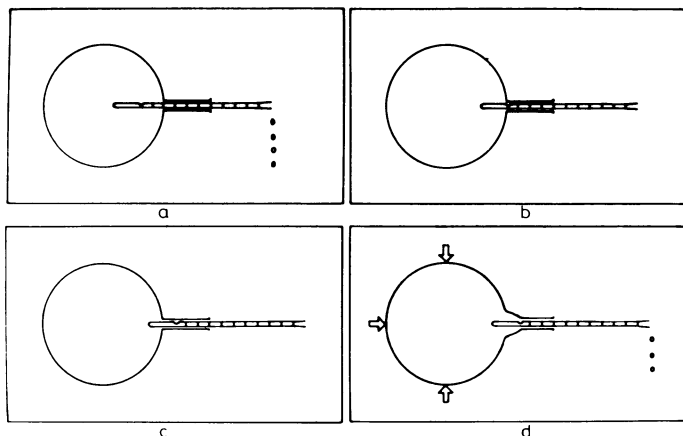


the catheter, however, it can be relocated at any time by repeating the procedure described above.

The figure shows a side-opening catheter, but the results we obtained with a catheter having a single hole at the tip appear to be the same.



Four stages of fluid bridge (flow) test: (a) catheter is passed up into bladder, (b) bladder neck is located, (c) test position is selected, (d) bladder neck opens during cough.

Comment

We used this method on more than 50 patients and found the results indistinguishable from those of the fluid bridge (pressure) test. The test is reproducible, though the distance from the bladder neck at which the result is positive may vary slightly with the strength of the cough.

The importance of the fluid bridge test has already been established and it appears to be a more sensitive indicator of bladder neck incompetence than other urodynamic tests, with the possible exception of pressure-cine-cystography.^{4,5} This simpler test permits wider use of work already done with more complex apparatus. Because no apparatus is required it should be possible to conduct this test in the outpatient clinic, avoiding referral of some patients to specialised units, saving time and effort.

¹ Asmussen M, Ulmsten U. Simultaneous urethro-cystometry with a new technique. *Scand J Urol Nephrol* 1976;**10**:7-11.

² Bates CP, Whiteside CG, Turner Warwick R. Synchronous cine/pressure/flow/cystourethrography with special reference to stress and urge incontinence. *Br J Urol* 1970;**42**:714-23.

³ Brown M, Sutherst J. A test for bladder neck competence: the fluid bridge test. *Urol Int* 1979;**34**:403-9.

⁴ Sutherst JR, Brown M. Detection of urethral incompetence. Erect studies using the fluid bridge test. *Br J Urol* (in press).

⁵ Sutherst JR, Brown M. Detection of urethral incompetence in women using the fluid bridge test. *Br J Urol* 1980;**52**:138-42.

(Accepted 17 June 1981)

Royal Liverpool Hospital, Liverpool L7 8XP

M SHAWER, MB, MRCOG, research registrar (now registrar, Kilton Hospital, Workson)

M BROWN, BSC, PHD, medical physicist

J SUTHERST, MD, FRCOG, senior lecturer in obstetrics and gynaecology

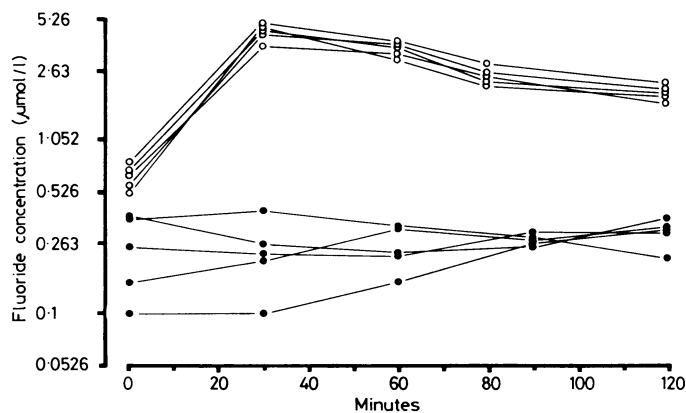
No evidence of transfer of fluoride from plasma to breast milk

Artificially fluoridated drinking water is supplied throughout the world as a mass-prophylactic agent against dental caries. No data are available, however, on the transfer of fluoride from maternal plasma to breast milk. We have therefore compared the fluoride concentrations in the plasma and breast milk of nursing mothers after an oral dose of fluoride.

Subjects, methods, and results

Five mothers aged 27-36 years were given fluoride by mouth on the third postpartum day. A dose of 1.5 mg was given as an aqueous solution of sodium fluoride in the morning after fasting for 10 hours. Blood and breast milk were sampled simultaneously in a non-glass system before and 30, 60, 90, and 120 minutes after the dose. Fluoride concentration in plasma was measured with a fluoride-sensitive electrode,¹ and in milk was determined using a modified microdiffusion technique.² Recovery experiments showed no evidence that fluoride binds to the constituents of breast milk. Hence the figures given for breast milk represent exclusively free fluoride.

The plasma fluoride concentration in all subjects rapidly increased after fluoride intake (figure). The highest plasma concentrations appeared 30 minutes after dosing, when they varied between 3.6 and 4.5 $\mu\text{mol/l}$ (70 and 86 ng/ml). This rapid absorption was in line with our results from oral single-dose studies in man.³ There was no corresponding increase in the fluoride concentrations in the breast milk, the values varying between 0.1 and 0.4 $\mu\text{mol/l}$ (2 and 8 ng/ml).



Plasma (open symbols) and breast milk (closed symbols) fluoride concentrations in five mothers after oral dose of 1.5 mg fluoride as sodium fluoride solution.

Conversion: SI to traditional units—Fluoride: 1 $\mu\text{mol/l} \approx 19 \text{ ng/ml}$.

Comment

These findings show that plasma fluoride is poorly transferred to breast milk and infants thus receive almost no fluoride during breast feeding. This is in contrast to another halogen, bromide, which reportedly accumulates in breast milk.⁴

In this study plasma and milk were sampled for a period of two hours after a single dose had been taken by the mother. The possibility of delayed transfer, not detected during the period of observation, was ruled out by other results from our laboratory, which showed that fluoride concentrations in breast milk remain steady, even when fluoride is given repeatedly and despite considerable variations in the maternal plasma fluoride concentrations.

The reason for the poor transfer of fluoride into the cells of the breast is obscure. Such a phenomenon has not been observed in other mammalian glands—for example, the salivary glands. The concentration in saliva follows that in plasma, and the ratio between salivary and plasma fluoride is around 0.65.³ Fluoride is excluded from certain cultured cells,⁵ but whether the same mechanisms are concerned in the mammary gland remains to be clarified.

Infants fed on milk substitutes receive higher fluoride doses, especially in areas where the drinking water is rich in fluoride. Thus in an area where the fluoride concentration is one part per million the daily fluoride dose in the newborn infant will be about 800-1000 μg when a milk substitute is used, whereas the fluoride dose for breast-fed children in the same area will not exceed 10 $\mu\text{g/day}$. The existence of a physiological plasma-milk barrier against fluoride suggests that the newborn is actively protected from this halogen. Hence the recommendation made in several countries to give breast-fed infants fluoride supplementation should be reconsidered.

This study was supported by grants from the Swedish Medical Research Council (project Nos 6002 and 522) and the Swedish Patent Revenue Research Fund.

¹ Ekstrand J. A micromethod for determination of fluoride in blood plasma and saliva. *Californian Tissue Research* 1977;**23**:225-8.

- ² Taves DR. Determination of submicromolar concentrations of fluoride in biological samples. *Talanta* 1968;15:1015-23.
- ³ Ekstrand J, Alván G, Boréus LO, Norlin A. Pharmacokinetics of fluoride in man after single and multiple oral doses. *Eur J Clin Pharmacol* 1977;12:311-7.
- ⁴ Kwit NT, Hatcher RA. Excretion of drugs in milk. *Am J Dis Child* 1935;49:900-40.
- ⁵ Holland RI, Hongslo JK. Fluoride, fluoride resistance and glycolysis in cultured cells. *Acta Pharmacol Toxicol* 1978;43:240-5.

(Accepted 19 June 1981)

Karolinska Institutet, School of Dentistry, Box 4064, S-101 04 Huddinge, Sweden

J EKSTRAND, ODONT D, assistant professor, department of cardiology

Karolinska Hospital, S-104 01 Stockholm, Sweden

L O BOREUS, MD, head, department of clinical pharmacology

P DE CHATEAU, MD, assistant professor, department of paediatrics

Fatal subarachnoid haemorrhage in young women: role of oral contraceptives

After a report was published in 1977 from the Royal College of General Practitioners' Oral Contraceptive Study,¹ which suggested a possible association between use of oral contraceptives and haemorrhagic stroke, a case-control study of fatal subarachnoid haemorrhage was carried out by Inman.² This showed a small, but not statistically significant, increased risk of subarachnoid haemorrhage in association with oral-contraceptive use in the absence of hypertension, though it was considered that use of oral contraceptives might be related indirectly by raising blood pressure. We report the results of a further study of this problem.

Methods and results

The methodology is discussed in detail elsewhere.³ We obtained death certificates for 446 women aged 15-44 years certified as dying of subarachnoid haemorrhage in England and Wales during 1978. Two hundred and seven cases were excluded; because there was insufficient evidence for the diagnosis (162), because the records could not be traced (32), or because death occurred after operation or during pregnancy and puerperium (13). Information about the remaining women and about two controls, selected at random³ for each woman and matched for sex, age, and marital status, was sought from their general practitioners. A further 71 deaths were not investigated fully because the general practitioner could not be traced or felt unable to help. Our results are therefore based on the 168 completed case-control sets.

Thirty-six (21%) cases were aged 15-29 years, 73 (43%) aged 30-39 years, and 59 (35%) aged 40-44 years. The controls were matched for age and marital status and had a similar social-class distribution. In 95 (57%) cases the diagnosis was based on post-mortem findings, in 8 (5%) on operative findings, in 13 (8%) on findings on diagnostic angiography or computed tomography scan and in 52 (31%) on clinical findings only

(results of lumbar puncture or the presence of subhyaloid haemorrhage). The table shows that there were no significant differences between cases and controls in their current or past use of oral contraceptives. Similar results were obtained when cases with only clinical evidence of subarachnoid haemorrhage were excluded and when separate age groups were analysed.

The known risk factors for subarachnoid haemorrhage were more prevalent in cases than controls: hypertension (33 cases (20%), 9 controls (3%)), a history of pre-eclamptic toxæmia (11 (7%) and 6 (2%)), renal disease (5 (3%) and 2 (1%)), and a previous subarachnoid haemorrhage (9 (5%) and none). Oral-contraceptive use in women with and without risk factors is shown in the table. The 33 cases diagnosed as hypertensive showed a higher rate of past use (55%) and a lower rate of current use (9%) when compared with non-hypertensive cases. Twelve of the 18 past users had been diagnosed as hypertensive when using oral contraceptives and had stopped using the pill for this reason. Data on smoking were available for only 75 (45%) cases and 95 (28%) controls, but among these women there were more smokers in cases (61%) than controls (32%). Although fewer cases who were using oral contraceptives were taking a preparation containing less than 50 µg oestrogen (9 out of 27 compared with 36 out of 65) the difference was not significant.

Comment

This study confirms the importance of known risk factors for subarachnoid haemorrhage. There have been five previous studies²⁻⁶ examining the role of oral contraceptives in the aetiology of subarachnoid haemorrhage. Three showed a statistically significant increase in risk associated with oral-contraceptive use,²⁻⁴ one a small but not significant increase in risk,² and one no association.⁵ The present study shows a small but not significant increase in risk. As Inman has suggested² oral contraceptives might act indirectly by raising blood pressure: 15 of the 33 patients with hypertension were first found to have raised levels of blood pressure while taking the pill. This effect was not great enough, however, to result in a significant difference in oral-contraceptive use. These findings taken with those of earlier studies suggest that both the relative and absolute risks of subarachnoid haemorrhage associated with use of oral contraceptives are small and are probably associated with the hypertensive effect of the pill.

We would like to thank the many people who have helped with this study and to acknowledge the financial support of the Medical Research Council.

¹ Royal College of General Practitioners. Mortality among oral-contraceptive users. *Lancet* 1977;ii:727-31.

² Inman WHW. Oral contraceptives and fatal subarachnoid haemorrhage. *Br Med J* 1979;ii:1468-70.

³ Adam SA, Thorogood M, Mann JI. The pill and myocardial infarction revisited: the effects of new preparations and prescribing patterns. *Br J Obstet Gynaecol* (in press).

⁴ Royal College of General Practitioners. Further analyses of mortality in oral contraceptive users. *Lancet* 1981;ii:541-6.

⁵ Vessey MP, McPherson KC, Yeates D. Mortality in oral contraceptive users. *Lancet* 1981;ii:549.

(Accepted 12 June 1981)

Department of Community Medicine and General Practice, Oxford OX1 3QN

M THOROGOOD, BSC, research assistant

S A ADAM, MB, MRCP, MRC research fellow (present appointment: senior registrar in community medicine, Oxford Regional Health Authority)

J I MANN, DM, PHD, university lecturer

Risk factors of cases and controls by use of oral contraception. Results are numbers (%)

	Cases	Controls*	With hypertension		With other risk factors		With no risk factors	
			Cases	Controls	Cases	Controls	Cases	Controls
Oral-contraceptive use:								
Never used	59 (37)	130 (43)	12 (36)	4 (44)	16 (48)	5 (45)	31 (34)	121 (43)
Used in past	64 (41)	94 (31)	18 (55)	3 (33)	9 (27)	3 (27)	36 (40)	88 (31)
Used currently†	27 (17)	65 (21)	3 (9)	1 (11)	7 (21)	3 (27)	17 (19)	61 (21)
Used at some time, current status not known	8 (5)	15 (5)		1 (11)	1 (3)		7 (8)	14 (5)
Total	158	304	33	9	33	11	91	284
Inadequate information available	10	27	1		4	2	5	25
Relative risk estimate for use (range)		1.25 (0.85-1.85)		1.40 (0.31-6.24)		0.89 (0.23-3.48)		1.44 (0.88-2.35)

*In five instances data on only one control were available.

†Currently = At the time of death for cases, and at the time of death of the relevant case for each control.