The Flu: Sorting Fact from Fiction

A Review of the Flu Vaccine Literature, Chiropractic and the Immune System

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Information obtained from Matthew McCoy DC, MPH; Editor – Journal of Pediatric, Maternal & Family Health - *Chiropractic*

Doubts About the Flu Shot?

If you question the wisdom of this annual rite of passage you are not alone in your disdain for the flu shot.

You'll be relieved to know that science is on your side and that respected researchers also question it.

Effectiveness – 2012-2013

Officials from the Centers for Disease Control and Prevention, speaking on a telephone news conference, again urged Americans to keep getting flu shots. At the same time, they emphasized that the shots are not infallible: **a preliminary study rated this year's vaccine as 62 percent effective**, even though it is a good match for the most worrisome virus circulating. That corresponds to a rating of "moderately" effective — the vaccine typically ranges from 50 percent to 70 percent effective, they said.

http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6202a4.htm?s_cid=mm6202a4_w

But Wait – There's More . . .

The findings in this report are subject to at least four limitations. First, VE can differ for patients of different ages, and age data were not yet available from all sites. However, VE estimates from one site (Wisconsin) differed little before (69%) and after age-adjustment (66%) (Edward Belongia, Marshfield Clinic Research Foundation, personal communication, January 2013). Second, vaccination status was self-reported; dates of vaccination were not available, except from one site; and vaccine formulation was not known. However, experience from prior seasons suggests that few persons are vaccinated <2 weeks from illness onset (*4*), a period when vaccine might not be effective yet, and self-reported influenza vaccine status was sensitive and fairly specific compared with documented vaccination at an immunization registry (*5*). Vaccination dates will be available for subsequent VE estimates. Third, VE estimates for prior seasons were reduced after adjusting for potential confounding factors (*4*), and the fully adjusted VE estimate for this season likely will be lower, also. Observational VE studies, such as those used for the current estimates, have greater potential for confounding and bias relative to randomized clinical trials, particularly when diagnostic test specificity is low (*8*). However, the U.S. Flu VE Network study design attempts to minimize bias and confounding through systematic screening of eligible patients and use of a highly sensitive and specific endpoint (rRT-PCR–confirmed influenza). Finally, subsequent VE estimates might change during the season if circulating viruses or population immunity change over the course of the season.

But Wait – There's More . . .

The findings in this report are subject to at least four limitations.

1. First, Vaccine Effectiveness (VE) can differ for patients of different ages, and age data were not yet available from all sites.

2. Second, vaccination status was self-reported; dates of vaccination were not available, except from one site; and vaccine formulation was not known.

3. Third, VE estimates for prior seasons were reduced after adjusting for potential confounding factors and the fully adjusted VE estimate for this season likely will be lower, also.

4. Finally, subsequent VE estimates might change during the season if circulating viruses or population immunity change over the course of the season.

http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6202a4.htm?s_cid=mm6202a4_w

Scientifically Flawed

The use of placebos most commonly used in vaccination trials is exceedingly important. In standard scientific methodology a placebo should be a very inert substance, such as water or a sugar substance, in order to accurately determine the tested substance's effects on human biology. According to Australian vaccine historian Dr. Viera Scheibner, vaccine trials do not employ an inert placebo. Instead, what is used as a placebo is "the vaccine with all the adjuvants and preservatives, certainly not inert substances, minus those viruses and bacteria… That is why when they compare the trial children who were given the lot and those who were given placebo, they have the same rate of reaction." This means that almost all vaccine efficacy and safety trials using a non-inert placebo are based on scientifically flawed design from the start. It is therefore evident that flawed methodology will inevitably result in flawed data. Yet that is the guiding principle the vaccine industrial complex relies upon, and our federal health establishment is all too ready to give a nod of approval and allow it to continue.

Interview with Dr. Viera Scheibner. Broadcast WPFW, Washington DC. September 21, 2009. Archived at http://garynull.org

Far from Perfect

"What we've known for a long time is that the flu vaccine is far from perfect," said Thomas R. Frieden, the CDC's director.

http://chronicle.com/blogs/percolator/flu-vaccine-gets-a-passing-grade-barely/32019?cid=pm&utm_source=pm&utm_medium=en

Not a Great Vaccine . . .

"It's not a great vaccine in terms of preventing infection, or even mild to moderate symptoms," said Paul A. Offit, a professor of vaccinology at the University of Pennsylvania.

Counterintuitive?

One sign of the lack of basic knowledge about the flu, Mr. Osterholm said, is that the CDC data show the vaccine gave 55-percent protection against H3N2, the main strain of flu sickening people right now, but gave 70-percent protection against a B strain known as B/Victoria, even though B/Victoria wasn't even in the vaccine. "Is that counterintuitive or what?" he said.

http://chronicle.com/blogs/percolator/flu-vaccine-gets-a-passing-grade-barely/32019?cid=pm&utm_source=pm&utm_medium=en

No Significant Difference

Also, while effectiveness is a measure of how many people get sick despite getting the vaccine, there's been little effort to measure whether people who got the vaccine suffer a lower grade of severity, Mr. Osterholm said.

"The data is sparse on this," said Joseph S. Bresee, chief of the Epidemiology and Prevention Branch of the CDC's Influenza Division. Some data, however, suggest those who have been vaccinated suffer a milder form of flu, Dr. Bresee said.

Mr. Osterholm disagreed, saying the few studies on the subject, including one soon to be released, show vaccination produces no significant difference in the severity of symptoms.

http://chronicle.com/blogs/percolator/flu-vaccine-gets-a-passing-grade-barely/32019?cid=pm&utm_source=pm&utm_medium=en

Worthless

In a recent interview with Dr. Thomas Jefferson, coordinator for the Cochrane Vaccine Field in Rome, Italy, he said that in 2009 he conducted a thorough review of 217 published studies on flu vaccines and found only 5% reliable. In other words, 95% of studies on flu vaccination are flawed and should therefore be ignored. This should not come as a great surprise; even CDC officials were forced to confess that "influenza vaccines are still among the least effective immunizing agents available, and this seems to be particularly true for elderly recipients." Dr. Anthony Morris, a distinguished virologist and a former Chief Vaccine Office at the FDA, found "there is no evidence that any influenza vaccine thus far developed is effective in preventing or mitigating any attack of influenza.' Dr. Morris states, "The producers of these vaccines know they are worthless, but they go on selling them anyway."

- Kidder D, Scmitz R. Measures of costs and morbidity in the analysis of vaccine effectiveness based on Medicare claims. In Hannoun C, et al. Eds. *Options for the Control of Influenza 11*. Amsterdam: Excerpts Medica, 1993; 127-33.
- Patrick, Jay. "Flu Vaccines 'Worthless' Says Eminent FDA Virologist."

A Sales Job

Last month,, in a step tantamount to heresy in the public health world, scientists at the Center for Infectious Disease Research and Policy at the University of Minnesota released a report saying that influenza vaccinations provide only modest protection for healthy young and middle-age adults, and little if any protection for those 65 and older, who are most likely to succumb to the illness or its complications. Moreover, the report's authors concluded, federal vaccination recommendations, which have expanded in recent years, are based on inadequate evidence and poorly executed studies.

"We have overpromoted and overhyped this vaccine," said Michael T. Osterholm, director of the Center for Infectious Disease Research and Policy, as well as its Center of Excellence for Influenza Research and Surveillance. "It does not protect as promoted. It's all a sales job: it's all public relations."

http://well.blogs.nytimes.com/2012/11/05/reassessing-flu-shots-as-the-season-draws-near/

Exaggeration of Effectiveness

While researching the report released last month, Dr. Osterholm said, the authors discovered a recurring error in influenza vaccine studies that led to an exaggeration of the vaccine's effectiveness. They also discovered 30 inaccuracies in the statement on influenza vaccines put forth by the expert panel that develops vaccine recommendations, all of which favor the vaccine.

http://well.blogs.nytimes.com/2012/11/05/reassessing-flu-shots-as-the-season-draws-near/

No Sound Data

A major finding from our review is that, since influenza vaccination programs were first implemented in the United States in the 1940s, influenza vaccination policies often have been developed with a strong intention to protect the population against influenza, but without compelling and scientifically sound data to support them. This was acknowledged in 1960, when influenza vaccine was recommended for certain high-risk populations. This was also acknowledged in the 1980s, when the concept of indirect benefit was introduced and implemented, even though limited information was available to support the strategy. Finally, various decisions from 1999 to 2010 to expand the groups for whom vaccine is recommended were at times made by the ACIP on the basis of group consensus and professional opinions from participating organizations, most notably the CDC, rather than on the body of scientific evidence.

http://www.cidrap.umn.edu/cidrap/files/80/ccivi%20report.pdf

Minimal Impact

Applying rigorous scientific methodology to this issue clearly shows that current influenza vaccines do not offer the level of protection necessary to significantly lessen influenza morbidity and mortality. In fact, despite significant increases in influenza vaccine coverage for those over 65 years of age since the late 1990s, a minimal impact on influenza morbidity and mortality has been noted in this country (see Chapter 3). Furthermore, influenza vaccination research has shown that this is a very complicated topic and that it is difficult to make general statements on the basis of the existing scientific data.

http://www.cidrap.umn.edu/cidrap/files/80/ccivi%20report.pdf

Overestimated Effectiveness

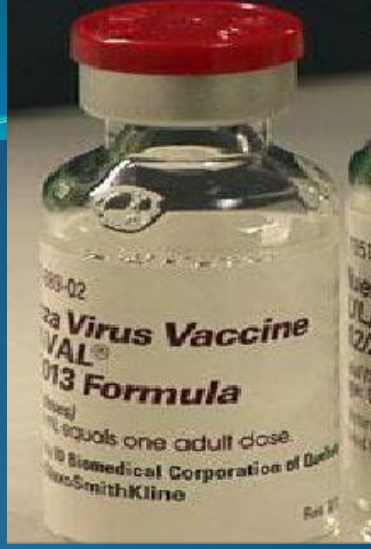
A third major finding is that federal policy documents and statements have overestimated the effectiveness of current influenza vaccines. We believe this is problematic for two reasons. First, overestimating vaccine effectiveness may cause the public to lose faith in vaccination recommendations. Second, if the current vaccines are considered to offer an acceptable level of protection, then little incentive exists for research and development companies and manufacturers to generate new and improved vaccines that could have a significant impact on the influenza disease burden.

http://www.cidrap.umn.edu/cidrap/files/80/ccivi%20report.pdf

Stable Income Source

Although the major pharmaceutical manufacturers of the current influenza vaccines are beginning to acknowledge the growing body of data supporting limited effectiveness of these vaccines, the existing vaccines represent a reasonably stable source of annual income for them. This steady income stream exists despite uncertainty regarding the antigen composition of the seasonal influenza vaccines each year and the annual variability in vaccine virus production and vaccine manufacturing. Given this reality, these companies have little incentive to change the status quo.

No Impact



- Giving young children flu shots appeared to have no impact on flu-related doctor visits or hospitalizations during two recent flu seasons, according to a study published in the Archives of Pediatric & Adolescent Medicine.
- The flu vaccine is no more effective for children under 2 than a placebo, according to a large-scale, systematic review of 51 studies, published in the Cochrane Database of Systematic Reviews.
- NO studies have conclusively proven that flu shots prevent flu-related deaths among the elderly.
- A study published in the Lancet found that influenza vaccination was NOT associated with a reduced risk of pneumonia in older people.
- Research published in the American Journal of Respiratory and Critical Care Medicine also confirms that there has been no decrease in deaths from influenza and pneumonia, despite the fact that vaccination coverage among the elderly has increased from 15 percent in 1980 to 65 percent today.

http://articles.mercola.com/sites/articles/archive/2010/11/04/big-profits-linked-to-vaccine-mandates.aspx

No Decline in Deaths

Epidemiological data seem to back up such anecdotes. According to an American Lung Association report from 2010, there was no sustained decline in influenza-associated deaths over the past decades. Among those older than 65, according to a *New England Journal of Medicine* review, flu hospitalization rates rose steadily between 1979 and 2001, despite an increase in vaccination rates among seniors from 32 percent in 1989 to 67 percent in 1997.

http://www.slate.com/articles/health_and_science/pandemics/2012/12/flu_vaccine_safety_tamiflu_and_vaccines_save_lives_and_show_public_health.html

That's a Miracle

Yet in the view of several vaccine skeptics, this claim is suspicious on its face. Influenza causes only a small minority of all deaths in the U.S., even among senior citizens, and even after adding in the deaths to which flu might have contributed indirectly. When researchers from the National Institute of Allergy and Infectious Diseases included all deaths from illnesses that flu aggravates, like lung disease or chronic heart failure, they found that flu accounts for, at most, 10 percent of winter deaths among the elderly. So how could flu vaccine possibly reduce total deaths by half? Tom Jefferson, a physician based in Rome and the head of the Vaccines Field at the Cochrane Collaboration, a highly respected international network of researchers who appraise medical evidence, says: "For a vaccine to reduce mortality by 50 percent and up to 90 percent in some studies means it has to prevent deaths not just from influenza, but also from falls, fires, heart disease, strokes, and car accidents. That's not a vaccine, that's a miracle."

http://www.theatlantic.com/magazine/archive/2009/11/does-the-vaccine-matter/307723/

No Rise in Mortality

THE HISTORY OF FLU VACCINATION suggests other reasons to doubt claims that it dramatically reduces mortality. In 2004, for example, vaccine production fell behind, causing a 40 percent drop in immunization rates. Yet mortality did not rise. In addition, vaccine "mismatches" occurred in 1968 and 1997: in both years, the vaccine that had been produced in the summer protected against one set of viruses, but come winter, a different set was circulating. In effect, nobody was vaccinated. Yet death rates from all causes, including flu and the various illnesses it can exacerbate, did not budge. Sumit Majumdar, a physician and researcher at the University of Alberta, in Canada, offers another historical observation: rising rates of vaccination of the elderly over the past two decades have not coincided with a lower overall mortality rate. In 1989, only 15 percent of people over age 65 in the U.S. and Canada were vaccinated against flu. Today, more than 65 percent are immunized. Yet death rates among the elderly during flu season have increased rather than decreased.

http://www.theatlantic.com/magazine/archive/2009/11/does-the-vaccine-matter/307723/

More PR than Science

Recently the British Medical Journal published an interesting article by Harvard medical graduate entitled 'Are US flu death figures more PR than science', 10 December 2005, http://bmj.bmjjournals.com/cgi/content/full/331/7529/1412. I quote a few extracts:

"US data on influenza deaths are a mess. The Centers for Disease Control and Prevention (CDC) acknowledges a difference between flu death and flu associated death yet uses the terms interchangeably. Additionally, there are significant statistical incompatibilities between official estimates and national vital statistics data. Compounding these problems is a marketing of fearóa CDC communications strategy in which medical experts "predict dire outcomes" during flu seasons..."

"CDC states that the historic 1968-9 "Hong Kong flu" pandemic killed 34 000 Americans. At the same time, CDC claims 36 000 Americans annually die from flu. What is going on?

Meanwhile, according to the CDC's National Center for Health Statistics (NCHS), "influenza and pneumonia" took 62 034 lives in 2001ó61 777 of which were attributed to pneumonia and 257 to flu, and in only 18 cases was flu virus positively identified. Between 1979 and 2002, NCHS data show an average 1348 flu deaths per year (range 257 to 3006)..."

"If flu is in fact not a major cause of death, this public relations approach is surely exaggerated. Moreover, by arbitrarily linking flu with pneumonia, current data are statistically biased. Until corrected and until unbiased statistics are developed, the chances for sound discussion and public health policy are limited."

http://www.bmj.com/content/331/7529/1412.full

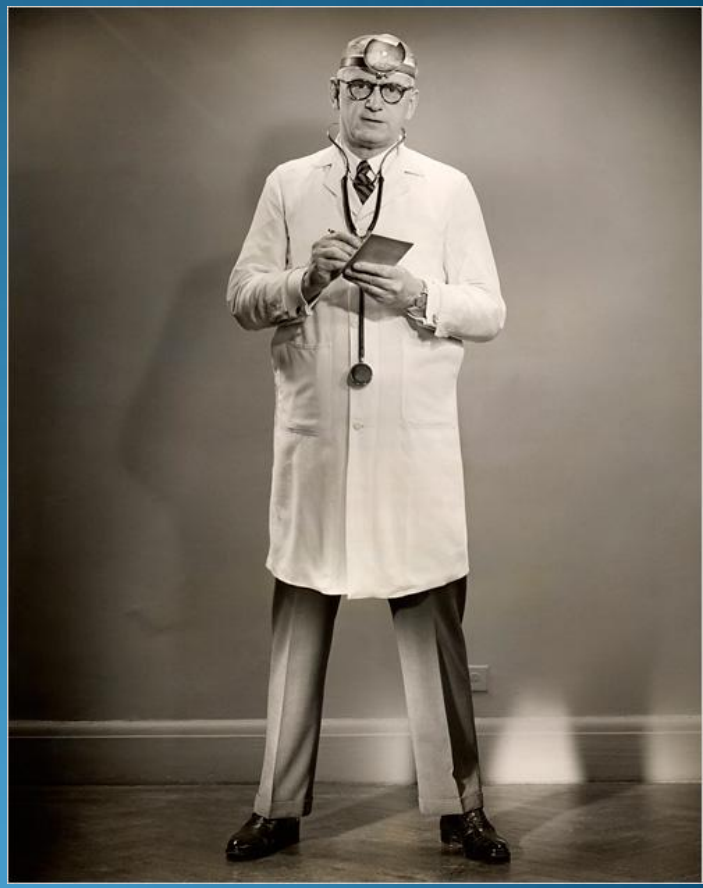
About that Epidemic . . .

"We have an epidemic of flu every year," said the New York City health commissioner, Thomas Farley. If there are alarming headlines, he added, it's because public officials are "trying to get out the message to get your vaccine." In a phone interview, Farley explained that the city declares an epidemic when more than 5 percent of the people going to emergency rooms are complaining of flu symptoms, which is unusual only in the sense that it doesn't happen in warm weather. He also managed to work "get your vaccine" into virtually every sentence.

http://www.nytimes.com/2013/01/12/opinion/collins-the-flu-who-knew.html

Doctors Don't Want Them

According to data from the Centers for Disease Control and Prevention, a significant number of health care professionals declined to get a flu shot during the 2006-07 flu season, with only about 40 percent opting for the shot.



Docs talk the talk but do they take flu shots?
http://abcnews.go.com/Health/ColdandFluNews/Story?id=6418974&page=2

Ontario Study

Done in Ontario to determine whether the incidence of influenza there decreased following the introduction of their Universal Influenza Immunization Campaign (UIIC) in 2000.

Researchers found that there has not been a decrease in the mean monthly influenza rate following the introduction of their campaign.

Groll DL, Thomson DJ. Incidence of influenza in Ontario following the Universal Influenza Immunization Campaign. Vaccine 24 (2006) 5245–5250

Ontario Study

Here's what the scientists who did the study concluded in their research paper:

"Despite increased vaccine distribution and financial resources towards promotion, the incidence of influenza in Ontario has not decreased following the introduction of the UIIC."

Groll DL, Thomson DJ. Incidence of influenza in Ontario following the Universal Influenza Immunization Campaign. Vaccine 24 (2006) 5245–5250

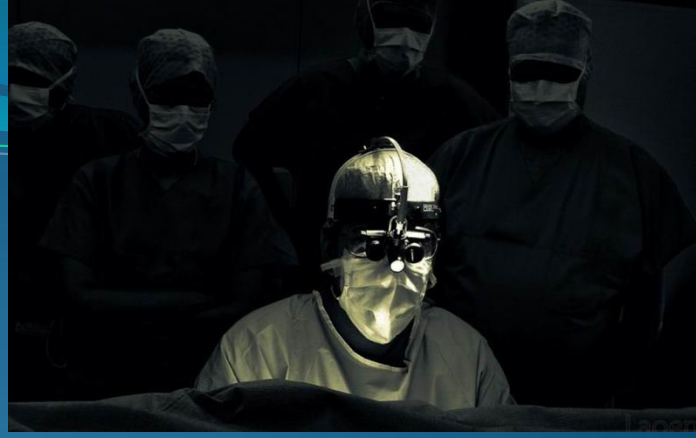
Archives Study

In this study published in the Archives of Internal Medicine researchers looked at the role of the flu vaccine in relation to benefit.

They looked at mortality among people aged 65 to 74 years in the decade after the 1968 pandemic.

Simonsen,L,. Reichert T, Viboud C, Blackwelder W, Taylor W, Miller M. Impact of Influenza Vaccination on Seasonal Mortality in the US Elderly Population ARCH INTERN MED/VOL 165, FEB 14, 2005

Archives Study



The scientists in the Archives study could not correlate increasing vaccination coverage after 1980 with declining mortality rates in *any age group* (emphasis ours).

Simonsen,L,. Reichert T, Viboud C, Blackwelder W, Taylor W, Miller M. Impact of Influenza Vaccination on Seasonal Mortality in the US Elderly Population ARCH INTERN MED/VOL 165, FEB 14, 2005

Archives Study

The researchers concluded that because fewer than 10% of all winter deaths were attributable to influenza in any season, that observational studies substantially *overestimate vaccination benefit (emphasis ours).*

Simonsen,L,. Reichert T, Viboud C, Blackwelder W, Taylor W, Miller M. Impact of Influenza Vaccination on Seasonal Mortality in the US Elderly Population ARCH INTERN MED/VOL 165, FEB 14, 2005

BMJ Study

Another study was published in the British Medical Journal in 2006.

It was funded by the Cochrane Collaboration, an independent non-profit foundation.

Researchers in this study challenged the safety and efficacy of the current flu vaccine recommended policy.

Jefferson T Influenza vaccination: policy versus evidence. BMJ VOLUME 333 28 OCTOBER 2006.

BMJ Study

The researchers in this study stated:

"Each year enormous effort goes into producing influenza vaccines for that specific year and delivering them to appropriate sections of the population. Is this effort justified?“

Jefferson T Influenza vaccination: policy versus evidence. BMJ VOLUME 333 28 OCTOBER 2006.

BMJ Study

The scientist's summary was alarming and they questioned the use of the flu vaccine as follows:

- Public policy worldwide recommends the use of inactivated influenza vaccines to prevent seasonal outbreaks
- Because viral circulation and antigenic match vary each year and non-randomized studies predominate, systematic reviews of large datasets from several decades provide the best information on vaccine performance
- Evidence from systematic reviews show that inactivated vaccines have little or no effect on the effects measured

Jefferson T Influenza vaccination: policy versus evidence. BMJ VOLUME 333 28 OCTOBER 2006.

BMJ Study

- Most studies are of poor methodological quality and the impact of confounders is high
- Little comparative evidence exists on the safety of these vaccines
- Reasons for the current gap between policy and evidence are unclear, but given the huge resources involved, *a re-evaluation should be urgently undertaken* (emphasis ours)

Jefferson T Influenza vaccination: policy versus evidence. BMJ VOLUME 333 28 OCTOBER 2006.

The Lancet

In another study published in *The Lancet* the researchers questioned the benefits of flu shots for elderly people stating that the benefits are “greatly exaggerated.”

The researchers stated that the public policy for the elderly getting flu shots is based on flimsy, even nonexistent, evidence.

Simonsen L, Taylor R, Viboud C, Miller M, Jackson L. Mortality benefits of influenza vaccination in elderly people: an ongoing controversy. Lancet Infect Dis 2007; 7:658–66 September 24, 2007

The Lancet

The lead scientist for the study, Dr. Lisa Jackson, was quoted in a news story about her research stating:

"The message is: We should not be basing our vaccine policy on data that is faulty“

Simonsen L, Taylor R, Viboud C, Miller M, Jackson L. Mortality benefits of influenza vaccination in elderly people: an ongoing controversy. Lancet Infect Dis 2007; 7:658–66 September 24, 2007

The Lancet

The researchers stated in their paper:

"We find it peculiar that the claims that influenza vaccination can prevent half, or more, of all winter deaths in elderly people have not been more vigorously debated."

Simonsen L, Taylor R, Viboud C, Miller M, Jackson L. Mortality benefits of influenza vaccination in elderly people: an ongoing controversy. Lancet Infect Dis 2007; 7:658–66 September 24, 2007

The Lancet

The researchers showed that unvaccinated seniors died at a higher rate for reasons unrelated to the flu.

The scientists also reported that increasing vaccination rates since 1980 *have not lowered death rates among the elderly*.

Simonsen L, Taylor R, Viboud C, Miller M, Jackson L. Mortality benefits of influenza vaccination in elderly people: an ongoing controversy. Lancet Infect Dis 2007; 7:658–66 September 24, 2007

The Lancet

Dr. Jackson, the lead scientist in this study calls for a more realistic assessment of the vaccine's benefits that may push researchers to begin studying other strategies to help the elderly avoid flu and its complications.

Simonsen L, Taylor R, Viboud C, Miller M, Jackson L. Mortality benefits of influenza vaccination in elderly people: an ongoing controversy. Lancet Infect Dis 2007; 7:658–66 September 24, 2007

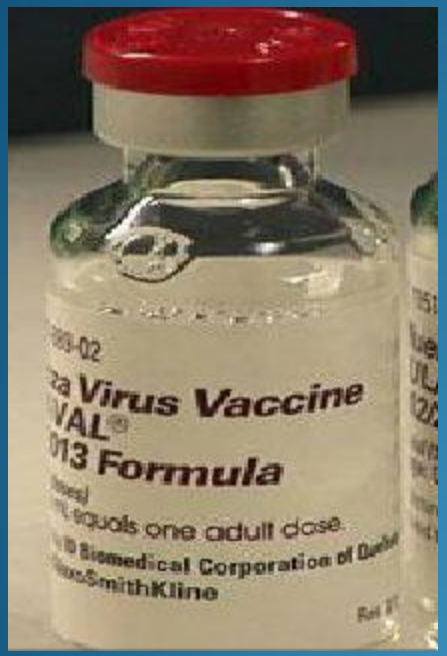
Osterholm Study

Osterholm performed a systematic review and meta analysis of the efficacy and effectiveness of influenza vaccines. A systematic review and meta analysis is one of the strongest ways to evaluate the level of evidence on a health care intervention. They are usually used to developed guidelines.

Osterholm and his team screened 5707 articles and identified only 31 eligible studies (17 randomized controlled trials and 14 observational studies).

Osterholm M, Kelley S, Sommer A, Belongia E. Efficacy and effectiveness of influenza vaccines: a systematic review and meta-analysis. The Lancet Infectious Diseases, Volume 12, Issue 1, Pages 36 - 44, January 2012.

Osterholm Study



Prior to this no published meta-analyses had assessed efficacy and effectiveness of licensed influenza vaccines in the USA with sensitive and highly specific diagnostic tests to confirm influenza.

Efficacy of inactivated vaccine was shown in only eight (67%) of the 12 seasons analyzed in ten randomized controlled trials in adults aged 18—65 years).

No such trials met inclusion criteria for children aged 2—17 years or adults aged 65 years or older.

Osterholm M, Kelley S, Sommer A, Belongia E. Efficacy and effectiveness of influenza vaccines: a systematic review and meta-analysis. The Lancet Infectious Diseases, Volume 12, Issue 1, Pages 36 - 44, January 2012.

Osterholm Study

Efficacy of attenuated vaccine was shown in nine (75%) of the 12 seasons analyzed in ten randomized controlled trials in children aged 6 months to 7 years.

No such trials met inclusion criteria for children aged 8—17 years.

Vaccine effectiveness was variable for seasonal influenza: only six (35%) of 17 analyses in nine studies showed significant protection against medically attended influenza in the outpatient or inpatient setting.

Osterholm M, Kelley S, Sommer A, Belongia E. Efficacy and effectiveness of influenza vaccines: a systematic review and meta-analysis. The Lancet Infectious Diseases, Volume 12, Issue 1, Pages 36 - 44, January 2012.

Osterholm Study

Influenza vaccines only provide moderate protection against virologically confirmed influenza, but such protection is greatly reduced or absent in some seasons.

Evidence for protection in adults aged 65 years or older is lacking.

Osterholm M, Kelley S, Sommer A, Belongia E. Efficacy and effectiveness of influenza vaccines: a systematic review and meta-analysis. The Lancet Infectious Diseases, Volume 12, Issue 1, Pages 36 - 44, January 2012.

Elderly - Jefferson

In another systematic review Jefferson and his team reviewed the evidence of efficacy and effectiveness of influenza vaccines in individuals aged 65 years or older.

They searched five electronic databases up to December, 2004, in any language, for randomized (n=5), cohort (n=49), and case-control (n=10) studies, assessing efficacy against influenza in laboratory-confirmed cases or effectiveness against influenza-like illness in symptomatic cases.

They analyzed the following outcomes: influenza, influenza-like illness, hospital admissions, complications, and deaths.

Jefferson T, Rivetti D, Rivetti A, Rudin M. Efficacy and effectiveness of influenza vaccines in elderly people: a systematic review. The Lancet, Volume 366, Issue 9492, Pages 1165 - 1174, 1 October 2005.

Elderly - Jefferson

In homes for elderly individuals (with good vaccine match and high viral circulation) the effectiveness of vaccines against influenza-like illness was only 23% and non-significant against influenza itself.

Jefferson T, Rivetti D, Rivetti A, Rudin M. Efficacy and effectiveness of influenza vaccines in elderly people: a systematic review. The Lancet, Volume 366, Issue 9492, Pages 1165 - 1174, 1 October 2005.

Elderly – 1 Percent

Government health projections confirm, and the CDC has had to acknowledge this, that elderly people, with or without the flu shot, show less than a one percent rate of being hospitalized for pneumonia and influenza. That means that 99 percent of elderly people manage to weather the storm.

Why You Should Not Get a Flu Shot
http://prn.fm/2013/01/18/gary-null-flu-vaccine/#axzz2HW0L8zGU

Elderly – Research Won't Be Done

But those may never be conducted on the elderly, in large part because of the way the vaccine was promulgated. Initially developed for soldiers and approved in 1945, the vaccine was approved for civilian use a year later. In 1960, the surgeon general, Leroy E. Burney recommended vaccinating three high-risk groups: pregnant women, the chronically ill and people 65 and over, Dr. Osterholm said. Once that recommendation was made, scientists felt that it would be unethical to run a trial that would essentially deny a recommended vaccine to participants assigned to the placebo group.

http://well.blogs.nytimes.com/2012/11/05/reassessing-flu-shots-as-the-season-draws-near/

Children - Jefferson

Jefferson also assessed the evidence of efficacy and effectiveness of influenza vaccines in children up to 16 years of age.

They included 14 randomised controlled trials, eight cohort studies, one case-control study, and one randomised controlled trial of intraepidemic use of the vaccines.

Live attenuated influenza vaccines had 79% efficacy and 38% effectiveness in children older than 2 years compared with placebo or no immunisation.

Inactivated vaccines had lower efficacy (65%) than live attenuated vaccines, and in children aged 2 years or younger they had similar effects to placebo.

Effectiveness of inactivated vaccines was about 28% in children older than 2 years.

Jefferson, Smith, Demicheli, Harnden, Rivetti, Di Pietrantonj. Assessment of the efficacy and effectiveness of influenza vaccines in healthy children: systematic review. The Lancet - 26 February 2005 (Vol. 365, Issue 9461, Pages 773-780)

Children - Jefferson

Efficacy and effectiveness of the vaccines differed strikingly. Only two small studies assessed the effects of influenza vaccines on hospital admissions and no studies assessed reductions in mortality, serious complications, and community transmission of influenza.

If influenza immunisation in children is to be recommended as public-health policy, large-scale studies assessing such important outcomes and undertaking direct comparisons of vaccines are urgently needed.

Jefferson, Smith, Demicheli, Harnden, Rivetti, Di Pietrantonj. Assessment of the efficacy and effectiveness of influenza vaccines in healthy children: systematic review. The Lancet - 26 February 2005 (Vol. 365, Issue 9461, Pages 773-780)

Children

When the CDC launched new swine flu vaccine in 2009, it recommended children as young as 6 months be vaccinated. All FDA-approved intramuscular flu vaccines comprise an inactivated virus. So is there any evidence that inactivated viral influenza vaccines are effective in very young children? In our own research, we have not found any convincing scientific evidence. However, some of the most damning evidence was reported in two studies performed by Dr. Tom Jefferson at the Cochrane Group and published in *The Lancet* and the prestigious *Cochrane Database Systems Review*. His first study was a systematic review of the effects of influenza vaccines in healthy children. The second was a review of all available published and unpublished safety evidence available regarding the flu vaccine. The authors of the study had also contacted the lead scientists or research groups for all the efficacy and safety trial studies under their review in order to gain access to additional unpublished trial studies the corporations may possess. The conclusions are shocking. The only safety study found for an inactivated flu vaccine was conducted in 1976. And that single study enrolled only 35 children aged 12-28 months. Every other subsequent inactivated flu vaccine study enrolled only children 3 years and older.

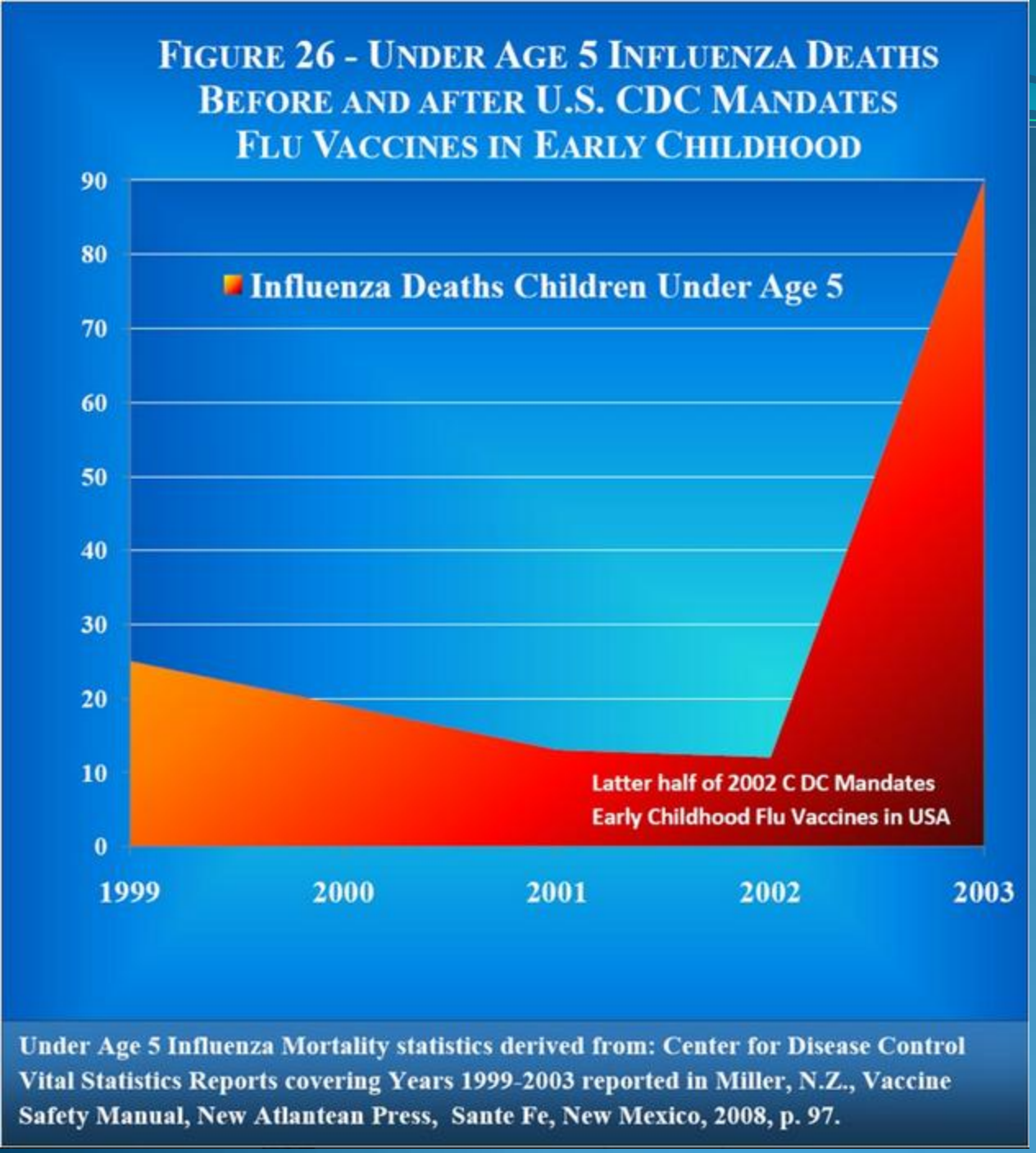
- Jefferson T, Smith S, Demicheli V, Harnden A, Rivetti A. Assessment of the efficacy and effectiveness of influenza in healthy children: systemic review. *The Lancet* 2005; 365: 773-780.
- Smith S, Demicheli V, Jefferson T, Harnden T. Matheson N, Di Pietrontonj C. Vaccines for preventing influenza in healthy children. Cochrane Database Syst. Rev. 2004. 3:CD004879.

Children

In a review of more than 51 studies involving over 294,000 children, there was "no evidence that injecting children 6-24 months of age with a flu shot was any more effective than placebo. In children over 2 years of age, flu vaccine effectiveness was 33 percent of the time preventing flu.
Dr. Jefferson told Reuters, "Immunization of very young children is not lent support by our findings. We recorded no convincing evidence that vaccines can reduce mortality, [hospital] admissions, serious complications and community transmission of influenza. In young children below the age of 2, we could find no evidence that the vaccine was different from a placebo."

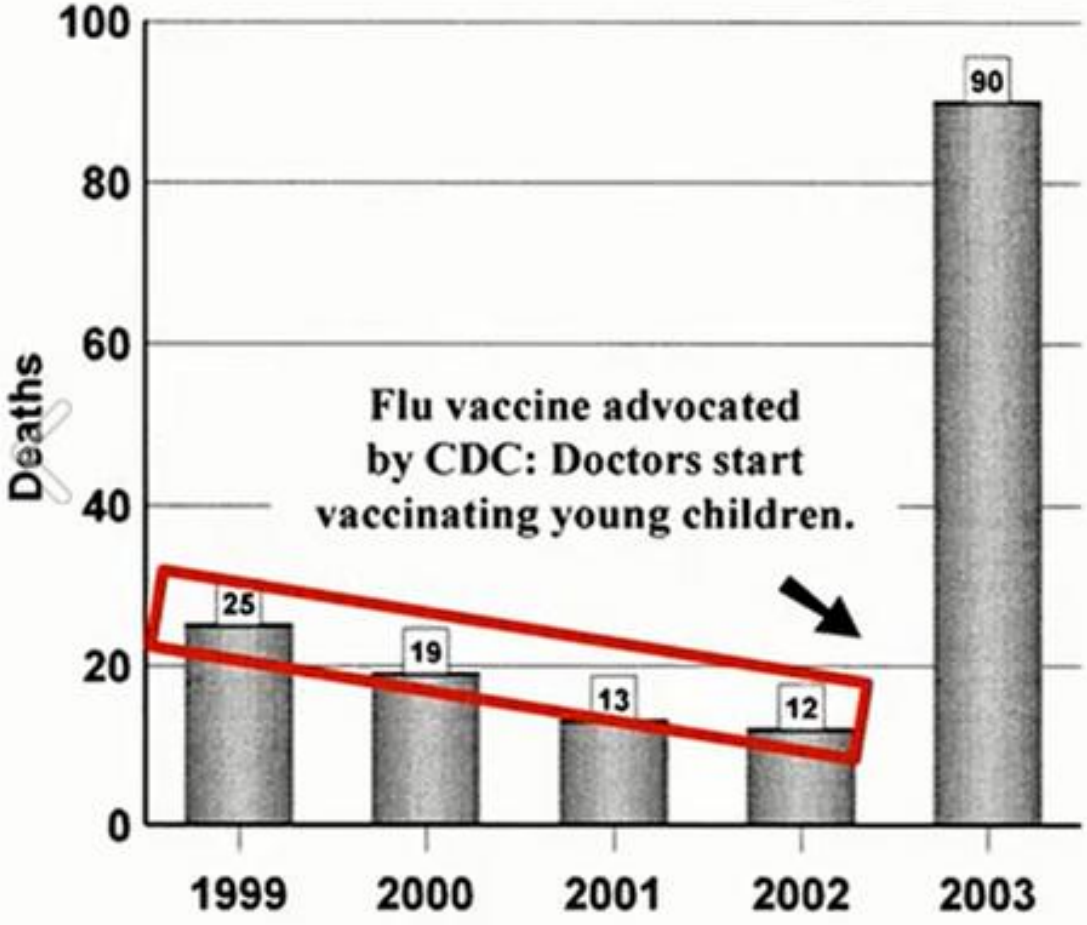
- Tenpenny, Sherri. "The Truth about Flu Shots". *Idaho Observer*, June 1, 2009.
- Reaney, Patricia. "No Evidence Flu Shots Work for Under-2s: Study. *Reuters*, September 22, 2005; Jefferson, Tom. "Safety of influenza vaccines in children." *The Lancet*, 2005. 366:803-804.

Figure 26 - Under Age 5 Influenza Deaths Before and after U.S. CDC Mandates Flu Vaccines in Early Childhood



Under Age 5 Influenza Mortality statistics derived from: Center for Disease Control Vital Statistics Reports covering Years 1999-2003 reported in Miller, N.Z., Vaccine Safety Manual, New Atlantean Press, Sante Fe, New Mexico, 2008, p. 97.

Influenza Deaths in Children Under 5 Years of Age



Source: *National Vital Statistics Reports, CDC.*

From 1999-2002, *before* the CDC advocated vaccinating young children, very few young children died from the flu. In 2003, *after* the CDC started vaccinating young children, flu deaths in this age group skyrocketed.

Pregnancy Research Negligible

First, very few vaccine studies have been performed on pregnant women. And none of them, according to Dr. Jefferson are "high quality" studies. While some extremely poor trials have been conducted, the CDC's National Institute for Allergies and Infectious Disease, research into the potential dangers and risks of the flu vaccine to both mom and fetus is negligible. After evaluating all flu vaccine studies on pregnant women, and finding them "artificial" in the way there designed and carried out, Dr. Jefferson concludes that "I would be very very cautious about vaccinating unborn babies."

Interview with Dr. Tom Jefferson, "The Gary Null Show" Progressive Radio Network, January 8, 2012 www.prn.fm

Pregnancy

Mak and his team reviewed the evidence for the risks of influenza and the risks and benefits of seasonal influenza vaccination in pregnancy.

They stated: Data on influenza vaccine safety in pregnancy are inadequate.

Influenza vaccination in pregnancy: current evidence and selected national policies. Tippi K Mak MD,Dr Punam Mangtani MD,Jane Leese FRCP,John M Watson MD,Dina Pfeifer MD The Lancet Infectious Diseases - 1 January 2008 (Vol. 8, Issue 1, Pages 44-52)

Pregnancy

Launay studied 877 women between 12 and 35 weeks of gestation. 320 received H1N1 vaccine.

None of the 877 study's women were hospitalized for flu. No difference on pregnancy outcomes was evidenced between vaccinated women, non-vaccinated women without seroconversion and non-vaccinated women with flu.

PLoS One. 2012;7(12):e52303. doi: 10.1371/journal.pone.0052303. Epub 2012 Dec 27. Low Rate of Pandemic A/H1N1 2009 Influenza Infection and Lack of Severe Complication of Vaccination in Pregnant Women: A Prospective Cohort Study. Launay O, Krivine A, Charlier C, Truster V, Tsatsaris V, Lepercq J, Ville Y, Avenell C, Andrieu T, Rozenberg F, Artiguebielle F, Tréluyer JM, Goffinet F; Inserm COFLUPREG Study Group.

Pregnancy

USE IN SPECIFIC POPULATIONS

Information is based on studies conducted with seasonal trivalent Influenza Virus Vaccine manufactured by IDB (FLULAVAL).

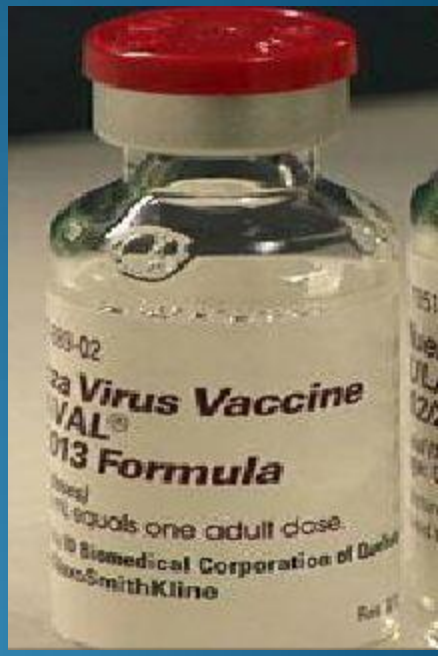
- Safety and effectiveness of Influenza A (H1N1) 2009 Monovalent Vaccine have not been established in pregnant women, nursing mothers, and children. (8.1, 8.3, 8.4)
- Geriatric Use: Antibody responses to FLULAVAL were lower in geriatric subjects than in younger subjects. (8.5)

http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM190377.pdf

Flu Vaccine Package Inserts

The next section of slides highlight the warnings, indications, contraindications and adverse effects of flu vaccines.

It is important to remember that despite what anyone says or what is written elsewhere – these are the statements REQUIRED by the FDA to be place in the package. Read carefully.



INDICATIONS AND USAGE

- Influenza A (H1N1) 2009 Monovalent Vaccine is an inactivated influenza virus vaccine, indicated for active immunization of adults 18 years of age and older against influenza disease caused by pandemic (H1N1) 2009 virus. (1)
- This indication is based on immune response elicited by the seasonal trivalent Influenza Virus Vaccine manufactured by IDB (FLULAVAL). Influenza A (H1N1) 2009 Monovalent Vaccine and FLULAVAL are manufactured by IDB using the same process. There have been no controlled trials demonstrating a decrease in influenza disease after vaccination with FLULAVAL. (14)

----------CONTRAINDICATIONS----------

Known systemic hypersensitivity reactions to egg proteins, or any other component of Influenza A (H1N1) 2009 Monovalent Vaccine, or life-threatening reaction to previous influenza vaccination. (4.1, 11)

---------- WARNINGS AND PRECAUTIONS ----------

- If Guillain-Barré syndrome has occurred within 6 weeks of receipt of a prior influenza vaccine, the decision to give Influenza A (H1N1) 2009 Monovalent Vaccine should be based on careful consideration of the potential benefits and risks. (5.1)
- Immunocompromised persons may have a reduced immune response to Influenza A (H1N1) 2009 Monovalent Vaccine. (5.2)

ADVERSE REACTIONS

Adverse reactions information is based on studies conducted with seasonal trivalent Influenza Virus Vaccine manufactured by IDB (FLULAVAL).

- Most common (≥10%) local adverse events for FLULAVAL were pain, redness, and/or swelling at the injection site. (6.1)
- Most common (≥10%) systemic adverse events for FLULAVAL were headache, fatigue, myalgia, low grade fever, and malaise. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact GlaxoSmithKline at 1-888-825-5249 or VAERS at 1-800-822-7967 and www.vaers.hhs.gov.

5.3 Preventing and Managing Allergic Vaccine Reactions

Prior to administration, the healthcare provider should review the patient's immunization history for possible vaccine sensitivity and previous vaccination-related adverse reactions. Appropriate medical treatment, including epinephrine, and supervision must be available to manage possible anaphylactic reactions following administration of the vaccine.

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse event rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine, and may not reflect the rates observed in practice. As with any vaccine, there is the possibility that broad use could reveal adverse events not observed in clinical trials.

Table 1. Solicited Adverse Events in the First 4 Days After Administration of FLULAVAL or Comparator Influenza Vaccine

	US Trial Adults 18 to 64 years of age (80% <50 years of age)		Canadian Trial Adults 50 years of age and older
Adverse Events	FLULAVAL N = 721	Comparator Influenza Vaccine[a] N = 279	FLULAVAL[b] N = 328
Local			
Pain	174 (24%)	85 (31%)	70 (21%)
Redness	76 (11%)	28 (10%)	48 (14%)
Swelling	71 (10%)	29 (10%)	21 (6%)
Systemic			
Headache	127 (18%)	48 (17%)	34 (10%)
Fatigue	123 (17%)	43 (15%)	33 (10%)
Myalgia	93 (13%)	44 (16%)	35 (11%)
Fever[c]	79 (11%)	28 (10%)	1 (1%)
Malaise	73 (10%)	28 (10%)	13 (4%)
Sore throat	64 (9%)	26 (9%)	17 (5%)
Reddened eyes	44 (6%)	15 (5%)	10 (3%)
Cough	44 (6%)	19 (7%)	11 (3%)
Chills	38 (5%)	6 (2%)	10 (3%)
Chest tightness	24 (3%)	4 (1%)	6 (2%)
Facial swelling	7 (1%)	1 (1%)	1 (1%)

Results >1% reported to nearest whole percent; results >0 but ≤1 reported as 1%.

[a] US-licensed trivalent, inactivated influenza virus vaccine (FLUZONE).

[b] Includes subjects who received FLULAVAL and a similar investigational formulation of FLULAVAL with reduced thimerosal.

[c] Fever defined as ≥37.5°C in the US study, and ≥38.0°C in the Canadian study.

Table 2. Adverse Events Reported Spontaneously[a] by ≥5% of Subjects in Either Clinical Trial of FLULAVAL

Adverse Events	US Trial (safety follow-up 42 days) Adults 18 to 64 years of age (80% <50 years of age)		Canadian Trial (safety follow-up 6 months) Adults 50 years of age and older
	FLULAVAL N = 721	Comparator Influenza Vaccine[b] N = 279	FLULAVAL[c] N = 328
Headache	49 (7%)	18 (7%)	63 (19%)
Cough	16 (2%)	5 (2%)	48 (15%)
Pharyngolaryngeal pain	17 (2%)	9 (3%)	38 (12%)
Upper respiratory infection	3 (1%)	2 (1%)	30 (9%)
Arthralgia	5 (1%)	3 (1%)	27 (8%)
Myalgia	4 (1%)	2 (1%)	23 (7%)
Nasopharyngitis	1 (1%)	1 (1%)	23 (7%)
Back pain	5 (1%)	3 (1%)	19 (6%)
Injection site erythema	2 (1%)	1 (1%)	18 (5%)
Diarrhea	5 (1%)	0	18 (5%)
Fatigue	6 (1%)	2 (1%)	17 (5%)
Nausea	5 (1%)	1 (1%)	17 (5%)
Nasal congestion	7 (1%)	2 (1%)	16 (5%)

Results >1% reported to nearest whole percent; results >0 but ≤1 reported as 1%.

[a] Adverse events reported spontaneously or in response to queries about changes in health status.

[b] US-licensed trivalent, inactivated influenza virus vaccine (FLUZONE).

[c] Includes subjects who received FLULAVAL and a similar investigational formulation of FLULAVAL with reduced thimerosal.

Blood and Lymphatic System Disorders: Lymphadenopathy.

Eye Disorders: Conjunctivitis, eye pain, photophobia.

Gastrointestinal Disorders: Dysphagia, vomiting.

General Disorders and Administration Site Conditions: Chest pain, injection site inflammation, rigors, asthenia, injection site rash, influenza-like symptoms, abnormal gait, injection site bruising, injection site sterile abscess.

Immune System Disorders: Allergic edema of the face, allergic edema of the mouth, anaphylaxis, allergic edema of the throat.

Infections and Infestations: Pharyngitis, rhinitis, laryngitis, cellulitis.

Musculoskeletal and Connective Tissue Disorders: Muscle weakness, back pain, arthritis.

Nervous System Disorders: Dizziness, paresthesia, hypoesthesia, hypokinesia, tremor, somnolence, syncope, Guillain-Barré syndrome, convulsions/seizures, facial or cranial nerve paralysis, encephalopathy, limb paralysis.

Psychiatric Disorders: Insomnia.

Respiratory, Thoracic, and Mediastinal Disorders: Dyspnea, dysphonia, bronchospasm, throat tightness.

Skin and Subcutaneous Tissue Disorders: Urticaria, localized or generalized rash, pruritus, periorbital edema, sweating.

Vascular Disorders: Flushing, pallor.

Neurological disorders temporally associated with influenza vaccination such as encephalopathy, optic neuritis/neuropathy, partial facial paralysis, and brachial plexus neuropathy have been reported.

Microscopic polyangitis (vasculitis) has been reported temporally associated with influenza vaccination.

8.1 Pregnancy

Pregnancy Category C

Animal reproduction studies have not been conducted with Influenza A (H1N1) 2009 Monovalent Vaccine or FLULAVAL. It is also not known whether these vaccines can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Influenza A (H1N1) 2009 Monovalent Vaccine should be given to a pregnant woman only if clearly needed.

8.3 Nursing Mothers

Neither Influenza A (H1N1) 2009 Monovalent Vaccine nor FLULAVAL has been evaluated in nursing mothers. It is not known whether Influenza A (H1N1) 2009 Monovalent Vaccine or FLULAVAL is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Influenza A (H1N1) 2009 Monovalent Vaccine is administered to a nursing woman.

8.4 Pediatric Use

Neither Influenza A (H1N1) 2009 Monovalent Vaccine nor FLULAVAL has been evaluated in children. Safety and effectiveness in the pediatric population have not been established.

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Neither Influenza A (H1N1) 2009 Monovalent Vaccine nor FLULAVAL has been evaluated for carcinogenic or mutagenic potential, or for impairment of fertility.

17 PATIENT COUNSELING INFORMATION

The vaccine recipient or guardian should be:

- informed of the potential benefits and risks of immunization with Influenza A (H1N1) 2009 Monovalent Vaccine.
- educated regarding potential side effects, emphasizing that Influenza A (H1N1) 2009 Monovalent Vaccine contains non-infectious killed viruses and cannot cause influenza.
- instructed to report any adverse events to their healthcare provider.
- informed that there are 2 influenza vaccine formulations for this influenza season, the monovalent vaccine against influenza disease caused by pandemic (H1N1) 2009 influenza virus and seasonal trivalent influenza vaccine.

Influenza Virus Vaccine
Fluvirin®
2012-2013 FORMULA

http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm123694.pdf

CONTRAINDICATIONS

- History of severe allergic reactions (e.g., anaphylaxis) to egg proteins, or any component of FLUVIRIN®, or life-threatening reactions to previous influenza vaccinations. (4.1, 11)

WARNINGS AND PRECAUTIONS

- If Guillain-Barré syndrome has occurred within 6 weeks of receipt of prior influenza vaccine, the decision to give FLUVIRIN® should be based on careful consideration of the potential benefits and risks. (5.1)
- Immunocompromised persons may have a reduced immune response to FLUVIRIN®. (5.2)

ADVERSE REACTIONS

The most frequently reported adverse reactions are mild hypersensitivity reactions (such as rash), local reactions at the injection site, and influenza-like symptoms. (6)

USE IN SPECIFIC POPULATIONS

- Safety and effectiveness of FLUVIRIN® have not been established in pregnant women, nursing mothers or children less than 4 years of age. (8.1, 8.3, 8.4)
- Antibody responses were lower in the geriatric population than in younger subjects. (8.5)

2.1 Preparation for Administration

Shake the syringe vigorously before administering the vaccine and shake the multidose vial preparation each time before withdrawing a dose of vaccine.

Inspect FLUVIRIN® syringes and multidose vials visually for particulate matter and/or discoloration prior to administration [see DESCRIPTION (11)]. If either of these conditions exists, the vaccine should not be administered.

Between uses, return the multidose vial to the recommended storage conditions between 2° and 8°C (36° and 46°F). **Do not freeze.** Discard if the vaccine has been frozen.

A separate sterile syringe and needle must be used for each injection to prevent transmission of infectious agents from one person to another. Needles should be disposed of properly and not recapped.

It is recommended that small syringes (0.5 mL or 1 mL) should be used to minimize any product loss.

For intramuscular use only.

4 CONTRAINDICATIONS

4.1 Hypersensitivity

Do not administer FLUVIRIN® to anyone with known history of severe allergic reactions (e.g., anaphylaxis) to egg proteins (eggs or egg products), or to any component of FLUVIRIN®, or who has had a life-threatening reaction to previous influenza vaccinations.

5 WARNINGS AND PRECAUTIONS

5.1 Guillain-Barré Syndrome

If Guillain-Barré syndrome has occurred within 6 weeks of receipt of prior influenza vaccine, the decision to give FLUVIRIN® should be based on careful consideration of the potential benefits and risks.

5.3 Preventing and Managing Allergic Reactions

Prior to administration of any dose of FLUVIRIN®, the healthcare provider should review the patient's prior immunization history for possible adverse events, to determine the existence of any contraindication to immunization with FLUVIRIN® and to allow an assessment of benefits and risks. Appropriate medical treatment and supervision must be available to manage possible anaphylactic reactions following administration of the vaccine.

5.4 Limitations of Vaccine Effectiveness

Vaccination with FLUVIRIN® may not protect all individuals.

6 ADVERSE REACTIONS

6.1 Overall Adverse Reaction Profile

Serious allergic reactions, including anaphylactic shock, have been observed in individuals receiving FLUVIRIN® during postmarketing surveillance.

6.2 Clinical Trial Experience

Adverse event information from clinical trials provides a basis for identifying adverse events that appear to be related to vaccine use and for approximating the rates of these events. However, because clinical trials are conducted under widely varying conditions, the adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine, and may not reflect rates observed in clinical practice.

TABLE 2

Solicited Adverse Events in the First 72-96 Hours After Administration of FLUVIRIN® in Adult (18-64 years of age) and Geriatric (≥65 years of age) Subjects.

	1998-1999*§		1999-2000*§		2000-2001*§	
	18-64 yrs N = 66	≥ 65 yrs N = 44	18-64 yrs N = 76	≥ 65 yrs N = 34	18-64 yrs N = 75	≥ 65 yrs N = 35
Local Adverse Events						
Pain	16 (24%)	4 (9%)	16 (21%)	-	9 (12%)	-
Mass	7 (11%)	1 (2%)	4 (5%)	-	8 (11%)	1 (3%)
Inflammation	5 (8%)	2 (5%)	6 (8%)	-	7 (9%)	1 (3%)
Ecchymosis	4 (6%)	1 (2%)	3 (4%)	1 (3%)	4 (5%)	-
Edema	2 (3%)	1 (2%)	1 (1%)	2 (6%)	3 (4%)	1 (3%)
Reaction	2 (3%)	-	2 (3%)	-	4 (5%)	1 (3%)
Hemorrhage	-	-	1 (1%)	-	-	-
Systemic Adverse Events						
Headache	7 (11%)	1 (2%)	17 (22%)	3 (9%)	4 (5%)	-
Fatigue	3 (5%)	2 (5%)	4 (5%)	1 (3%)	3 (4%)	-
Malaise	2 (3%)	1 (2%)	2 (3%)	1 (3%)	1 (1%)	-
Myalgia	1 (2%)	-	2 (3%)	-	-	-
Fever	1 (2%)	-	1 (1%)	-	-	-
Arthralgia	-	1 (2%)	-	1 (3%)	-	-
Sweating	-	-	3 (4%)	-	1 (1%)	1 (3%)

	2001-2002*^		2002-2003*^		2004-2005*^	
	18-64 yrs N = 75	≥ 65 yrs N = 35	18-64 yrs N = 107	≥ 65 yrs N = 88	18-64 yrs N = 74	≥ 65 yrs N = 61
Local Adverse Events						
Pain	12 (16%)	1 (3%)	14 (13%)	7 (8%)	15 (20%)	9 (15%)
Mass	4 (5%)	1 (3%)	-	-	-	-
Ecchymosis	2 (3%)	-	3 (3%)	3 (3%)	2 (3%)	1 (2%)
Edema	2 (3%)	1 (3%)	6 (6%)	2 (2%)	-	-
Erythema	5 (7%)	-	11 (10%)	5 (6%)	16 (22%)	5 (8%)
Swelling	-	-	-	-	11 (15%)	4 (7%)
Reaction	-	-	2 (2%)	-	-	-
Induration	-	-	14 (13%)	3 (3%)	11 (15%)	1 (2%)
Pruritus	-	-	1 (1%)	-	-	-
Systemic Adverse Events						
Headache	8 (11%)	1 (3%)	12 (11%)	9 (10%)	14 (19%)	3 (5%)
Fatigue	1 (1%)	1 (3%)	-	-	5 (7%)	2 (3%)
Malaise	3 (4%)	-	3 (3%)	4 (5%)	1 (1%)	1 (2%)
Myalgia	3 (4%)	-	5 (5%)	3 (3%)	8 (11%)	1 (2%)
Fever	-	-	-	1 (1%)	-	-
Arthralgia	-	-	2 (2%)	-	1 (1%)	-
Sweating	3 (4%)	1 (3%)	-	2 (2%)	-	-
Shivering	-	-	-	1 (1%)	-	-

Results reported to the nearest whole percent; Fever defined as >38°C

– not reported

* Solicited adverse events in the first 72 hours after administration of FLUVIRIN®

§ Solicited adverse events reported by COSTART preferred term

^ Solicited adverse events reported by MEDDRA preferred term

TABLE 3
Solicited Adverse Events in the First 72 Hours After Administration of FLUVIRIN® in Adult Subjects (18-49 years of age).

	2005-2006 US Trial FLUVIRIN® N = 304
Local Adverse Events	
Pain	168 (55%)
Erythema	48 (16%)
Ecchymosis	22 (7%)
Induration	19 (6%)
Swelling	16 (5%)
Systemic Adverse Events	
Headache	91 (30%)
Myalgia	64 (21%)
Malaise	58 (19%)
Fatigue	56 (18%)
Sore throat	23 (8%)
Chills	22 (7%)
Nausea	21 (7%)
Arthralgia	20 (7%)
Sweating	17 (6%)
Cough	18 (6%)
Wheezing	4 (1%)
Chest tightness	4 (1%)
Other difficulties breathing	3 (1%)
Facial edema	-

Results reported to the nearest whole percent
– not reported

TABLE 4
Adverse Events Reported by at least 5% of Subjects in Clinical Trials since 1998

	1998-1999§		1999-2000§		2000-2001§	
	18-64 yrs	≥ 65 yrs	18-64 yrs	≥ 65 yrs	18-64 yrs	≥ 65 yrs
	N = 66	N = 44	N = 76	N = 34	N = 75	N = 35
Adverse Events						
Fatigue	8 (12%)	2 (5%)	8 (11%)	2 (6%)	5 (7%)	-
Back pain	4 (6%)	3 (7%)	-	-	-	-
Cough increased	2 (3%)	2 (5%)	-	-	-	-
Ecchymosis	4 (6%)	1 (2%)	4 (5%)	1 (3%)	5 (7%)	-
Fever	3 (5%)	-	-	-	-	-
Headache	12 (18%)	5 (11%)	22 (29%)	5 (15%)	14 (19%)	2 (6%)
Infection	3 (5%)	2 (5%)	-	-	-	-
Malaise	4 (6%)	4 (9%)	4 (5%)	1 (3%)	-	-
Migraine	4 (6%)	1 (2%)	-	-	-	-
Myalgia	4 (6%)	1 (2%)	-	-	-	-
Sweating	5 (8%)	1 (2%)	-	-	-	-
Rhinitis	3 (5%)	1 (2%)	-	-	5 (7%)	2 (6%)
Pharingitis	6 (9%)	1 (2%)	10 (13%)	-	6 (8%)	-
Arthralgia	-	-	-	2 (6%)	-	-
Injection site pain	16 (24%)	4 (9%)	16 (21%)	-	9 (12%)	-
Injection site ecchymosis	4 (6%)	1 (2%)	-	-	4 (5%)	-
Injection site mass	7 (11%)	1 (2%)	4 (5%)	-	8 (11%)	1 (3%)
Injection site edema	-	-	1 (1%)	2 (6%)	-	-
Injection site inflammation	5 (8%)	2 (5%)	6 (8%)	-	7 (9%)	1 (3%)
Injection site reaction	-	-	-	-	4 (5%)	1 (3%)

	2001-2002^		2002-2003^		2004-2005^	
	18-64 yrs	≥ 65 yrs	18-64 yrs	≥ 65 yrs	18-64 yrs	≥ 65 yrs
	N = 75	N = 35	N = 107	N = 88	N = 74	N = 61
Adverse Events						
Fatigue	5 (7%)	4 (11%)	11 (10%)	8 (9%)	4 (5%)	2 (3%)
Hypertension	-	-	1 (1%)	4 (5%)	-	-
Rinorrhea	-	-	2 (2%)	5 (6%)	-	-
Headache	20 (27%)	2 (6%)	35 (33%)	18 (20%)	12 (16%)	1 (2%)
Malaise	6 (8%)	1 (3%)	13 (12%)	8 (9%)	-	-
Myalgia	4 (5%)	1 (3%)	10 (9%)	4 (5%)	-	-
Sweating	3 (4%)	3 (9%)	2 (2%)	5 (6%)	-	-
Rhinitis	4 (5%)	-	-	-	-	-
Pharingitis	-	-	-	-	6 (8%)	-
Arthralgia	-	-	5 (5%)	4 (5%)	-	-
Sore throat	4 (5%)	1 (3%)	5 (5%)	4 (5%)	-	-
Injection site pain	13 (17%)	3 (9%)	14 (13%)	7 (8%)	6 (8%)	2 (3%)
Injection site ecchymosis	4 (5%)	1 (3%)	4 (4%)	4 (5%)	-	-
Injection site erythema	5 (7%)	2 (6%)	11 (10%)	5 (6%)	4 (5%)	-
Injection site mass	4 (5%)	1 (3%)	-	-	-	-
Injection site edema	-	-	6 (6%)	2 (2%)	4 (5%)	1 (2%)
Injection site induration	-	-	14 (13%)	3 (3%)	7 (9%)	-

Results reported to the nearest whole percent; Fever defined as >38°C
– not reaching the cut-off of 5%
§ Solicited adverse events reported by COSTART preferred term
^ Solicited adverse events reported by MEDDRA preferred term

6.3 Postmarketing Experience

The following additional adverse reactions have been reported during post-approval use of FLUVIRIN®. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure. Adverse events described here are included because: a) they represent reactions which are known to occur following immunizations generally or influenza immunizations specifically; b) they are potentially serious; or c) the frequency of reporting.

- *Body as a whole*: Local injection site reactions (including pain, pain limiting limb movement, redness, swelling, warmth, ecchymosis, induration), hot flashes/flushes; chills; fever; malaise; shivering; fatigue; asthenia; facial edema.
- *Immune system disorders:* Hypersensitivity reactions (including throat and/or mouth edema). In rare cases, hypersensitivity reactions have lead to anaphylactic shock and death.
- *Cardiovascular disorders:* Vasculitis (in rare cases with transient renal involvement), syncope shortly after vaccination.
- *Digestive disorders:* Diarrhea; nausea; vomiting; abdominal pain.
- *Blood and lymphatic disorders:* Local lymphadenopathy; transient thrombocytopenia.
- *Metabolic and nutritional disorders:* Loss of appetite.
- *Musculoskeletal*: Arthralgia; myalgia; myasthenia.
- *Nervous system disorders:* Headache; dizziness; neuralgia; paraesthesia; confusion; febrile convulsions; Guillain-Barré Syndrome; myelitis (including encephalomyelitis and transverse myelitis); neuropathy (including neuritis); paralysis (including Bell's Palsy).
- *Respiratory disorders:* Dyspnea; chest pain; cough; pharyngitis; rhinitis.
- *Skin and appendages*: Stevens-Johnson syndrome; sweating; pruritus; urticaria; rash (including non-specific, maculopapular, and vesiculobulbous).

6.4 Other Adverse Reactions Associated with Influenza Vaccination

Anaphylaxis has been reported after administration of FLUVIRIN®. Although FLUVIRIN® contains only a limited quantity of egg protein, this protein can induce immediate hypersensitivity reactions among persons who have severe egg allergy. Allergic reactions include hives, angioedema, allergic asthma, and systemic anaphylaxis [see CONTRAINDICATIONS (4)].

The 1976 swine influenza vaccine was associated with an increased frequency of Guillain-Barré syndrome (GBS). Evidence for a causal relation of GBS with subsequent vaccines prepared from other influenza viruses is unclear. If influenza vaccine does pose a risk, it is probably slightly more than 1 additional case/1 million persons vaccinated.

Neurological disorders temporally associated with influenza vaccination such as encephalopathy, optic neuritis/neuropathy, partial facial paralysis, and brachial plexus neuropathy have been reported.

Microscopic polyangiitis (vasculitis) has been reported temporally associated with influenza vaccination.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C: Animal reproduction studies have not been conducted with FLUVIRIN®. It is also not known whether FLUVIRIN® can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. FLUVIRIN® should be given to a pregnant woman only if clearly needed.

8.3 Nursing Mothers

It is not known whether FLUVIRIN® is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when FLUVIRIN® is administered to a nursing woman.

8.4 Pediatric Use

The safety and immunogenicity of FLUVIRIN® have not been established in children under 4 years of age.

The safety and immunogenicity of FLUVIRIN® have been established in the age group 4 years to 16 years. The use of FLUVIRIN® in these age groups is supported by evidence from adequate and well controlled studies of FLUVIRIN® in adults that demonstrate the immunogenicity of FLUVIRIN® [see ADVERSE REACTIONS (6) and CLINICAL STUDIES (14)].

The 0.5-mL prefilled syringe presentation is formulated without preservative. However, thimerosal, a mercury derivative used during manufacturing, is removed by subsequent purification steps to a trace amount (≤ 1 mcg mercury per 0.5-mL dose).

The 5-mL multidose vial formulation contains thimerosal, a mercury derivative, added as a preservative. Each 0.5-mL dose from the multidose vial contains 25 mcg mercury.

Each dose from the multidose vial or from the prefilled syringe may also contain residual amounts of egg proteins (≤ 1 mcg ovalbumin), polymyxin (≤ 3.75 mcg), neomycin (≤ 2.5 mcg), betapropiolactone (not more than 0.5 mcg) and nonylphenol ethoxylate (not more than 0.015% w/v).

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

FLUVIRIN® has not been evaluated for carcinogenic or mutagenic potential, or for impairment of fertility.

Side Effects

In terms of side effects, some studies have shown an association between Guillian Barre' syndrome and flu shots. Interestingly the author of the second study - Jurrlink - was quoted in a news story as comparing the risk of getting GBS from the vaccine to being struck by lightning. Lightening, it turns out, killed 47 people in 2006.

1. Geier M, Geier D, Zahalsky A. Influenza vaccination and Guillain Barre syndrome. Clinical Immunology 107 (2003) 116–121
2. David N. Juurlink, MD, PhD; Therese A. Stukel, PhD; Jeffrey Kwong, MD, MSc; Alexander Kopp, BA; Allison McGeer, MD, MSc; Ross E. Upshur, MD, MSc; Douglas G. Manuel, MD, MSc; Rahim Moineddin, PhD; Kumanan Wilson, MD, MSc. Guillain-Barre´ Syndrome After Influenza Vaccination in Adults A Population-Based Study

Side Effects - Contamination

Meanwhile, Novartis is also currently defending its range of flu drugs, after they were banned in Italy earlier this week. Italy's health ministry banned the sale of four flu drugs for possible side-effects while Switzerland's regulator, Swissmedic, also suspended deliveries of Novartis' flu vaccines as a preventative measure against possible contamination.

http://www.pharmaphorum.com/2012/10/26/novartis-maintains-profit-q3-defends-flu-vaccines/

Risk Benefit Ratio

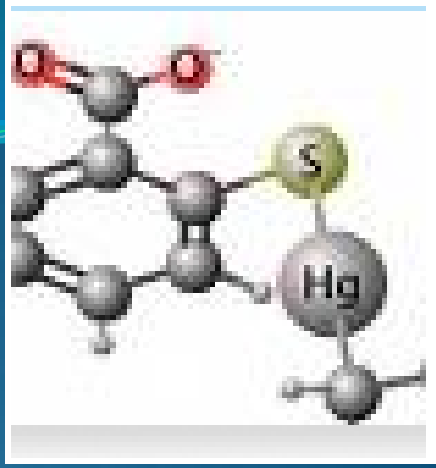
According to the Centers for Disease Control (CDC) they claim that influenza kills 30,000 to 40,000 Americans every year.

Though the CDC lumps the flu and pneumonia in together for these numbers.

According to Dr. Mercola the actual number of deaths attributable to the flu itself is less than 1000 a year

Flu Deaths Outrageously Exaggerated to Increase Vaccine Sales
http://www.mercola.com/2004/oct/30/flu_deaths.htm

Thimerosal



Add to all of this that the majority of influenza vaccines distributed in the United States contain Thimerosal and that while highly controversial, this methyl mercury based preservative has been claimed to be linked to autism, Alzheimer's, and ADD.

Autism, mercury poisoning, thimerosal and the flu vaccine
http://www.planetc1.com/cgi-bin/n/v.cgi?c=1&id=1162322544

Employment & the Flu Shot

More than 150 hospitals and health care systems in the United States are requiring their workers to be vaccinated against the flu, according to the Immunization Action Coalition, an organization that works to increase immunization rates. In many cases, if the worker refuses to be vaccinated, he or she might have to wear a mask for the duration of the flu season, might be reassigned away from patient care, or might be fired.

Mizra B. Is requiring flu vaccinations worth the risk? Society for Human Resource Management. February 23, 2012

Employment & the Flu Shot

Legislation and regulations are popping up in Colorado and Oregon. According to The Denver Post, the Colorado state board of health was scheduled to vote in February 2012 on rules that would require medical facilities to attain a 90 percent flu vaccination rate among their workers. And an Oregon bill would require health care workers to provide their employers with evidence that they received a flu shot or a declaration that they declined it. The measure has cleared the Oregon state Senate and was being considered by the state's House Committee on Health Care, according to Oregon Capital News.

Mizra B. Is requiring flu vaccinations worth the risk? Society for Human Resource Management. February 23, 2012

Employment & the Flu Shot

The Centers for Disease Control and Prevention (CDC) reported in November 2011 that 63.5 percent of health care workers reported receiving the flu vaccine during the 2010-2011 flu season. In hospitals and health care systems that required them to do so, 98.1 percent reported being vaccinated against the flu.

Mizra B. Is requiring flu vaccinations worth the risk? Society for Human Resource Management. February 23, 2012

Employment & the Flu Shot

Jordan Barab, deputy assistant secretary for the Occupational Safety and Health Administration (OSHA) in the U.S. Department of Labor, submitted comments to the NVAC in January 2012 saying mandatory vaccinations are not necessary and arguing against employees being fired for not receiving the flu shot.

Mizra B. Is requiring flu vaccinations worth the risk? Society for Human Resource Management. February 23, 2012

Employment & the Flu Shot

Barab wrote. However, “at this time, OSHA believes there is insufficient evidence for the federal government to promote mandatory influenza vaccination programs that may result in employment termination.”

Mizra B. Is requiring flu vaccinations worth the risk? Society for Human Resource Management. February 23, 2012

Employment & the Flu Shot

While vaccination protects health care workers from the flu, scientific literature does not support vaccinating the workers in order to protect patients,

Barab wrote. “High [health care personnel] influenza vaccination rates are generally desirable, but we are unaware of any evidence to support the notion that such a high influenza vaccination rate is also essential to protect patients, and should thus be mandatory.”

Mizra B. Is requiring flu vaccinations worth the risk? Society for Human Resource Management. February 23, 2012

Employment & the Flu Shot

Barab urged NVAC to rewrite its recommendations to remove references to firing employees who refuse the influenza vaccine. Instead, OSHA encourages employers to offer the vaccination to employees, educate them on the benefits and risks of the shot, and allow employees to sign statements declining the shot if that is their preference.

Mizra B. Is requiring flu vaccinations worth the risk? Society for Human Resource Management. February 23, 2012

Employment & the Flu Shot

The National Nurses United union agrees with OSHA's stance. Nurse DeAnn McEwen, vice president of the National Nurses United Executive Board, told SHRM Online that the union strongly recommends that all nurses receive all recommended vaccines. But any vaccination program "should include extensive education on risks and benefits with an emphasis on patient protection," she said. And nurses should have the right to refuse any treatment, including a vaccination, for religious or health reasons, she added.

Mizra B. Is requiring flu vaccinations worth the risk? Society for Human Resource Management. February 23, 2012

Employment & the Flu Shot

In addition, the nurses' union objects to forcing employees who decline the vaccine to wear a mask. "There's not good science to recommend masking," she said. "Masking is also targeting the individual for exercising her rights to refuse medical treatment and, I think, violates privacy laws. It's not good policy for hospitals, for patients seeing everyone wearing masks—it's a facade of protection that doesn't really benefit the public."

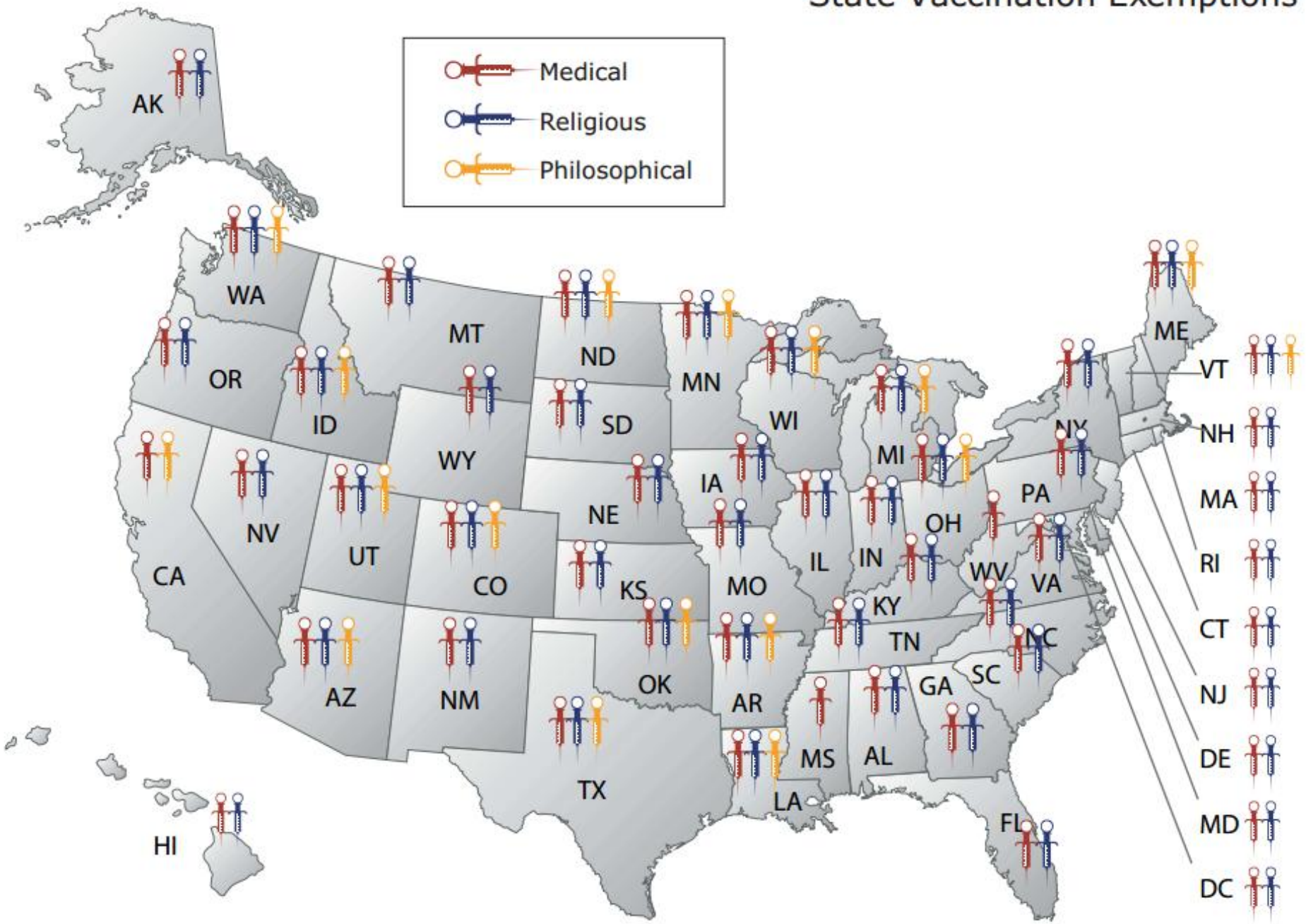
Mizra B. Is requiring flu vaccinations worth the risk? Society for Human Resource Management. February 23, 2012

Employment & the Flu Shot

In January 2012, a United States District Court ruled in favor of the Washington State Nurses Association, representing more than 600 registered nurses at Virginia Mason Medical Center in Seattle, in upholding an arbitrator's decision that stopped the hospital from forcing nurses to receive the flu shot. The hospital was one of the first health care systems to have a mandatory flu vaccine policy, starting in 2004

Mizra B. Is requiring flu vaccinations worth the risk? Society for Human Resource Management. February 23, 2012

State Vaccination Exemptions



What About Anti-Retrovirals?

CDC Recommends Anti-retrovirals for persons even SUSPECTED of having the flu – even if already vaccinated.

These early estimates indicate that some vaccinated persons will become infected with influenza, despite having been vaccinated. Therefore, antiviral medications should be used as recommended for treatment in patients regardless of their vaccination status (7).** Antiviral treatment can reduce the duration of illness and complications associated with influenza. Early antiviral treatment is recommended for persons with suspected influenza with severe or progressive illness (e.g., hospitalized persons) and those at high risk for complications from influenza, no matter how severe the illness. Antiviral treatment should be started as early as possible, preferably within 48 hours after illness onset. Among hospitalized patients, however, treatment should be initiated on admission; several studies suggest that antiviral treatment reduces mortality and illness severity among hospitalized adults, even when initiated ≥48 hours after illness onset (7). The decision to initiate antiviral treatment should not wait for laboratory confirmation of influenza and should not be dependent on insensitive assays, such as rapid influenza diagnostic tests.

http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6202a4.htm?s_cid=mm6202a4_w

Tamiflu & Other Retrovirals

In 2012 the Cochrane group, **the world's most respected organization devoted to synthesizing evidence and providing assessments on medical interventions**, updated their review of the Tamiflu studies. If you are wondering about taking Tamiflu, then here are 5 things you should know from their report . . .

Cochrane Database of Systematic Reviews: Plain Language Summaries.

A review of unpublished regulatory information from trials of neuraminidase inhibitors (Tamiflu - oseltamivir and Relenza - zanamivir) for influenza

First published: January 18, 2012; This version published: 2012; Review content assessed as up-to-date: April 12, 2011.

Plain language summary

We decided to update and amalgamate our reviews on the antiviral drugs zanamivir and oseltamivir for influenza on the basis of the manufacturers' reports to regulators (called clinical study reports) and regulators' comments (which we called regulatory information). Clinical study reports are extensive documents with exhaustive details of the trial protocol, methods and results. In view of the unresolved discrepancies in the data presented in published trial reports and of the substantial risk publication bias in this area, we elected not to use data from journal articles. Availability of documents generated by national and regional regulatory bodies during licensing processes in the UK, USA, continental Europe and Japan, partial trial reports from the manufacturers of oseltamivir and from the European regulator European Medicines Agency (EMA), enabled us to verify information from the trials. The authors have been unable to obtain the full set of clinical study reports or obtain verification of data from the manufacturer of oseltamivir (Roche) despite five requests between June 2010 and February 2011. No substantial comments were made by Roche on the protocol of our Cochrane Review which has been publicly available since December 2010. Based on our assessments of the documents we could obtain, we came to the conclusion that there were substantial problems with the design, conduct and availability of information from many of the trials. Due to these concerns we decided not to proceed with a meta-analysis of all the oseltamivir data as we had intended. Instead we carried out analyses of effects on symptoms (shortens them by 21 hours or so) and hospitalisations (no evidence of effect) of people with influenza-like illness ('flu') on data from all the people enrolled in treatment trials of oseltamivir. Other outcomes could not be assessed due to unavailability of data for all the people enrolled in treatment trials of oseltamivir. Our independent analysis concurs with the conservative conclusions regarding the effects of both drugs by the US Food and Drug Administration (FDA). The FDA only allowed claims of effectiveness of both drugs for the prevention and treatment of symptoms of influenza and not on other effects (such as interruption of person-to-person spread of the influenza virus or prevention of pneumonia). There is evidence to suggest that both drugs are associated with harms (oseltamivir: nausea, vomiting; zanamivir: probably asthma). The FDA described the overall performance of both drugs as "modest". We expect full clinical study reports containing study protocol, reporting analysis plan, statistical analysis plan and individual patient data to clarify outstanding issues. These full clinical study reports are at present unavailable to us.

Tamiflu – Cochrane Report

1. The manufacturer of the drug sponsored all the trials and the reviewers found evidence of publication and reporting biases. There are no prospective, placebo-controlled trials conducted that were funded by an **independent source**. Industry trials can be well conducted, but there are many situations where a lack of independence has had an influence on the way the study was designed and the results that are released. At the very least, it is worth noting that they were probably designed to have the best chance of showing benefit. And that the reviewers had concerned about whether all the information was released. In addition the experts found evidence of reporting bias. According to Tom Jefferson, one of the authors of the Cochrane study: 60% of randomized data from the Tamiflu treatment trials (i.e. in people with influenza-like-illness symptoms) have never been published including the biggest trial ever conducted (which was done in the US, so it's of great relevance to you)."

2. The studies did not show that Tamiflu reduced the risk of hospitalization. One of the reasons people might take an antiviral is to prevent the illness progressing to the point where they would need to be hospitalized. Unfortunately there was no evidence that the drug produced that benefit.

Tamiflu?

3. The studies were inadequate to determine the effect of Tamiflu on complications. Even though the drug did not reduce hospitalizations, some people may think it would prevent less severe complications. Unfortunately, the reviewers found that limitations in the design of the trials, their conduct, and the way they were reported precluded any conclusions about the effect of the drug on complications. To expect that Tamiflu can reduce complications would be a leap of faith currently unsupported by the available evidence. You should also know that the FDA requires Roche to print on the label: "Tamiflu has not been shown to prevent such complications [serious bacterial infections]."

4. The studies were inadequate to determine if Tamiflu reduced transmission of the virus. Same story. Some people might prescribe the drug to prevent the spread of the virus. The expert reviewers simply said that with what information they had available; they could not assess the effect of the drug on transmission. I asked Peter Doshi, one of the authors of the Cochrane report about this issue of transmission and here is what he wrote me: "Roche's prophylaxis trials were not designed to answer the question of transmission. The prophylaxis trials – and FDA approval of Tamiflu for prophylaxis – is based on its proven ability to reduce the chances of symptomatic influenza. (But since we don't know anything about asymptomatic influenza infections, we cannot say anything about whether or not Tamiflu reduces actual transmission of virus.)"

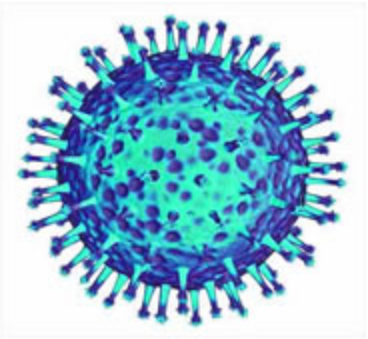
Tamiflu?

5. The use of Tamiflu did reduce the duration of symptoms by about a day. The reviewers found 5 studies that assessed the effect of Tamiflu on the duration of symptoms. They were fairly consistent in their findings – though the duration of the symptoms varied quite a lot across the studies.

   After conducting this review the reviewers felt that they needed access to more information to make firm conclusions about the drug. They asked Roche for full clinical study reports, with study protocols, the reporting analysis plan, the statistical analysis plan and individual patient data so that all they could more fully determine what could be concluded from the studies. Unfortunately, Roche has not complied .

British Medical Journal

The *BMJ's* **open data campaign** aims to achieve appropriate and necessary independent scrutiny of data from clinical trials. Working with others, we seek to highlight the problems caused by lack of access to data, and we welcome any suggestions on how to take things further.



The Tamiflu story

Our first open data campaign initiative relates to a public promise Roche made in 2009 to release full clinical trial reports in response to an investigation by the *BMJ* and Cochrane collaborators Peter Doshi and Tom Jefferson. [1][2][3][4]

The bottom line:

- WHO recommends Tamiflu, but has not vetted the Tamiflu data.
- EMA approved Tamiflu, but did not review the full Tamiflu dataset.
- CDC and ECDC encourage the use and stockpiling of Tamiflu, but did not vet the Tamiflu data.
- The majority of Roche's Phase III treatment trials remain unpublished over a decade after completion.
- In Dec 2009, Roche publicly promised independent scientists access to "full study reports" for selected Tamiflu trials, but to date the company has not made even one full report available.

Releasing the trial reports would allow independent academics to answer questions about this globally stockpiled drug. To date, the full data set has not been provided.

This page links to others listing open correspondence with Roche, and the various bodies around the world which licence or recommend drugs. This open correspondence of letters offers readers the chance to witness attempts to compel greater accountability and responsibility in public health decision making and policy. The *BMJ* plans to launch other campaigns linked to its investigations in the future. Find out more about the background to Tamiflu and open data by reading this feature and accompanying editorial.

What's new

- The campaign is gaining ground in the UK's parliament. MP's are planning an inquiry into clinical trials and data disclosure and there are calls for the powerful Public Accounts Committee to investigate the cost to the NHS of missing data
- See correspondence with the European Medicines Agency
- See the Cochrane Collaboration's complaint to the European Ombudsman

http://www.bmj.com/tamiflu

Complaints Filed

In October 2012 Cochrane Collaboration researcher Tom Jefferson made a maladministration complaint to the European Ombudsman. In his letter, (link below) he says the European Medicines Agency issued a market authorisation for oseltamivir on 20 June 2002. The EMA do not have and have never had a complete evidence set, he says.

http://www.bmj.com/tamiflu/ombudsman

Tamiflu Side Effects

Antiviral Medications Recommended for Treatment and Chemoprophylaxis of Influenza

Antiviral agent	Activity against	Use	FDA approved for	Not recommended for use in	Adverse Events
Oseltamivir (Tamiflu®)	**Influenza A and B**	**Treatment**	2 wks and older	N/A	**Adverse events:** nausea, vomiting. Sporadic, transient neuropsychiatric events (self injury or delirium) mainly reported among Japanese adolescents and adults.
		Chemo-prophylaxis	1 yr and older	N/A	
Zanamivir (Relenza®)	**Influenza A and B**	**Treatment**	7 yrs and older	people with underlying respiratory disease (e.g., asthma, COPD)	**Allergic reactions:** oropharyngeal or facial edema. **Adverse events:** diarrhea, nausea, sinusitis, nasal signs and symptoms, bronchitis, cough, headache, dizziness, and ear, nose and throat infections.
		Chemo-prophylaxis	5 yrs and older	people with underlying respiratory disease (e.g., asthma, COPD)	

http://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm

Follow the Money

In 2009 drug companies sold $1.5 billion worth of swine flu shots, in addition to the $1 billion for seasonal flu they booked earlier that year.

These inoculations are part of a much wider and rapidly growing $20 billion global vaccine market.

http://abcnews.go.com/Business/big-business-swine-flu/story?id=8820642

Follow the Money

"The vaccine market is booming," says Bruce Carlson, spokesperson at market research firm Kalorama, which publishes an annual survey of the vaccine industry. "It's an enormous growth area for pharmaceuticals at a time when other areas are not doing so well," he says, noting that the pipeline for more traditional blockbuster drugs such as Lipitor and Nexium has thinned.

http://abcnews.go.com/Business/big-business-swine-flu/story?id=8820642

Follow the Money

"Flu shots present a good opportunity to bring new customers into our stores," says Cassie Richardson, spokesperson for SUPERVALU, one of the country's largest supermarket chains. Drawing customers to the back of a store, where pharmacies are often located, offers retailers a chance to pitch products that might otherwise go unnoticed.

Even companies outside of the medical industry are benefiting: the UPS division that delivers vaccines in specially designed containers, for example, has seen a bump in business.

http://abcnews.go.com/Business/big-business-swine-flu/story?id=8820642

Follow the Money

The promise of profits has attracted new players into the business. Some of the world's largest drugmakers, who in the past avoided the vaccine market because of its limited scope -- its not easy to convince healthy adults to get a shot for measles -- are now jumping into the fray.

Last month alone saw three large vaccine deals. Abbott Labs bought a Belgian drug business, along with its flu vaccine facilities, for $6.6 billion. Johnson & Johnson invested $444 million in a Dutch biotech firm that makes and develops flu vaccines. Merck, which already makes vaccines for shingles and other diseases, struck a deal to distribute flu shots made by Australian CSL.

http://abcnews.go.com/Business/big-business-swine-flu/story?id=8820642

Follow the Money

Flu vaccines typically average $10 to $20 a dose. Despite their low price, analysts say companies like them because they provide a steady source of revenue. Vaccines are expected to generate $21.5 billion in sales by 2012, according to Sanofi-Aventis SA, a leading vaccine maker.

http://online.wsj.com/article/SB125417905531847679.html

Follow the Money

I believe the most evident beneficiaries are those companies involved in the production of flu vaccines and the businesses or hospitals that are administering those vaccines. In this case, I'm thinking about **AstraZeneca**-owned MedImmune with FluMist, **Novartis**' Fluvirin, **Sanofi**'s Fluzone, and **GlaxoSmithKline**'s Fluarix, which are annual vaccines given to persons either at high risk for flu-related complications or administered to those persons who choose to get a flu shot.

Hospitals and drugstores that are administering these shots should also see a surge in business. Large hospital operators like **HCA Holdings** would be expected to see a boost in revenue as more people visit the hospital with flu-related complications. For more proactive than reactive people, drugstores like **Walgreen** and **CVS Caremark** could clean up as the severity of this year's flu outbreak could necessitate consumers to rush in for a flu vaccination.

http://www.dailyfinance.com/2013/01/14/14-ways-to-play-the-flu-outbreak/?source=edddlftxt0860001

Follow the Money

Last updated: July 20, 2009 11:43 pm

Drug groups to reap swine-flu billions

By Andrew Jack in London

Some of the world's leading pharmaceutical companies are reaping billions of dollars in extra revenue amid global concern about the spread of swine flu.

Analysts expect to see a boost in sales from GlaxoSmithKline, Roche and Sanofi-Aventis when the companies report first-half earnings lifted by government contracts for flu vaccines and antiviral medicines.

http://www.ft.com/cms/s/0/375dde06-7559-11de-9ed5-00144feabdc0.html#axzz2IdxkVcRx

Follow the Money

A report last week from JPMorgan, the investment bank, estimated that governments had ordered nearly 600m doses of pandemic vaccine and adjuvant – a chemical that boosts its efficacy – worth $4.3bn (€3bn, £2.6bn) in sales, and there was potential for 342m more doses worth $2.6bn.

It forecast that fresh antiviral sales could boost sales for GSK and Roche by another $1.8bn in the developed world, and potentially up to $1.2bn from the developing world.

http://www.ft.com/cms/s/0/375dde06-7559-11de-9ed5-00144feabdc0.html#axzz2IdxkVcRx

Follow the Money

Company	Swine Flu Vaccine Sales (in millions)	Percent of Total Sales
GlaxoSmithKline (NYSE: GSK)	$1,306	3%
Novartis (NYSE: NVS)	$1,000	2.2%
AstraZeneca (NYSE: AZN)	$389	1.2%
Sanofi-aventis (NYSE: SNY)	$598	1.5%

http://www.fool.com/investing/value/2010/02/23/the-end-of-a-swine-flu-era.aspx

The Future?

FDA NEWS RELEASE

For Immediate Release: Jan. 16, 2013
Media Inquiries: Rita Chappelle, 301-796-4672, rita.chappelle@fda.hhs.gov
Consumer Inquiries: 888-INFO-FDA, OCOD@fda.hhs.gov

FDA approves new seasonal influenza vaccine made using novel technology

The U.S. Food and Drug Administration today announced that it has approved Flublok, the first trivalent influenza vaccine made using an insect virus (baculovirus) expression system and recombinant DNA technology. Flublok is approved for the prevention of seasonal influenza in people 18 through 49 years of age.

Unlike current flu vaccines, Flublok does not use the influenza virus or eggs in its production. Flublok's novel manufacturing technology allows for production of large quantities of the influenza virus protein, hemagglutinin (HA) – the active ingredient in all inactivated influenza vaccines that is essential for entry of the virus into cells in the body. The majority of antibodies that prevent influenza virus infection are directed against HA. While the technology is new to flu vaccine production, it is used to make vaccines that have been approved by the FDA to prevent other infectious diseases.

The Future?

11 DESCRIPTION

Flublok [Influenza Vaccine] is a sterile, clear, colorless solution of recombinant hemagglutinin (HA) proteins from three influenza viruses for intramuscular injection. It contains purified HA proteins produced in a continuous insect cell line (*expres*SF+®) that is derived from Sf9 cells of the fall armyworm, *Spodoptera frugiperda*, and grown in serum-free medium composed of chemically-defined lipids, vitamins, amino acids, and mineral salts. Each of the three HAs is expressed in this cell line using a baculovirus vector (*Autographa californica* nuclear polyhedrosis virus), extracted from the cells with Triton X-100 and further purified by column chromatography. The purified HAs are then blended and filled into single-dose vials.

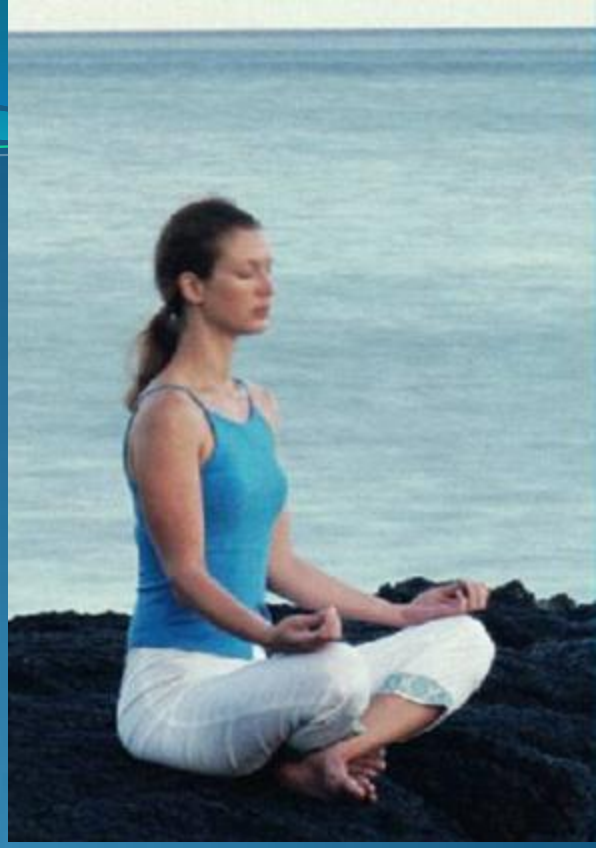
Flublok is standardized according to United States Public Health Service (USPHS) requirements. For the 2012 - 2013 influenza season it is formulated to contain 135 mcg HA per 0.5 mL dose, with 45 mcg HA of each of the following 3 influenza virus strains: A/California/7/2009 (H1N1), A/Victoria/361/2011 (H3N2), and B/Wisconsin/1/2010.

A single 0.5 mL dose of Flublok contains sodium chloride (4.4 mg), monobasic sodium phosphate (0.195 mcg), dibasic sodium phosphate (1.3 mg), and polysorbate 20 (Tween®20) (27.5 mcg). Each 0.5 mL dose of Flublok may also contain residual amounts of baculovirus and host cell proteins (≤ 28.5 mcg), baculovirus and cellular DNA (≤ 10 ng), and Triton X-100 (≤ 100 mcg).

Flublok contains no egg proteins, antibiotics, or preservatives. The stoppers used for the single-dose vials do not contain latex.

http://www.flublok.com/FlublokInsert.pdf

Alternative Strategies



The National Vaccine Information Center (NVIC) gives the following alternative strategies for dealing with the flu…

- If you have the flu, stay home until you are well
- If you know a person sick with the flu, avoid contact until they are well
- Wash your hands frequently
- Drink plenty of fluids, especially water
- Get adequate rest

National Vaccine Information Center
http://www.nvic.org/Default.htm

Flu? What flu? Chiropractors buck the trend by warning against flu shots

A survey of websites launched by licensed chiropractors reveal industry wide stance opposing flu vaccine.

BY DAVID KNOWLES / NEW YORK DAILY NEWS

THURSDAY, JANUARY 17, 2013, 1:21 PM

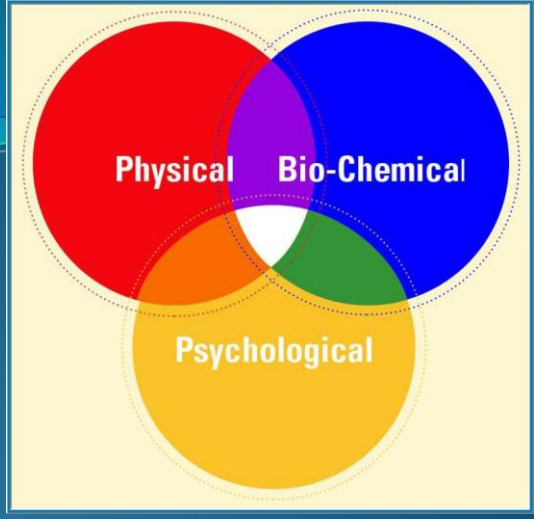
http://www.nydailynews.com/chiropractors-buck-trend-warning-flu-shots-article-1.1241886

Vaccination Policy

"Since the scientific community acknowledges that the use of vaccines is not without risk, the American Chiropractic Association supports each individual's right to freedom of choice in his/her own health care based on an informed awareness of the benefits and possible adverse effects of vaccination," the organization's policy states. "The ACA is supportive of a conscience clause or waiver in compulsory vaccination laws thereby maintaining an individual's right to freedom of choice in health care matters and providing an alternative elective course of action regarding vaccination."

American Chiropractic Association

Alternative Strategies



- Eat a wholesome diet rich in vitamins and minerals, especially foods containing vitamin D (such as cod liver oil)
- Spend a few minutes a day in sunlight to help your body make and store vitamin D.
- Consider ***chiropractic adjustments***, homeopathic remedies and other natural options for healing and maintaining health.
- Exercise regularly when you are well.
- Lower stress through meditation and other healthy lifestyle changes.

Wash Your Hands

Influenza Other Respi Viruses. 2012 Oct 8. doi: 10.1111/irv.12015. [Epub ahead of print]

Hand hygiene to reduce community transmission of influenza and acute respiratory tract infection: a systematic review.

Warren-Gash C, Fragaszy E, Hayward AC.

UCL Centre for Infectious Disease Epidemiology, Research Department of Infection & Population Health, Royal Free Hospital, London, UK. Department of Infectious Disease Epidemiology, Faculty of Epidemiology & Population Health, London School of Hygiene & Tropical Medicine, London, UK.

Abstract

Please cite this paper as: Warren-Gash et al. (2012) Hand hygiene to reduce community transmission of influenza and acute respiratory tract infection: a systematic review. Influenza and Other Respiratory Viruses DOI: 10.1111/irv.12015. Hand hygiene may be associated with modest protection against some acute respiratory tract infections, but its specific role in influenza transmission in different settings is unclear. We aimed to review evidence that improving hand hygiene reduces primary and secondary transmission of (i) influenza and (ii) acute respiratory tract infections in community settings. We searched Medline, Embase, Global Health and Cochrane databases up to 13 February 2012 for reports in any language of original research investigating the effect of hand hygiene on influenza or acute respiratory tract infection where aetiology was unspecified in community settings including institutions such as schools, and domestic residences. Data were presented and quality rated across outcomes according to the Grading of Recommendations Assessment, Development and Evaluation system. Sixteen articles met inclusion criteria. There was moderate to low-quality evidence of a reduction in both influenza and respiratory tract infection with hand hygiene interventions in schools, greatest in a lower-middle-income setting. There was high-quality evidence of a small reduction in respiratory infection in childcare settings. There was high-quality evidence for a large reduction in respiratory infection with a hand hygiene intervention in squatter settlements in a low-income setting. There was moderate- to high-quality evidence of no effect on secondary transmission of influenza in households that had already experienced an index case. While hand hygiene interventions have potential to reduce transmission of influenza and acute respiratory tract infections, their effectiveness varies depending on setting, context and compliance.

http://www.ncbi.nlm.nih.gov/pubmed/23043518

Chiropractic Care

Notice the recommendation by the NVIC that people add chiropractic to their strategy for warding off and fighting the flu and its effects this season.

Chiropractic Care

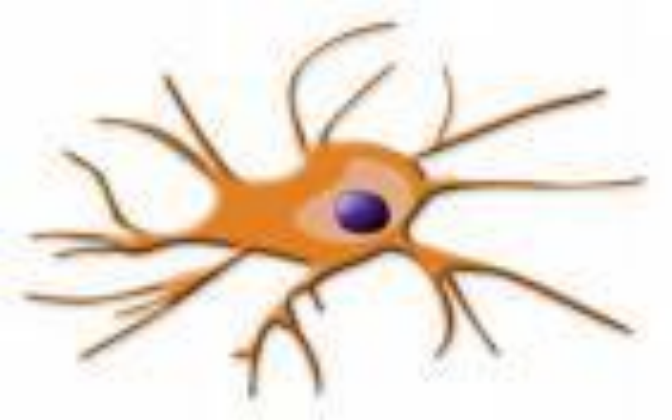
Spinal adjustments can have a positive effect on immune function, according to a growing number of researchers who are exploring the common denominators in disease processes, and the role of the nervous, immune, and hormonal systems in the development of immune related illnesses.

Chiropractic Care

Chiropractic corrects spinal abnormalities called vertebral subluxations that result in interference of the nervous system by affecting the function of nerves.

Since the nervous system controls all functions of the body -- including the immune system -- chiropractic care can have a positive effect on immune function.

Chiropractic Care



According to Dr. Christopher Kent, a leading chiropractic researcher:

"Contemporary research is beginning to shed light on the neurobiological mechanisms which may explain the outstanding clinical results chiropractors have experienced when managing patients with viral and infectious diseases."

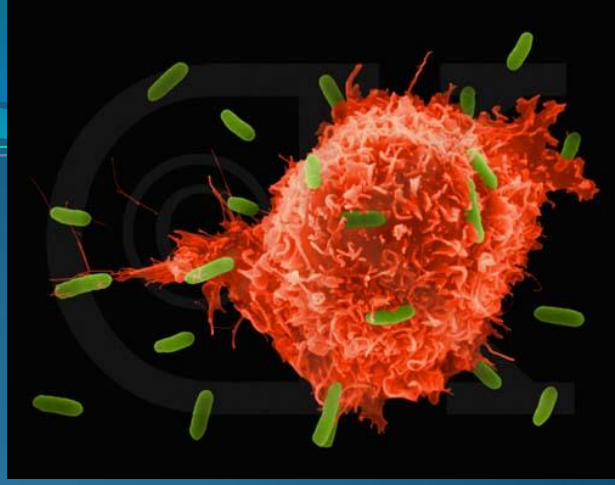
Chiropractic Care

A comprehensive review of the research literature reveals the current understanding that the brain and immune system are the two major adaptive systems in the body.

During an immune response, the brain and the immune system 'talk to each other' and this process is essential for maintaining homeostasis or balance in the body.

Elenkov IJ, Wilder RL, Chrousos GP, Vizi ES. The sympathetic nerve, an integrative interface between two supersystems: the brain and the immune system. Pharmacol Rev. 2000 Dec;52(4):595-638.

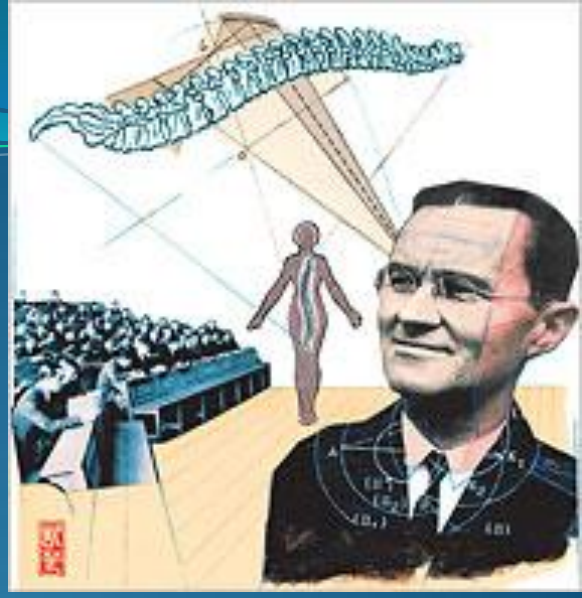
Chiropractic Care



Since its inception, chiropractic has asserted that viruses and microbes don't threaten us all equally and that a healthy immune system easily repels most invaders.

The immune system protects us from the flu, as well as any other infectious disease, and strives to get us well again when we do fall ill. Our immune system, like every other system in the body, is coordinated and controlled by the nervous system.

Chiropractic Lifestyle



Chiropractors are also aware of the importance of positive health life style practices (rest, drinking ample quantities of water, diet, exercise, proper food choices, use of high potency multivitamins and minerals, and stress reduction approaches) that can also positively influence the nervous system and immune response.

Chiropractic Lifestyle

A large study conducted by Robert Blanks Ph.D and his colleagues from the University of California studied nearly 3000 individuals undergoing chiropractic care.

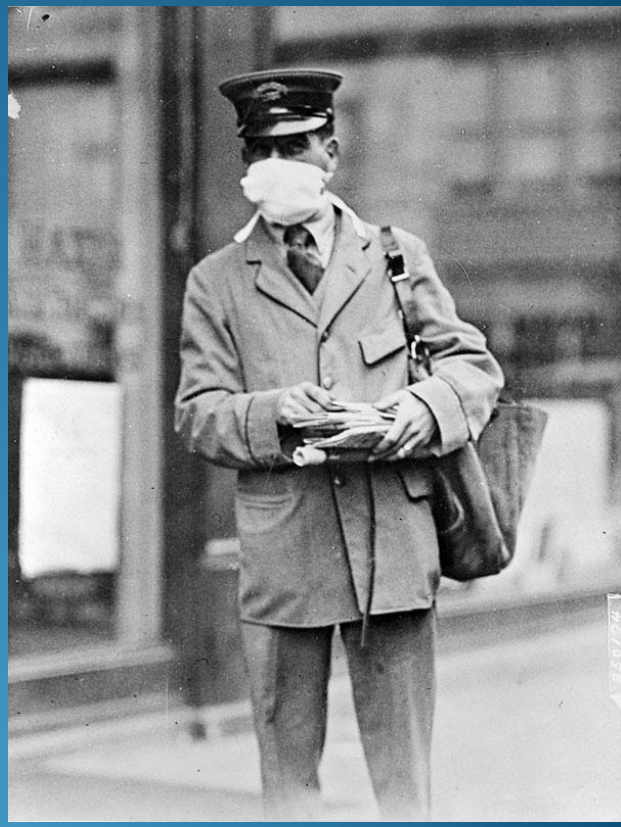
These individuals reported an average overall improvement, ranging from 7-28%, in a battery of physical symptoms including stiffness/lack of flexibility in the spine, physical pain, fatigue, **incidence of colds and flu**, headaches, menstrual discomfort, gastrointestinal disorders, allergies, dizziness and falls.

Blanks et al., 1997, Journal of Vertebral Subluxation Research

Chiropractic & Flu

Chiropractors helping patients battle the flu is not a new occurrence.

During the 1917-18 influenza epidemic, which brought death and fear to many Americans, it has been estimated that 20 million people died throughout the world, including about 500,000 Americans.



Chiropractic & Flu

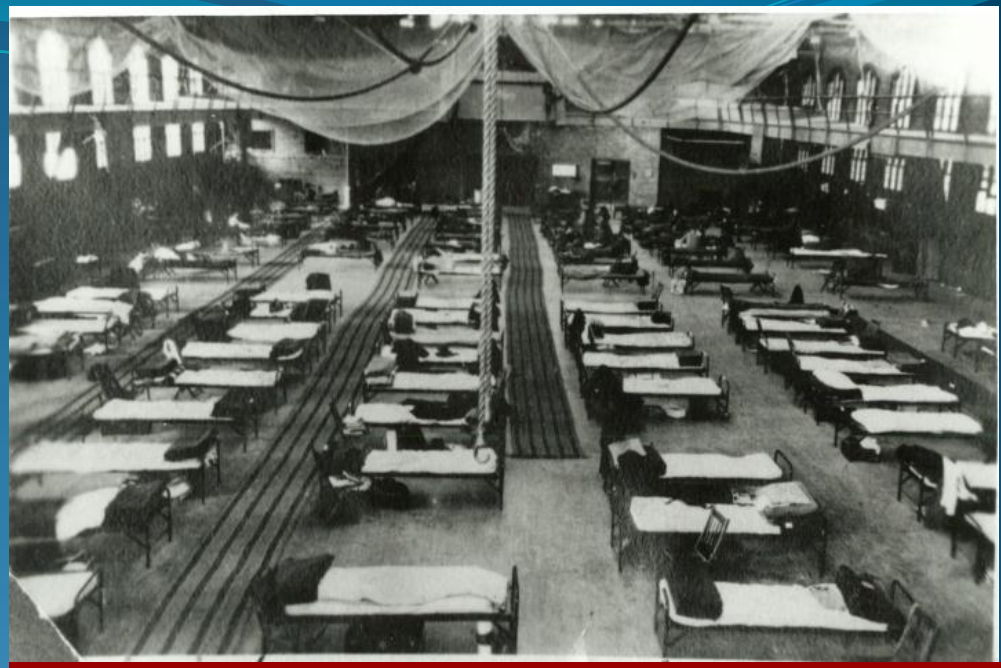
It was chiropractic's success in caring for flu victims that led to the profession's licensure in many states.

Chiropractic & Flu

Researchers reported that in Davenport, Iowa, out of the 93,590 patients treated by medical doctors, there were 6,116 deaths -- a loss of one patient out of every 15.

Chiropractors at the Palmer School of Chiropractic adjusted 1,635 cases, with only one death.

Outside Davenport, chiropractors in Iowa cared for 4,735 cases with only six deaths -- one out of 866.



Iowa State gymnasium, converted into hospital , (canvas partitions were used later between sections) 1918 flu epidemic

Rhodes WR: "The Official History of Chiropractic in Texas." Texas Chiropractic Association. Austin, TX. 1978.

"Chiropractic Statistics." The Chiropractic Research and Review Service. Burton Shields Press. Indianapolis, IN. 1925.

Chiropractic & Flu

During the same epidemic, in Oklahoma, out of 3,490 flu patients under chiropractic care, there were only seven deaths.

Furthermore, chiropractors were called in 233 cases given up as lost after medical treatment, and reportedly saved all but 25

1. Rhodes WR: "The Official History of Chiropractic in Texas." Texas Chiropractic Association. Austin, TX. 1978.
2. "Chiropractic Statistics." The Chiropractic Research and Review Service. Burton Shields Press. Indianapolis, IN. 1925.

Chiropractic & Flu

In another report covering 4,193 cases by 213 chiropractors 4,104 showed complete recovery.

1. Rhodes WR: "The Official History of Chiropractic in Texas." Texas Chiropractic Association. Austin, TX. 1978.
2. "Chiropractic Statistics." The Chiropractic Research and Review Service. Burton Shields Press. Indianapolis, IN. 1925.

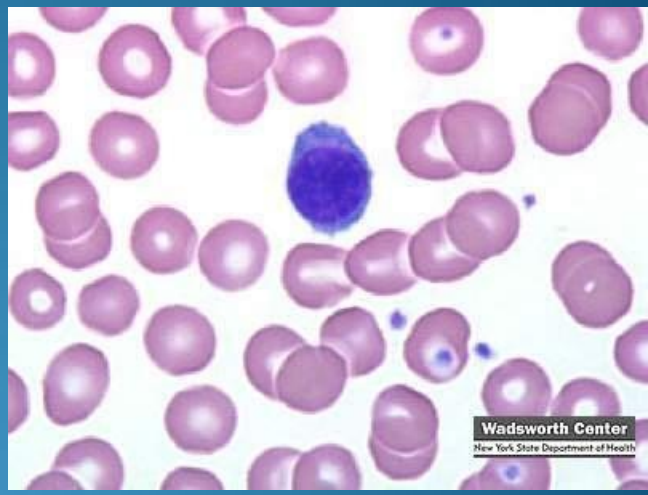
Chiropractic & Immunity

These results are not so surprising given what we now know about the interaction between the nervous system and the immune system.

Through research we know that chiropractic has beneficial effects on immunoglobulins, B-lymphocytes (white blood cells), pulmonary function and other immune system processes.

Chiropractic & Immunity

One series of studies, conducted by Patricia Brennan Ph.D and her team, found that when a chiropractic adjustment was applied to the middle back, the response of white blood cells taken from blood collected 15 minutes after the manipulation was significantly higher than blood collected 15 minutes before and 30 and 45 minutes after the chiropractic procedure.



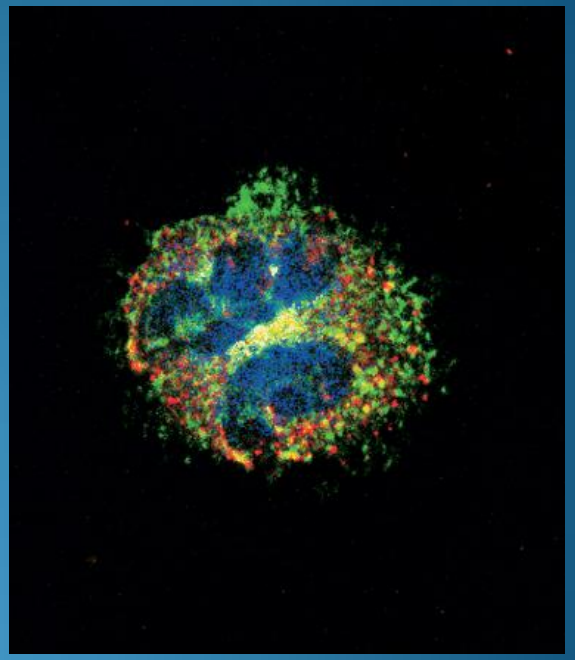
Brennan et al: Enhanced neutrophil respiratory burst as a biological marker for manipulation forces. J Manipulative Physiol Ther; 15(2)

Brennan PC, Kokjohn K, Kaltinger CJ, Lohr GE, Glendening C, Hondras MA, McGregor M, Triano JJ "Enhanced Phagocytic Cell Respiratory Burst Induced by Spinal Manipulation: Potential Role of Substance P" J Manipulative Physiol Ther 1991; 14(7): 399-407.

Chiropractic & Immunity

Brennan's research demonstrated an "enhanced respiratory burst" following the chiropractic adjustment.

This "burst" is needed for our immune cells to destroy invading viruses and bacteria



Chiropractic & Immunity

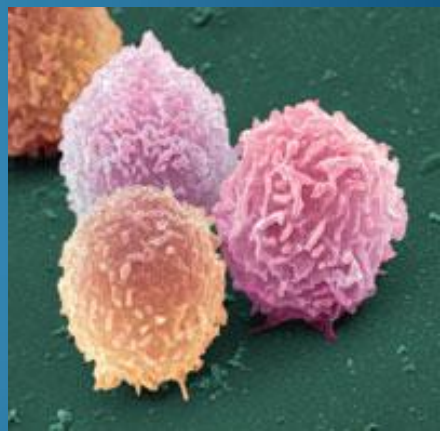
Another study of HIV positive patients was conducted to study the effects of specific chiropractic adjustments to correct vertebral subluxations in the upper neck on their immune systems.

Selano, Grostic et al: The effects of specific upper cervical adjustments on the CD4 counts of HIV positive patients. CRJ. Vol 3. # 1. 1994.

Chiropractic & Immunity

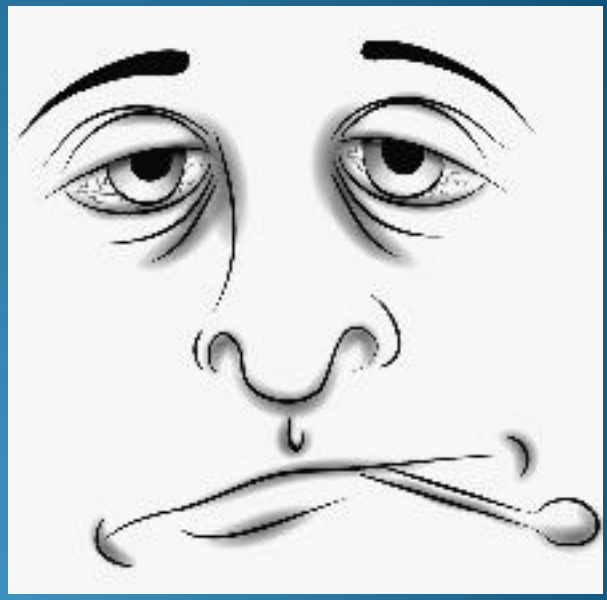
Over the six-month period of the study, the group that did not receive chiropractic care experienced a 7.96% decrease in CD4 cell counts.

The group that received chiropractic adjustments experienced a 48% increase in CD4 cell counts over the same period.



Chiropractic & Immunity

In the large study of nearly 3000 people talked about previously, physical symptoms including stiffness/lack of flexibility in the spine, physical pain, fatigue, incidence of colds and flu, headaches, menstrual discomfort, gastrointestinal disorders, allergies, dizziness and falls all improved.



Most significantly, the incidence of colds and flu were reduced by an average of 15% in this large population who were undergoing regular chiropractic care.

Blanks et al., 1997, Journal of Vertebral Subluxation Research

Immunity and Nerves

The relationship between the nervous system and the immune system was first reported by Researchers in 1993 in the journal Nature with The New York Times reported on it the day it was published:

"Scientists have found the first evidence of an anatomical connection between the nervous system and the immune system. Nerve cell endings in the skin and white blood cells of the immune system are in intimate contact, and chemicals secreted by the nerves can shut down immune system cells nearby."

J. Hosoi G. F. Murphy C. L. Egan†, E. A. Lerner, S. Grabbe, A. Asahina & R. D. Granstein. Regulation of Langerhans cell function by nerves containing calcitonin gene-related peptide. Nature 363, 159-163 (13 May 1993)

Kolata G. Nerve Cells Tied to Immune System. New York Times. May 13, 1993

Do it Today

Any person concerned about the upcoming flu season should add chiropractic to their list of things to do to remove interference to their nervous system, enhance their immune function and give their body every extra bit of security it needs.