Clinical response to deoxycoformycin

Case No	Neoplasm	Pheno-type	Response
1	Sézary syndrome	CD4+	Partial
2	Sézary syndrome	CD4+	Partial
3	Sézary syndrome	CD4+	None
4	Sézary syndrome	CD4+	None
5	T chronic lymphocytic leukaemia	CD8+	Partial
6	T chronic lymphocytic leukaemia	CD8+	Partial
7	T chronic lymphocytic leukaemia	CD8+	None
8	T chronic lymphocytic leukaemia	CD4+, CD8+	Partial
9	T prolymphocytic leukaemia	CD8+	Partial

clinical response.³ I agree with Dr Dearden and colleagues, however, that observations on this correlation should be confirmed by further clinical studies.

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Euthanasia

SIR,—There are two sides to every debate. Ms Madeline Simms (26 September, p 772) describes how a small determined group of people changed the law with regard to the termination of pregnancy. On the other hand, Margaret White in her book *Two Million Silent Killings* describes the results of the work of that pressure group.¹

Now 19 doctors use your columns (14 November, p 1276) to announce that they have formed a medical group within the Voluntary Euthanasia Society. The skilfully worded letter, which even raises the spectre of the acquired immune deficiency syndrome, urges other doctors to join them; paradoxically, as Dr Murray Parkes wrote, "It is often those who are most afraid of dying who demand euthanasia."² Arguments put forward to legalise euthanasia do not carry conviction among practitioners caring for the dying or among moral theologians.³

Conscious that one of the signatories had a similar surname to my own, I looked up the group in the medical directory; six are not listed, eight qualified before the second world war, and, of the remaining five, three are consultants—in orthopaedics, psychiatry, and geriatric medicine—and two are general practitioners.

Dame Cicely Saunders, who has done so much to improve care of the dying in recent decades, considered that terminal care in the 1970s bore little relation to care in the 1950s.⁴ Members of the Voluntary Euthanasia Society, founded in 1935, inform us that 30% of general practitioners favour legislation, which is a considerable change from the 8% that was recorded in a study I undertook for the Guild of Catholic Doctors in 1980. In that study 313 doctors in general practice (a third of the sample) responded to a questionnaire mailed by Gallup Polls Ltd. The survey concluded that doctors who dealt with the dying were overwhelmingly opposed to a change in legislation.⁵

The moral code that forbids killing by doctors has stood the test of time; we live in an ever changing world yet changing that law would lead to

the destruction of medicine as a caring profession. The ancient Greeks were aware of the dangers of listening to the sweet song of sirens and young doctors too should take care.

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SIR,—The letter from the medical members of the Voluntary Euthanasia Society stated that nearly 40% of general practitioners "would be prepared to administer voluntary euthanasia if it were legalised." The basis for this statement was a national opinion poll carried out this year in which 35% of the general practitioners responding said that they would be prepared to "consider" a signed request from a patient with incurable, intolerable illness to "end his/her life."

Willingness to "consider" such a request by no means implies willingness to "administer" legalised voluntary active euthanasia. The outcome of consideration may be a decision to withhold or withdraw active intervention (passive euthanasia). This might be the case even when active euthanasia had been specifically requested by the patient. The use of the term "administer" (implying prescription) is unjustified.

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SIR,—The letter by Dr Mary Bliss and others failed to identify the main group of people who request (and in my opinion deserve) euthanasia.

We all know that pain can be adequately controlled by correct medication, and people suffering painfully or otherwise from cancer know that they have a limited lifespan. The people who really want to die, and I have visited four of them in the past week, are old people suffering from stroke who are hemiplegic; the bedbound or chairbound; the aphasic; the incontinent; the deaf (never the blind); and those who are so old that they have grown too weak to move or even feed themselves. True, they can be nursed in one of the many homes for the elderly now available, and they are indeed often looked after with great care and devotion, with the result that their unhappy lives are further prolonged. They are often lonely, even in the midst of company, because all their loved ones have already departed. They feel guilty that, by living so long, they are consuming the family's financial resources to no good purpose; they feel that their lives are finished; they have no further contribution to make and they await death with eager anticipation. "I wish I could go" is a phrase constantly heard; it was constantly on the lips of my own mother during the three years in which she survived my father even though she played a keen game of bridge until a month before she died. Are we to continue to deny relief to our aged and weary patients?

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SIR,—The leading article by Dr Roger Higgs (14 November, p 1221) gives the impression that the profession is filled with doubt on the subject of treatment refusal by terminally ill patients or their relatives and that doctors need to pluck up courage and to seek legal subterfuges to accede to their wishes. The article goes on to argue that this should not be so.

I would like to argue that far from needing encouragement to accede to requests for treatment refusal or "death with dignity," we need encouragement to accede to the contrary request of providing treatment to prolong life to the last minute in the face of inevitable death when this is demanded by relatives.

In hospitals all over the country when a patient is in the terminal stages of illness "death with dignity" is allowed to take place and no further steps are taken to prolong life—indeed, it may be shortened by the administration of diamorphine ostensibly to keep the patient comfortable. No intravenous infusions are put up if the patient cannot take fluids by mouth and dehydration is allowed to play its part. As a general practitioner who has worked in a geriatric department I can vouch for this from personal experience. The British attitude to death is stoical and pragmatic, and, as stated in the article, too, "patients and relatives have a trusting relationship with doctors." Death with dignity appears to be acceptable.

The same cannot be said about some of our ethnic minorities such as orthodox Jews, who form a large part of my practice. To them life is all important and its preservation has to be attempted no matter how hopeless the outlook. A geriatrician I know holds uncompromising views on death with dignity, and if a terminally ill member of this minority is admitted under his care treatment is withheld even in the face of entreaties by the relatives. Once when in desperation the relatives approached me to do something I telephoned the senior house officer and explained that for the sake of appearances she should put up an intravenous infusion on an unconscious dying patient so that the relatives could be happier, but this was refused. The following day I was admonished by the consultant. There have been similar incidents with other consultants.

It is all very well to seek legal loopholes for death with dignity for those patients and relatives who request this, although from my experience this seems hardly necessary; what is really needed is an article to warn of the rights of those opposed to it.

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Graduated compression and its relation to venous refilling time

SIR,—The paper by Miss Julia Cornwall and colleagues (31 October, p 1087) describing the effect of graduated compression appears to be a careful study but the results do not agree with long term clinical experience. These unexpected findings could be due to defects in the methods.

The photoplethysmograph has failed to live up to its early potential. In normal legs the curves obtained are similar to the ambulatory venous pressure patterns but refilling times are inversely proportional. In venous disease, however, there is little change in a short refilling time, although the ambulatory venous pressure may vary from 80 to 40 mmHg.¹ The study was based on the refilling time with the stocking in situ and a 1 cm hole cut out to accommodate the photoplethysmograph probe. We have found in extensive tests that with

such a procedure the photoplethysmograph result is not reproducible.

The refilling time was obtained by squeezing the calf while the patient was sitting. An automatic tourniquet provides more accurate emptying because squeezing does not always empty the calf veins. Also, heel lifts with the patient standing give more reproducible results.¹

Only nine patients with assumed deep venous insufficiency and 10 patients with superficial vein incompetence were studied and the separation was based on Doppler ultrasound and photoplethysmography. It is not always possible to make such a precise diagnosis based on these two methods, especially when photoplethysmography is used without an ankle cuff to control reflux in the superficial veins. Calf and thigh tourniquets are not always adequate.

Because of these defects in the methods it is surprising that such clear cut results were obtained, and the work needs to be confirmed by others. The methodological defects would explain the unlikely conclusion that one type of stocking did not improve the venous refilling time. This was the stocking used in an earlier study, when a more accurate technique showed the stocking to provide a graduated compression in most legs and a great improvement in the ambulatory venous pressure.²

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Mania induced by biochemical imbalance

SIR,—The report of manic symptoms in an elderly hypertensive man with myxoedema and taking a milk only diet presented by Drs Gabriella Zolese and Rita Henryk-Gutt (24 October, p 1026) is interesting because of the many variables implicated. The authors considered the endocrine disorder, a reducing diet, and an underlying genetic predisposition to account for the development of inappropriate behaviour, hyperactivity, insomnia, irritability, flight of ideas, and pressure of speech. An important additional factor not discussed is the change in antihypertensive medication from atenolol to nifedipine one week before the development of the psychiatric symptoms.

Calcium channel blockers in general have a stimulating effect on the brain and have been proposed as treatment for different psychiatric conditions, including affective illness,¹ panic disorder,² and schizophrenia.³ While verapamil was originally reported to be effective in acute mania,⁴ there are also reports of its mood elevating effect in depression resistant to treatment.⁵ In schizophrenics verapamil may cause heightened emotional tone and worsen hostile and uncooperative behaviour.⁶ Diltiazem, a calcium channel blocker of the benzothiazepine class, may cause akathisia.⁷ The feeling of inner restlessness and the urgency to move may cause a clinical picture reminiscent of symptoms seen in mania. In one case a state of hyperexcitability, irritability, agitation, and belligerence seen in an elderly man was attributed to nifedipine.⁸

Myxoedema has not been associated with mania,

while depression is a common symptom in hypothyroidism.⁹ "Myxoedematous madness" is a well described psychotic syndrome, but it differs from the typical manic state. In contrast, several of the symptoms described by the authors have been reported with nifedipine or other calcium channel blockers so that an argument can be made for a drug induced syndrome. Because the drug is cleared by the liver the transient hepatic impairment with raised transaminase activities may have increased serum nifedipine concentrations. Furthermore, since 92-98% of nifedipine in plasma is protein bound the patient's low energy diet (3.2 MJ/day) could have increased the free pharmacologically active fraction of the drug and contributed to the adverse effects.

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Doctors and witchdoctors: Which doctors are which?

SIR,—Dr Larry Briskman (31 October, p 1108) is probably right to observe that many doctors support the popular notion of the scientist as an unprejudiced searcher after truth who collects facts and formulates hypotheses according to Baconian induction.

In the development of this theme it is proposed that Hume's refutation of inductivism as a circular argument is compensated for by the arrival of Popper with his proposal that a theory can be scientific only if it contains within it the means for its own falsification. Doctors would be confirmed in their disinterest if they knew that objections have been similarly lodged against Popper's falsificationism.¹ In particular, most classical scientific theories have historically not been falsified by contradictory observations. A contemporary example of this is the gate control theory of pain. One of the basic tenets of the theory was that the gate was closed by large fibre activity and that the selective loss of large fibres would be accompanied by pain. When this was found not to be so the theory was merely modified on an ad hoc basis.² By Popper's criterion the theory is therefore unscientific since it cannot be falsified.

To go further and use falsificationism to support a demarcation between orthodox and alternative medicine is a gross oversimplification. To take as an example from the BMA's report on alternative medicine I will cite the board of science's view of hypnosis.³ The report elaborates in detail the methods generally accepted as scientific. These include the application of double blind placebo controlled studies and statistical analysis and are in

accordance with Popper's criterion. No evidence for the efficacy of hypnosis in the terms defined by the board is presented, but hypnosis is supported for use under medical supervision. Ironically the board was apparently unaware of work which validates hypnoanalgesia according to the stringent criteria set out.⁴ The method necessitates the deception of both subjects and some experimenters and would now be unacceptable to an ethical committee. One might therefore be forgiven for concluding that the persuasiveness of interest groups and the need to accommodate to changing perceptions of alternative medicine have influenced the board of science's attitude. As Kuhn has said, there is no standard higher than the assent of the relevant community.⁵

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SIR,—Dr Larry Briskman's analysis of which doctors are witchdoctors (31 October, p 1108) presented a lucid account of Karl Popper's principle of falsifiability, but it contained an (unsupported) assertion—that the overwhelming majority of contemporary philosophers of science remain inductivists at heart—which cannot pass unchallenged. It may be true that most scientists (including doctors) are wedded to induction, but modern philosophers of science subscribe not to the theories of either Bacon or Popper but to the paradigms of Thomas Kuhn as set out in his influential treatise, *The Structure of Scientific Revolutions*.¹

Briefly, Kuhn describes science not as a steady progression towards some ultimate objective truth but as a process of intermittent evolution—of quiescent periods characterised by the pursuit of "normal" science punctuated by major paradigm shifts when a new, superior, theory replaces an existing one. This theory or paradigm provides the framework within which the puzzle solving of normal science is undertaken, including both verification and falsification experiments. The claims of the new theory succeed simply because it can explain more phenomena than the old and because it provides a more fruitful field for further research.

Although there are many other aspects to Kuhn's theories, their main appeal is that they describe more exactly the way that science is actually carried out. One needs only to think of the development of astronomy, which has matured over thousands of years, discarding several paradigms, such as astrology, on the way, and of theories of oxygen, evolution of the species, and more recently plate tectonics. Moreover, scientists generally do not perform falsification experiments per se—even the famous Michelson-Morley experiment on the speed of light aimed to confirm rather than deny the presence of an interplanetary ether. In any case is one falsification sufficient to invalidate a theory and if not then how many?

As regards modern medicine the point is not that it is true and alternatives are false. Rather, for the moment it works better, solves more problems, and provides greater opportunities for research. But just as Newtonian gravitation is adequate to send men to the moon, although it has been