Intradermal influenza vaccine delivery using skin-penetrating dissolvable vaccine microneedles

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Purpose:

To design and fabricate minimally skin-penetrating, dissolvable influenza vaccine microneedles for intradermal delivery to mice.

Methods:

A commercial trivalent influenza vaccine (Fluzone, 2004/2005) was dialyzed, concentrated, blended with dextrin and trehalose excipients, and lyophilized to powder formulations of 2% and 10% hemagglutinin (HA). The preservation of the HA's immunoreaction potency was confirmed by Western blot analysis. The vaccine powder reconstituted in deionized water was centrifugally cast in a mold having microneedle-shaped cavities. A cellulose gel was cast over the vaccine film to form a patch basal layer. The 1-cm-diameter disc carried 25–30 vaccine microneedles (Fig. 1a). The vaccine patch was administered by a spring-driven injector to the back of a shaved mouse. H1N1 antibody titers were assayed by ELISA. The results were compared with intramuscular (i.m.) and subcutaneous (s.c.) routes.

Results:

The two-step centrifugal casting reliably produced vaccine microneedles on the cellulose basal layer. The 30-µm-diameter needle tip was sufficiently strong to penetrate the mouse skin upon impulse. The estimated vaccine load per patch was approximately 80 µg for a 10% patch. Typically, one- to two-thirds of the needle length was dissolved in the skin after 15 min (Fig. 1b), which released an HA dose between 5 and 25 µg. Antibody titers were detectable by study day (SD) 14; at later SDs, the difference among all routes of administration was minimized (Fig. 2a). The reconstituted solid formulation produced antibody titers comparable to liquid bulk vaccine, indicating that the current vaccine solid formulation method is effective. Antibody titers increased with HA doses (Fig. 2b).

Conclusions:

Our results clearly demonstrate the utility of the vaccine microneedle patch. The exact amounts of antigen deposited in the skin were difficult to determine because of the administration method and the nature of the mouse skin. Methods for improving dose control are in progress.

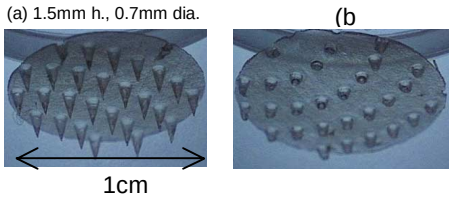

Figure 1. (a) Vaccine microneedles (b) after insertion for 15 min.

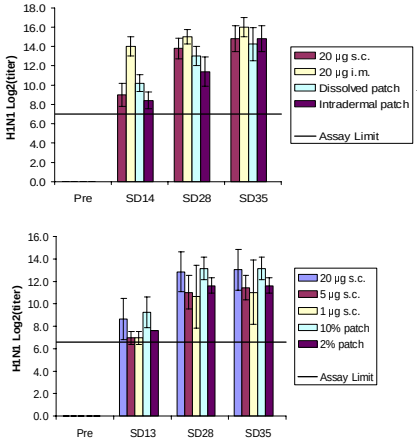

Figure 2. H1N1 antibody titers (a) administration route comparison (b) dose response. HA doses of 10% and 2% patches were between 5 and 25 µg and 1 and 5 µg, respectively.