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Physiological changes of pregnancy and monitoring

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Advances in medical care have led to increasing numbers of complex, high-risk obstetric patients. Specialist training and a sound knowledge of normal maternal physiology are essential to optimize outcomes. One of the earliest observed changes is peripheral vasodilatation; this causes a fall in systemic vascular resistance and triggers physiological changes in the cardiovascular and renal systems, with 40–50% increases in cardiac output and glomerular filtration rates. Safety concerns over Swan Ganz catheters have driven the increasing interest in alternative techniques, such as echocardiography, thoracic bioimpedance and pulse contour analysis, although their exact roles in future obstetric high-dependency care have yet to be established. Analysis of arterial blood gases is fundamental to the management of sick patients, and correct interpretation can be aided by a systematic approach. Observation charts are almost ubiquitous in all aspects of medicine, but little evidence exists to support their use in the high-dependency setting.

Key words: maternal physiology; high-dependency care; monitoring; observation charts.

Pregnancy represents a serious challenge to all body systems. The progressive physiological changes that occur are essential to support and protect the developing fetus and also to prepare the mother for parturition. This causes no major problems for healthy women; however, certain factors can affect an individual's ability to adapt to the demands of pregnancy, such as maternal age and multiple gestations. In the presence of clinical or subclinical pathology, the normal physiological changes of pregnancy

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can place significant strain on already compromised systems, threatening the lives of both mother and fetus.

MATERNAL PHYSIOLOGY

Cardiovascular physiology

Many of the most profound physiological changes occur in the cardiovascular system; therefore, cardiac disease can pose major difficulties in pregnancy. Most of these changes occur in the first trimester and plateau by mid-gestation, peaking again around the time of delivery.

Heart rate

Heart rate rises in pregnancy as a compensatory response to falling systemic vascular resistance (SVR).[1] Hormonal effects, possibly from the thyroid[2], may also play a role. This is seen as early as the seventh week of gestation and increases by up to 20% in the third trimester.[3] An increase in heart rate leads to decreased time for diastolic filling and can lead to reduced cardiac output (CO) and perfusion pressures. Rapid heart rates also reduce left atrial emptying and increase the risk of pulmonary oedema. This is a particular problem in rate-dependent conditions such as mitral stenosis.

Blood pressure

Blood pressure is the product of CO and SVR; put simply, pressure = flow × resistance. Like SVR, blood pressure falls early in pregnancy, decreasing by approximately 10% by 7–8 weeks of gestation.[4] This probably occurs secondary to peripheral vasodilatation[5], and although CO increases to compensate, this is not sufficient to prevent a fall in blood pressure during the first trimester. Thereafter, systolic and diastolic blood pressure continue to fall, reaching the nadir at 24 weeks of gestation[6,7] and returning to normal pre-pregnancy values around term.

Central haemodynamics

CO has been studied extensively in pregnancy using both invasive and non-invasive methodology. The general consensus is that CO rises in the first trimester, and peaks by the end of the second trimester at approximately 30–50% of non-pregnant values (3.5–6.0 L/min).[8–11] A study measuring CO longitudinally from preconception throughout pregnancy, where each patient was their own control, demonstrated an early rise in CO by 5 weeks of gestation (4.88 L/min, +17% mid-pregnancy values), increasing steadily and reaching a plateau at 32 weeks (7.21 L/min). Stroke volume was also increased by 8 weeks of gestation, reaching a plateau at 16–20 weeks (+32% mid-pregnancy values). CO rises at the onset of labour and declines rapidly after delivery[12], reaching normal values by 24 weeks post partum.[6]

SVR is the afterload against which the heart must pump. Studies have demonstrated a fall in SVR starting in early pregnancy, reaching a nadir at approximately 14–24 weeks of gestation, then rising to pre-pregnancy values by term.[8,9,13] The primary cause of the fall in SVR is likely to be peripheral arterial vasodilatation in early pregnancy, mediated by progesterone and vasodilators such as nitric oxide[14], although more recent data question the role of nitric oxide in this process.[15] The

conversion of the uteroplacental circulation from high to low resistance flow acts to further reduce afterload.

The observed decrease in SVR triggers the compensatory physiological mechanisms that sense the change as 'underfill', resulting in increased CO and the promotion of sodium and water retention in an attempt to maintain arterial blood pressure. Atrial natriuretic peptide (ANP) may play a role in this process. ANP is produced by the atrial cardiomyocytes, promotes sodium excretion and diuresis in non-pregnant subjects[16], and produces vasodilatation in angiotensin-II-treated vascular smooth muscle. Levels of ANP rise in pregnancy. Some workers have linked this with the early fall in maternal SVR[17,18], although there is little direct evidence to support ANP as a major cause of vasodilatation in pregnancy.

Peripartum cardiovascular changes

Uterine contractions have an important effect on maternal haemodynamics. Each contraction expels 300–500 mL of blood into the maternal circulation, increasing venous return and therefore CO by up to 30%.[19]

Maternal pain, anxiety, valsalva and positioning also have profound effects on CO in labour. Epidural anaesthesia helps to limit the effects of some of these factors by stabilizing the heart rate. Plasma expansion prior to insertion may also contribute. For this reason, epidurals are often recommended in some cardiac conditions where large fluctuations in CO are undesirable. CO also increases between contractions and with progress in labour.[12]

During and after the third stage of labour, large fluid shifts occur within the first 24 h. Haemodynamics alter significantly due to autotransfusion of approximately 500 mL of blood from the uterus back to the heart, relief of vena caval compression from the gravid uterus, and fluid shifts from the extravascular to the intravascular compartment. Whilst these changes are of no concern to normal healthy women, those with either pre-eclampsia or cardiac disease are at increased risk of cardiovascular decompensation.

CO (+59%), heart rate and stroke volume (71%) all rise within the first 10 min of delivery[20] and remain elevated at 1 h. These changes resolve over the next few weeks, falling by 28% (compared with 38-week values) at 2 weeks and 33% by 6 months post partum.[21]

Haematological system

In pregnancy, the haematological system undergoes changes in order to meet the demands of the developing fetus and placenta, with major alterations in blood volume, constituent cells and coagulation factors.

Blood volume

Plasma volume increases rapidly up to 10% above baseline by 7 weeks of gestation, and plateaus by 32 weeks at 45–50%.[4] Red cell mass expansion also occurs but to a lesser degree, and it is this differential that accounts for the dilutional anaemia of pregnancy despite adequate stores.[22] Haemodilution peaks by 30–32 weeks of gestation.

It is unclear whether or not this combination of changes gives a survival advantage, but the decrease in blood viscosity may improve placental perfusion and reduce the risk of local thrombosis[23] in the procoagulant state of pregnancy, and provide a degree of physiological reserve during haemorrhage.

Plasma volume may also be important for normal fetal development as pregnancies complicated by growth restriction have measurably lower mean maternal plasma volumes compared with normal fetuses.[24] There is also evidence that obstetric outcome and birth weight are correlated with the amount of plasma volume expansion.[25,26]

Blood components

The red cell 'mass' equates to the total volume of red blood cells in the circulation. It increases by 18–25%[27], perhaps secondary to a rise in erythropoietin[28], in early pregnancy, and then falls after delivery as a result of haemorrhage.[29] The degree of this increase is proportional to the size and number of the fetuses.

The increase in red cell volume provides for the extra oxygen demands of the mother and fetus, The lower end of the normal range for haemoglobin in pregnancy is 11–12 g/dL, and the World Health Organization recommends supplementation at levels <11.0 g/dL.

White cell count increases in pregnancy from the first trimester, and plateaus at approximately 30 weeks of gestation as a result of selective marrow erythropoeisis.[30] This causes a left shift with granulocytosis and more immature white cells in the circulation. The normal range for pregnancy is 5000–12 000/mm^3, although values as high as 15 000/mm^3 are not uncommon.[30]

The platelet count usually falls in pregnancy[31,32], possibly due to a dilutional effect and/or increased consumption secondary to endothelial-mediated activation. The consumption theory is supported by the observation that mean platelet volume, consistent with an immature platelet population, increases in pregnancy.[33]

Mild thrombocytopenia (100 000–150 000/mm^3), which is of no clinical significance, is present in approximately 8% of pregnancies and has been termed 'gestational thrombocytopenia'.[34]

Coagulation system

Pregnancy is a procoagulable state with alterations in both coagulation and fibrinolysis. The changes in the coagulation system during pregnancy appear to be aimed at minimizing blood loss at delivery. Unfortunately, these changes also predispose to thromboembolism, particularly in those with additional risk factors.[35]

In terms of absolute risk, pregnancy is associated with a four-to-six-fold increase in venous thromboembolism compared with non-pregnant age-matched controls.[36]

The circulating levels of factors VII, VIII, IX, X and XII, fibrinogen and von Willibrand factor increase, factor XI decreases, and prothrombin and factor V remain unchanged.[37]

The natural anticoagulants antithrombin III and protein C levels are unchanged or increase, and protein S levels fall.[37] Fibrinolytic activity is known to decrease, mainly due to the marked increase in plasminogen activator inhibitors, PAI-I and PAI-2[38], and the combination of all these changes increases the risk of thrombosis during pregnancy and the puerperium.

Respiratory physiology

The respiratory tract undergoes many changes during pregnancy, mediated initially by changes in the endocrine system and later by the enlarging uterus, in order to provide oxygen for increased maternal demands and for fetal physiology. These changes act to lower maternal PCO_2 to half that of the fetus, thereby facilitating more effective gas exchange.

Mechanics

As the pregnancy progresses, the uterus expands upwards and changes the chest shape.

The lower ribs 'flare' due to looser ligaments (influence of progesterone). The thoracic circumference increases by 8%[39], and both the transverse and anteroposterior diameters increase by 2 cm. These changes increase chest excursion and result in a 5-cm elevation of the diaphragm.[40] Lung compliance is unchanged but chest wall compliance decreases.

Physiology

Compared with the cardiovascular system, pregnancy places less stress on ventilation, which explains why all but the most severely compromised will cope reasonably well. Oxygen consumption increases by 30–50 mL/min[41,42], two-thirds of which covers additional maternal requirements (mainly the kidneys) and one-third is for the developing fetus. Despite this increase, pCO_2 does not vary greatly and is approximately 13.6 kPa at term.[43] pCO_2 is also lower in the supine position; therefore, blood gases should be collected while sitting.[44] Increased oxygen consumption is associated with a greater increase in carbon dioxide production, presumably due to the increase in carbohydrate to fat metabolism in pregnancy.[45]

The increase in oxygen consumption is associated with a 40% increase in ventilation secondary to a progressive rise in tidal volume of 200 mL (from 500 to 700 mL)[46], rather than an increase in respiratory rate which remains at 14–15 breaths/min.[47] Minute ventilation rises by approximately 40%, in parallel with tidal volume, from 7.5 L/min to 10.5 L/min.[48] Functional residual capacity, comprising residual and expiratory reserve volume (both of which fall), is reduced by approximately 500 mL, but it is the 20% fall in residual volume that further increases alveolar ventilation.

It is unclear what stimulates ventilation in pregnancy. The traditional view is that rising levels of progesterone drive the process, but an alternative hypothesis favours the increased metabolic rate of pregnancy.[50]

Progesterone may lower the threshold[51] and/or increase the sensitivity[52] of the respiratory centre to carbon dioxide, or act independently as a primary stimulant of these two mechanisms.[53]

Vital capacity, which is the maximum volume of gas expired after maximum inspiration, is unaltered in pregnancy.[41,46,54] Forced expiratory volume in 1 s and peak expiratory flow rate are indirect measurements of airways resistance, i.e. total resistance in the tracheobronchial tree plus work done to expand the lung and chest wall (compliance). Neither measurement is altered significantly in pregnancy[55], which is likely to be due to the additive effects of bronchodilatation and bronchoconstriction mediated by prostoglandins (E and $F_2\alpha$ acute, respectively), progesterone (smooth muscle relaxant) and the observed reduction in total lung capacity.[56]

To summarize, in healthy women, there is usually adequate maternal compensation for the increase in oxygen demands, with the increases in tidal volume leading to a significant fall in pCO_2. The whole process appears to be mediated by rising levels of progesterone and augmented by a decrease in residual volume.

Renal physiology

During pregnancy, the significant changes that occur are the result of functional and structural adaptations, which are imperative to support alterations in cardiovascular physiology.

The kidneys increase in length by approximately 1 cm[57] as a result of the increase in blood volume. The renal pelves, calyces and ureters[58] increase in size in response to rising progesterone levels. The enlarging uterus may also contribute to the mild to moderate hydronephrotic changes seen in pregnancy, by compression of the ureters at the pelvic brim[59], with the right-sided collecting system typically more dilated than the right. By the third trimester, 80% of women will have evidence of hydronephrosis.

The result of these changes is mild obstruction and urinary stasis, increasing the risk of infection and misinterpretation of diagnostic imaging.

Functional changes

Renal blood flow increases by 35–60%, increasing the functional capacity of the kidneys. The glomerular filtration rate (GFR) increases by 40–50% by the end of the first trimester, peaking at 180 mL/min.[60] It is then maintained at this level until 36 weeks of gestation. This reduces serum urea and creatinine compared with non-pregnant levels, as the GFR rises without a similar increase in production. This is important when interpreting the results of renal profiles in pregnancy. Timed urinary collections are also affected by alterations in GFR, causing an increase in urinary protein excretion up to 0.26 g/24 h[61], and creatinine clearance up by 25% at 4 weeks and 45% at 9 weeks of gestation.[62]

Loss of glucose through the kidneys is normal in pregnancy due to increased GFR and reduced distal tubular re-absorption; therefore, screening for gestational diabetes using urinalysis alone is unreliable. This glucose load also increases the risk of infection.

In pregnancy, resistance to the pressor effects of angiotensin II develops along with a rise in all components of the renin-angiotensin system. This results in a large increase in extracellular water volume (by 4–7 L)[63] and retention of sodium and water, which acts to maintain normal blood pressure. This water retention causes a decrease in plasma sodium from 140 to 136 mmol/L, and plasma osmolality from 290 to 280 mosmol/kg.[64]

The trigger for initiation of the changes discussed above is unknown. It may be that a primary fall in total vascular resistance leads to an 'underfill' signal which stimulates sodium retention and plasma expansion. This theory is consistent with the changes noted in renin-angiotensin-aldosterone levels during human and rat pregnancy, but an alternative proposal involves ANP, the sympathetic nervous system and the arginine vasopressin osmoregulatory system[65,66] re-adjusting and sensing the increase in plasma volume as normal.

A final and important point is that a pregnant woman's physiology does not recognize the renal system as a priority; therefore, when subjected to certain haemodynamic challenges such as massive haemorrhage, renal blood supply is preferentially reduced. This results in poor perfusion, a reduction in urine output and an inherent risk of acute tubular necrosis.

Gastrointestinal physiology

The gastrointestinal tract is affected by the expanding uterus during pregnancy. This, in combination with increased intragastric pressures and alterations mediated by the smooth muscle effects of progesterone on lower oesophageal sphincter tone, predisposes to reflux and heartburn.[67] Gastric and intestinal motility are also affected, causing lower transit times[68] and contributing to the sensation of bloating and constipation, which are common symptoms in pregnancy. Previous reports have suggested that gastric acid production is reduced in pregnancy and is, in some way, protective against peptic ulcer disease; however, recent studies refute this suggestion.[69]

Endocrine system

Thyroid

Pregnancy is a state of iodide deficiency due to inadequate intake and increased renal clearance. The thyroid gland undergoes significant but reversible hormone-driven changes in physiology during pregnancy, with moderate enlargement due to glandular, cellular and vascular hyperplasia.[2] Thyroid function tests change in pregnancy due to: (1) an oestrogen-mediated increase in thyroid globulin binding; (2) thyroid stimulation due to the 'spill-over' effect of human chorionic gonadotrophin, which is structurally similar to thyroid-stimulating hormone (TSH), during the first trimester; and (3) a decrease in the availability of iodide due to feto-placental losses and increased renal clearance.[2]

TSH falls in the first trimester, returning slowly to normal by term. Circulating levels of free T3 and T4 remain fairly constant throughout pregnancy and are preferred to total levels due to the effects of protein binding. The best laboratory test for monitoring purposes is a high-sensitivity TSH assay.

Pancreas

Changes in carbohydrate metabolism during pregnancy are achieved through increased production of insulin combined with resistance to its action. The B-islet cells undergo hyperplasia leading to increased insulin secretion, which may be responsible for the fasting hypoglycaemia common in early pregnancy. One of the main features of pregnancy is insulin resistance, which increases with placental enlargement and the release of insulin antagonists such as human placental lactogen. These changes may be adaptive, providing an optimal environment for fetal growth and development, as glucose is the major substrate for the fetus. Maternal blood glucose levels determine fetal levels, which are normally 10–15% lower.

Pregnancy is thus a diabetogenic state and susceptible individuals are at risk of developing gestational diabetes. A good knowledge of the profound metabolic changes of pregnancy is essential when providing care for diabetic mothers and their fetuses.

Pituitary

Like the other endocrine glands, the pituitary expands during pregnancy, increasing in size by 135%[70]; despite this, compression of the optic chiasma does not occur. Prolactin levels increase throughout pregnancy, peaking at term, and further changes may occur in the puerperium if breastfeeding is established. Prolactin appears to prepare the breasts for lactation by stimulating glandular epithelial cell mitoses and increasing production of lactose and lipids. Microprolactinomas (<10 mm) generally cause no problems in pregnancy, with the risk of symptomatic expansion of the order of 1.5%.[71] Macroprolactinomas (>10 mm) can be more troublesome, with symptomatic expansion in 4% of treated and 15% of untreated patients[71]; therefore, most physicians continue dopamine antagonists throughout the pregnancy.

BLOOD GAS ANALYSIS

Acid–base homeostasis

The concentration of hydrogen ions in the body is very tightly controlled, and this is reflected in its nanomolar range (36–43 nmol/L) rather than the usual millimolar range. This

degree of control is necessary as hydrogen ions, by virtue of their high charge density and large electrical field, influence nearly all biochemical processes, including protein structure and function, ionic dissociation and movement, and drug or chemical interactions.

The pH is the negative log of the hydrogen ion $[H^+]$ concentration; the normal value at $37\,^{\circ}C$ is 7.34–7.42, equivalent to the range discussed above. The primary source of acid is from cellular respiration as carbon dioxide from carbonic acid (15 000–20 000 nmol H^+/day), and the metabolism of proteins and fats provides a much smaller contribution (50 mmol/day).

Three different mechanisms act at different levels within the body to regulate pH:

- a rapidly responsive system – the respiratory centre regulates alveolar ventilation and controls PaCO2. As [H+] increases, ventilation increases and the amount of carbon dioxide expired from the lungs is increased.
- A slower system – renal control of bicarbonate and excretion of metabolic acids.
- The ever-present system – bicarbonate, sulphate and haemoglobin act as buffers to minimize acute change in acid–base homeostasis.

The Henderson-Hesselbach equation has been used to analyse and interpret clinical acid–base problems. It describes the carbonic acid buffer system, fundamental to the respiratory and renal control of pH. It defines pH as a function of carbon dioxide and bicarbonate in concentrations in aqueous solutions, but is limited as the bicarbonate concentration varies according to the amount of dissolved carbon dioxide. This is partly overcome using the anion gap or base excess.

pH is the ratio of bicarbonate to carbon dioxide; therefore, alterations in acid–base are due to changes in carbon dioxide (respiratory component) or bicarbonate (metabolic component), and various compensatory mechanisms exist to maintain this ratio at safe and functional levels (normally 20:1).

One of the main limitations of the Henderson-Hesselbach equation is in its inability to quantify metabolic derangement as clearly as respiratory derangement, because bicarbonate is dependent on pCO_2 in vivo. This led to the concepts of standard bicarbonate and base excess to help quantify metabolic derangements.

Stewart's strong ion theory of acid–base is a newer mathematically based concept that describes acid–base balance in the context of abnormalities in electrolytes and albumin. It helps to clarify the mechanisms of common metabolic disturbances seen in critically ill patients that are not easily explained by the conventional Henderson-Hesselbach model.[72]

Effect of pregnancy physiology

In normal pregnancy, the respiratory system undergoes significant changes; therefore, arterial blood gas analysis needs to take account of this at any stage of gestation.

Summary of important physiological changes:

- Increase in minute ventilation by 30–50%
- Decrease in alveolar and arterial pCO_2

The fetus relies on maternal respiration for excretion of carbon dioxide. As the maternal pCO_2 falls, this creates a gradient which allows the fetus to offload carbon dioxide. If the uteroplacental perfusion is normal, fetal pCO_2 is usually 10 mmHg higher than maternal pCO_2.

Despite these observed changes in ventilation, maternal pH is fairly constant throughout pregnancy. In order to compensate for the lower levels of pCO_2, the kidneys excrete more bicarbonate but serum bicarbonate levels remain between 18 and 21 mEq/L. The cumulative result of all these changes is that the metabolic state of pregnancy is a chronic respiratory alkalosis with a compensated metabolic acidosis.

Interpretation

Correct interpretation of blood gas results is fundamental to the management of patients requiring high-dependency care. The results can be very complicated, but in the vast majority of cases, interpretation can be aided by a systematic approach and several have been devised.[73,74]

Due to the unique physiology of pregnancy, a modification of the six-step approach of Morganroth[75] has been proposed, as follows.[76]

1. Acidaemia pH <7.36 or alkalaemia pH >7.44?
2. Is the primary aetiology respiratory or acidotic? For pCO_2 and bicarbonate, there are four basic types of disorder (Table 1).
3. If respiratory, is it acute or chronic? Mathematical formulae are used to calculate the expected change in pH, and the measured pH is compared with the pH that would be expected based on the patient's $PaCO_2$.

   Acute (pH Δ 0.08 per pCO_2 Δ 10 mmHg)
   Chronic (pH Δ 0.03 per pCO_2 Δ 10 mmHg)

4. If metabolic acidosis, is the anion gap increased? Different types of metabolic acidosis are classified according to the presence or absence of an 'anion gap'. The anion gap is calculated as $(Na^+ + K^+)$ $(Cl^- + HCO_3^-)$ although, in daily practice, K^+ is frequently omitted. The anion gap is representative of the unmeasured anions in the plasma, and these anions are affected differently based on the type of metabolic acidosis. The primary function of the anion gap measurement is to allow a clinician to narrow down the possible causes of a patient's metabolic acidosis.

The anion gap can be classified as either high, normal or, in rare cases, low. A high anion gap indicates that there is loss of bicarbonate without a subsequent increase in Cl^-. Electroneutrality is maintained by the increased production of unmeasured anions such as ketones, lactate, PO_4^- and SO_4^-; these anions are not part of the anion gap calculation and therefore a high anion gap results. In patients with a normal anion gap, the drop in bicarbonate is compensated by an increase in Cl^- and hence is also known as 'hyperchloraemic acidosis'. Causes of metabolic acidosis are shown in Table 2.

Table 1. Commonest acid-base disorders.

	Primary disturbance	Compensatory response
Metabolic acidosis	$\downarrow HCO_3$	$\downarrow pCO_2$
Metabolic alkalosis	$\uparrow HCO_3$	$\uparrow pCO_2$
Respiratory acidosis	$\uparrow pCO_2$	$\uparrow HCO_3$
Respiratory alkalosis	$\downarrow pCO_2$	$\downarrow HCO_3$

Table 2. Causes of metabolic acidosis.	
High anion gap >18 mmol/L	Normal anion gap <18 mmol/L
Ketoacidosis	Vomiting and/or diarrhoea
Lactic acidosis	Small bowel fistula
Acute renal failure	Renal tubular acidosis
Salicylate poisoning	Renal failure

5. If a metabolic component is present, is there adequate respiratory compensation? This is an important consideration because if there is adequate compensation, it implies that the patient has sufficient physiological reserve to mount a robust response to the underlying problem.

$pCO_2 = (1.5 \times$ serum $HCO_3) + (8 +/-2)$ if there is adequate compensation; if not, this suggests that a concomitant respiratory problem exists (Winter's formula).

6. If there is an anion gap metabolic acidosis (AGMA), is there a concomitant disturbance? Calculate the delta gap: $(= \Delta$anion gap $- \Delta HCO_3) = ($anion gap $- 12) - (24 - HCO_3)$

If the delta gap >6, there is a combination of AGMA and metabolic alkalosis. If the delta gap <-6, there is a combined AGMA and non-anion gap metabolic acidosis (NAGMA).

At this stage, we are entering rather advanced arterial blood gas (ABG) analysis and expert assistance is certainly recommended.

A basic knowledge of the common acid–base disorders is essential in the management of high-dependency patients. Adherence to a basic step-wise approach to blood gas interpretation should help attending personnel to understand metabolic disturbances and act quickly to treat the underlying cause.

PHYSIOLOGICAL MONITORING

Monitoring of physiological parameters is of vital importance in the high-dependency setting. Basic observations such as pulse, blood pressure and respiratory rate are the mainstay of physiological monitoring, but the newer, advanced monitoring systems can provide full central haemodynamic profiles, and the detection of changes in a patient's condition can facilitate the instigation of corrective treatments at the earliest opportunity.

Blood pressure

Blood pressure (or, more accurately, vascular pressure) represents the ability of the cardiovascular system to perfuse the maternal organs and the feto-placental unit. It is the product of CO and SVR. Systolic arterial pressure is defined as the peak pressure in the arteries, which occurs near the beginning of the cardiac cycle; the diastolic arterial pressure is the lowest pressure (at the resting phase of the cardiac cycle). The average pressure throughout the cardiac cycle is reported as mean arterial pressure; the pulse pressure reflects the difference between the maximum and minimum pressures measured.

Traditional methods

Several factors influence maternal blood pressure including gestational age, position and measurement technique. Despite the recommendations of several authorities to try and reduce measurement errors[77,78], evidence suggests that clinicians continue to make basic errors such as failure to use appropriate-sized cuffs[79] and rounding up of values to the nearest 5–10 mmHg.[80]

Debate has surrounded the best method of measuring diastolic blood pressure. Korotkoff Phase IV (muffled sound) is favoured by some groups as the most accurate measure of intra-arterial pressure in pregnancy, arguing that Phase V is very low or zero and therefore of little use, although this contention is not supported by more recent studies.[81] Invasive methods produce lower readings than conventional sphygmomanometry[82], and this is important to note in the high-dependency setting.

Automated methods

Due to the limitations of 'gold standard' mercury sphygmomanometers, a variety of auscultation-independent alternatives have been introduced. However, many systemically underestimate both systolic and diastolic blood pressure in pre-eclamptic patients, and are therefore not suitable for use in pregnancy.[83] The British Hypertension Society and the Association for the Advancement of Medical Instrumentation are the only bodies that have produced rigorous protocols for the assessment of devices for use in pregnancy, but neither of them make specific provision for pre-eclampsia. At present, only two devices have been validated for use in pre-eclampsia.[84,85]

Ambulatory methods

These overcome many of the limitations of conventional blood pressure monitoring by providing objective, accurate information away from the clinical setting. There are many ambulatory monitoring systems on the market, but is important that these are validated properly for use in pregnancy before they are introduced into routine clinical practice. Several systems have been tested in pregnancy and validated reference ranges are available.[86–88]

Pulse oximetry

This is a simple method of monitoring haemoglobin saturation via a small finger or ear lobe probe. The probes are linked to a computerized system which records and displays the estimated percentage of haemoglobin saturated with oxygen along with an audible signal. Normal levels can be programmed in, and alarms can be triggered if the results deviate from normal levels.

The systems are accurate for saturation readings of 70–100% ($+/-$ 2%), and alert the carer to falling levels of oxygenation before central cyanosis occurs. However, these systems do have several limitations, as follows:

- poor peripheral blood flows produce poor signals, e.g. hypotension;
- venous congestion, e.g. secondary to tricuspid regurgitation, can produce pulsatile flows with low readings in the ear probes;
- cannot distinguish between different forms of haemoglobin, e.g. carboxy-haemoglobin, which leads to overestimates of oxygenation;
- severe anaemia causes inaccurate readings;

- produce no information regarding level of carbon dioxide, limiting the assessment of patients with respiratory failure; and
- can be affected by bright lights, nail varnish and shivering.

The results obtained should always be interpreted in the context of the clinical condition, and low values should never be ignored. The technique is of value in the continuous monitoring of the adequacy of blood oxygenation, but cannot quantitate the level of impaired gas exchange.[89]

Maternal pulse oximetry readings are dependent on gestational age and position, e.g. supine/left lateral.

Haemodynamic monitoring systems

Management of CO is integral to providing effective care to high-risk peri-operative and critical care patients. Since this parameter cannot be assessed adequately by direct clinical examination, a reliable means of measurement is required.[90]

The 'Fick' principle refers to the concept of determining blood flow over time by measuring the dilution of a known substance in the blood. This led to the development of the thermodilution technique, using a pulmonary catheter, which remains the 'gold standard' approach to haemodynamic monitoring.

Traditional management consists of measuring physiological criteria and reacting to these with individual therapies rather than by maintaining optimal physiological goals prophylactically. 'Goal-directed' therapy is a relatively recent, and controversial, concept in the management of surgical or critically ill patients, which aims to increase oxygen delivery to tissues up to levels consistent with survivors of major surgery. The observation that survivors of high-risk surgical procedures tend to have higher CO and oxygen delivery[91] led to the assumption by Shoemaker that improved outcome can be achieved by manipulating the haemodynamics of surgical patients to 'supranormal' levels using fluids and inotropes.[92] A recent meta-analysis of haemodynamic optimization has demonstrated statistically significantly reductions in mortality.[93]

Invasive methods

Pulmonary artery catheters. In recent years, there have been major concerns regarding the risks of pulmonary artery catheters (PACs), either as a direct consequence of their insertion (e.g. damage to major vessels, pneumothorax, arrhythmias and trauma to the heart) or as a result of inappropriate treatments based on the results obtained.[94–96] These prompted the US Food and Drug Administration and the National Heart, Lung and Blood Institute to develop recommendations for the safe use of PACs, with particular emphasis on the education of those involved in catheter insertion and interpretation of results obtained. Nonetheless, PACs can provide a very large amount of accurate information, much of which is measured more directly than some of the newer systems, which derive most of their data via arterial waveforms using very complex mathematical algorithms.

Historically, PACs only measured pulmonary artery and pulmonary capillary wedge pressure (PCWP), but modifications now provide accurate measurement of CO and right ventricular ejection fraction by thermodilution, and allow infusion of drugs, blood sampling, pacing of the atrium and ventricle, and measurement of continuous mixed venous oxygen saturation, and have been shown to be valuable diagnostic and

monitoring tools in the critically ill.[97] The modern systems can also derive many other cardiorespiratory parameters including right ventricular end-diastolic volume.

Recent trial data have suggested that when the use of PACs is confined to the critically ill, mortality is not increased.[98] However, closer inspection of the data revealed a significant increase in renal failure and thrombocytopenia in the PAC group, which just adds to the confusion.

Pregnancy physiology, particularly those alterations that occur in pre-eclampsia, make the sole use of central venous pressure (CVP) monitoring to guide fluid therapy rather hazardous. In normal non-pregnant individuals, right atrial pressure is usually equal to CVP (right atrial filling pressure) and PCWP (left atrial filling pressure). In pre-eclampsia, where women are very fluid sensitive, the relationship is more variable.[99,100] One concern is that as CVP is often used in isolation, as a measure of volume status, pre-eclamptic women with significant CVP-PCWP gradients may develop iatrogenic pulmonary oedema as a result of small boluses of fluid. Wallenberg's study of 50 patients provided some reassurance[101]; he noted that in no case where CVP was ≤ 4 mmHg was PCWP >12 mmHg (a value >16 mmHg increases the risk of pulmonary oedema). It has been argued that resetting the CVP target from 8 mmHg down to 4 mmHg reduces the risk of fluid overload, although data from Cotton's group found that 23 of 51 (51%) women with pre-eclampsia were hypovolaemic (CVP <3 mmHg) but only one-third of them had a low PCWP.[102]

The use of pulmonary catheters in pregnancy has been restricted to either research into baseline haemodynamic data in normal and hypertensive pregnancies[9,99,103] or clinical use in the intensive care setting. In the wake of the negative press they have received in the last two decades, it is unlikely that such systems will flourish in modern obstetric high-dependency units.

Newer and less invasive monitoring systems are becoming increasingly available, but as with all new mechanical devices/techniques proposed for use in pregnancy, it is of utmost importance that they are properly validated prior to introduction into routine clinical practice.

Pulse contour/power analysis. Traditional invasive haemodynamic monitors do not produce real-time continuous beat-to-beat data for dynamic assessment of central haemodynamics in high-dependency or critically ill patients. By contrast, modern methods of assessing CO provide real-time data by utilizing arterial waveforms. There are three such systems in current use. PiCCO and LiDCO require calibration using indicator methods, and Flotrac operates without the need for calibration.

Arterial pressure waveform analysis. Arterial pressure analysis is not a new concept. It was first proposed in 1904[104] by Erlanger and Hooker, and has undergone many modifications and improvements over the last century. Most algorithms need to determine the systolic portion of the arterial pressure curve accurately, and estimate arterial compliance and its spontaneous or therapeutic changes over time.[105] Contour analysis, e.g. the PiCCO system, uses wave morphology to derive measures of stroke volume, whereas the PulseCO (LiDCO) system uses pulse power analysis. The main difference is that pulse power analysis is based on the assumption that the net power change in a heartbeat is the result of a mass of blood (stroke volume) minus the blood mass lost to the periphery during the beat, and it utilizes the whole beat and not just the systolic portion.[106]

This latter method has several theoretical advantages: central or peripheral arterial sites can be used, the effects of damping are less, and the system can be calibrated with

any form of accurate CO measurement. Few studies have assessed the value of pulse contour methods to track changes in unstable conditions.[107–110]

LiDCOplus (LiDCO Ltd, Cambridge, UK). The LiDCO*plus* system is combination of two innovative and novel monitors: the LiDCO System indicator dilution CO monitor and the PulseCO System real-time continuous arterial waveform monitor. The system has been validated extensively against thermodilution in paediatrics[111], adults[112] and horses.[113] It provides calibrated, continuous, real-time beat-to-beat CO with high precision and lower risk than pulmonary catheterization.[114]

The technique is simple to operate and requires the presence of an arterial line and either central or peripheral venous access.[115] For calibration, a small dose of lithium 0.3 mmol/L is injected, and a concentration time curve is generated by a lithium sensor attached to the arterial line. CO is calculated using the lithium dose and the area under the curve, prior to recirculation. Recent serum haemoglobin and sodium chloride measurements are also required for calibration purposes, plus maternal height and weight to generate indexed values.

Lithium is perfect for indicator dilution as there is no significant first-pass metabolism or loss from the pulmonary circulation, and it is redistributed rapidly.[116] The dose chosen has no pharmacogical effect and it would need to be exceeded many times before reaching toxic levels.[117]

The PulseCO system is used in conjunction with LiDCO to provide real-time, continuous CO. Stroke volume is calculated by a proprietary algorithm using beat duration, ejection duration, mean arterial pressure, and the modulus and phase of the first waveform harmonic.[118] The monitor clearly displays accurate haemodynamic information and remains accurate and reliable over a range of haemodynamic states in surgical, postoperative and intensive care settings.[119] Despite all these features, more recent experimental data from dogs draw into question the dynamic monitoring capabilities of the system during haemorrhage[119]; a problem which could be overcome by recalibration.

PiCCO system (Pulsion Medical Systems AG, Munich, Germany). This is a similar system to LiDCO*plus* in that it produces the same sort of continuous haemodynamic data, but there are two main differences: it uses a traditional thermodilution method for measurement of absolute CO, and pulse contour rather than pulse pressure analysis is used to generate continuous beat-to-beat CO. It also requires a central venous catheter, whereas LiDCO can calibrate via a peripheral line.

PiCCO is proven in clinical practice, and for many, this system has replaced the use of pulmonary catheters in the critically ill.[120] It also provides invaluable information on intrathoracic lung volumes (as does LiDCO*plus*), and extracellular lung volumes and evidence are emerging that volume-based assessment of intravascular filling associated with continuous CO can deliver levels of prediction of CO changes that might be superior to those obtained with older technology.[121]

FloTrac sensor and Vigileo monitor (Edwards Lifesciences, Irvine, CA, USA). This new system uses arterial pressure waveform analysis technology, based on the principle that aortic pulse pressure is proportional to stroke volume and inversely proportional to aortic compliance. This technology uses statistical analysis of 20-s windows of radial artery pressure waveforms in conjunction with estimates for compliance, and incorporates patient demographics into its calculations. It is unique in that it does not need calibration and is currently the least invasive of all the systems available. However, it is somewhat limited in comparison with LiDCO and PiCCO in that it fails to provide truly

continuous real-time data. Although relatively new, it has been validated against inter-
mittent thermodilution techniques and other PCA systems; some studies have
suggested reasonable correlations[122,123] and others have been less convincing.[124–126]

    None of these systems have been formally validated for use in pregnancy, and very
few articles have been published to date. The authors have recently finished evaluating
the LiDCO system in normal pregnancy – chosen as the least invasive of the systems
available at the time – and found it to be simple to use, safe, reliable and capable of
providing high-quality haemodynamic information in stable patients at term undergoing
caesarean section (unpublished data). With increasing knowledge and experience,
haemodynamic monitors and the information they provide may become integral to
the management of high-dependency obstetric patients. This may eventually enable
us to move away from the current protocol-driven, 'one fits all' approach.

Non-invasive methods

Thermodilution is the 'gold standard' against which all other methods are measured.
    Other non-invasive alternatives are now available and each will be discussed in turn.

Thoracic bioimpedance. This concept was first introduced in 1966 by Kubicek et al.[127]
Four electrodes are attached to the neck and chest, and a small electrical current is
passed across the thorax. Impedance plethysmography produces a waveform which
is then used to measure the pulsatile changes in resistance occurring during ventricular
systole and diastole. Stroke volume is calculated from changes in transthoracic imped-
ance, and CO is derived using this measurement and ventricular ejection fraction. This
method is simple to use, apparently safe and requires no specialist skills. It is, however,
potentially limited by lung fluid shifts and changes in haematocrit, and has failed to gain
widespread acceptance due to the large variations in methodology and electrode
placements used and signal processing issues.[128,129] It also seems to overestimate
low CO and underestimate CO in high output states, which could have serious
consequences in the clinical management of pre-eclamptic patients. Despite these
potential problems, thoracic electrical bioimpedance has been validated for use in
pregnancy.[130] Digital processing of the bioimpedance waveform plus modifications of
the Sramek-Bernstein equations have substantially increased the precision and reliabil-
ity of the 'new breed' of bioimpedance monitors, and in time, may ultimately make it
a realistic alternative to more traditional invasive methods.[131] Further developments
have made it possible for thoracic electrical bioimpedance to be used in longitudinal
assessments of haemodynamic variations in pregnancy[132], but although the method
continues to feature in the obstetric journals, it remains primarily a research tool.

Echocardiography
    Transthoracic echocardiography. The assessment of haemodynamic variables using
Doppler ultrasound began in the 1980s, and was formally validated for use in
pregnancy and pre-eclampsia by Easterling et al in 1987.[10] Estimation of flow and
pressure permits calculation of vascular resistance, and stroke volume is calculated
as the product of the cross-sectional area of the aortic outlet in systole and the
time velocity integral, either using pulsed-wave or continuous-wave Doppler.
    Various studies have utilized this technique in the study of both normal pregnan-
cies[133] and those complicated by hypertension.[10,13] Echocardiography has also been
validated against 'gold standard' invasive monitoring in critically ill patients[134]; however,
the value of this technique over and above pulmonary catheters is in its ability to

visualize the heart, thus gaining direct information regarding filling, ventricular perfor-
mance and valvular dysfunction.

With some basic training, useful assessments of left ventricular function, valve
dysfunction and diagnosis of effusions can be made by trainees with minimal experi-
ence[135,136], although consultation with an appropriate specialist is recommended prior
to the initiation or alteration of treatment on the basis of such scans.[137]

Handheld echocardiography is becoming established in adult intensive care, but has
not yet featured in the obstetric medical literature. However, the authors believe that
is only a matter of time before this very useful technique draws the attention of those
involved in high-dependency obstetric care to complement the current management of
massive haemorrhage and severe pre-eclampsia.

Transoesophageal echocardiography. This modality is extremely useful in non-
pregnant patients in the critical care setting, and provides quality data equivalent to
that produced by thermodilution.[138] In addition to information regarding the status
of the valves, its primary role in critical care is for haemodynamic monitoring, but it
has also been used to direct intra-operative fluid management.[139]

Data regarding transoesophageal echocardiography in pregnancy is rather scanty; to
date, only one study has attempted to compare this method with thermodilution,
consistently demonstrating underestimates of CO in up to 40% of cases.[140]

Modelflow (Portapres; Finapres Medical Systems, Amsterdam, the Netherlands)

This is a completely non-invasive haemodynamic monitoring system that uses finger
arterial pressure and algorithms to compute the aortic flow waveform from arterial
blood pressure. It is a reliable tool for providing beat-to-beat blood pressure readings
in non-pregnant adults[141] and pregnant women.[142] By using appropriate Beatscope soft-
ware, the system also provides some limited but continuous haemodynamic data via the
arterial pressure waveform.[143,144] It has been investigated for use in pregnancy, but con-
sistently underestimates stroke volume. Despite some adjustments made for alterations
in pregnancy physiology, there is still a 30% random variation between Modelflow and
Doppler echocardiography. However, as it is truly non-invasive, with further improve-
ments in waveform detection and analysis, it may prove attractive for research purposes.

OBSERVATION CHARTS

All areas of clinical care require an effective and efficient means of recording physio-
logical data from patients, regardless of whether it is derived from simple examination
or more complex medical devices. The accurate charting of this information allows
trends to be analysed over time, which can then be used to monitor a patient's
recovery or detect clinical deterioration.

The information charted is only useful clinically if the observations are correctly
obtained, recorded, shared and interpreted. Most clinical information in high-
dependency and critical care areas is now obtained automatically, but without correct
application and validation of pulse oximeters, blood pressure cuffs/machines and the
appropriate setting of ventilation equipment and invasive devices, the quality of the
observations obtained will be compromised.

It is interesting, although not surprising, that despite such widespread use in clinical
care, observation charts have not been validated, and research in this area is limited.
The authors could only find one publication addressing this issue, which focused on
evidence-based design and redesign of observation charts, in conjunction with staff

retraining.[145] The study demonstrated significant improvements in the detection rates of all parameters of physiological decline, by objectively quantifying chart performance and optimizing the presentation of data.

With the advent of sophisticated and fully networked electronic patient record systems, physiological information can now be recorded directly into individual patient monitors, which in theory will eliminate the risk of transcription errors and also provide an easily accessible historical archive, useful for both ongoing care and audit/research purposes.

SUMMARY

All those involved in the management of high-dependency obstetric patients should have a comprehensive knowledge of the normal physiological changes that accompany pregnancy. An awareness of these changes is vitally important when managing pregnancies that develop either de-novo complications, such as pre-eclampsia, or problems that result from pre-existing medical conditions.

Organization of care should be co-ordinated through a multidisciplinary team approach, and the use of appropriately validated, physiological monitoring systems should be encouraged, as per national recommendations. Furthermore, as technology advances, sophisticated haemodynamic monitors may become more readily available, enabling us to improve and optimize our patient's care. However, any proposed alterations to existing management protocols should only occur after an appropriate period of robust validation and assessment in pregnant populations.

Practice points

- a sound working knowledge of maternal physiology is an essential pre-requisite for all those involved in the care of high-risk obstetric patients
- the most profound physiological changes occur in the cardiovascular system, starting early in the first trimester
- CO rises by 30–50%, peaking at approximately 24 weeks of gestation, and SVR and blood pressure fall early in pregnancy, probably due to peripheral vasodilatation, returning to pre-pregnancy levels by term
- PACs are the 'gold standard' for haemodynamic monitoring, but have been associated with poorer outcomes in the critically ill. This may be secondary to complications of insertion or inappropriate interpretation of the measurements obtained
- newer, less invasive monitors are now available and may be of use in the management of high-risk patients, but these need to be formally evaluated and validated for use in pregnancy

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Research agenda

- determine the precise mechanism behind the peripheral vasodilatation seen in early pregnancy, which may increase understanding of pathological pregnancies
- establish the potential usefulness of minimally invasive monitoring systems to improve clinical outcomes in high-dependency obstetrics

CONFLICT OF INTEREST

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