Bacteriotherapy has also been used for other indications. Faeces or a mixture of faecal bacterial strains have been used to treat recurrent *Clostridium difficile* infection.[6] Although the efficacy of this treatment method still remains undecided because no randomised trials have been performed, *Saccharomyces bourlardii* yeast was used for the same indication in a randomised trial, with good results.[7] Milk containing *Lactobacillus* GG, given to children in day care centres, seems to reduce the rate and severity of respiratory infections.[8] Lactobacilli have been used in various clinical conditions—for example, for prophylaxis of antibiotic induced diarrhoea (decreasing the diarrhoea rate to one third compared with placebo) but also in promoting recovery from acute diarrhoea in children.[9] Moreover, non-pathogenic *Escherichia coli* have successfully been used to treat ulcerative colitis.[10]

Why are strategies such as bacteriotherapy arousing more interest in our attempts to combat antibacterial resistance? Although restrictions on use of antibacterial drugs in hospitals are effective in reducing bacterial resistance, the increasing number of immunocompromised patients in hospitals nevertheless tends to increase their use. And although we have shown that the reduction of antibiotics used in the community can reduce bacterial resistance,[11] this is a long row to hoe. Also, it may be that bacterial resistance is still too remote a problem for most physicians, patients, decision makers, and the medical industry to cause any concerted action in reducing antibacterial consumption. We do not even know the total consumption of antibacterial agents among humans in the European Union.[12]

In addition to bacteriotherapy, other strategies to reduce infection and bacterial resistance include improved hygiene measures, especially in hospitals but also in day care centres, and new bacterial vaccines.[12] In the future, treatment opportunities may include antibody treatment and bacteriophage therapy.

In the meantime bacteriotherapy seems to be a promising candidate for the future treatment and prevention of respiratory tract and gastrointestinal infections. Several questions remain open, however, such as safety. The α haemolytic streptococci chosen by Roos et al were selected for their superior ability to inhibit the growth of respiratory tract pathogens. Even if bacteriotherapy is safe for individual patients, the possibility remains that large quantities of active bacteria used clinically might change the human flora at population level.

Indeed, we still know very little about the complex system of human flora. There is an immediate need for basic research, and new molecular techniques should help.[13] This research is needed not only to develop bacteriotherapy and other medical treatments but also to better understand the role of human flora—for example, in food processing. Certainly the human microbiome will present plenty of challenges to eager explorers over the next few years.

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Phytoestrogen therapy for menopausal symptoms?

There's no good evidence that it's any better than placebo

Popular media would have us believe that plant constituents with a phenolic structure similar to oestrogen, known as phyto (plant) oestrogens, provide a natural alternative to the use of postmenopausal hormone replacement therapy. Are the popular media right?

Phytoestrogens, found in a wide variety of edible plants, may display both oestrogenic and antioestrogenic effects. Epidemiological studies, primarily comparing Asian and Western populations, have been interpreted to indicate that consumption of a diet rich in phytoestrogens ameliorates oestrogen deficiency symptoms in postmenopausal women—and may protect against breast cancer, bone loss, and cardiovascular disease. Consequently there is a global movement towards increased consumption of foods rich in phytoestrogens, and tablet formulations of concentrated isoflavone extracts are being heavily promoted. However, more recent intervention studies question the validity of the proposed benefits of phytoestrogen

BMJ 2001;323:354–5

supplementation, with little data in postmenopausal women to support a role for phytoestrogens as an alternative to conventional hormone replacement therapy.

The biological actions of these compounds are extremely complex. Their ultimate cellular actions are determined by many factors, including the relative levels of oestrogen receptors α and β, the diverse mix of coactivators and corepressors present in any given cell type, and the nature of the response elements with which the receptors interact on the oestrogen regulated genes.[1] Effects vary according to the phytoestrogen studied, cell line, tissue, species, and the response being evaluated. Hence results from in vitro and in vivo studies are inconsistent.

Japanese women are said to experience a lower frequency of hot flushes at the menopause than Western women, and this has been partly attributed to their high phytoestrogen consumption.[2] However, the apparently low frequency of hot flushes in Japanese women may be due to underreporting of symptoms rather than a genuinely lower prevalence.

The first study to show that certain dietary phytoestrogens can exert mild oestrogenic effects in postmenopausal women was published in 1990 and showed an increase in the vaginal cell maturation index (an indicator of oestrogenic activity).[3] Subsequent reports of their effects on vasomotor symptoms have not been consistent. Considerable differences exist between studies, with no clear correlation between oestrogenic changes in vaginal cytology and effects on vasomotor symptoms. In a placebo controlled study Murkies et al showed no benefit of soy over wheat flour supplementation for hot flushes and vaginal cytology after 12 weeks.[4] Similarly, in a study of soy versus linseed versus wheat supplemented diets the reduction in the rate of hot flushes after 12 weeks was greatest in the wheat diet phase, when the women had very low urine isoflavone excretion.[5] In contrast, a small reduction in hot flushes was reported in postmenopausal women treated with isolated soy protein versus casein. However about 25% of the participants dropped out of this study and the effects were not clinically significant.[6]

Two studies of an over the counter tablet preparation of isoflavones extracted from red clover (40 mg/tablet) versus placebo in postmenopausal women showed that doses of both 40 mg/day and 160 mg/day had no greater benefit than placebo for vasomotor or other menopausal symptoms.[7 8]

There are acknowledged difficulties in objectively assessing vasomotor symptoms in studies because of the natural resolution of these symptoms over time and the high placebo response rate. Nevertheless, conventional oestrogen therapy has been shown to reduce hot flushes effectively in comparison to placebo, and for phytoestrogens to be a viable alternative to hormone replacement therapy the same standard should apply. Phytoestrogens have not been shown to improve other symptoms that characterise the menopausal transition, such as anxiety, mood changes, arthralgia, myalgia, and headaches.

Some data indicate a cardioprotective effect of soy,[9 10] primarily due to favourable lipoprotein lipid effects, but whether the observed effects are due to the isoflavone component of soy or to other moieties is still unclear. There is little data to support the claim that phytoestrogens protect against bone loss, with published studies not having controlled for confounding factors such as exercise and the interventions having been relatively short term. That phytoestrogens prevent breast cancer also cannot be substantiated.

In vitro, concentrations of phytoestrogens equivalent to levels in humans with a moderate phytoestrogen intake stimulate cell growth in oestrogen positive, but not oestrogen negative, cells. In contrast, very high concentrations (probably greater than circulating levels achievable by diet) inhibit cell growth in both oestrogen positive and negative cell lines.[11] There is no evidence that phytoestrogen supplementation in tablet form protects against breast cancer, or is even safe. Furthermore, concurrent use of high dose phytoestrogen supplements and tamoxifen in women with breast cancer should also be discouraged, until further information is available, because of the potential for isoflavones to antagonise the desired antioestrogenic effects of tamoxifen.[12]

Women experiencing mild menopausal symptoms may gain relief by dietary modification and lifestyle changes, such as reducing smoking and consumption of caffeine and alcohol, stress management, and increased exercise. However, there is no evidence to support the belief that even a very high intake of soy products will alleviate hot flushes, night sweats, and other symptoms such as vaginal dryness, mood changes, and musculoskeletal symptoms. No absolute conclusions can be drawn from the few studies of the effects of phytoestrogens on bone. As with other interventions of unproved efficacy, long term randomised trials will be required to determine the place (if any) of phytoestrogens in the management of postmenopausal women.

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