



## H1N1 Vaccine Q & A's (October 28, 2009)

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CTV.ca, with the help of infectious disease expert Dr. Neil Rau, recently posted the following information regarding answers to common questions about the H1N1 flu vaccine.

### *What is Canada's new H1N1 swine flu vaccine called?*

The vaccine is being called Arepanrix and is manufactured by GlaxoSmithKline at its facility in Ste. Foy, Que. The vaccine was given official approval by Health Canada on Oct. 16, 2009, and is being recommended to almost all Canadians over the age of six months.

Should I get vaccinated against swine flu?

For some of the priority groups identified by The Public Health Agency of Canada, the vaccine is urgently and strongly recommended. The H1N1 flu vaccination will not be mandatory, so everyone will need to make an individual decision based on their assessment of available information. However, those who are most vulnerable, are recommended to receive the vaccine now, even as additional safety information becomes available.

The Public Health Agency of Canada has identified these groups as a priority for immunization:

- \* people with chronic medical conditions under the age of 65;
- \* pregnant women (see below for further details);
- \* children six months to under five years of age;
- \* people living in remote and isolated settings or communities;
- \* health care workers involved in pandemic response or who deliver essential health services;
- \* household contacts and caregivers of individuals who are at high risk, and who cannot be immunized (such as infants under six months of age or people with weakened immune systems).

Vaccine supplies will be limited in the first couple of weeks so patients may have to be prioritized. But the Public Health Agency of Canada has said that there will be enough vaccine for all Canadians who need or want the vaccine.

There are still questions about whether everyone will want to be vaccinated. Keep in mind that H1N1 causes only mild flu in most people; in fact, some Canadians may have already been "immunized" through an H1N1 infection. Determining who has been exposed already is a scientific challenge at this time (see next question). Otherwise healthy may choose to wait until vaccine manufacturers gather more safety and effectiveness data.

The vaccine is also not appropriate for infants under six months of age or anyone who currently has a fever.

### *Where can I get the vaccine and how much will it cost?*

The federal, provincial and territorial governments are footing the bill for the pandemic vaccine program, so there will be no cost to you.

### ***How effective will the new vaccine be?***

Trials conducted on the GSK vaccine in Europe have found the vaccine produces antibodies in 85 to 98 per cent of adults aged 18 to 64 -- an excellent though not perfect effectiveness rate. But then, even seasonal flu vaccination doesn't provide 100 per cent immunity. In years when the strains of the flu virus in the seasonal vaccine have been a good match for the dominant strains circulating in the community, seasonal flu vaccine has been shown to reduce infection by 70 to 90 per cent in healthy adults.

The vaccine may be somewhat less effective in children under 10 years of age. However, promising recent information from GSK indicates that one dose of adjuvanted vaccine may provide immunity to children over six months of age.

As things stand now, kids under the age of 10 will need two half-dose shots given 21 days apart. However, this recommendation may be revised in the future, based on the promising information just cited. In fact, adjuvanted vaccines may offer an advantage of giving one dose, rather than two doses to young children.

The vaccine also may not work as well in people who have problems with their immune systems or who are taking medication that affects their immune systems; however it is still important for these people to consider vaccination.

It should be noted that it takes about two weeks after vaccination for antibodies to develop in the body and provide protection, so a recipient is still at risk for infection in the two weeks after a shot.

### ***How safe is the new vaccine?***

The companies making H1N1 flu vaccine have been making seasonal flu vaccines for years and have good track records of safety. They are working alongside government bodies that will fund the complicated safety reviews needed for the swine flu vaccine.

Primarily, the safety trials are looking for side effects such as allergic reactions and something called "oculorespiratory syndrome," which would likely show up within a few days of administration and in relatively small numbers. At this point, at least 200,000 people have received a Canadian form of the vaccine worldwide.

Rarer side effects (see below), if associated with the vaccine, will not appear until many (i.e. millions) have received the vaccine. For this reason, Health Canada has said it will work with other world health agencies to monitor the safety and effectiveness of the vaccine in post-marketing surveillance, and "to ensure the timely communication of any potential adverse events following immunization." Time constraints mean that clinical data at the time will be limited before vaccine programs begin this fall.

### ***Are there side effects?***

Clinical trials have found the most common reactions after getting the adjuvanted vaccine included pain, swelling and redness at the injection site. These reactions occurred to less than 10

per cent of patients vaccinated. Such reactions are to be expected because the adjuvant helps the body develop a stronger immune response by increasing the inflammatory response.

Other reported reactions were fatigue, muscle and joint pain, and headache. In younger children, a fever, drowsiness, irritability and loss of appetite were also reported in low levels.

***Can I get the swine flu vaccine if I'm allergic to eggs, thimerosal or formaldehyde?***

People with egg allergies are generally told not to take flu shots because the vaccine is produced in eggs. But Canada's chief public health officer, Dr. David Butler-Jones, says the egg residue left in the vaccine after purification is small and that people with egg allergies who want to get an H1N1 shot can do so. He says, though, they should do it in a setting where they'll be cared for if they develop an allergic reaction.

Trace amounts of thimerosal or formaldehyde are also used in vaccine production too. Those who have had allergic reactions to other vaccines should not get the swine flu vaccine without talking to their doctor or allergist.

***I don't like needles. Can I get that vaccine that is sprayed up the nose?***

No, FluMist is not available in Canada. The company that makes it, MedImmune, only recently applied for a license to sell their seasonal flu vaccine in Canada. That application is still in the licensure process, so they cannot sell any flu vaccine in this country yet.

Canada is buying H1N1 vaccine from only one supplier, GlaxoSmithKline, whose vaccine is injectable.

***What is an adjuvant and why is Canada using one?***

An adjuvant is a chemical additive used in some vaccines to ramp up the response the immune system generates to a vaccine. Adjuvants aren't new in Canada; they're already used in pneumococcal and meningococcal vaccines, for example.

With an adjuvant, less pure vaccine antigens are needed, so one dose of vaccine can be stretched into four doses. An adjuvant boosts immune response so that recipients are more likely to develop antibodies to the swine flu virus. It also makes the immune response more "durable," so it lasts longer, and it creates a wider response, so that if the swine flu virus "drifts" or changes, this vaccine should still offer some protection.

While the U.S. is not using an adjuvant in its swine flu vaccines, Canada chose to use an adjuvant after there were initial problems with slow vaccine production and the WHO requested manufacturers use "antigen sparing strategies" to stretch out supplies.

Because flu vaccines don't normally use an adjuvant, GlaxoSmithKline could not use the "fast-track" vaccine approval system that allows seasonal flu vaccines to be tweaked every year with small adjustments to the strains. Adding the adjuvant made the Canadian version of the pandemic vaccine different enough from seasonal flu vaccine in its design that a new licence was required and more clinical trials were needed to assess safety.

GSK says its vaccine contains its own proprietary adjuvant system, called AS03. It is based on squalene, an organic compound obtained from fish oil and mixed with water and vitamin E that is safe, despite Internet-based rumours to the contrary.

***I'm pregnant or plan to be soon; should I get vaccinated?***

While pregnant women are not at higher risk of contracting swine flu, they are at higher risk for severe disease if they become infected in their second and third trimester. For that reason, they should consider getting their vaccine, especially if they have underlying disease. An added bonus is that mothers who are immunized while pregnant may help to protect their infant after birth. Because there hasn't been much data on the use of adjuvanted flu vaccines in pregnant women, these women may choose to wait for the unadjuvanted vaccine. If flu rates increase before the unadjuvanted vaccine is available, women more than 20 weeks pregnant should consider getting either adjuvanted or unadjuvanted vaccine.

Because pregnant women are recommended to get the unadjuvanted vaccine, this has led to the false perception that the adjuvant is not safe. This perception is untrue; all study data so far indicates adjuvanted vaccine is as safe as unadjuvanted vaccine in pregnancy. But because the numbers of pregnant women studied have been small so far, PHAC decided to "to err on the side of caution" in its recommendations to pregnant women.

***Can I opt to get the vaccine without adjuvant?***

Canada has ordered 1.8 million doses of unadjuvanted swine flu vaccine to offer to pregnant women. At this point, only pregnant women will be allowed to access the unadjuvanted vaccine. There is no evidence to suggest that the adjuvanted vaccine is unsafe, but there are studies that suggest the unadjuvanted H1N1 flu vaccine does not deliver as strong of an immune response. Even the best unadjuvanted flu vaccines protect only six out of 10 people who get the shot, studies have suggests. This may be modified, however, based on encouraging information from the manufacturer.

The PHAC, meanwhile, says the adjuvanted flu vaccine could boost protection rates to as high as nine in 10.

***If I've already had swine flu, will I need swine flu vaccine?***

If you're certain you've had swine flu, you won't need the vaccine, at least for this coming season. (The virus may change in future seasons, requiring the need for a new vaccine.) The problem is that only a small number of people can be so certain. They are those who underwent lab testing that confirmed they had swine flu. But since strain testing is not being routinely done for those infected with a flu-like illness, most people will not know if they have had H1N1 until an accurate blood test becomes available.

Even if you have been infected with swine flu already, it's likely safe to get the swine flu vaccine. Remember that seasonal flu vaccines are administered to the general population without the use of a blood test beforehand.

In future years, swine-origin H1N1 may "drift" from its current form and prior infection may not offer long-lasting immunity against any new version of the virus. By that point, we will have a much clearer idea of the seriousness of H1N1, the safety of the vaccine, and the need for ongoing annual, large-scale vaccination. It is remarkable that the virus has not yet "drifted." If the virus becomes a predominant seasonal strain circulating in the community (as often happens following a pandemic), the vaccine may require modification for future seasons.

***Will I still need the seasonal flu vaccine?***

The answer is still not clear. At the current time, swine flu is "crowding out" all other flu viruses and appears to be the dominant strain in the Northern Hemisphere at this time. That means Canadians who get flu illness right now are most likely becoming ill with swine flu.

We know that the seasonal flu vaccine is ineffective against swine flu. But it still has potential benefit for seniors over 65 who are most at risk of seasonal flu, but at minimal risk of swine flu. Therefore, most provinces are offering seasonal flu vaccine to people 65 and older and residents of long-term care facilities first, while the rest of the population is being advised to get the swine flu vaccine first.

However, as the season progresses, we might see a change in which swine flu no longer crowds out seasonal flu. In that case, seasonal flu may become a bigger player again and younger Canadians may be advised to get seasonal flu vaccine later in the season. However, this recommendation may change depending on which seasonal flu strain begins to circulate.

#### ***How is the vaccine made?***

Flu vaccine production is inherently slow; the total production and testing time is about 19 weeks. That's in part because the production begins with growing viruses in fertilized chicken eggs. For every shot, at least one egg has to be infected with the virus, where it then replicates before being extracted and purified into a vaccine.

Even after the vaccine is produced, it then has to be tested in clinical trials on different kinds of patient groups (adults first, then kids, etc.) Initial tests are meant to determine effectiveness and short-term safety, (i.e. safety one month after vaccine receipt). Then, larger numbers of volunteers are given the vaccine and the rate of disease and death from swine flu in vaccinated and unvaccinated communities is evaluated. Then, the vaccine has to go through regulatory approval.

#### ***Is there mercury in the swine flu vaccine?***

The flu vaccine contains a small amount of thimerosal. That's because the vaccine is delivered in multi-dose vials, so needles are inserted into the vial more than once to extract doses. For that reason, all flu vaccine bottles (seasonal and swine flu) contain small amounts of thimerosal as a preservative.

Thimerosal is a mercury-based preservative, but it's made of the ethylmercury, which is organic, not methylmercury, which has been linked to neurological damage.

The levels of ethylmercury in vaccines are minute and have not been shown to cause harm, says the Public Health Agency of Canada. It's estimated that there is four times as much mercury in a can of tuna fish than in the thimerosal in the H1N1 flu vaccine.

#### ***What about the 1976 flu vaccine?***

Many remember the Fort Dix outbreak flu in 1976, in which a number of Fort Dix recruits came down with a new strain of flu that turned out to be also partially swine-derived. A hastily-prepared mass vaccination program was undertaken in the ensuing panic. Millions of Americans and some Canadians got a shot for a virus that turned out not to be a good spreader and that quickly fizzled out. Among the millions who were immunized, about 500 came down with

Guillain-Barré syndrome, a paralyzing neuromuscular disorder that is generally temporary, and about 25 deaths were linked to the vaccine.

Although the vaccine had appeared safe in initial testing, the handful of rare neurological side effects became evident only after millions of doses had been given. What went wrong in that vaccine is still not clearly understood to this day.

Manufacturing processes are much improved in terms of purity today than they were in 1976. On the other hand, the 1976 swine flu vaccine did not use an adjuvant, raising concerns about whether the "swine" flu-derived vaccine are associated with higher risk of Guillain-Barre syndrome. For this reason, Health Canada has requested the manufacturer agree to "post-market commitments" surveillance.

Nevertheless, many argue that more lives were saved from flu prevented by the 1976 vaccine than were killed by the rare neurological side effects. And it should be noted that the kind of side-effects seen with the Fort Dix vaccine has not been seen with any subsequent seasonal flu vaccines used thereafter.

The WHO acknowledges that "special safety issues will inevitably arise during a pandemic when vaccine is administered on a massive scale." Some adverse events will be coincidental - that is, associated in time with vaccine administration, yet not directly caused by the vaccine. There could also be events directly caused by the vaccine, it said, but "given the safety record of seasonal vaccines, such events are expected to be rare."

***What about that Canadian study that suggested previous seasonal flu vaccination puts me at increased risk of swine flu?***

The decision to delay part of the seasonal flu vaccine programs this year in some provinces was fuelled in part by initial concerns raised by a controversial and unpublished Canadian study. The study, by scientists in British Columbia, Quebec and Ontario, suggested people who got a flu shot last year were twice as likely as those who didn't get a flu shot to catch swine flu.

It must be underscored that the data are yet to be confirmed. The research, led by researchers at the B.C. Centre for Disease Control and researchers at Laval University, is still being analyzed by a medical journal. As well, an independent panel set up at by the Public Health Agency of Canada is also reviewing the data.

It should also be noted that researchers in the U.S., Australia and Britain have looked for the same effect and haven't seen it. It's possible that there was something unique to the seasonal flu vaccine offered in Canada last year; or it's possible that the research is flawed in some way, such as selection bias, and the link isn't real.

A more recent Mexican study suggested that seasonal flu vaccine was partially protective against swine flu; the reality may lie somewhere in the middle: the seasonal flu vaccine neither protects nor increases swine flu.

***Can the seasonal vaccine and the novel H1N1 vaccine be given at the same time?***

Both vaccines can be given together if given at separate injection sites, according to the Public Health Agency of Canada. However, the immediate need is for swine flu vaccination which is crowding out seasonal flu strains.

In addition, it would be difficult to appraise potential adverse effects of this new vaccine if given simultaneously with the seasonal flu vaccine.