ANAESTHESIA FOR THE IRRADIATED PIG: A STUDY IN REMOTE CONTROL

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An investigation was planned to compare the biological effects of the neutron beam from a 45-inch cyclotron with the X-rays produced by an 8 MeV linear accelerator. The pig was chosen as the experimental animal because the structure of the human tissues concerned is closer to that of the pig than any other animal.

The investigation consisted of irradiating selected areas on the flank of the pig with neutrons and X-rays and comparing the doses necessary to produce the same biological effect. Some animals were irradiated once only, others twice a week for three or four weeks. Absolute immobility was essential, and the experimental animals had therefore to be anaesthetized throughout the periods of irradiation, which aggregated several hours. During exposure, the animals had to be enclosed within concrete radiation shields, which isolated them from the anaesthetist and the radiotherapist (fig. 1). The investigation was costly in time and effort, and it was important that no mortality or morbidity should be caused by the anaesthesia. These conditions posed some unusual problems.

THE CYCLOTRON AND THE LINEAR ACCELERATOR

In recent years the scope and character of the ionizing radiations available to the therapist have been enlarged by the development of various types of machines. Supervoltage X-rays in the energy range of 4–8 million volts have become available since the war by the development of the linear accelerator. The development of the cyclotron has made available for therapeutic purposes beams of protons, deuterons, alpha particles and neutrons.

Two of these machines, an 8 MeV linear accelerator and a 45-inch cyclotron, have been constructed at the Radiotherapeutic Research Unit of the Medical Research Council. The linear accelerator, producing 8 million-volt X-rays, has been in daily clinical use for the past seven years. The cyclotron produces a 15-million-volt deuteron beam which, impinging on a beryllium target, gives a beam of fast neutrons of sufficient intensity to make its clinical use a practical possibility. Before the neutron beam can be used clinically, however, it is of importance to compare its biological effects with those of a radiation with which the radiotherapist is familiar. Neutrons are unchanged particles of mass approximately equal to that of the hydrogen atom. The mechanism of energy transfer is dependent to a large extent on the number of hydrogen atoms present in tissue so that a layer of fat, of high hydrogen content, is likely to receive a higher absorbed dose of radiation than a layer of muscle exposed to the same beam.

CHOICE OF ANAESTHETIC TECHNIQUE

This was influenced by the nature of the experimental animal, and by the need for a nonexplosive agent (because of the proximity of high voltage electrical apparatus) which would provide safe anaesthesia for long periods by remote control.

The pig resents any form of physical restraint. Even if it can be held still it continues to squeal, and this shrill, penetrating noise is extremely disturbing to those concerned. Adequate premedication and a smooth rapid induction were therefore required.

Premedication.

For premedication phenothiazine derivatives were chosen because they produce sedation without undue respiratory depression and because their effects are long lasting. Promazine 2 mg and promethazine 1 mg per lb. (0.45 kg) body weight
were given together by intramuscular injection 1½ hours before induction of anaesthesia. Parasympathetic depression was also considered desirable, to avoid the possibility of respiratory obstruction due to bronchial secretion during the anaesthetic period. Atropine sulphate 1/200 grain (0.32 mg) was therefore given by intramuscular injection after induction.

Induction.

On the first occasions, anaesthesia was induced with intravenous thiopentone (250 mg for a 50-lb. pig). This proved satisfactory except for the difficulties of venepuncture. The only veins easily accessible in the conscious pig are those situated on the posterior aspect of the external ear. These veins may be easily damaged if the animal moves its head during the injection, or if any of the anaesthetic solution is injected perivenously. On subsequent occasions, to reduce the number of venepunctures, anaesthesia was induced with cyclopropane. A small-sized Hall dog mask was used with a flow of 1 litre per minute of cyclopropane and 2 litres per minute of oxygen into a Magill rebreathing attachment—the reservoir bag being filled with the mixture in advance. This presented no problem and restraint was not difficult in the premedicated animal.

Intubation.

Intubation was considered essential to maintain a clear airway (which is otherwise difficult in the pig) and to ensure that the animal inhaled only the selected anaesthetic mixture.

The nasal route was impracticable, since the nostrils of the pig are too small, and the turbinate bones too convoluted, to allow the passage of a tube of adequate size. Direct oral intubation was therefore required. A straight-bladed laryngoscope proved suitable for exposure of the glottis, but for large animals a blade longer than that of adult human laryngoscopes would be required.

The epiglottis was usually behind the soft palate, and often had to be brought forward with a blunt hook before the rima glottidis could be seen. The tube could then be introduced between the vocal cords but, because in the pig the larynx is set at an angle to the trachea, its onward passage brought it up against the anterior wall of the larynx at the cricothyroid junction. It could then be advanced only after slight withdrawal and rotation through 180°.

The provision of ideal conditions was found to be essential to overcome the difficulties of intubation in the pig. Suxamethonium 1 mg per lb. (0.45 kg) was therefore injected intravenously as soon as anaesthesia was established. This produced complete muscular paralysis for about 10 minutes. After it had taken effect, oxygen was administered through a mask placed over the snout. Intubation was carried out as quickly as possible and then artificial respiration was continued via the endotracheal tube by manual compression of the reservoir bag, until spontaneous respiration recommenced.

Maintenance.

Though maintenance of anaesthesia by a single intraperitoneal dose of a nonvolatile drug offered the advantage of simplicity, it was found to be unsatisfactory. An initial dose which was not dangerously large was often insufficient to prevent the return of reflex activity before the end of the procedure while the animal was still inaccessible.

It was felt that only the continuous administration of a nonexplosive inhalational anaesthetic could provide the safety and evenness required. Nitrous oxide seemed ideal in many respects, but its lack of potency required that it be supplemented. Possible supplementary agents were chloroform, trichloroethylene and halothane. The first was rejected because of the danger of ventricular fibrillation, the possibility that long repeated exposures would lead to liver damage, and its small margin of safety. Trichloroethylene was also considered to be too toxic for long repeated administrations. Furthermore, postanaesthetic nausea and anorexia were undesirable as each animal had to be subjected to anaesthesia once or twice weekly, and had in addition to contend with the general effects of irradiation. It was essential that it should be able to take food at least for one or two days between anaesthetics. Halothane appeared the best choice and in fact proved entirely suitable. The depth of anaesthesia could be readily controlled and maintained; recovery was rapid and the animal took its feeds soon after recovery.

Circuit.

To a flow of nitrous oxide (4 l./min) and oxygen (3 l./min) halothane (1–2 per cent) was
added from a Fluotec vaporizer. From the vaporizer the gas passed down 40 feet (12.1 m) of 0.5 cm bore p.v.c. tubing which went through an underground duct into the radiation chamber (fig. 1). It then passed via a normal Magill attachment, which was situated close to the animal, to the endotracheal tube. It was considered most unlikely that rebreathing could have occurred with a 50-lb. (22.5 kg) pig and a fresh gas flow of 7 l./min (Mapleson, 1954). Halothane undoubtedly passed into the wall of the long connecting tube, but this was of little practical importance as the linear flow rate was high enough to swamp the effect.

MANAGEMENT
The pig, which after premedication was usually not too vociferous, was brought to the “anaesthetic room”. This was a passage outside the cyclotron chamber. The animal was placed supine on a box of suitable height, and anaesthesia induced as quickly and gently as possible. Intubation was then performed, and the Magill attachment connected. When anaesthesia was stable the stethograph (see later) was applied. The circuit was then broken between the vaporizer and the Magill attachment, and the animal—still connected to the Magill attachment—was carried into the chamber and suspended in a hammock, which supported its chest and abdomen and allowed its legs to hang free. The anaesthetic supply and the Magill attachment were reconnected as soon as possible via the 40-ft. (12 m) tube, and the animal’s position was finally adjusted. The team then retired from the chamber and the motor operating the door was started. This door weighs 32 tons (31,500 kg) and takes 5 minutes to close or open. At the end of the period of neutron irradiation the procedure was reversed. Pig and anaesthetic apparatus were then conveyed about 100 metres along a passage and into the linear accelerator chamber, where the animal was irradiated with 8 MeV X-rays. The whole process of anaesthesia, transfer, positioning and irradiation took 5 to 6 hours, and during much of this time the animal was inaccessible to the operating team.

MONITORING AND CONTROL
Personnel had, of course, to remain outside the radiation chambers during exposure so that direct observation and adjustment of the animal were precluded. A closed-circuit television camera permitted indirect observation of the animal in the chamber. However, since it was trained on the portion of the animal being irradiated, it did not provide the anaesthetist with any useful information. Consequently, some device for monitoring the depth of anaesthesia was necessary. The cyclotron is supplied with 50 kilowatts of radio frequency power, so that any sensitive electrical monitor such as an electroencephalograph or electrocardiograph was impractical, and it was neces-
sary to use the respiration as the sole guide to the
depth of anaesthesia.

In less abnormal circumstances tidal exchange
could be accurately recorded with an integrating
pneumotachograph and capacitance manometer
(Hill, 1959), but this was not possible here be-
cause of the electrical capacitance of the long cable
required. The problem was solved by the con-
struction of a simple stethograph. This consisted
of a 6-inch length of anaesthetic corrugated tub-
ing securely corked at each end. The tubing was
tied around the pig's chest with webbing. It com-
municated with a pressure measuring capsule,
whose diaphragm was displaced by the pressure
changes arising from the pig's breathing. The
apparatus was used only to record relative changes,
since it is not well suited to measuring actual
tidal volumes.

The diaphragm's motion was converted into an
electrical signal by an RCA 5734 transducer valve.
This valve has a flexible anode which was mechani-
cally linked to the diaphragm. The consequent
motion of the anode gave rise to an electrical signal
across the valve. The valve was incorporated in a
simple circuit. The valve alone was close to the
pig, the power supplies and controls, outside the
chamber, being connected by a length of three
core screened cable. The circuit fed a 1 mA
recording milliammeter and gave a clear chart
trace of the pig's breathing. The floating 300-volt
supply was derived from a dry battery.

DISCUSSION

There was no mortality or morbidity attributable
to the anaesthetic. One pig of the first series of
seven animals died some weeks after exposure
from necrosis of the bowel, but this was con-
sidered to be due to radiation damage. Conscious-
ness was regained within 1 hour of the end of
the anaesthetic and feeding was resumed, often
at once, and never later than the following day.
However, pigs anaesthetized at twice-weekly in-
tervals failed to gain weight as rapidly as the
control animals. This was in part due to withhold-
ing food before anaesthesia.

The premedication made the pigs much easier
to handle. They were not asleep, but it made them
less resentful and noisy.

Venepuncture was very difficult in the conscious
pig because the prick of the needle prompted
violent rotation of the head by the powerful neck
muscles. Induction by inhalation was easier and
became the method of choice.

Intubation was difficult and required ideal con-
ditions, but the development of a hook for expo-
sure of the rima glottidis was helpful, and the
necessary skill was acquired with practice.

Maintenance of an even plane of anaesthesia
from observation of the stethograph record was
satisfactory. At no time did anaesthesia proceed
to the point of respiratory arrest, neither did reflex
activity ever interfere with the irradiation. On
two occasions the stethograph proved life-saving.
On the first, the endotracheal tube became kinked
shortly after the move from the cyclotron to the
linear accelerator. An irregular pattern was
noticed and the obstruction cleared before the
animal suffered any harm. On a second occasion
the oxygen fine adjustment valve was inexplicably
closed in transit to the linear accelerator. While
the pig was being positioned in the darkened
room, hypoxia proceeded to the point of apnoea
which was first detected on the stethograph trace.

In a second series of experiments extending
over the summer of 1961 several pigs died during
anaesthesia, death being attributed to heat stroke.
In these cases the rectal temperatures were
observed to rise to 41.7–42.8°C (the normal pig
temperature is 39.2°C), and on these occasions
the ambient temperature and humidity of the
cyclotron chamber were both unusually high.
Measures were therefore taken to reduce both
the ambient temperature and humidity, and subse-
quent animals have been managed without mis-
 hap. In particular, several animals have been anaes-
thesized twice weekly for a period of 3 weeks.

SUMMARY

In an experimental study on the effect of ionizing
radiations, a number of pigs were repeatedly
anaesthetized for several hours.

The animals were inaccessible to the anaes-
thesist for the greater part of this time, and anaes-
thesia had to be maintained by remote control.

The problems encountered are discussed, and
the technique adopted is described.

Halothane in nitrous oxide and oxygen was
used to maintain anaesthesia; and the condition
of the animal was assessed by a respiration moni-
tor constructed for the purpose.
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REFERENCES


SOMMAIRE

Dans une étude expérimentale de l'effet des radiations ionisantes, un nombre de porcs furent anesthésiés à plusieurs reprises pendant plusieurs heures. Les animaux étaient inaccessibles à l'anesthésiste pendant une grande partie de ce temps, et l'anesthésie devait être maintenue par contrôle éloigné.

Les problèmes rencontrés sont discutés, et la technique adoptée est décrite.

L'halothane dans le protoxyde d'azote/oxygène fut utilisé pour maintenir l'anesthésie; et l'état de l'animal fut enregistré par un indicateur de respiration construit pour cet usage.

ZUSAMMENFASSUNG

In einem experimentellen Versuch über die Wirkung ionisierender Strahlen wurden eine Anzahl Schweine wiederholt für mehrere Stunden narkotisiert.

Für den Anasthesisten waren die Tiere die meiste Zeit nicht erreichbar, die Narkose musste durch indirekte Steuerung aufrecht erhalten werden.

Die dabei auftretenden Probleme werden besprochen und die dem angepasste Technik beschrieben.

Halothan in Lachgas/Sauerstoff wurde verwendet, um die Narkose aufrecht zu erhalten; der Zustand des Tieres wurde durch ein für diesen Zweck gebautes Atemkontrollgerät überwacht.