

Does acupuncture relieve pain?

Interpreting the effects of sham acupuncture holds the answer



TIM MALYON AND PAUL BIDDLE/SPL

RESEARCH, p 330

Adrian White clinical research fellow, Peninsula Medical School, Universities of Exeter and Plymouth, Plymouth PL6 8BU
adrian.white@pms.ac.uk

Mike Cummings medical director, British Medical Acupuncture Society, Royal London Homoeopathic Hospital, London WC1N 3HR

Competing interests: Both authors are employees of the British Medical Acupuncture Society, a registered charity established to encourage the use and scientific understanding of acupuncture within medicine for the public benefit. AW is part time journal editor and MC is medical director.

Provenance and peer review: Commissioned; not externally peer reviewed.

Cite this as: *BMJ* 2009;338:a2760
doi: 10.1136/bmj.a2760

In the linked systematic review, Madsen and colleagues assess the analgesic effect of acupuncture and “placebo acupuncture” compared with usual care in 13 three arm studies.¹ Acupuncture has been used virtually unchanged for about 2000 years, although in contemporary practice needles are often stimulated electrically (electro-acupuncture). Traditional concepts of the mode of action have not been scientifically substantiated. Acupuncture is currently explained by neurophysiological mechanisms that are well established in research into experimental pain,² although the precise mechanisms of effects seen in clinical practice are more elusive.

The clinical effectiveness and cost effectiveness of acupuncture versus conventional treatment for chronic pain have been confirmed in large trials over the past 10 years. In particular, Germany’s Modellvorhaben Akupunktur (health insurance funded trials on acupuncture) provide evidence of effectiveness that has led to the integration of acupuncture into the management of osteoarthritis of the knee³ and back pain.⁴ In contrast, the evidence was insufficient to support such a policy for tension headache and migraine.

However, the nature of classic “acupuncture points” is an enigma. These anatomical locations have no unique physical or physiological explanation in Western science, but are often used to define the key difference between real and “placebo” (more correctly called “sham”) acupuncture in trials. Sham acupuncture often consists of superficial, off point needling, but this may still have a physiological effect. For example, sham acupuncture was statistically and clinically superior to guideline based conventional care for chronic back pain in a recent large (n=1162) randomised controlled trial.⁴

Placebo controlled studies have a very different role in the evaluation of physical treatments, such as acupuncture (and physiotherapy), than in the evaluation of new drugs. A placebo controlled trial of a drug gives an estimate of its efficacy in ideal conditions, whereas in everyday practice its effectiveness is often lower. In contrast, a sham controlled study of acupuncture gives an estimate just of the difference between one form of needling and another, and some rigorous systematic reviews conclude that acupuncture is superior to sham acupuncture.^{5,6} In everyday practice, this effect is augmented by other factors such as touch, expectation, and conditioning, so sham controlled studies of acupuncture are of little value in estimating benefit to patients. The review

by Madsen and colleagues starts from an academic research question about the size of the effect of the sham acupuncture but ends up tackling the perceived claim that acupuncture is a panacea for every kind of pain.¹ The authors included studies from a wide range of acute and chronic pain conditions, but specifically selected trials with three arms. They therefore restricted the search by trial methodology, not by clinical condition, which is an unusual approach in systematic reviews. They found a moderate difference between placebo acupuncture and conventional care (standardised mean differences -0.37, 95% confidence interval -0.56 to -0.19), corresponding to a reduction of 9 mm on a 100 mm visual analogue scale. However, heterogeneity was high. The effect was slightly larger in higher quality studies, but it varied across conditions, and seemed to be largest for musculoskeletal conditions.

The authors also found a small but significant difference between the effects of needling classic points and so called control points (-0.13, -0.22 to -0.04; no heterogeneity). The authors suggest that the difference could be explained by bias due to the subconscious influence of the unblinded practitioners. Another possible explanation for the difference, given its consistency across conditions, research groups, and countries, is that it could represent the physiological difference between two active treatments—needling classic points in deeper tissues and incorrect points in more superficial tissues.

The review covers such a broad range of pain conditions that it cannot directly inform clinical decisions about patients with particular conditions. The overall effect size of acupuncture in relation to usual care is moderate (a total of 12 mm on the visual analogue scale, including the placebo effect) and may be clinically relevant for musculoskeletal conditions, particularly in view of the limited treatment options and acupuncture’s safety record and patient preference.

The review also looks at the question of whether acupuncture has a specific effect beyond a placebo one—that is, a biological effect—and therefore whether it should be used at all. As we have seen, the evidence is open to interpretation.

Future research should define the optimum parameters and response variables for acupuncture,⁷ and then compare optimal acupuncture with best existing treatments for different conditions. It is unfortunate that placebo control acupuncture remains problematic. Even the use of non-penetrating needles may pose a

challenge—these needles may be potent modulators of target directed expectation,^{8,9} and therefore may condition responses to a greater extent than placebo pills.¹⁰ Further research is needed on the mechanisms of sham techniques, but comparison of acupuncture with sham techniques should be limited to single centre studies with tight control on all variables.

The role of patient expectation is coming under increased scrutiny and could be very relevant, for example, to individual variation in response.¹¹ Acupuncture seems, in part at least, to involve neurological pathways in common with placebo analgesia and studying these pathways may offer important insights into improving care.

- 1 Madsen MV, Göttsche PC, Hróbjartsson A. Acupuncture treatment for pain: systematic review of randomised clinical trials with acupuncture, placebo acupuncture, and no acupuncture groups. *BMJ* 2008;337:a3115.
- 2 Staud R, Price DD. Mechanisms of acupuncture analgesia for clinical and experimental pain. *Expert Rev Neurother* 2006;6:661-7.
- 3 Scharf HP, Mansmann U, Streitberger K, Witte S, Kramer J, Maier C, et al.

- Acupuncture and knee osteoarthritis—a three-armed randomized trial. *Ann Intern Med* 2006;145:12-20.
- 4 Haake M, Muller HH, Schade-Brittinger C, Basler HD, Schafer H, Maier C, et al. German Acupuncture Trials (GERAC) for chronic low back pain: randomized, multicenter, blinded, parallel-group trial with 3 groups. *Arch Intern Med* 2007;167:1892-8.
- 5 Furlan AD, van Tulder MW, Cherkin DC, Tsukayama H, Lao L, Koes BW, et al. Acupuncture and dry-needling for low back pain. *Cochrane Database Syst Rev* 2005;(1):CD001351.
- 6 White A, Foster NE, Cummings M, Barlas P. Acupuncture treatment for chronic knee pain: a systematic review. *Rheumatol (Oxford)* 2007;46:384-90.
- 7 White A, Cummings M, Barlas P, Cardini F, Filshie J, Foster N, et al. Defining an adequate dose of acupuncture using a neurophysiological approach. *Acupunct Med* 2008;26:111-20.
- 8 Benedetti F, Arduino C, Amanzio M. Somatotopic activation of opioid systems by target-directed expectations of analgesia. *J Neurosci* 1999;19:3639-48.
- 9 Pariente J, White P, Frackowiak RS, Lewth G. Expectancy and belief modulate the neuronal substrates of pain treated by acupuncture. *Neuroimage* 2005;25:1161-7.
- 10 Kaptchuk TJ, Stason WB, Davis RB, Legedza AR, Schnyer RN, Kerr CE, et al. Sham device versus inert pill: randomised controlled trial of two placebo treatments. *BMJ* 2006;332:391-7.
- 11 Lundeberg T, Lund I, Naslund J. Acupuncture—self-appraisal and the reward system. *Acupunct Med* 2007;25:87-99.

Follow-up by telephone after treatment for breast cancer

Patients are highly satisfied, even without clinical examination



MARK THOMAS/SPL

The numerous guidelines for following up women after treatment for breast cancer show little consistency. The lack of evidence to inform these guidelines means they are influenced by local economic concerns—prolonged and frequent follow-up is common for privately funded healthcare systems,¹ whereas state funded health services limit the frequency and duration of visits.² In the linked randomised controlled equivalence trial (doi:10.1136/bmj.a3147), Beaver and colleagues compare traditional hospital follow-up with telephone follow-up by specialist nurses in women treated for breast cancer.³

The National Institute for Health and Clinical Excellence recommends up to three years' hospital follow-up before discharge to the general practitioner (although the guidelines are under review).^{2,4} Few clinicians follow these guidelines.⁵ Rather than unify practice the guidelines have led healthcare practitioners to look for cost effective methods of providing longer follow-up care. A range of strategies has been investigated, including radiographer led follow-up,⁶ automated telephone follow-up,⁷ and several variations on nurse led follow-up.^{8,9}

Beaver and colleagues compare telephone follow-up by breast care nurses with follow-up by doctors within hospital clinics in 374 women treated for breast cancer with a low to moderate risk of recurrence. Women in the hospital group received 10 minute consultations and breast examination, and those in the telephone group received 20 minute consultations without clinical examination. Both groups had mammography performed according to local policy. The authors found that telephone follow-up was acceptable to most patients, it significantly improved satisfaction, and it produced no excess anxiety compared with hospital

follow-up.³ This agrees with previous studies finding that nurse led follow-up is not associated with reduced quality of life,^{8,9} and that nurses are better at detecting psychological distress than doctors.⁹ Small trials have found that not having a clinical examination does not increase anxiety^{8,10} or reduce patient satisfaction^{8,10} or quality of life.¹⁰

The study focuses less on survival and more on patient satisfaction. It is not the first study to show that follow-up without clinical examination results in high patient satisfaction. Many clinicians believe that routine breast examination is unnecessary. Others doubt that follow-up without examination provides equivalent outcomes specific to cancer and some patients are anxious about not being examined. About 40% of women approached to participate in Beaver and colleagues' trial refused—an undisclosed proportion said they were unwilling to forgo an examination.⁹ Alternative follow-up will not be implemented widely until clinicians have proof that the detection of relapse is not compromised by the lack of a clinical examination.

Lack of generalisability may also compromise implementation. Beaver and colleagues excluded patients classified as “high risk” on the basis of HER2 status and the Nottingham prognostic index,³ although this index does not predict local relapse. Metastatic relapse (which the index does predict) is not detected by routine breast examination and symptoms of metastatic disease can be elucidated over the phone. It would therefore be reasonable to include high risk women in trials investigating the need for clinical examination in future.

The costs of administering the intervention in Beaver and colleagues' trial are unknown, and we hope that an economic analysis of their trial will be under-

RESEARCH, p 337

David A Montgomery regional medical and research specialist, oncology, Pfizer Ltd, Tadworth, Surrey KT20 7NT
davidandrewmontgomery@hotmail.com

Competing interests: DAM is currently employed by Pfizer oncology and is also a co-investigator on a grant submission for a trial investigating clinical examination in follow-up after breast cancer. The views expressed in this editorial are those of the author and do not necessarily reflect those of Pfizer Ltd.

Provenance and peer review: Commissioned; not externally peer reviewed.

Cite this as: *BMJ* 2009;338:a2753
doi: 10.1136/bmj.a2753

taken. Expensive follow-up is unlikely to be adopted. Telephone follow-up may reduce the burden on clinics but may not, within this trial, prove more cost effective. Nurse led follow-up is not cheaper than traditional clinics because experienced nurses are required and they spend longer on each patient than doctors.⁹ In Beaver and colleagues' study, 30 minutes of senior nursing time was needed for each appointment (20 minutes for consultation and 10 minutes for dictation), compared with only 10 minutes for each consultation (provided mainly by increasingly inexpensive junior doctors) for women followed up in clinics.³

Beaver and colleagues' model may be more economical over longer periods of follow-up. Patients will need less time for each call as time since diagnosis and treatment increases. The extra information provided by longer, more structured, telephone consultation will deal with survivorship issues, which would help women return to normal function more quickly and benefit the wider economy.¹¹ As patients return to normal function, briefer consultations or even postal or online questionnaires can be combined with open access to clinic to facilitate rapid return if problems develop.

Follow-up is initially labour intensive and expensive but becomes less so later on. Crucially, it is focused on the individual patient's needs; psychosocial concerns should be detected and tackled early. If an economic analysis of Beaver and colleagues' study is undertaken it should be remembered that patients were included for a mean of only 24 months and all had prolonged consultations.

Beaver and colleagues' study adds to the growing body of evidence that alternative methods of follow-

up can be as or more acceptable to patients and can usefully provide the psychological support needed after diagnosis and treatment of breast cancer. It does not bring us closer to definitive proof that routine clinical breast examination is unnecessary. Only a large randomised controlled trial can answer this question and whether widespread implementation of alternative approaches will benefit patients.

- 1 Khatcheressian JL, Wolff AC, Smith TJ, Grunfeld E, Muss HB, Vogel VG, et al. American Society of Clinical Oncology 2006 update of the breast cancer follow-up and management guidelines in the adjuvant setting. *J Clin Oncol* 2006;24:5091-7.
- 2 National Institute for Health and Clinical Excellence. *Guidance on cancer services: improving outcomes in breast cancer. Manual update*. 2002. www.nice.org.uk/page.aspx?o=csgbcguidance.
- 3 Beaver K, Tysver-Robinson D, Campbell M, Twomey M, Williamson S, Hindley A, et al. Comparing hospital and telephone follow-up after treatment for breast cancer: a randomised equivalence trial. *BMJ* 2008;337:a3147.
- 4 National Institute for Health and Clinical Excellence. *Early and locally advanced breast cancer: diagnosis and treatment. Clinical guideline: draft for consultation*. 2008. www.nice.org.uk/nicemedia/pdf/EBCFullGuidelineConsultation120808.pdf.
- 5 Donnelly P, Hiller L, Bathers S, Bowden S, Coleman R. Questioning specialists' attitudes to breast cancer follow up in primary care. *Ann Oncol* 2007;18:1467-76.
- 6 Vaile D, Barrett-Lee P. Breast cancer follow-up: a radiographer-led service. *Breast Cancer Res* 2008;6(suppl 1):56.
- 7 Montgomery DA, Krupa K, Wilson CW, Cooke TG. Automated telephone follow-up after breast cancer: an acceptability and feasibility pilot study. *Br J Cancer* 2008;99:704-10.
- 8 Koinberg IL, Fridlund B, Engholm GB, Holmberg L. Nurse-led follow-up on demand or by a physician after breast cancer surgery: a randomised study. *Eur J Oncol Nurs* 2004;8:109-17.
- 9 Baildam AD, Keeling F, Thompson L, Bundred N, Hopwood P. Nurse-led surgical follow up clinics for women treated for breast cancer—a randomised controlled trial. *Breast Cancer Res Treat* 2004;88:S136-7.
- 10 Brown L, Payne S, Royle G. Patient initiated follow up of breast cancer. *Psychooncology* 2002;11:346-55.
- 11 Department of Health. *Cancer reform strategy*. 2007. www.dh.gov.uk/en/Publicationandstatistics/Publications/PublicationsPolicyAndGuidance/dh-081006.

New definition of myocardial infarction

Features new subtypes of infarction and puts high demands on diagnostic assays

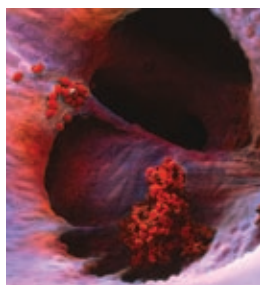
The evolution of the definition of acute myocardial infarction tells a fascinating story of medical progress. Between the publication of the initial World Health Organization's classification in 1979,¹ and that published by the redefinition committee of the American College of Cardiology, American Heart Association, and European Society of Cardiology in 2000, much of our diagnostic reasoning changed.² Biochemistry now takes centre stage, and the measurement of cardiac troponins has substantially increased diagnostic sensitivity.

Cardiologists predicted that these changes in diagnostic criteria and sensitivity would increase the incidence of acute myocardial infarction.³ They also predicted that the redefinition would have implications for individual patients and healthcare expenditure. Their predictions turned out to be correct, at least in part. A national registry in Norway found a 33% increase in acute myocardial infarction after the implementation of the 2000 criteria,⁴ and the Swedish Nationwide Centre of Epidemiology documented an abrupt 14% increase.⁵

Interest in the definition of acute myocardial infarction has recently been revived by the publication by the redefinition committee of the "universal definition of myocardial infarction."⁶ This guideline represents both consolidation and innovation—consolidation because the key importance of troponins is firmly established; innovation because for the first time the committee has established subtypes of infarction.

In principle, with regard to biomarkers, the 2007 definition of spontaneous acute myocardial infarction is the same as in the 2000 document. It requires a rise and fall of troponin values with at least one measurement above the upper 99th centile, a coefficient of variation (CV) <10% at this cut-off point, and the presence of myocardial ischaemia.

The subtypes of infarction are defined as follows (see box). Type 1 is the classic type of acute myocardial infarction triggered by rupture of an atherosclerotic plaque and subsequent thrombosis in a coronary artery. Type 2 reflects a mismatch between myocardial oxygen supply and demand, with no signs of coronary



PROF P. MOTTA/G. MACCHIARELLI/SPL

Dan Atar professor and head of cardiology, Division of Cardiology, Aker University Hospital and Faculty of Medicine, University of Oslo, 0514 Oslo, Norway
dan.atar@online.no

Competing interests: None declared.

Provenance and peer review: Commissioned; not externally peer reviewed.

Cite this as: *BMJ* 2008;337:a3078
doi: 10.1136/bmj.a3078

Clinical classification of different types of myocardial infarction

- Type 1—Spontaneous myocardial infarction related to ischaemia caused by a primary coronary event, such as plaque fissuring or rupture
- Type 2—Myocardial infarction secondary to ischaemia resulting from an imbalance between oxygen demand and supply, such as coronary spasm
- Type 3—Sudden death from cardiac disease with symptoms of myocardial ischaemia, accompanied by new ST elevation or left bundle branch block, or verified coronary thrombus by angiography. In this type of myocardial infarction death occurs before blood samples can be obtained
- Type 4—Myocardial infarction associated with primary percutaneous coronary intervention
- Type 5—Myocardial infarction associated with coronary artery bypass graft

thrombosis. Type 3 is reserved for acute cardiac arrest, which in most cases is an infarction. Types 4 and 5 are peri-procedural infarctions, which occur during primary percutaneous coronary interventions or a coronary artery bypass graft, respectively. This new classification is a bold innovation.

What are the weaknesses of the new definition? Many laboratories cannot achieve a diagnostic precision of <10% CV at the 99th centile for a given troponin I or troponin T assay. Moreover, clinicians are entirely dependent on the assay manufacturer's reported precision—the document refers readers to a website maintained by the International Federation for Clinical Chemistry,⁶ which lists the intra-lot variations established by the manufacturer. This has led to considerable uncertainty about whether to use the 99th centile as the cut-off point or whether to use a higher cut-off value. This decision is made more difficult by many assay manufacturers recommending their own cut-off value, regardless of the 99th centile and <10%

CV requirements. These challenges call for a close collaboration between clinical chemistry and cardiology departments, so that the new definition can be implemented under conditions that both parties feel comfortable with.

Because the ability to subclassify myocardial infarction increases our diagnostic repertoire considerably, we urgently need to update what the word “infarction” actually means. For instance, a type 2 infarction does not necessarily carry a poor prognosis, and drugs that are normally prescribed for infarctions may not be needed. This message must be conveyed to a wide range of people, including general practitioners, specialists, trialists, healthcare authorities, life insurers, epidemiologists, and politicians.

The new universal definition of myocardial infarction should be implemented in clinical practice as soon as possible. However, clinical chemical expertise will be needed to ensure that a given hospital laboratory can deliver the required diagnostic precision of a CV <10% at the upper 99th centile. Most importantly, knowledge should be disseminated about the new classification of infarctions.

- 1 WHO Task Force. Task force on standardization of clinical nomenclature. *Circulation* 1979;59:607-9.
- 2 JESC/ACC Committee. Myocardial infarction redefined—a consensus document of the Joint European Society of Cardiology/American College of Cardiology Committee for the redefinition of myocardial infarction. *Eur Heart J* 2000;21:1502-13.
- 3 Ferguson JL, Beckett GJ, Stoddart M, Walker SW, Fox KAA. Myocardial infarction redefined: the new ACC/ESC definition, based on cardiac troponin, increases the apparent incidence of infarction. *Heart* 2002;88:343-7.
- 4 Hagen T, Reikvam Å. Marked increase of the number of myocardial infarctions following introduction of the new diagnostic criteria. *Tidsskr Nor Lægeforen* 2003;123:3041-3.
- 5 The National Board of Health and Welfare of Sweden; Centre for Epidemiology: Statistics—Health and Diseases. *Myocardial infarctions 1987-2006*. www.socialstyrelsen.se/NR/rdonlyres/C06CE825-B163-400F-9F22-A5B18B2A4753/12898/200812521.pdf.
- 6 Thygesen K, Albert JS, White HD, on behalf of the Joint ESC/ACCF/AHA/WHF Task Force for the Redefinition of Myocardial Infarction. Universal definition of myocardial infarction. *Eur Heart J* 2007;28:2525-38.

Antibiotics for spontaneous preterm birth

Can cause harm, so should be used only after careful consideration

Andrew H Shennan professor of obstetrics, King's College London Division of Reproduction and Endocrinology, Department of Women's Health, London SE1 7EH andrew.shennan@kcl.ac.uk

Manju Chandiramani clinical research fellow, King's College London Division of Reproduction and Endocrinology, Department of Women's Health, London SE1 7EH

Competing interests: None declared.

Provenance and peer review: Not commissioned; externally peer reviewed.

Cite this as: *BMJ* 2008;337:a3015
doi: 10.1136/bmj.a3015

The incidence of preterm birth (<37 weeks' gestation) is rising. Preterm birth currently occurs in 7.6% of live births in England and Wales and 12.5% of births in the United States, where the annual cost exceeds \$26.2bn (£17.5bn; €20bn).¹ Up to three quarters of these births have a spontaneous onset. Evidence that labour is associated with an inflammatory process is increasing.²

Very preterm birth (<32 weeks) is commonly associated with infection³; micro-organisms usually gain access to the sterile uterine cavity by ascending from the vagina. Other routes include haematogenous spread, iatrogenic introduction, and retrograde spread through the fallopian tubes. The risk of preterm birth is higher with pyelonephritis and

bacterial vaginosis. Intrauterine activation of prostaglandins and phospholipase A2 by micro-organisms may cause contractions or preterm rupture of the membranes.⁴ Infection can also cause neurological damage and cerebral palsy.³

It would seem logical to use antibiotics to tackle this insult and thereby reduce preterm birth and improve outcome. Their benefit is not always clear, however, and evidence of adverse effects is increasing. Follow-up of participants in the ORACLE II randomised controlled trial found an increased risk of cerebral palsy at 7 years in the children of women with intact membranes who received antibiotics for spontaneous preterm labour.⁵ The original results showed no short term benefit in this group (contrary to women



A/PHOTO/SPL

with ruptured membranes). Children born to women who received antibiotics had a significantly increased incidence of cerebral palsy (odds ratio 1.93 (95% confidence interval 1.21 to 3.09) for erythromycin and 1.69 (1.07 to 2.67) for co-amoxiclav). When antibiotics were combined, risks were higher still than with erythromycin alone (4.55% *v* 2.29%). The implication is that treating women who may have subclinical infection could increase risk by masking this infection, so that the fetus has increased exposure to a hostile in utero environment. If infection goes unnoticed, the need for an early delivery will be missed. In the ORACLE I study, antibiotics did not increase the risk of cerebral palsy in the children of women with ruptured membranes, perhaps because morbidity caused by infection in these women is likely to result in delivery, which removes the baby from the adverse effects of infection. However, antibiotics resulted in significantly fewer babies being delivered within 48 hours in this group.⁶

Certain antimicrobials have been linked to adverse events. ORACLE I showed that co-amoxiclav was associated with an increased risk of neonatal necrotising enterocolitis, and thus erythromycin became the preferred choice for women with preterm ruptured membranes.⁶ However, the increased use of erythromycin has been linked to a substantial increase in antibiotic resistance.⁷ Metronidazole has been associated with an increased risk of preterm delivery when given prophylactically to high risk women,⁸ and vaginally administered clindamycin may be a better choice for bacterial vaginosis. The effects of antibiotics on neonatal gut flora have been linked to immune intolerance and increases in allergy, although breast feeding may help limit antibiotic induced abnormal colonisation of the neonatal intestine.⁹

Screening for or treating women with abnormal vaginal flora has no benefit.¹⁰ Treatment seems to eradicate bacterial vaginosis but has no effect on preterm birth and its consequences, although the results of different studies vary—different trials have reported that treatment both extended and reduced gestational age at delivery. As a result, more research is needed to elucidate the factors related to benefit, including the populations to be screened, antimicrobials to be used, and the gestational age to be targeted. The National Institute for Health and Clinical Excellence (NICE) does not recommend screening for bacterial vaginosis in pregnancy, even in women at high risk.¹¹

When should antibiotics be prescribed? Sepsis remains a common cause of maternal death globally, and antibiotics should be prescribed promptly if there is evidence of chorioamnionitis, which is more common with preterm pregnancy. Antibiotics should be and commonly are prescribed for specific infectious conditions, incidental to pregnancy, and few are contraindicated. Such an approach reduces preterm labour associated with general infectious morbidity in the mother. When the threshold for antimicrobial treatment is less certain—for example, in urinary frequency with dysuria in pregnancy—it is prudent

to wait for the results of culture (or at least ensure dipstick confirmation of nitrites) before starting treatment, unless the woman has overt signs of infection, such as pyelonephritis.

Prophylactic use of antibiotics is indicated to reduce the risk of preterm birth in well defined situations in pregnancy, as recommended by NICE.¹¹ All women should be screened in early pregnancy for asymptomatic bacteriuria, because treatment significantly reduces the incidence of maternal pyelonephritis and low birth weight.¹² Women with preterm rupture of the membranes before labour should still be given erythromycin because ORACLE I showed a reduction in the composite primary outcome (death or major cerebral abnormality or chronic neonatal lung disease).¹² Women at high risk of transmitting group B streptococcus to their baby, including those in preterm labour, should be treated prophylactically, although routine screening for group B streptococcus is not recommended.

Good clinical practice dictates that clinicians should treat only when clear evidence of benefit is available. It should not be assumed that, because of the association between infection and preterm birth, antimicrobial treatment is beneficial. Neurological damage after increased exposure to infection in utero may explain the results of increased cerebral palsy in ORACLE II.⁵ Treatment may also alter the natural vaginal flora, replacing this with opportunistic organisms more likely to cause adverse events. Clinical trials are needed to elucidate which populations will benefit from antibiotics, and with which agents. In the meantime, clinicians should be judicious in prescribing antibiotics in pregnancy and be aware of the potential adverse events.

- 1 National Centre for Health Statistics. *Preliminary births for 2004*. 2008. www.cdc.gov/nchs/products/pubs/pubd/hstats/prelimbirths04/prelimbirths04health.htm.
- 2 Norman JE, Bollapragada S, Yuan M, Nelson SM. Inflammatory pathways in the mechanism of parturition. *BMC Pregnancy Childbirth* 2007;7(S1):S7.
- 3 Goldenberg RL, Hauth JC, Andrews WW. Intrauterine infection and preterm delivery. *N Engl J Med* 2000;342:1500-7.
- 4 Mikamo H, Kawazoe K, Sato Y, Imai A, Tamaya T. Preterm labor and bacterial intraamniotic infection: arachidonic acid liberation by phospholipase A2 of *Fusobacterium nucleatum*. *Am J Obstet Gynecol* 1998;179:1579-82.
- 5 Kenyon S, Pike K, Jones DR, Brocklehurst P, Marlow N, Salt A, et al. Childhood outcomes after prescription of antibiotics to pregnant women with spontaneous preterm labour: 7-year follow-up of the ORACLE II trial. *Lancet* 2008;372:1276-8.
- 6 Kenyon SL, Taylor DJ, Tamow-Mordi W. Broad-spectrum antibiotics for preterm, prelabour rupture of the fetal membranes: the ORACLE I randomised trial. *Lancet* 2001;357:981-90.
- 7 Pearson A. Pyogenic and non-pyogenic streptococcal bacteraemias—England, Wales, and Northern Ireland. *CDR Weekly* 2004;15:4.
- 8 Simcox R, Sin WA, Seed PT, Briley A, Shennan AH. Prophylactic antibiotics for the prevention of preterm birth in women at risk: a meta-analysis. *Aust N Z J Obstet Gynaecol* 2007;47:368-77.
- 9 Bedford Russell AR, Murch SH. Could peripartum antibiotics have delayed health consequences for the infant? *Br J Obstet Gynaecol* 2006;113:758-65.
- 10 Nygren P, Fu R, Freeman M, Bougatsos C, Klebanoff M, Guise JM; US Preventative Services Task Force. Evidence on the benefits and harms of screening and treating pregnant women who are asymptomatic for bacterial vaginosis: an update review for the US Preventative Task Force. *Ann Intern Med* 2008;148:220-33.
- 11 National Institute for Health and Clinical Excellence. *Antenatal care: routine care for the healthy pregnant woman*. 2008. www.nice.org.uk/Guidance/CG62.
- 12 Small F, Vazquez JC. Antibiotics for asymptomatic bacteriuria in pregnancy. *Cochrane Database Syst Rev* 2007;(2):CD000490.

Doctors, patients, and the pharmaceutical industry

New report reflects a working party that has lost its way

NEWS, p 313, ANALYSIS, p 326
PERSONAL VIEW, p 359

Joe Collier emeritus professor of medicines policy, St George's, London SW17 0RE
jcollier@sgul.ac.uk

Competing interests: JC gave oral evidence to the RCP working party that produced *Innovating for Health*, was an adviser to the Health Select Committee in its 2005 inquiry into the influence of the pharmaceutical industry, and is a fellow of the RCP.

Provenance and peer review: Commissioned; externally peer reviewed.

Cite this as: *BMJ* 2009;338:b443
doi: 10.1136/bmj.b443

On 4 February 2009, the Royal College of Physicians of London (RCP) published a report entitled *Innovating for Health: Patients, Physicians, the Pharmaceutical Industry and the NHS*.¹ The report is the outcome of deliberations by a working party convened by the college in September 2007, chaired by Richard Horton (editor of the *Lancet*), and it comprises 70 pages and 42 recommendations. Despite its heritage the work is flawed, thereby diminishing the validity of the recommendations and the obligation to take them seriously.

The ideal working party has clear and understandable terms of reference; has a membership selected to tackle the problems at hand; concentrates primarily on resolving questions posed by its terms; produces a report that sets out the problems in such a way that each recommendation follows logically from the text; and finally, offers recommendations that are realistic and correctly targeted. In this instance, these ideals are often unmet.

Let us start with the terms of reference. Here the key request (presumably set by the RCP) is that the working party should “obtain evidence about the current and future prospects of the pharmaceutical industry” and about “the successes or failures in its relationships with the NHS and academic medicine.” Then, armed with such information the working party should “identify policies that would promote . . . a relationship between the NHS, academic medicine and the pharmaceutical industry, the purpose of which is to discover and deliver safe, effective and affordable new medicines to patients based on need.” Although time is spent on the delivery of safe and effective medicines, the group essentially ignores drug development, so almost no attention is paid to the direction of drug development. The report certainly has no regard for ideas of developing drugs to match patients’ needs and makes no recommendations relating to the affordability of drugs. These gaps, and the fact that the interests of patients seem to be a secondary consideration, give the report a hollow ring and its title an uneasy fit.

One possible explanation for the working party’s shift in direction is that its real agenda was to rehabilitate the image of the drug industry and its relations with clinicians and the NHS, which the group recognised were seriously hurt by the 2005 Health Select Committee’s report on the industry’s influence.² As part of this rehabilitation, there is little direct criticism of the workings of industry or serious enquiry into how the industry might do better. So, in a short section on “Medical journals: victims or assailants,” an opening salvo reads, “Editors of medical journals report examples of manipulation, distortion, bias, secrecy, overt promotion, and ghost

writing in publishing medical research” and goes on to give detailed examples of the “excesses” of industry. The subsequent recommendation does not ask drug companies to refrain from such behaviour but instead turns its attention to the journals, asking editors “to do more to strengthen public and professional confidence.” This stance defies logic.

If these problems were not enough, why do at least two recommendations (about the presentation of medicines) have essentially no supporting text? Why do some recommendations seem to be misdirected—why should doctors report a drug promotional violation to the Association of the British Pharmaceutical Industry’s code of practice authority, where it may be swept under the industry “carpet,” when reporting to the Medicines and Healthcare Products Regulatory Agency could lead to prosecution in a criminal court? Why did the committee make a key recommendation on patients’ access to medicines that covers much the same ground as the Pharmaceutical Price Regulation Scheme published on 1 January 2009,³ as if it knew nothing about the new scheme although members of the committee who work for industry or the Association of the British Pharmaceutical Industry would have seen all the details in good time for the proposals to be incorporated? Why are many of the recommendations far from new—why do we need 42 when half that number would suffice—and why are the recommendations not numbered?

Notwithstanding these concerns, we would do well to adopt several of the recommendations. So—for example, more impartial information about medicines and treatments should be available to patients; we should have a national day to promote public awareness of medicines; the teaching of clinical pharmacology should be strengthened; students and doctors should receive no industry perks and the provision of postgraduate education should not depend on industry “generosity”; healthcare professionals with links to industry should make these public; ways should be found to strengthen research or working collaboration; and the Medicines and Healthcare Products Regulatory Agency should be more transparent.

Despite these positive recommendations the product of the working party’s deliberations is weakened by a flawed process, and so a real opportunity has been lost.

- 1 Royal College of Physicians. *Innovating for health: patients, physicians, the pharmaceutical industry and the NHS*. Report of a working party. London: RCP, 2009.
- 2 House of Commons Health Committee. *The influence of the pharmaceutical industry*. Fourth Report of Session 2004-05. 2005. www.publications.parliament.uk/pa/cm200405/cmselect/cmhealth/42/42.pdf.
- 3 Collier J. Changes to the regulation of drug prices in the UK. *BMJ* 2008;337:a2735.