Eur Respir J 2000; 16: 1070–1074
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European Respiratory Journal
ISSN 0903-1936

Performance of forced expiratory manoeuvre in children

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ABSTRACT: The negative expiratory pressure (NEP) method has been previously used to assess the performance of forced vital capacity (FVC) manoeuvre in normal adults. The aim of the present study is to assess whether flow limitation is achieved during FVC manoeuvres in children aged 6–14 yrs.

NEP (-10 cmH_2O) was successfully applied in 177 normal children, the portion of FVC over which expiratory flow did or did not change with NEP being taken as effort-dependent and effort-independent, respectively.

In all children peak expiratory flow (PEF) and forced expiratory volume in one second (FEV1) increased with NEP, indicating that PEF was in the effort-dependent portion of FVC. This portion decreased significantly with age (50–20% of FVC from 6–14 yrs). It is suggested that this mainly reflects the poorer coordination of specialized motor acts in younger children because of incomplete morphological and functional maturation of the relevant central nervous system (CNS) mechanisms.

The results indicate that most unexperienced children aged 6–14 yrs can perform acceptable forced vital capacity manoeuvres, eventually achieving flow limitation over a portion of the forced vital capacity that increases with age. The negative expiratory pressure method can be used for online assessment of the performance of forced vital capacity manoeuvres and evaluation of treatment-related effects.
Eur Respir J 2000; 16: 1070–1074.

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Keywords: Detection of flow limitation
maximal expiratory flow-volume curve
negative expiratory pressure
normal values
upper airway collapsibility

Received: November 3 1999
Accepted after revision July 18 2000

This study was supported by the Ministry of University and Technological Research of Italy.

Forced expiratory manoeuvres including the forced expiratory volume in one second (FEV1) are routinely used to assess the maximal expiratory flows that a subject can achieve at different lung volumes [1, 2]. In adults, except at very high lung volumes, the maximal flows are usually determined by flow limitation (FL) due to dynamic airway compression [3–6]. One of the largest sources of within-subject variability of forced expiratory manoeuvres is the performance of the test with insufficient effort to reach expiratory FL [1, 2]. In the past, there was no online method available to assess whether expiratory FL was reached during the forced expiratory manoeuvre. Recently, however, the negative expiratory pressure (NEP) technique has been successfully applied in normal adults to assess FL during forced vital capacity (FVC) manoeuvres by VOLTA *et al*. [7]. They showed that adults with considerable previous experience in lung function testing performed FVC manoeuvres with sufficient effort to achieve FL over most of the vital capacity. In contrast, in subjects without previous experience multiple efforts may be required to obtain acceptable FVC manoeuvres [7].

Although in children aged ≥6 yrs FVC manoeuvres are routinely performed, the extent of FL, if present, has not been determined to date. The aim of the present study was to extend the use of NEP to detect expiratory flow limitation during FVC manoeuvres in a large population of healthy children aged 6–14 yrs.

Materials and methods

The study examined 220 Caucasian children, 140 males and 80 females, aged 6–14 yrs, from a private school in Milan, Italy. The outcome of a screening questionnaire [8] ensured that subjects with any known or suspected predisposition to pulmonary or upper airway disease were not included in the study. None of the subjects were aware of the purpose of the present investigation. The study was approved by the Institutional Ethics Commitee and informed consent was obtained from the parents.

The experimental setup consisted of a pneumotachograph connected through a rapid (displacement time of 45 ms) two-way solenoid valve either to the ambient or to a 220 L drum in which pressure was kept at -10 cmH_2O by means of a flow-through system. The high flow (~50 $L \cdot s^{-1}$), produced by two vacuum cleaners operating in parallel, ensured that the pressure in the drum increased negligibly when the subjects were made to expire maximally into the drum. With the solenoid valve inactive, the subject breathed into the ambient. Once activated, the solenoid valve connected the subject to the drum when the expiratory flow reached a preset threshold value (0.4–1.1 $L \cdot s^{-1}$) and the NEP was applied as long as the expiratory flow remained above the threshold value.

Flow was measured with a heated number 3 or 4 Fleisch pneumotachograph (Fleisch, Lausanne, Switzerland) connected to a differential pressure transducer (MP-45, ±2 cmH_2O; Validyne, Northridge, CA, USA). The signal from the transducer was amplified (Carrier; 20-3615-45; Gould, OH, USA) and recorded on a personal computer *via* a 16-bit analogue-to-digital converter at a sample rate of 200 Hz. The calibration of the pneumotachograph-transducer system was carried out by means of a rotameter before and after each session; the response was linear over the experimental range of flows. Data analysis was performed using the Anadat software (RHT-InfoDat, Montreal, Canada).

The subjects were studied sitting comfortably on a chair, wearing a noseclip; care was taken to ensure they felt comfortable and that they kept their neck at a fixed neutral position [9]. None of the subjects had previous experience with FVC manoeuvre. They were instructed to fully inspire, after a warning signal, from functional residual capacity (FRC) and then expire as fast and hard as possible. Tests were run according to established procedures [1, 8] by trained personnel between 15:00–17:00 h. The subjects performed two series of four FVC manoeuvres; each series consisted of two manoeuvres with and two without NEP performed randomly at a frequency of one every 40–60 s with an interval of 20–30 min between the two series.

The following parameters were assessed in subjects who were able to perform at least two technically satisfactory manoeuvres [1, 8, 10] with NEP and two without: 1) peak expiratory flow (PEF); 2) FEV1; 3) FVC; 4) time to reach PEF (*t*PEF); and 5) time from onset of expiration at which NEP was applied (*t*NEP). For PEF, FEV1 and FVC, the best value for each type of manoeuvre was selected, whilst *t*PEF and *t*NEP were taken from the manoeuvre with the largest PEF. Because NEP was applied for the time during which the expiratory flow remained above the preset threshold level, FEV1 with NEP was assessed only in the subjects in whom NEP was applied for at least 1 s.

Results are presented as mean±SD. Statistical significance of group mean values was established by analysis of variance (ANOVA) and a paired t-test where appropriate. Linear regressions were computed with the least square method and statistical assessment was made by covariance analysis (ANCOVA). A p-value of <0.05 was considered to be statistically significant.

Results

Of 220 subjects, 15 (10 in the 6–7 yr span and five in the 8–9 yr span) were unable to perform the FVC manoeuvre correctly because of the inability to: fully inspire, activate the expiratory muscles rapidly enough, exhale for at least 1 s, and avoid one or more interruptions during the expiratory effort. Lung function parameters of all 205 remaining subjects were within the limits of normality [11].

In 28 subjects, 18 males and 10 females, application of NEP decreased PEF by an average 0.34±0.05 $L \cdot s^{-1}$. These subjects exhibited a marked decrease in expiratory flow shortly after the application of NEP followed by a relatively slow increase to PEF. Hence, whilst timing of NEP application (TNEF=64±5 ms) was similar to that of the other subjects (table 1), *t*PEF (387±24 ms) was much longer.

Application of NEP during the FVC manoeuvre increased PEF in all 177 subjects, and FEV1 in 110 out of 127 subjects (91 male children and 36 female children) in whom NEP was applied for more than 1 s from the beginning of the expiratory effort. Figure 1 depicts the time course of flow during FVC manoeuvres with and without NEP of representative subjects, while the effects of NEP, classified according to age, are given in table 1. A significant negative correlation occurred between ΔPEF, expressed as per cent control PEF, and control PEF (slope=-1.14 $s \cdot L^{-1}$; p=0.006), as well as between Δ*t*PEF with NEP and control *t*PEF (slope=-0.334; p<0.001).

Nearly all the subjects inspired rapidly (0.8–1.2 s from FRC to full inspiration). In most of them the transition from inspiration to expiration (I-E) occurred with the same timing during FVC manoeuvres with and without NEP, *i.e.* either a short pause (<0.5 s) or a long pause (>1 s) preceded the expiratory effort (type A), but in some subjects the combination of the pauses was long-short (type B) or short-long (type C). The changes of PEF with NEP were similar for type A and B of I-E transition, but significantly smaller with type C (table 2), in line with previous observations in adults [12]. On the other hand, Δ*t*PEF was independent of the type of I-E transition.

Assessment of FL could be performed in 33 subjects, 20 males and 13 females, by superimposing the maximum expiratory flow-volume (MEFV) curves with and without NEP (fig. 1). This approach requires that total lung capacity (TLC) is reached in both manoeuvres [4]. To ensure that this was the case, the analysis was limited to those instances in which the FVC with and without NEP did not differ by >2% of the larger FVC. An additional requirement was that both the best PEF and FEV1 occurred for the same FVC manoeuvre with and without

Table 1. – Forced vital capacity variables with and without (control) negative expiratory pressure (NEP) of -10 cmH_2O

		Control			NEP			
Age yr	N	PEF $L \cdot s^{-1}$	FEV1 L	*t*PEF ms	PEF $L \cdot s^{-1}$	FEV1 L	*t*NEP ms	*t*PEF ms
6	8 (6)§	3.69±0.30	1.38±0.20	211±44	3.99±0.36*	1.52±0.29‡	51±34	185±59
7	20 (14)	4.23±0.59	1.57±0.14	195±80	4.62±0.70*	1.65±0.17+	57±36	181±65
8	25 (15)	4.24±0.44	1.62±0.21	199±68	4.59±0.46*	1.67±0.24+	57±22	188±65
9	17 (10)	4.49±0.43	1.76±0.32	208±64	4.92±0.46*	1.89±0.33+	71±32	224±79
10	20 (14)	4.85±0.52	1.98±0.29	189±68	5.37±0.53*	2.12±0.27*	68±23	172±56
11	24 (16)	5.41±0.60	2.37±0.30	172±59	5.77±0.69*	2.46±0.29+	59±29	187±55
12	27 (24)	5.87±0.54	2.53±0.30	171±65	6.36±0.56*	2.63±0.28*	54±24	170±75
13	19 (16)	6.29±0.93	2.66±0.32	165±58	6.72±1.09*	2.79±0.37+	53±19	159±66
14	17 (14)	7.08±1.04	3.20±0.55	158±46	7.60±1.16*	3.42±0.56*	47±21	151±53

Values are presented as mean±SD. *t*PEF: time to reach peak expiratory flow (PEF); *t*NEP: time from expiratory onset at which NEP is applied; FEV1: forced expiratory volume in one second. Value in parentheses represents the number of subjects in whom FEV1 was assessed both with and without NEP. §: applies to all age groups. Significant difference between NEP and control. *: p<0.001; +: p<0.01; ‡: p<0.05.

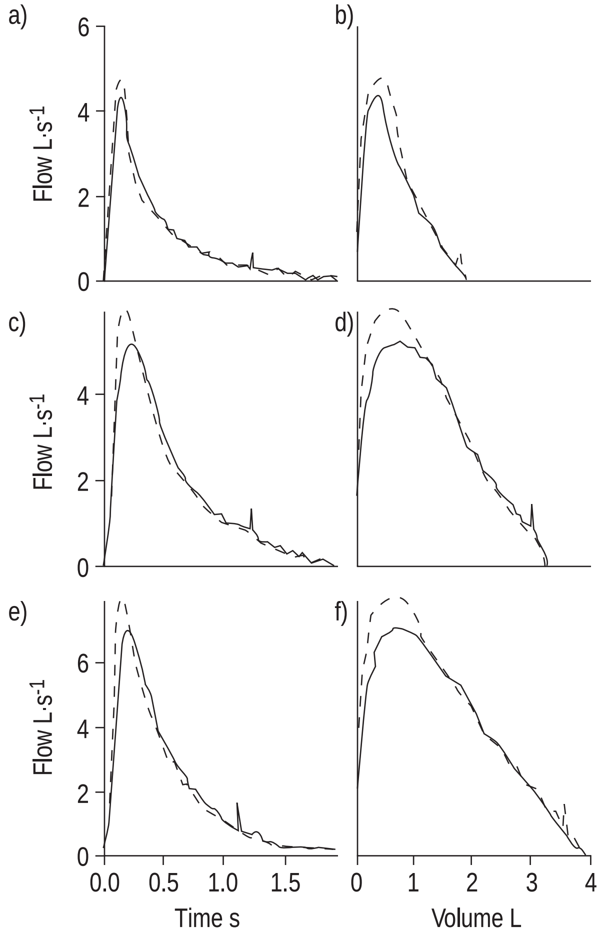

Fig. 1. – Time course of expiratory flow (a, c and e) and corresponding flow-volume curves (b, d, f) during forced vital capacity manoeuvres with and without negative expiratory pressure (NEP) observed in three children. Spikes on flow signal are artifacts that indicate application and removal of NEP. ——: control; - - - -: NEP.

NEP. In all these instances, NEP caused an initial increase in flow; however, the expired volume, expressed as per cent FVC, during which the expiratory flow with NEP exceeded that observed under control conditions decreased significantly both with increasing FVC and age, as shown in figure 2. Using the stepwise multiple regression analysis, age was the only significant contributor to the effort-dependent phase of FVC. In these subjects

Table 2. – Dependence of changes of forced vital capacity (FVC) variables with negative expiratory pressure (NEP) on the combination of end-inspiratory pauses preceding the FVC manoeuvre with and without NEP

Combination	N	ΔPEF $L \cdot s^{-1}$	Δ*t*PEF ms
A	139	0.42±0.25^{+}	-6±67
B	13	0.57±0.40*	-17±91
C	10	0.25±0.13	-5±45

Values are presented as mean±SD. *t*PEF: time to reach peak expiratory flow (PEF); ΔPEF: change in peak expiratory flow; A: same type of pause during FVC manoeuvre with and without NEP; B: pause (≤1 s) during FVC manoeuvre without NEP and no pause during FVC manoeuvre with NEP; C: opposite to B. Significant difference relative to C. *: $p<0.01$; $^{+}$: $p=0.001$.

the differences in PEF (ΔPEF) and FEV_1 (ΔFEV_1) between the forced expiratory manoeuvres performed with and without NEP were also computed. The relations of ΔPEF and ΔFEV_1, expressed as per cent of the corresponding values without NEP, PEF_c and FEV_1, respectively are plotted against age in figure 3. In both cases there was a significant correlation ($p<0.001$). On average, at an age of 6 yrs the values of PEF and FEV_1 were about 18 and 10% lower without NEP than with, while at an age of 12–14 yrs such differences became negligible. When computed from the data for all the subjects in table 1, the regression of $\Delta PEF/PEF_c(\%)$ to age was similar to that obtained in the subjects of figure 3 ($y=-26+1.53 \cdot x$; $r=0.559$; $p<0.001$). In contrast, the regression of $\Delta FEV_1/FEV_{1c}(\%)$ to age was not significant ($y=-10+0.8 \cdot x$; $r=0.13$). The latter was probably due to differences in TLC between the forced expiratory manoeuvres with and without NEP.

Discussion

The main new findings of the present study are that children aged 6–14 yrs eventually achieve expiratory FL during forced expiratory manoeuvres, and that the flow limited portion of FVC decreases significantly with decreasing age and FVC.

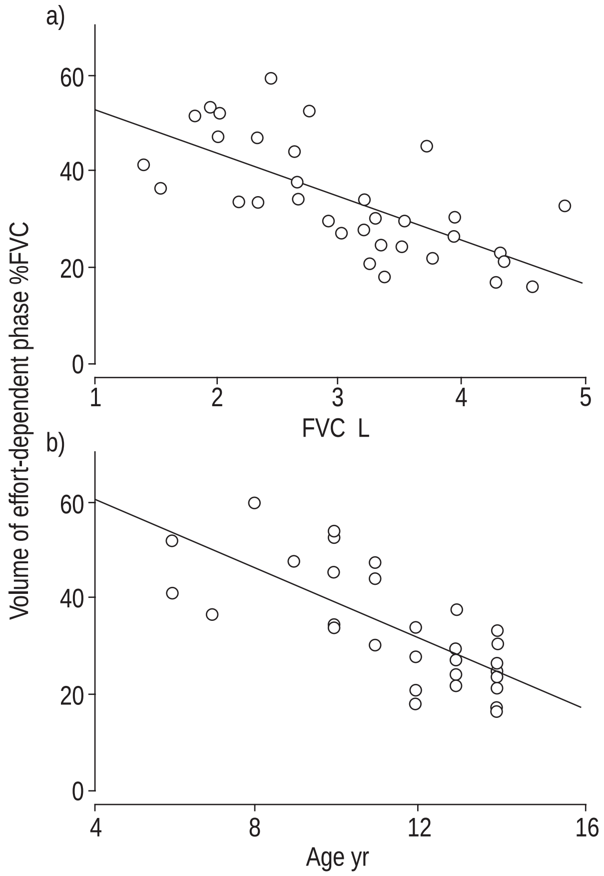

Fig. 2. – Relationships between forced vital capacity (FVC) and expired volume, expressed as per cent FVC, a) during which flow was larger with negative expiratory pressure (NEP) than without NEP (effort-dependent phase) ($y=61.7–9x$; $r=0.689$; $p<0.001$) and b) between age and expired volume, expressed as per cent FVC, during which flow was larger with NEP ($y=74.8–3.6x$; $r=0.725$; $p<0.001$).

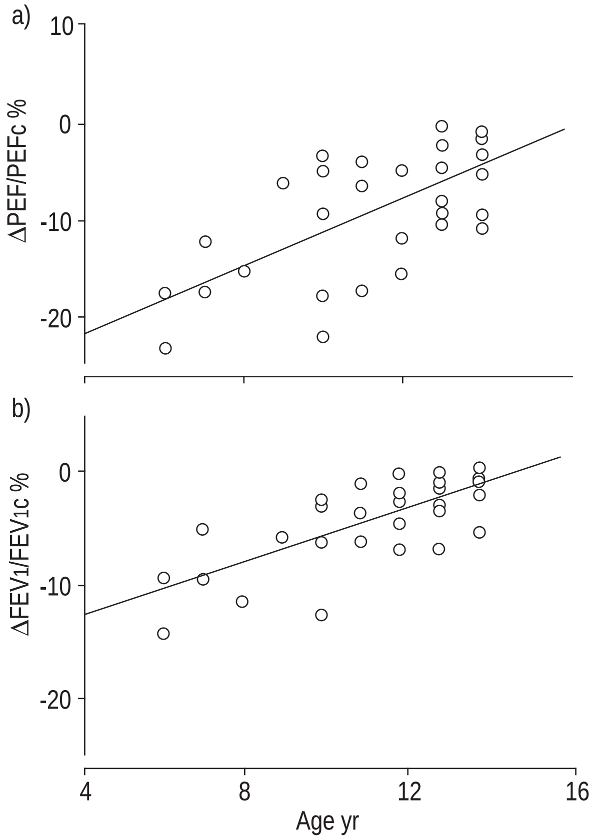

Fig. 3. – Relationships of age to the differences in a) peak expiratory flow (PEF) (y=-28.4+1.7x; r=0.654; p<0.001) and b) forced expiratory volume in one second (FEV_1) (y=17.1+1.11x; r=0.727; p<0.001) obtained during forced expirations with and without negative expiratory pressure (NEP), expressed as per cent of corresponding values without NEP (c) in same subjects of fig. 2.

Forced expiratory manoeuvres are routinely used to assess lung function in children aged ≥6 yrs [13, 14]. Only 15 of 220 children were unable to perform technically satisfactory FVC manoeuvres, their inability probably being due to the lack of cooperation, since it has been shown that some children aged 3–5 yrs can be coached to perform acceptable FVC manoeuvres [15].

The lung function (PEF, FEV_1, and FVC) of children who performed satisfactory forced expiratory manoeuvres was within normal limits [11]. In 28 of them, assessment of flow limitation with the NEP method could not be performed, since NEP caused a transient decrease in flow, reduced PEF, and markedly longer t_{PEF}. This pattern prevailed in the youngest children. A transient decrease in expiratory flow after application of NEP has been previously observed in normal adults during tidal breathing, and is believed to reflect upper airway narrowing [16, 17]. Such a phenomenon, however, has not been observed in normal adults with application of NEP of -10 cmH_2O during FVC manoeuvres, suggesting that young children have more collapsible upper airways than normal adults.

In most children PEF and FEV_1 increased significantly with NEP (table 1). The volume history preceding the FVC manoeuvre affects transpulmonary pressure [18] and maximal expiratory flows [12]; the increase of PEF with NEP was significantly smaller when the end-inspiratory pause preceding the FVC manoeuvre was long with NEP and short without NEP (table 2). However, the changes in PEF and FEV_1 with NEP could not be attributed to differences in the time course of maximal inspiration prior to the FVC manoeuvre, since in most children it was vitually the same with and without NEP (table 2). Thus, the higher PEF and FEV_1 values with NEP should reflect absence of FL during the initial part of FVC (effort-dependent phase). The effort-dependent phase decreased progressively from ~50% FVC at the age of 6 yrs to ~25% FVC at 14 yrs (fig. 2). HYATT *et al.* [5] originally estimated that in normal adults effort dependence encompassed 30–50% of FVC. This estimate was subsequently decreased to 20–30% FVC [6, 19], which is close to the values obtained in the older children in the present study, and to ~13% FVC in well trained adults [7].

Among the several factors that determine maximal expiratory flows (V'_{max}) [5], the following features could explain the greater extent of the effort-dependent phase in younger children (fig. 2), as they should limit the increase in alveolar pressure during the FVC manoeuvres. The total respiratory system compliance continues to decrease from age 5–16 yrs, with part of this change attributable to changes in the chest wall [20]. As a result the elastic recoil of the respiratory system should contribute less expiratory driving pressure in younger children than in older children and adults. Distortion of the chest wall occurs in normal adults during the FVC manoeuvre [21]; because of lower compliance of the chest wall and, most likely, lesser coordination of abdominal and ribcage expiratory muscles, the pressure losses due to distortion of the chest wall could also be greater in the younger children. Maximal expiratory pressures are smaller in younger children than in older children and adults [22], and this could also contribute to a lower rate of increase of expiratory pressure during the FVC manoeuvres. It is likely, however, that most of the age-dependent changes in the effort-dependent phase reflect the fact that younger children are unable to coordinate the activity of the various muscles involved in the FVC manoeuvre. While the peripheral nervous system and most central nervous system structures reach morphological maturity before the age of 6 yrs, the maturation of several structures involved in motor coordination occurs at the age of 10–15 yrs [23]. Moreover, the conduction time in the corticospinal tract also decreases with age, adult values being reached at the end of the first decade of life, and a similar maturational profile is exhibited in coordinated motor acts, such as tapping and aiming movements [24]. Kinesthetic reaction times have also been shown to attain adultlike values after 10 yrs of age [25]. The poorer coordination of specialized motor acts in young children is consistent with the observations that t_{PEF} (table 1) was markedly longer than that observed in normal, experienced adults (116±25 ms) [7], and that application of NEP significantly decreased t_{PEF} in those children who exhibited longer t_{PEF} under control conditions. It should also be noted that the children had no previous experience in FVC manoeuvres, and that lack of experience can affect the performance of the FVC manoeuvres in adults [7].

In adults, NEP has been used to assess the performance of FVC manoeuvre, *i.e.* for online recognition of whether the FVC manoeuvre is performed with sufficient effort to achieve FL over most of the expired volume [7]. In younger children the volume range over which FL occurs is considerably smaller (fig. 2) than in adults. Nevertheless, application of NEP in younger children is useful: a) to define the magnitude of the effort-independent range of FVC, and b) to assess if the changes in PEF and FEV1 due to treatment are the result of an improvement in FL or of an increase in expiratory effort. In the case of improvement of respiratory muscle function, V'_{max} would increase only in the effort-dependent volume range, whilst an improvement in FL (*e.g.* with bronchodilator administration) should be associated with an increase in V'_{max} over the effort-independent phase. Finally, since there is no evidence that over the effort-dependent phase of the FVC manoeuvre V'_{max} had been achieved with a NEP of -10 cmH_2O, there is the potential of a greater increase in PEF and FEV1 than that shown in figure 3 with development of larger expiratory driving pressures. This is of clinical interest to the extent that younger children could be trained to develop larger driving pressures. Asthmatic children, in whom PEF is often assessed on a daily basis, could exhibit such a training effect.

To conclude, the results of the present study indicate that most of the unexperienced children in the age group 6–14 yrs can perform acceptable forced vital capacity manoeuvres. All children eventually achieve flow limitation during the forced vital capacity manoeuvre, but the extent of the effort-independent portion of the forced vital capacity increases with age. The latter explains in part the larger intrasubject variability of peak expiratory flow and forced expiratory volume in one second exhibited by the children than by the adults. Application of negative expiratory pressure appears to be useful for the online assessment of the performance of the forced vital capacity manoeuvre and the evaluation of treatment related effects.

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