Vitamin K and childhood cancer

EDITOR,—The recent publication of another study on the possible relation between vitamin K and childhood cancer,¹ commented on by Minerva,² raises several questions. In this nested case-control study of the collaborative perinatal project's cohort of 54 795 children born at 12 centres in the United States during 1959-66 no association between vitamin K and childhood cancer was found. In contrast to the study of Golding *et al*, in which exposure was sometimes inferred from beliefs about policy,³ the collaborative perinatal project's study always had documentation of exposure to vitamin K in the notes: 68% of the 48 children with cancer and 71% of the 226 controls received vitamin K. For children who received intramuscular vitamin K the estimated relative risk of childhood cancer by age 7 or 8 was 0.84; the small number of cases in this study, however, resulted in wide 95% confidence intervals, the upper limit being 1.7.

The collaborative perinatal project's study, together with that of Tulchinsky *et al*,⁴ raises questions concerning the universality of prophylaxis with vitamin K in the United States, which Miller⁵ assumed when commenting on the study of Golding *et al*.³ In the collaborative perinatal project's study the proportion of children receiving vitamin K rose from 56% to 86% between 1959-60 and 1965-6.³ Tulchinsky *et al* found that, although universal prophylaxis with vitamin K had been recommended in the United States since 1961, until 1987 it was mandatory in only five states; in New York State as recently as 1987 there was no official policy of giving vitamin K.⁴ Hence vitamin K was not given universally at the collaborative perinatal project's centres, and it is possible that the rate was lower elsewhere in the United States. Thus the absence of an increasing trend in the incidence of childhood leukaemia in the United States reported by Miller,⁵ although a strong argument against there being an association with vitamin K, is perhaps less conclusive evidence against such an association than he, and we, originally believed.

Ekelund *et al*¹ were also unable to verify the association between vitamin K and childhood cancer reported by Golding *et al*. While, for reasons given previously, we are not persuaded that the association is causal,⁷ Ekelund *et al*'s paper should be interpreted cautiously (as indeed it is by its authors). Ekelund *et al*, following Golding *et al*, assume that Golding *et al*'s paper shows no association between oral vitamin K and childhood cancer. But if the findings regarding intramuscular vitamin K are accepted then the results of oral vitamin K are also compatible with a positive, albeit smaller, association between such prophylaxis and childhood cancer. Since Golding *et al* compared three groups of patients—those given vitamin K intramuscularly, those given it orally, and those not given it—but for most of the analyses combined the group given it orally and the group not given it, whereas Ekelund *et al* compared only the two forms of administration of vitamin K, the relative risks quoted in the two papers are not strictly comparable. The definitions of childhood cancer also differed between the two studies (Golding *et al* used 0-14 years for most of the analyses, Ekelund *et al* used 0-17 years). Both, however, looked at the subset of children who developed cancer by age 10. Although there are large differences between the estimates of relative

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risk from these studies, the estimates all have quite large confidence intervals attached. This variation in the estimates may be attributable to differences in the studies' methods, differences in the preparations of vitamin K used, or, at least in part, statistical imprecision in the estimates. If statistical imprecision is the case a carcinogenic effect of vitamin K remains possible, though if it exists it would seem to be considerably smaller than originally suggested by Golding *et al*.

We were puzzled also by the data on cumulative prevalence (actually, we assume, incidence) of cancer in Ekelund *et al*'s study: the figure gives a rate of about 2.5 cases per 1000 by age 15 compared with a rate for most European countries of between 1.5 and 1.9 per 1000 and the previously published rate of 2.0 per 1000 for Sweden.⁸

The debate on the possible carcinogenic effects of neonatal vitamin K should be settled by current studies with large enough numbers of cases to give a narrow confidence interval for the relative risk. Exposure to vitamin K should ideally be verified from individual records; failing that, beliefs regarding policy on administration of vitamin K should be checked from a sample of records from the areas and periods to which they are said to apply.

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Caution over journal supplements

EDITOR,—Recent reports on educational programmes that promote the financial interests of pharmaceutical companies^{1,2} have called to mind the experience of one of us of writing an editorial for the *BMJ*³ about a 1991 supplement to the *American Journal of Cardiology* entitled "The hypertriglyceridaemias: risk and management."⁴ The authors of the articles in the supplement are all listed as members of the International Committee for the Evaluation of Hypertriglyceridaemia as a

Vascular Risk Factor. A foreword notes that this official sounding committee was established by the Giovanni Lorenzini Medical Foundation of Milan and Houston, which is listed as the "scientific organizing secretariat."

The articles in the supplement propose a role for lowering triglyceride concentrations in the prevention of coronary artery disease. The concluding article, on the pharmacological management of patients with hypertriglyceridaemia,⁵ devotes nearly half its space to gemfibrozil (Lopid, Parke-Davis) and other fibrates but fails to mention either the increased total mortality ($p < 0.01$) among patients receiving clofibrate⁶ or the increased non-cardiovascular mortality after treatment with gemfibrozil.⁷ The discussion of fibrates is followed by a much shorter section on the less expensive nicotinic acid, which, in secondary prevention, may reduce total mortality.⁸ The supplement does not mention Parke-Davis.

The supplement was released after conferences in Geneva and New York and was accompanied by a lengthy press kit, which also did not mention Parke-Davis. The elaborate publicity material prompted us to make further inquiries. The editor of the *American Journal of Cardiology* told us that the peer review process for supplements differs from the process used in regular issues of the journal. Members of the international committee reviewed each other's work under the supervision of guest editors, who were the co-chairs of the international committee. The editor stated that the Giovanni Lorenzini Medical Foundation had paid for the supplement. A vice president of the foundation in Houston informed us that the foundation is a tax exempt, non-profit corporation financially supported by many pharmaceutical companies. These include Parke-Davis, which she said underwrote the international committee's conferences in Geneva and New York City. Staff in Parke-Davis's marketing department said that the company had not funded the supplement.

Bero *et al* examined the increasing number of symposiums published as supplements to medical journals and identified the *American Journal of Cardiology* as the leading publisher of such supplements.¹ The article noted that the supplements' outward appearance suggests that they have the same scientific independence and quality as regular issues of the journal, when in fact they are frequently supported by pharmaceutical companies, promotional in nature, and subjected to less stringent peer review.¹ A subsequent article described Parke-Davis's use of consensus development conferences to promote gemfibrozil.² Clinicians and researchers should thus exercise caution: some supplements and conferences that seem to be supported by disinterested international bodies designed to promote scientific exchange and formulate policy could in fact be indirectly supported by pharmaceutical companies.

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Surgical castration for sex offenders

An unlikely option

EDITOR,—Almost all the legal, ethical, and clinical aspects of the request for castration made by Mr K and discussed by various experts¹ revolve around his diagnosis and, specifically, whether in addition to his sexual deviancy he suffers from a broader personality disorder.

Legally, if he does not have a personality disorder he is excluded from any provisions under the Mental Health Act (because sexual deviancy as a sole disorder is specifically excluded from the act by section 1) and so all legal questions deriving from the act become irrelevant. Within common law, if he does have a personality disorder this may mean that he is less than fully competent to consent to treatment or at least that his motives for requesting treatment should be assessed with great care. Indeed, if his reasons for asking for surgical castration are not congruent with the reasons on which a doctor would rely to recommend it then there is no match between the perceptions of the doctor and the patient. Hence there is no valid basis for saying that both agree that he should be castrated. As a result, no question of (possibly illegal) mutilating surgery should arise.

Ethically, a patient with a personality disorder may have many reasons for requesting castration that have little to do with the simple choice of treatment for a well circumscribed disorder (the usual circumstance). Hence the choice between different treatments for his disorder may be influenced by things little to do with the disorder or the treatments themselves. Again, a doctor should not respond positively to such a request in these circumstances.

Clinically, if the man has a personality disorder this both reduces the likelihood of a successful outcome of castration (in terms of avoidance of further sexual offending) and increases the likelihood of an aberrant response after castration, such as suicide (as is referred to by John Gunn).

Some people argue that all paedophilic offenders, by virtue of the psychological background to their offending, have a personality disorder. If so it could be argued that no such offender should be surgically castrated. If some paedophilic offenders can be shown otherwise to have healthy personalities then they would be likely to opt for reversible chemical castration in the first instance; only after therapeutic failure occurred would they request, and should doctors consider, surgical castration. Even then some people would argue that there are broader public policy grounds for refusing voluntary castration. As the consultant forensic psychiatrist who treated Mr K commented in a *Heart of the Matter* programme on BBC1 television on 26 September, "I want no part of any public hygiene movement."

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- 1 Alexander M, Gunn J, Cook DAG, Taylor PJ, Finch J. Should a sexual offender be allowed castration? *BMJ* 1993;307:750-3. (25 September.)

No role for Mental Health Act Commission

EDITOR,—With regard to whether a sexual offender should be allowed castration,¹ I wish to clarify the role of the Mental Health Act Commission in orchidectomy: in essence it has no role. Its job is to monitor the operation of the Mental Health Act 1983 as it relates to patients detained in hospital under the act. The act provides safeguards for various types of medical treatment for mental disorder (electroconvulsive therapy and drug treatment) proposed for detained patients, who are either unwilling or unable to give their valid consent. In addition, it provides safeguards for psychosurgery and the surgical implantation of hormones to suppress male sexual drive when these can be categorised as medical treatments for mental disorder. These safeguards apply to any patient for whom these treatments are proposed; the commission administers them.

The only time that the commission would be statutorily entitled to become involved in any proposal to perform orchidectomy would be in the unlikely event that the procedure was proposed for a patient detained under the act. Even then, such involvement would arise from the commission's general obligation to protect detained patients and not because the act contains any safeguard about this specific procedure in relation to detained patients.

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- 1 Alexander M, Gunn J, Cook DAG, Taylor PJ, Finch J. Should a sexual offender be allowed castration? *BMJ* 1993;307:790-3. (25 September.)

Boundaries between surgery and mutilation are blurred

EDITOR,—There are no contemporary medical or legal precedents in Britain for voluntary or involuntary castration as a treatment for sex offenders.¹ We wish to comment on several related issues.

Firstly, there is the fundamental issue of whether Mr K was mentally disordered when he committed his offences. His periods of imprisonment suggest strongly that he had been found not to be—in which case the role of psychiatrists, and the Mental Health Act Commission, with respect to his request for castration is restricted to determining whether his decision is informed and made of a rational and sound mind. It should also be taken into account that section 1.3 of the Mental Health Act 1983 specifies that someone is not mentally disordered only by reason of sexual deviancy and that castration is not one of the treatments governed by section 57 of the act. Thus any further involvement of psychiatrists with respect to Mr K's request for castration reminds us of the question once raised by Gunn: "Is psychiatry about to over-sell itself in the field of sex offending?"²

Secondly, the fairly clear boundaries drawn between therapeutic surgery and mutilation have been criticised by many, especially with respect to male genital mutilation in the form of circumcision of male infants and children, when the question of consent is truly rhetorical.³ It can therefore be argued that if there is the smallest possibility of a reduction in libido then castration in this instance is not mutilation and, according to existing judicial policy, the procedure itself cannot be considered to be illegal or prohibited.

Thirdly, since patients have the right to refuse consent before examination or treatment under the common law, although the law itself can be challenged in certain instances,⁴ Mr K's refusal of chemical castration is legally valid. If he does undergo castration then before the procedure, he should be required to provide a legal statement to the effect that he has voluntarily refused the

chemical treatment offered and retains full responsibility for all his actions after the procedure.

Finally, the more general question of whether sexual contact with children is more deviant than forcing people to have sexual intercourse against their will must be considered. If Mr K does undergo castration that would set not only a medical precedent for non-mentally disordered offenders with multiple convictions for rape to request castration to prevent further recidivism but also a legal precedent for them to sue doctors for wilful negligence if they were to commit rape after having been refused their request.

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A ploy to deflect the blame

EDITOR,—Although the debate over whether a sexual offender should be allowed castration raises some interesting clinical and ethical issues,¹ the facts of the particular case lead me to suspect Mr K's motivation: Mr K is bluffing. His history would suggest to me that he is devious as well as deviant, and he has no intention of going through with his request for orchidectomy. I suspect he knows that his unreasonable demand for surgery will be refused when effective chemical castration is available, and therefore he can persist in his demands, which allows him to blame the medical profession for his future inevitable offending. To transfer the impotence of the doctors to Mr K, his bluff should be called with a minimum of delay and surgery arranged. I wager that he would not go through with it. Serious negotiation about his future treatment could then proceed.

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- 1 Alexander M, Gunn J, Cook DAG, Taylor PJ, Finch J. Should a sexual offender be allowed castration? *BMJ* 1993;307:790-3. (25 September.)

Urinary tract infection in childhood

Referral inconsistent

EDITOR,—Lyda Jadresic and colleagues draw attention to differences between recommended guidelines and current practice.^{1,2} I recently circulated a questionnaire to all the general practitioners and trainees in training practices in Tynedale, Northumberland, which covers a mixed urban and rural population. I asked which children they would refer for further investigation and after what number of urinary infections they would consider referring them. I also audited the management of childhood urinary tract infection in one of the practices, in which I was a trainee.

Eight of the 13 practices in Tynedale are training practices, with a total of 36 doctors; 32 doctors