

**Editorial I****Hypotension in obstetric spinal anaesthesia: a lesson from pre-eclampsia**

Vasopressor use to prevent hypotension occurs after 80% of spinal anaesthetics for Caesarean section.<sup>1</sup> The problem was first recognized 50 yr ago<sup>2</sup> when it was attributed to caval compression. This theory became accepted as the basis for clinical management, and it remains current today.<sup>3–4</sup> However, using this theory as a basis for the management of hypotension has proved disappointingly ineffective.<sup>5–6</sup> Important information from the 'natural experiment' of pre-eclampsia was overlooked, and fresh information from vascular biology now calls for a reconsideration of our management of hypotension in these circumstances.

Previously, the concept of compression of the vena cava and the aorta was linked to three features, which can coexist and are often considered together. However, each probably has a different mechanism. First, spinal anaesthesia almost always causes hypotension in normal pregnancy, and we will consider the reasons for this phenomenon later. Secondly, cardiac output can be reduced by aortocaval compression when some mothers lie in the supine position, although this is not necessarily clinically evident. Thirdly, a marked bradycardia with a reduction in cardiac output and severe hypotension can occur suddenly in a few subjects at some time after the mother moves to the supine position. This reflex effect is the relatively uncommon supine hypotensive syndrome of pregnancy (SHSP).<sup>7</sup>

Holmes<sup>8</sup> proposed that compression of the inferior vena cava by the gravid uterus caused hypotension after spinal anaesthesia because venous return was reduced and thus cardiac output decreased. Marx<sup>9</sup> developed the concept that blood was trapped in the legs, and introduced the treatment strategy of 'acute hydration' supported by a widely cited illustrative case history. Subsequently, fluid administration before spinal anaesthesia became the putative 'prophylaxis' and an almost universal therapy.<sup>10</sup>

The theory of caval compression and supine hypotension was based largely on studies by Scott and colleagues,<sup>11</sup> who measured cardiac output by dye dilution in eight

patients. Overall, cardiac output was 12% less in the supine compared with the lateral position. In three subjects, the mean reduction was only 6% and the investigators suggested that vena caval compression was relieved because the fetal head was engaged.<sup>11</sup> However, in two patients, there was sudden bradycardia, hypotension, and a decrease in cardiac output by more than 50%, suggesting a reflex response. Clearly, this study reported a heterogeneous group of patients, and the patients with bradycardia developed the supine hypotensive syndrome, which is a different phenomenon from the hypotension seen in the other patients in that study. An extensive review of SHSP found a wide range of case selection, clinical features, definitions, and degrees of hypotension.<sup>12</sup> Severe hypotension was reported in 2.5–20% of these patients. In some patients, hypotension only occurred after 20 min in the supine position. The possible reasons given for hypotension in these patients were either vena caval obstruction or a vagal reflex bradycardia, which is a well-known phenomenon associated with poorly filled heart.<sup>13</sup> Later studies found much less difference between supine and lateral positions. Using transcutaneous Doppler, a maximum change of cardiac output of 6% occurred with moving from supine to a left 15° tilt, and fetal head engagement made no difference.<sup>14</sup>

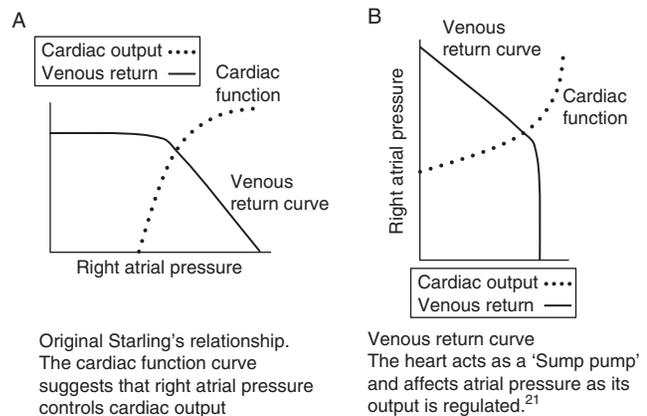
Undoubtedly, the vena cava is affected by the gravid uterus. Femoral venous and distal inferior caval pressures were greater in the supine position. In the lateral position, venous pressure was less, but still not as low as non-pregnant levels.<sup>15</sup> Angiography showed occlusion of the inferior vena cava and distension of the collateral azygos circulation in 12 supine patients having Caesarean section under general anaesthesia. The abdominal vena cava remained partly occluded in the lateral position.<sup>16</sup> However, in these studies, the link between changes in venous behaviour and hypotension was inferred rather than directly proved. No early studies involved spinal anaesthesia because general anaesthesia and increasingly epidural anaesthesia had, by that time, largely replaced spinals for Caesarean section in the UK.

The proponents of the caval compression theory suggested three ways to prevent hypotension after spinal block, but none has withstood careful examination. First, infusion of crystalloid or colloid was proposed to compensate for the venous blood said to be trapped in the legs, but initial reports of success in preventing hypotension<sup>17</sup> were not replicated in subsequent studies.<sup>1 5 6</sup> Colloid administration could increase cardiac output transiently, perhaps by haemodilution and reduced viscosity, but this effect was not sustained after sympathetic block with a spinal. Secondly, leg compression was attempted but was relatively ineffective, despite the success of the anti-G suit in preventing lower limb pooling and hypotension in aerospace medicine.<sup>18</sup> Finally, the tilt manoeuvre was advocated to reduce caval occlusion. Although widely used, this procedure is variably applied,<sup>19</sup> and does not prevent hypotension after spinal anaesthesia.<sup>6</sup> There is no escape from the fact that therapies based on the concept of caval compression do not reliably prevent hypotension after spinal anaesthesia in Caesarean section. Despite this, current books suggest routine use of strategies based on these putative explanations,<sup>4</sup> and current teaching uses these concepts.

The original hypothesis underlying the mechanism of hypotension was that a reduction in central venous pressure would reduce cardiac output, and thus reduce arterial pressure. This concept should be reconsidered. The hypothesis was based on the view that central venous pressure controls cardiac output, as suggested by the experimental studies of Paterson and Starling<sup>20</sup> and Guyton.<sup>21</sup> A clear understanding of the limits of Starling's studies is vital. They were of an isolated heart, supplied with blood from a venous chamber which could be raised or lowered to adjust the atrial pressure. In this 'open' system, output was not related to supply. The supply to the venous reservoir was externally adjusted by the investigator to keep the atrial pressure constant. By raising the reservoir to increase inflow pressure, the stretch of the ventricular muscle was increased, and thus ejection volume increased. To maintain the atrial pressure, the atrial reservoir had to be replenished more rapidly. In these circumstances, atrial pressure regulated cardiac output. This did not mean that the increased flow from the venous reservoir had increased the cardiac output, only that the flow had to be increased to sustain the reservoir pressure. The entirely separate studies of Guyton in which he related atrial pressure and venous return were equally artificial. Venous return was controlled using an adjustable pump. When the pump rate and thus the experimentally controlled 'venous return' was increased, a limit was reached where a decrease in venous pressure occurred and venous return did not change, implying upstream flow limitation.<sup>21</sup> In the whole body, the two factors of venous return and cardiac output are of course linked, in the long term, and neither is the 'cause' or 'effect' of changes in output or venous pressure, merely two sides of the same coin. The

inextricable link between venous return and cardiac output, and the unrealistic question concerning which is the cause and which is the effect, was recognized by Guyton, despite his considering venous pressure to be an independent variable. Even at the time, this highly artificial experiment was recognized as unlikely to be applicable to the intact animal.<sup>22</sup> In recent years, the relationship between venous pressure and cardiac output has been re-evaluated<sup>23 24</sup> and this has led to robust controversy.<sup>25 26</sup> Reddi and Carpenter<sup>27</sup> repeated previous suggestions<sup>23 25</sup> that it makes more sense to re-draw the Guyton plot with cardiac output on the abscissa (Fig. 1), to escape the common misconception that a decrease in right atrial pressure would act to increase blood flow through the veins. The important feature of the venous system is its compliance, not its resistance, and we can relate the central venous pressure to the volume held in the veins.<sup>28</sup> A recent helpful view is that the volume in the venous system is more relevant than the pressure, and that 'Venous Excess' is the important regulating factor on the venous side of the circulation.<sup>27</sup> Venous capacitance and its regulation in pregnancy may be an important element in understanding the haemodynamic response to spinal anaesthesia. For example, the splanchnic component of this capacitance drains directly into the vena cava via the hepatic vein which is not directly compressed by the uterus. However, we lack basic information on these aspects of venous dynamics.

The sensors that normally control arterial pressure, in the carotid sinus and the aorta, lie on the arterial side of the circulation, and are the sensors of the baroreflex. Why does this reflex fail to maintain arterial pressure after



**Fig 1** Comparison of cardiac function and venous return curves. (A) Cardiac function curve, after Guyton.<sup>19</sup> This relationship is based on the function of the isolated heart. An increase in central venous pressure causes an increase in cardiac output. The dependent variable (cardiac output) is plotted on the y-axis. (B) Venous return curve (also termed systemic or vascular function) which is the relationship found when the venous return is modified as the independent variable: under these circumstances, an increase in venous return reduces right atrial pressure.<sup>21</sup> Combining the two curves on one diagram condemns one of the relationships to have an independent variable expressed on the y-axis.

spinal anaesthesia in pregnancy? Part of the answer to this question can be found in the pathophysiology of pre-eclampsia. Remarkably, studies done in the 1950s showed that pregnant women with toxemia (severe pre-eclampsia) were far less likely to develop hypotension after spinal anaesthesia than normal pregnant or non-pregnant women. Similar differences were seen in response to autonomic ganglionic block, supporting the conclusion that withdrawal of sympathetic activity had less effect in the patient with pre-eclampsia.<sup>29 30</sup> For some reason, these studies were downplayed, although the proponents of the caval compression theory knew of them.<sup>2</sup> More recent studies corroborate the ability of pre-eclamptic patients to sustain arterial pressure after the spinal block.<sup>31</sup>

In pre-eclampsia, vascular epithelium is damaged by a process involving placental-derived proteins, leading to an imbalance between pro- and anti-angiogenic growth factors,<sup>32 33</sup> which results in persistent vasoconstriction. In contrast, the normal pregnant patient is very sensitive to spinal anaesthesia, because of an altered balance of vascular tone. Responses to endogenous pressors, particularly angiotensin II, are reduced. This is caused by an endothelium-dependent alteration of vascular smooth muscle function. Additionally, there is increased synthesis of vasodilator prostaglandins and nitric oxide. These effects increase dependence on sympathetic vascular tone in normal pregnancy.<sup>34 35</sup> The use of sympathomimetic vasopressors to sustain arteriolar tone and thus arterial pressure has become the most important strategy for safe spinal anaesthesia in contemporary practice, despite the prevailing theory of caval occlusion being responsible for hypotension after a spinal in normal pregnancy. Indeed, those who suggested that caval compression caused circulatory disturbances had advised against pressor agents to treat hypotension, suggesting that they would cause vasoconstriction but would not improve venous return.<sup>16</sup>

Nevertheless, aortocaval compression can reduce cardiac output and impair placental blood flow, so it remains rational to use tilt during anaesthesia, although the exact contribution of tilt to reducing hypotension in spinal anaesthesia is unclear.

After 40 yr, the relationship between spinal anaesthesia, pre-eclampsia, and hypotension can be properly acknowledged and put into clinical practice. These observations shed light on the circulatory effects of spinal anaesthesia in normal pregnancy. Research in obstetric anaesthesia can now move on from the legacy of an uncertain hypothesis by learning the lessons of pre-eclampsia and understanding how the features of this disorder illuminate our current concepts. Modern non-invasive methods such as ultrasound, MRI, and measures of skin blood flow<sup>36</sup> should be used in pregnancy to explain the effects of spinal anaesthesia more exactly. Better management and training based on logical theories should follow.

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## Editorial II

### Red cell transfusion in elective cardiac surgery patients: where do we go from here?

Transfusion of red blood cells (RBCs) is one of the most common interventions carried out upon the cardiac surgery population in the postoperative period. Of late, this practice has received increasing attention in terms of the appropriateness of the decision to transfuse, the deleterious consequences of unnecessary transfusion, and the possibility for viable alternatives.<sup>1</sup> We wish to highlight recent developments in these areas and suggest where the future may lie in terms of an evidence-based transfusion practice in cardiac surgery.

#### Appropriate use of RBCs

Since 1942, any decision to administer RBCs has largely been based upon a haemoglobin concentration [Hb] threshold with little consideration for any other patient variables.<sup>2</sup> Largely prompted by the availability of

high-quality data from the general intensive care unit population, this situation has gradually changed.<sup>3</sup> When considering [Hb] alone, there is considerable debate as to an appropriate threshold for the transfusion of RBCs. Experimental haemodilution studies in healthy volunteers suggest that [Hb] levels as low as 5 g dl<sup>-1</sup> may be adequately tolerated in healthy volunteers, albeit with the minor complication of a reversible cognitive deficit.<sup>4</sup> Although limited in sample size, several studies have attempted to examine the impact of acute anaemia on the outcome after cardiac surgery. Although it is not possible to extrapolate what an appropriate [Hb] might be, the strong suggestion is that in the absence of hypovolaemia, current levels of RBC transfusion are excessive.<sup>5 6</sup>

The premise behind any RBC transfusion is that it will improve the oxygen carrying capacity of the blood. Thus, investigators have attempted to identify several variables