RECENT ADVANCES IN

15

Anaesthesia and Analgesia

Edited by

R. S. Atkinson

A. P. Adams

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ANAESTHESIA AND ANALGESIA

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and
A. P. ADAMS

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Preface

The first and pleasant duty of the editors is to record their debt of gratitude to Dr Christopher Langton Hewer, the author and editor of *Recent Advances in Anaesthesia and Analgesia* from 1932 to 1982, a span of half a century seldom equalled in the history of medical writing. Volume 14, published in 1982, included a short history of the series and it is the hope and endeavour of the present editors to continue and build on the standard and tradition set by Dr Hewer.

Dr Atkinson has now been joined by Professor Adams, and together they have set out to produce a volume reflecting points of growing interest in the field of anaesthesia and intensive care. Once again, they have been fortunate to obtain the services of authorities in their respective fields and for the first time writers from North America have contributed.

The newer drugs isoflurane, atracurium and vecuronium have received individual attention, while the newer intravenous induction agents and narcotic analgesic drugs have been considered in the context of pharmacokinetics and pharmacodynamics. Calcium antagonists play an increasing part in the practice of anaesthesia and intensive care and they have been accorded a chapter in their own right. Techniques also change. High frequency positive pressure ventilation is now available in commercial form, but its place in the management of patients requiring ventilating support remains to be evaluated completely; it is therefore timely to review this topic, a task which has been undertaken by authorities in North America. Spinal analgesia, though not a new technique, has been the subject of increased study in recent years in an effort to understand better the factors governing spread of injected solution and site of action; it has therefore been considered here.

The anaesthetist's work in the general wards and intensive care units of our hospitals is inseparable from that in the operating room. The gastric acid problem is still a cause of worry to obstetric anaesthetists and others and so has been afforded a chapter. The problems of airway obstruction in infants and children, though uncommon, can tax the skill of the anaesthetist to his limits and so the subject has been reviewed. Thermal injuries are of increasing interest to anaesthetists involved in accident and emergency work, particularly in view of the lung damage which can be caused by smoke and fumes; though burns patients are often transferred to specialist centres, the importance of proper management is so vital to success that it has been thought appropriate to devote a chapter to the subject. Anaesthetists have been aware of the syndrome of malignant hyperpyrexia for some years, but its rarity in the average anaesthetist's practice, together with the need for skilled management should a case present unexpectedly, has made the subject of great interest, especially in view of possible links with other conditions. There have been considerable additions to the literature of this subject in recent years and the editors have been fortunate to obtain a comprehensive review from acknowledged leaders in this field.

No anaesthetist can be satisfied with the incidence of morbidity and mortality which, as recent surveys have indicated, are higher than desirable. The volume is rounded off by a chapter which draws attention to this problem. Fundamental teaching relating to safety in anaesthetic practice is of ongoing concern and importance and this final chapter does this in relation to some of the anxiety evident in recent surveys.

In a book of this kind, some overlap is inevitable, but the editors have allowed each author to express the subject in his own way believing that consideration of matters from more than one viewpoint is advantageous. It is their hope that the reader will find the subject matter interesting and informative whether he be clinical anaesthetist or examination candidate. It is hoped that the book will also appeal to anaesthetists working in many parts of the world where conditions are less privileged than in more affluent countries.

The editors would like to thank the contributors for their hard work and prompt delivery of manuscripts. The publishers are also thanked for their considerable help in getting this material to the readers in as rapid a manner as possible.

Southend and
London, 1985

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1. Isoflurane

R. M. Jones

One of the more positive aspects of the development of nuclear weapons in the early 1940s was the advance in fluorine chemistry which occurred during the early attempts to separate the isotopes of uranium. These advances in fluorine technology were to be put to use in the development of anaesthetics which fulfilled the hitherto seemingly incompatible goal of non-flammability coupled with minimal toxicity. It had previously been recognised that the halogenation of compounds with chlorine was associated with nonflammability. However, the relative instability of the carbon-chloride bond tended to increase toxicity (e.g. chloroform, $CHCl_3$). The carbon-fluoride bond is more stable and halothane, which contains a CF_3 moiety (Fig. 1.1) was developed

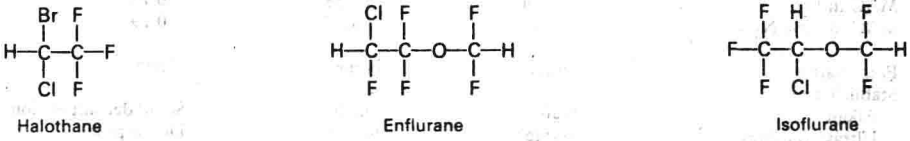

Fig. 1.1

after the second world war by Imperial Chemical Industries in the United Kingdom. Raventós[1] first published an account of its use as a general anaesthetic in 1956. The introduction of halothane marked a major advance in the quality and safety of anaesthetic care but the agent possesses some characteristics which fall short of the properties wanted in an ideal inhalational agent. Two of these — the sensitisation of the heart to endogenous or exogenous catecholamines and the rare, but potentially lethal, association with hepatitis — probably ensured that the search for a safer agent would continue. During the decade following the introduction of halothane a number of compounds having the same basic structure as halothane — alkanes — were studied.[2,3] However, none were clearly superior to halothane and all alkanes studied were associated with a tendency to cause dysrhythmias. In the early 1960s Ross Terrell and his co-workers in the United States were investigating a series of methyl ethyl ethers which seemed not to possess the dysrhythmic tendency of alkanes. The 347th compound synthesised by Terrell in 1963 was enflurane. Two years later its structural isomer isoflurane, a more difficult compound to synthesise, was isolated (the 469th compound that this group isolated). Halothane, enflurane and isoflurane are the principal potent volatile anaesthetic agents currently available in Europe and the United States. A number of factors, including the increasing developmental costs of agents, suggest that the likelihood of the introduction of any further inhalational agents in the foreseeable future is small.

STRUCTURE AND PHYSICIAL PROPERTIES

Isoflurane is 1-chloro-2,2,2,-trifluoroethyl difluoromethyl ether. Its structure, as well as those of halothane and enflurane is shown in Figure 1.1, whilst the more important physical characteristics of the three agents are shown in Table 1.1.

Table 1.1 Physical characteristics

	Isoflurane	Enflurane	Halothane
Molecular weight (g)	184.5	184.5	197.4
Boiling point (°C)	48.5	56.5	50.2
Specific gravity (25°C)	1.50	1.52	1.86
Vapour pressure at 20°C (mmHg)	238	172	243
Partition coefficients (37°C)			
Blood–gas	1.4	1.9	2.3
Water–gas	0.6	0.8	0.7
Oil–gas	97.8	98.5	224.0
Fat–gas	94.5	105.0	185.0
Conductive rubber–gas	62.0	74.0	120.0
MAC in O_2	1.28	1.58	0.75
MAC in 70% N_2O	0.56	0.57	0.29
Preservative	None	None	Thymol
Stability to:			
Alkali	Stable	Stable	Some decomposition
Ultraviolet light	Stable	Stable	Decomposes
Metal	Stable	Stable	May react
Per cent recovered as metabolites	0.2	2.4	20

Factors of note from Table 1.1

Vapour pressure. Halothane and isoflurane have similar vapour pressures. A vaporiser calibrated for halothane will provide acceptably accurate vapour concentrations of isoflurane. Using a Fluotec vaporiser in this way is not to be recommended because of the potential for an anaesthetic mishap should there be confusion about which agent is in the vaporiser.

Partition coefficients. Isoflurane has a lower blood–gas partition coefficient than either halothane or enflurane. Induction and recovery are thus more rapid, although the speed of induction is somewhat limited by the ethereal smell of isoflurane. Respiratory problems, such as coughing and breath holding, during induction are related to a high vapour concentration. There is no doubt that with experience using the agent (and only slowly increasing the vapour concentration) the incidence of respiratory problems can be minimised. In the writer's experience, respiratory problems during induction in suitably premedicated children occur in only a relatively small proportion of patients. The significantly lower fat solubility (about half that of halothane) also

facilitates a more rapid recovery. The lower blood and fat solubility also mean that the depth of anaesthesia is more readily adjusted by the anaesthetist to meet the changes in the degree of surgical stimulus.

The blood–gas partition coefficient of anaesthetic agents may vary with age (vide infra)[4] as does the minimum alveolar concentration (MAC). Children have a lower blood–gas partition coefficient than adults. Elderly patients (>75 yr) may also have a lower partition coefficient. Thus the rate of rise of alveolar partial pressure may be more rapid in the younger and older age groups.

Minimum alveolar concentration. A number of factors influence MAC. Each 1 per cent inspired N_2O decreases this index by approximately the same amount. Thus 50 per cent N_2O will decrease MAC by approximately 50 per cent. Depressant drugs in general—such as narcotics or alcohol—also decrease MAC. Interestingly pancuronium has been shown to decrease the MAC for halothane,[5] and thus may do so for other agents. Age has a marked influence on MAC. The MAC of isoflurane at various ages in 100 per cent O_2 and 70 per cent N_2O is:

Age (yr)	70% N_2O	100% O_2
26 ± 4	0.56	1.28
44 ± 7	0.50	1.15
65 ± 5	0.37	1.05

Stability. Isoflurane and enflurane are more stable molecules than halothane and no preservative is needed to prevent oxidative decomposition. The residue of the less readily vaporised preservative may cause mechanical problems and inaccuracy of vaporisers. Unlike halothane, isoflurane and enflurane do not react with metal and are stable in soda–lime and ultraviolet light. The lower solubility coefficients and rapid recovery coupled with great molecular stability suggest that the toxic potential (either organ toxicity in patients or toxicity due to long term exposure of trace amounts in theatre personnel) of isoflurane is likely to be very small.

EFFECTS ON THE HEART AND CIRCULATION

One index of the safety of an anaesthetic agent is provided by the difference between the concentration producing anaesthesia and the concentration producing lethal circulatory failure in animals. This has been defined as the cardiac index.[6] There seems little doubt that in these terms isoflurane provides a greater margin of safety than either halothane or enflurane.[6,7,8] However, isoflurane is a myocardial depressant. This has been demonstrated in vitro,[9,10] in vivo in intact laboratory animals[11] and in patients undergoing surgery.[12] There has been some controversy in the past concerning the degree of depressant activity of isoflurane. A much quoted and carefully performed study in human volunteers reported that 1–2 MAC isoflurane had no effect on a number of indices of myocardial performance.[13] These included cardiac output, the amplitude of the IJ wave of the ballistocardiograph, ejection time, mean rate of ventricular ejection and the pre-ejection period. However, a recent study in

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ASA I and II patients undergoing elective surgery utilised two dimensional trans-oesophageal echocardiography to estimate the velocity of circumferencial fibre shortening (V_{cf}) as an index of contractility.[12] Isoflurane (as well as halothane and enflurane) caused a decrease in Vcf and hence, it was concluded, was associated with some myocardial depressant effects even at relatively low concentrations (end tidal concentration of 1–1.5 per cent). Many factors have contributed to the variable results obtained from in vitro or in vivo animal work and human volunteer or patient studies. Amongst these must be numbered difficulties in defining and comparing parameters of contractility as well as the interdependence of certain indices (such as velocity of shortening or the pre-ejection period) with factors such as heart rate and afterload. For example, V_{cf} (circumferential velocity of shortening) is a proven estimator of contractility[12] but it is an ejection phase index and as such is directly dependent on heart rate and inversely related to afterload — both of which may be changed by isoflurane (vide infra). Current evidence would suggest that although isoflurane is undoubtedly a myocardial depressant it is less so than halothane (and probably enflurane too) especially at higher concentrations.[6,7,8,11,12]

Heart rhythm and rate

Cardiac dysrhythmias are due to an alteration in automaticity or to re-entry of the cardiac impulse. In the former, dysrhythmias may be due to reduced automaticity of the sino-atrial (SA) node or enhanced automaticity at a site outside the SA node — or a combination of these effects. The SA node normally serves as the cardiac pacemaker as it has the most rapid rate of spontaneous phase 4 depolarisation. Any factor which changes the rate of phase 4 depolarisation may produce alterations in heart rate and rhythm. It has been shown in the isolated spontaneously beating guinea pig SA node that halothane, enflurane and isoflurane influence the rate of discharge of the node primarily by their effect on the rate of phase 4 depolarisation.[14] There is a suggestion that these agents have different effects on phase 4 so that halothane more markedly decreases the slope of phase 4 depolarisation.[15] This effect may in part at least[14,16] be mediated by alterations in ion function — particularly calcium. The individual agents may thus interfere with calcium (and other ion) flux to a varying extent. This may explain the differing effect of agents not only on contractility (calcium is an essential intermediary in excitation–contraction coupling) but also on changes in phase 4 depolarisation — and hence of those dysrhythmias due to alterations in automaticity.

Re-entry is an underlying mechanism of many cardiac dysrhythmias. It may occur at many sites in the heart, for example the SA node (premature atrial depolarisation), the atria (atrial flutter or fibrillation), the atrioventricular node (paroxysmal supraventricular tachycardia) and the ventricles (premature ventricular depolarisation, ventricular tachycardia). Unidirectional block and slowing of conduction are prerequisites for the development of a re-entrant mechanism.[17] It is very likely that ventricular, His-Purkinje and AV nodal conduction are affected to different degrees by halothane, enflurane and isoflurane. There have been conflicting reports on the effect of these volatile agents on conduction.[18,19,20] However, it would appear that all agents cause some slowing of AV nodal conduction but that this is most marked with halothane and least marked with isoflurane.[18] Additionally, although enflurane may have some influence on His-Purkinje conduction — it is less marked than halothane. Isoflurane appears to have little or no effect on His-Purkinje conduction. Lastly,

halothane but not isoflurane or enflurane decreases ventricular conduction.[18] In their comprehensive review on anaesthetic agents and cardiac electromechanical activity, Pratila & Pratilas[21] have reviewed the underlying mechanism for the sensitisation of the myocardium to catecholamines during anaesthesia using volatile agents. They have suggested that catecholamine-induced dysrhythmias are probably due to a re-entry phenomenon. Agents which are associated with most slowing of conduction, will predispose to circumstances in which re-entry is most likely to occur. As isoflurane is associated with little disturbance of conductivity and enflurane only with some changes in His-Purkinje and AV nodal conductivity, on theoretical electrophysiological grounds isoflurane should cause little sensitisation of the myocardium to catecholamines and enflurane should cause less than halothane. This has been shown to be the case both in experimental animals[22] and in normocapnic anaesthetised patients.[23,24] The resistance to ventricular ectopic beats occurring during isoflurane anaesthesia seems to extend to other vasoactive agents such as metaraminol and phenylephrine[25] and to aminophylline.[26] This property of isoflurane is of particular clinical importance whenever it can be anticipated that plasma catecholamines will be increased — be these endogenous (e.g. phaeochromocytoma), or exogenous (any operation in which solutions containing adrenaline are infiltrated, e.g. thyroidectomy), and if infusions of vasopressors (e.g. during carotid surgery) or aminophylline are likely to be needed.

Although the heart rhythm is notably stable during isoflurane anaesthesia, the heart rate may increase. Three factors are probably involved in this. Firstly, isoflurane produces a dose related decrease in total peripheral resistance and hence of systemic arterial pressure.[8] Secondly, the baroreceptor reflex remains relatively intact, except at deeper levels of anaesthesia.[27] Thirdly, isoflurane has relatively little effect on the rate of spontaneous discharge of the SA node — unlike halothane which markedly reduces the rate of discharge. It might be anticipated that because baroreceptor activity decreases with advancing age,[28] reflex tachycardia will be less marked in an older age group. This is now established to be the case and an increase in heart rate during isoflurane anaesthesia is uncommon over the age of 50 years. The tendency of isoflurane to increase heart rate must be regarded as a disadvantage, although the use of a narcotic premedication or of intra-operative narcotic supplements are able to minimise heart rate changes.[29] The possible mechanisms behind the increase in heart rate associated with isoflurane can be contrasted to the mechanisms underlying the stable or reduced heart rate which accompanies halothane anaesthesia. Firstly, although isoflurane and halothane both cause a decrease in systemic arterial pressure this is primarily due to a reduction in cardiac output with halothane, rather than an alteration in total peripheral resistance, as it is with isoflurane.[30] Secondly, at less than 2 MAC halothane produces a signigcantly greater attenuation of the baroreceptor reflex than isoflurane.[27,31] Thirdly, halothane has the greatest effect on phase 4 depolarisation and hence most reduces automaticity and the rate of spontaneous discharge of the SA node.

In summary, isoflurane has a greater cardiac index than enflurane or halothane, suggesting a greater margin of cardiovascular safety. Although in common with other agents isoflurane is a myocardial depressant, there is little doubt that in clinical practice it has less effect on contractility than other agents. All three agents decrease systemic arterial pressure but this is primarily due to a decrease in systemic vascular

resistance with isoflurane and a decrease in cardiac output with halothane (enflurane may be regarded as having an intermediate position — it may have less of an effect on cardiac output than halothane, and less of an effect on systemic vascular resistance than isoflurane). Isoflurane does not alter heart rhythm (and in some circumstances may be regarded as anti-dysrhythmic) and does not sensitise the myocardium to catecholamines. This is an important advantage over halothane. Heart rate may increase in younger patients, but this may be attenuated by the use of a narcotic analgesic in the anaesthetic sequence.

EFFECTS ON THE RESPIRATORY SYSTEM

If unstimulated volunteers are anaesthetised with halothane, enflurane or isoflurane, there is an increase in arterial P_{CO_2}, indicating that these agents are respiratory depressants. In these terms it would appear that enflurane is the most depressant and halothane the least, with isoflurane being intermediate between the two.[30,32,33] Indeed the respiratory depression associated with enflurane and to a lesser extent isoflurane is such that a depth of anaesthesia sufficient to allow atraumatic tracheal intubation, may be difficult to achieve unless ventilation is assisted. Like halothane and enflurane, isoflurane increases respiratory rate and decreases tidal volume. Surgical stimulation decreases the degree of respiratory depression, probably due to the effect of catecholamines on the central control of respiration. Like other agents, isoflurane depresses the respiratory response to both hypoxia[31] and its augmentation by carbon dioxide,[8] thus reducing — and at deeper levels of anaesthesia (2MAC isoflurane) abolishing — the compensation of a spontaneously breathing patient to changes in arterial oxygen or carbon dioxide tension.

EFFECTS ON MUSCLE TONE

The ability of inhalational anaesthetics to produce and potentiate neuromuscular blockade has been recognised for seventy years.[35,36] Isoflurane and enflurane provide sufficient muscle relaxation so that at deeper levels of anaesthesia even abdominal surgery may be performed without the use of muscle relaxants. However, using these agents in such a manner is associated with a generally unacceptable degree of respiratory depression. Indeed the marked respiratory depression seen at deep levels of enflurane or isoflurane anaesthesia may — at least in part — be due to their (respiratory) muscle relaxant properties. Therefore, in most situations in which muscle relaxation is indicated, the administration of muscle relaxant drugs is to be preferred to deep isoflurane anaesthesia. Isoflurane and enflurane enhance the action of non-depolarising relaxants to a similar degree — and both do so considerably more than halothane. Thus the dose of relaxant needed to produce a sufficient degree of muscle relaxation is much reduced during isoflurane anaesthesia.

EFFECTS ON THE CENTRAL NERVOUS SYSTEM

In common with enflurane and halothane, isoflurane decreases cerebral metabolism and hence cerebral oxygen consumption. However, unlike enflurane, its isomer isoflurane does not produce any electroencephalograph (e.e.g.) or overt evidence of

convulsive activity in man. Unlike halothane or enflurane, low concentrations (< 1.0 MAC) of isoflurane do not cause an increase in cerebral blood flow if the arterial P_{CO_2} is normal.[8,30] At greater depths of anaesthesia all these agents will increase cerebral blood flow, and hence intracranial pressure, although isoflurane appears to increase flow less than halothane.[30] Another advantage of isoflurane is that even in patients with a space occupying lesion this increase in pressure will respond to hyperventilation.[37] If halothane is used hyperventilation needs to be performed prior to the introduction of the anaesthetic. Therefore isoflurane has some advantages over halothane and enflurane in neurosurgical anaesthetic practice. However, in common with other volatile agents isoflurane has no potential protective effect on the development of post-traumatic cerebral oedema[38] — unlike barbiturates and other intravenous anaesthetic agents.

Although isoflurane may not protect against post-traumatic cerebral oedema, there is evidence from animal studies to suggest that it may confer some protection from the cerebral effects of hypoxia or ischaemia[39], in the same way that barbiturates[40] have been shown to provide some protection in animal models of incomplete ischaemia. The underlying mechanism for this protection, conferred by either barbiturates or isoflurane, is presumably associated with the depression of cortical electrical activity and of cerebral metabolism. The clinical significance of these findings are unclear but there is the suggestion that a certain depth of isoflurane anaesthesia may be associated with some protection for the brain against periods of hypoxia — such as may occur during a transitory period of profound hypotension.

METABOLISM

As previously noted in the discussion on the physicochemical properties of isoflurane, the molecule is extremely stable. No preservative is needed to prevent oxidative decomposition and it does not react with metal, soda–lime or ultraviolet light.

A very small percentage of inhaled isoflurane is recovered as urinary metabolites (0.2 per cent)[41] which can be compared to an estimate of metabolism of approximately 2 per cent[42] for enflurane and some 20 per cent for halothane.[43] Renal toxicity is associated with a serum fluoride level of about 50 μmol/litre.[44] The plasma levels associated with 3 MAC hours exposure to isoflurane are 2–3 μmol/litre.[44] Coupling this molecular stability with a low solubility and rapid recovery leads one to anticipate that the toxic potential of isoflurane will be low. Isoflurane, enflurane and halothane reduce renal blood flow and glomerular filtration rate. However, exposure to isoflurane (either prolonged or repeated) is not associated with renal damage and pre-existing renal disease is not a contraindication to its use.

Although the precise mechanism linking hepatic toxicity to volatile anaesthetic exposure (especially halothane) remains a matter of some controversy,[45] the remarkably low metabolism and molecular stability of isoflurane suggests that isoflurane will not prove to be hepatotoxic. Previous exposure to halogenated anaesthetics or pre-existing liver disease are not at present considered to be contraindications to the use of isoflurane.

Just as the existence, frequency and mechanism of halothane induced hepatitis has been a controversial topic, so too has the association of volatile anaesthetic agents with carcinogenicity. Indeed the release of isoflurane for general clinical use was delayed by

a report linking isoflurane with an increased incidence of hepatic tumours in mice.[46] Subsequent work[47] (in which the author of the first report participated) failed to confirm the earlier findings. Although the study design of the second investigation was different (and improved) from the first it is possible that contamination of the food (by polybrominated biphenyls — known teratogens) of the mice in the original study was the cause of the erroneous finding.

Finally, although in vitro tests suggest that isoflurane (and enflurane) may be less potent than halothane in provoking malignant hyperpyrexia,[48] it is probably unwise to administer isoflurane to susceptible patients.

USE IN INFANTS AND CHILDREN

There is little published data on the use of isoflurane in infants and children. As previously noted the incidence of respiratory problems during isoflurane induction of anaesthesia in infants and children becomes less with experience using the agent. It is the writer's experience that problems such as coughing or laryngospasm, although somewhat more common than when using halothane, should not occur in more than about 5 to 10 per cent of premedicated patients. The effect of learning on the incidence of respiratory problems may account for the very high incidences that have been reported. Friesen & Lichtor of the Children's Hospital, Denver, reported an incidence of severe laryngospasm associated with copious pharyngeal secretions in 40 per cent of unpremedicated infants under 6 months of age.[49] Even with atropine premedication these authors experienced an incidence of laryngospasm of 23 per cent. Although these figures seem very high, there remains the possibility that young infants have a higher incidence of respiratory problems than older children. It would seem wise to prescribe an antisialogogue prior to anaesthesia with isoflurane if a gaseous induction technique is envisaged. Another study has noted that respiratory problems are more common in unpremedicated children (aged 8 months to 14 years) using isoflurane compared to halothane,[50] which would reinforce this suggestion. Infants induced with halothane or isoflurane were reported to have similar reductions in heart rate[49,51] — about 30 per cent — an effect which was lessened in both groups by atropine premedication. The surprising similarity in the reduction of heart rates in the infants receiving either agent may have as a basis the diminished baroreceptor response in the very young.

OBSTETRIC ANAESTHESIA

Studies using uterine muscle in vitro have demonstrated that halothane, enflurane and isoflurane cause a dose related decrease in contractility, there being no significant difference between the agents.[52] This is related to the clinical finding that all three agents are associated with an increase in blood loss during abortion procedures.[53,54] These volatile anaesthetics are probably unsuitable for use during this type of procedure,[8] especially if used in higher concentrations as the sole anaesthetic agent. The effects on uterine musculature have in the past lead to some reservations regarding their use during anaesthesia for Caesarean section. However, it is now well established that in low concentration any of these agents may be used to supplement a N_2O–O_2 technique to ensure that maternal awareness is prevented.[55] Warren and his

co-workers supplemented a 50 per cent O_2–50 per cent N_2O technique with either 0.5 per cent halothane, 1.0 per cent enflurane or 0.75 per cent isoflurane.[55] They measured maternal and neonatal blood–gas tensions, acid–base balance, blood lactate level, Apgar score and the early neonatal neurobehavioural scale to assess the inhuence of these anaesthetics on the maternal and neonatal condition. They demonstrated that any of these agents at the concentrations studied prevented maternal awareness, did not increase blood loss and maintained normal maternal and neonatal conditions. Low concentrations of isoflurane therefore appear to be safe for use during anaesthesia for Caesarean section delivery, although apart from the innate advantages of isoflurane (e.g. stability of cardiac rhythm and less interference with baroreceptor reflexes) it does not appear to have any specific advantage over halothane or enflurane.

DAY-STAY SURGERY

A useful characteristic for any drug used in the anaesthetic sequence for patients presenting for surgery on a day-stay basis is that it should not have a long duration of action and there should be few hangover effects. Hence, a short acting analgesic such as alfentanil is to be preferred to phenoperidine or morphine and relaxants such as atracurium or vecuronium are to be preferred to agents such as pancuronium or tubocurarine (Ch. 2 & 4). In these terms the low blood and fat solubility of isoflurane would seem to suggest that this agent might have a useful place in anaesthesia for day-stay surgery. Indeed, it is reasonable to assume, as Drummond has suggested,[56] that the decrement in mental function following exposure to volatile anaesthetics is in proportion to the concentration of the agent remaining. Davison and colleagues have studied the psychological effects of halothane and isoflurane anaesthesia and demonstrated that compared to halothane, isoflurane had less effect on mood and intellectual function—differences consistent with their different solubilities and metabolism.[57] Although this study was not designed to assess psychological function following brief exposure to the agents (by its very nature day-stay surgery tends to be of brief duration) the implications for day-stay surgery are clear. There is very little published data regarding the use of isoflurane in outpatients. Pandit and her colleagues at the Mott Children's Hospital in Ann Arbor have compared the induction and recovery characteristics of halothane and isoflurane in 74 children presenting for myringotomy on an outpatient basis.[50] They reported that both induction time and quality were less good with isoflurane compared to halothane and that although the 'alert time' with isoflurane was shorter than with halothane recovery after isoflurane was marked with coughing, salivation and thrashing about resulting in a significantly lower recovery score. Hence the previous suggestion that a gaseous isoflurane induction in the unpremedicated child is unsuitable, is reinforced. The study also raises the point that rapid recovery after surgery may be associated with some unwanted effects. Poor recovery characteristics have also been noted after isoflurane anaesthesia in adults especially following upper abdominal surgery in which analgesics have not been used in the anaesthetic sequence. The provision of adequate analgesia before awakening appears to prevent this phenomenon. However, the potential for minimal hangover following isoflurane anaesthesia is an attractive feature for day-stay patients.

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