The understanding of the mechanisms by which electro-anesthesia is produced could make it possible for this method of anesthesia to become clinically acceptable. Therefore, the proposed program to determine the information necessary to justify the extension of the use of electrical current for clinical anesthesia is submitted.

OBJECTIVES OF THE PROPOSED RESEARCH PROGRAM

The objectives of this proposal are to answer three major questions.

1. Where does the current go when it is applied to the cranium?
2. When is anesthesia present and at what depth?
3. What are the undesirable side effects of various currents and can they be eliminated?

PROPOSED STUDIES TO ACHIEVE OBJECTIVES

I. Electrical Mechanisms

- A. Determination of the frequency response curves and the external impedance levels of cranium.
- B. Determination of the degrees of linearity of these electrical responses.
- C. Determination of the impedance of the tissues of the brain.
- D. Determination of tissue voltage levels in the brain.
- E. Determination of the distribution of total electrical current in the cranium.

F. Determination of the convolution of dual electrical currents in the brain.

G. Determination of the role of the cerebral spinal fluid as a conductor of electrical currents.

H. Determination of the effects of induced brain lesions on the capability to produce electro-anesthesia.

I. Determination of methods to focus current to specific locations in the brain.

II. Biological Responses

A. Determination of the level of anesthesia.

B. Determination of the effect of electro-anesthesia on blood gases and blood pH.

C. Determination of the effect of electro-anesthesia on the circulatory system, including blood glucose levels.

METHODS

I. Animals to be Used

A. Calves.

B. Primates.

The calf has been selected as the experimental animal in the initial studies. Primates will be used after the evaluations are complete in the calf. For this purpose, the Rheus monkey and the Chimpanzee have been selected.

In vitro studies will be done on cadaver heads of calves, primates and humans in a related sequence to the in vivo studies.

C. Justification of Animal Selection.

The most repeatable results and the most stable level of anesthesia from the use of electrical currents have been achieved during bovine applications. There are specific problems associated with each of the other species as experienced by this investigator in studies on horses, sheep, pigs, dogs, cats, rabbits, rats, goats, and monkeys. The most accurate information on the mechanisms of electro-anesthesia can be obtained from animals that respond most favorable to electrical currents. Therefore, the calf was selected as the experimental animal for the first phase of the program.

Calves are available in adequate numbers and the facilities for handling them are adequate. Calves of a 175-200 pound weight range would be used. Twenty-five calves per year would be needed.

Primates are considered essential to the program, after completion of calf studies, since the anatomical structure of the head and the reactions to electro-anesthesia more closely resembles those of the human. Thus a link between bovine and human applications is formed to more clearly define the mechanisms involved.

II. Currents to be Used

A. Pulsed direct current with variable pulse duration, frequency of pulse and amplitude.

B. Sinusoidal alternating current with variable frequency and amplitude.

C. Dual sinusoidal with summation in the generator.

D. Dual sinusoidal with summation in the head.

E. Justification of Current Selections.

The review of the literature reveals that hypertension, cardiac and respiratory arrest and strong muscle contractions can occur. The cardiac and respiratory arrest can be permanent if the electrical currents are not properly applied.

1. Sinusoidal currents can be varied to produce a wide range of responses in the animal. These include electro-sleep with high-frequency-low amperage, electro-anesthesia with mid-frequency and amperage, and electro-convulsion with low-frequency-high amperage application. Thus by adjustment of the relationships between current amplitude and frequency, the differences in responses of the electro-biological parameters can be evaluated for the corresponding states of consciousness.

2. The sinusoidal waveform is a clean electrical wave unlike a number of other types, such as square and triangle waves which are composed of a number of sinusoidal waves at various frequencies in the harmonic mechanism. Therefore, less distortion should occur in sinusoidal applications.

3. Dual sinusoidal with summation in the generator produces superficial analgesia without sufficient depth in the deep tissues. It has the reverse effect of single sinusoidal, therefore the response of the mechanisms involved are changed.

4. Dual sinusoidal with summation in the head is a technique that opens new approaches to electroanesthesia. As the two currents are brought together inside the head, a number of possibilities exist which affects the response to current. If the phase angles are the same, the currents will combine in a true summation. However, variations in the relationship of phase angles of the applied currents can cause summation at locations in the brain and cancellations of the current in other areas. Thus if we can learn how to control this

mechanism to focus the current to specific locations in the brain rather than total brain stimulation, many of the unwanted side effects could possibly be eliminated.

III. Methods to be used in each Proposed Study

A. General Statement for All Studies:

Statistical consultation will be obtained for aid in the design of experiments and in the evaluation of data generated.

B. Specific Studies (Electrical)

1. Determination of the frequency response curves and external impedance levels of the cranium. In vitro studies will be made in cadaver calf heads and in vivo studies in calves of same size. The technique to be used consists of:

a. Applying electrodes to the head of the calf for current application. Both bitemporal and anterior-posterior types are to be used.

b. Placement of recording electrode by sterotoxic adjustment into the tissues of the cranium.