TABLE 3: PERCENTAGE OF PARTICIPANTS 18–55 YEARS OF AGE REPORTING SOLICITED ADVERSE REACTIONS WITHIN 7 DAYS FOLLOWING VACCINE ADMINISTRATION

	Menactra vaccine N*=1371			Menomune–A/C/Y/W-135 vaccine N*=1159		
Reaction	**Any**	**Moderate**	**Severe**	**Any**	**Moderate**	**Severe**
Redness‡	14.4	2.9	1.1†	16.0	1.9	0.1
Swelling‡	12.6†	2.3†	0.9†	7.6	0.7	0.0
Induration‡	17.1†	3.4†	0.7†	11.0	1.0	0.0
Pain§	53.9†	11.3†	0.2	48.1	3.3	0.1
Headache‖	41.4	10.1	1.2	41.8	8.9	0.9
Fatigue‖	34.7	8.3	0.9	32.3	6.6	0.4
Malaise‖	23.6	6.6†	1.1	22.3	4.7	0.9
Arthralgia‖	19.8†	4.7†	0.3	16.0	2.6	0.1
Diarrhea¶	16.0	2.6	0.4	14.0	2.9	0.3
Anorexia#	11.8	2.3	0.4	9.9	1.6	0.4
Chills‖	9.7†	2.1†	0.6†	5.6	1.0	0.0
Fever**	1.5†	0.3	0.0	0.5	0.1	0.0
Vomiting††	2.3	0.4	0.2	1.5	0.2	0.4
Rash‡‡	1.4			0.8		
Seizure‡‡	0.0			0.0		

* N = The number of subjects with available data; † Denotes $p < 0.05$ level of significance. The p values were calculated for each category and severity using Chi Square test; ‡ Moderate: 1.0–2.0 inches, Severe: >2.0 inches; § Moderate: Interferes with or limits usual arm movement, Severe: Disabling, unable to move arm; ‖ Moderate: Interferes with normal activities, Severe: Requiring bed rest; ¶ Moderate: 3–4 episodes, Severe: ≥5 episodes; # Moderate: Skipped 2 meals, Severe: Skipped ≥3 meals; ** Oral equivalent temperature; Moderate: 39.0–39.9°C, Severe: ≥40.0°C; †† Moderate: 2 episodes, Severe: ≥3 episodes; ‡‡ These solicited adverse events were reported as present or absent only.

Local and Systemic Reactions when Given with Typhim Vi Vaccine

The two vaccine groups reported similar frequencies of local pain, induration, redness and swelling at the Menactra injection site, as well as at the Typhim Vi injection site. Pain was the most frequent local reaction reported at both the Menactra and Typhim Vi injection sites. More participants experienced pain after Typhim Vi vaccination than after Menactra vaccination (76% versus 47%). The majority (70%–77%) of local solicited reactions for both groups at either injection site were reported as mild and resolved within 3 days post-vaccination. In both groups, the most common systemic reaction was headache (Menactra + Typhim Vi vaccine, 41%; Typhim Vi vaccine + Placebo, 42%; Menactra vaccine alone, 33%) and fatigue (Menactra + Typhim Vi vaccine, 38%; Typhim Vi vaccine + Placebo, 35%; Menactra vaccine alone, 27%). Between the groups, differences in rates of malaise, diarrhea, anorexia, or vomiting were not statistically significant. Fever ≥40.0°C and seizures were not reported in either group.

Post-Marketing Reports The following adverse events have been reported during post-approval use of Menactra vaccine. Because these events were reported voluntarily from a population of uncertain size, it is not always possible to reliably calculate their frequency or to establish a causal relationship to Menactra vaccine exposure. Immune system disorders - Hypersensitivity reactions such as anaphylactic/anaphylactoid reaction, wheezing, difficulty breathing, upper airway swelling, urticaria, erythema, pruritus, hypotension. Nervous system disorders - Guillain-Barré syndrome, vasovagal syncope, facial palsy, transverse myelitis, acute disseminated encephalomyelitis. Musculoskeletal and connective tissue disorders - Myalgia.

DOSAGE AND ADMINISTRATION

Menactra vaccine should be administered as a single 0.5 mL injection by the **intramuscular** route, preferably in the deltoid region. Do not administer this product intravenously, subcutaneously, or intradermally. The need for, or timing of, a booster dose of Menactra vaccine has not yet been determined. Parenteral drug products should be inspected visually for container integrity, particulate matter and discoloration prior to administration, whenever solution and container permit.

Concomitant Administration with Other Vaccines

Safety and immunogenicity data are available on concomitant administration of Menactra vaccine with Typhim Vi, and Td vaccines (see **ADVERSE REACTIONS** section). Concomitant administration of Menactra vaccine with Td did not result in reduced tetanus, diphtheria or meningococcal antibody responses compared with Menactra vaccine administered 28 days after Td.[4] However, for meningococcal serogroups C, Y and W-135, bactericidal antibody titers (GMTs) and the proportion of participants with a 4-fold or greater rise in SBA-BR titer were higher when Menactra vaccine was given concomitantly with Td than when Menactra vaccine was given one month following Td. The clinical relevance of these findings has not been fully evaluated.[4] Concomitant administration of Menactra vaccine with Typhim Vi vaccine did not result in reduced antibody responses to any of the vaccine antigens.[4] The safety and immunogenicity of concomitant administration of Menactra vaccine with vaccines other than Typhim Vi or Td vaccines have not been determined. Menactra vaccine must not be mixed with any vaccine in the same syringe. Therefore, separate injection sites and different syringes should be used in case of concomitant administration.

STORAGE Store between 2° to 8°C (35° to 46°F). DO NOT FREEZE. Product that has been exposed to freezing should not be used. Do not use after expiration date.

REFERENCES: 1. Ball R, et al. Safety Data on Meningococcal Polysaccharide Vaccine from the Vaccine Adverse Event Reporting System. CID 2001;32:1273-1280. **2.** CDC. Guillain-Barré Syndrome Among Recipients of Menactra® Meningococcal Conjugate Vaccine - United States, June 2005-September 2006. MMWR 2006;55(41): 1120-1124. **3.** CDC. General recommendations on immunization. Recommendations of the Advisory Committee on Immunization Practices (ACIP) and the American Academy of Family Physicians (AAFP). MMWR 2002;51(RR02): 1-36. **4.** Data on file, Sanofi Pasteur Inc. - 092503.

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Acceptance of H1N1 Flu Vaccine Was Poor

BY BRUCE JANCIN

FROM AN ANNUAL CONFERENCE ON PEDIATRIC INFECTIOUS DISEASES

VAIL, COLO. — Acceptance of the pandemic 2009 H1N1 influenza vaccine by U.S. health care workers was, in a word, "terrible," Dr. Adriana Weinberg declared.

A mere 37% of physicians and other health care workers were vaccinated against the pandemic virus, Dr. Weinberg reported at the meeting sponsored by the Children's Hospital, Denver.

VITALS

Major Finding: Only 37% of physicians and other health care workers were vaccinated against the pandemic virus.

Data Source: CDC data provided to the National Vaccine Advisory Committee.

Disclosures: Dr. Weinberg disclosed serving as a consultant to MedImmune, Astellas, GlaxoSmithKline, and Merck & Co. Inc.

Uptake of the vaccine by two notably high-risk patient groups—pregnant women, and children and adolescents aged 6 months to 17 years—was equally poor at 38% and 37%, respectively, said Dr. Weinberg, professor of medicine, pediatrics, and pathology, and medical director of the clinical virology laboratory at the University of Colorado Hospital, also in Denver. These data were provided to the National Vaccine Advisory Committee by the Centers for Disease Control and Prevention.

Among parents and other care providers for infants less than 6 months of age, vaccine acceptance was even worse at 14%. Moreover, only 25% of adults aged 24-64 years with immunosuppression or other chronic medical conditions placing them at elevated risk for increased flu morbidity got vaccinated. That was essentially the same rate as in the overall U.S. population, including both high-priority and non–high-priority individuals.

As a result of this low uptake, many millions of soon-to-expire doses of pandemic 2009 H1N1 influenza monovalent vaccine are being destroyed.

In several studies, the main reason cited by health care workers and pregnant women for not accepting the vaccine was fear of side effects, especially Guillain-Barré syndrome, which was an issue with the 1976 swine flu vaccine. The safety concerns proved baseless this time around, as evidenced by consistently reassuring findings from three separate sources: the Vaccine Safety Datalink, the Vaccine Adverse Event Reporting System, and the Emerging Infections Program.

For example, there were no deaths and no cases of Guillain-Barré syndrome among recipients of 438,376 doses of the vaccine in managed care organizations participating in the Vaccine Safety Datalink. And during surveillance for Guillain-Barré syndrome conducted through the Emerging Infections Program, the rate of cases was 1.92/100,000 person-years among vaccine recipients, compared with 1.21/100,000 person-years among nonrecipients. That 0.7/100,000 person-years excess of Guillain-Barré syndrome associated with the pandemic H1N1 vaccine is similar to that associated with the seasonal influenza vaccine, according to Dr. Weinberg.

One audience member said the reason lots more families in his practice didn't get vaccinated against H1N1 was not fear of side effects; it was that he and other office-based physicians in his community didn't get shipments of the vaccine until after the second and as it turned out, final, wave of the 2009 pandemic had passed.

Dr. Weinberg agreed that lack of timely vaccine availability caused by long delays in the cumbersome manufacturing process was a huge problem. A potential solution would be to produce influenza vaccines in cell culture instead of eggs, something the Food and Drug Administration is very reluctant to allow, although one such flu vaccine was recently approved in Europe. Another answer would be to identify common epitopes that confer cross-strain protection against all influenza strains, so a new vaccine wouldn't have to be created in advance of every flu season.

"There has been a big push on this. There are some good candidate epitopes emerging in the last year. We shall see," the virologist said.

The vaccine being manufactured for the coming 2010-2011 flu season contains antigens for a pandemic 2009 H1N1 influenza virus as well as a seasonal influenza A H3N2 Perth 2009 virus and an influenza B Brisbane 2008 virus. The immunization schedule recommended by the CDC calls for a single dose of the vaccine for adults and children older than age 10 years. Children aged 6 months to 9 years are to receive two doses 21 days apart unless they are in the minority who received the pandemic H1N1 monovalent vaccine last season, in which case they are to get a single dose of the trivalent vaccine. Despite this recommendation, a recent randomized controlled trial concluded that a single dose may be sufficiently immunogenic in young children (JAMA 2010;303:37-46).

"We do anticipate circulation of the pandemic H1N1 strain in the next flu season, but I have to caution you that in the Southern Hemisphere, where influenza season is going on right now, there is very, very little pandemic H1N1. What predominates are the A H3N2 and the B Brisbane," she said. ■