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Payments to healthy volunteers—ethical problems

Volunteers for drug trials may be recruited from amongst students, undergraduate or postgraduate, the public (now often unemployed), employees of drug companies or the staff of the investigating departments. Studies may take place in academic or clinical departments, contract houses or pharmaceutical company premises. Ethics committees vary widely in their requirements about payments to volunteers. In a survey organised by the clinical section of the British Pharmacological Society, it was found that only 53% of protocols for investigations had guidelines for payments to volunteers: 55% had to report funding to the ethics committee, though the survey included both academic units, where the guideline would be more likely to apply, and industrial units where the matter might be settled by negotiation with employees (Orme *et al.*, 1989). It is often assumed that payment should not be such as to constitute an inducement, and should be to recognise inconvenience but not risk. There is a marked divergence between payment to recruited volunteers and staff members in clinical units, who are often expected to volunteer and indeed often want to do so as part of their normal work.

Several issues arise. Payments to volunteers can cover several elements of varying justification, which include expenses, reward for inconvenience, or even reward for risk. Healthy volunteers are vulnerable if impecunious, but not usually otherwise; however they can be conditioned towards requesting or accepting payment. Is this right? Those who need volunteers may be wealthy and so have power. Is the combination of wealth and power with impecuniousness and vulnerability too strong at times, or not? What would informed consent truly be for volunteers of different levels of experience and understanding? And how informed can anyone be about a new chemical entity, when the whole aim of the study is to gain information? How much is this concealed human toxicology testing? And in giving much information to a volunteer can much also be concealed?

It is difficult to think of an ethical problem which is beset by more relativism than that of payment to healthy volunteers. No doubt aware of this, the recent guidelines of the Royal College of Physicians (1986) suggested that payments might range between a lower level set by the current student grant, and an upper level set by the mean current national wage, the set point being weighted by the inconvenience, but never the risks, of the study. A recent paper (Bigorra & Baños, 1990) sets out what happens in Spain in ways which show the relativities admirably. Two groups of volunteers were compared in an attitudinal survey. One group consisted of undergraduates without prior experience of drug trials, and the other were postgraduate students or employees who had previously volunteered. The amounts paid to the Spanish volunteers were stated to be some 10 to 20 times the student grant, and 1.5 to 5 times the wage earners' income per day. It is not stated whether this was in addition to normal pay. But it is stated that these rates are 'slightly higher than desirable', and that 'only a small number of the medical students would agree to volunteer solely for financial reasons', whereas 'by contrast, financial reward was the main reason for volunteering (90%) amongst the healthy subjects with previous experience of Phase I clinical trials'. What is not disclosed is how many of the latter group had once been members of the former group. Half of the experienced subjects were described as 'students', but they may of course have been postgraduates or predoctoral fellows. What then are the relativities? First, there has to be a relative effect of site, nation, culture. It is impossible to generalise from the Spanish study, interesting though it is. In Britain the known payments for volunteer studies are around £50–£100 per day which is currently 4 to 12 times the student grant and 1 to 2.3 times the mean national wage. Next, it seems very likely that despite their statements the Spanish students may have been conditioned to volunteer for the second time (if indeed those second volunteers were amongst the first) by the very large rewards, if only for the reason that half the 'experienced' volunteers had themselves been undergraduates shortly beforehand, and now said that they *did* volunteer for money, albeit of less value than formerly. Looked at from the standpoint of ethical analysis, though the students were indeed exercising apparently autonomous choice (there was no coercion), what is autonomy worth if it is so changeable in relation to the students' own professed values? By analogy, seduction does not respect the autonomy of the seduced, even if it seems to be their free choice. It is interesting that only 13.8% of the Spanish students believed that they were 'hired bodies'.

Next there is the question of informed consent; how informable is an undergraduate compared with a postgraduate student? One British study (Chaput de Saintonge *et al.*, 1988) showed that concern for biological risks in research studies fell in relation to that for loss of study time as students moved from their preclinical to the clinical course and as, presumably, their level of information about potential illness risks rose. In general, medical and science students of almost any kind seem likely to be more informed and informable than patients as a group. What determines reactions to risk? Is it just uncertainty, *vs* the utility to the subject of taking part? This problem does not involve the intelligence of subjects, which is beyond doubt. It is concerned with their beliefs about themselves and their feel for biological hazard and the efficacy of protections against it. Whatever the truth may be about either aspect, the findings in the Spanish students show that both change in the transition time between under- and post-graduate existence, in at least some individuals.

Risk acceptance by young people is an important aspect. Many pay considerable sums to be exposed to risk as part of pastimes, including alternative experience induced by drugs. The risks of clinical pharmacological tests are known to be very small (Royle & Snell, 1986), but can be extreme to the tiny minority who suffer

damage. The concept of 'double effect' operates here. This implies the notion that if someone contemplating an action with several possible outcomes, some good and some bad, does that deed willing the good, this justifies him even if the unlikely bad outcome eventuates. Surgical operations provide many good examples of this 'effect'. It is easy by 'double effect' to deny that payment is for risk but to assert that it is for inconvenience. (One actual example was payment of £90 for tympanic puncture).

The drug-testing industry now seeks to recruit volunteers by advertisement over a wide area, in colleges both medical and non-medical. They may therefore participate in tests in places remote from their site of study. The standards imposed by local ethics committees vary widely. It is easy for someone to become conditioned to volunteer repeatedly, even concurrently, despite the published warnings. When remote advertisements attract volunteers, they are exempt from the usual scrutiny by deans of schools, which is usually a responsibility delegated to a clinical pharmacologist on the college staff if such a person exists. Changes in student grants, perhaps combined with rising unemployment, were associated with a sharp increase in those asking to volunteer in 1989 and 1990. However no hard conclusion can be drawn since volunteering for remunerative experiments was increasing anyway as contract houses were established in London.

So, like the jellyfish in the bucket we have a picture of remarkable relativism. Bring together the impecunious provider and the wealthy purchaser of a scarce resource and there appears an internal market which satisfies both and defies external control. If good laboratory and clinical practice are assured, why try to control it anyway? Altruism can still be a luxury for those who want it. It can be eliminated from this discussion for all practical purposes, not because it should be but because it has been shown not to be a motive for volunteering in any but a tiny minority.

To state the positive side, it has to be a good thing in some degree for medical students at least to experience what patients endure. There seems to be no rooted objection in principle to student volunteering, just an area of ethical disquiet within the topic which is disturbing if only for the reason that the problems are insusceptible to control. One way to improve control would be for local ethics committees to adopt the scale of payments suggested by the Royal College. The disquiet is an amalgam of the relative lack of informed consent, the conditioning of subjects to want reward for accepting the inconvenience and small risks of testing, and the time and effort which they may expend on this whilst still accepting pay for their normal studies. Since it cannot be controlled from without, it can only be controlled by the testers themselves. How many volunteers do they decline to accept? For all these reasons, the guidelines from the Royal College of Physicians are very welcome as a step towards controlling abuse, whether deliberate or due to inadvertent enthusiasm, but they will only work in practice if they are known and adopted by local research ethics committees. Local ethics committees will need to accept the recommended guidelines, and enquire carefully into all aspects of payments to staff and volunteers before giving ethical approval.

A final matter is an appeal for evidence. Are things acceptable or not? I have only anecdotes, but I do know that students have turned down studies at one institution because the 'going rate' was said to be higher at another. And I do know two teachers who are concerned at student absences from teaching because those students are volunteers, although that may be relative to their perceived value of the teaching. Most students with whom I have discussed the issues, but not all, can see nothing wrong with volunteering as a way to earn money, and regard concern about any possible risks to them as paternalistic interference. I have encountered one student who had volunteered for several concurrent experiments. Three adverts for volunteers displayed the sums of money which were on offer at the top of the script. One of these was exhibited in an amusement arcade, one in a hospital casualty department, and one outside a nurses employment agency. In no case did the head of department know what had been done, and none was approved by an ethics committee. Clearly no general inferences can be drawn from such observations, but it would be helpful to collect the experiences of all who are involved in human drug experiments.

D. W. VERE
Department of Clinical Pharmacology and Therapeutics, The London Hospital Medical College, Turner Street, London E1 2AD

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