approved combination product contains one-third the dose of estrogen and about one-tenth the dose of progestin as was present in the original contraceptive. Steroids that are stored in and slowly released from adipose tissue after oral ingestion are currently under study with the aim of creating a pill that may require administration only once a month. Unpredictable uterine bleeding remains a problem, however.

Intramuscularly injected steroids with a prolonged effect that may last for one or more months have been widely studied. Although these compounds may suppress ovulation, uterine bleeding is often an unpredictable complication. The delay before resumption of ovulatory cycles often lasts from 12 to 21 months. There is considerable variation among patients. To regulate the uterine bleeding some investigators have administered oral or parenteral estrogen. Doing so, however, detracts from the simplicity of this purely progestational regimen.

Low-dose continuous progestin therapy has been investigated in several countries. Drugs of this kind exert their contraceptive effect without the addition of estrogen and without the inhibition of ovulation. The pregnancy rate appears to be approximately 2 per hundred women per year. Approximately two-thirds of the women studied have some cycle irregularity.

The contraceptive action of low-dose progestins provides for the first time the possibility of long-term, reversible control of fertility by single administration of a hormone. Steroids may be released at a low and constant rate from capsules, made of various silicones, that are small enough to be inserted under the skin with a hypodermic syringe and that may last possibly as long as three years. Such implants could be removed if subsequent fertility were desired. If the clinical studies that have recently been initiated prove fruitful, this form of hormone administration may well become an important development in contraception.

(e) *Thromboembolic disorders*

An etiologic relation between oral contraceptives and an increase in some thromboembolic disorders has been disclosed by several groups of investigators using retrospective methods of inquiry and studies of mortality trends. In 1967 the Royal College of General Practitioners in Great Britain undertook interviews of young women with vascular disease. By comparing patients with superficial thrombophlebitis with a suitably matched series of controls, it could be shown that the risk of developing thrombophlebitis was tripled in women who used oral contraceptives. In a second study, Vessey and Doll investigated young women admitted to several hospitals in the northwest of London with a diagnosis of idiopathic thrombophlebitis. These patients also were matched with suitable controls. A third study involved all of the deaths that occurred in England, Wales and Northern Ireland during 1966 in women between the ages of 20 and 44 whose death certificates referred to thrombosis or embolism of the pulmonary, cerebral or coronary vessels. The results of the second and third studies are summarized in Table 1.

TABLE 1.—USE OF ORAL CONTRACEPTIVES IN WOMEN SUFFERING FROM "IDIOPATHIC" THROMBOEMBOLIC DISORDERS (EXPECTED NUMBERS IN PARENTHESES)

Disorder	Source of data	No. of affected women with a history of oral contraceptives		No. studied		Relative risk: users to nonusers
		Used	Not used	Affected women	Control women	
Deep-vein thrombosis or pulmonary embolism	Inpatients	26 (5·0)	32 (53·0)	58	116	8·6 to 1
	Deaths	16 (4·2)	10 (21·8)	26	998	8·3 to 1
Cerebral thrombosis	Inpatients	5 (1·0)	4 (8·0)	9	[1]	10·0 to 1
	Deaths	5 (1·5)	5 (8·5)	10	[1]	5·7 to 1
Coronary thrombosis	Inpatients	0 (0·7)	13 (12·3)	13	[1]	----------
	Deaths	18 (11·4)	66 (72·6)	84	[1]	1·7 to 1

[1] As in the corresponding control groups for women with deep vein thrombosis or pulmonary embolism.

(From Doll, R.: Brit. Med. J. 2:69–76, 1969.)

According to these British investigators, in the absence of other predisposing causes the risk of developing deep vein thrombosis, pulmonary embolism, or