Antiplatelet therapy and atherosclerotic events. Commentary is inaccurate

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What do you think is a non-disease?

Pros and cons of medicalisation

Editor—The BMJ’s decision to extend participatory democracy to the question of disease is important not so much for the results but because it happened at all.1

To a previous generation the idea of asking consumers to decide on these matters would have been incomprehensible. Doctors decided which conditions were legitimate and which should be consigned to the outer darkness. In the debate about the nature of neurasthenia at the end of the 19th century all protagonists were in the medical profession and their debates were published in journals. The views of a few well educated and well heeled patients may be inferred from diaries and fiction, but their voices were largely unheard and unheeded.

Now of course medical authority is in retreat everywhere and the final arbiter of “non-disease” is fast becoming the patient. All this is well and good, so why the outrage of so many respondents? I suspect it comes from a failure to recognise the different concepts of illness and disease.

Taking chronic fatigue syndrome as an example from the debate, few could now question that it is indeed an illness. It has a nosological status and is clearly associated with suffering, ill health, and disability. The patient’s voice must be and is paramount. But is it a disease—that is, has a specific pathological process been identified to account for the above? Chronic fatigue syndrome is not yet a disease because no unambiguous evidence has yet been presented that has commanded widespread acceptance by the scientific community, which remains the arbiter.

Of course, the syndrome may plausibly make the transition from illness to disease like many other illnesses have done. Or it may not. The traffic is not entirely one way in which illness entities inevitably receive the stamp of scientific approval, usually after a period of being falsely labelled as psychological. Previously apparently sound entities have lost their disease status under the cold light of scientific scrutiny.

The concept of labelling also generated a lot of heat in this debate. People behave according to the labels that are ascribed to them, a process seen as largely negative. Some respondents rightly echo this, citing examples in which the act of labelling distress as something medical (pathological) carries with it a host of adverse consequences.1 w1-4

But more commonly the act of giving a name to symptoms and disability brings relief. The acknowledgement by the medical profession that a patient’s condition has a name and is a legitimate illness is immensely reassuring and enabling. It also ends the battle of diagnosis—“If you have to prove you are ill you can’t get well.”5 6

Giving a condition a name is an intervention in itself with costs and benefits.1 7 Cruelly handled, medicalisation can perpetuate disability and exclusion. But used constructively and appropriately it is the first step towards recovery.

Simon Wessely professor
Department of Psychological Medicine, Guy’s, King’s College, and St Thomas’s School of Medicine and Institute of Psychiatry, London SE5 8AF

s.wessely@iop.kcl.ac.uk

Defining non-diseases to avoid medicalisation is throwing the baby out with the bath water

Editor—Having read the list of non-diseases I am not sure I fully understand the rationale behind it.1 However, as a person who experiences chronic fatigue syndrome, fibromyalgia, obesity, and several other conditions included on the list I have a vested interest in the outcome.

I agree that the medicalisation of certain diseases, illnesses, and conditions has impacted negatively on those who experience them. I also accept that it might be better not to treat certain conditions in certain circumstances. This is true of both diseases and non-diseases and I see no automatic correlation between disease and treatment and non-disease and no treatment.

Few people would probably argue that having big ears is a disease, so its inclusion as a non-disease poses few problems. This does not mean, however, that it automatically requires no treatment. That decision surely depends on various factors, including the extent to which the condition impinges on the life of the person experiencing it. Conversely, cancer is (arguably) a disease that often benefits from highly aggressive treatment, but in some cases less aggressive treatment or no treatment at all might be better.

Moreover, despite the best efforts of certain egotistical members of the medical profession to convince us that they have all the answers, many conditions are not understood enough to be able to label them disease or non-disease. Perhaps a condition should be labelled a non-disease rather than erroneously be called a disease. I think, however, that any rush to label a condition of unknown origin a non-disease could have negative effects.

Historically, conditions that have no known origin have attracted labels such as psychosomatic and psychological, stigmatising those experiencing them as lacking or weak at best and mad at worst and defining treatment. For example, before the organic origin of multiple sclerosis was discovered patients were often labelled as having psychological difficulties and treated inappropriately. This is still the case with conditions such as chronic fatigue syndrome and myalgic encephalitis.

Labelling conditions as non-diseases could also have far reaching consequences. In the United Kingdom a person’s entitlement to receive state and other benefits when unable to work because of ill health is largely dependent on the recogni-
ation of a pre-existing condition. Clearly, the label of non-disease might well negatively affect the amount of benefit paid.

The classification of certain conditions as non-diseases to avoid the perils of medicalisation seems to be a case of throwing the baby out with the bath water. A holistic social approach to illness and disability that treats each person individually is far better than seeking a cover all solution replacing one label with another.

Dianna Dunbar  graduate in health and community studies
Yeovil BA2 3SN
uk_lox@h hint.com

Labels create legitimacy and produce dependence

Editor—The last decade has seen the development of an ever increasing role of patients as the primary decision maker in the management of illness. This approach has been encouraged by advocacy groups, the popular news media, and doctors who cater to the non-critical thinking population.

For those not trained to reign in their innate belief engines, the association of symptoms with a disease is encouraged only by the production of labels. A symptom complex described by physicians as fibromyalgia, which is nothing more than a descriptive term for pain in muscles and fibrous tissue, now has the legitimacy of a disease as opposed to a panoply of symptoms. The near mass hysteria displayed by like-minded believers when these labels are challenged adds to the dependency on the labels as being legitimate.

Having evolved a mind that is designed for pattern recognition, resists changing in the face of new information, and encourages the production of cause and effect relations in the presence of associative phenomena, some human beings will always need labels to support their continued suffering in an unfair world. These non-diseases clearly contribute to the development of co-dependent suffering.

Kevin C Murphy  medical oncoologist
BC Cancer Agency/Fraser Valley, 13750 96th Avenue, Surrey, British Columbia, Canada
V3V 1Z2
kmurphy@bcancer.bc.ca

Diet, lifestyle, exercise, spirituality, and the search for meaning are ignored at our peril

Editor—Much evidence supports the organic nature of many of the diseases mentioned in the list of non-diseases, particularly for myalgic encephalitis—chronic fatigue syndrome, fibromyalgia, and multiple chemical sensitivity. Evidence also supports shared symptoms in these and other medically puzzling and taxing disorders such as Gulf war syndrome and irritable bowel syndrome.

Linus Pauling argued that all diseases have a molecular basis. The validity of this statement is substantiated by many who advocate the existence of non-diseases. Yet in prescribing antidepressants, antiepileptic drugs, and agonists and antagonists of the major biogenic amines and neurotransmitters, they are changing the underlying physicochemical and physiological properties of organs and body systems, particularly the brain.

Illich has written perceptively about the medicalisation of life and its origins and consequences. Medical ignorance and arrogance dominated by rationalism seeks explanations of puzzling signs and symptoms and ends up creating spurious diseases and disorders that put the blame on patients or their caring family and friends.

The consequence of the triumph of such attitudes is now seen in the abandonment of any responsibility for one’s own health. Life-styles, however destructive, are pursued in the belief that medicine will somehow provide an answer. The drug industry and much of modern medicine seek new agents to modify or offset the consequences of excesses—for example, new anti-obesity agents for the epidemic of obesity and maturity onset diabetes.

The food industry also contributes to modern health problems with the widespread use of pesticides, plant and animal hormones, and genetically modified crops. Thus, even eating a healthy diet leads to an increasing burden of new man-made toxins, many of which have not been toxicologically assessed.

Diet, lifestyle, exercise, spirituality, and the search for meaning are all parts of our human condition. We ignore them at our peril.

What is required is a change of heart and mind leading to a change of practice that embraces human values of mutual respect, careful listening, and use of modern medicine as a byproduct of ageing, suggested Dirk Ulbricht of the Centre Hospitalier, Luxembourg, including osteoporosis. Yet, said Iona Collins, specialist registrar in trauma at the John Radcliffe Hospital, Oxford.

But de-medicalising disease could deny those who had them the right to research and treatment, said Alex McAulghlin, a writer from Red Hill in Australia, and they could be dismissed as “somatisers.” The hub of the issue, she said, was whether medicine had the capacity and the moral authority to define what is and what isn’t disease.

Others suggested that labels helped people cope better, gave them legitimacy, and signalled protected funding and physician time. Chronic fatigue syndrome was frequently suggested as rightfully belonging to the non-disease category, but it was also vigorously defended as having clear physiological changes.

And there were fears that state funding for disease that impaired mobility and the ability to work might be withheld if it were to lose its legitimate label. The UK government’s refusal to recognise repetitive strain injury as a disease, suggested Martin Wilson of Glasgow, denied people financial help.

Respondents worried that definitions were founded on shaky ground, guided as they are by constantly changing criteria: (lack of) knowledge, different cultural perspectives, where you lived.

And they were also subject to fads and fashion. A case in point is obesity, which was regarded as a sign of prosperity a century ago, pointed out research professor of chemistry, Joel Kaufmann, from Philadelphia. New Zealand patients’ rights cam-

Summary of responses

Editor—There were some who thought the exercise a joke, and in bad taste at that. Others couldn’t see the point and complained that deciding what was, or was not, a non-disease was unworthy of a serious medical journal and did little more than toy with semantics.

And some thought that the process trivialised genuine suffering and was an excuse for airing prejudice and ignorance. The stigma of having a non-disease could only make that suffering worse. But aside from the long list of possible contenders—from burnout to fibromyalgia, and high cholesterol—the issue provoked vigorous debate about the purpose of medicine and what some saw as a narrow understanding of illness and the limited scientific paradigm.

Respondents struggled with definitions of their own, and Kazem Zarrabi, a postdoctoral researcher at the University of Lund, Sweden, suggested that we should look to Darwin for guidance, regarding as disease any condition that interfered with our reproductive success and compromised our “inclusive fitness.”

Medicalising natural processes, such as normal childbirth, the menopause, and bereavement was not a healthy option, countered several correspondents, serving to boost the profits of drug companies.

And much of what we classify as disease is really a byproduct of ageing, suggested Dirk Ulbricht of the Centre Hospitalier, Luxembourg, including osteoporosis. Yet, said Iona Collins, specialist registrar in trauma at the John Radcliffe Hospital, Oxford.

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1 Non-disease. Results of ballot, and electronic responses. bmj.com 2002/03/bmj.com/cgi/content/full/324/7354/DC1; accessed 4 April 2002.
Medicalisation of life: the role of social factors, but their argument is disingenuous. I was pointing to the tension between aspects of British identity traditionally grounded in stoicism and composure and the emergent demands of an expressive individualism.

Mezey and Robbins pay lip service to the role of social factors, but their argument runs the other way. Their core defence is institutional: post-traumatic stress disorder must be valid because it is in the books—in psychiatric classification systems such as the International Classification of Diseases (ICD) and the Diagnostic and Statistical Manual of Mental Disorders (DSM). By this token they would happily have diagnosed homosexual identity as a mental illness during the years when it was classified as such in the ICD or DSM.

Psychiatrists serve neither society nor patients with psychiatric difficulties when they uncritically endorse the medicalisation of life.

ICD and DSM are contemporary cultural documents

Editor—In their riposte to my critique of post-traumatic stress disorder Mezey and Robbins cite me as advocating a “stiff upper lip” approach to adversity.1 This is disingenuous. I was pointing to the tension between aspects of British identity traditionally grounded in stoicism and composure and the emergent demands of an expressive individualism.

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Adequate investigation for other physical causes of chest pain must be part of a comprehensive approach to this difficult problem.

David S Coulshed staff specialist in cardiology Department of Cardiology, Nepean Hospital, Penrith, New South Wales 2751, Australia

Guy D Edick gastroenterology fellow eslcgk@med.usyd.edu.au

Nicholas J Talley professor of medicine Department of Medicine, University of Sydney, Nepean Hospital, PO Box 63, Penrith


Hormone replacement therapy and the breast

Studies must determine the evidence

Editor—As active members of the Australasian Menopause Society, we are disappointed at the conclusions that Dixon drew in his editorial on hormone replacement therapy and the breast.1 Although it may be true that hormone replacement therapy makes mammograms harder to interpret, it is far from clear that it causes breast cancer. A recent overview by Bush et al emphasises the weakness of Dixon’s argument, based, as it is, almost entirely on three observational studies.2 Unlike Dixon’s selection of studies with the highest odds ratio, Bush et al’s review was of 45 studies assessing the association between use of hormone replacement therapy and risk of breast cancer. It found that risk was reduced (relative risk <0.9) in 20% of the studies, did not change in 47% (0.9-1.1), and increased in 33% (1.1-2.0). In no study did relative risk increase above 2.0, and in the 20 studies where the relation between risk of breast cancer and combined oestrogen and progestin therapy was studied only four reported a significant difference in relative risk, with two showing an increased and two a decreased risk.

The heterogeneity of these data is in stark contrast to the homogeneity of the data on mortality from breast cancer in users of hormone replacement therapy that were reviewed: all 11 of the studies reported a reduction in risk. Unlike Dixon, the authors concluded that the likelihood of an adverse effect of hormone replacement therapy on breast cancer must be small.

The Australasian Menopause Society is a sponsor of the women’s international study of long duration oestrogen use after the menopause (the WISDOM trial), a large prospective 15 year randomised placebo controlled trial. The results of this trial, together with those of the women’s health initiative in the United States, will be used to answer the question of whether hormone replacement therapy has any effect (beneficial or adverse) on breast cancer.

Until then strong opinions will continue to be held about hormone replacement therapy and its relation to risk of breast cancer, often derived from selective quoting of the available literature. These opinions heighten the anxiety of women who have valid reasons for taking hormone replacement therapy and do not afford them the opportunity of informed choice.

Alastair H MacLennan professor of obstetrics and gynaecology Women’s and Children’s Hospital, University of Adelaide, Adelaide, South Australia, Australia

Beverley Lawton principal investigator WISDOM New Zealand, Wellington School of Medicine and Health Sciences, University of Otago, New Zealand

Rodney J Baber clinical senior lecturer in obstetrics and gynaecology University of Sydney, Royal North Shore Hospital, Sydney 2065, New South Wales, Australia


Competing interests: AHM is editor in chief of *Climacteric*, the journal of the International Menopause Society. He has received research grants to conduct phase 1 and phase 3 trials of various products for managing the menopause and its sequelae and is the principal investigator of WISDOM, Australia. IL is involved in three clinical trials of hormone therapy in postmenopausal women and receives funding from the Medical Research Council in the United Kingdom for the WISDOM trial. RB has received research grants to conduct phase 2 and phase 3 clinical trials on the effects of various types of hormone replacement therapy, selective oestrogen receptor modulators, and phytoestrogens in postmenopausal women.

The WISDOM trial in Australia is sponsored by the UK Medical Research Council, Australian National Health and Medical Research Council, Australian Heart Foundation, South Australian Anti-Cancer Foundation, Australasian Menopause Society, and Royal Australian and New Zealand College of Obstetricians and Gynaecologists.

1 Dixon JM. Hormone replacement therapy and the breast. *BMJ* 2001;323:1381-2. (15 December.)
3 Bush TL, Whiteman M, Flaws JA. Hormone replacement therapy in postmenopausal women and having received hormone therapy are considered to have an unknown factor proposed by Bush et al is the basis of the objections I drew on the development of breast cancer. Bush et al doubt whether oestrogen is important in breast cancer development and propose that some additional, as yet unidentified, factor is secreted from the ovary.

New data from over 9300 women with early breast cancer randomised to receive five years of treatment with adjuvant tamoxifen alone, anastrozole alone, or tamoxifen and anastrozole combined were presented last year by Baum. They show that after 33 months, there were five new invasive contralateral breast cancers in the 3112 patients taking anastrozole compared with 30 in 3116 women taking tamoxifen and 23 in 3125 in the combination arm—a significant reduction in contralateral breast cancers with anastrozole compared with tamoxifen (hazard ratio 0.42 [0.22-0.79], P = 0.0054). These data explode the myth of an unknown factor proposed by Bush et al and confirm the importance of oestrogen in the development of breast cancer.

It was not my intention to try to frighten women off hormone replacement therapy. The US Food and Drug Administration removed the treatment of oestrogen as an indication for oestrogen replacement therapy in 1999 because of lack of evidence from randomised trials. There are new specific and better drugs for this condition. “Hormone replacement therapy should not be prescribed for the express purpose of preventing cardiovascular disease.” In the heart and oestrogen/progestin replacement study women over 65 taking hormone replacement therapy had worsening urinary incontinence and an increased risk of fatal stroke.

Baum is inconsistent. He believes that women should be provided with all available data on screening so that they can make an informed choice yet he would deny them all available information on hormone replacement therapy. There is no doubt that oestrogen for women significantly improves the quality of many women’s lives. The challenge for women and their clinicians remains to control menopausal symptoms and to deliver the benefits of oestrogen while minimising the problems that continue to be reported with these preparations.

M Dixon consultant surgeon and senior lecturer Academic Office, Edinburgh Breast Unit, Western General Hospital, Edinburgh EH4 2XU jmd@wght.demon.co.uk

Competing interests: None declared.


### Schizophrenia in ethnic minority groups

**Selection bias in prevalence data is difficult to rule out**

Entroor—To sociologists, Boydell et al’s findings are counterintuitive. One would expect economic deprivation (at neighbourhood level) to be a decisive factor for an increased incidence of mental illness. But it is surprising to learn that the lower the proportion of non-white ethnic minorities in a local area the higher the incidence of schizophrenia in those minorities (controlled for economic deprivation).

As an explanatory hypothesis the authors point to overt discrimination and institutionalised racism as sources of stress, which can be alleviated by people making use of social capital within the ethnic group. This hypothesis surely necessitates further testing and debate. It is a pity that non-white ethnic minority groups had to be considered as one homogeneous group on an aggregate level. The social networks and levels of social cohesion may be different for different ethnic groups, and follow up research should be able to distinguish these.

Boydell et al assume that all people with schizophrenia will come into contact with psychiatric services, but this requires closer attention. Members of an ethnic minority with a mental disorder who live in predominately white neighbourhoods may be more likely to come into contact with psychiatric services. Probing for mental disorders might be more likely in predominantly non-white neighbourhoods than in non-white neighbourhoods.

This is not necessarily ruled out by the fact that there is job mobility of clinical staff, since institutional cultures can both consciously and uncon-
services.


Antithrombotic therapy and atherosclerotic events

Commentary is inaccurate

Editor—We endorse the response of Bai- gent and others to Cleland’s commentary on the Antithrombotic Trailists’ antithrombotic meta-analysis.1 We would like to add some further comments in response to Cleland’s article and the editorial in the same issue.

Both suggest that the data in the meta-analysis were revised retrospectively. But the overview methods were planned prospectively. Differences between the data in trial publications and the dataset used for the meta-analysis occurred where trialists provided additional information on the numbers of patients originally randomised, or on unpublished or subsequently available outcomes for small numbers of patients. Minor differences between the current and previous antithrombotic overviews generally relate to additional, unpublished data from a few trials and do not affect any of the results or conclusions.

The claim by Reilly and FitzGerald that the absolute reduction in vascular events with antithrombotic treatment is smaller in acute ischaemic stroke than in other high risk conditions is incorrect. For every 1000 patients treated, about 10 events are prevented in the first month after onset of stroke, and just over one event per month is prevented with long term treatment thereafter.

Cleland finds it remarkable how seldom trials of antithrombotic agents have shown benefit on their selected primary outcome. Many early trials of antithrombotic treatment were too small to detect moderate benefits reliably, which is why the first meta-analyses were needed. Reilly and FitzGerald suggest that meta-analysis is no longer needed because large enough trials are now being done. This view fails to acknowledge that, firstly, meta-analysis of large trials can assess not just whether a treatment works but also for whom and by how much, and, secondly, trials comparing different antithrombotic regimens have rarely been large enough to detect the small differences expected.

Cleland says that inconvenient trials are ignored in the discussion section of the meta-analysis, citing an unpublished anti-thrombotic trial, which included fewer than 200 patients and recorded only about 50 vascular events in its comparison between aspirin and control. Including this trial in the meta-analysis would make no difference to the results. Cleland also cites an economic appraisal of aspirin, which he co-authored. Its first sentence, that aspirin is a cheap drug that is effective for the prophylaxis of cardiovascular events, contrasts with the views in Cleland’s commentary.

Finally, unlike the Antithrombotic Trailists’ meta-analysis, neither the accompanying editorial nor the commentary has been endorsed by hundreds of collaborating trialists worldwide. Furthermore, Cleland’s commentary was published despite a reviewer pointing out that his views are maverick, and despite the fact that the conclusions of his article rely on basic errors of fact.2

Cathie Sudlow Welcome clinician scientist csudlow@skull.dcn.ed.ac.uk

Peter Sandercocx professor of medical neurology Department of Clinical Neurosciences, University of Edinburgh, Western General Hospital, Edinburgh EH4 2XU

Competing interests: CS, PS, and CW are members of the steering committee of the Antithrombotic Trailists’ Collaboration. CW participated in co-ordinating the current cycle of the collaborative overview and was a member of the writing committee for the antithrombotic meta-analysis.

3 Cleland JF. Preventing atherosclerotic events with aspirin. BMJ 2002;324:105-6. (12 January.)
4 Reilly M, FitzGerald GA. Gathering intelligence on antithrombotic drugs: the view from 30 000 feet. BMJ 2002;324:590-6. (12 January.)

Risks and patients' values need to be included in decision about aspirin for prevention of coronary heart disease

Editor—The updated meta-analysis by the Antithrombotic Trailists’ Collaboration confirms the benefits of aspirin in reducing non-fatal myocardial infarction, non-fatal stroke, vascular deaths, and total mortality in patients at high risk of vascular events.1 High risk was defined as patients with previous occlusive events or predisposing conditions (for example, diabetes) that led to risks of having a vascular event that were greater than 3% per year.

On the basis of these findings, the authors recommended aspirin for patients with high cardiovascular risks and low or average risks of gastrointestinal bleeding. In their discussion, they also recommended aspirin for patients at intermediate risk of vascular events (annual risk of 2%-3%), including those with peripheral vascular disease, stable angina, or atrial fibrillation. They then concluded by saying that for most healthy people, for whom the risk of a vascular event is likely to be substantially less than 1% per year, daily aspirin may well be inappropriate.

We performed a systematic review and meta-analysis of the effect of aspirin in adults with no previous history of cardiovascular events for the US Preventive Services Task Force.3 On the basis of the results of five large trials that evaluated the use of aspirin for patients without cardiovascular disease, we concluded that aspirin reduced the risk of non-fatal myocardial infarction and deaths from coronary heart disease by 28%,
Aspirin had little effect on thrombotic strokes or all-cause mortality over the three to seven year duration of the trials. The risk of coronary heart disease of patients in the five trials ranged from 0.36% to 1.24% per year, well below the high risk patients studied in the BMJ review. We found that the harms of aspirin included increased risks of haemorrhagic stroke and gastrointestinal bleeding that were similar to the levels found in the trials with patients at high risk.

We concluded that the number of potential reductions in events of coronary heart disease exceeded the number of potential precipitated adverse bleeding events when patients have an annual risk of 1% or greater of events of coronary heart disease. Numbers of adverse effects approached the numbers of beneficial effects when the annual risk of coronary heart disease was 0.2% or less. The balance of beneficial and adverse effects was closer for patients with risks of 0.2-1.0% per year. Providers and patients can easily measure such risks by using any one of several cardiovascular risk calculators available on the web, including our own site (wwwmed-decisions.com). We recommend that providers and patients incorporate both risk and patient values about those risks into their decisions regarding whether or not to use aspirin.

Michael Pignone assistant professor of medicine
University of North Carolina-Chapel Hill, 5039 Old Clinic Building, UNC Hospital, Chapel Hill, NC 27599-7110, USA
pignone@med.unc.edu

Can these problems with usually pharmacological doses of folic acid (1-50 mg daily) be avoided with minimum food fortification? The only evidence I know of is a review of 38 patients with vitamin B12 deficiency treated with ≤1 mg folic acid, 30% of whom showed a significant haematological response. None of 25 patients treated for 7-19 days developed nervous system disorder, whereas six of 12 treated for 90-930 days did. Isolated examples of a reticulocyte response and neurological deterioration occurred with doses as low as 0.3-0.5 mg daily. Because of the very active blood-brain barrier for folate the vitamin enters the nervous system slowly and the duration of the treatment is just as important as the dose, which is highly relevant to food fortification.3,4

Folic acid does much more than interfere with the metabolism of antiepileptic drugs. Experimental studies have confirmed that folates are highly convulsant if the blood-brain barrier is circumvented. The risk to patients is small because of the barrier mechanism, but the bigger the dose, the longer the duration, and the greater the damage to the blood-brain barrier then the higher the risk.

I do not agree that the benefits of fortification are clear. They may be relatively clear with respect to the prevention of neural tube defects, but not all such defects are preventable with folic acid. The Department of Health’s report estimates that fortification with 240 μg folic acid/100 g flour would prevent a further 74 cases (41%) in the United Kingdom. Given the potential risks to others, the policy of universal food fortification seems disproportionate.

Other, potentially much greater benefits of food fortification exist (including in vascular disease and to mental health), which have yet to be clarified. The possible benefits for mood, cognitive function, and ageing are considerable but have not been evaluated.2,3

For all these reasons field trials are advisable before the whole population is exposed to a prolonged increase in folate intake.

Edward Reynolds consultant neurologist
Institute of Epileptology, King’s College, Weston Education Centre, London SE5 9PJ
reynolds@backedus.net

Fortification of flour with folic acid

Fortification has several potential risks

Editor—Wharton and Booth recommend carrying out a field trial before a policy of fortifying flour with folic acid is implemented, but both they and the Department of Health’s report underestimate the potential risks of the policy to the nervous system.1

In people with vitamin B12 deficiency, giving folic acid does much more than mask any anaemia. The response of pernicious anaemia to folic acid is usually suboptimal and temporary and often followed by relapse. The vitamin precipitates not only neurological complications, sometimes after some initial temporary improvement, but also anaemia, although not necessarily to the same degree or in the same time scale.2,3

2 Dickenson MA, Dickenson J. Does folic acid harm people with vitamin B12 or folate deficiency? BMJ 2001;323:1198-9. (24 November.)
4 Reynolds EH. Neurological aspects of folic acid and vitamin B12 metabolism. In: Hoffbrand AV, ed. Clinical haematol-
5 Rottigatti T, Crevilin R, Reynolds EH. Folate and neuropsy-

Fortification is needed now

Editor—Wharton and Booth raise several points about the safety of fortifying food with folic acid to prevent neural tube defects.1 In my opinion, the negative effects of food fortification are overstated.

The risk of folate masking B12 deficiency leading to spinal cord degeneration is probably low.1 It is well known that neuropathies due to B12 or folate deficiency can occur without megaloblastic anaemia. Surely an increase in cord degeneration would have been seen by now in the United States, where food has been fortified since 1996. Even if it was increased, this risk could be abrogated by food fortification with vitamin B12 in addition to folate.1

Interference with antiepileptic drugs is unlikely to occur at the levels of fortification proposed. As the risk of fetal abnormality is increased in people with epilepsy who are taking drugs, especially in those taking sodium valproate, folate supplementation in this group is even more important.1

In my opinion, the negative effects similar to that estimated by case-control studies. As 10-20% of the population have high homocysteine concentrations, and this proportion increases with age, the potential health improvements are large and are likely to much outweigh the theoretical negative effects mentioned in the editorial.

A controlled trial of folate fortification, as suggested, would have to be conducted over an extended period to show the positive and negative effects adequately. During this time, preventable morbidity and death from atherosclerotic disease would be likely and many women would have unnecessary second trimester terminations. Folic acid fortification should be started as soon as possible.

Mark Sillender specialist registrar in obstetrics and gynaecology
Royal Berkshire Hospital, Reading, Berkshire RG1 5AN
mark.sillender@hotmail.com

2 Dickenson J. Does folic acid harm people with vitamin deficiency? A critical examination of the evidence, relevant to fortification of cereal grain. QJM 1995;88:357-64.
Treatment of intersex needs open discussion

Editor—It is excellent to see surgery for ambiguous genitalia and intersex being openly discussed.1-3 These articles prove what patients have been saying for years, that surgery can, and does, cause damage to sexual function. This research is long overdue and most welcomed by patients and parents. I agree that cosmetic genital surgery needs to be reassessed.

Parents and patients need to have all the facts explained before opting for irreversible genital surgery. This is especially so in the changing NHS that is aiming to be more patient led. Fully informed consent is important (particularly after the Bristol and Alder Hey scandals), and may be lacking in patients with ambiguous genitalia or intersex as surgery is often done on children before they can give consent. If parents are to make these decisions they need the full facts or they will end up with feelings of extreme guilt for damaging their child's sexual function by having early surgery. Ambiguous genitalia or intersex are nothing to be ashamed of; being more open can only help people lead better lives. More research is needed into whether leaving surgery until adolescence will have psychological effects compared with surgery in early infancy as is current practice in the thought that it reinforces sexual identity. This gives rise to the necessity for multidisciplinary treatment centres to treat the conditions with a more holistic approach encompassing surgery, endocrinology, and psychology.

Two conferences in 2000 brought together professionals and patient support groups to present their views. Universities have also invited patient groups to speak to medical students to learn from patients the effect on lives of people with ambiguous genitalia.

Support groups are professional and not disgruntled haters of doctors. They work closely with the medical profession to improve treatment, raise awareness, and support patients. Patients have the opportunity to air their views only in the media, which can often distort important issues.

When doctors come to our conferences and take time to listen to patients, parents, and support groups, they learn more than they do in the few minutes of a consultation. Patients are more likely to open up and talk to doctors who take an interest in how conditions affect people's quality of life and everyday living.

Melissa Cull,
son, Adrenal Hypoplasia Network
17 Newton Road, Lichfield, Staffordshire
WS13 7EF
melissa.cull@mcul.lcom

Letters

Advice to authors

We prefer to receive all responses electronically, sent directly to our website. Processing your letter will be delayed unless it arrives in an electronic form.

We are now posting all direct submissions to our website within 24 hours of receipt and our intention is to post all other electronic submissions there as well. All responses will be eligible for publication in the paper journal.

Responses should be under 400 words and relate to articles published in the preceding month. They should include ≤5 references, in the Vancouver style, including one to the BMJ article to which they relate. We welcome illustrations. Please supply each author's current appointment and full address, and a phone or fax number or email address for the corresponding author. We ask authors to declare any competing interest. Please send a stamped addressed envelope if you would like to know whether your letter has been accepted or rejected.

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Doctors’ knowledge of radiation exposures is deficient

Editor—We read with interest Adams’s personal view and share her concerns.1 At one of our hospitals a young boy with splenic trauma received serial computed tomography scanning of his upper abdomen to assess the degree of splenic laceration. The scans were discussed at a multiple disciplinary meeting, and a query was raised regarding the radiation dose received by that patient. It became clear that the requesting doctors were unaware of the dose.

We compiled a simple questionnaire and interviewed 130 doctors of all grades, including consultant radiologists. They were asked for an approximate dose of radiation to the average patient having chest radiography. This was then used as a unit of 1 to calculate how many units a patient would receive for a wide variety of investigations carried out in a busy radiology department of a district general hospital (17 examinations in total).

The results were appalling. With a pass mark of 50% only three doctors (2%) passed, and that was with a generous marking scheme—20% error allowed and no negative marking. Many doctors were able to score at all only because they realised that ultrasound examinations do not use ionising radiation. The degree of knowledge was inversely proportional to seniority, with consultants scoring less than junior colleagues.

It was clear and worrying that doctors have no real knowledge of radiation doses that their patients receive.

The fact that computed tomograms of the entire body can be performed on a single breath hold over a matter of seconds does not mean the patient is getting a lower radiation dose than they would have received 10 years ago. Although the Ionising Radiation (Medical Exposure) Regulations 2000 are in place, which means that it is a legal requirement to keep radiation exposures as low as possible and that they should be justifiable, it seems that knowledge is still seriously lacking.

K Gowers-Thomas Consultant radiologist
Kthomas@pr-tr.wales.nhs.uk

M H Lewis Consultant surgeon
Royal Glamorgan Hospital, Llwynymaer, Llantriant, Mid Glamorgan CF72 8XR

S Shiralkar Specialist registrar in radiology
University Hospital of Wales, Cardiff, CF14 4XW

M Snow Specialist registrar in Orthopaedics
Royal Gwent Hospital, Cardiff Road, Newport NP9 2UB

R B Galland Consultant surgeon
Bristol Royal Hospital, Reading RG1 5AN

A Rennie Specialist registrar in radiology
John Radcliffe Hospital, Oxford OX3 9DZ

Prevalence of surnames in each letter affects order of authors

Editor—Chambers et al’s study of the order of authorship in a study seems to be lacking in at least one way. I have observed that surnames, especially those with a British origin, tend to begin with letters from the first half of the alphabet. For example, among the research group to which I belong, surnames begin with A, B, C, H, J, K, L, M, P, R, S, and T. According to probability, a random drawing of three of my colleagues’ names to determine the order of authorship would be more likely to result in the first author having a surname beginning with a letter in the first half of the alphabet than in the second.

The graph in Chambers et al’s paper presents only the percentages of names in their study; it does not indicate (except for Q and X) what the prevalence was for surnames beginning with each letter. Thus it unfortunately does not allow us to evaluate whether adjustments are needed. This study could be enhanced by adjusting the analysis for the higher prevalence of surnames that begin with first letters from the first half of the alphabet.

Benjamin D Horne Epidemiologist
LDS Hospital, Salt Lake City, UT 84103, USA

ldshorne@iive.com

Rapid response

Correspondence submitted electronically is available on our website.