Toxicity and Complications

1. Stubbs and Pennybacker[19] report 5 cases of rigors during infusion in a series of 129 cases. They implicate too rapid infusion or decomposition of the solution through age or improper storage.

2. Change in tissue turgor, dry tongue, hypotension and tachycardia may present should there be excessive loss of fluid and electrolytes.[15,20]

3. Local venous complications varying from transient redness to superficial and deep-vein thrombosis have been reported in most series. Again stale solutions are implicated. It is emphasized that solutions deteriorate and decompose rapidly on heating, and under no circumstances must they be heated to body temperature before administration.[18]

4. Javid[8] reports skin blebs forming after subcutaneous leak of urea solution. These cleared up spontaneously. Mason and Raaf[15] relate a case of urea extravasation causing a 3 x 5 cm. slough which needed skin grafting.

5. Conscious patients will complain of nausea with pain at the infusion site.

6. Urea in the presence of a normotensive CSF may cause low-pressure headache such as is seen after lumbar puncture.[6,7]

7. In the past year we encountered 3 patients at the Groote Schuur Hospital presenting with ischaemic changes in the infusion forearm.[17,21] The main feature was a gross, blue discolouration of the forearm skin during the immediate post-infusion period. A demarcation line presented at the level of the sphygmomanometer cuffs which were attached to the infusion limbs. The first patient has developed a Volkmann's ischaemic contracture; the second recovered spontaneously without residual defect, and the third, on whom a brachial-block sympathectomy was done, died a few days postoperatively from other causes, but with an apparently normal arm. We advise the removal of all constricting bandages or blood-pressure cuffs from the infusion limbs before commencing infusion of the urea solution. Chemical sympathectomy may play a part in limiting or preventing the residual anatomical damage caused by this complication.

CONCLUSION

Thus, an old agent has returned in a new guise to take its place among the existing aids to anaesthesia in the management of patients receiving surgical treatment for neurological and ophthalmological conditions. Like the raised head, ventricular and lumbar CSF drainage, hypothermia, induced hypotension and controlled ventilation, it entails a certain degree of physiological trespass and the risk of systemic and local complications. That is the price we have to pay for progress. The art of anaesthesia, however, still lies in the hands of the administrator who understands both the scope and limitations of his equipment and can avoid turning it into a Frankenstein by blind devotion or physiological abuse.

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ELECTRONIC ANAESTHESIA

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The application of electrical currents to the brain for the production of narcosis was first observed by Mach[1] in experiments on animals in 1875. Of the earlier workers in this field Leduc[2] (1902) made the major contribution. In some of his experiments animals were narcotized for as long as 2 hours without any deleterious effect on their health.

It was only much later (1938) that electric currents were used for therapy in psychiatry. Insulin and metrazol convulsive comas, introduced by Sakel (1933) and Meduna (1936), were not easily controllable. Cerletti[3] overcame this by using electrically produced convulsions (ECT).

Some years later (1944) electric currents were used to produce prolonged narcosis without the shock effect. This form of therapy, called electronarcosis, was carried out on several thousands of patients with no adverse effects.[4-9] In 1961 the employment of electric currents for various forms of narcosis culminated in their being used for general anaesthesia in man.[10]

This paper deals with the production of general anaesthesia in animals using a current of a different frequency than previously described. We prefer to call this method of anaesthesia 'electronic anaesthesia' because, from the patient's point of view, it will be psychologically more euphonious than the term 'electrical anaesthesia'.

METHOD AND MATERIALS

Initially 36 animals, namely 14 rats, 7 guinea-pigs, 6 rabbits and 9 dogs, were subjected to electronic anaesthesia. An electric current at a constant frequency of 700 cycles per second (cps) was used in all the preliminary experiments. At this frequency narcosis was accompanied by increased muscle tone, tremor of the facial muscles and, in the smaller animals, twitching of the whiskers. Since these are undesirable side-effects attempts were made to eliminate them by varying the frequency of the current from 60 to 2,000 cps.

The most satisfactory frequency was subsequently found to be 1,500 cps. A current of this frequency was then used to anaesthetize another group of 53 animals which consisted of 27 rabbits, 22 dogs and 4 baboons.

The electrical apparatus consisted of a signal generator which produces a sinusoidally varying alternating current of variable frequency which is fed into a high-power distortion-less amplifier from which a current in the required range can be obtained. A milli-ammeter and voltmeter are included in the circuit.

The electrodes, which are similar to drawing-pins, were made of small circular metal discs with copper wire soldered to one surface. In these experiments the size of the electrodes was largely determined by the size of the head of the experimental animal. The diameter of the electrode varied from half an inch to one inch.

The passage of the electrical current from the electrodes into the tissue is proportional to the resistance of the skin-electrode interface. Without cutting the electrode size, the resistance was reduced by taking the following precautions:

The electrodes were covered by a thick gauze-cloth which

was kept moist during the electronarcosis, using a 5—20% saline solution.

The hair on the head at the proposed electrode sites was shaved off in all animals.

An electrode paste was applied between the skin and electrodes.

The electrodes were firmly applied to the skin using a suitable rubber band which fitted snugly to the head.

The sites chosen for the electrode placement were in a transverse position, comparable to those used for electroconvulsive therapy, one right and one left, just antero-medial to each ear.

Induction

All the small animals and a few of the large animals were anaesthetized without premedication. To simulate conditions applicable to humans, the larger animals (dogs and baboons) were premedicated.

For induction an initial high current, which varied for each species of animal, was maintained for about 2 — 3 seconds and then immediately dropped to a lower level which maintained anaesthesia.

During induction apnoea occurred. Respiration usually returned early, but when the apnoea was prolonged a 'pulsing' technique was used. This consisted of alternating the current between zero and the maintenance level, with 3-second intervals. This was repeated 3 times. The sudden rise and fall of current each time caused a generalized muscle contraction and relaxation which was accompanied by respiratory movements. A form of artificial respiration may thus be applied by 'pulsing' the apnoeic animal.

Premedication in dogs consisted of 1/300 gr. of intravenous atropine and ± 2 ml. of 2½% thiopentone, given about 5 minutes before the animal was subjected to electronic anaesthesia.

In the baboons premedication consisted of 1/300 gr. of intravenous atropine and ± 3 ml. of a 10% solution of transithal followed by 25 mg. of succinyldicholine to allow intubation with a cuffed endotracheal tube.

Maintenance

The best range of current for maintenance of anaesthesia was established by raising or lowering the amperage. It was found advisable to change the current slowly, especially while increasing it, to avoid convulsive movements. This maintenance range, although varying with the size of the animal, is relatively constant for each type of animal.

Oxygen was given to all the larger animals during anaesthesia *via* a nasal catheter or an endotracheal tube.

The state of analgesia and operability was tested by pinching the skin or foot pad with an artery forceps, incising and stitching of the skin, or in some cases by a laparotomy.

Recovery

The anaesthesia was terminated instantaneously by switching the current off.

OBSERVATIONS AND DISCUSSION

Induction

Without the aid of drugs the current which can maintain anaesthesia is not quite adequate for satisfactory induction of the electronic anaesthesia.

The higher current necessary for induction produces a generalized muscular rigidity and apnoea. Immediately the current was applied, the animal fell over on to its side with outstretched stiff limbs. Tremor and motor movements followed. Lowering the current immediately relaxed the animal and normal respiration began soon after.

The longer the application and the greater the strength of the induction current, the longer the apnoea lasted. If the apnoea was prolonged respiration was induced by the 'pulsing' technique.

The unwanted effects of the high current used for induction can be minimized by means of drugs. Ultra short-acting barbiturates and succinyldicholine given immediately before the application of the electric current allowed smoother induction at lower amperages.

The position of the electrodes may affect both induction and maintenance of anaesthesia. This will be the subject of further research. Most of the experiments were done with transversely placed electrodes. In a few experiments sagittally placed electrodes were used, the one placed in the midline of the vertex at the midpoint between the eye and the ear and the other at the occipital protuberance in the midline.

Induction done in this way was rapid and smooth with no convulsive movements.

Maintenance was continued with the electrodes either in the sagittal or transverse position. Where the sagittal position was used, the anaesthesia was equivalent to a high spinal anaesthesia. Analgesia and relaxation were good, but there was no analgesia of the face and head.

Maintenance

In these experiments the maintenance level of electronic anaesthesia was reached by carefully lowering or raising the current. Anaesthesia was also influenced by the frequency and skin-electrode resistance. At a frequency of 1,500 cps hypertonicity was lessened, and tremors were minimized by ensuring that the resistance at the skin-electrode interface remained low.

The anaesthesia at the maintenance level was good as measured in terms of narcosis, analgesia, and relaxation. But raising or lowering the current below this level led to the appearance of side-effects. Noticeable features were hypertonicity of muscles, limb movements, tremor, and difficulty with respiration. This suggests that there are probably 4 planes of electronic anaesthesia.

Plane 1. On lowering the current below the maintenance range a plane is reached where the animal, though still asleep, responds to painful stimuli by movement. The skeletal muscles may either be relaxed or show signs of tremor and, in the smaller animals, twitching of the facial musculature and whiskers may be present. The pupil reflex is present. On lowering the current still further the animal will awaken.

Plane 2. This is the plane of satisfactory general anaesthesia or 'surgical' anaesthesia where the animal is asleep, does not respond to painful stimuli, and operations can be performed. The respiration is satisfactory and the skeletal muscles are relaxed. The conjunctival and pupil reflexes are absent.

Plane 3. On raising the current above the maintenance range for plane 2, the animal remains asleep and analgesic, but increased muscle tone, tremor, and movements of the limbs may appear. In some rabbits running movements of the hind-legs may be seen. Difficulty with respiration may occur.

Plane 4. On raising the current still further convulsive movements occur. This usually occurs at the same current at which anaesthesia is induced.

In rabbits and dogs the average currents at 1,500 cps for the 4 planes of anaesthesia are shown in Table I. The average current required to maintain surgical anaesthesia, plane 2, in the baboons was 89.0 m. amps.

Paterson and Milligan[9] drew attention to a hyperkinetic stage during electronarcosis. They stated that 2 syndromes might develop after induction — a narcotic type or a hyperkinetic type, where the animal tried to right itself and violent movements occurred. These 2 syndromes may correspond to the signs of plane 2 and plane 3.

Recovery

The eyes usually remained open throughout electronic anaesthesia, and at the termination of anaesthesia they suddenly changed from a glassy stare to a lively sparkle. After a short period of time the animal would move and walk away unaided. There was an initial unsteadiness, but this soon disappeared.

The recovery was complete and rapid except where large doses of barbiturate were used for premedication.

TABLE I. PLANES OF ELECTRONIC ANAESTHESIA (AVERAGE CURRENTS IN M.AMPS. AT 1,500 CPS)

	Planes			
Animals	*1*	*2*	*3*	*4*
Rabbit	19.8	23.5	29.7	above 35
Dog	52.5	72.8	85.4	above 100

There was no post-anaesthetic vomiting. The animals often ate shortly afterwards.

There were no perceptible postanaesthetic mental effects either immediately or in those animals kept under observation for several months. Shortly after the electronic anaesthesia, one baboon carried out the correct sequence of events it had been taught when its weekly weight was taken. It sat on the scale as usual and was weighed. Thereafter, on command, it got off and returned to its cage.

Except for two instances no physical after-effects were observed. The first exception was a rabbit which, after the electronic anaesthesia, dragged its hind-quarters, but this cleared up shortly afterwards. The second physical change, which may be attributed to the electronic anaesthesia, was seen in one of the baboons. A female, who had had no sexual cycle for 3 years, had a swollen perineum one month later, but there was no bleeding. The other 3 baboons, also females, had no change in their sexual cycle, including one baboon that had had no sexual cycle for the past 8 years.

One baboon showed a weight loss of 12 oz. after a week, but this she soon regained. A second baboon showed a weight increase of 1 lb. after a week.

Two deaths, in a rat and a dog, occurred during the initial phase of the experiments. In our opinion these deaths were not attributable to the method of electronic anaesthesia described in this paper.

Corollary

Although the effects of electronic anaesthesia, as described for animals, are not necessarily applicable to human beings, the one human subject anaesthetized by this method followed a similar pattern.

Advantages

The advantages of electronic anaesthesia, compared to the standard forms of general anaesthesia, can only be surmised. Experimental evidence, however, indicates that this form of anaesthesia may yet prove to be a valuable aid to the anaesthetist. The following are some of its possible advantages:

The ease and speed of induction.

Rapid reversibility, which could reduce time in hospital required for recovery.

Absence of toxicity, side-effects, and after-effects, particularly useful for the poor-risk patients.

Its value in pulmonary disease, since no irritant vapours are inhaled.

Its value in liver disease or kidney disease, since no drugs need to be broken down or eliminated.

It does not involve the use of explosive gases.

Its value for veterinary and laboratory purposes.[2]

Its value in anaesthetizing battlefield patients without the use of bulky and expensive gas equipment.[10]

SUMMARY

1. Electronic anaesthesia was produced by currents of different frequencies in a total of 89 animals. The best anaesthesia was obtained at 1,500 cycles/second.

2. Induction and maintenance of anaesthesia were produced with the electrodes in the transverse position on the head.

3. The electronic anaesthesia produced is satisfactory for surgical procedures.

4. It is suggested that 4 planes of anaesthesia can be distinguished.

5. Recovery from anaesthesia was usually rapid and complete.

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EFFECT OF ADDITIONAL LEUCINE ON NITROGEN BALANCES OF MEN EATING MAIZE DIETS*

PRELIMINARY COMMUNICATION

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It is well established that the nutritive value of a food protein will be impaired if it contains too low a proportion of any of the essential amino acids. This *amino acid deficiency* is the main reason why the proteins of most vegetable foodstuffs are not as well utilized as animal foods, e.g. egg, for protein synthesis inside the body.

In the case of maize, our Group has previously shown by nitrogen balances in adults and children that its relatively low nutritive value[1] can be improved by giving small supplements of lysine plus tryptophan.[2,3]

A subsidiary concept of protein nutrition is the possibility that *excess* of an amino acid may impair nutritive value. The phenomenon is called *amino acid imbalance*. It has not really been confirmed in man yet, though isolated possible examples have been published.[3,4,5] Almost all the amino acid imbalances reported in rats have been produced by adding excess of a synthetic amino acid to natural proteins, usually ones already deficient in another essential amino acid.

Few natural foods contain an excess of any of the essential amino acids. Of the major foodstuffs, the one with the largest excess is maize; it contains 2·7 times the optimal proportion of leucine (the FAO provisional amino acid pattern). Put another way, leucine makes up 30% of the total of 8 essential amino acids in maize. The Protein Committee of FAO[6] have summarized the position as follows: 'The view has been generally held that imbalance among amino acids is unlikely to occur when only natural foods are ingested. Some evidence has been obtained indicating that the amount of leucine in maize may be sufficiently large to increase the requirement for isoleucine. The addition of an excess of leucine to a diet not deficient in isoleucine has been shown to depress growth in rats, and the depression in growth was eliminated only when the amount of isoleucine in the diet was increased.'

The relevant experiments were reported by Harper *et al.*[7] in 1955. Young rats fed on a low-protein (casein) diet *ad libitum* stopped growing when leucine was added to their ration. The effect was more marked with 3% than with 1·5% of additional L-leucine. It was partly counteracted by giving the isomeric amino acid, isoleucine, at the same time. Even without it, growth was resumed after about a week of continued leucine administration.

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