At the time of Mrs Boyes's death the existence of paradoxical pain was recognised by only a few pain specialists. Consultants such as Dr Cox would certainly not have been expected to be aware of it. The choice presented to Dr Cox was stark: either to walk away from his patient and leave her to it or to do what he did. Mr Justice Ognall told Dr Cox that his choice was "a total betrayal of his unequivocal duty as a physician." Most doctors faced with this dilemma may consider that Dr Cox did his medical duty despite the risk to himself.

Mr Justice Devlin set out the rules for doctors in *R v Adams*. "The doctor is entitled to do all that is proper to relieve pain and suffering, even if the measures he takes incidentally shorten life," but "if the acts are intended to kill, and do in fact kill, . . . it is still murder." In practical terms doctors are allowed to assist death by giving large doses of morphine or heroin. But what if heroin, normally the strongest pain killing drug available, increases pain and there is no rationale for using other drugs? Paradoxical pain induced by heroin was not known in Devlin's time. Does his dictum need to be brought up to date?

ALAN ST J DIXON

Tregisk,
Coverack, Cornwall TR12 6TQ

JACK S MORLEY

Pain Research Institute,
Liverpool L9 1AE

1 Correspondence. Euthanasia. *BMJ* 1992;305:951-2. (17 October.)

2 Morley JS, Miles JB, Wells JC, Bowsher D. Paradoxical pain. *Lancet* 1992;340:1045.

EDITOR,—The correspondence following the conviction of Dr Nigel Cox for attempted murder reflects the fact that suffering, including severe pain, is common in advanced disease, so that many doctors to some extent provide palliative care.¹ We suspect that the letters may also reflect the pain doctors feel when they are unable to help their patients.

We accept that not all patients in pain can be rendered pain free without drowsiness and that to suggest a specific combination of treatment that could serve as a universal panacea would be naive. We believe, however, that several important practical issues have not been covered.

The concept of "total pain" as proposed by Saunders is fundamental to the successful management of chronic pain,² yet the correspondents neglect the mental and social components of pain. Pain may be an expression of a need state³ and so may be at least as close to an emotion as to a sensation. Attempts to deal with it as a purely physical phenomenon are therefore likely to fail.

Even within the physical dimension, response to diamorphine and other opioids is often incomplete. Thus continuing pain does not necessarily imply an inadequate dose of opioids. We disagree with Lesley A M Willis's view that Lilian Boyes was "receiving a totally inadequate amount" of diamorphine.¹ Continuing severe pain despite up to 50 mg diamorphine an hour surely reflects pain that is not entirely responsive to opioids.

Like Will Tapsfield and Pat Amis,¹ we have found midazolam to be useful in controlling pain, although whether it treats physical aspects or mental aspects, or both, is unclear. Our aim is different from that of M Rosen,¹ who seems to suggest a technique of giving sedation until the patient develops a fatal bronchopneumonia. We would always aim to keep the patient comfortable but awake or at least easily aroused. To give more sedation than is necessary merely treats the staff's pain, and only in exceptional cases in which distress remains unrelieved after other expert advice has been sought would we consider aiming to achieve frank sedation.

When midazolam is used the intravenous route offers no advantages other than to achieve rapid

control when distress is acute and overwhelming. Although precise pharmacological data are not available, clinical evidence suggests that diamorphine and midazolam can be mixed in the same syringe and given by subcutaneous infusion with a syringe driver. This can be done with minimal supervision in the community as well as in hospital. We use an initial dose of 30 mg over 24 hours and then titrate according to response, the first reassessment being made within eight hours.

We hope that this broader view will help others to cope with severe pain and, perhaps, avoid another charge of attempted murder.

T MILLIDGE

S R KIRKHAM

Poole Hospital NHS Trust,
Poole, Dorset BH15 2JB

1 Correspondence. Euthanasia. *BMJ* 1992;305:951-2. (17 October.)

2 Saunders C. The philosophy of terminal care. In: Saunders CM, ed. *The management of terminal disease*. London: Edward Arnold, 1978:193-202.

3 Wall PD. The pain and circumstance march. Pain in relation to behaviour. *Horizons in medicine* No 3. London: Royal College of Physicians, 1991:411-6.

EDITOR,—The experience of Dr Nigel Cox¹ and the publicity surrounding it can be turned to good effect if we learn the lessons that come out of it. Though an experienced rheumatologist, Dr Cox was ignorant of the modern management of severe and intractable pain.² What this surely points to is the need for doctors of all grades, and perhaps especially consultants, to improve their therapeutic skills outside their own specialty.

Three steps toward improving pain relief and terminal care occur to me: firstly, these subjects should be emphasised more in undergraduate teaching; secondly, they should be included in a programme of mandatory refresher courses, as proposed recently by the Royal College of Physicians of Edinburgh³; and, thirdly, examples of poor terminal care should be given prominence, as in Alan Fenton's *Personal View*.⁴

I believe that in the future the reputation of our profession will hang more on how we care for those who are beyond cure than on all our brilliant successes.

DAVID SHORT

Aberdeen AB9 2PL

1 Dyer C. Rheumatologist convicted of attempted murder. *BMJ* 1992;305:731. (26 September.)

2 Correspondence. Euthanasia. *BMJ* 1992;305:951-2. (17 October.)

3 Royal College of Physicians of Edinburgh. *Continuing medical education for trained physicians*. Edinburgh: RCPE, 1992.

4 Fenton A. The ultimate failure. *BMJ* 1992;305:1027. (24 October.)

Ecstasy and dantrolene

EDITOR,—The editorial by John A Henry and, more recently, an article by Henry and colleagues of the National Poisons Information Service advocate the use of dantrolene in the acute management of patients who experience severe complications after ecstasy misuse.^{1,2} Although the precise mechanism of this toxicity is not known, it is suggested that a combination of ecstasy and the circumstances in which the drug is taken is of primary importance, with direct effects on central thermoregulatory mechanisms causing a fulminant hyperthermia and heat stroke.

Dantrolene is a peripherally acting muscle relaxant with no central effects and is presumably advised because it may reduce thermogenesis associated with muscular activity and perhaps, because it contains mannitol, which may contribute towards diuresis. If this is the case then the administration of dantrolene is ill advised since a non-depolarising neuromuscular blocking agent (for example, atracurium by infusion) would

similarly reduce muscle thermogenesis while being cheaper, easier to administer, and easier to titrate. Diuretics can be given separately after rehydration. In addition, there is no real evidence of the efficacy of dantrolene in ecstasy toxicity. Among the cases of ecstasy misuse reported in the medical literature only two patients have received dantrolene, and only one patient has survived.^{3,4} Indeed the survivor had no evidence of renal or hepatic impairment or disseminated intravascular coagulation, and unfortunately concentrations of ecstasy were not documented. Experience shows that, in severe cases, biochemical and haematological variables are often abnormal on presentation; they rapidly deteriorate, and disseminated intravascular coagulation is most frequently associated with death—therefore this patient may well have survived with supportive measures alone.⁴ The patient reported to have died of ecstasy toxicity received a small dose of dantrolene (1 mg/kg); the timing of its administration was not stated, and death followed the now well described clinical scenario.¹

Dantrolene may prove to be efficacious in ecstasy toxicity, but unless an association with the neuroleptic malignant syndrome or malignant hyperpyrexia is seriously suspected, the current proposed mechanism of toxicity provides no logical reason to administer dantrolene rather than a non-depolarising neuromuscular blocking agent.

P J BARRETT

Whiston Hospital,
Prescot,
Merseyside L35 5DR

1 Henry JA. Ecstasy and the dance of death. *BMJ* 1992;305:5-6. (4 July.)

2 Henry JA, Jeffreys KJ, Dawling S. Toxicity and deaths from 3,4-methylenedioxymethamphetamine ("ecstasy"). *Lancet* 1992;340:384-7.

3 Campkin NTA, Davies UM. Another death from ecstasy. *J R Soc Med* 1992;85:61.

4 Singarajah C, Davies NG. An overdose of ecstasy: a role for dantrolene. *Anaesthesia* 1992;47:686-7.

Confounding in epidemiological studies

EDITOR,—The clear presentation by George Davey Smith and Andrew N Phillips does not, however, provide credible support for their conclusion that "it is likely that many of the associations identified in epidemiological studies are due to confounding."¹ With a reasonable amount of scepticism and intelligence a hidden source of bias can be invoked in any epidemiological study. But empirical examples of suspected causal associations that have later been entirely attributed to a hidden confounding variable are rare. In the absence of empirical illustration of the practical importance of confounding bias it is possible to reverse their argument and say that "it is unlikely that many of the associations identified in epidemiological studies are due to confounding."

There is an omission in Smith and Phillips's paper that may explain why they were led to overemphasise the importance of confounding. Their argument does not take into consideration the magnitude of the bias that may result from unadjusted confounding. The size of the confounding effect varies with at least three factors: the strength of the relation between the confounders and outcome; the strength of the association between confounders and studied exposure; and the prevalence of the confounders in the studied population. Those elements must be taken into consideration when invoking a potential bias due to unadjusted confounding. It is unlikely that a strong confounding effect due to a factor highly related either to exposure or to disease, or frequent in the population compared to prevalence of the studied exposure, would remain undetected. It is also unlikely that a confounding bias would nullify