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Investigations in Progress

BIOMEDICAL

W. Keith C. Morgan and Earle P. Shoub

Although much is currently known about coal workers' pneumoconiosis, there are still many gaping voids in our knowledge. Thus although the inhalation of coal dust is essential to the development of this disease, a linear relationship between dust exposure and the development and progression of CWP is often not evident. There remain many unexplained anomalies, and much still remains to be done. The U. S. Public Health Service is currently involved in a number of studies which it is hoped will shed light on some of these mysteries. The more important of these are worth description.

National (Inter-Agency) Study of Coal Workers' Pneumoconiosis

In both Great Britain and Germany, long-term prospective studies attempting to relate the development and progression of coal workers' pneumoconiosis to the levels of dust prevailing in the coal mines have been in progress for many years. Workers from both countries presented their data at the Third International Conference on Inhaled Particles in London in September 1970, and the similarity of their findings, considering their varied methodology, was quite remarkable (1, 2). While the British use gravimetric sampling to measure respirable dust concentrations, the Germans use the Tyndalloscope. Despite this and other differences, the projected attack rates for given concentrations of dust were very similar.

In late 1968, it became apparent that no comparable prospective study was being carried out in the United States, and therefore, the U. S. Public Health Service and Bureau of Mines decided to remedy this deficiency by devising a similar study for coal mines in the United States. The data accumulated by the British and German workers have formed the basis for the permissible dust levels in their respective coal mines. Lacking comparable data here, it was realized that any health standards in the United States would have to be based on work carried out elsewhere.

The National Study of Coal Workers' Pneumoconiosis (Inter-Agency Study) is a joint effort of the Bureau of Mines and the Public Health Service. Over 30 coal mines in various parts of the United States have been selected for inclusion in the study. The criteria for selection were that the mines should have at least 100 miners, that they should have an estimated working life of at least 10, but preferably more years, that they should represent all the geographical areas of the United States in which coal mining remains a major industry, that different seams of coal with differing ranks and mineral content should be included, and finally that the mining methods used in the various mines should be diverse. The mines chosen for inclusion in the study are to be found in the following States: Pennsylvania, West Virginia, Virginia, Alabama, Tennessee, Kentucky, Ohio, Illinois, Indiana, Utah, and Colorado. It is expected that some 7500 to 8000 miners will be included; moreover, it is hoped to extend the study in the future. Up to now some 5000 active coal miners from Pennsylvania and West Virginia have been examined.

All the men employed in the selected mines either have been or will be asked to undergo a medical examination. This consists of a posteroanterior and left lateral chest film and some simple tests of ventilatory capacity. In addition, a questionnaire concerning the presence of cough, sputum, and shortness of breath is administered. A detailed smoking and occupational history is taken. Anthropometric measurements are made, and the subject is then asked to perform three forced vital capacity (FVC) maneuvers. Prior to the measurements being recorded, he is given two trial runs so that he understands what is required. The respiratory maneuvers are recorded as flow volume loops on a recording oscilloscope, and if all three appear satisfactory, they are photographed with a Polaroid camera. From the loop, the FEV_1, $FEV_{0.75}$, FVC, peak flow, and midflow are recorded. From the posteroanterior and lateral film, the total lung capacity (TLC) is measured and the residual volume (RV) is derived by subtracting the FVC from the TLC.

The medical examinations will be repeated at intervals of 5 years except on the first occasion when there will be only a 3-year interval. Comparison of the chest films taken at each examination will allow the Public Health Service to determine radiological progression over this period. In

addition, repetition of the pulmonary function tests will determine the annual decrement in ventilatory capacity over the same period. This can then be related to the presence or absence of pneumoconiosis, to the miner's smoking habits, and to various other factors.

The Bureau of Mines will be responsible for environmental measurements in the selected coal mines. Levels of respirable dust will be determined by several different instruments, including the Mining Research Establishment (MRE) horizontal elutriator and the Atomic Energy Commission (AEC) cyclone (personal sampler). Data will be developed which will permit estimation of the respirable dust exposure of underground workers in terms of milligram-years. A sufficient number of dust samples will be analyzed to estimate the influence of total ash, total combustibles, and total and free silica on the development and progression of pneumoconiosis, and at least 1% of all dust samples obtained from each mine will be subjected to a complete mineralogical analysis. The main purpose of the study will be to relate the radiological progression of the disease to the respirable dust levels that prevailed in the mines over the study period. It is expected that a relationship between the radiological findings and the magnitude of exposure to coal dust will be evident. Nonetheless, the British experience suggests that other factors play a role in the production of the disease, viz. the rank and mineral content of the coal mined, individual susceptibility of the exposed miners, and possibly the silica content of the coal (3). The relative importance of these factors should become more evident as the study progresses. The data accumulated should allow derivation of mathematical equations that predict the likelihood of men developing the various categories of the disease at differing levels of dust exposure for various periods. It is doubtful, however, that any sort of mathematical inferences of this type can be drawn with any certainty until an 8- to 10-year period has elapsed.

Studies of the Pathology and Biochemistry

While it has been known for some time that there is a fairly good correlation between the coal dust content of the lungs and the radiological category, that is to say, the more the dust, the higher the category, much debate is still taking place in regard to the material which is responsible for the radioopaque shadows seen in the chest film. In this context it is important to remember that carbon is nonopaque and does not cast a shadow. The Safety in Mines Research Establishment of Sheffield, England, has been carrying out a correlative study in which postmortem analyses of the lungs for various minerals and other agents, e.g., silica, iron, collagen, and coal are related to the antemortem radiographic appearances (4). They have shown that in addition to the corre-

lation between radiological category and coal-dust content there exists an almost equally good relationship with the total mineral content of the lungs. The same applies to the iron content of the lung. However, the best relationship of all is found when the radiographic category is plotted against a composite scale based on the combined coal, mineral, and iron contents. Rather surprisingly, the Sheffield group has shown that the coal content of the lung in progressive massive fibrosis is of the same order as that found in categories-1 and -2 simple CWP.

No explanation is available for the different sized opacities (pinhead or *p*, micronodular or *m*, and nodular or *n*) that may be found in films of subjects with simple pneumoconiosis with the exception of the nodular (*n*) variety. The latter are sometimes related to the presence of rheumatoid factor in the serum, and many of these subjects have a variant of Caplan's syndrome. It is possible that the type of opacity found in the chest film varies with the coal, mineral, and iron content of the lungs, and needless to say, this is worth further consideration.

It is becoming apparent that there seem to be certain distinctive physiological abnormalities associated with the different types of opacity. Thus Lyons and his colleagues have reported that the pinhead type of opacity tends to be associated with a lower diffusing capacity (5). These findings have been confirmed in the Appalachian Laboratory for Occupational Respiratory Diseases (ALFORD). In addition, a few subjects with the pinhead opacity have been found to have mild pulmonary hypertension in the absence of any cause for it other than simple pneumoconiosis. There is a great need for studies designed to correlate changes in the various physiological indices with varying types of pulmonary opacity seen on the chest film. The reasons why irregular opacities predominate in certain films and why other films show only rounded regular opacities remain a mystery. It seems possible that the extent of focal emphysema or fibrosis may vary with the type of small opacity present in the lungs. Work along these lines is presently being carried on in ALFORD.

The pathological features of CWP are fairly well recognized, and the main argument today centers around the specificity of the bronchiolar dilatation or focal emphysema that is found in the center of the coal macule. This type of emphysema has been described in urban dwellers and is claimed by both Lynne Reid and Heard not to be specific for CWP. The other features of the coal macule seem to be well accepted, and most pathologists maintain that the pathology of CWP is the same the world over and that it is impossible to differentiate pathologically the lesion found in soft-coal workers from that found in anthracite miners, provided the latter have not developed classical silicosis from exposure to coal mine dust with a high silica content. When the quartz content of

the total lung dust exceeds 18%, then the microscopic appearances are those of silicosis and not CWP. Yet despite the common histological features, epidemiological studies have shown wide regional differences in the prevalence of simple and complicated pneumoconiosis. Moreover, Heppleston has shown that dusts which have identical size and surface characteristics but are prepared from coals of different rank are treated differently in the lungs (6). There is a need for studies in which the deposition and clearance of various types of coal are characterized. In addition, the effects on biological systems of coal and other dusts that produce pneumoconiosis need to be studied. This can be best achieved by studying the action of the various dusts on tissue cultures of cells found in the lungs, e.g., macrophages and fibroblasts.

Many pneumoconioses are associated with changes in the laying down of the fibrous proteins of the lungs, viz. collagen, elastin, and reticulin. The factors governing the disposition of these proteins in the lungs of subjects with pneumoconiosis have barely been considered, and a fertile field exists for the interested biochemist. In this connection, the pathogenesis of progressive massive fibrosis still remains a matter of speculation despite the several theories put forward to explain its development. It is not known whether the disease is a single entity, and the recent demonstration that some subjects with PMF have rheumatoid factor in their serum and histological evidence of vasculitis in the conglomerate lesion raises the possibility that these subjects have an autoimmune process. Further evidence in favor of this hypothesis is the demonstration of lung autoantibodies in the serum of many of these subjects.

There is little doubt that the pathological process that leads to PMF starts long before the "one-centimeter" opacity becomes evident on the chest film. Attempts should be made to detect the lesion before it is evident on the chest film as a one-centimeter shadow. Were it possible to study the very early lesions by means of light and electron microscopy, some clues in regard to the pathogenesis of the condition might be found.

The factors that determine whether or not PMF progresses are of paramount importance, yet are completely unknown. The vast majority of subjects who develop PMF have small lesions which grow exceedingly slowly. In many instances, the lesion reaches a limited size and remains unchanged thereafter. A detailed study of the immunology and immunochemistry of subjects with PMF is likely to be rewarding in this regard.

Physiological Studies

The numerous epidemiological studies performed on coal miners have mostly relied on simple screening tests of pulmonary function, such as

the forced expiratory volume in 1 second (FEV_1), or some other test derived from a forced vital capacity maneuver. While the normal inclination of the epidemiologist is to study large numbers of subjects inadequately, the physiologist studies a few subjects—usually the wrong ones—in meticulous detail. Somewhere between lies a happy medium which is hopefully represented by some of the current studies taking place in ALFORD.

Studies of Ventilation and Pulmonary Mechanics

It is commonly accepted that miners as a whole have a lower ventilatory capacity than do nonminers. The cause of this reduction remains a matter of speculation, however. Several hypotheses have been put forward to explain it. First, it has been suggested that the inhalation of dust by itself produces a form of chronic obstructive airway disease, and indeed there is some evidence that this is so. Nonetheless, the effects of cigarette smoking so outweigh all other factors in the production of bronchitis that confirmation of this theory is difficult. This problem can be approached by comparing the annual decrement in pulmonary function in nonsmoking miners with a similar group of nonminers. Another possible explanation for the low FEV_1 is related to coal miners having smoking habits different from the general male population. The miner smokes slightly fewer cigarettes than does his nonminer counterpart; however, he manages to do so in half the time since he is unable to smoke while underground. It is conceivable that the more intense insult is responsible. A third possible explanation is that of differential migration. Were the more fit miners more prone to leave the occupation of coal mining, then those who remain would be less fit and would probably have a lower ventilatory capacity and more symptoms. Finally, the possibility exists that the coal macule itself is responsible for the effect. The radiological appearance of CWP depends on the superimposition of numerous macules upon each other; yet it must be remembered that macroscopic macules are present in the lungs some time before they become radiologically evident. Relevant in this connection is the fact that airway resistance may be partitioned into central and peripheral components and that most of the resistance is to be found in the larger airways, the smaller airways being responsible for less than 20%. Yet the coal macule is peripherally situated and thus can only affect flow in the peripheral airways. It is, therefore, apparent that were 50% or even more of the distal airways obstructed, the total airway resistance would not be appreciably affected, and this would probably not be detected on con-

ventional spirometry. The distensibility of the lung would, nevertheless, be changed to such an extent that the subject might well be short of breath. The resistance to flow in the peripheral airways can be studied by means of the expiratory flow volume loop and also by determination of the pulmonary compliance at different frequencies. Some indication of changes in the peripheral resistance also might be detected from a study of the full curve of airway resistance plotted against volume of thoracic gas. Finally there is a need for studies of static pressure volume curves of the coal miners' lungs to determine the possible presence of early lung destruction. All these studies are currently underway at ALFORD.

Studies of Gas Transfer and Diffusion

The reduced diffusing capacity found in United States coal miners with the pinhead type of simple pneumoconiosis has been mentioned elsewhere. There seems little doubt that this is a valid observation since the British and the Belgians have reported similar findings. This finding needs to be supplemented by further studies of oxygen and carbon dioxide exchange, especially during exercise, and the latter should be related to the presence of pulmonary disability. Additional studies of the pulmonary circulation are recommended in order to evaluate possible changes in the pulmonary capillary bed. These can be best effected by perfusion scans with radioactive iodinated human serum albumin. Radioactive xenon offers a sophisticated, but as yet unutilized approach to the investigation of ventilation perfusion abnormalities found in coal workers' pneumoconiosis.

REFERENCES

1. Jacobsen, M., *et al.* (in press). Proceedings of the 3rd International Symposium on Inhaled Particles, London, 1970.
2. Reisner, M. T. R. (1970). "Relationship between pneumoconiosis and dust exposure in British coal mines," presented at the Third International Symposium on Inhaled Particles, London.
3. Jacobsen, M., *et al.* (1970). *Nature* **227**, 445.
4. Rossiter, C. E., *et al.* (1967). Dust Content, Radiology, and Pathology in Simple Pneumoconiosis of Coalworkers *in* "Inhaled Particles and Vapours II," p. 419. Pergamon, New York.
5. Lyons, J. P., *et al.* (1967). *Brit. Med. J.* **4**, 772.
6. Heppelston, A. G. (1970). "Effects of duration and intermittency of exposure on the disposal of high and low rank coal in SPF rats," presented at the Third International Symposium on Inhaled Particles, London.

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Edited by MARCUS M. KEY

DIRECTOR
BUREAU OF OCCUPATIONAL SAFETY AND HEALTH
U. S. DEPARTMENT OF HEALTH, EDUCATION AND WELFARE
ROCKVILLE, MARYLAND

LORIN E. KERR

DIRECTOR
DEPARTMENT OF OCCUPATIONAL HEALTH
UNITED MINE WORKERS OF AMERICA
WASHINGTON, D. C.

MERLE BUNDY

MEDICAL DIRECTOR
U. S. STEEL CORPORATION
PITTSBURGH, PENNSYLVANIA

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