Inhalation Anaesthesia: From Diethyl Ether to Xenon

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Abstract  Modern anaesthesia is said to have began with the successful demonstration of ether anaesthesia by William Morton in October 1846, even though anaesthesia with nitrous oxide had been used in dentistry 2 years before. Anaesthesia with ether, nitrous oxide and chloroform (introduced in 1847) rapidly became commonplace for surgery. Of these, only nitrous oxide remains in use today. All modern volatile anaesthetics, with the exception of halothane (a fluorinated alkane), are halogenated methyl ethyl ethers. Methyl ethyl ethers are more potent, stable and better anaesthetics than diethyl ethers. They all cause myocardial depression, most markedly halothane, while isoflurane and sevoflurane cause minimal cardiovascular depression. The halogenated ethers also depress the normal respiratory response to carbon dioxide and to hypoxia. Other adverse effects include hepatic and renal damage. Hepatitis
occurs most frequently with halothane, although rare cases have been reported with the other agents. Liver damage is not caused by the anaesthetics themselves, but by reactive metabolites. Type I hepatitis occurs fairly commonly and takes the form of a minor disturbance of liver enzymes, which usually resolves without treatment. Type II, thought to be immune-mediated, is rare, unpredictable and results in a severe fulminant hepatitis with a high mortality. Renal damage is rare, and was most often associated with methoxyflurane because of excessive plasma fluoride concentrations resulting from its metabolism. Methoxyflurane was withdrawn from the market because of the high incidence of nephrotoxicity. Among the contemporary anaesthetics, the highest fluoride concentrations have been reported with sevoflurane, but there are no reports of renal dysfunction associated with its use. Recently there has been a renewed interest in xenon, one of the noble gases. Xenon has many of the properties of an ideal anaesthetic. The major factor limiting its more widespread is the high cost, about 2,000 times the cost of nitrous oxide.

1 Introduction

On the morning of Friday 16th October 1846, in front of an invited audience in the Bullfinch operating theatre of the Massachusetts General Hospital in Boston, the dentist William Morton administered diethyl ether to Edward Abbott for the excision of a tumour from his neck. This was the first successful demonstration of anaesthesia with ether in man, although anaesthesia with nitrous oxide had been used in dentistry 2 years before. Although the patient subsequently admitted being conscious during the procedure, he had experienced no pain. A newspaper reporter was present in the audience, and the discovery of surgical anaesthesia soon spread worldwide, and ether anaesthesia soon became commonplace. Chloroform was introduced as an anaesthetic almost simultaneously with ether (1847) and for a time largely replaced it in popularity. It was not until the introduction of halothane in 1956 that the popularity of ether waned.

The first half of the twentieth century saw the introduction of a variety of volatile liquids and gases as anaesthetics, most of which are now only of historical interest. Developments in organic fluorine chemistry in the 1950s paved the way for the synthesis of the fluorinated anaesthetic alkanes and ethers used in modern anaesthesia.

2 Physical Properties

2.1 Vapour Pressure

Inhalational anaesthetics are either gases or the vapours of volatile liquids. A substance is a gas when above its critical temperature (the temperature above which it cannot be liquefied irrespective of how much pressure is applied), and a vapour