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The cardio-respiratory effects of a thoracic epidural anaesthetic as is given for pain relief following upper abdominal surgery were examined in thirteen surgical patients studied in the immediate pre-operative period, following an overnight fast and without premedication. The focus of interest was on its effects on FRC and on gas exchange (measured as $A\text{-}aD_{O_2}$ and $Q_S/Q_T\%$), which have not been previously reported. All subjects were given 10 ml/Kg glucose in saline I.V. during the pre-epidural period. Lidocaine 1.5% was used in all cases, plain lidocaine for the first eight and lidocaine with epinephrine 1/200,000 in the other five subjects. This agent was given to achieve a sensory block to both pin-prick and ice up to $T_4$. Neither FRC nor gas exchange showed any consistent changes following the epidural anaesthetic. These findings are in keeping with what was anticipated from a consideration of the basic physiology and pharmacology concerned and with a review of the pertinent literature.

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# CARDIO-RESPIRATORY EFFECTS OF THORACIC EPIDURAL ANAESTHESIA

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DEDICATION

To Rosy, Ricky and Phlippy

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# CHAPTER I

## INTRODUCTION

The challenge of instituting effective pain relief that is satisfactory both subjectively and objectively concerns physicians from all disciplines. Of particular interest to anaesthetists is the pain leading to ventilatory disturbances, such as that following upper abdominal surgery and trauma, an interest reflected in the large number of publications on the subject (7, 12, 13, 14, 15, 21, 34, 48, 59, 72, 82, 83).

Attention has focussed on the problem of enabling the patient to breathe deeply and cough effectively. These manoeuvres would respectively reverse the tendency to alveolar collapse that follows breathing at low lung volumes, and would favour the removal of secretions to aid in the prevention of atelectasis and postoperative pneumonia (2a, 34, 48, 94).

Pain relief can be accomplished by (a) systemic analgesia; (b) local infiltration of nerves; or (c) epidural or spinal anaesthesia.

The use of systemic analgesics, although subjectively good, is however, objectively unsatisfactory, because of central sedation and respiratory depression, and

the fact that the patient does not spontaneously take a deep breath (53). Peripheral nerve blocks are not practical if the area to be blocked is extensive. The ideal solution appears to be to use a technique whereby the sensory fibres are blocked at the level of the spinal cord, a result which can be achieved by either spinal or epidural anaesthesia. The latter, thought to be safer (65, 70), has been shown to be effective in terms of pain relief (12, 14, 25, 83). However, its acceptability depends on clearcut evidence that it is accompanied by little or no upset of cardiovascular and respiratory function. There are a number of studies reporting the physiological effects of epidural anaesthesia which will be reviewed later. But information on an important aspect of cardio-respiratory function is minimal, namely the effect on pulmonary gas exchange. This is particularly important in view of the possible use of epidural anaesthesia postoperatively, when gas exchange may be impaired for other reasons (4, 64, 75a, 77, 78, 79).

The purpose of this study was therefore to examine the effects of epidural anaesthesia on some unreported aspects of cardio-respiratory function, with

particular reference to its effect on end-expiratory lung volume (Functional Residual Capacity, FRC) and gas exchange.

The interest in FRC stems from its relation to closure of airways and alveolar collapse (30, 31, 32, 61, 75b). Leblanc et al have described the relationship of airway closure, FRC and gas exchange (32). The supine position decreases FRC but not the closing volume (61), while FRC has been shown to be decreased following abdominal surgery (2b, 5b). If this places end-expiratory volume below closing volume, hypoxaemia would be expected. If an epidural anaesthetic can help restore a normal FRC by abolishing the sensation of pain, and thus permit a normal pattern of breathing rather than the "clenched-fist thorax," then it will have served two purposes, namely subjective pain relief and off-setting the possible effects of a low FRC on gas exchange (60, 73). For these reasons the epidural anaesthetic must have no detrimental effects on FRC. A knowledge of the effects of epidural anaesthesia on gas exchange would help delimit its functional consequences.

The studies on the effects of epidural anaesthesia on gas exchange published to date (11, 68, 87) report on arterial blood gases as the only measure of the effects on gas exchange. Arterial $P_{O_2}$ is a reliable measurement of gas exchange upon which to base clinical decisions. It is, however, affected by many factors which include minute ventilation, mixed venous $P_{O_2}$, cardiac output and true right to left shunt. Alveolar-arterial oxygen difference ($A\text{-}aD_{O_2}$) is a more precise measure of gas exchange than arterial $P_{O_2}$ alone in that it takes into account these factors. However, only if these other factors mentioned above are unchanged can a change in $A\text{-}aD_{O_2}$ be equated with changes in the efficiency of gas exchange. This study planned to measure all these factors in order to make the measurement of gas exchange efficiency as meaningful as possible.

## CHAPTER II

## PHYSIOLOGICAL AND PHARMACOLOGICAL CONSIDERATIONS

The effects of an epidural anaesthetic up to the level of the fourth thoracic segment as instituted in this study can be anticipated by an examination of the pertinent physiological and pharmacological aspects involved.

### A. Effect of Agent on Nerve Fibres.

The basic effect of local anaesthetic agents on nerve fibres is to block impulse conduction, with the abolition of the usual ionic fluxes across the cellular membrane that follow depolarization and repolarization (91). This block does not occur in a haphazard fashion, but rather in an orderly and sequential manner depending on fibre size and myelination.

TABLE I: NERVE FIBRE SIZE AND FUNCTION

| TYPE | | DIAMETER (μ) | FUNCTION |
|---|---|---|---|
| A | ALPHA | 12-20 | Proprioception, somatic motor sense |
| | BETA | 5-12 | Pressure |
| | GAMMA | 3-6 | Motor to muscle spindle |
| | DELTA | 2-5 | Pain and temperature |
| B | | 3 | Pre-ganglionic sympathetic |
| C | | 0.4-1.2 | Pain (Dorsal Root C Fibres) |
| | | 0.3-1.3 | Post-ganglionic sympathetic |

Adapted from GANONG (42)

anaesthetic
When bathed in the same solution, the thinner and unmyelinated fibres are blocked before, and more completely, than the larger and myelinated nerve fibres. The degree of nerve block also depends on the amount of local anaesthetic available, while in the context of epidural anaesthesia the extent of segmental blockade is, in part, determined by the mass of drug injected (i.e. the product of volume and concentration) (16, 17). By taking fibre size and drug concentration into consideration, a selective block can be performed. For instance, incremental doses of a given dilution can be shown to block the thinnest fibres, such as those carrying pain, before the thicker fibres, such as the fibres concerned with somatic motor function. It is in this manner that one can give amounts of local anaesthetic sufficient to block pain fibres only, while avoiding a motor block. Individual factors, such as length of back, age, pregnancy, posture and site of injection also play a role in determining the extent of the block, but since these concern the patient and the technique, they need not be examined further.

B. Relation of Sensory and Sympathetic Levels.

In considering the effects of an established epidural

anaesthetic, it is important to correlate the level of sensory blockade to that of sympathetic block.

During spinal anaesthesia, Greene (45) reported his observations that the upper level of "pin-prick block" was at least 2 segments lower than that of ice. He reasoned, on the basis of fibre size, that the autonomic effects would be at the level of temperature blockade, if not higher. He warned against the assumption that the level of sensory block to pin-prick was equal to that of sympathetic block. However, with epidural anaesthesia, Wugmeister and Hehré (93) found that the two levels of pin-prick and temperature coincided very closely, and therefore suggested that the sensory level would indicate the level of sympathetic blockade. In our study, therefore, we will assume that the level of sympathetic block coincides with the sensory level.

C. <u>The Effects of Sympathetic Blockade</u>.

(i) Cardiovascular System.

In order to appreciate the effects of sympathetic denervation on cardio-vascular function, it is necessary to first delimit the extent of the block. If this block involves only the thoraco-lumbar region from

$T_8$-$L_2$, then peripheral vasodilatation in the distribution of the blocked segments will be observed, with no direct effect on myocardial function. The sympathetic fibres supplying the upper limb ($T_2$-$T_8$) (9) will cause a vasoconstriction in the vessels they supply and therefore little or no change in total peripheral resistance (TPR) will occur. If the block extends up to, but not including, the cardiac sympathetics ($T_1$-$T_4$) (9), then this compensatory vasoconstriction may not be found and a fall in TPR would be evident. However, should the sympathetic block extend cephalad to include the cardiac sympathetics, then a more profound fall in cardiac output and TPR will be noted (76).

(ii) Respiratory System.

Bromage has advanced the concept of neuraxial spread of local anaesthetics within the spinal cord (17). Thus local analgesics could conceivably reach the cerebrospinal fluid (CSF) and cause a direct effect on the medullary respiratory centres. However, unless there is inadvertant subarachnoid injection, the volume and the rate of entry of the agent into the CSF should be minimal, because the major proportion of the injected drug will first be fixed to nerve tissue. Autonomic

block could have effects on both pulmonary blood volume and the tracheo-bronchial tree. The effect on pulmonary circulation would be related to the effect on cardiac output.

If sympathetic block of the bronchial tree is established, then there should be broncho-constriction due to the unopposed parasympathetic tone. But such is not the case, as shown by Bromage (19). A possible explanation could be offered by referring to the work of Daly and Schweitzer (33). They report that, in dogs, vascular hypotension is accompanied by reflex bronchodilation, through activation of the carotid sinus baroreceptors. The fall in blood pressure could be followed by a fall in pulmonary vascular pressure, better oxygenation and relief of the broncho-spastic state. But it must be remembered that Bromage's original observation was on subjects with abnormal airways, and may not be true of normal individuals.

D. Relation of Sensory and Motor Levels.

The relation between sensory and motor levels has been demonstrated by Freund (40). Using 2% lidocaine he reported that motor blockade was 4.6 neurotomes below the sensory level, with epidural block, in contrast

to the 2.8 neurotome difference during spinal anaesthesia. Therefore it seems that in the case of spinal anaesthesia there is a segmental difference between sensory and both motor and sympathetic levels. On the other hand, for epidural anaesthesia, such segmental differences exist only for the motor blockade.

As far as the degree of motor block is concerned, Morris (71) stresses the fact that a 1.5% solution will have less marked motor effects than a 2% solution. This point was also raised by Freund (40).

E. Role of Muscles of Respiration.

The muscles of respiration play different roles during the act of breathing. Using electromyography to detect muscular activity, Campbell (22, 23) found that maximal inspiration involved the diaphragm and the fifth to ninth external intercostals, while forced expiration was brought about principally by the action of the abdominal muscles and diaphragm. From these considerations, it is evident that any reduction of respiratory muscle activity will depend on the amount of anaesthetic injected and the extent of the blockade.

F. Systemic Effects of the Agents used.

Although injection of the local anaesthetic is in

the epidural space, systemic effects can be noticed to a greater or lesser extent, depending on the plasma concentration. To prolong the effect of the anaesthetic agent, adrenaline is sometimes used. This will decrease the local blood flow and therefore decrease vascular uptake and biodegradation and elimination of the anaesthetic agent. Systemic effects due to the adrenaline can also be seen. These systemic effects will be examined separately.

(i) Local anaesthetics.

These produce their pharmacological effects by acting on excitable membranes. The most prominent and important effects are on the central nervous and the cardio-vascular systems.

a - The Central Nervous System Effects: These are initially stimulation, even up to convulsions, followed by progressive depression, which starts at the cortex first. Deepening coma follows and when the vital medullary centres are affected, progressive cardio-vascular and respiratory collapse will be evident. However, it must be noted that during epidural anaesthesia, barring the mishap of direct venous injection, these effects are minimal. This is due to the fact

that these agents reach the circulation slowly and there is sufficient time for their metabolism. The critical plasma level is said to be 12 $\mu$g/ml for lidocaine (16).

(i)b -The Direct Cardio-vascular Effects:

These are due to a reduction in myocardial excitability, conduction time and contractility, together with direct vasodilatation (43). These effects will lead to a reduction in stroke volume and heart rate, with a resultant fall in cardiac output. The direct central stimulating effects of lidocaine may, however, predominate and offset the direct myocardial effects. At the critical plasma level this balance may be lost and a general cardio-vascular collapse would follow. The effects of combined cardiac depression and sympathetic blockade, such as after gross overdosage with an epidural injection, would be additive.

(ii) Epinephrine.

When epinephrine is incorporated in the anaesthetic solution, it can lead to marked cardio-vascular effects, if there is significant vascular uptake. The interesting point about epinephrine is that the effects are dose related, in that smaller amounts give $\beta$ stimulatory

effects, while larger amounts have $\alpha$ effects. The differences between $\alpha$ and $\beta$ effects are given in Table II.

TABLE II: DIFFERENCES IN CIRCULATORY RESPONSE OF $\alpha$ AND $\beta$ STIMULATION

| COMPONENT | | | RECEPTOR TYPE | RESPONSE |
|---|---|---|---|---|
| A. | Heart | S.A.Node | $\beta$ | Increase in heart rate |
| | Atria | | $\beta$ | Increase in contractility and conduction velocity. |
| | A.V.Node | | $\beta$ | Increase in conduction velocity |
| | Ventricles | | $\beta$ | Same as atria |
| B. | Vessels | Muscles | $\alpha + \beta$ | |
| | Abdominal viscera | | $\alpha + \beta$ | |
| | Cerebral | | $\alpha$ | Vasoconstriction |
| | Skin | | $\alpha$ | " |
| | Pulmonary | | $\alpha + \beta$ | " |

From: Goodman and Gilman (43)

A low plasma level of epinephrine causes $\beta$ stimulation, whereas $\alpha$ effects would be seen only if the plasma level were higher. The effects of higher concentrations of epinephrine led Moore to abandon the use of 1/125,000 dilution in favour of the 1/200,000 (70).

Finally, it is important to discuss the rôle of hydration. The vasodilatation which follows sympathetic block will be accompanied by a certain degree of peripheral pooling. If the subject is well hydrated before the block, then the effective intravascular volume will not be grossly affected. But if, on the other hand, a state of under- or de-hydration exists even a small degree of pooling will be a cause for a fall in the effective circulating volume and hence cardiac output.

From the above discussion, the cardio-respiratory effects of an epidural anaesthetic will depend on the following factors:

1. Segmental spread, which will determine the level of sympathetic and motor blockade.

2. Mass of drug injected, which will determine the profoundness of the motor blockade.

3. The systemic effects of the local anaesthetic agent and/or the vasoconstrictor.

4. The state of hydration of the subject.

# CHAPTER III

## REVIEW OF THE LITERATURE

A. CARDIOVASCULAR SYSTEM

I. Effects of Cardiac Sympathetic Blockade

II. Effects of Peripheral Sympathetic Blockade

III. Effects of Epinephrine

IV. Effects of Combined Blocks

V. Effects of Circulating Lidocaine

VI. Effects on Renal Circulation

VII. Effects During Nitrous Oxide Supplementation

VIII. Effects on Subjects with Vascular Disease

B. RESPIRATORY SYSTEM

I. Lung Volumes and Capacities

II. Blood Gases

# LITERATURE REVIEW

The literature available regarding the effects of epidural anaesthesia can best be reviewed by considering cardio-vascular and respiratory changes separately, followed by a review of the functional effects on gas exchange. Some of the articles deal with spinal anaesthesia also, and as will be shown later, there is a difference between the two forms of anaesthesia. It is important, therefore, to keep in mind that the effects may be similar but the difference is in the extent or degree of the changes caused by these two types of anaesthetics.

## A. CARDIO-VASCULAR SYSTEM

From the review of the physiological effects presented in Chapter II, one can anticipate that the effects of cardiac and peripheral sympathetic blockades would be quite different.

### 1) Effects of Cardiac Sympathetic Blockade

The cardiac effects were studied by Otton and Wilson (76), by giving an appropriate dose of 1% mepivacaine (1 mgm/Kg) via a catheter placed at the seventh cervical - first thoracic inter-space. In this manner they hoped to

block the cardiac sympathetics only. The end-point of sympathetic denervation was the disappearance of sympatho-galvanic response in the arm (63). The most significant and consistent findings were a fall in cardiac output and a rise in central venous pressure, with an increase in total peripheral resistance (TPR). They concluded that the sympathectomised heart was unable to respond to its filling pressure, due to a reduction in myocardial contractility. A second effect of the sympathectomy was a slowing of the heart rate due to unopposed action of the vagus. The increase in TPR could be due to an increase in vasomotor tone in the intact blood vessels.

II) Effects of Peripheral Sympathetic Blockade

In a series of articles Bonica and his colleagues report their findings when the epidural anaesthetic is given in the lumbar space (8, 11, 55, 86, 87). By this technique it is the peripheral sympathetic outflow that is blocked primarily, with cardiac sympathetic block being a result of cephalad spread of the agent. They compared subarachnoid (spinal) anaesthesia and epidural anaesthesia given to the same patient (87). Before discussing their findings, it is appropriate to make some remarks on their

study. Their subjects were, for the major part, healthy young volunteers aged 21-42. They do not mention the volume or type of intravenous fluid given, if any. The stated level of sensory block to "at least $T_5$" poses the question of the extent of involvement of the cardiac sympathetics, as they do not mention the upper limit of their sensory blockade. This means that the cardiac sympathetic blockade could have been anywhere from minimal to total. The dosage regimen of an initial 25 ml bolus of 2% lidocaine, plus an extra 15 ml in a few instances, means that the degree of block must have been fairly extensive.

The results are given in tabular form as follows:-

TABLE III: CARDIO-VASCULAR EFFECTS REPORTED BY BONICA et al.(87)

| | Subarachnoid | Epidural | 2% Lidocaine |
|---|---|---|---|
| | 5% Lidocaine | No Epinephrine | + Epinephrine |
| Mean Blood Pressure | -21.3% | -8.9% | -22.0% |
| Total Peripheral Resistance | -5.0% | -2.9% | -39.6% |
| Cardiac Output | -17.7% | -5.4% | +30.2% |
| Stroke Volume | -25.4% | -10.2% | +7.9% |
| Heart Rate | +3.7% | +6.7% | +15.8% |

Thus the effects of subarachnoid and epidural anaesthesia (using plain lidocaine) on cardio-vascular

parameters were in the same direction, but differed in degree and were significant only following spinal anaesthesia. The authors invoke a reflex vasomotor response following the epidural injection to explain this difference in the degree of change. This response, also supported by Bromage (16), would be initiated by the sudden increase in CSF pressure following the epidural injection.

It would be pertinent, at this point, to examine the rôle played by the venous system in circulatory dynamics under epidural anaesthesia. Shimosato and Etsten (81) carried out such a study on 5 normal subjects who were given 1.5% lidocaine for an epidural anaesthetic and on 15 other subjects who received 0.3% tetracaine for a spinal anaesthetic. The sensory level achieved was between $T_4$ and $T_7$. The results obtained showed an increase in blood flow, an increased vascular distensibility, with a decrease in vascular resistance in the anaesthetized calf muscles. The ratio of calf blood flow to cardiac output increased, with changes in cardiac output not affecting this ratio. From this work, it appears that the effects of sympathetic denervation are (a) an increased distensibility of the capacitance vessels and (b) a decreased resistivity in the pre- and post-capillary

resistance vessels. These two effects led to the fall in blood pressure, which follows epidural and spinal anaesthesia. Thus, their results suggest that the changes in blood pressure do not correlate with changes in either cardiac output or total peripheral resistance alone, but rather with the interaction of changes in these two parameters.

III) Effects of Epinephrine

The incorporation of epinephrine in the anaesthetic solution given for epidural anaesthesia leads to very striking differences between the effects of that solution and those following the use of plain solutions.

Bonica et al. (87) reported an increase in cardiac output (CO) of about 30% when epidural anaesthesia was instituted with lidocaine plus epinephrine. This increase seemed to be due to an increase in both stroke volume and heart rate. That this effect is mainly due to $\beta$ stimulation by epinephrine is stressed by the authors in their commentary. This is not surprising when it is recalled that these subjects received at least 25 ml of anaesthetic solution, which means that 125 micrograms of epinephrine were injected. Although plasma levels of lidocaine and epinephrine were not recorded, one can assume that the plasma level was not sufficient to cause $\alpha$ type responses.

In another paper (8), they report essentially the same sort of changes both in direction and degree.

In a study of the effects of epinephrine (1/200,000) incorporated in the local anaesthetic solution (56) the same group of authors report statistically significant increases in cardiac output when epinephrine is used for epidural and brachial plexus blocks, but not when used for subarachnoid anaesthesia.

It is clear from the above reports that the effects of epinephrine can be very important.

The reported differences between thoraco-lumbar ($T_5$ - $L_2$) and upper thoracic ($T_1$ - $T_4$) epidurals can now be reviewed. A thoraco-lumbar block would lead to a fall in total peripheral resistance, but the heart can still maintain its inotropic action adequately. However, a thoracic block of $T_1$ - $T_4$ would cause a significant fall in cardiac output and the heart cannot respond to either increased loads or sympathetic stimulation. At the same time peripheral resistance increases. Should the block be extensive enough to block <u>both</u> peripheral and cardiac fibres, then one can expect that there would be a generalised cardio-vascular deficit.

IV) Effects of Combined Blocks

A study of the combined cardiac and peripheral effects was reported by McLean et al (65) who studied the effects of upper thoracic followed by lumbar epidural anaesthesia in the same patient. They studied 7 fit adults aged 31-72 years. Following the injection of 1 mgm/Kg mepivacaine via a thoracic catheter, the changes observed were the same as those reported in an earlier study by Otton and Wilson (see page 16). The addition of peripheral sympathetic blockade resulted in a further fall in cardiac index and stroke volume, with now, however, a fall in CVP and TPR.

In a recent publication, Bonica et al (11) reported their findings when epidural anaesthesia progressed cephalad from the lumbar region, and at the same time plasma lidocaine levels were measured. When the block reached $T_{4-5}$, they reported no changes in all cardiovascular parameters measured except heart rate which increased by 5.8 beats/min. and arm blood flow which decreased by 2.1 and leg blood flow which increased by 8.6 ml/100 ml.tissue/min. The anticipated fall in cardiac output was noted when the level extended beyond $T_2$. However, a striking finding was that cardiac

output, heart rate and stroke volume increased between $T_{4-5}$ and $T_{2-3}$ levels. This suggests that other mechanisms, apart from sympathetic blockade or plasma levels of epinephrine may affect the cardio-vascular system when the sensory level extends to $T_{2-3}$. The authors proposed that lidocaine may exert direct effects, and so increase CO and BP at the moderate plasma levels of 4-7 µgm/ml, which they presumed was the plasma level achieved when this segmental block was established.

V) Effects of Circulating Lidocaine

It is important that the exact cardio-vascular effect of lidocaine be defined. Bonica et al attempted to clarify this point by studying the effects of intravenously administered lidocaine to eight healthy volunteers (10). These subjects were given 0.3 mgm/Kg/min. for 10 and 20 minutes. A subarachnoid block using 2-3 mgm tetracaine followed, attempting to block $C_{6-7}$ to $T_{5-7}$. In this manner they set out to determine the effects of two dosage levels of lidocaine and the effect of sympathetic block by a subarachnoid anaesthetic.

In their preliminary report, they presented their findings after 10 minutes of intravenous infusion of lidocaine and after the addition of a subarachnoid block.

The changes induced by the lidocaine alone, presented as changes of the means from control values for some of the parameters are as follows:-

| | | |
|---|---|---|
| MBP | (mm Hg.) | $+10.5^{x}$ |
| CVP | (cm $H_2O$) | $+3.0^{x}$ |
| CO | (L/min) | +0.6 |
| HR | (beats/min) | +12.3 |
| SV | (ml/beat) | -9.9 |
| TPR | (dynes/sec/$cm^5$) | +27 |

($x = p < 0.05$)

The subarachnoid block resulted in the abolition of these changes and a return to near-control values.

It appears that the main haemodynamic effects of intravenous lidocaine are an increase in HR, TPR, MBP and CVP, with a fall in stroke volume (SV). The CO increased mainly as a result of the increase in heart rate. The plasma lidocaine level achieved ranged from 2.5-6.5 $\mu$gm./ml. The effects of the 20 minute infusion were not reported.

An earlier study along the same general lines was reported by Jorfeldt (51). In that study, 4 volunteers were given 5 mgm/Kg over 20 minutes (i.e. 0.25 mgm/Kg/min). The plasma concentration of lidocaine was, on an

average, 4.9 mg/μgm/ml. In two subjects CO increased, but was unchanged or slightly reduced in the other two subjects. Heart rate increased in all subjects, as did MBP. Central venous pressure did not, however, increase as it did in Bonica's study. One of these 4 subjects developed convulsions at a comparatively low plasma lidocaine level. The authors suggested that an augmentation in sympathetic tone may be reflected in the observed tachycardia with an associated increase in myocardial contractility. Such a central increase in sympathetic activity due to lidocaine was reported by Kao and Jalar from their work on dogs (52). These authors reported an increase in HR and SV, and therefore CO, after 1-2 mgm/Kg lidocaine were injected. This effect on CO was abolished in both decerebrate and vagotomized dogs.

However, D'Amato (35) has proposed that local anaesthetics act peripherally by potentiating the effects of epinephrine on blood vessels.

Binnion and his co-workers (6) reported their findings while studying patients undergoing cardiac catheterization. A 1 mgm/Kg bolus led to insignificant changes in cardiac output. The mean plasma level

obtained was 1.96 (± 0.28) μgm/ml. They also reported that maximum left ventricular dp/dt did not rise significantly. From this it seems that lidocaine in lower concentrations has insignificant effects on cardiac output. It must be remembered, also, that Binnion was dealing with diseased myocardia while both Bonica and Jorfeldt were working on healthy volunteers.

From the data presented, it would seem that lidocaine exerts its actions on cardio-vascular dynamics in a dose related manner. The comparatively smaller blood levels (2 μgm./ml) reported by Binnion (6) led to insignificant changes. Greater dosage ranges, such as those used by Jorfeldt, caused an increase in CO in half the subjects (51). A slightly bigger dose, such as that in Bonica's study led to an increase in CO by 0.6 L/min, mainly due to an increase in heart rate (10). This together with the significant increase in MBP could be due to central stimulation. However, Bromage, in his review article (16), came to the conclusion that a considerable degree of the cardiac depression noted with epidural anaesthesia could be due to circulating local anaesthetics. Therefore, one can assume that with lower plasma levels central stimulation offsets direct

cardio-vascular depression, but that this balance is lost with higher plasma levels. Such a possibility was seen in the review of pharmacology (Chapter II). The critical plasma level has been reported to be 12 μgm/ml. (16). In Bonica's study the plasma level was 4-7 μgm/ml and therefore below this critical level. Another mechanism which may explain the changes reported in Bonica's study (11) is the transient increase in vasomotor tone and cardiac output following the sudden rise of epidural pressure due to the rapid injection of the drug (16). This effect has, however, been disputed by Akamatsu et al (1). These authors observed no significant cardio-vascular response to the rapid epidural injection of 20 ml of normal saline in seven male surgical patients. This is in direct contrast to the dramatic cardio-vascular response reported by Galindo while working with dogs (44).

In summary, in order to explain the rise in CO when the epidural block involved $T_{2-3}$, reported by Bonica, two explanations have been offered. The first one is that the effect is due to circulating lidocaine in amounts sufficient to cause central stimulation. The alternative explanation is a response to an increase

in epidural pressure. This last possibility has been disputed by Akamatsu.

It seems reasonable that the pharmacological explanation is the better one. This is because cephalad spread beyond that segmental level, which can mean a higher plasma lidocaine concentration, resulted in a fall in cardiac output. However, one can conjecture that at the $T_{2-3}$ level the subjective feeling of inability to breathe (similar to that observed with spinal anaesthesia) and the apprehension that is bound to follow may have caused the release of catecholamines and thus the observed effects. This is possible because up to that moment, the sympathetic system was still functioning relatively adequately as evidenced by the cardio-vascular parameters. Beyond that segmental level it may be that the sympathetics were totally paralysed and thus CO fell. It must be remembered too, that the increase in CO during that period was due, in greater part, to an increase of HR (14.5 $\pm$ 3.8 beats/min) rather than an increase in SV (0.6 $\pm$ 6.2 ml/beat).

This striking observation reported by Bonica (11) is worthy of further investigation and underscores the many factors that enter into play when an epidural

anaesthetic is given. Such a change in cardiac output, however, need not be anticipated when an epidural anaesthetic is given to cause a sensory block up to $T_4$ only.

VI) Effects on Renal Circulation

The work surveyed so far concerned the general systemic cardio-vascular effects. Kennedy et al (55) studied the renal haemodynamic alternations together with the cardio-vascular effects in a group of 20 volunteers. Half the subjects received 2% plain lidocaine while the other 10 received 2% lidocaine with epinephrine 1/200,000. The changes in cardio-vascular dynamics were identical with those reported previously and which have already been reviewed. Renal haemodynamics were studied using $^{57}$Co-cyanocobalamin and $^{125}$I-Hippuran to asses Glomerular Filteration Rate (GRF) and Effective Renal Plasma Flow (ERPF). They found no significant difference in the fall of GFR in both groups, whereas the fall in ERPF in their Group II (lidocaine and epinephrine) was significant as compared with that in Group I (lidocaine alone). The difference appears to be primarily due to the decrease in Mean Blood Pressure.

VII) Effects During Nitrous Oxide Supplementation

The cardio-vascular effects of epidural block combined with $N_2O$ general anaesthesia were studied by Stephen et al (84). Following thiopentone induction, an epidural catheter was inserted, four control measurements of cardiac output were made and, following injection of 30 ml of 2% lidocaine (plain), repeat measurements of cardiac output every 2 minutes were made for 20 minutes, i.e. when the arterial pressure stopped falling. In six of their series of eleven subjects, no significant changes in cardiac output, central venous pressure, heart rate, stroke volume, peripheral resistance or mean arterial pressure were found. In four, a significant fall in mean blood pressure following a lowering of peripheral resistance, was noted, but, with little change in cardiac output. The last patient in their series showed a marked fall in output following a significant bradycardia. This was not compensated for by an increase in total peripheral resistance. From their discussion, the authors were impressed with the fact that falls in blood pressure do not mean falls in cardiac output, whereas hypotension plus bradycardia was accompanied by a 40%

reduction in cardiac output. An important observation they made was that ephedrine can increase both blood pressure and cardiac output. Prior to injecting ephedrine, they raised the patients legs vertically to promote drainage of the pooled blood. This had the effect that CVP and MBP rose but not the cardiac output. This could mean that the heart was sympathetically denervated and could not handle the extra load. It is unfortunate that no mention of sensory levels was made. It would have been very interesting indeed to have had this study performed before and after the general anaesthetic was given, in order to define the effects of these manoeuvres and those of the nitrous oxide. However, a light general anaesthetic using only $N_2O$ can be assumed to have minimal cardio-vascular effects.

In summary, they report, (1) falls in MBP do not mean falls in CO unless there is marked hypotension and bradycardia; (2) raising the legs raises the B.P. only; (3) ephedrine reverses the changes in both cardiac output and blood pressure.

VIII) Effects on Subjects with Vascular Disease

So far we have considered the effects on healthy individuals. If, however, the subject has arterio-

sclerotic vascular disease, one can anticipate that this pathological state may have some bearing on the picture. Bromage has found that diabetes or arteriosclerosis caused a reduction of dosage requirements below the amount calculated on the basis of age (16, 18). In a study, recently concluded, Cousins et al (29) report their findings of the effects on graft blood flow, muscle blood flow and skin in human legs following epidural blockade. They noted an increase in skin temperature, a fall in muscle flow with an associated overall increase in limb blood flow. These subjects were undergoing reconstructive vascular surgery for peripheral arteriosclerotic disease. The significant result reported in this study is the increase in graft flow, which, interestingly enough, correlated highly with the reduction in muscle blood flow. In other words, epidural blockade seems to improve graft flow and this could conceivably have significant clinical benefit in the immediate post-operative period when intense vasoconstriction is dominant and graft blood flow is still poorly established.

B. RESPIRATORY SYSTEM

The review of the literature will, for the sake of clarity, be undertaken by considering lung volumes and capacities and peak flow rates separately from the studies on blood gases.

I) Lung Volumes and Capacities

Moir (69) studied the effects of epidural anaesthesia with 1.5% lidocaine in 12 "bronchitic" and 30 "normals" in the pre-operative period. The parameters measured were tidal volume ($V_T$), minute volume ($\dot{V}$), vital capacity (VC) and Peak Flow. The level of analgesia was above $T_6$ in all cases and ranged from $T_2$-$T_5$. The mean percent changes calculated in the normal group were:-

| | |
|---|---|
| $V_T$ | -1.1% |
| $\dot{V}$ | -1.0% |
| VC | -7.1% |
| Peak Flow | -5.0% |

The changes in the 12 subjects with broncho-pulmonary disease were:-

| | |
|---|---|
| $V_T$ | +3.5% |
| $\dot{V}$ | +3.2% |
| VC | -8.5% |
| Peak Flow | -9.7% |

The 8.5% reduction in VC in the second group was significant ($p < 0.01$) but not the 7.1% fall observed in the normal group. The author concluded that epidural anaesthesia does not significantly alter resting ventilation, but the reduction in peak flow rates in both groups were found to be statistically significant ($p < 0.01$).

To compare the effects of spinal and epidural anaesthesia on ventilatory reserve, Freund (40) studied 18 subjects who received both spinal (5% lidocaine) and epidural (1.5% lidocaine + epinephrine 1/200,000) anaesthetics. In essence they compared the spread of motor block (electromyographically determined) and that of sensory block (to pin-prick) for each type of anaesthetic. There are several noteworthy findings in this study.

(i) Motor block was 4.6 segments below sensory block with epidural anaesthesia but only 2.8 segments lower during spinal anaesthesia. Thus one could estimate the level of motor block from a knowledge of the sensory level.

(ii) During epidural anaesthesia, inspiratory capacity (IC) was reduced by 3% and expiratory reserve volume (ERV) by 21%. The changes in these

measurements during spinal anaesthesia were 8% and 48% respectively. This can be interpreted to mean that the reduction in motor power following sub-arachnoid anaesthesia is more profound than that following extradural anaesthesia.

(iii) In seven of their subjects the sensory level achieved was $T_4$. These subjects had a 2% reduction in IC and a 13% reduction in ERV.

(iv) As motor block proceeded cephalad, the reduction in these 2 parameters was progressive.

A fairly comprehensive report on the effects of epidural anaesthesia for pain relief was made by Simpson et al (83). Their group included sixty patients, with ages ranging from 18 to 77 years, scheduled for intra-abdominal surgery and herniorrhaphies. However it is unfortunate that they did not perform the measurements after the epidural anaesthetics and before surgery. They only performed pre-operative, post-operative and then post-pain-relief measurements. In other terms, they really measured the "respiratory restorative" effects of epidural anaesthesia. Their results are interesting enough in that respect. When their subjects were in pain, VC was found to be 35.2%

of control and after pain relief 69% of control in the upper abdominal group. In the group undergoing lower abdominal surgery, the values for VC were 55.5% and 84.8% of the pre-operative value during pain and after pain relief respectively.

Although they measured FRC pre-operatively in 9 subjects, no report is made either after epidural anaesthesia or in relation to pain and it relief.

They report a widely varying percent change in lung compliance after pain relief. This ranged from -32% to +37%. It must be noted that some of their subjects had chronic obstructive lung disease and this fact alone makes the study difficult to assess as the results are not reported as "normal" or "abnormal " chests.

II) Blood Gases

In a study of healthy volunteers, Ward et al (87) reported the changes in blood gases following spinal and epidural anaesthesia. For the latter they used 2% lidocaine (plain) in half their subjects and 2% lidocaine with epinephrine in the other half. The oxygen tension rose by 14.9 mmHg in the spinal group, while the epidural group, as a whole, showed a rise of 2.6

mmHg only, which was not significant. The mean carbon dioxide tension fell by 6.5 and 0.6 mmHg in the two groups respectively, while the changes in pH were +0.05 and 0.01.

The changes in gas tensions in the spinal group can be explained on the basis of hyperventilation due to the apprehension that is frequently noticed during high spinal block. On the other hand, this did not seem to occur during epidural anaesthesia.

Moir and Mone (68) studied the effects of epidural anaesthesia on blood gases in 12 normal subjects and 8 patients with chronic bronchopulmonary disease. All the subjects received 1.5% plain lidocaine. In this study the sensory level achieved ranged from $T_2$ to $T_4$. The 12 normal subjects showed no change in pH, $Pa_{02}$ or standard bicarbonate. The changes in the second group were also minimal.

de Jong (36), while studying the effects of spinal and epidural anaesthesia, found no significant changes in blood gases ($Pa_{02}$ and $PaCO_2$) even when sensory levels were as high as $T_2$.

The obese patient represents a problem to anaesthetists for many reasons, one of the most important

being the potential post-operative pulmonary complications. In such patients, epidural analgesia is definitely indicated, but great care must be taken to avoid further reduction of respiratory muscle performance.

In a study comparing the vital capacities in obese and non-obese patients following spinal anaesthesia, Catenacci et al (24) found no changes in the non-obese group. A reduction in VC and a small increase in arterial $P_{O2}$ were noted in the obese group. In these obese subjects, the arterial $P_{CO2}$ fell slightly, and a state of hyperventilation is in agreement with Ward's study (87). However, it must be pointed out that the sensory level achieved ranged anywhere from $T_{10}$ to $T_4$ while the weight range was from 77 to 121 Kgs, so that it is quite difficult to reach conclusions as regards effects in relation to sensory levels and patient weights.

In their study on the effects of cephalad progression of epidural anaesthesia, Bonica and his co-workers (11) present some interesting data. Up to the $T_{4-5}$ level no clinically significant changes were noted in blood gases. During the period of spread

to $T_{2-3}$ levels however, $Pa_{O_2}$ increased by 8.8 ± 2.3 mmHg from control levels while $PaCO_2$ dropped by 1.4 ± 0.7 mmHg. Although the absolute change is not very large, it may, however, indicate some hyperventilation due to apprehension. What is more striking is the change following the next step, i.e. extension of the block beyond $T_1$. At that stage $Pa_{O_2}$ increased by 20.8 ± 13.1 mmHg and $PaCO_2$ dropped by 3.9 ± 2.1 mmHg. This again could quite easily be due to hyperventilation. The accompanying changes in haemodynamic parameters have already been discussed. Apprehension and catecholamine release were suggested as possible mechanisms to explain the reported changes.

It appears, therefore, that an epidural anaesthetic per se does not lead to significant changes in blood gases unless it spread beyond $T_{4-5}$. Above that level significant changes may be noted with a fall in $PaCO_2$. and a rise in $Pa_{O_2}$.

The effects of epidural and spinal anaesthesia with supplemental 1.5% Halothane in oxygen were reported by James and Fisher (50). They studied 11 patients and measured $A\text{-}aD_{O_2}$. Eight subjects received 0.5% cinchocaine and the three epidural studies received

1.5% lidocaine in a dose calculated to produce an estimated sensory level below $T_6$.

The initial readings were taken when the patients were already under the effects of general anaesthesia, without pre-operative control determinations. Once the epidural or spinal agent was injected, the patients were turned into the supine, 5° head-down position. The sensory level could not therefore be accurately known or even predicted, because the dose was calculated on an age-height-basis. The results are given as means of all subjects studied, with no individual data or the means of each group alone.

The authors reported a mean decrease in $PaO_2$ of 82 mmHg and a mean increase in $A\text{-}aD_{O2}$ of 85 mmHg. The mean blood pressure fell by 21 mmHg. The fall in MBP correlated positively with the increase in $A\text{-}aD_{O2}$. The changes in $V_D/V_T$ and $PaCO_2$ were not significant. From this it would seem that the changes in MBP presumably reflected changes in cardiac output which can explain the increase in $A\text{-}aD_{O2}$. This presumes that all other factors such as shunt, ventilation/perfusion, and diffusion remained constant, together with an unaltered oxygen consumption.

It is interesting to note that a correlation was found between the maximum A-a$D_{O_2}$ and body weight, with the heavier patients having the bigger values for oxygen gradients. These patients also showed the more severe falls in blood pressure. But, considering that weight entered in the calculation of their dosage, presumably the heavier ones got bigger doses, showed bigger falls in blood pressure and cardiac output and therefore the larger oxygen gradients.

Thus, although these workers measured the changes in A-a$D_{O_2}$, no firm conclusions about the effects of epidural anaesthesia can be drawn for the reasons mentioned above.

## CHAPTER IV

## SUBJECT MATERIAL

The subjects studied were patients scheduled for elective upper abdominal surgery. The epidural anaesthetic was selected for the purpose of post-operative pain relief by the anaesthetist in charge of the case; operative management was with general anaesthesia, muscle relaxation being achieved by either curare or epidural anaesthesia.

The patients studied were free of cardio-respiratory disease on the basis of the history and physical examination.

On the day before the operation, the patients were visited and the purpose, content and extent of the study explained to them. Each patient was specifically asked about symptoms referable to a condition which would contra-indicate an epidural anaesthetic, such as lumbar disc disease, drug allergy and neurological disease.

The physical characteristics of the subjects studied are given in table number IV.

TABLE IV: PHYSICAL CHARACTERISTICS OF PATIENTS STUDIED.

| GROUP | PATIENT | AGE yrs | HT m | WT Kg | SEX | OPERATION | LIDOCAINE ml | LIDOCAINE mgm | EPIN. μgm. | I.V. FLUIDS L |
|---|---|---|---|---|---|---|---|---|---|---|
| A. LIDOCAINE 1.5% | 1. A.F. | 44 | 1.65 | 55.5 | F | Cholecystectomy | 19 | 285 | - | 0.90 |
| | 2. F.P. | 26 | 1.73 | 70.0 | M | Pyloroplasty | 26 | 390 | - | 1.00 |
| | 3. M.V. | 40 | 1.62 | 100.5 | F | Cholecystectomy | 20 | 300 | - | 0.95 |
| | 4. V.L. | 35 | 1.54 | 88.0 | F | " | 33 | 495 | - | 1.00 |
| | 5. G.R. | 45 | 1.68 | 82.0 | F | " | 22 | 330 | - | 1.00 |
| | 6. D.S. | 34 | 1.83 | 84.0 | M | " | 17 | 255 | - | 1.00 |
| | 7. R.H. | 67 | 1.51 | 58.0 | F | " | 8 | 120 | - | 0.60 |
| | 8. A.P. | 36 | 1.52 | 55.5 | F | " | 15 | 225 | - | 0.60 |
| B. LIDOCAINE 1.5% + EPINEPHRINE 1/200,000 | 9. P.G. | 31 | 1.58 | 71.0 | F | Cholecystectomy | 17 | 255 | 85 | 0.80 |
| | 10. M.C. | 47 | 1.62 | 65.0 | F | " | 15 | 225 | 75 | 0.65 |
| | 11. H.L. | 71 | 1.68 | 76.6 | M | Lt. Hemicolectomy | 14 | 210 | 70 | 0.75 |
| | 12. J.G. | 20 | 1.65 | 65.0 | F | Cholecystectomy | 23 | 245 | 115 | 0.70 |
| | 13. E.C. | 59 | 1.57 | 65.0 | F | " | 15 | 225 | 75 | 0.80 |

# CHAPTER V

## METHODS

A. Lung Volumes

1. Functional Residual Capacity

a. Basic Principle

b. Apparatus

c. Determination of Apparatus Dead Space

d. Actual Experimental Steps

e. Calibration of Measured Volume

2. Vital Capacity

B. Forced Expiratory Volume

C. Cardiac Output

D. Expired and Blood Gas Analyses

E. Physiological Dead Space

F. Venous Admixture

## A. LUNG VOLUMES

The determination of the subdivisions of total lung capacity will be described under the headings:-

1. Functional Residual Capacity (FRC)
2. Vital Capacity (VC)

### 1. FUNCTIONAL RESIDUAL CAPACITY.

There are three available methods for the determination of FRC:-

i. Body Plethysmography
ii. Nitrogen Washout Technique
iii. Closed Circuit Helium Technique

In this study the closed circuit Helium technique (27a, 28a, 66, 67) was employed and will be described fully.

#### A) Basic Principle

The basic principle of this technique is to switch the subject at end-expiration into a spirometer containing a known volume with a known helium concentration. Helium is chosen because it is insignificantly absorbed from the lungs. Its concentration can be measured by a catharometer, which is basically a Wheatstone bridge (66, 67) and the voltage change can be calibrated as concentration. If the patient is switched into the circuit at end-expiration,

then the unknown volume which will mix with the known helium mixture will be FRC. After complete mixing of these two volumes, the concentration of helium will be indicated on the helium meter. FRC can be calculated simply, the equation deriving from the fact that the volume of helium in circuit initially = volume of helium in lungs plus that in circuit at equilibrium. Thus:

$$V_C \times F_{HeI} = (V_C + V_{FRC})\, F_{HeF}$$

where: $V_C$ = Volume of circuit

$F_{HeI}$ = Initial helium concentration

$F_{HeF}$ = Final helium concentration

FRC = Functional residual capacity

$$FRC = \frac{F_{HeI} - F_{HeF}}{F_{HeF}} \times V_C$$

However, the above formula only explains the principle involved. In actual practice one must take into account

a. Dead space of the mouthpiece

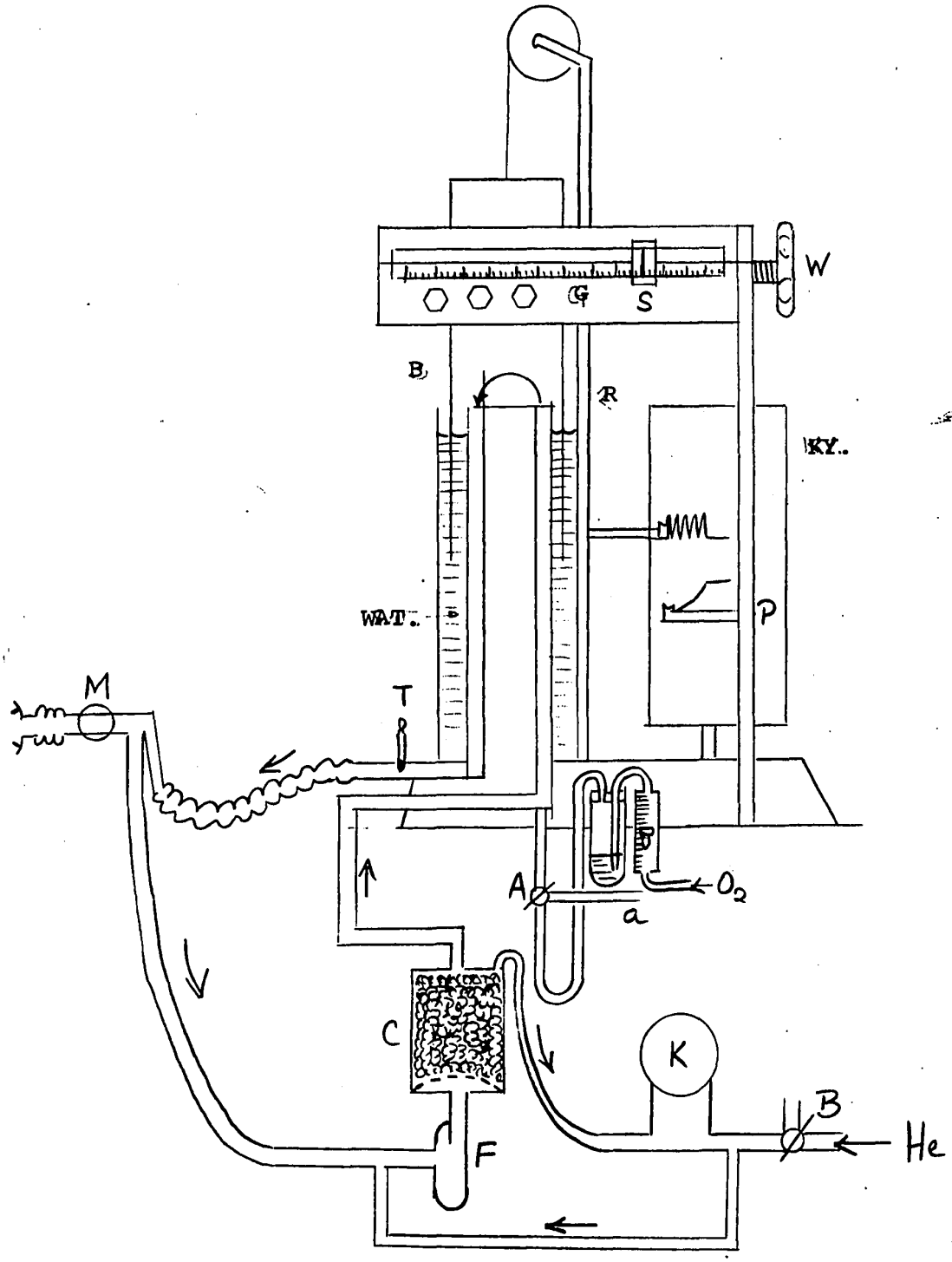
b. Oxygen consumption and $CO_2$ absorption

c. Accuracy of timing at "switching in".

These considerations will be dealt with later at the appropriate place. The actual formula used, which includes corrections for the above three factors is:

$$FRC = \left( \frac{F_{HeI} - F_{HeF}}{F_{HeF}} \times V \right) \pm \emptyset_2 D - Sw.D - V_D/M.P.$$

FIG. 1. APPARATUS USED FOR DETERMINING FRC.




Description in text. Arrows indicate direction of gas flow.

Where: $V_D$/M.P. = Dead space of mouthpiece

$F_{HeF}$ = Fractional concentration of helium (final)

V = Volume of air in spirometer system (Dead space + added volume)

$O_2D$ = Oxygen difference to allow for either excess or deficient addition of $O_2$ during the test to make up for oxygen consumption.

SwD = Switch difference, if switching in was not exactly at end-expiration.

After equilibration, only one side of the equation remains to be calculated. There is a temperature correction of 25 ml/°C change during the period of measurement to balance the change in volume should the temperature change.

B) Apparatus

The basic design is shown in figure I.

It consists of a ball (B) ensheathed in a water jacket, (WAT.), the bell containing the breathing mixture. By appropriate manipulation of the tap at the mouthpiece (M), the bell can be filled or emptied, flushed with either room air or oxygen from an oxygen source through tap A.

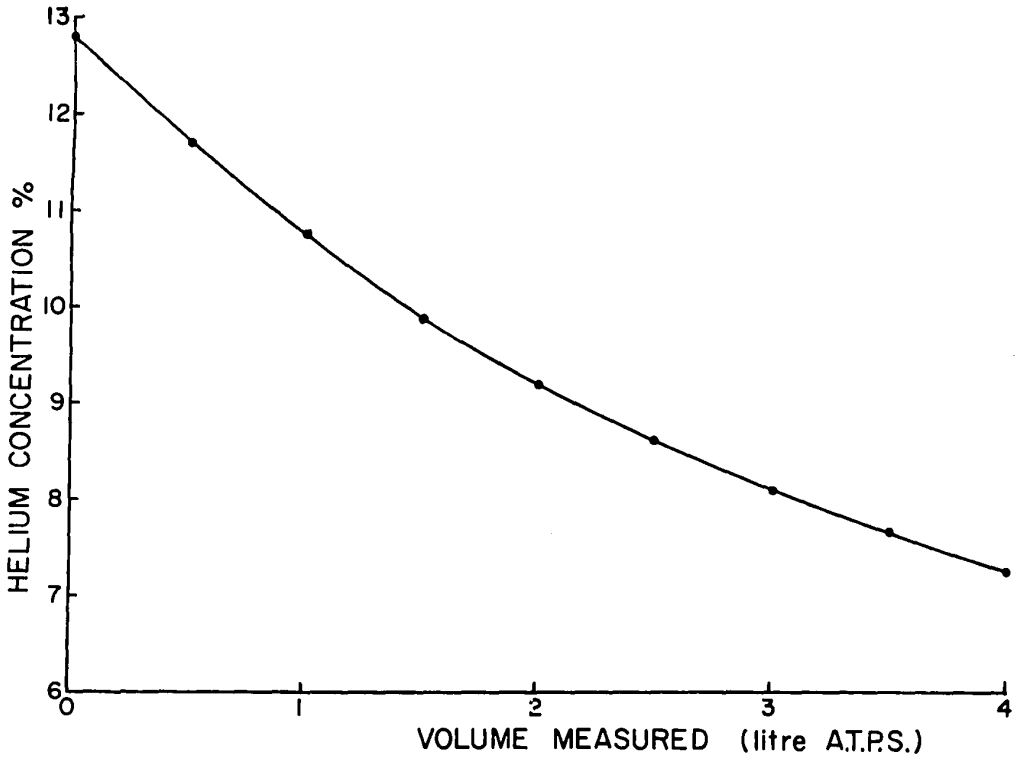



FIG. 2 : CHANGES IN HELIUM CONCENTRATION AFTER ADDITION OF ALIQUOTS OF AIR.

Derivation explained in text.

When the subject is switched into the circuit at end-expiration, this bell moves with respiration and mixing between FRC and the breathing mixture occurs.

A fan (F) maintains unidirectional flow. The expired gases pass through a $CO_2$ absorber to avoid $CO_2$ accumulation with its effects on the respiration and on the catharometer readings (8). This catharometer (K) analyses the helium concentration, the changes being reflected on the galvanometer (G) which is factory calibrated to read in % helium on the scale (S).

There are two inlets, one for helium from a cylinder into the circuit and the other for oxygen through flow meters. The importance of adding basal oxygen is twofold:

1. To keep the concentration of oxygen in the mixture constant and thus avoid the respiratory effects of a lower $F_IO_2$.

2. A reduction of oxygen will cause changes in the thermal conductivity of the mixture and thus false readings for helium.

It is also important to test for possible leaks.

The accuracy of the volume scale was determined by adding known volumes of air from an accurately calibrated

5000 ml syringe and noting the change of the volume scale.

C) Determination of Dead Space of Apparatus

This was determined by analysis of $P_{O_2}$ of the mixture resulting from the addition of accurately measured volumes of 100% oxygen. The samples obtained from this mixture were analysed for $F_{O_2}$ by the Scholander technique. This determination was performed by adding 1000 ml of $O_2$ to the circuit. These additions of 1000 ml of $O_2$ gave a mean final $F_IO_2$ of 0.3755. The value of $V_{DAPP}$ was then calculated as follows:

$$(V_D \times .2093) + (1000 \times 1.0) = (V_D + 1000) \times .3755$$

$$\therefore V_D \times .2093 + 1000 = (V_D \times .3755) + 375.5$$

$$\therefore 1000 - 375.5 = .3755\ V_D - .2093\ V_D$$

$$624.5 = .1662\ V_D$$

$$\therefore V_D = \frac{624.5}{.1662} = 3.755L.$$

D) Actual Experimental Steps

After the usual preparation of the equipment, 800 ml air, 700 ml of helium and 200 ml oxygen are added to the mixture. This gives a breathing mixture of 21% oxygen.

At end-expiration the subject is switched into the breathing circuit, the nose clip having been placed previously. The importance of $CO_2$ absorption and the

and the addition of basal $O_2$ have already been mentioned.

The temperature of the water bath is noted for later conversion of the measured volume to BTPS by the usual equation (28c). In practice, the conversion factor used was obtained from Cotes (28d). Correction for switch difference and oxygen difference were made where necessary.

E) Calibration of Measured Volume

Aliquots of air were introduced into the system prepared in the above mentioned manner. By adding volumes within the expected range of FRC values, we determined the dilution effect of each aliquot.

The mean of 5 experiments was used to construct a curve of volume/He concentration. After noting the final helium concentration, the diluting volume (i.e. FRC) could be determined directly from the curve. (Figure 2).

2. VITAL CAPACITY

After equilibrium was reached in the FRC determination, the subject was asked to completely empty his lungs two or three times with four to five normal breaths in between. This measures the expiratory reserve volume (ERV). The spirometer was then filled to the 5 litre mark with room air and the patient asked to completely fill his lungs, also two or three times to measure inspiratory capacity.

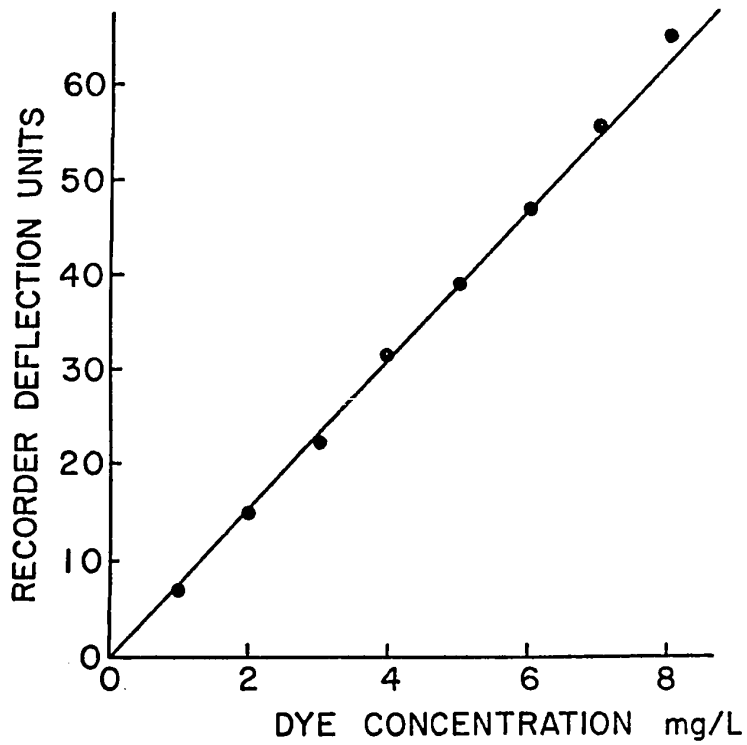



Figure 3.: Response of cardiac output densitometer to solutions of indocyanine green in blood.

Tidal volume was measured from the tracing during the FRC measurement.

From these measured volumes and capacities the remaining subdivisions of total lung capacity were determined.

B) Forced Expiratory Volume 1.0

The apparatus used was a Stead-Wells spirometer which consists of a very light plastic bell ensheathed in a water bath. The interior of the plastic bell is connected by wide-bore tubing to a mouthpiece. The air expired forcefully by the subject is introduced into the bell at its bottom end. This volume change is traced by a marker pen system directly on a revolving kymograph (kymograph speed: 4.0 cm/sec) with 1.0 sec. markings vertically and litre markings horizontally. A specially fashioned "mask" is used to read the value of FEV 1.0. The subject is asked to take a maximal breath in, hold it, then blow out as hard and as fast as possible into the mouthpiece, while the operator insures no leaks by aiding the subject to hold the mouthpiece firmly between the lips. A nose-clip is placed for each test. This test was performed in duplicate.

The curve obtained was analysed from start of upstroke rather than by disregarding the first 100 ml (28e).

C) Cardiac Output

The technique used was that of dye dilution using Indocyanine green (Cardio-green: Hynson, Westcott and Dunning) as the indicator. Through the central venous catheter a bolus of 1 ml containing 5 mgm was injected rapidly and flushed with 6-8 ml of normal saline. Arterial sampling was by a Beckman infusion - withdrawal pump, at a rate of 19 ml/minute. The sample was aspirated through a Waters VC-302 cuvette. The signal from a Waters D-400 Densitometer was recorded on a Honeywell Electronik 194 ten-inch chart recorder. Duplicate output curves were obtained both before and after establishment of epidural anaesthesia. The mean of these readings are reported. The response of the cuvette-densitometer system was determined for blood with dye concentrations ranging from 0 to 8 mgm/L and found to be linear (32). (Figure 7). Individual calibrations after each study were performed using the subject's own blood and dye from the same bottle used for the output determination. A Hamilton PB600 repeating dispenser with a micro-syringe system

was used to deliver dye into 10 ml aliquots of blood drawn by a pipette. Three concentrations were prepared in this way and a calibration factor obtained using the best-fit straight line through zero and the three points. The curves obtained were analysed by the Stewart Hamilton replot technique (47, 85). The area under the curve was determined by using a compensating polar planimeter (Keuffel and Esser, Model 620005) with the readings in square centimeters.

A modification of the standard dye dilution equation, derived by Dr. E. Housley, the Royal Infirmary, Edinburgh, was used. This derivation was a personal communication to Dr. D. B. Craig and is reported separately (32).

$$C.O. = f * p.s./A$$

Where: C.O. = cardiac output in L/min

f = calibration factor: the deflection in cm. produced by a dye concentration of 1 dose per litre

p.s. = paper speed of recorder in cm/min

A. = area under the dye curve in sq. cms.

D) Expired and Blood Gas Analyses

During a three minute expired gas collection into a 50 L meteorological balloon, an arterial blood sample was

withdrawn into a heparinized glass syringe and packed in ice. The expired gas sample was analysed for $P\bar{E}O_2$ and $P\bar{E}CO_2$ and its volume determined. The arterial blood sample was analysed for $PaO_2$, $PaCO_2$, pH and haematocrit. These analyses were performed by the Clinical Blood Gas Laboratory, Royal Victoria Hospital, Montreal. The apparatus employed was an Instrumentation Laboratory model 113 pH/Gas Analyser, equipped with Clark and Severinghaus electrodes for oxygen and carbon dioxide respectively, and a combined glass electrode for pH. The water-bath temperature of the electrode system was 37 C. Body temperature was assumed to also be 37 C., and therefore, no temperature correction factors were required. Because sampling was into syringes packed in ice-water and analysis was performed within 15 minutes, no correction for metabolic changes was felt necessary (54).

E) Physiological Dead Space

This was calculated from Bohr's equation:

$$V_{DPHYS} = V_T \left( \frac{PaCO_2 - P\bar{E}CO_2}{P\ CO_2} \right)$$

Correction was made for the apparatus dead space and the results are presented as $V_D/V_T$ ratio.

F) Alveolar-Arterial Oxygen Gradient

Analysis of expired gases was employed to calculate alveolar $P_{O_2}$ using a version of the ideal alveolar air equation (27b, 75d).

$$P_AO_2 = P_IO_2 - P\bar{a}CO_2 \times \left( \frac{P_IO_2 - P\bar{E}O_2}{P\bar{E}CO_2} \right)$$

Where: $P_AO_2$ = Ideal alveolar $P_{O_2}$

$P_IO_2$ = Inspired $O_2$ tension = $(P_B - 47)\ F_IO_2$

$PaCO_2$ = Arterial $CO_2$ tension

$P\bar{E}CO_2$ = Mixed expired $CO_2$ tension

$P\bar{E}O_2$ = Mixed expired $O_2$ tension

Arterial blood was analysed for $PaO_2$. The oxygen tension gradient reported is the difference between the calculated alveolar $P_{O_2}$ and the measured arterial $P_{O_2}$ $(A - a\ D_{O_2})$.

F) Venous Admixture

This was obtained by using the standard shunt equation and expressed as $Q_S/Q_T\%$ (27c).

The "shunt" so calculated really reflects the degree of venous admixture which would be required to account for the observed differences between the calculated pulmonary end-capillary $P_{O_2}$ and the measured arterial $P_{O_2}$. It is also called the "physiological" shunt and includes

a component attributable to the true shunt (i.e. anatomical) as well as a component attributable to those parts of the lung with low regional $\dot{V}/\dot{Q}$ relationships.

$$\frac{Q_S}{Q_T} = \frac{C\acute{c}O_2 - CaO_2}{C\acute{c}O_2 - C\bar{v}O_2}$$

Where C = content

$\acute{c}$ = end-capillary, a = arterial, $\bar{v}$ = mixed venous

Oxygen content can be obtained by applying the following equation:

$$C = (SaO_2 \times 1.34 \times \text{H3 content}) + (PaO_2 \times \lambda)$$

Where S = saturation %

$\lambda$ = solubility factor for $O_2$ = 0.00003 ml/ml plasma/ mm Hg $P_{O_2}$

These saturations were obtained from blood $P_{O_2}$ and pH using a Severinghaus blood gas calculator (80). Oxygen content for arterial and end-capillary blood was then calculated. The oxygen content of mixed venous blood was obtained indirectly by applying Ficks principle:

$$CO = \dot{V}O_2/(CaO_2 - C\bar{v}O_2)$$

Cardiac output was determined by dye dilution. Oxygen consumption was calculated separately from the following equation:

$$\dot{V}_{O_2} = \dot{V}_I \times F_I O_2 - \dot{V}_E \quad F\bar{E}O_2$$

Where $\dot{V}_I = \frac{F_E N_2}{F_I N_2} \cdot \dot{V}_E$

Where $\frac{F_E N_2}{F_I N_2} = \frac{P_B - 47 - P_E O_2 - P_E CO_2}{P_B - 47 - P_I O_2}$ (28)

Having in this way calculated $\dot{V}_{O_2}$, the value for $CaO_2 - C\bar{v}O_2$ was calculated, and since $CaO_2$ was known, $C\bar{v}O_2$ was then determined.

## CHAPTER VI

## EXPERIMENTAL DESIGN

On the day of the operation the patients were brought to the Recovery Room of the Department of Anaesthesia, Royal Victoria Hospital in their hospital beds.

The first step in the study was placement of the epidural, arterial, and venous catheters, in that order. This was performed after preparation of the skin using 0.5% Iodine in alcohol, and the site infiltrated (intradermally and subcutaneously) with 1% Lidocaine. The epidural catheter was placed in the epidural space, after it was located by the loss of resistance test using a Tuohy needle (62). Correct placement was ascertained by a negative aspiration test. A polyethylene catheter was threaded one needle-length cephalad, beyond the needle tip, and the needle withdrawn. The catheter was anchored in place in the usual manner using 2" wide tape. The site of introduction was an intervertebral space between the last thoracic and 2nd lumbar vertebrae.

The subjects then lay supine for the placement of the arterial and venous cannulae.

Cannulation of the radial or brachial artery was performed using an ARGYLE MEDICUT (R) 18 gauge (2") intravenous cannula. This was kept patent using small volumes of heparinised saline (1,000 U in 250 ml). The venous catheter (C.V.P. INFUSOR, SORENSON RESEARCH CO. 15 gauge (21") radio opaque catheter) was introduced in a vein in the antecubital fossa and advanced an appropriate distance. This catheter was used to infuse the precalculated dose of 5% saline in Dextrose, and for the injection of Cardio-green (R) (Indocyanine Green) used for the cardiac output determination. The arterial catheter was used to withdraw samples for blood gas analyses and the cardiac output determinations. Once these preparatory steps were made, the patient was left for 10-15 minutes to rest.

The sequence of tests was as follows:-

1) Determination of lung volumes
2) Determination of cardiac output (in duplicate)
3) A three-minute collection of expired gases into a 50 litre meteorological balloon, with concomitant arterial blood sampling during the second minute.
4) Determination of F.E.V.$_{1.0}$ second (in duplicate)

During this control study, a pre-determined volume of normal 5% saline in Dextrosewas infused into a central vein, this volume being 10ml/Kg body weight. This was given to minimize any hypotension due to the epidural anaesthetic following the over-night fast, part of the normal pre-operative preparation. The importance of adequate hydration has been stressed by Wollman and Graves (92, 44).

The next step was the injection of the 1.5% Lidocaine in incremental volumes such as to obtain a sensory block up to the fourth thoracic segment. During this time, frequent determinations of the pulse and blood pressure were made. The need to inject a vasopressor never arose. However, in 3 of the subjects an extra volume of the infusate was required to keep the blood pressure stable.

The level of sensory loss was frequently determined using both ice and pin-prick. Once the desired level was obtained, the tests were repeated in the same sequence as above. The arterial catheter was then withdrawn, firm pressure applied for 5 minutes and a sterile dressing applied.

The intravenous catheter was left in place for use during the intra-operative and post-operative periods.

The epidural catheter was subsequently used for either intra- or post-operative injection of local anaesthetic as required for the clinical management.

The epidural catheter was removed by an anaesthetist at the appropriate time post-operatively.

Sequelae of Cannulations

There were no major complications following the arterial cannulations. Mild pain during flushing of the catheter was experienced by some patients. A properly padded plaster of Paris slab placed on the dorsal aspect of the fore-arm prevented pain produced by movement at the joints.

One patient required heparinization following phlebitis of the right cephalic vein, aaconsequence of the venous catheter being left in place for 3 days. The patient was discharged from hospital on oral anti-coagulants, which were continued for 2 weeks. Follow-up at 2 months after surgery indicated clinical improvement, with no sequelae.

No complications due to the epidural catheterizations occurred.

# CHAPTER VII

## RESULTS

The results are reported in tables V-VIII which show the individual pre-epidural values, changes (in absolute values) the mean percent change and the standard deviation of the mean (S.E.). The values before epidural anaesthesia were compared with the post-epidural values using Student's t-test for paired measurements. Significance was set at the 5% level.

### A. LUNG VOLUMES AND CAPACITIES

#### I) Functional Residual Capacity

a) Group A (Figs. 4 and 6, table V)

The mean pre-epidural value for FRC in Group A was 1.921s (± 0.22). The two components, Residual Volume (RV) and Expiratory Reserve Volume (ERV) were found to be 1.34 (± 0.14) 1s and 0.58 (± 0.11) 1s respectively. After the desired level of epidural anaesthesia was achieved FRC showed a mean increase of 0.091s (± 0.07), The changes in its two components were +0.101s (± 0.07) and -0.011s (± 0.05) for RV and ERV respectively. The observed changes in FRC, RV and ERV showed individual variation in both magnitude and direction with no

consistent pattern; and none of its mean changes reached the 5% level of significance.

b) Group B (Figs. 5 and 6, table VI)

In this group, the mean pre-epidural FRC was 1.96 ls (± 0.24) with RV and ERV having mean values of 1.53 ls (± 0.22) and 0.44 ls (± 0.12) respectively. These values were not statistically different from the Group A control figures. The mean changes noted after epidural anaesthesia for FRC, RV and ERV were -0.04 ls (± 0.06), +0.04 ls (± 0.08) and -0.09 ls (± 0.06) respectively, and these did not reach the 5% level.

Thus the effect of epidural anaesthesia on FRC and its two components (ERV and RV) was found to be minimal.

II) Vital Capacity (VC)

Group A. (Figs. 4 and 6, table V)

The changes in ERV have already been considered. The mean pre-epidural value for Inspiratory Capacity (IC) was 2.97 ls (± 0.23) and the mean change was +0.21 ls (± 0.09), or 5.7% (± 0.07) which was found to be insignificant at the 5% level. It must be pointed out, however, that in most instances IC increased, and in one subject (no. 4) this increase was by +23%. If this one change is excluded

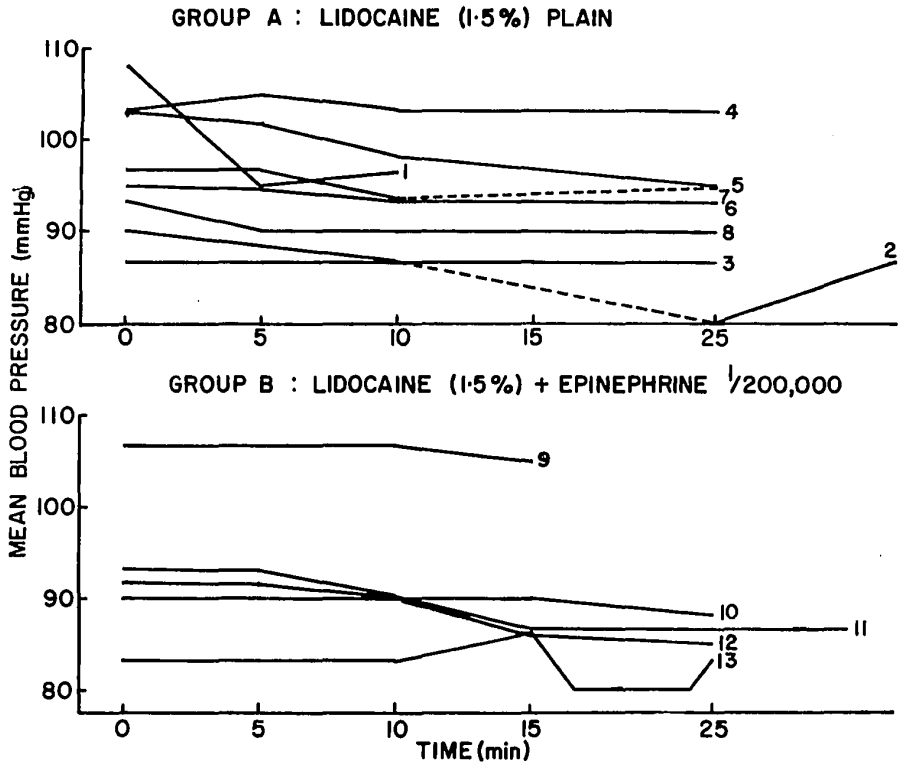



FIG. 7: CHANGES IN MEAN BLOOD PRESSURE (MBP) WITH TIME (BOTH GROUPS)

from the study, the mean change would then be +4.1%. It seems, therefore, that an epidural anaesthetic given in the stated circumstance not only leads to no decrease in VC but may actually increase IC. In addition there appeared to be a direct relationship between increases in IC and in FEV 1.0 (Fig. 12) which will be discussed in Chapter VIII.

Group B (Figs. 5 and 6, table VI)

The mean pre-epidural value for IC in Group B was 2.84 ls (± .14) with a mean change of -0.04 ls (± 0.22), which was insignificant. Thus the mean change in IC following epidural anaesthesia is a small increase in Group A and a small decrease in Group B, but in both instances the mean changes are largely determined by marked changes in one individual. Thus if subject 11 is omitted from Group B then the mean change would be +5.5%, which is quite similar to the 4.1% increase seen in Group A after exclusion of subject no. 4.

III) Forced Expiratory Volume (FEV 1.0)

a) Group A (Figs. 4 and 6, table V)

The mean figure during the control study was 2.48 and the mean change was +0.111s/min. There was a con-

siderable difference in the range in the changes observed (from +0.85ls/min to -0.45ls/min). It must be remembered that this test depends to a greater extent than other lung volume measurements on the subjects willingness and co-operation. It is of interest that during the post-epidural study, some subjects spontaneously reported a subjective feeling of being able to breathe more easily, in spite of a fall in $FEV_{1.0}$.

b) Group B (Figs. 5 and 6, table VI)

In this subject-group the mean control value was 2.41 ls/min with a mean change of -0.01. Data for subject no. 10 is missing due to the patients unwillingness to perform the test. The mean changes in $FEV_{1.0}$ following epidural anaesthesia were not significant at the 5% level in either of the two groups (A and B).

B. MEAN BLOOD PRESSURE AND CARDIAC OUTPUT

I) Mean Blood Pressure (Fig. 7)

This shows the changes in MBP with time from the time of injection of lidocaine (0 mins.). In both groups, MBP stayed relatively stable in most cases. In subject 2 the almost continuous fall in MBP was reversed by extra intravenous fluid. Unfortunately, no cardiac

output measurements were made due to inability to catheterize an artery. The other two subjects who required supplementary infusion to correct a fall in MBP were subjects no. 1 and 5. In both cases cardiac output fell, but these falls were not large.

II) Cardiac Output (CO)

a) Group A (Figs. 8 and 10, table VII)

The mean value for this measurement was 5.7 L/min (± 0.34). The mean change was +0.3 L/min (± 0.4) or +4.8% (± 0.07). These figures are for 6 subjects only, and were not significant at the 5% level. Attention must be drawn to two points: i) the fact that there were individual variations in both magnitude and direction of change. ii) the impressive increase noted in subject no. 8. This patient was seen to be shivering towards the end of the experiment.

The observed changes stress the importance of adequate hydration. The regimen of an extra dose of IV fluid was effective in reversing falls in MAP. It seems probable that the vascular bed expanded following the epidural anaesthetic (presumably because of removal of sympathetic tone). The increased IV infusion was thus capable of filling up the vascular space and maintaining a relatively stable cardiac output.

b) Group B (Figs. 9 and 10, table VIII)

Data is available for 3 out of 5 subjects only. Pre-epidural values for Group A and B were similar. In Group B the mean value was 5.9 L/min (± 0.34) with a mean change of +0.1 L/min, but the individual values varied strikingly.

C. ALVEOLAR-ARTERIAL OXYGEN GRADIENT ($A\text{-}aDO_2$)

(Figs. 8, 9 and 10, tables VII and VIII)

The mean in Group A was 27.3 mmHg (± 4.6) and this fell by 1.1 mmHg (± 2.4) after epidural anaesthesia. The changes ranged from -8.2 mm to +8.7 mm.

In Group B the mean change from a control value of 33.2 (± 5.3) was -0.59 (± 3.26), changes ranging from -10.9 mm to +8.5 mm.

Changes of this order are not generally thought to be important clinically, i.e. epidural anaesthesia as used in this study does not result in any apparent derangement in overall oxygen transfer. Nor did there appear to be any direct relationship between changes in CO and $A\text{-}aDO_2$ or between changes in CO and $Q_S/Q_T$ in either Group A or Group B.

D. VENOUS ADMIXTURE ($Q_S/Q_T$)

(Figs. 8, 9 and 10, tables VII and VIII)

Although reported as $Q_S/Q_T$, the figures really represent venous admixture, rather than "true" right to left shunt. However, changes in this measurement are probably the best reflection of changes in the efficiency of gas exchange since CO and $\dot{V}_{O_2}$ may also be affected by the epidural anaesthesia.

The mean value for Group A was 11.5% (± 2.83) and the change was 1.6% (± 1.64). The mean for Group B was 11.54% (± 5.45) and the change was -1.5% (± 2.86). There were no significant differences between the control values for Groups A and B, nor did the anaesthesia result in significant changes in $Q_S/Q_T$% in either group. However, it should be noted that subjects 5 and 7 (Group A) and subject 11 (Group B) all had unusually high values before anaesthesia which showed some improvement thereafter.

## E. ALVEOLAR VENTILATION

(Tables VII and VIII)

In spite of relatively wide variation in individual control values, the means were quite similar being 5.24 l/s (± .89) for Group A and 4.92 l/s (± 1.02) for Group B. Only small changes were noted after anaesthesia, +.2 l/s (± .93) and +4 l/s (± 0.59) for Groups A and B respectively.

F. OXYGEN CONSUMPTION

(Tables VII and VIII)

There was some variation in individual values and changes in both groups in this parameter. However, the means were quite similar (224 ml (± 16.0) and 201 ml (± 9.79) for Groups A and B respectively, and the changes were slight, namely +2 ml. (± 15.89) for Group A and -8.4 ml. (± 9.4) for Group B.

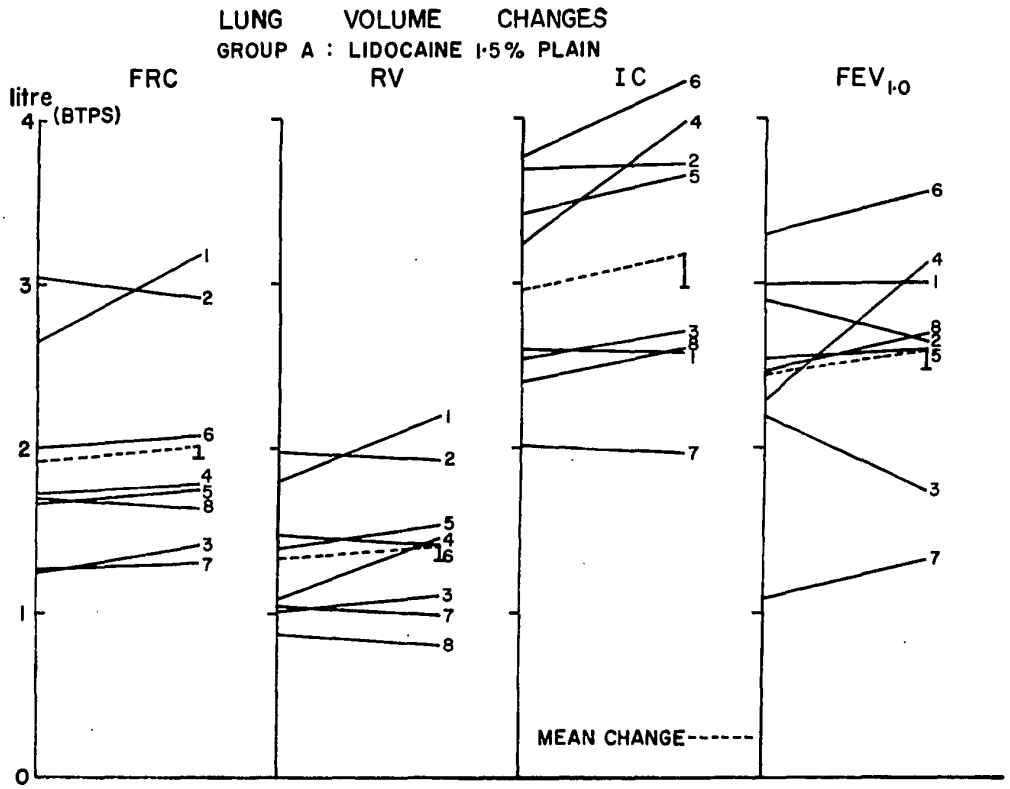



FIG. 4: LUNG VOLUME CHANGES IN GROUP A (PLAIN LIDOCAINE)

Continuous lines: individual changes (with subject numbers)

Interrupted lines: changes in the mean (-1 S.E.)

V. EFFECTS OF EPIDURAL ANAESTHESIA ON LUNG VOLUMES GROUP A: LIDOCAINE 1.5% PLAIN

| SUBJECT | RESIDUAL VOLUME (L) PRE-EPID | CHANGE | EXP.RES.VOL.(L) PRE-EPID | CHANGE | FUNCT.RESID.CAPAC. PRE-EPID | CHANGE | INSPIR. CAPAC. PRE-EPID | CHANGE | VITAL CAPACITY PRE-EPID | CHANGE | FORCED EXP.VOL. (1.0) PRE-EPID | CHANGE |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 1.81 | +0.40 | 0.87 | +0.10 | 2.68 | +0.50 | 2.60 | -0.02 | 3.47 | +0.08 | 3.00 | 0.00 |
| 2 | 1.99 | -0.06 | 1.05 | -0.06 | 3.04 | -0.12 | 3.69 | +0.04 | 4.74 | -0.02 | 4.74 | -0.25 |
| 3 | 1.01 | +0.10 | 0.24 | +0.08 | 1.26 | +0.18 | 2.55 | +0.16 | 2.80 | +0.23 | 2.20 | -0.45 |
| 4 | 1.11 | +0.37 | 0.64 | -0.32 | 1.74 | +0.05 | 3.24 | +0.74 | 3.88 | +0.42 | 2.30 | +0.85 |
| 5 | 1.40 | +0.13 | 0.28 | -0.06 | 1.68 | +0.07 | 3.42 | +0.22 | 3.70 | +0.16 | 2.55 | +0.05 |
| 6 | 1.44 | -0.04 | 0.54 | +0.10 | 2.01 | +0.06 | 3.78 | +0.44 | 4.32 | +0.54 | 3.30 | +0.25 |
| 7 | 1.06 | -0.06 | 0.22 | +0.11 | 1.27 | +0.04 | 2.03 | -0.06 | 2.24 | +0.04 | 1.10 | +0.23 |
| 8 | 0.88 | -0.07 | 0.83 | +0.01 | 1.70 | -0.06 | 2.41 | +0.19 | 3.24 | +0.19 | 2.48 | +0.22 |
| S.E. | 0.14 | 0.07 | 0.11 | 0.05 | .22 | 0.07 | .23 | 0.09 | .28 | 0.07 | - | - |
| MEAN | 1.34 | +0.10 | 0.58 | -0.01 | 1.92 | +0.09 | 2.97 | +0.21 | 3.55 | +0.20 | 2.48 | +0.11 |
| MEAN % CHANGE | | +6.9% | | +4.1% | | +4.7% | | +6.5% | | +5.7% | | +2.2% |
| S.E. | | 0.05 | | 0.11 | | 0.03 | | 0.03 | | 0.02 | | - |

All volumes at B.T.P.S.

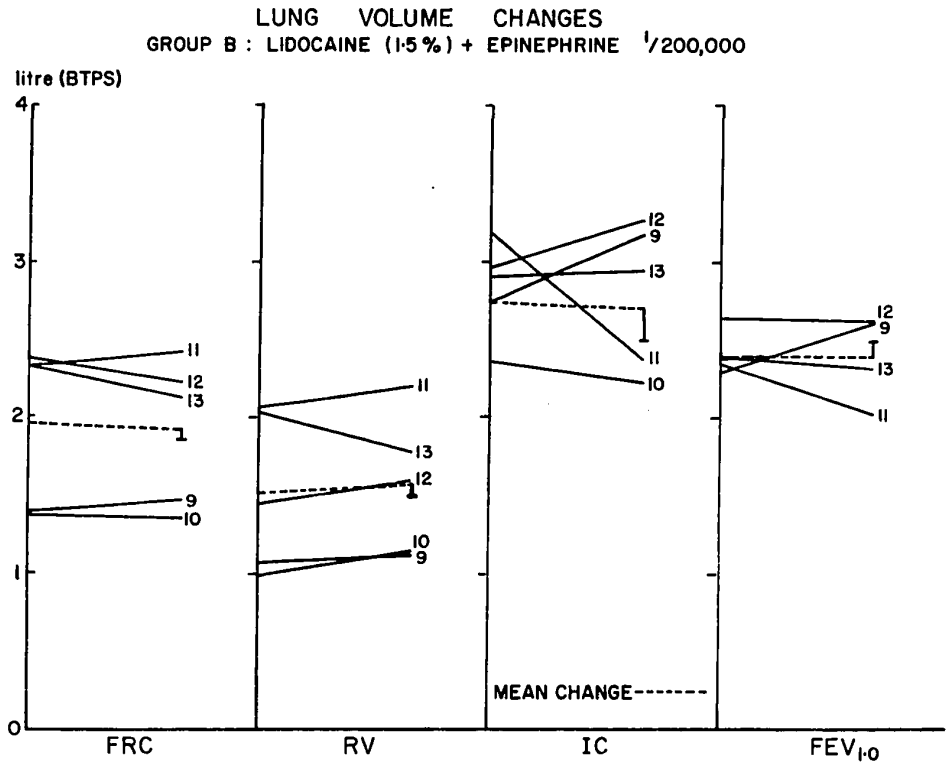



FIG. 5: LUNG VOLUME CHANGES IN GROUP B (LIDOCAINE + EPINEPHRINE

Continuous lines: individual changes (with subject numbers

Interrupted lines: change in the mean (± 1 S.E.)

VI EFFECTS OF EPIDURAL ANAESTHESIA ON LUNG VOLUMES GROUP B: LIDOCAINE 1.5% + EPINEPHRINE 1/200,000

| SUBJECT | RESIDUAL VOLUME | | EXP.RES.VOL. | | FUNC. RESID. CAPAC. | | INSPIR. CAPAC. | | VITAL CAPACITY | | FORCED EXP. VOL. | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | PRE-EPID | CHANGE | PRE-EPID | CHANGE | PRE-EPID | CHANGE | PRE-EPID | CHANGE | PRE-EPID | CHANGE | PRE-EPID | CHANGE |
| 9 | 1.08 | +.05 | 0.33 | +.02 | 1.40 | +.03 | 2.74 | +.43 | 3.07 | +.45 | 2.30 | +.33 |
| 10 | 0.99 | +.15 | 0.38 | -.17 | 1.37 | -.01 | 2.38 | -.13 | 2.76 | -.29 | - | - |
| 11 | 2.06 | +.14 | 0.27 | -.06 | 2.34 | +.08 | 3.20 | -.82 | 3.47 | -.87 | 2.34 | =.31 |
| 12 | 1.46 | +.13 | 0.92 | -.28 | 2.38 | -.15 | 2.97 | +.30 | 3.89 | +.02 | 2.65 | -.02 |
| 13 | 2.04 | -.26 | 0.30 | +.05 | 2.33 | -.21 | 2.90 | +.04 | 3.20 | +.08 | 2.35 | -.03 |
| MEAN | 1.57 | +.04 | 0.44 | -.09 | 1.96 | -.04 | 2.84 | -.04 | 3.28 | -.13 | 2.41 | -.01 |
| S.E. | .22 | 0.08 | .12 | 0.06 | .24 | 0.06 | .14 | 0.22 | .19 | 0.22 | - | - |
| MEAN % CHANGE | | +4.7% | | -14.6% | | -1.5% | | -0.9% | | -3.7% | | -0.2% |
| S.E. | | 0.05 | | 0.11 | | 0.03 | | 0.07 | | 0.07 | | - |

All vds. in ls. at B.T.P.S.

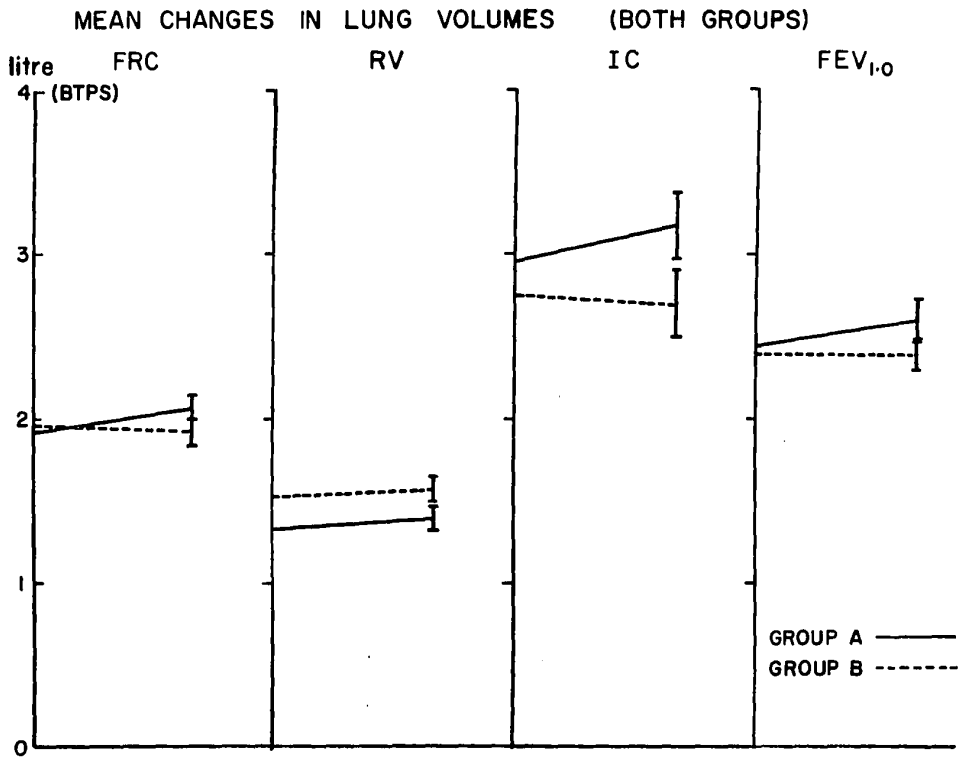



FIG. 6: LUNG VOLUME CHANGES (BOTH GROUPS)

Continuous line: changes in the mean in Group A (± 1 S.E.)

Interrupted line: changes in the mean in Group B (± 1 S.E.)

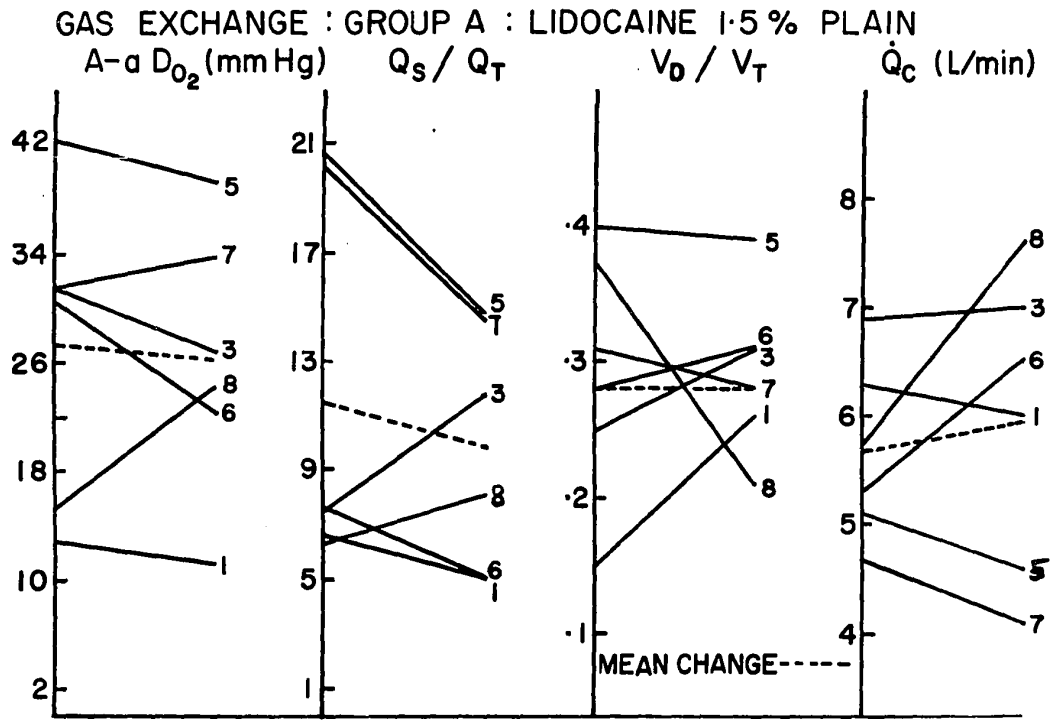



FIG. 8: CHANGES IN GAS EXCHANGE PARAMETERS (GROUP A)

Continuous lines: individual changes ( with subject numbers)

Interrupted lines: changes in the mean

VII EFFECTS OF EPIDURAL ANAESTHESIA ON GAS EXCHANGE GROUP A: LIDOCAINE 1.5% PLAIN

| SUBJECT | $\dot{Q}_C$ (L/min) | | $A-aD_{O_2}$ (mmHg) | | $Q_S/Q_T$ (%) | | $V_D/V_T$ | | $\dot{V}_A$ (L/min) | | $\dot{V}_{O_2}$ (ml/min) | | R. | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | PRE | CHANGE | PRE | CHANGE | PRE | CHANGE | PRE | CHANGE | PRE | CHANGE | PRE | CHANGE | PRE | CHANGE |
| 1 | 6.3 | -0.3 | 12.7 | -1.5 | 6.7 | -1.7 | .25 | +.06 | 4.15 | -0.9 | 118 | -3 | .87 | +.04 |
| 3 | 6.9 | +0.1 | 31.6 | -4.8 | 7.6 | +4.2 | .11 | +.14 | 8.92 | -3.8 | 285 | -27 | 1.18 | -.28 |
| 5 | 5.1 | -0.5 | 42.2 | -3.0 | 20.7 | -5.9 | .40 | -.01 | 4.30 | -0.2 | 234 | -5 | .78 | +.01 |
| 6 | 5.3 | +1.2 | 30.6 | -8.2 | 7.7 | -2.6 | .28 | +.03 | 6.90 | +2.4 | 253 | +65 | 1.05 | +.13 |
| 7 | 4.7 | -0.6 | 31.5 | +2.2 | 20.2 | -5.7 | .31 | -.03 | 3.81 | +0.2 | 187 | -43 | .84 | -.02 |
| 8 | 517 | +1.8 | 15.3 | +817 | 6.3 | +1.8 | .38 | -.17 | 3.36 | +2.4 | 205 | +27 | .68 | +.18 |
| MEAN | 5.7 | +0.3 | 27.3 | -1.1 | 11.5 | -1.6 | .29 | -.01 | 5.24 | +.2 | 224 | +2 | .90 | +.01 |
| S.E. | 0.34 | 0.4 | 4.6 | 2.4 | 2.83 | 1.64 | .04 | .04 | .89 | .93 | 16.8 | 15.89 | 007 | 0.06 |
| MEAN % CHANGE | | +4.8% | | +0.5% | | -5.1% | +17.6% | +17.6% | +10.6% | +10.6% | | +0.4% | | +3.0% |
| S.E. | | 0.07 | | .12 | | .15 | | 0.23 | | 0.10 | | 0.07 | | 0.07 |

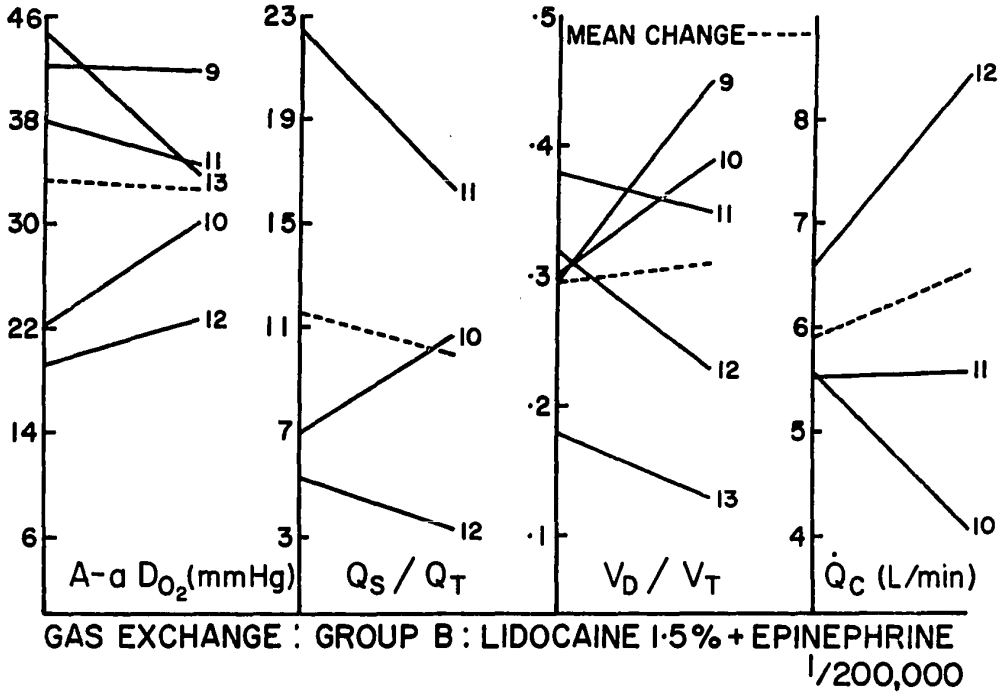



FIG. 9: CHANGES IN GAS EXCHANGE PARAMETERS (GROUP B)

Continuous lines: individual changes (with subject numbers)

Interrupted lines: changes in the mean

VIII EFFECTS OF EPIDURAL ANAESTHESIA ON GAS EXCHANGE GROUP B: LIDOCAINE 1.5% + EPINEPHRINE 1/200,000

| SUBJECT | $Q_C$ (L/min) | | $A\text{-}aD_{O_2}$ (mmHg) | | $Q_S/Q_T$ (%) | | $V_D/V_T$ | | $\dot{V}_A$ (L/min) | | $\dot{V}O_2$ (ml/min) | | R. | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | PRE | CHANGE | PRE | CHANGE | PRE | CHANGE | PRE | CHANGE | PRE | CHANGE | PRE | CHANGE | PRE | CHANGE |
| 9 | - | - | 42.2 | -.5 | - | - | .30 | +.15 | 4.67 | -1.3 | 202 | -12 | .93 | -.23 |
| 10 | 5.6 | -1.5 | 22.2 | +8.5 | 7.0 | +3.4 | .30 | +.08 | 3.74 | -0.61 | 197 | -39 | .87 | -.05 |
| 11 | 5.5 | -0.1 | 38.0 | -3.5 | 22.4 | -6.2 | .38 | -.03 | 4.06 | +0.65 | 194 | +18 | .98 | -.03 |
| 12 | 6.6 | +1.9 | 19.2 | +3.5 | 5.22 | -1.9 | .18 | -.05 | 8.89 | +2.0 | 236 | -12 | 1.28 | +.11 |
| 13 | - | - | 44.6 | -10.9 | - | - | .32 | -.09 | 3.22 | +1.13 | 176 | +3 | .83 | +.21 |
| MEAN | 5.9 | +.1 | 33.2 | -.59 | 11.54 | -1.5 | .30 | +.01 | 4.92 | +.4 | 201 | -8.4 | .98 | +.0 |
| S.E. | 0.34 | .96 | 5.3 | 3.26 | 5.45 | 2.86 | .03 | .04 | 1.02 | 0.59 | 9.79 | 9.4 | .08 | .07 |
| MEAN % CHANGE | | +0.9% | | -4.3% | | -3.8% | | +3.6% | | +6.9% | -4% | -4% | | +0.2% |
| S.E. | | .16 | | 0.10 | | 0.28 | | 0.10 | | 0.13 | | 0.15 | | 0.08 |

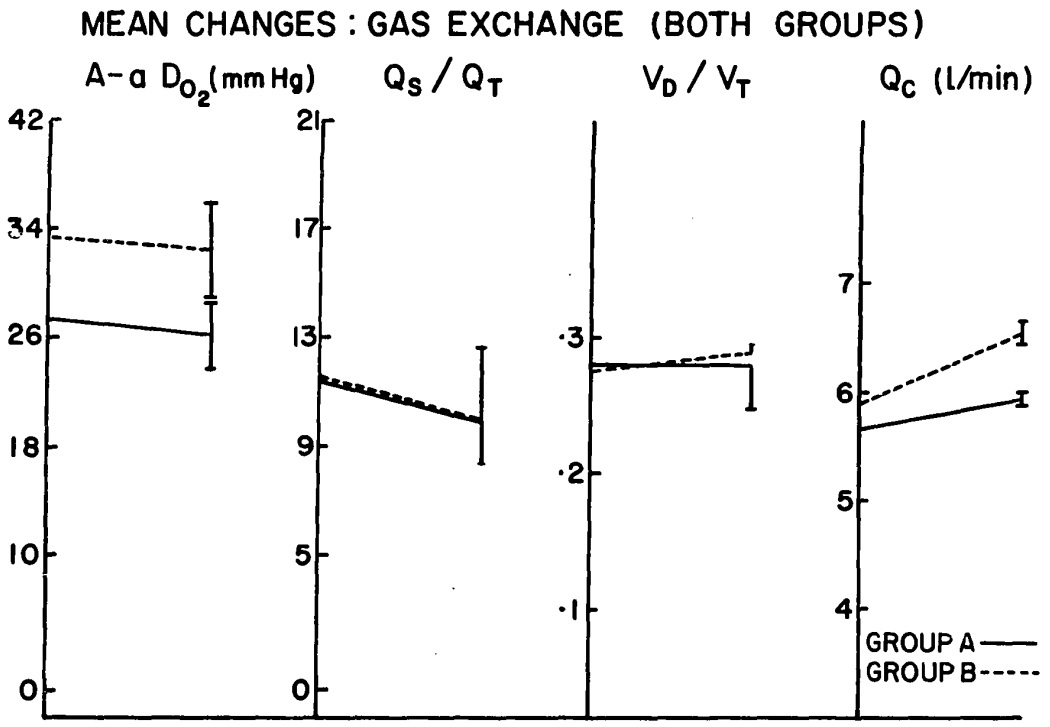



FIG. 10: CHANGES IN GAS EXCHANGE PARAMETERS (BOTH GROUPS)

Continuous lines: changes in the mean in Group A (± S.E.)

Interrupted lines: changes in the mean in Group B (± S.E.)

# CHAPTER VIII

# DISCUSSION

The results of the present study will be discussed in relation to the published studies and the review of relevant physiology and pharmacology. Following that, the incidence of post-operative pulmonary complications, and the post-operative pulmonary pathophysiological changes will be briefly reviewed with the aim of placing the usefulness of epidural anaesthesia during the post-operative period in proper perspective.

## A. THE EFFECTS OF EPIDURAL ANAESTHESIA ON CARDIAC OUTPUT AND MEAN BLOOD PRESSURE

If epidural anaesthesia is to be used for post-operative pain relief, it is extremely important to establish that the procedure itself does not affect gas exchange adversely by diminishing cardiac output (CO).

Because of the effects of epinephrine on the circulatory system, epidural anaesthesia without epinephrine will be considered first.

Studies performed by Bonica and his colleagues (8, 55, 56, 87) suggested that the procedure resulted in a fall of cardiac output (CO) by 5.4% and in mean blood

pressure by 8.9%. These studies were on volunteers, using 2% plain lidocaine and the sensory level was only defined as to at least $T_5$. They did not mention whether intravenous fluids were given to their subjects. In their later study (11), they reported insignificant changes in CO when the sensory level was up to $T_{4-5}$. In this study, they maintained an intravenous infusion, and gave the lidocaine in incremental doses. In the present study following the same procedure, a mean change of +5% was found. The discrepancies between the present study and their earlier ones are thus probably due to the fact that there were fundamental differences in the experimental set up, specifically in hydration of the patients and in the manner of injecting the lidocaine. In the present study, the subjects were in-patients, 1.5% lidocaine was used and they were given a stated dose of I.V. fluids before the epidural anaesthetic. The lidocaine was injected in incremental doses to achieve a sensory block to a well defined level, and not injected as a bolus. Because of these differences in the amount of lidocaine injected, it is quite conceivable that sympathetic blockade was more extensive in Bonica's earlier studies than in either his later study or in the present report. Analysis of individual changes in the present

study shows some variation in both direction and magnitude of change of CO. The only case (No. 8, Group A) to show a marked increase in CO also showed marked increases in alveolar ventilation ($\dot{V}_A$) and oxygen consumption ($\dot{V}O_2$), and was shivering at the time the post-epidural measurements were made. If that subject were not included in the results, then the mean change in cardiac output in Group A would have been -0.02 L/min, which is insignificant clinically. This then would be in even closer agreement with the better defined study reported by Bonica (11).

Thus, it is of interest that the small decreases in CO noted in Cases 5 and 7 were not associated with any decrease in gas exchange efficiency (as reflected by $Q_S/Q_T$.) This is of importance since $Q_S/Q_T$ values in these individuals were higher than is usually found in health (75f) before anaesthesia. However, it is possible that our range for health will have to be enlarged in view of recent work showing higher values for $Q_S/Q_T$ and $A\text{-}aD_{O_2}$ in the supine position in subjects in whom airway closure involves the tidal breathing range in this position (32). These two individuals may well be in that category. The same holds true for case 11 in Group B. It is interesting to note that their ages were 45, 67 and 71 respectively.

From closer scrutiny of our data and that of Bonica (11), in which a sensory level is stated, it seems that changes in CO using either 1.5% or 2.0% lidocaine plain will not be clinically significant. This is important not only for tissue perfusion and overall cardio-vascular function but because of the rôle that CO plays in determining the efficiency of overall pulmonary gas exchange, as reflected in $A\text{-}aD_{O_2}$ and $Q_S/Q_T$ (54, 79).

Epinephrine is believed to have an important and significant effect on cardiac output. This was reviewed in earlier chapters. Since complete measurements were obtained in only 3 subjects in Group B (i.e. epidural anaesthesia with epinephrine) firm conclusions cannot be reached about effects from the present series. However, the increase in cardiac output did appear to relate to the amount of epinephrine administered and is in agreement with the findings reported by Bonica (8a, 55, 56, 87).

In three subjects (1, 2 and 8), an initial fall in mean blood pressure was noted and I.V. fluids were given to correct that fall (Fig. 8). This observation stresses again the value of adequate hydration which has been reported by various authors (92, 86, 44).

B. ALVEOLAR ARTERIAL OXYGEN GRADIENTS AND VENOUS ADMIXTURE

There are, to date, no published studies on the effects of epidural anaesthesia (as administered in this study) on the above measurements. The only reports are for blood gas determinations, reviewed previously in Chapter III.

In the present study, there was a small mean reduction in both $A\text{-}aD_{O_2}$ and $Q_S/Q_T$ in both groups of patients, indicating no consistent deterioration, and perhaps even a small improvement in pulmonary gas exchange. By deduction, it appears, therefore, that regional $\dot{V}_A/\dot{Q}$ relationships were not deleteriously affected to any degree and one may draw the tentative conclusion that an epidural anaesthetic does not adversely affect gas exchange. This is particularly important because an epidural anaesthetic to relieve postoperative pain would be of little value if it caused an increase in shunting and an enlarged $A\text{-}aD_{O_2}$. However, if a significant fall in cardiac output should occur with the epidural anaesthetic, which can occur in an inadequately hydrated patient, an enlargement of the $A\text{-}aD_{O_2}$ may occur.

Despite the fact that mean values for $A\text{-}aD_{O_2}$ and $Q_S/Q_T$% changed little, there were individual exceptions. Of particular importance were Case 8 (Group A) and

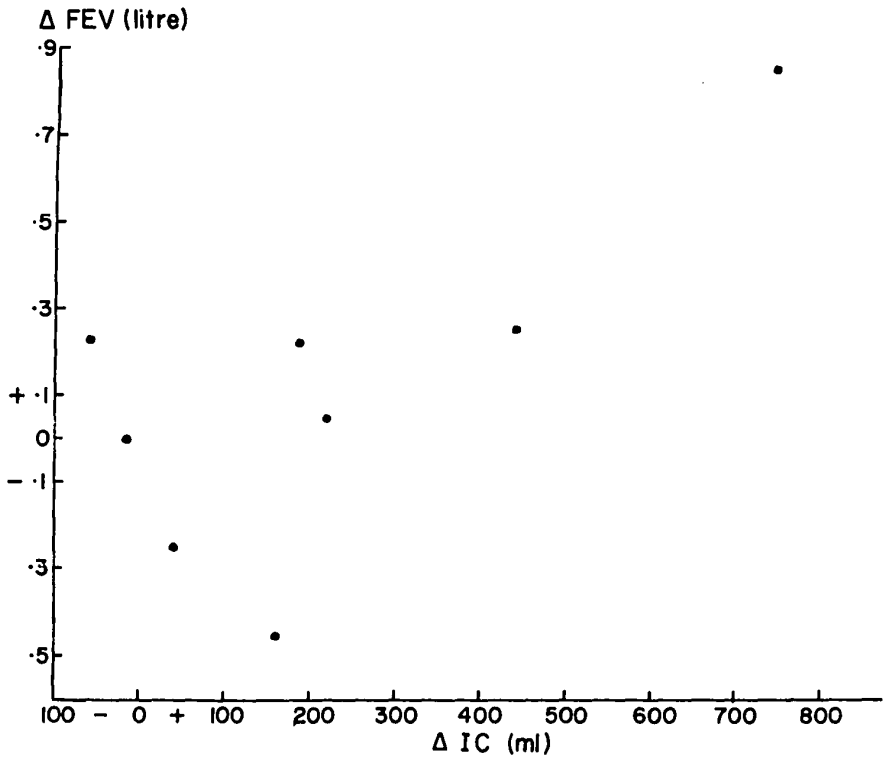



FIG. 11: CHANGES IN $FEV_{1.0}$ (ORDINATE) AND I.C. (ABSCISSA)

(GROUP A)

Case 10 (Group B) in whom both $A\text{-}aD_{O_2}$ and $Q_S/Q_T\%$ increased to a degree which could well be important clincically.

Case 8 was shivering towards the end of the post-epidural measurements and this shivering would explain these findings.

However, this was not the case in subject 10, and no obvious explanation of this observation can be found. In subject 8, cardiac output increased by 31%, while in subject 10 CO fell by 27%. It is also interesting to note that MBP was fairly stable in both cases. This points to the fact that a fall in MBP is not necessarily indicative of a reduction in cardiacoutput, a point raised by Stephen et al (84).

C. PHYSIOLOGICAL DEAD SPACE

This measure of wasted ventilated showed, on the whole, insignificant changes following epidural anaesthesia. Bronchodilatation can lead to an increase in $V_D/V_T$ ratios. If lidocaine is absorbed to any clinically significant degree, and if it causes bronchodilatation (91), an increase in $V_D/V_T$ would have been observed. Though mean changes were not impressive it was of interest that $V_D/V_T$ increased to a rather marked degree in two cases (9 and 10)

in Group B both of whom showed a fall in $\dot{V}_A$ which would explain the results obtained. This also holds true for subject 3 in Group A.

D. FUNCTIONAL RESIDUAL CAPACITY

There are no reports in the literature on the effects of epidural anaesthetic on this measurement despite its clinical importance (see page 3 in Introduction). A reduction in FRC can be very detrimental to gas exchange if airway closure occurs above FRC. A reduction in FRC will also signify a derangement in pulmonary mechanics. If the elastic recoil of the chest wall is reduced, then the lung recoil factors will function unopposed. This change could then be reflected in closure of some lung units and an increase in shunting. Absorption of residual gas will then be evident as atelectasis. It is for these reasons that it was felt important to measure the changes in FRC and in gas exchange.

In spite of individual variations, the changes were insignificant. This is useful practical information because of the implication that derangements in gas exchange due to a reduction of FRC will not occur following epidural anaesthesia. If the FRC is already reduced post-operatively, the epidural anaesthetic may help in reversing that change by alleviating the pain and/preventing the "guarded"

breathing pattern which is presumably due to pain and thus allow free breathing (14). It is interesting to note that although FRC was unchanged, there was, in general, an increase in residual volume (RV) with a slight reduction in expiratory reserve volume (ERV), a finding which could have been anticipated from the rôle of the muscles of respiration during a vital capacity manoeuvre, mentioned previously. The study by Freund (40) also has shown a reduction in ERV following an epidural anaesthetic. But this reduction was minimal and insignificant. Freund (40) has stated that a 1.5% solution could lead to less effects than the 2.0%.

E. VITAL CAPACITY

By limiting cephalad spread of anaesthesia and by using a weaker solution, it appears that in the present study, inspiratory capacity was not only unchanged, but even increased in most of the subjects. Although these changes are small, they may be of clinical importance, because they suggest an unchanged deep breathing and coughing ability, in itself very important in the post-operative period for the purpose of reversing changes in surfactant and for the removal of secretions. From the review of the literature and the discussion of the

physiological and pharmacological aspects, it was anticipated that there would not be any serious reduction in VC if the epidural anaesthetic is administered strictly according to the present schema, and this is confirmed by these results. Although Moir (69) has reported a slight fall in VC, this does not necessarily contradict our results. In his series the sensory level was at $T_2$ in some instances and this accounts for the difference in results. The results reported by Freund (40) were with the use of 2% lidocaine, which will probably make the degree of motor paresis more profound (71, 40).

F. FORCED EXPIRATORY VOLUME

The effects of epidural anaesthesia on $FEV_{1.0}$ varied from case to case, within a range of -5% to +9%, but these changes are clinically unimportant. Because neither VC and $FEV_{1.0}$ changed to any extent one therefore assumes that bronchial calibre did not change. It is, however, at least theoretically, possible to get bronchodilatation (91) due to the lidocaine. It is of interest that there appeared to be a direct relationship between increases in IC and in $FEV_{1.0}$ (Fig. 1[illegible]).

These findings are of clinical importance because the manoeuvres involved in doing an $FEV_{1.0}$ are similar to those

of a cough, and it is important to establish that they are not impaired following an epidural anaesthetic.

GENERAL COMMENT

It is disconcerting to learn that the incidence of pulmonary complications following surgery is about the same today as it was almost 30 years ago. In 1933, King (58) reported the incidence to be 8.9% for the period of one year, while in 1968 Wightman (89) reported a 6.2% incidence over a 7 month period. In the latter series infection (bronchopneumonia, pneumonia and bronchitis) accounted for 56% of cases while atelectasis (collapse either alone or with superimposed infection) accounted for 42%. It is interesting to note that the incidence of such complications following abdominal operations was 19.2% and that for non-abdominal operations was 12.7%, indicating that pulmonary complications following non-abdominal surgery constitute an important clinical problem. Equally interesting is the higher incidence of such complications in smokers (14.8%) compared to the 6.3% incidence in non-smokers (89). This virtually unchanged incidence of post-operative chest complications over the past thirty years is a stimulus to further study of the pathophysiological changes that occur in the post-operative

period, in the hope that better understanding will enable us to institute more effective measures to reduce that incidence.

During the post-operative period, particularly following abdominal surgery, there is a reduction in vital capacity and functional residual capacity (2, 5a, 5b) and arterial hypoxaemia. This arterial hypoxaemia may be caused by $\dot{V}_A/\dot{Q}$ inequalities (74, 77) which are possibly due to the shunting of blood in partially collapsed alveoli (34, 48). Diament has proposed that this partial collapse arises spontaneously (37) and Williams has proposed that this could be due to inactivation of pulmonary surfactant (90), although the evidence suggests that this inactivation may follow rather than preceed the collapse (38). It appears, therefore, that the reduction in FRC could be due to absorption atelectasis with a loss of lung volume. On the other hand, it is also possible that abdominal pain due to surgery may, by causing a "clenched-thorax" pattern of ventilation, cause the reduction of FRC. Both mechanisms could contribute to the impairment of gas exchange. Breathing below FRC can cause veno-arterial shunting as has been shown by Nunn (73). The reduction in VC will of necessity decrease the

effective propulsive power required to expectorate and remove secretions. Also because of the inability to breathe deeply, the changes in surfactant cannot be reversed. In this manner, the atelectasis and accummulation of secretions would be the starting point for post-operative pneumonia.

It seems, from this discussion, that the appropriate measures required to reduce this incidence of pulmonary complications should be directed towards reversal of as many as possible of the pathophysiological changes mentioned above. Thus pain must be effectively alleviated to allow better ventilation and more adequate expectoration. The subject must be able to deep-breathe in order to restore normal compliance. The assumption can now be made, therefore, that an improvement in ventilation would reduce the incidence of post-operative pulmonary complications. In order to help achieve such an improvement pain relief must be adequate but not cause any undesirable side effects of its' own. The effectiveness of epidural anaesthesia in improving ventilation has been reported (14, 15, 21). It remained therefore, to determine the cardio-respiratory effects of epidural anaesthesia such as would be given for the purpose of pain relief following upper abdominal surgery. The desired level would then be a sensory block

up to T4. It is important that epidural anaesthesia itself have no detrimental effects on gas exchange, because it will be given during a period when gas exchange is often already deranged and cardiac output is unstable.

Once these effects are known, and if found to be innocuous, asstudy of gas exchange following pain relief can then be made. Such a study should be a controlled one comparing systemic analgesics and epidural anaesthesia in terms of subjective pain relief, gas exchange and the incidence of pulmonary complications. Although such a study was envisaged, it was felt that an examination of the effects of epidural anaesthesia alone must be made before performing the equally important controlled study outlined above.

# CONCLUSIONS

The basic aim of this study was to determine whether epidural anaesthesia, an effective measure for post-operative pain relief, has any harmful effects on FRC and through FRC on pulmonary gas exchange (as measured by $A\text{-}aD_{O_2}$, $Q_S/Q_T$ as well as $Pa_{O_2}$). Should it have no adverse effects on these important measurements, than it can quite safely be recommended for post-operative pain relief, specially in the patient requiring extra-ordinary care during the post-operative period.

From the basic physiological and pharmacological considerations and in the light of a review of the literature, it was postulated that epidural anaesthesia need not be accompanied by any derangement of gas exchange. The present study, undertaken to establish or disprove that postulate, was carried out on a group of patients considered to be a reasonable representation of hospital surgical material.

From our findings, it is evident that only insignificant changes in $A\text{-}aD_{O_2}$ and FRC and VC will occur. However, it is important to re-stress some points. The patients must be adequately hydrated and cardiac output must be adequate.

That is, blood loss during surgery must be corrected, and any residual effects of agents or drugs used during surgery must be taken into account. The local anaesthetic used should be a relatively dilute solution, such as 1.5% lidocaine (with or without epinephrine). The dosage of the local anaesthetic agent must be incremental to achieve a satisfactory analgesic level, up to the fourth thoracic segment, if necessary. These two last considerations are important to minimize muscular effects and to avoid affecting the cardiac sympathetic nerves.

In conclusion, it can be stated that an epidural anaesthetic given for pain relief following upper abdominal surgery has been shown to be quite safe in terms of gas exchange. But care regarding hydration of the patient and in the choice of the concentration and dosage of the anaesthetic agent must be very strict.

# GLOSSARY OF ABBREVIATIONS

# AND

# BIBLIOGRAPHY

## GLOSSARY OF ABBREVIATIONS USED

The abbreviations adopted are based on those currently accepted in respiratory physiology as recommended by Pappenheimer et al: Standardization of definitions and symbols in respiratory physiology. Federation Proceedings 9: 602, 1950.

| | | |
|---|---|---|
| General | V | Gas Volume in general |
| | $\dot{V}$ | Gas volume per unit time |
| | P | Gas pressure in general |
| | $\dot{Q}$ | Volume flow of blood |
| | C | Concentration or content in blood phase |
| | F | Fractional concentration in dry gas phase |
| | f | Respiratory frequence; breaths/unit time |
| | R | Respiratory exchange ratio; $\dot{V}_{CO_2}/\dot{V}_{O_2}$ |
| Gas Phase | I | Inspired gas |
| | E | Expired gas. $\bar{E}$ = Mixed expired |
| | A | Alveolar |
| | T | Tidal |
| | D | Dead space |
| | B | Barometric |
| Blood Phase | a | Arterial |
| | v | Venous $\bar{v}$ = mixed venous |
| | c | Capillary $\bar{c}$ = End capillary |

| | | |
|---|---|---|
| Lung Volumes | TLC | Total lung capacity |
| | VC | Vital capacity |
| | IC | Inspiratory capacity |
| | FRC | Functional residual capacity |
| | ERV | Expiratory reserve volume |
| | RV | Residual volume |
| | $FEV_{1.0}$ | Forced expiratory volume (1.0 sec) |
| Miscellaneous | BTPS | Body temperature, pressure, saturated with water vapor. |
| | STPD | Standard temperature, pressure dry. (0 C., 760 Torr) |
| | ATPS | Ambient temperature, pressure, saturated with water vapor. |
| | $A\text{-}aD_{O_2}$ | Alveolar-arterial oxygen gradient |
| | S | Saturation, percent |
| | CO or $Q_C$ | Cardiac output |
| | $\%Q_S/Q_t$ | Percent shunt |
| | $\dot{V}_A/Q$ | Ventilation Perfusion Ratio |

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