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Doing Research on the Ethics of Doing Research

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Commentary

Doing research on the ethics of doing research

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See related research by Chenaud *et al.*, <http://ccforum.com/content/10/6/R170>

Abstract

In the previous issue of *Critical Care* Chenaud and colleagues found that most intensive care unit patients who had given informed consent for their participation in a clinical trial could not recall either the purpose of the trial or its related risks several days later. These findings should remind us that informed consent is a process, not an event, but they should not be interpreted to mean that recall is, of itself, a useful criterion for evaluating either the validity or the quality of the informed consent process. On an entirely separate note, the decision of the authors not to obtain informed consent for this study itself raises interesting questions about the ethics of doing research on the ethics of doing research.

Chenaud and colleagues [1] are to be commended for their interest in achieving a better understanding of 'informed consent for research obtained during the intensive care unit stay'. Because intensive care medicine consumes an ever increasing percentage of total health care expenditure, research to define both its benefits and limitations is a moral imperative. Ironically, ethical concerns about informed consent for clinical studies in the intensive care unit (ICU) are making this research increasingly difficult to conduct, especially in Europe [2-5].

The essential finding of this study is that research participants in the ICU may have limited capacity to retain and remember elemental aspects of studies in which they have enrolled. The authors showed that most ICU patients, when questioned 10 to 12 days after having given their consent for participation in a study (involving six blood draws over the course of a month), could not recall the purpose of the trial or its related risks. These findings are similar to results previously reported by this same team of investigators in ICU patients who underwent elective cardiac surgery [6].

What is the message of this study? As emphasized by the authors, we must remember that informed consent for research is a process, not an event, and that we have an obligation to

make sure that participants are continually reminded of the purposes and risks of a study and of their right to withdraw at any time.

However, does this study call into question the validity of the informed consent process itself? The authors remind us of the three mandatory conditions for informed consent for research, as outlined in the Belmont report [7]: communication of information about the purposes and procedures involved in the trial, including its associated risks and benefits; ensuring that subjects comprehend this information; and ensuring that subjects are able to provide consent voluntarily. Of note, none of these conditions require subjects to be able to recall this information at a later time. In other words, whether subjects can recall elemental information at a later date has no bearing on whether the informed consent was valid. In fact, there are good reasons why this should not be a factor in determining the quality of the informed consent process.

First, whether a patient has given a valid informed consent is a question that can only be asked and answered at the time when the consent is obtained. Events that happen later in the patient's hospitalization cannot make the consent more or less valid.

Second, ICU patients commonly experience neurologic derangements that limit their capacity for recall, caused both by their illnesses and by the medications they have been administered. Patients who have given their genuine informed consent under ideal circumstances may therefore be unable to recall the specifics at a later time.

Third, the severity of the risks associated with the research may affect whether they can be recalled by subjects at a later time. For patients with a critical illness, a request for six blood

ICU = intensive care unit.

draws (as in this study) might have seemed trivial and not worth remembering.

The irrelevance of recall to the quality of informed consent can be illustrated by considering a hypothetical clinical trial that involved administration of a medication that would induce retrograde amnesia. If subjects could theoretically provide fully valid consent for a study of this type, as I believe they could, then the capacity to recall the informed consent process clearly cannot be a criterion for its validity.

To sum up, this study should remind us that informed consent is not just an event that occurs at the beginning of a study, but a process that needs to be continually revisited with patients during the course of a trial. It would be a mistake, however, to claim that the inability of patients to recall elemental features of a trial at a later time is relevant to judging the quality and validity of the initial consent.

As a final note, it is curious that this study on informed consent was itself conducted without informed consent. The authors defend their decision not to obtain informed consent by noting that they obtained all of their data from the research database and from administrative files. Clearly, however, the

subjects had given consent only for their data to be used for the original purposes of the clinical research, and the investigators neither informed the subjects nor obtained their permission for these data to be used in a separate study for an entirely different purpose. As one part of the study, the investigators asked the subjects questions about their recall of earlier conversations. Subjects who were asked these questions were not aware that they were participating in a research study and were not asked for their informed consent. Other information was taken from 'administrative files' for research purposes without approval from an ethical review board. Although I acknowledge that it is very unlikely that any patients were harmed by their participation in this research, the question remains as to whether this study on the ethics of doing research itself satisfied the requirements of the Belmont report.

The report provides an opportunity to discuss and debate a great many interesting issues, from the question of how we measure the quality of the informed consent process to the issue surrounding the ethical standards that should be applied to this type of research, and as such is very deserving of our interest and attention.

Authors' response

Catherine Chenaud, Paolo Merlani and Bara Ricou

We are grateful to Robert Truog for his interesting and judicious comments on our report.

Our research article [1] actually resulted from an interesting finding identified during the conduct of a study on inflammation, in which we had to re-contact the patients 10 to 12 days after their inclusion in order to plan for blood sampling on day 28. All patients had consented to this blood sampling. We realized that some patients did not remember having consented to participate in the study, its purpose, or its risks. In these cases, we reviewed the study information and asked the patients whether they agreed to continue their participation in the study. This made us reconsider the way in which we were obtaining informed consent. We therefore established an informed consent procedure based on a protocol to ensure that patients were adequately informed by all investigators. We additionally noted whether patients read the information leaflet and asked questions during the procedure. Our objective in initiating this procedure was to ensure full adherence to the principle of autonomy. We were surprised to discover that so many patients did not remember their inclusion in the study, its subject, or the related risks.

Because problems stemming from the informed consent procedure may be frequent, we felt that it would be worthwhile to add to the debate on informed consent in

critically ill patients by sharing our findings with the medical community.

It is not unusual for multiple reports to come from a single protocol, and this also applies to studies on informed consent conducting during studies on other issues. Some of these studies require informed consent only for the main study, whereas in others the need for informed consent is waived for all aspects of the study [8-11]. We are not aware of a specific informed consent procedure being in place in these situations. Respect for fundamental ethical principles, embodied in the Belmont report [7], is essential in protecting the human research subject. It also is interesting, however, to balance the importance of informed consent, acquisition of knowledge, and study-related risks or burdens. The most important safeguard for research subjects - more so than informed consent - is a conscientious, responsible, and caring investigator.

In conclusion, we not only believe that 'the patients were not harmed by their participation', but we also feel that we tried to respect our patients' autonomy by examining our informed consent procedure. By sharing our experience with the scientific community, we hope to contribute to improvements in protection of human research subjects in future studies conducted in critically ill patients.

Competing interests

The authors declare that they have no competing interests.

References

1. Chenaud C, Merlani P, Luyasu S, Ricou B: **Informed consent for research obtained during the intensive care unit stay.** *Crit Care* 2006, **10**:R170.
2. Druml C, Singer EA: **The European Directive: a further blow to science in intensive care medicine in Austria.** *Intensive Care Med* 2004, **30**:335.
3. Silverman HJ, Druml C, Lemaire F, Nelson R: **The European Union Directive and the protection of incapacitated subjects in research: an ethical analysis.** *Intensive Care Med* 2004, **30**:1723-1729.
4. Lemaire F: **The European Directive 2001/20 for clinical research: friend or foe?** *Intensive Care Med* 2006, **32**:1689-1690.
5. Truog RD: **Will ethical requirements bring critical care research to a halt?** *Intensive Care Med* 2005, **31**:338-344.
6. Chenaud C, Merlani P, Ricou B: **Informed consent for research in ICU obtained before ICU admission.** *Intensive Care Med* 2006, **32**:439-444.
7. National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research: *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research.* Washington, DC: Government Printing Office; 1979.
8. Gammelgaard A, Mortensen OS, Rossel P: **Patients' perceptions of informed consent in acute myocardial infarction research: a questionnaire based survey of the consent process in the DANAMI-2 trial.** *Heart* 2004, **90**:1124-1128.
9. Williams BF, French JK, White HD: **Informed consent during the clinical emergency of acute myocardial infarction (HERO-2 consent substudy): a prospective observational study.** *Lancet* 2003, **361**:918-922.
10. Harvey SE, Elbourne D, Ashcroft J, Jones CM, Rowan K: **Informed consent in clinical trials in critical care: experience from the PAC-Man Study.** *Intensive Care Med* 2006, **32**:2020-2025.
11. Annane D, Outin H, Fisch C, Bellissant E: **The effect of waiving consent on enrollment in a sepsis trial.** *Intensive Care Med* 2004, **30**:321-324.