

## Measurement of sniff nasal and diaphragm twitch mouth pressure in patients

Philip D Hughes, Michael I Polkey, Dimitris Kyroussis, Carl-Hugo Hamnegard, John Moxham, Malcolm Green

### Abstract

**Background** – Inspiratory muscle weakness is a recognised cause of unexplained dyspnoea. It may be suggested by the finding of a low static inspiratory mouth pressure (MIP), but MIP is a difficult test to perform, with a wide normal range; a low MIP may also occur if the patient has not properly performed the manoeuvre. Further investigation conventionally requires balloon catheters to obtain oesophageal (Poes) and transdiaphragmatic pressure (Pdi) during sniffs or phrenic nerve stimulation. Two non-invasive tests of inspiratory muscle strength have recently been described – nasal pressure during a maximal sniff (Sn Pnas) and mouth pressure during magnetic stimulation of the phrenic nerves (Tw Pmo). The use of these two tests in combination might identify patients without inspiratory muscle weakness who are unable to produce a satisfactory MIP, therefore avoiding the need for investigation with balloon catheters.

**Methods** – Thirty consecutive patients with clinically suspected inspiratory muscle weakness and a low MIP underwent both conventional (Sn Poes and Tw Pdi) and non-invasive testing (Sn Pnas and Tw Pmo). Weakness was considered to be excluded by a Sn Poes of  $\geq 80$  cm H<sub>2</sub>O or a Tw Pdi of  $\geq 20$  cm H<sub>2</sub>O. The limit values used to test the hypothesis were Sn Pnas  $\geq 70$  cm H<sub>2</sub>O or Tw Pmo  $\geq 12$  cm H<sub>2</sub>O.

**Results** – Inspiratory muscle weakness was excluded in 17 of the 30 patients. Fifteen of these would have been identified using Sn Pnas and Tw Pmo, with better results when the two tests were combined. The cut off values selected for Sn Pnas and Tw Pmo were shown by ROC plots to indicate normal strength conservatively, avoiding failure to detect mild degrees of weakness. No patient with global weakness was considered normal by Sn Pnas or Tw Pmo.

**Conclusions** – In most patients with normal inspiratory strength and a low MIP, Tw Pmo and Sn Pnas used in combination can reliably exclude global inspiratory muscle weakness, reducing the number of patients who need testing with balloon catheters.

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Keywords: sniff nasal inspiratory pressure, magnetic stimulation, mouth pressure.

Accurate assessment of inspiratory muscle strength in patients is of value in the investigation of dyspnoea unexplained by cardiac or respiratory disease.<sup>1</sup> Although measurement of maximum static inspiratory mouth pressure (MIP) is a simple and commonly applied test, the normal range is wide even in experienced subjects.<sup>2,3</sup> Thus, although attainment of a high MIP probably excludes significant inspiratory muscle weakness, patients frequently generate low values which fail to differentiate between genuine mild weakness or difficulty with the technique. Moreover, the MIP does not discriminate specific diaphragm weakness. For these patients it is usual to obtain a more accurate assessment of inspiratory muscle strength by measuring pleural and transdiaphragmatic pressure during a sniff<sup>4,5</sup> and during phrenic nerve stimulation.<sup>1,6</sup> These measurements require the pernasal passage of balloon catheters into the stomach and oesophagus which may be mildly uncomfortable; this technique also requires experience which is not widely available.

It has recently been shown in subjects with normal airways that the pressure developed at the nose during a sniff (Sn Pnas) is closely related to the pressure in the oesophagus (Sn Poes).<sup>7,8</sup> Similarly, the pressure developed at the mouth during phrenic nerve stimulation (Tw Pmo) is also closely related to the twitch oesophageal (Tw Poes) and twitch transdiaphragmatic pressures (Tw Pdi).<sup>9,10</sup> We therefore hypothesised that Sn Pnas and Tw Pmo used in combination might enable inspiratory muscle weakness to be excluded in patients who were unable to achieve a satisfactory MIP for reasons other than respiratory muscle weakness. If so, the discomfort and technical difficulty of balloon catheters could be avoided in these patients without overlooking the diagnosis of inspiratory muscle weakness.

### Methods

#### PATIENTS

The subjects were 30 consecutive patients referred for suspected respiratory muscle weakness (table 1). They were unable to achieve a MIP which confidently excludes significant inspiratory weakness, defined in our laboratory as more than 80 cm H<sub>2</sub>O for men and 70 cm H<sub>2</sub>O for women.<sup>1</sup> The use of Tw Pmo and Sn Pnas in patients has been approved by our ethical committee and they now form part of the standard evaluation of patients referred for clinical assessment.<sup>1</sup> All patients gave informed consent to respiratory muscle assessment.

Respiratory Muscle Laboratory, National Heart and Lung Institute, Royal Brompton Hospital, London SW3 6NP, UK  
P D Hughes  
D Kyroussis  
M Green

Respiratory Muscle Laboratory, King's College Hospital, London SE5, UK  
M I Polkey  
J Moxham

Department of Pulmonary Medicine, Sahlgrenska University Hospital, Goteburg, Sweden  
C-H Hamnegard

Correspondence to: Dr P D Hughes.

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Patients with contraindications to magnetic nerve stimulation – that is, the presence of a cardiac pacemaker or cerebral aneurysm clips – were excluded from the study. Patients with potential swallowing difficulty such as motor neurone disease were carefully assessed prior to passing the balloons.

#### MEASUREMENTS

Mouth pressures were measured using a flanged mouthpiece attached to a brass tube incorporating a valve and 2 mm leak to prevent glottic closure. Oesophageal (Poes) and trans-diaphragmatic pressures (Pdi) were measured from latex balloons mounted on 100 cm polythene catheters passed pernasally and positioned in the oesophagus and stomach. Pressure at the nose (Pnas) was measured via an 80 cm catheter held in the nostril by a soft, hand fashioned nasal plug (Optosil P, Bayer, Leverkusen, Germany).<sup>8-11</sup> All pressures were measured with Validyne MP-45 transducers ( $\pm 200$  cm H<sub>2</sub>O) and Validyne amplifiers (Validyne Corporation, Northridge, California, USA). Signals were passed via a 12 bit NB-MIO-16 analogue-digital converter (National Instruments, Austin, Texas, USA) to a Macintosh Centris computer (Apple Computers, Cupertino, California, USA) running LabView software (National Instruments) and sampling at 100 Hz. The signals were neither filtered nor smoothed. The transducers were shown to be linear over the range of pressures measured in this study and the frequency response of the balloon and catheter-transducer system, determined by a pop test, was approximately 14 Hz.

#### MANOEUVRES

MIP was measured from residual volume while seated and wearing a nose clip.<sup>12</sup> Maximum inspiratory effort was encouraged verbally with

simultaneous visual feedback from a monitor. Manoeuvres were separated by at least 30 seconds rest and continued until no further increase in pressure could be obtained.

Sniffs were performed with the subject seated at functional residual capacity (FRC). Similarly, the monitor screen was visible to the subject and sniffs were recorded until no further increase in pressures could be obtained.<sup>5</sup>

Phrenic nerve stimulation was performed seated at FRC with the neck flexed using a Magstim 200 HP stimulator (Magstim Co, Whitland, Dyfed, UK) with a circular 90 mm coil positioned dorsally over the cervical spine.<sup>13</sup> Subjects rested for 20 minutes before stimulation to minimise twitch potentiation.<sup>14</sup> To obtain Tw Pmo an automatic triggering mechanism was used.<sup>9</sup> While the subject breathed quietly through the mouthpiece and tube the operator positioned the stimulator coil on the neck. After relaxing at FRC the valve was closed and the subject was then asked to exhale gently. The stimulator was automatically triggered as the mouth pressure reached 5 cm H<sub>2</sub>O.

#### ANALYSIS OF DATA

The MIP was defined as the greatest (most negative) value that could be sustained for one second; the best effort was selected for analysis. Sniffs were only accepted if the trace showed a rapid upstroke to a sharp peak. The greatest value obtained after instruction and with verbal encouragement was selected for analysis. Since in clinical practice Sn Pnas would be performed without an oesophageal balloon and the relation to FRC would be unknown, the baseline for Sn Poes and Sn Pnas was determined as the pressure at end-expiration immediately before the onset of the sniff upstroke, and the amplitude was the difference between this level and the nadir.

Table 1 Clinical and pulmonary function data on patients studied

Patient no.	Age	FEV <sub>1</sub> (% predicted)	FVC (% predicted)	TLC (% predicted)	Diagnosis
1	57	58	81	81	Elevated hemidiaphragm, COPD
2	61	100	101	90	Elevated hemidiaphragm
3	55	76	97	94	Dyspnoea, previous diaphragm surgery
4	56	23	67	145	Ventilatory failure, COPD
5	33	82	85	84	Elevated diaphragm
6	69	52	48	70	Ventilatory failure, motor neurone disease
7	48	47	49	55	Bilateral diaphragm paralysis
8	36	60	55	58	Dystrophia myotonica
9	61	81	91	90	Dyspnoea of unknown origin
10	68	55	50	51	Elevated hemidiaphragm
11	48	83	86	91	Elevated hemidiaphragm
12	74	58	54	75	Bilateral diaphragm paralysis
13	68	30	51	77	Elevated diaphragm, ventilatory failure, COPD
14	42	117	126	117	Friedrich's ataxia, dyspnoea
15	33	75	73	77	Ventilatory failure
16	56	58	83	71	Elevated hemidiaphragm
17	33	31	31	44	Elevated diaphragm
18	29	84	98	103	Dyspnoea of unknown origin
19	64	73	75	74	Dyspnoea of unknown origin
20	60	46	54	84	Ventilatory failure, COPD
21	65	60	57	69	Motor neurone disease
22	38	98	98	94	Dyspnoea of unknown origin
23	33	56	57	55	Elevated hemidiaphragm
24	54	67	68	67	Muscular dystrophy
25	52	94	98	97	Elevated hemidiaphragm, asthma
26	69	92	114	103	Familial myopathy
27	58	35	85	117	Familial myopathy, asthma
28	40	65	70	78	Elevated hemidiaphragm
29	32	66	68	70	Dyspnoea of unknown origin
30	64	82	94	95	Elevated diaphragm

FEV<sub>1</sub> = forced expiratory volume in one second; FVC = forced vital capacity; TLC = total lung capacity. Patients 1–17 are men.

Table 2 Inspiratory muscle strength data (units are cm H<sub>2</sub>O)

Patient	MIP	Sn Poes	Sn Pnas	Tw Pdi	Tw Pmo
1	64	92	78	21	10
2	56	90	71	21	12
3	58	125	96	23	8
4	22	76	31	16	7
5	64	72	64	35	21
6	15	24	7	5	3
7	27	47	38	0	0
8	36	46	46	2	1
9	19	75	58	20	9
10	53	89	60	20	13
11	58	84	51	9	10
12	37	37	26	3	2
13	43	36	35	7	6
14	57	96	109	30	21
15	66	82	60	37	27
16	22	52	49	16	8
17	8	37	33	60	23
18	60	111	87	22	19
19	35	88	82	21	17
20	11	70	58	13	6
21	8	35	31	8	7
22	15	47	41	38	30
23	42	72	52	11	8
24	18	32	27	5	3
25	22	51	42	23	20
26	44	69	63	16	8
27	32	87	76	24	12
28	65	70	55	17	10
29	33	46	40	25	24
30	35	72	68	22	13

MIP=inspiratory mouth pressure; Sn Poes=sniff oesophageal pressure; Sn Pnas=sniff nasal pressure; Tw Pdi=twitch transdiaphragmatic pressure; Tw Pmo=twitch mouth pressure.

For twitch Pdi, traces were accepted for analysis if the subject was at FRC. For Tw Pmo, where FRC would also have to be estimated without an oesophageal balloon, traces were accepted if there was a smooth pressure profile with no evidence of poor mouth seal. Amplitude was defined as the difference between baseline and peak; the mean of at least three stimulations was used.

The relationship between Sn Pnas and Sn Poes, and between Tw Pmo and Tw Pdi, was examined using linear regression. Our aim was to identify subjects in whom balloon catheter investigation would serve no useful purpose; we therefore intentionally set conservative limit values which would certainly exclude important weakness: Sn Poes  $\geq 80$  cm H<sub>2</sub>O or a Tw Pdi of  $\geq 20$  cm H<sub>2</sub>O. The limit values used to test our hypothesis were: Sn Pnas  $\geq 70$  cm H<sub>2</sub>O or Tw Pmo  $\geq 12$  cm H<sub>2</sub>O. The sensitivity and specificity of the limit values for Sn Pnas or Tw Pmo were calculated by defining a true positive result as a patient with normal strength correctly identified by these two tests. The effect of varying these limit values on the detection of normal strength was considered using receiver-operator characteristic (ROC) plots.

## Results

Pulmonary function data are presented in table 1. Full inspiratory muscle measurements are shown in table 2 and plotted in fig 1. Using the predetermined criteria for the tests with balloon catheters (Sn Poes  $\geq 80$  cm H<sub>2</sub>O or Tw Pdi  $\geq 20$  cm H<sub>2</sub>O), significant inspiratory muscle weakness was confidently excluded in 17 of 30 patients (57%). Both Tw Pmo and Sn Pnas were above the limit values in five of the 17 patients, in two the Sn Pnas was above the limit value, and in eight Tw Pmo exceeded the limit value. Thus, in 15 of the 17 subjects (88%) with a low MIP normal strength could

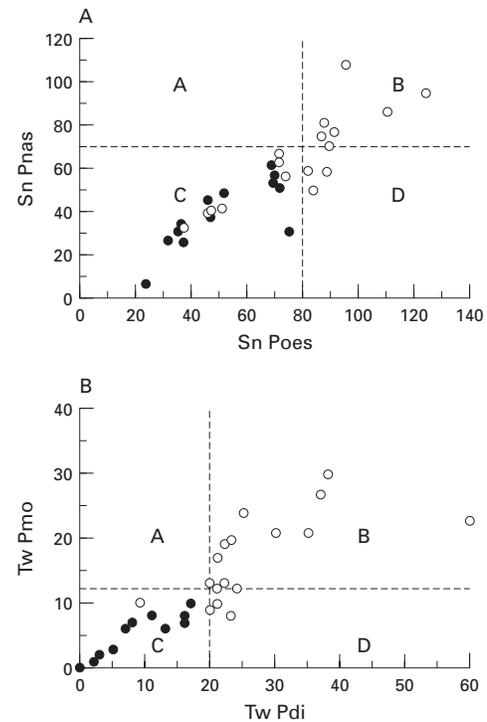


Figure 1 (A) Values of Sn Poes and Sn Pnas for each patient ( $R^2=0.786$ ). Dashed lines represent limit values for exclusion of significant weakness. Open circles represent patients with normal strength (Sn Poes  $\geq 80$  cm H<sub>2</sub>O or a Tw Pdi of  $\geq 20$  cm H<sub>2</sub>O), closed circles represent weak patients. Box A represents patients who would be defined as normal by Sn Pnas, while Sn Poes would suggest weakness. No patients fall into this category. Box B contains patients exceeding the limit values for Sn Poes and Sn Pnas. This box therefore represents patients in whom testing with balloon catheters is unnecessary, as Sn Pnas has excluded significant weakness. Box C contains the patients who were unable to attain the limit value with either Sn Poes or Sn Pnas, therefore defined as weak by both tests. Box D contains the three patients unable to reach the limit values for Sn Pnas in whom Sn Poes excluded inspiratory weakness – that is, Sn Pnas suggested weakness, refuted by balloon catheter testing. (B) Values for Tw Pdi and Tw Pmo for each patient ( $R^2=0.845$ ). Open and closed circles as for (A). Box A represents patients who would be defined as normal by Tw Pmo, while Tw Pdi would suggest weakness. No patients fall into this category. Box B represents patients in whom Tw Pdi and Tw Pmo are above the limit values, therefore excluding weakness. Passage of balloon catheters is unnecessary as Tw Pmo exceeds the limit value. Box C contains patients in whom Tw Pmo and Tw Pdi are low, therefore defined as weak by both tests. Box D contains patients with Tw Pmo below the limit value, suggesting weakness. In these patients Tw Pdi confirms normal diaphragm strength.

be confirmed without tests requiring balloon catheters. The confirmation of normal strength when Sn Pnas and Tw Pmo were used in combination (15 of 17) was greater than when either Sn Pnas (seven of 17) or Tw Pmo (13 of 17) were used alone. Two of the 17 patients subsequently found to have normal inspiratory muscle strength would not have been spared formal investigation using the limit values of Sn Pnas  $\geq 70$  cm H<sub>2</sub>O or Tw Pmo  $\geq 12$  cm H<sub>2</sub>O.

Figure 2 shows ROC curves for Sn Pnas and Tw Pmo when used individually and in combination. The effect of applying differing cut off values on the sensitivity and false positive rate (defined as 1 – specificity) for confirming

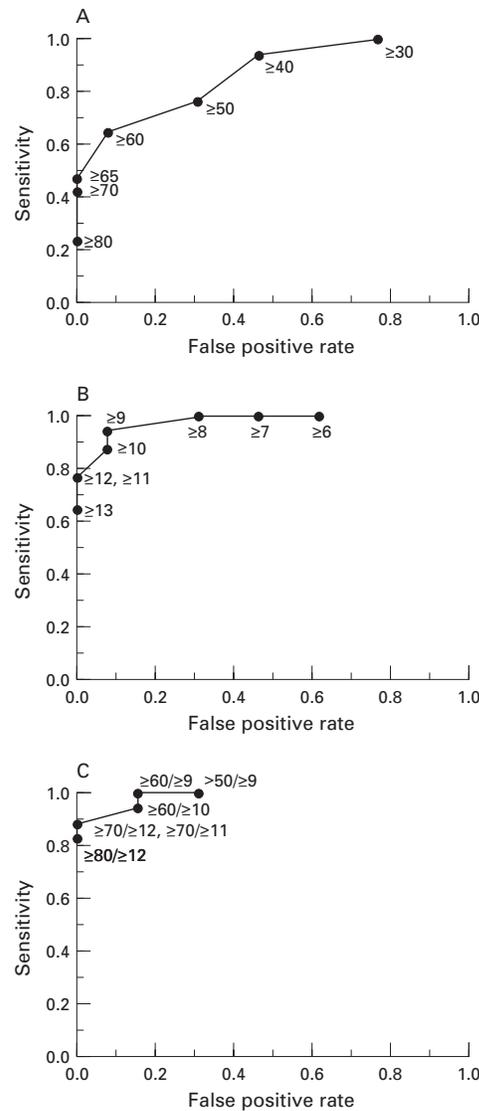


Figure 2 ROC plot for (A) Sn Pnas, (B) Tw Pmo, and (C) Tw Pmo and Sn Pnas in combination for the detection of normal respiratory muscle strength. Points represent cut off values (cm H<sub>2</sub>O) for each test or tests.

strength are shown. The curves demonstrate the empirical observation that the greatest sensitivity and lowest false positive rate for confirming normal strength is achieved by combining Tw Pmo and Sn Pnas.

### Discussion

We conclude that Sn Pnas and Tw Pmo can satisfactorily exclude inspiratory muscle weakness in a substantial proportion of patients with suspected muscle weakness and a low MIP. Although very safe, the passage of balloon catheters is mildly uncomfortable and requires the experience and expertise of a specialist laboratory. By using these tests clinicians may be able to avoid tests with balloon catheters for a significant number of patients.

The validity of this approach rests on the predefined limit values used for this study. The exclusion of muscle weakness after formal

testing was based on values previously reported in the literature from our laboratories.<sup>4-6,15</sup> For the non-invasive tests we chose values slightly higher than those previously reported<sup>9,16,17</sup>; the rationale for this was that we wanted to set a level which would allow us confidently to avoid placement of balloon catheters. Our cut off values were based on the principle of detecting the greatest proportion of subjects who are truly strong, while keeping as small as possible the possibility of falsely declaring normal strength as this implies failure to detect weak respiratory muscles. The ROC plots show that our selected cut off points achieved this aim, although slightly lower values would have achieved similar results. Equally, specific cut off values for each sex (or, indeed, age group) might refine the determination of strength by Sn Pnas and Tw Pmo, but our patient numbers are insufficient for meaningful analysis in this regard. Indeed, the two false negative cases were both men, suggesting that, in our data at least, reduced cut off values for women are unnecessary.

The clinical application of Sn Pnas and Tw Pmo assumes that pressure is well transmitted from the pleura to the mouth. This may be a particular problem in chronic obstructive pulmonary disease (COPD) during phrenic nerve stimulation<sup>18</sup> and, to a lesser extent, during sniffs.<sup>19</sup> In COPD this is compounded by the altered geometry of the diaphragm which causes a disproportionate reduction in the capacity of the diaphragm to lower intrathoracic (and hence mouth) pressure<sup>20</sup> and is demonstrated by patient no. 1. Although Sn Pnas and Tw Pmo may falsely suggest weakness if used in patients with severe airflow obstruction, this does not alter our conclusion that inspiratory muscle weakness may be excluded if the cut off values are achieved with these tests. A protocol for suspected respiratory muscle weakness using mouth pressure measurements followed by Sn Pnas and Tw Pmo and finally Sn Poes and Tw Pdi is a logical stepwise progression<sup>1</sup> as these tests are increasingly specific but more complex and demanding at each level. An alternative strategy whereby Sn Pnas and Tw Pmo replace balloon tests in diagnosing weakness cannot be recommended with confidence. Technical limitations might falsely label a few patients as weak, diverting the clinician from the correct diagnosis. Furthermore, placement of balloon catheters provides additional valuable physiological data in truly weak patients such as lung compliance and hemidiaphragm twitch Pdi. Patients with diaphragm weakness are uncommon in clinical practice and it is therefore important to investigate them thoroughly and diagnose them accurately. Selecting out patients with low MIP and normal Sn Pnas or Tw Pmo will substantially reduce the numbers requiring balloon tests which relatively few clinicians have immediately available.

Although we have shown the benefit of Sn Pnas and Tw Pmo, especially when used together, there are likely to be difficulties in adopting these tests, particularly Tw Pmo, as widely as MIP because of the cost and technical

difficulty in setting up a suitable system outside a specialist laboratory.<sup>17</sup> However, oesophageal pressure is routinely measured in many standard lung function laboratories. Sn Pnas or Sn Poes are therefore likely to be the first logical step in the investigation of patients with low MIP, although Sn Poes, Sn Pnas and MIP share the failings of a volitional manoeuvre – specifically, that patients do not always make a maximal effort.<sup>21</sup> Lowering the threshold for MIP while using Sn Pnas does not further improve the detection of normal strength in our group of patients. Magnetic nerve stimulators are increasingly used by departments of neurology and neurophysiology in place of electric nerve stimulators and may therefore become more widely accessible to respiratory physicians.

Although mildly unpleasant for the subject, in experienced laboratories balloon catheters may be satisfactorily positioned in more than 95% of patients. The use of balloon catheters requires both training and skill in correct technique and in the interpretation of traces and therefore adds to the time and cost of achieving a diagnosis. We believe that such an assessment is justified in patients with genuine respiratory muscle weakness even when mild. However, the avoidance of unnecessary examinations in patients without respiratory muscle weakness is beneficial to all concerned. Our results show that the use of Tw Pmo and Sn Pnas in combination (using limit values of Sn Pnas  $\geq 70$  cm H<sub>2</sub>O or Tw Pmo  $\geq 12$  cm H<sub>2</sub>O) is of value in the exclusion of inspiratory muscle weakness. The data support their use in patients with low MIP before proceeding to further investigation with balloon catheters. If appropriately used this approach could save both time and inconvenience to patients and clinical staff.

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