

## Capillary blood gases - to arterialize or not

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The 'gold standard' sample for blood gas analysis is arterial blood obtained via an indwelling arterial catheter or by arterial puncture. For a number of reasons capillary blood is an attractive substitute sample that is routinely used in some clinical settings.

The purpose of this article is to examine the evidence that blood gas parameter values (pH,  $p\text{CO}_2$  and  $p\text{O}_2$ ) obtained from a capillary blood sample accurately reflect arterial blood.

There is conflicting opinion that increasing local blood flow (by warming or application of vasodilating agent) prior to capillary blood sampling is necessary for most accurate results and this controversial issue will be addressed.

Note: The unit of  $p\text{CO}_2$  and  $p\text{O}_2$  measurement used in this article is kPa - to convert kPa to mmHg divide by 0.133.

Blood gas analyzers measure blood pH and the oxygen and carbon dioxide tensions of blood ( $p\text{CO}_2$  and  $p\text{O}_2$ ).

These measurements along with parameters (bicarbonate, base excess etc) derived by calculation from these measurements allow evaluation of acid-base status and adequacy of ventilation and oxygenation.

Thus blood gas analysis is helpful for assessment and monitoring of patients suffering a range of metabolic disturbances and respiratory diseases both acute and chronic; it is an important component of the physiological monitoring that critically ill patients, particularly those being mechanically ventilated, require.

The 'gold standard' sample for blood gas analysis is arterial blood obtained anaerobically via an indwelling arterial catheter (most often sited at the radial artery in adults and the umbilical artery in neonates), or arterial puncture.

In an intensive care setting where patients may require frequent (perhaps two hourly) blood gas testing, arterial catheterization may be justified because it allows not only convenient and painless access to arterial blood but also continuous blood pressure monitoring.

Placing an arterial catheter is however an invasive, painful and technically difficult procedure [1], which is associated with risk of serious complications including systemic infection, hemorrhage, thrombosis and ischemia [2].

Technical and safety considerations determine that for most patients who require blood gas analysis placement of an arterial catheter is either not justified or justified for only a limited period, so that arterial blood is most often sampled by arterial puncture using needle and syringe.

The most usual puncture site is the radial artery in the wrist; alternative sites include the brachial artery in the arm and femoral artery in the groin. Although arterial puncture does not place patients at risk of the serious complications associated with arterial catheterization, it is potentially hazardous and certainly not risk free [3].

Furthermore it is a painful procedure that is reported by patients to be significantly more painful than venous puncture [4]. Specialist training in arterial puncture is essential for patient safety and comfort, and in many countries obtaining arterial blood is the almost exclusive preserve of medically qualified staff.

Capillary blood can be obtained by near painless [5] skin puncture using a lancet or automated incision device that punctures the skin to a depth of just 1mm [6,18]. It is the least invasive and safest blood collecting technique and can be performed by all healthcare personnel after minimal training [9].

The relative simplicity and safety profile of capillary blood sampling and the necessity for only small volumes (100-150  $\mu$ L) of blood for pH and gas analysis make capillary blood an attractive substitute for arterial blood, particularly among neonates and infants, but also adults.

However the clinical value of capillary blood gas results depends on the extent to which pH,  $p\text{CO}_2$  and  $p\text{O}_2$  of capillary blood accurately reflect pH,  $p\text{CO}_2$  and  $p\text{O}_2$  of arterial blood.

## Capillary and arterial blood - some theoretical considerations

With a diameter of just 8  $\mu$ m, capillaries are the smallest blood vessel. They are the connection between arterioles (the smallest artery) and venules (the smallest vein) and thus between the arterial and venous sides of the circulatory system.

The capillary network (see FIGURE 1) is the site of nutrient and waste exchange between blood and tissue cells, made possible by the single cell (1  $\mu$ m) thickness of the capillary wall.

Oxygenated arterial blood arriving via arterioles at the capillary network yields up its oxygen and other essential nutrients to tissue cells as carbon dioxide and other waste products of metabolism are added to blood for transport from tissue cells via venules and the venous system.

As a consequence of these exchanges there is a pH,  $p\text{CO}_2$  and  $p\text{O}_2$  gradient across the capillary network (from arteriole to venule), known as the arteriovenous (AV) difference.

Thus for example, the  $p\text{O}_2$  of blood in arterioles is normally 13 kPa, but following loss of oxygen to tissues only 5 kPa in venules, giving an AV difference for  $p\text{O}_2$  of approximately 8 kPa [7]. The normal AV differences for pH and  $p\text{CO}_2$  are of the order 0.02–0.03 pH units and 0.6–0.7 kPa, respectively [8].

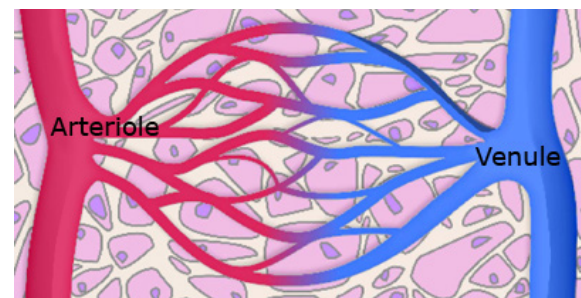


FIGURE 1: Capillary Network

Arterial blood		AV Difference		Venous Blood	
pH	7.40	pH	0.02	pH	7.38
$p\text{CO}_2$	5.3 kPa	$p\text{CO}_2$	0.7	$p\text{CO}_2$	6.0
$p\text{O}_2$	13.0 kPa	$p\text{O}_2$	8.0	$p\text{O}_2$	5.0

Given the anatomical relationship of capillaries to arterioles and venules, it might be supposed that the pH,  $p\text{CO}_2$  and  $p\text{O}_2$  of capillary blood would lie roughly midway between arterial and venous values.

That is however not the case because blood obtained by skin puncture is not actually pure capillary blood, but a mixture of blood from punctured arterioles, capillaries and venules (along with a small but variable contribution of interstitial fluid and intracellular fluid from damaged tissue cells) [9].

Due to the relative high pressure on the arterial side of the circulation, this blood mixture contains a relatively greater proportion of blood from the arteriole side of the capillary bed than from the venule side, and thus a 'capillary' blood sample obtained by skin puncture approximates closer to arterial blood than venous blood.

This is the theoretical justification for the use of capillary blood as a substitute for arterial blood.

AV difference is clearly a major theoretical determinant of difference between arterial and capillary blood gas values. The greater the AV difference the worse the agreement [10].

By this argument it can be predicted that  $p\text{O}_2$  (which exhibits a relatively high AV difference) is less likely to show good agreement between capillary and arterial blood than  $p\text{CO}_2$  and pH (which both, by comparison, have a low AV difference).

Furthermore reduced  $p\text{O}_2$  (hypoxemia) is associated with reduction in AV difference and hyperoxemia with increased AV difference [7]. Thus there is good theoretical reason to suppose that capillary and arterial blood  $p\text{O}_2$  will agree more closely if arterial  $p\text{O}_2$  is reduced than if arterial  $p\text{O}_2$  is normal or raised.

So long as tissue oxygen consumption and carbon dioxide production remains unchanged, as is the case in the resting state, increasing blood flow through the capillary bed has the effect of reducing AV difference and thereby the difference between arterial and capillary pH,  $p\text{CO}_2$  and  $p\text{O}_2$ .

This provides the rationale for strategies such as pre-warming the puncture site or treating the puncture site with vasoactive agents prior to capillary blood sampling.

The increased local blood flow that is presumed to occur when these pre-sampling strategies are adopted, theoretically at least, leads to so called 'arterialization' of capillary blood and pH,  $p\text{CO}_2$  and  $p\text{O}_2$  values that more accurately reflect those of arterial blood.

### Arterial and capillary blood gas pH, $p\text{CO}_2$ & $p\text{O}_2$ - study findings

Several studies of healthy individuals have defined reference ranges for capillary blood pH,  $p\text{CO}_2$  and  $p\text{O}_2$  [11,12]. The results of at least one [11] demonstrate that for healthy adults, sampling 'arterialized' capillary blood provides results that are not significantly different from those obtained from arterial blood (see TABLE 1).

Of greater significance are the many more studies conducted over the past 40 years [10,13-27] that have compared blood gas values of simultaneously collected capillary and arterial blood in patients whose clinical condition demands blood gas analysis.

In general they have revealed that whilst capillary blood pH and  $p\text{CO}_2$  reflects arterial pH and  $p\text{CO}_2$  sufficiently accurately for clinical purposes, that may not be the case for  $p\text{O}_2$ . Studies in this area have focused exclusively on either pediatric patients (mostly neonates) [13-21] or adult patients [10,21-27].

	Arterial	Capillary
pH	7.35-7.45	7.402 (mean only)
Hydrogen ion conc (mmol/L)	35-45	37-43
$p\text{CO}_2$ (kPa)	4.7-6.0	4.8-6.0
$p\text{O}_2$ (kPa)	10.6-13.3	11.2-14.5
Capillary values derived from 103 healthy adults (aged 18-24 yrs) Ref [11]		

TABLE 1: Reference ranges for arterial and "arterialised" capillary blood

## Studies of pediatric patients

The capillary blood for all studies of neonates and young infants [13–16,18,20] was sampled by heel stab. The method of arterialization was almost exclusively heel warming, usually by immersing the heel in warm water (40–45 °C) for 5–10 minutes prior to heel stab, or using a warmed surgical plastic device [18].

The rather cumbersome method of histamine iontophoresis was used to arterialize capillary blood of neonates in one early study [15]. Finger stab was the preferred site for sampling capillary blood from children [17,19].

The vast majority of studies reveal clinically acceptable agreement between capillary and arterial pH - a difference of less than 0.05 pH units being considered clinically insignificant [16,17].

In one study [19] of 75 paired samples the mean of capillary pH results was identical to the mean of arterial results and in all other studies the mean difference ranged from 0.001 pH units [14] to 0.02 pH units [20].

One of the larger studies in which 158 paired samples from 41 preterm neonates were compared [16], despite a mean difference of just 0.001 pH units, 24 % of paired samples gave clinically discrepant results (i.e. a difference of > 0.05 pH units).

This however did not detract the authors from the conclusion that capillary blood is a 'satisfactory' alternative to arterial blood for measurement of pH. Closer agreement was revealed by a later study [17] of 50 babies and children being cared for in a pediatric intensive care unit.

Here the mean difference between capillary and arterial pH was just 0.009 pH units (95 % limits of agreement  $\pm$  0.032) and in no patient was there a difference greater than 0.05 pH units. Johnson *et al* [18] and Hunt [15] reported no significant difference between capillary and arterial pH of 21 sick neonates (aged from three hours to seven days) and 44 sick babies (aged 3.5 days to 10 weeks).

In common with pH, most studies reveal clinically acceptable agreement between 'arterialized' capillary  $p\text{CO}_2$  and arterial  $p\text{CO}_2$  - a difference of less than 1 kPa [16] or less than 0.87 kPa [17] being considered clinically insignificant.

All studies revealed the same bias with mean of capillary  $p\text{CO}_2$  values greater than the mean of arterial  $p\text{CO}_2$ , although this difference was in most studies small, ranging from 0.04 kPa [20] to 0.21 kPa [17].

This last study [17] showed clinically discrepant results (difference greater than 0.87 kPa) in only 2/50 (4 %) paired samples. One of few studies to have revealed poor agreement was that of Hunt [15]. Here the mean difference between capillary and arterial  $p\text{CO}_2$  was 2.0 kPa.

All studies reveal a bias with regard to  $p\text{O}_2$  with mean of arterial  $p\text{O}_2$  values greater than mean of capillary  $p\text{O}_2$  values. Most studies reveal that this difference is of sufficient magnitude to conclude that there is an unacceptably low level of agreement between capillary and arterial  $p\text{O}_2$ .

McClain *et al* [16] found a mean  $p\text{O}_2$  difference of 2.4 kPa, with 84 % of paired samples differing by more than 1 kPa, 56 % differing by more than 2 kPa and 24 % differing by more than 3 ka.

They judge that difference of > 1 kPa has clinical significance. Harrison *et al* [17] found a mean difference in  $p\text{O}_2$  between the sample types of 3.3 kPa. In 42/50 (84 %) of paired samples the difference exceeded 0.87 kPa, the difference limit they had set for clinical acceptability.

Bland-Altman plot revealed that the magnitude of the difference between arterial and capillary  $p\text{O}_2$  depends on arterial  $p\text{O}_2$ . As arterial  $p\text{O}_2$  increases so too does the difference between capillary and arterial  $p\text{O}_2$ .

Conversely as arterial  $p\text{O}_2$  decreases the difference decreases. So striking was this effect that Harrison *et al* found acceptable agreement between capillary and arterial  $p\text{O}_2$  in all paired samples with arterial  $p\text{O}_2$  less than < 8 kPa.

This is in agreement with other studies that have included sufficient numbers of severely hypoxemic neonates [16,15].

### Arterialization strategies not effective

Several of these studies [15,16,18] tested the effectiveness of strategies aimed at arterializing capillary blood. Hunt *et al* [15] simultaneously collected arterialized (by histamine iontophoresis) and non-arterialized capillary samples from each study subject for comparison with arterial blood and found no difference in pH,  $p\text{CO}_2$  and  $p\text{O}_2$  results for arterialized and non-arterialized capillary samples.

Likewise Johnson *et al* [18] found that warming babies heels in a plastic molded heating device for on average seven minutes had no arterializing effect; there was no significant difference in pH,  $p\text{CO}_2$  and  $p\text{O}_2$  for capillary blood sampled from a warmed heel compared with capillary blood sampled at the same time from the contralateral unwarmed heel.

The greatest arterializing effect of heel warming was found by McLain *et al* [16], but although mean values for pH,  $p\text{CO}_2$  and  $p\text{O}_2$  of warmed heel blood were all slightly closer to mean values for arterial blood than were mean values derived from unwarmed heel blood, on statistical analysis the differences were again found to be insignificant.

These results are in accord with other recent studies [28,29] that have found heel warming has no effect in terms of improved blood flow, an indication of effective arterialization.

A study conducted nearly 50 years ago [30] provides limited evidence that heel warming is effective. This compared capillary with arterial blood pH,  $p\text{CO}_2$  (but not  $p\text{O}_2$ ) in 106 neonates (all less than two weeks old).

In total 149 sample pairs were obtained for comparison. The heel was warmed before collection of capillary blood in 126 instances. For the remaining 23 pairs, capillary blood was collected without prior heel warming.

Superior agreement was observed for both pH and  $p\text{CO}_2$  for the 126 arterial versus warmed capillary blood pairs compared with the 23 arterial versus unwarmed capillary blood pairs.

The Clinical and Laboratory Standards Institute (CLSI) document H4-A5 on the subject of capillary blood sampling states that: "The need for heel warming is not universal in the literature.

The cited references provide data showing no significant difference of analyte measurement (pH, blood gas, electrolytes) between warming and nonwarming for capillary collection.

Although studies show that prewarming may not be necessary when using a skin incision device, increasing blood flow may be necessary to prevent hemolysis and/or contamination with tissue fluids when using other devices or as a general practice."

### Studies of adult patients

The fingertip or, more commonly, the lower tip of the earlobe are the usual sites of capillary blood sampling in adults, and the most common method of arterialization is application of a vasodilating cream (e.g. Algipan) to the puncture site 5-10 minutes prior to blood sampling.

Of many studies [22–27] that have compared 'arterialized' capillary blood gases with arterial blood gases in adults, probably the most informative is a recently published meta-analysis by Gerald Zavorsky and colleagues at McGill University [27].

The database that this group recovered from 29 previously published studies comprised 664 paired samples for comparison of earlobe capillary with arterial blood and 222 paired samples for comparison of fingertip capillary blood with arterial blood. The pH of these 886 paired samples ranged from 6.77–7.74;  $p\text{CO}_2$  from 1.3–15.1 kPa and  $p\text{O}_2$  from 2.8–20.6 kPa.

Both fingertip and earlobe capillary pH were found to accurately reflect arterial pH. The mean difference

between arterial and earlobe capillary pH was  $0.01 \pm 0.02$  pH units. Regression analysis for this comparison revealed a coefficient of determination ( $r^2$ ) = 0.94 and a residual standard error of 0.025. Very similar results were found for analysis of fingertip capillary versus arterial pairs.

Capillary  $p\text{CO}_2$  values were also found to be very close to those of arterial blood.

Mean difference between arterial and earlobe capillary blood  $p\text{CO}_2$  was  $0.01\text{kPa} \pm 0.38$ . Coefficient of determination ( $r^2$ ) = 0.94; residual standard error 0.4 kPa. Although judged acceptable, agreement between fingertip capillary and arterial  $p\text{CO}_2$  was not as close as that between earlobe capillary and arterial  $p\text{CO}_2$ .

There was poor agreement between fingertip capillary and arterial  $p\text{O}_2$ . Mean difference was  $1.4 \pm 2.0$  kPa. Coefficient of determination ( $r^2$ ) = 0.48; residual standard error 2.0 kPa. By comparison, better agreement was evident between earlobe capillary and arterial  $p\text{O}_2$ .

Here mean difference was  $0.3 \pm 0.8$  kPa. Correlation of determination ( $r^2$ ) = 0.88; residual standard error 0.8 kPa. There was unequivocal evidence that agreement between capillary (both types) and arterial  $p\text{O}_2$  improves as arterial  $p\text{O}_2$  falls.

The authors of this significant study conclude that capillary blood sampled from either the fingertip or earlobe (preferably), accurately reflects arterial pH and  $p\text{CO}_2$  over a wide range of values. Sampling blood from the earlobe (but never the fingertip) may be an appropriate substitute for arterial  $p\text{O}_2$  unless precision is required.

The large standard error associated with earlobe capillary  $p\text{O}_2$  measurement limits its clinical usefulness.

## Summary

There is consensus that capillary blood is a clinically acceptable sample alternative to arterial blood if only acid-base parameters (pH and  $p\text{CO}_2$ ) are of interest.

Most studies conducted prior to the mid-1990s [5,13,22,23] suggested that capillary blood  $p\text{O}_2$  reflected arterial  $p\text{O}_2$  sufficiently accurately for clinical purposes and that capillary blood could justifiably be used as a substitute for arterial blood, not only to assess patient acid-base status, but also oxygenation status.

The results of recent studies [10,18-21,24-27] have challenged that view and the relatively poor agreement between capillary and arterial  $p\text{O}_2$ , most marked if  $p\text{O}_2$  is raised and least marked if  $p\text{O}_2$  is low, revealed by these studies, suggest that capillary  $p\text{O}_2$  results have limited clinical value and should be interpreted with caution.

Capillary blood sampled from the fingertip is particularly unsuited for assessment of oxygenation status [27]. There is really no substitute for arterial blood if accuracy of  $p\text{O}_2$  measurement is important, for example, for the prescription of long-term oxygen therapy [26].

There is evidence from several studies to suggest that the ritual of warming the heel of babies prior to sampling capillary blood is not effective in 'arterializing' capillary blood. There is little, if any, contrary evidence to suggest it is effective. The effectiveness of vasodilating agents in 'arterializing' earlobe capillary blood samples seems not to have been formally assessed.

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