INTRAVENOUS ANAESTHESIA

THESIS

Submitted in Partial Fulfilment
For The Master Degree in
Anaesthesia

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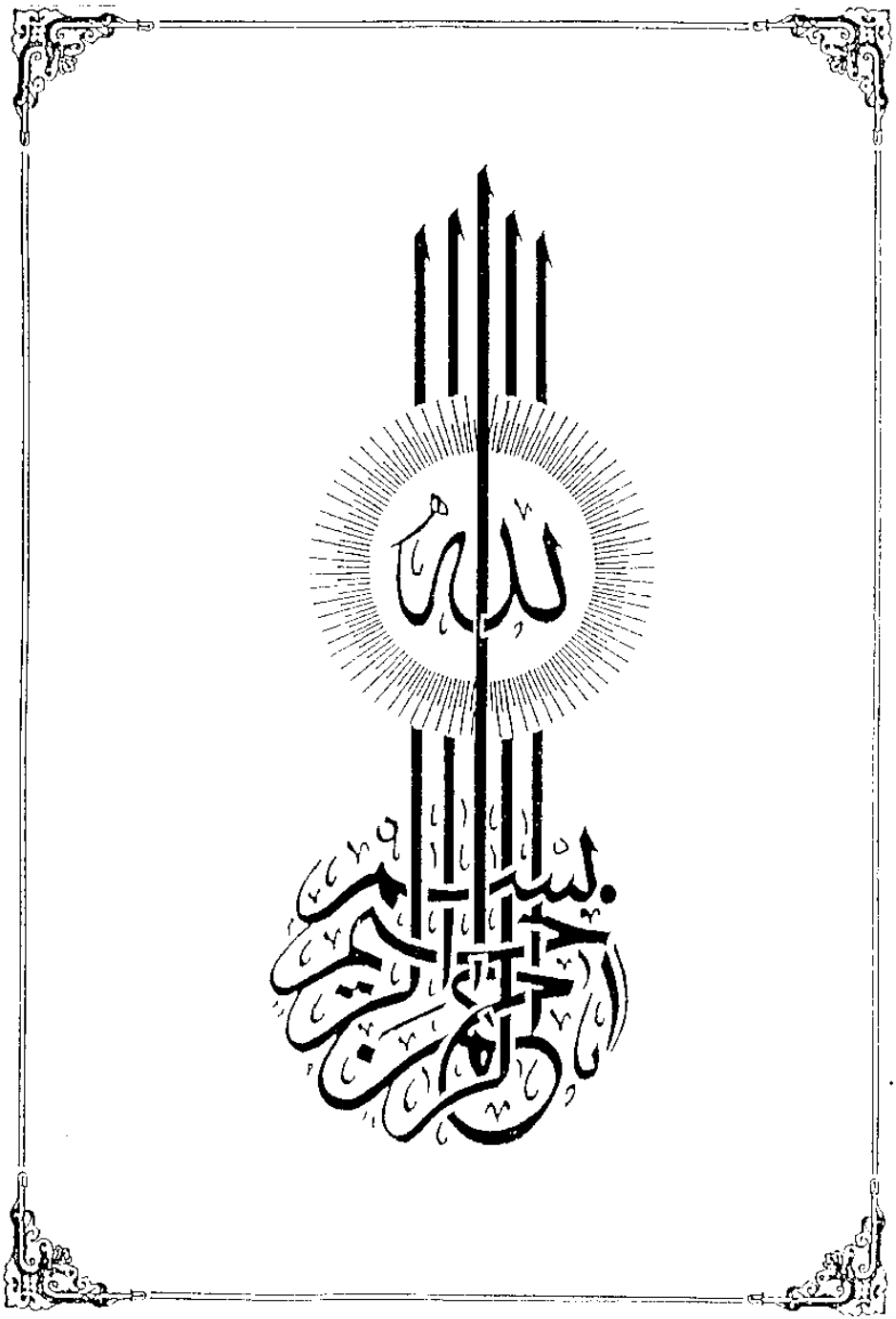
Cairo 1982



ACKNOWLEDGEMENT

I wish to express my deep gratitude to prof. Doctor **SALAH EL DIN EL HALABI**, professor of anaesthesia, Ain Shams University for his keen supervision and precious instructions, feeling a great honour for being his resident.

I am also greatly endebted to Ass. Prof. **AHMED GAMAL EISSA AHMED** for suggesting and supervising the details of this work.

I would also like to thank all the members of the department of Anaesthesiology, Faculty of Medicine, Ain Shams University for their great help and encouragement feeling deep pleasure and much honour to work under their supervision.

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HISTORY

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The first attempt at an intravenous injection in man was made by Christopher Wren in 1656, unconsciousness followed his intravenous injection of opium.

Fisher and Von Mering had synthesised barbitone in 1903. In 1905, Krawkow in St.Petersburg injected Hedonal (methyl-propyl-carbinol-urethane) which gained a measure of popularity in Russia and in other parts of Europe.

Noel and Souttar in 1913 reported the intravenous use of paraldehyde followed in 1916 by magnesium sulphate (Peck and Meltzer). In 1929 Kirschner described intravenous tribromethanol (Avertin). The German obstetrician, E. Bumm, first introduced pernostone (Sodium 2-butyl-B-bromallyl barbiturate) in 1927 and this achieved a measure of popularity. Zefras and McCallum reported in 1929 on the intravenous use of the sodium salt of amylobarbitone (Amytal). Intravenous anaesthesia truly came of age in 1932 with the first published report by Weese and Scharpff of hexobarbitone. In 1934 Laundy started clinical trials of thiopentone (pentothal). The acceptance of intravenous anaesthesia has varied somewhat from country to country. The early popularity of intravenous anaesthesia outside the United Kingdom may be due to

the fact that hexobarbitone was of German origin while thiopentone was an American product. The disastrous results which followed the administration of hexobarbitone and thiopentone of Pearl Harbour in December 1941 may have been responsible for the decrease of their popularity in the United States during the later War years.

Thiopentone in British civilian hospitals during the war years limited by the lack of trained anaesthetists. However, when the experienced specialists returned, the popularity of intravenous anaesthesia increased enormously and even today this form of induction appears to be used more widely in the United Kingdom than in the United States or in some European countries. Despite some competition from other barbiturates, thiopentone has remained essentially unchallenged. Thiamylal, an equally good agent, was passed over for another 15 years (Dornette, 1954). Thialbarbitone, the use of which was first reported by Carrington and Raventos in 1946. Methohexitone, first known as compound 25388 (Stoelting, 1957), is the barbiturate which probably offers most competition to thiopentone. In recent years techniques have been evolved which aim at producing sedation or light sleep with intense analgesia, a ' lytic cocktail'was used comprising a potent analgesic and was termed artificial hibernation.

A few non barbiturate agents have been discovered but having a limited field of use and thiopentone remains on the top of these agents till this day. Selye (1941) described the hypnotic properties of steroids on rats. P'An et al (1955) showed that hydroxydione had a wider safety margin than thiopentone. The end of ninteen-fifties, neurolept analgesia was introduced and was first described by Castro and Mundeleer 1959. The most recent development in this field is "dissociative" anaesthesia e.g. Ketamine which was first synthetised by Steven (1963).

Etomidate is a new non barbiturate intravenous anaesthetic which was synthetised and studied by Janssen and his colleagues (1971) under the number RI 6659. A related development has been the use of the tranquilliser diazepam, and various combinations were developed e.g. pentazepam (1971) which is a combination of diazepam "hypnotic" and pentazocine "analgesic". Lastly, at 1978 long term sedation has been introduced in clinical practice e.g. lorazepam "hypnotic" and buprenorphine "analgesic".

CLASSIFICATIONS

CLASSIFICATION

The classification of intravenous anaesthesia can be approached from the pharmacokinetics, chemical or clinical views.

The terms ultra-short and short are misleading and these descriptive terms should be reserved for drugs which have rapid recovery due to rapid breakdown in the body rather than redistribution to non-nervous tissues. On this basis, the only applicable drugs are ultra short acting - propanidid (epontol, fabontal) and short acting althesin (CT 1341, alfatesine) and etomidate. In contrast with these, return of consciousness following intravenous barbiturates occur with a large amount of active drug remaining in the body and there is a tendency for patient to lapse back to sleep if left undisturbed.

It is desirable for induction agents to be rapid acting, to cause sleep in one arm-brain circulation time in adequate dose. There are two classifications :

(A) Drugs fall into two groups:

1- Those used primarily for induction of anaesthesia e.g. barbiturates, eugenol, steroids.

2- Those used either alone or in combination to produce a particular state, such as dissociative anaesthesia, neuroleptanalgesia, sedation or tranquility.

The second classification :

(B) Intravenous anaesthesia are classified as follows:

a- Barbiturates:

1. Thiopentone (intraval, pentothal, nesdonal).
2. Hexobarbitone (evipan, hexonal).
3. Thiobutobarbitone (inactin).
4. Thialbarbitone (kemithal).
5. Thiamylal (surital).
6. Buthalitone.
7. Methohexitone (brietal, brevital).
8. Methitural (nerval).
9. Enibomal.

b- Non Barbiturates:

A- Eugenols;

1- Propanidid.

2- Propinal.

3- G 29505.

B- Steroids;

1- Althesin.

2- Hydroxydione.

3- Minaxolone.

C- Neurolept techniques;

1- Droperidol.

2- Phenoperidine.

3- Fentanyl.

D- Dissociative anaesthesia;

1- Ketamine.

2- Phencylidine.

3- Cyclohexamine.

4- Etoxadol.

E- Tranquillisers;

1- Diazepam.

2- Midazolam.

3- Flunitrazepam (Ro 5-4200).

F- Miscellaneous;

1- Bromethol.

2- Dolitrone.

3- Sodium gamma-hydroxybutyrates (gamma-OH).

4- Chlormethiazole.

5- Intravenous opiates (narcotics).

6- Methaqualone.

7- Volatile inhalation anaesthetics.

8- Etomidate.

9- ICI 35868.

Recently, Dundee (April, 1979) classified intravenous anaesthetics according to their chemistry, speed of onset and clinical acceptability.

(A) Rapidly acting (induction agents):

- Thiobarbiturates, methylbarbiturates.
- Eugenols.
- Steroids.
- Imidazole derivatives.
- Di-isopropyl phenol.

(B) Slower acting (basal hypnotics and sedatives):

- Phenyl cyclohexamines.
- Benzodiazepines.
- Opiates - neuroleptic/tranquilliser combination.
- Large doses of opiates.

In addition to the above the rapidly acting barbiturates can be classified either according to their chemistry or clinical acceptability.

Chemistry:

a) Thiobarbiturates:-

- Thiopental (pentothal,intraval,ne sdonal).
- Thiamylal (surital, thiobut)
- Thiobutobarbitone (inactins).
- Buthalitone.
- Methitural (nerval).
- Thialbarbitone (kemithal).

b) Methyl barbiturates:-

- Hexobarbitone (evipan, hexonal).
- Methohexitone (brietal, brevital).
- Enibomal.

Clinical acceptability:-

(1) Very satisfactory and equally acceptable:-

Thiopentone, thiamylal, thiobutobarbitone and thialbarbitone.

(2) Unsatisfactory with high incidence of side effects and not used clinically:-

Buthalitone, methitural & hexobarbitone.

(3) Compromise with unique advantages & side effects:-

Methohexitone, enibomal.