ANAESTHETIC-INDUCED MALIGNANT HYPERPYREXIA AND A METHOD FOR ITS PREDICTION

BY


SUMMARY

The clinical syndrome of anaesthetic-triggered malignant hyperpyrexia occurring in pigs is described. This condition in the pig is considered to be the same "explosive thermal idiosyncrasy" to general anaesthesia that is manifested by humans. The condition has a strong genetic factor occurring in 25 per cent of Landrace pigs used by us. Sex has no influence on its appearance. The clinical syndrome consists of: (1) tachycardia; (2) muscle rigor; (3) tachypnoea and hyperventilation progressing to apnoea; (4) blotchy cyanosis of the skin; (5) rapid, sustained and extreme rise in temperature; (6) gross acidosis. Prognosis, once the condition is well established, is extremely poor. All attempts at treatment have failed. Histological investigation has shown change in muscle only. The significance of this change is unknown. The muscle of affected pigs shows, in comparison to normal pigs, an abnormal fall in ATP content in response to incubation and to "in vitro" exposure to halothane. This reaction provides a method of predicting the development of the syndrome. Halothane, chloroform and suxamethonium have been identified as triggering agents. The mechanism of heat production is unknown.

Cases of malignant hyperpyrexia or fulminant hyperthermia occurring during the course of clinical general anaesthesia have been described with disturbingly increasing frequency over the last few years (Leading Article, 1968; Hawthorne, Richardson and Whitfield, 1968; Marx et al., 1968). The most frightening aspects of this condition are that:

(1) Mortality is in excess of 70 per cent.
(2) Occurring most frequently in young healthy patients undergoing relatively minor surgical procedures, its occurrence appears to be completely unpredictable.
(3) The stimulus, or trigger, appears to be directly related to the administration of a general anaesthetic.
(4) Because of the complete ignorance of pathogenesis, treatment is empirical, symptomatic and, in general, unsuccessful.

The discovery by Hall and associates (1966) and ourselves (1968) of what we have become convinced is exactly the same abnormal response to general anaesthesia—malignant hyperpyrexia—in the pig is of interest, for quite fortuitously we have been provided with an animal experimental model in which to investigate this frightening condition.

The pig is used by us as the experimental model in a research programme on liver transplantation and isolated liver perfusion. Three breeds of pig have been used: Landrace, Landrace/Large White Cross, and Large White. Pigs of each breed come to us from separate farms. The pigs are used between the ages of 6-10 weeks, weighing between 30 and 45 kg.

ANAESTHETIC TECHNIQUE

Two anaesthetic techniques which differed only in the drugs used were employed. Certain events and manoeuvres were common to both. These were:

Pre-anaesthetic starvation of 16 hours.
Induction of anaesthesia.
Orotracheal intubation with cuffed endotracheal tube.
Maintenance of anaesthesia with nitrous oxide and oxygen administered by an IPPR non-rebreathing technique utilizing a Bird ventilator (Voss, 1967).
Passage of oesophageal thermometer lead and large-bore stomach tube.
Establishment of arterial and venous pressure and blood-gas monitoring by means of femoral artery and jugular venous catheterization.
The two techniques differed in the inclusion or omission of halothane.

**Technique 1.**
Halothane with nitrous oxide and oxygen was used both for induction and maintenance of anaesthesia. For induction 3 per cent halothane vapour was utilized, while for maintenance 0.5-2 per cent depending upon the demands of the surgery.

**Technique 2.**
Anaesthesia was induced with thiopentone sodium (5 per cent solution) administered by an ear vein. During maintenance of anaesthesia with nitrous oxide and oxygen supplemental doses of thiopentone, with in some cases the addition of 3-5 mg doses of tubocurarine, were administered.

In a group of 7 pigs which survived aborted episodes of malignant hyperpyrexia and were the subject of further specific experiment, e.g. identification of triggering agents, monitoring was first established under thiopentone-nitrous oxide-oxygen anaesthesia.

**Incidence of malignant hyperpyrexia.**
With the two anaesthetic techniques used, the syndrome of malignant hyperpyrexia occurred only in those pigs which were exposed to halothane. The incidence of occurrence of the syndrome in the three breeds of pig when anaesthetized with halothane (technique 1) is set out in table I.

<table>
<thead>
<tr>
<th>Breed</th>
<th>Total No.</th>
<th>Malignant hyperpyrexia</th>
<th>% incidence</th>
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<tbody>
<tr>
<td>Landrace</td>
<td>85</td>
<td>21</td>
<td>24.7</td>
</tr>
<tr>
<td>Landrace/Large White</td>
<td>59</td>
<td>2</td>
<td>3.4</td>
</tr>
<tr>
<td>Large White</td>
<td>16</td>
<td>0</td>
<td>0</td>
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</table>

"An explosive thermal idiosyncrasy" (Wilson et al., 1967) is present in response to exposure to halothane in one quarter of the pure Landrace pigs we have used. It is pertinent to note that the pigs in which Hall and co-workers (1966) found this trait in response to suxamethonium were of the Landrace/Wessex breed (Woolf, N., 1969, personal communication). The appearance of the syndrome in the cross-breed Landrace/Large White pigs we have used has been rare.

As in reported human cases, the sex of the animal had no influence on the appearance of the syndrome.

**THE CLINICAL SYNDROME**
The clinical syndrome in pigs develops with dramatic speed. The onset, with rare exception, occurs within minutes of exposure to halothane. The changes in physiological parameters are gross and all the manifestations appear almost simultaneously. These are:

1. **Tachycardia.**
2. Stiffness and hardening of the muscles.
3. Tachypnoea and hyperventilation which rapidly progresses to apnoea.
5. A rapid sustained rise in temperature up to as much as 45°C.

**Tachycardia.**
With the onset of this syndrome a sinus tachycardia of 200-300 beats/min develops and is maintained until very shortly before the death of the animal. Arterial blood pressure is maintained for 30-60 minutes, thereafter declining progressively due to falling cardiac output. Terminally, ventricular arrhythmias, coupling, and finally gross bradycardia precede asystole. Asystole has occurred at varying periods from the commencement of the condition, the shortest being 10 minutes, the longest 165 minutes. Mean survival time was 106 minutes.
Fig. 1
Susceptible pig anaesthetized with thiopentone. Note relaxed hind limbs.

Fig. 2
Same pig as fig. 1, 4 minutes after administration of halothane. Note extension of hind limbs.
**Muscle rigor.**

Rigor of the muscles occurs rapidly. Though generalized, it is most obvious in the limbs which become rigidly extended, as in rigor mortis (figs. 1 and 2).

The administration of tubocurarine in doses of 6–10 mg has had no effect on this rigor, which is maintained until the death of the animal and beyond. Observation of animals up to 18 hours postmortem has revealed no softening or autolysis of the muscle rigidity.

**Tachypnoea and hyperventilation.**

Tachypnoea commences with the onset of the syndrome and is rapidly succeeded by apnoea. When attacks of the syndrome have been successfully aborted by the discontinuance of halothane within minutes of its introduction, before the onset of apnoea, the tachypnoea has persisted for up to 30–45 minutes. This tachypnoea is extreme with respiratory rates up to 125 b.p.m.—panting is a better description. In some survivors, if apnoea has ensued following discontinuance of the halothane, tachypnoea has resumed after a period of IPPR with oxygen. In these pigs, though exposure to halothane was extremely brief, deep coma has persisted until the tachypnoea has recommenced.

**Blotchy cyanosis.**

Cyanosis of the skin, described in some human cases, is a constant early feature in the pig. As measured arterial Po$_2$ at this stage is not reduced (vide infra) it indicates skin vasoconstriction, with areas of stagnant hypoxia. The skin soon becomes hot to the touch.

**Rapid, sustained rise in temperature.**

Rise in temperature is rapid and extreme. An example is presented in figure 3. In this experiment a pig which previously survived an aborted attack of the syndrome was re-challenged with halothane after anaesthesia had been induced with thiopentone and monitoring established. The first change in oesophageal temperature was recorded at 6 minutes, with a subsequent rise at a rate of 1°C every 7 minutes. Other examples are to be seen in figures 4 and 5. In these examples, the rate of rise was as fast as 1°C in 5 minutes at one stage. When unmodified by cooling, oesophageal temperatures reached 45° in some pigs before death; 43–44° was the common end point.

**Acid base and blood-gas state.**

Acidosis was profound and invariable with both gross metabolic and respiratory components; 15–20 minutes from the first signs of the syndrome the arterial acid base state has been typically: pH 6.8; Pco$_2$>150 mm Hg; BE<-22 m.equiv/l.

No primary respiratory reason for the gross hypercapnia—pulmonary, lesion or underventilation—was apparent in any animal. As soon as the syndrome commenced IPPR with oxygen was instituted with tidal volumes of 500 ml and minute ventilatory volumes of the order of 10 l./min. Clear air entry to both lungs was noted in all animals. This gross hypercapnia, with its probably accompanied high carbon dioxide output is paralleled in human cases in which carbon dioxide absorbers were observed to become rapidly very hot (Cullen, 1966; Davies and Graves, 1966; Hogg and Renwick, 1966).

Arterial oxygen tension values (Clarke electrode) were above normal in all animals, ranging from 145 mm Hg in pigs breathing 30 per cent nitrous oxide and oxygen to 400 mm Hg when IPPR with oxygen alone had been instituted. These values fell off later when there was evidence of progressive circulatory failure. Mixed venous blood always appeared extremely desaturated. Values observed ranged from 30 to 60 mm Hg.
FIG. 4
Record of oesophageal temperature and other events during administration of suxamethonium to a susceptible pig anaesthetized with thiopentone.
Thiop. = thiopentone; S.C. = suxamethonium; Intubn. = intubation.

FIG. 5
Record of oesophageal temperature and other events during administration of suxamethonium and cyclopropane to a susceptible pig. Control period anaesthesia-thiopentone.
Thiop. = thiopentone; S.C. = suxamethonium; Cyclo. = cyclopropane; Intubn. = intubation.
Electrolyte changes.
Limited investigation of serum sodium and potassium changes has shown the development of a marked hyperkalaemia. Levels as high as 11–12 m.equiv/l., which could well have accounted for the ultimate cardiac asystole, were observed in some animals.

Blood cultures.
Blood from 2 pigs which died of the syndrome was submitted to bacteriological culture with negative results.

Histology.
Postmortem examination of pigs dying of malignant hyperpyrexia showed no macroscopic abnormalities. Tissue from 4 such pigs was examined histologically (Prof. C. J. Uys); sections of brain, liver, kidney and adrenals showed no changes of note. Only striated muscle showed demonstrable changes (fig. 7). In these sections the majority of fibres appeared normal. However, isolated fibres were shortened and shrunken. At their ends these fibres were separated from adjacent fibres, and in some instances they appeared to have ruptured transversely. These shortened fibres were more intensely eosinophilic than normal fibres. Similar fibres were observed in muscle sections from normal pigs, but in the affected pigs they were more frequent and readily observed.

CARBOLGEN + HALOTHANE
CARBOLGEN
WATER
BATH
38°C
AGITATION
KREBS RINGER
SOLN.
MUSCLE

FIG. 6
Method of incubation and exposure of muscle to halothane “in vitro”.

PROGNOSIS AND TREATMENT
As with human cases (Wilson et al., 1967), the prognosis in the pig, once the syndrome is established, is extremely poor. Ten minutes after exposure to halothane and commencement of the syndrome, discontinuance of this agent, IPPR with oxygen, active cooling, treatment of the acidosis, and other measures, have had no influence on the inexorably fatal outcome of the condition. Cooling has failed to prevent mortality, even on those few occasions when a drop in temperature was achieved. Doses of sodium bicarbonate, sufficient to correct base deficits, of the order of 40–50 m.equiv/l. of extracellular water administered over 30 minutes have had little effect in changing pH. If this has been shifted up at all, it has rapidly reverted to less than 7. Attempts at hyperventilation have met with no success in lowering the raised Pco₂, boosted as it is, no doubt, by the infusion of sodium bicarbonate. Administration of up to 0.3M of THAM over 20–30 minutes has had as little success in terms of survival.

In the light of some unproven hypotheses of the biochemical lesion, we have administered the following drugs with complete lack of therapeutic effect:

1. Adrenergic blocking agents: (a) propranolol; (b) propranolol and phentolamine. These drugs were given to block any possible adrenaline-induced or mediated rise in calorigenesis (Havel, 1968; Depocas, 1960; Hsieh, Carlson and Gray, 1957). Pretreatment with these drugs did not prevent the onset of the syndrome, nor did they control it once established.

2. Promethazine. This drug is known to have an “in vitro” antioxidant effect (Slater, 1968). Pretreatment with the drug did not prevent the onset of the syndrome nor did it control the condition once established.

3. Magnesium sulphate. This drug has an inhibitory effect on mitochondrial respiration (Chance, 1959) and was used because of the suggested role of uncoupling of oxidative phosphorylation in this syndrome (Wilson et al., 1966).

4. Insulin and glucose. This combination was used in an attempt to combat the observed hyperkalaemia.
Muscle of susceptible pig under control thiopentone anaesthesia.

Fig. 7
Histological sections of striated muscle. H. & E. stain; magnification ×100.

(a) Normal pig.

(b) Muscle of susceptible pig under control thiopentone anaesthesia.

(c) Muscle biopsied during malignant hyperpyrexia following halothane anaesthesia.
ANAESTHETIC-INDUCED MALIGNANT HYPERPYREXIA

(5) ATP. We observed a fall in muscle ATP during this syndrome (vide infra) and sought to replace it.

Prompt discontinuance of the agent at the earliest moment either of the three major signs appeared (tachypnoea, muscle rigor, tachycardia) left us with 7 initial survivors in 23 examples of this syndrome. These survivors had no treatment. Their survival depended entirely on extremely early diagnosis with discontinuance of halothane within a matter of minutes. In that survival only occurred in cases in which the triggering stimulus —halothane—was discontinued at so early a stage that the syndrome was not properly established, identification of the syndrome could be called in question. However, all survivors developed the full-blown syndrome fatally on a subsequent occasion when re-challenged with halothane or other triggering agent.

THE TRIGGERING AGENT

All 23 instances we have experienced of this syndrome have followed a first exposure to halothane. In the 7 survivors of aborted attacks we have tested other possible triggering agents.

The anaesthetic techniques used in the reported human cases have, in each case, involved multiple agents. These have included thiopentone, halothane, methoxyflurane, cyclopropane, ether, nitrous oxide, and the relaxants suxamethonium and tubocurarine.

We have challenged known susceptible pigs with all these agents individually. Because of the apparent importance of the halogenated hydrocarbon anaesthetic agents, we have tested, in addition, trichloroethylene and chloroform. In the case of a negative response, anaesthesia, temperature and blood-gas monitoring were continued for 1 hour.

A negative response followed administration of thiopentone, nitrous oxide, ether, trichloroethylene, methoxyflurane and tubocurarine. As thiopentone was shown neither to prevent the onset of the syndrome nor to influence its progress once established, monitoring for subsequent specific experiments in survivors was first established under anaesthesia with this agent.

In an experiment complementary to that in which adrenergic blocking agents were administered (vide supra) we challenged a susceptible pig with an intravenous infusion of adrenaline 1:103,000. The syndrome was not triggered.

Positive triggering of malignant hyperpyrexia followed administration of halothane (our standard triggering agent), chloroform, suxamethonium (see fig. 4) and possibly cyclopropane.

The muscle fasciculations that followed administration of suxamethonium were, as in the reported human cases, extremely coarse and tonic, causing the legs to be rigidly extended. The muscle fasciculations that followed the second dose of suxamethonium were the most intense.

A question-mark must be left next to cyclopropane. This drug was tested in a known susceptible pig only after two test doses of suxamethonium had been given (see fig. 5). Malignant hyperpyrexia commenced the moment cyclopropane was administered. But subsequently we demonstrated that fulminant hyperthermia could follow the administration of suxamethonium alone.

AN ASPECT OF MUSCLE FUNCTION

One of the most obvious clinical manifestations of this condition is muscle stiffness, reminiscent of rigor mortis. Szent-Gyorgyi (1944) in his classical studies on muscle concludes that “... rigor and insolubility of the actinomyosin are the different consequences of one and the same condition—a lack of adenosine-triphosphate (ATP)”. This, and the observation that muscle taken from one of our pigs during a fatal episode of malignant hyperpyrexia showed a low ATP content, led us to study the concentration of ATP in the muscle of susceptible pigs and its behaviour “in vitro” to exposure to halothane.

Twelve Landrace pigs were submitted under thiopentone anaesthesia to muscle biopsy. Two biopsies of approximately 2 g each were taken of the gluteal muscle. Each piece of muscle was immediately divided into three aliquots which were blotted, weighed and then treated as follows.

(1) One aliquot was immediately frozen in liquid nitrogen.

(2) A second aliquot was incubated for 30 minutes at 38°C in 15 ml of Krebs-Ringer solution through which carbogen (oxygen 95 per cent, carbon dioxide 5 per cent) was bubbled (see fig. 6). Thereafter it was frozen in liquid nitrogen.

(3) A third aliquot was treated exactly as the second except for the addition to the carbogen of
4 per cent halothane vapour. This resulted in concentrations of halothane in the solution which ranged between 19 and 29 mg/100 ml. Concentrations of halothane in the solution were estimated by gas chromatography (Gadsden, Risinger and Bagwell, 1965).

Following extraction of the muscle in TCA, the concentration of ATP in mM/g of muscle was now measured in each aliquot using a kit supplied by Boehringer (Kit Ref. CAT. No. 15979TWAC). The aliquot duplicates were then averaged to give the concentration of ATP, (i) in fresh muscle, (ii) after incubation without halothane, (iii) after incubation with halothane.

Following muscle biopsy the pig was allowed to recover consciousness and was returned to its pen. Two days after the muscle biopsy each pig was anaesthetized with halothane, nitrous oxide and oxygen, and its reaction was observed.

RESULTS

Of 12 pigs used, 7 showed no abnormal response to halothane, whilst 5 developed malignant hyperpyrexia. The concentrations of ATP measured in muscle are presented in table II, grouped in relation to the pig’s subsequent response to the exhibition of halothane.

The concentration of ATP in fresh muscle was the same in both groups of pigs. Incubation of the muscle with and without halothane caused a fall-off in ATP concentration. In these circumstances, but especially after halothane, fall-off in ATP concentration was greater in muscle from pigs with the hyperpyrexia trait. The constancy of this reaction permitted prediction of the pig’s ultimate response to halothane.

DISCUSSION

Anaesthetic-triggered malignant hyperpyrexia poses a nightmare situation for the clinical anaesthetist. We believe that certain susceptible pigs of the Landrace strain suffer precisely the same “explosive thermal idiosyncrasy” to anaesthetic agents as humans and provide an important, if fortuitous, experimental model for the investigation of this condition.

From our experience, it would appear that the one hope for the patient exhibiting this abnormal response lies in its very early recognition, allowing discontinuance of the triggering stimulus. Early signs which presage the onset of the condition are:

(1) Tachycardia.
(2) An abnormal response to suxamethonium such as coarse fasciculations or sustained muscular contraction.
(3) Abnormal muscle tone that does not respond to reasonable doses of tubocurarine.
(4) Tachypnoea and hyperventilation.
(5) Blotchy general skin cyanosis.
(6) A rapid rise in temperature.

Two accompaniments of this syndrome have been identified: (a) gross acidosis; (b) a fall in muscle ATP.

<table>
<thead>
<tr>
<th>Table II</th>
<th>ATP concentration in muscle.</th>
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<tr>
<td></td>
<td>ATP concentrations in mM/g</td>
</tr>
<tr>
<td></td>
<td>Fresh muscle</td>
</tr>
<tr>
<td>Normal pigs</td>
<td>n=7</td>
</tr>
<tr>
<td>&quot;Hot&quot; pigs</td>
<td>n=5</td>
</tr>
<tr>
<td>Significance of difference between similar means (Student's t test)</td>
<td>0.05&lt;P&lt;0.10</td>
</tr>
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[0.05<P<0.10 Not significant]
Acidosis.

The acidosis which occurs in the presence of an above normal arterial Po$_2$ is characterized by a rapid fall in base and rise in Pco$_2$. The former has recently been shown to be due to a severe rapidly developing lactacidosis, and in the absence of any obvious respiratory cause, the latter is assumed to result from buffering of this acid load (Bennan et al., 1969). Whether this is the primary result of the heat-producing mechanism, a secondary or coincidental occurrence, remains to be investigated. The high Pco$_2$ recorded does serve to explain two clinical observations: (1) hyperventilation progressing to apnoea with the reappearance of hyperventilation should the animal survive; (2) persistent unconsciousness of the animal long after the anaesthetic agent has been discontinued and while the animal is being artificially respired with oxygen only. The former is the normal respiratory response to hypercarbia while the latter is probably carbon dioxide narcosis.

Though we have had no success with it in the pig, it would appear reasonable, from the above observations, to use THAM rather than sodium bicarbonate in treating this acidosis.

The fall in muscle ATP.

In vitro study of pig muscle showed a greater fall-off in ATP concentration in affected pigs after simple incubation as well as an even greater fall-off after exposure to halothane. This may indicate that not only is the response of these pigs to halothane abnormal, but that the muscle cells have an even more basic abnormality. The fall in ATP may be due to either inhibition of mitochondrial respiration (Fink and Kenny, 1968), or perhaps to uncoupling of oxidative phosphorylation (Snodgrass and Piras, 1966; Wilson et al., 1966) or perhaps to the triggering of energy formation via a non-phosphorylating pathway (Challoner, 1966). Whatever its genesis, the fall in ATP content may be an explanation of the rigor-mortis-like rigidity of the muscle (Szent-Gyorgyi, 1944). Though we are ignorant of its theoretical implications this reaction does have a useful practical application. It provides us with a method of predicting which pig will develop malignant hyperpyrexia when exposed to halothane.

The identity of the triggering mechanism remains an enigma. First, some genetic factor appears necessary to provide the environment in which the triggering substances can act. In our pigs, and those of Hall and associates (1966), this genetic factor appears to be associated with the Landrace breed. A genetic factor has been implicated in reports of human cases involving near relatives (Barlow, 1968; Britt, Lochner and Kalow, 1969; Denborough et al., 1962; Purkis et al., 1967). Given this genetic environment, there appears to be no single triggering agent. We have identified halothane, chloroform and suxamethonium. There are probably others. Though a comforting molecular similarity may be seen between halothane and chloroform, the intrusion of the chemically dissimilar suxamethonium is bewildering. This seems to rule out any direct chemical triggering mechanism, leaving us the likelihood of some biophysical phenomenon (Allison and Nunn, 1968).

One thing is certain. If by some quirk of fate Raventós (1956) had used Landrace pigs instead of rats, mice, dogs, cats and monkeys on which to test his new-found anaesthetic, halothane, it would never have emerged from the laboratory to become the most widely used anaesthetic in the world. For who would dare suggest the clinical use of an agent that killed a quarter of those animals exposed to it?

ACKNOWLEDGEMENTS

This research programme is financially supported by the following donors, whom we gratefully acknowledge: the Anglo-American and De Beers Anaesthetic Research Fund; the University of Cape Town Staff Research Fund; and the South African Council of Scientific and Industrial Research.

We acknowledge also our indebtedness to Professor A. B. Bull, Head of the Department of Anaesthetics, for figures 1 and 2 and much helpful, constructive criticism; the Department of Chemical Pathology for serum electrolyte estimations, and Dr. Berman of this department for figure 3; the Department of Pathology for histological sections and Professor C. J. Uys of this department for figure 7; S. Wicht, L. Frith and A. Munroe for technical assistance and the J. S. Marais Laboratory for Surgical Research (Director, Professor C. N. Barnard) for the facilities placed at our disposal.

REFERENCES


ANAESTHETIC-INDUCED MALIGNANT HYPERPYREXIA


BOOK REVIEWS


This is one of the Oxford handbooks for medical auxiliaries. Its author, Dr. Brenda Vaughan, is Reader in Anaesthetics at Makerere University College and Head of the University Department which is situated in Mulago Hospital, Kampala, Uganda. She has written this book based on her experiences in Uganda and other African countries for the medical auxiliaries who are training to become anaesthetists but it should be said right away that it is suitable for a much wider readership.

Medical auxiliaries in Uganda are persons of reasonable educational standard who have generally had a three-year training in medicine and subsequently receive a further course in a specialty, if they adopt one. In the case of auxiliary anaesthetists this subsequent training extends for eighteen months. They are much more akin to the Russian "feldsher" than to the nurse-anaesthetist. In these countries, anaesthetists do work which varies from community medicine to specialties such as anaesthesia and even in some instances they carry out minor surgical procedures. In countries which are incredibly under-doctored they do extremely valuable work and it is indeed difficult to see how the health service in those regions could carry on without them. It may be in time that the local medical schools which are developing in many countries where there have been no such schools, for example, in Africa, will produce an adequate number of doctors in the years to come to make the existence of such auxiliaries unnecessary. The facts of the matter at present are that they exist, that very often the anaesthetic stuff of a hospital consists of only one such auxiliary who works for perhaps two or three surgeons and may, as the writer has seen, have to look after two theatres operating at the same time. Such auxiliaries in training will indeed be grateful for this book.

Dr. Vaughan has written an enlightened text which is based upon a modern approach to the subject and in which there is evidence of an adequately scientific approach for those who must inevitably be mainly "technicians". The physiological and pharmacological principles are clearly and simply stated and generally accurate. As an example of simple basic, clear and admirably direct teaching, the chapter on blood trans-

fusion, haemorrhage and shock would be difficult to beat; but it is really invidious to choose one chapter, for all show the same characteristics. An appendix contains conversion tables for length, volume and weight and pressure, the normal physiological and biochemical values, an excellent glossary, and it even lists some manufacturers of anaesthetic equipment and sundries.

Dr. Vaughan has probably been right in deciding to use the familiar proprietary names rather than the often unfamiliar approved names in the context of the readership she has in view.

The writer has no hesitation in recommending that this book is very suitable indeed for undergraduates, and even for those who are taking their first steps in the specialty, as a primer during the preliminary introductory few weeks. Certainly they could not find a better elementary text.

T. Cecil Gray


Apart from the addition of two short chapters—one on the electrocardiograph in intensive care and the other on the electrocardiograph in anesthetic research—the 2nd edition of this monograph is essentially similar to the first. Only one of the new chapters carries illustrative electrocardiograms which depict the changes induced by lethal hypotension in a dog. The first four chapters deal with the human electrocardiogram in health and disease, the fifth with the various changes attributable to anaesthesia and surgery, and the remainder with the limitations of electrocardiography and the various types of apparatus suitable for use in operating theatres. The quality of the illustrative electrocardiograms is variable—most are good but quite a few are almost indecipherable because of their relatively minute size and too much background shadow. Generally speaking this is a useful little book which presents in compact form, albeit sketchily, the essentials of surgical electrocardiography. As such it is an acceptable and inexpensive introduction to more detailed studies of the subject.

Michael Johnstone