Do subjects investigated for occupational asthma through serial peak expiratory flow measurements falsify their results?

Jean-Luc Malo, MD, Carole Trudeau, RT, Heberto Ghezzo, PhD, Jocelyne L'Archevêque, RT, and André Cartier, MD
Montreal, Quebec, Canada

Background and aim: *Serial assessment of peak expiratory flow (PEF) rates has been advocated as a sensitive and specific means of investigating occupational asthma. The possibility that, for several reasons, subjects do not accurately report their values has been raised. The availability of portable instruments that assess PEF and store timings and values now makes it possible to estimate compliance and accuracy of results.*
Methods: *Twenty-one subjects consecutively investigated for occupational asthma were asked to assess their PEF every 2 hours during the day, both at work and away from work, with a VMX instrument (Clement Clarke International, Columbus, Ohio) and record the times and values on a sheet of paper. The subjects were not aware that the data were also being stored on a computer chip. The diagnosis was occupational asthma in eight subjects, personal asthma in four subjects, and neither condition in nine subjects.*
Results: *The mean duration of recording was 36 days (range, 14 to 79 days). At least 6048 values should have been recorded, but only 4839 (80%) were either recorded or stored. Reported values corresponded precisely to stored values in 2533 of 4839 recordings (52%). The timing of the recording was also examined in relation to the time at which the recording was solicited; values recorded within 1 hour of the solicited time were judged as acceptable. Of the total of 3342 recordings stored, 2375 (71%) satisfied this criterion. Compliance was significantly less satisfactory in those referred by the Workers' Compensation Board* (n = *11).*
Conclusion: *In this survey of 21 subjects investigated for possible occupational asthma, compliance with PEF recording, as assessed by comparing recorded and stored results and the time at which the recording was solicited, was poor. (J ALLERGY CLIN IMMUNOL 1995;96:601-7.)*

Key words: *Compliance, patient compliance, occupational diseases, respiratory function tests*

A diagnosis of occupational asthma depends on the use of several tools. Inspired by serial recording of peak expiratory flow (PEF) in asthma as an example,[1, 2] Burge et al.[3, 4] were the first to propose it in the investigation of occupational asthma. As reviewed recently, they found it was satisfactorily sensitive and specific in the diagnosis of occupational asthma.[5] These findings were confirmed more recently.[6, 7] As compared with specific inhalation challenges, which can only be done in specialized centers, PEF monitoring has the advantages of being readily available, simple, and less costly. However, there are pitfalls: it is less sensitive than forced expiratory volume in 1 second (FEV_1) in assessing airway caliber[8]; interpretation of results must be done by experts and depends on visual analysis, which is more satisfactory than

Abbreviations used
FEV_1: Forced expiratory volume in 1 second
PC_{20}: Provocative concentration causing a 20% fall in FEV_1
PEF: Peak expiratory flow
WCB: Workers' Compensation Board

From the Department of Chest Medicine, Hôpital du Sacré-Coeur, Montreal. Dr. Malo is a research fellow with the Fonds de la Recherche en Santé du Québec and the Université de Montréal School of Medicine.
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Reprint requests: Jean-Luc Malo, MD, Department of Chest Medicine, Hôpital du Sacré-Coeur, 5400 West Gouin, Montreal, Canada H4J 1C5.

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arithmetical indices[7]; values must be assessed at least four times a day[9]; and it is possible to falsify results because the values are recorded by subjects with no direct supervision by a technician.

The recent availability of instruments that can assess PEF and store data made it possible for us to assess compliance, in terms of recordings, of 21 subjects prospectively assessed for possible occupational asthma. The hypothesis was that compliance would not be satisfactory and less than satisfactory in those subjects referred by a medicolegal agency because they would be aware of possible financial consequences.

METHODS

Subjects

The data kept for analysis came from 21 prospectively recruited subjects who attended a specialized occupational asthma clinic and who met the following criteria: at least 2 weeks of PEF monitoring at work and 2 weeks away from work in the case of subjects with a diagnosis of occupational asthma and at least 2 weeks of PEF monitoring at work in the case of subjects without a confirmed diagnosis of occupational asthma. Patients were either referred by their general practitioner or a specialist or by the Workers' Compensation Board (WCB).

Protocol

Subjects were not aware that data were being collected on a computer chip in the VMX instrument (Clement Clarke International, Columbus, Ohio). They were asked to record their PEF values every 2 hours from the time they woke up until they went to bed. If they required an inhaled β_2-adrenergic agent, they were asked to record their values 15 minutes after taking it. They were instructed in how to perform the maneuvers and record their results at the time of the first visit and again 2 weeks later in the case of subjects who also recorded their values for 2 extra weeks. Three expirations were assessed and recorded each time. The VMX is a portable instrument, which uses the standard mini-Wright peak flow meter (Ferraris Medical, Inc., Holland, N.Y.) as its prime mover. From the mini-Wright peak flow meter, a static pressure bleed operates an analog pressure transducer, which signals the peak flow attained. The VMX also has a built-in memory and clock. The signal generated by the standard mini-Wright peak flow meter is digitized, processed, and memorized by an on-board computer together with the time and the date. Therefore the absence of an expiration cannot generate a signal that could be wrongly stored. The VMX has a computer connection to transfer the data to a standard IBM-compatible personal computer. Data obtained in our laboratory in 48 subjects with asthma and a wide range of airway caliber (uniform distribution of PEF from 150 to 700 L/min) showed good reproducibility in PEF values assessed by the standard mini-Wright peak flow meter and the VMX-stored PEF value (r^2 of 0.94, mean ± SD difference = 5 ± 32 L/min), between PEF values assessed by the standard mini-Wright peak flow meter and VMX written values (r^2 of 0.96, mean ± SD difference = 3.3 ± 26 L/min), and between the VMX stored and digitalized values (r^2 of 0.97, mean ± SD difference = 1.5 ± 23.5 L/min).

When they visited the hospital laboratory, the subjects underwent spirometry according to American Thoracic Society standards[10] and methacholine inhalation challenges by using a standard procedure with the Wright's nebulizer (Ferraris Medical, Inc.; output = 0.14 ml/min), breathing at tidal volume for 2 minutes.[11] Dose-response curves were drawn on a semilogarithmic noncumulative scale and the provocative concentration causing a 20% fall in FEV_1 (PC_{20}) was interpolated. A PC_{20} of 16 mg/ml or less was considered to represent significant bronchial hyperresponsiveness.[12] Subjects also underwent skin prick tests with a battery of 15 common inhalants. Atopy was defined as the presence of at least one positive reaction (wheal of 3 mm or more) in the absence of reaction to a control diluent and a positive reaction to histamine phosphate at 1 mg/ml concentration 10 minutes after skin testing.

Analysis of results

The diagnosis of asthma was based on a suggestive history and a PC_{20} value of 16 mg/ml or less.[12] The diagnosis of occupational asthma was based on the results of specific inhalation challenges in the laboratory ($n = 9$) or at work ($n = 5$) in a total of 14 subjects.[13] Specific inhalation challenges in the laboratory were carried out by exposing the subject to the relevant occupational agent as previously described.[13] In the other subjects, the diagnosis was rejected on the grounds that there was no significant bronchial hyperresponsiveness after a period of at least 2 weeks at work.[14] At the end of the investigation, subjects were classified as having either occupational asthma or personal asthma or as having neither occupational nor personal asthma.

The protocol was accepted by a local ethics committee with the understanding that the data would not be used to blame those subjects with poor compliance or those for which differences in the stored and written values would be observed.

Concordance between accuracy of results in terms of values and timing was analyzed by multivariate analysis.[15] Differences in compliance for subjects referred and not referred by the WCB was assessed by chi square analysis. A p value of less than 0.05 was considered significant.

RESULTS

Some of the baseline anthropometric, clinical, and functional results are listed in Table I. The majority of subjects were men under 55 years of age and taking either no medication or an inhaled β_2-adrenergic agent only as needed. The most commonly incriminated agents at work were isocyanates (hexamethylene diisocyanate only) among spray

TABLE I. Baseline anthropometric, clinical, and functional results

Patient No.	Sex	Age (yr)	Atopy	Medication	Diagnosis	Duration of exposure (yr)	Duration of symptoms after exposure (yr)	Agent	FEV_1 (% pred)	PC_{20} (mg/ml)	Referred by the WCB
1	M	21	+	B2	OA	3	0.5	Flour	88	6	No
2	M	26	−	None	No OA, no PA	10	1	Flour	94	22	No
3	F	47	+	None	OA	1	0.5	Morphine	91	56	No
4	M	21	+	B2	PA	2	1	Chemical products	50	0.5	No
5	M	21	+	B2; Be	OA	2	1.5	Chicken	98	4	Yes
6	M	51	−	B2; Be	OA	20	1	Isocyanate	59	1	Yes
7	M	41	+	None	No OA; no PA	7	3	Isocyanate	100	>128	No
8	F	30	+	None	No OA; no PA	0.8	0.7	Methacrylate	118	46	Yes
9	F	53	+	B2; Be	OA	18	2	Cloth	102	0.2	Yes
10	M	40	+	None	PA	12	0.25	Soldering	72	5	Yes
11	M	32	−	B2	OA	14	4	Isocyanate	102	3	No
12	M	40	+	B2; Be	OA	8	3	Clam	97	0.8	Yes
13	M	31	+	B2; Be	PA	6	1	Formaldehyde	64	3	Yes
14	M	54	−	None	No OA; no PA	29	0.5	Inks	104	>128	Yes
15	M	48	+	None	PA	6	3	Cereals	49	2	No
16	M	29	+	B2	No OA; no PA	10	0.3	Isocyanate	95	>128	No
17	M	45	+	B2; Be	PA	13	10	Dyes	48	0.3	Yes
18	M	28	+	B2	No OA; no PA	18	3	Isocyanate	83	>128	Yes
19	F	48	+	B2; Be	OA	6	4	Flour	73	0.2	Yes
20	M	23	+	B2; Be	No OA; no PA	5	1	Formaldehyde	68	64	No
21	M	53	−	B2; Be	No OA; no PA	25	2	Inks	129	42	No
Mean		37				10	2		85		
SD		12				8	2		23		

Atopy was defined as at least one immediate skin reaction to any of 15 common inhalants.
B2, β_2-Adrenergic agent; *OA,* occupational asthma; *PA,* personal asthma; *Be,* inhaled beclomethasone; *SD,* standard deviation.

painters in body shops and flour among bakers. A diagnosis of occupational asthma was retained in eight subjects, of personal asthma in five subjects, and of neither condition in eight subjects.

The mean duration of recording was 36 days (range, 14 to 79 days), which included 20 days (range, 10 to 52 days) at work and 17 days (range, 4 to 44 days) away from work. At least one value was recorded in this interval, and at least one value was stored in 33 days (range, 10 to 80 days). A minimum of 6048 recordings should have been made (excluding values that were requested on an as-needed basis, i.e., when subjects had symptoms and might have taken an inhaled β_2-adrenergic agent), that is: mean duration of 36 days × 21 subjects × 8 assessments each day. However, only 4839 values (80%) were either stored or recorded. Two features of recording were examined: the accuracy of values written by the subjects and the accuracy of their timing. Table II summarizes the results according to these two criteria. We considered that subjects should have written down the precise value shown on the digital screen. This was the case in 2533 of 4839 recordings (52%) with 427 written values (9%) being within ± 20 L/min of the stored value, a threshold considered to be the upper limit of the within-subject reproducibility for the test,[3, 4] and in 204 recordings (4%) within 21 to 50 L/min and 178 values (4%) beyond 50 L/min, a threshold considered to be physiologically rele-

TABLE II. Accuracy of results

	Total no. of cases			Timing					
				Subjects referred by the WCB			Subjects not referred by the WCB		
	0 to 1 hr	>1 hr	Total	0 to 1 hr	>1 hr	Total	0 to 1 hr	>1 hr	Total
Value									
Identical	**1749**	784	2533	**968**	437	1405	**781**	347	1128
±20 L/min	347	80	427	259	53	312	88	27	115
±21 to 50 L/min	146	58	204	118	46	164	28	12	40
>50 L/min	133	45	178	111	43	154	22	2	24
Total	2375	967	3342	1456	579	2035	919	388	1307

Figures exclude 1209 values that were neither recorded nor stored, 156 values that were recorded on the VMX apparatus but not reported on paper, and 1341 values that were reported but not stored. Numbers in boldface type show perfect accuracy in terms of timing and reported result. This was the case in 52% of total occasions for which values were reported and recorded, that is, 1749 of 3342. The two columns on the right distinguish between subjects referred and those not referred by the WCB. Significantly better compliance was found in those not referred by the WCB (781 of 1307 or 60% as opposed to 968 of 2035 or 48%) (chi square = 47, $p < 0.001$). The same was found by adding values that were either recorded but not stored or not recorded but stored (781 of 1639 or 48% as opposed to 968 of 3198 or 30%) (chi square = 160, $p < 0.001$).

vant. There were as many occurrences in which the written values overestimated and underestimated the stored values by 20 L/min or more (167 as opposed to 215). Fourteen hundred ninety-seven of 4839 recordings (31%) were either not stored or not recorded correctly; this includes 156 values that were stored but not recorded by the subject and 1341 values that were recorded but not stored. The timing of the recordings was also examined in relation to the time at which the recording was solicited, that is, from the time of awakening and every 2 hours until subjects went to bed. Values that were recorded within 1 hour of the solicited time were judged as acceptable. Of a total of 3342 stored recordings, 2375 (71%) satisfied this criterion. Only six subjects (29%) recorded values at least four times a day on 80% of days; 9 subjects did so between 61% and 80% of days; and six subjects did so on less than 50% of days.

There was no concordance between accuracy of the timings and accuracy of the recordings. Ten subjects were significantly more accurate (>20% difference in the type of accuracy) in the timing or in the precision in terms of exact value of reading, written or stored (by multivariate analysis, correlation coefficient = 0.01 [not significant]; Kappa agreement coefficient = 0.11, standard deviation = 0.21, not significant).[15]

Compliance was less satisfactory in those referred by the WCB ($n = 11$) as compared with those not referred by the medicolegal agency (Table II). Only 30% of values were correct, that is, exact values recorded within 1 hour of the requested time interval in those referred by the WCB, as opposed to 48% of values recorded by subjects not referred by the WCB (these figures include values either not stored but recorded or recorded but not stored) (chi square = 168, $p < 0.001$). These differences cannot be accounted for by differences in educational level between the two groups: 10 of the 11 subjects referred by the WCB had a secondary school level education in comparison with eight of the 10 subjects not referred by the WCB. The proportions of stored to written values were not different in those subjects having French or English as their first language ($n = 15$, 0.7 ± 0.3) in comparison with those ($n = 6$, 0.8 ± 0.3) who had other languages as their first. The percentages of inaccurate values in terms of written and stored values were also not significantly different according to primary languages (24% ± 19% for subjects with French or English as their primary language as compared with 32% ± 19% for other subjects). There was also no difference in compliance among those with a diagnosis of occupational asthma ($n = 8$) (36%) as opposed to those with personal asthma or with neither asthma nor occupational asthma ($n = 13$) (37%).

Figs. 1 and 2 show examples from two subjects for whom there was satisfactory and unsatisfactory concordance between reported and stored PEF data.

DISCUSSION

This study shows that the compliance with PEF monitoring in the investigation of occupational asthma was poor in our sample of 21 asthmatic subjects prospectively assessed. Subjects were asked to record three PEF values eight times per

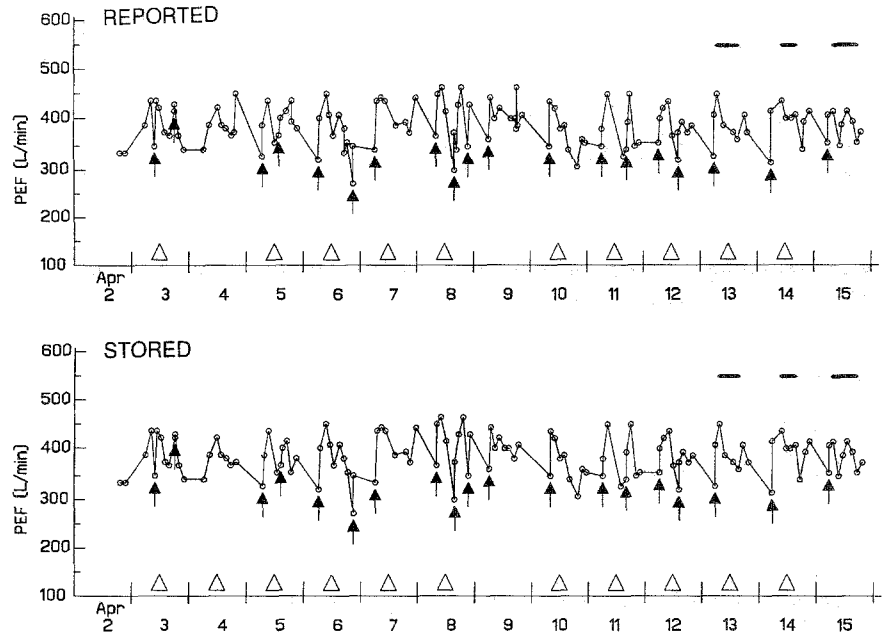

FIG. 1. Almost perfect correspondence between reported and stored values. Subject no. 6 (Table I). *Triangles* (▲) indicate days on which there were daily fluctuations (maximum − minimum value ÷ maximum value × 100) ≥20%. *Arrowheads* (△) show timing of inhaled β_2-adrenergic agent. *Horizontal bars* correspond to periods at work.

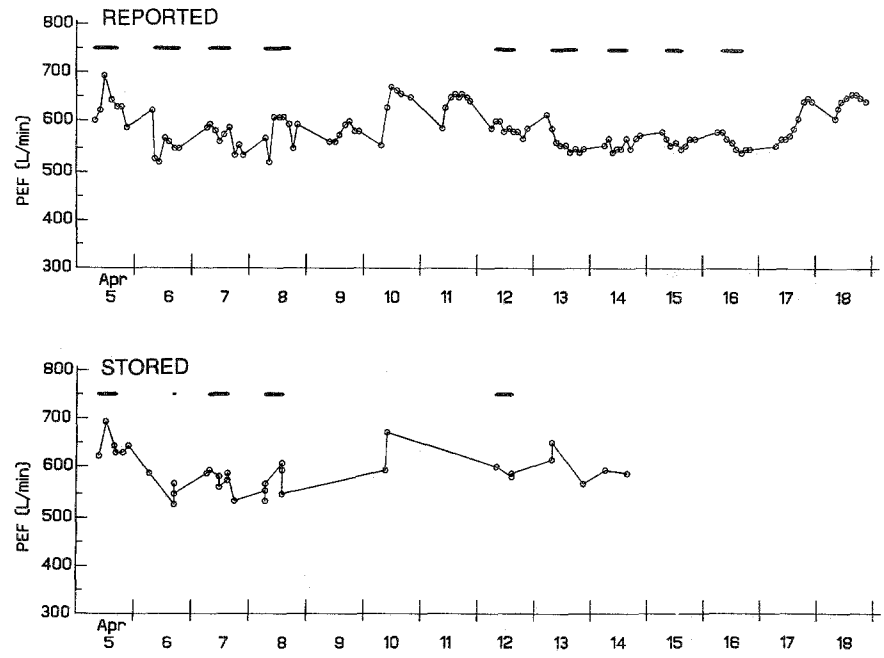

FIG. 2. Unsatisfactory correspondence between reported and stored values. Subject no. 7 (Table I). *Horizontal bars* correspond to periods at work.

day for a mean duration of 36 days. This is the method for which we previously showed a sensitivity of 81% and a specificity of 74%.[7] At least 6048 values should have been recorded and stored in the VMX apparatus (this excludes some values, which should have been recorded after a β_2-adrenergic agent was used on an as-needed basis), but only 4839 values were either stored or recorded (80%).

A total of 1341 values (28% of all stored or recorded values) were recorded but not stored, suggesting that they were in fact invented. Only 2374 values (49% of all stored or recorded values) were accurate in terms of the same value being reported on paper and stored and assessed within 1 hour of the time at which it was solicited.

Reasons for this poor compliance are hypothetical. First, asking subjects to record their results every 2 hours is demanding, and in this context it is not surprising that 20% of values were neither recorded nor reported. The original method suggested by Burge et al.[3, 4] was to record every hour or every-2-hours. Recording values four times a day may be sufficient. We recently showed that recording four times a day was almost as satisfactory as recording every 2 hours in terms of sensitivity and specificity in diagnosing occupational asthma as compared with the gold standard, which was the result of specific inhalation challenges. However, in this study we showed that, even considering only those subjects who recorded their values at least four times a day, only six subjects did so on 80% or more of days.

What was more perplexing was the proportion of values that were clearly invented, 33% of those recorded by subjects referred by the WCB (1052 of 3198 values recorded or stored) and 17% (289/1639) of those recorded by subjects not referred by the WCB. This can be explained by the fact that patients with occupational asthma are compensated in Quebec. Claimants with occupational asthma can receive benefits of up to 2 years of full salary if they are under 55 years of age, and up to 10 years of full salary if they are 55 or older.[16-18] They can also get extra money for impairment or disability, which is assessed 2 years after the end of exposure.[19] Although this information was not checked prospectively, workers who were referred to the clinic might have been aware of the potential benefits. This might explain why subjects referred by the WCB may have tended to invent recordings.

Finally, what was also perplexing, although to a lesser extent, was the proportion of the remaining values that were not precise, either in terms of the value itself or the timing. Only 52% of the values that were recorded and stored fulfilled the criterion for accuracy, that is, the same value being recorded and stored within 1 hour of the requested time. Although not recording a value at the time requested can be explained, it is harder to understand why subjects did not record the value that was shown on the digital screen of the VMX apparatus. Again, this proportion was more significant among subjects referred by the WCB (31%) as opposed to those not referred by the WCB (14%).

Diagnosing occupational asthma with PEF graphs depends on many aspects, which can undermine the accuracy of the method. First, it can be difficult for illiterate patients to record values unless a more expansive apparatus (such as the VMX), which stores data, is used. Second, compliance can be poor at times, as was demonstrated by our study. Compliance may be dependent on sociocultural factors or medicolegal aspects, which can vary from one country to the next. It would therefore be interesting to have comparable data from another country. Third, plotting PEF graphs has not been standardized. Comparison of individual recordings with graphs including mean, highest, and lowest daily values has not been done. Mathematical indices are clearly not as satisfactory as visual analysis ("eye balling").[7, 20] We and others are currently investigating the validity of automated methods of plotting PEF graphs; the rationale is that the resulting graphs could be read by physicians not specializing in the field. Finally, interpreting the graphs is not that clear-cut, although there is generally satisfactory reproducibility from one expert to the next.[9, 21] Interpretation of graphs can be especially difficult for subjects who are not continuously exposed to the "sensitizing" agent at work, as we suggested previously.[7]

The results of this study throw serious doubt on the accuracy of PEF monitoring in subjects referred to specialized clinics because of suspected occupational asthma. It would be interesting to know whether accuracy is more satisfactory in subjects with asthma, because many physicians and guidelines suggest that patients with asthma use such monitoring.[22, 23] It would be relevant to have this information for both personal and occupational asthma.

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