able to bypass the stratum corneum, as reflected in the decreased time to maximum blood flux (Figure 40.3), but the pointed needle may deliver more methyl nicotinate into the skin over the 30-second injection period. Hollow microneedles designed with a lumen different from the pierce and entry zone may increase drug injection efficacy.

All volunteers were asked to describe what they felt during the injection, and all responded by saying that they felt pressure but no pain, in agreement with Kaushik et al. (4).

These results show that hollow microneedles can painlessly bypass the stratum corneum during injections and deliver drugs to the skin capillaries in humans. Traditional hypodermic needle injections will continue to be advantageous in treatments requiring deeper penetration past the epidermis, like subdermal, muscular, or intravenous injections. However, hollow microneedles offer distinct advantages: they are painless and can reduce needle phobia in patients, are simpler to use than traditional injections, and can be integrated into devices for controlled, continuous drug delivery. Another advantage for hollow microneedles among transdermal drug delivery systems is the potential to inject large-sized protein formulations, such as sustained-release insulin formulations that range from 2 to 30 μm (24). The lumens of the hollow microneedle are 35 to 300 μm (10–13) and could successfully inject these formulations. Microneedles will be beneficial from a public health perspective too, because more people may be willing to receive vaccinations due to the increased convenience and comfort of the microneedle injection.

The design of the microneedle can affect how quickly drugs can be introduced through the needles. Microneedles can serve as a painless alternative to hypodermic vaccine injection and to administer drugs that may normally be administered in a topical manner. Revolutionary continuous and controlled drug therapies can be possible when pumps and sensors are mounted onto microneedle arrays.

Recent studies have evaluated the use of microneedles for multiple clinical application within immunology and dermatology.

Vaccinations have been explored as one possible application of microneedle technology. In fact, two pilot clinical studies have evaluated the use of microneedle-based delivery of vaccines in human participants (25, 26). In both studies microneedles that were shorter than 700 microns were used and compared against intramuscular vaccine delivery, and both studies showed that microneedle injections lead to as much immunogenicity as intramuscular injections. In both studies, pain was noted to be less with the microneedle-based delivery but local redness was increased in the microneedle injection group, suggesting that a sufficient immune response could be elicited from microneedle-based vaccinations. Further studies are needed, but both of these studies are promising.

Two studies evaluated if microneedles could assist with topical anesthesia. In one study, anesthesia was injected through hollow microneedles and achieved the same level of anesthesia as hypodermic needles (27). Moreover, 77% of participants preferred the self-administered microneedle injection rather than a hypodermic needle. In the other study, solid microneedles were used as a pretreatment on the forearm before applying topical 4% lidocaine and compared against the contralateral forearm with sham treatment (flat surface with no microneedles). The investigators found that pretreatment with microneedles enhanced topical anesthesia by 30 minutes in all participants and by 10 minutes in those that had greater pain sensitivity.

Finally, microneedles have been adapted for use in photodynamic therapy for actinic keratoses where topical 5-aminolevulinic acid is typically applied to the skin and allowed to incubate for one hour prior to exposing the skin to blue light. One study utilized a split-face design in 48 participants to show that the standard 60-minute incubation was comparable to microneedle pretreated skin that was incubated for only 20 or 40 minutes (29). Another study evaluated lowered incubation times of 10 and 20 minutes in a split-face design for the treatment of actinic keratoses (30). The 10-minute incubation did not show statistically significant improvement from the sham-treated side of the face (roller with no microneedles); However, the 20-minute incubation after microneedle treatment was significantly improved compared to the sham-treated side. The two studies suggest that microneedle pretreatment may enhance the transcutaneous penetration of 5-aminolevulinic acid and warrant more study in an expanded group of participants to better assess the role of microneedle pretreatment.