RADIOLOGY

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BASIC CONCEPTS IN RADIOLOGY

Historical Background

In 1895, when Roentgen discovered the x-ray, there followed a burst of scientific activity never before equaled. In medicine, the potential of this new form of radiation was recognized at once, and before the turn of the century, x-ray equipment was in active clinical use in every corner of the civilized world.

From these early times, the growth of medical radiology has been remarkable. The excitement that accompanied Roentgen's discovery has continued undiminished ever since. New techniques and methods employing x-rays have followed one another in rapid succession; today radiology finds itself at the center of clinical medicine.

The universal enthusiasm with which radiological methods have been accepted in medicine stems largely from the wealth of diagnostic information these methods provide. Nowhere is this more evident than in radiography of the chest where the information is of such fundamental importance that the chest radiograph has become an essential element in the clinical investigation of almost every patient and an epidemiological tool of great value in the study of dust-related occupational disease.

Properties of X-rays

In many respects, x-rays are similar to light. They travel in straight lines with a speed of 300,000 km per second. They blacken photographic film and cause certain crystalline materials to fluoresce. They tend to scatter when interacting with matter. They are composed of myriads of discrete bundles of energy, called photons. However, unlike light, whose photons contain only a small amount of energy (a few electron-volts), x-rays are very energetic (tens of thousands of electron-volts per photon). This difference causes x-rays to exhibit a number of distinct properties.

X-rays have the ability to penetrate matter, the fraction of radiation either transmitted or absorbed by an object being dependent on (a) the object's density and thickness, (b) the object's elemental composition, and (c) the radiation's energy. This differential transmission and absorption of x-rays causes them, after passing through an object, to bear an image of the object's internal structure. Such an image can be converted to a visible image by means of an appropriate photographic film or fluorescent screen.

Radiation Hazards

In the beginning, the hazards of excessive x-ray exposure were not known. Although a few reports of x-ray "burns" began to appear in the medical literature as early as 1896, the first radiologists took few precautions to protect themselves from exposure to this new form of radiation. On the contrary, many of these pioneers fluoroscoped their hands each day to test their apparatus before their first patients were examined. It did not occur to them that such a practice might be unwise. Soon, the hands of these physicians became inflamed and underwent changes that often degenerated into skin cancer.

From these experiences, it was quickly realized that large exposures to ionizing radiation can be harmful and that radiologists should take measures to protect themselves from unnecessary exposure. Appropriate means were quickly developed and implemented and, for a while at least, the problems associated with excessive radiation exposure were resolved and concern for them faded.

A few decades later, Muller reported that even small doses of ionizing radiation produced

genetic aberrations within the progeny of irradiated species of fruit flies. Moreover, the changes seemed to be linearly related to radiation dose; were cumulative; and were not reversible (14).

Muller's work went largely unnoticed until shortly before World War II when scientists associated with American atomic energy research began to worry about the genetic effects of ionizing radiation received by large population groups. At the same time, interest in the somatic effects of ionizing radiation, including the development of malignant disease, was rekindled. Since then, studies of Japanese nuclear bombing survivors and of various clinical groups exposed during multiple x-ray procedures have added greatly to our knowledge of the small-dose effects of ionizing radiation.

In chest x-ray examinations, radiation hazards are fortunately small. With respect to possible genetic damage, the amount of radiation reaching the testes in men and the ovaries in women is vanishingly minute as long as examinations are carried out with the x-ray beam limited to the thorax (chest) by collimation. Collimation is widely used in practice today and is a requirement of all NIOSH providers.

With respect to possible somatic damage, chest x-ray examinations deliver relatively small doses of ionizing radiation to the thorax due to the low density of the air-containing pulmonary tissues. As a consequence, approximately 20 posteroanterior radiographs of the chest may be performed on an individual in a given year, with the delivery of a mean radiation dose to the intrathoracic tissues no greater than that received annually from natural background sources at sea level. Although unnecessary radiation is something to be avoided at all times, present knowledge indicates that radiological examinations of the chest, judiciously planned and executed, do not constitute a significant hazard to health.

TECHNICAL ASPECTS OF RADIOGRAPHY

The Formation of Radiographic Images

X-ray Production

X-rays are produced whenever electrons impinge on matter at high velocity. To take advantage of this phenomenon, an x-ray tube consists of an evacuated glass envelope in which are mounted a source of electrons and a metallic target on which the electrons can be projected. Conventionally, the electron source is a filamentary wire which, when electrically heated to incandescence, emits electrons into the surrounding vacuum. These electrons are attracted to the target and x-rays are generated when a high electrical potential (several kilovolts), positive in polarity, is applied to the target.

In radiography of the chest, x-ray tubes must be operated at very high capacity. This is to assure that exposure times will be sufficiently short (e.g., 1/60 sec.) to avoid blurring of the radiographic images from heart motion. This requirement creates serious problems for the x-ray design engineer because x-ray production is a relatively inefficient process. Only a small fraction of the electronic energy developed in an x-ray tube is converted to x-radiation. The remaining energy is converted to heat, and when a tube is operated at high capacity, means of dissipating this heat must be provided before damage to the tube occurs. The problem is made particularly difficult by the fact that the tube's electrons must be focused on a very small area of the target (e.g., 1.5 mm sq. or less) if the radiographic images of all structures, both moving and stationary, are to be clear and sharp.

Because of these considerations, the targets of today's x-ray tubes are made of tungsten, a metal that is not only a relatively efficient x-ray emitter but a metal that has a high melting point. Moreover, the tungsten is arranged in the form of a disc which rotates in front of the electron source in a manner such that electrons fall successively on different areas of the disc during x-ray emission. Heat is thereby distributed over a large area of the target while x-ray emission appears to occur from a fixed locus. By these provisions, x-ray tubes with small focal spots can be operated at high capacity to yield x-ray images of excellent quality even in the presence of vigorous heart motion.

X-rays are emitted in all directions when electrons impinge on the target of an x-ray tube. For this reason, it is necessary to encase such tubes in leaded enclosures which prevent the escape of radiation except that coming through a small opening in the enclosure located close to the tube's target. This emerging radiation is further restricted by appropriate collimating devices—external to the tube—that prevent anatomical structures, other than those under exami-

nation, being irradiated. Moreover, aluminum filters, 2 mm to 3 mm in thickness, and placed directly in the emerging x-ray beam, remove components of the radiation which do not contribute significantly to the formation of x-ray images but which otherwise would add to the radiation dose received by the subject under examination.

Image Formation

Although x-rays have the ability to penetrate matter, only a fraction of the radiation falling on an object emerges from the opposite side. The remaining radiation is either absorbed in or scattered by the object. The fractions of radiation transmitted, absorbed, or scattered by an object (such as an anatomical structure) depend on the density and thickness of the structure its elemental composition, and the energy of the photons comprising the x-ray beam. Consequently, the x-rays transmitted by an object bear an image of the object's internal components.

For example, when x-rays are projected through a person's chest, the amount transmitted in the regions of the lungs is relatively large, because only small fractions of the incident radiation are absorbed or scattered by the air-containing pulmonary tissues. On the other hand, the amount of radiation transmitted in the region of the heart is relatively small, because the heart and its contents are quite dense. The radiation transmitted by the ribs is smaller still, because ribs contain calcium salts which absorb incident radiation to a much greater degree than the surrounding tissues, despite their short path length.

If the radiation transmitted by the chest falls on a photographic film, a visible image is created when the film is processed, with the areas of the film under the lungs being relatively dark and the area under the heart much lighter. Images of ribs superimposed upon the lung fields and heart are comparatively lighter still.

In addition to gross outlines of the lungs, heart, and ribs, fine detail within these structures can also be recorded if the x-ray tube has a small target area from which x-rays are emitted (i.e., a small focal spot); is operated with a short exposure time; and is placed a long distance (e.g., six feet) from the patient and film. Under these circumstances, images of the lungs' branching blood vessels can be recorded, appearing as relatively light structural patterns against the dark background of the air-filled pulmonary tissues.

No images of the peripheral bronchi or of their branches are seen under normal circumstances. Because these structures are air-containing, they transmit the same amount of x-rays as the lungs' air sacs; hence, no images of them are produced. However, if the air sacs contain fluid (as in pneumonia), and consequently become dense, the air-containing bronchi then create images that stand out in sharp contrast to those of the surrounding air-filled lung.

Recording Media

Photographic films, including those developed specifically for the recording of x-ray images, absorb very little of the x-radiation projected on them (about 2%). Consequently, large amounts of radiation are needed to produce satisfactory radiographic images unless some means is provided to make greater use of the available x-ray energy. Intensifying screens constitute just such a means. They are thin, yet rigid, sheets of radiolucent material, the size of an x-ray film, which are coated with a thin layer of fluorescent material composed of heavy-element crystalline salts whose x-ray absorption is relatively high (30% or more).

X-ray film, unlike conventional photographic film, is coated on both sides. Intensifying screens are normally produced in pairs, with one screen placed in apposition to the front surface of an x-ray film and the other in apposition to the film's rear surface. This duplication of screens increases the efficiency of x-ray capture. When exposed to x-rays, the intensifying screens fluoresce, converting the absorbed x-rays to light. The light then exposes the film.

A wide variety of films and intensifying screens are available to the radiologist. These range in sensitivity or speed from very slow, which require the delivery of a relatively large radiation dose to a patient, to very fast, requiring the delivery of a relatively small dose. In general, a film-screen combination's resolution (i.e., ability to record fine detail) varies inversely with its sensitivity or speed. In chest radiography, particularly when pneumoconiosis is a possible diagnosis, it is usually advisable to employ medium-speed films and screens. Such a combination should record the images of small pneumoconiotic lesions with sufficient detail to assure their easy recognition and yet not cause the de-

Table I-54

REPRESENTATIVE FILM-SCREEN COMBINATIONS OF THE MID-SPEED CLASS, SUITABLE FOR RADIOGRAPHY OF THE CHEST

Film	Screens	Rel. Speed#	QMI*
Class A	DuPont Par Speed	0.40	2.8
Class A	G.E. Blue Max I	1.00	4.2
Class A	Kodak X-Omatic Reg.	0.80	4.2
Class A	USR Rarex BG Detail	0.50	2.7
Class B	DuPont Par Speed	0.80	3.9
Class B	G.E. Blue Max I	2.00	6.0
Class B	Kodak X-Omatic Reg.	1.60	4.6
Class B	USR Rarex BG Detail	1.00	3.8
Class C	Kodak Lanex Fine	1.00	5.5
Class C	3_M Alpha—4	1.50	4.9
Class D	Kodak Lanex Fine	1.30	6.3
Class D	3_M Alpha—4	2.00	5.7

*Quantum Mottle Index, a measure of film granularity due to the discreet nature of x-ray photons.
Class A Films:—DuPont Cronex 7, Kodak XG
Class B Films:—DuPont Cronex 4, DuPont Cronex 6+, Kodak XRP and 3M, Type R
Class C Film:—Kodak Ortho G
Class D Film:—3M, Type XD

#Measured as the reciprocal of the radiation exposure in milliroentgens required to produce an optical density of 1.0 in the processed film.

livery of large radiation doses to patients.

Table I-54 lists a number of film-screen combinations of the mid-speed class that are suitable for chest radiography (15). Many physicians and technologists prefer combinations using class A and class B films because of the greater number from which to choose. Moreover, these films are sensitive only to blue light, in contrast to the green-sensitive class C and D films. Darkroom fogging tends to be encountered less frequently with such films.

Table I-55 lists the gradient and latitude characteristics of the films included in Table I-54. The gradient of a film is a measure of its contrast-recording ability. Latitude is a measure of the extent to which technical errors of exposure may be made without causing deterioration of image quality. These two parameters vary inversely with one another, i.e., films with high gradients generally exhibit less latitude than those with low gradients and vice versa.

Table I-56 lists resolution and absorption characteristics of the intensifying screens included in Table I-54. Resolution is a measure of a screen's ability to record detail; absorption a measure of the amount of radiation available for image production. It is wise to use screens with a high percentage absorption, so long as resolution is not sacrificed, because the radiation dose delivered to a subject during radiography is inversely related to the amount of radiation absorbed by the intensifying screens.

Generally speaking, it is desirable to use

Table I-55

CHARACTERISTICS OF REPRESENTATIVE FILMS OF THE MID-SPEED CLASS

Film	Gradient	Latitude
DuPont Cronex 4	3.0	0.58
DuPont Cronex 6+	2.6	0.67
DuPont Cronex 7	3.0	0.58
Kodak XG	3.0	0.58
Kodak XRP	2.8	0.62
Kodak Ortho G*	2.4	0.73
3M Type R	2.4	0.73
#M Type XD*	2.9	0.50

*Green sensitive, for use with green emitting screens.

Table I-56
CHARACTERISTICS OF REPRESENTATIVE INTENSIFYING SCREENS OF THE MID-SPEED CLASS

Screens	Rel. Resolution	% Absorption
DuPont Par Speed	1.4	21
GE Blue Max I*	1.5	32
Kodak Lanex Fine* +	2.1	34
Kodak X-Omatic Reg.	1.5	37
3M Alpha—4* +	1.7	42
USR Rarex BG Detail*	1.4	34

*Rare earth screens; + green emitting screens.
**These values apply to conditions in which an 80 kVp x-ray filtered with 3.5 cm Al, is used.

film-screen combinations with relative speeds ranging from 1.0 to 2.0, with quantum mottle indices of 5.0 or less and with screen absorption values of 30% of more. Under these conditions, the clarity of recorded images should be excellent and subject exposure small.

Image Quality

Image quality is the attribute of a radiographic film denoting the clarity with which recorded images are perceived, and hence, is as much an attribute of the observer as of the roentgenogram. Image quality is governed by a large number of factors, including characteristics of the structure under examination, a number of physical factors associated with the exposure, processing and visualization of the radiographic film, and the educational background and psychological state of the observer. Although many of these factors can be measured objectively, image quality is a parameter amenable only to subjective measurement due to the psychological element involved in its evaluation. Hence, the image quality of a particular radiograph may be perceived quite differently from one observer to another. This obviously creates problems for the technologist who serves a group of physicians, or who makes films that may be reviewed by a number of observers. Frequently, a film is judged acceptable by one physician, only to be rejected as unreadable by another. Image quality appears to bear a strong, inverse relationship to the interpretive difficulty a physician experiences with pathological changes recorded in a film. Often, films of excellent quality on purely technical grounds are rejected as "unreadable" when they contain patterns difficult to evaluate clinically.

So image quality is a parameter of enormous complexity. The more important aspects of the way radiographic technique can be used to enhance the quality of images seen in chest radiography follow:

Image Detail and Contrast

Two of the principal factors controlling image quality are the detail and contrast with which images are recorded. For purposes of this discussion, image detail is defined as the minimum limit of image size perceptible in a film. For radiographic films made with medium-speed intensifying screens, this limit is a diameter of 0.1 to 0.2 mm *when the images are of high contrast,* and when films are made under ideal technical conditions. Image detail is considerably poorer when images are blurred by movement of anatomical structures under examination, or by the use of an x-ray tube whose focal spot is excessively large. Image blurring and degradation also occur if the intensifying screens of a film-screen combination are not in uniformly firm contact with the film.

Image detail is also affected by image contrast, decreasing as contrast diminishes. In radiography, it is convenient to recognize two types of contrast: specific and gross. Specific image contrast is the difference between the blackness or optical density of the image of a given anatomical structure (or lesion) and the blackness or optical density of the immediate surrounding field. Gross image contrast, on the other hand, is the difference between the blackness or optical density of the darkest image of diagnostic interest in a film and the blackness or optical density of the lightest image of diagnostic interest.

Parenthetically, optical density is a quantitative measure of a film's blackness. Specifically, optical density at a given point in a film is the negative logarithm of the film's fractional light transmission. For example, a film which transmits one-tenth of the light incident on it has an optical density of 1.0; a film which transmits one-hundredth of the light has an optical density of 2.0.

Radiographic Exposure and Film Density

A radiographic film's blackness or optical density is a function of the x-ray exposure received by the film, rising from a value of zero, when no exposure is given, to values in excess of 3.0, when exposures are large (see Figure

I-15). This entire range of blackness or optical density, however, is not useful for clinical radiographic purposes. For example, if film receives an exposure (with characteristics shown in Figure I-15) of 1 mR directly under a subject's pneumoconiotic lesion, and the exposure received by the film from the region immediately adjacent to the lesion is 25% greater or 1.25 mR, the contrast between the lesion's recorded image and its surrounding field will be 0.3 units of optical density (Figure I-16). If the film under the lesion receives an exposure of 0.4 mR, the surrounding field receives 25% more or 0.5 mR. The contrast of the lesion's image under these circumstances will only be 0.15 units of optical density, due to the shallowness of the film's density vs log exposure curve at low exposure levels (Figure I-17). This loss of contrast is detrimental to image clarity and should be avoided. In practice, image contrast is usually judged unacceptable when a film's optical density is less than 0.2.

If the film under the lesion receives an exposure of 2.5 mR and the surrounding area 25% more or 3.125 mR, the image contrast will now be 0.275 units of optical density or closely the same as that when the exposure was 1 mR (Figure I-17). Under these circumstances, one might assume image clarity to be good. Such, however, is not the case under conventional viewing conditions. As images become darker, an observer's contrast discrimination diminishes noticeably. Moreover, even though the image contrast recorded by a film is good when the film's optical density is 1.7 or 1.8 and greater, the radiographic images are so dark that ambient light in the viewing room entering the observer's eyes and diffused by particulate material in the eyes, fogs the visual images and reduces their contrast to unacceptable levels. Ambient light in the viewing area should be maintained as low as possible. Otherwise, image contrast at the retina may fall to unacceptable levels at optical densities well below 1.8.

Useful Range of Optical Density

The useful range of film blackness for radiographic purposes extends from an optical density of about 0.2 at its lower limit to a density of 1.8 at its upper limit.* Such a range would be adequate for all radiographic purposes if, in practice, physicians were interested only in seeing images of simple anatomical structures, recorded one at a time. Under these circumstances, technologists would merely expose film to a point where a desired image produced (in the processed film) a density somewhere in the middle of the useful range and a good film would *a priori* be produced.

However, the chest is not a simple structure. It is extremely complex, and its radiographic images must be recorded all at once. Moreover, these images produce optical densities within the film that extend through wide limits. Hence, depending on what structures a physician wishes to see, a film's useful density range is often more than filled. For example, some physicians feel it would be desirable if, on a single film, one could record with excellent detail and contrast the images of the peripheral lung fields, the hilar blood vessels and lymph nodes, the heart and other mediastinal tissues, all of the osseous structures of the thorax and more. Unfortunately, this ideal cannot be reached because it is impossible to crowd images of all of these structures into the limited range of optical density available, and still retain levels of image contrast sufficiently high to permit these images to be seen well. Physicians must be satisfied with much less, and most find it acceptable if only images of the lung fields and hilar regions are included within the useful range of film density.

Because image contrast and clarity are closely related, it is generally important that as much of a film's useful range of optical density as possible be filled by images of diagnostic interest. Under these circumstances, both specific and gross image contrast levels approach their maxima. However, when the useful range is fully occupied, the technologist is left with little latitude in estimating the proper exposures to be given when radiographic films are made. Small errors of over- or underexposure will yield unacceptable films. Therefore, it is usually wise to limit gross image contrast to a level moderately below its maximum (i.e., moderately less than 1.6 units of optical density). Figure I-18 illustrates the amount of latitude available to the technologist when the gross image contrast is 1.2 units of optical density. Even under these conditions, the technologist has relatively little latitude for error.

*Useful information is also recorded above a density of 1.8 and can be recovered with the use of a high intensity illuminator. However, this procedure is impractical when dealing with large numbers of films as in the interpretation of pneumoconiosis radiographs.

Scattered Radiation Effects

Under some circumstances, optical densities of images of diagnostic interest fall far short of filling the useful range of film density, due to the presence of one or more factors impairing image contrast. The most serious of these is scattered radiation which, when excessive, fogs the film and sharply impairs image quality.

Scattered radiation increases rapidly as patient size and thickness increase. To a lesser extent, scattered radiation levels become greater when the electrical potential (kilovoltage) of the x-ray tube is raised.

The amount of scattered radiation reaching a radiographic film can usually be reduced to acceptable levels by the use of a grid—a device composed of alternating sections of radioluscent and radiopaque materials—which attenuates the scattered radiation while allowing image-bearing x-rays to pass through. Scattered radiation can also be reduced by increasing the distance between patient and film, but this can cause loss of image detail and a disproportionate increase in the radiation exposure of the patient.

High Kilovoltage Techniques

In recent years, the electrical potentials or kilovoltages applied to x-ray tubes during chest radiography have been raised substantially to improve the image quality of pulmonary and other nonosseous structures. By the use of potentials of 300 kVp and more, in contrast to conventional voltages of 80 to 125 kVp, x-ray absorption of the ribs is sufficiently reduced, and the tendency of these structures to obscure underlying pulmonary tissues is almost wholly alleviated. This trend may be expected to continue.

Miscellaneous Factors Affecting Image Quality (also, see Table I-57)

This discussion of the technical aspects of chest radiography would be incomplete without mentioning the importance of a number of tech-

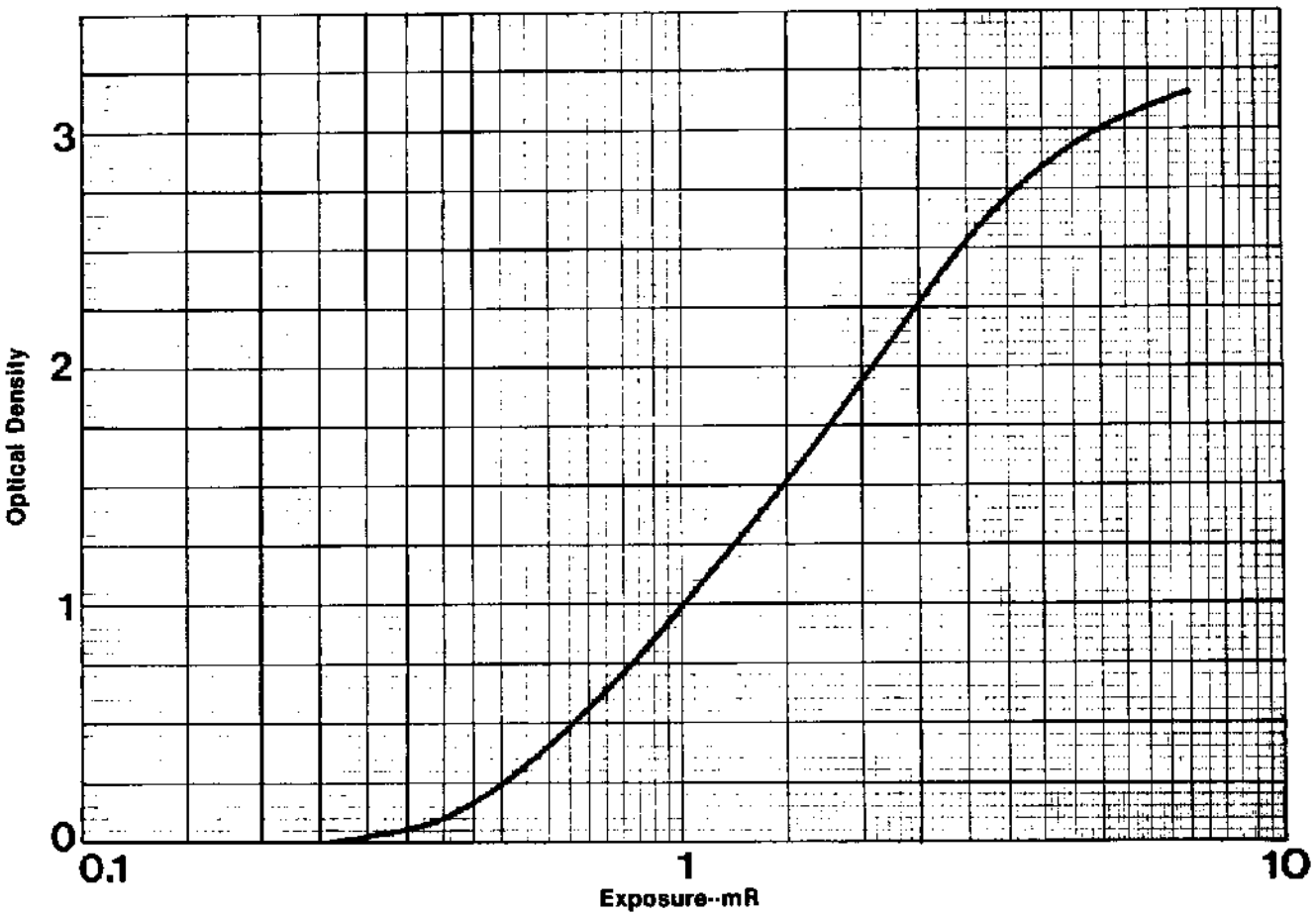

Figure I-15. Relationship between the exposure received by a typical film-screen combination and the optical density or blackness of the processed film.

Table I-57

CRITERIA FOR EXCELLENCE OF TECHNICAL QUALITY IN CHEST RADIOGRAPHS

The following rules may be helpful to those seeking technical excellence in radiography of the chest:

A. Optical Density

1. Hilar regions should exhibit a minimum of 0.2 units of optical density above fog.
2. Parenchymal regions should exhibit a maximum of 1.8 units of optical density above fog.

B. Gross Image Contrast

The difference in optical density between the darkest segment of the lung parenchyma and the lightest portions of the hilar region should fall within a range of 1.0 and 1.4 units of optical density.

C. X-ray Tube Potentials and Use of Grids

1. Potentials of 70 to 100 kVp: Use grid for all subjects whose posteroanterior dimension exceeds 22 cm.
2. Potentials over 100 kVp: Use grid for all subjects.

D. Exposure time: Not greater than 0.1 sec., and preferably 0.05 seconds or less.

E. Film-Screen Combination: Use medium-speed films and screens to assure adequate image detail. Good screen-film contact is essential; periodic testing mandatory.

F. Processing: Maintain strength and temperature of processing chemicals within limits recommended by manufacturer.

G. Assumptions

1. Cleanliness of films and screens and of processing fluids and equipment is maintained.
2. Care in subject positioning is taken.
3. Subject movement is prevented.

nical requirements that must be met for the attainment of optimum image quality. One is the respiratory phase of the patient when a chest radiograph is made. It is essential that the patient be in deep inspiration with respiration arrested. This is to maximize image clarity and contrast and to reduce patient exposure. Films exposed during expiration or shallow inspiration are almost always unacceptable.

Another requirement concerns the position of the patient during exposure. He or she should be upright and placed facing the cassette in such a way that all portions of the lung fields, including the apices of the lungs, the lateral chest walls and the costophrenic angles, are recorded on the film. Moreover, the shoulders must be rotated forward so that the scapulae are moved to the sides and away from positions in which they obscure the lung fields.

Darkroom cleanliness and adherence to strict time-temperature processing is elementary but fundamentally important. All too often radiographic films are spoiled by poor darkroom technique. The repeated films occasioned by such spoilage represent the worst kind of unnecessary radiation exposure; radiation that with disciplined darkroom practices can be avoided entirely.

Major Problems in the Radiographic Technique

Experience gained from the pneumoconiosis programs of the National Institute for Occupational Safety and Health and of the Department of Labor, indicates that the most serious problem found by physicians and their technologists in producing satisfactory films of the chest is the estimation of proper radiographic exposure. There is little room for error when such estimates are made; overexposure or underexposure, with resultant loss of image quality, can easily occur.

The correction of this problem lies in improved training programs for both physicians and technologists. The need for professional ex-

cellence in radiographic technology cannot be overemphasized. Unfortunately, many of radiology's practitioners currently fail to recognize its importance.

Another technical problem, almost as serious as that pertaining to radiographic exposure, is the inadequate control of scattered radiation, particularly in large patients. Since satisfactory methods of control are readily available, this problem's correction seems to be a matter of improved training and supervision of radiographic professionals. When scattered radiation is not controlled properly, image contrast falls quickly to unacceptable levels.

Three other technical problems also reflect inadequate radiographic skills and/or lack of professional discipline and supervision among physicians and their technologists: unsatisfactory patient positioning, failure to correct radiographic cassettes in which there is poor film-screen contact, and failure to maintain minimum standards of cleanliness in the darkroom.

Taken together, these problems cause—in the best of settings—about 10% of chest radiographs to fall below optimal quality standards. In the worst situations, failure rates exceeding 50% are not uncommon.

STANDARDS OF INTERPRETATION AND CLASSIFICATION OF CHEST RADIOGRAPHS IN PNEUMOCONIOSIS

The Radiology of Pneumoconiosis (5)

When dusts containing one or more of the many compounds of silicon are inhaled, pathological changes occur within the lungs and pleural coverings that are detectable radiographically. As the dust particles find their way into the lungs' alveolar sacs, a localized reaction takes place about each particle or group of particles that ultimately leads to the formation of a small fibrous nodule. Such nodules appear in the lung fields of a chest radiograph as small discrete opacities, rounded and/or irregular in shape, a few millimeters in diameter, and distributed widely throughout the lungs.

When dust exposure is limited, the number or profusion of opacities is likely to be small and their distribution localized. However, if the exposure continues, the opacities will increase in number until ultimately, adjacent lesions coalesce to form large opacities several centimeters

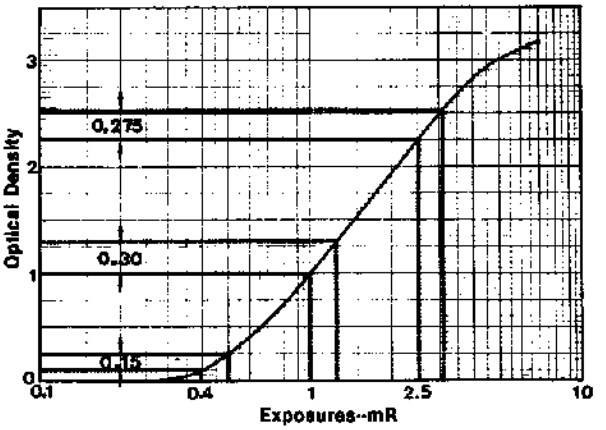

Figure I-16. Illustration of the effect of optical density on the contrast exhibited by an image recorded by a radiographic film.

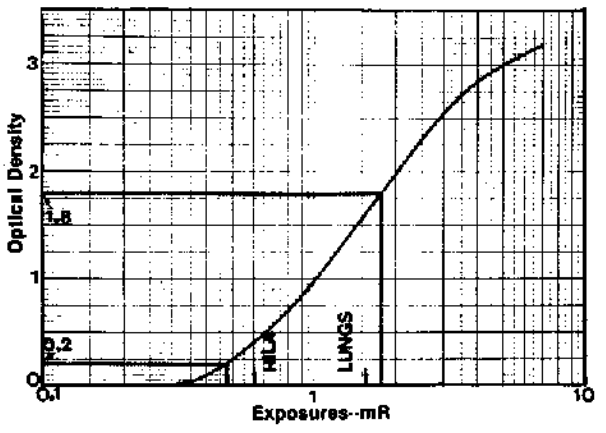

Figure I-17. Graphic illustration of how the latitude of a technologist in estimating the exposure to be given during radiography of the chest diminishes as the useful range of optical density becomes increasingly filled by images of diagnostic interest.

in diameter and often distributed widely throughout the lungs. At this stage, serious lung damage has occurred.

With many silicic materials, such as those encountered in coal mining, radiographic opacities tend to reside in the upper lung fields. In other cases, especially when asbestos fibers are inhaled, changes are more commonly observed in the lung bases and are more irregular or linear in shape. Asbestos fibers tend to migrate to pleural surfaces by way of lymphatic channels to create localized fibrous thickenings of pleural tissues. These lesions characteristically occur

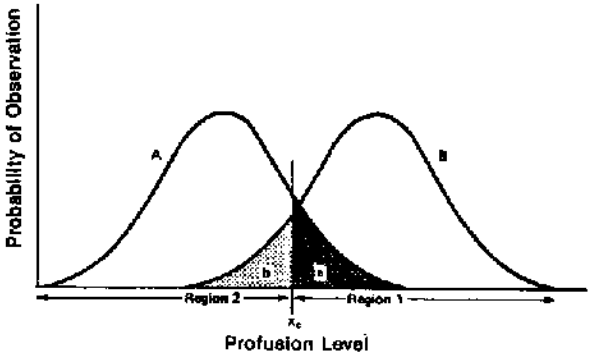

Figure I-18. Representation of the decision problem in pneumoconiosis. Hypothetical population distributions in which the ordinate depicts the probability of one's observing a given profusion level in a population free of pneumoconiosis (curve A) and in a population with pneumoconiosis (curve B).

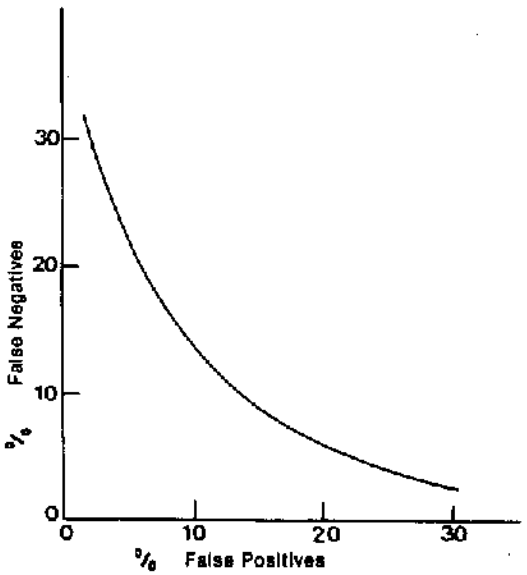

Figure I-19. Curve illustrating reciprocal relationship between percentage false negative and false positive interpretations of chest radiographs for pneumoconiosis (derived from data given in Figure I-18).

along lower chest walls, on diaphragmatic surfaces, and in pleural and pericardial surfaces adjacent to the heart. Frequently, they become calcified.

In advanced cases of pneumoconiosis, there is usually no question, radiographically, regarding the disease's diagnosis. However, when only small opacities are present and their profusion is limited, interpretation can be difficult (12). This is because small opacities can occur in a wide variety of situations, both normal and abnormal, as well as in pneumoconiosis. For example, as individuals become older, periodic respiratory infections often leave them with pulmonary fibrotic changes that appear radiographically as small irregular opacities. These changes are particularly prevalent in cigarette smokers. Also, individuals who suffer from congestive heart disease, in time, develop extensive fibrotic findings in the lungs that may be confused with early stages of pneumoconiosis. Finally, many pathological conditions unrelated to dust (e.g., sarcoidosis) manifest, at various times in their courses, radiographically as small opacities.

So radiographic findings in early pneumoconiosis are not unequivocally interpretative. This has led to the suggestion that chest radiographs always be evaluated with the assistance of the clinical information provided in the patient's history. Superficially, the suggestion appears to have merit. However, it must be recognized that such clinical data usually exhibit as many uncertainties as the radiographic findings. Hence, it is wise in most instances to evaluate history and radiography independently of one another and only afterward bring the two bodies of information together for a clinical judgment. Such a process tends to maximize clinical objectivity and minimize interpretative errors of the history and radiographic information.

Because of the difficulties that exist in the interpretation of chest radiographs, it is not surprising that inconsistencies arise when a number of physicians independently evaluate a series of radiographs or when an individual physician evaluates the series a number of times. Such inconsistency is unavoidable and indeed is characteristic not only of radiographic procedures but all clinical testing (including history taking, physical examinations, and physiological tests) due to uncertainties inherent in all methodologies in which human judgment is a factor (8)(19).

To illustrate graphically the manner in which interfering patterns affect the decision processes and observer error in the interpretation of chest radiographs for pneumoconiosis, consider the profusion of small rounded or irregular opacities (i.e., the number of opacities per cm^2) that might be observed in the films of

a representative sample of individuals who are free of the disease: Curve A, Figure I-18, plotting the number of films prevailing at each profusion level, depicts data that might result from such a study. The profusion of similar opacities in the radiographs of individuals who have pneumoconiosis are greater; the corresponding probability distribution generated by those cases might be characterized by Curve B. The two curves overlap and diagnostic uncertainty will prevail for cases included in the overlapping region. If an interpreter selects a profusion level of x_c as his operating point—separating cases he will call positive for pneumoconiosis from those he will call negative—cases to the right of x_c in region 1 will be called positive for the disease. Of these, the cases under the unshaded portion of Curve B will be correctly diagnosed; i.e., they will be true positives. However, cases included under the shaded portion of Curve A (a) will also be called positive, in spite of the fact that they actually are free of the disease. Such cases will, therefore, be false positives.

Cases to the left of x_c in region 2 will be interpreted as normal. Of these, cases under the unshaded portion of Curve A will be correctly diagnosed as negative, whereas those under the shaded portion of Curve B (b) must represent false negative interpretations, since disease is actually present in these cases.

It will be evident from an examination of Figure I-18 that the percentages of false positive and false negative interpretations will depend upon where the operating point (x_c) is placed. If it is placed to the left of the position shown, the number of false negatives will diminish but at the expense of an increasing number of false positives. If the operating point is moved to the right, the number of false positives will diminish but at the expense of an increasing number of false negatives. The reciprocal relationship between the percentage of false positive and false negative interpretations as one moves the operating point (x_c) along the profusion axis is illustrated graphically in the Figure I-19.

Significant inconsistencies among readers in the radiographic interpretation of pneumoconiosis have been documented (1)(2)(6)(7)(16)(17). Reger found that three American readers who interpreted 498 coal miners' radiographs of profusion according to the UICC Classification agreed as to the major x-ray category on 48% to 71% of the films, while on these same films five British readers agreed on 83% to 90% (3)(16). Felson similarly documented the level of agreement among readers who interpreted the radiographs of 55,730 coal miners examined under the Federal Coal Mine Health and Safety Act of 1969. Felson found the 'A' readers (the first readers to interpret the miner's X-ray) agreed with 'B' readers (members of radiology departments at three hospitals who were experienced at classifying pneumoconiosis) on 41,493 (74.5%) of the 55,730 films interpreted. In both Reger's and Felson's studies approximately 87% to 89% of the films were interpreted as normal.

Inconsistencies in radiographic interpretation can probably be reduced by multiple readings carried out independently by a number of physicians with results examined for consensus (18). Inconsistency can also be minimized by training programs in which physicians are taught to recognize subtle differences between normal and abnormal radiographs. Finally, it is important that physicians responsible for interpreting chest radiographs in national pneumoconiosis programs have opportunities to apply their knowledge sufficiently often to maintain diagnostic acuity. If these criteria are carefully observed, the chest radiograph can be relied upon to be of great value in the evaluation of individuals suspected of having dust-related disease.

ILO Classification System (9) (11)

In clinical practice, it is customary for physicians reporting radiological findings recorded in chest films to do so in nonquantitative, narrative form. For most clinical purposes this is satisfactory. However, when the information is to be used epidemiologically or to evaluate pulmonary disability in workmen's compensation programs, the reporting must be more quantitative.

The need for this was first recognized officially by the International Conference on Silicosis held in Johannesburg in 1930. Since then, the system devised during that meeting has evolved through a series of revisions until the current system, known as the ILO 1980 International Classification of Radiographs of the Pneumoconioses, was recently adopted by the International Labor Office in Geneva (9). The current system has been designed not only to permit codification of coal workers' pneumoconiosis (CWP) and silicosis but also of asbestosis. Ex-

pansion of the system to include the latter entity occurred in 1967 with the assistance of a subcommittee of the Committee on Asbestos and Cancer of the International Union Against Cancer (UICC), members of the McGill University Asbestos Study, and the panel of Radiology Consultants to the Bureau of Occupational Safety and Health, U.S. Public Health Service (USPHS) meeting in Cincinnati.

The ILO-80 Classification System requires the codification of a chest radiograph according to its pulmonary and pleural findings and to its technical quality. With respect to pulmonary findings, the system divides lung opacities into two categories: small and large with each defined in specific quantitative terms.

Small Opacities

The system requires the recording of data on the following four characteristics: shape, size, profusion, and extent. Two shapes are recognized; small rounded and small irregular. For each shape, opacity size is graded in three categories. For example, rounded opacities are classified according to the approximate diameter of the predominant lesions into:

(p) opacities up to about 1.5 mm in diameter

(q) opacities exceeding 1.5 mm and up to about 3 mm in diameter

(r) opacities exceeding about 3 mm and up to about 10 mm in diameter

Irregular opacities are classified according to the approximate width of the predominant lesions into:

(s) fine linear opacities up to about 1.5 mm width

(t) medium opacities exceeding about 1.5 mm and up to about 3 mm in width

(u) coarse, blotchy opacities exceeding about 3 mm and up to about 10 mm in width

To record shape and size, two letters must be used. If the reader considers that virtually all of the opacities are of one shape and size, this should be noted by recording the appropriate symbol twice, separated by an oblique stroke (e.g., q/q). If, however, another less predominant shape (or size) is observed, this should be recorded as the second letter (e.g., q/t). Hence, q/t would mean that the predominant small opacity is round and of a size q, but that significant numbers of small irregular opacities are present of size t. In this scheme, the recording of no more than two kinds of size and shape is permissible.

The term profusion refers to the concentration or number of small opacities per unit area observed within the lung fields. In early versions of the system, profusion was graded only in four major categories:

Category 0: small opacities are absent or less profuse than Category 1

Category 1: small opacities are present, but few in number; the normal lung markings (i.e., the images of the vascular structures) are usually visible

Category 2: small opacities are numerous; the normal lung markings are partially obscured

Category 3: small opacities are very numerous; normal lung markings are usually totally obscured

In 1968, this codification of small-opacity profusion was modified by the further division of each major category into three minor divisions to provide a 12-point scale or continuum. The current notation designating the several divisions of this scale is as follows:

0/−	0/0	0/1
1/0	1/1	1/2
3/2	3/3	3/+

The first number in each division indicates the major category to which the division belongs; the second number indicates whether the profusion level is judged to be somewhat less than, equal to, or somewhat greater than the profusion level corresponding to the major category indicated. Thus, the notation 2/1 is used to indicate a profusion level that is definitely category 2 but somewhat less than the midpoint of that major category.

Although this 12-point scale of profusion implies a high degree of quantification for the recording of profusion levels, the definition of the major profusion categories on which the scale is based is nonspecific. Hence, when the profusion levels of a series of radiographs are evaluated by a group of physicians, substantial differences of opinion can be expressed.

The problem is particularly bothersome when profusion levels are near the lower end of the scale. This is because films in major category 0

(i.e., profusion categories 0/−, 0/0, and 0/1) are usually regarded as normal or as exhibiting essentially no evidence of pneumoconiosis, whereas films in major category 1 (i.e., profusion categories 1/0, 1/1, and 1/2) are generally regarded as poitive for pneumoconiosis. The radiological findings of pneumoconiosis in its early stages are difficult to differentiate from the findings of normal individuals. Both may have similar small-opacity profusion levels. Physicians generally have difficulty in separating a series of radiographs into normals and abnormals when profusion levels are near the divisions 0/1 and 1/0. A given physician will exhibit some inconsistency in his or her codification of profusion in such instances.

Physicians of limited experience, or physicians who do not have the opportunity to see (in their practices) the range of appearance normal films may exhibit, tend to codify their films into higher profusion levels than those classified by their more experienced colleagues. This circumstance constitutes a serious problem for administrators of workmen's compensation programs because consistency between readers is difficult to obtain when readers of different backgrounds and experience interpret films. It is a problem that can be resolved only by the development of improved training standards for all physicians involved in such programs and by the use of multiple readings to resolve interpretive differences when they occur.

The fourth characteristic of small opacities that must be codified in the ILO-80 Classification System is the spatial distribution of pulmonary disease. To record this parameter, lung fields are divided into six zones, three on each side, corresponding to the upper middle and lower thirds of the lung fields. In reporting the extent of disease, the physician simply checks off the zones affected.

Of the four characteristics of small opacities requiring codification, profusion is the most important for it is the best indicator of the seriousness of any disease that may be present. When profusion levels vary from one portion of the lung fields to another, the category of profusion to be recorded is determined by considering the profusion as a whole, over the affected lung zones. Where there is a marked (three minor categories or more) difference in profusion in different zones, the zone or zones showing the lesser degree of profusion are ignored for the purpose of classifying profusion.

Large Opacities

These lesions are codified in three categories of size:

Category A: a single opacity whose greatest diameter exceeds about 1 cm but is no more than about 5cm, or several opacities, each greater than about 1 cm in diameter, the sum of whose diameters does not exceed about 5 cm.

Category B: one or more opacities larger or more numerous than those in Category A whose combined area does not exceed the equivalent of the right upper zone.

Category C: one or more opacities whose combined area exceeds the equivalent of the right upper zone.

Pleural Thickening

With respect to pleural thickening, the ILO-80 Classification System requires that the site (chest wall, diaphragm, costophrenic angle), width, and extent of the thickening be recorded separately. In the case of site, pleural thickening of the chest wall must be recorded separately for right and left sides.

For pleural thickening observed in profile (edge on), width is measured from the inner border of the chest wall to the inner margin of the parenchymal-pleural boundary seen most sharply. The ILO system recognizes three gradations of width:

a. a maximum width up to about 5 mm

b. a maximum width over about 5 mm and up to about 10mm

c. a maximum width over about 10 mm

The presence of pleural thickening observed face on (en face) is recorded even if it cannot be seen in profile. If pleural thickening is observed face on only, width cannot be measured.

The extent of pleural thickening is defined in terms of its maximum length, whether seen in profile or face on. Three gradations of extent are recognized:

1. total length equivalent to up to one quarter of the projection of the lateral chest wall.

2. total length exceeding one quarter but not one half of the projection of the lateral chest wall.

3. total length exceeding one half of the projection of the lateral chest wall.

With respect to involvement of the diaphragmatic pleura, localized thickening (plaque) is recorded separately as present or absent, and right and/or left. Obliteration of the costophrenic angle is recorded in a similar manner.

When pleural calcification is observed, its site (chest wall, diaphragm, and other locations) and extent are recorded separately for the two sides of the thorax. Three gradations of extent are recognized:

1. a region of calcified pleura with a maximum diameter of up to about 2 cm or a number of such regions, the sum of whose diameters does not exceed about 2 cm.
2. a region of calcified pleura with maximum diameter exceeding about 2 cm and up to about 10 cm, or a number of such regions, the sum of whose maximum diameters falls within this range.
3. a region or number of regions of calcified pleura, the sum of whose maximum diameters exceeds 10 cm.

Obligatory Symbols

The ILO Classification System includes a number of symbols (whose use is obligatory) to permit the recording of important radiographic features (see Table I-58).

Table I-58

OBLIGATORY SYMBOLS

ax	—coalescence of small pneumoconiotic opacities
bu	—bullae
ca	—cancer of lungs or pleura
cn	—calcification in small pneumoconiotic opacities
co	—abnormal cardiac size and/or shape
cp	—cor pulmonale
cv	—cavity
di	—marked distortion of intrathoracic organs
ef	—effusion
em	—definite pulmonary emphysema
es	—eggshell calcification of hilar or mediastinal lymph nodes
fr	—fractured rib(s)
hi	—enlargement of hilar or mediastinal lymph nodes
ho	—honeycomb lung
id	—ill-defined diaphragm
ih	—ill-defined heart outline
kl	—septal (Kerley) lines
od	—other significant abnormality
pi	—pleural thickening in the interlobar fissure or mediastinum
px	—pneumothorax
rh	—rheumatoid pneumoconiosis
tb	—tuberculosis

Technical Quality

The ILO Classification System recognizes four gradations of technical quality as follows:

1. Good
2. Acceptable, with no technical defect likely to impair classification of the radiograph for pneumoniosis
3. Poor, with some technical defect but still acceptable for classification purposes
4. Unacceptable

If the technical quality of a radiograph is not Grade 1, the technical defects should be commented upon.

Standard Radiographs

To enhance consistency in the application of its classification system, the ILO has made available to physicians sets of standard chest radiographs, which illustrate various stages of pneumoconiosis and which have been codified by an international panel of experts. These films provide examples of the classification system and are useful for comparison purposes when a physician examines a series of chest films. The availability of these standard films has been an important contribution to occupational medicine. They may be obtained in the United States at a cost of $275 per set from the International Labour Organization, 1750 New York Avenue, NW., Washington, DC. 20006.

Full size reproductions of pertinent sections of the standard films are illustrated in Figures I-15 through I-19. These examples provide graphic demonstrations of small opacity profusion, size, and shape, and attributes of large opacities and pleural thickening defined in prior sections of this chapter.

TRAINING OF PHYSICIANS AND TECHNOLOGISTS

The usefulness of any medical procedure is markedly dependent upon the skills of the individual performing the technical work involved in the procedure and of the physicians who interpret the procedure's derived information. For that reason, the National Institute for Occupational Safety and Health (NIOSH) has been vitally interested in the training and professional standards of physicians and radiographic technologists who participate in its pneumoconiosis programs. For many years, NIOSH, with the assistance of the American College of Radiology, has provided radiologists, chest physicians, occupational health specialists, and their associated technologists short courses (of several days' duration) designed to improve the skills of these individuals both in producing and classifying chest radiographs. The courses are offered at frequent intervals throughout the United States to enable as many individuals as possible to take them.

Courses designed for physicians have been particularly effective. Over 2,500 doctors in a variety of specialties have attended these courses since their inception in the early 1970's. Those who attend one or more of the courses are designated as "A" readers by NIOSH. All of the physicians who participate in its pneumoconiosis programs are "A" readers.

At about the time its training programs for physicians were begun, NIOSH, as well as the Social Security Administration, began the practice of multiple readings of chest radiographs submitted to them by coal workers seeking benefits under the 1969 Federal Coal Miners Health and Safety Act (PL 91-713). Although this practice has been frequently misunderstood, it was instituted with the single purpose of improving the validity of medical information gained from these radiographs. Physician inconsistency can occur in the interpretation and classification of chest radiographs for pneumoconiosis; one of the methods by which such inconsistency can be reduced is the process of multiple readings of films. It is a meritorious practice: it not only benefits the coal miner by increasing the value of information provided by his chest radiograph, it also protects the public against fraudulent reports of disease that are occasionally submitted for adjudication. For these reasons, the practice of multiple reading has been mandated by NIOSH regulations.

In an effort to assure that readings of coal workers' chest films are performed by physicians having the highest possible credentials, NIOSH, in 1973, contracted the Johns Hopkins School of Medicine to develop an examination the Institute could use to test the proficiency of physicians employing the ILO Classification System. Since that time, the examination has been given to over 200 physicians, about 120 of who have been given passing (i.e., 50 or better) grades (13). Those who have passed are called "B" readers and, unless their skill decays from disuse, collectively constitute a superb resource of established competence, available for the evaluation of the increasing number of chest radiographs of individuals who may have been occupationally exposed to hazardous levels of inorganic dusts.

Periodically, the merits of using properly trained lay persons to classify chest radiographs in accordance with the ILO system are considered. If this were practical, it would reduce the burden on physician manpower and might reduce costs. A number of experiments have been carried out to determine the effectiveness of such readers after an appropriate training period. The results of these tests are encouraging. In a recent experiment in the United Kingdom, a group of lay readers, after a period of one year's training, performed as well as a group of experienced physician cohorts (10).

Although training programs developed to augment physician proficiency in the use of the ILO Classification System have been successful, the same cannot, regretfully, be said of efforts to improve the skills of technologists in producing chest radiographs of consistently high quality. Currently, upward of 10% to 25% of the chest films submitted to the Department of Labor and the Social Security Administration are unreadable for technical reasons and many more are less than satisfactory. This is particularly reprehensible because a high proportion of readable films can be achieved given proper equipment, training, and administrative control.

The problem is not only a matter of technologist skill, but of the supervision technologists receive from physicians for whom they work. Since many physicians, including radiologists, receive little or no training in the technical aspects of radiography, their supervision is often of doubtful value. The problem is particularly serious because the radiographic characteristics

of the human chest are such that a technologist has precious little latitude for error in estimating the proper exposure to be given a particular patient during chest radiography.

Much greater effort must be expended on radiographic technology training, not only for the technologist, but for the radiologist and practicing physician who uses radiographic equipment as well. All government agencies having responsibility for the administration of coal workers' benefits must establish, as rapidly as possible, minimum technical standards for personnel who wish to provide chest radiographs to them. Some years ago, NIOSH developed and implemented the use of a series of standards which have been instrumental in substantially reducing the number of unreadable films submitted to it (less than 1%). Other government agencies, which have not yet established similar standards of acceptability, should do so with all deliberate speed. Without such efforts, and the will to apply them rigorously, coal workers, as well as the taxpaying public, will continue to suffer inconvenience and loss.

OTHER RADIOGRAPHIC TECHNIQUES USEFUL IN THE EVALUATION OF PNEUMOCONIOSIS

Limitations of Conventional Radiographic Methods

Radiographic methods primarily record anatomical structure. With limited exception, they do *not* record function. Information provided by a chest radiograph on lung structure and on pathological changes that may exist within them is more useful than information on how the lungs may be functioning. In short, the chest radiograph is better in evaluating pathological characteristics of disease than in assessing any impairment the disease may have caused.

These limitations of chest radiography in the evaluation of pulmonary impairment are not difficult to understand. In pneumoconiosis, the disease, particularly in its early stages, is frequently confined to small portions of the lungs (e.g., the upper lobes); large segments can be relatively unaffected. Unaffected regions are likely to function reasonably well, and therefore, regardless of how extensive the disease may be in the diseased zone, pulmonary function may not be significantly impaired. On the other hand, there are times when the disease initially involves much of the lung parenchyma with fibrotic changes that may not be impressive radiographically, but because they are so widespread, may impair function and cause disability relatively early.

The physiological limitations of the chest radiograph should in no way deprecate its value —either from a clinical or public health standpoint—in the evaluation of persons suffering from pneumoconiosis. Its objectivity in accurately and reliably assessing the disease's pathological anatomy is unequalled. Often it represents the best data available on the clinical status of a patient.

Other Radiographic Techniques

The simple chest radiograph, taken with the radiation projected through the subject in a posteroranterior direction, is the keystone of all radiographic examinations of the chest. However, there are occasions when a more extensive examination is called for. For instance, pleural thickening can be detected most easily when seen in profile. Therefore, when localized thickenings exist, as is frequently the case in asbestosis, it may be desirable to take oblique and lateral views of the chest in an effort to bring the lesion into profile.

When pneumoconiosis is complicated by coexisting disease, there are additional radiographic measures that may be useful in evaluating the nature and extent of the pathological processes and their relationships. One of these is tomography, a technique in which thin slices of pulmonary tissues are recorded in cross-section or longitudinally. The images may be presented either in conventional or computerized form. When many such films are made, each depicting a different section of the lungs, pulmonary architecture can be displayed in remarkable detail and without the confusing, superimposed patterns of other structures. The technique is particularly valuable when pulmonary cavities and masses are to be evaluated.

Another technique, useful in the evaluation of bronchial disease, is bronchography. In this procedure, radiopaque materials are instilled or blown into the bronchial tree to demonstrate irregularities, dilations, and obstructive lesions of the respiratory system.

Finally, a battery of radiological tests employing radioactive nuclides has been devised in recent years to study vascular problems associ-

ated with the lungs. Some of these show promise in the evaluation of pulmonary function.

All together, radiologic procedures constitute an enormously valuable group of diagnostic tools for use by clinicians and public health physicians when dust-related occupational disease is evaluated. One may expect the number and scope of these techniques to become even greater in the years ahead as medicine profits from this fast-growing science.

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PULMONARY FUNCTION TESTING

Benjamin Burrows

Pulmonary function studies are an essential part of any respiratory evaluation. Capable of detecting abnormalities not evident on chest radiography and not associated with symptoms, lung function tests are relatively objective and provide a quantitative index of impairment. They are invaluable for investigating dose-effect relationships, for studying progression of abnormalities, and for evaluating disability. Some individual lung function studies are specific for particular types of lung alternations and are thereby useful in determining the mechanism of a noxious agent's effect.

Critical to pulmonary function testing is the expertise of the staff administering the tests. The capabilities of the pulmonary function technician can often determine the accuracy of test results. It is also essential that standardized procedures be used and that tests of quality control be included whenever lung function studies are carried out.

CONSIDERATIONS IN THE SELECTION OF TESTS

A large number of lung function tests are available. They measure different aspects of lung function and vary greatly in complexity. Some of the more commonly used tests are listed in Table I-59. Some are readily applicable to epidemiological studies; others are restricted to inlaboratory studies of small groups of selected subjects.

Determining the mechanism of a known noxious agent's action in affected subjects may require pressure-volume curves to assess a loss of lung recoil from emphysema or a decrease in compliance owing to diffuse fibrotic changes. Studies of airways resistance may be needed to determine the extent and localization of airways abnormalities. However, since complete evaluation of lung mechanics requires an esophageal balloon and relatively sophisticated technology, these tests are not applicable to epidemiological investigations.

Arterial blood gas measurements provide less specific information about disease mechanisms but are useful in disability evaluations. Arterial oxygen and carbon dioxide tensions provide important information about the physiological impact of disease. The use of arterial blood gases in epidemiological studies is limited, however, by the wide intrasubject variability of arterial oxygen measurements, as well as by the need for arterial puncture which involves some patient discomfort and a small risk of complication (42).

The Timed Spirogram

The forced expiratory volume in one second (FEV_1) and the forced vital capacity (FVC) are the simplest, most reproducible, and most widely employed lung function tests. They primarily reflect the mechanical function of the lung and have been regarded as essential for all respiratory epidemiological studies (14). To perform these tests, the subject takes a deep inspiration and then exhales as rapidly and completely as possible into a recording device. A "timed spirogram" is thus obtained. It is recommended that at least three technically satisfactory tests be recorded and that the maximum values for FEV_1 and FVC be reported (14). Recently published recommendations in regard to instrumentation and test procedures are summarized in Table I-60 (14)(36). Traditionally, the test has been carried out with a relatively inexpensive, internally calibrated instrument—such as a water-sealed spirometer recording on a simple kymograph. Measurements are then made from the obtained tracings by a technician.

Measurement errors may be eliminated and the procedure simplified by automated analyses (using computer technology). A variety of electronic devices are available which are easier to use and more portable than the traditional water filled spirometer. While automated measure

Table I-59
SUMMARY OF LUNG FUNCTION TESTS

A. Minimal tests, useful for detecting abnormalities in groups or in individuals:
   Timed spirometry with measurement of FVC and FEV_1
   (Measurement of FEF 25-75% optional)

B. Sensitive tests, useful for detecting subtle abnormalities in groups but of questionable significance in individuals:
   1. MEFV curve with measurement of $Vmax_{50\%}$ and $Vmax_{25\%}$
   2. Closing volume test with measurement of CV/VC and Slope III

C. Tests especially useful for detecting diffuse interstitial diseases:
   Single breath diffusing capacity

D. Tests used primarily in disability evaluations:
   1. Arterial blood gases at rest and exercise
   2. Maximum voluntary ventilation

E. Tests which may be useful for determining the nature of a physiological abnormality but not generally recommended for population surveys:
   1. Total lung capacity measurements
   2. Pressure-volume curves with measurements of lung compliance and recoil
   3. Airways resistance measurements
   4. Helium vs. air MEFV curves

F. Tests for determining the degree of airways reactivity:
   1. Methacholine or histamine inhalation challenge
   2. Exercise provocation test

ments and newer recording devices have many desirable features, they do impose the need for careful apparatus calibration. Also, special consideration must be given to determining the onset of the test in a manner analagous to the "back extrapolation method" used in hand calculations (14). Algorithms to accomplish this have been reported both for volume (39) and flow sensitive devices (22).

The FEV_1 and FVC are highly reproducible within individuals; show little variation with time of day or season; and involve relatively little subject cooperation or discomfort (42). Generally, an inadequately performed test is immediately recognized by an experienced technician. A complete study can be performed within five to ten minutes, and tests are readily performed in the field.

As with virtually all lung function tests, there is wide intersubject variability in test results. Much of this is related to the age, sex, and body size of subjects and can be accounted for by prediction formulae. However, even among totally asymptomatic nonsmoking subjects in the general population, obtained data show a standard deviation of approximately 15% around predicted values (22). Also, the FEV_1 and FVC tests may not detect very mild changes in the airways, changes which can be detected by more "sensitive" tests of lung function.

Additional data are available from the maneuver carried out to obtain the FEV_1 and FVC. The average flow over some segment of the forced exhalation (e.g., between exhalation of 25% and 75% of the FVC (FEF 25-75%)) can be measured. It has been claimed that the FEF 25-75% is more sensitive than the FEV_1, but newer data refute this (14). Nevertheless, since determination of the FEF 25-75% requires no additional effort or time on the part of the subject; no additional instrumentation; and little ex-

Table I-60

STANDARDS FOR SPIROMETRIC TESTING

A. ***Instrument***

1. Minimum usable volume 7+ L. (for volume sensitive devices).
2. Must measure volume with an error ±3% of reading or ± 50 ml, whichever is greater.
3. Must be able to accumulate volume for 10+ seconds.*
4. Must produce a graphic record of volume vs. time or of volume vs. flow for the entire forced expiration.
5. Time display must be 2+ cm per second, volume display at least 10 mm per liter, and flow at least 4 mm per L/sec.
6. A volume sensitive device should be equipped with a thermometer.
7. The recorder must have reached calibrated speed by the onset of the forced expiration.

B. ***Test Procedure***

1. Nose clips are needed with closed circuit testing.
2. At least three apparently satisfactory tracings must be obtained and the FVC and FEV_1 of the best two should vary by no more than 5% of reading or 100 ml, whichever is greater.
3. The largest FVC and FEV_1 are reported even if they do not come from the same maneuver.

*This is deemed adequate for field work but not for clinical studies. Clinically ill subjects may not complete their expiration by 10 seconds (14).

tra effort in calculation, the test has been recommended for epidemiological investigations (14).

The Maximum Expiratory Flow-Volume Curve

Still more information may be procured if data obtained during and FVC manuever is displayed as a maximum expiratory flow-volume (MEFV) curve, plotting instantaneous flow ($\dot{V}$max) against volume exhaled. The flow after exhaling half of the ($\dot{V}$max 50%) is generally measured. It is closely related to the FEF 25-75% and has about the same sensitivity (20). Flow later in expiration, as when only 25% of the FVC remains to be exhaled ($\dot{V}$max 25%), should detect more subtle abnormalities. The small airways contribute a greater fraction of the total airflow resistance at low lung volumes, and abnormalities resulting from inhaled irritants often begin at the level of these small airways. Also, preferential slowing late in expiration would be expected, regardless of the site of disease, since almost all abnormalities develop in a nonuniform fashion, and the most obstructed, slowest emptying regions are preferentially represented late in the MEFV curve.

The $\dot{V}$max shows increasing variability late in the MEFV curve. The standard deviation around predicted of the $\dot{V}$max 25% is in the range of the 30% in asymptomatic nonsmokers (22), and intrasubject variability is much higher than for the FEV_1 (42). Despite its variability, the $\dot{V}$max 25% does reveal a greater number of abnormalities in smokers and in symptomatic subjects than does the FEV_1, and it may have a role in the detection of mild airways abnormalities (19).

In measuring the Vmax 25%, it is essential that a complete expiration be obtained. Failure to empty the chest fully will affect the point at which $\dot{V}$max 25% is measured and may lead to a falsely high value. The possibility of a falsely high value exists with any flow measurement made at a given fraction of the FVC (or expressed

as a fraction of FVC) including the FEF 25-75%, any Vmax measurement, and the FEV_1/FVC ratio. With the FEV_1 or FVC, a poor test performance usually leads to a falsely low value. On the other hand, an excessively slow start of exhalation, with a large back-extrapolated volume, may result in a falsely high FEV_1.

There are some technical problems in obtaining valid MEFV curves. Apparatus must be capable of measuring both flow and volume with fidelity. The MEFV display requires X-Y recording; standard X-Y recorders are generally too slow to respond satisfactorily to on-line signals unless these signals are markedly attenuated. Curves may be photographed from an oscilloscope screen, stored on magnetic tape for subsequent computer processing, or held in temporary storage and given to the recorder at a reduced rate. This raises the cost considerably above that of timed spirometry. Also, it has not yet been demonstrated that Vmax values are independent of measurement techniques.

The Closing Volume and Slope of Phase III

The closing volume (CV) is the point in exhalation at which basal airways are believed to close. An increased closing volume is regarded by some as a sensitive indicator of airways disease. Certainly, it does reveal abnormalities in smokers even when spirometric tests are normal. It may be measured either by inhaling a bolus of an inert gas such as helium (18), or by the so-called "resident nitrogen" technique (2). The latter technique is more popular because of its relative simplicity and because it provides an index of alveolar gas uniformity as well as a CV measurement.

To perform the resident nitrogen test, the subject exhales fully, takes a maximum inhalation of oxygen, and exhales slowly and steadily back to residual volume. Specific recommendations in regard to methodology have been published (30). The type of data obtained is shown in Figure I-20. The closing volume is usually expressed as a fraction of the vital capacity (VC). If the residual volume (RV) is known, a "closing capacity" (CC) can be calculated. This is simply the sum of RV and CV; it is usually expressed as a fraction of the total lung capacity (CC/TLC).

Unfortunately, the measurement of CV is invalid unless the subject exhales fully both before the inhalation of oxygen and on the subsequent slow expiration. Exhaling to the same point on both occasions and/or sustaining a slow, steady exhalation is difficult for some subjects. For these reasons, many technically unsatisfactory tests occur in field studies.

The test requires more expensive and sophisticated equipment than simple spirometry. Determination of the inflection point which marks the CV is subjective and not readily amenable to automation, leading to possible observer variation and even bias. The test shows wide intersubject variation even when age and sex are taken into account, with reported standard estimate errors as high as 50% of predicted values (21). The significance of an abnormal CV remains unclear. On the other hand, the CV is occasionally normal even when there is frank spirometric abnormality.

The slope of phase III (Slope III), which can be measured from data obtained during the resident nitrogen technique (Figure I-20), may be a more useful indicator of functional abnormality than the CV measurement itself. It provides an index of alveolar gas uniformity, thereby detecting nonuniform function throughout the lung. Theoretically, it should be less susceptible to poor test performance or to observer error than the CV. It should also be relatively independent of such factors as chest size and thoracic muscle function—factors which probably increase the variability of spirometric measurements. The test is a better discriminator of smokers and symptomatic subjects than the CV/VC or FEV_1, despite the fact that it shows wide intersubject variability (21) and that its intrasubject variability is greater than any of the other tests discussed thus far (42).

Helium Response of the MEFV Curve

The helium response of the MEFV curve is supposedly a specific test of small airways function. It does appear capable of detecting abnormalities in the airways which do not lead to frank spirometric abnormalities (13). The test is based on the fact that helium is less dense but at least as viscous as nitrogen. Replacing nitrogen with helium improves flow characteristics when flow is turbulent, but not when flow is laminar. When the lung is near full inflation, the maximum flow which can be generated (Vmax) is limited by the large airways where flow is turbulent. As lung

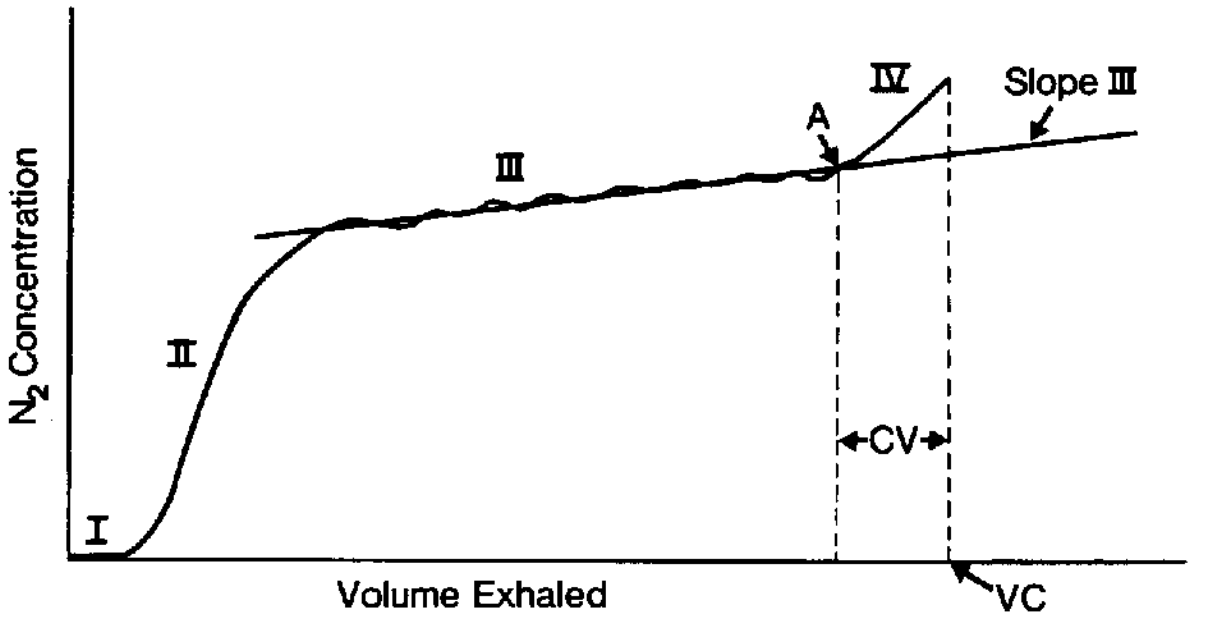

Figure I-20. Data obtained in a resident nitrogen closing volume test. The first gas exhaled (Phase I) is from the anatomic dead space which contains the pure oxygen previously inhaled. This is followed by a rapid rise in exhaled N_2 (Phase II) as alveolar gas begins to appear. A relative plateau of N_2 concentration then occurs (Phase III) reflecting a relatively constant alveolar air composition. Toward the end of the curve, a sudden upward deflection may occur (Point A) reflecting closing of basal airways. The closing volume (CV) is the amount of air exhaled following this inflection point (Phase IV) and is usually expressed as a fraction of the total gas exhaled (the CV/VC ratio). The slope of Phase III (Slope III) can also be measured by drawing a visually fit line through the relative plateau of N_2 concentration noted during that phase of the test.

volume decreases, the small airways, where flow is laminar, become increasingly important in terms of airways resistance and flow limitation. Normally, when one repeats the MEFV curve obtained on air after a subject has breathed a mixture of 80% helium and 20% oxygen, $\dot{V}$max is markedly increased early in forced expiration. But post-helium $\dot{V}$max tends to become similar to the air value as one approaches residual volume (Figure I-21). If there is disease of the small airways, the point at which helium fails to improve flow (the volume of iso-flow) occurs at a higher than normal lung volume, and the increase in flow after 50% of the FVC has been exhaled ($\Delta\dot{V}$max 50%) is less than normal.

While this test has certain theoretical attractions and probably can detect small airways abnormalities at an early stage, its applicability to epidemiological surveys has not been adequately evaluated. Certain features of the test make it less than ideal for field studies. Unless subjects are able to (almost exactly) reproduce their air FVC after breathing helium, measurements of the volume of iso-flow and of the Δ $\dot{V}$max 50% are unreliable. This problem results in a large number of technically unsatisfactory tests. Measuring the volume of iso-flow depends on determining the point at which two converging lines meet and is subject to considerable observer error. Intrasubject variability of the test has not been adequately studied; intersubject variability in a field situation has not been tested.

As originally described, the test was carried out with the subject in a body plethysmograph (13). The volume axis was measured plethysmographically, thereby accounting for any gas compression in the thorax which occurred during forced exhalation. The apparatus needed to perform the test in this way is cumbersome and the technology relatively complex. Although both flow and volume can be measured with spirometric type apparatus, this fails to account for differences in gas compression during the air test compared with the helium-oxygen test, which possibly changes normal limits and affects the maneuver's reproducibility. The helium response of the MEFV curve needs further methodological research before it can be recommended for

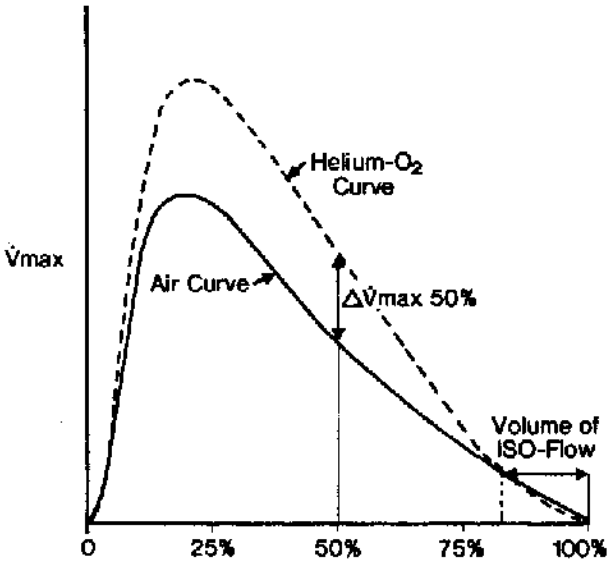

Figure I-21. Data obtained during a test of the helium response of the MEFV curve. The MEFV curve obtained on air breathing is shown as a solid line; that obtained after equilibrating with a He-O_2 mixture as a broken line. The improvement in flow after exhaling 50% of the FVC ($\dot{V}$max 50%) can be measured and is usually expressed as a fraction of the air $\dot{V}$max 50%. Also, the gas exhaled following the point at which air and He-O_2 $\dot{V}$ values become identical is sometimes measured and is called the volume of iso-flow. It is generally expressed as a fraction of the FVC.

survey use. It may, however, be of considerable importance in detailed evaluations which attempt to localize the site of disease.

Other "Sensitive" Tests

Measurement of frequency dependence of compliance is sensitive to nonuniform airways abnormalities, but it requires use of an esophageal balloon and is technically difficult (44). The test is totally unsuited to survey work and probably has few applications of any type at the present time.

Inert gas washout or equilibration curves, while theoretically capable of revealing subtle function changes, are seldom used in epidemiological studies. They are time consuming, require considerable subject cooperation, and have technical problems as well as an uncertain range of normal.

The Maximum Voluntary Ventilation

The maximum voluntary ventilation (MVV) is the volume of air breathed per minute with a maximum voluntary effort. This test has been used extensively in clinical laboratories and is still favored by some clinicians as a guide to the overall function of the ventilatory pump. However, it requires considerable effort by the patient and is affected by the technician's coaching. Results depend to some extent on the instrumentation used and on the breathing pattern adopted by the subject. Furthermore, a properly performed MVV is closely correlated with the FEV_1. Indeed, an "indirect" MVV has been calculated in the past by multiplying the FEV_1 by a constant value (14). In view of the problems with the test and the fact that it provides no unique information about the physiological state of the lungs, it has little place in studies of occupational lung diseases except, perhaps, in disability evaluations.

Pulmonary Diffusing Capacity and Lung Volume Measurements

When occupational exposure is thought to produce a diffuse interstitial lung disease, measurement of pulmonary diffusing capacity should be considered as an addition to timed spirometry. Nearly a fifth of subjects with interstitial disease, who have normal spirometric tests, are classified as having abnormal diffusing capacities (14). Various methods for measuring diffusing capacity have been introduced. Steady state methods are technically difficult; may need to be carried out during exercise; and show great inter- and intrasubject variability. The single breath carbon monoxide method (Dsb), is more suited to epidemiological studies and has been recommended for investigations of interstitial diseases (14).

The Dsb requires a subject to exhale fully and then breathe in a mixture of approximately 0.3% carbon monoxide, 10% helium, 21% oxygen, and the remainder nitrogen. The breath is held at full inflation for 9 to 11 seconds, after which the patient exhales. The first 500 to 1,000 ml of the expirate is discarded. The remainder is collected and analyzed for helium and carbon monoxide. From a recording of the ventilatory maneuvers, knowledge of the inspired gas concentrations, and measurements on the expired gas, Dsb can be calculated—provided the volume of the lung during breath holding is known. The procedure can be automated, simplifying its use in field situations (16).

Most working subjects are able to cooperate well enough to exhale a sufficient volume of the gas mixture so that Dsb measurements can be

made. The test requires only moderate subject cooperation, and the duplicate measurements needed can be obtained within 15 minutes. Under ideal conditions, the intrasubject coefficient of variation on successive tests can be brought below 5% (14). However, this requires scrupulous attention to equipment calibration and proper test performance. Standardized procedures for the Dsb test have been published (14). Regardless of techniques, there is wide intersubject variability even when age, sex, and body size are taken into account; "normal limits" for the test are not well established.

As already noted, calculation of Dsb requires an estimate of the lung volume (V_L) during breath holding. The simplest method for calculating V_L is from the dilution of helium observed in the course of the Dsb test. This method appears as satisfactory as any for studies of subjects with normal lungs, with interstitial lung disease, or even with mild airways obstruction (14). In severe airways obstruction, this method may underestimate both V_L and Dsb.

To obtain accurate Dsb, total lung capacity (TLC), and residual volume (RV) measurements in subjects with severe airways obstruction, the plethysmographic method for determining thoracic gas volume is recommended (14). Standardized techniques have been described (27). It is uncertain, however, what place the test has in epidemiological studies. Although the RV and RV/TLC would be expected to be elevated relatively early in obstructive disorders, these measurements show so much intra-subject variability over time that they are not recommended for epidemiological investigations (42). And although the test is relatively quick and simple to perform, body plethysmography requires cumbersome and expensive apparatus and considerable technical expertise.

There are alternative methods for measuring lung volume, including nitrogen washout and inert gas rebreathing techniques (14). These methods are time consuming, require considerable subject cooperation, and are more suited to clinical than to epidemiological studies. Lung volume may also be estimated from the nitrogen dilution noted during the resident nitrogen closing volume test (4). While all these methods can be used for studies of subjects without severe airways obstruction (14), none have the reliability of body plethysmography. Radiographic measurements are a reasonable alternative to plethysmography when a chest radiograph is being obtained for other reasons (14). If radiographs are to be used for lung volume calculations, however, subjects must be at full lung inflation when the films are taken.

INTERPRETATION

Determining Normal Limits

Most pulmonary function tests show wide intersubject variability which is in part related to sex, age, body size, and race. These factors must be taken into account before attempting to interpret a test result.

One method of reducing variability is to calculate the ratio of two measurements which normally bear a relatively fixed relationship to one another. Common examples include the FEV_1/FVC, CV/VC, and RV/TLC ratios. A somewhat similar type of size correction is made when $\dot{V}max$ is measured at a fraction of the obtained FVC rather than after some absolute expired volume. While relating two measurements reduces the range of values and the coefficient of variation, it does not necessarily fully account for sex, age, or even body size relationships. Ratios also fail to reveal proportional changes in the two values being considered.

Another method of reducing variability is to adjust obtained values to a standard age and a standard body size. This technique is especially useful when comparing groups of subjects in a research report. In other settings, sex, age, and body size are usually accounted for by expressing data as a percent of some predicted value. Formulae to calculate predicted values are determined by multiple regression techniques applied to data from some reference population. Ideally, a presumed healthy subset of the population actually under study should be used. In a general population sample, the reference population might consist of subjects who have no respiratory complaints or known lung disease and who have never smoked cigarettes. When using such presumed healthy individuals, the apparent effects of age, sex, body size, and race—independent of disease—are evident from the prediction equations, and deviations from predicted in groups of subjects can be assumed to reflect their degree of abnormality.

Some of the more commonly used prediction formulae derived in this way for the FEV_1 and FVC are shown in Table I-61. Three are

based on findings in asymptomatic nonsmokers in general population samples (9)(22)(31). Some asymptomatic smokers or ex-smokers were included in other studies. In one study, subjects aged 15 to 20 were included in the reference population (9). It is now known that FEV_1 and FVC increase with age in this group before beginning an age dependent decline (22). Inclusion of teenagers may have led to the relatively slight (apparent) age effect in the study of Cherniack and Raber (9). Most other studies show that in men over age 25, there is a fall in FEV_1 of approximately 25 to 30 ml per year and a fall in FVC of about 20 to 25 ml. For women over age 20, both values appear to decline somewhat less rapidly, but they are similar to those of males when considered as fractional declines.

Relatively few prediction formulae have been published for the FEV_1/FVC ratio. It has been common practice to calculate the predicted ratio as 100 x Predicted FEV_1/Predicted FVC. Certainly, the ratio does show a decline with age. While it generally exceeds 80% up to the age of 55, mean values fall as low as 70% to 75% after age 60 (38). In order to more validly predict the FEV_1/FVC ratio, investigators should probably use the actual value obtained from the reference population of observed FEV_1 divided by observed FVC for each subject, and develop a regression equation in the same way as has been done for the predicted FEV_1 and the predicted FVC. Recently published prediction formulae for this ratio expressed as percent are as follows:*(22)

Males:	103.6—0.14 Age—0.087 Ht (cm)
Females:	107.4—0.11 Age—0.11 Ht (cm)

These predictions are all based on cross-sectional analyses. They may be useful for predicting values within the existing population, but because of cohort effects, they do not necessarily indicate longitudinal changes. It is possible that individual age changes in function are less in magnitude and more nonlinear than those found in cross-sectional studies.

Occasionally, the total study sample is used to predict lung function levels. One must then be cautious in interpreting percent predicted values, especially if a large proportion of the population may be at risk for a pulmonary disorder. For example, the cumulative effects of smoking in a general population sample would increase the apparent effect of age and lead to a large standard error of the estimate (SEE). When predictions are based on the entire study group, healthy individuals will show mean percent predicted values greater than 100% while deviations from predicted will be minimized in affected subjects. In this situation, effects of exposure to a suspected noxious agent must be evaluated by comparing percent predicted findings in exposed and nonexposed subjects. "Predicted" cannot be equated with "healthy" if the reference population includes presumed unhealthy subjects.

When there are too few subjects to allow age, sex, and body size regressions in the study group itself, prediction equations derived from some other population must be used. However, prediction formulae are *never* strictly applicable to any population other than the one from which they were derived. Differences in race, ethnic background, socioeconomic conditions, time of study, test technique, subject motivation, and a myriad of other factors can affect predicted levels. If one must use prediction formulae derived from another reference population, that population should resemble the one under study as closely as possible, and only comparisons between different groups within the study sample are meaningful. Absolute deviations from predicted can be misleading. A recent report by Lanese noted several studies confirming "normal" black subjects have significantly lower FVC and FEV_1 values than whites—even when age, sex, and height are taken into account (24). It has been recommended that values predicted for these measurements derived from predominantly or wholly white populations (see Table I-61) be reduced by 13.2% when applied to blacks (11)(37). Since the forced vital capacity ranges 10% to 15% lower for blacks (1), this recommendation appears reasonable until better race specific prediction formulae are developed. The FEV_1/FVC ratio shows less difference between blacks and whites and probably does not require an adjustment for race, although it may be slightly higher in black than in white men.

When comparing results of different lung function tests, predicted values for all tests must be derived from the same reference population.

*The relationship to height is of interest, and suggests that large subjects, expected to have large FVC's, tend to get out a smaller fraction of their total volume during the first second of exhalation.

Table I-61
PREDICTION FORMULAE

A. For FEV_1 (liters)

	Coefficients		Constant	Reference
	Age (Years)	Standing Ht. (cm)		
Males	−.028	.037	−1.93	(23)
	−.032	.036	−1.26	(31)
	−.023	.036	−1.507	(9)
	−.031	.033	−0.897	(38)
	−.027	.052	−4.203	(22)
Females	−.021	.028	−0.87	(40)
	−.025	.035	−1.932	(31)
	−.019	.024	−0.187	(9)
	−.027	.026	−0.525	(38)
	−.021	.027	−0.794	(22)
B. For FVC (liters)				
Males	−.022	.052	−3.60	(23)
	−.025	.058	−4.24	(31)
	−.014	.048	−3.18	(9)
	−.022	.047	−2.82	(38)
	−.029	.065	−5.46	(22)
Females	−.018	.041	−2.69	(40)
	−.024	.045	−2.85	(31)
	−.015	.031	−1.05	(9)
	−.022	.037	−1.92	(38)
	−.022	.037	−1.77	(22)

NOTE: All reference populations were restricted to whites except for that of Smith and Kory (40).

If a new test's predicted values are derived from a "healthier" group than predictions from established tests, the new test will invariably appear to be a more sensitive disease detector.

Having taken into account the effects of sex, age, body size, and race by relating findings to a predicted value, it may be important to determine whether a percent predicted or adjusted value for an individual is "within normal limits." Limits of normal for lung function tests are totally arbitrary. If prediction formulae are derived from the total population being studied and normal limits based on deviations around predicted data, the number of "abnormalities" in the total sample will be predetermined. When predicted values are derived from presumed healthy subjects in the sample, the same procedure results in a predetermined number of abnormalities in that reference group. The number of "abnormal" tests in the total sample will then depend on the difference in values obtained in other subjects compared to those in the reference group. The more carefully screened the reference population, the more "abnormalities" will be found in the remainder of the sample.

When obtained data in the reference population are distributed in a Gaussian fashion around predicted data, "normal limits" are usually set on the basis of the SEE of the prediction equation. For values reduced by disease (such as the FEV_1), setting normal limits at 2 SEE below predicted will result in approximately 2.5% abnormalities in the reference group. If one is willing to accept a higher rate of abnormalities in that group, limits of "normal" can be set at 1.64 SEE below predicted, giving an approximate abnormality rate of 5%. This assumes that the SEE is independent of the predicted level. In fact, the SEE may be approximately proportional to the predicted value, and

in this case, "normal limits" are more appropriately expressed as a percent of predicted.

Deviations from predicted do not always follow a Gaussian distribution. For example, the Vmax 25% tends to show marked skewness toward above predicted values. If "normal limits" are set at 2 SEE below predicted, zero may appear to fall within the "normal range" (22). Either the data must be transformed (perhaps made into a logarithmic function) or "normal limits" must be set by some method which does not assume a known distribution pattern. If numbers allow, one may simply examine obtained data to find the level at which a given fraction of the reference population is arbitrarily classified as abnormal. This technique has the advantage of fixing quite precisely the number of apparent abnormalities in the reference population. It has been used effectively when examining the relative ability of different tests to detect excess abnormalities in smokers or symptomatic subjects (19).

Regardless of the specific method used to set "normal limits," they should not be interpreted as separating health from disease. Even within the normal range there will be an increasing probability that disease exists as one progresses from above predicted to low-normal values. In research studies, enumeration of "abnormalities" in population groups should be regarded only as an illustrative procedure. Determining that a functional test is different in one group than another requires examination of the overall distribution of values in the two groups.

When it is necessary to decide whether an individual lung function test is "normal" or not, the following procedure may be used. If the test is more than 2 SEE below predicted, it is generally presumed to be "abnormal," provided the low value is confirmed on retesting. When the measurement being examined falls in the range of 1.64 to 2 SEE below predicted, a second measurement may be examined. In the case of a borderline percent predicted FEV_1, for example, the FEV_1/FVC ratio or $FEF_{25-75\%}$ can be examined. If the second test is also more than 1.64 SEE below predicted, it is reasonable to assume disease is present. On the other hand, it is inappropriate to use an abnormality in any one of multiple measurements as an indication of abnormal lung function. As more tests are considered, more subjects in the reference population will show at least one "abnormal" measurement. This is true even when measurements are closely related, as in the case of multiple indices of forced expiratory flow (19).

There are more scientifically defensible ways to express the extent to which a lung function test resembles measurements found in a reference population than by calling it "normal" or "abnormal." The actual number of SEE's by which the value differs from predicted gives an index of the likelihood of finding such a value in the reference population. One may also readily convert the SEE information into probability figures. Thus, a value which is 1.3 SEE below predicted can be interpreted as follows: "This low a value is found in approximately 10% of asymptomatic nonsmokers in the population."

Assessing the possible effects of other exposures in cigarette smokers is a complex problem. Clearly, even asymptomatic current or exsmokers show lower lung function values than nonsmokers and the effect appears to be related both to intensity and duration of cigarette use (7). While published data might allow an adjustment for smoking, the adjustment's reliability would be uncertain, The range of "normal" in smokers has not been, and perhaps cannot be, determined with precision.

Finally, it should be remembered that prediction equations are derived from a selected portion of some general population—usually asymptomatic nonsmokers. No unscreened population would be expected to have this level of function. Even if smoking habits are taken into account, almost any unscreened population, even if not exposed to noxious agents, will contain some portion of symptomatic subjects whose lung function is impaired. Thus the fact that some unscreened industrial population has average lung function values below predicted does not necessarily indicate that it is different from any other general population sample.

Patterns of Abnormalities

Airways obstructive disorders are characterized by a reduction in forced expiratory flow which is out of proportion to any reduction in the total volume of gas exhaled, and leads to a low FEV_1/FVC ratio. There is also an increased RV and a high RV/TLC ratio. This is the pattern of "obstructive lung disease" and is characteristic of asthma, emphysema, and chronic obstructive bronchitis. Other physiological findings in these diseases depend on the anatomi-

cal abnormalities underlying the airways obstructive problem as well as on the stage of the disease (6). With advanced anatomic emphysema, the TLC is large, pulmonary diffusing capacity markedly reduced, lung recoil very low, and resistance of the large airways (measured by body plethysmography) near normal. There may be relatively mild hypoxemia and no elevation of the arterial carbon dioxide tension until late in the disease. Patients with this type of disorder have been called "Type A" or the "emphysematous type" of chronic obstructive lung disease, or "pink puffers." In contrast, patients with minimal emphysema, but severe intrinsic disease of the airways, show less pulmonary hyperinflation, less consistent reduction of diffusing capacity, little loss of lung recoil, and high airways resistance measurements. They tend to have severe hypoxemia, chronic hypercapnia, and cor pulmonale relatively early in their disease. Such patients have been called "blue bloaters," or characterized as "Type B" or as a "bronchial type" of chronic obstructive lung disease. In fact, these distinctions are quite artificial. Classical examples of either type of disease are relatively rare since most subjects with chronic irreversible airways obstruction have both emphysema and intrinsic airways disease.

Asthma can be distinguished from chronic irreversible airways obstructive disorders only by the reversibility of the physiological abnormalities. The improvement which occurs within minutes of inhaling a potent beta adrenergic bronchodilator should be observed. When an obstructive abnormality is markedly improved by bronchodilator inhalation, some asthma must have been present. However, many severe asthmatics prove refractory to a single dose of inhaled medication. The reversibility of their abnormality may be seen only after a prolonged program of medical management. Thus, the type of testing which is usually done in field situations does not permit differentiation of asthma from irreversible airways obstructive diseases.

Special care must be taken in assessing acute changes in lung function after bronchodilator inhalation or with challenge tests. The total FVC as well as flow rates may change. Thus, alterations may be missed if the FEV_1/FVC ratio is examined. Also, $\dot{V}max$ values can be misleading unless they are examined at the same absolute volume of exhalation (29).

It has been recently reported that subjects with late onset "intrinsic" asthma are more likely to show diminished response of the MEFV curve to helium/oxygen inhalation than are "extrinsic" asthmatics (3). This suggests that the problem in "intrinsic" disease is located in more peripheral airways. However, the reliability of the helium-oxygen test in distinguishing different types of asthma needs to be confirmed.

A different pattern of abnormalities is noted in subjects whose airways are not obstructed, but whose lungs are less compliant than normal because of inflammatory changes or fibrosis. Here, the vital capacity, FVC, and TLC are reduced, but expiratory flow rates are relatively unimpaired. Thus, the FEV_1/FVC ratio is not decreased. This pattern of "restrictive lung disease" is totally nonspecific. It occurs with any disorder which limits inspiration—abnormalities of the chest wall, any type of parenchymal lung disease except emphysema, and even poor patient effort. When it is the result of diffuse interstitial disease, additional abnormalities often occur, including a marked reduction in diffusing capacity and increased lung stiffness noted on pressure-volume studies. There may also be arterial hypoxemia which is made worse by exertion, corrected by small supplements of oxygen, and accompanied by a normal or even low arterial carbon dioxide. This constellation of findings has been called an "alveolar-capillary block syndrome." While doubt has been expressed that a true alveolar-capillary block exists in most patients, the described pattern of abnormalities is characteristic of diffuse interstitial lung diseases.

When only spirometric data are available and TLC is not known, interpretation is limited. If the FEV_1 is reduced out of proportion to the FVC, producing a low FEV_1/FVC ratio, "obstructive ventilatory impairment" can be said to exist. If the FVC or VC is below normal limits, but the FEV_1/FVC ratio is not reduced, a "restrictive ventilatory impairment" is present.

There are many diseases which produce both a small lung as well as a problem with airflow. In this case, both the FEV_1/FVC ratio and the total lung capacity are reduced, and a "mixed" type of abnormality is present. All in all, pulmonary function tests are of limited value in diagnosis beyond distinguishing diseases which primarily affect airways function from those

which increase the stiffness of the lung and therefore decrease its distensibility.

THE MEANING OF PULMONARY FUNCTION ABNORMALITIES

The relationship of lung function tests to symptoms and prognosis in patients with severe irreversible airways obstruction is reasonably well documented. In these patients, the FEV_1 shows a crude but definite relationship to the severity of clinical illness. For example, most patients note dyspnea only on moderate exertion when their FEV_1 exceeds 1.25 liters, even though this value is less than half of predicted. Dyspnea on slight exertion and complications of the disease are seen more frequently as the FEV_1 falls below 1.0 liters. Complete invalidism generally occurs as the FEV_1 approaches .5 liters. Survival shows a relationship to a great variety of lung volume measurements, but is best correlated with FEV_1 obtained after bronchodilator inhalation (43). The median survival is less than three years when the FEV_1 is below 30%, approaches five years when the FEV_1 is in the range of 30% to 40%, and is near ten years when the FEV_1 is close to 50% of predicted. While there are wide variations around these median survivals, a lung function test does provide a crude index of a disease's stage.

In asthma, fluctuating symptom severity is reasonably well reflected by changes in the FEV_1, but longevity has not been studied in relationship to function tests. There is some correlation between vital capacity and survival in patients with idiopathic diffuse interstitial fibrosis, but the relationship is not close. Evidence relating symptom severity or survival to lung function measurements are lacking for most other diseases, but nearly all clinicians would agree that severe blood gas or spirometric abnormalities are poor prognostic signs in any progressive respiratory insufficiency state.

Work status has been shown to have some relationship to measured funtional impairment in patients with chronic airways obstruction who are not applying for disability benefits (12). Most subjects continue to work at sedentary jobs until their FEV_1 falls below a liter. Work status is also related to certain psychological factors (10); in disability applicants, there appears to be little correlation between measured impairment and self-perceived disability (28).

It is important to remember that pulmonary function tests do not necessarily measure the specific functional characteristics which lead to symptoms. Indeed, the actual mechanism of dyspnea remains unclear. Thus, although function tests are useful for confirming the presence of disease, for following its course, and sometimes for determining the type of anatomical abnormality present, such tests cannot measure the total impact of the disease. Also, disease progression rates are generally variable, and lung function studies can be expected to produce only crude estimates of longevity.

It has become popular to use lung function tests for "early detection" of chronic airways obstructive diseases. This is based on the theory that these diseases develop slowly and gradually throughout adult life, and that the subject who will have severe airways obstruction at age 60 should show a mild subclinical impairment of lung function by age 40 or 45. It has been shown that middle-aged subjects with mildly diminished FEV_1's do tend to have relatively rapid declines in lung function over a period of several years. The decrements in lung function of subjects with lower test values have been described as the "horse-race effect" (15). However, there is wide variability in reported data and the precision with which spirometric test can detect the individual who will later develop incapacitating disease remains unclear.

The use of more sensitive tests to detect "early" disease is problematical. $\dot{V}max$ 25%, slope of Phase III, and closing volume detect more abnormalities in smokers than the FEV_1 (21)(22). However, the significance of such abnormalities is uncertain. It is not known if they are predictive of later development of progressive disabling illness; it is not even known if they persist within individuals. According to the "horse-race effect," a good FEV_1 in middle-age should preclude succeeding severe disease regardless of findings on more sensitive tests. At our present state of knowledge, isolated abnormalities in $\dot{V}max$ 25%, slope III, closing volume, or helium/oxygen response of the MEFV curve are best regarded as indicative of mild lung dysfunction but not necessarily of an "early" stage of a progressive disease.

When an abnormality is found in a more clinically relevant measurement such as the FEV_1, the abnormality should be confirmed and its irreversibility demonstrated. Response to inhalation of an adrenergic bronchodilator should be

observed. A high proportion of mildly abnormal tests, detected in a population survey, increased to "within normal limits" after isoproteranol inhalation (29). An FEV_1 persistently below 60% of predicted is generally associated with some clinically significant symptoms; in the presence of a low FEV_1/FVC ratio, it is compatible with frank airways obstructive disease. A persistently low FEV_1 (i.e., 60% to 75% of predicted) indicates a subject at high risk of later developing more severe ventilatory impairment, but the magnitude of this risk remains to be determined.

Assessing Severity of Abnormality

There tends to be confusion between the clinical and statistical significances of a test abnormality. The CV/VC may be several SEE above predicted, and therefore, "definitely abnormal" in a statistical sense. However, this hardly indicates a "severe abnormality" in clinical terms. The clinical importance of an isolated abnormality in CV/VC remains unclear. To avoid confusion, it might be reasonable to accept certain conventions. When referring to the statistical confidence of abnormality, tests might be classified as normal, low normal, borderline, or definitely abnormal. Terms such as mild, moderate, and severe abnormality are probably best restricted to assessments of clinical significance. This can only be determined by empiric observations relating symptoms and prognosis to test results.

Possible guidelines for expressing the relationship of a test to findings in a reference population, using terms understandable to most clinicians, are shown in Table I-62. For the FEV_1, FVC (or VC), and blood gases, a clinical appraisal may also be provided based on empiric observations, but this is possible for few other tests. In clinical terms, an FEV_1 in the range of 60% to 75% of predicted might be considered a mild abnormality, whereas tests in the ranges of 45% to 60%, 30% to 45%, and less than 30% might be considered moderate, severe, and very severe abnormalities respectively. The $FEF_{25-75\%}$ tends to stabilize in late stages of disease. It is therefore less satisfactory than the FEV_1 for assessing either the stage or course of an airways obstructive disease. The same must be true of Vmax values, slope III, and even the FEV_1/FVC ratio (5).

CHALLENGE TESTING

Challenge tests have been used for two distinct purposes. The first is to evaluate the general state of bronchial reactivity. For this purpose, inhaled histamine or methacholine may be used, or the response to vigorous exercise may be observed. A standardized protocol must be followed to obtain meaningful results (8). Most asthmatics show falls in lung function after inhaling much smaller doses of histamine or methacholine than are required to affect the lung function of normal subjects. Similarly, most asthmatics show excessive fluctuation in lung function during severe exercise. Intermediate responses noted in patients with allergic rhinitis and relatives of asthmatics are presumed to indicate a milder degree of bronchial hyperreactivity than is seen in overt asthma (17). Such challenge tests have been used to confirm the diagnosis of asthma during remissions of illness. They are of substantial research interest because of their potential to identify the individual who will be most affected by exposure to a bronchial irritant or allergen, but this has not yet been documented.

Table I-62

RELATIONSHIP OF RESULTS TO A REFERENCE POPULATION

Number of SEE from Predicted*	Interpretation
<1	Normal
1—1.64	Low normal range
1.64—2	Borderline abnormality
<2	Definite abnormality

*Based on findings in an asymptomatic, nonsmoking general population sample.

It is technically possible to use histamine and methacholine challenges in the field. Theoretically, these tests might even be applied to large population groups. There are certain problems, however. Considerable patient cooperation is required. The tests are time consuming and require a physician's attendance. Also, there is a risk of inducing a first asthmatic attack in a predisposed subject. Were this to happen, the subject might interpret the test as a cause of his disease. Unfortunately, exercise testing is not practical for field use. Vigorous exercise is required, and many subjects cannot complete

the protocol.

The second use of provocative testing is to confirm that a specific inhalant provokes symptoms and physiological abnormalities. This is most often used to identify factors leading to acute bronchospasm (8) but has also been used in regard to hypersensitivity pneumonitis (34). This type of testing is totally unsuited to large scale studies and should only be carried out under an experienced physician's direct supervision.

While as crude a measure as peak flow (measured with a Wight Peak Flow Meter) has been effectively used in assessing exercise responses (17), airways resistance measured in a body plethysmograph is more sensitive to acute bronchospastic changes than measurements from the timed spirogram or the MEFV curve. When using this technique, subjects must be exposed to an inert material as well as the suspected noxious agent in a blind fashion since placebo effects do occur, and mild bronchospasm may be induced by suggestion (41).

Even without a formal challenge test, the acute effects of a suspected provocative factor may be studied by checking lung function studies before and after a subject is naturally exposed. This technique has been used to determine whether exposure to air pollutants affects the lung function of exercising school children (26). It has also been widely used to see if occupational exposures cause lung function to decline over the course of a work shift, or when a subject returns to work after an absence of several days (32). A fall in the FEV_1 of greater than 15% is generally considered indicative of significant bronchospasm.

Some investigators consider it important for overall quantitative accuracy that tests be performed at the same time of day and same season of the year, especially if workers are to be monitored for longitudinal studies. Whether the use of pulmonary function tests in shift studies and air pollution detection effects ought to include this aspect of seasonal and diurnal variability is debatable because (1) the variability is usually so small as to be statistically insignificant and (2) scheduling tests pursuant to this possible variability is only sporadically feasible.

Research Needs

Research needs in the application of pulmonary tests to occupational disease studies include:

1. Determination of simple, accurate prediction formulae for commonly used pulmonary tests for nonwhites.
2. Investigation of the prognostic significance of "sensitive" tests of lung function, including instantaneous flow measurements toward the end of the flow-volume curve, closing volume and Slope III measurements, and the response of the flow-volume curve to helium inhalation.
3. Determination of the usefulness of tests of bronchial reactivity (bronchial challenge test) in identifying workers who may be especially sensitive to occupational exposures.
4. Investigation of the relationship of "shift changes" to longitudinal changes" in lung function.
5. Improvement in our ability to distinguish smoking effects from those of occupational exposures. At a minimum, this would require more accurate prediction equations for smokers with varying smoking habits and varying pack-years of cigarette use.
6. Improved statistical methods for dealing with longitudinal observations of lung function where the variability of measurements generally far exceeds the true annual decline.

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