In general the current view, and the practice, of
the concept of balanced anaesthesia consider only
the i.v. and the inhalation agents. It is certainly
just as reasonable to consider regional anaesthesia
as one of the components (Thomson, 1980; Scott,
1983).

The combination of regional anaesthesia (iliac
crest and rectus sheath block) with light general
anaesthesia offers certain advantages in anaes-
thesia for laparoscopic investigations in gynaecol-
ogical surgery. The author’s (R.S.N.) personal
experience extends to more than 300 patients.
The regional nerve block produces anaesthesia of
the abdominal wall and underlying peritoneum,
light general anaesthesia prevents the response
from stimulation of the visceral peritoneum (Lee
and Atkinson, 1982; Scott, 1983). The combined
technique retains spontaneous ventilation and
maintains a firm abdominal wall, giving a more
definite end-point to the insertion of the trochar
(Seed, Shakespeare and Muldoon, 1970; Collins,
Docherty and Plantevin, 1984), and decreases the
volume of gas required to create the pneumo-
peritoneum.

Competitive myoneural blockade in a dose
sufficient to permit tracheal intubation may be
complicated by delayed antagonism, if the pro-
cedure is less than 20 min duration (Pearce,
Williams and Jones, 1984) or associated with an
unacceptably high percentage of difficulty in
intubation if the dose is reduced (Collins, D Hoch-
erty and Plantevin, 1984; Pearce, Williams and
Jones, 1984; Sosis, 1986).

**SUMMARY**

Following local anaesthesia of the lower abdomi-
nal wall, in patients undergoing laparoscopic
sterilization (n = 16), using 0.5% plain bupiv-
acaine 40 ml (n = 8), or 0.5% bupivacaine
with 1:200000 adrenaline (n = 8), venous
plasma (total) bupivacaine concentrations were
measured (gas-liquid chromatography) at inter-
vals up to 2 h after the local anaesthetic was
injected. Mean peak plasma venous concen-
tration achieved following 0.5% plain bupiv-
acaine was 2.23 ± 0.24 µg ml⁻¹ (mean ± SEM),
while the mean peak concentration following
0.5% bupivacaine with adrenaline was 0.98 ±
0.10 µg ml⁻¹ (mean ± SEM). At all sampling
times up to and including 45 min after the
injection of local anaesthetic, the plasma con-
centrations were significantly less in the bupiv-
acaine with adrenaline group when compared
with the group in whom a plain solution was
used.

Insufflation of carbon dioxide to the peritoneal
cavity leads to an increase in PaCO₂, with either
spontaneous or controlled ventilation, with the
possibility of exceeding the arrhythmia threshold
(Hodson, McClelland and Newton, 1970; Seed,
Shakespeare and Muldoon, 1970).

The combination of regional anaesthesia with
light general anaesthesia reduces the concentra-
tion of volatile agent to the absolute minimum
(Scott, 1983), thus decreasing the likelihood of
cardiac arrhythmia in the presence of an increased
PaCO₂. If nitrous oxide is used as the insufflating
gas a much lower incidence of arrhythmias has
been reported (Scott et al., 1972): 4% as com-
pared with 17% with carbon dioxide. Patients in
both groups breathed spontaneously.
Regional anaesthesia is a recommended technique for repair of inguinal hernia in outpatients. Large volumes of local anaesthetic agents have been prescribed and used (Glasgow, 1976; Lee and Atkinson, 1982). Bupivacaine has been recommended in combination with dextran and adrenaline (Simpson, Hughes and Long, 1982); the extended duration of action ensures a more comfortable postoperative period. Plasma concentrations of lignocaine have been measured following its use for anaesthesia of the abdominal wall (Scott and Cousins, 1980); a similar study of the plasma profile of bupivacaine has not been performed.

Scott (1984) highlighted the need for careful investigation of the use of local anaesthetic agents in various clinical situations and for accurate reporting and analysis of any toxic reaction.

This study was undertaken to measure the circulating concentration of bupivacaine following regional nerve block of the lower abdomen, and to determine the effects of using adrenaline on subsequent systemic absorption.

PATIENTS AND METHODS
Sixteen women (ASA I) aged 25-35 yr, undergoing laparoscopic sterilization were informed of the nature of the study, and consent was obtained for venous blood sampling.

All patients were anaesthetized in a standard manner, the only deviation from normal practice being that the trachea was intubated in all patients. This was performed to minimize the possibility of an increase in $P_{\text{aco}}_2$, resulting from any element of airway obstruction.

Premedication was with temazepam 30 mg unless the patient was a day-case. Following a precurarizing dose of alcuronium 2.5 mg, anaesthesia was induced by the i.v. administration of thiopentone via an indwelling cannula in the dorsum of the hand, and tracheal intubation was facilitated with suxamethonium. Anaesthesia was maintained with nitrous oxide and halothane in 33% oxygen using a Bain anaesthetic system; spontaneous ventilation was permitted for the duration of the procedure (average 20 min).

The patients were allocated to one of two groups and local anaesthesia was performed using either 0.5% plain bupivacaine ($n = 8$) or 0.5% bupivacaine with adrenaline 1 in 200000 ($n = 8$). Bilateral ilioinguinal, iliohypogastric and modified iliac crest blocks were performed: with the patient lying supine, a 20-gauge, 76-mm short bevelled needle was introduced at 45° to the skin surface 1 cm medial to the anterior superior iliac spine, aimed in an infero-medial direction, parallel with the inguinal ligament. The aponeurosis of the external oblique muscle was appreciated, and on advancing the needle, a distinct "click" felt as the needle entered the plane between the external and internal oblique muscles. The needle was then moved more horizontally and advanced between the tissue layers. Ten millilitre of local anaesthetic solution deposited in this plane anaesthetized both the ilioinguinal and iliohypogastric nerves (fig. 1). Before withdrawal of the needle, it was re-directed to lie subcutaneously, cephalad from the point of skin entry and a further 5 ml of anaesthetic agent injected while the needle was withdrawn; this achieved blockade of the cutaneous branches of the lateral divisions of the 11 and 12 spinal nerves. The region of the rectus muscle was blocked by depositing local anaesthetic in the plane between the posterior surface of the recti and the posterior rectus sheaths (fig. 2), bilaterally, two to three finger-breadths below the umbilicus. A total of 40 ml of local anaesthetic was used (200 mg).

Samples of venous blood were obtained from an indwelling cannula in the contralateral arm. Following a baseline sample of 10 ml of venous blood, 10-ml heparinized samples were taken at 5, 10, 15, 20, 30, 45, 60, 90 and 120 min after the block was completed, continuing for 90 min into the postoperative period. The samples were centrifuged and the plasma frozen until analysed for bupivacaine using gas-liquid chromatography. An adaptation of the method of Zylber-Katz, Granit and Levy (1978) was used; this had been described fully elsewhere (Neill and Watson, 1984).

Statistical analysis of the results was performed using Student's $t$-test.

RESULTS
Anaesthesia was uneventful in all patients, and no evidence of a toxic reaction to the local anaesthetic was observed. After recovery from anaesthesia, all the patients had a sensory loss to pinprick over the lower abdominal wall and of the upper thigh. Some patients, however, complained of abdominal cramp, and some of shoulder tip pain; these can be attributed to tubal spasm (tubal clips were used) and peritoneal irritation, respectively.
BUPIVACAINE CONCENTRATIONS: LOWER ABDOMINAL BLOCK

The results of plasma analysis are demonstrated in table II. The mean peak plasma bupivacaine concentration using the plain solution was 2.23 μg ml⁻¹ ± 0.24 (mean ± SEM); that for the solution with adrenaline was 0.98 mg ml⁻¹ ± 0.10 (mean ± SEM). The difference is statistically significant (P < 0.001).

Plasma concentrations following the injection of plain bupivacaine were significantly greater at all sampling times from 5 to 45 min inclusive. Peak concentration also was reached in a shorter time with a plain solution (fig. 3).

DISCUSSION

The study demonstrates that, for anaesthesia of the lower abdominal wall, 0.5 % bupivacaine 40 ml (3 mg kg⁻¹ in this series) neither resulted in clinical evidence of toxicity, nor achieved serum concentrations equal to those considered to cause

<table>
<thead>
<tr>
<th>Group</th>
<th>Weight (kg)</th>
<th>Age (yr)</th>
<th>Dose of bupivacaine (mg kg⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plain bupivacaine (n = 8)</td>
<td>64 ± 6.2</td>
<td>28 ± 3</td>
<td>3.38 ± 0.127</td>
</tr>
<tr>
<td>Bupivacaine with adrenaline (n = 8)</td>
<td>60 ± 2.2</td>
<td>30 ± 4</td>
<td>3.29 ± 0.22</td>
</tr>
</tbody>
</table>
The potential toxicity of local anaesthetic drugs lies not only in the inherent toxicity of the drugs themselves, but also in the many aspects of their clinical use which determine the circulating concentration of the local anaesthetic, for example, the site of injection (Scott, et al., 1972; Neill and Watson, 1984), rate of injection (Scott, 1975), concentration of drug used, and the use of vasoconstrictors to reduce systemic absorption (Scott et al., 1972; Scott and Cousins, 1980).

It has been argued that one of the most important factors contributing to the toxicity of local anaesthetic agents is the vascularity of the area to which they are injected (Sheen and Michenfelder, 1979; Neill and Watson, 1984). The tissue planes to which bupivacaine was injected in this study are not highly vascular; furthermore, direct intravascular injection—another reason for toxicity—is unlikely, as the inferior epigastric vessels are the only vessels of significant size in the area to which the injections are made.

No patient in the study exhibited any sign of cardiovascular or neurological toxicity. Measurements and observations were made during the surgical procedure and continued into the postoperative recovery period. All patients were awake and co-operated fully during the testing of cutaneous anaesthesia which concluded the study.

It is possible that general anaesthesia could have masked signs of minor toxicity during the surgical procedure and the early recovery phase, but the effect must have been minimal or absent in the later period of the study at a time when the plasma concentrations were still at a plateau concentration (fig. 3).

Jorfeldt and colleagues (1968) infused bupivacaine i.v. to mean arterial plasma concentration of 2 μg ml⁻¹ with no neurological or cardiovascular side effects, the subjects spontaneously remarking that they experienced fewer symptoms than following lignocaine or mepivacaine. Following extrapolation from the plasma concentrations which produced convulsions in dogs they suggested that, in man, the "danger level" was 4 μg ml⁻¹—a figure supported by blood concentrations in patients during convulsions (Moore, Balfour and Fitzgibbons, 1979).

Reynolds (1971) infused bupivacaine i.v. and
BUPIVACAINE CONCENTRATIONS: LOWER ABDOMINAL BLOCK

Fig. 4. Venous bupivacaine (total) concentrations up to 2 h after injections. × = Plain bupivacaine 200 mg. ○ = bupivacaine with adrenaline 1:200000 200 mg; —— = mean. Dashed line represents lower limit of concentration range at which toxic effects might be anticipated.

described toxic symptoms of a minor nature at an arterial concentration of 1.5–2.0 µg ml⁻¹. Depending on various factors, such as speed of infusion and site of injection, arterial concentrations may be 10–20% greater than venous concentration (Moore et al., 1976).

A recent review (Reynolds, 1987) contained a compilation of data from various sources which indicated that mild toxicity may occur at plasma concentrations of 1.6–2 µg ml⁻¹, with risk of serious toxicity at 2.3–5 µg ml⁻¹.

In this study the mean venous, measured plasma concentration never exceeded 2 µg ml⁻¹ (2.5 µg ml⁻¹ arterial, derived using a correction factor of 25%). In the steady state achieved during the later part of the study, this correction factor is possibly excessive. The scattergram (fig. 4) demonstrates that 11 individual measurements, all in the plain bupivacaine group, lie within the 2.3–5.0 µg ml⁻¹ band in which major toxic effects might be anticipated. No measurement in the bupivacaine-adrenaline group exceeded 1.5 µg ml⁻¹ (venous).

Adrenaline is known to decrease peak plasma concentration after all common nerve blocks (Wildsmith et al., 1977), but does not always prolong time to peak concentration (Tucker, 1986). This study confirms the finding of decreased peak plasma concentration, but also demonstrates a delay in reaching peak concentration.

Tucker (1986), using 2 µg ml⁻¹ as a conservative estimate of safe plasma bupivacaine concentration together with data on peak concentration after various blocks, has calculated that accurate injection of much greater doses than 2 µg kg⁻¹ should not exceed the toxic threshold. The results of this study support this calculation, in that the mean dose administered (3.3 mg kg⁻¹) did not result in mean venous plasma concentrations of more than 2 µg kg⁻¹, nor did any patient exhibit signs of toxicity.

Toxicity is related to the concentration of the drug which is free and active in the plasma. Bupivacaine has been shown to be highly protein bound: 90% at concentrations up to 5 µg ml⁻¹ in in vivo experiments (Tucker and Mather, 1975). The part played by protein binding in the in vivo situation has not been studied in detail, and more information is required on the free concentrations of bupivacaine occurring after nerve blocks. It would, however, seem prudent to use adrenaline-containing solutions when large volumes of drugs are required to complete a specific nerve block, in order to reduce the peak plasma concentration and minimize the risk of toxicity.
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