Letters

Informed consent

The central problem is often poor design and conduct of trials

EDITOR—We are concerned about some aspects of the recent articles on consent.[1 2] Len Doyal claims that informed consent may not be necessary for three most vulnerable groups: young children, patients with learning difficulties, and unconscious or semiconscious patients. Yet young children (unlike all adult groups) have the protection of their parents' consent, and this should always be respected.[3] The other two groups show the limitations of applying Kantian respect for autonomy, designed for property owning 18th century gentlemen, to vulnerable dependent patients. There is an urgent need to agree new ways of making research decisions with and for these minority groups.

As is usual in arguments against seeking informed consent, there is a tendency to concentrate on dramatic extremes: patients with severe mental impairment and patients receiving heroic cancer treatment. The development of principles from extremes is dangerous and should be discouraged. Difficulties with relatively small groups should not be used to excuse researchers from requesting the consent of the vast majority of the millions of people every year who help with research into mundane pharmaceutical trials of treatments of arthritis or everyday misery.

A deeper problem with the articles is the assumption that consent is the central problem in research. We suggest that, more often, the central problem is the poor design and conduct of trials which alienate or distress people on whose practical support researchers depend. The solution here is not to tinker with consent but to clean up research. Health service users could help at every stage of clinical research: the selection of questions worth investigating; the design and conduct of trials, including the information materials; the interpretation and reporting of the evidence; dissemination; and working with practitioners to put findings into practice. Consumers for Ethics in Research has been working with health service users, researchers, and practitioners on these issues for the past eight years, partly through regular open meetings, during which many practical ideas have been advanced.

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1 Doyal L. Journals should not publish research to which patients have not given fully informed consent—with three exceptions. *BMJ* 1997;314:1107-11. (12 April.)
2 Tobias JS. BMJ's present policy (sometimes approving research in which patients have not given fully informed consent) is wholly correct. *BMJ* 1997;314:1111-4. (12 April.)
3 British Paediatric Association. *Guidelines for the conduct of medical research with children.* London: BPA, 1992.

Journals should require routine reporting of consent rates

EDITOR—We wish to contribute to the debate on informed consent.[1] Two of us (HC, SAMS) have recently conducted a review of randomised control trials published in the *Archives of Diseases in Childhood* from 1982 to 1996. We found that 112 (45%) of 249 trials did not report whether informed consent had been obtained. Of the trials that did note that informed consent had been obtained, 111 (81%) of 137 quoted consent rates of 100%. This proportion varied by study setting and paediatric subspecialty and was particularly high in trials in inpatients (90%) and trials in neonates (96%). Two of the trials that reported 100% consent rates included over 500 children.

Some of the trials may have considered obtaining patients' consent to be part of the inclusion criteria for participation. We are concerned, however, that investigators may have been following the letter of the law but not the spirit of the law. The process of obtaining consent should include the elements not only of information, comprehension, and consent but also of voluntariness—which includes absence of persuasion. It is important that investigators understand that patients' dependency can lead to absence of participation and choice, and that non-verbal behaviour and the setting can exert considerable influence.[2]

Beyond our immediate concern about the legitimacy of consent rates of 100% in large trials, we believe that a perceived lack of care in obtaining consent may lead to the imposition of a legalistic approach to gaining consent in paediatric research. Concern exists in several quarters that parental consent may not be sufficient to justify research with children. It could be argued that the individual circumstances of each specific study should be assessed by investigators and local research ethics committees. In law, however, research with children remains a grey area, and a shift towards greater emphasis on individual autonomy could restrict research much more than at present.

Such a shift is made more likely if the process of obtaining consent is perceived to be less than fully empowering to the subjects concerned. In this context, local research ethics committees and editors of medical journals should be alert to the possibility of informed consent that is not freely obtained, should require routine reporting of consent rates, and should challenge investigators to explain or comment on extremely high consent rates. Even more importantly, however, investigators should be encouraged to regard the process of obtaining informed consent not as an irritating chore but as an opportunity to use their clinical skills to secure the subject's wholehearted cooperation in an important task.

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1 Smith R. Informed consent: the intricacies. *BMJ* 1997;314:1059-60. (12 April.)
2 English DC. *Bioethics: a clinical guide for medical students.* London: W W Norton, 1994.

Advice to authors

We receive more letters than we can publish: we can currently accept only about one third. We prefer short letters that relate to articles published within the past four weeks. We also publish some "out of the blue" letters, which usually relate to matters of public policy.

When deciding which letters to publish we favour originality, assertions supported by data or by citation, and a clear prose style. Letters should have fewer than 400 words (please give a word count) and no more than five references (including one to the BMJ article to which they relate); references should be in the Vancouver style. We welcome pictures.

Letters, whether typed or sent by email, should give each author's current appointment and full address. Letters sent by email should give a telephone and fax number when possible. We encourage you to declare any conflict of interest. Please send a stamped addressed envelope if you would like to know whether your letter has been accepted or rejected.

We may post some letters submitted to us on the world wide web before we decide on publication in the paper version. We will assume that correspondents consent to this unless they specifically say no.

Letters will be edited and may be shortened.

Other societies have different concepts of autonomy

EDITOR—There is a disturbing undertone of cultural imperialism in the debate about informed consent. It shows itself most starkly in the tacit assumption that the whole world shares the same philosophical meanings as those that underpin our own shaky Judaeo-Christian-liberal ethic. That this is far from so is vividly illustrated in the very different concepts of autonomy held by different societies. In many traditional African cultures, and certainly in Bantu culture, the individual does not take his or her autonomy from "cogito, ergo sum" ("I think, therefore I am"), as in the West, but from "sumus, ergo sum" ("we are, therefore I am")—membership of an intensely important group that enhances the individual. In many parts of Africa it is simply not possible, especially for women, to make important decisions without reference to the group; any clinician or researcher who believes that a "yes" given by a terrified and lonely patient, in or out of a hospital bed, amounts to anything approaching informed consent is either naive or a knave. Add to this the very real social difficulty in ever saying "no" and thus threatening a relationship and you have the perfect situation for doing anything you like.

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British institutions collaborating in projects overseas may face dilemma

EDITOR—We agree with the principle that medical research that does not include informed, individual consent should not be published[1] unless it falls into one of the three categories detailed by Len Doyal.[2] We would, however, argue for an additional guiding principle requiring community consultation over difficult ethical issues. Satish Bhagwanjee and colleagues might have sought opinions about HIV testing without consent from former patients of the intensive care unit in South Africa (and their relatives) before putting the study protocol to the ethics committee.[3] It might also have been more appropriate for a local HIV support group to be consulted instead of the subcommittee of the institutional ethics committee comprising a bioethicist, a clinician, and an AIDS expert.[3]

We would also argue that a properly constituted ethics committee should remain the final arbiter of the extent to which informed consent should be sought for a given study. This committee must be independent, as suggested by the Declaration of Helsinki, and as close to the community involved in the research as possible.

One problem is that, particularly in developing countries, many ethics committees remain to be set up or exist but are not properly constituted to include lay representation. Bhagwanjee and colleagues' study was reviewed by a subcommittee of the postgraduate committee.[3] However carefully that committee agonised over the fact that informed consent was not to be sought, the independence of its judgment must be questioned until its constitution is clarified.

As researchers based in a British institution but collaborating in many projects overseas, we are constantly faced with a dilemma. While it is presumptuous to impose an ethical opinion on research that will take place in circumstances very different to our own, it is unethical to be associated with research that does not come under any independent ethical scrutiny at all. All our research is reviewed by our own ethics committee, which includes independent lay representation from a variety of religious and cultural backgrounds. We emphasise that ethical approval from this committee does not absolve researchers from seeking local ethical approval. We recognise that this situation is not ideal and are building up a database of the ethics processes present in those countries with which we have links.

We hope that the debate on informed consent in the *BMJ* will encourage the development of independent ethics review processes in those places where they currently do not exist. Otherwise, medical journals will continue to have difficulty in judging whether, on ethical grounds, to publish some research.

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1 Smith R. Informed consent: the intricacies. *BMJ* 1997; 314:1059-60. (12 April.)
2 Doyal L. Journals should not publish research to which patients have not given fully informed consent—with three exceptions. *BMJ* 1997;314:1107-11. (12 April.)
3 Bhagwanjee S, Muckert DJJ, Jeena PM, Moodley P. Does HIV status influence the outcome of patients admitted to a surgical intensive care unit? A prospective, double blind study. [With commentaries by R Kale, S Bhagwanjee et al, and Y K Seedat.] *BMJ* 1997; 314:1077-84. (12 April.)

Research studies in diving medicine are considered by Ministry of Defence research ethics committee

EDITOR—In his letter Peter Wilmshurst made some general comments on the use of human volunteers for medical research; however, he singled out his concern about the adequacy of the ethical control of research in diving medicine, most of which, he asserts, "is performed outside hospitals and without the safeguard of hospital ethics committees."[1] Diving medicine is a highly specialised branch of medicine covering basic physiological, operational, and commercial aspects of the subject. It is appropriate, therefore, that ethical considerations of non-clinical research in diving medicine should be dealt with by committees that are independent of hospital ethics committees but nevertheless conform with the codes of practice outlined by the Royal College of Physicians.[2] Examples are the procedures that are adopted by the Ministry of Defence at its two experimental diving establishments: DERA (Defence Evaluation and Research Agency) Alverstoke and the Institute of Naval Medicine at Alverstoke, where non-clinical aspects of diving are dealt with.

Each research project is first scrutinised from the scientific and ethical points of view by local advisory committees. It is then considered by the Ministry of Defence (navy) personnel research ethics committee for final assessment. The membership of this committee is constituted according to the guidelines recommended by the Royal College of Physicians[2] and consists of nine civilian personnel, all but one being independent of the Ministry of Defence. In addition, Royal Navy personnel and others with a specialist knowledge of diving medicine are coopted.

The volunteers are drawn from Royal Navy or Ministry of Defence personnel, and there is no question of their services being obtained by coercion. Before being invited to sign the consent form they receive in writing a description of the project and an account of their proposed participation in it, the methods to be used, the benefits likely to accrue from the project and any possible risks to their own health. They are given the opportunity of discussing the project with the project officer and independent medical officer, and it is emphasised to them that they can withdraw from the project at any time, either before it starts or during it, without having to give a reason why. Their decision does not entail any loss of earnings or seniority and does not affect their prospects of promotion. All volunteers are examined for medical fitness by the independent medical officer.

I hope that these details will help to allay any fears that ethical aspects of the use of human volunteers in naval diving medicine in Britain have not been properly addressed.

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1 Wilmshurst P. Informed consent in medical research. *BMJ* 1997;314:1481. (17 May.)
2 Royal College of Physicians of London. *Guidelines on the practice of ethics committees in medical research involving human subjects.* 3rd ed. London: RCP, 1996.

Subjects may not understand concept of clinical trials

EDITOR—We agree with Richard Smith that the issue of informed consent is not simple.[1] Even when a paper clearly states that information was given and consent obtained, readers cannot assume that the information given was "full" or that the consent was "fully informed."

We recently conducted a qualitative interview study with the parents of 21 babies enrolled in the United Kingdom collaborative trial of extracorporeal membrane oxygenation.[2 3] The trial compared two methods of life support in critically ill newborn babies: conventional management (ventilatory support) and oxygenation of the blood through an external circuit.

In the qualitative study the parents were asked about their reactions to the offer to participate in the trial and to randomisation. The findings showed that they often had difficulty with the idea of randomisation and the rationale for its use. An example of a difficulty in explaining the scientific method is the use of the word "trial." The concept of a clinical trial was unfamiliar to most parents and the term did not necessarily convey the crucial information that two treatments (allocated on a random basis) were being compared. The trial was seen by some parents more as "a trial period." There were other areas of difficulty for the parents. For example, where parents did not know that medical uncertainty was the basis for the trial they sought other means to explain the use of randomisation (perhaps as a way for doctors to circumvent a difficult choice between treatments, or to decide between babies competing for scarce beds).

We generated three hypotheses from the data: (*a*) that parents were given accurate information but did not retain the details; (*b*) that parents were given partial information at the discretion of the caregiver, so that if they were perceived to be under too much stress the caregiver withheld or softened certain details; and (*c*) that parents were given inaccurate information, which reflected the caregivers' own beliefs about the trial. These hypotheses are not mutually exclusive.

We are continuing our research in other trials to try to develop strategies to support caregivers and to ease the process of obtaining and giving informed consent. We would be interested to hear from others working in this or related fields.

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1 Smith R. Informed consent; the intricacies. *BMJ* 1997;314:1059-60. (12 April.)
2 Snowdon C, Garcia J, Elbourne D. Understanding randomisation: parental responses to the allocation of alternative treatments in a clinical trial involving their critically ill newborn babies. *Soc Sci Med* (in press).
3 UK Collaborative ECMO Trial Group. UK collaborative randomised controlled trial of neonatal extracorporeal membrane oxygenation. *Lancet* 1996;348:75-82.

Informed consent is not always obtained in United States

EDITOR—A code of silence and a spirit of denial surround one of the oldest and most perplexing conundrums in medical research: how to recruit large numbers of fully consenting subjects. So it was refreshing to note the *BMJ*'s pioneering willingness to devote much of the issue of 12 April to questions of informed consent. "Rather than restrict the debate to ourselves," as the editor, Richard Smith, put it, the *BMJ* dared to display publicly what institutional review boards and healthcare professionals usually handle with discretion or denial.

Our own analysis, published in *The (Cleveland, Ohio) Plain Dealer* and other American newspapers late last year, suggests the extent to which questions of consent persist.[1] This is despite the American government having apologised formally recently to survivors of a study of the natural course of syphilis in black men in Tuskegee, Alabama.[2] President Clinton has diverted the mandate of the National Bioethics Advisory Commission (which was formed to grapple with issues such as informed consent) to take up the more sensational if speculative topic of human cloning. Headlines have overtaken the issue before; in 1995, on the day that the Advisory Committee on Human Radiation Experiments warned of questions of consent in contemporary medical research, public interest focused on the verdict in the case of O J Simpson. In the past few months, disclosures in Augusta, Georgia, and Orange County, California, raised questions of consent, illustrating that the topic is more than a matter of distant history.[3 4]

Since 1977 the US Food and Drug Administration (FDA) has conducted 4154 inspections of clinical trials. Our analysis of records of those inspections showed that 53% of the investigators were cited by the FDA for failing clearly to disclose the experimental nature of their work. In 46 trials involving at least 1000 men, women, and children, drugs were tested without any written evidence that subjects had consented.

We also found evidence that the US government, which makes annual payments to survivors of the study in Tuskegee, has sponsored experiments on unsuspecting subjects well into the 1990s. Among our case studies were tests by the Centers for Disease Control and Prevention, begun in 1990 in Los Angeles, of the immunogenicity and efficacy of the Edmonston-Zagreb measles vaccine, which the centres knew had earlier caused excess mortality in Africa; and a study in 1991 of hepatitis A vaccine, conducted on a Sioux reservation, in which the letterhead on the consent form implied an established prevention programme rather than the safety and efficacy trial it was.

Nor does the record overseas appear any better. Foreign and internal FDA documents that we reviewed contained accounts of fraud, concealed side effects, experiments diverging from protocols, and questions of consent. Consent forms were incomplete or inadequate in 65 of 137 inspections by the FDA of trials conducted in countries other than the US. In Canada, consent forms were inadequate in 21 of 36 inspections. Verifiable scientific data were missing from 53% of the international research submitted to support a US new drug application.

Our analysis of FDA data also showed that internal review boards, the front line in protecting test subjects, cannot be counted on to ensure that people know they are being used in medical research. At 942 internal review boards between 1990 and 1996, FDA inspectors found multiple violations: no evidence of continued safety monitoring (at 20% of the review boards); no copies of consent forms, injury reports, or protocols (19%); and that patients were not clearly told when procedures were experimental (16%), not offered proved alternative treatments (13%), not informed of expected risks and pain (10%), and not told of likely benefits (6%).

Some people—among them US senator John Glenn and Gary Ellis, director of the office for protection from research risks at the National Institutes of Health—have argued for stronger controls. Glenn has proposed legislation to close many regulatory gaps. But until more researchers and their publications are willing to come out publicly about what they know and what they believe should be done to better advance medical research without sacrificing—and documenting—consent of the fully informed test subject, prospects appear dim for meaningful reform. And questions of consent can be expected to recur with disturbing frequency.

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1 Epstein K, Sloat B. Drug trials: do people know the truth about experiments? *The (Cleveland) Plain Dealer* 1996 Dec 15-18:a1. [Articles and charts are posted at www.spj.org/sdxawards/03invrptg/index.htm#top or can be requested from: epstein@dgsys.com]
2 Harris JF, Fletcher MA. Six decades later, an apology. *Washington Post* 1997 May 17:a1.
3 Teegardin C, Whitt R. FDA inspection finds violations in Augusta studies. *Atlanta Constitution* 1997 May 11:a3.
4 Marsh B, Romney L. Hospital accused of violating consent rules. *Los Angeles Times* 1997 May 30:a3.

Research in pregnancy brings special considerations

EDITOR—The debate on informed consent stimulated by the *BMJ* must be welcomed by anyone interested in the ethics of medicine and research.[1] Subsequent correspondence has highlighted the differences between consent to treatment that benefits only the individual and consent to participation in research that aims to benefit other people.[2] For pregnant women, however, both treatment and research involve third parties, which might influence decision making. When treating pregnant women or offering them the chance to participate in research we must ensure that consent is truly informed and freely given.

Women feel responsible for the fetus they carry to the extent that they often modify their habits and lifestyle during pregnancy. Pregnancy may affect their ability to make a free choice: they may feel bound to accept interventions that might benefit the fetus which they would rather decline, or they may refuse treatment for themselves in case it should harm the baby. If the risks and benefits to the fetus are not carefully explained they may not give their consent for research to which they feel a personal obligation or in which they are interested.

Research in pregnancy brings special considerations. The "two patient" model of pregnancy disallows the imposition of possible harm on one party for the sake of the other,[3] which is particularly important, for example, in studies on the mode of delivery. The father may have an opinion that will

influence whether the mother participates. Previously independent women may be vulnerable and dependent on their doctor, whom they need to trust and whom they may want to please by entering research projects. If they are to forgo the "good" of personal care they must trust that the trial truly is based on the null hypothesis—that there is no known difference between the proposed treatments or interventions. Some patients will prefer to assume that "[My] doctor knows best [about me and my baby]" and not be happy to enter into the discussion of uncertainty that a trial and the issue of informed consent will raise.

These challenges sometimes lead to the exclusion of pregnant women from clinical trials. For work on drugs such as tocolytic agents, however, only pregnant women can help. Pregnancy does not remove a woman's competence to give informed consent, but it does bring extra considerations that researchers must bear in mind when trying to encourage these women to participate.

These views arose out of interviews with women who had been invited into research projects while pregnant; the work was supported by a grant of £5000 from the NHS Executive (West Midlands) research in primary care initiative.

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1 Smith R. Informed consent: the intricacies. *BMJ* 1997; 314:1058-60. (12 April.)
2 Informed consent in medical research [letters]. *BMJ* 1997; 314:1477-83. (17 May.)
3 Tauer C. When pregnant women refuse interventions. *AWHONN'S Clinical Issues* 1993;4.4:596-604.

Explicit guidance is required on valid exemptions for need for ethical review

EDITOR—We welcome the recent attention to the ethical conduct of human experimentation.[1 2] But we believe that an overzealous interpretation of what are intended to be general guidelines can make it difficult to communicate non-experimental case reports, reviews of case notes, and clinical series. We are often asked for advice on whether studies require review by an ethical committee. To advise that a study does not need ethical review is to make an ethical judgment; that is, of course, the function of the committee. Thus it falls to the investigators to decide whether to seek approval of the ethics committee. We believe that when an author submits a manuscript for publication the editor should consider a statement giving valid reasons for exemption from the general need for ethical approval. We find the guidelines issued by the Royal College of Physicians both lucid and helpful.[3] We suggest that editors could adopt these or similar statements making clear what types of report need not be reviewed by a research ethics committee.

In essence, the grounds for exemption could include:

- that the information emerged from clinical practice and so does not constitute research (section 3.1 in the Royal College of Physicians' guidelines)
- that the information concerns innovative treatment applied with the patients' informed consent and so does not constitute research (section 3.2)
- that the investigation was considered to be a quality control or medical audit exercise exempt for the need for ethical review (section 4.8).

The editor should decide whether the claim for exemption is valid and also ensure that the manuscript respects the confidentiality of the patients.

As an example of the difficulties that arise, we are aware of a case in which an editor refused to consider a manuscript because the work had not been reviewed by an ethics committee. The authors were describing five years of clinical experience with a technique generally accepted as a therapeutic option and which they considered to be the method of choice for a life threatening condition. In our opinion, the authors, who were also the patients' medical practitioners, did not need approval of a research ethics committee to provide what they considered to be the best care for their patients or to refer back to the original case notes in order to aggregate the data. In response to an appeal, the editor concerned asked whether the authors could obtain retrospective approval from the local ethics committee. But it is that committee's policy not to consider retrospective applications.

More explicit guidance on valid exemptions for the need for ethical review would be invaluable in preventing or resolving this type of impasse.

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1 Rennie D. Disclosure to the reader of institutional board approval and informed consent. *JAMA* 1997;277:922-3.
2 Smith R. Informed consent: the intricacies. *BMJ* 1997;314:1059-60. (12 April.)
3 Royal College of Physicians of London. *Guidelines on the practice of ethics committees in medical research involving human subjects.* 2nd ed. London: RCP, 1990.

Lack of respect for patients in medical research may reflect wider disrespect in clinical practice

EDITOR—I do not think that the *BMJ* should continue to publish papers that do not include informed consent.[1] Martin Dennis and colleagues, who studied the effect of contact with a stroke family care worker, did not ask patients to consent to randomisation.[1] As Sheila McLean points out in her commentary on Dennis and colleagues' study, none of the considerations that the authors faced were unique.[1] I suggest that they are in fact faced by many trialists. Certainly none of them were of such importance as to override fundamental ethical principles. In Dennis and colleagues' study it would have been possible, by using multivariate analysis, to determine whether initial preference (assessed, for example, by a question posed before randomisation) had a significant impact on satisfaction or other variables. This is an approach that colleagues and I used in a randomised controlled trial.[2] I sympathise with the desire to remove as much bias as possible, but we would do well to heed the philosopher Xenophanes (6th century BC), who said: "Through seeking we may learn and know things better, but as for certain truth no man hath known it, for all is but a woven web of guesses."

The situation faced by Satish Bhagwanjee and colleagues was certainly more complex.[3] Nevertheless, Len Doyal rightly suggests that "assent" from relatives of incompetent patients should be sought.[4] Bhagwanjee and colleagues' concern to maintain confidentiality posthumously might have been satisfied by their making clear to the assenting relatives that the result would be destroyed and not disclosed to them if the patient died.

I wonder whether a lack of respect for patients in medical research reflects a wider, subtle, disrespect in clinical practice: how many general practitioners, midwives, or obstetricians, for example, can honestly say that they seek the informed consent of all women for antenatal screening for syphilis? The draft revision of the Hippocratic oath recently circulated by the BMA states: "I will ensure patients receive the information and support they want to make decisions about disease prevention and improvement of their health."[5] Our duty as medical researchers is clear.

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1 Dennis M, O'Rourke S, Slattery J, Staniforth T, Warlow C. Evaluation of a stroke family care worker: results of a randomised controlled trial. [With commentaries by S McLean and M Dennis.] *BMJ* 1997;314:1071-7. (12 April.)
2 Clement S, Sikorski J, Wilson J, Das S, Smeeton N. Women's satisfaction with traditional and reduced antenatal visit schedules. *Midwifery* 1996;12:120-8.
3 Bhagwanjee S, Muckart D, Jeena P, Moodley P. Does HIV status influence the outcome of patients admitted to a surgical intensive care unit? A prospective double blind study. [With commentaries by R Kale, S Bhagwanjee et al, and Y K Seedat.] *BMJ* 1997;314:1077-1084. (12 April.)
4 Doyal L. Informed consent in medical research. *BMJ* 1997;314:1107-11. (12 April.)
5 BMA. Draft revision of the Hippocratic oath. *BMA annual report of council 1996-97.* London: BMA, 1997.

Rigorous studies are needed to determine values of interventions

EDITOR—Richard Smith's editorial and the accompanying papers concerning informed consent have considerable implications for research on the "softer" areas of medicine.[1] There are important differences between trials looking at, say, distribution of an information leaflet or provision of a specialist nurse and studies of a new drug or of a surgical procedure.

If offered the choice of receiving an information leaflet or specialist nursing, few patients would opt for the equivalent of no treatment. Results from any such trial requiring informed consent would therefore be extremely unrepresentative and possibly misleading or meaningless.

In her commentary on Martin Dennis and colleagues' study Sheila McLean states: "If certain research cannot be undertaken to the maximum standards of scientific inquiry the question is not how much information should be withheld, it is whether the research should be done in the first place."[2] Many members of the legal profession, whose primary information base is case law, presumably hold this view. Medicine must, in

contrast, be based on more than individual case histories.

As well as expecting to be kept informed by their doctors, patients expect their doctors to be informed. If we cannot perform rigorous studies we shall continue to be pressurised to provide interventions of little or no value to patients, and harm may result.

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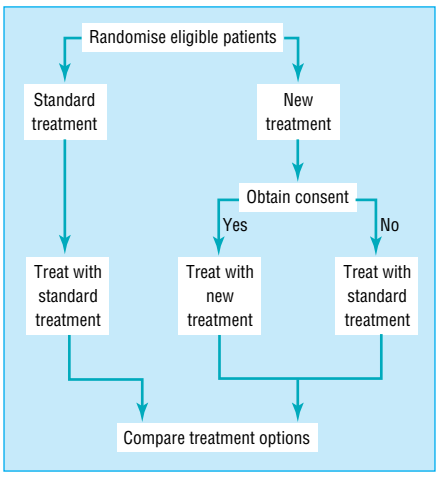
1 Smith R. Informed consent: the intricacies. *BMJ* 1997;314:1059-60. (12 April.)
2 Dennis M, O'Rourke S, Slattery J, Staniforth T, Warlow C. Evaluation of a stroke family care worker: results of a randomised controlled trial. [With commentaries by S McLean and M Dennis.] *BMJ* 1997;314:1071-7. (12 April.)

Trials that use Zelen's procedure should be acceptable

EDITOR—In his editorial on the ethics of obtaining consent in trials, Richard Smith describes the Edinburgh evaluation of family stroke care workers as one "in which informed consent was not sought," a description taken up in the lay press.[1 2] In fact, Martin Dennis and colleagues make it clear that they did seek consent, using a variant of Zelen's procedure, the single randomised consent design (figure).[3]

In her commentary criticising the Edinburgh trial Sheila McLean says: "Anyone who is to be studied must be given the fullest possible information." [2] Len Doyal seems to agree, using the terms informed consent and fully informed consent interchangeably.[4] What is fully informed consent? Does it include details of all the evidence justifying the mounting of a trial and details of the financing of the study, how the sample size was derived, and the methods that will be used to analyse the results? If taken literally, the idea is absurd; consent can never be fully informed. In any case, an attempt at implementation—that is, at ensuring that everybody knows everything—would defeat its purpose. To paraphrase Zelen, what we want is not fully informed subjects but fully understanding ones. We must choose what information to impart, or we only confuse. It is adequately informed consent that is the hallmark of ethical research.



Single randomised consent design

In decisions of what constitutes adequately informed consent, the conflict is not simply between researchers' convenience and the moral rights of subjects. Insisting on consent to randomisation in pursuit of one ethical aim may lead to the conduct of an unethical trial for another reason. As willingness to consent to randomisation is a psychological characteristic it may be associated with other characteristics that themselves determine the outcome of treatment. This applies particularly to trials of psychosocial interventions. If refusals are substantial but the trial is completed, sampling bias will be large but uninterpretable. Research that is useless or yields misleading results because of design faults is unethical, just as much as inadequately informed consent is.

It does not help the ethical argument to talk about informed consent, fully informed consent, and consent to randomisation as if they were the same thing. Nor does it help to argue that seeking consent to randomisation is always ethical while not doing so is simply self serving. A good case has not been made for obligatory adherence to consent to randomisation, and until it has, the *BMJ* should continue to publish trials that use Zelen's procedure.

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*The authors are conducting a trial of psychological intervention after stroke, funded by the NHS research and development programme, that uses a randomised consent design.

1 Smith R. Informed consent: the intricacies. *BMJ* 1997;314:1059-60. (12 April.)
2 Dennis M, O'Rourke S, Slattery J, Staniforth T, Warlow C. Evaluation of a stroke family care worker: results of a randomised controlled trial. [With commentaries by S McLean and M Dennis.] *BMJ* 1997;314:1071-7. (12 April.)
3 Zelen M. Randomised consent designs for clinical trials: an update. *Stat Med* 1990;9:645-56.
4 Doyal L. Journals should not publish research to which patients have not given fully informed consent—with three exceptions. *BMJ* 1997;314:1107-11. (12 April.)

Not seeking informed consent breaches patient's charter

EDITOR—The patient's charter has not been mentioned in the recent debate about informed consent.[1] The charter tells patients that they have the right to choose whether or not to take part in medical research.[2] Thus, not to seek patients' informed consent before entering them into research is to breach the charter and to nullify patients' legitimate presumptions. Journals should not publish research whose design depends on avoiding consent or that fails to give particulars of how consent was sought.

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1 Smith R. Informed consent: the intricacies. *BMJ* 1997;314:1059-60. (12 April.)
2 Department of Health. *The patient's charter.* London: HMSO, 1991.

Ethical principles may need to be adapted when research subject is not an individual subject

EDITOR—Most commentaries on consent have centred on the individual research subject. In public health, however, the "subject" is often a population or unit of service, and both the study design and ethical principles may need adaptation. This gets especially tricky when the style of informing people about a service, and inviting them, is itself the focus of study.

For example, the effect of inviting women aged 65-69 for breast screening is currently being studied in East Sussex, Leeds and Wakefield, and Nottingham. We have argued, and our local research ethics committees have agreed, that the benefit to individual women is already sufficiently proved (and similar to that for women aged 50-64) that the same routine style of invitation to and acceptance of screening are sufficient to achieve informed consent to the procedure. The research question—the area of "therapeutic uncertainty"—is whether those benefits (set against the costs) justify such screening as a national policy. Response to invitation will be one of the key end points; it would be difficult to predict the national response to a standard form of invitation if the trial districts had used a non-standard invitation involving consent.

We could not, in the present state of knowledge, have advanced a similar argument for women aged over 70, and it is a moot point at what stage in the accumulation of evidence our argument became valid for 65-69 year olds. (It is not clear from published accounts how informed consent was secured in previous trials.) The chairman of Wakefield's local research ethics committee thought that one justification for our approach was that the beneficial intervention was being offered to an entire population, with no randomisation or non-intervention group. We hope that journal editors will accept the line taken when the time comes to publish the results.

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Study in which patients had HIV tests could have been designed differently

EDITOR—We share Rajendra Kale's view that failing to seek patients' consent to HIV testing is always wrong.[1] In a bronchoscopy study of patients with HIV infection in Harare the patient's consent was sought in every case. It was only rarely declined, and even when this occurred the data were still acceptable for publication.[2]

Satish Bhagwanjee and colleagues' study could have been designed differently. HIV testing could have been done anonymously,

with matching of the results of the tests and patient data done by a third party not involved in the patients' care. Alternatively, serum samples from all the patients admitted to the intensive care unit could have been stored and survivors asked for their permission for testing. Serum samples from non-survivors could have been tested and given a number that would render them unidentifiable to anyone outside the study. Testing without consent and then informing the patients can be an unfortunate combination. The fact that only three out of 402 patients wished to know the result of their HIV test suggests some unconscious resistance to being tested, and of course by then they were not in a position to refuse testing. Were all patients asked whether they objected to being included without prior testing, and if so how was this question posed?

We believe that the ethics committee that considered this proposal did the investigators a disservice by not pointing out alternative ways of doing this study while protecting patients' rights.

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1 Bhagwanjee S, Muckart D, Jeena P, Moodley P. Does HIV status influence the outcome of patients admitted to a surgical intensive care unit? A prospective double blind study. [With commentaries by R Kale, S Bhagwanjee et al, and Y K Seedat.] *BMJ* 1997;314:1077-1084. (12 April.)
2 Malin AS, Gwanzura LEC, Klein S, Robertson VJ, Musvaire P, Mason PR. Pneumocystis carinii pneumonia in Zimbabwe. *Lancet* 1995;346:1258-61.

Informed consent is light years away for black African patients

EDITOR—We wish to cross swords with Y K Seedat over the wild and presumptuous assertions in his commentary about testing subjects without their consent.[1] His piece is apt to mislead and presents a one sided picture for any doctor who has no idea of South African society.

Seedat is professor of medicine at the University of Natal, an almost exclusively Asian and black medical school. This medical school's main hospital is King Edward VIII Hospital, a black hospital. We find it astounding that no mention is made of the racial breakdown of those tested anonymously for HIV without their consent. We assume that they were almost exclusively black African patients in social classes IV and V (black working class). As black doctors whose medical studies began at the University of Natal, we find Seedat's wild assertions insulting not only to black Africans but to humanity as a whole. His claim that there is no harm or injury to the subjects has never been tested.

The subjects who were tested have never had any rights in South Africa and are forever grateful and indebted to anyone with a white coat and a stethoscope—anyone in authority. Our experience with South Africa during apartheid and since its abolition suggests that true informed consent as part of ethics is light years away for black African patients. Although we are British medical practitioners, we are South African nationals, and we find it unacceptable that black South African patients become subjects of dubious laboratory tests without their knowledge for the benefit of doctors and other races.

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1 Bhagwanjee S, Muckart DJJ, Jeena PM, Moodley P. Does HIV status influence the outcome of patients admitted to a surgical intensive care unit? A prospective double blind study. [With commentaries by R Kale, S Bhagwanjee et al, and Y K Seedat.] *BMJ* 1997;314:1077-84. (12 April.)

Research suffers if patients suspect that their rights may be breached

EDITOR—Debate on informed consent has drawn attention to situations in which scientific reliability—specifically, avoiding subjective reporting bias—conflicts with the obligation fully to inform subjects in a clinical trial.[1 2] When there is a conflict of principles we have to choose which principle will take precedence. The majority opinion both in the medical profession and among ethicists is that the patient's right to choose takes precedence over the researcher's right to seek knowledge, and this involves rights to refuse participation and to request information. Weakening or abandoning the requirement for informed consent on the grounds that bias may result if patients know that they are in a trial is a potentially serious erosion of the protection afforded by the principle of informed consent. It therefore requires careful, and in our view sceptical, review.

In recent years there has been a tendency to argue that badly designed research is inherently unethical. While we have sympathy with this view, the consequence of regarding some methods as carrying moral value is to devalue the patient as the prime source of moral authority. We are approaching a situation in which the requirements of a method may once again take precedence over patients' consent, as, for example, in Dennis and colleagues' study of the introduction of a stroke worker.[1] While the authors argue that the intervention was harmless, we believe that the cost of condoning research that lacks consent will always outweigh any possible benefit.

Even if one ignores the philosophical argument, simply in practical terms research suffers if patients suspect that their rights may be breached. One development that might help patients and researchers is to expand the role that patients have in the research design and reviewing processes. Professional researchers may regard this as unrewarding. We suspect that forms of research other than clinical trials may provide more insight into the effectiveness of interventions than a randomised controlled trial in precisely those cases in which researchers believe that patient subjectivity may confound results.

When consent is a matter of bald choice, it is unsurprising that many patients refuse to participate in trials that seem to be in their own or society's interests and that the results of trials are hard to apply to non-experimental medical situations. Evidence from trials in breast cancer suggests that good consent processes benefit patients and result in improved outcome measures. Surely this indicates that more and better consent and involvement of patients are needed in research, not less.

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1 Dennis M, O'Rourke S, Slattery J, Staniforth T, Warlow C. Evaluation of a stroke family care worker: results of a randomised controlled trial. [With commentaries by S McLean and M Dennis.] *BMJ* 1997;314:1071-7. (12 April.)
2 Bhagwanjee S, Muckart D, Jeena P, Moodley P. Does HIV status influence the outcome of patients admitted to a surgical intensive care unit? A prospective double blind study. [With commentaries by R Kale, S Bhagwanjee et al, and Y K Seedat.] *BMJ* 1997;314:1077-1083. (12 April.)

Patients' knowledge that they are participating in trial may not bias results

EDITOR—In his commentary on his and colleagues' study Martin Dennis puts forward arguments as to why patients in a trial of the effect of a stroke family care worker were not asked for their consent before being entered into the trial.[1] We question whether seeking consent would necessarily have biased the results. We are currently involved in a randomised controlled trial in Oxford of a family support organiser for patients with stroke and their families. As in Edinburgh, patients are randomised in our study before consent has been obtained. At the time of randomisation, however, we write to the closest carers of all patients, inviting them to take part. The letter explains the purpose of the study and that whether or not the carers see the family support organiser will be determined by chance. Altogether, 18 of the 179 families contacted so far have elected not to take part, either in response to the letter or when contacted by a researcher six months after the stroke. The proportion of families not taking part is the same (10%) in both the intervention and control group. At the follow up visit the researcher does not specifically remind patients or their family that the purpose of interviewing them is to evaluate the possible effects of a family support organiser. Our study was approved by the Central Oxford Research Ethics Committee.

The theoretical concern is that patients and their families will realise which group they are in and that this might influence the results.[1] Our experience, however, suggests that patients and families do not discriminate between different community services. Prompted by the issues raised by Dennis, we decided to do a limited interim analysis of our (ongoing) study. At the end of the follow up interview the researcher asks what services have been received since the stroke. Only eight of 80 families in the intervention group have mentioned the family support organiser at this time. The researcher then records which of the two groups she thinks the family was in. She has so far guessed correctly for 102 (64%) out of 159 families (95% confidence interval 57% to 72%).

While higher than would be expected by chance, this is not significantly more than the 59% recorded by the researcher in the Edinburgh study. This provides circumstantial evidence that many families were effectively blind to their treatment allocation. Therefore, it would seem that consent can be obtained in trials of this sort without compromising the validity of the results.

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Funding: The Oxford family support organiser trial is supported by the Stroke Association.

1 Dennis M, O'Rourke S, Slattery J, Staniforth T, Warlow C. Evaluation of a stroke family care worker: results of a randomised controlled trial. [With commentaries by S McLean and M Dennis.] *BMJ* 1997;314:1071-7. (12 April.)

Two stage randomisation and consent would overcome many problems

EDITOR—We believe that two stage randomisation procedures potentially provide a solution to the ethical concerns arising from Martin Dennis and colleagues' study evaluating a stroke family care worker.[1 2] A two stage randomisation procedure requires that all patients give full consent to their particular role in the trial rather than to a hypothetical scenario. In the first stage of randomisation all patients are asked to give consent for follow up. Consent for additional (non-standard) treatment is sought only from a random sample selected to be offered the study intervention. Therefore, patients—whether they are in the control or intervention group—consent to the assessments and treatment that they will actually receive. This contrasts with the usual one stage consent procedure in randomised controlled trials, whereby patients consent to two or more possible forms of care which they may or may not get. When a one stage procedure is used patients randomised to standard care may feel disadvantaged as a result of not receiving the intervention, particularly if it is a new clinical service. A two stage randomisation clearly would be unethical if the control group were receiving non-standard care. In her commentary on the study Sheila McLean argues that patients should consent to the project rather than their role within it. Surely, however, it is more appropriate that they give personal consent to their assessment and treatment in a project and what will be required of them in the study. We believe that this approach, centred on the patient, is consistent with the highest of ethical standards in medical research.

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1 Dennis M, O'Rourke S, Slattery J, Staniforth T, Warlow C. Evaluation of a stroke family care worker: results of a randomised controlled trial. [With commentaries by S McLean and M Dennis.] *BMJ* 1997;314:1071-7. (12 April.)
2 Zelen M. A new design for randomised clinical trials. *N Engl J Med* 1979;300:1243-5.

Ability to be informed is separate from ability to give consent

EDITOR—The debate over the need for research subjects' informed consent lacked the patients' perspective. It is true that many people would be reluctant to take part in a randomised controlled trial if they knew that they were doing so. And why is this? It is because they have at best only a 50% chance of being in the group with the most positive outcomes, if there is indeed a difference, and because, by the time the trial has established such distinctions, their own treatment may be compromised. Their reasons are rational; they are just inconvenient for the researcher.

I am concerned by Len Doyal's and others' ready exclusion of consent for people "not competent" to give consent.[1] In the case of a person with a learning difficulty, a juvenile, or a person with a severe mental health problem (my own field of research), what may perhaps be compromised is the ability to be informed. I would argue that this is separate from the ability to give consent, and failure to recognise the distinction allows researchers to take the arrogant view that the only reason why people refuse to cooperate is because they have failed to understand the information offered.

It is easy in practice for researchers to be "economical" with the information, volunteering only those aspects of the study that they suspect are most acceptable to patients. The smaller the potential sample the more likely this subterfuge is, to maximise participation.

Jeffrey S Tobias suggests that there is often a conflict of interests between the best interests of the individual patient and those of society as a whole.[2] But it hardly seems appropriate to leave the research community to decide what the interests of society as a whole are, for we would expect their conclusions to be biased.

It is undeniable that offering truly informed consent will skew outcomes in most cases, though it will not necessarily affect the outcome variables that are being measured. No research design involving human subjects can avoid the human factor. Perhaps we need to accept, as the average sceptical but rational layperson did a long time ago, that scientific research rarely provides unequivocal outcomes. What it does is substantiate reasonable hypotheses, which will help predict outcomes in most cases. Let's not kid ourselves that we work under laboratory conditions; and let's remember that you can't treat people like rats.

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1 Doyal L. Informed consent in medical research. *BMJ* 1997;314:1107-11. (12 April.)
2 Tobias JS. *BMJ*'s present policy (sometimes approving research in which patients have not given fully informed consent) is wholly correct. *BMJ* 1997;314:1111-4. (12 April.)

"Blanket" consent to trials would be a good idea

EDITOR—In his editorial on informed consent, Richard Smith discusses the contrasting views of Len Doyal and Jeffrey S Tobias.[1] He highlights Tobias's suggestion that a patient could give "blanket" consent when admitted to a hospital where several randomisation studies are in progress.[2] I supported this idea some years ago, but also suggested that much work would have to be done explaining the need for it and gaining public trust.[3] It could be a useful third option, added to the options of requesting and not requesting informed consent; thorough safeguards and approval of an ethics committee would be necessary.

In all walks of life, when one person seeks help from another, consent based on trust is surely just as valid as consent based on information. There is always a blend of the two, but the proportions vary. Lord Scarman, a judge with liberal views, said, "It may be sensible to trust your doctor and feel that the risks are for him to assess."[4] We all know that "fully informed" consent is often nothing of the kind; there may well be more trust than information. With blanket consent the average amount of trust would have to be even greater, but there would be many advantages.

Those who want the *BMJ* to take a rigid view that might overrule the opinion of ethics committees should spend a day in a ward full of elderly people. They would probably find many who, though far from being mentally incompetent, are at times confused and forgetful. What could be more unrealistic than to refuse to recognise this for fear of being called patronising or paternalistic? Suppose a doctor approaches such a patient, who perhaps feels ill and wants only sensitive care, with a view to gaining his or her fully informed consent to, say, two studies—the randomising of the patient's sleeping tablets and the randomising by the surgeon of a new suture material. Who can be sure that concern or confusion will not follow? Where is the sense in this? Some people underestimate both the danger of not comparing treatments in a reliable way and the harm that can be done to many sick patients when fully informed consent for every trial is sought, no matter how tense or difficult the situation.

There are many grey areas, but we should start thinking seriously about the idea of some general form of consent to the fact that a treatment is being randomised. The result would be fewer misconceptions, less fundamentalism, more trust, less detail, and more time to attend to patients' real needs.

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1 Smith R. Informed consent: the intricacies. *BMJ* 1997;314:1059-60. (12 April.)
2 Tobias JS. BMJ's present policy (sometimes approving research in which patients have not given fully informed consent) is wholly correct. *BMJ* 1997;314:1111-4. (12 April.)
3 Brewin TB. Valid comparison is the key. In: Razis DV, ed. *Medical ethics and/or ethical medicine.* Paris: Elsevier, 1989.
4 Scarman, Lord. Consent, communication and responsibility. *J R Soc Med* 1986;79:697-700.

Respect for autonomy may conflict with principle of beneficence

EDITOR—The argument of Len Doyal[1] and Sheila McLean (in her commentary[2]), that respect for patients' autonomy demands that they should be informed about possible alternative treatments, should be applied not just to clinical trials but to any situation in which there is uncertainty about which treatment is best. As Martin Dennis and colleagues' trial evaluating the introduction of a stroke family care worker shows, any new treatment or care service, no matter how apparently benign, has the potential to do harm, yet many are introduced without formal evaluation.[2] For example, when coronary care units were introduced few people would have questioned their intrinsic benefits in promoting better monitoring and early treatment of complications, yet how many deaths may have been caused by overenthusiastic use of prophylactic antiarrhythmic drugs?[3] We therefore have a duty to evaluate rigorously not just new practices but many of those that have already come into widespread use.

If uncertainty still exists about the value of coronary care units or about the patients most likely to benefit, should we respect the autonomy of patients with acute chest pain (regardless of age or other commonly applied eligibility criteria) by explaining all the potential advantages and disadvantages of specialised coronary care? Alternatively, should we conduct a randomised trial and explain to patients allocated to care in a general ward exactly what special facilities will not be made available to them? The bias in expectations introduced by such an approach would not only weaken the conclusions of the study, as Dennis points outs in his commentary,[2] but could lead to the wrong conclusions, possibly misleading clinicians for years to come.

Rigid insistence on full disclosure risks undermining the confidence of patients that they are getting the best possible treatment. We know that this can have a substantial adverse effect, so respect for autonomy may thus conflict with the principle of beneficence. Why should one ethical principle take precedence over another, and why should different standards be applied to "normal" clinical practice and research? Could it be because the informed consent procedure is easier to audit, particularly in a clinical trial, and is therefore more susceptible to legal challenge? If we submit to such thinly veiled legalistic threats then not only will reliable scientific evaluation of health care services be impossible (as Dennis and colleagues have shown) but we will no longer be able to deal with the inevitable uncertainties of clinical practice in a way that protects patients from serious potential harm.

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1 Doyal L. Informed consent in medical research. *BMJ* 1997;314:1107-11. (12 April.)
2 Dennis M, O'Rourke S, Slattery J, Staniforth T, Warlow C. Evaluation of a stroke family care worker: results of a randomised controlled trial. [With commentaries by S McLean and M Dennis.] *BMJ* 1997;314:1071-7. (12 April.)
3 Cardiac Arrhythmia Suppression Trial (CAST) Investigators. Effect of encainide and flecainide on mortality in a randomised trial of arrhythmia suppression after myocardial infarction. *N Engl J Med* 1989;321:406-12.

⁂We have received an unprecedented response to our cluster of articles on informed consent. Readers can see from these letters and the previous group that we published that correspondents hold very different views on what policy we should set. Because we think that the voices of patients have not been adequately heard we plan to publish further responses from them. We will also publish brief responses from the two authors who introduced the debate.

We plan then to hold a meeting of all interested parties—including researchers, ethicists, and patients—to discuss what policy we should adopt. We hope that that meeting will be able to reach a consensus, but if (as seems likely) it cannot then the editorial team will decide our policy. We will report on the meeting and our decision in the journal.—EDITOR

French committee will investigate proposed link between activities of nuclear reprocessing plant and leukaemia

EDITOR—Alexander Dorozynsky states inaccurately that the international scientific committee established by the French government to review the studies of leukaemia among children and young adults living near the La Hague nuclear reprocessing plant has validated the conclusions of Dominique Pobel and Jean-Francois Viel.[1] These authors proposed a causal link between the incidence of leukaemia and the plant's activities.[2]

The committee, which I chair, noted that the reported incidence of leukaemia in children and young adults in the Nord-Cotentin region was unremarkable (25 cases observed *v* 22.8 expected), although there was a small excess of cases in the Beaumont-Hague canton, which contains the reprocessing plant (4 cases observed *v* 1.4 expected).[3] The case-control study, based on the Nord-Cotentin region as a whole, reported associations between leukaemia and the reported recreational use of local beaches, consumption of local seafood, and residence in a home constructed from granite.[2]

The incompatibility of some findings of the incidence and case-control studies was also noted. For example, recreational use of beaches was reported by 39% of control mothers. If this behaviour were causally related to the incidence of leukaemia with a true relative risk of 4.5 (as estimated in the case-control study) then one would expect a large numerical excess of leukaemia in the region as a whole. No such excess was observed. Because the published results do not permit resolution of this and other anomalies the committee recommended that these studies be reanalysed and the incidence study extended to cover the period 1993-7. The committee has also recommended strengthening the registration of cancer, particularly childhood cancer, in France and establishing a unit, similar to that in areas of Britain, to manage epidemiological data for small geographic areas.

The committee also assessed the available radiological data. The maximum annual effective radiation dose received by members of the public from emissions from all nuclear installations in Nord-Cotentin is estimated at 0.3 mSv, but this estimate is based on the maximum permitted emissions, which are probably much higher than the actual emissions. The committee has therefore recommended obtaining specific information about the dispersion of radionuclides from the plant into the environment, re-evaluating doses received by the general population on the basis of environmental monitoring data, and undertaking a detailed study of the exposure of critical groups in the population.

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1 Dorozynsky A. Links with leukaemia confirmed for French nuclear plant. *BMJ* 1997;314:1854. (28 June.)
2 Pobel D, Viel J-F. Case-control study of leukaemia among young people near the La Hague nuclear reprocessing plant: the environmental hypothesis revisited. *BMJ* 1997; 314:101-6. (11 January.)
3 Viel J-F, Pobel D, Carré A. Incidence of leukaemia in young people around the La Hague nuclear waste reprocessing plant: a sensitivity analysis. *Stat Med* 1995;14:2459-72.

Plans are needed on how to cope with demand for ventilation during pandemic influenza

See editorial by Mayou-White

EDITOR—A document entitled *Multiphase Contingency Plan for Pandemic Influenza* has just been issued by the United Kingdom's health departments for consultation.[1] Sadly, this document reflects the current state of thinking in NHS management nationally, in that 71 pages of text include only seven sentences relating to secondary care (one of which deals with mortuary arrangements). The document predicts a pandemic, which may well occur before 2010, and attempts to develop a strategy. The only statement about how the secondary care sector will cope is the terse sentence, "Supplies of relevant drugs (eg, antibiotics) and equipment (eg, ventilator equipment) will need to be secured." There is no indication of how this might be done and no comment on where the professional staff will come from (if they themselves do not succumb to influenza). We already know of the dire shortage of ventilator equipment and of beds and staff to deal with ventilated patients even during a normal winter. The general public will soon be aware that ventilation can save lives, yet the British government is apparently giving no thought to how Britain will cope with a

demand for ventilation hugely in excess of the provision presently available.

We are making strong representations to the Department of Health, and we would encourage an urgent and wide debate on measures that need to be taken to deal with such a disastrous possibility.

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1 UK Health Departments. *Multiphase contingency plan for pandemic influenza.* London: Department of Health, 1997.

Scientists should inform public of risks of transgenic experimentation

EDITOR—Robert Winston dismisses fears of a moral threat from cloning by presenting cloning as an exciting scientific endeavour which has been in progress for 20 years.[1] This tells us nothing about its potential for good or ill: atomic and nuclear weapons are no less terrible because they emanated from decades of challenging scientific research.

Winston implies that current disquiet about transgenic research is merely the product of a "scientifically illiterate" society. Yet David Weatherall reminds us that the unresolved technical problems of transferring human genes include ensuring that "the process does not result in any deleterious effects on the transfected cell population."[2] Germ line experimentation obviously has even more far reaching and unquantifiable consequences than somatic gene transfer, including the possibility of irreversible changes to the human genome, our food supply, and our environment.

Winston's editorial assures us of the adequacy of regulation in Britain and says there is "no particular urgency" in tightening it up. Even if this is true, research on cloning conducted in Britain could well be open to abuse in other parts of the world—we have an equal moral responsibility to people outside Britain. An editorial in the *Lancet* concludes: "The only way to reinforce an international prohibition of human cloning is to stop any research headed in that direction."[3]

Winston's lament about sensational press coverage is ironical given the way that genetic technology has been promoted through the popular media. As Weatherall notes: "There can be few fields of medical research that have gained so much publicity ... than what is still rather hopefully called 'gene therapy.'...Yet it is still to produce a genuine clinical success story."[2] Coverage in the financial press of biotechnology companies is revealing; an article in the *Times* recently stated: "Stock market valuations running into hundreds of millions of pounds are supported, it often seems, by little more than promises of future success." Significantly, the article emphasised that "News flow—announcements about trials, discoveries, and new research partnerships—is one of the main drivers of share prices."[4]

With such huge commercial pressures at work, the limitations and dangers of genetic research have been consistently underplayed. If our society really is scientifically illiterate then it is even more incumbent on scientists to inform the public about the serious risks inherent in transgenic experimentation.

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1 Winston R. The promise of cloning for human medicine. *BMJ* 1997;314:913-4. (29 March.)
2 Weatherall D. Gene therapy [book review]. *BMJ* 1997;314:1057. (5 April.)
3 One lamb, much fuss [editorial]. *Lancet* 1997;349:661.
4 Durman P. Biotech's potent investment formula. *Times* 1997 April 3:31.

Public should know of efficacy of early hospital treatment of paracetamol overdose

EDITOR—In response to our editorial on paracetamol overdose[1] Simon J Taylor argues that raising public awareness of drug toxicity will increase the number of deliberate paracetamol overdoses.[2] We are not aware of any published research showing the impact of public education on preventing overdose. To our knowledge, none has focused on people who considered paracetamol for overdose but decided against this on the basis of prior knowledge of toxicity.

We agree that prior knowledge of potential death does not seem to deter people because overdoses are mainly taken on impulse. Consequently, many people reverse their wish to harm themselves soon after taking an overdose. Increasing public safety information should make attendants as well as those who overdose aware of the efficacy of early hospital treatment, especially with the antidote acetylcysteine. We believe that respect for autonomy includes making public all options. Such campaigns should be monitored to study their impact as a deterrent or encouragement, whether for paracetamol in overdose, alcohol, smoking, or use of recreational drugs.

Quentin Spender finds it extraordinary that our editorial did not mention the possible benefits of including the antidote methionine in all available preparations of paracetamol. We omitted to mention methionine on grounds of brevity. The costs of using methionine would probably be considerable, especially as any antidote would have to be included in all proprietary preparations containing paracetamol. In addition, the efficacy of methionine has not been tested in field studies.

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1 Fagan E, Wannan G. Reducing paracetamol overdoses. *BMJ* 1996;313:1417-8. (7 December.)
2 Taylor SJ. Reducing paracetamol overdoses. *BMJ* 1997; 314:750-1. (8 March.)

Balance in long term follow up between secondary and primary care is necessary

EDITOR—Alan Rodger described the considerable gains to patients with breast cancer who are followed up in specialist hospital clinics.[1] He observed the educational importance to himself and his juniors of acquiring experience especially in identifying long term morbidity, which led to developments in treatment.

The debate about the long term follow up of diabetic patients has a similar ring to it. Increasingly, general practitioners—often rightly—wish to take over the long term care of their patients, and I have long supported the principles of shared care, especially with help from a diabetes resource team now established in south London. Yet, increasingly, purchasers press for the discharge of patients to primary care, and Lambeth, Southwark and Lewisham Health Authority currently requires the number of outpatients to be reduced by a further fifth.

If this trend continues, experience will be denied to consultants and their trainees. Long term observations, which lead to improved understanding and eventually better treatment, would become progressively less viable. The existing system of hospital follow up has enabled us to describe the outcome of specific and uncommon complications of diabetes over more than a decade—painful neuropathy,[2] truncal radiculopathy,[3] femoral neuropathy,[4] and symptomatic autonomic neuropathy.[5] These observations could never have been made if most patients were discharged to primary care only to reappear when new problems arose. Studies of this kind abound in the British literature but are lacking in other health care systems such as that in the United States, where such long term follow up is almost impossible.

Balance in the long term follow up of patients between secondary and primary care is necessary, and during recent years liaison has vastly improved. But the balance should remain, and managers should not dictate changes that could ultimately damage patients' health by denying specialist teams the education that they acquire from long term follow up and observation.

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