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APPENDIX 4

REPORT OF THE TASK FORCE ON BIOLOGIC EFFECTS

P. A. Corfman, M.D., Chairman

INTRODUCTION

Many important studies of the biological effects of oral contraceptives have been published since the 1966 FDA Report on Oral Contraceptives (55) and the results have been summarized in part by Diczfalusy (45), Jeffrey and Klopfer (83), and others (74, 103, 184). A detailed review of the nonendocrine effects was undertaken at a four-day conference in December, 1968, organized by the Harvard Center for Population Studies and supported by the National Institute of Child Health and Human Development. The proceedings of the conference are published under the title "The Metabolic Effects of Gonadal Steroids and Contraceptive Agents" (147).

This comparatively brief Task Force report does not attempt to include all of the extensive literature on the biological effects of oral contraceptives but identifies certain topics that the Task Force believes to be of particular importance. The effects of these agents on blood coagulation and thromboembolism are covered in another portion of the report. It is clear, however, that oral contraceptives have many varied effects on many organ systems. Indeed, there appears to be no organ system tested that is not affected in some way.

The ubiquitous effects of oral contraceptives probably relate to their high degree of contraceptive effectiveness, brought about through interference with several phases of the reproductive process. An influence on the hypothalamus or higher brain centers is probably responsible for the suppression of pituitary production of gonadotropins, leading secondarily to the inhibition of ovulation.

The second major effect is on the endometrium. The progestin acts as an antiestrogen, causing alterations in endometrial glands, and as a progestin, causing a pseudodecidual reaction. Both of these effects alter the ability of the endometrium to participate in the process of implantation.

The third effect is on the cervical mucus through prevention of the alterations that normally occur at the time of ovulation and appear to permit the ascent of sperm into the uterine cavity. Oral contraceptives cause the cervical mucus to remain thick and apparently hostile to the transmission of sperm. Oral contraceptives may affect tubal motility also and may alter the local ovarian response to gonadotropic hormones.

A consideration of the biological effects of oral contraceptives is complicated by the facts that there are many different compounds and several modes of