degree. Present evidence indicates that the frequency of pregnancies occurring with the patients on sequential medication remained unchanged over the 2½-year period, thus supporting the contention that tolerance to or escape from the medication probably does not occur.

B. Treatment of Amenorrhea

The efficacy of oral contraceptives in the treatment of amenorrhea could not be readily ascertained from the material available to the Committee because of the endpoint used. Treatment was considered successful when uterine bleeding followed cyclic withdrawal of the medication. Such an endpoint does not specifically measure the efficacy in treating amenorrhea, since cyclic withdrawal bleeding and menstrual periods are different biologic phenomena. If efficacy in the treatment of amenorrhea is claimed, it must be based on evidence that menstrual cycles are maintained following discontinuation of drug therapy. Such information was not contained in the submitted material. If, however, the objective of the therapeutic effort is to produce cyclic withdrawal bleeding in the amenorrheic patient, the oral contraceptive drugs can be considered efficacious, since this result was achieved in 80 to 90 percent of treated patients.

C. Treatment of Dysmenorrhea

The comments pertaining to efficacy of the drugs in the management of patients with dysmenorrhea were similar to those cited in the previous paragraph. The situation was even more complicated because of the difficulty in quantitation of the principal variable. Dysmenorrhea is known to disappear spontaneously, and relatively high "cure rates" have been obtained with placebos. No followup data were available in the submitted material; the reports thus pertained to the evaluation of pain during cyclic withdrawal bleeding rather than during a menstrual period. Although the data suggest that in certain patients the progestational agent might be of value in the treatment of dysmenorrhea, additional information is required before the therapeutic efficacy can be proved. Statistically, the submitted material was considered unsatisfactory because of the small number of patients in the individual series. It was surprising to find that a very small sample had been utilized in the study of such a common phenomenon. The members were aware of the difficulties in designing controlled studies, since placebos do not provide contraception, a fact that cannot remain undisclosed to the patient.

D. Treatment of Endometriosis

In evaluating the material in which the diagnosis of endometriosis was established by histologic examination, the Committee finds continued and prolonged (6 to 12 months) progestational therapy valuable to conservative management of the affected patient. In the well-documented cases it is reasonable to expect a favorable response in 75 to 90 percent. It must, however, be pointed out that recurrence might be expected in an appreciable proportion of patients after cessation of medication. In contrast, the therapeutic efficacy in subjects in which the diagnosis of endometriosis had been made by physical examination or history alone, was uncertain. This population undoubtedly comprises a variety of diseases that should not be expected to improve during therapy with progestational agents.

E. Treatment of Functional Uterine Bleeding

The claims for therapeutic efficacy in treatment of functional uterine bleeding were met with criticism similar to that applied to treatment of dysmenorrhea and amenorrhea. The Committee considers the joining of a variety of conditions under the heading "Functional Uterine Bleeding" inappropriate because the individual diseases have specific and different causes. The index of general efficacy might not therefore reflect the favorable results achieved in certain categories, or conversely might create the impression of therapeutic merit in diseases that are not susceptible to therapy. Irregular menstrual periods will respond in a high percentage of cases to therapy if cyclic withdrawal bleeding is considered synonymous with menses, whereas menorrhagia might be and appears to be considerably more resistant to the advocated therapy. Patients with hypermenorrhea appear to have shorter periods and less loss of blood when placed on cyclic therapy with these compounds. Difficulty in constructing a meaningful endpoint for the various categories was evident since most of the conditions causing functional bleeding are known to be self-limiting.

F. Habitual Abortion

The Committee found no data to indicate that any of the oral contraceptives are effective in altering the natural history of patients with habitual abortion. Although the reasons for habitual