TABLE VII—*Unadjusted and joint relative risks for term births, age at last term birth, menopausal state, use of oral contraceptives, and cigarette smoking**

Factor	Unit of change	Unadjusted risk (B)	Joint risk			
			B	Relative risk	t=B/SE(B)	p (Two sided significance)
Term births	1	−0·269	−0·220	0·80	−2·79	0·005
Age at last term birth	5 years	−0·283	−0·250	0·78	−2·74	0·006
Postmenopausal	Yes	−1·735	−1·733	0·18	−2·71	0·007
Use of oral contraceptives	5 years	−0·193	−0·184	0·83	−2·14	0·032
Weight	10 kg	0·185	0·190	1·21	2·66	0·008
Cigarette smoking	10/day	−0·211	−0·200	0·82	−2·10	0·036

*Parameters estimated from logistic regression model. Basic parameters (B) are such that relative risk=exp(B). SE(B)=standard error of B.

These factors modifying the risk of fibroids—protective effects of term births, use of oral contraceptives, cigarette smoking, and a harmful effect of increased body weight—are also the major factors associated with the risk of endometrial cancer. "Unopposed" oestrogen—that is, oestrogen exposure unaccompanied by a progestogen—has been clearly identified as the major cause of cancer of the endometrium, and all these risk factors can be interpreted in terms of the hypothesis of unopposed oestrogen.[11,12] This strongly suggests that unopposed oestrogen is also the underlying cause of fibroids.

After the menopause increased weight is associated with increased concentrations of circulating oestrogen, presumably because the major source of postmenopausal oestrogens is conversion of androstenedione to oestrogen in fat cells.[13] Before the menopause this oestrogen source is fairly unimportant in the face of ovarian production, but increasing weight is still closely associated with decreasing concentrations of sex hormone binding globulin and thus presumably with increasing concentrations of bioavailable oestradiol. Cigarette smoking has also been found to be associated with lower concentrations of urinary oestrogens.[14] If infertility is associated with a high risk of fibroids an oestrogen mechanism could also be proposed; this association could be due to high concentrations of unopposed oestrogen related to a high frequency of anovulatory cycles in such women. According to this hypothesis, the decreased risk associated with term pregnancies and use of oral contraceptives would be explained most readily by the oestrogen modifying effect of progestogens.

The data on the possibly increasing protective effect with increasing progestogen dose of oral contraceptives with the same ethinyloestradiol content (table IV) also provide some support for the unopposed oestrogen (protective effect of progestogens) hypothesis. The data on oral contraceptives containing ethynodiol diacetate are puzzling and need confirmation. Direct studies of the effect of different brands on the myometria may be informative.

Blood or urine concentrations of oestrogens in women with or without uterine fibroids appear not to have been measured. Alterations in oestrogen concentration and in oestrogen metabolism in leiomyomatous versus normal myometrium have been reported by some,[15] but not all investigators.[16] Further work may help explain why, unlike endometrial cancer, we have been unable to find any data linking oestrogen replacement therapy in postmenopausal women to an increased risk of fibroids; this apparently anomalous observation needs to be investigated closely. It would also be useful if future studies on women with endometrial cancer could report on the prevalence of fibroids in such women. We would, of course, expect women with endometrial cancer to have a raised risk of fibroids but we know of no data that address this issue.

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Corrections

Intramuscular loading dose of quinine for falciparum malaria: pharmacokinetics and toxicity

An error occurred in this paper by Dr Yupaporn Wattanagoon and others (5 July, p 11). The conversion of traditional to SI units is incorrect; the values for quinine should have been expressed in μmol/l, not mmol/l since, for quinine base, 1 mg/l is equivalent to 3 μmol/l.

Divided dose intramuscular regimen and single dose subcutaneous regimen for chloroquine: plasma concentrations and toxicity in patients with malaria

An error occurred in this paper by Dr R E Phillips and others (5 July, p 13). The conversion of traditional units to SI units is incorrect; for chloroquine base 1 mg/l is equivalent to 3 μmol/l. The values for chloroquine should have been in μmol/l, not mmol/l.