4

EPIDEMIOLOGY AND OCCUPATIONAL LUNG DISEASE

W. Keith C. Morgan

The identification of both acute and chronic occupational hazards depends for the most part on the intelligent use of epidemiological studies. Epidemiology is the study of the etiology of disease states through the acquisition and analysis of appropriate data by statistical methods. It concerns itself in the main with large populations, and for this reason many of the diagnostic methods that are used at the bedside or in the hospital-based laboratory are not applicable in the field.

For a test to be suitable in field work it must be relatively easy to perform, it should not require much in the way of skill or complex maneuvers on the part of the patient, and the equipment or apparatus necessary for its performance should be as simple and sturdy as possible. If complex and sophisticated apparatus is to be used, then the necessary technical and electronic supporting facilities must be available. The ideal test for use in field work should take a short time to carry out, should be reproducible and sensitive, and should not involve invasive techniques. Whenever possible a direct readout of the test should be available since this will allow an immediate rough check on the results. Should the discovery subsequently be made that a number of measurements were technically unsatisfactory, it is often difficult to persuade the whole population to return for retesting. Finally, as far as possible the test should be independent of the effort the subject puts into it.

Epidemiological surveys are of two types, cross-sectional and longitudinal. In the former a sample of the population is selected and is studied once over a relatively short time. From such a study it is possible to define the prevalence of a disease and of certain symptoms. The term prevalence signifies the frequency of a disease or a symptom in a particu-

Epidemiology and occupational lung disease (1975)
ACL Doc 25357 · Page 1 of 10
Published by AsbestosClaims.Law
asbestosclaims.law/library/25357/1

lar population at a particular time. It does not help to define how often or over what time period a disease develops. If such a study is repeated at regular intervals, it becomes a longitudinal study, and it is possible by these means to identify how many subjects develop a particular condition, symptom, or disease over a designated time. Such information allows the incidence of a disease to be determined. Longitudinal studies suffer from the fact that subjects are lost to study and in many instances these losses leave the study with an unrepresentative sample. In epidemiological studies it has to be borne in mind that large numbers of persons are studied and errors in the collection of physiological or other data and in the answering of specific questions can be assumed to occur at random. Such errors or inaccuracies, while acceptable in epidemiology, would be more serious if they occurred in the clinical investigation of a patient.

Field surveys of respiratory disease commonly utilize three methods for the collection of data, namely, a standard questionnaire on respiratory symptoms, the performance of certain pulmonary function tests, and radiographic examination of the chest.

THE USE OF A STANDARD QUESTIONNAIRE

An excellent questionnaire has been devised by the Medical Research Council of Great Britain.[1] This records the prevalence of the most important respiratory symptoms, viz., cough, sputum production, and shortness of breath. It also takes a smoking history and includes an abbreviated occupational history with particular emphasis on past dusty exposure. The questionnaire has been tested in a variety of different conditions and has been shown to be a reproducible and accurate way of collecting such information. However, the questions have to be asked as written, and the subject being interviewed must not be intimidated or "bullied" by the tone of the interviewer. In this context, it has been shown that subjects who smoke will, when interviewed by a physician who is very much against the habit, confess more often to cough and sputum than they would had they been interviewed by a nurse or more disinterested person. For these reasons, the MRC have published a set of instructions which describe how the questionnaire should be administered.[2] In addition, some form of training in the administration of the questionnaire is advisable for all potential interviewers prior to its use.

The questionnaire can be supplemented if necessary. Thus if a survey is being done on coal miners, a more detailed occupational history can be added in order to quantify dust exposure. Such a history would ask where the miner worked, viz., at the face, on transportation, on the surface, and so on.

To be an effective instrument in the accumulation of reliable data, a

Published by AsbestosClaims.Law
asbestosclaims.law/library/25357/2

questionnaire should not be too long. A current fad at many hospitals and clinics is to administer a long detailed questionnaire to all referred patients before they are seen by the physician. Such exercises are in the main futile. They often take 30 to 60 minutes to complete and the patient becomes bored and resentful by the time he has completed the questionnaire. This leads to incompleteness and the acquisition of useless and inaccurate data. It is also vitally important to realize that patients who seek medical help because of symptoms want to see a physician as soon as possible. If instead they are greeted by a tedious and prolonged questionnaire, they become resentful and uncooperative. The need for simplicity cannot be overemphasized.

Finally, the use of the same questionnaire in different countries may result in some anomalous responses that are related to translation and cultural differences. Nonetheless, such differences can frequently be controlled or at least limited, and it only remains to be said that much important epidemiological information can be acquired by the correct application of a standard questionnaire.

TESTS OF PULMONARY FUNCTION

Spirometry and Standard Tests of Ventilatory Capacity

Any spirometric or other equipment used in the field should be simple, accurate, and reliable. Many spirometers are currently available; some are excellent, others mediocre, and an appreciable number completely unreliable. Even with the acceptable spirometers, it must be remembered that the response characteristics differ and that a person's FEV_1 and FVC may differ by as much as 5 to 10 per cent or more according to the instrument used. The accuracy of the spirometer is mainly dependent on its resistance and inertia, and when disparate readings are obtained, they can usually be related to faults in these features. For these reasons, one cannot compare the absolute values for various ventilatory tests of two field studies using different spirometers unless they have been calibrated against each other so that a conversion factor is available. For similar reasons, differing predicted values may be obtained on the same population if differing apparatus is used. To obviate such problems, many United States government agencies that are currently sponsoring research in pulmonary physiology are now insisting that spirometric values be "corrected" to the values which would have been obtained had a standard Stead-Wells spirometer* been used.

No matter what type of spirometer is used, a permanent record of

*Warren E. Collins, Inc., 220 Wood Road, Braintree, Mass. 02184.

Published by AsbestosClaims.Law
asbestosclaims.law/library/25357/3

several forced expiratory volume maneuvers is desirable. Such a tracing provides an opportunity to see that the subject has been fully cooperative and that there were no technical misadventures. If the subject produces three closely similar curves, then it can be assumed that cooperation and effort have been satisfactory. All spirometers that are used in field studies should be fitted with a temperature probe. While it may be justifiable to use a constant temperature correction factor in a hospital-based laboratory, it is certainly not when the measurements are being performed in the field where the temperature may be near freezing or well over 80° F., depending on the season and circumstances.

When performing spirometry in the field, we recommend that the subject be allowed two practice maneuvers first. These allow him to become familiar with the apparatus. Three real maneuvers are then recorded. If all three appear similar, all well and good, but if one tracing appears different, then the subject should be asked to repeat the maneuver. Ideally, the values for FEV_1 and FVC from three forced expirations should be within 5 per cent of each other. This is a stringent requirement and it is probably reasonable to regard measurements as valid if two out of three are within 5 per cent and all three within 10 per cent. The tests can be performed either standing or sitting, but in either instance the patient must be comfortable, not bent over, and with his clothing reasonably loose. Under normal circumstances, spirometric values are similar whether the subject is standing or sitting. This does not apply, however, to grossly obese subjects in whom the sitting value may be significantly lower. Nose clips may be used but are not necessary.

There are differences of opinion as to which value to record. Many persons feel that the average of the last three should be used. Others take the mean of the two greater values. We use the largest value of the three.[3] In practice, it seems to make little difference which value is used. It should, however, be stressed that in subjects with severe obstructive airways disease, the largest FEV_1 may be obtained in the two practice maneuvers, most commonly the first. Despite numerous repeat maneuvers, the subject will usually fail to reproduce the first high figure and there is reason to believe that this inflated value is "a freak." For these reasons, if the highest FEV_1 is obtained in the two practice maneuvers, it should be discarded.

In regard to the most appropriate indices, we recommend the FEV_1, FVC, and MMF. The FEV_1 should be obtained by extrapolating the steepest part of the curve to zero volume. This is to correct for variations related to the time the subject started his forced expiration. All values should be corrected to BTPS. Measurement of the MVV is not practical in field studies as it is difficult to obtain maximal cooperation. Peak expiratory flow rates may be measured with a Wright peak flow meter.[4] This instrument requires constant calibration and peak flow is a far less useful measurement than is a complete forced expiratory volume maneuver. With this instrument, values should be expressed as ATPS. The

Published by AsbestosClaims.Law
asbestosclaims.law/library/25357/4

main advantage of peak flow measurement is that the maneuver is extraordinarily simple and the instrument requires no power. For these reasons, peak flow measurements are useful in children.

Flow volume loops may prove to be useful means of detecting small airways disease. The theory behind this has been alluded to previously. It is possible with some electronic ingenuity to devise a time-pulse generator that will superimpose suitable signals on the flow volume loop, thereby enabling the FEV_1 and FVC to be measured from the loop.[6]

Other Pulmonary Function Tests

Oscillation Method of Determining Respiratory Resistance.[7, 8] The equipment used for determining resistance is complex. This method relies on the fact that it is possible to superimpose on the respiratory flow pattern a secondary pressure oscillation at the mouth. This results in another flow and the relationship between pressure and flow can be seen on an oscilloscope. The frequency of the oscillations is adjusted in order to narrow the loops as much as possible. Complete closure is possible in normal subjects. The resistance is then measured from a photograph made from the oscilloscope.

The methodology can be modified using a fixed pressure and frequency. The pressure is set automatically so that a flow pattern is superimposed on the top of the normal breathing pattern. If the airway pressure is constant, oscillatory flow must thus be inversely related to resistance. Hence resistance can be calculated for each breath. An excellent description of these methods has been given by Ferris.[8] In our experience, the method is far from satisfactory because many subjects cannot cooperate. The added pressure oscillation leads to the patient closing his glottis and tensing his respiratory muscles. The early hopes of the widespread applicability of this test to field studies appear unlikely to be fulfilled.

Measurement of Airways Resistance with a Plethysmograph.[9] This is an objective test which requires little patient cooperation. Extensive and complicated equipment is necessary and many patients are reluctant to sit inside the "box." Nonetheless, Dr. George Wright has used a plethysmograph in field studies.[10] It is our opinion that very little additional information beyond that which can be obtained by spirometry is made available from the plethysmographic determination of airways resistance.

Measurement of Diffusing Capacity. This measurement has only recently been used in field studies. The steady state method is not practical for field studies because of the time involved. In addition cigarette smoking and ventilation-perfusion inequalities affect the results. The single breath method is more suitable. Automated modules are in existence which allow this determination to be made in the field.* Suffice it

*Collins Modular Lung Analyzer, Warren E. Collins, Inc., 220 Wood Road, Braintree, Mass. 02184.

Published by AsbestosClaims.Law
asbestosclaims.law/library/25357/5

to say that the results are affected by hemoglobin concentration and that the latter often varies according to populations examined. Cigarette smoking in the 15 minutes prior to testing also influences the results. It seems doubtful whether the measurement of diffusing capacity will add greatly to the information that is available from simpler tests; however, further studies to assess its usefulness are desirable.

Total Lung Capacity. This may be estimated from the alveolar gas volumes obtained when the diffusing capacity is measured with a module such as is described above. The values obtained are lower but seem to be reproducible.[8]

Total lung capacity may also be determined by radiographic methods. The most accurate method was originally described by Barnhard.[11] It is derived from a series of measurements made from posteroanterior and left lateral chest films. In essence the chest is divided into a series of elliptical cylindroids and the volume of each is calculated. Appropriate subtractions are made for the heart, vertebral column, and so forth. The measurements take some time to make and the calculations take somewhat longer. Nonetheless, the values derived by this method are closely similar to those obtained with the plethysmograph. An abbreviated and simpler method has been devised by Reger, Young, and Morgan.[12] Although the latter is simpler and takes far less time, it is only slightly less accurate and is quite acceptable for epidemiological surveys.

Ideally, in any investigation of the respiratory function of a group of exposed subjects, a comparable group of controls should also be studied. In this way a comparison can be made of the respiratory status and function of the control and exposed groups. Should this not be possible, it is customary to compare the various indices of pulmonary function to predicted figures for the normal population. Such a comparison may introduce bias in that the smoking habits of the exposed group may differ from those of the population from which the predicted figures were derived. More importantly, ethnic differences in lung volumes, flow rates, and certain other indices of pulmonary function are often present and may be as large as 10 to 15 per cent. Thus, black Americans have smaller lungs and lower flow rates than white Americans of European origin.[13] Such ethnic differences must be borne in mind when conducting epidemiological surveys.

RADIOGRAPHIC EXAMINATIONS

The chest radiograph has for many years been one of the mainstays in the epidemiological investigation of the pneumoconioses. It remains the sole means of detecting pulmonary retention of certain dusts, e.g., silica and coal. For these and other reasons, an abnormal chest film is frequently accepted as the only legal evidence of dust exposure in work-

Published by AsbestosClaims.Law
asbestosclaims.law/library/25357/6

men's compensation cases and similar industrial litigation. Seldom, however, is the chest film useful in the assessment of pulmonary impairment. It does nevertheless provide a measure of the amount of dust retained in the lungs and is especially useful in conditions such as silicosis and coal workers' pneumoconiosis.

Before embarking on a respiratory disease survey which relies on chest radiography as one of the means for the acquisition of epidemiological data, it is imperative that the techniques for taking and interpreting the films be standardized as far as possible. This is especially important in longitudinal studies. The reasons for this are several.

The chest radiograph is used as a means of quantifying the amount of dust that is retained in the lungs. The retention of dust leads to the development of certain shadows or opacities in the chest film, and in general, the more the opacities, the more retained dust. While the radiographic opacities may not always be produced by the dust itself—rather, they may be produced by the fibrogenic response to the retained dust—it is reasonable to assume that the more fibrosis present, the more retained dust. Thus it is evident that there is a continuum from no dust in the lungs to maximal dust, whatever that might happen to be. In an attempt to quantify the amount of dust in the lungs, various radiological classifications of the pneumoconioses have been introduced. The classifications rely on the arbitrary selection of certain films as being typical of the various stages of the disease. Thus, the pneumoconioses were originally divided into the simple and complicated forms of the disease. The former was defined according to the presence of either regular or irregular opacities less than 1 cm. in diameter. When the opacities were more than 1 cm. in diameter, then complicated coal workers' pneumoconiosis was said to be present. Simple pneumoconiosis was further divided into categories 1, 2, and 3, according to the extent and profusion of the opacities, and, similarly, complicated pneumoconiosis was divided into stages A, B, and C, according to the size of the large opacities.[14] A group of physicians then selected chest films which in their opinion could be used as standards for these various stages or categories. It was moreover suggested that any chest film that was being categorized should be assessed by comparing it to the standards. While such an exercise is a help in approximating the unknown with a standard, it must be realized that no other radiograph exactly resembles the standard since the amount of dust retained in the lungs of the subject whose film is being categorized is either slightly more or less than that retained in the lungs of the subject from whom the standard film was made.

It subsequently became apparent that a classification that relies only on major categories, viz. 1, 2, and 3, lacked sufficient sensitivity for longitudinal studies. Thus a 12 point scale was introduced.[15] This subdivided each major category of simple pneumoconiosis into three subcategories. Category 0 was divided into subcategory 0/−, in which the film was absolutely normal and under no conceivable circumstances would anyone

Published by AsbestosClaims.Law
asbestosclaims.law/library/25357/7

call it otherwise; 0/0 where the film was normal, 0/1 where the interpreter decided it was category 0 but considered category 1 as well. Category 1 was made up of subcategories 1/0, 1/1, and 1/2. In the case of subcategory 1/0, it was decided the film should be placed in category 1 but category 0 was also considered, 1/1 represents a typical category 1 when neither category 0 nor category 2 was considered; and so on. The numerator represents the category in which the radiograph was placed while the denominator describes any other category that was considered. By this means, it is possible to divide the continuum into a 12 point scale. An assumption is made that the scale is of equal intervals and that the weight of additional dust retained for each increase in subcategory is the same; viz., it takes the same amount of dust to change a 0/1 to 1/0 as it does to change a 2/2 to 2/3. This assumption may not be entirely valid but it has much to recommend it practically, especially when it comes to the assessment of progression of pneumoconiosis. Studies have been carried out which have related radiographic subcategories to the coal dust content of the lungs.[16] These have shown that for the most part there is a straight line relationship.

Granted all the above, the radiographic interpretation of pneumoconiosis still remains a subjective exercise.[17] Marked interobserver and intraobserver variations occur, as they do also in the interpretation of chest films for tuberculosis, barium enemata for colitis, and electrocardiograms for myocardial infarction. Interobserver is usually greater than intraobserver variation, and it is essential in any epidemiological survey to compare and standardize the radiographic interpretation of the various readers. Those readers who differ greatly from their colleagues should be excluded. Multiple readings are to be preferred to single readings but even then the panel of readers should be tested at regular intervals to see that their reading habits do not change. This can be done by having them reread the same series of films at regular intervals. Such a series should range over all categories and should have at least 200 films in it. During the interpretation of a series of unknown films, standard films should always be used for comparison.

The interpretation of films for pneumoconiosis is greatly influenced by technique and as such this should be standardized as far as possible prior to starting the survey.[18] Individual radiologists can no more agree on an optimal technique than they can on the stage of pneumoconiosis present in an individual film. For these reasons, some uniform technique should be adopted, since were each radiologist allowed to use his own preference, the range would be infinite. Such recommendations have been published and while certainly not ideal can, with intelligent application, do much to reduce interobserver variation.[19]

The depth of inspiration, the technique used to take the film, and the method of developing the film all may influence interpretation. We have shown that "overpenetrative" films are likely to lead to a lower category being given to a particular film, while if the film is unduly "soft,"

Published by AsbestosClaims.Law
asbestosclaims.law/library/25357/8

then a higher category is likely to be awarded.[18] The effects of such changes may be profound and may change prevalence and progression rates by as much as 50 per cent.

Unless readers and techniques are all standardized and rendered comparable, it is impossible to compare prevalence rates between different studies and different countries. The determination of progression is likewise influenced by the radiographic techniques employed when the films were taken. Unless the technique used to take both of the films is similar, falsely high or falsely low progression rates may result.

It is often assumed that the interpretation of films for pneumoconiosis requires profound knowledge and perspicacity and that the ideal interpreter is a happy blend of Sherlock Holmes, Albrecht Durer, and Socrates. The interpretation of a film for pneumoconiosis is a glorified guess or estimate of the number of "dots" present on it. The more educated the observer, the more rigid he is in his interpretation. If he happens to coincide with an accepted consensus, this is ideal, but if he does not, then it is most unlikely that he will change his reading habits. Should the latter state of affairs be the case – a frequent occurrence with eminent radiologists – then he must be excluded from such epidemiological surveys. We have shown that lay readers can be trained to read films for pneumoconiosis.[20] In many ways, they are to be preferred since they are more open-minded and more likely to "record" than to "interpret."

REFERENCES

1. Medical Research Council Committee on the Aetiology of Chronic Bronchitis, Definition and classification of chronic bronchitis, Lancet *I*, 775, 1965.
2. Medical Research Council Committee on the Aetiology of Chronic Bronchitis, Instruments for the use of the questionnaire on respiratory symptoms, Dawlish, Devon, W. J. Holman Ltd., 1966.
3. Stebbings, J. H., Jr., Chronic respiratory disease among non-smokers in Hagerstown, Maryland. II. Problems in the estimation of pulmonary function values in epidemiological surveys, Environ. Res. *4*, 163, 1971.
4. Wright, B. M., and McKerrow, C. B., Maximum forced expiratory flow rate as a measure of ventilatory capacity, Brit. Med. J. *II*, 1041, 1959.
5. Lapp, N. L., and Hyatt, R. E., Evaluation of lung mechanics in epidemiological studies, Bull. Physio-Path. Resp. 6, 595, 1970.
6. Hankinson, J. L., and Lapp, N. L., Time-pulse generator for flow-volume curve, J. Appl. Physiol. 29, 109, 1970.
7. Fisher, A. B., Dubois, A. B., and Hyde, R. W., Evaluation of the forced technique for the determination of resistance to breathing, J. Clin. Invest. *47*, 2045, 1968.
8. Ferris, B. G., Use of pulmonary function tests in epidemiologic surveys, Bull. Physio-Path. Resp. 6, 595, 1970.
9. DuBois, A. B., Botelho, S. Y., and Comroe, J. H., A new method for measuring airway resistance in man using a body plethysmograph, J. Clin. Invest. 35, 327, 1956.
10. Wright, G., Lloyd, T. C., Hamill, P., and Prindle, R.: Epidemiologic study of obstructive pulmonary disease in two small towns, Amer. Rev. Resp. Dis. 86, 713, 1962.
11. Barnhard, H. J., Pierce, J. A., Joyce, J. W., and Bates, J. H.: Roentgenographic determination of total lung capacity, Amer. J. Med. 28, 51, 1960.
12. Reger, R. B., Young, A., and Morgan, W. K. C., An accurate and rapid radiographic method of determining total lung capacity, Thorax *27*, 163, 1972.

Published by AsbestosClaims.Law
asbestosclaims.law/library/25357/9

13. Lapp, N. L., Amandus, H. E., Hall, R., and Morgan, W. K. C., Lung volumes and flow rates in black and white subjects, Thorax 29, 185, 1974.
14. International Labour Office: Meeting of experts on the international classification of radiographs of the pneumoconioses, Occup. Safety Health 9, 2, 1959.
15. Liddell, F. D. K., and May, J. D., Assessing the radiological progression of simple pneumoconiosis, London, National Coal Board (Medical Service), 1966.
16. Rossiter, C. E., Rivers, D., Bergman, I., Casswell, C., and Nagelschmidt, G., Dust content, radiology and pathology in simple pneumoconiosis of coal workers, in Davies, C. N., ed., Inhaled Particles and Vapours II, New York, Pergamon Press, 1967, Section 5, pp. 419–437.
17. Reger, R. B., and Morgan, W. K. C., On the factors influencing consistency in the radiologic diagnosis of pneumoconiosis, Amer. Rev. Resp. Dis. *102*, 905, 1970.
18. Reger, R. B., Smith, C. A., Kibelstis, J. A., and Morgan, W. K. C., The effect of film quality and other factors on the roentgenographic categorization of coal workers' pneumoconiosis, Amer. J. Roent. *115*, 457, 1972.
19. Jacobson, G., Bohlig, H., and Kiviluoto, R., Essentials of chest radiology, Radiology 95, 445, 1970.
20. Peters, W. L., Reger, R. B., and Morgan, W. K. C., The radiographic categorization of coal workers' pneumoconiosis by lay readers, Environ. Res. 6, 60, 1973.

Published by AsbestosClaims.Law
asbestosclaims.law/library/25357/10