warnings advising health professionals and women patients that the risk is much reduced if estrogens are taken at the lowest possible dose and if chronic administration is avoided.[2,3]

Jick et al.'s[2] study of patients in a large prepaid group practice in the Seattle area found parallel sharp declines in both the incidence of uterine cancer and in the number of prescriptions for replacement estrogens. This recent report suggests that when patients discontinue taking estrogens, the risk of developing endometrial cancer decreases markedly within one year. A possible alternative explanation suggested by Jick is that the time of diagnosis is postponed when patients discontinue estrogens. Jick concluded the correct explanation will emerge as the population and nationwide statistics continue to be monitored.

A downward trend for estrogen use began in 1976 after announcements of epidemiological findings on the risk in late 1975. Nationwide, FDA data indicates that estrogen use declined by 18 percent from 1975 to 1976, and by another 10 percent from 1976 to 1977. According to Jick and others, the incidence of endometrial cancer fell about 27 percent nationwide from 1975 to 1977. In 1977 approximately 5 percent of women in the United States, or 4.1 million, were taking estrogen therapy.

The papers by Jick et al.[2] and Antunes et al.[3] agree on two issues important to physicians prescribing estrogens and to women taking these drugs:

- The increased risk of endometrial cancer in estrogen users is proportional to the duration of use and is particularly high with use of 5 years or longer. It should be noted, however, that Antunes, Stolley et al., and Ziel and Finkle[4] reported an increased risk even with use of estrogens for a period of 1 to 5 years. No definite evidence of increased risk of cancer from estrogen use less than 1 year has been reported.
- The use of cyclic therapy or progestins for 7 days each month does not meaningfully protect against the risk of endometrial cancer. Whether use of progestins for longer periods each month will provide protection has not been adequately studied.

The only established way to use estrogens with minimum risks in women with intact uteri is to prescribe low doses for relatively short periods—i.e., months, rather than years.

A recent study by Horwitz and Feinstein sparked controversy about certain aspects of estrogen therapy and cancer link. They maintained that the risk of endometrial cancer in estrogen users may be overestimated, because women who have uterine bleeding after estrogen therapy receive increased diagnostic attention, and, therefore, their cancer is detected earlier than in women not taking the drugs. Using a procedure different from that of previous researchers, these authors found only a slight increase in risk of uterine cancer in estrogen users.

Hutchison and Rothman challenge Horwitz and Feinstein's findings,[5] maintaining that although women who take estrogens may be diagnosed with endometrial cancer somewhat earlier, nearly all women with invasive endometrial cancer ultimately will have their disease diagnosed. These researchers conclude that even if screening advances that date of diagnosis, it will have little effect on the number of cases ultimately found.

Antunes, et al. used a methodology that compensates for the possible screening problem, and they still found a strong association between estrogen use and endometrial cancer.

FDA since 1977 has required estrogen patient labeling to carry the warning about the association between prolonged estrogen use and a 5-15-fold increase in risk for uterine cancer. The warning label and FDA's information campaign to medical professionals aim at reducing uses of estrogen in treating conditions for which it is neither effective nor medically justified, such as for treatment of simple nervousness and depression during menopause, or to help women feel younger.

Estrogens are effective, however, for vasomotor symptoms of the menopause and can be used with no known increase in risk for the treatment of this common problem if doses are kept low and the period of treatment is less than 1 year.

References

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Syrup of Ipecac

National Poison Prevention Week is March 18-24, 1979, and FDA believes this is an appropriate time for health professionals to discuss with their patients the use of ipecac syrup in cases of accidental poisonings.

With proper use, syrup of ipecac is a safe and effective emetic. The recommended labeling for ipecac syrup was published on September 8, 1978, as part of FDA's tentative final monograph on emetic drug products. Syrup of ipecac is indicated "only to cause vomiting in case of poisoning."

The labeling warns consumers *not* to use syrup of ipecac if strychnine or corrosives (such as lye and strong acids) have been ingested. Because consumers may not know if the poisonous substance is highly toxic, a corrosive, or a petroleum distillate, the labeling stresses that they should contact a physician, poison control center, or emergency room for advice *before* using ipecac syrup. The drug should not be used if the patient is convulsing, semiconscious, unconscious, or has lost the gag reflex.

If ipecac syrup and activated charcoal (which is often given to prevent poison absorption in the stomach) are used together, vomiting must be induced with the ipecac syrup before the patient takes the activated charcoal. Activated charcoal adsorbs ipecac syrup and may reduce its effectiveness.

If vomiting does not occur within 20 minutes, the dose may be repeated once. If vomiting doesn't occur within 20 minutes after a second dose is given, the physician, poison control center, or emergency room should be called again.