Brian Schrag's Commentary on "Ethical Issues in Research with Children"

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Ethical Issues in Research with Children

Assessment of Risk

Benefits

Voluntary, Informed Consent

Special ethical and regulatory considerations are involved in investigator design and IRB review of research on children. I will focus on these special concerns.

One step is to identify which of four categories of research the study belongs to: 1) research that does not involve greater than minimal risk to children; 2) research involving greater than minimal risk but presenting the prospect of direct benefit to the individual child-subject; 3) research involving greater than minimal risk and no prospect of benefit to the child; 4) research not otherwise approvable under one of the above categories, but the IRB determines that the study presents a reasonable opportunity to further the understanding, prevention or alleviation of a serious problem affecting the health or welfare of children. (OPRR Reports 1981)

The study in this case calls for eighth graders to take a skin prick test of 12 different allergens including those for cockroaches and dust mites. The children are divided into three groups for the purpose of the experiment based on the following characteristics. 1) children who have self reported a diagnosis of asthma; 2) children who have wheezing but have not been diagnosed with asthma, and 3) children who have neither wheezing nor asthma.

Assessment of Risk

The first category of research does not involve greater than "minimal risk" to children. Minimal risk means "the probability of and magnitude harm or discomfort anticipated in the research are not greater in and of themselves that those ordinarily encountered in daily life or during performance of routine physical or psychological tests." Allergy scratch tests are included in the category of minimal risk. (Office of Human Subjects Research 1993, p. 3) There is a possibility that a child will go into anaphylactic shock from the skin prick tests. Anaphylactic shock can lead to death in minutes if not treated. The probability in the general population of anaphylactic shock from the skin prick tests is 1 in 1 million; the magnitude of harm is great, but the probability is small.

However, the aim of the research is to determine whether asthma and wheezing are associated with exposure and sensitivity to cockroaches and dust mites. If that turns out to be the case, then there is a possibility that children in groups 1) and 2), who have asthma or wheezing, may have already developed a sensitivity to these allergens. Hence, the probability of anaphylactic shock may be higher for them. That probability is, presumably, unknown. The probability of risk for subjects in these two groups may thus be higher than for the general population and those in the control group who do not have asthma or wheezing. However, the risk for those in the two experimental groups is no higher than it would be if their parents had decided, because of the children's symptoms, to take them in for allergy testing on their own. The control group, on the other hand, might not otherwise undergo the scratch tests and hence incur the 1 in 1 million risk of the scratch test.

It is also the case that the tests will be conducted in a setting prepared to deal with such reactions and perhaps with heightened awareness to the possibility of reactions. Does this set of experimental conditions move the research subjects to a category higher than minimal risk? It is not clear that it does.

Benefits

There are some direct material benefits for all participants from participating in the program. 1) All participants would receive a free allergy test. 2) All participants would receive free assessment of levels of these allergens in their homes. 3) All would receive some inexpensive materials for control of dust mites and cockroaches.

Who stands to benefit from results of this research? If it should turn out that asthma and wheezing in children in groups 1) and 2) is caused by dust mites or cockroaches or both, then children in these two groups would presumably benefit significantly and directly from the findings since the source of their problem will have been identified and thus may be alleviated. For them, this study falls in the category of therapeutic research. The population of all children who are at risk when exposed to these elements also may benefit significantly from this knowledge. Recent publicity suggests that the number of children with wheezing and asthma is substantial and increasing and may be linked to allergies to dust mites and cockroaches. The benefits to the two experimental groups may well be said to offset the risks.

The results presumably would not directly benefit those in the control group who are resistant to these allergens, unless, of course, even they could become sensitized given high enough allergen levels. Children in the control group might have siblings who are sensitive to these allergens, and the siblings might benefit directly from the research results. The benefits for the control group are minimal. Children in the control group will be exposed to the risk of anaphylactic shock, which they would presumably not otherwise incur, but that risk is deemed minimal.

Voluntary, Informed Consent

A second consideration in the study is the process of obtaining voluntary, informed consent. The case does not indicate the socioeconomic level of the participants. If they are from a low socioeconomic and educational background, there is a possibility that they will be unduly swayed by the offer of free allergy tests and modest environmental interventions. That possibility must be taken into consideration.

Human subjects research guidelines for children require that the permission of parents or guardians must be obtained, since children are considered unable to give legally valid informed consent. However, the children in this case are in the eighth grade and are capable of providing assent. Hence, they should be asked if they assent to participating in the research.

The information given to subjects and parents should certainly include the purpose of the experiment and the risks and benefits involved. In the case of the control group, it should be made clear to both parents and children that their involvement is

not for their own benefit but for the benefit of others.

The information must be made available in a manner easily understood by both parents and children, particularly if they are from a disadvantaged population. It would be appropriate to include some general educational information on problems associated with asthma and allergies so all can understand the significance of the research and, in the case of groups 1) and 2), they can learn something about the conditions they have.

If a participant experiences anaphylactic shock at some point during the allergy tests, it would be appropriate to inform the other participants and give them the option of withdrawing from the experiment.

References

- Office of Human Subjects Research Information, National Institutes of Health. "Research Involving Children," Sheet 10. Revised 10/93. N. p.: National Institutes of Health, 1993.
- OPRR Reports, "Protection of Human Subjects," Title 45 Code of Federal Regulations, Part 46 Subpart D -- Additional Protections for Children Involved as Subjects in Research. Revised June 18, 1981.