RESEARCH ETHICS

Ethical reflections on Edward Jenner's experimental treatment

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In 1798 Dr Edward Jenner published his famous account of "vaccination". Some claim that a Research Ethics Committee, had it existed in the 1790s, might have rejected his work. I provide the historical context of his work and argue that it addressed a major risk to the health of the community, and, given the devastating nature of smallpox and the significant risk of variolation, the only alternative preventative measure, Jenner's study had purpose, justification and a base in the practice of the day.

In 1798 Dr Edward Jenner published an account of "vaccination",¹ arguing that this gave safer protection against smallpox than the existing treatment, variolation. Proponents of immunisation, a technique that developed from Jenner's work, often claim that a research ethics committee, had it existed in the 1790s, might have rejected his work.

Is it therefore possible, more than 200 years later, to assess this claim and the ethical standard of Jenner's work in its historical context? This paper looks at a (hypothetical) review of Jenner's experiment and discusses its ethical dimensions.

THE BERKELEY LOCAL RESEARCH ETHICS COMMITTEE 1795

DRAMATIS PERSONAE

Chairman of the Berkeley REC
The rector of Berkeley
Zebediah Cowstock, a local farmer
Mr John Moore
Archibald Turner, the town apothecary
Dr Reginald Arbuthnot, a local doctor
Lady Sarah Wright
Dr Edward Jenner
CHAIRMAN

"Members, thank you for attending. Dr Jenner has kindly agreed to attend and discuss his application."

EDWARD JENNER

"Mr Chairman, my work is designed to explore how we might prevent people contracting smallpox, and I believe cowpox, a disease in our countryside, may hold the answer. What I have suggested in my application may seem dangerous but I would propose it is no more than an improvement of current preventive measures based on our modern experimental methods. Let me place my work in context. Smallpox is a serious threat to our community and our current methods for prevention carry significant risk of death and disfigurement. This technique is called "variola-tion" and uses fluid from smallpox vesicles. I

believe that fluid from cowpox vesicles could protect more safely and that there are persuasive theoretical reasons to believe inoculation for the cowpox will be of greater benefit than current variolation. My modification to this technique is based on a long history of country folklore, supported by my own observations.

Much effort has been spent in trying to prevent smallpox, starting in this country when Lady Mary Montague, wife of our ambassador in Constantinople, brought the technique of inoculation for the smallpox (variola-tion) to England. Variolation is achieved by placing a small amount of the fluid from a smallpox blister into a small cut on the recipient's skin. It suffered setbacks, the deaths of the Earl of Sunderland's 2 yr old son the Hon William Spencer and a 19 yr old son of the footman of Lord Bathurst, but, subsequently, Dr James Jurin, secretary of the Royal Society, established annual reports.² He reported a death rate for smallpox of 1 in 5 or 6 and a corresponding lower fatality rate for variolation of 1 in 48 or 60. Dr Nettleton added further evidence in 1722. He reported 3405 cases of smallpox, of which 636 died. At the same time he reported 61 variolations with no fatalities.³ In 1752, Mr Brown, apothecary in Salisbury, reported his experience of variolation. He inoculated 422 persons of whom 4 died.⁴ Dr Maty FRS reported his experience from Geneva, vaccinating foundlings. All recovered.⁵ In 1754, Monsieur Bonnet (FRS) of Geneva wrote to John Clephane reporting his experience in Geneva.⁶ This author reported good results in 70 people but wrote "But I presume that the French will be a long time in adopting the practice of inoculation. The clergy there throw a terrible obstacle in its way."

Thus, while variolation can provide protection against the smallpox, it carries a significant risk. In 1767 Josiah Wedgwood decided to variolate his two children Sukey and John. Both had convulsions as the rash developed and he wrote:

"they have had a pretty smart pox as our doctor terms it, but both have been so very ill that I confess I repented what we had done, and I much question whether we should have the courage to repeat the experiment".⁷

There is an illness to which the horse is subject that is called the "grease" which seems to generate disease in the human after it has gone through modification in the cow. This human disease is called the cowpox. Any person so affected seems to be secure from smallpox.⁸⁻¹⁰ I also have cases that support this commonly held belief. In fourteen cases under my supervision, variolation failed to take, and all had previously contracted cowpox.

I now wish to collect fluid from a human cowpox vesicle and inject it into the skin of a

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suitable child subject. I have found two references to a similar process in my researches."¹¹⁻¹²

RECTOR OF BERKELEY

"Dr Jenner I must express disquiet. I believe that your project interferes with the natural order. You will know and have mentioned that many religious men raised objections. You refer to only a few of many condemnations."

EDWARD JENNER

"Current experiments don't question the divinity, rather they try to explain His workings. The great Sir Isaac Newton, the greatest scientist our country has produced, sought to explain our world as God has created it. Our motive is to undertake this work for the benefit of mankind."

ZEBEDIAH COWSTOCK

"I myself am most concerned. I lose several of my farm hands a week at a time when they go down with this contagion cowpox, and we know that they can contract it again and again."

EDWARD JENNER

"I thank you for your comments, but I ask you to think of the benefit you will accrue from the eradication of the smallpox. I believe that any reduction in illness will help your farms".

JOHN MOORE

"I'm very concerned about injecting material, particularly when it has come from an animal such as a horse or a cow. It is unnatural and might it not introduce animal spirits?"

EDWARD JENNER

"None in my practice of variolation have thus suffered. We now have 80 years of experience. Furthermore I see enormous benefit coming from my work, and a small risk is justified."

ARCHIBALD TURNER

"Dr Jenner, after injecting the cowpox fluid, I understand you intend to challenge your patient with smallpox? How could you possibly justify this deliberate exposure to a disease you have just admitted carries such a terrible possibility of death or disfigurement?"

EDWARD JENNER

"I would be offering my patients variolation anyway. The design of my project allows me to use this not only as therapy but also the end point of my experiment."

DR REGINALD ARBUTHNOT

"Dr Jenner, how will you know it is the treatment that has effected the protection? Recent studies have talked about the need for patients that "have been treated exactly the like in every respect besides (the experimental process)".¹³⁻¹⁵ Shouldn't your study be similar?"

EDWARD JENNER

"Such work requires the doctor to be in doubt as to which treatment is better, to be in "equipoise". I am not in this position. I would be offering some of my patients inferior treatment. Not only would this be unethical but also my practice would suffer. My arguments convince me that vaccination will be safer than variolation, I therefore can't justify a control group."

THE CHAIRMAN

"How will you seek consent?"

EDWARD JENNER

"As a doctor I offer my professional skills to any who attend and I assume consent. I have no monopoly. I do, however, recognise that my method is experimental and I have followed the example of Doctors Warrick and Cowper who discussed their experiments with colleagues first and obtained their agreement before offering it to their patients.¹⁵⁻¹⁶ They clearly felt that patients might not be in a position to balance the value and risk of what they were being offered."

CHAIRMAN

"Dr Jenner, might I ask how whether you would identify your patient?"

EDWARD JENNER

"At the moment, I propose to follow current practice and use full names but I would appreciate the committee's advice as there seems to be no consensus. I have found some that don't divulge subjects names¹⁷⁻²¹ although others do.²²⁻²⁵ Some do both.²⁶"

LADY SARAH WRIGHT

"Dr Jenner, I'm really very unhappy about your proposal to experiment on children. Don't you think your early work should be on adults?"

EDWARD JENNER

"I understand your concerns but I can be more certain whether children have or have not had either the smallpox or the cowpox, factors which would obviously affect my results. The results of my experiment will therefore be easier to interpret. Secondly children are more vulnerable to the smallpox than adults. Remember I do not start from any position of equipoise."

CHAIRMAN

"If Lady Sarah is happy with that answer, I don't think there are any more questions. Dr Jenner, perhaps you could withdraw, we will finish our deliberations. Our Secretary will let you know our decision."

Dr Jenner leaves.

CHAIRMAN

"I believe we have given Dr Jenner a fair hearing and to aid our decision perhaps I could crave the committee's indulgence and summarise our interview with Dr Jenner. I might divide it into some key areas."

Purpose and justification for doing this research

We must ask ourselves whether we feel this research is worthwhile. Does it improve care or deepen our understanding of disease/illness? Does it address an important area of the health of our people and will it answer the question the researcher has posed?

Demonstration of the validity of the project

Does this project fit in with our current understanding and is it a logical development of our practice today and management of disease and can we see that it is founded upon current based on?

To address this, we may wish to ask if any respected doctors have looked at Dr Jenner's proposal, to look at his method and help us assess the potential risks and possibility and nature of any harm. We may also wish to consider his arguments against a placebo arm to the study.

Delineation of possible adverse consequences for any subject

We need to ask ourselves if there are ways these might be recognised and what would be done if a patient was harmed.

We might also wish to think about the criteria for suspending or terminating the research study as a whole.

Delineation of potential benefits

Dr Jenner feels there will be enormous benefit. Will these be fairly and dispassionately explained? We might be concerned that these, along with their relationship with Dr Jenner, may coerce families to be recruited against their best interests.

Method(s) of recruitment

We need to assure ourselves that any subject is able to agree to take part without being forced or deceived.

We might wish to know how initial contact and recruitment will be conducted, how information will be given and whether the extra procedures are to be clearly explained.

Do Dr Jenner's explanations satisfy us?

Using children as research subjects

Is it acceptable that he will start this study with children and, if so, is their recruitment, consent (presumably from parents) and care adequately detailed?

Dissemination of results

Are the arrangements for dissemination satisfactory and should they be fed back to the subject?

However this is planned, is it explained to the subject before entry?

Confidentiality

Who will have access to the personal data of the patients that Dr Jenner will recruit, and are the arrangements for confidentiality adequate?

Does Dr Jenner have any conflicts of interest?

Arrangements at the end of the study

If this technique is successful, will it be available to the community? Will the community benefit from the study?

When we have deliberated, we have four possible decisions.

APPROVE or give FAVOURABLE OPINION

APPROVE CONDITIONAL UPON SPECIFIED CHANGE (and what would these be?)

NO DECISION POSSIBLE (requiring expert review)
REJECT"

Email your decision to the journal.

Competing interests: None.

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