Nearly a century after its discovery, most insulin is still delivered via a needle, which many people with diabetes find painful and inconvenient. Researchers and companies are developing both needle technology and new ways of insulin delivery. However, needles will be an important part of the insulin regimen for some time yet and there is room for improvement in the way they are used, says Dr Susan Aldridge.

The first insulin syringe was introduced in 1924, but there was little change in needle design and use until the 1960s. And it is only recently that there has been a focus on the technical aspects of injections, and on the relationship of needle selection and good injection technique to glycaemic control and care optimisation. Evidence and experience-based updated recommendations were published last year by the Forum for Injection Technique and Therapy: Expert Recommendations (FITTER)1, following the publication of the Injection Technique Questionnaire (ITQ) survey2,3*.

The survey covered over 13,000 patients in 42 countries, making it the largest-ever study of insulin injection. The new recommendations also draw on the experience of over 150 of the world’s injection and infusion experts, and the collective contribution of over 15,000 healthcare professionals around the world.

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Improving pain scores. "In the last skin leakage, with the shortest needles shows equivalent glucose control and patient groups, including the very obese, 5mm and 8mm needles in different IM injection. Research comparing 4mm, subcutaneous tissue with little risk of glucose variability and they increase the risk 8mm, children ≥ 6mm) needle lengths (adults ≥ needle, pen and insulin dose, and found thinner and safer. “Several companies, including ourselves, are interested in developing smart or digital needles,” says Dr Strauss. These may have chips embedded which can remember where and when you injected. They can also tell you how much you injected by being linked to the pen. “The smart needle is a form of telemedicine. It will close the loop, with the pen ‘talking’ to the glucose meter, thereby creating a robotic, artificial pancreas style system for the patient.”

Another significant development has been the introduction of safety-engineered needle devices, with the aim of protecting healthcare professionals, and others, from needlestick injuries. One example is the Microlot Safety Pen Needle, which has a shield that locks automatically after injection and is being supplied to 41 major trusts in the UK, according to the company, with take-up now expanding rapidly.

These devices play an important role in the safe use and disposal of the most commonly used sharps in the world (many of which, according to the survey, still find their way into public refuse). Debbie Hicks, Nurse Consultant and Diabetes/Service Lead, Enfield Health Adult Community Health Services and FITTER Scientific Advisory Board member, says: “Always dispose of used sharps in a Sharpsguard, which is available on prescription.”

There is more to needle technology than just making the devices shorter, thinner and safer. "Several companies, including ourselves, are interested in developing smart or digital needles,” says Dr Strauss. These may have chips embedded which can remember where and when you injected. They can also tell you how much you injected by being linked to the pen. “The smart needle is a form of telemedicine. It will close the loop, with the pen ‘talking’ to the glucose meter, thereby creating a robotic, artificial pancreas style system for the patient.”

One key issue is lipohypertrophy (LH) which the ITQ survey found occurring in 30 per cent of patients, with many still injecting into the same site, instead of rotating sites. The survey also showed that LH is associated with higher HbA1c, more glucose variability and more unexplained hypoglycos, as well as with increased insulin use and the accompanying healthcare costs. Training in good injection technique was linked to lower HbA1c, fewer hypos and less glucose variability. Furthermore, more recent instruction in injection technique is associated with lower levels of needle reuse and fewer hospitalisations for hypoglycemia.

“At the bare minimum, injection techniques and sites should be checked at least once a year. It should only take five to 10 minutes,” advises Dr Strauss. “Where there are difficulties, such as lipohypertrophy or swelling, it should be done more often until the problems are sorted out. One of the most disturbing findings in our survey is how infrequently this is done. Many patients had never had their injection sites checked. This is one of the most cost-effective things you can do for your patients in terms of avoiding hypos and getting good HbA1c. It pays dividends and, although it may cost a bit of time – especially with older patients – it really is worth it.”

Hicks adds: “I strongly believe that healthcare professionals can make a significant difference to the lives of people with diabetes by raising and reinforcing the importance of correct injection technique at every opportunity.”

Download the recently published UK Injection and Infusion Technique Recommendations 4th edition from www.fit4diabetes.com

"NICE guidance on Type 1 and Type 2 diabetes highlights the need for rotation of sites, good injection technique and regular checking of injection sites"
Recent developments in insulin pump technology have played an important role in moving the artificial pancreas into the real-life setting. But the infusion set appears to be the weak link in the insulin pump set up, with patients frequently reporting problems. One particular issue is the occurrence of silent occlusions, which can lead to unexplained hyperglycaemia. Studies show that the use of a side-ported catheter can reduce the incidence of silent occlusions by 75 per cent compared with a conventional insulin infusion set.

**INFUSION SETS**

Recent developments in insulin pump technology have played an important role in moving the artificial pancreas into the real-life setting. But the infusion set appears to be the weak link in the insulin pump set up, with patients frequently reporting problems. One particular issue is the occurrence of silent occlusions, which can lead to unexplained hyperglycaemia.

Medtronic is close to introducing its new MiniMed Pro Infusion Set, with BD’s Flow Smart Technology, featuring a side opening in the catheter, which improves insulin flow. Studies show that the use of a side-ported catheter can reduce the incidence of silent occlusions by 75 per cent, compared with a conventional infusion set.

**TRANSDERMAL DELIVERY AND MICRONEEDLES**

Transdermal delivery of insulin through a microneedle array in patch format has many potential advantages – minimal, or no, pain, minimal training and attention and more discreet application. These devices are designed to penetrate to the dermal layer, while avoiding the dermal nerves.

The arrays can be used in several ways. They can be applied to the skin, to create tiny pores, before the drug itself is applied. Or the drug can be coated onto the needles and administered when the needles are applied. There are also hollow microneedles, through which the drug is directly injected into the skin. Research into transdermal insulin delivery in human subjects is, however, at an early stage, although indications are that insulin can be delivered in a more predictable and painless (or significantly less painful) than with a needle.

One interesting development is the Smart Insulin Patch, in development by Dr Zhen Gu at the University of North Carolina, which has recently attracted funding from JDRF and Sanofi. The patch contains 121 microneedles, loaded with insulin-containing nanoparticles and glucose oxidase. The enzyme senses high blood glucose and triggers the release of insulin – thus mimicking the action of beta cells. The patches are several years away from clinical trials at present (currently being tested in minipigs) but Dr Gu says they are intended as a complete replacement for insulin injections.

Finally, there is the OneTouch Via from Calibra Medical Inc., one of the Johnson & Johnson diabetes care companies, which is a wearable on-demand insulin delivery system allowing delivery of bolus insulin at mealtimes by just pressing two buttons on the device, even through clothing. The device contains an insulin reservoir, a cannula, a pump and a valve and is applied like a patch to the body, with a provided inserter, which places the Teflon cannula subcutaneously. The pump controls the movement of insulin from the reservoir through the cannula, allowing the transfer of insulin into the subcutaneous tissue. The valve regulates the precise delivery of insulin from the reservoir into the user.

In a study reported at last year’s American Diabetes Association conference, patients reported missing fewer doses and feeling less stressed, compared with being on multiple daily injections. Calibra has enrolled a clinical outcomes study, across 60 sites in the US and Europe to measure HbA1c, glycaemic variability and quality of life with the patch compared with pens. A spokesperson for the company says they are awaiting FDA approval, and evaluating options for a limited US launch.
Needle-free injector technology has been around for 75 years or so, but has run into problems such as bruising and transmission of infection. Some of these issues have been addressed recently, and there are two needle-free insulin pens on the UK Drug Tariff.

The INJEX30 has a patient-activated trigger, consisting of a spring-loaded mechanism built into the device. The trigger forces insulin through a micro-orifice and through the top layer of the skin, from where it spreads into the subcutaneous layer.

The mechanism of the InsuJet pen releases the insulin at a certain pressure, when the device is pushed against the skin at the injection point. Insulin is pressed at high speed through a small orifice in the nozzle, creating a fine stream of insulin that easily penetrates the skin to reach the subcutaneous layer.

In both devices, the administration of insulin is virtually painless (the jet itself is thinner than a needle), and pharmacokinetics is similar to, or even better than, that for insulin administered by needle, as the insulin enters the skin in a cone-shaped pattern. And, of course, there is no scar tissue and no needles to dispose of.

ORAL INSULIN

Oral insulin remains a goal worth pursuing, because there would be no pain, or fear of pain, in administration, which could also be done more discreetly. These advantages might, in turn, improve adherence with overall long-term improved clinical outcomes for people with both Type 1 and Type 2 diabetes. A further advantage is that oral insulin reaches the circulation in a way more similar to endogenous insulin than subcutaneous insulin, which may have some clinical benefit.

The search for oral insulin began almost as soon as the discovery of insulin itself. Early experiments revealed two major challenges — namely, high variability insulin pharmacodynamics and low bioavailability of the insulin molecule. These continue to be tough obstacles, yet intense interest in oral insulin remains. A recent review11 shows that several companies are actively involved in the development of oral insulin formulations, but most research remains at the preclinical stages. Review author Dr Eric Zijlstra, Director of Project Development at Profi l, a contract research organisation in diabetes and obesity based in Neuss, Germany, notes that there has been little by way of scientific publications on the topic in recent years. It is therefore most unlikely that there will be any oral formulations on the market before 2019 at the very earliest, although he believes that a basal insulin for Type 1 diabetes might stand a better chance of success than an oral mealtime insulin.

This prediction is surely borne out by Novo Nordisk’s discontinuation of its oral insulin programme last year. Citing a challenging payer environment, Kenneth Strømdahl, Novo Nordisk’s Senior Vice President, Device R&D, says: “We had a very good oral insulin project, but the problem lay in the yield. We haven’t put oral insulin out of our minds and may pick it up at some point. We are always interested in making insulin more user friendly.”

“…several companies are actively involved in the development of oral insulin formulations, but most research remains at the preclinical stages”
NEEDLE PHOBIA

For some people with diabetes, the injection process can be very distressing. Clinical psychologist Dr Jen Nash, Director of Positive Diabetes, describes needle phobia and how to help patients manage it.

A phobia is an extreme or irrational fear or aversion to something. A small degree of dislike of needles is perfectly normal – most people would avoid them if they possibly could. But this fear is greatly heightened in people with needle phobia, to the point where they cannot bear the thought of injections. Some studies suggest that the rate of occurrence of needle phobia in the general population is at least 10 per cent. The actual figure may be higher, as many of those with needle phobia simply avoid all medical treatment.

The main feature of needle phobia is anxiety at the thought of injections or blood glucose testing. This may be associated with feeling dizzy and light-headed, a dry mouth, palpitations, sweating, trembling, over-breathing, feeling sick and even fainting, and lead to avoiding injections or testing.

Why does needle phobia occur?
The most common causes of needle phobia are thought to be:
• an upsetting experience of needles when young (for example, a painful procedure at the hospital or at the dentist)
• a fear that has been modelled by an adult close to the child, either through actual observation of their fear, or being told a story that implied injections and needles were very painful.

There is also an evolutionary value to a fear of needles. In the past, an individual who feared being stuck with a thorn or a knife was less likely to die in accidents or in encounters with hostile animals or other humans. Before the 20th century, even an otherwise non-fatal puncture wound had a reasonable chance of causing a fatal infection. So a trait that had positive survival value throughout evolution now has the opposite effect, as it means people struggle to engage in using the needle that will save their life.

Needle phobia and diabetes
Fear of self-injecting or of self-testing are associated not only with poorer adherence to the diabetes treatment regimen, but with more diabetes-related distress overall and poorer general wellbeing. Helping your patient gain skills of relaxation and confidence is the key to making injections less painful than it is now, and less anxiety-provoking. Reassure them that they can gain confidence over time and with practice, using a combination of relaxation and developing their own personal ‘fear hierarchy’.

There is more on this, and how to help people with diabetes manage needle phobia, in my book Diabetes and Wellbeing (Chicester, Wiley-Blackwell) 2013 pages 95–103.

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6 Aronson R. Gibney MA, Oza K et al (2013). Insulin pen needles: effects of extra-thin wall needle technology on preference, confidence and other patient ratings. Clinical Therapeutics 35 (7); 923–933

*BD sponsored the ITQ survey and FITTER*

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