WATCH COMMITTEE

Health significance of occupationally-induced declines in FEV$_1$

Issue
1. Health significance of declines in FEV1 caused by workplace exposures to dusts, fumes, and irritant gases/vapours.

Timing Considerations
2. Routine.

Recommendation
3. WATCH is invited to consider the issues noted in this cover paper and to respond to the actions in paragraph 15.

Background
4. Occupational respiratory disease (ORD) is a priority within HSC/E’s Chemicals Programme. There is a high prevalence of chronic obstructive pulmonary disease (COPD) in the UK. The latest statistics reveal 900,000 diagnosed cases and half as many again undiagnosed cases$^1$ (1.5 million cases in total). Cigarette smoking is the main cause, but occupational exposures to dusts, fumes and irritant gases can cause COPD independently of smoking, and can increase the risk of COPD in those who smoke. A self-reported household survey carried out in the UK in 2001/02 (SW101/02)$^2$ showed that 168,000 people attributed breathing and lung problems to work. The American Thoracic Society (2003)$^3$ estimates that the population attributable risk for work-related COPD is 15%, suggesting 135,00-180,000 work-related cases in the UK.

5. FEV1 (forced expiratory volume in one second) is a widely used measure of pulmonary function in epidemiological studies. It is a relatively robust and reliable measure of airway calibre, and is important in confirming a diagnosis of COPD. The criteria for diagnosis$^4$ are a reduction in FEV1 to 80% of the predicted value in combination with an FEV1/FVC ratio of less than 0.7. FEV1 may also be used in the diagnosis of asthma: a 20% decline in FEV1 following bronchial challenge with a putative asthmagen may be taken as a positive response. An accelerated annual decline in FEV1, over and above that due to ageing, is an indicator of COPD development. However, the interpretation of FEV1 data from occupational studies may not be straightforward (and hence the appropriate regulatory interventions may be
subject to challenge). One issue concerns the magnitude of decline in FEV1, over and above the normal age-related decline, that should be regarded as clinically significant in human health terms. Other potential issues concern the lack of ability to identify a threshold for exposure-induced declines in FEV1, individual variability in susceptibility/resistance; the combined effects of cigarette smoking and workplace exposures; and how to interpret the importance of corresponding data on respiratory symptoms. WATCH members may also identify other issues that merit consideration in addition to those listed above.

**Argument**

6. The Leicester IEH report (R13) provides background information on the factors that influence FEV1 and its variability in the population (pp 72-79). A copy of this report is provided with this cover paper. The IEH report notes that FEV1 declines in adulthood by about 30 ml per year as a result of normal ageing. In subjects who develop COPD, FEV1 decline by more than 40 ml per year.

**FEV1 and premature mortality**

7. The IEH Report notes that low FEV1 is a powerful predictor of premature death. Evidence was cited from a 20-year follow-up study of nearly 3000 British men. Analysis of the results showed that the risk of dying of COPD was 50-fold higher in those whose FEV1/height was 2 SDs or more below the average value, and 20-fold for those whose value was between 1 and 2 SDs below the average.

**FEV1 and chronic obstructive pulmonary disease (COPD)**

8. COPD is a disease state that encompasses chronic bronchitis and emphysema. Signs and symptoms include chronic cough and sputum production, and shortness of breath. The diagnosis is confirmed by spirometry as indicated in paragraph 5 above. Usually, the presence of symptoms precedes the onset of COPD by some years. However, in some individuals there can be quite a marked decline in pulmonary function before symptoms develop.

**Occupationally-induced declines in FEV1**

9. “Dusty trades” have been associated with chronic bronchitis (and by implication, COPD) since the 19th century. It is recognised that coalmine dust, quite independently of cigarette smoking, is a cause of COPD. In this review, the results of a study in over 4000 British coalminers are cited, which suggest a loss of FEV1 of 104 ml after a 40-year working lifetime exposed to respirable dust at 2 mg.m⁻³ (8-hr TWA). The HSE review of kaolin, assessed by WATCH in 1992, included a study of English china clay workers where the results showed that 40 years exposure to respirable dust at 2.5 mg.m⁻³ would lead to a decline in FEV1 of 220 ml. An HSE review of carbon black, assessed by WATCH in 2002, indicated that 40-year exposures to respirable carbon black at 1, 2 or 3.5 mg.m⁻³ would lead to declines in FEV1 of 48, 96 and 169 ml respectively.
10. However, it was not possible in any of the above case examples for WATCH to identify a “threshold” level of exposure below which there would be no dust-induced decline in FEV1. To some extent, this may be a feature of the linear models used in epidemiological studies. However, the existence of “background noise” and considerable inter-individual variability may also preclude the identification of a threshold of effect. The OES was set for kaolin at a level predicted to cause a stated reduction in FEV1, not at a “no-effect” level. The same issue surfaced in the more recent WATCH discussions on carbon black but remains unresolved. This issue is likely to emerge time and time again with substances considered in the ORD sub-programme. Hence, there is a need for an agreed generic approach to deciding where, on the dose-response curves for substance-induced declines in FEV1, regulatory interventions are needed, and how stringent these interventions need to be.

11. HSE summary documentation on grain dust, cotton dust and wool process dust indicate that the problem is not restricted to mineral dusts, that organic dusts, perhaps to some extent due to endotoxin content, are also causes of COPD. Apart from workplace dusts, there is evidence for the ability of certain gases, ammonia, ozone, nitrogen oxides, and sulphur dioxide to cause effects such as chronic lung inflammation, emphysema, and/or chronic bronchitis. This emphasises the generic importance of establishing a position on the health significance of occupationally-induced declines in FEV1.

Variability in susceptibility

12. Cigarette smokers have higher death rates for COPD than non-smokers. However, not all smokers develop clinically significant COPD; this may be due to factors such as dietary status and levels of physical exercise, but possibly genetic factors might also modify individual risk. This raises the question as to whether or not these same genetic factors might either increase resistance or enhance susceptibility to the respiratory effects of workplace dusts. Individuals with deficiencies in alpha-1 antitrypsin are at increased risk of emphysema; this supports the potential for genetic susceptibility to inhaled substances that might cause COPD. The WATCH review of kaolin noted that some individuals might suffer a greater dust-induced decline in FEV1 than others, emphasising the importance of health surveillance.

Interaction with cigarette smoking

13. Analysis of results from a US population study showed that the excess risk of COPD from the combined effects of smoking and workplace exposures was about 2-fold higher than would be expected from a purely additive relationship. A cross-sectional study in refractory ceramic fibre (RCF) manufacturing workers from six European sites showed an inverse relationship between cumulative exposure to RCFs and FEV1 and FVC. The estimated loss of FEV1 in male smokers was 100 ml for a cumulative exposure of 5 fibre.ml⁻¹.years. However, there were no significant declines in FEV1 in non-smokers. These results also support the existence of an interaction between smoking and dust exposure.

Interpreting occupational data on FEV1
14. Difficulties may arise due to the design of the study; most occupational studies are cross-sectional but ideally longitudinal studies are needed to explore annual changes, and to avoid the “healthy worker effect”. Another difficulty may arise due to lack of correlation between subjectively reported respiratory symptoms and objective measures of pulmonary function. Also, uncertainties may arise because FEV1 data are usually reported as a percentage of predicted values; the prediction is based on average reference values from the European Respiratory Society\(^9\), but workers in manual trades might be expected to have better than average values. Hence, the use of the European reference values might lead to an underestimation of effect.

Consultation

15. No wider consultation on the content of this cover paper beyond HSE has been undertaken at this stage.

European Context

16. None.

Action

17. WATCH is asked to consider the issues described in this paper and to:
   a. Provide views on the interpretation and strength of evidence that can be placed on occupational studies, which are frequently subject to numerous weaknesses and limitations. The relative importance of symptoms data is also relevant to this point.
   b. To decide whether or not it can recommend a particular magnitude of decline in FEV1 at which regulatory interventions are needed, and to comment on the nature and required stringency of such interventions.
   c. If a precise recommendation for b) cannot be made at this meeting, to advise what approach could be jointly taken by WATCH and HSE to develop a position that would be of generic applicability to dusts, gases and fumes dealt with in the course of the ORD sub-programme.

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References


