

DIS News

College of Health Professions and Biomedical Sciences
Drug Information Service

Battle of the Influenza Vaccines

Vaccination decreases the incidence of influenza infection, and vaccination is more effective in patients aged 15-64 (70-90%) than patients aged ≥ 65 (30-40%).¹ A higher dose vaccine may trigger a stronger immune response, resulting in an increased number of antibodies produced and enhancing the body's ability to fight off an infection.² A high dose (HD) vaccine was developed containing 60 mcg of hemagglutinin (HAI), which is four times the concentration of the standard 15 mcg dose (SD) vaccine.³

In the pre-licensure trial comparing HD to SD influenza vaccine in patients ≥ 65 years old, higher rates of seroconversion were seen in patients given the HD vaccine.⁴ Seroconversion indicates the body's ability to produce antibodies to the antigen in the vaccine. Patients given the HD vaccine (n=2575) had seroconversion rates 25.4% and 18.4% higher for the two influenza A strains and 11.8% higher for the B strain compared to patients who received the SD vaccine (n=1262). Superiority was established for the HD vaccine for the influenza A strains, but the HD vaccine was nonsuperior for influenza B. The most common adverse reactions were pain, myalgia, and headache, but the rates were not significantly higher in the HD group than in the SD group. Due to higher rates of seroconversion and similar rates of adverse effects, HD influenza vaccine is recommended for patients ≥ 65 years old; however further evaluation is necessary to determine an association of HAI value with the vaccine efficacy. This study was limited by its small sample size relative to the US population. Sampling less than one percent of the population may misrepresent the actual incidence of influenza infection in the vaccinated population.⁴

The results from the above trial allowed Fluzone[®] High-Dose to receive accelerated approval by the FDA in December 2009 in elderly patients.⁵ Despite these promising results, the reception by the medical community and willingness to incorporate this new vaccine

has been underwhelming. HD vaccines represented only 20% of flu shots administered last year to patients ≥ 65 years old. A post-licensure study was recently conducted, and healthcare professionals are waiting for its outcomes before encouraging widespread use of the HD vaccine.⁵

The complete post-licensure trial has not yet been published, but results have been summarized and are available for review.⁵ The study enrolled 31,803 patients ≥ 65 years old; 15,892 were given HD influenza vaccine and 15,911 were given SD influenza vaccine. The primary outcome was the number of laboratory-confirmed cases of influenza. The occurrence of cardio-respiratory conditions and their association with HD vaccine use were evaluated. Efficacy and safety of the HD vaccine was greater than the SD vaccine in the post-licensure study. During the two-year study, 227 patients given the HD vaccine and 300 patients given the SD vaccine developed influenza. Fluzone[®] High-Dose was 24.2% (95% CI, 9.7-36.5%) more effective than Fluzone[®] at preventing influenza in patients ≥ 65 years old. In addition, fewer cardio-respiratory conditions occurred within 30 days of a respiratory illness in the HD group compared to the SD group. Serious adverse events occurred more often in the SD group than the HD group (9.02% vs. 8.27%). The authors concluded that the results were consistent with the pre-licensure trial and the HD vaccine was more effective at vaccinating against all three influenza strains than the SD vaccine. Until the full study has been published, limitations cannot be discussed.⁵

Current literature and the preliminary results for the major post-licensure study provide evidence that Fluzone[®] High-Dose is superior to standard-dose Fluzone[®] in patients ≥ 65 years old.^{4,5} Publication of the post-licensure study is anticipated after full statistical evaluation has been made, and will provide a more complete picture of the risk/benefit profile of the HD vaccine.

By Nathan Jensen, PharmD Candidate

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We welcome any comments and suggestions for future newsletter topics.

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Do you remember drinking that soda? BVO and memory loss

Bromine exposure from brominated vegetable oil (BVO), an ingredient found in some sodas, may cause memory loss.^{1,4}

The extent of memory loss and the amount of BVO required to induce the memory loss remains unknown.¹⁻³ The typical American diet does not include bromine, but a regular source is citrus flavored sodas.^{4,5} Mountain Dew[®], Squirt[®], Fanta[®] Orange, Powerade[®] Strawberry Lemonade, and Fresca[®] all still contain BVO.^{4,5}

BVO, unsaturated vegetable oil with a bromine atom attached to the double bonds, stabilizes the lipophilic fruit flavorings and carbonated-water mixture.⁴⁻⁷ BVO was removed from the Food and Drug Administration generally regarded as safe list in the 1970s, but it was permitted to remain in beverages at an arbitrary concentration of less than 15 parts per million (ppm) in the interim pending results from future safety studies.^{5,8} Almost 40 years later, those studies still remain to be performed in humans.^{4,5,7,9} The European Union has banned products with BVO since toxicities remain unknown.^{4,5} Increased public awareness forced PepsiCo[™] to reformulate Gatorade[®] last year when consumers demanded a change.⁹

Three BVO-containing sodas rank on the top 10 sodas consumed list in the United States. Companies manufacturing these sodas are required to include BVO in the ingredient list, but are not required to report the concentration.⁵ One study sought to determine how much BVO is actually contained in citrus sodas. After extraction of all isomers, three unnamed sodas contained an average of eight ppm of BVO. Americans consume an estimated 217 liters of soda per person per year which amounts to 272 mg of BVO ingested per year.⁵

After ingestion, BVO is absorbed and hydrolyzed by pancreatic lipase before distributed to fat tissue for storage.^{5,7} Two mechanisms exist that may explain the mental changes experienced with bromine toxicity.¹ Bromine replaces

chloride in the body resulting in decreased neuronal conductance leading to psychiatric changes. Another possible mechanism involves bromine and its effects on GABA neurons. When GABA binds to its receptor, bromine passes through the GABA-linked ligand gated chlorine channel in greater quantity than chlorine would. This ultimately increases inhibitory effects of the nerve and increases GABA-ergic effects like sedation and relaxation.¹

Animal studies demonstrate BVO may cause memory loss.³ Mice exposed to bromine during the neonatal period develop behavior, learning, and memory dysfunctions which become evident during adulthood. The quantity of cholinergic receptors was decreased by 31% compared to control. Decreases in quantity of cholinergic receptors are common during the aging process of humans. However, it is unclear how an unnatural decrease in these receptors will affect humans. Additional studies on how bromine can affect these cholinergic receptors and how they may affect the normal aging process in humans are necessary to determine the true consequences of bromine in beverages.³

Even though no controlled studies on the effects of BVO in humans exist, case reports reveal some of the consequences of its use.^{1,2,4} Bromine toxicity has occurred in patients who consume excessive amounts of soda over a long duration of time.^{1,2} These cases include a man drinking between two and four liters of Ruby Red[®] daily for a couple months, a video gamer drinking a 12 oz Mountain Dew[®] can every hour for six hours during sessions, and patients abusing medications that used to contain bromine.^{1,2,4} Although BVO may be damaging the body in small quantities, currently only side effects from toxicity are recognized.^{1,2,4,6} Side effects can include sedation, lethargy, slurred speech, confusion, hallucinations, depression, mania, ataxia, visual changes.^{1,2} Short-term memory loss was present in all of these cases.^{1,2,4}

Without the clinical studies to assess the true consequences of BVO, consumers could continue to damage their mental function.^{3,7} Accumulated bromine may lead to detrimental loss in movement, behavioral, learning, and memory dysfunction in adulthood.^{1,2,4,5,7} BVO may damage the body in small quantities, but currently only side effects from toxicity are recognized.^{1,2,4,6} Even with the severe side effects associated with bromine toxicity, diagnosis is difficult and often delayed.¹ Until more research is available on the long-term safety of BVO for humans, BVO consumption should be avoided, and other ingredient options explored.



By Alivia Ready, PharmD Candidate

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PATIENT INFORMATION:

Which Emergency Contraception (EC) Will Work For You?

Nearly half of all pregnancies in America are not planned, and of those, another 40% are terminated by abortion. There are various options available for preventing an unplanned pregnancy for up to 120 hours after sexual intercourse.

Mediocre: the Yuzpe Regimen

- ◇ Developed in 1974.
- ◇ Women can take two doses of 2-6 tablets (depending on the type used) of their estrogen and progesterone birth control pills about 12 hours apart.
- ◇ Prevents the egg from being released from the ovary.
- ◇ About 74% effective; should be used within the first 72 hours after sexual intercourse.

Good: Plan B® (levonorgestrel)

- ◆ 1999—developed as two 75 mg tablets taken together or 12 hours apart; available by prescription only.
- ◆ 2006—available without prescription behind the pharmacy counter to women ≥18 years; women <17 years still needed a prescription.
- ◆ 2009—the age was lowered to ≥17 years for the sale behind the counter and included the sale to men ≥17 years. Plan B One-Step®, a one tablet dose of levonorgestrel 150 mg, became available.
- ◆ 2013—the sale of Plan B® allowed for women and men of any age without a prescription; still available behind the pharmacy counter.
- ◆ Prevents the egg from being released from the ovary. May also alter the activity of sperm by producing a thick mucus fluid and reduce the thickness of the uterine lining preventing egg implantation.
- ◆ About 88% effective when used within 72 hours after sexual intercourse.

Better: Ella® (ulipristal acetate)

- * 2010—Available only with a prescription.
- * Formulated as one 30 mg tablet.
- * Like Plan B®, Ella® prevents the egg from being released from the ovary. May also alter the activity of sperm by producing a thick mucus fluid and reduce the thickness of the uterine lining, pre-

venting egg implantation.

- * Unlike Plan B®, Ella® is effective when used up to 120 hours after sexual intercourse.
- * The pregnancy rate for women using Ella® may be as low as 1.9%.

Best: Copper Intrauterine Device (IUD)

- First developed in the 1970s.
- Copper is toxic to sperm and kills sperm prior to fertilization.
- Prevents the egg from implanting on the uterine wall when inserted within 120 hours after sexual intercourse.
- 99.9% effective at preventing pregnancies.

Cautions

- ⊗ Hormonal methods are only truly effective 2-5 days before the egg is released from the ovary
- ⊗ When women take EC the day before or the day after ovulation, the pregnancy rate is the same as in women who do not take EC.
- ⊗ It is unknown if Plan B® and Ella® keep the egg from implanting into the wall of the uterus.

How effective is EC for you?

Body weight may play an important role in the effectiveness of EC. The risk of pregnancy in overweight and obese women is increased >4 times when using Plan B® and >2 times when using Ella®, compared to normal weight women. The copper IUD, however, has the same efficacy in women of all sizes.

The use of EC can be avoided altogether, depending on the timing of your ovulation cycle. If you are unsure of the approximate time of your cycle, the use of EC may be recommended. If you are overweight, the most effective type of EC is the copper IUD, but it requires a professional to insert and timing can be difficult due to business hours if the request is on a weekend. When the copper IUD is not an option, the next best alternative for overweight patients is

Ella®, but a prescription can also be difficult to obtain outside of business hours, although it is effective for up to 120 hours after intercourse.

By Nathan Jensen, PharmD Candidate

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PATIENT INFORMATION:

Vitamin B12 - Staying Healthy and Staying Vegetarian in Pregnancy

Vegetarians are as capable of having healthy pregnancies as those who include animal products in their diets. Sufficient quantities of protein are found in the vegetarian diet, but if meals are not properly planned, all vegetarians—especially pregnant women—are at risk for vitamin B12 deficiency. Vitamin B12 is predominately found in animal products, so vegetarians may have difficulty getting enough B12 in their diet.

Where to get vitamin B12

Since vitamin B12 is not common in plant products, vegetarians must get it from either vitamin B12 fortified foods or supplements. Foods fortified with vitamin B12 include soy and rice milk, cereals, meal substitutes, and Red Star Vegetarian Support Formula Nutritional Yeast[®]. The recommended daily intake for vitamin B12 increases during pregnancy and breastfeeding. Pregnant women need 2.6 mcg/day, and breastfeeding women need 2.8 mcg/day. Check the Nutrition Facts on food labels to verify that vitamin B12 has been added. Vegan vitamin B12 supplements are also available. Long-term vegetarians are typically deficient in vitamin B12 and should consider supplementation.

Vitamin B12 Supplements

Vitamin B12 in supplements is not well absorbed by the body. Therefore, higher doses than the recommended daily intake are required. Take between 25 – 100 mcg of vitamin B12 at the same time each day with or without food. Side effects from vitamin B12 supplements include elevated blood pressure, reddening of the skin, and hives if an allergic reaction occurs.

If considering supplementation, it is important to remember that more is not always better. Some vitamins and minerals used in excess during pregnancy have been linked to preterm delivery or high blood pressure in the mother. Talk with your healthcare provider to help determine if vitamin B12 supplementation is right for you.

Benefits of B12 in pregnancy

Since vitamin B12 passes through the placenta from mother to child, if the mother has enough vitamin B12, then so does the baby. Adequate levels of vitamin B12 in the mother

allows the baby to be born with a healthy weight, prevents complications with the baby's spinal cord, and prevents delays in the child's physical and mental growth.

In the mother, vitamin B12 helps develop and support function of brain and nerve cells. Vitamin B12 also prevents anemia and replaces old cells by helping make new DNA and red blood cells.

Low B12 levels in pregnancy

Problems associated with low vitamin B12 levels during pregnancy can be apparent at birth and continue throughout the child's life. Infants born to mothers who were deficient in vitamin B12 are more likely to be irritable and lethargic. Physical problems may also appear like difficulty standing and walking. These children may have trouble forming sentences and difficulty with problem solving and short-term memory. Studies have indicated that these mental problems continue through adolescence.

Low levels of vitamin B12 during pregnancy may impact the child for life. Although it is not completely understood, vitamin B12 deficiency during the second trimester may also be linked to the development of type 2 diabetes.

The long-term effects of vitamin B12 deficiency are still being discovered. By eating a balanced diet and supplementing when needed, pregnancy outcomes in vegetarian women can be as optimal as those in non-vegetarian pregnant women.

Symptoms of B12 deficiency

To decrease problems from low vitamin B12, it is important to notice symptoms that suggest vitamin B12 deficiency. A multitude of vague symptoms are common with vitamin B12 deficiency, such as fatigue, depression, anemia, numbness or tingling in the extremities, and difficulty concentrating. If any of these symptoms occur, it may be reason to see your healthcare professional and

have blood levels of vitamin B12 checked.

A well-balanced diet

To insure the best nutrition for you and your growing fetus, it is important to eat a well-balanced diet. A healthy diet for vegetarians should include 1-2 servings of dark green vegetables, 4-5 servings of other vegetables and fruit, 1-2 servings of nuts and seeds daily, and whole-grains and beans or soy served at each meal. In addition, a pregnant mother should also increase her calcium and iron intake, take 1 tablespoon of ground flax seed, and eat 4 servings of vitamin B12 fortified foods per day.

By Alivia Ready, PharmD Candidate

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