as carried out with cigarette smokers would be required to indicate a possible relationship between oral contraceptives and cancer. Results of a mass study concerning carcinogenesis would probably not be of any value until well into the 1970's.

In the area of mutagenicity, it is virtually impossible to determine a cause and effect relationship.

Animal testing probably is the only practical means for determining the relation between chemicals and their long range genetic effects. This conclusion can be inferred, of course, from the preceding statements. The need to rely on animal data is especially imperative with the oral contraceptives that have been in use for a comparatively short time.

The universal nature of the hereditary material allows one to extrapolate between species with some assurance. In lieu of epidemiological data, which usually cannot be accumulated until a compound has been on the market for a prolonged period, heavy reliance must be placed on definitive and extensive animal studies in this area. We simply don't have an alternative.

I would like now to specifically talk about the oral contraceptive and teratogenic effect, that is developmental abnormalities.

The steroid hormones such as the corticosteroids are known to have a number of effects on the developing embryo in both animal and man. Women using hormones for contraceptive purposes may become pregnant either during the course of treatment or shortly after discontinuing the pill. The number of women who use the drug during pregnancy or shortly after becoming pregnant, may be sufficiently high enough to warrant careful consideration of the potential teratogenic effects of oral contraceptives.

The progestin, chlormadinone acetate, produced cleft palate in mice and contracture of the wrist joint, defect of the abdominal wall and cleft palate in rabbits at high concentrations and I think it is important to emphasize the extremely high concentrations used. These contrations are considerably higher than those required to inhibit ovulation in rabbits and humans. High dose of norethynodrel with 2 percent mestranol also produced cleft palate in mice. Norethisterone with 1 percent mestranol showed no teratoganic effects, in the same study. An increase in dead or reabsorbed fetuses with the two progestins that produced malformations was also reported in this study.

In studies with rhesus monkeys, high doses of norethindrone were administered orally for 5 days per week from approximately 30 days to term. Eight of 10 fetuses were stillborn; all five females were virilized; males showed a greater degree of cryptorchidism than expected. However, six rhesus mothers treated with 50 mg. progesterons I.M. daily during the same period of pregnancy suffered no deleterious effect. Again, we are talking about very high concentrations when we did find a response with the steroids.

In humans, two investigators have shown, that progestins increase the risk of masculinization of female embryos during the first 16–18 weeks of inadvertent pregnancy. In certain instances a dose-related response was recorded. I might say that this particular manifestation is rather easy to correct surgically, and masculinization has been seen with other materials and also occurs spontaneously in our population.

The steroids vary as to their teratogenic potency and the compound