Pneumatic tube transport of blood samples – an update

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The significance of good practice during the preanalytical phase of clinical laboratory investigation cannot be overemphasized. One aspect of the preanalytical phase – the transport of samples – is considered here; in particular the transport of samples via pneumatic tube systems.

This is an update of a previous article [1] that focused on pneumatic tube transport of samples destined for blood gas analysis, and aimed through literature-based research to address the question: *to what extent, if any, does transport of specimens via a pneumatic tube system invalidate blood gas results?*

This article will briefly summarize the findings of the first article and discuss two studies relevant to the question that have been published since the first article was written, a decade ago.

The scope of this updated article is extended beyond transport of samples for blood gas analysis by consideration of other recent studies that have examined the potential for pneumatic tube transport to cause *in vitro* hemolysis of any blood sample.

The article begins with a brief discussion of the impetus to reduce sample turnaround time (TAT) that underpins the rationale for transporting samples via pneumatic tube systems.

Turnaround time (TAT)
– A key indicator of laboratory performance

Modern healthcare is characterized by unrelenting pressure to provide more care at less cost. This has placed demands on clinical staff to reduce length of hospital stay and facilitate early patient discharge.

Speedy assessment and diagnosis for patients admitted to hospital emergency departments

allows higher patient throughput, i.e. higher productivity and thereby cost saving. For a minority of emergency room patients, who are critically ill, speedy assessment and diagnosis may of course be essential to patient survival.

In this high-pressure hospital environment, it is perhaps not surprising that of all measures of clinical laboratory performance, clinicians regard timeliness as of great significance [2] and may be willing to sacrifice a degree of analytical quality (the prime preoccupation of laboratorians) for a speedier service [3].

Turnaround time (TAT) is the universally accepted way of expressing the timeliness of laboratory services. There remains lack of consensus on the precise definition of TAT, but so far as clinicians are concerned the most valid definition is the interval between the time a test is requested by the physician and the time the test result is available to that physician or others caring for the patient [4].

This definition of TAT includes the preanalytical phase of the testing process, and therefore the time taken to transport samples to the laboratory.

The clinical demand to continuously reduce TAT persists [5]. The relative success of various strategies adopted (including those directed at reducing sample transport time) is discussed in a recent review [3].

Pneumatic tube systems (PTS) allow speedy and reliable automated transport of samples to the central laboratory. A number of studies have demonstrated that replacing human-courier transport of samples with PTS significantly reduces TAT [6, 7].

As a recent study [8] has demonstrated, point-of-care testing rather than PTS transport of samples and central laboratory testing can further reduce TAT.

Pneumatic tube transport of samples for blood gas analysis

So far as blood gas analysis is concerned, the clinical desirable goal is a TAT of around 5 minutes [9], which is usually achievable if the blood gas analyzer is sited at the point of care.

An early study [10] demonstrated that this demanding TAT could also be achieved if blood gas analysis is centralized in the laboratory, so long as blood is transported to the laboratory via PTS.

Centralized laboratory testing of blood gases, made possible by PTS, has become a preferred option for many hospitals, and a number of studies [11-19] have been directed at establishing the effect PTS has on the measured parameters, pH, pCO_2 and pO_2.

Discussion of these studies [11-19] was the main focus of the original companion article [1] of this updated article. Here is the bullet point summary of that original article:

- PTS has no effect on pH or pCO_2 [11-16]
- PTS does not affect pO_2 so long as pO_2 is close to that of ambient air (~20 kPa) [19]
- PTS can cause an increase in pO_2 for samples whose pO_2 is significantly less than 20 kPa, and a decrease in pO_2 for samples whose pO_2 is significantly greater than 20 kPa [19]
- The main cause of these changes in pO_2 induced by PTS is contaminating air (i.e. bubbles in syringe) [17, 19]
- Clinically significant aberrant pO_2 results can occur if samples are not purged of air bubbles before transport via PTS [19, 15, 20]
- If air could be reliably excluded from an arterial sample before transport, the changes in pO_2 induced by PTS would be clinically insignificant [15, 19, 20]
- Protocols aimed at purging air from arterial specimens are neither 100% effective nor universally applied [15, 16, 19]

- The effect of PTS on pO_2 values can be ameliorated by reducing the speed at which samples are sent via PTS [19] and by sending samples in pressure-sealed containers [16]

Recent studies examining the effect that PTS has on blood gas values

Since the first article [1] was written in 2005, two further relevant studies [21, 22] have been published.

For the first [21] of these, conducted in a German hospital, a total of four blood samples were taken for blood gas analysis from 54 patients. Three of each sample series was transported to the laboratory by PTS and the fourth by human courier.

Results of blood gas analysis of all samples from the 54 patients revealed "no statistically significant differences" between samples transported via PTS and samples transported by courier.

The authors conclude that "[transport of samples for blood gas analysis via a modern pneumatic tube system is safe when samples are correctly prepared]". (The full study report is in German - with just an abstract in English – so unfortunately the detail of this study cannot be provided or discussed further here).

The second study [22] was conducted soon after installation of a modern PTS in a large (2200-bed) tertiary-care teaching hospital in Vellore, India. (This was, according to the authors of this report, the first PTS installation in any Indian hospital).

The study cohort was a convenience sample of 50 intensive care patients who had an indwelling arterial line and required blood gas analysis. Two samples of arterial blood were collected from each of the 50 study patients.

After ensuring all visible air bubbles had been expelled from the samples, one was transported to the central laboratory via PTS and the other via human courier. Blood gas analysis of all samples revealed excellent agreement between samples transported via PTS and those transported by courier, for pH and pCO_2.

The mean difference in pH between the two samples was just 0.001 pH units, and 95% limits of agreement (LOA) were –0.028 to +0.030 pH units. The mean difference in pCO_2 between the two samples was 0.232 mmHg (0.03 kPa) and 95% LOA –3.37 to +3.83 mmHg (–0.45 to +0.51 kPa).

So the authors of this study were able to conclude that their results suggest that PTS has no effect on pH or pCO_2; this is in line with results of many previous studies [11-16].

Agreement was less satisfactory for pO_2, although the overall mean difference between PTS and courier samples was small (–0.9 mmHg or –0.12 kPa), suggesting good agreement. Some individual pairs, however, had significantly different pO_2 reflected in the wide 95% LOA: –40.8 to +39.0 mmHg (–5.4 to +5.2 kPa).

The relationship between PTS- and courier-sample pO_2 was found not to be uniform across the range of pO_2 values. For pO_2 values <160 mmHg (21 kPa) PTS values tended to be higher than courier values, but for pO_2 values <160 mmHg (21 kPa) PTS values tended to be lower than courier values.

These findings reflect a previous study [19] and are consistent with the notion that micro bubbles of air remained in the syringe of some samples in this study, and in these affected samples equilibration of blood with this air occurred during PTS transport, causing the erroneous pO_2 values.

In discussion of their study the authors speculate that the effect of PTS on pO_2 values could also be due in part to the use of plastic syringes.

What is the significance of the two new studies?

The results of these two studies nicely reflect a pre-existing controversy surrounding the use of PTS to transport blood gas samples. They both confirm that PTS has no effect on pH and pCO_2, a notion supported by many previous studies. But they also reflect an unresolved issue concerning the effect of PTS on pO_2.

The results of one suggest that pO_2 is unaffected by PTS, but the other suggests that PTS can cause erroneous pO_2 results. So the literature suggests, as it did a decade ago, that there is no consensus on the advisability of using PTS to transport blood gas samples.

The authors of the German study advise that so long as samples are correctly prepared, it is acceptable to use PTS. The authors of the Indian study, who report diligence in their preparation of samples, do not hold this view.

In the event they decided to abandon the use of PTS to transport samples and instead installed a blood gas analyzer at the point of care in their intensive care units. This decision was based not only on the potential for erroneous pO_2 results revealed by the study, but also on the prolonged TAT (~38 minutes) associated with use of their PTS – a secondary finding of the study.

In line with previous study the two studies suggest that if PTS is used, any effect of PTS on pO_2 values can be minimized by scrupulous adherence to the protocol of removing any air bubbles from the sample prior to transport.

There have been no further published studies over the past decade to support or refute the notion suggested in 2002 [16] that any effect of PTS on pO_2 values can be minimized by transport of samples via PTS in pressure-sealed containers.

In vitro hemolysis – a common pre-analytic problem

In vitro hemolysis is the release of hemoglobin and other contents of erythrocytes to plasma/serum following damage to cell membranes during sample collection or handling. It is the most common reason for specimen rejection [23].

The main deleterious effect of hemolysis is artefactual increase in serum/plasma concentrations of potassium, phosphate, and lactate dehydrogenase (LD). These parameters are particularly sensitive to the effect of hemolysis because of their high intracellular concentration relative to extracellular (plasma/serum) concentration.

Spectrophotometric measurement of plasma/serum hemoglobin concentration provides a convenient and highly sensitive way of determining if a sample is affected by hemolysis. Some modern instrumentation allows this assay to be applied during routine chemical profiling of plasma/serum samples.

The result is by convention reported as hemolysis index (HI) [23]. Prior to the relatively recent introduction of routine determination of HI, the only way of determining the presence of hemolysis was visual inspection of serum/plasma (the presence of hemoglobin causes pink-to-red discoloration) but this is a less sensitive method that continues to be used at some laboratories.

Recent studies examining the potential for PTS to cause *in vitro* hemolysis

The first ever study to examine the feasibility of transporting blood samples via PTS was conducted in 1964 and revealed evidence of hemolysis in all PTS-transported samples studied [24]. So since its inception there has been awareness that PTS has the potential to cause *in vitro* hemolysis.

Later studies [11, 12, 14] helped establish the now widely held view that the extent to which samples suffer cell (erythrocyte or leukocyte) membrane damage during transport via PTS is to a large degree a function of the particular system.

The system-dependent factors that affect the risk of hemolysis include: the speed and distance samples travel through the system, the number of changes of direction (switches) samples have to suffer, and the intensity of gravitational force that samples endure during acceleration and deceleration phases of the transport.

Improvements in PTS design (e.g. padded containers, soft cushioned deceleration) have helped to minimize the extent of hemolysis but the issue remains a concern and there is expert agreement that all laboratories should investigate the susceptibility of their particular PTS to cause hemolysis [25].

A number of such studies are recently published [7, 26-31].

Fernandes et al [7] studied the PTS link between the emergency department and central laboratory of a Canadian tertiary-care hospital. This system transports samples in high-impact-resistant carriers with padded liners.

The system traverses just one floor and involves only one switch (change in direction). Average speed is 7.6 m/sec, and at destination the carrier is decelerated by an air cushion, and drops gently into a receiving bin.

The study revealed that some degree of hemolysis was visibly evident in 7 of 121 (5.8%) of samples transported via PTS and in 20/200 (10%) of samples transported by courier.

The authors determined that this was a statistically insignificant difference (p>0.15) and concluded that use of their PTS was not associated with increased risk of hemolysis.

That was not the case for the PTS system studied by Kara et al [26] that transports samples over a distance of 80 m at an average speed of 3 m/sec from the emergency department to the laboratory of a Turkish hospital. For this study 49 samples were transported manually and 53 samples transported via PTS.

Spectrophotometric analysis revealed that some degree of hemolysis was present in all 53 samples transported by PTS but only in 8 of 49 (16%) of samples transported manually.

Mean potassium concentration of samples transported via PTS was significantly higher than that of samples transported manually (4.6 ± 0.4 versus 4.4 ± 0.5 mmol/L). Mean LD level of PTS samples was also significantly higher than that of manually transported samples (284, range 16-220 U/L versus 190, range 228-384 U/L).

Tiwari et al [28] examined the effect that PTS speed and distance have on risk of hemolysis using three indices of hemolysis: plasma/serum concentration of hemoglobin (Hb), potassium (K^+) and lactate dehydrogenase (LD).

The study was conducted in three phases. For the first phase (short distance/high speed), paired samples of blood were taken from 52 volunteers. One of each of the pairs was sent by courier and the other sent via the PTS over a distance of 115 m at a speed of 3 m/sec.

For the second phase (long distance/high speed), 215 paired samples were collected. As before one of each of the pairs was sent via courier and the other by PTS. But for this phase, PTS samples were sent via a longer route (225 m) at the same speed, 3 m/sec.

For the third and final phase (short distance/slow speed), PTS samples were sent over the same

short route used in phase 1 (115 m) but at a slower speed, 2 m/sec. All blood samples were centrifuged on arrival at the laboratory and serum submitted for Hb, K$^+$ and LD determination.

These analyses revealed that in the first phase there was no significant difference between courier and PTS samples so far as Hb and K$^+$ are concerned, but the mean LD of PTS samples was significantly higher than that of courier samples 582 U/L (SD 158) versus 532 U/L (SD 109).

In the second phase, mean of all three indices (Hb, K$^+$ and LD) was significantly higher in the PTS samples than in the courier-transported samples. By contrast there was no significant difference for any of the three indices between samples transported by courier and samples transported by PTS during the final third phase.

In summary the study discovered no evidence of PTS-related hemolysis for samples transported over a distance of 115 m at low speed (2 m/sec) but clear evidence of hemolysis for samples transported over a longer distance (225 m) and at greater speed (3 m/sec).

Minimal degree of hemolysis (increase in LD only) was evident in samples transported over short distance but at high speed. Results of this and other studies [29] suggest that of the three hemolysis indices used, LD is the most sensitive.

A second study of similar design [27] confirms that the rate of hemolysis in PTS-transported samples is affected by PTS speed and distance. This study [27] in common with others [29, 31] also provides evidence that blood collected into tubes containing anticoagulant is more susceptible to PTS-related hemolysis than blood collected into gel tubes without anticoagulant.

The notion that PTS design can have major impact on the risk of hemolysis is nicely demonstrated by a case study report [30] of a particularly high rate of hemolysis-affected samples (54%) due to defective (malfunctioning) PTS.

The defects included missing felt "O" rings around the outside of specimen carriers (these "O" rings are necessary to ensure slow deceleration of canisters on arrival). After correction of this and other found defects the proportion of hemolysis-affected samples declined to <10%.

A novel way of monitoring PTS for risk of hemolysis

Since it is now clear that risk of PTS-related hemolysis is largely system dependent and each system installation is unique, all laboratories should assess and monitor their particular PTS for risk of hemolysis. The split-sample method (one sent by courier the other by PTS) used in all the above studies is cumbersome and time consuming.

An alternative, much simpler, method is promised by the results of a recent German study [32].

Investigators responsible for this study exploited miniaturized data loggers that can be sent through a PTS system recording in real time the environmental condition (temperature, pressure, humidity and acceleration forces) that blood samples are exposed to during their journey through the PTS.

They demonstrated that the magnitude of peak accelerations as recorded by the data logger correlates with the degree of hemolysis in samples sent at the same time, and conclude that their approach could be used to predict the risk of hemolysis of any PTS system, without the need for blood sampling or laboratory analysis.

Sample specific effect of PTS – a cautionary case study

There is recent evidence to suggest that not all blood samples, when exposed to the same PTS, suffer the same degree of hemolysis even if the

blood is collected into identical sample collection tubes [33].

Those with hematological malignancy represent a patient group whose "leukemic" blood cells are particularly susceptible to damage (lysis) if exposed to the mechanical trauma induced by PTS.

This is well illustrated by recent case-study reports of PTS-related pseudohyperkalemia [34-37].

One of these case reports [34] is representative and concerns a previously well 12-year-old boy who presented at emergency department complaining of breathlessness, fever and neck swelling.

Initial laboratory results of a sample transported to the laboratory via PTS included very high white cell count (396 x 109/L) and grossly elevated plasma potassium concentration (16.6 mmol/L). All other U&E results were normal as was a 12-lead electro-cardiogram (ECG).

As the ECG trace provided no confirmatory evidence of hyperkalemia, pseudohyperkalemia (falsely raised potassium) was suspected. Two further samples were taken for potassium estimation. The first was transported to the laboratory via PTS and the second submitted for potassium estimation using the blood gas analyzer sited at the point of care.

The potassium concentration of the sample analyzed at the point of care was just 3.1 mmol/L but the sample transported via PTS had, as before, a grossly elevated value, 15.8 mmol/L. This pattern was found on further testing.

Following further hematological investigation a diagnosis of acute lymphoblastic leukemia was made, and it was concluded that PTS had caused tumor cell lysis with massive influx of potassium from cells to plasma, and consequent (pseudo) hyperkalemia.

The authors of this [34] and other case reports [35-37] caution that blood samples from patients with high-white-cell-count malignancies should not be transported to the laboratory via PTS.

Summary

- PTS has no effect on pH and pCO_2 measurement but may cause erroneous pO_2 values; this remains a contentious issue.
- Particular scrupulous attention must be paid to removing air bubbles from blood gas samples if PTS is used to transport samples.
- The mechanical trauma that specimens suffer during transport via PTS predisposes them to hemolysis.

The extent to which samples transported via PTS are affected by hemolysis is largely system dependent and each system should be assessed and monitored. Miniaturized data loggers may prove a simple and convenient method for individual PTS assessment

- Serum samples are more prone to PTS-related hemolysis than plasma samples.
- Some samples, most notably those from patients with high-white-cell-count malignancies, should not be transported via PTS.

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