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Editorial

Ethics and evidence based research: Is there a conflict?

No, not only is it possible for a plastic surgeon to conduct ethical evidence based research, but also it is mandatory. How are ethics defined and how is high quality research defined?

PLASTIC SURGERY RESEARCH ETHICS IN THE 19TH AND 20TH CENTURIES

Plastic surgery research dates back to the beginning of the 19th century. Joseph Carpue, the father of modern plastic surgery, only had second hand knowledge of the techniques of nasal reconstruction that had been perfected over the course of centuries in India. Carpue was a scientist and as a scientist, he knew that for any scientific claim to be valid, it had to be independently duplicated. How did Carpue act ethically? Ask yourself the questions, what would you do if you had a patient who would benefit from an operation that you had neither seen nor done before and the surgeon most experienced in the technique was unavailable. What would you tell your patient? What Carpue did was to first practice forehead flap nasal reconstruction on cadavers and then he told his patient what he had learned and truthfully admitted that he had never done the operation on a live patient.[1]

Carpue had only his curiosity and conscience to guide him. Looking to America 50 years ago and we find a different ethical solution published in Plastic and Reconstructive Surgery almost half a century years ago. A 28 year-old quadriplegic, who was being treated for a sacral pressure sore, had skin flaps created on his posterior calves. The flaps were supposedly identical and were purposely designed so that there would be flap necrosis! One flap was treated with dimethyl sulfoxide (DMSO) while the other flap was not.[2] One year later the same authors published their definitive research on rats and referenced their unblinded n of 1 study, in which one flap may have inadvertently been a sural artery flap and the other skin only. They had either the ignorance to believe or the audacity to claim: 'In the clinical case described in our previous report, *the obvious beneficial effect* of DMSO on pedicle flap tissue in man was shown'.[3] (Emphasis mine)

What clinical benefit did this patient who had entrusted the care of his sacral pressure sore gain from being a guinea pig who had flaps created that were destined to die? We do know that the alleged benefits of DMSO were insufficient for the drug to be used.

What beneficial effect did DMSO have for the patient? Who profited from this controlled clinical trial? The paper's financial disclosure stated that Merck Sharpe and Dome, a predecessor of Merck, and a local cancer association had funded the research. Was the patient paid to be a guinea pig? Was he told that his flaps were purposely designed to die? Were the authors paid for their clinical case? Were there any repercussions for the authors?

The only objection to be raised was by John Remensnyder, who was then a young trainee and who would eventually become the chief of plastic surgery at Massachusetts General Hospital. Remensnyder wrote an editorial in Plastic and Reconstructive Surgery where he noted that the 1945 Nuremberg Code was the standard that existed for defining the ethical requirements of human research.[4] He did not state that the experiment on the paraplegic patient violated the Nuremberg Code, but that would have been obvious to anyone who reads the code.[5] Rather Remensnyder recommended that 'we must keep intact not only his right of voluntary consent but also his unfettered right of dissent'.

History has shown that this ethical lapse was ignored by or unknown to the plastic surgery establishment in

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the United States. Years later, one author was elected to the presidency of the American Society of Plastic and Reconstructive Surgeons while his partner another author was elected to a 7-year term on the American Board of Plastic Surgery culminating in his chairing that board.

Now, it is easier to do clinical trials of high quality in an ethical manner if for no other reason that we now have universally available definitions of what are clinical trials, what constitutes quality, and what is ethical.

WHAT IS A CLINICAL TRIAL?

The most widely accepted definition of what is a clinical trial is that adopted by the World Health Organization.[6] It states:

'For purposes of registration, a clinical trial is any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on the health outcomes. Clinical trials may also be referred to as interventional trials. Interventions include, but are not restricted to drugs, cells and other biological products, surgical procedures, radiologic procedures, devices, behavioural treatments, process-of-care changes, preventive care, etc'.

For plastic surgeons, the most relevant points in the definition are that a clinical trial is prospective, that there need not be a control group and that it is not limited to the use of drugs or surgery.

WHAT CONSTITUTES QUALITY?

Last year, the Centre for Evidence Based Medicine in Oxford updated its levels of evidence that had grown too complex and unwieldy with it having grown to 10 evidence levels. The 2011 levels of evidence have been reduced to five.[7]

The 2011 levels for treatment useful for plastic surgeons are:

- Level 1: Systematic review of randomized control studies
- Level 2: Randomized trials
- Level 3: Non-randomized controlled cohort/follow-up studies
- Level 4: Case-series, case-control studies, or historically controlled studies
- Level 5: Mechanism-based reasoning

In general, the lower the number of the level the higher the quality of the research.

WHAT IS ETHICAL?

Determining what is ethical is much simpler in 2012 than it was in Carpue's time. The Nuremberg Code was developed in response to the Nazi's human experiments during World War II. The Declaration of Helsinki (DOH) was adopted by the World Medical Association in 1964.[8] It has undergone a number of amendments with the latest version having been adopted in Seoul in 2008.[9] Most major plastic surgery journals, including this one, require that as a condition of publication that all submissions comply with the latest version of the DOH. In other words, all prospective studies must comply with the DOH.

It is imperative that any physician planning to be involved in plastic surgery research from the earliest stage of formulating a project to the final stage of peer-reviewing it read and understand the DOH.

WHAT MUST PLASTIC SURGEONS NOT FORGET ABOUT MAKING THEIR CLINICAL RESEARCH ETHICAL?

The following points are those where plastic surgery research has been lacking:[10,11]

- Authors forget to note in their submissions that they have complied with the DOH. (DOH Article 14)
- Authors do not realize that the DOH is not limited to research on patients alone but also includes research on a human material and data. (DOH Article 1)
- Authors forget to note that their clinical trials have been approved by an independent research Ethics Committee before the trial begins. (DOH Article 15)
- Authors forget to provide proof, such as the trial registration number, that their clinical trials have been registered in a publicly accessible database before the first patient is enrolled. (DOH Article 19)
- Authors forget to note that they have received informed consent from their patients. (DOH Article 24)
- Authors forget to note that they have received informed consent from their patients' data or clinical material. (DOH Article 25)
- Authors believe that they can retroactively correct their omissions such as registering a trial after it has been completed and still have their research be published.

Editors and publishers have ethical obligations too. The DOH states, 'reports of research not in accordance with the principles of this Declaration should not be accepted for publication'. (DOH Article 30)

M. Felix Freshwater

Voluntary Professor of Surgery University of Miami School of Medicine, 9155 S. Dadeland Blvd. Suite 1404, Miami FL 33156-2739, USA
E-mail: mfelix.freshwater@gmail.com

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