

inserted into the skin, could detect a specific antigen, or antigens, alongside result validation. An additional benefit is this test can produce results in less than five hours [206]. MNs have been used to detect nitric oxide levels in the body using a dual diagnostic system of an endomicroscope and MN biosensor, giving fast and accurate diagnoses of cancer [207]. Peptide aptamer-based MNs can also be used for detection of cancer by measuring vascular endothelial growth levels (VEGF) levels in the blood [208]. Point-of-care diagnostics using disposable MNs coupled with a wristwatch-type portable analyzer can measure blood oxygen levels, or other systems can measure potassium levels using an on-chip system, both giving rapid results, which lead to increased standards of patient care [209, 210]. Alternatively, MNs can be loaded with antigens and adjuvants, such that when inserted attract specific tissue-resident immune cells which can be sampled and analyzed. Changes in antibody levels can be tracked to assess immune responses over time [211].

MNs arrays were originally developed as a method of enhancing transdermal drug delivery, and the principle can be adapted to deliver diagnostic molecules across the skin. An example is with the Mantoux test, or tuberculin skin test (TST), for tuberculosis which involves intradermally injecting tuberculin purified protein derivative (PPD) from *Mycobacterium tuberculosis* [212]. Intradermal injections are painful for the patient and difficult to perform and require adequately trained health care workers. A MN array made from chitosan and coated with the PPD was subsequently developed, with the test being simplified to simply inserting the MN under thumb pressure [213]. This enables the PPD to be delivered to the correct depth consistently, with far greater ease, and with minimal training. The TST has also been carried out using the aforementioned MicronJet600 [214]. Comparing this device to traditional hypodermic needles used in the Mantoux test showed there was no significant difference in the TST reaction rates; however, the MN device exhibited significantly less pain and no additional adverse effects due to the device [214]. Allergen testing is often performed using skin patch tests, where traditionally different allergens would be injected into the patient's skin and the reaction to each allergen assessed for hypersensitivity. Along with the disadvantages mentioned previously (Section 39.1), the test also covers a substantial area of skin, which can be unsightly and uncomfortable. MNs have the potential to overcome this. Solid MNs could be coated with the allergen of choice, or the allergen could be incorporated into a dissolving MN array [215]. Both of these methods give quick responses, and when combined with an integrated sensor, give instantaneous results [216]. In an applicator device the numerous needle heights can be adjusted to deliver the allergen to various skin depths, or a different allergen could be combined with each needle to give multiple results at once.

MNs, and in particular hydrogel-forming arrays, are self-disabling and therefore can only be single use. Continuous monitoring is an area of great interest, with blood glucose monitoring alone worth an estimated \$12 billion globally in 2020, and so it is no surprise that MNs have been explored for this purpose [197]. Arrays used for continuous glucose monitoring can be formulated from hollow MNs integrated with an enzyme-based flow-through sensor to give real-time data, which is essential for blood glucose control [217]. A different group has shown their hollow needles, which are coupled to an amperometric detector, to be clinically accurate at measuring glucose levels for up to 72 hours [218]. MNs coated in platinum and silver have been used to quantify glucose levels by acting as electrodes. They have been shown to have a low limit of detection and exhibit a strong linearity with a fast readout time; however, the patch did not perform at the required level for more than four days due to biofouling [219]. Away from glucose monitoring, MNs have been developed for use as continuous monitors for alcohol in the body via enzyme-coupled arrays, as well as platinum- and gold-coated arrays for continuous monitoring of free cholesterol [220, 221]. Outside of the health care setting, continuous sweat monitoring has potential in elite athletes and sports teams. A wearable system has been developed to selectively and simultaneously measure metabolites of choice (e.g., lactate) and electrolytes (e.g., sodium), as well as pH and temperature. This device can transmit data wirelessly for real-time data analysis [222]. Other groups have explored wearable MN metabolite testing systems that would enable training programs to be tailored to, or by, each individual athlete [223, 224]. As wearable technology such as Fitbit and Apple Watch continue to grow commercially, there is