# Contraceptive Gel Appears Safer Than Nonoxynol-9

## *Cellulose sulfate, an experimental vaginal gel, is reported effective in preventing HIV, pregnancy.*

BY FRAN LOWRY
*Orlando Bureau*

WASHINGTON — Cellulose sulfate, a new vaginal gel that is being developed as both a contraceptive and as a means of preventing human immunodeficiency virus and other sexually transmitted infections, is as effective as nonoxynol-9 in preventing pregnancy, and also appears to be safer, researchers wrote in a poster presented at the annual meeting of the American College of Obstetricians and Gynecologists.

The cumulative probability of pregnancy during "typical" and "perfect" use of cellulose sulfate was 13.9 and 3.9, respectively, in a population of 200 heterosexual, fertile couples who used the gel as their primary method of birth control for 6 months as part of a phase II, noncomparative contraceptive effectiveness trial, wrote Dr. Christine Mauck, of the Contraceptive Research and Development (CONRAD) program at the Eastern Virginia Medical School in Arlington, and associates.

Cellulose sulfate is an antimicrobial that stimulates acrosomal loss, inhibits hyaluronidase, and impedes sperm penetration into cervical mucus. Animal studies in rabbits have demonstrated its contraceptive ability. Cellulose sulfate is active against cell-free and cell-associated HIV-1 because it blocks glycoprotein 120–CD4-coreceptor interaction, thereby inhibiting HIV cell entry. Cellulose sulfate has been studied in multiple safety studies of both HIV-free and HIV-infected men and women in which it has been found to be safe, and is currently being studied in two phase III HIV prevention trials, Dr. Mauck wrote.

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In this study, the 200 couples were demographically similar with regard to age (27 years for females; 29 years for males), race, and education. Clinic visits were scheduled at enrollment, after one menstrual cycle, and after 6 months or six menstrual cycles, whichever occurred later. Study participants were also asked to phone the clinic 7-10 days after the onset of the first menstrual period, and at the onset of each menses thereafter throughout the study.

There was a mean of 11.5 coital acts per cycle, and 78% of the study subjects used the cellulose sulfate gel alone, as instructed. The gel was used alone, but incorrectly, in 4% of subjects, with an additional contraceptive method in 5% of subjects; 10% of subjects used another method alone, and 4% had unprotected intercourse, Dr. Mauck and her associates wrote.

At the end of the study, 18 women (9%) were pregnant, and 82 (41%) had not become pregnant. Another 14 women (7%) discontinued the study for gel-related reasons; 66 (33%) stopped for other reasons, 18 (9%) said they never used the gel, and 2 patients (1%) were lost to follow-up.

Nonoxynol-9 (N-9), currently the only vaginal contraceptive gel approved for use in the United States, has been associated with an increased risk of HIV, compared with placebo, when used frequently by women at high risk for HIV, Dr. Mauck commented in an interview. "This is why we need a new contraceptive gel. N-9 was found in a previous trial to be associated with a greater risk of HIV seroconversion when used frequently by women at risk of HIV because it's a surfactant and may cause damage to the vaginal epithelium. [Cellulose sulfate gel] appears to be safer than N-9 and may be safer than sexual lubricants like K-Y and at least as effective as N-9," she said. ■

# Physicians Debate Conservative Versus Aggressive Treatment of CIN 2 Lesions

BY ROXANNE NELSON
*Contributing Writer*

LAS VEGAS — Experts are divided on how aggressively cervical intraepithelial neoplasia grade 2 should be treated, and on whether observation is an acceptable option, especially in low-risk populations.

Cervical intraepithelial neoplasia (CIN) has been regarded as a preinvasive condition, with progressively higher grades being associated with an increasing risk of cancer. As most CIN 1 lesions regress without treatment, it has been suggested that CIN 2 may also have limited potential to progress to a more invasive disease.

"The goal of treatment for CIN is to prevent cancer by eliminating lesions with true malignant potential," Dr. Mark Spitzer said at a meeting of the American Society for Colposcopy and Cervical Pathology. "And we also want to avoid unnecessary treatment of lesions with little or no premalignant potential."

The data are mixed, said Dr. Spitzer of New York University, New York. Some studies show that CIN 2 is an intermediate entity that lies between CIN 1 and CIN 3 and has some premalignant potential although not as great as that of CIN 3. Other studies show that it is much closer to CIN 1 or benign disease, so it does not have real premalignant potential.

That raises the question, "Is the diagnosis of CIN 2 a reliable or reproducible diagnosis?" Dr. Spitzer said.

He pointed out that a few studies have assessed that question, and one concluded that interobserver variation is fair to good for the diagnosis of benign conditions, CIN 3, or invasive cancer, but poor for the diagnosis of CIN 1 or CIN 2. There is also poorer correlation between colposcopic and histologic diagnosis with CIN 2, compared with CIN 1 and CIN 3.

"The problem with CIN 2 is that we don't really know what it is," Dr. Spitzer said. Any system of grading an intraepithelial lesion, in which there is a lesional continuum, is essentially artificial. A grading system that is based on light microscopy is subject to inter- and intraobserver variations in reporting, and treating all patients with CIN 2 will clearly result in the overtreatment of many of them.

There's also a question of age, when making the decision to treat cervical lesions. CIN 2 in adolescents is different than it is in adults, he explained. Some preliminary results showed that after 1 year, the behavior of CIN 2 in adolescents was the same as that of CIN 1.

"If you're under 20 the risk of invasive cancer is zero," Dr. Spitzer said. "If you're in the cohort under age 25, it still is really very low. So not treating CIN 2 in younger patients really makes a lot of sense."

However, Dr. Edward John Mayeaux Jr., of Louisiana State University, Shreveport, disagreed with the assumption that CIN 2 isn't a real entity. "This has been debated before," he said, "And the data do show that it is different in its progression and regression potential than CIN 1. It has a biological activity that is different from both CIN 1 and CIN 3.

"In adolescents it is often transient, and the risk of cancer is small. And our guidelines already say that observation for 1 year is acceptable for adolescents with CIN 2," he said.

Dr. Mayeaux also pointed out that in the United States, CIN 2 and 3 are managed in a similar fashion, primarily because the potential for progression is higher than that of CIN 1 and reliable histologic differentiation in CIN 2 and 3 is only moderate.

Overall, CIN 3 has about a 12% progression to cancer, but CIN 2 has about a 5% progression to cancer. These estimates do vary significantly, and at this time, most authors, guidelines, and professional organizations do recommend treatment for both CIN 2 and 3 lesions.

"We do need a better way to tell who is going to progress, and I agree with that," he said. "The difference in our point of view is that I don't think we're there yet. And until we get there, we don't know what those changes are going to mean for patient outcome. We still need to treat it until we reach that point."

Given the current variations in equipment and practice and the greater potential of CIN 2 to progress, compared with CIN 1, Dr. Mayeaux recommends no changes in current treatment protocols.

In rebuttal, Dr. Spitzer said that while CIN 2 has premalignant potential, overtreatment with loop electrosurgical excision can also have consequences. ■

# *Vaginal Cytology Deemed a Poor Endometrial Ca Screen*

PALM SPRINGS, CALIF. — Routine vaginal cytology as a surveillance test for endometrial cancer recurrence is costly, inefficient, and benefits less than 1% of patients, Dr. Robert E. Bristow and his associates reported in a poster session at the annual meeting of the Society of Gynecologic Oncologists.

"The rationale for intensive surveillance of endometrial cancer patients in clinical remission is based on the premise that early detection of an asymptomatic recurrence will translate into improved survival outcomes," the researchers of the Kelly Gynecologic Oncology Service at Johns Hopkins Medical Institutions, Baltimore, wrote in their poster.

Although this premise is widely held, studies have not demonstrated a significant survival advantage for patients whose recurrences are detected during routine follow-up, compared with symptomatic patients presenting for interval evaluation, they noted.

The researchers reviewed the medical records of 377 endometrial cancer patients who were treated at the Kelly Gynecologic Oncology Service between July of 1997 and June of 2005. They calculated the total number of Pap tests performed during surveillance or until the time of recurrence. Costs were based on 2005 Pap test costs adjusted retroactively via the consumer price index.

Of the 337 patients, most (63.7%) had stage I cancer; 10.1% had stage II; 18.8% had stage III, and 7.4% had stage IV. The median follow-up was 30 months. A median of five Pap samples per patient were collected during the study period, for a total of 2,134 Pap tests.

The researchers found that endometrial cancer recurred in 61 patients (16.2%), while 11 (2.9%) had an isolated vaginal recurrence. Of the isolated recurrences, seven were detected by physical examination alone, two were detected by interval CT, and two asymptomatic vaginal recurrences were detected by routine vaginal cytology, for a rate of 0.5%.

"Detection of each asymptomatic vaginal recurrence required 1,067 Pap tests, generating $44,049 in cumulative charges," the researchers noted in their poster.

They concluded that "elimination or reduction in the use of vaginal cytology for this purpose offers an opportunity for significant cost savings in gynecologic oncology health care."

Dr. Bristow directs the Kelly Gynecologic Oncology Service.

**—Doug Brunk**