Case Two: Experimental Blood Substitute on First Response Vehicles

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Clinical trials in a number of countries are now underway to evaluate experimental, non-human blood substitute.[1] One scenario calls for the blood substitute to be available on board emergency vehicles. This allows first responders the opportunity to provide transfusion support at an accident site and on the way to the hospital. However, many of the patients who would most benefit from the use of this material may be unconscious and unable to comprehend or sign an informed consent. One possible solution would be to eliminate the need for informed consent.

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History testifies to the need for protecting human beings who serve as subjects of experimentation.[1] Requiring voluntary *informed consent* is intended to protect the life, health, dignity, and autonomy of subjects. However, in the case of first responders, waiving informed consent is justified in some cases. Understandably, the mere thought of waiving the informed consent requirement causes the entire world to shudder. The prospect reminds us of the inhumane Nazi and Tuskegee experiments.

The Nazis performed heinous experiments that included freezing and thawing humans, testing various poisons and methods of sterilization, injecting humans with typhus and malaria, testing bone, nerve and muscle regeneration, and bone transplantation. There were seemingly fetishist experiments conducted under the supervision of researchers such as Josef Mengele.[2] These experiments were justified by the "important information" they produced for furthering the German war effort, purifying the German race, and affirming German superiority. When the world learned of the horrors of these experiments, there was a collective determination to protect human beings from exploitation in the name of science. International documents such as the Nuremberg Code and the Declaration of Helsinki were composed to require the voluntary, informed consent of all human subjects.[3]

The infamous Tuskegee experiments in Alabama began in 1932, some 10 years before the Nazi experiments. They continued 25 years after the 1947 creation of the Nuremberg Code. The experiments documented the progression of syphilis in African American males. The men were not told they had syphilis, nor were they told they were subjects of an experiment. Ten years after the initiation of the study, it was discovered that penicillin cured the disease; however, the men were not treated, and the experiment continued. Many subjects died, and those who did not suffered the debilitating effects of the untreated disease. Wives were infected by their unsuspecting husbands, and children were infected by their mothers. The experiments were finally put to an end in 1972, as a result of front page articles featured in the *Washington Star* and *The New York Times*.[4] The Tuskegee experiments prompted Congress to impose federal regulations on human experimentation, requiring voluntary, informed consent of human subjects involved in federally funded experiments.[5]

To avoid the horrors of the past, informed consent is required for experiments involving humans. However, federal regulations allow for a narrowly tailored exception which permits research in emergency settings without informed consent. To fall within the exception, the research must meet the following criteria: (a) informed consent is not feasible; (b) the human subjects must be in a life-threatening situation; (c) available treatments are unproven or proven unsatisfactory; (d) participation in the research carries the prospect of direct benefit to the subjects; (e) the collection of valid scientific evidence is necessary to determine the safety and effectiveness of the particular intervention; and (f) the clinical investigation could not practicably be carried out without the waiver.[6] Allowing first responders to administer blood substitute to unconscious patients when blood loss is critical

and there is no legal representative to consent for the patient meets these criteria.

In emergency cases informed consent may not be feasible if the patient is unconscious and there is no legal representative. Moreover, there is no way for researchers to prospectively identify who in the community will suffer massive blood loss at an emergency site. When first responders determine that blood loss is life-threatening, blood transfusion is necessary to ensure patient survival during transportation. Currently, first responders administer volume expanders to increase the patient's blood volume. However, these do not support tissue oxygenation. Administering a blood substitute may benefit the patient by simulating the properties of a blood transfusion. The safety and effectiveness of the blood substitute can only be assessed without a waiver because patients suffering massive blood loss would not be able to comprehend the information being supplied to them even if they were conscious.

Of course, the fact that the law allows an exception to the informed consent requirement does not mean waiving the requirement is the right thing to do, but waiving informed consent in emergency cases is consistent with the principles underlying the requirement. Given the unthinkable treatment of human beings during the Nazi and Tuskegee experiments, the world cannot trust that all of humanity will view fellow human beings as ends in themselves, that is, as autonomous individuals who innately possess value and natural rights.[7] Instead, history has proven that at least some researchers view their subjects as means to gain scientific knowledge, or as expendable for the greater good of society. However, in the case of unconscious patients who will die without a first response transfusion, administering the blood substitute affirms the patient's value as a human being. Unlike the Nazi and Tuskegee experiments, waiving informed consent in these emergency cases attempts to benefit the patient and acknowledges his/her welfare as the most important objective.

Exceptions to informed consent are dangerous, no matter how narrowly tailored. Still, in first response situations where death is imminent due to blood loss, the humane course of action is to administer the blood substitute. To safeguard against abuses, the experimental protocol should detail the conditions under which informed consent is waived. The institutional review board (IRB) should discuss the proposed clinical trial with members of the participating communities. These discussions should include the risks and benefits of the trial, identifying groups that should be excluded from the trial, including community consultants on the IRB, and discussing other mechanisms for ensuring community involvement. The IRB should also publicly disclose information about the clinical trial to the communities involved before the trials begin. Lastly, an independent data monitoring committee should be established to oversee the clinical trials.[8]

ENDNOTES

1. In addition to the Nazi and Tuskegee experiments discussed in the comment, controversial experiments continue. Three examples include the gene therapy experiment at the University of Pennsylvania, the skin cancer vaccine experiment at the University of Oklahoma, and the AZT experiment in Africa. See: Charrow R, Bramlage JC. Biomedical research: human subjects protection. The National Law Journal. Oct. 30, 2000:B10. This reports the FDA found that researchers at the University of Pennsylvania failed to fully comply with informed consent requirements and that researchers at the University of Oklahoma misled subjects into thinking the experimental skin cancer vaccine would shrink their tumors. Also see: Lurie P, Wolfe S. Unethical trials of interventions to reduce the transmission of the human immunodefeciency virus in developing countries. New Eng J Med 1997;337:853. This explains ethical violations in fifteen of sixteen studies on AZT performed in third world countries.
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