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 flow limitation and/or airway hyperresponsiveness due to causes and conditions attributable to a particular occupational environment and 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 relationship between the workplace and the symptoms, to relate the symptoms to a specific agent, and 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 symptoms.

PEF monitoring has been used in the investigation of asthma since 1969 [6]. Burge and co-workers, however, were the first, in 1979, to propose this method for the assessment of occupational asthma [7, 8]. Because of its simplicity, the popularity of the method has increased greatly in recent years, but it soon became clear that, despite simplicity, several aspects, both methodological and conceptual, had to be carefully defined. A lot 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 have still to be clarified, there are enough data to allow a first 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 of PEF and instruments

PEF is the maximum flow achieved during a forced expiration starting from the level of maximum lung inflation. Like other indices derived from the forced expiratory manoeuvre, it is usually considered to be an indirect index of airway calibre. On the flow volume curve, PEF is measured on the first effort-dependent portion of the forced expiratory manoeuvre, unlike other indices which can be partially or primarily determined by the dynamic effort-independent properties of the airways. Thus, PEF, forced expiratory volume in one second (FEV1) and maximal expiratory flows are not interchangeable indices of airway calibre 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 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 using a computer driven syringe [17]. There should be a linear relationship between the flow delivered to and that recorded by the instrument. Peak flow meters should be capable of giving values in the range of 60–800 L·min⁻¹, except those models designed for the low range of 30–350 L·min⁻¹. There are concerns about the accuracy of instruments [19, 20]. Although the meters give reasonably accurate readings at low flows, they may overread by about 70 L·min⁻¹ in the middle of the range, and underread by about 50 L·min⁻¹ in the high range. Thus, currently available instruments may distort flow rates.

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 to 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 Instruction to the patient

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

Prior to the actual recording, the patient should practice the forced expiration manoeuvre under supervision until the measurements are accurate. Careful instructions for the correct performance of the test are detailed in [17] (see below).

Briefly, subjects should be at rest. The test can be performed in a standing or sitting position, but the neck must not be fixed. Having taken a maximal inspiration, and after only a momentary pause at total lung capacity, the subject is to blow as hard as possible, maintain 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 not be taken not to squeeze or obstruct the orifices of the peak flow meter with the fingers, and not to impede 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$^{-1}$ of another [9].

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 reported 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 going to and coming from work should be reported every day. Moreover, any major change in the regular rhythm of life, unexpected events, and diseases should also be recorded (date and time of the day).

#### 2.2 Frequency of assessment

The ideal frequency of daily assessment is debatable. Measurements are usually taken every two hours during waking hours [2, 5, 9, 10, 13, 21] during periods at work and periods off work in order to detect short episodes of bronchoconstriction.

Some authors use a six-times-a-day assessment [12, 15]. A recent paper compared graphs recorded every two hours with a four-times-a-day recording [14]. It was found that, although graphs of PEF recorded every two 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 possibly result in higher compliance and more reliable readings [14]. To enhance the reliability of four-times-a-day assessment, which does seem more advantageous in clinical practice, a suggestion is to take measurements four times a day during waking hours regularly, the first one immediately on waking, plus additional measurements in the presence of symptoms [16].

It must be stressed, however, that the number of readings needed for analysis depends on the degree of changes seen due to 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, the more readings are better.

#### 2.3 Period of self-monitoring

Periods at work are compared with periods off work. The duration of periods at work and off work differs depending on the author. Burge first proposed at least a week at work followed by ten days off work followed by two more weeks at work [9] and, thereafter, [21] about 4 weeks at work. Other groups suggested 3 working periods separated by periods away from work with at least one of the periods off work longer than one week [2]; yet 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 off work [13, 14]. It is up to the physician's experience to indicate the duration and the sequence of periods at work and off work of PEF monitoring. In general, there is a difference in the length of record required for somebody who has a normal PEF diurnal variation within the normal range (no asthma) and records where asthma is present with increased diurnal variation, which is not so obviously related to work. In the former situation (no asthma), quite short periods can exclude occupational asthma, in the latter instance, much longer periods, including two 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 due to a lack of exposure to the suspected offending agent(s), 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 two-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, as in this case there is no need to maintain exposure. Periods off 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 favourable relationship between the nurse/technician and physician, and the patient is an important prerequisite. Patients are usually seen every two weeks and their records checked. However, if the patient needs to contact the nurse or technician more frequently during the measurement period, he should be encouraged to do so. In addition, the patient should not feel obliged to alter
his entire life style due to 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 PEF L·min⁻¹, the scale of the y axis being identical for each individual subject. The graph is plotted on the diary card where days at work and off work are marked. Since days at work are not always identical, days of exposure to the suspected offending agent(s) can be indicated as well. Days should be taken as morning-till-morning periods rather than calendar days. Graphs can be analysed qualitatively by simple visual assessment or quantitatively by calculating intra-day and/or within-day indices of variability [13], comparing periods at work and periods off work.

3.2. Analysis and interpretation of PEF records

3.2.1. Visual analysis vs 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; difficult to manage in clinical practice. Calculation of monitoring for long periods results in a bulk of data that are

3.2.2 Pattern of reactions emerging from PEF monitoring. BURGE [9] described typical patterns of changes in PEF that are due largely to the speed of recovery: the hourly pattern, i.e. changes occurring from hour-to-hour within one day; the daily pattern, i.e. changes occurring from day-to-day within each work week; and the weekly pattern, i.e. changes occurring from week-to-week.

Changes within one work day (the hourly pattern) resemble the immediate and late response to a specific bronchial challenge [4]. They are only seen when there is reasonable recovery by the next day. Repeated exposure often reduces this recovery, resulting in a flat pattern where 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 week-end 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 at the weekend. Daily patterns are only seen when there is substantial recovery during breaks (usually two-day weekends).

When recovery takes longer than 2–3 days, the pattern that results (weekly pattern) depends on the time it takes for recovery to start and the worker’s resilience to repeated exposure. The start of recovery is sometimes very delayed after leaving 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 using visual assessment as a method of graph analysis and different gold standards. In the original works of BURGE and co-workers [7, 8], using the combination of history and specific challenges as the gold standard, the sensitivity of visual analysis of PEF monitoring varied from 77% in colophony-induced occupational asthma to 100% in isocyanate-induced asthma, whilst 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], whilst specificity varied from 89% [12] to 74% [13].

One group evaluated the sensitivity and specificity of PEF monitoring using either diurnal variation ≥20%,
when it was relatively more frequent, or with greater variation on working days than days off work as the criteria for PEF-interpretation of occupational asthma and a combination of history and/or changes in bronchial responsiveness to methacholine and/or skin test and/or bronchial challenges as the gold standard [21]. In this study, the sensitivity of PEF monitoring was found to be 72% and specificity 53%.

The poor sensitivity and specificity of PEF monitoring in some subjects, compared to 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 of occupational asthma, linking the measurement of nonspecific bronchial responsiveness to methacholine and/or skin test and/or bronchial challenges as the gold standard [21]. In this study, the sensitivity of PEF monitoring was found to be 72% and specificity 53%.

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, due to weakening compliance, fear of job loss, or malingering 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 do not exclude mild airway lability.

3.2.4. The problem of the "gold standard". As reported above, all the data of 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. All of these gold standards, however, have shortcomings and specific challenges, which, at present, are considered the best [2, 5], can result in a percentage of false negative results due to technical or methodological problems. This could be a bias in evaluating 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 diagnosing 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 suggested [11] and is widely used in clinical practice. However, two studies [12, 13] have shown that this does not improve the sensitivity nor 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 (longer monitoring of PEF, specific bronchial challenges) to further confirm the diagnosis.

3.2.6. Interference from therapy. Theoretically, an optimal PEF reading is taken where there is no therapy in progress. In practice, as many subjects are already undergoing therapy when they are referred for the investigation of occupational asthma, it is debatable whether treatment should be discontinued or not. In the original works of Burge [8, 9], the use of antiasthma medications (steroids or cromoglycate) resulted in lower PEF sensitivity. By contrast, recent data have shown that use of common antiasthma medications, both bronchodilators and inhaled anti-inflammatory drugs, does not affect the sensitivity and specificity of PEF readings, determined using specific challenges as the gold standard [14]. Reduction of, or changes in, the usual therapy could be associated with a deterioration in asthma and a decrease in PEF upon 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 beta2-agonists should be taken only as needed [22] and reported on the diary cards. The important point is that treatment be the same at work and away from work [9].

3.2.7. Objectivity of PEF self-monitoring arbitration. All the assessments performed are based on subjective judgement and/or empirical experiences, fixed days or percentages during, or for, which a certain parameter has to be lower in the work period than during the off-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 interpreting PEF-monitoring data, taking into account all the measurements during both periods. Based on the pool of data collected during the off work period, the criterion is set for a significant change of the values during the at-work period, allowing for an objective assessment of records.

4.0. Advantages of PEF self-monitoring

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 manoeuvre: measurements by means of cheap and handy devices.
3) Feasibility in nonspecialized centres where specific challenges cannot be performed.
4) Useful in differentiating between non-occupational and work-related asthma.
5) If specific bronchial challenges are negative due to a worker being away from work for too long, then serial PEF provides a means to prove the relationship between asthma and workplace.

5.0 Limitations

1) Patient's motivation and honesty is a crucial prerequisite, and can often be a serious hindrance-aggravation
in compensation-oriented patients. Compliance could be low due to the frequency of daily assessments or a loss of interest due to the long period of monitoring (four or more weeks). Patients with low intellectual ability can encounter serious difficulties. New instruments available that store data, thereby preventing falsification, may overcome these disadvantages.

2) Re-exposure of the patient to the work environment is necessary, and could be potentially dangerous.
3) It takes a relatively long time to obtain the results (long duration of the recording period before a reliable assessment can be made).
4) There are organizational difficulties - arranging for the off-work period can mean that the monitoring period is postponed for several months, delaying the end of the diagnostic protocol and operative decisions.
5) The need for the patient to be at work can, under certain circumstances, be a major drawback - if the patient is not operating any more, if the worker is not employed any more, 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 non-characteristic patterns and borderline results.
7) Its poor sensitivity 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, generally, the method cannot 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, work has to be done in the following areas:
1. Instruments that can record PEF and FEV1 and store the data, with accurate recording of flow rates;
2. Further studies on the required frequency of daily assessments;
3. Computer programs to generate graphs in a standardized way;
4. More objective ways to analyse graphs other than "eye balling" (visual analysis); such graphs would not require interpretation from a specialist or a physician; they could be interpreted automatically via a computer program, although the diagnosis will still remain the physician's interpretation and responsibility;
5. Further studies comparing the results of specific inhalation challenges and serial PEF monitoring in subjects exposed continuously and intermittently to an offending agent at work;
6. Further studies to assess the effect of therapy (anti-inflammatory preparations) on the results;
7. The applicability of the methods to epidemiological studies ("field studies") as opposed to an individual clinically-oriented approach.

These questions should be addressed in multicentre, 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 centres 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 diagnosing 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 centres, but the interpretation of PEF data for confirming a diagnosis of occupational asthma should be given to a specialized centre. The low sensitivity of PEF monitoring means there is a considerable percentage of false negative results, thus, a "stable" PEF does not exclude 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 aetiological diagnosis, except in the minority of cases of occupational asthma where 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 to a strongly positive IgE antibody assessment is sufficient to make a precise aetiological diagnosis.

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References


PEFR IN OCCUPATIONAL ASTHMA

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