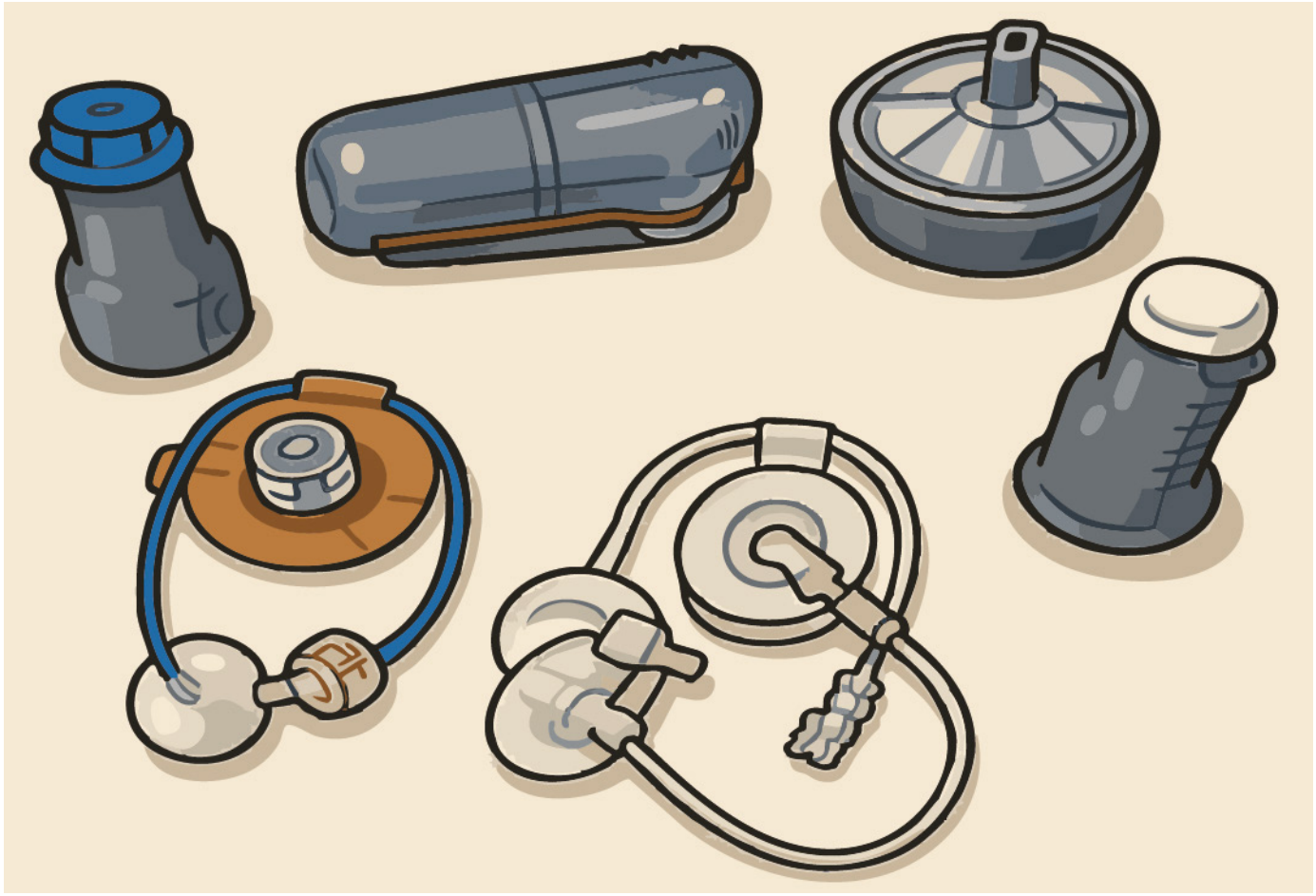
Soraya Carpintero Lozano.
Pediatric Diabetes Nurse Educator at Hospital Universitario Ramón y Cajal (Madrid, Spain).
Member of the Spanish Diabetes Society and the "Women and Diabetes" working group.

Pilar María García Mondéjar.
Pediatric Diabetes Nurse Educator at Hospital Universitario Ramón y Cajal (Madrid, Spain).



Advances in Insulin Pump Infusion Sets:

What's New?

Infusion sets are a crucial part of continuous subcutaneous insulin infusion (CSII) systems and can be a source of glycemic control issues due to mechanical problems (occlusion, kinking, or adhesive detachment) and skin-related complications, which negatively impact the quality of life of individuals with type 1 diabetes mellitus (T1DM). New models have gradually been developed and marketed to meet patient needs—most notably, the ability to safely extend the use of infusion sets up to 7 days without compromising glycemic control.

It has been demonstrated that glycemic control in people with type 1 diabetes mellitus (T1DM) has improved thanks to closed-loop systems, which are recommended by both the ADA (American Diabetes Association) and ISPAD (International Society for Pediatric and Adolescent Diabetes) for all pediatric and adult patients at any stage of the disease for T1DM management (1, 2).

A closed-loop system integrates 3 components: an insulin pump or CSII, a continuous interstitial glucose monitoring sensor (CGM), and a control algorithm. One of the insulin pump components that significantly impacts the quality of life in people with T1DM is the infusion set. The infusion set serves as an essential interface, composed of a thin and flexible tube that connects the pump to the patient via a stainless steel needle or a Teflon cannula, secured to the skin by an adhesive patch. In addition to the material (steel needle or Teflon cannula), users can also choose the needle/cannula length, tubing length, and insertion angle (perpendicular or oblique), allowing personalization of the infusion set based on the patient's characteristics and needs.

Problems related to infusion sets can lead to unexplained hyperglycemia, which increases the risk of diabetic ketoacidosis. The most common issues are mechanical: occlusion, kinking, and adhesive detachment. Other undesirable effects include local skin reactions and immune responses, possibly worsened by insulin and its preservatives. These effects may be associated with the duration of infusion set use (3). As a result, patients need to rotate insertion sites to avoid skin damage, making it difficult—especially for children—to find suitable areas to place the devices.

HISTORY OF INFUSION SETS

In the early 1960s, Dr. A. Kadish designed the first IV insulin delivery system using a peripheral venous access. Later, in 1978, J. Pickup et al. (4) conducted a small study in T1DM patients that first demonstrated the clinical efficacy of continuous subcutaneous insulin infusion (CSII). This first registered infusion set for subcutaneous insulin delivery consisted of a nylon cannula inserted via a 16-gauge introducer needle 6–9 cm long, after prior local anesthesia.

In 1986, the implantable insulin pump was introduced for intraperitoneal delivery, along with *"insulin-friendly tubing"*—a catheter tunneled through the lower abdominal subcutaneous tissue and into the liver via the peritoneum.

Since the 1990s, insulin pumps have evolved to become smaller, more practical, and more precise, along with the development of more efficient infusion sets. Currently, a wide variety of infusion systems are available, enabling customization according to cannula material, insertion angle, and tubing/cannula length.

Significant advances have aimed to increase comfort and flexibility, such as the introduction of the first "patch pump" in 2011, which included an integrated infusion set without tubing (5).

Until recently, infusion sets were limited to 2–3 days of use, depending on the material (steel needle or Teflon cannula). Extending infusion set duration was a critical unmet need—until now.

We currently have an extended-use infusion set model lasting up to 7 days per catheter, with other models under development (6,7).

This new extended-use **infusion set features** changes to the tubing material and a redesigned connector to reduce preservative loss while maintaining the insulin's chemical and physical stability for 7 days (8). One special consideration is that the reservoir may need to be changed before the full 7 days, depending on the patient's total daily dose (TDD) of insulin.

EVALUATING THE SAFETY AND EFFICACY OF THE EXTENDED INFUSION SET

Studies have assessed the potential adverse effects of these new systems in adults using insulin lispro and aspart. The most common concerns include device-induced unexplained hyperglycemia, adhesive strength, and skin reactions.

Device-induced unexplained hyperglycemia

Studies on extended infusion systems share a concern about unexplained hyperglycemia. »

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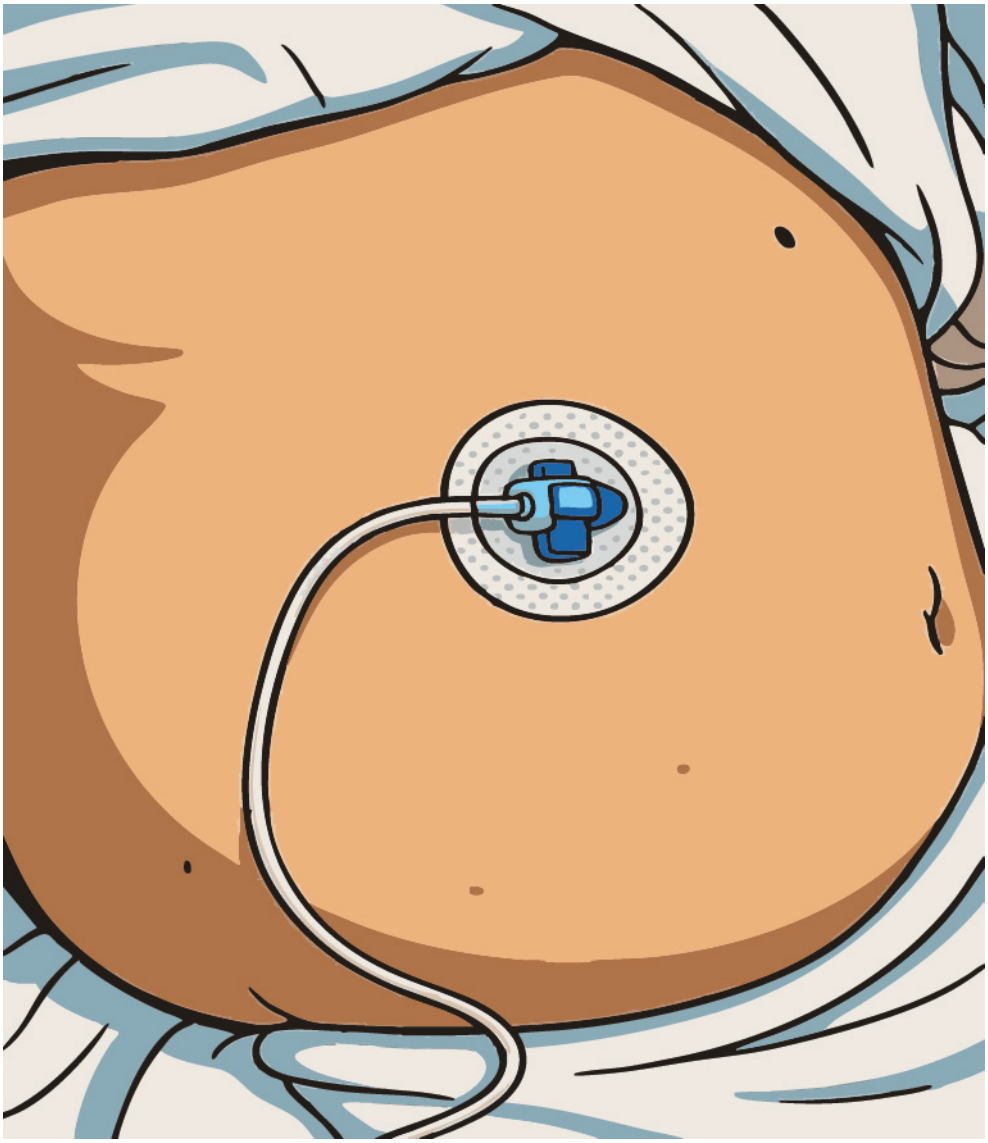
ISSUES RELATED TO INFUSION SETS CAN LEAD TO UNEXPLAINED HYPERGLYCEMIA, WHICH CARRIES A HIGHER RISK OF DEVELOPING DIABETIC KETOACIDOSIS



» This was defined as a blood glucose meter reading >250 mg/dL (at least 3 hours post-meal), followed 60 minutes after a corrective bolus with an additional increase of ≥ 50 mg/dL. The failure rate was defined as the number of device removals associated with unexplained hyperglycemia divided by the total number of device insertions (7).

Results show that the rate of unexplained hyperglycemia due to the infusion sets is very low.

Furthermore, some studies conclude that mean glucose levels and time-in-range remained stable over the 7-day use, with no significant changes in glucose variability or TDD (7,9).

Adhesive strength

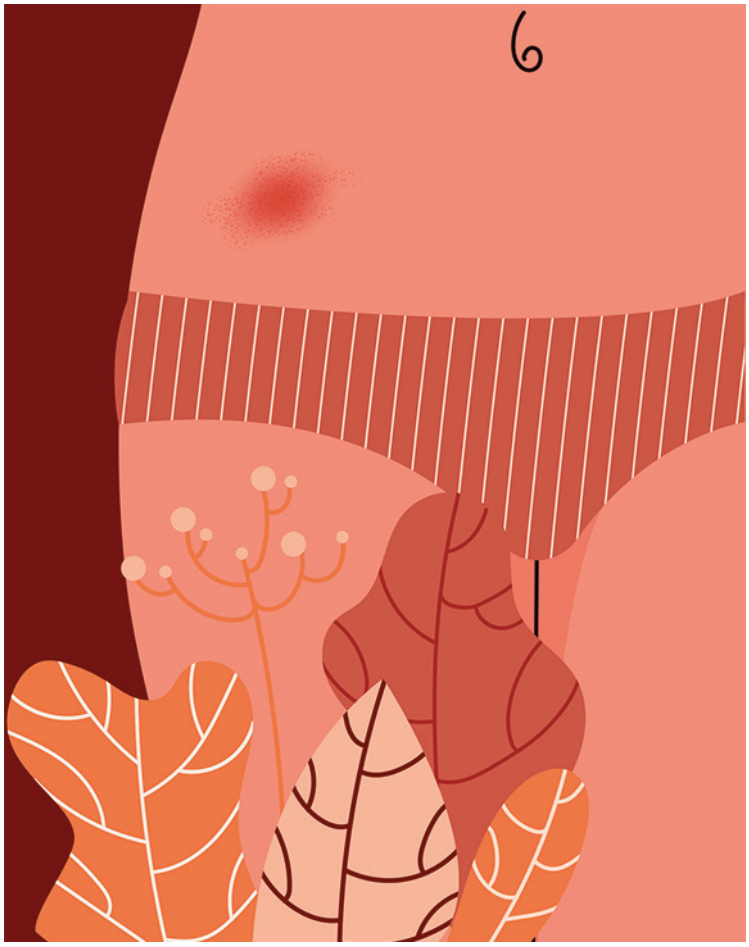
The adhesive-related survival of infusion sets appears to vary by user. The adhesive in this new system is stronger, allowing for longer wear time.

Skin reactions

While dermatological issues with adhesives are common, especially in children, no studies have yet addressed this area. Similarlu, no evidence has been found regarding the impact of infusion set biomaterials and designs on subcutaneous tissue response (3).

USER SATISFACTION WITH THE EXTENDED INFUSION SET

User satisfaction in terms of comfort and ease of use of the extended infusion set was found to be higher than with previously used standard sets (7,10). D



CONCLUSIONS

Infusion systems have evolved significantly throughout time. One of the most recent and impactful advances is the extension of their use to seven days, improving the quality of life for CSII users. This extended duration also translates into cost savings, thanks to reduced insulin waste from fewer set changes. Available studies on extended-use infusion sets report positive outcomes in user satisfaction without compromising safety or glycemic control. However, data are lacking for pediatric and pregnant populations, whose body composition might affect the efficacy proven in adults. Another limitation is that existing studies have only used insulin lispro or aspart.

Currently, experience with extended infusion sets remains limited, highlighting the need for further research to enable personalized selection of infusion systems for people with T1DM, based on population and phenotypic results.

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