All of the oral contraceptives now on the market are designed to mimic pregnancy. Since a pregnant woman does not ovulate, there are no subsequent eggs to fertilize and hence no multiple pregnancies. Normally, the female part of the reproductive process starts with physiologically timed stimuli that reach the brain (cortex), which, via the hypothalamus, stimulates the pituitary to secrete follicle-stimulating and luteinizing hormones (FSH and LH). These hormones are involved in the growth of ovarian follicles, rupture of the follicle to release its egg, secretion of the female sex hormone estradiol (an estrogen), change of the follicular cell into the corpus luteum, and secretion of progesterone. Estradiol is involved in the growth of the uterine lining (endometrium); progesterone is involved in preparing the lining for implantation and nutritive support of the fertilized egg and in preventing the development of more follicles and eggs. The natural estrogens and progesterone, secreted by the ovary and later the placenta, inhibit the secretion of FSH and LH during pregnancy and thus prevent ovulation. When a nonpregnant woman ovulates and fertilization does not take place, secretion of progesterone stops, the uterine lining breaks down, and sloughs off. This is menstruation. The entire cycle in the nonpregnant woman takes about 28 days. The synthetic estrogens and progestins in the birth control pills produce the same effects as the natural hormones. Their basic difference is that they are modified chemically so that they can enter the woman's system when taken orally. Two types of birth control pills (and treatments) are on the market: combined and sequential. In combined treatment, each pill contains both estrogen and progestin. Generally, the woman takes one pill a day for 21 days, stops for seven days (menstruation period), and resumes taking the pills. In sequential treatment, she takes only an estrogen for 16 days, then a combination pill for five or six days (depending on the product). She then stops until the 28th day before resuming.

Some months ago, Dr. Mueller and his group showed that estrogen sparked the growth of uterine tissue by direct effect on protein synthesis, through stepped-up production of RNA (ribonucleic acid) in the nucleus. They noticed that there was an increase in RNA polymerase activity—the enzyme which catalyzes the RNA synthesis—just after estrogen was added. But of much interest, in their opinion, is that this higher polymerase activity correlated with the production of protein elsewhere in the cell. In other words, two events were taking place: Protein was being produced somewhere else in the cell; it was affecting the synthesis of RNA via its polymerase.

"We interpret this to mean," Dr. Mueller says, "that this other protein is modifying the activity of the polymerase because if we decrease protein we stop the activity of the polymerase."

Where does estrogen fit into this process? Mueller thinks that it's either facilitating the manufacture of the other protein or helping to transport it to the polymerase area. As for the receptor protein, it could well be acting as a carrier of the estrogen to the site of action.

Progesterone's action is an even bigger mystery. But work by Dr. Walter G. Weist of Washington University (St. Louis) medical school is uncovering some clues. In labeling experiments, he has found that progesterone, like estrogen, also encounters a receptor in uterine cells during the progesterone-dependent proliferative phase of endometrial growth (when the endometrium is being readied to receive the fertilized egg).

Studies of the type being done by Dr. Jensen, Dr. Mueller, and Dr. Weist—as well as the related research of Jack Gorski of the University of Illinois and Sheldon Segal of the Population Council—are indeed scarce in endocrinology today because they're at the level of molecular biology. But this is the trend, and rather a necessary one, in the opinion of Dr. Weist. "Steroid distribution studies, too, are a must," he says. "That is, it must be determined where they tend to distribute in the target cell, how and to what they are bound, and their metabolic fate. The big hooker is how you assess the physiological results of cell hormone interaction."

Hookers do indeed abound in this field. For example, in vitro studies of steroid metabolism could clear away dozens of parameters that muddy results obtained with whole tissue. But all attempts to isolate reaction systems in the necessary lipid environment have meant destruction of one enzymic component or another. Moreover, cell biologists haven't succeeded in growing target tissue outside the cell. Some work along this line is being pursued at Worcester