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# The 1996 Continuous Negative Extrathoracic Pressure (CNEP) Trial: Were Parents' Allegations of Research Fraud Fraudulent?

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SPECIAL ARTICLE

**Editor's Note**

**Abuse of Child Abuse Experts in England**

*I have watched with dismay this story evolve in England for over a decade. It's a complicated story described in detail in the Chadwick et al and Hey articles in this issue.*

*In my opinion neither of these doctors should ever have been put through this ordeal. There is something grossly wrong with the medical and legal system, which allowed this to happen.*

**—Jerold F. Lucey, MD**

# The 1996 Continuous Negative Extrathoracic Pressure (CNEP) Trial: Were Parents' Allegations of Research Fraud Fraudulent?

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The author has indicated he has no financial relationships relevant to this article to disclose.

PEDIATRICIANS in Britain have been watching with increasing incredulity the convoluted and dysfunctional way that their regulatory authorities have investigated allegations that fraud occurred during the conduct of a randomized, controlled trial reported in *Pediatrics* in December 1996.[1] The study under scrutiny took place at Queen Charlotte's Hospital (London, United Kingdom) and the North Staffordshire Hospital (Stoke on Trent, United Kingdom). It was designed to determine whether the use of continuous negative extrathoracic pressure (CNEP) reduced the number of preterm infants with respiratory failure needing tracheal intubation, the length of time they needed intubation, and the time it took for them to be weaned from supplementary oxygen. It reported a marginal but statistically significant improvement in early respiratory outcomes and an even more marginal, nonsignificant increase in the number of infants in the CNEP group who did not survive to discharge.

However, at least 1 family lodged a formal complaint over the way the trial had been conducted 5 months after the research article appeared, and even today, 9 years later, the issues raised by that complaint still remain unresolved. The proper conduct of clinical research, and the proper conduct of investigations into allegations of research misconduct, are rightly issues of concern to clinicians everywhere. It is worth recounting, therefore, what went wrong with the investigation of those allegations by the United Kingdom's various regulatory authorities.

The initial complaint was widely reported. Indeed, 1 early headline in a national Sunday article read "Parents say 'guinea pig' trial killed their babies,"[2] and headlines like this soon attracted the attention of a small but very active and well-organized pressure group[3] that was already extremely hostile to the work of Professor David Southall, one of the principal instigators of the CNEP trial. The hostility stemmed from his use of covert video surveillance (under a police-approved protocol)[4] to investigate why some infants suffered repeated episodes of apparently inexplicable life-threatening apnea.[5] Their input gave added publicity to the first family's allegations, and it was not long before other mothers came forward to voice similar concerns. One family eventually persuaded their Member of Parliament to take their concerns to a government minister, and soon after that, the Department of Health instituted a formal inquiry into what was going on in Stoke on Trent. The panel of 3 conducting the inquiry (which included a pedia-

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The author readily admits to a concern that clinical research designed to safeguard the interests of people who need medical care could have been jeopardized by some of the events mentioned in this commentary. He asked but was not allowed to see any of the original case notes and consent forms for children involved in this trial, but he has had access to much photocopied material and to all the material that has appeared in the press and on various campaign Web sites.

**Key Words**

continuous negative extrathoracic pressure, Guinea pig babies, consent forms

**Abbreviation**

CNEP—continuous negative extrathoracic pressure

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trician, Professor Terry Stacey) thought that they had found enough concern to recommend root and branch reform of the whole of the country's existing framework for regulating clinical research.[6] The report stressed that it had never "sought to determine if allegations of poor practice were true," but that was not how the media[7] and the medical press[8] interpreted the findings, and the government has never taken any action to correct the general public's perception that the report was a direct attack on the clinicians in Stoke on Trent. It also has not ever managed to admit, in public, any of the report's many errors and deficiencies.[9]

The Department of Health has always been remarkably anxious to stress that its report never influenced the hospital's abrupt decision to suspend Dr Martin Samuels and Professor Southall (the only clinicians running the CNEP trial also involved in child abuse work) in November 1999. Given that the first draft of the department's report had only been completed a few weeks earlier, this is hard to believe. Local management must have received some intimation of what it contained. Both pediatricians remained under suspension for 2 years and only returned to work after 3 additional internal inquiries led hospital management to conclude that there had been "no misconduct, and no incompetence."[10] What those inquiries found has never been made public. Neither has the public ever been told what happened after 7 families asked the police to investigate their claims that consent documents had been forged.

However, the outcome of an independently conducted follow-up study of the children in the CNEP trial is soon to appear in *Lancet*,[11] which shows just how willfully and blatantly early press reports distorted the known facts.[1] Claims that "[t]wenty eight infants died after suffering appalling injuries in controversial experiments conducted by one of Britain's top consultants" appearing under the banner headline "X-files of the Guinea Pig Babies"[12] were frankly libelous, although they went unchallenged at the time. The follow-up study, conducted as recommended by the government enquiry, makes it clear that "hospital trials" did not "kill premature babies." Four fifths of the infants survived, although most were born with lungs so immature that that they would have died without respiratory support from birth. Infants assigned to receive standard treatment with a tube through the larynx were marginally less likely to die than those in whom CNEP was used to minimize pulmonary atelectasis, but marginally more of the survivors were disabled. Both the differences were small and well within what might be expected by the play of chance.

## DEALING WITH THE CORE ACCUSATION

The *Lancet* report, however, does not address the most serious of the criticisms leveled at the clinicians in Stoke on Trent—that consent documents had been forged. The General Medical Council (the United Kingdom body that can strip a doctor of the right to undertake any medical work) is known to have had these allegations under review for 9 years now, but neither the profession nor the public has ever had much idea what was under investigation until the Court of Appeal (the country's second highest appeal court) finally lifted the veil slightly at the end of last year.[13] We now know that 3 of the authors of the 1996 article (Dr Samuels, Professor Southall, and Dr Andrew Spencer) still face accusations that, among other things, they (1) deceived the local research ethics committee (the United Kingdom's equivalent of an institutional review board) about the benefits and safety of the CNEP technique, (2) performed unnecessary cesarean sections specifically to ensure an adequate supply of premature infants for the trial, (3) fraudulently misrepresented the trial's results to further their personal financial interests in the development of CNEP equipment, (4) conspired to misreport postmortem results to prevent any death being treated as caused by trial treatment, and (5) forged 1 woman's signature on the consent forms or, alternatively, (6) entered her daughters into the trial without first giving her an information leaflet and obtaining her informed consent.

The United States has a body capable of mounting a rigorous investigation into such allegations of research misconduct, but many countries do not. The United Kingdom's General Medical Council has not managed to mount a competent investigation into these allegations, and the "research governance" bureaucracy that the government set up in the aftermath of its own flawed enquiry into the "CNEP affair" has also failed to meet this need. Yet, without a body capable of investigating allegations of research misconduct fairly, efficiently, and quickly, it is very difficult not only to identify misconduct when it has occurred[14] but also to reassure the public when it has not and thus protect the reputation of those wrongly impugned.[15] An alert institutional review board or ethics committee can usually stop poor and unethical research before it gets started, and a case can be made for monitoring the progress of research studies after approval, although it is difficult to do this effectively without incurring costs that make it difficult to mount trials that lack a commercial sponsor.[16] There is little good evidence that the United Kingdom government's current governance strategy has improved the way that medical research is currently conducted and plenty to suggest that it is making research more difficult. The best deterrent to research misconduct is a fear of being found out and the sure knowledge that misconduct will be treated with the utmost severity. If you trust someone, they are much more likely to behave in a trustworthy way[17]; if they do not, you sack them. It could, and ought, to be as simple as that.

## SO WERE CONSENT FORMS FABRICATED?

Thirty-four doctors must still be wondering if they could face allegations of fraud >12 years after they recruited infants into the CNEP trial in Stoke on Trent, so it is easy to understand why many United Kingdom clinicians have become reluctant to undertake neonatal research in the last few years. Therefore, it is of some interest to try and assess just how plausible the various currently unresolved allegations of consent fraud really are. The government panel, which was the first to look into some of these allegations, is recorded as having agreed with parents that 3 of the signatures it was shown while interviewing families "could have been fabricated." The panel is also known to have passed these allegations on to the hospital authorities for additional investigation in mid-1999, but there is no published evidence to suggest that those authorities found the allegations well founded.

On the basis of what parents told others, including the press, hospital managers may have been asked to look into 10 claims that consent forms were not genuine. Eight children had been in the neonatal CNEP trial, 1 was in the small parallel trial of the use of CNEP for bronchiolitis, and 1 had been treated with CNEP for bronchiolitis without the context of a research study. All 9 of the trial children had, somewhat improbably, been randomly assigned to receive treatment with CNEP, and all had died or been left with a serious disability. Seven different doctors are believed to have signed the relevant consent forms, and none yet report having been interviewed. Is it really likely that 7 different junior doctors were involved in research fraud when none of them had anything to gain by compromising themselves in this way? One family is said to have claimed that forms relating to 2 different children were both false. Another is thought to have claimed that 3 different consent forms were not genuine. The families alleging fraud were obviously upset and distressed, but they also stood to gain much if their claims were upheld.

The stance taken by the first family to claim that forms had been forged has been particularly complex and inconsistent. One of their claims is that the form giving consent to "a research investigation," which was supposed to have been signed when their child was 6 hours old, must be a forgery because the child's first name is on it, and they had still not decided on a name at that stage. That is hard to reconcile with the fact that the child's first name is also on several nursing charts that were started within hours of birth, as the parents must know because they possess copies of all the relevant case notes. These parents (like most families in the trial) also later received a letter from some of the nurses involved in the trial. This letter reminded them that they had "agreed to enroll [their child] into [the] study comparing negative pressure respiratory support and standard treatment" and asked what they thought of the care received. The mother's reply shows that she clearly knew that 2 approaches to care were undergoing comparison because she says in a long, detailed, freehand comment that, having had children cared for both ways, care in a CNEP tank seemed "more effective than in a normal incubator." This is hardly the response of a family who did not know that their child was in a research study, although that is what they now claim.

Doctors are happy to be held accountable for their actions, but they also look to have managers and administrators held publicly accountable. Civil servants and their political masters should also face public scrutiny. That has not happened in this case. What has happened is Kafkaesque. I conclude that at least some of the accusations of consent fraud may have been fraudulent, and it is high time the public was told the truth about these allegations.

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