Tubercle and Lung Disease (1992) **73**, 7–12

Tubercle and Lung Disease

Occupational lung diseases in the industrializing and industrialized world: commonalities and contrasts: measurement tools

D. C. Christiani

Harvard School of Public Health, Boston, Massachusetts, USA

SUMMARY. **Research on occupational lung disease has been a growing challenge over the past 4 decades. Exposure to respiratory toxins has increased in many industrializing countries of the world while new and old hazards continue to exist in the industrialized world. The focus of this paper is on measurement tools commonly used in the study of occupational lung diseases. The emphasis is on epidemiology, a discipline which has contributed much to the understanding and control of occupational lung disease. An examination of these tools reveals that (1) there are more commonalities than contrasts in available methods; (2) researchers in industrializing settings can contribute much to our understanding of occupational lung diseases; (3) international collaboration is needed in refining measurement tools; and (4) international collaboration should proceed on studies of preventive strategies.**

RÉSUMÉ. **Pendant les quatre dernières décennies, la recherche sur les maladies pulmonaires professionnelles a été l'objet d'un interêt croissant. L'exposition aux nuisances respiratoires a augmenté dans beaucoup de pays en développement, tandis que des risques nouveaux et anciens continuent à exister dans le monde industrialisé. Le présent article traite des méthodes d'évaluation habituellement utilisées pour étudier les maladies pulmonaires professionnelles. L'accent est mis sur l'épidémiologie, discipline qui a beaucoup contribué à la compréhension et au contrôle des maladies pulmonaires professionnelles. L'examen de ces méthodes révèle que: (1) les procédés disponibles ont davantage d'éléments en commun que de contrastes; (2) les recherches poursuivies dans des régions en développement peuvent aider à la compréhension des maladies pulmonaires professionnelles; (3) une collaboration internationale est essentielle pour une mise au point des methodes d'évaluation; et (4) cette collaboration internationale devrait être poursuivie par l'étude de stratégies préventives.**

RESUMEN. **La investigación en enfermedades pulmonares ocupacionales ha sido un desafío cada vez mayor durante las 4 últimas décadas. La exposición a tóxicos respiratorios ha aumentado en muchos países industrializados, mientras persisten nuevos y antiguos riesgos en el mundo industrializado. Este artículo se refiere a las herramientas de medición utilizadas habitualmente en el estudio de enfermedades pulmonares ocupacionales. Se da énfasis a la epidemiología, una disciplina que ha contribuido enormemente a la comprensión y al control de las enfermedades pulmonares ocupacionales. Un examen de estas herramientas revela que: (1) existen mucho más semejanzas que diferencias entre los métodos disponibles ; (2) las investigaciones en los países en industrialización pueden contribuir mucho a nuestra comprensión de las enfermedades pulmonares ocupacionales; (3) la colaboración internacional es necesaria para afinar las herramientas de medición; y (4) la colaboración internacional debería proseguir estudiando estrategias preventivas.**

Correspondence to: David C. Christiani, MD, MPH, Associate Professor, Harvard School of Public Health, Boston, Massachusetts 02115, USA.

INTRODUCTION

The study of occupational lung diseases in populations has been an evolving challenge over the past 4 decades. There are actually more commonalities than contrasts among the industrialized and industrializing worlds when considering occupational lung diseases. My objective in this paper is to focus on measurement tools, with an emphasis upon epidemiologic methods.

Epidemiologic study of workers exposed to respiratory hazards can contribute to our understanding of occupational lung disease in several ways:

1. Discovery of new causes of lung disease.
2. Determining exposure-response relationships.
3. Identification of the relationship between acute and chronic lung disease.
4. Clarification of pathogenesis in early stages of disease.
5. Development of medical surveillance techniques.

Characterization and quantification of exposure are crucial to the attribution of a measure of health outcome to an occupational exposure. Hence, knowing *exposure* is as important as the *effect* (disease, early physiological changes).

Measures of both exposure and health effects must be expanded. This is particularly true in industrializing settings, but is still important in the industrialized setting. Specifically, measurement tools should, in general, be relatively simple, reproducible, safe and amenable to epidemiologic field study. These simple rules apply to air sampling and other measures of exposure, as well as to tests of lung function.

MEASURING EXPOSURE

'Exposure' does not equal 'dose'. However, as Smith has pointed out, using a pharmacologic approach can help characterize human dose-response relationships for toxic materials in the workplace.[1] In this context, an individual's exposure is quantified by measuring the time profile of the agent at the portal of entry, such as air concentration at the breathing zone. However, it may not be practical to measure each individual's exposure. Hence, the exposure associated with a given job title may be quantified instead and used with the assumption that all workers performing that job have the same average intensity of exposure. The exposure assessment for an epidemiologic study of a population of workers would be the estimation of time profiles of concentration for all agents associated with the jobs and/or work sites for a time period relevant to the health effects.

In most settings in the industrializing world, an exposure assessment based on the detailed personal sampling I have just described is impossible at this time. Instead, other techniques are available, some old, some new.

1. The first approximation for exposure is a simple, dichotomous variable: *exposed* versus *non-exposed.* This can be obtained on questionnaire and/or employment records. For example, studies which demonstrated the associations between asbestos exposure, smoking and lung cancer were done using job title alone (i.e. asbestos worker *vs* non-asbestos worker (Table 1).

2. Years employed can be used as a surrogate for *duration* of exposure. Duration of exposure as a surrogate for cumulative exposure may or may not be helpful in assessing a hazard. For example, one study of TDI[3] exposure among polyurethane workers revealed no relationship between acute, across-shift decrement in FEV, and duration of exposure revealed (Table 2). When direct measurement of TDI was done cross-sectionally at the time of spirometric testing, and exposure groups recategorized, a good relationship was found (Table 3).

3. Job history. Usual job and all jobs in chronology can be very useful in constructing a cumulative exposure history. Collapsing job titles with common exposure can be done. However, assumptions regarding constant intensity of exposure often severely limit this approach.

4. Subjective indicators of exposure may be helpful when air sampling is not feasible. A recent study from South Africa by Myers et al[4] has shown that subjective indicators of exposure (dustiness), as determined on

Table 1. Synergistic effect of smoking and asbestos exposure on lung cancer (per 100000 person-years of observation)

Group	Exposed asbestos	Smoking	Death rate	Mortality ratio
Control	No	No	11.3	1.00
Asbestos worker	Yes	No	58.4	5.17
Control	No	Yes	122.6	10.85
Asbestos worker	Yes	Yes	601.6	53.24

Source: Hammond E C et al. Ann N Y Acad Sci 1979; 330: 473.

Table 2. Acute FEV-1 change in polyurethane production workers

Duration of employment (months)	N	Mean ΔFEV-1 (ml)
< 4	28	155
4–15	21	40
16–27	32	127
28–39	13	82
40+	17	84

Source: Wegman D H et al. J Occup Med 1974; 16: 258.

Table 3. Acute FEV-1 change in polyurethane production workers

Exposure group (PPB)	N	Mean ΔFEV-1(ml)
3	51	78
4–5	43	108
6–13	17	180

Source: Wegman D H et al. J Occup Med 1974; 16: 258.

careful questionnaire administration, are predictive of respiratory abnormalities.

The importance of reliably estimating respiratory hazard exposure by means of questionnaire has obvious importance for studies in industrializing nations. It also has importance in industrialized nations where the choice may be to do personal sampling or none at all.

5. Biologic measures of exposure exist for some occupational settings such as inorganic lead exposure. Unfortunately, we do not have such techniques available for respiratory hazards except in very select circumstances. Examples include blood, urine and salivary cotinine for measures of tobacco fume exposure.[5] Another example is measuring cytogenetic changes in peripheral blood after exposure to known or potential lung carcinogens such as asbestos, tobacco smoke, or coke oven emissions.[6] These cytogenetic changes may include sister chromatid exchange (SCE), DNA or hemoglobin adducts. These pathophysiologic alterations are being used with increasing frequency to estimate the internal, biologically effective dose of toxins and, hence, are both measures of exposure and of preclinical disease in some instances. This fledgling field of 'biochemical' or 'molecular' epidemiology is just developing in the industrialized world, and the techniques utilized are not widely available.[7] It is also important to note that the health significance of some of these findings (e.g. SCE) is unknown at this time.

MEASURING EFFECTS

Questionnaires

Respiratory symptom questionnaires have been in use for 30 years — since the British Medical Research Council developed a standardized format. In the USA, the American Thoracic Society (ATS) adopted the MRC questionnaire in 1969 and made recommendations on study design for epidemiological surveys.[8] The questionnaire was revised in a workshop held by the Division of Lung Diseases (DLD) of the National Heart and Lung Institute. Subsequent workshops led to additional recommendations. Problems with proposed standards for questionnaires, lung function testing and radiography remained and this led to an additional effort called the ATS's Epidemiology Standardization Project.[9] Other organizations, such as the World Health Organization (WHO), have also made recommendations for epidemiological research.

As Samet has pointed out, a questionnaire's utility is determined by its validity — the extent to which it measures what it was designed to measure — and by its reliability — the extent to which responses are repeatable.[10] Assessment of validity has been limited to sputum, dyspnea and chest illness since appropriate standards for other variables are not available. Short-term reliability varies in different studies from about 60–90% for sputum production.

A recent international comparison of the ATS-DLD questionnaire by Enarson et al[11] presented at the 1990 World Conference on Lung Health, illustrates the cross-cultural usefulness of this tool for determination of chronic bronchitis prevalence. However, there are limitations to the standardized questionnaire. It is important to note that the ATS-DLD questionnaire is inadequate in regard to wheezing and other manifestations of airway hyperreactivity.[12] Moreover, simple translation and back-translation does not necessarily ensure accurate assessment of symptoms such as dyspnea, wheeze or chest tightness. The perception and reporting of symptoms is not only language-dependent, but also culturally determined. Finally, the standardized respiratory questionnaire has not been adequately evaluated as a tool in longitudinal studies of workers. Limited data suggest significant variability over time in reports of chronic sputum and other symptoms. Hence, the respiratory symptom questionnaire may not be as useful in longitudinal studies as it is in cross-sectional, or prevalence studies. There needs to be work done in both the industrializing and industrialized nations to:

1. Validate a symptom questionnaire that addresses airway reactivity,
2. Assess the determinants of longitudinal variability in symptom reporting.

Despite the limitations of the standardized respiratory questionnaire, it remains a very valuable tool for occupational respiratory epidemiology. It is an inexpensive, safe, and a generally reliable instrument. In the future we will likely see further revisions which will enhance its utility.

Physical chest examinations

The chest examination is not a reliable tool in the study of occupational lung disease. In the absence of amplification equipment, there is low reproducibility for rales; and the significance of expiratory wheeze heard on one examination *vis-à-vis* airway hyperreactivity is questionable.[13] Unfortunately, when adventitious sounds are consistently present, pathophysiologic changes are relatively advanced.

Chest X-ray radiography

The International Labor Organization (ILO) 1980 Classification System provides a method of systematically recording radiographic abnormalities of the lung and pleura resulting from the inhalation of all types of inorganic dusts.[14] The objective is to codify the abnormalities in a simple, reproducible manner without definition of pathologic entities or to assess physiologic derangements. It has been a useful epidemiologic tool in the study of pneumoconioses such as silicosis, coal workers' pneumoconiosis (CWP) and asbestosis.

The application of this epidemiologic classification scheme is based upon a set of standard postero-anterior chest radiographs illustrating radiographic stages of pneumoconioses. Parenchymal changes are quantitatively divided into two main categories: small and large opacities. Small opacities are further divided into round or irregular, which are recorded according to size, extent and profusion (density).

Parenchymal opacities are graded on a 12-point scale of 'profusion', an estimate of opacity density. Although the coding system has improved consistency in the reading of parenchymal disease, which is subject to large reader variability, limitations remain even after the various technical requirements for obtaining a satisfactory chest radiograph are met. These include:

1. The coding scale is continuous, not discreet. So, the border line between certainly normal and certainly abnormal may be confusing in many cases.
2. Assessment of small opacities is much influenced by radiologic techniques, as well as body habitus, level of inspiration and age of subject.
3. There is particular intra-observer and inter-observer variability in low profusion readings (e.g. 1/0 and 0/1).
4. There are no standard films provided for low profusion conditions (e.g. 1/0).

In addition to parenchymal abnormalities, there is also a coding scheme for pleural abnormalities and other changes associated with pneumoconioses (e.g. eggshell calcification of hilar nodes).

Since the goal of occupational epidemiology is the prevention of occupational disease, the utility of measurement tools such as radiography must be judged in that context. We need further clarification as to the usefulness of detecting early parenchymal opacities, and pleural abnormalities, in workplace interventions that will result in decreasing disease progression.

The use of chest radiography in the study of occupational asthma or Chronic Obstructive Pulmonary Disease (COPD) is discouraged, as the relationships among X-ray findings,lung function and pathology are complex. This fact, plus the feasibility, cost, and technical considerations make the routine use of chest X-ray situations other than fibrogenic dust exposure impractical.

Lung function tests

Lung function testing is an essential tool in the detection of occupational lung disease. There are a variety of tests available including:

1. Spirometry (FEV_1, FVC, PEFR, FEF_{50}, FEF_{25-75}).
2. Isolated peak-flow rate measurement (PEFR).
3. Tests of airway responsiveness (e.g. histamine).
4. Special tests, e.g. nitrogen washout (small airways), lung volumes determination (FRC, TLC), and diffusion capacity (DLCO).

To be most useful, pulmonary function tests must be accurate, reliable (repeatable), sensitive (able to detect disease), and readily applicable at the workplace.

The usefulness of pulmonary function testing to quantify hazardous effects of occupational exposures are influenced by several factors.

Choice of test

The forced expiratory spirogram still appears to be the best single test available! Spirometry can be used cross-sectionally and longitudinally. Longitudinal applications may take place over years, as in pneumoconiosis research, or across a workshift, or in studies of acute airways disease (e.g. asthma, byssinosis). The across shift technique has been used effectively in developing countries, as demonstrated in a study of textile workers in Shanghai, China[15] (Table 4).

Table 4. Regression analysis of change in across-shift FEV_1 (ΔFEV_1 %) in 767 textile workers

Outcome: ΔFEV_1 %		
Variable	Beta	P>t
Intercept	+0.276	0.73
Age	+0.004	0.86
Smoking*	+0.526	0.41
Gender†	–0.574	0.39
Exposure‡	–2.32	<0.01

* Smoking = 0 if no, = 1 if yes.
† Gender = 0 if female, = 1 if male.
‡ Exposure = 0 if non-cotton, = 1 if cotton worker.

Source: Christiani D C et al. Scand J Work Environ Health 1986; 12: 46.

Recent data also suggest that use of a simple, portable peak flow meter can yield very valuable information and can be used as part of a multiple or serial test design in the study of airways disease.[16] For example, 3 peak flow measurements are taken at frequent intervals ranging from times per day to hourly using a mini-Wright® or comparable instrument. Exposure is measured continuously, or relatively continuously, and can be characterized for short intervals with peaks of varying frequency, intensity and/or duration. Individual dose-response curves can be generated for each subject and these curves can be examined in relation to confounders and effect modifiers. Furthermore, Ryan et al have shown that an examination of alterations in diurnal peak flow variability can also be helpful in assessing bronchial reactivity.[17] Repeat measures of peak flow are simple, inexpensive and do not cause discomfort to the subject. Most importantly, there is no requirement for electricity, enhancing utility in the developing country setting.

Instrument standardization

It is essential to have equipment that meets accuracy and repeatability criteria, such as those elaborated by the ATS[18].

Instrument calibration
Quality control is essential. Field conditions in any country may be quite unfavorable as contrasted with the laboratory. Careful and frequent calibrations must be performed regularly.

Test procedure standardization
An ATS committee has recently updated its statement on standardization of spirometry.[19] The statement provides both instrument and performance guidelines, with waveform illustrations. Epidemiologic studies by Eisen and associates have shown that strict performance reproducibility criteria may result in selection bias, with the result that subjects with poor test performance had lower, unobserved, spirometric values and were excluded from analysis.[20] Hence, reproducibility of spirometry performance is a goal, not a requirement, for assessing occupational lung disease in populations.

Data interpretation; reference values
Interpretation of pulmonary function results requires consideration of many factors such as smoking history, gender, height and race, as well as occupational exposures. Reference value determination is clearly an area that needs further investigation. In the USA alone, there are over 20 reference value equations for spirometry in common use. Few data are available for several race and age groups. Data are scarce in most developing countries. However, there have been equations published from several regions in China, from Singapore, and from parts of Africa. Recently, a project was completed in Nicaragua, Central America, which generated the first prediction equations for that region and will be published in the near future. There has been, in fact, a considerable amount of data collected in the developing world using standard spirometers, which is yet to be analyzed fully.

TESTS OF AIRWAY RESPONSIVENESS

Bronchial provocation testing has become an important tool for epidemiologic and clinical assessment of asthma. It can be a safe, reliable and technically feasible approach for evaluating bronchial reactivity. Several methods are available, including histamine, methacholine (comparable to histamine), cold air, exercise and specific antigen challenge. Standardized techniques have been developed since 1975.[21] Methacholine testing has been adopted for field use, outside of the laboratory and used successfully.[22] On the other hand, specific antigen challenge can be dangerous, is not standardized, and, hence, should only be done in hospital.

Biomarkers of early disease

As noted above, in many occupational settings, attention has turned to defining early *pathophysiologic* changes which precede clinical disease. Early biological responses may include bronchial hyperreactivity, evidence for sensitization(RAST), evidence for inflammation (BAL lavage fluid, nasal lavage, etc.).[6] Most of these approaches require considerable resources, including laboratory support, making them inappropriate for most industrializing settings.

CONCLUSIONS

There are actually many commonalities, and fewer contrasts, in measurement tools available to us for the study of occupational lung disease in industrializing and industrialized settings.

Colleagues in industrializing settings can make a major epidemiologic contribution to our understanding of occupational lung disease by wider application of the basic tools of epidemiology already available.

Refinement in measurement tools (and in analysis of data) can proceed in a collaborative fashion with colleagues from around the world concentrating efforts on identifying and eliminating occupational lung disease. I would like to stress that it should not be our common goal to use the industrializing settings as a laboratory for the study of the effects of chronic exposure to respiratory toxins. On the contrary, these settings should be the sites of active intervention for reduction of harmful exposures and disease prevention. Hence, together we can study *intervention*, particularly in relation to halting disease progression, or reversing disease which is reversible.

References

1. Smith T. Exposure assessment for occupational epidemiology. Am J Ind Med 1987; 12: 249–268.
2. Hammond E C, Selikoff I J, Seidman H. Asbestos exposure, cigarette smoking and death rates. Ann N Y Acad Sci 1979; 330: 473–479.
3. Wegman D H, Pagnotto L D, Fine L J. A dose-response relationship in TDI workers. J Occup Med 1974; 16: 258.
4. Myers J E. Respiratory health of brickworkers in Cape Town, South Africa: appropriate dust exposure indicators and permissible limits. Scand J Work Environ Health 1989; 15: 198–202.
5. Jacob P, Wilson M, Benowitz N C. Improved gas chronatographic method for the determination of nicotine and cotinine in biologic fluids. J Chromatogr 1981; 222: 61–70.
6. National Research Council. *Biologic Markers in Pulmonary Toxicology*, National Academy Press, Washington, D. D., 1989.
7. Hulka B S, Wilcosky T C, Griffith J D. Methodologic issues in molecular epidemiology. In: Biologic markers in epidemiology. New York: Oxford University Press, 1990.
8. American Thoracic Society. Committee on Standards for Epidemiologic Surveys in Chronic Respiratory Disease. New York, National Tuberculosis and Respiratory Disease Association.
9. Ferris B G, ed. Epidemiology standardization project. Am Rev Respir Dis 1978; 118(6, part 2): 1–20.
10. Samet J M, Speizer F E, Gaensler E A. Questionnaire reliability and validity in asbestos exposed workers. Bull Eur Physiopathol Respir 1978; 14: 177–188.
11. Enarson D A, Christiani D C, Ernst P et al. The prevalence of chronic bronchitis: an international comparison. Am Rev Respir Dis 1990; 141: A327.

12. Samet J M. Epidemiologic approaches for the identification of asthma. Chest 1987; 91: 74s–78s.
13. Gandevia B. Clinical techniques. In: Weil H, Turner-Warwick M, eds. Occupational lung diseases. New York: Marcel-Dekker, 1984.
14. Guidelines for the Use of ILO International Classification of Radiographs of Pneumoconiosis. Occupational Safety and Health Series 22 (Rev 1980). Geneva: International Labor Office, 1980.
15. Christiani D C, Eisen E A, Wegman D H, et al. Respiratory disease in cotton textile workers in the People's Republic of China. Scand J Work Environ Health 1986; 12: 46–50.
16. Wegman D H, Eisen E A. Design for epidemiologic studies of acute effects of respiratory irritants. In: Hogstedt C, Reuterwall C, eds. Progress in occupational epidemiology. Amsterdam: Exerpta Medica, 1988: pp 297–300.
17. Ryan G, Latimer K, Dolovitch J et al. Bronchial responsiveness to histamine: relation to diurnal variation of flow rates and improvement after bronchodilator. Thorax 1981; 37: 423–427.
18. Nelson S B, Gardner R M, Crapo R O, Jensen R L. Performance evaluation of contemporary spirometers. Chest 1990; 97: 288–297.
19. Gardner R M, Hankinson J L, Clauses J C, Crapo R O, Johnson R L, Epler G R. ATS statement on standardization of spirometers — 1987 update. Am Rev Respir Dis 1987; 136: 1285–1298.
20. Eisen E A, Oliver L C, Christiani D C, Robins J M, Wegman D H. Effects of spirometry standards in two occupational cohorts. Am Rev Respir Dis; 1985; 132: 120–124.
21. Chai H, Farr R S, Froehlich L A. Standardization of bronchial inhalation challenge procedures. J Allergy Clin Immunol 1975; 56: 323–328.
22. Hendrick D J, Fabbri C M, Hughes J M et al. Modification of the methacholine inhalation test and its epidemiologic use in polyurethane workers. Am Rev Respir Dis 1986; 133: 600–604.