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Exploring the functionality of the adult's venous compartment is of interest to the field of obstetrics

W. Gyselaers, MD PhD

Dept. Obstetrics & Gynaecology, Ziekenhuis Oost Limburg, Genk Belgium
Dept. of Physiology, Hasselt University, Diepenbeek Belgium

Correspondence at: wilfried.gyselaers@zol.be

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Normal characteristics of venous blood flow and implications of abnormal venous hemodynamics are much less understood than arterial vascular (dys)functionality. This is mainly due to limitations of methods to study the venous system, especially when they are performed in clinical conditions. Methods to study body venous tone have been reviewed by Pang (2000): they include mean circulatory filling pressure technique, constant CO reservoir technique, plethysmography, blood-pool scintigraphy, linear variable differential transformer technique and intravascular ultrasound. Recently, duplex sonography has been reported to be a simple, non-invasive and easily-accessible method to study venous hemodynamics, especially in pregnant women (Karabulut *et al*., 2003; Bateman *et al*., 2004; Roobottom *et al*., 1995; Gyselaers *et al*., 2009/1; Gyselaers *et al*., 2009/2).

The venous compartment has two important physiologic functions. It is a large capacitance reservoir, containing 65-75% of the total blood volume. Of this, 75% is in the small veins and venules (Pang, 2000). The splanchnic bed is the most important blood reservoir of the body, containing up to 25% of the total blood volume (Pang, 2000), of which the majority is in the liver bed (Berne *et al*., 2001; Pang, 2001). The venous vascular walls contain collagen and elastin fibres, together with a circular layer of smooth muscle cells (Juncqueira *et al*., 2005). This histological structure serves physiologic properties as expansion, visco-elasticity and active contraction (Pang, 2000). Active vasoconstriction of the venular bed and passive emptying of the venous capacitance reservoir following arteriolar constriction are two basic physiologic mechanisms by which the venous compartment contributes to the regulation of cardiac output (Gelman, 2008; Boulpaep *et al*., 2005; Berne *et al*., 2001) In the control and regulation of cardiac output, the heart and venous compartment cooperate as one functional unity (Berne *et al*., 2001).

Both under experimental conditions and in clinical syndromes, it is illustrated that venous hemodynamic dysfunction predisposes to renal and/or liver dysfunction. This organ dysfunction occurs through (a) increased intravenous pressure with subsequent congestion at the level of the microcirculation, and (b) reduced organ perfusion following reflex induced arterial constriction (Gelman, 2008). Increased renal venous pressure but not increased renal parenchymal pressure in swine kidney preparations evoked reduced glomerular filtration and proteinuria (Doty *et al*., 1999; Doty *et al*., 2000). In rats, increase of renal venous pressure by partial renal vein ligation was associated with reduced glomerular filtration (Dilley *et al*., 1983) and arterial vasoconstriction due to a renorenal neural reflex (Corradi, 1985). In a sheep model, reflex arterial hypertension at unchanged venous return was observed after bilateral occlusion of uterine veins; this was not present after occlusion of inferior vena cava with reduction of venous return (Lotgering *et al*., 1986). Thrombosis or external compression of Inferior Vena Cava, Hepatic Veins, or Renal Veins is associated with dysfunction or even failure of liver and/or kidneys (Horton *et al*.,

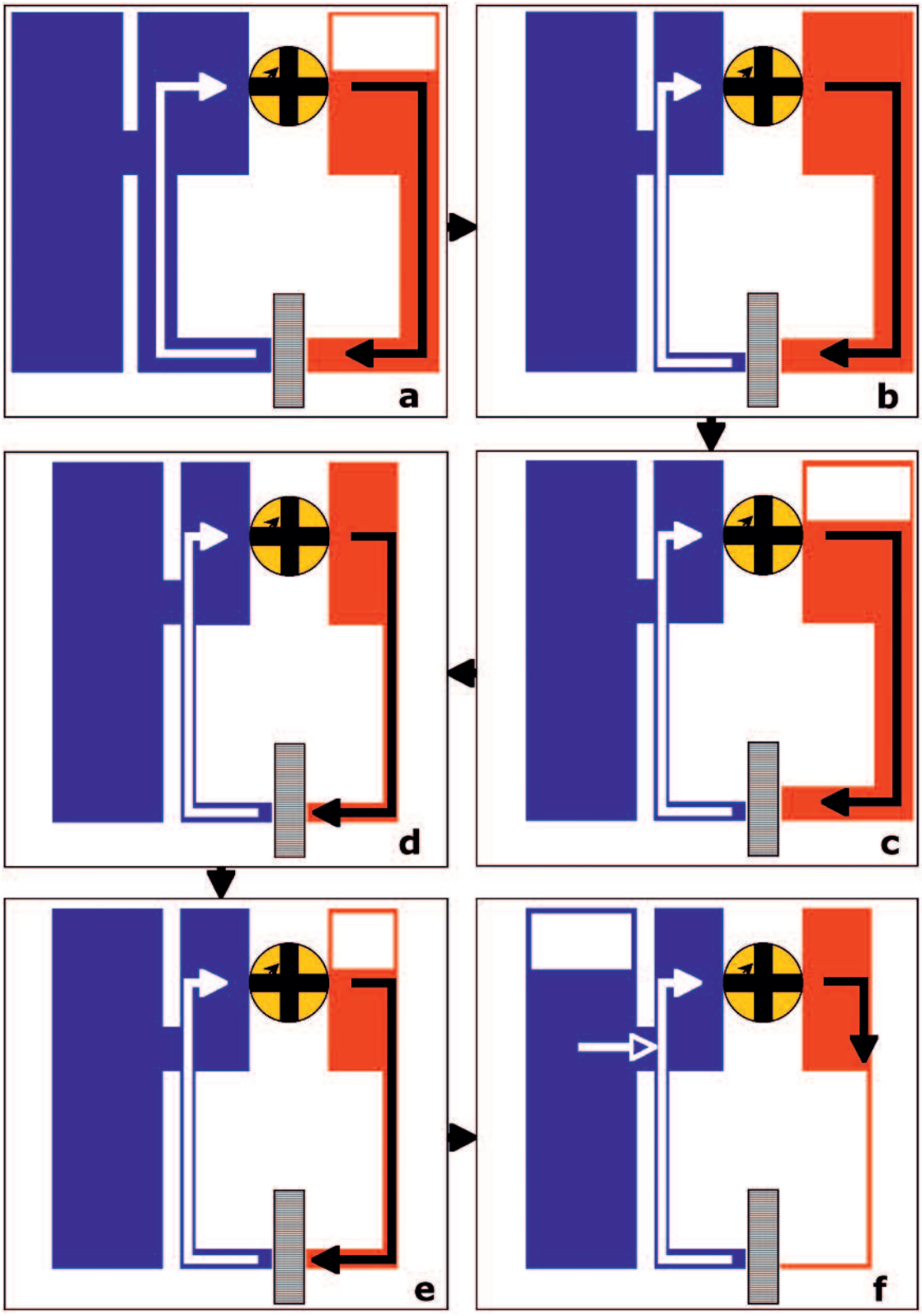

Fig. 1. — Schematic presentation of the normal physiologic control of flow-pressure-volume relations in the human systemic circulation (Gelman, 2008). The red elements on the right hand side in every panel represent the arterial system with a circulating volume (upper) and an arteriolar volume (lower). The arterioles drain into the capillary system, represented by the shaded rectangle at the bottom of each panel.
This in turn is connected to the venular system (lower blue) and the large veins (upper blue). The circulation is indicated by arrows and is maintained by the heart (yellow circle with rod).
Next to a circulating volume, the venous system also contains a capacitance reservoir (blue box on the left hand side in each panel). A reduction of cardiac output (panel a) evokes a reflectory constriction of the venous compartment (panel b), which actively mobilises blood from the venous to the arterial compartment. In further control of organic blood perfusion, there is a dynamic process maintaining a balance between blood volume and vascular tone of veins and arteries (panels c and d). However with increased reduction of cardiac output (panel e), constriction of the arteriolar system reduces influx of blood into the capillary and venous system (panel f). Venous blood then is mobilised passively from the venous capacity reservoir into the circulation due to the pumping activity of the heart (panel f).

2008; Zigman *et al*., 2000; Ahmed *et al*., 2006; Itoh *et al*., 1997). Acute or chronic heart failure can induce cirrhosis with liver dysfunction (Naschitz *et al*., 2000) and/or renal insufficiency (Ronco *et al*., 2008; Tang *et al*., 2010). Venous congestion in decompensated heart failure has been recognised as the most important hemodynamic factor contributing to renal dysfunction. (Tang *et al*., 2010; Mullens *et al*., 2009; Wencker, 2007).

Similar to the arterial compartment, the venous compartment is subject to gestational adaptive changes. During uneventful pregnancy, venous distensibility is increased, which serves the increased capacitance function of the venous system necessary to accommodate the increase in plasma volume. (Sakai *et al*., 1994) Venous capacitance returns to nonpregnant values in the first three months postpartum. (Skudder *et al*., 1990) Venous compliance also increases by 30% and the diameter of the inferior vena cava increases up to 70% above nonpregnant values. (Krabbendam *et al*., 2007) A dilatation of the left atrium occurs already in early gestation, (Duvekot *et al*., 1998) whereas a rise of Atrial Natriuretic Peptide (ANP) is observed in the second half of pregnancy. (Krabbendam *et al*., 2007) This rise of ANP originates from extension of the atrium due to expansion of the plasma volume, and prevents overfilling of the cardiovascular system. Despite an overall increase of venous capacitance, a decrease of compliance of splanchnic veins has been reported in pregnant rats as compared to nonpregnant controls. (Hohmann *et al*., 1992) Considering the splanchnic vascular bed as the most important blood reservoir of the body, the combination of both increased capacitance and reduced compliance in the splanchnic veins allows for punctual control of cardiac output. Under these conditions, subtle changes of splanchnic arteriolar or venular tone have a prominent impact on mobilisation of stored blood volumes into the circulation. As such, gestation induced changes of the venous compartment seem to upgrade its physiologic properties towards regulation of cardiac output, in which it becomes more powerful than in nonpregnant conditions.

Preeclampsia is known as a maternal cardiovascular maladaptation syndrome with diminished plasma volume expansion, (Ganzevoort *et al*., 2004) decreased cardiac output, (Rang *et al*., 2008) and reduced dilation of the left atrium already present in the first trimester (Krabbendam *et al*., 2007; Duvekot *et al*., 1998). Reduced plasma volume expansion occurs before increase of progesterone or reduction of aldosterone in women, destined to develop preeclampsia (Salas *et al*., 2006). The adaptation of the venous compartment, as explained above, is also blunted in preeclampsia: venous distensibility, (Sakai *et al*., 1994) capacitance, (Goodlin, 1986) and compliance are reduced (Krabbendam *et al*., 2007). Nearly half of women with a history of preeclampsia show postpartum persistence of subnormal plasma volume, (Spaanderman *et al*., 2000) which is associated with low venous capacitance (Aardenburg *et al*., 2005) and impaired venous drainage of the conjunctival microcirculation (Houben *et al*., 2007). For these women in nonpregnant condition, the autonomic response to volume expansion (Krabbendam *et al*., 2009) and cardiovascular adaptation to exercise (Aardenburg *et al*., 2005) is blunted. These women are also at higher risk for recurrence of preeclampsia in subsequent pregnancy, (Aardenburg *et al*., 2003) and they show a condition of relative overfill already present at the very early beginning of pregnancy, leading to atrial stretch and overshooting of ANP-release (Krabbendam *et al*., 2007). In pregnant women who subsequently develop early-onset preeclampsia, first trimester cardiac output is lower than normal, whereas this is higher in women destined to develop late-onset preeclampsia (Valensise *et al*., 2008). Uptil now, this preeclampsia – related dysregulation of cardiac output hasn't been linked to the function of the venous comparment.

The information presented above can be summarised as follows:

- the venous compartment is one of the most important systems in the human body towards control and regulation of cardiac output
- gestation induced changes of the venous compartment upgrade the physiologic properties of the venous system towards regulation of cardiac output
- in pregnant women who subsequently develop early-onset preeclampsia, first trimester cardiac output is lower than normal, whereas this is higher than normal in women destined to develop late-onset preeclampsia
- arterial hypertension and liver and/or renal dysfunction can be secundary to abnormal venous hemodynamics

Today it is not yet fully understood what the exact role is for the venous compartment in physiologic conditions with changing patterns of cardiac output, such as normal pregnancy. It is even less clear to what extend the venous compartment is involved in the preclinical and clinical stages of preeclampsia. The information summarised above reveals a new and tempting hypothesis: the clinical stage of preeclampsia, a condition generally considered as one of the most serious gestational complications of which background mechanisms are not yet fully understood, might be a systemic response to a preced-

ing failure of the venous system to regulate cardiac output appropriately. In order to accept or refute this hypothesis, data from more studies and observations are needed. This is why the exploration of the adult's venous compartment, both in non-pregnant and pregnant conditions, is of interest to all obstetricians, cardiologists, sonographers and scientists involved in research on gestation- induced maternal cardiovascular adaptation mechanisms and/or background mechanisms behind preeclampsia.

Glossary

Distensibility: The general definition of the ability of a vessel to distend in response to volume and/or pressure changes

Compliance: The relation between distensibility and transmural pressure (inside minus outside pressure). It is quantified as the change in volume (ΔV) divided by the change in pressure (ΔP).

Capacitance: The relationship between the intravascular blood volume and the pressure distending the vascular walls.

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