MEDICAL PRACTICE

*Contemporary Themes***Medical ethics and the potentialities of the living being**

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In a recent discussion of medical ethics in *The Times* over the problems of the law and test tube babies, Professor Ian Kennedy somewhat hesitantly suggested that the human embryo must be regarded in terms of its "potentialities"—that is, that it must be seen as a living being.¹ To many European philosophical biologists this would present no problems.² To the thinker in the existentialist stream of thought it would seem obvious that we must see biological entities as beings. But to the mind trained in the atmosphere of British science the embryo is only a "blob of cells" or even a mere conglomeration of molecules. At what moment does it become a "child"? At 14 days? At birth? It is (in this paradigm) as though something magical happens, as at midnight on the 14th day, when that which is non-living suddenly becomes living, or that which was mere "chemistry" becomes a being. But may it not have been a living being from conception?

Confounding influence of scientism

Problems here may be traced to evolutionary theory. Mechanistic darwinism is so deep and ingrained that its proponents can no longer even open up the fundamental questions. As Professor Marjorie Grene points out, we even fall into the assumption that only the non-living is real, because our paradigm is one which believes that it can explain all in terms of "molecules": conversely, all that belongs to life is not real.³ As E W F Tomlin has said, mechanism remains the orthodoxy, even though it has in fact substituted thanatology for biology: "If life is to be defined and explained," says Michael A Simon in *The Matter of Life*, "it will have to be in terms of what is not alive."⁴ The definition of life in terms of what is not alive is now influencing medical ethics at a deep level.

Some scientists seem unable to begin to see that what we need is a new ontology which allows to life its due place in the natural world: as Marjorie Grene puts it, "an account of reality in general is such that it makes sense to talk about living things at all"; and "We are so used . . . to identifying

enlightenment with the reduction of all else to 'moleculaw and atoms,' that to admit, *au fond*, the reality of living nature seems a betrayal of science itself. What is real is by definition the *non-living*."⁵

That what is real is the non-living lies like a heavy stone behind utilitarian philosophies of being, and has done since the nineteenth century. As Kierkegaard saw, many problems arise from the fundamental error which is to apply the modes and procedures of natural scientism to human nature and existence—a procedure he declared to be a "blasphemy."

It is this blasphemy which now emerges to bewilder us over problems of embryology. For in our very modes of thinking about "life" we cannot find *being*—that is, the autonomy, dynamic organisation, and potentiality of the living creature.

Attitudes to the new being

In the early weeks of 1980 *The Times* carried a discussion on abortion. Professor W H Thorpe, a distinguished biologist and also a Christian, wrote:

Sir, It seems to me that a curious mistake permeates much of your correspondence on abortion. What is of supreme value to mankind is the existence, not of ova and sperm, but of persons. The physical basis of a person can only be brought about by union of the two. In normal human beings one ovum is lost every month of adult life and millions of sperm. Once the two come together the *basis* for a human person is provided. But surely no one can argue that the foetus is more than a *potential* person.

A foetus which has barely started to be able to coordinate its sense, and certainly cannot make choices, cannot be described as a person. The miracle of person building comes gradually, not by sudden fiat; but in it parental care and love will later play a crucial role. It is surely irresponsible, if not worse, for a couple to proceed with parenthood unless they feel able and willing to provide for their offspring the loving environment needed.

I believe that the vast majority of responsible people would agree that pregnancy should be terminated if there is a clear risk of a handicapped or deficient child being born. But I would agree with Professor Glanville Williams (January 31) and with I believe most medical men, that to make *serious* damage to the health of the mother the only justification for abortion would be a disastrous step; the future infant should surely be considered as well.

Contraception, whether by physical or medical methods or simple abstinence is not murder. It is a gift and responsibility which has been bestowed upon mankind mainly in the twentieth century, and we should indeed be grateful for it.

Obviously the longer a pregnancy has lasted the more reluctant a normal woman will be to terminate it; and if the outlook for a reasonably good childhood is present she will rightly hesitate to do so. But it is the parent's ineluctable responsibility to make the choice as soon as the situation is clear. This is primarily what Christian marriage is about.⁶

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We may leave the issue of contraception aside and the question of the common wastage of ova and sperms which never meet. The moral issues of abortion and in vitro fertilisation obviously require us to attend to the question of our attitudes to the new *being* formed when a sperm fertilises an ovum.

Professor Thorpe regards the fertilised ovum as only a "physical basis" for a person and the fetus as no more than a "potential" person.

This is a strange position for a biologist, since it seems to deny all those capacities of a living creature, which I have indicated above. By Thorpe's account it is as if "life" of a "person" has yet to be breathed into the fertilised egg from outside it (from parental care and love). Yet, as we know, the primal consciousness in the fertilised cell has already in it the potentiality to become a certain physical size and shape, a certain kind of character, a certain kind of spirit (as when we speak of "the spirit of Beethoven," say), and a certain novelty, a certain creative movement towards fulfilment. Tomlin speaks of the "primary consciousness" which directs the form and development of a living creature. This dynamic organises the growth of different parts of the organism and its functions (fetuses kick, move their heads and hands, weep, and recent research suggests that they can hear and recognise their parents' voices). Professor Thorpe, however, implicitly denies all this: to him there is only a physical basis—that is, the reality of the fetus is only that of the non-living, of the assemblage of molecules; the essentially living primal consciousness and intentionality of the fetus are not real to him:

A foetus which has barely started to be able to coordinate its sense, and certainly cannot make choices, cannot be described as a person. The miracle of person building comes gradually, not by sudden fiat; but in it parental care and love will later play a crucial role.

In this account there is no "miracle" in the first conception: the miracle somehow comes later, as if the potentialities were not there in the beginning. We may agree that parental care and love are fundamental to the process of full human development, and that growth of such a full adult is a miracle. But wasn't the first mystery in the creation of a new being directed by its "primary consciousness"? Must we not realise that the potentialities for a new *being* are there "biologically" from the moment of conception? If they are, then if we experiment with a fetus we may be destroying a potential being, and the implicit and indirect effects on all our attitudes to life will be seriously affected.

The question of abortion

In abortion the first moral question is whether a setting in which love and care seem doubtful or unpropitious is good enough reason for destroying the potentialities of a life that is striving to come into being. Of course a person does not develop by a "sudden fiat": but the fertilisation of the ovum has been a sudden fiat. A completely new situation has appeared, in which a living being has been begun and exhibits a primal consciousness which is governing its behaviour from the moment of conception. (That there is natural loss does not solve the problem, since what we are discussing are deliberate human acts.)

The fetus may not make "choices" but it responds to noises, even the mother's moods, and moves into comfortable positions very early on: it is already progressing through complex stages of becoming. It may not be possible to describe "it" as a person, but it is not merely a "physical basis": it is a living creature of promise. If we were able to find intentionality in our biology we should be able to see that it displayed this propensity towards a future coming into being. In this we need to consider very carefully the dimension of time and the uniqueness of being in time.

The way in which we behave towards such a being will indicate the degree to which we are capable of developing a whole adequate sense of man's relationship with the natural world. This is more important than our attitudes to, say, the extinction and preservation of species, the preservation of the atmosphere, the avoidance of nuclear pollution, the control of war, and the contest against disease: of course, the need for us to find a new understanding of man's relationship with nature underlies all these. But it underlies especially our attitude to our own fetuses. And everything about this issue affects what we think of ourselves: all our moral attitudes.

We shall never be able to solve these problems if we cannot form an adequate attitude to the unborn fetus, to "life." Professor Thorpe's view seems seriously overmechanistic and so inadequate. Of course "the future infant should surely be considered as well." But even with children who look as if they are likely to be "handicapped or deficient," is destruction an acceptable solution?

Another reader replied thus in *The Times* exchange:

Professor W H Thorpe evidently has very little use for handicapped persons even if they are absolutely sane; he suggests that the "vast majority of people"

would approve of any abortion in which there was a possibility that the child would be handicapped. I wonder if he has consulted with any handicapped men, women or children, or those who care for them, and asked them whether they regard their lives as useless?

More worrying still is his assertion that "A foetus which has barely started to be able to coordinate its senses and certainly cannot make choices cannot be described as a person." What, therefore, can be Professor Thorpe's opinion of *mentally* handicapped persons—children and adults? Are they non-persons in his vocabulary? Wasn't this the thinking behind Hitler's extermination of the insane?

I leave aside the kind of argument represented by Professor Thorpe's phrase "vast majority of people": the delicate question of the legality of abortion cannot be left to "vast" majorities. It requires extremely careful moral consideration: something certainly more subtle and responsible than the political horse trading which accompanied David Steel's Bill, over which, as Mr Leo Abse, MP, has disclosed, there was a good deal of compromise—leading to the present situation in which, whatever the intentions of the "vast majority" in parliament, we have virtually abortion on demand.

As we know, legislation has meant that some women are having abortions not for any grave reasons of health of the mother or child, or any diagnosis of handicap—or, indeed, any forecast of a loveless upbringing—but because the bringing of this life into the world is inconvenient to them. This is a bodily parallel, surely, to the pollution of the natural world, a radical failure of man's relationship with nature.² The acceleration of technology, as with surrogate motherhood, is deepening the mechanistic model in its hold on our minds while outstripping our thinking about our real nature as beings.

Relevance of "uniqueness"

Another letter, by Professor R J Berry, which appeared on the same day in *The Times*, showed further the failure of the scientific mind to find "life":

Sir, Your correspondence on abortion has repeatedly referred to every fertilized egg as unique. This is probably true, but it is a poor argument against abortion, since there is no moral value in uniqueness *per se*.

The sense in which a fertilized egg is unique is entirely a combinatorial one of re-assorted chemical molecules. Moreover, both the sperm and the egg which fuse are unique in exactly the same sense, and no one worries about the millions of sperm and eggs which never achieve any further development.

Even worse, a cancer cell usually results from a mutation in a cell of a unique individual, and is therefore also unique, but such a cell is never a cause for ethical concern.

The present confusion is probably a hangover from the days when a fertilized egg was believed to contain the adult in miniature. (It is not all that long ago when the sperm was thought to contribute all the *form* of the next generation; the female merely nourished the all-important homunculus provided by the male.)

This is now known to be incorrect: almost any cell of an individual has the genetical potential to function as a fertilized egg, and this potential has been experimentally realized in experiments with amphibia in which the nucleus of an adult cell has functioned as an egg nucleus. The egg is merely a cell which is "switched on" for development.

The essence of the Christian (as opposed to the medical or sociological) argument against abortion is that every person is an immortal soul. It is false extrapolation to assume that the "life" from God which transforms a biological being into a spiritual one is automatically given to every fertilized egg. Such an assumption is far too all-embracing and denies the sovereignty of God, who is the giver of life.

The Church of England agnosticism as to when (and, by implication, if) a foetus acquires immortality is much better. After all, every petunia or tapeworm has perfectly good biological life, and is almost certainly generically unique. Bad biology will not make good ethics.³

Here, it seems to me, if we begin at the end of this letter, we are able to see how totally irrelevant Christianity and religious beliefs seem to have become to the essential problem. According to such beliefs as are expressed here, God may or may not give every biological being an immortal soul. So all we have to do presumably is to give a dog a bad name and hang him: with Professor Thorpe a human fetus is not a "person" until . . . until when?—presumably until the moment we decide that it is too late to perform an abortion: mechanical time provides the basis for a definition. With Professor Berry we might declare that a fetus with spina bifida is not one of those to which God has allocated a soul.

"Immortality" as a relevant concept may be dismissed: we shall not get very far if we decide the issue of abortion on whether the fetus's soul will be met in heaven.

But what about "uniqueness"? This seems about as much of a gesture as the mechanistic scientist can grant to the demand that he should recognise the special *category of life*: there is just the possibility that the molecules in the "physical basis" may be twisted in a way which is unlike every other cell. There is no moral value in that kind of mechanistic, mathematical uniqueness.

But there is if we recognise the existential uniqueness of a living being. To

Professor Berry the use of "unique" in physical terms means "just like any other physical entity": something quite different is meant by unique in terms of the individual experience of a being (in Kierkegaard's sense—in the existentialist view). My life is unique: and my experience of self and world cannot be quantified without blasphemy (again in Kierkegaard's sense) to my living reality. This was Dickens's point in *Hard Times*, that marvellous moral fable directed against utilitarianism: statistics about the "Kalmucks of Tartary" are nothing to us when we contemplate our own suffering and joy, in our one unique experience of existence, alive.

This existential insistence that "life" and "society," that all human reality, exist only in terms of unique experiencing beings can be avoided by sticking to the scientific-darwinian model. Nature is only a self-perpetuating machine: life is only the concatenation of molecules. The problems of "life" are avoided by this mechanistic paradigm.

This is what Professor Berry is able to do, by invoking the physicochemical meaning of "unique." When a fetus is destroyed, as by being torn apart (taking 10 minutes) by the new suction process, the whole miraculous capacity for an "I," a human consciousness to experience the world, is destroyed: the whole wink of heaven to which the minute creature aspires is annihilated. This is briskly dismissed by Professor Berry, from the heart of university free medicine: "The sense in which a fertilized egg is unique is entirely a combinatorial one of re-assorted chemical molecules." This is analogous, metaphysically, to the statement, "we are only DNA making more DNA." Think of the living being—which is an awkward mystery, with its capacity to grow eyes, ears, heart, breasts, brain, toes, toenails, and future—as only "reassorted chemical molecules" and you leap a gap. The being in question could become future men and women for ever and ever, or at least till Doomsday; think of that miraculous being as only a "combinatorial one of reassorted chemical molecules"—that is, as essentially non-living entities—and you have solved all the moral problems, since moral problems belong to life, and that we cannot find. (And what, pray, are "chemical" molecules?—the term is simply introduced surely to blind us with science: wouldn't "molecules" do?)

Biology and ethics

"Bad biology will not make good ethics": that is true. But Professor Berry's is bad biology and does not deserve the term "life sciences" since he fails to find "the category of life." He even goes as far as to pervert the biological truth by adding, "both the sperm and egg which fuse are unique in *exactly* the same sense" (my italics). If we consider even a simple protozoon, perhaps a hundredth of an inch long, moving at 600 micrometres a minute, it exhibits *behaviour* and *autonomy*, which mechanism cannot explain. Combinatorial molecules change their forms in a mysterious way—but since Professor Berry has reduced them simply to twisted strands of atoms we may let that "coding" miracle pass and agree with his "unique." But as soon as sperm and ovum fuse there is no such chemical uniqueness here to be reduced to the merely mechanical; and it cannot be so reduced, because to do so ignores the reality of the existence of an experiencing being with that primary consciousness. What needs to be introduced here is the sense of the intrinsic worth of a living creature—a different kind of uniqueness. In this we have a uniqueness which, in all good biology, is simply not so reducible without falsifying truth. Already the new being is on to becoming Napoleon, or a professor of medicine, or some village Hampden. It moves into the womb wall and by its primal consciousness begins to unfurl the beauty of its human form; by incredibly complex processes. (And the biologist is interested in the living creature because of its intrinsic qualities.)

The parallel with a cancer cell carries very little weight: there are, I believe, very occasionally cancerous fetuses. With such pathological biological entities there can be no doubt: it is true that with them there is no ethical problem as there is with a fertilised human egg. There is, no doubt, another philosophical problem, of how we regard destructive and pathological phenomena in the world: but what we are discussing are healthy potential human beings and their *trivial* destruction or mechanistic manipulation.

It used to be believed, says Professor Berry, that the sperm contained all the form of the next generation and that there was an adult in miniature in the homunculus. But these were ways of explaining what is actually true: that in the fertilised egg are the morphogenetic dynamics which will produce your unique child. It may well be that every cell of an individual could be "switched on" to become a mature adult. But why that "merely"? Is it not a great mystery (for example) that Driesch's sea urchins could repair themselves? And even more so that a minute speck can become an Einstein or crossing sweeper?

Again it is the reference to "switched on" which exhibits a scientific hubris. We have discovered some of the secrets of DNA coding, but we have by no means solved the secrets of how a living being becomes. As Francis Crick wrote in his *The Encyclopaedia of Ignorance*: "How an organism constructs a hand with its thumb and four fingers, with all the bones, the

muscle, and the nerve cells assembled and correctly connected together, that we cannot yet explain with the force and finality which characterises a successful piece of science." Professor Berry, in giving the impression that we can explain the development of a living cell into a human being, and by using his "merely" implying that it is all a matter of genetic "switching on," is exhibiting the worst biology.

Mysteries of "life"

It is true that living substances obey the laws of physics and chemistry. But they also obey other laws, and despite the brilliance of recent work in molecular biology it would seem that something is still lacking. As the late Professor Michael Polanyi pointed out, the dynamics of a living cell cannot be explained by reduction to the laws governing DNA molecules. All that would produce would be "noise"; in fact, what we have in the molecules of life is a fantastic configuration of forms and activities which require to be studied in yet another dimension. The physical-chemical forms represent the characteristic boundary conditions of the system. But the shaping of the boundaries establishes a "controlling principle," while the system is put under the control of a non-physical-chemical principle by a "profoundly informative intervention."⁸ Others who have pointed to the need to take into account the dimension of activities in living creatures have not yet, as it is often declared, found "the secret of life," for large areas of that secret are still mysterious and unfathomable. For example, the development of the individual from its beginnings is no straight path because there are climacteric changes, as at adolescence and so on, and it seems that we are far from understanding how these are coded for or how the "codes" can change for each stage. The overall controlling principle in life still escapes our knowledge.

The human individual is far from being a mere assemblage of atoms, which is how Professor Berry presents him. Some biologists like Polanyi believe that "life strives" and this is its especial quality, and that there is a "gradient" in life towards higher forms and self-consciousness. The high level of genetic possibilities in man as compared with a lower animal is a manifestation of that striving, and each individual, as it comes into being, is a fresh manifestation of the attempt by life to develop potentialities. Fascinated by structure, many biologists have in recent years forgotten activities and forms by which life is manifested. In our ethical debates the important thing is for us to have reverence for the mystery of this unfolding of potentialities and to determine how best human acts can serve it. In this, the mechanistic oversimplifications and the metaphysic that goes with all this, as manifested in Professor Berry's letter, are a serious threat, since they make it seem that all we are is molecules blindly running in a universe left to mere chance and necessity and that therefore our life is futile and without meaning. Yet the mere emergence of life, and especially of mind, are mysteries which we cannot explain and which seem to suggest that they could not have come into existence simply by the collision of matter. Debate here, however, has hardly begun, even as sensitive issues like abortion are crudely politicised embryo technology advances into disturbing areas and outstrips our philosophical capacities to deal with it.

Debate continues

The issue surfaced again in *The Times* in April of this year. Writing about embryo research, Sir Andrew Huxley, president of the Royal Society, tells us that the early embryo is a mass of cells nearly all of which are destined, during normal development, to form parts of the afterbirth.⁹ Sir Andrew seems to be saying that at a certain moment in the original growth of a human being there is nothing but a collection of cells. Then, at a certain point, there is a different situation and this entity becomes a human being. In the "mass of cells," according to him, "a potential human being has not even begun to take form." But this surely is either playing with words or implies a kind of magic, by which what seems merely primary life is suddenly transformed into a human being? Surely the process must be continuous and the overall control and development must be inherent in the original "mass"?

In a biological textbook we are told that "this process involves a complex sequence of relative cell movements whereby the cells of the blastula rearrange themselves, eventually resulting in the transformation of the blastula into the intricate folded form of the early embryo, or gastrula, which consists of three basic germ cell layers: the ectoderm, which gives rise to the skin and nervous system; the mesoderm, which gives rise to muscle and skeletal tissue; and the endoderm, which gives rise to the lining of the gut with its associated glands. . . ." To a layman these marvellous processes seem as though they must be governed by some overall design, a "primary consciousness" as Tomlin calls it—otherwise how could that mass of cells become a president of the Royal Society? The potentiality must be there from the beginning, from conception. The "cells" "*know*," whatever that may mean, what they are to become, and become it according to plan and

impulse, which are there in the beginning, even if we do not know how and where. The dynamic of the "information content" in living things is not and cannot be explained by physics and chemistry, since if physics and chemistry were all there were to it all we should have is "noise": some overall principle guides and controls, and this we do not yet have the disciplines to apprehend; and yet by logical fallacies we suppose that we have explained "life" by mechanistic analysis.

Conclusion

I have written this article as a non-believer: I am not invoking any religious beliefs. I am simply aware, as a literary man who has read a little science and philosophy, that there is a need to find a mode of thinking that can understand and find "the category of life" and the special dimension of being in time of which the existentialists are aware. This must surely be acknowledged by those who argue that the central issue is that of childless couples: one understands their grief and dismay, but it will not do to argue that all those whose destiny is grim have the "right" to put their circumstances right even at the expense of other lives and at the expense of moral principles. We are "in" our conditions, and we must recognise that not all can be overcome: we cannot stop growing old and dying, for instance. (I was amazed to hear Lady Warnock, discussing surrogate motherhood, say that she would find the *in vitro* fertilisation and parturition of infants less worrying than surrogate motherhood because money was implicated in the latter. In both there is a dangerous denial of the realities of parturition and *being*.)

Since there are so many mysteries that we do not yet understand (like the extension of the mother's personality to provide *psychic*

parturition for the infant long before birth—to which the great paediatrician D W Winnicott gave the name "primary maternal preoccupation") it is important to provide protection for the natural processes by which a human being comes into this world, against the Faustian ambitions of some of mechanistic science and of technology which has outstripped ethics and is reckless with its own ignorance. We may only be able to glimpse some of the philosophical fallacies—but they ought to be enough to warn us that in this realm we could cause the kind of disaster we have caused in the past, from soil erosion to dangerous forms of radioactivity, by our manipulation of life without fully understanding its special properties. And the intuitive support given to Bills like that of Mr Enoch Powell shows that people recognise this, by a kind of common sense.

References

- 1 Kennedy I. *The Times* 1984 May 26:6 (col 1).
- 2 Grene M. *Approaches to a philosophical biology*. New York: Basic Books, 1968.
- 3 Grene M. *The knower and the known*. London: Faber and Faber, 1966:185.
- 4 Tomlin EWF. The concept of life. *Heythrop Journal* 1977;18:No 3.
- 5 Simon MA. *The matter of life* (1971). Quoted by Tomlin.⁴
- 6 Thorpe WH. *The Times* 1980 Feb 7 (col 5).
- 7 Berry RJ. *The Times* 1980 Feb 6:15 (col 6).
- 8 Polanyi M. *Chemical and Engineering News* 1967;45:54-66.
- 9 Huxley A. *The Times* 1985 April 6:9 (col 4).

Further reading

- Holbrook D. *Education and philosophical anthropology*. London and Cranbury: Associated Universities Presses (in press).
- Holbrook D. *Evolution and the humanities*. Aldershot: Gower (in press).

What is the optimum dose of aspirin for use as an antiplatelet agent? Does dipyridamole add to its antiplatelet effect and if so what is the optimum dosage for it?

The optimal dose of aspirin for use as an antiplatelet agent has not yet been clearly defined and it may to some extent depend on the clinical condition. Aspirin acetylates and thereby inactivates the enzyme cyclo-oxygenase. In platelets cyclo-oxygenase is responsible for the synthesis of thromboxane A_2 , which induces platelet aggregation and vasoconstriction, but in vascular endothelium it is responsible for the synthesis of prostacyclin, which inhibits platelet aggregation and produces vasodilatation. The antithrombotic effect of aspirin is thought to be due to its effect on platelet thromboxane A_2 synthesis, and there has been concern that this might be offset by its effect on vascular prostacyclin synthesis. The concept of an optimal dose of aspirin is based on the premise that endothelial prostacyclin synthesis is less susceptible to aspirin inhibition than is the synthesis of platelet thromboxane A_2 . In theory the optimal dose of aspirin would be that which inhibits thromboxane A_2 synthesis but has minimal effects on prostacyclin synthesis. A single dose of 325 mg of aspirin almost completely inhibits platelet thromboxane A_2 synthesis but also significantly reduces the formation of prostacyclin. Single doses of less than 100 mg also largely inhibit thromboxane A_2 synthesis but appear to have less effect on prostacyclin synthesis.¹

The clinical importance of these theoretical considerations is uncertain. Most clinical trials have used doses greater than 325 mg daily and some have shown benefit. It is not known whether greater benefit would have been shown if smaller doses had been used. One hundred milligrams of aspirin daily increases the patency rate after coronary artery bypass surgery,³ but it is not known whether this dose is effective in other conditions. Recently, it has been suggested that an increase in platelet sensitivity to prostacyclin may be an additional and important property of aspirin; and this may be shown after several weeks' treatment with as little as 1 mg of aspirin daily. These authors suggest that the optimal daily dose of aspirin for prolonged antithrombotic treatment may lie between 1 mg and 25 mg.² There are other good reasons for attempting to define a minimum effective dose. Large doses of aspirin are associated with a 10-20% incidence of side effects, and the use of perioperative aspirin increases the risk of bleeding. Nevertheless, general recommendation of doses of 100 mg daily or less must await the results of further clinical trials. For the time being it seems reasonable not to exceed 325 mg daily.

The antiaggregatory effect of prostacyclin on platelets is due to the production of cyclic-AMP. Dipyridamole potentiates this effect by inhibiting platelet phosphodiesterase, thus preventing breakdown of cyclic-AMP.

Dipyridamole and small doses of aspirin have additive effects on platelet function⁴ but, as the effect of dipyridamole depends on the presence of prostacyclin, it might be prevented by high doses of aspirin. The optimal dose of dipyridamole has not been defined but 50-75 mg three times daily in combination with low doses of aspirin may be sufficient to provide a maximal additive effect on platelet function.⁴ This sort of dose has been used in the few clinical trials showing benefit from the combination.—LINDA BEELEY, consultant clinical pharmacologist, Birmingham.

- 1 Weksler BB, Pett SB, Alonso D, *et al*. Differential inhibition by aspirin of vascular and platelet prostaglandin synthesis in atherosclerotic patients. *N Engl J Med* 1983;308:800-5.
- 2 Sinzinger H, O'Grady J, Fitscha P, Kaliman J. Extremely-low-dose aspirin (one milligram per day) renders human platelets more sensitive to antiaggregation prostaglandins. *N Engl J Med* 1984;311:1052.
- 3 Meister W, Schacky CV, Weber M, *et al*. Low dose acetylsalicylic acid (100 mg/day) after aortocoronary bypass surgery: a placebo-controlled trial. *Br J Clin Pharmacol* 1984;17:703-11.
- 4 Rajah SM, Penny AF, Crow MJ, Pepper MD, Watson DA. The interaction of varying doses of dipyridamole and acetylsalicylic acid on the inhibition of platelet functions and their effect on bleeding time. *Br J Clin Pharmacol* 1979;8:483-9.

Acidosis is thought to be the cause of abdominal pain in diabetic ketoacidosis. I have had two patients whose pain quickly responded to intravenous bicarbonate. Might abdominal pain with acidosis be another indication for bicarbonate?

I do not agree that acidosis is the main cause of abdominal pain in diabetic ketoacidosis. Using himself as the experimental subject, Haldane induced acidosis by taking ammonium chloride¹ on one occasion and calcium chloride² on another, and abdominal pain did not feature among the resulting symptoms. Similarly abdominal pain is not characteristic of even severe renal acidosis. On the other hand, abdominal pain is found with ketoacidosis due either to diabetes or to cyclical vomiting in children. The administration of intravenous sodium bicarbonate to patients with diabetic ketoacidosis also lowers resistance to insulin³ by reducing the acidosis, and so any improvement in abdominal pain may be largely attributable to improved insulin action. Doctors should be cautious in using sodium bicarbonate to treat diabetic ketoacidosis, since it tends to increase urinary losses of potassium and provides a stable alkali to neutralise metabolisable and therefore transient ketoacids.—J M STOWERS, professor of diabetes and endocrinology, Aberdeen.

- 1 Haldane JBS. Experiments on the regulation of the blood's alkalinity II. *J Physiol* 1921;55:265-75.
- 2 Haldane JBS, Hill R, Luck JM. Calcium chloride acidosis. *J Physiol* 1923;4:57:301-30.
- 3 Mackler B, Lichtenstein H, Guest GM. Effects of ammonium chloride acidosis on the action of insulin in dogs. *Am J Physiol* 1951;166:191-8.