Waiving informed consent for unconscious patients

Aboard the Starship *Enterprise* in the 24th century: Beverly Crusher, the ship's chief medical officer, suspends a visiting clinical researcher because she administers an experimental treatment to an unconscious patient, severely injured in an accident. The patient dies. Crusher is outraged because the researcher did not first try conventional therapy. The researcher argues that the conventional approach was unlikely to save the patient, and, anyway, she now has data about the drug that will benefit others in future.

Clearly someone forgot to pick up a copy of the waiver of the regulation governing informed consent for experimental therapies in emergency circumstances, which will be published some time this month in the *Federal Register* (where regulations and other Federal agency documents are published).

In drawing up the regulations for research (which the new waiver will supplement), neither the Office for Protection from Research Risks (OPRR) nor the US Food and Drug Administration (FDA) anticipated routine research on acute-care patients (accident and heart attack victims) unable to give consent. Yet science is uncovering therapies that researchers argue need to be evaluated. For example, animal studies and limited human trials suggest that an enzyme that scavenges free radicals of oxygen that are released in the brain after a severe head injury might prevent subsequent brain damage. Researchers now want to enroll patients in a randomized, placebo-controlled trial to discover just how effective this treatment is and at what dosage.

Unfortunately, many of the potential participants will be unconscious, and thus unable to give informed consent. Sometimes the next of kin (or legal representative) are either unknown or cannot be contacted, and so are unable to provide consent by proxy. Yet the need for informed consent before any medical research remains what Thomas Murray, a bioethicist at Case Western Reserve University in Cleveland, Ohio, terms, the "gold standard".

But is it fair to exclude an unconscious patient from a potentially beneficial trial? And, if unconscious patients are to be included, how can they be protected from the overenthusiastic researcher embodied in popular culture from Frankenstein to Star Trek?

In recent years when researchers have written a protocol for experimental therapies, they have turned to both the FDA's and OPRR's regulations. Their provisions for a waiver of informed consent, however, are not compatible, and in neither case were intended as guidance for the enrollment of possibly unconscious, acute-care patients.

The FDA's regulatory exception to obtaining informed consent allows for an experimental therapy to be tried when all else has failed, and it cannot easily be applied to research. The OPRR's regulation regarding waiver of informed consent was really intended to apply to research for which the risk and degree of intervention are minimal. Two examples are research involving behavioural studies, where prior knowledge of the study might influence the outcome, and the use of data from patient records.

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Informed consent and acute-care patients: Federal agencies have clarified the circumstances in which informed consent can be waived.

Faced by regulatory confusion on the one hand and the emergence of promising therapies on the other, some researchers started using the term 'deferred consent', meaning that they enrolled patients and sought permission later for what they had already done. With a disapproving grimace, Wendy Baldwin, deputy director for extramural research at the US National Institutes of Health, calls deferred consent, "a non-concept". (The OPRR reports to Baldwin and carries out the regulations of the Secretary of Health and Human Services.)

The practice of deferred consent prompted Representative Ron Wyden (Democrat, Oregon) to hold congressional hearings last year on informed consent. The issues of research on acute-care patients and on those suffering from mental disorders were raised specifically. (If the new National Bioethics Advisory Commission is formed during the coming fiscal year, which begins this October, one of its first stated tasks will be to examine the issue of informed consent in patients suffering from mental disorders.)

Under pressure from the US Congress and researchers, the OPRR (whose regulations apply to all research funded by the Department of Health and Human Services) and the FDA have reconciled their differences in the secretarial waiver of the informed consent provision appearing this month. For the first time, patients in emergency circumstances are identified as a vulnerable population in a special category — as are fetuses and children. The secretarial waiver of the regulations quashes any notion of deferred consent, but will allow a waiver of informed consent, as long as no conventional therapy is withheld. As soon as patients can be consulted, the researcher must ask if they wish to continue with the experimental therapy.

To obtain a waiver of informed consent, researchers will have to convince the local Institutional Review Board of the scientific validity of the study and of its potential benefit. Researchers must also show, says Baldwin, that it would take too long if they can recruit only those patients able to give their informed consent before treatment. Responsibility for defining what constitutes 'too long' will, in each case, rest with the local review boards. These boards already play a key role in assessing the safety of research protocols, and, says Baldwin, will now provide oversight of research involving patients unable to give consent in emergency circumstances.

The regulations also call for researchers to educate local communities of the potential benefits of research with such patients. Says Baldwin, "If I were contemplating research on experimental therapies for, say, gun-shot victims, I'd be out there now trying to inform the local community about the plans."

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