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Remodelling the regulation of postmodern innovation in medicine

David Price
Professor of Medical Law, De Montfort University School of Law, Leicester

Abstract

'Therapy' is a legal concept of considerable import, traditionally juxtaposed with, but separate from, research and also, to some degree, marking the boundaries of legitimate medical intervention. The recent case of Simms *highlighted these issues, in addition to which novel clinical interventions were the subject of specific recommendations in the Bristol Royal Infirmary Inquiry Report. This article subjects the notion of therapy to analytical scrutiny and considers the extent of proper clinician discretion to innovate and, albeit much more superficially, how medicine should itself evolve. It advocates a new, more (patient) protective model which should generate confidence in the ethical character of contemporary innovatory practices.*

Introduction

'Innovative therapy' has been treated as a discrete concept in legal and ethical, as well as clinical, discourse. 'Therapy', or 'medical treatment',[1] is typically self-legitimating and distinguished from research, thereby avoiding the regulatory oversight and ethical review usually associated with research procedures. The recent case of *Simms v. Simms and another; A v. A and another*[2] touched on these rather neglected issues and put into relief the now urgent imperative for greater prospective regulation of experimental procedures in order principally to protect patients. The Bristol Royal Infirmary Inquiry Report's recommendation for research ethics committee (REC) review of *all* novel invasive clinical interventions has yet to be properly implemented.

More precisely, this paper focuses on three issues which, whilst separate, overlap to some degree. First, it probes the boundaries and nature of (innovative) 'therapy' as a conceptual construct; an issue of great consequence in so far as non-therapeutic research is an activity entirely distinct from medical treatment,[3] and would typically be illegitimate if administered to seriously ill patients.[4] It has been charged that, historically, very vulnerable patients (in reality 'subjects') were unknowing recipients of what were in fact 'non-therapeutic' procedures, thereby using them, in the Kantian sense, merely as a means to the ends of others. Included were the first artificial and human heart transplants and early xenotransplants (e.g. Baby Fae) (Annas, 1987).[5] Therapy may also be *combined*

1 The root of the word 'treatment' (from the Latin *tractare*) is 'to deal with' or 'to handle', whilst the root of 'therapy' is 'to cure'. Nothing significant appears to hang on this difference, and the Law Reform Commission of Canada has stated that 'The word "treatment" both in everyday language and in law carries the connotation of therapy': Law Reform Commission of Canada (1980, p. 57).

2 (2002) 71 BMLR 61.

3 Kong (2004, p. 166).

4 Kennedy and Grubb consider that non-therapeutic research would only permissible in regard to patients suffering from minor illnesses, see Kennedy and Grubb (2000, p. 1721).

5 There have also transparently been various supposedly therapeutic *research* procedures where the (lack of any) real prospect of benefit was hidden from patients, see Annas (1996, p. 305).

with research, reflected in the distinction between therapeutic and non-therapeutic research.[6] Beauchamp and Childress have similarly counselled that 'Attaching the favourable term "therapeutic" to research can be dangerous, because it suggests "justified intervention" in the care of particular patients and may create a misconception'.[7] Various commentators claim that the very terminology of 'gene therapy' for instance serves to confuse, if not obfuscate, the reality that such procedures essentially constitute non-therapeutic research (McLean, 2000).[8] Where the procedure falls within the latter category, this not only influences the maximum degree of permissible risk but may mandate a greater obligation to disclose information.

Secondly, it examines the relationship and distinction between 'therapy' and 'research'. This requires further elucidation, deconstruction and re-evaluation, especially in view of the norm for prospective review of research procedures by RECs in this country and Institutional Review Boards (IRBs), etc., abroad. Indeed, new medicinal products may not generally enter medical practice without licensing and rigorous evaluation by way of clinical research trials and independent ethical review (governed by statute since May 2004),[9] overseen domestically by the Medicines and Healthcare products Regulatory Agency (MHRA) (formerly the Medicines Control Agency), and the Food and Drugs Administration (FDA) in the U.S. New surgical procedures in particular have, on the other hand, historically been introduced in haphazard and unregulated fashion into medical practice without independent 'objective' assessment of their value, based on the largely unencumbered discretion of medical practitioners. The divergence, and anomalies, are highlighted in the fact that many transplant clinicians in the U.S. have argued that xenotransplantation does not fall within the oversight of the FDA because it is a surgical procedure as opposed to a regulatory product. Katz asserted some while ago that '. . . the establishment of regulations for the conduct of human research has led investigators both wittingly and unwittingly to label their interventions "therapy" rather than "research" in order to avoid the requirement of protocol review'.[10] It has been frequently maintained that it is difficult to distinguish research and innovative therapy.[11] It is submitted, however, that this dichotomy is in fact fallacious, the real distinction being between (innovative) 'therapy' and 'non-therapy'. Innovative therapy *is*, also, (therapeutic) research.

Thirdly, the question is asked whether therapeutic innovation should occur in the context of traditional treatment regimes or instead by way of a systematic research methodology. King opines:

> 'Maybe the right question to ask is whether experimental treatment is more like standard therapy or more like research. Considering it like one or other essentially has to do with the way medical progress is conceptualised. To view it as therapy is to place one's faith in the individual physician's desire to help patients, and to view it as research is to claim that only the scientific method holds out the hope of benefit, even to the individual patient currently in need.'[12]

There is a tension here between the clinical model of treatment and the scientific evidence-based medicine model. This raises issues relating to the nature of medicine itself and indeed how medicine should fundamentally evolve and new techniques and practices diffuse into clinical practice.

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6 The revised version of the Declaration of Helsinki in 2000 abandoned the distinction, but the majority of commentators still find it useful.

7 Beauchamp and Childress (2001, p. 320).

8 McLean (2000, p. 211). See also Kong (2004, p. 165).

9 The Medicines for Human Use (Clinical Trials) Regulations 2004, SI 2004/1031 implementing the EU Clinical Trials Directive 2001/20/EC.

10 Katz (1987, pp. 5–6).

11 See e.g. Fox (2002, p. 253).

12 King (1995).

The common thread is the ambit of clinical discretion in relation to innovation, which historically has been generally unfettered. A new framework for managing and regulating innovation is advanced here which, although considered in an Anglo-American context, has relevance across all jurisdictions. This revised regulatory model emphasises novelty and its attendant uncertainty, attempts to constrain innovatory excess and risk so as to protect patients, whilst avoiding substantial disincentives to innovate for the benefit of patients as well as society in general. It is submitted that the relevance of clinicians' intentions have been overstated in this sphere. The parameters of medicine must be something other than professional self-limitation (Illich, 1995). A more protective, patient-orientated, analytical axis is required with an enhanced emphasis upon communication.

Innovative therapy

Medical interventions have traditionally been viewed as falling within one of four categories: accepted or beneficial treatment; experimental or innovative treatment; futile treatments; and research procedures.[13]

Legitimacy

Ormrod J said of novel procedures (sex reassignment procedures in that instance) in *Corbett v. Corbett* that '. . . if they are undertaken for genuine therapeutic reasons, it is a matter for the decision of the patients and the doctors concerned in the case'.[14] This is not, of course, to say that innovative procedures are outside the jurisdiction of the law. They may become the subject of a civil suit for negligence where damage results. In early cases, such as *Slater v. Baker*[15] in England and *Carpenter v. Blake*[16] in the U.S., experimental procedures were viewed with suspicion and scepticism, but the imperative in these earlier times was to avoid the dangers of quackery by censoring deviations from standard practice. Contemporary judicial institutions are tolerant, indeed approving, of such innovations,[17] focusing instead on the degree of risk and danger posed by them.[18] Where a patient is injured as a consequence of an experimental procedure, any deviation from standard practice requires justification,[19] which will principally centre on the views of peers and the supporting scientific evidence. King neatly summarises the contemporary position: 'An experimentation case based in malpractice would condemn as experimental new or unproven treatments that deviate unreasonably far from the standard of care, especially when standard treatment is available'.[20] However, such judicial assessment necessarily occurs retrospectively and thus tends to shut the stable door after the horse has bolted.

Procedures amounting to 'proper medical treatment' do not constitute offences against the person as a consequence of a recognised public interest exception. This was re-emphasised by Lord

13 Schneidermann and Jecker (1996, p. 249).

14 [1971] P 83 at 99.

15 *Slater v. Baker* (1767) 95 ER 860.

16 *Carpenter v. Blake* 60 Barb NY 488 (1871).

17 A milestone case in the U.S. is *Fortner v. Koch* 261 NW 2d 762.

18 For a recent British example of judicial condemnation of an experimental procedure, see *Hepworth v. Kerr* [1995] 6 MLR 139.

19 In *Hunter v. Hanley* 1955 SLT 213 at 217 Lord Clyde said that a negligent procedure departing from accepted practice is one which 'no professional man of ordinary skill would have taken if he had been acting with ordinary care'.

20 King (1995, p. 7).

Mustill in the House of Lords in *R v. Brown.*[21] The English Law Commission stated in its Consultation paper *Consent in the Criminal Law*, 'Conventional medical and surgical treatment for a therapeutic purpose by qualified practitioners gives rise to no particular difficulties'.[22] Although innovative procedures are not 'conventional', ordinarily speaking, the Law Commission appears to be referring to 'conventional treatment' in the generic sense. 'Medical treatment' may even lie outside the purview of the criminal law entirely. The Law Reform Commission of Canada once recommended that the administration of 'treatment' should not constitute bodily harm or injury at all i.e. procedures performed for therapeutic purposes would be legal per se.[23]

Thus the therapeutic *purpose* of a procedure justifies it a priori where the treatment is 'conventional',[24] at least where consent has been given, and even where there are substantial risks attaching to it. Non-therapeutic procedures, including research, require a wholly different public interest justification, one which has rightly been described as 'undefined and poorly analysed'.[25] It is not legally possible to provide a valid consent to certain non-therapeutic procedures at all, which are therefore inherently unlawful. The Law Commission stated though that 'properly approved medical research' (i.e. approved by a local research ethics committee or other body charged with the supervision and approval of medical research in the relevant jurisdiction)[26] is also legitimate, where consent is given. Where what is involved is *exclusively* research, as opposed to therapy, however, the risks to which a person may be exposed are considerably less than where therapeutic benefit is anticipated.

Hope springs eternal

As has already been noted, critics view procedures which offer little prospect of either cure or remission as 'non-therapeutic' despite clinicians perceiving themselves as administering therapy. Intention has nonetheless been the dominant criterion in this sphere. What constitutes therapeutic benefit should not be solely a matter of medical judgement however.[27] Chadwick considers that in determining whether a procedure is therapeutic, it is not enough that there was an intention to benefit the patient; there must be *some good reason for believing* it will be beneficial to the patient (Chadwick, 1994). She cogently contends that a therapeutic objective is at best a necessary, but not *sufficient*, condition for legitimacy. Indeed, in the U.S. the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (Belmont) Report defined 'therapies' as 'interventions that are designed solely to enhance the well-being of an individual patient . . . *and* that have a reasonable expectation of success' [*my emphasis*] (Belmont Report: 1978). Such expectation must be 'scientifically well-founded'. King opines that 'Perhaps the desire for the patient's benefit ought instead to be classed with hope: necessary and inevitable, but having meaning only when success is reasonably possible'.[28]

The recent case of *Simms* provides some interesting insights into the foundation for the belief, and the threshold of expectation of benefit, for determining what is therapy under English law.

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21 [1994] 1 AC 212 at 266F-G.

22 Law Commission (1995, p. 109).

23 Law Reform Commission of Canada (1980, p. 55).

24 Seemingly, according to the Law Commission, because it is likely to be in the patient's best interests in that it may prolong the patient's life or hold out the prospect of a better quality of life, para. 8.39.

25 Kong (2004, p. 168).

26 This would apparently rule out such research on mentally incapacitated persons despite some leeway being conventionally permitted here, although proxy consent by a 'legal representative' is catered for in the EU Clinical Trials Directive in respect of the investigation of medicinal products.

27 Kong (2004, p. 168).

28 King (1995). This would be based on the perspective of the hypothetical reasonable person.

Necessity is the mother of invention

In *Simms v. Simms and another; A v. A and another*[29] decided in the Family Division of the High Court at the conclusion of 2002, two defendants, JS (Jonathan Simms) and JA, aged 18 and 16 years respectively, suffered from (probably) variant Creutzfeldt-Jakob disease (vCJD).[30] Whilst there was no cure available, nor any recognised approved drugs available to arrest or prolong the continuing neurological deterioration, research in Japan had recently identified a treatment, Pentosan Polysulphate (PPS),[31] which inhibited the progress of abnormal prion proteins being deposited in the brain (which in turn cause neurological damage) of rodents and dogs.[32] It had not been tested on humans at the time of the hearing and there had been no validation of the experimental work done abroad. It was intended to infuse the PPS intracerebrally, which in turn required a surgical procedure to facilitate this. Both sets of parents applied to the court for declaratory relief that each defendant lacked capacity to make a decision relating to PPS and that it was lawful as being in their best interests that they receive it.

JS and JA were at a broadly similar stage of the disease. Both remained aware of their surroundings and able to make slight movements, although permanently bedridden. It was nevertheless agreed by all involved that the patients still had some enjoyment from, and quality of, life worth preserving. Dame Elizabeth Butler-Sloss initially considered whether the procedure came within the *Bolam* test,[33] finding that responsible medical opinion did not reject such a procedure and that in any event it was 'consistent with the philosophy that underpins' the test. This is defensible not just in so far as strict reliance on the test might be viewed as inhibiting medical progress but also because it has come to be viewed as being based on 'supported (accepted)' as opposed to 'customary' practice.[34] Her Ladyship then proceeded to find that the procedure could be viewed as being in the two patients' best interests,[35] stating 'Even though the patients will not recover, it seems to me that the concept of "benefit" to a patient suffering from vCJD does encompass an improvement from the present state of illness, or a continuation of the existing state of illness without deterioration for a longer period than might otherwise have occurred, or the prolongation of life for a longer period than might otherwise have occurred'.[36] The declarations were granted.

Whilst the question of whether the procedures constituted 'therapy' did not explicitly arise, there was nonetheless the implicit assumption that the prospect of clinical benefit was a necessary threshold for legitimacy, i.e. that it could be properly viewed as *treatment* or *therapy*.

In receipt of benefits: evidential thresholds

The court reviewed the scientific basis for assertions of prospective benefit. It was noted that '[t]here are gaps in the present knowledge of the mechanisms of the disease and in the precise relationship between the abnormal proteins, the loss of nerve cells and neurological dysfunction',[37] but evidence from animal studies that PPS was a direct inhibitor of the formation of abnormal prion protein, the

29 *Simms v. Simms and another; A v. A and another* (2002) 71 BMLR 61.

30 It is believed that Jonathan Simms contracted the disease from eating BSE-infected meat. He was first diagnosed as suffering from vCJD in December 2001.

31 PPS is a blood thinning agent.

32 The mice were infected with scrapie, another prion disease closely related to CJD, found in sheep.

33 *Bolam v. Friern Hospital Management Committee* [1957] 2 All ER 118.

34 She observed that if one waited for *Bolam* to be complied with to its fullest extent, neither the use of penicillin nor heart transplant surgery could have been attempted: (2002) 71 BMLR 61 at 74.

35 The *Bolam* test is no longer decisive as regards the best interests of adults lacking capacity, see *Re SL (Adult Patient) (Medical Treatment)* [2000] 2 FCR 452 (CA), i.e. it is not a purely clinical issue.

36 (2002) 71 BMLR 61 at 76.

37 (2002) 71 BMLR 61 at 65.

cause of vCJD. As regards safety, it was stated that there was some evidence of serious side-effects in dogs, although not in mice, but apparently only from higher doses. The court regarded this evidence as sufficient to generate a sound basis for anticipating the possibility of success. Although a *theory* alone should not suffice, a plausible hypothesis based on a proper foundational scientific basis of laboratory and/or animal testing [I make no implicit assertion regarding the appropriateness of such procedures here] should typically be sustainable. As regards the *probability* of benefit accruing to the patient, the Royal College of Physicians (RCP) proffer the conventional view in the context of research that therapeutic research is an intervention which *may* benefit the patient, whereas non-therapeutic research is an intervention which *is unlikely* to benefit the person, i.e. a dichotomy founded on an *objective* evidential basis for anticipating a likelihood of efficacy.[38] In *Simms*, Her Ladyship stated only that the possibility of benefit 'could not be entirely ruled out', that there was 'some chance of benefit' and that it was not 'treatment which is clearly futile'.[39] Whilst the threshold of anticipated benefit laid down in *Simms* was undoubtedly fairly minimal, this was seemingly tolerable, enabling innovation to thrive and patients potentially to gain from advances in medicine. The issue of *who* should assess the basis for evidence of potential efficacy in situations across the board is addressed below.

There are clearly borderline cases in practice. Critics have alluded to the 'phase I-doublespeak' used in the context of cancer trials where patients or the parents of patients are provided with unrealistic or false expectations (Annas: 1996).[40] They object to the description of such trials as 'potentially therapeutic' despite the prospect of benefit being extremely small;[41] they are non-therapeutic and thus not able lawfully to be carried out. The same is often said in relation to novel treatments for AIDS. Indeed, in one sense such Phase I trials are 'intended to harm' patients by way of increasing dosage until an intolerable level is reached.[42] There is nevertheless the, albeit limited but plausible, prospect of some benefit to patients who have generally exhausted all other options, with the evidence suggesting that the real likelihood of a tumour response in an average Phase I cancer trial in patients is around 5%.[43] The Law Reform Commission of Canada opined that '[t]here is no ready solution to the overlapping borders of treatment and non-therapeutic interventions', and suggested that decisions should be made on a case-by-case basis.[44] It has been argued that the tendency to conflate medical treatment and research, particularly where such research involves dependant patients, has prevented consent from being a meaningful exercise of self-determination.[45] How things are 'dressed up' and presented may undoubtedly be important. However, if honest and realistic information was provided as to the prospect of benefit then many objections would fall away, and this might even be better achieved without the use of labels.

Nothing to lose?

Even if the procedure constitutes therapy, it will only satisfy the best interests test applicable to mentally incapacitated patients where there is net benefit to be potentially achieved. Dame Elizabeth Butler-Sloss stated in *Simms* that:

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38 Royal College of Physicians (2000, para 6.12). See generally Beh and Diamond (2000, p. 13).

39 (2002) 71 BMLR 61 at 76. Whilst 'futile treatment' is seemingly a contradiction in terms, in the research context it has been equated with there being no reasonable prospect of benefit.

40 These Phase 1 clinical trials of medicinal products will henceforward also be subject to regulatory approval and ethical review, under the EU Clinical Trials Directive 2001/20/EC.

41 The National Cancer Institute researchers in the U.S. have dubbed such trials 'therapeutic'.

42 Montgomery (2003, p. 215).

43 Tattersall and Simes (1992, p. 86).

44 Law Reform Commission of Canada (1980) 59.

45 Kong (2004, p. 165).

> 'Where there is no alternative treatment available and the disease is progressive and fatal, it seems to me to be reasonable to consider experimental treatment with unknown benefits and risks, but without significant risks of increased suffering to the patient, in cases where there is some chance of benefit to the patient'.[46]

Prima facie it might seem that the potential deleterious effects and the fact that success was improbable were minimised by the court in view of the patients' desperate plight. Her Ladyship remarked:

> 'I think it is reasonable . . . to put into the balance that, if there is a possibility of continuation of a life which has value to the patient and the patient is bound to die sooner rather than later without the treatment, these two young people *have very little to lose* in the treatment going ahead.' [*emphasis added*].[47]

Jonas rightly asserts, however, that one must fight the tempting sophistry that the hopeless case is expendable and therefore especially usable, as the opposite is true.[48] But whilst it is certainly inappropriate to permit procedures to be carried out based on such a specious rationale, a lack of other choices and the fact of an impending death are undoubtedly very material factors to weigh in the balance.[49]

Although an experiment does not become therapy simply because no conventional intervention exists and a subject's desperate circumstances cannot increase the likelihood of benefit,[50] the 'principle of proportionality' is applicable here. It is broadly accepted that greater risks may be warranted where a patient is desperate and without other feasible alternatives.[51] Whereas new medicinal products are tested on patients in Phase II and Phase III trials, Phase I trials are typically carried out on healthy volunteers. As a consequence, the involvement of cancer *patients* in Phase I dose tolerance testing is, as has been noted, criticised by some as being unethical. Evans and Evans, however, note that such cytotoxic drugs are tested on patients rather than healthy subjects because these *are* very toxic substances and the chances of a serious adverse event are high. They state:

> 'But given that such patients are *in extremis* and that the trial substance might hold out some slender hope of palliating their symptoms or slowing the progress of their disease, the balance between risk and benefit to the subject is totally different from that involving healthy volunteers.'[52]

This is not a different view of the potential efficacy of the procedure, an essentially scientific question, but an ethical question relating to the proper balancing of (uncertain) risks and benefits. Even an extremely modest benefit viewed in 'objective' terms may be of enormous experiential relevance for a severely compromised patient.[53] The clinicians in *Simms* intended only a 'cautiously low dosage', being

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46 (2002) 71 BMLR 61 at 76.

47 (2002) 71 BMLR 61 at 77.

48 Jonas (1969). Annas goes so far as to argue that subjects who believe they have nothing to lose should be ineligible for such interventions and that clinicians who hold such a view should be disqualified from participation in them, see Annas (1996, p. 323).

49 A lack of 'less restrictive alternatives' in such scenarios is of course an *additional* criterion to satisfy.

50 See Annas (1996, p. 321).

51 Law Reform Commission of Canada (1980, p. 59).

52 Evans and Evans (1996, p. 26).

53 For instance, patients with paralysis and lack of movement may view any restoration of mobility as being of huge significance, and may be prepared to assume risks that 'objectively' would be viewed as disproportionate, see 'A Life Worth Living', *The Times*, 6 August 2002 (T2), p. 11.

only 3% of the higher dose used in the animal research. The dose-dependent risks posed by the infusion were consequently viewed as small; with an overall risk of haemorrhage of 5%. But even if the risks had been greater they would have needed to be weighed against the potentially significant benefits.

Fair labelling

Where the individual possesses decision making capacity,[54] the patient is able to weigh these risks and benefits for him- or herself. Even where the potential for significant harm, disability or debilitation is high, as arguably in respect of the first intended permanent artificial heart given to Barney Clark in 1982 (his 112 days following surgery and prior to his death were riddled with serious medical difficulties), it would nevertheless typically be appropriate to allow the, fully and properly informed, patient to decide, *if* the chance of benefit was real and provided no false hope was instilled or 'self deception' practised. Patient vulnerability, however, demands additional protections which are discussed below.

Thumb screws[55]

The existence of a basic human instinct to cling to life and the absence of other realistic alternatives for avoiding death lead some to contend that no *voluntary* decision to consent to innovative treatment can be given by desperate individuals. In *Simms* it was nevertheless opined that both patients, had they been competent to consent, would probably have done so, suggesting such a consent would have been legally valid.[56] It is difficult to see this as being 'coercive' in the absence of any pressure or influence being exerted from another human agency.[57] An additional option is being offered rather than any available option being foreclosed. 'Situational coercion' generated by health factors may impair freedom, but not autonomy (King and Henderson: 1991). There is no denying the dependency of *patients* upon their carers in such contexts though, rendering them vulnerable to clinicians especially.[58] The Medical Research Council guidelines appropriately assert that in such circumstances consent may not be properly voluntary and that an independent doctor, not involved in the procedures, should be involved in obtaining consent.[59]

Non-therapy

King asserts that:

> 'It is especially important to try and determine whether there is a real chance of benefit to subjects because, under the current regulatory scheme, so much hinges on distinguishing

54 In some instances, the person's illness will undermine decision-making capacity. Terminally or extremely ill individuals may be in denial and suffering from feelings of helplessness, depression, etc.

55 Ingelfinger has spoken of the 'thumb screws of coercion' being applied to patients with disease in respect of experimental procedures, see Ingelfinger (1992, p. 466).

56 It has similarly been alleged that parents of chronically sick children will 'clutch at any last straw' (as in the case of Laura Davies, who underwent a seven-organ entire digestive system transplant) and that this cannot constitute any kind of voluntary decision. However, parents do refuse such procedures, as can be seen from *Re T (a minor) (wardship: medical treatment)* [1997] 1 All ER 906 (CA), where the parents refused a potentially life-sustaining liver transplant for their young child.

57 In *Kaimowitz v. Michigan Department of Mental Health* 42 USLW 2063 (Mich. Cir. Ct. 1973) the court implied that the institutionalised mental patient involved would have been unable to give a valid voluntary consent, even if competent, to experimental psychosurgery. However, the outcome was contingent upon the fact that the procedure was highly dangerous and the patient involved was involuntarily institutionalised. The disempowerment associated with 'total institutions' has been conveyed by Goffman (1961).

58 Capron states 'Any illness may undermine a person's normal ego strength; a crippling disease which puts a patient in a sickbed without prospect of recovery can call forth ultimate dependence, cooperation, and devotion to the all-powerful physician who possesses the magical means of curing him' (1974, p. 381).

59 Medical Research Council (1998, Appendix 1, Article 10).

between research that does offer subjects the potential for direct benefit and research that does not.'[60]

Nonetheless, non-therapeutic *research* may also be permissible, subject to a significantly more limited ceiling on permissible risks; the individual is now instead embarked on altruism. Capron has asserted that:

'There is certainly a place in medical innovation for the brave subject who, realizing that his life is near its end, decides selflessly to participate in research so that more can be learned about the disease that is killing him or about new possibilities of treating it.'[61]

Whilst some would confine such research to patients suffering from minor illnesses,[62] others foresee the likelihood of greater future societal acceptance of non-therapeutic experimentation with regard to seriously ill patients who are made aware of the foreseeable risks.[63] By virtue of the absence of potential clinical benefit and the irrelevance of therapeutic privilege or waiver as reasons for withholding information, it is generally assumed that there should be *full* disclosure of information relating to non-therapeutic research, including the risks involved, as there is only 'one level' of consent.[64] The decision of the Saskatchewan Court of Appeal in *Halushka v. University of Saskatchewan*[65] reflects this view. Some non-therapeutic research procedures are even permissible with respect to mentally incapacitated adults and children. However, the risks involved would seemingly need to be no more than minimal.[66]

External appraisal

The question arises whether there should be any external assessment of these matters beyond the doctor/patient relationship. Where there are risks to society as a whole from a particular procedure, by way of disease transmission or otherwise, as in respect of xenotransplantation, society should certainly evaluate these risks prior to it being offered to individual patients.[67] Indeed, the (non-statutory) Gene Therapy Advisory Committee and the United Kingdom Xenotransplantation Interim Regulatory Authority have been established in such circumstances, and where it has been determined a priori that procedures should initially be introduced by way of formal research trials. By contrast, xenotransplantation has historically been characterised by one-off procedures or very small 'series' of patients, without a formal research protocol, the risks in relation to which cast doubt retrospectively on their legitimacy (Price, 2000). Whereas in *Simms* prospective societal evaluation took place through the agency of the courts, there would typically be no prior external review however outside the context of a formal research trial. Clinical discretion and informed (patient or parental) consent, or a best interests assessment, would essentially suffice. It was noted in *Simms* that

60 King (2000, p. 333).

61 Capron (1974, p 392). There may even be strong motivations to entertain such procedures. Jonathan Simms' father stated on television that . . . 'at least society will learn from the experience so that others can benefit in the future'.

62 Kennedy and Grubb (2000, p. 1721).

63 See Tunkel (1992, p. 15).

64 This was how the Nuffield Council on Bioethics Working Party put it (1995, para. 7.7).

65 *Halushka v. University of Saskatchewan* (1965) 53 DLR (2d) 436.

66 Principally because of the invariable application of the best interests test. Regulations implementing the EU Clinical Trials Directive insist that there should be 'no risk' at all. However, the Mental Capacity Act 2005, which applies to intrusive research outside the clinical trials environment, refers to 'negligible risk', see s. 31.

67 See Fox (2002, pp. 269–271).

PPS was about to be tested in Japan without any impediment whatever. Patients so situated are peculiarly vulnerable, however, and require additional protection.

Therapy versus research?

Surprisingly, there is a pervasive failure by central agencies such as the Medical Research Council and the Central Office for Research Ethics Committees (COREC), and within pertinent legislation, to define 'research'. This definitional vacuum is especially regrettable, since labelling a procedure only as therapy tends to evade prospective independent evaluation, regulation and on-going monitoring. Moreover, such procedures will tend to enter medical practice without prior validation by way of controlled comparative trial, thus raising broader issues as to how procedures should become integrated into medical practice generally.

Research is typically distinguished from therapy on the basis of the intent of the physician.[68] The Royal College of Physicians (RCP) asserts[69] that

> 'The distinction between medical research and innovative medical practice derives from the *intent*. In medical *practice* the sole intention is to benefit the *individual patient* consulting the clinician, not to gain knowledge of general benefit, though such knowledge may emerge from the clinical experience gained. In medical *research* the primary intention is to advance knowledge so that *patients in general* may benefit: the individual patient may or may not benefit directly.'

Once more it is submitted that the relevance of subjective intent is overstated.[70] Clinical innovators have ever-present mixed motives and personal/institutional incentives. Gaze and Dawson observe that:

> 'The physician's motives . . . may not always be separable. Motives . . . are not necessarily clear, or easily identified or distinguished from one another, especially where no established treatment exists. For example, while the doctor undoubtedly wishes to heal the patient, if the new treatment works, it will inevitably benefit others as well as the patient, and the doctor must be aware of this. If the test turns on subjective motivation, there is the problem of proving or establishing what was in a person's mind at some time in the past.'[71]

Quite apart from the evidential difficulties in isolating intention(s), it is submitted that intentions, in and of themselves, are insufficient to categorise research and distinguish it from therapy.[72]

The 'design'

The Belmont Report (1978) expressed the view that:

> '[T]he term "research" designates an activity designed to test an hypothesis, permit conclusions to be drawn, and thereby to develop or contribute to generalisable knowledge . . . The fact that a

68 Stauch, Wheat and Tingle (2002, p. 552) distinguish 'foresight' that new knowledge (from innovative therapy) will be generated from the intention to generate knowledge which is the essential aim of a research procedure.

69 Royal College of Physicians (1996, para. 6.4).

70 The Institute of Medical Ethics Working Party Report (1986, pp. 36–37) states that '*Innovative therapy* consists in the performance of a new or non-standard intervention as all or part of a therapeutic activity and not as part of a formal research project. Innovative therapy may therefore be quite haphazard, starting just when a doctor has a bright idea that he wants to try out. If the bright idea seems to be any good, then innovative therapy can become research as soon as the bright idea is examined in a systematic manner.'

71 Gaze and Dawson (1989, p. 307). Motives should not be bifurcated from intentions in such remarks.

72 Caplan (1990, p. 153).

> procedure is "experimental", in the sense of new, untested or different, does not automatically place it in the category of research. Radically new procedures of this description should, however, be made the object of formal research at an early stage in order to determine whether they are safe and effective.'

From this perspective, the intent, and thus the purpose of the procedure, is implicit in the inherent design of the study, as opposed to residing in the subjective motivation of the investigators.

The Belmont Report's comments, which emphasise the contribution to generalisable knowledge, principally envisage highly formalised, paradigmatic research involving comparator groups and in particular the 'gold standard' randomised controlled trial (RCT). Even formal research in fact comes in various guises, with varying degrees of extrapolation of data required. Furthermore, innovative procedures of every hue contribute to generalisable knowledge to some degree or other, regardless of the actual purpose of the actors or the design of the study, and the largely anecdotal nature of the evidence generated. Whilst it has been maintained that '[o]utcomes simply are not in the realm from which generalisable conclusions can be made',[73] it is now very clear from the huge number of kidney transplants performed to date, for instance, that outcomes are *invariably* better for most patients than long-term renal dialysis, even though the intention from their inception was merely to benefit individual recipients. In *Simms* it was recognised and commented that:

> 'Although this cannot be a research project, there would be an opportunity to learn, for the first time, the possible effect of PPS on patients with vCJD and to have the opportunity to compare it with the treatment about to be given to patients in Japan.'[74]

The testing of a scientifically plausible hypothesis is one of the supposed hallmarks of research. Evans and Evans have, however, observed:

> 'If the first patient to receive the modified treatment provided the occasion for forming a hypothesis, the second patient (and many subsequent patients) provided the opportunity for the hypothesis to be tested. Both the initial forming and the subsequent testing of the hypothesis look ahead to a more general future. We think that this broad account remains essentially true even when the looking forward is informal, unsystematic and when the clinician in question might more naturally have chosen the word "hunch" than the grander-sounding "hypothesis".'[75]

They suggest that the evolution of medical practice has in reality consisted of undeclared or unrecognised research. In fact, one might go further and suggest that in all novel medical procedures a hypothesis is being tested even *in the first clinical applications* of new pharmaceuticals, transplants, etc., as they are all underpinned by prior work in animals, laboratory testing, etc., which in turn generated hypotheses as to efficacy in humans. The Belmont Report considers that research is usually described in a formal protocol that sets forth an objective and a set of procedures designed to reach that objective.[76] Margo alludes to this perception of research as adhering to a particular *form* (i.e. a formal research protocol) and without regard to its substance, and points to the danger that 'In the United States and elsewhere, a gap exists between the formal federal definition of human

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73 Dossetor (1990, p. 967).

74 (2002) 71 BMLR 61 at 79.

75 Evans and Evans (1996, p. 54).

76 Belmont Report (1978). In like vein, Kennedy has asserted 'To qualify as research, an intervention must form part of a programme of enquiry based on a scientifically plausible hypothesis, must follow a scientifically valid methodology, and be intended to produce data of a generalisable nature', see Kennedy, 'Research and Experimentation' in Kennedy and Grubb (eds) (1998, para. 13.01).

research and what the public perceives as human experimentation'.[77] It is true, however, that by virtue of the fact that systematised research protocols take into account the general interest to some degree, a 'new contract' needs forging. Gillon states that the patient/subject must know that '. . . the normal therapeutic doctor-patient relationship either does not exist or has been modified to include objectives that may compete with the patient's best medical interests'.[78] The notion of conflict of interest looms large here, i.e. the doctor is acting *qua* scientist as well as *qua* doctor. Information disclosure and consent are therefore crucial to enable individuals to protect their own interests and to make informed decisions as to whether to submit to such research or not. This is vital because the procedure will often carry risks, other forms of treatment may be denied or deferred, benefit may be dubious, etc. However, information about *all* experimental procedures is essential to the same ends, regardless of whether it constitutes traditional 'research' or not.

McNeill maintains that informed consent is inadequate (i.e. necessary but not sufficient) in itself to deal with the complexities of experimentation on human subjects, and advocates that all experimental procedures, not just research projects, should be required to undergo prior review (McNeill, 1993). The consequences of a one-off experimental procedure may be even *greater* than under a properly conducted research trial.[79] Johnstone and Elliott, for instance, contend in respect of the drastic practice of healthy limb amputation for the relief of psychological suffering caused by a body dysmorphic disorder known as apotemnophilia, that '[b]y operating outside a framework of oversight by a research review board, [the clinician concerned] blurred an already fuzzy line between innovative therapy and clinical research'.[80] In so far as innovative therapy and research do not differ in their essential nature, and the fact that it is the *novelty* and *inherent uncertainty* of the intervention which are the crucial elements, scrutiny through RECs and IRBs should be a legal pre-requisite for all such procedures.

Controlling evolution

Ethical tension is generated by the simultaneous desire to allow clinicians the freedom to think and act creatively in the interests of their patients whilst at the same time protecting patients from being subjected to poorly conceived and designed therapeutic interventions with potentially harmful consequences. There is a tension here between the ideology of science and the ideology of treatment, the latter being more obviously patient-orientated. Innovative therapies are deviations from common practices which have not been studied formally, and therefore lack the safety and efficacy validation that a research protocol would secure.[81] There is no doubting that various procedures[82] should have been evaluated earlier by means of a formal research trial. Safety doubts have arisen with regard to the use of artificial reproductive procedures around the world, for example,[83] leading to criticism that further safety and efficacy research testing should have been undertaken at the outset.[84]

77 Margo (2001, p. 42).

78 Gillon (1991, p. 53).

79 Levine similarly considers that innovative procedures involving substantive deviations from standard practice should be subject to review by an IRB in the same way as if they were research: Levine (1978, Appendix vol. 2).

80 Johnstone and Elliott (2002, p. 434). Keyhole surgery has also been subject to opprobrium. Radial keratotomy to correct refractive errors of the eye and episiotomy is another example historically raised, see Grimes (1993, p. 3031).

81 Morin (1998).

82 It has even been observed that the optimum method of performing a hysterectomy remains unclear, due to lack of rigorous comparative study, see Garry (1998).

83 See *The Guardian*, 23 November, 2004.

84 Noah (2003).

Similarly, surgical intervention for infants with ambiguous genitalia or who suffer traumatic genital injury, which occurred against the backdrop of a very limited and dubious theoretical and scientific foundational basis, has resulted in considerable injury and trauma.[85] Improvised ad hoc uses of medical devices have also led to significant injury in some instances.[86] We are, of course, considering therapy alone here. Where the procedure is *non*-therapeutic, a generalisable knowledge maximising strategy should *always* be adopted.

The development of surgical practice has generally been 'experiential', i.e. largely by trial and error. The introduction of the philosophy of evidence-based medicine (EBM) in the 1980s has, however, transformed the general paradigm of medical practice. Agich observes that 'Innovation tolerates, even thrives on, intuition, experience, and uncertainty whereas scientific research proceeds under methodological constraints from a base of established knowledge toward its goal of hypothesis confirmation or disconfirmation'.[87] A distinct advantage of EBM is the lesser importance accorded to clinician authority and unconstrained discretion.[88] Formalised research comparing new procedures with currently accepted methods should ostensibly be the norm as knowledge procured for the benefit of future patients and society as a whole is most reliably generated in a systematic manner having controlled for confounding factors.[89] Once innovative, but unvalidated, practices become widely adopted, the standard of care in law which relies heavily on accepted practice will tend even further to entrench and protect many potentially harmful and dubious interventions.[90] There are also issues of justice here with regard to who should be able to *access* new procedures and methodologies. It has been observed that the public policy debate has 'paradigmatically shifted'[91] over the years from a central focus on subject *protection* to issues as to who should be afforded the possibility of *benefiting* from such novel interventions. Access to certain novel drugs is often only available within the context of a clinical trial e.g. for HIV/AIDS. Should we be insisting then that *all* new procedures enter medicine by way of formal clinical trials? The Declaration of Helsinki asserts that

> In the treatment of a patient, where proven prophylactic, diagnostic and therapeutic methods do not exist or have been ineffective, the physician, with informed consent from the patient, must be free to use unproven or new prophylactic, diagnostic, and therapeutic measures, if in the physician's judgement it offers hope of saving life, re-establishing health or alleviating suffering. *Where possible* measures should be made the object of research, designed to evaluate their safety and efficacy [*emphasis added*] (World Medical Association: 2000).[92]

85 See Beh and Diamond (2000). The accepted wisdom was that sexual identity was a function of rearing, nurturing and socialisation rather than any inherent or genetic predisposition.

86 The MHRA has warned staff not to use medical devices for unintended medical purposes, see *The Times*, 5 February 2004.

87 Agich (2001, p. 296).

88 See Stirrat (2004).

89 It has, in fact, recently been reported that a research drug trial for vCJD is being set up by the Medical Research Council. However, this will be of an anti-malarial drug, quinicrine. Some experts have argued that the trial should have instead focused on PPS: see *The Times*, 5 August 2004.

90 Although the interpretation of the *Bolam* principle in the House of Lords in *Bolitho v. City and Hackney Health Authority* [1998] AC 232 has recently introduced a greater critical element here. Once procedures have been attempted 'informally', it may also be difficult to assert 'equipoise' to embark on a later comparative clinical trial, with potentially detrimental consequences for society as a whole.

91 To use the words of Fox (2002, p. 267).

92 World Medical Association (2000, *Declaration of Helsinki*, at para. 32).

Whilst RCTs are the paradigmatic interventional strategy for innovative procedures, they should not be viewed as the only proper ethical or 'scientific' methodology.[93] The constraining effects of formal research protocols such as RCTs may inhibit patient benefit,[94] whereas treatment regimes are able to be modified as and when required in the patient's best interests.[95] Moreover, RCTs may be inappropriate where a new treatment with modest risk ostensibly offers vastly better prospects than conventional alternatives (there would be no *equipoise*). Regulatory schemes on both sides of the Atlantic have 'fast tracking' procedures[96] or 'compassionate' or 'emergency' treatment use provisions for medicinal products, and allow 'off label' uses of drugs in certain circumstances. These are typically applicable where the condition concerned is either seriously debilitating or life-threatening and there are no other available options (a policy compatible with the Helsinki Declaration, above). In *Simms* it was noted that although PPS is not licensed in the U.K., the Medicines Control Agency (as then was) would have been unlikely to object to its use in such specific instances provided the treating doctor took personal responsibility in respect of its administration. Whilst accusations are made that this has the effect of shifting unproven interventions from the category of 'research' to 'therapy', with its associated risks and falsely raised expectations, I have sought to argue that the dichotomy between research and therapy in respect of novel procedures is false; they exist along a spectrum.

Kennedy and Grubb note that the case law both in England and in the U.S. has sought to give some 'leeway' to clinicians to develop medical practice incrementally outside the context of systematic research whilst placing limits on the 'leaps' that clinicians may engage in.[97] They cautiously suggest that the notion of 'minimal risk' may be of some assistance here, whilst asking rhetorically whether such a criterion would unnecessarily inhibit the doctor from trying new techniques outside the ambit of systematic research? It is submitted that such a ceiling would indeed be too constraining, as can be gleaned from the early organ transplants, recent maxillo-facial surgical procedures and attempts to separate conjoined twins. Whilst the Iranian adult Bijani twins died after the first attempt to separate them, there have been several recent successful separations of similar craniopagus twins, including the two-year old twins Ahmed and Mohamed in Dallas and Carl and Clarence Aguirre in New York.[98] Yet each case is virtually unique, as is the case in respect of certain very rare neurological conditions.[99] But whilst some discretion in terms of methodology is appropriate, it has been submitted already that prospective review should be obligatory regardless of the methodology adopted.

The view that RCTs are productive of generalisable scientific evidence applicable to the treatment of individual patients is itself debatable on account of the 'average' results and differences which result from such trials – science after all deals in generalities rather than individuals.[100] This is

93 See Liberati and Vineis (2004).

94 Mason, McCall Smith and Laurie (2002, p. 573) maintain that: 'Research and experimentation are commonly used as interchangeable terms – we, however, believe that there is a distinction to be made. Research implies a predetermined protocol with a clearly defined end-point. Experimentation, by contrast, involves a more speculative, ad hoc, approach to an individual subject. The distinction is significant in that an experiment may be modified to take into account the individual's response; a research programme is more likely to tie the researcher to a particular course of action until such time as its general ineffectiveness is satisfactorily demonstrated.'

95 Sham surgical procedures are also especially contentious.

96 For instance, the FDA approved the use of zidovudine to treat AIDS patients in the U.S..

97 Kennedy and Grubb (2000, p. 1743).

98 See *The Times*, 13 October 2003 and *The Times* 6 August 2004, respectively.

99 Half of a teenager's brain was removed (hemispherectomy) in a pioneering operation performed at the Johns Hopkins Medical Center in Baltimore in 1999. The girl suffered from Rasmussen's syndrome, a progressive, previously thought to be inevitably fatal, disease: see *The Times*, 15 July 1999.

100 Aronowitz (1998). Lind (1988, p. 547) states: '. . . the conclusions of major trials may not be as revealing as hoped, for a variety of reasons.'

consequently not just a debate about the best way of ensuring efficacy and safety, but part of a broader debate about the nature of medicine itself, about the generalisability and transferability of therapies, etc. Aronowitz even questions the extent to which '. . . clinical reality can be adequately understood as a set of uniform and predictable encounters between patients suffering specific ailments and physicians who apply specific diagnostic and therapeutic technology and practices'.[101] Science is ultimately in the service of medicine which subsumes it. Innovation is inherent in the very practice of medicine, and medicine would partially stagnate if every advance had to constitute part of the *regulatory ethics paradigm.*[102]

Independent review

There is a need to enhance the autonomous nature of patient decision-making and introduce further review ex ante of therapies with potential for significant harm and/or questionable benefit. Indeed, the Bristol Royal Infirmary Inquiry Report recommended that before any new and hitherto untried invasive clinical procedure (whether a variation of an existing procedure or a genuinely new innovation) could be undertaken for the first time, the clinician should previously have satisfied a local research ethics committee (LREC) that it is justified and in the patient's interests to proceed, and each NHS trust should have in place a system for ensuring that this process is complied with.[103] At the same time as accepting that new interventional procedures require special oversight and scrutiny, the Government, however, rejected giving LRECs the function of reviewing all new interventional procedures, preferring instead to provide a national system of appraisal, able to harness expert knowledge with respect to safety and efficacy. The National Institute for Health and Clinical Excellence (NICE) now issues guidance on interventional procedures,[104] having taken over responsibility for the Safety and Efficacy Register of New Interventional Procedures (SERNIP) from February 2003.[105] Notified procedures are considered by NICE's Interventional Procedures Advisory Committee (IPAC), which ultimately produces guidance on them. Where there is 'inadequate evidence' of safety and efficacy (as opposed to evidence that the procedure is either safe and efficacious for use or not safe and efficacious enough), patients should be made aware that there is current uncertainty as to its safety and efficacy. NICE review and evidence gathering will facilitate the use of EBM in assessing safety and efficacy in a more coherent, comprehensive and objective fashion. However, NICE only considers procedures which fall *outside of a Research Ethics Committee approved protocol.*

Medical practitioners planning to undertake new interventional procedures must seek approval from their NHS trust's Clinical Governance Committee.[106] This Committee will ascertain whether NICE has issued guidance with respect to it. Medical practitioners would be expected to follow any such guidance,[107] although the Committee may approve its use even in the absence of such guidance

101 Aronowitz (1998, p. 179).

102 It has been argued that the best methodology for testing surgical procedures and techniques differs from the assessment of new drugs and that in many circumstances carefully performed observational studies ought frequently to suffice, see Stirrat (2004) *Journal of Medical Ethics*, 163.

103 Report of the Public Inquiry (2001, Recommendations, para. 100).

104 Defined as any procedure involving making a cut or hole in the body, gaining access to a body cavity without cutting into the body or using electromagnetic energy or ultrasound.

105 Previously, the safety and efficacy of new interventional procedures was registered with the Academy of Royal Medical Colleges (SERNIP), but this was voluntary rather than compulsory, see 'Remedying bias in surgical trials' (1997) 314 BMJ 916.

106 See Health Service Circular HSC 2003/011, at www.dh.gov.uk.

107 Compliance can only be made mandatory through trusts' clinical governance schemes, although compliance by clinicians would ordinarily be expected in any case.

being available where, inter alia, patients are made aware of the lack of experience with the procedure.[108] The aim is for clinical innovation to be 'responsibly managed' henceforth.

However, whilst these are extremely laudable, important and seemingly robust developments, the uniqueness and novelty of innovative, invasive interventions create an imperative for independent *ethical* review, over and above the scientific safety and efficacy appraisal undertaken by NICE and management scrutiny by local NHS trusts under its clinical governance remit. REC review considers individual patient circumstances, whereas NICE investigates the (efficacy and safety of the) procedure itself without reference to either the specific clinicians or patients implicated. Moreover, it is not generally within the remit of IPAC to consider the ethical issues, thus leaving a lacuna which was anticipated in the Bristol Inquiry Report, to which the government's Response to the Report rather obliquely asserted 'Ethical expertise will be needed within the system and we will discuss cross-membership with research ethics committees and to ensure good governance' and 'LRECs will need to consider any studies of new procedures as advised by NICE'.[109] However, IPAC seemingly only has the power to *suggest* that the procedure be carried out on a 'research' basis, and RECs will only consider novel clinical interventions which meet the traditional model of 'research', presumably involving a comparison of therapeutic options.[110] The systems therefore appear to be running in parallel, whereas the need for nationally reliable efficacy and safety assessment and localised ethical review *both* appear to be crucial, generating good scientific evidence and a system for protecting vulnerable individuals. The two separate, scientific and clinical, elements can be seen in the decision making in *Simms*.

Patients are exposed to the risk of more than minimal harm from a novel invasive clinical intervention whether this fits the traditional model of research or not. In New Zealand *every innovative practice* must be prospectively reviewed and approved by an ethics committee, demonstrating that it is justifiable in terms of its potential contribution to medical knowledge and that it has the potential to be of direct benefit to individuals, based on pre-clinical evaluation, clinical evidence, etc., and that it does not expose participants to undue harm. Requirements of consent and justice must also be considered prior to its initiation.[111] REC review should utilise and subsume scientific review by NICE into its determinations in the same way as it presently uses peer review with regard to all research protocols.[112] This model should be adopted more widely and embedded within a statutory framework, despite certain commentators emphasising the breadth of innovations within medicine, some being no more than minimal dose variations or timing.[113] Certainly, bureaucracy and delay must be minimised where time is of the essence, especially where there is no other efficacious

108 NICE has produced information sheets for the guidance of patients on consent for experimental procedures, *Consent – procedures for which the benefits and risks are uncertain*, Department of Health (2003).

109 Department of Health (2002, para. 5.19 and 158).

110 Central Office for Research Ethics Committees (2004, para. 4.27). In this event, a site-specific assessment (SSA) will also be required for any investigational medicinal product or any physically invasive clinical intervention which is not already established as routine clinical practice, where there is no 'local investigator'.

111 *Operational Standard for Ethics Committees*, New Zealand Ministry of Health, Wellington, 2002, available at http://www.moh.govt.nz. 'Innovative practice' is defined as including any clinical intervention, whether a drug, device or clinical procedure, that is untested, unproven or not in common use, see para 112.

112 But see Cave and Holm (2002, p. 321).

113 In *Brook v. St. John's Hickey Memorial Hospital* 380 NE 2d 72 at 76 (1978) the Supreme Court of Indiana stated: 'Too often courts have confused judgmental decisions and experimentation . . . The everyday practice of medicine involves constant judgmental decisions by physicians as they move from one patient to another in the conscious institution of procedures, special tests, trials and observations recognized generally by their profession as effective in treating the patient or providing a diagnosis of a diseased condition.'

therapy available, or one without substantial burdens or problems, but even extremely radical and risky interventions have traditionally evaded prior review.[114]

The need to ensure that informed consent has been properly given by competent patients is especially essential in experimental contexts. Even though competent, the thinking of the extremely sick is frequently impaired and partially compromised, thus necessitating sensitive and responsive information giving processes. RECs should have particular regard to this to facilitate experimental therapies on chronically ill individuals under protective conditions.[115] The Bristol Royal Infirmary Inquiry Report stated that patients were entitled to know the extent to which the procedure they are about to undergo is innovative or experimental, to which the Government responded that it endorsed such a view which was captured in the Department of Health's *Reference Guide to Consent for Examination or Treatment.*[116] In *R v. Mental Health Act Commission, ex p X*, Stuart-Smith L. J. stated *obiter* in the Divisional Court of the Queen's Bench that '. . . it was important that the applicant should realise that the use on him was a novel one and the full implications with use on young men had not been studied, since trials had only been involved with animals and older men'.[117] However, this occurred in a specific statutory context, and there is a more pervasive and probable reliance upon a negligence/malpractice basis for recovery here. For instance, in *Estrada v. Jaques*,[118] the North Carolina Court of Appeals stated that '. . . the health care provider has a duty, in exercising reasonable care under the circumstances, to inform the patient of the experimental nature of the proposed procedure'.[119] The Alberta Court of Appeal held similarly in *Zimmer v. Ringrose.*[120] There should be substantial disclosure obligations in this context as such procedures carry an especially high level of inherent risk due to their novelty. It is crucial that patients involved in all forms of experiment, whether formal research or otherwise, have detailed information regarding the extent of existing knowledge relating to the procedure, the currently approved treatments available, and the foreseeable risks attaching to it and to research in general.[121] Informed consent must be a shield rather than a sword here.

Concluding remarks

Simms puts many unresolved issues in relief, including how innovation in medicine should proceed and what scientific evidence base should exist prior to clinical application in patients. Commenting

114 Although drastic deviations are usually submitted to IRBs in the U.S., despite not formally being considered 'research', and RECs in this country occasionally review such procedures on an informal basis.

115 It has been alleged that patients *in extremis* cannot make *informed* decisions regarding potentially risky new technologies in view of either the uncertainties involved or the weight and complexity of salient information. Uncertainty is an inherent feature of all experimental/research procedures though and whilst sick patients may undoubtedly find assimilating and assessing a substantial volume of information difficult, sensitivity, reinforcement and gradually building understanding are essential constituents of a properly informed consent here.

116 Department of Health (2001). Similarly, in the U.S. in *Gaston v. Hunter* 588 P 2d 326 (Ariz. Ct. App. 1978) the Arizona court asserted that the physician '. . . must inform his patient of the novel or investigational nature of the procedure'.

117 (1988) 9 BMLR 77. The court implied that the consent given would have been invalid on this basis, but was satisfied that the applicant did know these matters.

118 321 SE 2d 240 (N.C.Ct.App. 1984).

119 See also *Karp v. Cooley* (1974) 493 F 2d 408 (US CA, 5th Cir). Steve Winter is currently suing the federal government for damages for a failure to reveal the extent of the procedure being performed upon him to restore movement to his legs, involving the insertion of 180 wires many of which have become infected but are unable to be removed, see *The Times*, 20 September 2003.

120 (1981) 124 DLR (3d) 215.

121 See Giesen (1995, p. 28).

on the *Simms* scenario, Brazier states, without likelihood of contradiction, that the line between using a patient as a research subject and 'doing your utmost for him', is blurred, i.e. the dichotomy between clinical practice and research.[122] However, I argue that this dichotomy is an artificial and unhelpful one. There is no clear division between either therapy and research or therapeutic and non-therapeutic research. It is the quality of communication with the patient which is frequently most critical. King contends that what is required is the offer of 'meaningful justification for . . . recommendations to patients in every case'.[123] Rigid pigeon-holing and labelling serve largely to obfuscate rather than clarify.

This arena clearly displays a tension between autonomy and beneficence. Churchill et al., however, note that genuine beneficence always grounds an intent to benefit with some reasonable evidence that such intent is a well-founded and reasonable expectation.[124] It might be objected that existing practice permitting experimentation outside the formal trials context exploits the vulnerability of already desperate individuals, who will grasp at any straw of hope.[125] King and Henderson say that '[t]his is not an argument that desperate people are not decisionally capable. It is an argument that a reasonable world does not offer desperate choices, because some options are inhumane, even when they appear to hold a promise other than death.'[126] But to deny patients interventions even where potential benefit is a slim prospect is to undermine patient self-determination and to invite paternalism. Indeed, *quaere* whether withholding such a measure on wholly clinical grounds merely because of its only limited lifesaving potential might infringe Article 2 of the European Convention on Human Rights? Arguably, such individuals are not being used instrumentally merely as means to the ends of others, having voluntarily acceded to the risks and uncertainties.[127] Even where patients lack decision-making capacity, radical last resort procedures may sometimes be justified on the basis of beneficence.

It has been observed that, historically, therapy remained grounded in trust rather than consent, and was, therefore, somewhat resistant to the increased supervision applied to research with human subjects.[128] The 'freedom to innovate' based upon trust reposed in clinicians in every instance is, however, misplaced, and independent scrutiny is required, not only as a bulwark against excessive clinical zeal and pre-emption, but as a screening for what new procedures enter medical practice at all and in what way. Retrospective legal censure is insufficient patient protection in many instances, and this may be contrasted adversely with the kind of prospective evaluation undertaken in *Simms*. It is nonetheless crucial not to undermine innovation by excessive regulation. Greater engagement of the public is required, to negotiate a proper balance of creativity and protectionism.

As a postscript, it was reported shortly after the procedure was eventually applied that Jonathan Simms, then aged 19, had mercifully made a small but significant improvement, according to both his parents and clinicians, as a result of improved brain stem and swallowing function. A microbiologist specialising in vCJD, Stephen Dealler, described Jonathan's improvement as of April 2003 as 'incontestable'. Jonathan showed more responsiveness and had lowered blood pressure and heart rate, and had gained almost two stone in weight. It has more recently been reported by his father, Don Simms,

122 Brazier (2003, p. 405).

123 King (1995, p. 13).

124 Churchill, Collins, King, et al. (1998, p. 41).

125 Oberman and Frader (2003).

126 King and Henderson (1991, p. 1049).

127 Article 2 of the Council of Europe Convention for the Protection of Human Rights and Dignity of the Human Being with Regard to the Application of Biology and Medicine 1997 states that the interests of individuals must be accorded precedence over those of society.

128 Churchill, Collins, King, et al. (1998, p. 41).

that, whilst there has been no further improvement, Jonathan has remained stable and is no longer terminally ill.[129] He said that without PPS treatment there was a 100% certainty that Jonathan would already have died. Indeed, evidence of Jonathan's encouraging progress formed the backdrop to further declarations being made in analogous situations, in *An NHS Trust v. HM*[130] and *EP v. Trusts A, B & C*[131]. In fact, in the former case, the patient, a young man of 19 years, was not as gravely afflicted as Jonathan Simms. There are apparently at least eight similarly situated patients currently receiving PPS.

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129 *The Times*, 5 August 2004.

130 [2004] Lloyd's Rep Med 207 (Fam Div).

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