

## Title page

**Assessment of maximum inspiratory pressure (P<sub>I</sub>max): prior submaximal respiratory muscle activity ('warm-up') enhances P<sub>I</sub>max and attenuates the learning effect of repeated measurement.**

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**Short title: The effect of 'warm-up' upon P<sub>I</sub>max.**

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## **Abstract**

*Background* -The variability of maximal inspiratory pressure (P<sub>I</sub>max) in response to repeated measurement affects its reliability; published studies have used between three and twenty P<sub>I</sub>max measurements in a single occasion.

*Objective* - This study investigated the influence of a specific respiratory 'warm-up' upon the repeated measurement of inspiratory muscle strength and attempts to establish a procedure by which P<sub>I</sub>max can be assessed with maximum reliability using the smallest number of manoeuvres.

*Methods* - Fourteen healthy subjects, familiar with the Mueller manoeuvre, were studied. The influence of repeated testing on a single occasion was assessed using an 18 measurements protocol. Using a randomised cross-over design subjects performed the protocol, preceded by a specific respiratory warm-up (RWU) and on another occasion without any preliminary activity (Control). Comparisons were made amongst 'baseline' (best of the first 3 measurements), 'short' series (best of 7<sup>th</sup> to 9<sup>th</sup> measurement) and 'long' series (best of the last 3 measurements).

*Results* - Under control conditions the mean increase ('baseline' vs. 'long' series) was 11.4 (5.8%); following the RWU the increase (post RWU 'baseline' vs. 'long' series) was 3.2 (10.0)%. There were statistically significant differences between measurements made at all 3 protocol stages ('baseline', 'short' and 'long' series) under control conditions, but none following the RWU.

*Conclusions* - The present data suggest that a specific RWU may attenuate the 'learning effect' during repeated P<sub>I</sub>max measurements which is one of the main contributors of the test's variability. The use of a RWU may provide a means of obtaining reliable values of P<sub>I</sub>max following just 3 measurements.

## **Introduction**

Maximal inspiratory pressure (P<sub>I</sub>max) is a commonly used index of inspiratory muscle strength; it reflects the combined force-generating capacity of the inspiratory muscles during a brief, quasi-static contraction (Mueller manoeuvre)[1]. The reliability of P<sub>I</sub>max has been questioned, particularly in the context of its variability in response to repeated measurement. Day to day fluctuations similar to those seen with other measures of strength have been reported to be  $\pm 10$  percent [2]. However, the variability relating to the number of manoeuvres that are performed can result in an underestimate of P<sub>I</sub>max of as much as 1.96 kPa (20 cmH<sub>2</sub>O) [3]. Reports suggest that a learning effect can be significant in both short series (3-5 measurements) and longer series (up to 20 measurements) protocols [3, 4].

In a recent study, we have shown that prior activity of the inspiratory muscles, i.e., breathing against a modest threshold load using an inspiratory muscle trainer, induced a statistically significant increase in P<sub>I</sub>max [5].

Thus, the aims of the present study were to investigate the influence of a specific respiratory ‘warm-up’ upon the repeated measurement of inspiratory muscle strength and to attempt to establish a procedure by which P<sub>I</sub>max can be assessed with maximum reliability using the smallest number of manoeuvres. The influence of repeated testing was assessed on a single occasion using a protocol which consisted of a total of 18 maximal efforts.

## **Material and Methods**

### **Subjects**

Fourteen healthy subjects were studied following informed, written consent and local Ethics Committee approval. Their mean (SD) characteristics were: age 26 (3) yrs; weight 72 (9) kg; and height 1.80 (0.06) m. None reported any history of respiratory or neuromuscular disease. Subjects were removed from the study if they reported a respiratory tract infection within the two weeks of data collection because of the potential effects upon respiratory muscle strength [6].

## **Procedure**

Subjects were experienced with the nature of the Mueller manoeuvre or had visited the laboratory at least twice for familiarisation prior to data collection. These two preliminary sessions were designed to allow for the initial learning effect and to assess test-retest reliability. Larson *et al.* [1] reported that performance plateaus between the 3<sup>rd</sup> and 4<sup>th</sup> test session. The familiarisation sessions consisted of the same protocol as in the actual data collection. The influence of repeated testing on a single occasion was assessed using a protocol consisting of a total of 18 measurements, performed in 6 sets of 3 efforts. One minute rest was allowed between individual measurements and a 3 min rest between sets to minimise the effects of fatigue.

Subjects performed the protocol under two conditions, in a randomised cross over design. On one occasion, the test protocol was preceded by a specific respiratory warm-up (RWU); on another occasion, the protocol was performed without any preliminary activity (Control). Both data collection sessions (Control and RWU) were performed at the same time of the day and within 5-7 days of each other.

## **Maximum Inspiratory Pressures**

Peak maximum inspiratory pressure (P.PI<sub>max</sub>) and maximum inspiratory pressure averaged over 1 sec (PI<sub>max</sub>) were recorded using a portable hand held mouth pressure meter, (Morgan Medical, UK). This device, equipped with a flanged mouthpiece, has been demonstrated to measure inspiratory efforts accurately and reliably [7]. A small hole in the system was preventing closure of the glottis during inspiration and a noseclip was used in all efforts. The subjects were asked to sustain a maximal inspiratory effort for 2-3 sec.

The initial length of the inspiratory muscles was controlled by initiating each effort from residual volume (RV). Subjects were instructed to take their time and to slowly empty their lungs to RV. All manoeuvres were performed in the upright standing position and verbal encouragement was given to help the subjects

perform maximally. The trials which did not represent the subjects' maximum effort, according to their subjective feeling, were discarded.

Comparisons were made according to the following definitions: 'baseline' series measurement was defined as the highest of the first 3 measurements. The 'short' series measurement was defined as the highest among the 7<sup>th</sup> to the 9<sup>th</sup> efforts [3]. The 'long' series measurement was defined as the highest value amongst the last 3 of the 18 measurements.

### **Specific respiratory warm-up (RWU)**

Two sets of 30 breaths were performed with a POWERbreathe<sup>®</sup> inspiratory muscle trainer (IMT Technologies Ltd., Birmingham, UK), with mouth pressures being measured within 2 minutes of completion of each set. The pressure load was set at 40% of the P<sub>Imax</sub> measured before the commencement of the protocol. This level of recruitment has been suggested to approximate the upper loading limit before fatigue of the diaphragm occurs [8].

POWERbreathe<sup>®</sup> is a pressure-threshold device which requires continuous application of inspiratory pressure throughout inspiration in order for the inspiratory regulating valve to remain open. Subjects were instructed to initiate each breath from RV and to continue the inspiratory effort up to the lung volume where the inspiratory muscle force output for the given load limited further excursion of the thorax. Because of the increased tidal volume, a decreased breathing frequency was adopted in order to avoid hyperventilation and the consequent hypocapnia.

### **Analysis**

Student's t-test for paired samples was used to compare differences before and after the two conditions. The coefficient of variation ( $CV = 100\% \times SD/mean$ ) and the coefficient of repeatability for agreement [9] was used to evaluate the within-sessions reproducibility of the baseline and final maximum values. One-way ANOVA with repeated measures and Scheffé post-hoc test was used to detect differences between the 'baseline', 'short' and 'long' series values.  $P < 0.05$  was considered statistically significant.

## RESULTS

### *Test-retest reproducibility*

The group mean (SD) 'baseline' and 'long' series P<sub>I</sub>max and P.P<sub>I</sub>max values measured under the two test conditions are summarised in Table 1 (note that the 'baseline' value presented here for RWU is the value recorded prior to the RWU). The mean (SE) coefficient of variation (CV = 100% x SD/mean) and the repeatability coefficient [9] of the 'baseline' and 'long' series P<sub>I</sub>max and P.P<sub>I</sub>max values for the two conditions are shown in Table 2.

### *Response to the RWU*

Following the RWU, there was a significant increase in the mean baseline values of both P<sub>I</sub>max and P.P<sub>I</sub>max (P < 0.01) which, in absolute values, was 1.4 (0.5) kPa (13.8 (5.6) cm H<sub>2</sub>O) and 1.6 (0.6) kPa (15.9 (5.8) cm H<sub>2</sub>O), or 10.1 (8.1)% and 11.2 (9.0)%, respectively.

### *Response to repeated measurement*

The development of P<sub>I</sub>max and P.P<sub>I</sub>max values during the 18 measurement protocol under both conditions is summarised in Table 3 and for P<sub>I</sub>max in Figure 1. Under control conditions the mean increase ('baseline' vs. 'long' series) was 11.4 (5.8)%; following the RWU the increase (post RWU 'baseline' vs. 'long' series) was 3.2 (10.0)%. There were statistically significant differences between measurements made at all 3 protocol stages ('baseline', 'short' and 'long' series) under control conditions, but none following the RWU.

## DISCUSSION

The main finding of the present study was that following a specific RWU the response to repeated measurement of both P<sub>I</sub>max and P.P<sub>I</sub>max was attenuated such that there was no statistical difference between the post-RWU 'baseline' measurement and the 'long' series measurement.

This finding confirmed our original hypothesis and has important implications for the administration of the Mueller manoeuvre and the measurement of inspiratory muscle function. In the control condition, both P<sub>I</sub>max and P.P<sub>I</sub>max continued to increase throughout the 18 measurements with significant differences in all stages (Table 3). These data are in agreement with previous reports on the ‘learning effect’ of P<sub>I</sub>max [3, 4] but in contrast with reports of no effect for P.P<sub>I</sub>max [10]. When the ‘baseline’ measurement was preceded by a RWU, P<sub>I</sub>max and P.P<sub>I</sub>max showed only modest increases of the order of 0.2-0.4 kPa (2-4 cm H<sub>2</sub>O) across the 18 measurements. This difference was not significant statistically nor, it could be argued, is it significant functionally.

Our data show that following preliminary submaximal activity of the inspiratory muscles (RWU) a reliable baseline value can be measured, for both P<sub>I</sub>max and P.P<sub>I</sub>max, with the first trial. However, it is acknowledged that all of our subjects were well acquainted with the Mueller manoeuvre before the 18 trial protocol was initiated. It is possible that, for subjects that are more naïve, the RWU may be insufficient to fully enhance P<sub>I</sub>max. However, the mean increase in P<sub>I</sub>max over the 18 measurements was around 12% in our subjects, which is comparable with that observed by others in more naïve subjects over a similar number of trials [3, 4].

The within-session reproducibility of the two conditions was assessed using the coefficient of variation. The coefficient of variation for P<sub>I</sub>max were similar or smaller than those reported previously [11, 12], whilst those for P.P<sub>I</sub>max were considerably smaller than the 11.2 % reported by Wijkstra and others [10]. The coefficient of repeatability for P<sub>I</sub>max for the maximum value (‘long’) was similar to that reported previously [11], 2.5 kPa (25 cm H<sub>2</sub>O) compared to 2.7 kPa (28 cm H<sub>2</sub>O). The coefficient of repeatability for the ‘baseline’ measurement was larger than Maillards' [10], but this can be attributed in part to the differing absolute values of P<sub>I</sub>max of our subject populations. Our group had mean P<sub>I</sub>max of 13.5 kPa (138 cm H<sub>2</sub>O) whilst Maillards' was 11.3 kPa (115 cm H<sub>2</sub>O). Since the coefficient of repeatability is expressed in absolute values a larger absolute biological variability will be expressed in its values.

It is difficult to identify the mechanism(s) responsible for the increase in P<sub>I</sub>max and P.P<sub>I</sub>max following the RWU, but it is unlikely that it was due to the learning effect reported previously [1]. Whilst the Mueller manoeuvre is a highly effort-dependent test, earlier studies have shown that in well motivated healthy subjects full activation of the diaphragm is possible [13, 14]. However, a recent study by McKenzie et al.[15] found that voluntary activation of the diaphragm declines during maximal Mueller efforts at volumes below FRC. They conclude that amongst a number of mechanisms which could contribute to the influence of lung volume on voluntary drive to the diaphragm, reflexes dependent on muscle afferents might be involved.

In common with other skeletal muscle, the development of maximal force by the inspiratory muscles requires substantial reflex facilitation (most likely from muscle spindle afferents) in addition to the descending drive [16]. It has been suggested that the sudden loading of the inspiratory muscles experienced during the Mueller manoeuvre may produce a reflex inhibition of motoneurons [17]. It is possible that the preliminary respiratory activity of the RWU improves the intramuscular co-ordination and removes some of the reflex inhibition, resulting in greater force generation. Alternatively, even though the two conditions are different in terms of muscle contraction pattern, the muscle length specificity between the RWU and the Mueller manoeuvre may have contributed to the changed inspiratory muscle performance following RWU. In both test conditions, due care was taken to ensure that the manoeuvres were initiated from RV. This volume represents a specific muscle length of the inspiratory muscles that is not normally involved during quite breathing. It is quite possible that when a particular movement is repeated many times, alterations occur in the complex interactions amongst muscles, with the result that performance is enhanced [18]. Further work is required in this area and the response of trans-diaphragmatic pressure to bi-lateral phrenic nerve stimulation with and without RWU would be of particular interest.

Whilst there were no statistically significant differences between any of the 18 measurements following RWU, there is a suggestion that the RWU may have induced a small degree of fatigue which appeared to recover after about 15 measurements (see figure 1). We were not able to calculate the Tension-Time Index



(TTI) because the duty cycle ( $T_i/T_{ot}$ ) of the breathing pattern was not measured during the RWU. However, as can be seen in the methods, the breathing frequency adopted during the RWU was reduced. The subjects following expiration were pausing at FRC until they felt an urge to breath. This breathing pattern was characterised by a breathing frequency of about 6/min and an estimated  $T_i/T_{ot}$  value of around 0.1. Therefore, we are reasonably confident that the TTI was below the fatigue threshold of 0.15 suggested by Bellemare and Grassino (19). Even if we accept that some level of fatigue was induced by the RWU the effect that we report is still significant. If the suggested fatigue was prevented the warm-up effect would have been even larger. Therefore we don't believe that the presence, or not, of fatigue is a fundamental limitation of our study or that it should alter our conclusions. In any case, since both protocols resulted in the same absolute inspiratory pressures we can assume that RWU did not induce any additional fatigue than that, if any, induced by the 18 MIP manoeuvres. Clearly, further work is necessary to identify an optimal RWU which retains the properties of the warm-up utilised in our study.

The present study confirms our previous observation that the inspiratory muscles exhibit a 'warm-up' phenomenon following prior submaximal activity. Further, the present data suggest that a specific RWU may negate the so-called 'learning effect' which is one of the main contributors of the test's variability. In both the clinical and academic fields, the use of a RWU may provide a means of obtaining reliable values of  $P_{Imax}$  and  $P.P_{Imax}$  following just 3 measurements.

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Table 1 Mean (SD) values of PImax and P.PImax (kPa): difference between baseline series values without RWU and long series values with and without RWU.

	PImax		P.PImax	
	Baseline	Long	Baseline	Long
Control	13.5 (2.4)	14.7 (2.8)	13.5 (2.4)	15.9 (2.8)
RWU	13.5 (2.4)*	14.7 (3.0)	13.9 (2.1)*	15.7 (2.9)

Baseline: highest of the first 3 measurements, \* recorded prior to the RWU; Long: highest of the last 3 measurements; PImax: Maximum inspiratory pressure averaged over 1s; P.PImax: Peak maximum inspiratory pressure; RWU-Respiratory warm-up. Note: Baseline value for RWU in the value recorded prior to the RWU.

Table 2 Reproducibility data for the ‘baseline’ and ‘long’ series measurements of PImax and P.PImax.

	PImax		P.PImax	
	Baseline	Long	Baseline	Long
CV (%)	8.4 (3.7)	5.3(3.1)	8.2 ( 4.7)	5.6(3.7)
CR (kPa)	3.7	2.5	3.7	3.0

CV-Coefficient of variation, mean (SD); CR-Coefficient of repeatability for agreement.

	PImax			P.PImax		
	Baseline	Short	Long	Baseline	Short	Long
Control	13.2(2.2)	*13.8(2.7)	**14.7(2.8)	14.2(2.3)	*15.0(2.8)	**15.9(2.8)
RWU	14.3(2.9)	14.2(2.3)	14.7(3.0)	15.5(2.7)	15.5(2.8)	15.7(2.9)

Table 3 Mean (SD) development of PImax and P.PImax values (kPa) throughout the 18 measurement protocol for the two conditions (\* P< 0.05, \*\* P< 0.01).

Figure 1 Development of P<sub>I</sub>max during the Warm-up and the following 18 measurement protocol under both conditions. Comparisons are between RWU and control conditions. (\* P< 0.05, \*\* P< 0.01) (&: 'baseline' values of the trial without RWU are repeated for comparison purposes).

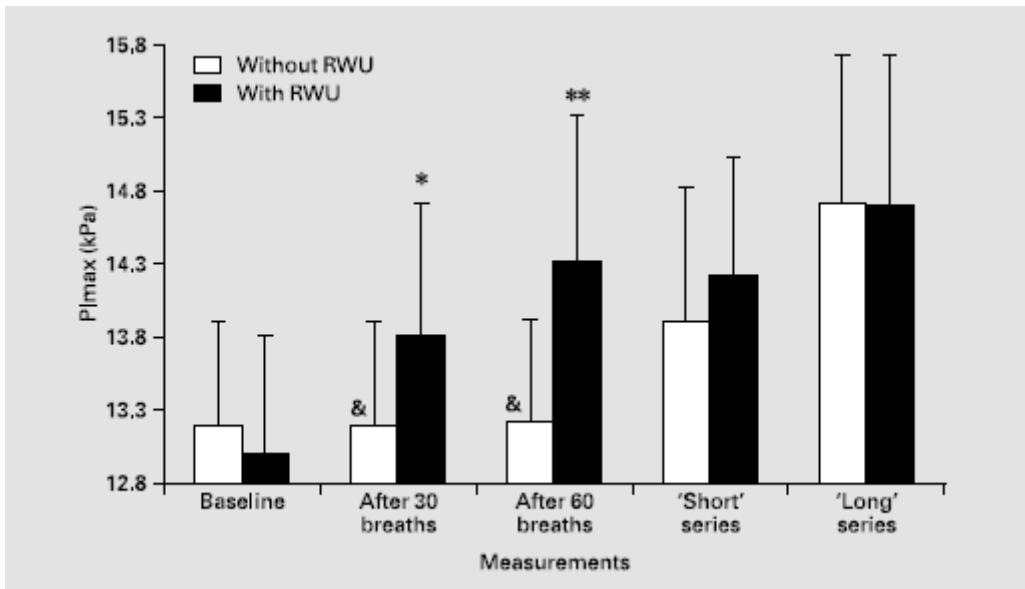


Figure 2 Development of P<sub>I</sub>max during the 18 measurement protocol without RWU.

