Respiratory Medicine (2000) **94,** 350–355
doi:10.1053/rmed.1999.0714, available online at http://www.idealibrary.com on IDEAL®

Use of transcutaneous oxygen and carbon dioxide tensions for assessing indices of gas exchange during exercise testing

R. Carter and S.W. Banham

Department of Respiratory Medicine, Glasgow Royal Infirmary, North Glasgow University NHS Hospitals Trust, U.K.

The slow response characteristics of the combined transcutaneous electrode have been viewed as a major disadvantage when compared with other types of non-invasive assessment of gas exchange during exercise testing. We have previously shown that by using the highest recommended temperature of 45°C to reduce response times, and combining this with an exercise protocol of gradual work load increments, that this allows changes in arterial blood gases to be closely followed by transcutaneous values. In the present study we have validated the use of a transcutaneous electrode for estimation of alveolar–arterial oxygen gradient (aaO_2) and dead space to tidal volume ratio (V_D/V_T) during exercise, against values calculated from direct arterial blood gas analysis. One hundred measurements were made in 20 patients with various cardiopulmonary disorders who underwent exercise testing. Exercise testing was performed by bicycle ergometry with a specific protocol involving gradual work load increments at 2 min intervals. Transcutaneous gas tensions were measured by a heated combined O_2 and CO_2 electrode. Arterial blood was sampled at the midpoint of each stage of exercise and transcutaneous tensions noted at the end of each stage. The mean difference of the aaO_2 gradient calculated from blood gas tensions obtained by the two methods was 0.14 kPa. The limits of agreement were −0·26 and 0·63 kPa. The same values for V_D/V_T calculated from gas tensions measured by the two methods were: mean difference 0·001; limits of agreement −0·0242 and 0·0252. For both these parameters there was an even scatter around the mean value on Bland and Altman analysis. The findings of this study suggest that estimation of parameters of gas exchange using transcutaneous values during exercise testing is reliable, provided the electrode is heated to a slightly higher temperature than usual and the work load increments are gradual, allowing for the latency in the response time of the system. This system allows the assessment of the contribution of ventilation/perfusion inequality to breathlessness on exertion in patients, provided an initial arterial or ear lobe capillary sample is obtained for calibration purposes. This technique is particularly valuable in patients undergoing repeat exercise tests as it circumvents the need for arterial cannulation.

Key words: gas exchange; transcutaneous gas; exercise testing.

Respir. Med. (2000) **94,** 350–355

Introduction

It has been suggested that the slow response characteristics of transcutaneous electrodes would render them unsuitable for use during exercise testing. An electrode temperature of approximately 43°C is required to maintain adequate skin perfusion (1) but even at these temperatures the oxygen electrode, with its recording delay during the warm-up period and slow response times, has been demonstrated to miss rapid changes in arterial PO_2(2–4). Several previous studies, however, have demonstrated that the transcutaneous oxygen electrode provides a reliable method of continuously monitoring the changes in arterial oxygen tension in adults undergoing exercise tests (5–8) but difficulties were encountered in other studies (9).

More controversy surrounds the use of the transcutaneous carbon dioxide electrode to monitor arterial carbon dioxide tensions during exercise testing. It has been shown that $tcPCO_2$ reflects arterial PCO_2 in haemodynamically stable patients at rest using an electrode temperature of 39–40°C (10–12). At this temperature, however, there is a slow response time for monitoring changes which, in some cases, was as long as 3 min thus precluding its use in exercise testing (13). The use of a higher electrode temperature produces a systematically higher skin surface carbon dioxide tension and, in addition, a more rapid response time (14,15). In our own laboratory the use of an electrode temperature of 45°C produces response times of the $tcPO_2$ and $tcPCO_2$ electrode to a change in breath pattern or inspired gas of 30 and 55 sec, respectively (16,17). In addition, we have assessed the combined transcutaneous

Received 9 June 1999 and accepted in revised form 28 September 1999.

Correspondence should be addressed to:
Roger Carter, Principal Clinical Scientist, Department of Respiratory Medicine, Queen Elizabeth Building, Glasgow Royal Infirmary, Alexandra Parade, Glasgow, G31 2ES, U.K.

0954-6111/00/040350+06 $35·00/0

monitor following an *in vivo* calibration against direct arterial sampling during exercise testing. This study showed that by using the highest recommended temperature of 45°C to reduce response times, and combining this with an exercise protocol of gradual work load increments of 2 min periods, this allows changes in arterial blood gases to be closely followed by transcutaneous values (18).

The accurate non-invasive assessment of arterial gas tensions has important implications during cardiopulmonary exercise testing since, with the measurement of mixed expired gases and minute ventilation, this allows the calculation of sensitive indices of ventilation/perfusion inequality at all stages during the exercise test.

The good agreement between arterial and transcutaneous values of oxygen and carbon dioxide during exercise testing following an *in vivo* calibration allows the calculation of these standard indices of ventilation/perfusion inequality from these non-invasive measurements. This would allow the assessment of the contribution of these indices to exertional breathlessness with circumvention of the need for arterial cannulation. We have therefore validated the use of the combined transcutaneous electrode for the estimation of the alveolar–arterial oxygen difference (AaO_2) and dead space to tidal volume ratio (V_D/V_T) during exercise testing against values calculated from direct arterial blood gas analysis.

PATIENTS

Full exercise and blood gas data was available for 14 patients (10 men, four women) from our original study who were referred from respiratory or general medical clinics for a symptom limited progressive exercise test. The group comprised patients with a range of cardiopulmonary disorders of varying degrees of severity, and also included patients with unexplained breathlessness. A further six patients were referred from the Scottish Cardiopulmonary Transplant Unit who had progressive cardiopulmonary exercise testing with full gas exchange as part of their assessment for cardiac transplantation. Informed consent was obtained from the patients prior to the exercise tests. Ethical committee approval had been granted for the original study from which this data is derived and for the cardiac transplant patients for a cardiopulmonary exercise test with full gas exchange as part of their routine assessment for consideration of transplantation.

The characteristics of these patients are shown in Table 1.

Methods

The AaO_2 gradient and V_D/V_T were calculated using standard formulae (19) described below at rest and during a progressive cardiopulmonary exercise test.

The AaO_2 gradient is calculated from the alveolar gas equation:

$$P_AO_2 = P_IO_2 - \frac{PaCO_2}{R} - [F_IO_2.PaCO_2.(1 - R)/R]$$

where P_IO_2 is the inspired oxygen tension; $PaCO_2$ is the arterial (transcutaneous) carbon dioxide tension; F_IO_2 is the fractional concentration of oxygen in the inspired air; and R is the respiratory exchange ratio.

The respiratory exchange ratio (R) is the volume of carbon dioxide evolved divided by the volume of oxygen consumed; it was calculated from the following formula:

$$R = P_ECO_2/P_IO_2.[P_EN_2/P_IN_2] - P_EO_2$$

Where P_I denotes the partial pressure in the inspired gas mixture and P_E denotes the partial pressure in the mixed expired gas mixture.

The transcutaneous or arterial oxygen tension was subtracted from the calculated alveolar oxygen tension to produce the gradient at rest and at each work load increment.

The dead space/tidal volume ration was calculated from the following formula:

$$V_D/V_T = (PaCO_2 - P_ECO_2)/PaCO_2$$

where Pa denotes arterial (transcutaneous) partial pressure and P_E denotes the partial pressure in the mixed expired gas mixture.

The combined transcutaneous electode (TCM3, Radiometer, Copenhagen, Denmark) was initially calibrated *in vitro* at two points; the first calibration gas contained 5% carbon dioxide and 20·9% oxygen and the second 10% carbon dioxide in nitrogen. The electrode temperature was set to 45°C. The combined sensor was then attached to the skin of the upper quadrant of the chest with an adhesive ring after a drop of contact fluid was placed in the ring. The TCM3 monitor automatically corrects the $tcPCO_2$ output back to 37°C according to the Siggaard–Andersen equation (14). After the output of the TCM3 monitor was stable (approximately 10 min) an arterial sample was obtained from a previously inserted arterial cannula. These samples were analysed immediately for oxygen and carbon dioxide tensions using an ABL5 blood gas analyser (Radiometer, Copenhagen, Denmark). The gain controls of the TCM3 monitor were then altered so that the output of the $tcPO_2$ and $tcPCO_2$ corresponded to the measured PaO_2 and $PaCO_2$ (*in vivo* calibration).

Symptom limited exercise tests were performed using an electrically braked bicycle ergometer, with the patient breathing through a low dead space, low resistance valve box (Benchmark exercise test system, Morgan Medical, Kent England). The valve box contains a flexible pneumotachograph for the calculation of inspired and expired flows which are integrated to calculate minute ventilation. The expired limb is fed through a mixing chamber from which mixed expired gas concentrations can be analysed for carbon dioxide (infra-red gas analyser) and oxygen (fuel cell reference and rapidly responding zirconium analyser)

The averaged mixed expired concentrations of oxygen and carbon dioxide and minute ventilation over the last 30 sec of a 2 min resting period were used to calculate the respiratory exchange ratio by the formula described above. An arterial blood sample was obtained from a previously inserted arterial cannula during the middle period of the resting phase and the values of $PaCO_2$ and PaO_2 measured

TABLE 1. Characteristics of the study population

Diagnosis	*n*	Age range (years)	Sex	Summary of cardiorespiratory function
Unexplained breathlessness	2	29 and 54	2M	Normal cardiorespiratory function
Chronic obstructive pulmonary disease (COPD)	8	57–67	6M, 2F	Mean FEV_1 45% predicted (range 36–66%)
Pulmonary thromboembolic disease	2	31 and 45	2F	Angiographically proven pulmonary thromboembolism. Normal lung volumes reduced *T*LCO
Hyperventilation syndrome	2	27 and 45	2M	Normal FEV_1, TLCO Normal ECG
Ischaemic heart disease	4	53–64	3M, 1F	ECG and coronary angiography evidence of IHD; on active treatment. Transplant assessments
Cardiomyopathy	2	38 and 41	2M	Normal lung volumes, no airflow obstruction, reduced *T*LCO. Transplant assessments

(Radiometer ABL5 Blood gas analyser). The tcPO_2 and tcPCO_2 values were noted at the end of the resting period to take account of the previously measured lag and response time of the transcutaneous electrode. The arterial and transcutaneous values obtained, together with the mixed expired concentrations of oxygen and carbon dioxide, were used to calculate resting values of AaO_2 gradient and V_D/V_T using the standard equations previously described. A progressive exercise test was then performed in 20 patients with various cardiopulmonary disorders on an electrically braked bicycle ergometer with a specific protocol involving gradual work load increments (10–25 watts) at 2 min intervals until symptomatic limitation of exercise. The AaO_2 gradient and V_D/V_T were calculated for each work load increment as described above using both the arterial and transcutaneous oxygen and carbon dioxide tensions. The measurement of the indices of ventilation/perfusion inequality obtained by arterial and transcutaneous monitoring were compared by regression analysis and the analysis of Bland and Altmann (20).

Results

In this study the range of arterial PO_2 and PCO_2 measured was 6·0–14·0 kPa and 3·5–7·0 kPa respectively. The 20 patients investigated produced 100 measurements of gas exchange indices during cardio-pulmonary exercise testing. In these 20 patients the AaO_2 gradient calculated using direct arterial oxygen tension ranged from 0·9–9·6 kPa. There was a significant correlation (Fig. 1) between the AaO_2 calculated from direct arterial sampling and from transcutaneous PO_2 measurements derived from these 100 simultaneous measurements ($r = 0{\cdot}98$, $P < 0{\cdot}001$). The mean difference of the AaO_2 calculated from blood gas tensions obtained by the two methods was 0.14 kPa (limits of agreement −0·26 and 0·63 kPa) with an even scatter around the mean value (Fig. 2). The V_D/V_T calculated from arterial carbon dioxide tension ranged from 0·15–0·64. There was a significant correlation (Fig. 3) between the

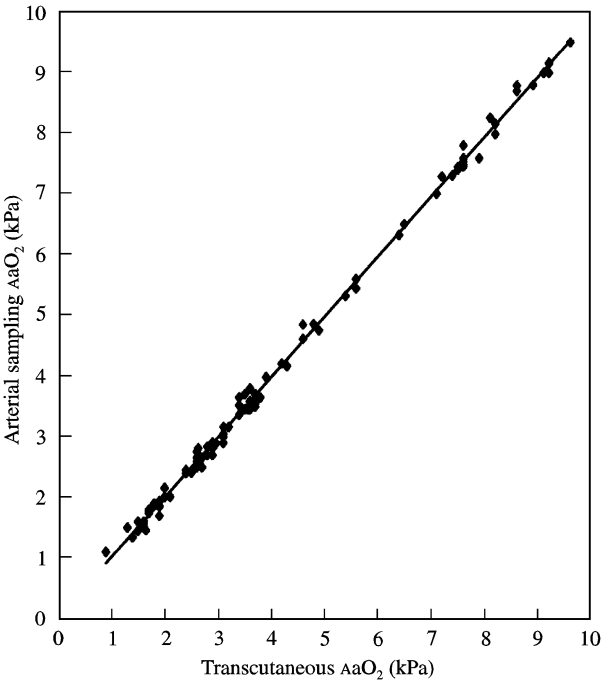

FIG. 1. AaO_2 gradient: transcutaneous against direct arterial sampling. $y = 0{\cdot}9905x + 0{\cdot}0226$; $R^2 = 0{\cdot}9977$.

V_D/V_T calculated from direct arterial sampling and from transcutaneous PCO_2 measurements derived from 100 simultaneous measurements ($r = 0{\cdot}99$, $P < 0{\cdot}001$). The values for V_D/V_T calculated from gas tensions measured by the two methods (Fig. 4) gave a mean difference of 0·001 (limits of agreement 0·0252 and −0·0242) with an even scatter around the mean value.

Discussion

The slow response characteristics of the combined transcutaneous electrode has been viewed as a major disadvantage

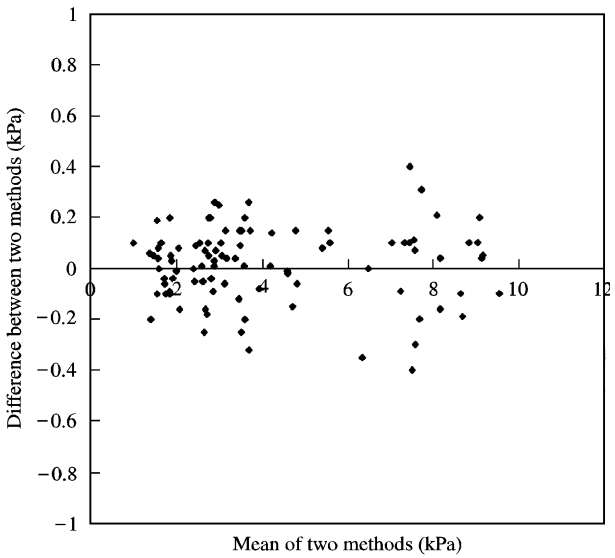

FIG. 2. Bland and Altman analysis: AaO_2 gradient—transcutaneous against direct arterial sampling.

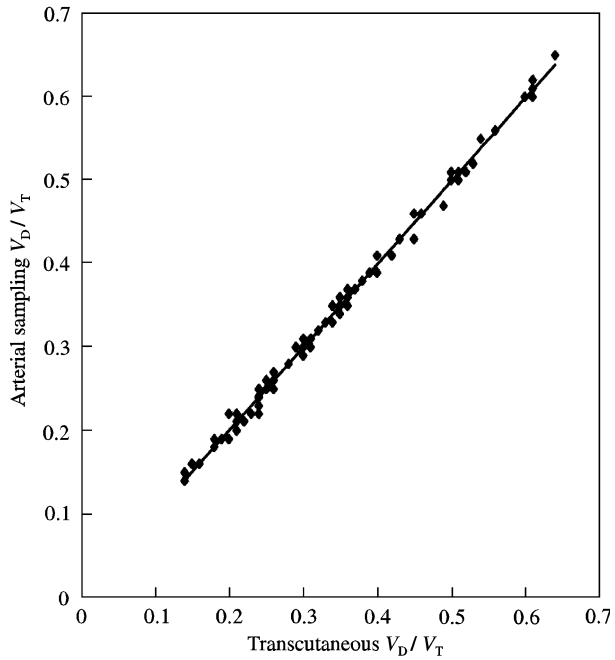

FIG. 3. V_D/V_T: transcutaneous against direct arterial blood sampling. $y = 0{\cdot}9956x + 0{\cdot}0009$; $R^2 = 0{\cdot}9954$.

when compared with other types of non-invasive assessment of gas exchange during exercise testing using pulse oximetry (21) or end tidal measurement of carbon dioxide (22). Some of these difficulties may have been caused by the different temperature settings used with the transcutaneous electrode (42–44°C) producing a range of response times. Furthermore, the transcutaneous system may have been calibrated using a dry gas mixture, or an *in vivo* calibration may have depended on a single arterial stab prior to the

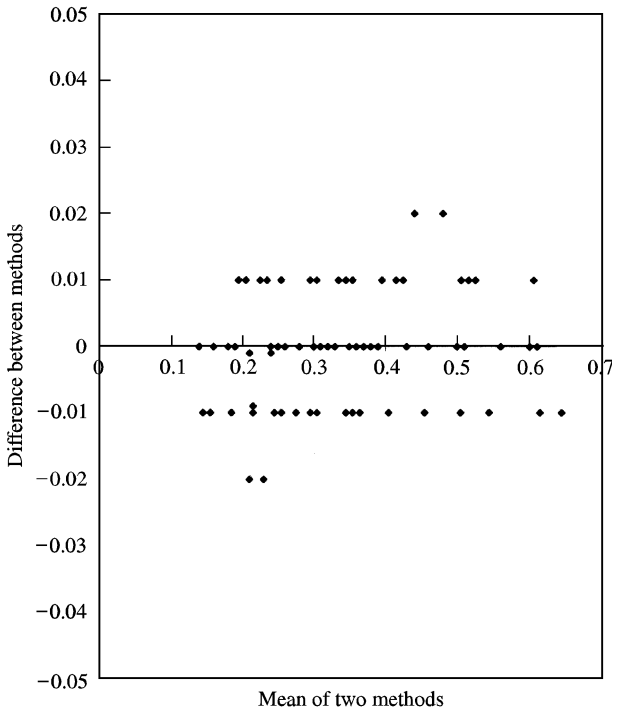

FIG. 4. Bland and Altman analysis: V_D/V_T—transcutaneous against direct arterial sampling.

exercise tests. The present study has shown that indices of gas exchange measured by transcutaneous monitoring closely follows those assessed by direct arterial sampling during cardiopulmonary exercise testing.

The response time of the transcutaneous oxygen electrode has previously been assessed in a study by Schonfield *et al.* (6). This group reported a 90% response time for $tcPO_2$, with an electrode temperature of 42°C, after a step change in inspired oxygen concentration to be 182·5 ± 7·9 sec during exercise which would preclude the use of transcutaneous monitoring during rapidly progressive exercise protocols. However, using a higher electrode temperature of 45°C, Gray *et al.*, in a comparison with pulse oximetry, showed that both transcutaneous and ear oximeter responded to changes in inspired oxygen significantly more slowly than end-tidal measurements, but that during exercise there was no significant difference between the response characteristics of the ear oximeter and $tcPO_2$ electrode (8). This study showed a 90% response time of 25–30 sec for the transcutaneous oxygen monitor which would make it suitable for monitoring arterial PO_2 during exercise testing. These findings were confirmed in our own laboratory: using an electrode temperature of 45°C, the $tcPO_2$ electrode responded to changes in breathing pattern, inspired gas or changes on exercise testing in 30 sec (16,17).

With the use of a combined electrode, higher electrode temperatures produce an increase in the temperature of capillary blood which leads to a systematically higher skin surface carbon dioxide tension than when measured at 37°C although a temperature correction can be applied (14). In

addition, the increased temperature leads to a more rapid response time so that using an electrode temperature of 44°C, Nickerson *et al*. (15) showed a lag time of 30 ± 2 sec and a 50% response time to changes in carbon dioxide of 33 ± 2 sec during vigorous exercise. They concluded that changes in ventilation will not be reflected by the CO_2 electrode for at least 1 min. This was again confirmed by our previous studies which showed that using an electrode temperature of 45°C, with a temperature correction applied, changes in carbon dioxide tension would be reflected at 55 sec (16,17). The combination of the transcutanoeous electrode at its highest temperature setting and the use of a progressive exercise test incorporating gradual work load increments of 2 min, therefore, allows arterial blood gases to be monitored by transcutaneous values during cardiopulmonary exercise testing (18).

Full gas exchange assessment during progressive exercise testing has previously relied upon the insertion of an arterial line (23) which may be associated with significant complications (24). The validation of the transcutaneous method against directly measured arterial oxygen and carbon dioxide tensions during an exercise test has led to the possibility of non-invasive, apart from a single arterial blood sample (arterialized earlobe capillary sample), monitoring of indices of gas exchange during exercise testing. The indices of alveolar–arterial oxygen gradient and dead space/tidal volume ratio are more specific indicators of the function of the pulmonary gas exchange mechanism and are important determinants of the ventilatory requirement on exertion (25). An increase in the ratio of dead space to tidal volume (V_D/V_T) ratio, for example, compromises the effectiveness of the ventilatory capacity in maintaining adequate alveolar ventilation on exertion and in this way contributes to breathlessness. An additional stimulus to ventilation is the development of arterial hypoxaemia during graded exercise. This results in a widening alveolar–arterial oxygen gradient (AaO_2) which is one of the best indicators of pulmonary gas exchange abnormalities. An increased ventilatory requirement on exertion may, therefore, be a contributory factor to exertional dyspnoea in patients with cardiac or pulmonary disease (25–31). The use of the transcutaneous electrode during cardiopulmonary exercise testing in our laboratory has allowed assessment of the contribution of gas exchange abnormality, without arterial cannulation, to aerobic capacity in patients with ankylosing spondylitis (32). Currently this method is being used to assess the contribution of gas exchange abnormality to the ventilatory response on exertion in patients with COPD prior to and following a programme of pulmonary rehabilitation with nutritional supplementation. In addition this method is being used to assess the effects of cardiac transplantation on the raised ventilatory response to exertion in patients with cardiac failure (33).

In conclusion, this study suggests that a combined $tcPO_2$ and $tcPCO_2$ electrode can be used to provide a reliable non-invasive estimate of indices of gas exchange on exercise testing provided the maximal permissible temperature is selected, together with gradual work load increments at 2 min intervals. The technique circumvents the need for arterial cannulation, but requires an initial *in vivo* calibration using a single arterial puncture or arterialized ear-lobe capillary sample (34) for accurate monitoring of arterial blood gas values during exercise. The system allows the non-invasive, apart from this single arterial puncture, assessment of the contribution of ventilation/perfusion inequality to breathlessness on exertion in patients and is, therefore, particularly valuable in patients undergoing repeat exercise tests.

References

1. Clark SJ, Votteri B, Ariagno RL, *et al*. Non-Invasive assessment of blood gases. *Am Rev Respir Dis* 1992, **145:** 220–232.
2. Huch A, Huch R. Transcutaneous, non-invasive monitoring of PO_2. *Hosp Pract* 1976; **11:** 43–52.
3. Monaco F, Nickerson BG, McQuitty J. Continuous transcutaneous oxygen and carbon dioxide monitoring in the paediatric ITU. *Crit Care Med* 1982; **10:** 765–766.
4. Versmold HT, Linderkamp O, Stuffer KH, Holzmann M, Riegel KP. *In vivo vs. In vitro* response times of transcutaneous PO_2 electrodes. In: Severinghaus JW, Peabody J, Thunstrom A, Eberhard P, Zappia E, eds. *Workshop on methodologic aspects of transcutaneous blood gas analysis. Acta Anaesthesiol Scand* 1978; **68** (Suppl): 40–48.
5. McDowell JW, Thiede WH. Usefulness of the transcutaneous PO_2 monitor during exercise testing in adults. *Chest* 1980; **78:** 853–855.
6. Schonfield T, Sargent CW, Bautista D. Transcutaneous oxygen monitoring during exercise stress testing. *Am Rev Respir Dis* 1980; **121:** 457–462.
7. Hughes JA, Gray BJ, Hutchison DCS. Changes in transcutaneous oxygen tensions during exercise in pulmonary emphysema. Thorax 1984; **39:** 424–431.
8. Gray BJ, Barnes NC, Heaton RW, Callaghan JM. Response characteristics of a transcutaneous oxygen electrode and an ear oximeter compared at rest and during exercise. Thorax 1984; **39:** 715.
9. Steinacker JM, Wodick RE. Transcutaneous PO_2 during Exercise. *Adv Exp Med Biol* 1984; **169:** 763–774.
10. Greenspan GH, Block AJ, Haldeman LW. Transcutaneous non-invasive monitoring of carbon dioxide tension. Chest 1981; **80:** 442–446.
11. Tremper KK, Shoemaker WC, Shippy CR. Transcutaneous PCO2 monitoring on adult patients in the ICU and the operating room. *Crit Care Med* 1981; **9:** 752–755.
12. McLellan PA, Goldstein RS, Ramcharan V, Transcutaneous carbon dioxide monitoring. *Am Rev Respir Dis* 1981; **124:** 199–201.
13. Hazinski TA, Severinghaus JW. Transcutaneous analysis of arterial PCO_2. *Med Instrum* 1982; **16:** 150–153.
14. Siggaard-Andersen O. *The acid-base status of blood*. Munksgaard, Copenhagen 1976: 89.

15. Nickerson BG, Paterson C, McCrea R, Monoaco F. In vivo response times for a heated skin surface CO_2 electrode during rest and exercise. *Ped Pulmonol* 1986; **2:** 135–140.
16. Carter R. Transcutaneous oxygen and carbon dioxide monitoring in the adult patient. *Care Crit Ill* 1988; **4:** 13–15.
17. Carter R. The measurement of transcutaneous oxygen and carbon dioxide tension during exercise testing. *Breath* 1989; **38:** 2–6.
18. Sridhar MK, Carter R, Moran F, Banham SW. Use of a combined oxygen and carbon dioxide electrode in the estimation of gas exchange during exercise. *Thorax* 1993; **48:** 643–647.
19. Riley RL, Cournand A. ''Ideal'' alveolar air and the analysis of ventilation-perfusion relationships in the lung. *J Appl Physiol* 1949; **1:** 825–847.
20. Bland MJ, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986; **1:** 306–310.
21. Saunders NA, Powles ACP, Rebuck AS. Ear Oximetry: accuracy and practicality in the assessment of arterial oxygenation. Am Rev Respir Dis 1976; **113:** 745–749.
22. Yamaka MK, Sue DY. Comparison of arterial end-tidal PCO2 difference and deadspace/tidal volume ratio in respiratory failure. *Chest* 1987; **92:** 832–835.
23. Mckelvie RS, Jones NL. Cardiopulmonary exercise testing. *Clin Chest Med* 1989; **10(2):** 277–291.
24. Bedford RF, Wollman H. Complications of percutaneous radial artery cannulation: an objective prospective study in man. *Anaesthesiology* 1973; **38:** 228–236.
25. Wasserman K, Whipp BJ. Exercise physiology in health and disease. *Am Rev Respir Physiol* 1975; **112:** 219–249.
26. Watt J. Cardiopulmonary stress testing: A review of non-invasive approaches. *Chest* 1986; **90:** 504–510.
27. Webber KT, Janicki JS, McElroy PA, Reddy HK. Concepts and applications of cardiopulmonary exercise testing. *Chest* 1988; **93:** 843–847.
28. Eschenbacher WL, Mannina A. An algorithm for the interpretation of cardiopulmonary exercise tests. *Chest* 1990; **97:** 263–267.
29. Sue DY, Wasserman KT. Impact of integrative cardiopulmonary exercise testing on clinical decision making. *Chest* 1991; **99:** 981–992.
30. Weber KT, Janicki JS. Cardiopulmonary exercise testing: Physiologic principles and clinical applications. Philadelphia: WB Saunders, 1986.
31. Wasserman K, Diagnosing cardiovascular and lung pathophysiology from exercise gas exchange. *Chest* 1997; **112:** 1091–1101.
32. Carter R, Riantawan P, Banham SW, Sturrock RD. An investigation of factors limiting aerobic capacity in patients with ankylosing spondylitis. *Respir Med* 1999; **93:** 700–708.
33. Al-Rawas OA, Carter R, Richens D, Stevenson RD, Naik SK, Tweddel A, Wheatley DJ. Ventilatory and gas exchange abnormalities on exercise in chronic heart failure. *Eur Resp J* 1995; **8:** 2022–2028.
34. Dawson S, Cave C, Pavord I, Potter JF. Transcutaneous monitoring of blood gases: is it comparable with arterialized earlobe sampling. *Respir Med* 1998; **92:** 584–587.