

Medical experiments on human beings

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Author's abstract

Throughout the scientific age it has been increasingly realised that the path to knowledge is through carefully-controlled experimentation. Medicine must never, however, treat human beings as objects, or as the means to achieving increased knowledge.

Ultimately the goal of human evolution will be served by the willing collaboration of members of society in the advancement of knowledge through carefully planned experimentation. As of now, however, many safeguards must be built into the system to ensure that no exploitation occurs. Experimenters are charged with the task of designing the most ingenious experiments, to give maximum information with a minimum of trauma and always to ensure the fully informed consent of the participants. This paper was read to a conference on human rights in relation to forensic science organised by Centro Internazionale di Ricerca e Studi Penale e Penitanzari, in cooperation with UNESCO, held in Messina, Italy, in March 1980.

Ever since I began my medical studies – more years ago than I care to remember – and throughout my career as a physician, experimental researcher and university teacher, I have been convinced that medicine is or ought to be the most humane and most humanistic of all the professions. We are given the privilege of studying our fellow human beings at all stages of life, in all conditions of health and disease (physical, psychological and spiritual) and to see them safely home (at whatever age it may come) on that journey we are all making, the journey towards death. Medicine ought to be, I said, the most humane of all the professions. It very often is. After listening to Dame Cicely Saunders, Medical Director of St Christopher's Hospital, London, in a previous session, my faith in the good practice of the art and science of medicine was fully reactivated. One needs such demonstrations from time to time, because it is sadly true that much of current medical practice is less than humane, and at times borders on the inhumane. The 'organised' medical profession, as represented by its local and national official bodies, seems often unaware of, or uncaring about, the sometimes flagrant breaches of ethics or the law that may be perpetrated by its members. Years ago I observed, in print, (1) that organised medicine

represents the most powerful trade union in the world. Like all trade unions, its principal concern appears very often to be the economic well-being of its members and the maintenance or improvement of what it conceives to be the appropriate social status of the profession. There are many signs that this policy, pursued over many decades, has now become or is becoming counterproductive. The profession has good reason to feel fearful for its future.

If medicine is, or ought to be, the most humane of the professions, the law is the most important, the most fundamental, one for society. The law is concerned to establish and maintain the principles of justice, without which a good society cannot function. Society can function without medicine but not without law. And yet there are many 'crooked' lawyers, and again the Bar Associations and other official legal bodies often fail to censure them. The law is the final embodiment of society's mores; medicine is the servant of society as it develops and modifies its mores in the course of evolutionary change. Transdisciplinary studies between not only practitioners of medicine and law but between those two specialities and all the rest of society are essential if societal unrest is to be avoided. 'Transdisciplinary' vs. 'interdisciplinary,' represents to me Clark Kerr's distinction between 'university' and 'multiversity'. (2)

I am very much disturbed by the wave of legalism and bureaucratic controls which, developing especially in the last decade, now threatens to engulf medical science and to prevent its further advance. I recognise the current need for legislation on abuses, but I deplore its necessity. If the wave of criticism forces the medical profession to re-evaluate its positions and attitudes towards human rights, human freedom, human values, then all may not be lost, and we may at some time in the future experience the full flowering of the art and science of medicine dedicated to the well-being of individual persons and to that collective personality that represents society.

In this talk I will speak only of 'ordinary' patients, in highly developed countries, as subjects of experimental procedures. I will not concern myself with the special needs and special rights (which are greater than those of ordinary patients) of the underprivileged such as prisoners and the very poor, especially in the developing countries.

My friend, Dr Bankowski, Executive Secretary, Council for International Organisations of Medical Sciences (CIOMS), Geneva, will speak especially about the latter.

The importance of medical experimentation on human subjects for the advance of knowledge, learning and understanding, is beyond dispute. The technological advances that have been made since the dawn of the scientific era in the 17th century have been truly remarkable. It is true that medicine *as science* has been pursued with great vigour only during the last half century, and it is true that there has been acceleration in the number of soundly based advances (and some not so soundly based) for only a little over a quarter century. It may well be that we have already passed the zenith. It may be that future advances will be hard to make and very slow to be realised. I doubt if Edward Jenner would have had the temerity to carry out his first experimental vaccination (especially on a child) if the climate of opinion had been as it is today. He surely would not have had the patience to battle the bureaucracy of Institutional Review Boards and Granting Agencies, Human Subject Protection Committees, and all the rest. The criticism evoked by his *successful* demonstration of the efficacy of vaccination guarantees that a research *proposal* would have been rejected. And yet Jenner had observed and properly understood that local milkmaids who had contracted cowpox were immune to the ravages of smallpox; he dared deliberately to give that mild disease – the cowpox – to a healthy youngster as a protection against the much more serious smallpox; as a result of his insight the year 1979 saw the astonishing success of the campaign of WHO to eradicate smallpox from the entire human community – forever, unless a viral mutagen turns up again.

I seriously doubt if, with regulations as thick and dense as they currently are in the advanced countries, we shall ever get such a breakthrough again. I doubt if we shall see developed any extension of the current range of highly-successful vaccines against a host of diseases. Think of the fiasco of the swine flu vaccine in America during President Ford's incumbency. It was only because of the political 'hoo-ha', and the publicity that it generated, that the cases of Guillain-Barré syndrome (always a risk with *any* vaccine) came to light. Government involvement required that it pay the consequences – it has done so to the tune of many millions of dollars in compensation to real and imagined victims of Guillain-Barré disease. The *Government* didn't pay, of course; the American taxpayer paid. In future circumstances (and who can doubt that now that a precedent is set all future instances of Guillain-Barré syndrome will be pursued with vigour by that cadre of lawyers the ranks of which are swelling every year in the US!) it will be the pharmaceutical company that has to pay up, at

highly inflated rates, for what is often a very mild disturbance of physical well-being. What company will risk the marketing of a new vaccine no matter how good the research and clinical trials have proved it to be?

The same is true with new drugs, which represent much the largest component in the field of experimental medicine. The use of diethylstilbestrol for prevention of abortion or threatened miscarriage, is a case in point. In the 1940s it was confidently regarded as being entirely safe. True, by the late 50s it was realised that there were health problems associated with it. But it was not until the 1970s that increased vaginal and cervical cancer came to light in the daughters of women who had had the drug during the embryogenesis of their offspring. Serious defects in the genitourinary tracts of males are now being observed some 20–30 years after exposure to the drug. Now normally, in order to bring a successful prosecution, one has to identify the specific product and its manufacturer. Thirty years ago there were some forty firms distributing DES in the US. In early March the California Supreme Court gave permission to two women victims, who could not specify the particular brand that their mothers had taken, to bring an action against all forty companies. If damages are awarded the companies will be required to contribute in proportion to their share of the market at the relevant time.

It may be that we *are* a drug-obsessed community. It may be that there are too many firms making too many drugs with potential for harm to the patient. Maybe their activities should be curtailed for the common good. Whether the profits they make are good or bad for society I leave to the economists and politicians to judge in the full knowledge that there will be deep differences of opinion.

Let us look at a few more recent and currently relevant problems:

KIDNEY TRANSPLANTATION

This initially was a highly experimental procedure with a very low success rate. Renée Fox has written perceptively about the early days in her book *Experiment Perilous*. (3) More recently she has written (with Judith Swazey) under the title *The Courage to Fail*. (4) Whose courage? Not primarily the physicians', nurses', social and psychiatric workers'. Rather it is the courage of the patients and their families that is most striking. The battle over kidney transplants is not over – Dr Robert Sells, Secretary of the British Transplantation Society, tells me that current success-rates for cadaveric kidney transplants vary from 80 per cent down to 20 per cent depending on a number of variables. Each case is still 'experimental' of course; in strict analysis, *any* therapeutic intervention for *any* patient is theoretically experimental. Haemodialysis

for kidney disease is much safer, at least in the short run – but emotional, psychiatric and organic disturbances are beginning to turn up in increasing numbers with chronic dialysis patients. And the US Government paid out more than two billion dollars last year to support the dialysis programme it started to fund less than a decade ago.

HEART TRANSPLANTATION

Today, we regard this procedure as even more 'experimental' than it was ten years ago. Very few centres (Stanford, Paris) are performing these operations with any measure of success. One recalls the media-blitz that followed Christiaan Barnard's first human heart transplant. I personally will never forget the horror I felt when I saw the smiling face of Mr Washkansky on my TV set in England a few days after his 'successful' operation. He was sitting up in bed cracking a boiled egg and joking with the nurses. It was a miracle, he said. And yet, to anyone with biological knowledge there were only two courses ahead of him at that time and both involved an early death: either his immunological system was not properly suppressed, in which case his new heart would soon be rejected. Or his immunological system *was* suppressed, and he was prey to all the attendant germs of the nurses and doctors and camera crew and everyone else who crowded round him for publicity purposes. Was it ignorance or self-aggrandisement that led Dr Barnard to do what he did? But what *he* did was nothing to what was done immediately by doctors in virtually every country in which technical facilities existed for the relatively simple surgery involved. It was scandalous, and showed up a lack of mature thinking, and of ethical concern, by many members of the world-wide medical community.

BONE-MARROW TRANSPLANTATION

Today it is the turn of bone-marrow transplants – but we have grown wiser and more mature even if only at the behest of government funding agencies and the incredible bureaucratisation that that involves. There are only five centres in the US that are 'licensed' to carry out BMT, and records of the regimens employed (all experimental) have to be rigorously kept. Survival rates for aplastic anaemia have moved from 10 per cent to about 70 per cent. That is great for a disease which previously was uniformly fatal. For myelogenous leukaemia success rates, which were looking good some 3–4 years ago, now appear not much better than the rates for spontaneous remission. Death after BMT does not come easy: 'the sickest patients I've ever seen' was how a resident described them during two panel discussions we held (and recorded on videotape) at UCLA. Panelists included a paediatrician and an oncologist, both actively engaged in the programme; a senior haematologist to take a more objective view; a psychiatrist who

had donated blood platelets to his sister after another histocompatible sister had donated marrow; a distinguished moral philosopher; and a renowned medical sociologist. These were just two of a series of more than 60 recorded panel discussions we have held at my institution under the title 'Medicine and Society Forum.' I hope, in the discussion on the teaching of human rights in medical schools, to give you more information about this series of in-depth discussions of complex ethical and legal problems in medicine. The meetings are open to all members of the university and to the general public. Some of the best contributions have come from the audience, including an impassioned plea from a victim of leukaemia to be given the option of transplantation before his disease became unresponsive to chemotherapy. With a prognosis of twelve months before he would reach that state his wish was granted – and he was dead in two months.

How does one get informed consent to a procedure which may help but which may prove worse than the disease? It is not enough for a doctor to give a simplified clinical description. Patients and families need to talk to experienced nurses, social workers, psychiatric counsellors and to the families of other patients. All too often the doctor, unduly proud of his own image, takes all the responsibility for informing – and *fails* to inform fully. The consent then is invalid. But patients will often clutch at a merest wisp of a straw (especially when they are young) and they often show an almost unbelievable degree of the 'courage to fail'.

We have discussed other clinical/ethical problems in our Medicine and Society Forum, such as a double-blind study to test the effectiveness of the powerful cytotoxic drug chlorambucil for the chronic and usually fatal connective tissue disease known as *scleroderma*. The drug was tested against placebo. If the patient group had been large enough to give statistically significant results a third subgroup might have been formed. These might have been given (unknown of course to the medical team as well as to the patient) a normal anti-inflammatory drug such as aspirin or phenylbutazone. The ethics of patient choice to enter the study, and the ethics of sound guarantees that the code would be broken or the regimen changed if there was clear deterioration, are profound indeed. The physician's responsibility is to patient care *and* to scientific enquiry if *and only if* this does not compromise patient care. Conflict of interest clearly abounds in such situations.

An experimental procedure which worries me right now is one that is becoming so common that it might be thought to be routine. I refer to the use of ultrasound as a non-invasive technique for the detection by echo of abnormalities within the interior of the body. It is especially valuable for

diagnosis of fetal abnormalities, and is regarded as so safe that it is done routinely (and very effectively) prior to amniocentesis. Now it is true that this is non-ionising radiation. But it involves at least some heat-dispersion at the organic interfaces from which the echos bounce back. Scientific reports of damage to cells in tissue-culture when exposed to ultrasound tend to be discounted because the sources used have been powerful ones, and the layer of cells is so thin in culture.

And yet we thought the same about the safety of X-rays in the early days. X-ray damage takes a while to show itself. How do we know that the delicate, growing tissues of embryos and fetuses might not suffer damage (as they clearly did with diethylstilbestrol) which will not manifest itself for many years? The clinical procedure is in full swing and growing rapidly. To my mind much more testing should be done on fetuses of other species whose natural life-span is short to see if exposure in fetuses produces sickness in the adult phase of life.

Scientific research and development in medicine followed the discovery that by the use of penicillin an actual disease could actually be cured by medication. Since then the pharmaceutical industry has had financial motivation for the production of any and all potentially effective drugs. Free market economy clearly produces conflicts of interest which may and often do produce harm for patients. After the success of the Russian sputnik, American pride led to a vast outpouring of funds through NASA and HEW for scientific research and development. It was thought that if we could put a man on the moon we could do *anything*. Little did the politicians know about the relative simplicity of the science of physics and the enormous complexity of the science of human biology. We were going to 'lick' heart disease, stroke and cancer; we are still trying, with only some modest successes.

Now a word about the reasons for society's currently increasing concern that has led to increasing legislative constraints on further scientific advance.

First is the fact that commitment to objective, quantifiable science *tends* to dehumanize practitioners to the point where they may regard the patient as an experimental creature, the researchers' so-called 'animal of necessity'.

Secondly, there is the inevitable competitiveness within the scientific community: competitiveness for grants and promotions and the ultimate goal of a Nobel Prize. While Nobel Prizes for Literature and Peace surely do no harm, I am suspicious, for instance, of those in Economics, a discipline which represents an unholy alliance between academia and politics. Prizes for Science and Medicine, though, have produced the most seriously harmful results in terms of vicious competition for advancement, not infrequently leading to secrecy, cheating

and theft. I hesitate to think what future historians will make of all this.

Thirdly, it is government funds that have largely supported biomedical science. Such funds are essentially political and subject to all the vagaries of political opinion. When a public scandal emerges, such as the Tuskegee experiments where chronic syphilitics were untreated to serve as an experimental control group, political reaction is swift and ruthless. (5, 6)

Fourthly, the Medical-Scientific-Industrial complex has not yet put its ethical house in order. There are too many conflicts of interest to permit the regular practice of a sound medical deontology.

As a result of all these four factors we now see increasing controls over, and bureaucratisation of, biomedical research. In the past, physicians have demanded the right to self-determination for all their activities, but in turn have been very paternalistic – or *parentalistic* as I prefer to say – towards their patients. Now, it is society's turn to be parentalistic, through regulation and control, towards physicians and biomedical scientists. Patients used to expect to be treated like children, and they seemed to like to be passive and dependent. Patients are always, of course, ambivalent in their feelings toward paternalistic physicians. John Owen, the 16th century writer, composed an epigram which sums it up:

God and the doctor we alike adore,
But only when in danger, not before.
The danger o'er, both are alike required:
God is forgotten, and the doctor slighted.

We are now in a phase of backlash where the older, passive role of patients is concerned. There is an increasing rejection of paternalism by our patients. Especially is this true in California, that crucible of human evolution where everything is tried until it is found wanting. The movement of patients towards self-help and 'holistic' medicine is very striking. We, in medicine, must readjust towards self-determination on the part of our patients. Some of us will find it difficult, but it must be done if we are to survive.

There is an urgent need for a thorough evaluation of professional ethics in medicine. The study must be truly transdisciplinary, because simple interdisciplinary contact between medicine and law leaves each discipline more or less where it was; more heat than light tends to be generated in interdisciplinary studies, especially when they are conducted on an adversarial basis. The medical problem is really a societal one, involving people as persons at all levels. To become again the most humane and most humanistic of the professions we must, in medicine, reawaken concern for human values – which of course include scientific values.

In 1968 I attended an international conference on human experimentation at the Château de Bossy,

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Switzerland. We drew up and published (7) suggested modifications to the Helsinki Code, some of which were incorporated into the 1975 Tokyo revision. A whole new section was added, but this was ignored in Tokyo. This section concerned the need to educate medical students and practitioners concerning human values and human rights. I am glad to see that this present conference will devote its last day to this topic. We also suggested, at Bossey, that the promulgation and implementation of guidelines concerning human experimentation would obviate the need for extensive legislation. I wish that action had been taken on that wise suggestion.

Ultimately our theme in this session requires the development of a satisfying theory of philosophical anthropology, equally acceptable to all, of whatever religious persuasion or none. For more than a hundred years the concepts of evolution in general, and of man in particular, have been seriously misinterpreted by society. We still seem to believe, as Tennyson said before Darwin, that Nature is 'red in tooth and claw'. The phrase 'survival of the fittest' has been seriously misinterpreted to mean 'survival of the strongest or the most aggressive'. The idea that evolution is random and meaningless, in light of the 19th century physical law of increasing entropy, has led to much of the nihilism and pessimism of our present age. If the 1960s represented the Decade of the Naked Ape and his Territorial Imperative, it is not surprising that the phrase 'the weakest go to the wall' represents the dominant current theory of appropriate human behaviour. Far from being human it is anti-human. It is also anti-evolutionary when we look at evolution properly.

In two recent papers (8, 9) I have tried to examine evolution properly, particularly from the point of an attempted development of an evolutionary ethic that can satisfy the deepest longings of all mankind for peace and justice and human rights. We need to see 'Teilhard's Law' which he called the law of 'increasing complexity-consciousness in evolution' (10) as the basis for development of a hopeful dynamism to replace the passive despair of much of the last half century.

It is incumbent on all academics of good will to

research, write and teach on these themes. When mankind (including physicians, scientists and lawyers) begins to act according to the golden rule of all philosophies, namely 'do unto others as you would have them do unto you,' then the need for stringent regulations governing human experimentation will become redundant; they will quietly disappear.

References

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- (2) Kerr C. *The uses of the university* (1963 Godkin Lectures, Harvard University) Harvard University Press, 1964. See especially Chap 1, The Idea of a Multiversity, which opens with 'The University started as a single community—a community of masters and students. It may even be said to have had a soul in the sense of a central animating principle. Today the large American university is, rather, a whole series of communities and activities held together by a common name, a common governing board, and related purposes. This great transformation is regretted by some, accepted by many, gloried in, as yet, by few. But it should be understood by all.'
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