
Marc Van de Velde
Anesthesiology
UZLeuven - KULeuven
Content

- Adaptation to pregnancy:
  - Body weight.
  - Respiration.
  - Circulation.
  - Hematology.
  - Gastrointestinal system.
  - Nervous system.
  - Other.

- Analgesia for normal labor and delivery.

- Anesthesia for Cesarean section in normal pregnant patients.

- Anesthetic implications.
Weight gain throughout pregnancy.

**Table 1.5. DISTRIBUTION OF WEIGHT GAIN DURING PREGNANCY**

<table>
<thead>
<tr>
<th>Tissue Fluid</th>
<th>Increase in Weight in Grams (and Pounds) up to:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>10 wk</td>
</tr>
<tr>
<td>Fetus</td>
<td>5 (0.01)</td>
</tr>
<tr>
<td>Placenta</td>
<td>20 (0.04)</td>
</tr>
<tr>
<td>Amniotic fluid</td>
<td>30 (0.07)</td>
</tr>
<tr>
<td>Uterus</td>
<td>140 (0.3)</td>
</tr>
<tr>
<td>Breasts</td>
<td>45 (0.1)</td>
</tr>
<tr>
<td>Blood</td>
<td>100 (0.2)</td>
</tr>
<tr>
<td>Extracellular extravascular fluid (no edema present)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Subtotal</td>
<td>340 (0.7)</td>
</tr>
<tr>
<td>Maternal reserves</td>
<td>310 (0.7)</td>
</tr>
<tr>
<td>Total weight gain</td>
<td>650 (1.4)</td>
</tr>
</tbody>
</table>

Respiratory physiology.

- Oxygen consumption: + 60%.
- Increased thoracic cage circumference.
- Elevated position of the diaphragm.
- Capillary engorgement nasopharynx and larynx.
- Airway dilation due to progesterone and relaxin.

Table 2-2  Changes in respiratory physiology at term gestation

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Change*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung volumes</td>
<td></td>
</tr>
<tr>
<td>Inspiratory reserve volume</td>
<td>+5%</td>
</tr>
<tr>
<td>Tidal volume</td>
<td>+45%</td>
</tr>
<tr>
<td>Expiratory reserve volume</td>
<td>−25%</td>
</tr>
<tr>
<td>Residual volume</td>
<td>−15%</td>
</tr>
<tr>
<td>Lung capacities</td>
<td></td>
</tr>
<tr>
<td>Inspiratory capacity</td>
<td>+15%</td>
</tr>
<tr>
<td>Functional residual capacity</td>
<td>−20%</td>
</tr>
<tr>
<td>Vital capacity</td>
<td>No change</td>
</tr>
<tr>
<td>Total lung capacity</td>
<td>−5%</td>
</tr>
<tr>
<td>Dead space</td>
<td>+45%</td>
</tr>
<tr>
<td>Respiratory rate</td>
<td>No change</td>
</tr>
<tr>
<td>Ventilation</td>
<td></td>
</tr>
<tr>
<td>Minute ventilation</td>
<td>+45%</td>
</tr>
<tr>
<td>Alveolar ventilation</td>
<td>+45%</td>
</tr>
</tbody>
</table>

# Blood Gas Values

| Table 2-3  Blood gases during pregnancy |
|-----------------|-----------------|-----------------|-----------------|-----------------|
|                 | Nonpregnant     | First           | Second          | Third           |
| Paco₂ (mm Hg)   | 40              | 30              | 30              | 30              |
| Pao₂ (mm Hg)    | 100             | 107             | 105             | 103             |
| pH              | 7.40            | 7.44            | 7.44            | 7.44            |
| [HCO₃⁻] (mEq/L)| 24              | 21              | 20              | 20              |
Respiratory physiology during labor.

- Minute ventilation: +100 – 300 %
- \( \text{PaCO}_2 \): 10 – 20 mmHg
- Oxygen consumption: + 75 %
- Epidural analgesia blunts these changes
Central Hemodynamics.

- Accentuation of the first heart sound
- Mild tricuspid regurgitation
- ECG-changes:
  - P-R interval shorter
  - Q-T interval shorter
  - Depressed S-T segments in the left-sided pre-cordial leads
- Left ventricular hypertrophy
- Mild pericardial effusion

### Table 2-4  Central hemodynamics at term gestation

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Change*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac output</td>
<td>+50%</td>
</tr>
<tr>
<td>Stroke volume</td>
<td>+25%</td>
</tr>
<tr>
<td>Heart rate</td>
<td>+25%</td>
</tr>
<tr>
<td>Left ventricular end diastolic volume</td>
<td>Increased</td>
</tr>
<tr>
<td>Left ventricular end systolic volume</td>
<td>No change</td>
</tr>
<tr>
<td>Ejection fraction</td>
<td>Increased</td>
</tr>
<tr>
<td>Left ventricular stroke work index</td>
<td>No change</td>
</tr>
<tr>
<td>Pulmonary capillary wedge pressure</td>
<td>No change</td>
</tr>
<tr>
<td>Pulmonary artery diastolic pressure</td>
<td>No change</td>
</tr>
<tr>
<td>Central venous pressure</td>
<td>No change</td>
</tr>
<tr>
<td>Systemic vascular resistance</td>
<td>−20%</td>
</tr>
</tbody>
</table>

*Relative to nonpregnant women.

Aortocaval compression.
Cardiac output during labor and delivery.

- Elevation sympathetic nervous system activity.
- Autotransfusion during contractions from intervillous space.
- Epidural analgesia blunts these changes.
Hematology.

- 1% platelet count < 100000/mm³
- Increased platelet aggregation
- Relative hypercoagulability
- Leucocytosis, especially during labor
  - 10000 – 15000/mm³
- Plasmacholinesterase concentration decreased with 25%

---

Table 1.7. COAGULATION FACTORS AND INHIBITORS DURING NORMAL PREGNANCY

<table>
<thead>
<tr>
<th>Factor</th>
<th>Nonpregnant</th>
<th>Late Pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor I (fibrinogen)</td>
<td>200–450 mg/dL</td>
<td>400–650 mg/dL</td>
</tr>
<tr>
<td>Factor II (prothrombin)</td>
<td>75–125%</td>
<td>100–125%</td>
</tr>
<tr>
<td>Factor V</td>
<td>75–125%</td>
<td>100–150%</td>
</tr>
<tr>
<td>Factor VII</td>
<td>75–125%</td>
<td>100–250%</td>
</tr>
<tr>
<td>Factor VIII</td>
<td>75–150%</td>
<td>200–500%</td>
</tr>
<tr>
<td>Factor IX</td>
<td>75–125%</td>
<td>100–150%</td>
</tr>
<tr>
<td>Factor X</td>
<td>75–125%</td>
<td>150–250%</td>
</tr>
<tr>
<td>Factor XI</td>
<td>75–125%</td>
<td>50–100%</td>
</tr>
<tr>
<td>Factor XII</td>
<td>75–125%</td>
<td>100–200%</td>
</tr>
<tr>
<td>Factor XIII</td>
<td>75–125%</td>
<td>35–75%</td>
</tr>
<tr>
<td>Antithrombin III</td>
<td>85–110%</td>
<td>75–100%</td>
</tr>
<tr>
<td>Antifactor Xa</td>
<td>85–110%</td>
<td>75–100%</td>
</tr>
<tr>
<td>Platelet count</td>
<td>↔ or ↓</td>
<td>↓</td>
</tr>
<tr>
<td>PT</td>
<td>↓ 20%</td>
<td>↓</td>
</tr>
<tr>
<td>PTT</td>
<td>↓ 20%</td>
<td>↓</td>
</tr>
<tr>
<td>Fibrin split products</td>
<td>↑</td>
<td></td>
</tr>
</tbody>
</table>

Colloid oncotic pressure.

- 14 – 20 % decrease
- Further decrease after delivery
- Increased risk of pulmonary edema
# Gastrointestinal system.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Trimester</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>First</td>
<td>Second</td>
<td>Third</td>
<td>Labor</td>
<td>Postpartum (18 hr)</td>
</tr>
<tr>
<td>Barrier pressure†</td>
<td>Decreased</td>
<td>Decreased</td>
<td>Decreased</td>
<td>Decreased</td>
<td>?</td>
</tr>
<tr>
<td>Gastric emptying</td>
<td>No change</td>
<td>No change</td>
<td>No change</td>
<td>Decreased</td>
<td>No change</td>
</tr>
<tr>
<td>Gastric acid secretion</td>
<td>Decreased</td>
<td>Decreased</td>
<td>No change</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Proportion of women with gastric volume &gt; 25 mL</td>
<td>No change</td>
<td>No change</td>
<td>No change</td>
<td>Increased</td>
<td>No change</td>
</tr>
<tr>
<td>Proportion of women with gastric pH &lt; 2.5</td>
<td>No change</td>
<td>No change</td>
<td>No change</td>
<td>Decreased</td>
<td>No change</td>
</tr>
</tbody>
</table>

*Relative to nonpregnant women.
†Difference between intragastric pressure and tone of the lower esophageal high pressure zone.
Nervous system.

- Pregnancy induced analgesia
  - Endorphins, enkephalins increase in plasma, brain and CSF

- Sympathetic nervous system: sympathetic nervous system becomes more important
Lumbar lordosis.

Fig. 2-6. Changes in posture during pregnancy. The first figure and the subsequent dotted-line figures represent a woman's posture before growth of the uterus and its contents have affected the center of gravity. As the uterus enlarges and the abdomen protrudes, the lumbar lordosis is enhanced and the shoulders slump and move posteriorly. (From Beck AC, Rosenthal AH. Obstetrical Practice. Baltimore, Williams and Wilkins, 1955:146)

Fig. 2-9. Effects of pregnancy on the lumbar spine. A, Non-pregnant; B, pregnant. There is a marked increase in lumbar lordosis and a narrowing of the interspinous space during pregnancy. (From Bonica JJ. Principles and Practice of Obstetric Analgesia and Anesthesia, Volume 1. Philadelphia, FA Davis Company, 1967:35)
Musculoskeletal – nervous changes.

- Stretching nervus cutaneus femoris lateralis
- Brachial plexus neuropathy
- Carpal tunnel: relaxin
- Pelvic instability: relaxin
  - Low back pain
  - pelvic discomfort
Content

- Adaptation to pregnancy.

- Anesthetic implications:
  - Positioning
  - Endotracheal Intubation:
    - Difficult intubation
    - Aspiration prophylaxis
    - Maternal oxygenation
  - Anesthetic drugs
  - Regional anesthesia

- Analgesia for normal labor and delivery.

- Anesthesia for Cesarean section in normal pregnant patients.
Positioning: left lateral tilt.

- Always from second trimester
- Improved fetal heart rate
- Improved fetal pH
- Improved UA pH
- Improved Apgar scores
Endotracheal intubation.

- **1:280 failed intubation vs 1:2230 in non-pregnant**
  - Capillary engorgement
  - Weight increase
  - Breast volume
- **Rapid hypoxemia: 3 vs 7 minutes**
  - Increased oxygen consumption
  - Decreased FRC
  - **PaCO₂ at 30 mmHg**
  - **Higher minute volume**
Aspiration prophylaxis.

Figure 22.2. (A) Division of gastric pH and volume conditions into four quadrants indicating risk level. Patients in quadrant IV (pH < 2.5, and volume > 25 ml) should be at greatest risk for the development of acid pneumonitis after aspiration of gastric contents. (B) Gastric volume and pH in laboring parturients receiving only 0.3 M sodium citrate before emergency cesarean delivery. Fifteen received 15 ml of sodium citrate and 15 received 30 ml. (C) Gastric volume and pH at cesarean delivery in laboring parturients receiving ranitidine, 50 mg IM, every 6 hours during labor. (D) Gastric volume and pH at cesarean delivery in laboring parturients receiving ranitidine, 50 mg IM, every 6 hours during labor and every dose of 0.3 M sodium citrate, 15 ml, immediately before the induction of anesthesia. (Kolker RD, Frank M, Longman SA, Collier RG, Catanzariti A. Use of ranitidine for the prophylaxis of aspiration pneumonitis in obstetrics, Br J Anaesth 1988;61:720)
Aspiration prophylaxis.

- Metoclopramide: 10 mg IV 30’ voor inductie.
- Natriumcitraat 0.3 M 30 ml po 15’ voor inductie.
- Ranitidine:
  - Geplande sectio: 150 mg po avond voordien en po 2 uur voor de ingreep.
  - Dringende sectio: 50 mg IV zo snel mogelijk.
Anesthetics: inhalational agents.

- MAC reduced by 30%:
  - Progesterone effect
  - Increased serotonergic activity
  - Endorphins

- Rate of anesthetic induction increased:
  - Increased minute ventilation
  - Reduced FRC
Anesthetics: intravenous agents.

- Thiopental: 30% dose reduction, longer half-life
- Propofol: induction dose ????, pharmacokinetics unaffected
- Opioids: unaffected pharmacokinetics
Anesthetics: succinylcholine.

- Reduction plasma cholinesterase activity clinically irrelevant
- Faster recovery:
  - Increased volume of distribution
  - Less sensitive
Anesthetics: non-depolarizing.

- 50% reduction in $ED_{50}$
- Increased sensitivity

- Cisatracurium and atracurium unaffected pharmacokinetics ????????
Anesthetics: local anesthetics.

- Reduced epidural dose requirements: Large dose unaltered – low dose reduced
  - Enhanced neural sensitivity
  - Epidural vein distention
- Reduced spinal dose requirements:
  - pressure CSF
  - reduced CSF protein
  - elevated CSF pH
  - enhanced neural sensitivity
  - increased rostral spread
Anesthetics: local anesthetics.

- Cardiotoxicity: estrogen and progesterone increase the sensitivity of the myocardium to bupivacaine and not to lidocaine and ropivacaine.
Pain during childbirth.

Fig. 18-5. The visceral and somatic pain pathways associated with parturition. (*The paravertebral somatic block and the sacral nerve root blocks are not used in contemporary obstetric anesthesia practice, but they were important in identifying and defining the pain pathways.) (Modified from Bonica JJ. The Management of Pain, 2nd ed. Philadelphia, Lea & Febiger, 1990:1336)
Adrenergic response.
Adrenergic response.

The graph shows the uterine activity (%) of control in response to different concentrations of catecholamines. The x-axis represents the log of [catecholamine] (M), and the y-axis represents uterine activity (% of control). Three lines are depicted:

- Norepinephrine
- Epinephrine
- Norepi + Epi

As the concentration of catecholamines increases, the uterine activity varies accordingly, indicating the adrenergic response.
Effect of epidural analgesia.
Pain can result in.....

- Increased fetal heart rate
- Fetal hypoxia
- Reduced progress of labor
- Maternal cardiovascular and respiratory distress
Content

- Adaptation to pregnancy.
- Anesthetic implications.

- Analgesia for normal labor and delivery.
  - Low dose epidural analgesia
  - Addition of opioids
  - PCEA vs continuous infusion vs intermittent top-ups
  - CSE
  - New local anesthetics
  - Other adjuvant drugs

- Anesthesia for Cesarean section in normal pregnant patients.
Epidural Analgesia: low doses of local anesthetics.

- Lidocaine 2%.
- Bupivacaine 0.25 - 0.5 – 0.75%.
- Intermittent top-ups.

- Bupivacaine 0.125 % in obstetric epidural analgesia.
Addition of Opioids.

Extradural bupivacaine with sufentanil for vaginal delivery.

The effects of the addition of sufentanil to 0.125% bupivacaine on the quality of analgesia during labor and on the incidence of instrumental deliveries.
Addition of opioids.

Fig. 1. The median effective local analgesic concentration of bupivacaine, and with addition of sufentanil 0.5, 1, and 1.5 μg/ml as determined by the technique of up-down sequential allocation. The minimum local analgesic concentrations are 0.104, 0.048, 0.021, and 0.009% wt/vol, respectively. Error bars represent the 95% confidence interval. The testing interval was 0.01% wt/vol.
Addition of Opioids.

- Decreased total and hourly consumption of local anesthetics.
- Decreased motor block.
- Decreased shivering.
- Less instrumental deliveries.
- Increased patient satisfaction.

- Increased incidence of pruritus.
PCEA vs CEI vs top-ups: Quality of pain relief

Less anesthetist interventions.

Fig. 2. Pain scores (mean ± S.D.) obtained throughout the study as measured by visual analog scale (mm).

Local anesthetic requirements.

- Gambling et al.  
  *Can J Anaesth* 1988; 35, 249  -26%
- Ferrante et al.  
  *Anesth Analg* 1991; 73, 547  -55%
- Purdie et al.  
  *Br J Anaesth* 1992; 68, 580  -24%
- Gambling et al.  
  *Can J Anaesth* 1993; 40, 211  -44%
- Ferrante et al.  
  *Anesth Analg* 1994; 79, 80  -48%
- Sia et al.  
  *Anaesth Intens Care* 1999; 27, 154  -15%
- Boutros et al.  
  *IJOA* 1999; 8, 236  -12%

Less Motor Block
Incidence of spontaneous delivery.

<table>
<thead>
<tr>
<th>Study</th>
<th>Journal</th>
<th>CIE vs PCEA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eddlestone et al.</td>
<td>Br J Anaesth 1992; 69, 154:</td>
<td>47% vs 60%</td>
</tr>
<tr>
<td>Gambling et al.</td>
<td>Can J Anaesth 1993; 40, 211:</td>
<td>21% vs 51%</td>
</tr>
<tr>
<td>Ferrante et al.</td>
<td>Anesth Analg 1994; 79, 80:</td>
<td>60% vs 87%</td>
</tr>
<tr>
<td>Curry et al.</td>
<td>Pain 1994; 57, 125:</td>
<td>47% vs 57%</td>
</tr>
</tbody>
</table>

Less outlet forceps deliveries
Meta-analysis on PCEA in labour.

- Less anesthetic interventions: RD of 27%.
- Less motor block: RD of 18%.

CSE: Why bother to use CSE?

Problems with epidurals........

- Slow onset, especially in late labor.
- Failure: patchy, unilateral block,.....: 1-10%.
- Motor block, effects on labor outcome.
- Late labor: ineffective.
- Local anesthetics required.
- Sometimes high doses required to produce analgesia.
Shorter onset time.


Quality of Analgesia.

Reliability epidural catheters.

<table>
<thead>
<tr>
<th></th>
<th>EA</th>
<th>CSE</th>
<th>CSE 27G</th>
<th>CSE 29G</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=661</td>
<td>N=2075</td>
<td>N=349</td>
<td>N=1726</td>
</tr>
<tr>
<td>Failed spinal</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>56 (2.70%)</td>
<td>9 (2.58%)</td>
<td>47 (2.72%)</td>
<td></td>
</tr>
<tr>
<td>Failed epidural</td>
<td>21 (3.18%)</td>
<td>31 (1.49%)</td>
<td>6 (1.72%)</td>
<td>25 (1.44%)</td>
</tr>
</tbody>
</table>

EA: data on patients treated with epidural techniques; CSE: data on patients treated with combined spinal-epidural techniques; CSE 27 gauge: data on patients treated with CSE using a 27 gauge spinal needle; CSE 29 gauge: data on patients treated with CSE using a 27 gauge spinal needle. Values are number (% of subgroup). *P<0.05 versus EA.
Analgesic requirements.

Table 2
Characteristics of analgesia following combined spinal epidural analgesia (CSE, n = 55) or epidural analgesia (EPI, n = 55) for women in labor

<table>
<thead>
<tr>
<th></th>
<th>CSE</th>
<th>EPI</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>VAS-score</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VAS-score Baseline</td>
<td>73 ± 2</td>
<td>70 ± 1</td>
<td>NS</td>
</tr>
<tr>
<td>VAS-score at satisfactory analgesia</td>
<td>14 ± 2</td>
<td>18 ± 2</td>
<td>NS</td>
</tr>
<tr>
<td>Lowest VAS-score</td>
<td>0.4 ± 0.1</td>
<td>4 ± 1</td>
<td>p &lt; 0.05</td>
</tr>
<tr>
<td><strong>Time to satisfactory analgesia</strong> (sec)</td>
<td>326 ± 22</td>
<td>766 ± 79</td>
<td>p &lt; 0.01</td>
</tr>
<tr>
<td><strong>Analgesic requirements</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bupivacaine (mg)</td>
<td>23.5 ± 2.3</td>
<td>33.9 ± 2.9</td>
<td>p &lt; 0.05</td>
</tr>
<tr>
<td>Sufentanil (μg)</td>
<td>12.5 ± 1.0</td>
<td>16.5 ± 1.7</td>
<td>p &lt; 0.05</td>
</tr>
<tr>
<td><strong>Satisfaction (scale 1-4)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poor (1 &amp; 2)</td>
<td>2</td>
<td>7</td>
<td>NS</td>
</tr>
<tr>
<td>Good (3 &amp; 4)</td>
<td>53</td>
<td>48</td>
<td>NS</td>
</tr>
</tbody>
</table>

Satisfactory analgesia: VAS-score reduction > 50%, or VAS-score < 25 mm.
Data are presented as a mean ± SEM.

CSE and side-effects.

- **Less motor block.**
Labor progress.

Labor outcome no different from low dose epidural techniques.

Fig. 1. The initial cervical dilation rate for each patient are shown. Lines connect the most recent cervical examination before and the first cervical examination after analgesia. The heavy plot symbol and lines indicate the mean and SD for each group. The slopes of the mean lines equal the mean initial cervical dilation rates (see the text and table 1 for details).

Tsen et al Anesthesiology 1999; 91, 920 - 925.
Pruritus.

- 50 – 100 % incidence with IT opioids.

- Incidence also 25 – 70 % with epidural opioids.
Infection

- Several case reports.
- Always “un-sterile” technique.
- New technique: gets lots of attention.
- Our own experience:
  - no infection in >6000 CSE-treated patients for labor.
  - 1 infection of a subcutaneous collection several weeks after the CSE in >1200 CSE-treated patients for cesarean section.
# Post dural puncture headache.

<table>
<thead>
<tr>
<th></th>
<th>Total N=2736</th>
<th>EA N=661</th>
<th>CSE N=2075</th>
<th>CSE 27G N=349</th>
<th>CSE 29G N=1726</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>144 (5.26%)</td>
<td>29 (4.39%)</td>
<td>115 (5.54%)</td>
<td>30 (8.60%)</td>
<td>85 (4.93%)</td>
</tr>
<tr>
<td>Dural tap</td>
<td>18 (0.65%)</td>
<td>5 (0.75%)</td>
<td>13 (0.62%)</td>
<td>2 (0.57%)</td>
<td>11 (0.52%)</td>
</tr>
<tr>
<td>PDPH</td>
<td>12 (0.44%)</td>
<td>3 (0.45%)</td>
<td>9 (0.43%)</td>
<td>1 (0.29%)</td>
<td>8 (0.48%)</td>
</tr>
<tr>
<td>Intravenous catheter</td>
<td>91 (3.33%)</td>
<td>20 (3.01%)</td>
<td>71 (3.42%)</td>
<td>13 (3.72%)</td>
<td>58 (3.36%)</td>
</tr>
</tbody>
</table>

Total: data on all patients; EA: data on patients treated with epidural techniques; CSE: data on patients treated with combined spinal-epidural techniques; CSE 27 gauge: data on patients treated with CSE using a 27 gauge spinal needle; CSE 29 gauge: data on patients treated with CSE using a 27 gauge spinal needle; Cath: catheter; PDPH: post-dural puncture headache. Values are number (% of subgroup). There were no statistically significant differences between the groups.

*Anaesthesia and Intensive Care, Vol. 29, No. 6, December 2001*
Respiratory depression.

- 5 case reports of severe respiratory depression.

- Characteristics:
  - Sufentanil 10 µg or more.
  - Previous IV opioids in 3/5 patients.
  - Small patients < 155 cm.
  - Somnolence as first sign.
  - Within the first 30 minutes.
  - Reversible with naloxone.

- 1 case of altered consciousness.
Fetal heart rate changes.

10 – 20 minutes after CSE initiation with opioids
Uterine hyperactivity
No hypotension

Fetal bradycardia
Late decelerations

Lasts for 5 – 15 minutes
Treatment is conservative
Neonatal outcome is good
FHR changes: prospective data.

FHR changes: prospective data.

Mechanism?

- Hypotension.
- Uterine hyperactivity due to rapid analgesia.
- Uterine hyperactivity due to direct effect on oxytocin release.
- Direct effect on the fetus.
Which intrathecal drugs?

- Fentanyl or sufentanil.
- Local anesthetics combined with opioids.
- Addition of clonidine ?
- Addition of neostigmine ?????
Gasthuisberg protocol.

- Ropivacaine 3.5 mg + sufentanil 1.5 µg in 2 ml saline.
- PCEA ropivacaine 0.175 % + sufentanil 0.75 µg/ml: 0 – 4 ml continuous and bolus 4 ml/lock-out 15 minutes.
Why combining drugs?

- Additive effects.
- Synergistic effects.

Adjuvant drugs.

- Opioids:
  - Fentanyl.
  - Sufentanil.
- $\alpha_2$ - adrenergic agents:
  - Clonidine.
  - Epinephrine.
- Neostigmine.
- Adenosine.
- Magnesium.
Opioids
α₂-agonists

Primary Afferent Neuron

Dorsal Horn Neuron

Thalamus
Hypothalamus Cortex

PAG / PAV
PONS
Medulla Oblongata

Acetylcholine
Norepinephrine
Serotonin

Neostigmine

Stimulation

Pain transmission

Inhibition

Descending Inhibitory Tract

Curtosy to Erik Vandermeulen
Opioids added to epidural local anesthetic agents.

Polley et al. Anesthesiology 1998; 89, 626 - 632.

Fig. 1. The median effective local analgesic concentration of bupivacaine, and with addition of sufentanil 0.5, 1, and 1.5 μg/ml as determined by the technique of up-down sequential allocation. The minimum local analgesic concentrations are 0.104, 0.048, 0.021, and 0.009% wt/vol, respectively. Error bars represent the 95% confidence interval. The testing interval was 0.01% wt/vol.
Opioids and local anesthetics combined for intrathecal use.

<table>
<thead>
<tr>
<th></th>
<th>MLAD (95% CI, mg)</th>
<th>Duration of Analgesia (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bupivacaine plain</td>
<td>1.99 (1.71 – 2.27)</td>
<td>43.1</td>
</tr>
<tr>
<td>Bupivacaine + fentanyl 5 µg</td>
<td>0.69 (0.35 – 1.02)</td>
<td>56.1</td>
</tr>
<tr>
<td>Bupivacaine + fentanyl 15 µg</td>
<td>0.71 (0.00 – 1.53)</td>
<td>68.5</td>
</tr>
<tr>
<td>Bupivacaine + fentanyl 25 µg</td>
<td>0.85 (0.58 – 1.13)</td>
<td>77.2</td>
</tr>
</tbody>
</table>

Stocks et al. Anesthesiology 2001; 94, 593 – 598.
Epidural clonididine 75 µg.

Epidural clonidine 75 µg.

- No differences in hypotension.
- No increase in sedation.
- No differences in the incidence of FHR changes.
- Similar neonatal outcome.


- 15 – 50 µg clonidine added to a local anesthetic/sufentanil spinal mixture prolongs analgesia duration.
- Significant hypotension develops.

<table>
<thead>
<tr>
<th>Duration (min)</th>
<th>No clonidine</th>
<th>Clonidine</th>
</tr>
</thead>
<tbody>
<tr>
<td>D’Angelo</td>
<td>132 ± 39</td>
<td>197 ± 70</td>
</tr>
<tr>
<td>Sia</td>
<td>111 ± 22</td>
<td>144 ± 28</td>
</tr>
<tr>
<td>Paech</td>
<td>99 (91–134)</td>
<td>116 (102-142)</td>
</tr>
<tr>
<td>Van de Velde</td>
<td>90 ± 36</td>
<td>122 ± 56</td>
</tr>
</tbody>
</table>

Epinephrine: disadvantages.

- Motor block.
- Adverse effects on labour outcome:
  - Tocolysis: β-agonist actions.
- Adverse fetal and neonatal effects:
  - Direct effects on the uteroplacental perfusion.
- Storage problems - Price.
Spinal epinephrine - motor block.

<table>
<thead>
<tr>
<th>Motor block (%)</th>
<th>No epinephrine</th>
<th>epinephrine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Okutomi et al. 100 µg epinephrine</td>
<td>6</td>
<td>22</td>
</tr>
<tr>
<td>Vercauteren et al. 2.25 µg epinephrine</td>
<td>28.5</td>
<td>30.4</td>
</tr>
<tr>
<td>Campbell et al. 200 µg epinephrine</td>
<td>0</td>
<td>20</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Duration Analgesia (min)</th>
<th>No epinephrine</th>
<th>epinephrine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goodman et al. 100 µg epinephrine</td>
<td>125</td>
<td>134</td>
</tr>
<tr>
<td>Vercauteren et al. 2.25 µg epinephrine</td>
<td>79</td>
<td>94</td>
</tr>
<tr>
<td>Campbell et al. 200 µg epinephrine</td>
<td>145</td>
<td>188</td>
</tr>
</tbody>
</table>

Epidural neostigmine: 4 μg/kg.

Epidural neostigmine + clonidine.

- Clonidine 75 µg + neostigmine 500 – 750 µg.
- Effective analgesia > 90 minutes.
- No significant side-effects.

Roelants et al. Anesthesiology 2005; 102, 1205 - 1210.

<table>
<thead>
<tr>
<th>Owen</th>
<th>No neostigmine</th>
<th>Neostigmine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of Analgesia</td>
<td>123 ± 21</td>
<td>165 ± 32</td>
</tr>
<tr>
<td>Hypotension</td>
<td>27</td>
<td>7</td>
</tr>
<tr>
<td>Nausea</td>
<td>0</td>
<td>33</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>D’Angelo</th>
<th>No neostigmine</th>
<th>Neostigmine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of Analgesia</td>
<td>215 ± 60</td>
<td>205 ± 62</td>
</tr>
<tr>
<td>Hypotension</td>
<td>87</td>
<td>67</td>
</tr>
<tr>
<td>Nausea</td>
<td>7</td>
<td>53</td>
</tr>
</tbody>
</table>

The “ideal” local anaesthetic.

- Reversible loss of conduction and thereby loss of sensation in the innervated region.
- Acceptable difference between therapeutic and toxic doses.

Bupivacaine ?
My proposition......

- Bupivacaine should be replaced by ropivacaine or levobupivacaine as the local anaesthetic of choice for obstetric anaesthesia and analgesia.

- Why? Because
  - They have lower toxic potential and thus are “safer” drugs.
  - They have greater sensory – motor differentiation resulting in
    - Less motor block.
    - Increased patient satisfaction.
    - Improved labour outcome.
    - Improved neonatal outcome.
  - The benefits outweigh the increased costs.
Epidural ropivacaine versus bupivacaine for labor: number of patients with motor block using similar, low concentrations of local anaesthetic in both groups.

<table>
<thead>
<tr>
<th>Study</th>
<th>Bupivacaine</th>
<th>Ropivacaine</th>
<th>Number of study subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Campbell et al.</td>
<td>5</td>
<td>0 *</td>
<td>40</td>
</tr>
<tr>
<td>Meister et al.</td>
<td>18</td>
<td>8 *</td>
<td>50</td>
</tr>
<tr>
<td>Gautier et al.</td>
<td>15</td>
<td>3 *</td>
<td>90</td>
</tr>
<tr>
<td>Lee et al.</td>
<td>21</td>
<td>10</td>
<td>346</td>
</tr>
<tr>
<td>Owen et al.</td>
<td>12</td>
<td>8</td>
<td>50</td>
</tr>
<tr>
<td>Gogarten et al.</td>
<td>11</td>
<td>4</td>
<td>109</td>
</tr>
<tr>
<td>Chua et al.</td>
<td>5</td>
<td>3</td>
<td>32</td>
</tr>
<tr>
<td>Fischer et al.</td>
<td>19</td>
<td>10</td>
<td>189</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>106</strong></td>
<td><strong>46</strong></td>
<td><strong>906</strong></td>
</tr>
</tbody>
</table>

Number of patients with motor block. * P < 0.05 versus bupivacaine.
Epidural ropivacaine versus bupivacaine: Incidence of motor block using higher ropivacaine concentrations.

Gautier et al Anesthesiology 1999; 90, 772 - 778.
MLAC studies and potency of new local anaesthetics.

MLAC studies: criticism…..

- Choice of initial drug dose is critical.
- No information on the slope of the dose-response curve => so traditional dose response studies remain necessary.
- Difficult to control for confounders: stage of labour, parity, etc….
- What about maintenance of analgesia ?
- VAS score less then 10 mm is the end point, in most clinical studies it is 20 or 30 mm.
- It studies concentration and not dose.
Clinicians are interested in the ED95…..

- We want solutions and standard doses in routine clinical practice that apply for most of our patients.
- So, yes, in the real world we will overdose some patients…….
- But we should overdose with the drug that then gives least side effects.
Dose response relationship for racemic bupivacaine and levobupivacaine.

Racemic bupivacaine was found to be 1.388 times more potent than levobupivacaine at the ED50 and 1.487 times (1.06 – 1.91; 95% confidence intervals) more potent at the ED95 (p=0.0006).

Figure 1: predicted (lines) and observed (dots) dose response relationship of racemic bupivacaine and levobupivacaine in 300 labouring women.

Dreelinck et al. IJOA 2005; 14 (supplement), S4, O01.
Dose response relationship for ropivacaine and levobupivacaine.

The potency ratio between ropivacaine and levobupivacaine was found to be 1.035.

Figure 1: predicted (lines) and observed (dots) dose response relationship of racemic bupivacaine and levobupivacaine in 300 labouring women.

Epidurals cause dystocia.

Table II. Comparison of course of labor and delivery in patients in narcotic and epidural groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>Narcotic group (n = 45)</th>
<th>Epidural group (n = 48)</th>
</tr>
</thead>
<tbody>
<tr>
<td>First stage of labor (min)</td>
<td>519 ± 279</td>
<td>676 ± 394* (n = 41)†</td>
</tr>
<tr>
<td>Second stage of labor (min)</td>
<td>54 ± 45</td>
<td>115 ± 71* (n = 41)†</td>
</tr>
<tr>
<td>Oxytocin augmentation</td>
<td>12/45 (26.7%)</td>
<td>28/48 (58.3%)*</td>
</tr>
<tr>
<td>Oxytocin after first analgesic dose only</td>
<td>9/42 (21.4%)</td>
<td>19/39 (48.7%)*</td>
</tr>
<tr>
<td>Malposition</td>
<td>2/45 (4.4%)</td>
<td>9/48 (18.8%)*</td>
</tr>
<tr>
<td>Spontaneous vaginal delivery</td>
<td>39/45 (86.7%)</td>
<td>27/48 (56.2%)*</td>
</tr>
<tr>
<td>Low-forceps vaginal delivery</td>
<td>3/45 (6.7%)</td>
<td>4/48 (8.3%)</td>
</tr>
<tr>
<td>Vacuum-assisted vaginal delivery</td>
<td>2/45 (4.4%)</td>
<td>5/48 (10.4%)</td>
</tr>
<tr>
<td>Total cesarean delivery</td>
<td>1/45 (2.2%)</td>
<td>12/48 (25.0%)*</td>
</tr>
<tr>
<td>Cesarean section for dystocia</td>
<td>1/45 (2.2%)</td>
<td>8/48 (16.7%)*</td>
</tr>
<tr>
<td>Cesarean section for fetal distress</td>
<td>0</td>
<td>4/48 (8.3%)</td>
</tr>
</tbody>
</table>

Data are reported as mean ± 1 SD or as proportions.

* A p value < 0.05 by χ², Fisher exact, or Student t as appropriate.
† In seven patients complete dilatation was never achieved, and therefore by definition the duration of first and second stages of labor cannot be calculated. If n is different from the group sample size, it is noted in parentheses. Proportions in percent are also noted in parentheses.
Modern forms do not.

<table>
<thead>
<tr>
<th>Study and Year</th>
<th>OR (95% CI, Random)</th>
<th>Epidural, n/N</th>
<th>Opioid, n/N</th>
<th>OR (95% CI, Random)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Philipsen and Jensen et al, 1989</td>
<td></td>
<td>10/57</td>
<td>6/54</td>
<td>1.70 (0.57-5.06)</td>
</tr>
<tr>
<td>Thorp et al, 1993</td>
<td></td>
<td>12/48</td>
<td>1/45</td>
<td>14.7 (1.82-118)</td>
</tr>
<tr>
<td>Ramin et al, 1995</td>
<td></td>
<td>39/432</td>
<td>17/437</td>
<td>2.45 (1.36-4.41)</td>
</tr>
<tr>
<td>Muir et al, 1996</td>
<td></td>
<td>3/28</td>
<td>2/22</td>
<td>1.20 (0.18-7.89)</td>
</tr>
<tr>
<td>Bofill et al, 1997</td>
<td></td>
<td>5/49</td>
<td>3/51</td>
<td>1.82 (0.41-8.06)</td>
</tr>
<tr>
<td>Sharma et al, 1997</td>
<td></td>
<td>13/358</td>
<td>16/357</td>
<td>0.80 (0.38-1.70)</td>
</tr>
<tr>
<td>Barry et al, 1997</td>
<td></td>
<td>15/156</td>
<td>22/162</td>
<td>0.68 (0.34-1.36)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>97/1183</td>
<td>67/1186</td>
<td>1.50 (0.81-2.76)</td>
</tr>
</tbody>
</table>

Halpern et al. JAMA 1998; 280, 2105 - 2110.
Modern forms do not.

<table>
<thead>
<tr>
<th>Method of Delivery</th>
<th>Epidural Analgesia (N = 358)</th>
<th>Patient-controlled Intravenous Analgesia (N = 357)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spontaneous</td>
<td>319 (89)</td>
<td>326 (91)</td>
<td>NS</td>
</tr>
<tr>
<td>Instrumental vaginal total</td>
<td>26 (7)</td>
<td>15 (4)</td>
<td>NS</td>
</tr>
<tr>
<td>Low forceps*</td>
<td>22 (6)</td>
<td>12 (3)</td>
<td>NS</td>
</tr>
<tr>
<td>Outlet forceps†</td>
<td>4 (1)</td>
<td>3 (1)</td>
<td>NS</td>
</tr>
<tr>
<td>Cesarean delivery total</td>
<td>13 (4)</td>
<td>16 (5)</td>
<td>NS</td>
</tr>
<tr>
<td>Dystocia</td>
<td>9 (3)</td>
<td>10 (3)</td>
<td>NS</td>
</tr>
<tr>
<td>Nonreassuring FHR tracing</td>
<td>4 (1)</td>
<td>6 (2)</td>
<td>NS</td>
</tr>
<tr>
<td>Overall operative delivery</td>
<td>39 (11)</td>
<td>31 (9)</td>
<td>NS</td>
</tr>
</tbody>
</table>

Data are N (%).
FHR = fetal heart rate.
* Low forceps: +2 cm to +4 cm below the ischeal spines.
† Outlet forceps: fetal head at the perineum.
Content

- Adaptation to pregnancy.
- Anesthetic implications.
- Analgesia for normal labor and delivery.
- Anesthesia for Cesarean section in normal pregnant patients.
  - General anesthesia.
  - Regional techniques.
Failed Intubation: 1/249  
- Barnardo and Jenkins Anaesthesia 2000; 55, 690 – 694.

Life-threatening situations: 1/885 versus 1/2728 with regional anesthesia.  
Mendelsohn syndrome.
Confidential enquiries into maternal deaths in the UK: DIRECT DEATHS DUE TO ANAESTHESIA
Awareness.

- Thio 4 mg/kg, Lachgas 50%, isoflurane 0.2%.
- BIS-index: 76.
- All 34 subjects: Memory of presented words was possible.
- High risk for awareness.
Awareness.

Awareness during general anaesthesia: a review of 81 cases from the Anaesthetic Incident Monitoring Study

I. J. Bergman,¹ M. T. Kluger² and T. G. Short³

1 Department of Anaesthesia, Auckland Hospital, Auckland, New Zealand
2 Department of Anaesthesia, North Shore Hospital, Private Bag 93-503, Takapuna, Auckland, New Zealand

Kluger et al. Anaesthesia 2002; 57, 549 - 556.

■ 5% of all awareness cases is obstetric.
Hemodynamic instability.
General anesthesia and stroke risk.

Relative Risk
GA vs RA:
2.81 (1.69-4.64)

General anesthesia

- Aspiration prophylaxis.
- Rapid sequence induction.
- Induction of anesthesia.
- Maintenance of anesthesia.
Aspiration prophylaxis.

- 40% NO aspiration prophylaxis.
- 30% NO aspiration prophylaxis with general anesthesia.
- 50% NO aspiration prophylaxis with regional anesthesia.

**Table 2. Scheduled Cesarean Sections**

<table>
<thead>
<tr>
<th></th>
<th>All hospitals</th>
<th>≤500</th>
<th>501–1000</th>
<th>&gt;1000</th>
</tr>
</thead>
<tbody>
<tr>
<td>GA</td>
<td>63</td>
<td>72</td>
<td>59</td>
<td>55</td>
</tr>
<tr>
<td>Gastric emptying</td>
<td>6</td>
<td>6</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>Chemoprophylaxis</td>
<td>69</td>
<td>59</td>
<td>72</td>
<td>79</td>
</tr>
<tr>
<td>RA</td>
<td>37</td>
<td>28</td>
<td>41</td>
<td>45</td>
</tr>
<tr>
<td>EDA</td>
<td>60</td>
<td>50</td>
<td>63</td>
<td>63</td>
</tr>
<tr>
<td>SpA</td>
<td>40</td>
<td>49</td>
<td>36</td>
<td>36</td>
</tr>
<tr>
<td>Chemoprophylaxis</td>
<td>52</td>
<td>45</td>
<td>52</td>
<td>60</td>
</tr>
</tbody>
</table>

Values are expressed in percentages.

GA = general anesthesia, RA = regional anesthesia, EDA = epidural anesthesia, SpA = spinal anesthesia.
Aspiration prophylaxis.

- Sodium citrate / H2-blocker / metoclopramide.
  - Highest pH.
  - Smallest volume of gastric contents.
- With EVERY C-section.
- Also in case of an urgent C-section !!!!!!!
  - 50% of cases of aspiration occurs with extubation.
Cricoid cartilage
Esophagus
Do we still need succinylcholine?

**Table 5** Efficacy data after exclusion of major study violations (mean (SEM)). *P < 0.05

<table>
<thead>
<tr>
<th></th>
<th>Rapacuronium 2.5 mg kg⁻¹ (n = 20)</th>
<th>Succinylcholine 1.5 mg kg⁻¹ (n = 22)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset time (s)</td>
<td>80.4 (14.1)</td>
<td>63.9 (5.6)</td>
</tr>
<tr>
<td>Maximum effect</td>
<td>96 (1.9)</td>
<td>99 (0.4)</td>
</tr>
<tr>
<td>Return of T1 to 25% (min)</td>
<td>16.9 (1.5)*</td>
<td>9.6 (1.1)</td>
</tr>
</tbody>
</table>

Do we still need succinylcholine?

- Onset time 90 – 120 seconds; dose of 0.6 mg/kg.
- Time to block which is reversible: > 30 minutes.
- End of the procedure: reversal required in > 90% of patients.

Rocuronium (Org 9426) for Caesarean section

E. ABOULEISH, T. Abboud, T. Lechevalier, J. Zhu, A. Chalian and K. Alford

Remifentanil for general anesthesia: Why?

- To improve the quality of anesthesia – avoid awareness.
- Improve hemodynamic stability – avoid hypertension and tachycardia:
  - High risk patients with medical disease.
  - Severe preeclampsia.
- Avoid inhalational anesthesia – reduce the risk of uterine atony and bleeding.
Remifentanil for general anesthesia: Case reports.

- 17 published case reports involving 22 patients in which remifentanil was given prior to delivery of the fetus.
  - 5 reports (6 patients) from French and Spanish literature.
  - Reasons for remifentanil use/general anesthesia:
    - 15 patients with cardiac disease (mostly valvular).
    - 4 patients neurologic disease.
    - 2 patients with coagulopathy.
    - 1 patients severe preeclampsia.
**Remifentanil for general anesthesia: Case reports.**

<table>
<thead>
<tr>
<th>Case report + year</th>
<th>A1</th>
<th>A5</th>
<th>A10</th>
<th>Weight (g)</th>
<th>Mask</th>
<th>Duration mask</th>
<th>ETT</th>
<th>Naloxone</th>
<th>NICU</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scott et al. 1998</td>
<td>6</td>
<td>8</td>
<td>8</td>
<td>NR</td>
<td>No</td>
<td>0</td>
<td>No</td>
<td>No</td>
<td>NR</td>
</tr>
<tr>
<td>Bedard et al. 1999</td>
<td>7</td>
<td>8</td>
<td>NR</td>
<td>2970</td>
<td>No</td>
<td>0</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Johannsen et al. 1999</td>
<td>3</td>
<td>5</td>
<td>10</td>
<td>635</td>
<td>Yes</td>
<td>NR</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Johnston et al. 2000</td>
<td>8</td>
<td>10</td>
<td>NR</td>
<td>1960</td>
<td>No</td>
<td>0</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Manullang et al. 2000</td>
<td>6</td>
<td>9</td>
<td>NR</td>
<td>NR</td>
<td>No</td>
<td>0</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Mertens et al. 2001</td>
<td>3</td>
<td>7</td>
<td>9</td>
<td>NR</td>
<td>Yes</td>
<td>1 minute</td>
<td>No</td>
<td>No</td>
<td>NR</td>
</tr>
<tr>
<td>McCarroll et al. 2001</td>
<td>6</td>
<td>8</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>Yes</td>
<td>NR</td>
</tr>
<tr>
<td>Imarengiaye et al. 2001</td>
<td>6</td>
<td>9</td>
<td>NR</td>
<td>2830</td>
<td>Yes</td>
<td>4 minutes</td>
<td>No</td>
<td>Yes</td>
<td>NR</td>
</tr>
<tr>
<td>Wadsworth et al. 2002</td>
<td>3</td>
<td>9</td>
<td>NR</td>
<td>3100</td>
<td>Yes</td>
<td>6 minutes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Wadsworth et al. 2002</td>
<td>3</td>
<td>7</td>
<td>NR</td>
<td>2150</td>
<td>Yes</td>
<td>NR</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Orme et al. 2004</td>
<td>10</td>
<td>10</td>
<td>NR</td>
<td>3500</td>
<td>No</td>
<td>0</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Orme et al. 2004</td>
<td>9</td>
<td>10</td>
<td>NR</td>
<td>3200</td>
<td>No</td>
<td>0</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Orme et al. 2004</td>
<td>6</td>
<td>10</td>
<td>NR</td>
<td>3000</td>
<td>Yes</td>
<td>1 minute</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Orme et al. 2004</td>
<td>5</td>
<td>10</td>
<td>NR</td>
<td>2400</td>
<td>No</td>
<td>0</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Carvalho et al. 2004</td>
<td>7</td>
<td>9</td>
<td>NR</td>
<td>3027</td>
<td>Yes</td>
<td>2 minutes</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Richa et al. 2005</td>
<td>8</td>
<td>10</td>
<td>10</td>
<td>2050</td>
<td>No</td>
<td>0</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Restrepo et al. 2005</td>
<td>7</td>
<td>10</td>
<td>NR</td>
<td>NR</td>
<td>No</td>
<td>0</td>
<td>No</td>
<td>No</td>
<td>NR</td>
</tr>
<tr>
<td>Restrepo et al. 2005</td>
<td>8</td>
<td>10</td>
<td>NR</td>
<td>NR</td>
<td>No</td>
<td>0</td>
<td>No</td>
<td>No</td>
<td>NR</td>
</tr>
</tbody>
</table>

10/18 neonates Apgar at 1’ < 7 (56%); at 5’ only 1/18 neonates (6%); 7/18 required mask ventilation (39%).
Remifentanil for general anesthesia: Prospective case series.

- Unblinded, prospective evaluation of 10 women undergoing C-section under general anaesthesia.
- Reasons for general anaesthesia:
  - 7 coagulopathy.
  - 1 patient refusal.
  - 1 failed regional block.
  - 1 extensive spinal surgery.
- Induction: remifentanil 0.5 µg/kg bolus + infusion 0.2 µg/kg/min, target controlled infusion of propofol set at 5 µg/ml, succinylcholine 1.5 mg/kg.
- Maintenance: remifentanil 0.2 µg/kg/min, target controlled infusion of propofol set at 2.5 µg/ml.
- Measurement of:
  - Obstetric – demographic data.
  - Haemodynamics.
  - Neonatal outcome: umbilical artery blood gas analysis, Apgar scores, need for assisted ventilation, need for intubation, need for naloxone.

### Remifentanil for general anesthesia: Prospective case series.

Base Exc: base excess; ND: not done, UA: umbilical artery.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Apgar 1'</th>
<th>Apgar 5'</th>
<th>Apgar 10'</th>
<th>Weight (g)</th>
<th>Mask (min)</th>
<th>UA pH</th>
<th>UA pCO2</th>
<th>Base Exc</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7</td>
<td>9</td>
<td>10</td>
<td>1250</td>
<td>1</td>
<td>7.364</td>
<td>50.2</td>
<td>2.1</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>6</td>
<td>9</td>
<td>1410</td>
<td>5</td>
<td>7.233</td>
<td>64.5</td>
<td>-2.6</td>
</tr>
<tr>
<td>3</td>
<td>7</td>
<td>9</td>
<td>9</td>
<td>3830</td>
<td>None</td>
<td>7.370</td>
<td>54.2</td>
<td>4.3</td>
</tr>
<tr>
<td>4</td>
<td>7</td>
<td>8</td>
<td>9</td>
<td>1187</td>
<td>None</td>
<td>7.318</td>
<td>52.9</td>
<td>-0.2</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td>9</td>
<td>10</td>
<td>3100</td>
<td>2</td>
<td>7.297</td>
<td>57.0</td>
<td>-0.3</td>
</tr>
<tr>
<td>6</td>
<td>5</td>
<td>9</td>
<td>10</td>
<td>3050</td>
<td>3</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>7</td>
<td>9</td>
<td>9</td>
<td>10</td>
<td>3370</td>
<td>None</td>
<td>7.319</td>
<td>53.3</td>
<td>-1.7</td>
</tr>
<tr>
<td>8</td>
<td>8</td>
<td>9</td>
<td>9</td>
<td>1750</td>
<td>None</td>
<td>7.270</td>
<td>54.2</td>
<td>-3.0</td>
</tr>
<tr>
<td>9</td>
<td>2</td>
<td>6</td>
<td>8</td>
<td>2135</td>
<td>3</td>
<td>7.322</td>
<td>50.1</td>
<td>-1.1</td>
</tr>
<tr>
<td>10</td>
<td>1</td>
<td>9</td>
<td>9</td>
<td>3600</td>
<td>2</td>
<td>7.205</td>
<td>52.8</td>
<td>-1.3</td>
</tr>
</tbody>
</table>

General anesthesia.

- Acid aspiration prophylaxis.
- Rapid sequence induction.
- Induction: remifentanil 0.5 µg/kg bolus + infusion 0.2 µg/kg/min, target controlled infusion of propofol set at 5 µg/ml or thiopenthal 4 mg/kg, succinylcholine 1.5 mg/kg.
- Maintenance: remifentanil 0.2 µg/kg/min, target controlled infusion of propofol set at 2.5 µg/ml.
- Normo-ventilation: pCO₂ of 30 – 32 mmHg
- Pediatrician present at delivery.
- Postoperative analgesia: start during surgery as early as possible after delivery of the baby.
Regional anesthesia.

- Epidural anesthesia.
- Top-up existing epidural.
- Spinal anesthesia.
- CSE anesthesia.
- Always acid aspiration prophylaxis.
Epidural anesthesia. Topping-up an existing epidural.

- New local anesthetic:
  - ➔ reduced toxicity.
  - ➔ reduced duration of motor block.

- Addition of opioids.
How to reduce cardiotoxicity.

- Safer local anaesthetics.
- Technique related toxicity:
  - Incremental dosing.
  - Test dose.
  - Lower total doses.
  - Slow administration.
  - Frequent aspiration of catheters.
  - ...........
Are toxic events rare?

Incidence of potentially toxic events.

- Studies performed by AstraZeneca to develop and study ropivacaine:
  - 1/650 anaesthetics performed was potentially toxic.

- 2/38 accidental IV injection of ropivacaine during anaesthesia for C-section.
  
Are toxic events rare?
Reports of toxicity with new local anaesthetics.

Ropivacaine and levobupivacaine: Evidence of reduced toxicity.

Epidural anaesthesia with ropivacaine, levobupivacaine and bupivacaine.

- Duration of motor block is reduced with the new local anaesthetics, especially with ropivacaine.

Spinal anaesthesia.

- Duration of motor block is reduced with ropivacaine.

Spinal anesthesia: hypotension.

% of patients without hypotension.

% of patients with hypotension.

Tercanli et al.: 46 %.
Jouppila et al.: 100 %.
Karinen et al.: 23 %.
Rout et al.: 50 – 60 %.

Pathophysiology.

(Co)mplete sympathetic blockade
Preganglionic neurones

Several segments higher than sensory blockade

Arterial arteriolar vasodilation.
Venodilation \( \rightarrow \) decreased venous return \( \rightarrow \) decreased CO.
Bradycardia or loss of cardioaccelerator function.

+ Aortacaval compression: decreased venous return and 50% reduction in cardiac output.
### Risk of fetal acidemia.

<table>
<thead>
<tr>
<th></th>
<th>General</th>
<th>Epidural</th>
<th>CSE</th>
<th>Spinal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants (n)</td>
<td>371</td>
<td>286</td>
<td>659</td>
<td>231</td>
</tr>
<tr>
<td>UA pH &gt;7.2</td>
<td>97 %</td>
<td>88 %</td>
<td>82 %</td>
<td>76 %</td>
</tr>
<tr>
<td>UA pH &lt;7.2</td>
<td>4 %</td>
<td>9.6 %</td>
<td>15 %</td>
<td>19 %</td>
</tr>
<tr>
<td>UA pH &lt;7.1</td>
<td>0 %</td>
<td>2 %</td>
<td>3 %</td>
<td>4 %</td>
</tr>
<tr>
<td>UA pH &lt; 7.0</td>
<td>0 %</td>
<td>0.4 %</td>
<td>1 %</td>
<td>2 %</td>
</tr>
</tbody>
</table>
Fetal acidemia.

- Severity of hypotension.
- Duration of hypotension.
- Condition of the fetus:
  - Chronic distress.
  - Acute distress.
Factors associated with fetal acidosis: regression analysis.

<table>
<thead>
<tr>
<th>Factor</th>
<th>UA pH decreased</th>
<th>UA BE decreased</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use of ephedrine</td>
<td>0.003</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>U-D time</td>
<td>0.008</td>
<td>0.12</td>
</tr>
<tr>
<td>Maximum decrease SBP</td>
<td>0.006</td>
<td>0.76</td>
</tr>
<tr>
<td>Duration hypotension</td>
<td>0.34</td>
<td>0.34</td>
</tr>
<tr>
<td>Ephedrine x duration</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Block height</td>
<td>0.78</td>
<td>0.84</td>
</tr>
<tr>
<td>Pre loading</td>
<td>0.98</td>
<td>0.57</td>
</tr>
<tr>
<td>No vasopressor</td>
<td>0.49</td>
<td>0.15</td>
</tr>
<tr>
<td>Metaraminol</td>
<td>0.09</td>
<td>0.29</td>
</tr>
</tbody>
</table>

N = 337

Onset of hypotension.

Cumulative % of patients with hypotension following spinal anesthesia

Van der Walt et al. SASAC 1991.
Representative baseline blood pressure.

- Immediate pre-operative: 51%.
- Most recent antenatal: 39%.
- Booking blood pressure: 3%.
- ........

- Preeclampsia – baseline blood pressure?

Allowable drop in blood pressure.

- < 110 mmHg SBP: 1.5 %.
- < 100 mmHg SBP: 44 %.
- < 90 mmHg SBP: 41 %.
- < 80 mmHg SBP: 8 %.

Depending on the individual patient baseline value:
- Within 10 %.
- Within 20 %.
- Within 30 %.

# How low can we tolerate?

<table>
<thead>
<tr>
<th></th>
<th>Group 80</th>
<th>Group 90</th>
<th>Group 100</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose PE (µg)</td>
<td>790</td>
<td>1070</td>
<td>1520</td>
</tr>
<tr>
<td>pH UA</td>
<td>7.30</td>
<td>7.30</td>
<td>7.32</td>
</tr>
<tr>
<td>UA Base excess mmol/litre</td>
<td>-2.3</td>
<td>-1.8</td>
<td>-1.9</td>
</tr>
<tr>
<td>Hypotension (%) &lt; 80% of baseline</td>
<td>96 %</td>
<td>72 %</td>
<td>29 %</td>
</tr>
<tr>
<td>Nausea (%)</td>
<td>40 %</td>
<td>16 %</td>
<td>4 %</td>
</tr>
</tbody>
</table>

Fluid pre-loading.
Factors associated with fetal acidosis.

<table>
<thead>
<tr>
<th>Factor</th>
<th>UA pH decreased</th>
<th>UA BE decreased</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use of ephedrine</td>
<td>0.003</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>U-D time</td>
<td>0.008</td>
<td>0.12</td>
</tr>
<tr>
<td>Maximum decrease SBP</td>
<td>0.006</td>
<td>0.76</td>
</tr>
<tr>
<td>Duration hypotension</td>
<td>0.34</td>
<td>0.34</td>
</tr>
<tr>
<td>Ephedrine x duration</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Block height</td>
<td>0.78</td>
<td>0.84</td>
</tr>
<tr>
<td>Pre loading</td>
<td>0.98</td>
<td>0.57</td>
</tr>
<tr>
<td>No vasopressor</td>
<td>0.49</td>
<td>0.15</td>
</tr>
<tr>
<td>Metaraminol</td>
<td>0.09</td>
<td>0.29</td>
</tr>
</tbody>
</table>

N = 337

Why do we think fluid loading works?

  - UBF in pregnant sheep (spinal anesthesia) restored following IV fluids.

  - Small number of patients, some patients in labor in the fluid group.

  - Preload prevented hypotension and hypotension produced fetal acidosis.
Crystalloids: qualitative literature review.

“Crystalloid loading will not reliably prevent hypotension.”


Figure 1. The l’Abbé plot of crystalloid preload is shown. The treatment group received a larger volume of preload than the control group, who received a smaller volume or no preload. The dot size is proportional to the sample size of each study. The reference number is in parentheses after the first author’s name.
Moment of infusion: co-load!

Are colloids more effective?

“... indicate that colloid is superior to crystalloid in preventing postspinal hypotension for elective C-section.”

--> Intravascular half life!

Hypotension is not completely eradicated.

- Problems:
  - Anaphylaxis: 0.085% to starches.
  - Cost.

Ephedrine: vasopressor of choice.

- Does not produce uteroplacental vasoconstriction.
- Preserves uteroplacental blood flow.
- OK for fetus.
Does ephedrine prevent hypotension?

Ephedrine: dose response effects.

% of patients without hypotension.

Prophylactic ephedrine: meta-analysis of benefits and risks.

Figure 1. Risk of maternal hypotension in patients receiving various doses of IV ephedrine in randomized controlled trials included in the meta-analysis. The plotted line is the summary regression line (significant dose response).

Figure 2. Change in umbilical arterial pH in patients receiving various doses of ephedrine IV in randomized controlled trials included in the meta-analysis. The reference group was the control group (0 mg). The plotted line is the summary regression curve (significant dose response). The umbilical arterial pH was assumed to be linearly related to the natural logarithm dosage of ephedrine. The equation is as follows: change in umbilical arterial pH = 0.06 - 0.03 \times \ln (dose), R^2 = 0.36.

Figure 3. Risk of fetal acidosis (pH <7.2) in patients receiving various doses of ephedrine IV in randomized controlled trials included in the meta-analysis. The plotted line is the summary regression line (no significant dose response).

Figure 4. Benefit (hypotension) compared with harm (hypertension) for ephedrine IV doses between 0 and 30 mg. The baseline risk of hypotension was assumed to be 80% (13) and that of hypertension to be 11% (1). The threshold at which benefit and harm were equal was at 14 mg.
Phenylephrine.

- Equally effective in preventing hypotension, if not better.

- No detrimental effects on fetal and neonatal outcome.

Figure 1. Meta-analysis of trials. The effect of phenylephrine versus ephedrine on umbilical cord arterial blood pH. Data are mean difference with 95% confidence intervals.

## Phenylephrine

<table>
<thead>
<tr>
<th></th>
<th>Group 80</th>
<th>Group 90</th>
<th>Group 100</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose PE (µg)</td>
<td>790</td>
<td>1070</td>
<td>1520</td>
</tr>
<tr>
<td>pH UA</td>
<td>7.30</td>
<td>7.30</td>
<td>7.32</td>
</tr>
<tr>
<td>UA Base excess</td>
<td>- 2.3</td>
<td>- 1.8</td>
<td>- 1.9</td>
</tr>
<tr>
<td>mmol/litre</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypotension (%)&lt; 80% of baseline</td>
<td>96 %</td>
<td>72 %</td>
<td>29 %</td>
</tr>
<tr>
<td>Nausea (%)</td>
<td>40 %</td>
<td>16 %</td>
<td>4 %</td>
</tr>
</tbody>
</table>

Low dose CSE.

- 6.6 mg bupivacaine + sufentanil 3.3 µg.
- Hyperbaric – Sitting.
- Epidural volume expansion.
- IV fluid – and if necessary 5 to 10 mg ephedrine.

**Results:**
- SBP < 100 mmHg: 16 %.
- SBP < 90 mmHg: 6 %.
- SBP < 80 mmHg: 2 %.

Own experience: % decrease in MAP, DAP, SAP.

Incidence of severe hypotension:
➢ 20% decrease in MAP

High: 85 %.
Low: 20 %.

UZ Gasthuisberg unpublished results.
Hyperbaric vs hypobbaric.

Hyperbaric vs hypobaric.

Patient position: lateral versus sitting.

Ephedrine (mg)
Conclusion: proposed algorithm for prevention and treatment of spinal hypotension during C-section.

- Hyperbaric bupivacaine.
- Low dose CSE: 1.5 ml HB bupi + 0.5 ml sufentanil
  \[\Rightarrow 0.1 \text{ ml/10 cm patient height.}\]
  eg. Patient 168 cm = 1.7 ml of mixture = 6.375 mg bupi.
- Sitting.
- Epidural volume expansion
  - with 10 ml saline if block < T10 after 5 minutes.
  - with 5 ml saline if block > T10 after 5 minutes.
- Wedge under right hip !!!!!!
Conclusion: proposed algorithm for prevention and treatment of spinal hypotension during C-section.

- Prophylactic IV fluid: 500 – 1000 ml Voluven.
- Prophylactic vasopressor: 5 – 10 mg ephedrine in Voluven.
- More then 10% decrease in SAP: initiate therapy.
  - Therapy: phenylephrine boli.

- LABOUR: continue to use ephedrine.
Final point: spinal after failing epidural?

- Yes but reduce the dose even further.