Studies conducted in Great Britain and reported in April 1968[1, 2] estimate there is a seven to tenfold increase in mortality and morbidity due to thromboembolic diseases in women taking oral contraceptives. In these controlled retrospective studies, involving 36 reported deaths and 58 hospitalizations due to "idiopathic" thromboembolism, statistical evaluation indicated that the differences observed between users and non-users were highly significant. The conclusions reached in the studies are summarized in the table below:

COMPARISON OF MORTALITY AND HOSPITALIZATION RATES DUE TO THROMBOEMBOLIC DISEASE IN USERS AND NON-USERS OF ORAL CONTRACEPTIVES IN BRITAIN

Category	Mortality rates		Hospitalization rates (morbidity)
	Age 20–34	Age 35–44	Age 20–44
Users of oral contraceptives	1.5/100,000	3.9/100,000	47/100,000
Nonusers	0.2/100,000	0.5/100,000	5/100,000

No comparable studies are yet available in the United States. The British data, especially as they indicate the magnitude of the increased risk to the individual patient, cannot be directly applied to women in other countries in which the incidences of spontaneously occurring thromboembolic disease may be different.

2. Discontinue medication pending examination if there is sudden partial or complete loss of vision, or if there is a sudden onset of proptosis, diplopia or migraine. If examination reveals papilledema or retinal vascular lesions, medication should be withdrawn.

3. Since the safety of * * * in pregnancy has not been demonstrated, it is recommended that for any patient who has missed two consecutive periods, pregnancy should be ruled out before continuing the contraceptive regimen. If the patient has not adhered to the prescribed schedule the possibility of pregnancy should be considered at the time of the first missed period.

4. A small fraction of the hormonal agents in oral contraceptives has been identified in the milk of mothers receiving these drugs. The long range effect to the nursing infant cannot be determined at this time.

PRECAUTIONS

1. The pretreatment physical examination should include special reference to breast and pelvic organs, as well as a Papanicolaou smear.

2. Endocrine and possibly liver function tests may be affected by treatment with * * *. There, if such tests are abnormal in a patient taking * * *, it is recommended that they be repeated after the drug has been withdrawn for 2 months.

3. Under the influence of estrogen-progestogen preparations, pre-existing uterine fibromyomata may increase in size.

4. Because these agents may cause some degree of fluid retention, conditions which might be influenced by this factor, such as epilepsy, migraine, asthma, cardiac or renal dysfunction, require careful observation.

5. In breakthrough bleeding, and in all cases of irregular bleeding per vaginum, nonfunctional causes should be borne in mind. In undiagnosed bleeding per vaginum, adequate diagnostic measures are indicated.

6. Patients with a history of psychic depression should be carefully observed and the drug discontinued if the depression recurs to a serious degree.

7. Any possible influence of prolonged * * * therapy on pituitary, ovarian, adrenal, hepatic or uterine function awaits further study.

8. A decrease in glucose tolerance has been observed in a significant percentage of patients on oral contraceptives. The mechanism of this decrease is obscure. For this reason, diabetic patients should be carefully observed while receiving * * * therapy.

[1] Inman, W. H. W. and M. P. Vessey, British Medical Journal 2:193–199, 1968.
[2] Vessey, M. P. and R. Doll. British Medical Journal, 2:199–205, 1968.