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**Statement on self-monitoring of peak
expiratory flows in the investigation of
occupational asthma**

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Occupational asthma is a disease characterized by variable airflow limitation and/or airway hyper-responsiveness caused by factors attributable to a particular occupational environment but not to stimuli encountered outside the workplace.¹ The investigation of occupational asthma requires a stepwise approach, but the crucial point is to confirm the cause-effect relationship between occupational exposure and asthma.^{2,3} Specific inhalation challenge tests,⁴ either in the laboratory or in the workplace, are used to confirm this relation-

Abbreviation used

PEF: Peak expiratory flow

ship^{2,3,5} because they are able to simultaneously confirm the relationship between the workplace and the symptoms, to relate the symptoms to a specific agent, and to reproduce the temporal relationship between exposure and the onset of symptoms.

The use of serial peak expiratory flow (PEF) monitoring has also been advocated in the diagnosis of occupational asthma as an objective confirmation of the relationship between the workplace and the symptoms.

PEF monitoring has been used in the investigation of asthma since 1969.⁶ Burge et al.,^{7,8} however, were the first, in 1979, to propose this method for the assessment of occupational asthma. Because of its simplicity, the popularity of the method has increased greatly in recent years, but it soon became clear that despite its simplicity, several aspects, both methodological and conceptual, had to be carefully defined. A lot

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of work has been done by several researchers to clarify the different aspects of PEF monitoring in the investigation of occupational asthma,⁹⁻¹⁶ and although several points must still be clarified, enough data are available to allow for an initial summing-up of the results.

This document is intended for use by physicians dealing with occupational asthma. The main points addressed are:

- 1.0. Definition and instruments
- 2.0. Means of PEF self-monitoring
- 3.0. Expression and interpretation of data
- 4.0. Advantages
- 5.0. Limitations
- 6.0. Recommendations
- 7.0. Conclusions

1.0. DEFINITION OF PEF AND INSTRUMENTS

PEF is the maximum flow achieved during a forced expiration starting from the level of maximal lung inflation. Like other indices derived from the forced expiratory maneuver, it is usually considered to be an indirect index of airway caliber. On the flow-volume curve, PEF is measured on the first effort-dependent portion of the forced expiratory maneuver, unlike other indices, which can be partially or primarily determined by the dynamic effort-independent properties of the airways. Thus PEF, FEV₁, and maximal expiratory flows are not interchangeable indices of airway caliber, and the sensitivity of these parameters in detecting airway obstruction is different, with PEF generally having a low sensitivity.^{16, 17}

Various types of instruments can be used to measure PEF, including pneumotachometers, spirometers, turbines, and anemometers. For PEF self-monitoring, the most suitable instruments are portable peak flow meters, which measure only PEF, indirectly deriving it from pressure generated in a forced expiration. These instruments are mass-produced and relatively inexpensive. They should satisfy recently detailed criteria.^{17, 18} In particular, all peak flow meters should be carefully calibrated with a computer-driven syringe.¹⁷ There should be a linear relationship between flow delivered to and flow recorded by the instrument. Peak flow meters should be capable of measuring values in the range of 60 to 800 L/min, except for those models designed for the low range of 30 to 350 L/min. There are concerns about the accuracy of the instruments.^{19, 20} Although the meters provide reasonably accurate readings at low flows, they may

overestimate a value by about 70 L/min in the middle of the range and underestimate it by about 50 L/min in the high range. Thus currently available instruments may distort flow measurements.

Recently, new portable instruments derived from standard peak flow meters have been developed. These instruments are able to assess PEF and store timings and values on a computer chip. Their ability to estimate compliance and the accuracy of the results balances the disadvantage of their higher cost compared with standard peak flow meters.

All instruments come with clear instructions about care, cleaning, and disinfection of the instrument and the detachable mouthpiece.

2.0. MEANS OF PEF SELF-MONITORING

2.1. Instructions to the patient

Each patient should be given detailed written and verbal instructions on how to perform PEF self-monitoring. Nurses or technicians can be responsible for supervising the test.

Before the actual recording, the patient should practice the forced expiration maneuver under supervision until the measurements are accurate. Careful instructions for the correct performance of the test are detailed in the report by Quanjer et al.¹⁷ Subjects should be at rest. The test can be performed in a standing or sitting position, but the neck must not be flexed. Having taken a maximal inspiration, and after only a momentary pause at total lung capacity, the subject must blow as hard as possible, maintaining an airtight seal between the lips and the mouthpiece, which should be gripped by the teeth. Dentures should not be removed unless they fit very poorly. Care should be taken to avoid squeezing or obstructing the orifices of the peak flow meter with the fingers and to avoid impeding the progress of the pointer. Three technically satisfactory blows should be performed each time. At least two of the three should be within 20 L/min of each other.⁹

Ideally, the patient should record all three measurements, and the graph should be plotted by the nurse or technician. Ideally, subjects should not be asked to select the best PEF and should not plot the graph.

Measurements are recorded on a diary card. Patients should be instructed to fill in the diary card carefully. In particular, medication taken, respiratory symptoms, respiratory tract infections, exercise, and time of going to and coming from work should be reported every day. Moreover, any major change in the regular rhythm of life, unex-

pected events, and diseases should also be recorded (date and time of day).

2.2. Frequency of assessment

The ideal frequency of daily assessment is debatable. Measurements are usually taken every 2 hours during waking hours* during periods at work and periods away from work to detect short episodes of bronchoconstriction.

Some authors use a six-times-a-day assessment.^{12, 15} A recent article compared graphs recorded every 2 hours with a four-times-a-day recording.¹⁴ It was found that although graphs of PEF recorded every 2 hours have some advantages over less frequent recordings (e.g., optimal sensitivity and specificity), four-times-a-day assessment is almost as satisfactory and may result in higher compliance and the most reliable readings.¹⁴ To enhance the reliability of four-times-a-day assessment, which does seem more advantageous in clinical practice, one suggestion is to take measurements four times a day during regular waking hours, the first one immediately on waking and additional measurements when symptoms are present.¹⁶

It must be stressed, however, that the number of readings needed for analysis depends on the degree of changes seen as a result of work and the inherent instability of asthma. For those with obviously normal or abnormal records, two to three readings a day are sufficient. For those with variable asthma and smaller changes at work, more readings are better.

2.3. Period of self-monitoring

Periods at work are compared with periods away from work. The duration of periods at work and away from work differs depending on the author. Burge⁹ first proposed at least a week at work, followed by 10 days away from work, followed by 2 more weeks at work, and thereafter²¹ about 4 weeks at work. Other groups suggested 3 working periods separated by periods away from work with at least one of the periods away from work longer than 1 week²; others suggested 3 weeks at work and 2 weeks away from work.^{12, 15} Several authors use 2 weeks at work and at least 2 weeks away from work.^{13, 14} The duration and sequence of periods at work and away from work for PEF monitoring should be based on the physician's experience. In general, there is a difference in the length of recording required for a subject who has PEF diurnal variation within the normal range (no

asthma) and that for a subject in whom asthma is present with increased diurnal variation that is not so obviously related to work. In the former situation (no asthma), quite short periods can rule out occupational asthma; in the latter instance, much longer periods, including 2 weeks away from work, are required. In any case, periods at work should be prolonged enough to permit a careful evaluation of the pattern of response (see item 3.2.2) and to avoid false-negative results caused by a lack of exposure to the suspected offending agent or agents, particularly when exposure is only intermittent. In some instances this may take only hours, but before the conclusion of a negative recording is made, a 2-week period of monitoring at work under usual conditions is advocated. However, the period at work should be stopped when a significant pattern of occupational asthma is observed because in this case there is no need to maintain exposure. Periods away from work should be prolonged enough to allow for recovery, the start of which could be delayed and take a long time to complete.⁹

To overcome one of the major problems of PEF self-monitoring, (i.e., inadequate patient compliance), a favorable relationship between the nurse, technician, or physician and the patient is an important prerequisite. Patients are usually seen every 2 weeks, and their records are checked. However, if a patient needs to contact the nurse or technician more frequently during the measurement period, he or she should be encouraged to do so. In addition, the patient should not feel obliged to alter his or her entire lifestyle because of the monitoring regimen and should be told that being occasionally late or early for a measurement does not really matter as long as the measurements are recorded on the diary card.

3.0. MEANS FOR INTERPRETING RESULTS

3.1. Summarizing PEF self-monitoring data

PEF readings are plotted on a graph where the x axis represents days and the y axis represents PEF in liters per minute; the scale of the y axis is identical for each subject. The graph is plotted on the diary card on which days at work and away from work are marked. Because days at work are not always identical, days of exposure to the suspected offending agent or agents can be indicated as well. Days should be counted as morning-to-morning periods, rather than calendar days.

Graphs can be analyzed qualitatively by simple visual assessment or quantitatively by calculating

*References 2, 5, 9, 10, 13, and 21.

intra-day and/or within-day indices of variability,¹³ comparing periods at work and periods away from work.

3.2. Analysis and interpretation of PEF records

3.2.1. Visual analysis versus variability indices. PEF monitoring for long periods results in a bulk of data that are difficult to manage in clinical practice. Calculation of variability indices requires a lot of time by the readers; besides, it is not clear which index is more indicative for a significant variation. Burge et al.^{7,8} first used visual assessment to analyze PEF monitoring data. They described several patterns of changes in PEF (see item 3.2.2) but did not give the quantitative change required for diagnosis. In subsequent works they considered a record with a mean peak flow in the normal range and a diurnal variation of less than 15% as normal.²¹ Visual assessment is a more direct method of analysis, but it is based on subjective criteria rather than any well-established ones. Despite this, recent studies have shown that visual assessment of PEF records is a satisfactory means of investigating occupational asthma caused by various agents.¹³⁻¹⁵

With the specific challenge as the gold standard, visual analysis has been found to have higher sensitivity and specificity levels than various other objective PEF-derived indices. Only in Western red cedar-induced asthma¹⁵ did the difference in mean PEF between the maximum value during weekends and the minimum value on workdays have a sensitivity greater than that of visual assessment, and a similar specificity was observed. Complete concordance between different readers in interpreting PEF graphs by visual inspection has been found in a percentage of cases, varying from 69%¹⁰ to 78%¹³ and 82%.¹⁴ Visual analysis therefore seems to be a satisfactory method for interpreting PEF data in most cases with typical patterns.

Difficulties in the visual inspection of PEF can arise when patterns are not typical (see item 3.2.2), particularly when asthma is severe or when exposure to the offending agent is intermittent.²² In these cases the interpretation of the monitoring can be difficult and requires careful case-by-case consideration. It is believed that the possibility of a more objective method of analysis, based on the use of one or more numerical indices such as moving average or exponentially weighted moving average,^{24,25} should be explored.

3.2.2. Pattern of reactions emerging from PEF monitoring. Burge⁹ described typical patterns of changes in PEF that are largely due to the speed of

recovery: the hourly pattern (changes occurring from hour to hour within 1 day), the daily pattern (changes occurring from day to day within each work week), and the weekly pattern (changes occurring from week to week).

Changes within 1 workday (the hourly pattern) resemble the immediate and late response to a specific bronchial challenge.⁴ They are only seen when reasonable recovery occurs by the next day. Repeated exposure often reduces this recovery, resulting in a flat pattern in which the peak flow is depressed fairly uniformly for the whole day.

The daily patterns depend on the cumulative effect of repeated exposure and on the time it takes for recovery. Repeated daily exposure can result in an equivalent deterioration each day, if recovery is substantial on the day after exposure. Equivalent daily patterns are usually associated with immediate asthmatic reactions and rapid weekend recovery. If recovery is incomplete by the day after exposure, repeated daily exposure can result in a progressive daily deterioration. Each day is worse than the day before. Sometimes a plateau is reached at the end of the week. Recovery is usually longer over the weekend. Daily patterns are only seen when there is substantial recovery during breaks (usually 2-day weekends).

When recovery takes longer than 2 to 3 days, the pattern that results (weekly pattern) depends on the time it takes for recovery to start and on the worker's resilience to repeated exposure. The start of recovery is sometimes delayed after the subject leaves work and continues for a prolonged time.⁹

3.2.3. Sensitivity and specificity of PEF monitoring. The sensitivity and specificity of PEF monitoring in diagnosing occupational asthma have been evaluated in most studies by use of visual assessment as a method of graph analysis and different gold standards. In the original works of Burge et al.,^{7,8} in which the combination of history and specific challenges was used as the gold standard, the sensitivity of visual analysis varied from 77% in colophony-induced occupational asthma to 100% in isocyanate-induced asthma, whereas specificity was found to be 100% in both. In more recent studies,^{12,13} with specific challenges as the gold standard, the sensitivity of visual analysis of PEF monitoring varied from 86%¹² to 81%,¹³ whereas specificity varied from 89%¹² to 74%.¹³

One group evaluated the sensitivity and specificity of PEF monitoring by using diurnal variation ($\geq 20\%$), when it was relatively more frequent or showed greater variation on working days than on days away from work, as the criterion for PEF interpretation of occupational asthma; and a com-

bination of history, changes in bronchial responsiveness to methacholine, skin tests, and/or bronchial challenges was used as the gold standard.²³ In this study the sensitivity of PEF monitoring was found to be 72%, and specificity was 53%.

The poor sensitivity and specificity of PEF monitoring in some subjects, compared with specific bronchial challenges, can be explained by the lower sensitivity of PEF in detecting mild bronchial obstruction,¹⁶ particularly during the late response to occupational sensitizers.²⁶ It is difficult to evaluate what percentage change in PEF would correspond to a significant change in FEV₁, but an attempt to identify a correspondence between PEF changes and FEV₁ changes in absolute values during bronchial challenges was made in a recent study.²⁷

Another possible explanation for the lower sensitivity and specificity of PEF monitoring is that prolonged monitoring requires strong motivation and good collaboration on the part of the subject; both can diminish over a long period because of weakening compliance, fear of job loss, or malingering in order to receive compensation benefits.²²

In any case, these sensitivity figures result in a considerable percentage of false-negative results, and it should be strongly emphasized that "stable" PEF values do not rule out mild airway lability.

3.2.4. The problem of the "gold standard." As reported above, all of the data on the sensitivity and specificity of PEF monitoring have been referred to a gold standard (e.g., history with specific challenges, specific challenges alone, or a combination of various tests). As a matter of fact, all of these gold standards have shortcomings; and specific challenges, which at present are considered the best gold standard,^{2,5} can result in a percentage of false-negative results caused by technical or methodological problems. This could represent a bias in evaluation of PEF monitoring sensitivity and specificity data.

3.2.5. Association between PEF monitoring and measurement of nonspecific bronchial responsiveness. To improve the reliability of PEF monitoring and to provide more objective criteria for diagnosis of occupational asthma, linking the measurement of nonspecific bronchial responsiveness to PEF self-monitoring at the end of a period at work and at the end of a period away from work has been suggested¹¹ and is widely used in clinical practice. However, two studies^{12,13} have shown that this does not improve the sensitivity or the specificity of visual analysis of PEF. When changes in PEF are associated with parallel changes in nonspecific bronchial responsiveness, the diagnosis of occupational asthma is highly probable. If there is disagreement

between PEF monitoring and nonspecific bronchial responsiveness, it may be prudent to do more testing (e.g., longer monitoring of PEF, specific bronchial challenges) to confirm the diagnosis.

3.2.6. Interference from therapy. Theoretically, an optimal PEF reading is taken when no therapy is in progress. In practice, because many subjects are already undergoing therapy when they are referred for investigation of occupational asthma, whether treatment should be discontinued is debatable. In the original works of Burge et al.,^{8,9} the use of antiasthmatic medications (steroids or cromoglycate) resulted in lower PEF sensitivity. In contrast, recent studies have shown that use of common antiasthmatic medications, both bronchodilators and inhaled antiinflammatory agents, does not affect the sensitivity and specificity of PEF readings, determined with specific challenges as the gold standard.¹⁴ As a matter of fact, reduction of or changes in the usual therapy could be associated with a deterioration in asthma and a decrease in PEF on the subject's return to work, which could be erroneously interpreted as work-related. Therefore a patient's usual therapy, particularly inhaled steroids or theophylline, should not be interrupted or varied during monitoring, whereas inhaled β_2 -agonists should be taken only as needed²² and reported on the diary cards. The important point is that treatment should be the same at work and away from work.⁹

3.2.7. Objectivity of PEF self-monitoring arbitration. All of the assessments performed are based on subjective judgment and/or empirical experiences, fixed days or percentages in or for which a certain parameter must be lower in the work period than in the away-from-work period, although this is not entirely justified. Attempts have therefore been made to apply methods of trend analysis (moving average or exponentially weighted moving average)^{24,25} to interpretation of PEF monitoring data, taking into account all the measurements during both periods. On the basis of the pool of data collected during the away-from-work period, the criterion is set for a significant change of values during the at-work period, allowing for an objective assessment of the records.

4.0. ADVANTAGES OF PEF SELF-MONITORING

The advantages of PEF self-monitoring are:

1. Ability to assess patient's lung function outside the laboratory: in a natural setting, at work, at night, on weekends and holidays
2. Simplicity of PEF measurement; maneuver by means of inexpensive and handy devices

3. Feasibility in nonspecialized centers where specific challenges cannot be performed
4. Usefulness in differentiating between nonoccupational and work-related asthma
5. If specific bronchial challenges are negative because a worker is away from work for too long, then serial PEF provides a means to prove the relationship between asthma and the workplace.

5.0. LIMITATIONS

The limitations of PEF self-monitoring are:

1. Patients' motivation and honesty are crucial prerequisites and can often be a serious hindrance or aggravation in compensation-oriented cases. Compliance could be low because of the frequency of daily assessments or a loss of interest because of the long period of monitoring (4 or more weeks). Patients with low intellectual ability can encounter serious difficulties. The new instruments available store data, thereby preventing falsification, and may overcome these disadvantages.
2. Re-exposure of the patient to the work environment is necessary and potentially dangerous.
3. It takes a relatively long time to obtain the results (long recording period before a reliable assessment can be made).
4. There are organizational difficulties: arranging for the away-from-work period can mean that the monitoring period shifts for several months and delays the end of the diagnostic protocol and operative decisions.
5. The need for the patient to be at work can, in certain circumstances, be a major drawback; if the plant is no longer operating, if the worker is no longer employed there, or if the technology has changed, the monitoring cannot be performed. (Requests for compensation claims require re-evaluation.)
6. There are interpretation difficulties: reading of PEF plots is not objective; there are noncharacteristic patterns and borderline results.
7. The poor sensitivity of PEF self-monitoring leads to a high percentage of false-negative results.
8. PEF self-monitoring can confirm the relationship between symptoms of asthma and occupational exposure, but it cannot relate the asthmatic condition to a specific agent unless one deals with a worker exposed to one agent only and with significantly increased specific IgE antibodies (generally high molecular weight agents). Therefore in general, the method can-

not distinguish between occupational asthma (i.e., asthma caused by a specific agent present at work) and so-called work-related asthma (i.e., bronchoconstriction induced by nonspecific exposure to irritants in the workplace in a subject with bronchial hyperreactivity).

6.0. RECOMMENDATIONS

PEF monitoring is a satisfactory tool for providing objective evidence of work-related asthma. However, more research is needed in the following areas:

1. Instruments that can record PEF and FEV₁ and store the data, with accurate recording of flows
2. Required frequency of daily assessments
3. Computer programs to generate graphs in a standardized way
4. More objective ways to analyze graphs, other than "eye balling" (visual analysis) (Such graphs would not require interpretation by a specialist or a physician; they could be interpreted automatically through a computer program, although the diagnosis will still remain the physician's responsibility.)
5. Comparison of the results of specific inhalation challenges and serial PEF monitoring in subjects exposed continuously and intermittently to an offending agent at work
6. Assessment of the effect of therapy (antiinflammatory preparations) on the results
7. The applicability of the method to epidemiologic studies ("field studies") as opposed to an individual clinically oriented approach

These questions should be addressed in multicenter international studies.

7.0. CONCLUSIONS

PEF monitoring is a reliable method for confirming the relationship between occupational exposure and symptoms of asthma. It is feasible in nonspecialized centers, and it is simple and safe to perform. Nevertheless, it is time-consuming and requires collaboration and honesty on the part of the subject.

Analysis of PEF graph-derived data is still based on subjective evaluation, and the development of more objective methods of analysis is needed.

Interpretation of PEF data in the diagnosis of occupational asthma is a critical point, and it should be carefully considered in every case. PEF monitoring could be useful as a first-level confirmation of a history of suspected occupational

asthma in nonspecialized centers, but the interpretation of PEF data for confirming a diagnosis of occupational asthma should be done by a specialized center. The low sensitivity of PEF monitoring means that there is a considerable percentage of false-negative results, so a "stable" PEF does not rule out the presence of occupational or work-related asthma. However, even in the case of a pattern of PEF monitoring indicative of a positive relationship between symptoms and occupational exposure, it should be emphasized that PEF monitoring cannot relate symptoms to a specific agent. Thus PEF monitoring is not useful in etiologic diagnosis, except in the minority of cases of occupational asthma in which there is a clear demonstration of specific sensitization (i.e., strongly positive for IgE antibody) to agents present at work.² In these cases (for instance, bakers), a strongly positive peak flow record associated with a strongly positive IgE antibody assessment are sufficient to make a precise etiologic diagnosis.

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