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Complementary and Integrative
Medical Therapies

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Alan Lisbon, MD
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Beth Israel Deaconess Medical Center
330 Brookline Avenue
Boston, MA 02215

Dear Dr. Lisbon,

I write in response to the February 13, 2003 letter from Christina C. Borrer, PhD, Director of the Division of Compliance Oversight, Office for Human Research Protections. Listed below are responses to the allegations included in that letter regarding research protocol 96-12-10-0486, "Survey of Two Homeopathic Practices Documenting the Treatment of Acute Otitis Media," originally submitted in December 1996.

(1) The research project failed to ensure that risks to subjects are minimized by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and that risks to subject are reasonable in relation to anticipated benefits, if any, to subjects, as required by HHS regulations at 45 CFR 46.111(a)(1) and (2).


This was an observational study. The study design was to observe the usual practice in the offices of two physicians, one a board certified family physician the other a board certified pediatrician, who routinely use homeopathic medicine in diagnosis and treatment. Parents chose these physicians because they desired homeopathic medicine. All of the subjects in the study were established patients in these physicians' practices.

There was no treatment intervention as part of the study. Study subjects received usual care from their physician of choice. The

role of the investigators was to document and summarize these practices in order to inform subsequent research.

Treatment was prescribed according to the usual practice of the participating physicians. Homeopathic medicines were used for analgesia and temperature control as well as the treatment of the infection. All homeopathic medicines used in the course of this study were included in the Homeopathic Pharmacopeia of the United States. There was no prohibition of the use of other analgesics or anti-pyretics. Antibiotics were available and, indeed, were used to treat two study subjects.

A diagnosis of otitis media was made by standard methods (pneumatic otoscopy) and confirmed by additional non-invasive techniques available to the study used for differentiating air filled "normal" or fluid filled (abnormal) middle ear space (acoustic reflectometry and tympanometry).

Although the informed consent mentions that a nasal swab would be obtained, in fact, both MD homeopaths decided not to proceed with nasal swabs and none was obtained for any of the research subjects. In retrospect, this should have been identified as a modification of the protocol (i.e. the omission of a diagnostic test) and should have been reported to the IRB. 

Study subjects were contacted one day, two days and three days after their initial entry to this observational study, and were seen again two weeks after their initial visit. They were seen for a third time four weeks after entry into the observational study. As such, study participants received closer follow-up from their chosen physician than would have normally been the case outside of this observational study.

(1) The informed consent document for the research project failed to adequately address the following elements required by HHS regulations at 45 CFR 46.116 (a):

(a) Section 46.116(a)(2): A desc

(b) ription of the reasonably foreseeable risks and discomforts.

A description of risk and discomfort is present in Section D4 of the consent form and reads as follows: "Taking part in the study may take more of your time than a routine office visit for an ear infection. Your child may experience discomfort when his/her nose is swabbed." (As mentioned, although consent was obtained to perform nasal swabs, these were not performed).

(c) Section 46.116(a)(3): A description of any benefits to the subject or others that may reasonably be expected from the research.

The potential benefit of the physician having information about bacterial pathogens present in the child's nose is listed in Section D5 of the consent form. The informed consent also states that the principal purpose of this study was to, "learn about how ear infections are treated by medical doctors who practice homeopathy."

(d) Section 46.116(a)(4): A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subjects.

A description of alternative procedures is present in Section D6, and includes the following: “You may choose whether or not your child will take part in this research. Whatever your decision, you understand that your child’s care is independent of taking part in this study. You are free to change your mind about your child’s participation at any time during the study. If you chose for your child not to take part, your child will be treated in the usual manner for his/her condition by your physician.”

(e) Section 46.116(a)(6): For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained.

A statement of availability of treatment in the event of research injury is present in the consent form at the bottom of page 3 and reads as follows: “I understand that the Beth Israel Deaconess Medical Center has no formal program for compensating patients for medical injuries arising from this research. Medical treatment will be provided for injuries at the usual charge to me or my insurer unless payment is otherwise provided for in this consent form.”

A statement about where further information can be obtained can be found at the end of the consent form and reads as follows: “If I wish additional information regarding this research and my rights as a research subject, or I believe I have been harmed by this study, I may contact the Chairman of the Medical Center’s Committee on Clinical Investigation at (617) 667-4272.”

(2) The research involved children; the risk of the research was more than a minor increase over minimal risk; the research had no prospect of direct benefit to the subjects; the intervention was not likely to yield generalizable knowledge about the subjects’ disorder or condition which is of vital importance for the understanding or amelioration of the subjects’ disorder or condition; and therefore was not approvable under HHS regulations at 45 CFR 46.406.

The objective of this study was to observe usual practice of the treatment of otitis media by medical doctors who routinely use homeopathic methods. The research component included recording: (a) the diagnosis (by methods outlined above); (b) the treatment chosen by the physician when practicing in his/her usual standard of care (i.e. which includes homeopathy); and, (c) the clinical course of each study subject. A research assistant called study subjects at frequent intervals (days one, two and three following entry into the study) to document each subject’s clinical status. Children were also seen again in follow-up at two weeks and four weeks after entry into this observational study. Antibiotics were prescribed when deemed appropriate by the physicians caring for these patients.

Parents of study subjects were accustomed to and had chosen these particular practicing physicians because the parents desired homeopathic care. The study subjects were being cared for by their parents’ selected physicians. There were no additional treatment interventions, but rather, an observation of usual practice by medical doctors who routinely use homeopathic care in the treatment of otitis media. The purpose of this study, namely, “to learn about how ear infections are treated by medical doctors who practice homeopathy” is clearly stated at the beginning of the informed consent.

The investigators' goal was to use data from this study to identify study criteria for any subsequent scientifically-based randomized trial to assess the efficacy (or lack thereof) of homeopathic medicines compared with standard allopathic medicines (i.e. anti-microbial agents).

At the time the study was proposed (1996), the medical literature included epidemiologic evidence of the frequent use of alternative medicine (including homeopathy) by children. In an article by Spiegelblatt, et al (Pediatrics, 1994 94;6:811, "The use of alternative medicine by children"), a survey of 1,911 children in a pediatric outpatient department of an urban university general hospital suggested that 11% of children previously consulted one or more alternative medicine practitioners. More specifically, chiropractors, homeopaths, naturopaths and acupuncturists accounted for 84% of the alternative medicine professionals consulted by parents of children. Homeopathy was second only to chiropractic in the frequency of use. Moreover, ear, nose and throat conditions were the second most commonly cited reason for using alternative medicine in this survey of a pediatric ambulatory population. As mentioned in our initial IRB application, our long-term objective was to use information from this observational study to inform the design of prospective interventional double-blind controlled trials to assess the efficacy (or lack thereof) of homeopathic treatments for acute and/or chronic otitis media.

In light of these facts and because study subjects received the usual and customary care of their chosen physicians, this observational study did not involve "more than a minor increase over minimal risk."

(3) The subjects were vulnerable to coercion and undue influence but additional safeguards were not included in the study to protect the rights and welfare of these subjects, in contravention of HHS regulations at 45 CFR 46.111(b).

Study subjects' ages ranged from 8 – 77 months. Parents of these children agreed, upon enrollment in the study, to the manner in which their child was to be treated and observed for the purpose of this observational study. Parents were told, and agreed in the consent form, that they could choose not to participate or could withdraw from this observational study at any time. The actual wording is as follows: "I understand that participation in this study is voluntary and I may refuse to participate or may discontinue participation at any time without penalty, loss of benefits, or prejudice to the quality of care which I will receive." Moreover, the informed consent also states: "I acknowledge that no guarantees have been made to me regarding the result of the treatment involved in this study, and I consent to participate in the study and have been given a copy of this form."

Parents also agreed to have the diagnosis of otitis media in their child confirmed with the additional noninvasive diagnostic techniques mentioned in the consent form. They also agreed to have nasal swabs taken; however, these were not performed.

As requested by you, we also provide the following additional information:

- (1) All correspondence between the IRB and the investigators.
- (2) All continuing review reports.
- (3) A list of subjects (code numbers only) and dates of enrollment.

(4) A copy of any publications or presentations which were derived from this research project. These include:

- (a) An abstract entitled, "Challenges of evaluating homeopathic treatment of acute otitis media," Elizabeth D. Barnett, et al. presented at The American Pediatric Society and the Society for Pediatric Research, 1999.
- (b) A peer reviewed medical publication entitled, "Challenges of evaluating homeopathic treatment of acute otitis media," Elizabeth D. Barnett, et al. The Pediatric Infectious Disease Journal 2000 19;4:273-275.
- (c) Abstract and presentation by Janet Levitan, MD at the 7th International Symposium on Recent Advances in Otitis Media, June 1-5, 1999 in Fort Lauderdale, Florida.

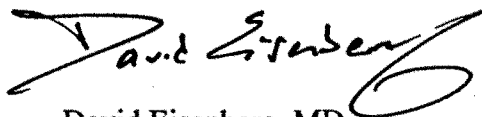
(4) Other pertinent information:

The research protocol was submitted in December 1996 to the IRB of the Beth Israel Deaconess Hospital. The protocol was not submitted to the IRB at Boston Medical Center based on our understanding in 1996 of the role of Drs. Klein and Barnett as "engaged in research". Based on the guidelines for Engagement in Research published on January 26, 1999, Drs. Klein and Barnett will in the future submit such studies to the IRB at Boston Medical Center based on (1) intervene or interact with living individuals for research purposes (not applicable to the December 1996 protocol); or (2) obtain individually identifiable private information for research purposes (applicable to the December 1996 protocol).

This letter has been reviewed and approved by the following co-investigators:

David Eisenberg, MD
Elizabeth Barnett, MD
Jerome Klein, MD
Ted Kaptchuk
Janet Levatin, MD
Ted Chapman, MD

Sincerely,



David Eisenberg, MD