

Myth of the menopause paradox

Sir—In his viewpoint, Hugh Tunstall-Pedoe (May 9, p 1425)¹ reinvents a paradox about menopause and risk of coronary heart disease (CHD) that has been known for 30 years.² He concludes that menopause is not a risk factor for CHD, on the basis of the observation that a semilogarithmic plot of CHD mortality rates by age does not show an increased acceleration in women after the age of 50. We believe that this approach is not justified for examination of the effect of menopause.

First, an increased acceleration of CHD mortality rates at or after the age of menopause implies that the relative risk associated with menopause continuously increases with age, which is not seen for any CHD risk factor, including hypertension and smoking. Second, since the acceleration of CHD mortality rates declines with age in men, an increased acceleration in women is unlikely, even when menopause raises the risk. We have examined the effect of menopause on CHD in a simulation model with more realistic assumptions.

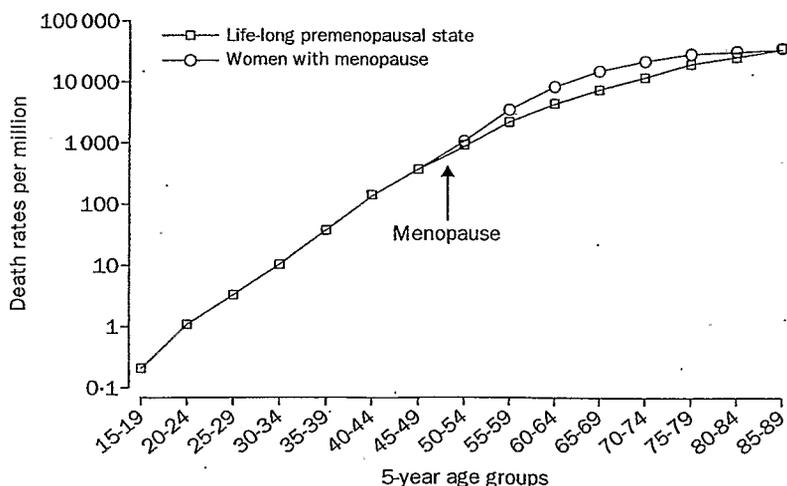
We used mortality rates of UK men,¹ the Framingham risk function,³ and estimates of relative risks at young ages from the MRFIT Study,⁴ to construct a graph of CHD mortality rates in men in the first decile of the Framingham risk score to represent women premenopausal until the end of life (figure). On the basis of estimates of the effect of age at menopause,⁵ we assumed menopause to enhance CHD mortality by 20, 60, and 100% at ages 50–54, 55–59, and

60–69 years, respectively, taking age and a lagtime into account. We assumed that the menopause-related variation in menopausal risk falls gradually thereafter until no excess risk at age 85–89. The upper curve in the figure represents the curve when an effect of menopause is imposed on the curve reflecting the lifelong premenopausal state. The constructed curve does not show a change in slope around the age of menopause and is similar in shape to that of UK women.¹ Although we will probably never know the true effect of menopause, and cannot be certain that our assumptions are correct, our data suggest that the observed CHD mortality pattern in women in the population is not incompatible with an effect of menopause.

*J C M Witteman, C J Moerman,
I C D Westendorp

*Department of Epidemiology and Biostatistics, Erasmus University Medical School, Rotterdam 3000 DR, Netherlands; and Department of Women's Health Studies, Amsterdam Medical Center, University of Amsterdam

- 1 Tunstall-Pedoe H. Myth and paradox of coronary risk and the menopause. *Lancet* 1998; 351: 1425–27.
- 2 Tracy RE. Sex differences in coronary disease: two opposing views. *J Chronic Dis* 1966; 19: 1245–51.
- 3 Anderson KM, Wilson PWF, Odell PM, Kannel WB. An updated coronary risk profile: a statement for health professionals. *Circulation* 1991; 83: 356–62.
- 4 Kannel WB, Neaton JD, Wentworth D, et al. Overall and coronary heart disease mortality rates in relation to major risk factors in 325,348 men screened for the MRFIT. *Am Heart J* 1986; 112: 825–36.
- 5 Schouw van der YT, Graaf van der Y, Steyerberg EW, Eijkemans MJC, Banga JD. Age at menopause as a risk factor for cardiovascular mortality. *Lancet* 1996; 347: 714–18.



Coronary heart disease mortality rates by age on a logarithmic scale

Lower curve gives mortality rates in women staying premenopausal till the end of life. Upper curve gives mortality rates when an effect of menopause is imposed on the curve reflecting the lifelong premenopausal state.

Meningococcal immunisation and protection from epidemics

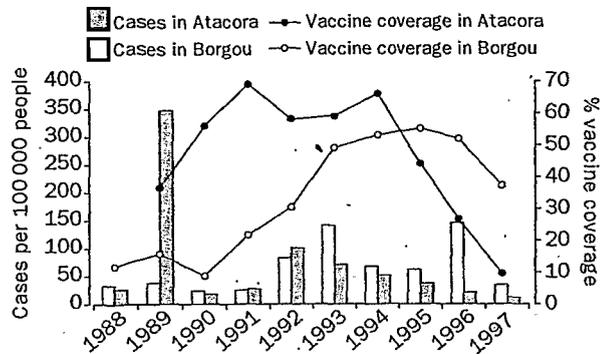
Sir—Some researchers question universal preventive immunisation versus mass vaccination started after the outbreak of epidemics.¹ Epidemics in West Africa in 1994–97 confirm that necessary conditions for an efficient riposte to such vaccination in case of epidemics are far from being achieved. As noticed by J B Robbins and co-workers,² the early detection of the epidemic followed by mass vaccination will prevent, at best, only 50% of cases, which is not acceptable. Even in this scenario, it would be necessary to ensure that the surveillance system is functioning perfectly, alert thresholds are pertinent, resources are immediately obtainable, vaccine stocks available, and vaccination teams operational.³

Two kinds of arguments are made to discredit the preventive immunisation against meningitis epidemics. The first are theoretical and usually speculative. The induction of an immunological memory by the polysaccharide vaccine⁴ and its effect on the carriage of *Neisseria meningitidis*⁵ remains largely questioned and do not seem to offer good protection of subjects in the context of expanded programme.⁶ The second are logistical, but do not take account of all the possible strategies. The preventive vaccination is discounted by some specialists because of difficulties of organisation that would entail a poor vaccine coverage.

In the Republic of Benin, two departments, the Atacora and the Borgou, are included in the meningitis belt and present a high risk of meningococcal epidemics. Since 1988, the vaccine strategy consists in placing polysaccharide vaccine at the disposal of the whole population with cost recovery (300 F CFA, about US\$0.5). This vaccination is distributed in health centres or distributed by mobile teams before the season of epidemics and in areas at greatest risk.

The vaccine coverage has reached or exceeded 60% of the population between 1991 and 1994 in the Atacora and exceeded 50% in the Borgou between 1993 and 1996. During the same period no meningitis epidemics have been observed in Bénin (figure), whereas in neighbour states, severe epidemics have been declared between 1994 and 1997. Niger, North of Benin (1995, 1996), Nigeria East of Benin (1996, 1997), Burkina Faso North of





Incidence of meningitis and vaccine coverage in North Benin (1989–97)

Benin (1996, 1997), and Togo, West of Benin (1997). The epidemic wave skirted North Benin without including a severe outbreak as in adjacent countries.

The situation in north Benin does not constitute proof that the preventive immunisation has avoided epidemics, but we think that it has largely contributed to reduce the number of cases and their brutal appearance, and to limit their geographical extension. The cost for the community has been negligible, and the rational organisation of the preventive immunisation avoids the disorder induced by the installation of a mass vaccination after the onset of epidemics.

We are concerned about the reduction of the vaccine coverage since 1996, which leads to an underestimate of the risks of meningitis outbreak. Reduction of coverage can arise from the false impression that the risk is past and that the epidemic is no longer a danger or from ignorance of the duration of protection by the vaccine. Individuals already vaccinated since 1988 may believe they are definitively protected. A large campaign of information is therefore vital to eliminate these erroneous beliefs.

Jacques Hassan, Achille Massougbodji,
*Jean-Philippe Chippaux, Bruno Massit,
Richard Josse

Ministère de la Santé Publique du Bénin,
Laboratoire de Microbiologie du Centre
Hospitalier Universitaire, Cotonou, Bénin;
Mission Française de Coopération, Cotonou,
Bénin; *Centre de Recherche sur les
Meningites et les Schistosomoses, BP
10887, Niamey, Niger; and Centre ORSTOM
de Niamey, Niger

- 1 Robbins JB, Towne DW, Gotschlich EC, et al. "Love's labours lost": failure to implement mass vaccination against group A meningococcal meningitis in sub-Saharan Africa. *Lancet* 1997; 350: 880–82.
- 2 Robbins JB, Schneerson R, Gotschlich EC. Meningococcal vaccine in sub-Saharan Africa. *Lancet* 1997; 350:1709–10.
- 3 Chippaux JP, Soula G, Campagne G, et al. Optimiser la riposte aux épidémies de méningite à méningocoque: rapport d'un

atelier d'experts au CERMES de Niamey du 12 au 14 janvier 1998. *Cahiers Santé* (in press).

- 4 Higham JH. Meningococcal vaccine in sub-Saharan Africa. *Lancet* 1998; 350: 1701.
- 5 Perkins BA, Broome CV, Rosenstein NE, et al. Meningococcal vaccine in sub-Saharan Africa. *Lancet* 1997; 350: 1707–08.

Patients' use of complementary medicine

Sir—There is much debate about the need for clinical trials to prove the efficacy of complementary medicine. The UK Foundation for Integrated Medicine held a joint meeting of medical practitioners and complementary therapists in May, 1998. Two discussion documents^{1,2} have repeated the call for further research. However, research takes time, and these demands do not take account of the fact that patients are seeking out and using these remedies irrespective of the absence of scientific evidence of efficacy or safety. We are concerned that medical practitioners may not take adequate notice of the use of complementary remedies by their patients.

Since 1991, we have assessed reports of suspected adverse health effects of traditional and herbal remedies. We found that these remedies are fairly safe,³ but that many patients are afraid to inform their doctors of their use of herbal treatments for fear of a negative response.

Physicians should seek to identify what complementary medicine is being taken whilst keeping an open-mind—negative and dismissive attitude to these medicines will not prevent their use. Lack of information exchange between doctor and patient may have many adverse outcomes. For example, doctors may not be kept informed of what herbal medicines their patients use, patients may stop using their prescribed medicines without informing their doctors, drug interactions between pharmaceuticals

and herbal medicine may not be recognised, and adverse or beneficial effects may not be correctly attributed or investigated. Discussion between medical professionals and herbal practitioners when treating the same patient would reduce the chance of interactions and would also give the patient the confidence to discuss treatments with both therapists.

Concern about the competence of the practitioners has been a barrier to the acceptance of complementary medicine.¹ A system of registration of herbal practitioners to ensure standards and professional standing would ease dialogue and improve mutual respect.

Doctors and herbal practitioners should look for ways to collaborate in the care of patients to provide the most effective treatment.

*Debbie Shaw, Christine Leon,
Virginia Murray, Glyn Volans

Medical Toxicology Unit, Guy's & St Thomas' Hospital Trust, London SE14 5ER, UK

- 1 NHS Confederation. Complementary medicine in the NHS: managing the issues. Birmingham: NHS Confederation, 1997.
- 2 Coates JR, Jobst KA, eds. Foundation for Integrated Healthcare 1997. Integrated healthcare—a way forward for the next five years. *J Altern Complement Med* 1998; 4: 209–47.
- 3 Shaw D, Leon C, Kolev S, Murray V. Traditional remedies and food supplements—a 5 year toxicological study (1991–1995). *Drug Safety* 1997; 17: 342–56.

DEPARTMENT OF ERROR

Warring parties continue to ignore health care in southern Sudan (Nov 15, p 1455)—In this Dispatch by Anderson Wachira Kigotho, a statement on the health of children in Sudanese government-held displaced-civilian camps was incorrectly attributed to Médecins Sans Frontières.

Expression of genes that contribute to proliferative and metastatic ability in breast cancer resected during various menstrual phases—In this early report by Zahida Saad and colleagues (April 18, p 1170), figures 2 and 3 should be transposed.

Tackling thorny issues of herbal medicines worldwide—In this news piece (April 18, p 1190), in the panel *Botanical products seeking standards of pharmaceuticals* by Rachelle H B Fishman, Clive R Taylor was incorrectly called Clive R Thomas.

Prope tolerance, perioperative campath 1H, and low-dose cyclosporin monotherapy in renal allograft recipients—In this research letter by R Calne and colleagues (June 6, p 1701), the mention of anti-CD53 in line 16, should have been anti-CD52.

Belief in the face of evil—In this book review (June 6, p 1745), the name and address of the reviewer should have read: Kathleen A Clanon, Division of HIV Services, Alameda County Medical Centre, 1411 East 31st Street, Oakland, CA 94602, USA.

THE LANCET



Volume 352, Number 9125 • Founded 1823 • Published weekly • Saturday 1 August 1998

EDITORIAL

- 335 **Shaken babies**

COMMENTARY

- 336 **Antenatal screening for Down's syndrome: where are we and where next?** J E Haddow
- 337 **Thin line between research and audit**
V Choo
- 338 **Implantable cardioverter defibrillators—for whom?**
S J Connolly
- 339 **Axon loss in multiple sclerosis**
N Scolding, R Franklin
- 341 **Room air or oxygen for asphyxiated babies?**
W O Tarnow-Mordi
- 342 **Low-dose aspirin not for pre-eclampsia** M Darling

ARTICLES

- 343 **UK multicentre project on assessment of risk of trisomy 21 by maternal age and fetal nuchal-translucency thickness at 10–14 weeks of gestation**
R J M Snijders and others, for the Fetal Medicine Foundation First Trimester Screening Group
- 347 **Macrophagic myofasciitis: an emerging entity**
R K Gherardi and others, for the Groupe d'Etudes et Recherche sur les Maladies Musculaires Acquises et Dysimmunitaires (GERMMAD) de l'Association Française contre les Myopathies (AFM)
- 353 **Outbreak of epidemic typhus associated with trench fever in Burundi**
D Raoult and others

EARLY REPORTS

- 359 **Electropotential measurements as a new diagnostic modality for breast cancer**
J Cuzick and others
- 364 **Introducing a placebo needle into acupuncture research**
K Streitberger, J Kleinhenz

CASE REPORT

- 366 **Fractured rib, pleural effusion, and ascites** S Thomas and others

RESEARCH LETTERS

- 367 **Fulminant neurogenic pulmonary oedema with hand, foot, and mouth disease**
L-Y Chang and others
- 368 **Treatment of Guillain-Barré syndrome with interferon- β**
A Créange and others
- 369 **Human Dobrava hantavirus infections in Estonia**
Å Lundkvist and others
- 369 **Effect of starch-free bread on metabolic control in type 2 diabetes**
B Stilling and others
- 370 **Telencephalin as an indicator for temporal-lobe dysfunction**
P Rieckmann and others
- 371 **Salivary antibodies to lipopolysaccharide antigens of *Escherichia coli* O157**
H Chart, C Jenkins
- 371 **Effect of arginine on mucociliary function in primary ciliary dyskinesia**
S Loukides and others
- 372 **Effects of luteinising-hormone-releasing hormone on nervous-system tumours**
J C van Groeninghen and others
- 373 **Severe nausea and vomiting with timolol eye drops**
F H J Wolfhagen and others
- 373 **A cyclophosphamide-induced autoimmune diabetes**
C Atlan-Gepner and others
- 374 **Implications of chills**
J T Van Dissel and others

NEWS

Science & medicine

- 375 Lyme disease vaccines are safe and effective
Autoimmunity from Lyme disease
- 376 Shellfish point to cystic-fibrosis therapy
Adult cardiac myocytes do divide
- 377 Human albumin controversy
New flu database
First antisense drug approved in USA

Feature

- 378 Extending the targets for antihypertensive drugs

Dispatches

- 379 UK's big budget faces big demands
Cyanide poisoning in Japan

Policy & people

- 380 IOM considers breast-implant safety
Report highlights India's health failings
- 381 Health service for China's peasants
US House backs patients' rights bill
Bid to stop assisted suicide in USA
- 382 Cadavers' gametes and artificial fertilisation
Genetically engineered foods debate

SEMINAR

- 383 **Medical causes of seizures**
N Delanty and others

ELECTROLYTE QUINTET

- 391 **Magnesium and phosphorus**
J R Weisinger, E Bellorín-Font

HYPOTHESIS

- 397 **Aetiology of transient global amnesia**
S L Lewis

Contents list continues inside

All literary matter in The Lancet is copyright. © The Lancet Ltd, 1998. Registered as a newspaper. ISSN 0140-6736.

£3.95

PH 18 - 3 AOUT 1998

Trisomy 21
pages 336, 337, 343