teams with that of staff such as district nurses and health visitors. Acute services trusts are also trying to be more responsive to the needs of general practitioners, such as by offering to provide specialist outreach clinics in their surgeries. As this happens, integration between primary care and community health services staff is developing in parallel with specialisation as general practitioners are encouraged to offer services in fields where they have particular expertise. An example is the Birmingham Multifund, in which general practitioners with specialist skills and training receive referrals from their colleagues as an alternative to hospital referral (G Corser, personal communication).

These initiatives show how collaboration between general practitioners is developing in parallel with competition to provide services. Yet if competition is to develop further, there must be a move away from the current national contract for general practitioners to greater discretion on the part of health authorities to negotiate agreements at a local level. The agreements between health authorities and general practitioners for the latter to provide services beyond those covered by the national general medical services contract indicate the shape of things to come. Extending this approach to part or all of the general medical services could quite rapidly stimulate a market in primary care as general practitioner partnerships, NHS trusts, and the new primary care organisations compete to win business from health authorities. There is every prospect of this happening in the light of the government's consultation document on the future of primary care,² which signals support for local flexibility in the provision of primary care services.

Increased competition could also occur if the government accepts the BMA's argument that the core of the general medical services contract should be defined more clearly. This raises the possibility of providers other than general practitioners entering the market to deliver non-core services. In effect general practitioners would become specialists in family medicine and much greater reliance would be placed on other staff

(including general practitioner assistants) to carry out work that is currently the responsibility of general practitioners. This outcome may not be the one envisaged by the medical profession but it has obvious attractions to politicians concerned to squeeze ever increasing efficiency out of limited health care budgets.

The potential benefits of a primary care market are greater choice for patients and increased responsiveness to their needs. There may also be gains in efficiency. These could arise through competing general practitioner based delivery systems or from the substitution of nurses for doctors where this is appropriate. Quality of care may rise too as new entrants to the market stimulate existing providers to improve their performance and as innovative approaches are adopted to tackling low standards of service provision in deprived areas. But a major risk is that transaction costs will increase as local contracting replaces national negotiation. There is also a danger that competition will set doctor against doctor and make it difficult to build a culture of cooperation and collaboration and to break down professional isolation still further. And at a time when policy makers seem increasingly disillusioned with experience of market oriented reforms,³ any attempt to promote competition in primary care should be viewed with caution. All of this suggests that localised contracts and the primary care market need to be thought through carefully. At a minimum, they should be accompanied by evaluation to ensure that the effects are properly assessed and that policy making is evidence based.⁴

CHRIS HAM
Director

Health Services Management Centre,
University of Birmingham

1 Meads G, ed. *Future options for general practice*. Oxford: Radcliffe Medical Press, 1996.

2 NHS Executive. *Primary care: the future*. Leeds: Department of Health, 1996.

3 Ham C. Contestability: a middle path for health care. *BMJ* 1996;312:70-1.

4 Ham C, Hunter DJ, Robinson R. Evidence based policymaking. *BMJ* 1995;310:71-2.

Vitamins in early pregnancy

Not too little, not too much

Two vitamins have been making headlines in recent years because of their relation to congenital malformations: folic acid because it can prevent some, and vitamin A because it can cause them. In both cases the crucial issues are how much should be consumed in early pregnancy, and whether the vitamins should come from food, pills, or both.

There is now unimpeachable evidence that an adequate consumption of folic acid before conception and during the first two to three months of pregnancy significantly reduces the risk of neural tube defects.^{1,2} There is increasing evidence that folic acid may also reduce the risk of some other birth defects.³ The health departments of many countries have advised women who may become pregnant to increase their folic acid intake by 0.4 mg (400 µg) daily. This amount seems to be both safe and effective.

Unfortunately, although surveys show that the implementation of these policies is gradually increasing, only a minority of women are aware of them. There are also difficulties in achieving the desired results by adjusting diets. It is not easy to find out exactly how much folic acid there is in food, especially when high speed shopping. Foods which declare their folic acid content do not indicate the proportions of free folate, which can be absorbed immediately, and polyglutamates, which must first undergo enzymatic breakdown in the gut. The final difficulty is that 0.4 mg extra folate from food seems

not to raise plasma folate concentrations as effectively as the same dose in a pill.⁴

Vitamin A was the first vitamin to be shown to be teratogenic in animals, initially in pigs⁵ and later in several smaller species. Occasional case reports have linked human birth defects with large doses of vitamin A in early pregnancy, but it was the incrimination of the vitamin A analogues isotretinoin and etretinate, used for the treating severe acne, as a teratogen in the 1980s⁶ that renewed interest in naturally occurring vitamin A (retinol). It is now accepted that vitamin A in sufficient dose is teratogenic in humans, although carotenoids, which are vitamin A precursors, are not.

A recent cohort study by Rothman *et al* analysed birth defects in the offspring of almost 23 000 mothers in relation to their vitamin A intake shortly before and during early pregnancy.⁷ A total daily intake from all sources in excess of 15 000 IU was associated with a significantly increased risk of birth defects, notably of structures arising from the cranial neural crest (craniofacial, central nervous system, thymic, and heart defects). (3.33 IU = 1 µg retinol equivalent.) Very few women achieved an intake in excess of 10 000 IU from food alone, and, although there was a suggestion of an increased rate of birth defects in their offspring, the exact vitamin A intakes of the five mothers of abnormal babies were not specified.

When the effects of vitamin A supplements are examined, a dose-response relation is more evident, the risk of birth defect being increased with intakes above 10 000 IU, although how far above is again not clear. With vitamin A from all sources, the risks, especially of cranial neural crest defects, increase significantly with intakes above 15 000 IU. Again, it is uncertain how far above 15 000 IU constitutes a real danger, but daily intakes below 10 000 IU seem to carry no significant teratogenic risk.

Rothman *et al*'s interpretation of their findings has been widely challenged,⁸ and the actual teratogenic risk from large doses of vitamin A may not be as great as they suggest. Nevertheless, it seems sensible to err on the safe side until further work has been done.

In terms of practical advice, dietary sources may not provide enough folate to do good or enough vitamin A to do harm, although pregnant women should still be advised to avoid liver and liver products because of their variable vitamin A content. Vitamin supplements increase the possible benefit from folate and the possible harm from vitamin A. Women who are planning pregnancy or have very recently become pregnant should not take vitamin supplements without medical advice. The simplest advice is to take only folic acid, 0.4 mg daily, starting before or soon after conception. Any woman who wishes to take a multivitamin supplement should ensure that it contains

0.4-1.0 mg folic acid and not more than 5000 IU vitamin A. This is the limit recommended by the American College of Obstetricians and Gynecologists in 1993.⁹ Although health food shops no longer stock very high dose vitamin preparations, some of their products include more than 10 000 IU vitamin A in the recommended daily dose, and small print pregnancy warnings are easily missed. It may be wiser to purchase vitamin preparations from a retail chemist.

DICK SMITHELLS
Director

International Centre for Birth Defects,
Via Sabotino 2,
00195 Rome

- 1 MRC Vitamin Study Research Group. Prevention of neural tube defects: results of the MRC vitamin study. *Lancet* 1991;338:132-37.
- 2 Czeizel AE, Dudas I. Prevention of the first occurrence of neural-tube defects by periconceptional vitamin supplementation. *N Engl J Med* 1992;327:1832-5.
- 3 Czeizel AE. Prevention of congenital abnormalities by periconceptional multi-vitamin supplementation. *BMJ* 1993;306:1645-8.
- 4 Cuskelly GC, McNulty H, Scott JM. Effect of increasing dietary folate on red-cell folate: implications for prevention of neural tube defects. *Lancet* 1996;347:657-9.
- 5 Hale F. Pigs born without eyeballs. *J Hered* 1933;24:105-6.
- 6 Rosa FW. Teratogenicity of isotretinoin. *Lancet* 1983;iii:513.
- 7 Rothman KJ, Moore LL, Singer MR, Nguyen UDT, Mannino S, Milunsky A. Teratogenicity of high vitamin A intake. *N Engl J Med* 1995;333:1369-73.
- 8 Correspondence. Teratogenicity of high vitamin A intake. *N Engl J Med* 1996;334:1195-7.
- 9 American College of Obstetrics and Gynecology. Vitamin A supplementation during pregnancy. ACOG opinion: committee on obstetrics: maternal and fetal medicines. *International Journal of Gynecology and Obstetrics* 1993;40:175.

Postmenopausal cystitis

Urinary problems, including infection, are common and distressing in older women

Recurrent lower urinary tract infections are common after the menopause and occur in more than 10% of women over the age of 60.¹ A rise in vaginal pH promotes an alteration in the normal vaginal flora, with decreased lactobacilli leading to increased colonisation by pathogenic faecal flora. This increases the incidence of urinary tract infections, especially in sexually active women. Oestrogen deficiency also results in generalised urogenital atrophy, and postmenopausal women are therefore at increased risk not only of recurrent urinary tract infections but also of dyspareunia, vaginal irritation, pruritus, pain, and symptoms of urgency, frequency, dysuria, and urinary incontinence.²

Unfortunately, urogenital atrophy is a late manifestation of the menopause and is consequently often underdiagnosed and undertreated. Many older women fear the side effects of systemic oestrogen therapy, and few wish to suffer monthly withdrawal bleeds from the commonly used hormone replacement therapy of oestrogen and cyclical progestogen. However, oestrogen therapy does promote recolonisation by vaginal lactobacilli, reducing both vaginal pH and proliferation of Gram negative faecal uropathogens.³

Uncontrolled studies have shown that low dose oestrogen therapy decreases the incidence of recurrent urinary tract infections.⁴ In the largest controlled study of its type to date Raz and Stamm showed that vaginal oestriol cream was significantly more effective than placebo in reducing the incidence of urinary tract infections, suggesting that treatment with low dose topical oestrogen may be adequate for this condition.⁵

For those women in whom oestrogen therapy is ineffective or inappropriate, it is important to exclude underlying pathology. This should include a pelvic examination, cystoscopy and bladder biopsy, intravenous urography, and, where indicated, urodynamic studies. Thereafter, antibiotic treatment should be based on microscopy, culture, and sensitivity testing of a midstream specimen of urine. Sometimes a long course of low dose antibiotics is required to eradicate infection. Symptoms may be caused by fastidious organisms, which will not be

identified unless their culture is specifically requested. *Ureaplasma urealyticum* and *Mycoplasma hominis* require long term treatment (about three months) with low dose tetracyclines or erythromycin. Those women who suffer from postmenopausal cystourethritis in association with sexual intercourse may be advised to use a vaginal lubricant and a prophylactic antibiotic such as norfloxacin 400 mg at the time of sexual intercourse, as well as general hygienic measures including voiding to completion after sexual activity.⁶

Not all postmenopausal cystitis is bacterial, and interstitial cystitis should be identified at cystoscopy and by an increased mast cell count on bladder biopsy. This condition is difficult to treat, but patients may benefit from hexamine hippurate 1 g twice daily and a tricyclic antidepressant such as imipramine or amitriptyline given at night. Alternatively, low dose corticosteroids (prednisolone 15 mg daily for the first month, 10 mg daily for the second month, and 5 mg daily for the third month) may be used. Finally, it is important to remember that irritative bladder symptoms, including urgency, frequency, and dysuria, may not necessarily be caused by cystitis. Medical conditions such as diabetes should be considered, and pelvic pathology such as fibroids must be excluded. In those women who do not respond to simple measures further investigations should be undertaken, including urodynamic studies.

LINDA CARDOZO
Professor of urogynaecology

8 Devonshire Place,
London W1N 1PB

- 1 Romano JM, Kaye D. UTI in the elderly. Common yet atypical. *Geriatrics* 1981;36:113-5.
- 2 Bachmann GA. Vulvovaginal complaints. In: Lobo RA, ed. *Treatment of postmenopausal women: basic and clinical aspects*. New York: Raven Press, 1994:137-42.
- 3 Molander U, Milson I, Ekelund P, Mellstrom D, Eriksson O. Effect of oral oestriol on vaginal flora and cytology and urogenital symptoms in the post menopause. *Maturitas* 1990;12:113-20.
- 4 Cardozo LD, Kelleher CJ. Sex hormones, the menopause and urinary problems. *Gynecol Endocrinol* 1995;9:75-84.
- 5 Raz R, Stamm WE. A controlled trial of intravaginal estriol in postmenopausal women with recurrent urinary tract infections. *N Engl J Med* 1993;329:753-6.
- 6 Gillespie L. *You don't have to live with cystitis*. New York: Avon Books, 1986.