be injected into the abdomen.
If by accident an intramuscular injection of rapid-acting insulin is given in the thigh, this can lead to hypoglycaemia. A study has shown that if insulin is injected intramuscularly, and then exercise is done, e.g. cycling, the increase in plasma insulin during and after the exercise is more than double the increase after subcutaneous injection of insulin. This led to a considerable fall in blood glucose with a risk of hypoglycaemia. To avoid the situation outlined above, it is recommended that patients inject into a skin fold and/or use shorter needles <8 mm (Frid et al. 1990III, C).

INTRAMUSCULAR INJECTION AND INTERMEDIATE-ACTING INSULIN
Vaag et al. (1990bIII, C) investigated whether uptake of intramuscularly injected NPH insulin is faster than for subcutaneously injected insulin, and they evaluated intrapatient and interpatient variations in absorption rates. They found that intramuscular injection of insulin was taken up almost twice as fast as subcutaneously injected insulin and produced much greater variation in day-to-day uptake. In order to achieve the longest effect for the intermediate-acting insulin and the lowest variation in uptake, it is recommended that the thigh be used for subcutaneous injection of intermediate-acting insulin rather than intramuscular injection. Vaag et al. (1990bIII, C) therefore recommend that needles shorter than 5 mm be used and/or injection be into a skin fold in order to avoid intramuscular injection, as intramuscular injection of intermediate-acting insulin must be avoided.

RISK OF INTRAMUSCULAR INJECTION
Over the past 10 to 15 years many studies have been performed using radiological methods. These have produced a great deal of information concerning the many risks involved in injecting insulin intramuscularly, as the distance from skin to muscle is often shorter than was previously supposed. In addition, the distance varies considerably within and between different anatomical areas. Using computer tomography, Frid and Lindén (1992III, C) measured the thickness of the subcutaneous adipose tissue at injection sites in 91 normal-weight (BMI=22.8) diabetics:

The thickness of adipose tissue from skin to muscle:
- **Thigh:** the upper lateral quadrant of the thigh was 7 mm in men and 14 mm in women. They calculated that 48% of the women and 91% of the men would inject into muscle with a 12.5 mm needle without a lifted skin fold. In the uppermost quadrant and medially on the thigh the risk of intramuscular injection was less, though still present.
Abdomen: 28% of the women and 44% of the men had less than 13 mm subcutaneous adipose tissue lateral to the navel, which is the area with the largest layer of fat on the abdomen.

Hip: the subcutaneous adipose tissue measured where the layer of fat is thickest – on a vertical line from the hip bone – was 55 mm from skin to muscle in women and 38 mm in men, which means that injection into the hip can take place without using a skin fold.

Upper arm (1/3 of the distance between shoulder and elbow). Here the subcutaneous adipose tissue was 15.1 mm in women and 12.2 mm in men. This means that there is a high risk of intramuscular injection. It is also difficult to lift up a skin fold, meaning an injection into the arm using a 12.5 mm needle can therefore not be recommended (Frid & Lindén 1992III, C). This study was confirmed by Thow et al. (1992III, C), who found that the average thickness of the subcutaneous adipose tissue on the arm in 50 people with diabetes (BMI=24.6) was 5.8 mm in men and 10.1 mm in women, so injection into the arm cannot be recommended due to the high risk of intramuscular injection.

Similar studies have been carried out on children and young people by a number of people, including Birkebaek et al. (1998III, C), who found that:

- Abdomen: 32-84% of the girls and 55-95% of the boys had subcutaneous adipose tissue less than 8 mm thick over the central abdomen.
- Thigh: 16-44% of the girls and 41-95% of the boys had a fat layer less than 8 mm. The subcutaneous adipose tissue was significantly thicker in girls than in boys due to an increase in the subcutaneous adipose tissue in girls after the start of puberty.

In addition, Frid and Lindén (1986III, C) found that in a single individual, subcutaneous adipose tissue varies a great deal, depending on the anatomical site. For example, in a slim woman, it was found that the subcutaneous adipose tissue on the abdomen was 26 mm, 25 mm in the middle of the thigh and only 5 mm laterally on the thigh. They studied 14 patients (of whom 3 were women). They found that the average thickness of the subcutaneous adipose tissue varies a great deal from person to person, as the average thickness of the subcutaneous adipose tissue on the abdomen in the thickest place was 14 mm (with a variation of 4-26 mm). The average thickness on the thigh was laterally 6 (2-19 mm), at the top 8 mm (3-15 mm) and medially 14 mm (4-25 mm).
Using the correct injection technique and right needle length can minimize the risk of injecting intramuscularly, and reduce day-to-day variation in insulin absorption.

The effect of intramuscular injection can sometimes be made use of by practitioners and people with diabetes, for example, in an acute situation involving high blood glucose levels, where rapid uptake of rapid-acting insulin is required. Intermediate-acting insulin must never be injected intramuscularly.

**CONSEQUENCES OF INTRACUTANEOUS INJECTION**

The full consequence of intracutaneous insulin injection is unknown and it should therefore be avoided. Intracutaneous injection may give rise to greater insulin leakage due to the short distance to the surface of the skin and perhaps more pain due to direct nerve stimulation. There are several unresolved questions, for example, what is insulin uptake like? Could it be possible that there may be a stronger immunological reaction to the insulin?

Correct injection technique and the right needle length can minimize the risk of intracutaneous injection (Strauss 1998IV, D).
Adherence

It has been demonstrated that those patients who are the most satisfied with the communication they have with their doctor are in the best position to maintain the recommended treatment recommendations. In such cases, 53% of patients follow the doctor’s advice after asking him or her, when they are satisfied with communication and the consultation (Thompson 1984). Empirical studies have also shown that only 50% adhere to the recommendations following a diagnosis of the disease. Furthermore, more and more people eventually stop following the advice, despite the fact that they are being treated with insulin and/or tablets (DiMatteo and DiNicola 1982). These studies date from the 1980s, but they are supported by a more recent study from the Danish Diabetic Association. Here it proved to be the case that those who were most satisfied with those treating them were also the best regulated (Danish Diabetic Association (Diabetesforeningen) 2000). The studies show that there are problems associated with following the recommended lifestyle advice. However, it is crucial that good glycaemic control be maintained in order to prevent and delay the incidence of late diabetic complications. In this, ongoing blood glucose measurements, a diabetic diet and exercise, together with insulin treatment, play a crucial role in reducing day-to-day variations in blood glucose levels. People with diabetes therefore need education in order to learn what they need to do, when and why. At the same time they need to be supported and encouraged in these treatments, so it becomes part of their daily routine. This also applies in connection with learning about insulin injection, where there is a great need for instruction and care, particularly at the start of insulin treatment. But for the rest of their lives there will still be a need for education and support, because new forms of treatment and new devices for injection technique are constantly appearing (Diabetesbehandling i Danmark. Redegørelse 1994; Sct. Vincent Deklaration 1991). For many people with diabetes, insulin treatment can initially be more traumatic than the actual diagnosis of diabetes. Diglas et al. (1999Ia, B) asked people with diabetes how they found having to start insulin treatment and found that 45.8% were very worried about the needles and troubled by them at the start of insulin treatment, while 37.5% were somewhat worried and troubled by needles. Since the publication of the DCCT trial in 1993 there has also been a more active focus on achieving optimal regulation of diabetes, which means that people with diabetes must inject themselves several times daily. It can therefore be a huge challenge to achieve good levels of adherence among people who fear injections.
It is important for health care professionals to be sure to assess whether a person has needle-phobia. If this is the case, the health care professional in question must recommend devices and techniques to reduce the perception of pain, so that good glycaemic control can be maintained.

PEOPLE WITH DIABETES WHO HAVE NEEDLE PHOBIA

Many people dislike having injections or having to inject themselves. A Swedish study showed that around 10% of 7-15-year-olds had needle phobia, which means that a vasovagal reflex of shock is triggered when they are injected with a needle or when they inject themselves. In addition, needle phobia can give rise to fainting, a choking sensation, headache, cold sweat, a drop in blood pressure, a rise in the secretion of stress hormones and cardiac disorders. It can be difficult to measure fear of needles, but an objective measurement may be to record how long it takes before the patient takes the injection (Hanås 1998 IV, D). Needle phobia has recently been defined as a medical condition and has been included in the fourth edition of the American Psychiatric Association’s Diagnostic and Statistical Manual of Mental Disorders (DSM-IV). Needle phobia can result in the individual avoiding the health authorities, which can have catastrophic consequences. For people with diabetes who are dependent on daily insulin injections, needle phobia can affect adherence and blood glucose levels. Needle phobia is linked to people’s perception or experience of pain. Hanas and Ludvigsson (1997 III, C)) have shown that pain associated with injections in children and adults who have reported anxiety concerning needles has a significant link with poor metabolic control.

DEVICES FOR DEALING WITH NEEDLE PHOBIA

Insulin pens are perceived as being less painful than syringes and needles (Hanas & Ludvigsson 1997). It has proved to be the case that finer, shorter needles produce significantly less pain (Lytzen et al. 1993 III, C). If patients cannot see the needle during the injection, the actual needle length makes no significant difference to the perception of pain. However, patients prefer a shorter needle (6 mm or 8 mm needles compared with 12 mm needles) when the needle is visible. This emphasises the significance of the psychological effect of the perception of pain, as shorter needles are perceived as less painful because they appear less threatening than longer ones (Lawton 2000 IV, D). Special devices
that conceal the needle and inject it automatically have proved to be a boon for
needle-phobic patients (Diglas et al. 1999IIa, B). For example, PenMate is a use-
ful accessory to Novo’s Junior 3 pen and a great help to those patients who are
frightened of injections. PenMate reduces the perceived pain of an injection by
diverting attention away from the needle. Diglas et al. (1999IIa, B) performed
a comparison between the NovoPen 3 insulin pen with and without PenMate.
The needle is injected automatically by pressing a button on the device. The
result of the study was that the perception of pain was significantly lower with
PenMate, and that it was easy to use. In addition, 84% of patients said that they
would recommend PenMate to someone who was afraid of needles (Diglas et
al. 1999IIa, B). There are other devices to help patients with a fear of needles,
e.g. insuflon. This is like a small venflon that is positioned in the subcutaneous
adipose tissue in the abdomen. It is then possible to inject insulin through a
small silicone membrane. Insuflon can remain in place for 3-6 days before
being replaced. Up to 75 injections can be administered through one insuflon. In
Sweden everyone newly diagnosed with diabetes is offered an insuflon before
their first insulin injection, and pre-school-age children are always given an
insuflon. This makes it easier for the child to accept multiple injection therapy
and for the parents to regulate their child’s diabetes. Metabolic regulation is
not affected when an insuflon is used (Hanås 1998 IV, D). Hanas et al. (1997III,
C) have shown that use of a catheter for insulin injection for up to 4 days does
not affect uptake of rapid-acting insulin when the catheter is placed in an area
without lipo hypertrophy.

In Denmark there is little experience of insuflon use. But in cases of needle
phobia where other devices have not helped, further literature on insuflon
could be looked for, or Sweden could be approached for further information on
their experiences with insuflon.

The NovoFine Autocover needle could be useful for helping with needle pho-
bia, because the needle is not visible.

Poor adherence often has several causes, for example:

- inadequate or forgotten knowledge
- contact with diabetes team/health care professionals is insufficient
- no up-to-date instruction
- fear of needles and inadequate knowledge of devices to help with this
- failure to accept the fact of having a chronic disease.
The insulin injection process

**WHICH AREAS CAN BE USED FOR INSULIN INJECTION**

Insulin has different absorption rates at different areas on the body. This is presumably due to the difference in the number of blood capillaries and/or their permeability, as well as differing blood flow at the different anatomical sites on the body. Studies have shown that rapid-acting insulin is absorbed 86% faster from the abdomen than from the femur, and 30% faster from the abdomen than from the arm. Absorption from the upper arm is approximately 40% faster than from the thigh. In other words, insulin is absorbed fastest from the abdomen, than from the arm and thigh (Koivisto & Felig 1980III, C). The aforementioned study emphasises the importance of not switching between injection sites at different anatomical points on the body but instead between different injection sites within the same anatomical area. The finding stated above is confirmed by Binder et al. (1984IV, D) who found that absorption of rapid-acting insulin was fastest from the abdomen, than from the arm, followed by the hip and, finally, the thigh.

**Abdomen**

Insulin is absorbed more quickly when it is injected into the subcutaneous adipose tissue in the abdomen than into the subcutaneous adipose tissue in the thigh. One study has shown that following injection into the subcutaneous adipose tissue in the femur it took almost three hours for 50% of the quantity of insulin to be absorbed, while it took one and a half hours for it to be absorbed from injection into the abdomen. It also proved to be the case that considerable day-to-day variations in blood glucose were observed despite careful control of insulin doses, food quantities and exercise. There was less variation in blood glucose when the insulin was injected into the abdomen (Zehrer et al. 1985IV, D).

Another study carried out by Frid and Lindén (1992III, C) showed the same results. The half-life for insulin in the thigh was more than 240 minutes compared with the abdomen, where the half-life was 180 minutes. This makes the thigh unsuitable for injection if rapid-acting insulin absorption is required. The same study also showed that there were large differences in the absorption rate within the abdominal area. The insulin was absorbed significantly more quickly from a spot 120 mm above the navel than 40 mm below it. It proved to be the case that there was 36% residual insulin 120 mm above the navel versus 49%
On the basis of the aforementioned studies, the abdomen is recommended as the preferred injection site for rapid-acting insulin and insulin analogues. The injection areas should be within approximately 12 cm on both sides of the navel, and approximately 4 below the navel, because the subcutaneous adipose tissue is much thinner further away from the navel. It is also easy to lift a skin fold in these areas. If an area up to 12 cm above the navel is used you should be aware of the fact that uptake of insulin is faster (see chart 1).

Chart 1
Thickness of subcutaneous adipose tissue and residual insulin 175 min. after injection

| Depth of subcutaneous fat layer and residual 125I radioactivity after 175 min at various injection sites after subcutaneous injection of 125I-labelled unmodified human insulin (5 U; 100 U ml-1) in nine type 1 diabetic patients |
|---------------------------------|-----------------|
| Fat depth (mm)                  | Residual 125I-radioactivity (%) |
| 40 mm below umbilicus           | 20 ± 3          | 49 ± 4 |
| 120 mm above umbilicus          | 16 ± 1          | 36 ± 4 |
| 120 mm lateral to umbilicus     | 14 ± 1          | 54 ± 2a|
| thigh                           | 13 ± 1          | 62 ± 4 |

Mean ± SE.
ap<0.01 compared with above umbilicus. (With permission from Frid A, Lindén B: Diabetic Medicine 1992;9:236-239III, C)

On the basis of the aforementioned studies, the abdomen is recommended as the preferred injection site for rapid-acting insulin and insulin analogues. The injection areas should be within approximately 12 cm on both sides of the navel, and approximately 4 below the navel, because the subcutaneous adipose tissue is much thinner further away from the navel. It is also easy to lift a skin fold in these areas. If an area up to 12 cm above the navel is used you should be aware of the fact that uptake of insulin is faster (see chart 1).
Femur
Rapid-acting insulin is absorbed very slowly from the subcutaneous adipose tissue of the femur, as only approximately 50% is absorbed after five hours (Vaag et al. 1990a, C; Henriksen et al. 1994a, B). In fact, the absorption of rapid-acting insulin from the subcutis of the abdomen closely resembles the absorption that is seen following intramuscular injection into the femur (Vaag et al. 1990a, C). Henriksen and Vaag (1991, C) found that if rapid-acting insulin is injected subcutaneously into the thigh, a lower average blood glucose level is seen at night with a far greater number of incidences of hypoglycaemia (blood glucose under 3 mmol/l).

Not only is intermediate-acting insulin absorbed slowly from the thigh, but the absorption rate is more constant with less day-to-day variation compared with injection into the abdomen (Henriksen et al. 1991, C). This is particularly important when intermediate-acting insulin is injected at bedtime (22.00-23.00), where the aim is to create a stable insulin profile at night. It is crucial that the insulin effect remains stable at night, because the need for insulin at night is very constant. Injecting intermediate-acting insulin into the thigh at bedtime encourages more uniform absorption through the night, producing a more constant insulin profile. This helps to reduce the risk of night-time hypoglycaemia and hyperglycaemia before breakfast (Henriksen et al. 1991, C).

Hip
As the hip has an insulin absorption profile equivalent to that of the thigh (155 minutes compared to 164 minutes for subcutaneously injected insulin to be absorbed (Binder et al. 1984 IV, D), the hip may be an excellent alternative as an injection site for intermediate-acting and slow-acting insulin. The thickness of the subcutaneous adipose tissue on the hip, particularly the upper lateral quadrant of the hip, is generally significantly thicker than on the thigh, and this makes the hip an ideal injection site. In a study of 50 people with type 1 diabetes (BMI=24.6) it was found that the average thickness of the subcutaneous
adipose tissue in the mid-hip area was 12 mm in men and 24 mm in women (Thow et al. 1992). Another study of normal-weight children showed that no girls and only 5% of boys had skin and subcutaneous adipose tissue that was less than 6 mm combined over the central section of the hip (Birkebaek et al. 1998 III, C). The risk of unintentionally performing an intramuscular injection into the hip is small compared with the thigh; nevertheless the thigh is the site most frequently used for insulin injections. This is linked to the fact that many people find it uncomfortable or awkward to inject themselves in the hip.

**Upper arm**

The upper arm is **not recommended** as an injection site for insulin, because there is often only minimal distance from skin to muscle (Frid & Lindén 1992III, C, Thow et al. 1992III, C). This gives rise to a high risk of intramuscular injection. In one study of 50 normal-weight children (3-18 years old) it was found that even if they injected into a lifted skin fold, 88% injected into muscle with a 12.7 mm needle when they used the upper arm. Even using an 8 mm needle, 48% would still hit muscle. This study emphasises the importance of selecting the right needle length (Tubiana-Rüfi et al. 1999Ib, A).

If the upper arm is to be used nonetheless, it is essential to inject into a lifted skin fold. This requires help from another person, as it is impossible for the patient to both hold up a skin fold and inject the insulin using just one hand.

**THE OPTIMUM INJECTION SITE FOR PREMIXED INSULIN**

If a rapid effect is required from premixed insulin, it should be injected into the abdomen. If a slower effect is required, it should be injected into the thigh. A consensus document from 40 diabetes experts recommends that when premixed insulin is used it should be injected into the abdomen in the morning. When premixed insulin is used in the evening, it should be injected into the
Insulin injections should be performed at the same time every day and within the same anatomical area to ensure uniform insulin absorption. Rotation within the same anatomical area reduces variations in blood glucose levels (Bantle et al. 1993). Individual advice based on the above should be given, as guidance must always be adapted to suit the individual concerned. It may be difficult, for example, to remember to inject the same insulin type in two different sites.

**ROTATION OF INJECTION SITES WITHIN THE SAME ANATOMICAL AREA TO PREVENT LIPOHYPTERTROPHY**

Within each key area where insulin is injected, it is extremely important to ensure that you alternate between the injection sites within the same anatomical area to prevent lipohypertrophy. It is possible to create a systematic system of rotation so that the same site is not used all the time. It is recommended that there be three cm between each injection site (Zehrer et al. 1985). A study of 150 people with type 1 diabetes showed that women with a high BMI who did not distribute their injections had the highest incidence of lipohypertrophy. Therefore, women with a high BMI and type 1 diabetes should take additional care when choosing injection site (Saez-de Ibarr & Gallego 1998). It might be supposed that this also applies to women with type 2 diabetes, but until this is investigated it remains merely an assumption.

In a major European study of 22 diabetes centres with 1.002 people with type 1 and type 2 diabetes, it is proved to be the case that the incidence of Lipohypertrophy was not related to needle length, gender, lifted or not lifted skin folds, injection angle, swabbing of the skin prior to injection or how long the needle remains in the subcutis before being withdrawn (Strauss K, De Gols H. Hannet, 2002).

Use of an injection chart is recommended to aid choosing of the injection sites.
Charts 2 a and b

Injection charts for thigh and abdomen that show how to distribute the injections.
Young man with lipohypertrophy of the abdomen. He has always injected himself in the same area and only changed needle when he changed the pen.

Injection in Lifted Skin Fold

Many patients with diabetes have a high risk of unintentionally injecting insulin into muscle, because the subcutaneous adipose tissue is often very thin at the injection areas normally used. Even overweight patients risk injecting into muscle on the thigh or in the abdomen (see page 41 for a more detailed description).

One method for reducing the risk of intramuscular injection is to pinch a skin fold between two fingers. The optimum skin fold is created by pinching the skin between the thumb and index finger, which raises the subcutaneous adipose tissue. (Figure 3). This technique helps to ensure that the muscle fascia is not raised, which can happen if several fingers are used to create a skin fold (Polak et al. 1996III, C). The patient must also be taught how to move the fold of skin carefully from side to side before the injection is performed, because this will increase the likelihood that it is the subcutaneous adipose tissue being lifted and not the underlying muscle fascia. The underlying muscle must be relaxed during the injection (Lawton 2000IV, D). The skin fold must remain lifted throughout the injection and for 5-10 seconds afterwards, before the needle is withdrawn (Strauss 1998IV, D)
A study has recently been published of 50 normal-weight children (3-18 years) with diabetes. In this, the average distance from skin to muscle fascia was increased by 80% when using two fingers to create a skin fold (Tubiana-Rufi et al. 1999b, A).

<table>
<thead>
<tr>
<th>A: Correct method for lifting a fold of skin between 2 fingers</th>
<th>B: Incorrect method, in which muscle fascia is picked up when skin is lifted using several fingers</th>
</tr>
</thead>
</table>

![Image](image.png)


**Injection without a skin fold**

If the distance from skin to muscle is greater than the needle length, it is not necessary to inject into a lifted skin fold. However, as described previously, the distance from skin to muscle is often less than the needle length (Frid & Lindén 1992III, C). And even for an experienced practitioner, it is difficult to judge the distance from skin to muscle without a radiological examination, e.g. computer tomography or ultrasound scan. As skin thickness varies a great deal both within the same anatomical area and between areas (Frid & Lindén 1986III, C), injections should always be performed using a two-finger fold of skin when it is possible for the patient to do this. When recommendations are made, there will always also be exceptions. There will be patients who are unable to lift a skin fold due to problems with their hands, perhaps having impaired hand strength or being afflicted with arthritis. If a patient is unable to lift a skin fold, the thickness of the subcutaneous adipose tissue on the femur should be assessed with a view to selection of needle length and injection angle, or alternatively the abdomen or hip can be used with shorter needles (e.g. 6 mm needles). (See chart 3 p. 45).
It has been shown that compression on the injection site can reduce the average distance from skin to muscle by up to 35% (Birkebaek et al. 1998III, C). This underlines the importance of not putting excessive pressure on the injection site, particularly if injection is not to be into a lifted skin fold. An insulin injection device with a “support shoulder”, e.g. InnoLet from Novo Nordisk, can probably reduce the risk of compression by distributing the pressure over a larger area at the injection site.

**INJECTION WITHOUT A SKIN FOLD IN THE HIP**
Thow et al. (1992III, C) used ultrasound scanning to show that everyone except the leanest adults (BMI under 24.6) can inject into the upper lateral quadrant of the hip without a lifted skin fold, using a 6 mm needle. Here the subcutaneous adipose tissue averages 11.8 mm in men and 24.8 mm in women, so there is no risk of injecting into muscle when using a 6 mm needle.

**INJECTION WITHOUT A SKIN FOLD IN THE ABDOMEN**
A study has recently been published in which slim (average BMI 22.4) and overweight (average BMI 27.8) adults injected themselves in the abdomen using a 6 mm needle without a skin fold. All the overweight subjects injected subcutaneously, while 15% of the normal-weight subjects hit muscle. The best technique with a 6 mm needle was injection into a lifted skin fold at a 90 degree angle. With this technique, 97.8% of the injections went into the subcutaneous adipose tissue. With a 12 mm needle, the best technique was to inject at an angle of 40-60 degrees into a lifted skin fold. This resulted in 93.7% of the injections going into the subcutaneous adipose tissue (Solvig et al. 2000III, C). Other studies also support the hypothesis that a large proportion of normal-weight individuals have a high risk of injecting into muscle if they do not inject into a lifted skin fold in the abdomen.

Normal-weight individuals are recommended to inject into a lifted skin fold
(Spraul et al. 1998III, C; Frid & Lindén 1986III, C; Strauss 1998IV, D).
INJECTION ANGLE

If a 12 mm needle is used, it is recommended, on the basis of the aforementioned studies, that injection be at an angle of 45 degrees to reduce the risk of intramuscular injection (Spraul et al. 1988III, C; Frid & Lindén 1986III, C; Solvig et al. 2000III, C). The development of shorter needles makes it possible to inject at an angle of 90 degrees. It has proved to be the case in practice that it is easier to inject at a 90-degree angle than at a 45-degree angle. It was also found that although children were taught to inject at an angle of 45 degrees into a lifted skin fold, they often injected at an 90-degree angle without a lifted skin fold (Birkebaek et al. 1998). Injecting at an oblique angle reduces the risk of injecting into muscle. But even minor changes to the injection angle can result in the insulin being placed significantly deeper or closer to the skin’s surface than intended. If, for example, a patient injects using a 12 mm needle at a 60-degree angle instead of the planned 45-degree angle, the insulin will be placed 2 mm deeper than planned, which increases the risk of hitting muscle (Lawton 2000IV, D). One possibility could be to recommend 90-degree injection and different needle lengths for different areas on the body, depending on the thickness of the subcutaneous adipose tissue and the fatty tissue distribution of the individual concerned. This can only remain an opinion until it becomes standard procedure to perform ultrasound scans on patients in order to determine the thickness of the subcutaneous adipose tissue at the various injection sites.

The rationale behind recommending perpendicular (90-degree angle) injection with a shorter needle can be illustrated by comparing 8 mm and 12 mm needles, which must always be injected at a 45-degree angle due to the risk of intramuscular injection. If the 8 mm needle is injected at a 90-degree angle the insulin will be placed at the same depth as with a 12 mm needle injected at a 45-degree angle (Figure 4).

It has proved to be the case that there are often major differences in what patients say they will do and what they actually do. Observation of 30 individuals with diabetes revealed that only 10 used the injection technique they had previously said they would use. For example, 11 of them said they would inject at a 90-degree angle without a skin fold, but only 4 of them did so in practice (Thow et al. 1992III, C).
Choosing needle length

Everyone with diabetes has their own individual needs, and only through choice of the right injection technique and the correct needle length the insulin will be placed in the subcutaneous adipose tissue.

Choice of needle length depends on:

- patient’s gender
- BMI (clinical assessment of adipose tissue thickness)
- injection site
- injection technique with or without a lifted skin fold
- injection angle

Ultimately, it is increased knowledge and evidence concerning insulin absorption and the thickness of the subcutaneous adipose tissue that has led to the development of shorter needles in order to optimise the injection of insulin. As described previously, children and lean adult men in particular are at high risk of injecting into muscle if they use a 12 mm needle, and therefore 6 mm and 8 mm needles are those used most often.

12 mm needle: Previously, the 12.7 mm needle was the one most frequently used, but today it is not used much due to the risk of intramuscular injection. For example, a study of children who used a 12.7 mm needle found that 30.5% injected into muscle (Polak et al. 1996III, C). This is supported by another study of normal-weight children, which found that 84% of injections hit muscle in the thigh when a 12.7 mm needle was used at a 90-degree angle into a lifted skin fold. With an 8-mm needle, 28% still hit muscle (Tubiana-Rufi et al. 1999Ib, A). Another study supports this. This showed that 15% of normal-weight adults with diabetes (BMI = 22.4) injected into muscle in the thigh with a 12 mm needle despite using an angle of 40-60 degrees and a lifted skin fold. Among overweight individuals (BMI=27.8), only 7% injected into muscle (Lawton 2000IV,D).

If the patient is used to a 12 mm needle, and for whatever reason it is decided that he or she should continue with a 12 mm needle, injection should always be into a lifted skin fold at an angle of 45 degrees due to the risk of intramuscular injection.
8 mm needle: The safety and effectiveness associated with the use of 8 mm needles is well documented, and this type has now replaced the 12 mm needle as the most frequently used needle length.

The published results of a study involving 106 adults with diabetes show that both normal-weight and overweight patients can switch from a 12.7 mm needle to an 8 mm needle without any significant change in glycaemic control. The results also show that switching from 12.7 mm to 8 mm needles did not result in any significant rise in insulin leakage (diffusion/backflow) at the injection site. However, more insulin leakage was seen in overweight patients using an 8 mm needle. In addition, a larger volume of injected insulin was also significant for insulin leakage, as more leakage was seen with increasing quantities of insulin among overweight individuals. However, this did not affect metabolic control, and the shorter needle was less painful to use (Ross et al. 1999Ia,B).

Two further studies involving a total of 70 normal-weight patients (age 5-65 years) show that, compared with 12 mm needles, 8 mm needles do not affect metabolic control or give rise to increased insulin leakage (Lawton 2000IV, D).

Another study involving normal-weight children showed that, compared with 12 mm needles, 8 mm needles reduced the risk of intramuscular injection by 58%, and that there was no significant difference in insulin leakage whether 8 mm or 12.7 mm needles were used. Therefore, 8 mm needles are recommended for normal-weight children and adult patients with type 1 diabetes (Tubiana-Rufi et al. 1999Ib, A). With an 8 mm needle it has proved to be the case that it is extremely important for patients to keep the needle in the skin for at least 10 seconds before withdrawing it, as otherwise there is a high risk of insulin leakage (Annersten & Frid, 2000III, C).

Frid and Lindén (1996III, C) investigated whether the insulin is placed subcutaneously or intramuscularly when using an 8 mm needle with or without a lifted skin fold injected at a 90-degree angle. There were no intramuscular injections when injection was into a lifted skin fold. However, intramuscular injections into the thigh were seen when a fold of skin was not used, even among overweight patients. In addition, intramuscular injections in the abdomen occurred in slim patients. The study showed that intramuscular injection often occurs in both normal-weight and overweight people, male and female, when injection is at a 90-degree angle using an 8 mm needle. Injecting into a lifted skin fold reduces the risk of intramuscular injection (Frid & Lindén 1996III, C).
But even when using an 8 mm needle, there is still a risk of intramuscular injection. For example, 13% of children injected into muscle with an 8 mm needle, and 6% injected just under the skin. It is recommended that lean children inject into a lifted skin fold at an angle of 45 degrees (Birkebaek et al. 1998 III, C). This is supported by another study, in which 28% of injections into the thigh done by normal-weight children using an 8 mm needle hit muscle despite injection into a raised fold of skin but at a 90-degree angle. Researchers found that use of an 8 mm needle did not eliminate the risk of intramuscular injection. They recommend 8 mm needles for normal-weight children and adults with type 1 diabetes (Tubiana-Rufi et al. 1999Ib, A).

The risk of intramuscular injection is greatest among normal-weight adults, boys and prepubescent girls. It can therefore be argued that 8 mm needles should be injected at an angle of 45 degrees for these groups.

6 mm needle: As far back as 1989, researchers recommended the use of 5-6 mm needles for most patients, because a 12-13 mm needle would result in intramuscular injection for some patients, leading to unpredictable insulin uptake. These recommendations were made following ultrasound scans of the three most commonly-used injection sites (Pemberton & Holman 1989III, C). 6 mm needles were previously recommended for normal-weight adults and normal-weight children. However, there are now studies that show that 6 mm needles can also easily be recommended for overweight patients. A study was carried out involving 24 normal-weight (average BMI 22.4) and 24 overweight (average BMI 27.8) adults, who injected using a 6 mm needle at a 45 or 90-degree angle with and without a skin fold. The positioning of the injections was localised using ultrasound. The study showed that the most effective technique was for the 6 mm needle to be injected into a lifted skin fold at a 90-degree angle. This technique resulted in 97.8% of all the injections being positioned subcutaneously. In normal-weight individuals it was observed that all injections were delivered subcutaneously both in the thigh and the abdomen when needles were injected into a lifted skin fold at a 90-degree angle. In overweight individuals it was found that all injections were delivered subcutaneously when the needle was injected at a 90-degree angle into a lifted skin fold in the thigh and at a 90-degree angle without a skin fold in the abdomen. Intracutaneous injections were seen in 8.6% of injections using a 6 mm needle when injection was at 45-degree angle (Solvig et al. 2000III, C).
Another study compared the use of 12 mm and 6 mm needles among adults with either type 1 or type 2 diabetes. This showed that 6 mm needles were just as safe in clinical use as 12 mm needles, as there was no significant difference in insulin leakage or changes in glycaemic control.

Also, 70% of patients who had previously used a 12.7 mm needle preferred after the study to use a 6 mm needle. However, there were still 11% who continued to prefer a 12.7 mm needle (Van Doorn et al. 1998Ib, A). A similar study was carried out among 60 children/young people aged 10-18 (average = 13.4 years). In this, 6 mm and 8 mm needles were compared. The results showed that there was no significant difference between the two needle lengths with regard to insulin leakage, pain perception, reactions at the injection sites, glycaemic control and cases of hypoglycaemia. Average insulin leakage at the injection sites was very minor for both needle types, as it was less than 1% of the total insulin dose, seen as the backflow of insulin on the skin. Although there was no difference between the two needle types, 44% of patients preferred the 6 mm needle to the 8 mm one. The patients stated that the 6 mm needle penetrated the skin more easily, and that it was easier to inject the insulin and perform the injection (Chiarelli et al. 2000Ib, A).

The 6 mm needle can be used on the same basis as the 8 mm needle (see chart 3 p. 45)

5 mm needle: Although the 5 mm needle was only launched a few years ago, there have already been studies among both children and adult patients with type 1 and type 2 diabetes comparing it with the 8 mm needle. For example, 23 adults injected themselves using a 5 mm needle without a lifted skin fold. They were compared with another 23 patients who injected using an 8 mm needle into a lifted skin fold for a total of 3 weeks, after which time the two groups switched over to the other form of treatment. It became clear that there was no difference in glycaemic control or in insulin leakage, and the perception of pain was the same for the two needle lengths. In another study of 13 adults with diabetes, glycaemic control was slightly better with the 5 mm needle, but the insulin dose also increased by 3 units of insulin on average per day (Strauss et al. 1999IV, D)Frid has carried out a study involving a total of 28 adults (25
Choice of needle length must be assessed in relation to injection angle and thickness of the subcutaneous adipose tissue in each individual person (see chart below).
### Chart 3

Needle length and injection technique for different patient types.

<table>
<thead>
<tr>
<th>Patient type</th>
<th>Needle length</th>
<th>Injection angle</th>
<th>Skin fold</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal weight (BMI &lt; 25)</td>
<td>6 mm</td>
<td>90 degrees</td>
<td>lifted</td>
</tr>
<tr>
<td></td>
<td>8 mm</td>
<td>45 degrees</td>
<td>lifted</td>
</tr>
<tr>
<td>Above average weight (BMI &gt; 25)</td>
<td>6 mm</td>
<td>90 degrees</td>
<td>without lifted skin fold in abdomen</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>lifted skin fold in thigh</td>
</tr>
<tr>
<td></td>
<td>8 mm</td>
<td>90 degrees</td>
<td>lifted</td>
</tr>
<tr>
<td></td>
<td>12 mm</td>
<td>45 degrees</td>
<td>lifted</td>
</tr>
</tbody>
</table>
Swabbing skin prior to injection

As far back as 1982 it was stated that swabbing the skin prior to insulin injection was not recommendable, because repeated use of spirit on the skin hardens it (Watkins 1982IV, D).

A study of 50 people with diabetes, who performed a total of 600 injections to the abdomen using an insulin syringe that was used 4 times, looked at three different methods:

1)  dry the skin and swab with spirit for 5 seconds prior to injection.
2)  dry the skin and wash using tap water and a cotton wool pad prior to injection.
3)  do nothing prior to injection.

There was no difference between the three methods. No infection or other injection complications were observed, even though the insulin syringe was used 4 times. However, there were complaints that the needle was blunt by the fourth injection (McCarthy et al. 1993IIa, B). When using these methods it is essential to practice good personal hygiene, as otherwise infections could arise (Gorman 1993IV, D).

In another study involving a total of 50 people with diabetes receiving insulin treatment, the usual subcutaneous injection technique including wiping the skin was compared with an experimental injection technique that involved injecting through various kinds of clothing material (from nylon to denim). A total of 13,720 injections were performed over a 20-week period. The study showed:

- no rash
- no hardness of the skin
- no infections/abscesses at the injection site.

HbA1c and the leucocyte count were measured at the start and end of the study, and there was no difference between the two injection methods. There were a very small number of problems involved in injecting through clothing, e.g. blood spots on the clothing and bruises. On the other hand, participants
Swabbing of the skin prior to injection in hospital is recommended.

Statens Serum Institut has been contacted in connection with the updating of this publication. They now also recommend swabbing the skin prior to injection at home (Råd og Anvisninger. Statens Serum Institut, Denmark 2004).

stated that there were advantages to injecting through clothing; for example, it was convenient and saved time when they were eating out (Fleming et al.1997 Ib,A)

Although there is no risk involved in injecting through clothing as above, the method cannot be recommended, as it is important to check the skin for signs of infection and bruises prior to injection. It is not possible to do this if you are injecting through clothing. Furthermore, it is difficult to lift a skin fold and ensure that the injection angle is correct when performing an injection through clothing.

According to the studies described above, it is not necessary to swab the skin prior to injection of insulin. Advice and guidance from Statens Serum Institut, Denmark, recommends that in hospitals, a 5x5 cm area of skin be disinfected. The disinfectant must be allowed to dry before the skin is perforated. Factory-produced pre-injection swabs may be used (Statens Serum Institut, Denmark, 1997).
Re-use of insulin needles for pen systems

A study has been carried out in Germany involving 20 people with diabetes receiving insulin treatment. The study investigated whether or not it is safe to re-use insulin needles for pen systems under normal day-to-day conditions. Previously patients had re-used needles from 2 to over 10 times, and prior to the study, a total of 33,000 injections were carried out without any sign of infection at the injection site. During the study, which lasted 2-4 weeks, needles were re-used 1, 3, 6, 9 and 12 times, before undergoing a bacteriological examination. The pens were kept at room temperature. Eighty-seven needles were subjected to a bacteriological examination, and there were bacteria on one needle. No signs of infection were observed at the injection sites at any time during the study period. Thirteen patients used their needle 9 times before it became blunt, and 7 patients used their needle 12 times. The conclusion was that it is safe to store pens at room temperature and re-use needles, and that there is no connection with any greater risk of skin infections when they are re-used a limited number of times. Needles should be re-used no more than 5-10 times, because the tip of the needle becomes blunt, making any subsequent injection more painful (Schuler et al. 1992III, C). Although the study did not reveal any risk of infection when re-using needles, the question of whether needles can be re-used is difficult to answer. If needles are re-used, the injections can become more painful, because the silicone coating wears off. Experience shows that the needle can bend and become hook-shaped if it is re-used, which can result in a higher risk of bleeding, bruises and damage to the adipose tissue. There is also a risk that the needle might snap once in the skin, which has actually happened. In a study in which 60 people with diabetes had to grade their level of pain following injection of a test medium, it was proven that there was most post-injection pain when needles were re-used that had punctured a rubber membrane protecting an insulin vial 5 times. This is because the tip of the needle had become blunt through puncturing the rubber membrane. Post-injection pain had no relation to the quantity of injected fluid, when this was between 0.025 ml and 0.50 ml (Chantelau et al. 1991Ib, A).

A major European study involving 1,002 people with diabetes demonstrated that re-using needles more than once increases the risk of Lipohypertrophy by 31% (Strauss K, De Gols H, Hannet I et al. 2002.III.C).
The needles are disposable and it is therefore recommended that they be used once only (CAS-NYT, no. 90, July 2001. Statens Serum Institut, Denmark). It is recommended that needles always be removed immediately after the injection when using NPH insulin or mixtures containing NPH insulin. This is done to avoid leakage of solvent (fluid) through the needle, which can gradually cause the concentration of insulin in the remaining mixture to increase (Houtzagers 1989IV, D).
Disposal of needles and insulin pens

A UK study involving 50 patients receiving insulin treatment found that around half of patients did not dispose of their needles in a safe manner. For example, 12% of patients threw their needles straight into the rubbish bin without using a sharps bin. The study concluded that it is essential that health care professionals regularly instruct patients in how to dispose of pens and needles safely (Bain & Graham 1998III, C). Used needles should be placed in an unbreakable sharps bin, which can be purchased from pharmacies. To avoid needlestick injuries, it is not necessary to put the protective cap on the needle. When the container is full it should be taken to a pharmacy. Insulin pens that are empty or partially empty should be taken to a pharmacy, which will then deal with their disposal (Danish Environmental Protection Agency, 2006).
Risk of infection

It has proved to be the case that use of insulin pens can aid the transfer of biological material. A French study that examined pens and needles after injection of insulin showed that:

- 30% had biological material in the needles
- 58% had biological material in the insulin pen
- 25% had biological material in both pen and needle.

The insulin pen may only be used by one person, which is to say that an insulin pen is personal (LeFloch et al. 1998III, C).

It is recommended that at hospitals the membrane on the insulin pen be swabbed before inserting the needle (Statens Serum Institut, Denmark, 2006).
General guidelines for insulin injections in adults

1. Wash your hands before preparing the injection.

2. The pen is to be used for one person only.

3. Check that it is the right type of insulin at the right time. The insulin should be at room temperature.

4. With intermediate-acting insulin or premixed insulin containing intermediate-acting insulin, the pen is turned at least 10 times back and 10 times forth, until the insulin is uniformly milky white in colour.

5. At the hospital the membrane is swabbed with spirit, the needle is attached and the pen’s function is checked. This is done by allowing a drop of insulin to appear at the tip of the needle (follow the guidelines for the various pen systems). If no insulin appears at the tip of the needle, repeat the procedure. Set the pen to the correct insulin dose.

6. The correct anatomical area for this type of insulin is checked. Rapid-acting and very rapid-acting insulin is always injected in the abdomen within an area 4 cm below the navel, 12 cm to the sides or 12 cm above the navel. The uptake rate is quicker above the navel. Slow-acting insulin analogues and intermediate-acting insulin is always injected into the outer thigh area one hand’s breadth above the knee and away from the groin. A recommended alternative site is the hip. Normally, premixed insulin is administered in the abdomen in the mornings and in the thigh in the evenings.

7. Check that the injection site is without injury, signs of infection, bruises and lipohypertrophy. Ensure that the new injection site is at least three centimetres from the previous injection site.

The choice of needle length and injection angle varies from patient to patient in order to ensure that the insulin is injected subcutaneously (see the table below). Usually an 8 mm or 6 mm needle is required for the insulin and is injected at a 45 or 90 degree angle in a lifted skin fold (lifted by thumb and forefinger). Keep the skin fold lifted for the duration of the injection. When you need to administer more than 40 IU insulin at a time, the dose is divided into two injections.
8. Swab the skin with spirit before injecting the needle subcutaneously. If the needle is positioned correctly, the tip of the needle can move freely from side to side in the subcutis.

9. Inject the insulin and release the skin fold at the same time as drawing the needle halfway out. Count to at least 10 (equivalent to 10 seconds) before withdrawing the needle completely.

10. Remove the needle and place it in an unbreakable sharps bin.

The clinical guidelines are designed for use in daily practice, but they do not exempt the practitioner from using clinical judgement in specific situations, e.g. in connection with major transplants, oedema, etc.

<table>
<thead>
<tr>
<th>Needle length and injection technique for different patient types.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient type</strong></td>
</tr>
<tr>
<td>-----------------------</td>
</tr>
<tr>
<td>Normal weight</td>
</tr>
<tr>
<td>(BMI &lt;25)</td>
</tr>
<tr>
<td>Above average weight</td>
</tr>
<tr>
<td>(BMI &gt;25)</td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>
Bibliography

Annersten M., Frid A. Insulin pens dribble from the tip of the needle after injection. Practical Diabetes International 2000; 17: 109-111. (III, C)


Bantle JP, Neal L, Frankamp LM. Effects of the anatomical region used for insulin injections on glycaemia in type 1 diabetes subjects. Diabetes Care 1993; 16: 1592-1597. (1b, A)

Beck-Nielsen H, Henriksen JE, Hermansen K, Madsen LD, Olivarius NdF, Mandrup-Poulsen T et al. Type 2 diabetes og det metaboliske syndrom-Diagnostik og behandling. Klaringsrapport nr. 6, 2000; ISSN 1398-1560. (1a, A)


Chiarelli F, Severi F, Damacco F, Vanelli M, Lytzen L, Coronel G. Insulin leakage and pain perception in IDDM children and adolescents, where the injections are performed with NovoFine 6 mm needles and NovoFine 8 mm needles. Based on a Novo Nordisk sponsored clinical trial. Abstract presented at FEND meeting i Jerusalem, Israel. 2000. (1b, A)

De Meijer PHEM, Lutterman JA, van Lier HJJ, van’t Laar A. The variability of the absorption of subcutaneously injected insulin; effect on injection technique and relation with brittleness. Diabetic Medicine 1990; 7: 499-505. (IIa, B)


Gorman KC. Good hygiene versus alcohol swabs before insulin injections (Letter). Diabetes care 1993; 16: 960-961. (IV, D)


Hanås R. “Måste det göra ont att sticka sig?” Incitament 1998; 7: 84-88. (IV, D)


Lauritzen T, Faber O. K and Binder C. Variation in 125 I-insulin absorption and blood glucose concentration. Diabetologia 1979; 17: 291-295. (Iia, B)


Lytzen L, Hansen B, Sørensen TK. Pain perception and frequency of bleeding. A single-blind randomised investigation comparing NovoPen Gauge 27/12 mm needle, NovoFine Gauge 28/12 mm needle, and NovoFine Gauge 30/12 mm needle. Hormone Metabolisme Research 1993; 25: 61. (III, C)

McCarthy JA, Covarrubias B, Sink P. Is the traditional alcohol wipe necessary before an insulin injektion? Dogma disputed (Letter). Diabetes Care 1993; 16: 402. (IIa, B)


Nielsen BB, Musaeus L, Gæde P, Steno Diabetes Center, Copenhagen, Denmark. Attention to injection technique is associated with a lower frequency of lipohypertrophy in insulin treated type 2 diabetic patients. Abstract præsenteret som poster ved EASD kongres i Barcelona, Spanien 1998. (1b, A)


Van Doorn LG, Alberda A, Lytzen L. Insulin leakage and pain perception with NovoFine 6 mm and NovoFine 12 mm needle lengths in patients with type 1 or type 2 diabetes. Diabetic Medicine 1998; 1: suppl 1: S50. (1b, A)


Appendix 1
Standard for injection technique

AIM: FOR PERSONS WITH DIABETES RECEIVING INSULIN TREATMENT TO BE GIVEN THE CORRECT INJECTION OF INSULIN

<table>
<thead>
<tr>
<th>Problem formulation</th>
<th>Criterion</th>
<th>Standard</th>
<th>Indicator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Studies have shown that lipohypertrophy can result in poor metabolic control and unstable blood glucose levels</td>
<td>Everyone with diabetes receiving insulin treatment is free from lipohypertrophy</td>
<td>80% of people with diabetes receiving insulin treatment are free from lipohypertrophy</td>
<td>Inspection and palpation of injection areas</td>
</tr>
<tr>
<td>Studies have shown that insulin positioned intramuscularly increases absorption rates, with a risk of hypoglycaemia and fluctuating day-to-day uptake</td>
<td>Everyone with diabetes receiving insulin treatment should inject insulin into the subcutis</td>
<td>95% of all insulin injections are positioned in the subcutis</td>
<td>Clinical assessment of the thickness of the subcutaneous adipose tissue compared with the selection of needle length and injection angle</td>
</tr>
<tr>
<td>Studies have shown that there are different absorption rates for different types of insulin. Similarly the absorption rate for the subcutis is different in the abdomen, femur and hip region, with consequences for the effectiveness of the insulin</td>
<td>All insulin injections are placed in one anatomical area, where the intended effect can be achieved</td>
<td>90% of all insulin injections are positioned so that the desired effect can be achieved</td>
<td>Identify insulin type, anatomical injection area and glucose levels</td>
</tr>
</tbody>
</table>
**TOPIC:**
**LIPOHYPERTROPHY**

<table>
<thead>
<tr>
<th>Structure</th>
<th>Procedure</th>
<th>Results</th>
</tr>
</thead>
</table>
| The nurse knows:  
- that repeated use of the same injection site can lead to lipohypertrophy  
- insulin injections must be administered at sites at least 3 cm apart  
- that lipohypertrophy gives rise to fluctuating blood glucose levels and worse metabolic control  
The nurse is familiar with clinical guidelines for injection of insulin for adults with diabetes mellitus | The nurse must:  
- inspect and palpate the injection areas at least once a year  
- analyse and assess habits with regard to changing needles, needle length, distribution of injection sites  
- ensure that insulin doses larger than 40 IU are divided into two injections  
- analyse and assess blood glucose levels  
- provide guidance and instruction in relation to the observations made  
- recommend use of an injection chart |  
- Avoids lipohypertrophy  
- People with diabetes, the people treating them and their relatives understand the significance of systematic distribution of injection sites  
- Achieves good glycaemic metabolic control |
**TOPIC:**

**SUBCUTANEOUS INJECTION OF INSULIN**

<table>
<thead>
<tr>
<th>Struktur</th>
<th>Procedure</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>The nurse knows:</td>
<td>The nurse must:</td>
<td>• The insulin is positioned correctly in the subcutis</td>
</tr>
<tr>
<td>• the structure of the skin and how insulin is absorbed in subcutaneous tissue</td>
<td>• Analyse and assess the thickness of the subcutis in the injection area(s)</td>
<td>• Fluctuating blood glucose levels can be avoided</td>
</tr>
<tr>
<td>• that insulin should be administered subcutaneously</td>
<td>• Analyse and assess injection technique</td>
<td>• Hypoglycaemia can be avoided</td>
</tr>
<tr>
<td>• that insulin positioned intramuscularly can lead to hypoglycaemia</td>
<td>- needle length</td>
<td>• People with diabetes, the people treating them and relatives position the insulin in the subcutis</td>
</tr>
<tr>
<td>The nurse is familiar with clinical guidelines for injection of insulin to adults with diabetes mellitus</td>
<td>- injection angle</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- that the needle can move freely in the subcutis with and without a lifted skin fold</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Analyse and assess blood glucose levels</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Provide guidance and instruction on the basis of observations</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Recommend use of an injection chart</td>
<td></td>
</tr>
</tbody>
</table>
**TOPIC:**

**ABSORPTION RATES FOR DIFFERENT INSULIN TYPES AND DIFFERENT ANATOMICAL AREAS**

<table>
<thead>
<tr>
<th>Struktur</th>
<th>Procedure</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>The nurse knows:</td>
<td>The nurse must:</td>
<td></td>
</tr>
<tr>
<td>• the effect of the insulin types</td>
<td>• Provide guidance concerning the right anatomical area for the prescribed insulin type and the desired effect in relation to diet, exercise, and lifestyle</td>
<td>• Insulin injection is positioned for optimal effect</td>
</tr>
<tr>
<td>• that insulin absorption varies from different anatomical areas</td>
<td>• Identify habits with regard to injection methods for the various types of injection</td>
<td>• Stable blood glucose levels are achieved</td>
</tr>
<tr>
<td>• that insulin absorption varies according to insulin type</td>
<td>• Provide guidance for dividing insulin doses over 40 IU</td>
<td>• People with diabetes, their relatives, and people treating them understand the significance of consistent selection of an anatomical area for insulin injection</td>
</tr>
<tr>
<td>The nurse is familiar with the clinical guidelines for injection of insulin for adults with diabetes mellitus</td>
<td>• Possibly provide the patient with guidance in injection technique</td>
<td></td>
</tr>
</tbody>
</table>

- Insulin injection is positioned for optimal effect
- Stable blood glucose levels are achieved
- People with diabetes, their relatives, and people treating them understand the significance of consistent selection of an anatomical area for insulin injection
## Appendix 2

### Evidence Table

<table>
<thead>
<tr>
<th>Type of publication</th>
<th>Strength</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meta-analysis, systematic overview</td>
<td>Ia</td>
<td>A</td>
</tr>
<tr>
<td>Randomised, controlled study</td>
<td>Ib</td>
<td></td>
</tr>
<tr>
<td>Controlled, non-randomised study</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>Cohort study</td>
<td>IIb</td>
<td></td>
</tr>
<tr>
<td>Diagnostic test (direct diagnostic method)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Case-control study</td>
<td>III</td>
<td>C</td>
</tr>
<tr>
<td>Diagnostic test (indirect nosographic method)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decision analysis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Descriptive study</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minor series, overview article</td>
<td>IV</td>
<td>D</td>
</tr>
<tr>
<td>Expert assessment, leader</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
