

Articles Question Wide Use of 2 Vaccines

By ELISABETH ROSENTHAL

Two vaccines against cervical cancer are being widely used without sufficient evidence about whether they are worth their high cost or even whether they will effectively stop women from getting the disease, two articles in this week's New England Journal of Medicine conclude.

Both vaccines take aim at the human papillomavirus, or HPV, a common sexually transmitted virus that usually causes no symptoms and is cleared by the immune system, but which can in rare cases become chronic and cause cervical cancer.

The two vaccines, Gardasil by Merck and Cervarix by Glaxo-SmithKline, take aim at two strains of the virus that together cause an estimated 70 percent of cervical cancers. Gardasil also prevents infection with two other strains that cause some proportion of genital warts. Both vaccines have become quick best sellers since they were licensed two years ago in the United States and Europe, and are given to tens of millions of girls and women.

"Despite great expectations and promising results of clinical trials, we still lack sufficient evidence of an effective vaccine against cervical cancer," Dr. Charlotte J. Haug, editor of The Journal of the Norwegian Medical Association, wrote in an editorial in Thursday's issue of The New England Journal. "With so many essential questions still unanswered, there is good reason to be cautious."

In her article, Dr. Haug says the vaccines have been studied for a relatively short period — both were licensed in 2006 and have been studied in clinical trails for at most six and a half

years. Researchers have not demonstrated how long the immunity will last, or whether eliminating some strains of cancer-causing virus will decrease the body's natural immunity to other strains.

More to the point, because cervical cancer develops only after years of chronic infection with HPV, Dr. Haug said there was not absolute proof that protection against these two strains of the virus would ultimately reduce the

Concerns in a journal about effectiveness against cervical cancer, and the cost.

rates of cervical cancer, although in theory it should do so.

Dr. Richard Haupt, medical director at Merck, called these concerns "very theoretical," noting that continuing research and monitoring suggested that immunity would be long lasting and that the vaccine would not lead to problems with other strains.

Dr. Haupt added that cervical cancer was "just the tip of the iceberg" and that HPV caused a huge amount of expensive and stressful testing in developed nations that could be avoided with vaccination.

The vaccines, which require three shots for a complete series, cost \$400 to \$1,000, depending on the country and the fees for doctors' visits. Unlike older vaccines that save money by preventing costly disease, these vaccines cost health systems money.

The second paper published this week, a study by Jane J. Kim and Dr. Sue Goldie of Harvard, looks at the issue of costs and concludes that the vaccines will be cost effective only if used in certain ways. In particular, the researchers say the vaccines will

be worth the cost only if they prove to protect girls for a lifetime, and if current methods for screening for cervical cancer using Pap smears can be safely adjusted to reduce costs there. Further research is required in both areas.

"I believe the vaccine is a great advance," said Dr. Philip Davies of the European Cervical Cancer Association, "but we have to implement it properly to get the benefits, and that hasn't happened."

In developed countries, Pap smear screening and treatment have already effectively reduced cervical cancer death rates to low levels. There are roughly 3,600 deaths annually from cervical cancer in the United States, 1,000 in France and 400 in Britain.

Cervical cancer, like skin cancer, can generally be caught at precancerous or noninvasive stages and treated. Because the vaccine prevents infection with only some of the cancer-causing strains, Pap smear screening must continue even in those who are vaccinated.

The Harvard study concluded that giving the vaccine to 12-year-olds would cost \$43,600 for every "quality adjusted year of life" it saved by preventing a cancer death; that price would often be considered acceptable by health officials in wealthy countries, experts say.

Dr. Haupt said the study proved it was best to vaccinate early. "It underscores the value of vaccinating preadolescent girls," he said, since the vaccine works fully only in girls who have not been exposed to HPV.

But if the vaccine were given to all girls and women up to age 21, the cost per year of life saved would be far higher — \$120,400, the Harvard study concluded. And if the vaccines prove to require a booster shot, as many critics believe, that cost rises to \$140,000. In such cases it might make more economic sense to rely on Pap smear screening alone, the researchers said.

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