ON GUARD – GARDASIL

A critical look at a new and controversial vaccine

by

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Despite vocal opposition from some religious groups and worried parents, on February 2, 2007, the Republican governor of Texas Rick Perry signed an executive order requiring all 11- and 12-year-old Texas schoolgirls to be vaccinated with Gardasil. This is a newly approved vaccine, manufactured by the pharmaceutical giant, Merck, Inc. It is designed to prevent infection with four strains of the human papillomavirus (HPV): types 6 and 11, which cause genital warts, and types 16 and 18, which are among the 30 or more strains that are capable of causing cervical cancer.

By signing this executive order, Gov. Perry bypassed the Texas legislature, and thereby avoided an open political debate on this controversial issue. Grassroots opposition in the Texas legislature may yet reverse this unilateral decision (see below). But at this writing the order stands: any girl who wants to enter sixth grade next September in the Lone Star State will have to show proof that she has received three Gardasil injections before school begins.

According to a front-page article in the *New York Times*, at least 31 other states are currently debating bills that would require Gardasil vaccination; appropriate funds for such vaccination; or require information on HPV to be distributed to children and their parents (Saul 2007). Eighteen of these states are considering legislative action mandating Gardasil vaccination. Eventually, if the drug's advocates have their way, the entire female population of the US – around 150 million girls and women – will be compulsorily vaccinated. Vaccination of the male population may then follow.

HPV is a sexually transmitted virus that is nearly universal in the human population. Unlike the H5N1 virus that causes avian influenza (bird flu), it is not a potentially airborne infection that threatens to tear through our communities, causing disease and death. It is more of a risk factor for disease than a disease-causing agent in itself. Why, then, such an urgent need to vaccinate at least half the entire population? Has there been some unexpected outbreak of HPV-related illnesses? Why should vaccination against cervical cancer suddenly be made mandatory? After all, cervical cancer is not a contagious illness that can be passed along by casual contact. It is a slowly progressing disease process, which is readily preventable by current means, so that no one needs to die of it.

The main scientific rationale for inoculating large segments of a susceptible population is to confer what scientists call "herd immunity." When a sufficiently high proportion of an at-risk population has been inoculated, this confers a degree of resistance to the spread of the infectious agent, thereby protecting the whole population by reducing the likelihood

of an epidemic. The effectiveness of herd immunity depends, among other things, on maintaining a high vaccination rate in the at-risk population and ensuring that vaccinations are kept current.

But in the case of HPV, herd immunity cannot be achieved without also inoculating the entire male population, since males constitute the primary reservoir of the virus and are the source of continual re-infection for females – and also sometimes (in the case of homosexual males) for infecting one another. In addition, one would have to inoculate the 50 million or more people who visit the US each year (tinet.ida.doc.gov), as well as the 11-12 million illegal immigrants who are often beyond the reach of the education system (pewhispanic.org). This is a nearly impossible task. Therefore, since the acquisition of herd immunity cannot be a realistic goal, there is no compelling medical justification for inoculating half the population with Gardasil.

The goal of eliminating cervical cancer – and the other illnesses with which these viruses are associated – is certainly laudable (although in the case of cervical cancer it is, in fact, attainable by means other than vaccination). But there remain many unanswered questions concerning Gardasil, especially those pertaining to its safety, cost and effectiveness. In this report I discuss the reasons why I believe that the precipitous drive to vaccinate every girl child in America has more to do with generating profit for Merck, the manufacturer of the vaccine, rather than with any genuine drive to reduce the number of women contracting cervical cancer.

First, some facts.

Human papillomavirus (HPV) may be relatively unfamiliar to most people, but it is actually one of the most common viruses to affect human beings and is nearly ubiquitous in the human species. There are more than 100 different strains and at least 30 of these are transmitted through sexual activity. The virus can be spread via sexual intercourse, through any genital contact between men and women, or through homosexual activity of either sex.

A February 2007 study from the Centers for Disease Control and Prevention (CDC) showed that just over one in four US women aged 14 through 59 are infected with some form of the human papillomavirus (Dunne 2007). In fact, almost *80 percent* of American women become infected with HPV by the time they reach 50 years of age. This certainly sounds scary. However, it is crucial to understand that the vast majority of these infections are with harmless strains and most women will *never* experience any symptoms, much less succumb to cervical cancer or any other serious disease, as a result of having been exposed to any strain of this virus.

In fact, although there are more than 20 oncogenic strains (i.e., strains which have the potential to cause cancer), few women are actually infected with these. According to the same February 2007 CDC study just cited, infection with HPV types 6, 11, 16, or 18 (the types prevented by Gardasil) were detected in just 3.4 percent of the study participants. Of these four, types 16 and 18 are the most carcinogenic. But they were found to be

relatively rare in the American population. In fact, the CDC study put prevalence of each of the four relevant strains of HPV – 6, 11, 16 and 18 - at under 1.6 percent.

Aside from the two carcinogenic strains against which Gardasil is designed to be active, HPV strains 31, 33 and 45, and at least 9 others, are also strongly associated with increased cancer risk. Gardasil does not claim to protect against these, nor does it protect against the remaining strains that are also believed to be associated with cancer.

The so-called 'viral ecology' of HPV infection is also unclear: no one knows whether, by preventing infection with the two most currently prominent oncogenic strains, HPV 16 and 18, we may inadvertently be creating an opportunity for one or more of the remaining 18 or so oncogenic strains to take up the slack. The European Medicines Agency report on Gardasil rather fleetingly mentions that the incidence of HPV disease due to non-vaccine types of the virus was 5.5 percent *higher* overall in the vaccinated group compared to those receiving placebo (EMA 2006)**.** This may be an early warning signal that other strains of HPV (including other carcinogenic strains) are already moving into the ecological niche left vacant as HPV 16 and 18 are suppressed.

To reiterate: while HPV is certainly widespread in the population, the vast majority of people who contract it, to quote the Centers for Disease Control, "will not have any symptoms and will clear the infection on their own" (CDC 2004). In fact, one surprising finding from the February 2007 CDC study was that the strains of the virus that are most closely linked to cervical cancer are found in fewer than one in 30 women.

An infection that almost always causes no symptoms and clears up on its own is hardly a cause for alarm, still less for a campaign of mandatory vaccination aimed at schoolchildren.

For a small minority of American women, however, HPV infection, left undetected and untreated, may cause a number of illnesses, the most serious of which is cervical cancer. It is said that HPV strains 16 and 18 cause up to 80 percent of all cervical cancer. This may well be true. But a more relevant question is, why do so *few* women contract this disease, when millions are able to successfully fight it off? Which women are most susceptible to long-term infection with the oncogenic strains of this virus? Are there are other, less drastic ways of reducing the risk of cervical cancer in susceptible women, short of inoculating the entire female population?

There are answers to these questions. Indeed it turns out that science has already discovered effective ways of identifying those at greatest risk and detecting the disease in its early pre-malignant phases. In fact, so effective are current screening tests – notably the Pap test (see below) – that ***cervical cancer incidence has decreased by 80 percent in the US over the past few decades,*** and continues to decline steadily. This is largely attributable to the effectiveness of the Pap test, one of the great success stories in public health. Simply by fostering sensible health habits, and increasing the access of poor women to relevant information about Pap tests, we could all but eliminate cervical

cancer, at a reasonable cost to society, with attendant side benefits, and certainly without recourse to mass vaccination with Gardasil.

HPV, Cervical Cancer and Gardasil

The American Cancer Society (ACS) estimates that there will be 11,150 new cases of cervical cancer and 3,670 deaths in the US in 2007. If Gardasil is as effective as the manufacturer claims, it will prevent up to 80 percent of these cases.

But the story does not end there. Fortunately, cervical cancer usually has a very long latency period. While it is necessary to be vigilant against this disease, its progression is typically so slow that there is ample time to discover and cure it. Over 3,000 deaths may seem like a lot. But consider how rare this disease is, compared to the tens of millions of women who are infected each year with HPV.

By some reports there are as many as 24 million US women infected with HPV at any given time (NPIN 2007). But out of these 24 million women, as we have said, only a tiny fraction (maybe one in several thousand) actually goes on to develop cervical cancer as a result of this infection, and typically this process is extremely slow. It may take *decades* for an HPV-infected woman to develop an outright cervical malignancy, and oftentimes the process spontaneously reverses itself and the woman's immune system clears up the infection on its own. In its public relations campaign, Merck has tried to depict HPV as a major threat to women's health (see below). But getting worried (much less panicked) about the mere presence of HPV is totally misguided, since almost all of us have it, yet few of us will ever develop a disease on account of it.

What happens when an infection with HPV does result in pre-malignant changes to the cervix? These precursor lesions, termed epithelial dysplasia, cervical intraepithelial neoplasia (CIN) and/or carcinoma in situ (CIS), are not true malignancies. Rather, they are warning signs that the cervical tissues are not perfectly normal and that cancer may ultimately develop there. The important point is that such conditions are easily and routinely treated. The US National Cancer Institute Web site (www.cancer.gov) states: "Properly treated, tumor control of in situ cervical carcinoma should be nearly 100 percent."

In other words, there are few things in oncology as certain as the cure of pre-malignant changes in the cervix!

How much time does a woman have between the detection of such pre-malignant changes (usually found as a result of routine screening) and the appearance of actual cancer? According to the US National Library of Medicine's Health Services/Technology Assessment text:

> "Generally, the progression to invasive cancer follows a slow, predictable pattern…. 30 percent to 70 percent of untreated patients with cervical

> intraepithelial neoplasia (CIN) will develop invasive carcinoma in 10-12 years" (NLM 2007).

Thus, typically, cervical cancer has at least a decade-long latency period. During this 10- or 12 year time span a woman would normally have three consecutive Pap tests (see below). Since the false negative rate of the modern day Pap test is extremely low, the odds of this pre-malignant condition not being detected by a series of consecutive tests is very small. There is near-certainty that the first Pap test, not to mention a second or third one, would detect this condition with more than sufficient time to successfully prevent the development of an outright malignancy.

In a small minority of CIN patients (about 10 percent of the total, according to the NLM Health Services/Technology Assessment text), lesions do progress to invasive carcinoma in under one year. However, even these more aggressive tumors are eminently treatable. What is the cure rate for such tumors? Historically, the five-year disease-free survival rate for all stage I cervical cancers has been 92 percent (ACS 2007). But if the tumor is discovered in stage IA, then the results are even better. According to the University of Florida Shands Cancer Center Web site:

> "Approximately 95% of patients with stage IA cervical cancer survive without evidence of cancer recurrence 10 years after surgery or radiation therapy. Less than 5 percent of patients with stage IA cervical cancer experience recurrence."

And even such recurrences can often be treated successfully. So the actual number of women who would need to deal with advanced cervical cancer after being properly screened is a tiny minority of a tiny minority – again, hardly cause enough to inoculate the entire population.

The Pap Test

For the past half century or so, cervical cancer incidence and mortality have been in a steep and steady decline. There is perhaps no other cancer whose natural history is so well understood and whose diagnosis and treatment has been so thoroughly mastered. One only wishes that the other major killers, such as cancers of the lung, breast, colon and prostate, could be controlled in a similar manner and with an equal degree of success.

The conquest of cervical cancer began decades ago with the introduction of the Pap test, named after its inventor, Dr. George Papanicoulau (1883-1962). Papanicoulau is one of the true medical heroes of the 20th century. Born in Greece, for most of his career he was a researcher at Cornell Medical Center in New York. He first proposed a version of his test in the 1920s, but his medical colleagues were skeptical. Faced with stiff opposition and even mockery from his colleagues, it took 30 years for his ideas to eventually prevail. The Pap test became so deservedly famous that its inventor was featured on a 1978 commemorative postage stamp in his adopted country, the US, and on the 10,000 drachma bill in Greece, his native land (below).

The Pap test is basically a microscopic examination of cells that have been shed (exfoliated) by the uterine cervix. Abnormal or pre-malignant cells show up years before any true malignancy has had a chance to develop. While early Pap testing was plagued by a relatively high rate of both false positive and false negative results, modern Pap tests have overcome these earlier shortcomings and have become extremely accurate.

Since the mid-1990s, in fact, the Pap test has been improved by putting the sample into a vial containing a liquid medium that preserves the cells. (The two best known of these tests are called Sure-Path and Thin-Prep.) The sample is processed in a laboratory into a cell thin-layer, then stained and examined by light microscopy. The same liquid sample can also conveniently be used to test for the presence of HPV. (HPV testing can be added to the Pap smear in women over the age of 30 to reduce the risk of false negatives even further.) In this way, the sensitivity of the Pap smear has been improved to nearly 100 percent.

So, let me reiterate this crucial point: through regular cervical Pap smears, taken according to a predetermined schedule (most women are on a three-year cycle), ***almost every case of cervical cancer can be detected in its precancerous phase,*** and appropriate treatment can then be initiated. For the relatively few women who slip through this screening regimen, conventional treatment of early-stage cervical cancer is still between 95 and 100 percent effective. Thus, armed with the Pap test, and a few other simple protective measures (which I shall describe below), no woman need fear dying of cervical cancer. Even without Gardasil, if a woman has adequate health care, there is no reason to fear this disease, provided that proper preventive and diagnostic procedures are followed.

Life Style Issues

In addition to having regular Pap tests, there are several other things that a woman can do to reduce her risk of ever contracting long-term HPV infections, cervical dysplasia, or cervical cancer. Some of these relate to sexual habits. Short of life-long celibacy, it is difficult to avoid HPV entirely. But women (or men) who want to diminish the risk of getting HPV infections should avoid:

- Having sex at an early age
- Having many sexual partners
- Having a partner who has had many sex partners
- Having sex with uncircumcised males

The use of condoms as a way of preventing HPV has been controversial. Some religious conservatives have argued against condom use, claiming that only sexual abstinence can protect women against HPV infection. But a 2006 study, published in the *New England Journal of Medicine*, found that consistent use of condoms could cut the risk of male-to-female transmission of HPV by 70 percent. On the other hand, this study gave no comfort to the pro-vaccination side of this debate, since the implication was that the need for vaccination against HPV had been overstated, and that there was an alternative way – i.e., condoms – of preventing most HPV infections.[1]

There are other life style changes that may also reduce the risk of cervical cancer. Cigarette smoking is a major cofactor in the development of this cancer, as in many other diseases. Tobacco byproducts decrease the ability of the cervical tissue to defend itself against HPV infection. In a population-based study in Utah, women who smoked had a 3.42 times greater chance of developing cervical cancer than did nonsmokers. Nearly identical risk was found among those who were exposed to the smoke of others for three or more hours per day – so-called passive smokers (Slattery 1989). Thus, in addition to reducing the risk of lung cancer and heart disease, among other maladies, smoking cessation is a way of reducing one's chance of developing cervical cancer.

Diet also plays a role. According to a study published in the journal *Cancer Epidemiology, Biomarkers & Prevention*, women whose diets were high in vegetables were 50+ percent less likely to have long-lasting HPV infections than women with low vegetable intake. They were therefore less likely to develop cervical cancer. In this study, Dr. Rebecca L. Sedjo and her colleagues at the University of Arizona found that in addition to high vegetable intake, the presence of one particular nutrient, lycopene – found primarily in tomatoes, watermelon and pink grapefruit – guarded against long-lasting HPV infections (Sedjo 2002).

Finally, there is a definite link between one's immune status and the odds of developing precancerous lesions following infection with the HPV virus. A leading microbiology textbook states:

> "The virus is ubiquitous….[but] precancerous lesions and cervical cancer occur in immunosuppressed patients" (Baron 1996). In one rare disease (epidermodysplasia verruciformis) that is associated with HPV infection, it has been shown that patients' cell-mediated immunity is significantly impaired.
>
> "The exact role of the host immune response in patients with CIN and cervical cancer is not clear," the textbook authors continue, "but the immune system could be involved in the disease process and immunosuppression appears to lead to an increase in cervical cancer and CIN" (Baron, 1996, p. 617).

[1] The condom should cover the entire shaft of the penis, since the virus can be present in any part of that organ.

Similarly, suppression of the immune system by the human immunodeficiency virus (HIV) is an important risk factor for cervical cancer, because it renders the cells lining the lower genital tract more readily infected by the cancer-inducing types of HPV (Stentella et al 1998).

It is well-known that long term use of corticosteroids, which are commonly prescribed for the treatment of asthma and autoimmune diseases, can also lead to immunosuppression. This increases the risk of cervical infections. Women may also increase their risk of CIN or outright cervical cancer through the use of recreational drugs, alcohol and, as mentioned earlier, tobacco products (Ylitalo et al 1999).

There are certain good-sense things that women (and men) can do to keep their immune systems functioning well. Positive ways to improve immunity include ingesting certain foods and dietary supplements. Here, I will mention just one example among many - shiitake mushrooms (*Lentinus edodes*). Chinese scientists have shown that the polysaccharide L-II, isolated and purified from the fruiting body of shiitake, significantly increased almost every parameter of normal immunity, and was capable of shrinking sarcomas in experimental animals. These researchers concluded that "the antitumor activity of the polysaccharide L-II on mice-transplanted sarcoma 180 was mediated by immunomodulation in inducing T-cells and macrophage-dependent immune system responses" (Zheng 2005).

Needless to say, the topic of immune modulation and cancer is a huge one, but the basic principle seems clear: to a certain extent, the health of the immune system, and its ability to ward off potentially dangerous viruses, is amenable to change by life-style factors.

If a woman wants to avoid cervical cancer she can reduce her risk almost to zero by the following healthy and prudent life style measures:

- Follow standard medical guidelines on having periodic Pap tests. Have your doctors supplement these with tests for HPV, when necessary.
- Practice safe sex: avoid promiscuity and use condoms, if appropriate.
- Do not smoke and do not allow yourself to be exposed to passive smoke;
- Eat a diet that is rich in nutrient-dense vegetables, especially tomatoes and other lycopene-containing produce.
- If necessary, take supplements or special foods such as Asian mushrooms to boost immunity.

While nothing in life is certain, taken together these should cut the risk of contracting long-lasting HPV infections and/or invasive cervical cancer significantly. If cervical cancer by some chance does occur, prompt treatment can almost always arrest this disease completely. If every woman in America followed these simple and inexpensive guidelines death from cervical cancer would be exceedingly rare – and certainly there would be no need to inoculate every schoolgirl in order to prevent it.

HPV As a Risk Factor for Other Diseases

But, it will be argued, Gardasil does other things. It also prevents up to 90 percent of the genital warts caused by HPV. Genital warts are highly contagious. The National Institute of Allergy and Infectious Diseases Web site states that "about two-thirds of people who have sexual contact with a partner with genital warts will develop warts, usually within 3 months of contact" (NIAID 2006). While genital warts are never themselves fatal, they are a significant and fairly common venereal disease. They particularly occur in the 20-24 year age group. It is said that there has been a fourfold increase in the past 20 years, although it is not known if this increase is due, in part, to a heightened awareness and willingness on the part of young people to present for treatment.

Genital warts, like other HPV infections, seem related to one's immunological status. NIAID's Web site also states that they "often disappear even without treatment" (NIAID 2006). A Finnish study followed 532 women with HPV infections for 45 months. They found that even among those with pre-malignant lesions the rate of spontaneous remissions was 41.8 percent (Kataja 1989).

In a randomized trial in Manchester, UK, researchers found that even in women who had precancerous conditions "spontaneous regression of cytological abnormality occurred in 26 per cent…of untreated women." The authors concluded "the substantial rate of spontaneous regression suggests…that intervention is frequently unnecessary" (Woodman 1993).

For those who do not recover spontaneously, there are various treatments. Surgical excision has a cure rate of 63 to 91 percent. Even resistant infections have been cured by subcutaneous injections of interferon-alpha-2b (the synthetic form of an immune-system component). The cure rate in one study was 52 percent (Petersen 1991).

While highly unpleasant, genital warts are a warning flag for HPV infection and bring the affected persons into the clinic for treatment, and this offers the opportunity for Pap testing and education.

Gardasil is seemingly a very effective way of preventing most cases genital warts. One wonders, though, how many parents – or state legislatures – would approve of making such a vaccine mandatory simply on the basis of its activity against sexually-transmitted warts.

It would seem more appropriate for doctors to offer Gardasil, on a voluntary basis, to young people - including possibly young men - who are becoming sexually active and seem at high risk for contracting this infection**.** In no case, however, can this vaccine substitute for safe sex practices, since there are other infections (such as HIV) in the sexual arena that are most appropriately prevented by condoms.

Anal and Penile Cancer

It is also known that HPV infection often precedes several other serious diseases, the most dangerous of which penile cancers in men and anal cancers in both sexes. Because of the risk of penile cancer, and because boys and men represent a great reservoir for the strains of HPV that cause cervical cancer, there have been calls for the universal vaccination of male Americans, as well.

"We need to move toward a paradigm where this is a universal vaccine," said Bradley Monk, MD, associate professor in gynecologic oncology at the University of California at Irvine, in an often-cited commentary in the journal *Obstetrics & Gynecology* (Reuters 2007).

The official CDC position is as follows:

> "We do not yet know if the vaccine is effective in boys or men. It is possible that vaccinating males will have health benefits for them by preventing genital warts and rare cancers, such as penile and anal cancer. It is also possible that vaccinating boys/men will have indirect health benefits for girls/women. Studies are now being done to find out if the vaccine works to prevent HPV infection and disease in males. When more information is available, this vaccine may be licensed and recommended for boys/men as well" (CDC 2006).

We should emphasize that Gardasil at this point is only being recommended for girls and women and has not been tested or approved for use in men. So even if every female in America were vaccinated, the disease could still be widespread in men, and could continue to spread via male-to-male sex.

How effective would a male Gardasil vaccine be in regard to cancer prevention? Penile cancer represents about 0.2 percent of the total number of diagnosed malignancies in men. There will be an estimated 1,280 cases of cancer of the penis and genitalia in men in 2007, with a total of 290 deaths. HPV alone may not be the only – or even the direct – cause of penile cancer: other cofactors may contribute, as they do with cervical cancer. For example, one study has shown that cigarette smoking is associated with an astonishing 4.5-fold risk of invasive penile cancer (Daling 2005).

In this same study, DNA from the HPV virus was detected in 79.8 percent of tumor specimens, and most of these (69.1 percent) specifically for HPV strain 16 (Daling 2005). Yet consider how truly rare penile cancer is. Despite the near ubiquity of HPV infection among young men, invasive penile cancer is almost unknown as a disease in the United States especially among men who do not smoke tobacco. In addition, it appears that circumcision in childhood reduces – although it does not eliminate – the risk of penile cancer later in life.[2]

[2] The experts differ, sometimes quite vehemently, on the advisability of circumcision as a cancer prevention strategy. It is beyond the scope of this report to comment on this ongoing controversy.

Another class of malignancies that has been associated with HPV is cancer of the anus, anal canal and anorectum. Together, these afflict a total of 4,650 Americans per year, 1,900 of whom are male and 2,750 are female. There are a total of 690 deaths (260 male, 430 female). The risk of anal and anorectal cancer is higher among men who have been the passive partners in homosexual sex, and the risk is higher still in men who are infected with the HIV virus and have compromised immune systems. Among non-homosexual men and among non-HIV positive women, anal cancer is another very rare disease.

The exact relationship between anal cancer and anal HPV infection remains uncertain. According to a University of California Web site:

> "What is the natural history of anal HPV infection? We don't really know since long-term studies have never been done. What is clear though is that most people don't run into trouble from HPV infection. Some people develop AIN [anal intraepithelial neoplasia – a premalignant lesion, essentially the equivalent of CIN in the uterine cervix, ed.] due to HPV infection, but most of the cases of AIN will not progress to cancer. In most people the AIN will go away by itself and they will not even have been aware of it…" (www.analcancerinfo.ucsf.edu).

This parallels the natural course of HPV infection in genital warts, with its relatively high rate of spontaneous remissions. ***So inoculating the entire population against HPV in order to prevent anal or penile cancer makes even less sense than it does as a policy to prevent cervical cancer.*** The number of cases is relatively small to begin with and the connection of HPV to anal cancer has not been established with the same certainty that it has for much cervical cancer. And of course inoculating females will not be sufficient to stop the occurrence of anal cancer among men, which is most prevalent among HIV-infected passive homosexuals.

Shortcomings of the Gardasil Clinical Trials

Like all new drugs, Gardasil was approved after a series of clinical trials. In my opinion, however, there were some serious limitations to the trials on which FDA based its approval of this new agent.

One of the key questions that must be answered when considering any proposal for mass vaccination is this: What are the long-term consequences, positive as well as negative, of such vaccination? But in the clinical trials that led to the approval of Gardasil, the follow-up of participants was relatively short: test subjects were only monitored over a period ranging from 18 months to 4 years. Thus we have no data on which to base an assumption of long-term safety.

While the immediate side effects of vaccination were minor (largely limited to tenderness at the injection site and mild fever) doctors also acknowledge that severe side effects are typically only seen in the so-called "post-marketing period," when the vaccine has been administered to a larger number of people over a protracted length of time.

Furthermore, we currently do not have any evidence concerning the *durability* of Gardasil's immunity beyond 5 years. In other words, it is simply not known how long this immunity will last. At the time of approval (2006), follow-up from the initial clinical trials had only continued for at most 5 years. It appeared that immunity was still present after this time, but the future is a question mark. A document from the European Medicines Agency (EU equivalent of the FDA) states: "However, the durability of response in this target group as well as long-term persistence of efficacy and immunogenicity requires close monitoring for 10 to 15 years. This will be critical for the decision of the optimal age to vaccinate sexually naïve subjects" (EMA 2006). In the US, however, the vaccine was rushed through with at most five years of follow up observation and a decision was made, in Texas, at least, to vaccinate all 11- and 12-year olds.

Should the vaccine's effectiveness weaken over time, as is very possible, then periodic booster shots will be necessary in order to maintain adequate levels of immunity. This, however, will lead to a concomitant increase in potential side effects and costs.

FDA approval was based on clinical trial involving just over 20,000 young women. This may seem like a considerable number. But less than 1,200 of these were under 16 years of age and few of them were at the sensitive age of puberty – typically 10-12 years in American girls – which happens to be the age suggested as the optimum target group for mandatory inoculation in Texas. (This is not coincidental, as the goal is to inoculate girls before they become sexually active.)

As mentioned above, the follow up of clinical trial participants was for 4 years at most; and only 18 months for many of the subjects, including the 1,200 in the youngest age group. ***So we have a situation in which the very group that is being singled out for mandatory vaccination is actually the group that was conspicuously under-represented in the clinical trials, and followed up for the shortest time.***

Alum Adjuvant

In the clinical trials, only 10 percent of the control group was given a genuine placebo (i.e., an inert saline solution). The remaining 90 percent were given a solution containing the same alum (aluminum hydroxide) adjuvant that is contained in Gardasil. Hence the vast majority of the control group was also exposed to the adjuvant, whose purpose is to act as an immunological "kick" in order to elicit a heightened immune response.

Both the experimental and the placebo groups complained of numerous post-vaccination events, most of which were minor. As expected, the incidence of such events was higher in the experimental (full vaccination) group, but what is more disturbing is that among the small true placebo group (i.e., those who received nothing but saline, without the alum adjuvant) the incidence of side effects and post-vaccination events was very markedly less than in the other groups. *This suggests that the vaccine itself, with its alum adjuvant, can cause side effects.*

It remains to be seen whether other, more serious side effects will develop over time. There is no reason to doubt that immediate adverse reactions to vaccination were generally minor in the clinical trials that led to approval; however, a small number of participants (9 in the Gardasil group vs. 3 in the placebo group) did develop more serious symptoms, which Merck acknowledges are potentially indicative of vaccination-triggered systemic autoimmune disease. (An autoimmune reaction is an immune response by the body against one of its own tissues.)

There were over 21,000 patients enrolled in the five Gardasil trials: 11,813 received Gardasil itself, while 9,701 received placebo. There were nine cases of arthritis in the Gardasil group, vs. 3 in the placebo group.

Potential Autoimmune Dx	**Gardasil (No. = 11, 813)**	**Placebo (No. = 9,701)**
Juvenile arthritis	1	0
Rheumatoid arthritis	2	0
Systemic lupus eryth.	0	1
Arthritis	5	2
Reactive arthritis	1	0
Total serious events	**9**	**3**

Admittedly, the absolute number of serious adverse effects is small. But when you are talking about vaccinating up to two million people, each and every year, even small numbers add up. For instance, 9 out of 11,813 represents a serious adverse event rate of just 0.076 percent. But if 2,000,000 girls are inoculated nationwide each year, as advocates propose, the number of anticipated cases of arthritis would climb to around 1,520 cases per year. Arthritis in young people can vary in intensity. But in its worst form, juvenile rheumatoid arthritis (JRA), it can be totally debilitating. Here is a description of JRA from the kidshealth.org, a Web site of the Nemours Foundation:

> "Systemic JRA affects the whole body. Symptoms include high fevers that often increase in the evenings and then may suddenly drop to normal. During the onset of fever, the child may feel very ill, appear pale, or develop a rash. The rash may suddenly disappear and then quickly appear again. The spleen and lymph nodes may also become enlarged. Eventually many of the body's joints are affected by swelling, pain, and stiffness."

Even a relatively small percentage of adverse effects like this would be a very high price to pay for the prevention of a disease that is entirely preventable by other means. Lawsuits stemming from what are perceived as after effects of the vaccine could also represent a major financial challenge to the manufacturer and a political problem for all those who mandated its use.

The Case of the Rota Vaccines

Since large-scale and long-term data are not yet available, we do not know if serious adverse events will occur. Perhaps not. Perhaps Gardasil will turn out to be as safe as its manufacturer, the FDA and almost the entire medical establishment assures us it will. However, experience teaches us to remain vigilant, if not skeptical, on this point.

It is rarely mentioned that the FDA has already had to acknowledge major problems with the safety of at least one other vaccine, after initially approving it. In the 1990s, FDA approved Wyeth's RotaShield as a vaccine against rotavirus, which can cause serious diarrhea in infants. But FDA withdrew its approval for RotaShield in 1999 after doctors established that vaccinated infants suffered an increase in the incidence of intussusception, a serious and potentially life-threatening condition in which a section of the intestine telescopes into itself, and becomes blocked or twisted.

Not to be deterred, in February 2006, FDA subsequently approved RotaTeq, another anti-rota vaccine, after 70,000 infants were enrolled in a clinical trial in which half got the active vaccine and half a placebo. Those studies showed "no significant increased risk of intussusception," according to an FDA public health notice at the time. An FDA official called the results "reassuring." But more recently – on Feb. 13, 2007 – FDA announced that 28 babies in the United States had developed the identical problem, potentially deadly intussusception, after receiving the newer RotaTeq vaccine (Hitti 2007).

Parents have been asked to notify FDA if their child suffers intussusception after receiving RotaTeq. However, the manufacturer continues to deny the association and claims that intussusception is a natural event unrelated to use of its product (Hitti 2007). The name of the manufacturer? Merck.

This doesn't prove, of course, that Merck's other vaccine, Gardasil, is harmful. But it does illustrate that vaccines are not necessarily without serious health repercussions. Such adverse effects sometimes only show up in the years after the FDA has approved an inoculating agent. When one is proposing administration of such an agent to millions of people, as in the case of Gardasil, even a relatively rare but serious side effect can have disastrous public health consequences.

Does Gardasil 'Cure' Cervical Cancer?

I wish to clear up some issues of terminology. Texas governor Perry has misleadingly – and outrageously -- spoken of Gardasil as a "cure for cancer." According to the NCI's Dictionary of Cancer Terms, a cure is a treatment that heals or restores health. But Gardasil, even according to its proponents, cannot cure any existing disease. It simply prevents infection in most cases with four potentially dangerous viruses.

Strictly speaking, Gardasil it also has *not* been shown to prevent cervical cancer: it has simply been shown to confer immunity against two strains of HPV that are associated with the development – in particular individuals – of this disease.

As mentioned, cervical cancer is generally a slow-growing tumor, and the test period for Gardasil was not a lengthy one. Therefore, it is hardly surprising that ***not a single case of cervical cancer*** occurred in the test groups during the clinical trials. In the trials, the development of genital warts and CIN were used as "stand-ins" for cervical cancer – but that is not the same thing as truly demonstrating the prevention of cervical cancer. Even the FDA has been forced to admit that.

According to the FDA:

> "The results [of the clinical trials] showed that in women [ages 16-23] who had not already been infected with the type of HPV contained in the vaccine, Gardasil was nearly 100 percent effective in preventing precancerous cervical lesions, precancerous vaginal and vulvar lesions and genital warts caused by infection with the HPV types against which the vaccine is directed" (FDA 2006).

Approval was given based on an extrapolation from conditions known only to be associated with an increased risk of cervical cancer. The best the FDA can do now is to sidestep this issue by saying: "It is *believed* that prevention of cervical precancerous lesions is *highly likely* to result in the prevention of those cancers" (FDA 2006, emphasis added). ***So, are we now mandating vaccines for half the population based on an unproven premise that is 'believed' to be 'highly likely'? Where is the science in that?***

Cervical cancer was not prevented in these trials. Cervical cancer can take decades to become clinically apparent, and does not always arise out of a pre-existing lesion. Claims for the vaccine's effectiveness are therefore based only on surrogate markers (stand-ins that indirectly reflect a patient's clinical condition), and not on any demonstration of preventing cervical cancer itself.

Neither genital warts nor CIN is the equivalent of full-blown cervical cancer: both conditions can be present, and can persist over many years without progressing to cervical cancer. Unlike cancer, these lesions often resolve spontaneously. They do not predictably and always progress to outright cancer. So the claim that the vaccine prevents cervical cancer is based on the decidedly shaky assumption that CIN is the equivalent, on a 1:1 basis, with cervical cancer.

Also, it should be noted that nearly 30 percent of the trial participants were not immunologically naïve – i.e., they showed evidence of prior exposure to, or ongoing infection with, at least one of the four strains of HPV against which Gardasil is said to be protective. Put another way, almost one-third of the trial participants had already been challenged with, and had mounted an immune response to, one or more components of the vaccine. But the 100 percent efficacy in preventing the surrogate lesions (CIN, VIN, warts, etc.) was only seen in those participants who were *not* already infected at the start of the trial and these made up only about 70 percent of the trial participants. Merck's own report on the clinical trial states "There was no clear evidence of protection from disease caused by HPV types for which subjects were PCR [polymerase chain reaction, ed]

and/or seropositive at baseline" (Merck 2006). Yet the vaccine has been approved by the FDA for administration to women between the ages of 9 and 26.

Merck's product information states: "Gardasil has not been shown to protect against the diseases caused by all HPV types and will not treat existing disease caused by the HPV types contained in the vaccine. The overall efficacy of Gardasil, described above, will depend on the baseline prevalence of HPV infection related to vaccine types in the population vaccinated and the incidence of HPV infection due to types not included in the vaccine."

If the prevalence of existing infection in the clinical trial population is representative of the prevalence in the population at large, one can reasonably assume that in the general population *only two-thirds of those vaccinated will be fully protected*. One can also reasonably expect that pre-existing exposure/infection will be even more prevalent in the age groups above those tested in the clinical trials (i.e., 25 yrs +), representing women at their most sexually active.

Therefore claims of 100 percent protection against oncogenic (cancer-causing) strains that cause 70 percent of cervical cancer apply only to about 70 percent of those likely to be vaccinated. The compounding effect of these two 70 percents certainly reduces the attractiveness of the efficacy statistics!

False Sense of Security?

One point that has been repeatedly made by critics of compulsory inoculation is that youngsters who have been vaccinated against HPV may acquire a false sense of security about their subsequent risk, and this may cause them to engage in risky sexual behavior or to forego regular Pap testing.

"If they think they are protected against one venereal disease, they may think they're protected against all venereal diseases," said Ravinder Khaira, a Sacramento pediatrician. "That's just the way some kids think" (quoted in Stein 2006).

This point of view, put forward by many skeptical parents, has been ridiculed by some scientists. UC Irvine's Dr. Bradley Monk, for instance, characterizes it as follows:

> "Just because you wear a seat belt, does that mean you drive recklessly? Or just because you give your son a tetanus shot, does that mean he is going to go out and step on a rusty nail? Of course not" (Reuters, 7/30/06).

But what is really known about effect of Gardasil vaccination of sexual behavior? This is an unknown area. It seems that both sides in this public debate are arguing more from analogy than from fact. Are there sociological studies of teenage behavior to suggest whether they are more – or less – likely to engage in risky behavior after being vaccinated? Or are people just arguing based on their preconceptions about the benefit or

harm of the product in question? (Dr. Monk, for instance, believes the entire US population, males included, should be inoculated. He has said that "To have a vaccine that prevents cancer and not use it would be one of the greatest tragedies," again conflating the prevention of HPV infections with "preventing cancer.")

Parents and pediatricians (who know children's behavior best) are certainly right that teenagers sometimes engage in very risky behavior and do not always draw logical conclusions, especially when it comes to sex. Some youngsters may in fact believe that once they have submitted to the ordeal of three consecutive Gardasil injections they have been "vaccinated against cervical cancer," and no longer need to worry about it. We simply don't know what the "takeaway message" will be for most teenagers.

When an academic expert cannot distinguish between preventing infection with four strains of HPV and preventing cervical cancer, and when the governor of Texas outrageously refers to Gardasil as a "cure for cancer," can we expect the average teenager to make such fine distinctions?

We do know that many teenagers do not have a strong grasp on possible dangers associated with sexual behavior. For instance, a 2003 Kaiser Family Foundation study of showed that one in four American adolescents and young adults contracts a sexually transmitted disease annually! This same study found that 70 percent of women ages 15 to 24 consider forms of contraception other than condoms – such as birth control pills – to be a form of "safer sex," while 80 percent consider oral sex "safer" than vaginal or anal intercourse (Kaiser 2004). (Of course, we recently had a President of the United States who didn't consider oral sex to be sex at all.) How being inoculated with Gardasil will affect girls' and women's sexual behavior seems to me to be a perfectly legitimate – in fact, urgent – area for scientific investigation.

In particular, it will be important to see if taking Gardasil has an impact on awareness of the need for Pap testing in the entire female population. Gardasil advocates cede that the need for Pap tests continues regardless of vaccination, since the vaccine only protects against 70 percent of the risk. But if a false sense of security were to develop among young people, and Gardasil were even marginally to reduce the perceived need for routine Pap tests, then the vaccine might paradoxically contribute to an *increased*, rather than a decreased, risk of cervical cancer and death.

Economic Issues

Merck charges a base price of $360 for the required series of three Gardasil injections. This is considered an unprecedentedly high charge, making it unsuitable for sale in underprivileged countries, where most of the cervical cancer occurs worldwide.

In the US (as in most countries) the associated costs of providing the injections (medical administration fees, etc.) will add approximately $100-$150 to this base price. A more realistic per-person cost would therefore be in the range of $450-$550. Since each year's

cohort of schoolgirls in the US is about 2 million, the annual national cost of administering Gardasil will therefore approach $1 billion (2,000,000 x $500). This cost will have to be shared among insurance companies, parents' out-of-pocket expenses, and various government agencies. Note that this billion dollar expenditure will have to be repeated each year, *ad infinitum*, to cover each cohort of 2 million sixth graders.

We do not yet know if Gardasil provides lifetime immunity or if it will have to be re-administered periodically, at some as yet undetermined interval. However, the possible cost of providing such booster shots has rarely been figured into the calculation of total costs. Merck acknowledges that the duration of immunity following immunization will only be discovered after a substantial number of girls and young women have been vaccinated and followed for up to a decade. However, it is to be expected that booster shots will indeed be needed. The first cohorts of vaccinated girls will therefore be the *de facto* proving ground.

Let us say, hypothetically, that the vaccine effectiveness diminishes after ten years, the way that the tetanus vaccine does. Then girls who received the vaccine initially at 11-12 years of age will have to be re-inoculated at age 21-22, and probably every ten years thereafter. Without regular booster shots, immunity will decrease, and possibly even disappear entirely, and these females will have been repeatedly inoculated in vain. Since the risk of being infected by a partner is always a possibility, booster shots will have to be administered for as long as the woman is sexually active. Being in a monogamous relationship is no guarantee that one will not be infected by one's spouse (since between half and three-quarters of the population is HPV-infected.)

So the cost of inoculating each individual woman will not be just the initial $500, but $500 plus the cost of administering each booster series over the course of a woman's sexually active lifetime. If we hypothesize that booster shots will be necessary every ten years, then each woman will need vaccinations at ages 11, 21, 31, 41, 51, and possibly beyond (depending on her sexual activity).

Thus, if Gardasil immunity does periodically wear off (as is widely anticipated), and if a course of re-inoculation is called for, the cost of protecting each woman will be closer to $2,500 than $500, and the cost of inoculating *each year's* cohort of two million females will rise from one billion to somewhere closer to five billion dollars per year, each and every year. And this will be just in the US (presuming that the cost of the vaccine remains the same).

Let us for the moment calculate on a strictly economic basis the likely cost and benefit of Gardasil inoculation. What is the potential anticancer benefit? This year in the US, 11,150 women will be diagnosed with cervical cancer and 3,670 women will die of the disease. If HPV 16 and HPV 18 do indeed cause 70 percent of the annual cases (and if no other opportunistic strains of HPV move into the ecological niche vacated by these two), we can calculate that, in the best case scenario, Gardasil will prevent 7,805 cases of cervical cancer. At the current rate of death, this will save around 2,569 lives annually.

Of course *every* life saved is an unequivocally desirable outcome. But if the cost of providing this benefit is $1 billion per year (my projected cost for each cohort-year, i.e. $500 x 2 million girls, receiving a single course of injections), then the cost of saving each life will be $389,257**.** If, however, we take into account the fact that women will possibly need at least one course of booster shots then the price for each life saved will rise accordingly to around $650,000. Should she need five inoculations over the course of a lifetime, then the cost for each life saved would be almost two million dollars ($1,946,280).

If the goal is to save women's lives, there are certainly more cost-effective ways of doing so. And, as is well known, cervical cancer deaths are almost entirely preventable. Women generally only die of the disease because they have failed to get regular Pap smears, and other diagnostic tests, which detect pre-malignant growths and cancers in their earliest and most curable stages. The universal use of such tests would obviate the need for expensive vaccines administered to girls as young as 9 years old. Providing free and easily obtainable Pap tests would also draw more underprivileged women into the health care system, which would have the additional benefit of allowing other diseases and conditions to be discovered and treated early.

Poverty Is A Barrier

Why then are women still dying of cervical cancer? In the US, it is mainly because of a deplorable lack of gynecological care for poor women, especially in minority communities. A 2001 study found that 12 percent of women aged 18-64 had not received any Pap screening within the previous 3 years. But the actual figures may be higher. The US National Cancer Institute says that "the current death rate is far higher than it should be and reflects that, even today, Pap smears are not done on approximately 33 percent of eligible women."

This is hardly surprising, as over 20 million women lack health insurance, and are far less likely to have regular Pap tests than those with private insurance. Among less affluent women of Mexican-American, Puerto Rican or Vietnamese heritage, cervical cancer is two to three times more common than among non-Hispanic white women (Chu 2001). A lack of proper educational efforts by doctors and public health officials may be responsible for this problem. A study in California and Texas found that "Vietnamese-American women have low rates of Pap test awareness, intention, and receipt….Efforts to increase Pap test utilization in this population need to be directed at encouraging physicians to offer the Pap test and empowering women to ask for the test (Nguyen 2002).

Women who get regular Pap tests almost never die of cervical cancer. The real targets of Gardasil – although this is rarely articulated – are therefore the children of the poor, especially minorities and underprivileged communities. But is Gardasil really the answer to *their* health problems? Wouldn't these young people be far better served by gaining access to a comprehensive national health insurance program, one that includes Pap tests

on a prescribed schedule? Doesn't mandating vaccination for cervical cancer evade the urgent need to implement such a system?

One has to question why there is such widespread enthusiasm for Gardasil but so little enthusiasm for bringing the benefits of Pap tests to the 33 percent of the population that currently doesn't (or cannot) avail itself of them? Could this disparity have something to do with that $4 billion in annual sales that Wall St. projects for Gardasil (Simons 2006)?

Meanwhile, in its 2006 budget the Bush Administration proposed a $1.4 million cut in funding for the National Breast and Cervical Cancer Early Detection Program, run by the Centers for Disease Control, which provides free Pap tests to uninsured, underserved and low income women. According to *New York Times* columnist Bob Herbert, this would mean that 4,000 fewer women would have access to early detection. "This makes no sense," said Herbert. "In human terms, it is cruel. From a budget standpoint, it's self-defeating," since, as is well known, prevention is more economical than cure (Herbert 2006).

The money being allocated for Gardasil could – and should – go into stepped-up cervical cancer screening for the poor. And while the Administration's health agencies pay lip service to the need for Pap tests among all Gardasil recipients, it simultaneously proposes cutting access to those tests among those who need them the most!

"We're going backwards," said Wendy Selig, vice president of legislative affairs for the American Cancer Society, in reference to these cuts. "There are so many avenues in research to combat cancer, we should be increasing the investment into research, not cutting it" (CancerCompass.com, Jan. 11, 2007).

Rush To Vaccinate

There is an unseemly political dimension to the story unfolding in Texas. Opponents of mandatory Gardasil vaccination point out that Merck employs as its lobbyist Gov. Perry's former chief of staff, Mike Toomey. According to the *Wall St. Journal*, the company has also bankrolled the influential lobbying group, Women in Government, which has been among the most vociferous advocates of compulsory Gardasil vaccination at the level of the states. Gov. Perry's present chief of staff's mother-in-law, Deirdre Delisi, also happens to be the Texas state director of Women in Government. An executive from Merck's vaccine division has also served on the board of Women in Government. The *Wall St. Journal* further revealed that that many of the bills to mandate Gardasil were introduced into several state legislatures by members of this group.[3]

In late February, 2007, the Associated Press reported that Gov. Perry's present chief of staff met with key aides about the vaccine on Oct. 16, 2006. This happened to be the

[3] See also Janice Hopkins Tanne's informative article in the British Medical Journal 2007;334:332.

same day that Merck's political action committee (PAC) donated $5,000 to the governor's campaign (Peterson 2007b).

Gov. Perry defended his Gardasil decision in the following terms:

> "When a company comes to me and says we have a cure for cancer, for me not to say, 'Please come into my office and let's hear your story for the people of the state of Texas, for young ladies who are dying of cancer,' would be the height of irresponsibility. Whether or not they contributed to my campaign, I would suggest to you, are some of those weeds that we are trying to cut our way through" (Stinebaker 2007).

Reporters, not satisfied with this rather incoherent statement, pressed Gov. Perry on the question of precisely when he had decided to issue the February 2 executive order that requires the vaccination of all sixth-grade girls. He snapped back: "I wish you all would quit splitting hairs, frankly, and get focused on 'Are we going to be working together to find the cure for cancers?' No, I can't tell you when" (Stinebaker 2007).

Gov. Perry's spokeswoman Krista Moody claimed that his order was effective until he or a successor changed it, and the Legislature had no authority to repeal it. But, according to the Associated Press, even before these campaign contributions became known, the House public health committee had voted 6-3 to override Perry's executive order and had sent the revised bill to the full House. This bill – undoing Perry's order – was cosponsored by two-thirds of the state representatives. The Texas House was not expected to take up the measure until mid-March. A repeal measure has also been introduced in the state Senate, with nearly half of that chamber cosponsoring, as well.

At this writing, Perry had not decided whether he would veto the repeal bill, when and if it reaches his desk.

"I highly respect the legislative process that we have, and so I would respectfully tell you that we will let it play its way out," said the governor. It is classic Orwellian doublespeak to say that one "respects" the legislative process while at the same time bypassing the deliberations of the state's elected representatives and issuing an executive order!

"But do you think we would be having the debate today on HPV if I had said, 'Let's pass some legislation?'" asked Perry. If I understand that last sentence, the governor seems to be admitting that he if he had gone to the legislature with a bill for mandatory Gardasil vaccination, it would have been rejected, and that his decision to issue an executive order was therefore designed specifically to avoid such a rejection. The more he speaks, the deeper the hole he digs for himself.

When Merck's connection to Women in Government became public, it led to further charges that the company was bankrolling vaccination efforts in various states (Peterson 2007a). In the face of increasing public awareness of its intense lobbying efforts, the company ostentatiously announced that it was backing down. On Feb. 21, 2007, it

declared that it would stop lobbying state legislatures to adopt Gardasil. As the *New York Times* quoted a Merck official: "Merck would continue to provide health officials and legislators with education about the vaccine and would continue to lobby for more financing for vaccines in general" (*New York Times*, Feb. 21, 2007). One would need to be extremely naïve to believe that this retrenchment was the end of the company's campaign to achieve mandatory vaccination in as many states as possible.

Enter Cervarix

Merck's "education" is likely to be as tendentious as its public service announcements about HPV. They are all part of a campaign directed towards one end – the rapid adoption of Gardasil as a compulsory vaccine for children. When Gardasil was approved by the FDA in June 2006, it was called a "potential blockbuster with no competition." But now a strong competitor has appeared on the horizon, GlaxoSmithKline (GSK) with its own vaccine, Cervarix (Smith 2006). Merck's frantic lobbying effort seems to be directed towards having Gardasil mandated for school admission in the fall of 2007, thereby shutting GSK out of this lucrative market.

According to Wall Street analysts, Merck is attempting to corner the market on the vaccine while it can, and to make its use a *fait accompli* before serious competition arrives. This is a clash of economic Titans that has nothing whatsoever to do with saving women's lives.

Religion and Science

The mainstream media has generally portrayed the struggle over Gardasil as a battle between rational scientists on the one hand, and religious conservatives on the other. Certainly some parents feel that a vaccine directed against sexually transmitted diseases (STDs) interferes with the way they raise and educate their children about sexual morality. Some feel that if they teach their children to avoid promiscuous sexual contacts, to form exclusively monogamous and heterosexual relationships, and to live a healthy lifestyle, their children will necessarily be free of the risk of sexually transmitted diseases.

This may be true for some STDs, such as syphilis or gonorrhea, but it is certainly not true for HPV. HPV is so prevalent in the human population that if one's sexual partner has ever had intercourse with another person there is a risk of infection. One would have to know the exact sexual history of one's partner in order to be sure that he or she is not infected, and people are not always truthful about their sexual histories! Furthermore, you can't always tell if a person is infected. Although HPV infection may manifest itself in the form of genital warts, it doesn't always do so, and oftentimes there are no particular signs or symptoms. There is simply no way to be certain that your son or daughter will be guarded against HPV solely by living a 'clean' life-style.

For that reason, it seems to me that this sexual morality argument is the least persuasive one being leveled against widespread use of the vaccine. Parents who rely on this argument underestimate the pervasiveness of the various forms of HPV.

More relevant is the fact that HPV infection, by itself, is not a life-threatening concern. As we have discussed, the great majority of HPV strains are harmless. Even exposure to the carcinogenic strains is not *ipso facto* a cause for alarm. The medical literature indicates that one's chance of contracting a long-lasting HPV infection can be reduced by simple life-style modifications, such as the use of condoms. And if all else fails, the necessary triennial Pap tests can and will pick up any atypical changes in cervical cells long before they can become cancerous. Such changes can be dealt with through routine measures that are nearly 100 percent effective. So the argument for the vaccine fails on scientific grounds.

Wielding Ockham's Razor

The 14th century English philosopher, William of Ockham, once proposed a principle of logic known as "Ockham's razor." This held that the explanation of any phenomenon should eliminate (or "shave away") all portions of an explanation that make no difference to the ultimate outcome. It is a very useful principle that applies to the issue of Gardasil.

1. It is universally agreed that every woman needs to have periodic gynecological exams (including Pap tests) in order to detect pre-malignant lesions, and thereby preclude the development of cervical cancer.

2. It is also universally agreed that even women who are vaccinated with Gardasil will continue to need regular Pap tests.

3. But by taking such Pap tests, the overwhelming majority of cervical cancers can be precluded by standard medical procedures. So, wielding Ockham's razor, one can eliminate the redundant Gardasil injections from the equation, since they add virtually nothing to the successful fight against cervical cancer.

The mainstream media have tended to ignore the scientific weaknesses of the argument for Gardasil and have instead promulgated the view that only religiously conservative parents, or those who habitually oppose the use of all vaccines, are resisting compulsory vaccination with Gardasil.

In fact, in deference to religious scruples, the Texas mandatory vaccination law was written to include an opt-out clause exempting people from mandatory vaccination, but *only* on religious or conscience grounds. Ironically, you cannot opt out because you reject the dubious science behind this financially-motivated promotion.

Despite the limited nature of this opt-out clause, the medical profession does not seem to want the fact that there is such a clause to become widely known. By and large, leading

doctors would rather leave parents with the impression that Gardasil is mandatory and there is nothing that can be done about it.

"A lot of us are concerned that if you allow people to opt out of one vaccine they will opt out of other vaccines that are due at the same time," said Dr. Mark Myers, executive director of the National Network for Immunization Information, a pro-vaccination group (*New York Times*, Feb. 17, 2007). So the fate of Gardasil has become tied up with the larger and even more acrimonious debate on the merits or dangers of vaccination in general.

Can We Trust Merck?

Gardasil may indeed be as safe as advertised. Only time will tell. But Merck's track record in revealing the dangerous side effects of its drugs is hardly stellar. Take, for example, Merck's infamous anti-arthritis drug, Vioxx (rofecoxib). This was another allegedly safe product, which Merck was urgently forced to withdraw on Sept. 30, 2004 – a date referred to by in a *New England Journal of Medicine* perspective piece as "a day of infamy for drug safety" (Avorn 2006).

After that withdrawal, FDA concluded that between 1999 and 2003, Vioxx had caused an astonishing 27,785 heart attacks and sudden cardiac deaths. Merck has been besieged by lawsuits stemming from the Vioxx fiasco. In one case alone, a jury fined the company $253 million in damages (Berenson 2005). J.P. Morgan Chase has estimated that Merck's liabilities for Vioxx could range from $8 to $25 billion (Smith 2005). On January 31, 2007, Merck reported that its fourth-quarter profit had plunged 58 percent despite higher revenue, mainly to cover its legal reserves for Vioxx lawsuits (SignOnSanDiego.com). This is a company in deep trouble.

To skeptics, the promotion of Gardasil is a major part of Merck's recovery strategy. One activist critic, Vera Hassner Sharav, of the Alliance for Human Research Protection (www.ahrp.org) has humorous said that the abbreviation "HPV" stands for Merck's plea to "Help Pay for Vioxx" litigation (Saul 2007).

Wall Street analysts project $4 billion in annual sales for Gardasil, which is enough to pay for over 11 million three-dose courses of Gardasil (at $360 a course). Such astronomical numbers can only be attained if Gardasil is forced on parents and children by compliant governments, in the US and abroad. After all, how many parents do you think would *volunteer* their sixth graders to be vaccinated against a disease that can be entirely prevented by a simple and effective screening test, which even those who are vaccinated will continue to require?

Propaganda Campaign

Until recently the public had never even heard of HPV, and most people could have cared less. This lack of concern led to an all-out propaganda campaign to "educate" public opinion on the topic. Last year, Merck launched a $27.4 million ad campaign called "Tell

Someone," softening up the public for the impending vaccine rollout. The "Tell Someone" HPV awareness campaign was designed to prime the US market for Gardasil's approval and subsequent launch.

In November 2006, came an even more massive print, TV and Internet ad campaign for Gardasil, this time centered around the theme, "One Less," as in "one less life affected by cervical cancer." The underlying idea was female empowerment. This campaign has been equally successful. There are now almost one million Web sites discussing human papillomavirus. HPV has been the subject of front-page articles in almost every newspaper. The *New York Times* has editorialized twice in favor of compulsory vaccination against the disease.

In effect, Merck has cast HPV almost as a new disease, one that was to all intents and purposes unknown before last year. This is a prime example of what the late medical writer Lynn Payer once described as "disease mongering" (Payer 1994). A 2006 Australian conference on this topic identified the key techniques of disease-mongering, such as (a) the expansion of the boundaries of disorders, (b) the medicalization of normal life events, and (c) the portrayal of risk factors as diseases in themselves (www.diseasemongering.org).

Merck knows how to play this game skillfully, and fear is its foremost weapon. The *New York Times* quoted Margaret McGlynn, Merck's president for vaccines, as saying: "Each and every day that a female delays getting the vaccine there is a chance she is exposed to human papillomavirus" (Saul 2007).

Technically true, but medically irrelevant. Let me reiterate that we are all exposed to up to 100 forms of HPV from birth onwards. Eighty percent of all women (and probably at least the same, if not more, men) have been exposed to more than one form of this virus and are immune to them, without ever exhibiting any clinical symptoms whatsoever. Nature inoculates us with – and against – this virus. It can be considered an inevitable part of being human and, in itself, is not to be feared. Thus, to say that each and every day that you delay getting Gardasil you are putting yourself at risk is scientific gobbledygook.

"The immune system is constantly challenged by ubiquitous viruses," said two pathologists at the University of Nebraska. "Multiple immune defenses have evolved to meet these challenges, and thus immunocompetent individuals successfully respond to infection without sequela" [a sequela is a condition following as a consequence of disease, ed.] (Purtilo 1983).

Recommendations

With the health of millions of girls and women potentially at stake, extreme caution is in order in evaluating all claims of Gardasil's safety and efficacy. It is axiomatic that corporations like Merck are in business to make money for their employees and

stockholders. Obviously, we should not reject scientific claims on those grounds alone. But Merck has a spectacularly poor record in regard to the safety of at least one of its erstwhile leading brands, Vioxx. I think this alone provides ample reason to be cautious.

Remember that 20 million Americans took Vioxx and only one quarter of one percent of them suffered serious cardiovascular damage as a result. But this statistical 'blip' created 50,000 medical catastrophes. This is the equivalent of a small American city getting wiped off the map. When huge numbers of consumers are put at risk, it only takes a relatively tiny fraction of a percent to add up to a big problem, dwarfing the alleged benefit of the drug.

Government officials, egged on by the mainstream media, are now talking seriously about forcing the inoculation of millions of children, using a largely unnecessary vaccine whose long-term effects are unknown.

Should we make the entire female population, first of Texas, and then of the other states and countries, into human guinea pigs to test the long-term safety of the latest moneymaking product from Big Pharma?

Wouldn't it be more effective and economical, rather than spending enormous sums on Gardasil, to spend those same resources on a stepped-up campaign to provide basic gynecological services to all women, with special emphasis on minorities, the poor and the uninsured? Even Gardasil advocates readily admit that inoculated women are still going to need regular gynecological exams, including Pap tests – but they offer no solution to the fact that a third of US women do not get such exams. In fact, the more government and private money that is spent on Gardasil the less will be available for basic gynecologic care for the poor, who suffer the brunt of cervical cancer incidence and death.

Fundamentally improving the public health system so that every woman has access to routine and regular gynecological exams (including Pap tests) makes more sense. But reforming American health care will require considerable political will. How much simpler, then, to mandate a dubious vaccine, while simultaneously refreshing the coffers of one of the world's most powerful drug companies.

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