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RESEARCH—BIOCHEMISTRY OF THE PILL LARGELY UNKNOWN

MOLECULAR BIOLOGY AND INTERMEDIARY METABOLISM ARE SLOWLY BECOMING CRITICAL AREAS FOR STUDYING MECHANISMS OF ORAL CONTRACEPTIVES

The 5 to 7 million women in the U.S. who practice birth control by oral contraception have two new versions of "the pill" to choose from: Orthos 1 mg. Ortho-Novum and Syntex's 1-mg. Norinyl-1 (see table). Yet, for all the interest and energy that companies are putting into developing oral contraceptives (the Food and Drug Administration is studying about 30 more possibilities), and for all the efforts to upgrade safety surveillance, nobody knows fundamentally how the drugs work. For the biochemistry of inhibiting conception by taking drugs remains one of reproductive physiology's more fogbound research areas.

And little wonder. Each woman who uses the pill is daily swallowing tablets containing various synthetic formulations of sex hormones of the type she would routinely produce during pregnancy. Being biochemically pseudopregnant, therefore, she fails to ovulate. Failing to ovulate, she can't conceive. When faced with comprehending this biochemical interplay of brain, glands, and genitalia, most scientists turn to work that leads to quicker publication—such as extrapolating the results of urine and blood analyses.

Fortunately, all is not blood and urine. Molecular biology and intermediary metabolism are slowly becoming the critical areas for studying the mechanisms of both the natural sex hormones and their oral contraceptive counterparts. Work of this type is moving ahead at such centers as the Population Council in New York City; the Universities of Chicago, Wisconsin, and Michigan, and Washington University in St. Louis. Also, to a limited extent, at FDA, the National Institutes of Health, the Worcester Foundation for Experimental Biology, Oxford University (England). San Diego Naval Hospital, and Canada's Food and Drug Directorate.

Several laboratories are probing the action of estrogens and progesterone at the protein synthesis level. Some are at long last tracing steroidal pathways through the cell with tritiated agents. Other groups are trying to relate neurochemical triggering mechanisms to hormone production. Still others are studying the effects of estrogens, progesterone, and their synthetic counterparts on the structural chemistry of target tissue such as uterus, ovary, and pituitary. All this activity, though really just beginning, could one day lead to a sort of biochemical systems analysis of steroidal interactions. It also could help to clear up the mass of confusion over the pill's long-term effects in connection with diabetes, cancer, diseases of the circulatory system, and various interactions possibly too subtle to be noticed now.

And confusion there is. The chemical manipulation of the woman's sex cycle by synthetic estrogens, synthetic progesterones (progestins), and future non-steroidal contraceptives has posed questions of ultimate effects on her biochemistry and physiology. Moral questions aside, millions of women, their husbands, and a high percentage of their physicians express qualms over whether several unresolved possible risks outweigh the convenience.