APPENDIX VII

Physical Examination Protocol

Field Operations Manual
NIOSH Contract No. 210-76-0175

INSTRUCTIONS TO PHYSICIANS ON GRAIN HANDLERS' FIELD STUDY

The physician's assessment of the health status of the patient will include an interview during which the salient points of the questionnaire will be reviewed with particular emphasis on the manifestations related to the cardiovascular system to the symptoms related to exposure to grain dust and those symptoms related to exposure to detectable pesticides.

The questionnaire will be reviewed for completeness by one of two trained assistants before you see the worker, but you are required to recheck it to assure it is complete. Pay particular attention to the following:

- Check to see that the Consent Form is signed and obtain necessary permission for release of information from other physicians if necessary.

- Check work history, particularly whether the patient has worked in mining, farming, in a foundry, steel mill, with asbestos, in a shipyard, chemical plant, quarry, grain flour industry, welder, etc.

- Question 13e--be sure that the number of years that he/she has had the cough is entered.

- Is his/her cough better when non-exposed?

- Question 20--be sure that he/she understands that "only once" means only once in a lifetime and not once a day.

- Be sure that he/she enters the number of years on Questions 23 and 24.

I. Interview:

The interview should emphasize the clarification of complaints in the questionnaire, but answers to questions should not be modified. Questions 46 and 47 should be verified using Work Sheet provided (Appendix V).

The information you obtain from the patient should be written on the margins or at the end of the questionnaire. This anecdotal information will serve to clarify interpretation of historical, physical or laboratory findings in individuals if necessary. Analysis of symptoms felt in relation to his/her work should be done to rule out cardiac disease as the cause of the usual symptoms of cough, dyspnea, wheezing and chest tightness. Be sure to answer the following question:

In your opinion is his dyspnea from heart disease?

Yes ____ No ____ Not sure ____

- Obtain more details on pesticide exposure symptoms.

- On Question 64d--if he/she has had tuberculosis, did he/she receive treatment; did he/she receive a vaccine for tuberculosis?

- On Question 64e--specify age and treatment for the cancer.

- On Question 64f--specify reason for surgery, what was done, when.

- On Question 64i--how was Farmer's Lung disease diagnosed?

- If yes to Question 65a--pneumonia diagnosed by a doctor. Obtain detailed history for each pneumonia.

  Pneumonia #1: Did he/she have a chest x-ray, to be hospitalized, cough, phlegm, chest pain, wheezing, dyspnea, sore throat, earache, stuffy nose, muscle aches.

  Pneumonia #2: Did he/she have a chest x-ray, to be hospitalized, cough, phlegm, chest pain, wheezing, dyspnea, sore throat, earache, stuffy nose, muscle aches.

  Pneumonia #3: Did he/she have a chest x-ray, to be hospitalized, cough, phlegm, chest pain, wheezing, dyspnea, sore throat, earache, stuffy nose, muscle aches.

- Question 67a--type of heart disease or heart trouble. Therapy, if any.

- Questions 67d and 67e--what trouble, when, doctor's diagnosis, what doctor, what tests were done, was he/she hospitalized, where.

II. The physical examination will include:

a. The measurement of height, weight, blood pressure and heart rate, which will be performed by a technician.

b. The description of the chest configuration as outlined in the physical examination form.

c. Auscultation of the chest to be done in the upper and lower lung fields posteriorly while the patient breathes deeply through open mouth followed by auscultation during forced expiratory maneuvers. These will be reported as: 1) none, 2) obvious and common, or 3) on forced expiration only. If present, whether bilateral and diffuse or unilateral and localized. Rales will be reported as: 1) none, 2) bilateral, or 3) unilateral. The anterior or ventral chest will be auscultated over the four usual precordial areas, that is, the apex of the heart, the left sternal border, the aortic valve area and the pneumonic valve area. The findings will be reported as: 1) normal heart, 2) murmur and specify, 3) abnormal rhythm, or 4) other and specify. Also, specify whether in your opinion the murmur is "functional" rather than "organic" in origin. With the patient then lying down, palpate the liver at the mid-clavicular line. If palpable, the span should be measured by percussion and palpation. If the span is greater than 14 cm., hepatomegaly is present. Any other obvious physical findings should be reported under "Other Findings."

PHYSICAL EXAMINATION RECORD

STUDY ID # / / / / / / / / / / / /

BLOOD SAMPLE

URINE SAMPLE

WEIGHT / / / / / / Pounds

BLOOD PRESSURE / / / / / /-/ / / / / (SYSTOLIC) (DIASTOLIC)

HEIGHT / / / / / / Inches

PULSE RATE / / / / / / Beats/Min

RECORDER _____

CHEST CONFIGURATION (Check ONLY one that pertain)

/ / 1. Normal

If NOT Normal:

/ / 2. Kyphoscoliosis

/ / 3. Scoliosis

/ / 4. Pectus Excavatum

/ / 5. Other

AUSCULTATION - POSTERIOR CHEST

Rhonchi and/or Wheezes (Check ONLY one)

/ / 1. None

Or obvious on deep but not forced expiration: (Check ONLY one)

/ / 2. Bilateral-diffuse

/ / 3. Unilateral-localized

Or if ONLY on forced expiration:

/ / 4. Bilateral-diffuse

/ / 5. Unilateral-localized

IV AUSCULTATION - ANTERIOR CHEST (Check ALL

/ / 1. Normal

If NOT Normal:

/ / 2. Murmur (Specify: _____

/ / 3. Abnormal rhythm

/ / 4. Other (Specify: _____

_____

V. ABDOMEN (Palpate liver at mid-clavicular line

If palpable, measure span. If greater than 14 cm. = hepatomegaly.)

Liver

/ / 1. Not palpable

If palpable, span = ___ ___ . ___cm

/ / 2. Hepatomegaly absent

/ / 3. Hepatomegaly present

PHYSICAL EXAMINATION RECORD (continued)

Rales (Check ONLY one)

/ / 1. None

/ / 2. Bilateral

/ / 3. Unilateral

OTHER FINDINGS: (ANY other abnormal physical findings)

APPENDIX VIII

Pulmonary Function Studies

Field Operations Manual
NIOSH Contract No. 210-76-0175

FORWARD

This manual contains a description and detailed procedures of the standardized techniques used in conducting the on-site pulmonary function tests specific to this study. Recorded data will be appropriately filed in data storage folders and subsequently measured and transcribed to computer input forms in Madison, Wisconsin, following completion of the field testing. Frequent on-site measurements and computations on a programmable calculator (TI SR-52 with PC 100 Printer) will be performed to spot check technical procedures and measurements.

Since prior to 1977 our epidemiological studies were supported by an NHLI Specialized Center for Lung Research Grant. Our laboratory had standardized pulmonary function testing in accordance with the recommendations of the NHLI, Division of Lung Disease, report of workshops on epidemiology of respiratory disease, October, 1972, and November, 1973. In addition, for measurements of FEV_1 and FVC we have considered the preliminary information available from the ATS Committee on Standardization of Spirometry.

TABLE OF CONTENTS

STANDARDS FOR PULMONARY FUNCTION TESTING

I. Spirometry, FEV_1, FVC, and MMF for Studies I & III

1. Instrumentation - Studies I & III (Rolling bar 840 will be used for Studies II, IV, & V.)

Standard equipment utilized for these procedures includes:

A. 13.5ℓ chain-linked, water-sealed, spirometer (W. E. Collins), with 3 speeds (32, 160, 1920 mm/min).

B. Mouthpieces - large rubber

C. Two-way bypass valve

D. Two 34" lengths of 1 1/2" ID corrugated wire wound flexible plastic tubing with 1 3/8" ID rubber coupling ends

E. Recording pens and ink

F. Noseclamp

With nose occluded, the subject is connected to the spirometer through the rubber mouthpiece attached to a large free breathing bypass valve and two lengths of corrugated tubing. Any CO_2 absorbent is removed from the system to minimize resistance to air flow.

2. Calibration

Weekly check for:

A. Deformities in spirometer bell

B. Leaks around water seal

C. Accuracy of kymograph drum speed

Forced Expiratory Volume (FEVt) - the volumes exhaled in 1.0 and 3.0 sec. total. (See Fig. 1)

3. Procedure

Record:

1. a. Date

b. Subject name, sex*

c. Ht. (cm)*

d. Wt. (kg)*

e. Age (yrs)*

f. Barometric pressure (mmHg)

g. Spirometer temperature (^{o}C)

*b-e optional if recorded elsewhere

2. Seat subject in a comfortable upright posture

3. Loosen any tight clothing

4. Explain test procedure

5. Install nose clip

6. Go onto mouthpiece, breath normally to room air

7. Fill drum approximately 2/3 full

Turn subject into spirometer (kymograph speed of 160 mm/min) and followng a few quick breaths request a maximal inspiration – (hold at TLC for ~1 second while switch is turned to 1920 ml/min paper speed); then request a maximal expiration (vigorously encourage subject to breathe out as hard and fast as possible).

Repeat steps 8 & 9 until at least three acceptable curves are obtained.

4. Criteria of Acceptability

Acceptability is based upon the technician's observation that the subject understood the instructions and performed the test with a smooth, continuous exhalation with apparent maximum effort and without: a) coughing; b) Valsalva maneuver; c) premature expiratory termination (in normals, before completion of the breath; in obstructed individuals this would be assumed if expiratory time was less that 5 seconds); d) a leak; e) an obstructed mouthpiece (e.g., tongue becoming positioned in front of mouthpiece); f) unsatisfactory start of expiration from TLC, characterized by excessive hesitation or false starts thus preventing accurate back extrapolation to time 0. (Extrapolated volume on the volume time tracing (spirogram) must be less than 10% of the FVC); g) excessive variablilty among the three acceptable curves i.e., exceeding $\pm$ 10% of the reading or 100 +mm.; whichever is greater, between the two best curves.

5. Measurements/Calculations

(a) FEV_t - volume of gas exhaled over a given time interval during the performance of a vital capacity maneuver. (See Fig. 1) FEV 1.0 is the volume expired in the first 1.0 sec. of the FEV_t. FEV 1.0 as well as FEV 2.0 and 3.0 are obtained from the spirogram by determining the time intervals on the spirometer chart paper. FEV and FEV_1 volumes are expressed as a % of total (i.e., FEV 1.0%), the values for which may be determined from different acceptable curves.

$$\text{FEV 1.0 (\%)} = \frac{\text{FEV}_1 \text{ (ml)} \times 100}{\text{FVC (ml)}}$$

The maximum FVC and the maximum FEV_1 (BTPS) will be computed following examination of data from all the acceptable curves even if the two values do not come from the same curve. From these values the $FEV_{1.0}$ (1%) will be calculated. In addition, the maximum FVC and FEV_1 from the maximum FVC as well as the ratio of this FEV_1/FVC X 100 will be recorded for purposes of the three year follow-up study.

Volumes expressed in absolute terms must be converted from ATPS to BTPS. $FEV_{BTPS} = FEV_{ATPS}$ X BTPS factor.

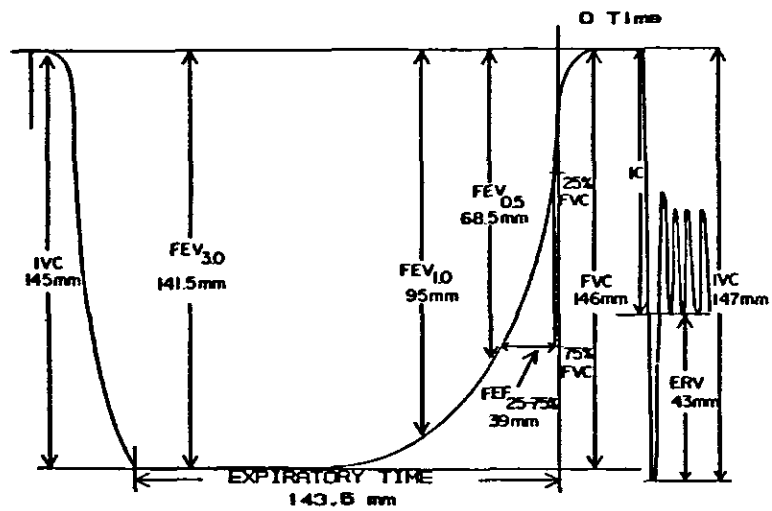

Fig. 1 Forced Expiratory Spirogram

(b) FEF 25-75% - the average flow rate during the middle two quarters of the volume segments of the forced expiratory spirogram (i.e., from 25-75% of the volume -- Fig. 2)

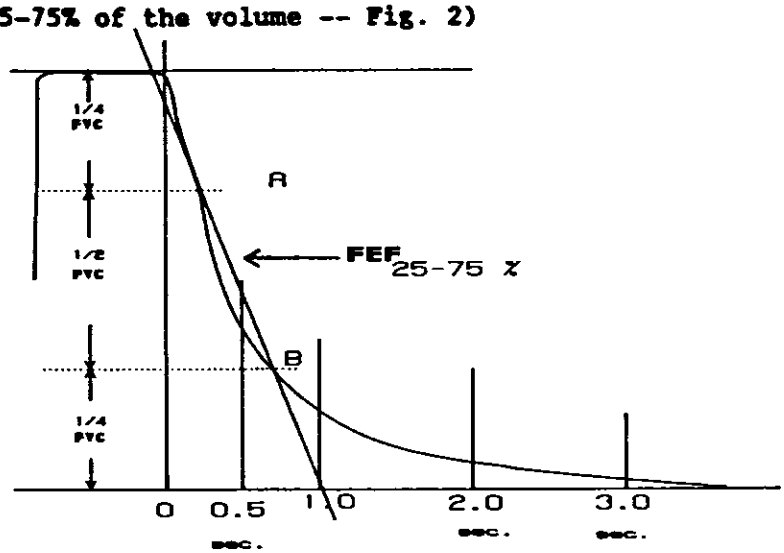

Fig. 2 Forced Expiratory Spirogram

"A" represents the intersection of the FEF with the line between the first and second quarter of the FVC volume (25%); "B" is the intersection of the FEF with the line between the third and fourth quarter of the FVC volume (75%). Points "A" and "B" are determined by measurement or with preset quadrant calipers from the point of commencement (0 time) of forced exhalation. Zero (0) time is determined by the back extrapolation method (Fig.3). Extrapolated volumes that exceed 10% of FVC are suboptimal and should be so noted for subsequent interpretations.

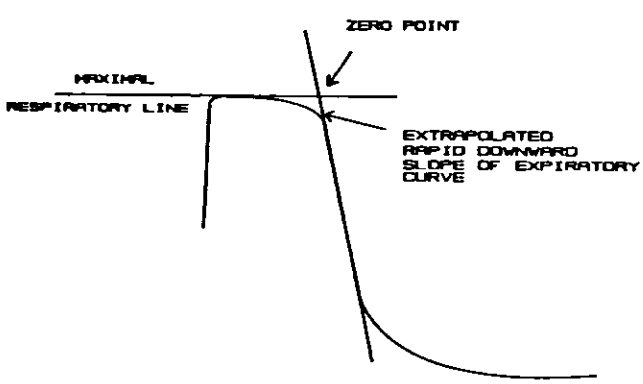

Fig. 3 Back Extrapolation Method of Establishing 0 Time Point

The slope of the line connecting "A" and "B" is the forced mid-expiratory flow (FEF 25-75%) which is determined by extending line "AB" until it crosses two time lines (i.e., 1 sec. apart). The distance between where the line crosses the two time lines represents the FEF 25-75% volume. Therefore:

$FEF\ 25\text{-}75\%_{ATPS}$=_____ℓ/sec x 60 = _____ℓ/min

$FEF\ 25\text{-}75\%_{BTPS}$=$FEF\ 25\text{-}75\%_{ATPS}$ x BTPS factor = _____

The $FEF_{25-75\%}$ will be calculated from the curve producing the largest sum of FVC and FEV_1. In addition, the MMF that corresponds with the largest FVC will be recorded for purposes of the 3 year follow-up study.

Prediction Values:

Absolute values of FEV_1, FVC, and MMF will be compared with the following prediction equations of Knudson, et al.

$FEV_{1.0}$ <25 years old = .045 Age (yrs) + .046 Ht (cm) - 4.808

(men) <25 years old =-.027 Age (yrs) = .052 Ht (cm) - 4.203

FVC <25 years old = .078 Age + .05 Ht - 5.508

(men) >25 years old = -.029 Age (yrs) + .065 - .065 - 5.459

MMF >25 years old = .059 Ht (cm) - 5.334

(men) >25 years old = - .031 Age + .045 Ht (cm) - 1.864

For Studies II, IV, and V:

The instrumentation is described under "Flow-volume Curve." Forced expiratory volume-time will be obtained using an Ohio 840 Rolling Bar Spirometer. The FVC-time curve will be displayed on an HP 1046A X-Y-Y recorder and measured on the paper record as explained above.

References

Kanner, R.E. and A.H. Morris, eds., Spirometry, Ch. 1, "Clinical Pulmonary Function Testing," 1975.

Kory, R.C., J. Rankin, G.L. Snider, and J.F. Tomashefski. Clinical Spirometry (recommendations of the section on pulmonary function testing, Committee on Pulmonary Physiology, Am. Col. of Chest Phys.), Dis. of the Chest, (43):214-219, 1963.

Frayser, R. and J.C. Ross. Clinical Spirometry. Laboratory Procedure Manual, Dept. Medicine, Indiana Univ. School of Medicine,:11-19, 1966.

Knudson, R.S., Slatin, R.C., Lebowitx, M.D., Burrows, B. The maximal expiratory flow volume curve, normal standards, variability and effects of age. Am. Rev. Resp. Div. 113:587-600, 1976.

National Heart and Lung Institute, Report on Workshop on Standardization of Methods used in Epidemiologic Studies, 1973.

IIa. CLOSING VOLUME - NITROGEN METHOD

1. Instrumentation: Standard equipment utilized for this procedure includes:

A. Wedge Spirometer (Med. Science 570)

B. Nitralyser (Med. Science 505)

C. XYY recorder (Hewlett-Packard 7046A)

D. Two-way bypass valve

E. Tubing (corrugated) 24-30 " length 1-7/8 " ID

F. Mouthpiece - large rubber

G. O_2 cylinder (100% O_2), with pressure regulator

H. Recording paper (Hewlett-Packard 9270-1024)

I. Recording pens

J. Nose clamp

With nose occluded, the subject is connected to the Wedge spirometer through a large rubber mouthpiece, corrugated tubing and bypass valve. The output of the spirometer is monitored by a Nitralyser connected to one axis of the XY_1Y_2 recorder allowing for simultaneous recording of the flow volume and N_2 concentration curve.

2. Calibration:

A. Y_1Y_2 recorder: according to Ch. V, in Maintenance, Performance, Checks and Adjustments of the Operating and Service Manual for XY_1Y_2 Recorder 7046A.

B. Nitralyser: Weekly with concentrations ranging from 0-80% dry N_2 from calibrated tanks. (Monthly calibrations may prove adequate.)

C. Wedge Spirometer: Calibration of volume (ℓ) + N_2 concentration (%), is performed against a built-in electronic reference and displayed on each subject's record of CV tracings.

3. Procedure

A. Flush the Wedge Spirometer with 100% O_2 until N_2 concentration reads 0.

B. Install noseclip and have subject come onto the mouthpiece with the two-way valve turned to room air.

C. The subject takes a deep breath and exhales to residual volume(RV).

D. At RV the subject is turned into the spirometer and slowly inspires a vital capacity breath of pure O_2 and, without breath holding, slowly expires a second time to RV.

During inhalation of O_2 the Y_2 channel of the recorder is switched from .5 V/cm to 25 mv/cm. The subject is instructed to maintain expiratory flow rate (monitored from the Y_1 display channel) at 0.4 lps.

E. At the end of the second expiration to RV, the subject is turned into room air.

F. The operator urges the subject repeatedly at both extremes of vital capacity; during exhalation of the measurement, however, it must be only after the Phase IV deflection is apparent (See Fig. 2).

G. A minimum of 3 and maximum of 6 measurements are made; the number of measurements determined by visual acceptance of the curves.

H. Complete O_2 washout is not necessary between measurements. This necessitates accurate F_AN_2 measurements. A delay in repeating the test is advised if, during the preliminary air breathing phase, F_IN_2 and F_EN_2 differ by more than 5%.

4. Criteria for Acceptability of Single Breath N_2 Closing Volume Curves

The following criteria must be met for acceptability, failure to satisfy any one of these leads to rejection of the curve:

A. Mean expiratory flow after the first 500 ml is expired must equal or be less than 0.5 lps (the subject is instructed to aim for 0.4 lps).

B. Except for the first 500 ml of expiration during closing volume measurement, expiratory flow transients must not exceed 0.7 lps. Unacceptable flow transients are defined as deviation from the required flow which persists during expiration of more than 300 ml.

C. Difference between inspired and expired VC must be less than 5%.

D. Differences in VC between blows must not exceed 10%.

E. There must not be a step change in the expired N_2 concentration with continued cardiogenic oscillations after the step. The causes of such step changes are obscure but are probably not related to airway closure. If such curves are accepted the onset of Phase IV will frequently be read as the volume at which the step occurs.

5. Measurements/Calculations

Ideally on all subjects 3 acceptable tracings will be obtained. The mean of the 3 values of each measurement is taken as the final value. When only 2 readable tracings are obtained, the mean of the 2 values is used. When only one readable tracing is obtained, the subject is discarded from the series. Readers must keep a careful track of the number of individuals with 3, 2, 1, and 0 readable curves. Figure 4 depicts a sample closing volume tracing.

CLOSING VOLUME AND CLOSING CAPACITY

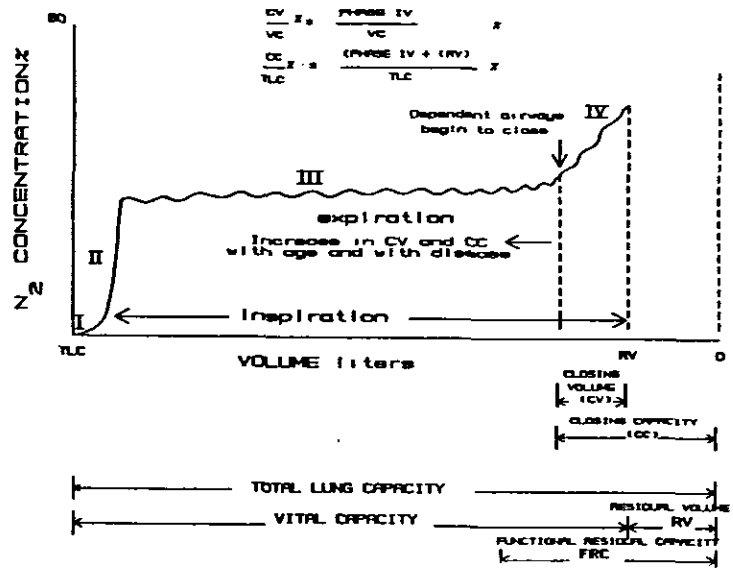

Fig. 4 - Characteristic changes in expired nitrogen concentration which occur during a vital capacity maneuver following an inhalation of 100% oxygen.

A. Closing Volume (CV)

The onset of phase IV should be determined by the best-fit line drawn by eye through the latter half of phase III. The point of final departure from this line is the onset of phase IV. In some subjects there is a sharp drop in N_2 concentration after the onset of phase IV. Occasionally this can intersect the line drawn through phase III. Under these circumstances the onset of phase IV is taken as the first definite point of departure of the N_2 tracing from the best-fit line. The closing volume is the volume from the onset at phase IV to residual volume (RV). CV is expresses as % of the expired vital capacity (VC).

B. Slope of phase III

The slope of phase III is determined by the best-fit line, between 70% VC and the onset of phase IV. The slope is reported as the angle formed by the line of best fit with the horizontal axis.

The analysis of these curves cannot always be made in a totally objective manner. On some curves in particular, the onset of phase IV is difficult to determine and when the same reader blindly reads such curves twice, there is not very good agreement between the two measurements. This appears to be due to differences between individuals, because when a subject generates such a curve, it is likely that all curves that he generated will be difficult to analyze. On the other hand, if a subject generates a curve which is easy to analyze, in all likelihood, all curves obtained from him will be easy to analyze. Obviously, curve readers will have to use good judgment and they may decide that some curves, although conforming to the criteria of acceptability, are unreadable and therefore must be rejected. It is impossible at present to establish a set of rigid rules governing such cases.

Prediction Values:

For purposes of comparison with general population studies, CV and Phase III slope values will be compared with the predictions of Buist.

Buist: Closing Volume:

CV/VC % = 0.318 Age (yrs) + 1.919 $\pm$ SEE 4.61 (MEN AND WOMEN)

Phase III Slope:

$\Delta N_2/L$ = 0.710 + 0.010 Age (yrs) $\pm$ SEE 0.43 (Men)

$\Delta N_2/L$ = 1.036 + 0.009 Age (yrs) $\pm$ SEE 0.57 (Women < 60)

$\Delta N_2/L$ = 1.777 + 0.058 Age (yrs) $\pm$ SEE 1.30 (Women > 60)

REFERENCES

Suggested Standardized Procedures for Closing Volume Determinations (Nitrogen Method), Division of Lung Diseases, National Heart and Lung Assoc. 1973

Buist, A.S. and B.B. Ross. Predicted values for closing volume using a modified single breath N_2 test. Am. Rev. Resp. Dis., 107:744-752, 1973.

Buist, A.S. and B.B. Ross. Quantitative analysis of the alveolar plateau in the diagnosis of early airway obstruction. Am. Rev. Resp. Dis., 108:1078-1087, 1973.

EXPIRATORY FLOW-VOLUME CURVE

IIb. 1. Instrumentation:

A. An Ohio 840 Rolling Bar Spirometer

B. Hewlett-Packard X-Y Recorder HP 7046A for volume-time curves.

C. Hewlett-Packard X-Y Recorder HP 7046A for flow volume curves. (slowing speed Y axis = 76 cm/sec and acceleration Y axis = 6350 cm/sec).

D. Large base flexible plastic tubing and large rubber mouthpiece. If during the performance of a forced vital capacity maneuver expired airflow is plotted against expired (or lung) volume, the resultant relationship has a characteristic configuration as depicted in Fig. 5. Expired flows increase readily to a peak and then decrease relatively linearly with decreasing lung volume. Obstructive and restrictive lung disease results in flow patterns different from the normal response (Fig. 5), providing a clear, graphical display of characteristic patterns of pulmonary disease.

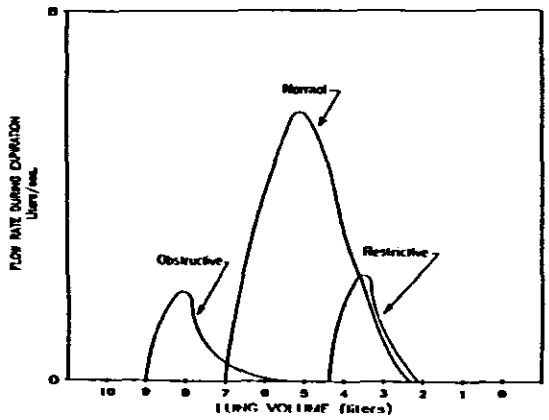

Fig 5 - Schematic representation of typical maximal expiratory flow volume curves from a normal subject and from patients with restrictive and obstructive lung disease. Airway obstruction results in low expired flows both in absolute terms and relative to the lung volume. In contrast, restrictive disease results in low flow in absolute terms, but normal or slightly high flows when corrected for lung volume.

With nose occluded, the subject is connected to the spirometer through a large rubber mouthpiece and corrugated tubing. Simultaneous monitoring of expired air flow against: a) lung volume and b) time are traced on the XY axis of individual recorders.

2. Calibration:

Initial calibration of volume is done using the 1 liter glass syringe previously checked against a 13 liter Collins spirometer. Flow rate is determined with a Fisher rotometer which has been previously calibrated against a Tissot spirometer with room air. Individual calibration will be done by the operator for each patient, using the function known on the Ohio 840 spirometer.

3. Procedure:

A. Set function knob at operate, BTPS at the appropriate setting, and piston variation knob at 5 liters.

B. With nose occluded, have subject go onto mouthpiece and breathe normally on room air.

C. Following 2-3 normal breaths, instruct subject to inspire maximally (TLC).

D. Lower pens of both recorders to contact surface and request a maximal effort of fast exhalation followed by a maximal inspiration.

E. Disconnect subject; remove nose clip; let subject relax and flush spirometer.

F. Repeat steps A-E until three acceptable curves have been obtained.

4. Criteria for Acceptability of Measured Data:

A. Inspired and expired volumes must check within 5% and duplicate curves within 5%.

B. Three acceptable curves are required.

5. Measurements/Calculations:

Measurement of maximum instantaneous flow over portions of the expiratory volume are determined by the linear distances (mm) of the excursion height, converted to volume (ℓ) with the appropriate conversion factor determined from the electrical calibration. FEV_1, FVC, and MMF will be measured as explained in "Spirometry" section. These values will be used in Studies II, IV, and V. Measurements of maximum instantaneous flows will be made on three acceptable vital capacity loops that do not vary by more than ± 5% (that is, not less than 5% of the largest EVC). Flow will be measured after a volume equal to 50% and to 75% of the EVC has been expired. $V_{max}50$ and $V_{max}75$ corresponding to: I) the largest EVC and, II) the mean V_{max} of the two or three acceptable curves (II) will be measured and recorded. V_{max} by method (I) will be used in studies I, IV, V, and by method (II) in studies II and III.

Prediction Values:

Values for VC and MEF flow measured with the rolling bar spirometer in these studies will be compared with the following predicted values of Knudson et al.

Vmax50 Table:

<25 years old 0.081 Age + 0.051 Ht - 4.975

>25 years old 0.015 Age + 0.069 Ht - 5.400

Vmax75 Table:

<25 years + .032 Ht - 2.455

>25 years old -0.012 Age + .044 Ht - 4.143

NOTE: Applies to Studies II, IV, and V - when Ohio 840 output was taped for later display and analysis. Regarding Instrumentation: add 1) 4 channel Hewlett-Packard tape recorder (multiple speed); 2) Tetronix storage oscilloscope.

3.D Add "Turn on tape recorder, identify patient and time of day," clear storage oscilloscope screen.

E.E Add "Turn off tape recorder."

Additions to Above:

Study I. FEV_1 and FVC measured from Ohio 840 records will be compared to those obtained on Collins spirometer and used for future prospective studies.

Study II. Add to above instrumentation procedures and measurement: During Study II flow and volume signals from Ohio 840 spirometer were also recorded on a Superscope 301A cassette recorder. The taped data were analyzed using a micro-processor based on an Intel 8080 system with 4 analog to digital channels and 4 digital to analog channels and a 2K circulating memory for each channel. The data was displayed on a two channel oscilloscope with cursor signal on the two channel. The operator used the cursor, under control of a basic program, to mark the curves to be analyzed.

Studies IV and V. Add to above technique description: Flow and volume from Ohio 840 spirometer was displayed on a Tetronix 411 storage oscilloscope and recorded on magnetic tape using a Hewlett-Packard 3960 instrumentation recorder at speed of 3.75 ms/sec. From the taped data played back at 15/16 ms/sec we obtained a paper record using a Hewlett-Packard X_Y_Y 7046A recorder to measure FVC, V_{50}, V_{75}, and ΔV_{50} $He\text{-}O_2$.

III. SINGLE BREATH CARBON MONOXIDE DIFFUSING CAPACITY

1. Instrumentation

Equipment required:

A. 30 liter test bag for gas containing approximately 0.2% CO, 10% He, 21% O_2, 69% N_2

B. A bag-in-box respirometer (W. E. Collins)

C. Infared CO analyzer, or gas chromatograph

D. Linear He analyzer (15% full-scale)

E. Solenoid valve for direction of expiratory volume into a 5 liter sample bag or to room air

F. Mouthpiece - large rubber

G. 9 liter Collins Spirometer

H. Gas Cylinder and regulator

I. Recording supplies - paper, pens, ink

J. Stopwatch

K. 5 liter rubber sample bags

The measurement of diffusion capacity is the rate at which CO disappears from the lung into the blood. The nature of this disappearance beginning at the initiation of inspiration is exponential with time, the slope of the curve being dependent upon the diffusivity of the CO molecule along the whole diffusion pathway from alveolus to hemoglobin molecule.

The bag-in-box system (See Fig. 6) is completely flushed and the bag filled with the test gas mixture from which a sample is analyzed. The subject is seated, nose occluded, and kymograph drum speed set at 160 mm/min. The subject inspires to TLC, holds breath, goes onto the mouthpiece, exhales to RV, then inspires to TLC as rapidly as possible and holds his breath for 8-12 secs. He then exhales rapidly to RV during which the first 800-1000 ml. of VC is expired to room air and the remainder directed to a collection bag for subsequent analysis. From the changes in gas concentration between inspired

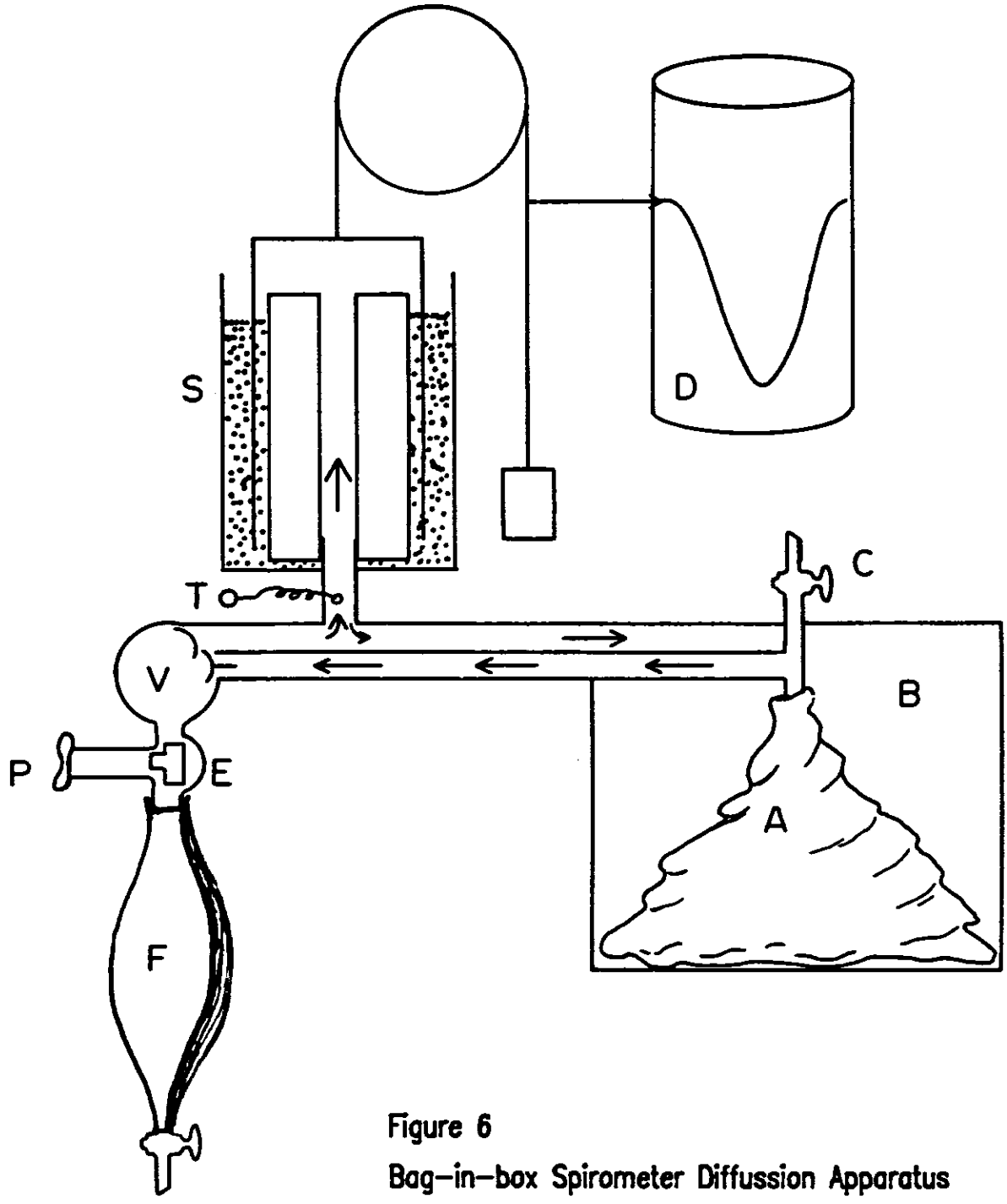

Figure 6
Bag–in–box Spirometer Diffussion Apparatus

A – 30 litre bag of test gas
B – rigid box
C – stopcock for filling A
V – solenoid valve permitting expiration into the spirometer (s) and inspiration from the bag (A) via flexable rubber tubing
E – large bore – 3 – way valve
P – mouthpiece
F – 5 litre sample bag
S – 8 litre recording soirometer
D – kymograph drum revolving 2.66 mm/sec.
T – thermometer

and expired gas and the associated spirometric tracing, the $D_L CO$ and He dilution lung volumes may be calculated.

2. Calibration

(1) Testing for leaks:

Check Spirometer weekly for:

A. Deformities in spirometer bell

B. Leaks around water seal

C. Accuracy of kymograph drum speed

D. Leaks in the 30 liter test gas bag

E. Solenoid valve operation

(2) CO and He meters

Calculation of single breath D_L requires calculations of ratios of two measurements of He concentration and two measurements of CO concentration. Since only the ratios of He and CO are important, precise measurements of either He and CO concentration is not essential.

CO meter calibration and He meter linearity procedure:

A. Scales should read zero with no power, adjust mechanical zeros as required

B. Following several hours of warm-up, flush system with room air and zero both instruments

C. Introduce sample of test gas and adjust CO analyzer gain controls to approximately 90% of full scale deflection. Thus, a slightly higher CO% (e.g., 0.3) will not read greater than 100% full scale. Once set, do not alter gain control further.

Whenever a non-linear CO analyzer is used, it is necessary to carefully construct a calibration curve from which meter

deflections can be used to determine the actual concentration of CO in the test sample. Once the calibration curve is established, the gain adjustment of the reference gas should always be set at the identical reference value.

Alternately, if CO samples are analyzed using gas chromatography, then the recorded peak heights of reference gas curves are used to establish a proportionality for determination of test sample concentrations.

With 10% He, the He meter should read 8-12% with appropriate adjustment of the gain control as required.

K. Repeat zero and test gas checks; readjust zero and upper scale deflections as necessary. Verify further with test gases of different concentrations.

3. Procedure

(1) Check depletion level of CO_2 absorber system

(2) Flush system rebreathing circuit leaving test gas bag completely evacuated

(3) Fill the reservoir balloon (bag-in-box) with test gas

(4) Seat subject and occlude nose

(5) Set kymograph speed at 160 mm/min

(6) Have subject inspire to TLC, go onto mouthpiece, exhale to RV, then inspire to TLC as rapidly as possible. Hold breath at end of inspiration for approximately 10 secs then expire forceably to RV

(7) After discarding the initial "dead space" (800-1000 ml portion) of the expired volume into room air, activate the solenoid switch and collect the remainder of the expirate.

(8) Have subject come off mouthpiece and breath room air

(9) Clamp, remove alveolar sample balloon and analyze contents.

(10) Flush rebreathing circuit thoroughly

(11) Repeat steps (1-10) following a minimum of 5 minutes before retesting to insure complete washout of CO and He from lungs. Repeat test 3 times.

4. Criteria for acceptability for single breath D_L.

Acceptable tracings will have a sharp and rapid inspiration, level hold for 8-10 seconds from the beginning of inspiration to start of sample collection. Rapid expiration of the appropriate volume will show about the same vital capacity and expired gas values from trial to trial.

5. Measurements/Calculations:

$D_L CO$ is determined according to the following equation:

$$D_L CO \text{ (ml/min/mmHg)} = \frac{VA \times 60}{(PB - 47)_t} \times \ln \frac{F_A CO_9}{F_A CO_t}$$

where:

$$F_A CO_O = F_I CO * \frac{F_A He}{F_I He}$$

where: VISTPD = volume inspired corrected to STPD

VD = assumed dead space volume of .150 ℓ

$F_I He$ = % inspired He

FeHe = % expired He ($F_A He$)

60 = # secs in one min.

Bp-47 = Barometric pressure - water vapor pressure at body temperature of $37^{o}C$.

t = time in secs of breath held

F_ICO - % inspired CO

F_ACO_t = % expired CO

ln = natural log raised to power of expression in parenthesis

Prediction Values:

For purposes of comparison with general population studies, DL values will be compared with the following predictions of Ogilvie, et al. and Rankin, et al.

Ogilvie:

DL (ml/min/mm) = 18.85 surface area - 6.8

Rankin:

DL (ml/min/mm) = 2.0474 Ht (in.) - .166 Age (Yrs) - 102.62

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HELIUM-OXYGEN FLOW VOLUME TEST

1. Instrumentation

   A. An Ohio 840 Spirometer

   B. Esterling Angus X-Y Recorder

   C. Ohio Demand Valve

   D. Large bore 3-way stopcock

   E. Appropriate tubing and connectors

   Following completion of three flow volume loops, the subject inspires four slow VC breaths of an 80% Helium/20% O_2 mixture. At RV of the fourth breath the subject is turned into a spirometer containing the same 80% Helium/20% O_2 gas mixture, and instructed to inspire to TLC followed by a maximal forced expiration. Following this maneuver, the subject returns to the He/O_2 circuit for several more breaths and the process is repeated.

2. Calibration

   Initial calibration of volume is done using the 1 liter glass syringe previously checked against a 13 liter Collins spirometer. Flow rate is determined with a Fisher rotometer which has been previously calibrated against a Tissot spirometer both with air and with the 80% Helium/20% O_2 mixture. Individual calibration will be done by the operator for each patient, using the function knob on the Ohio 840 spirometer.

3. Procedure

   A. Set function knob at operate, BTPS knob at the appropriate temperature setting, and piston variation knob at 5 liters.

   B. Have subject perform three flow volume loops (see Section 11a).

   C. Flush spirometer and fill with 80% He, 20% C_2 mixture.

D. Turn 3-way stopclock connecting subject to the inspired gas mixture via the demand valve.

E. Request four slow deep breaths to TLC expiring to RV each time.

F. At the end of expiration, turn subject into spirometer with the 3-way stopcock.

G. Request a maximal inspiration (to TLC) followed by a maximal forced expiration (to RV).

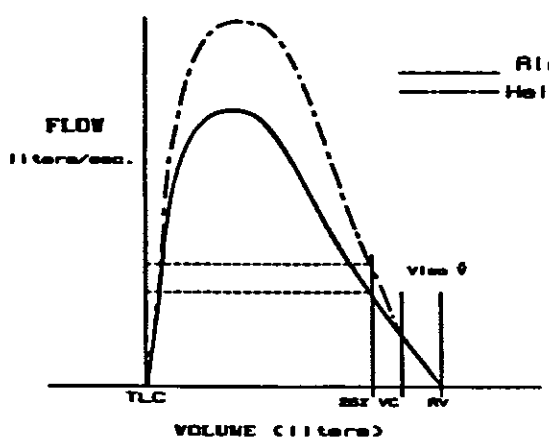
H. Return subject to He/O_2 mixture for several more breaths (while spirometer is rinsed) and repeat steps C-G.

4. Criteria of Acceptability

A minimum of three acceptable tracings are required. The EVC and IVC must correspond within 10% of each other. The agreement between the helium-oxygen curve and the curve on room air must be within 5% of each other in regard to EVC. If the curves are not identical, they are lined up at RV. If after a group of test runs there is lack of agreement in EVC, the loop that has the largest EVC, meeting the requirement of EVC/IVC being within 10% of each other, is chosen as the test run.

5. Measurements/Calculations:

The helium/oxygen curve is superimposed on the room air curve at RV (Fig. 7). The point of intersection of flow is found. The volume at which the flow rates were identical (isovolume point) on both He + O_2 air, that is, independent of density, is identified and expressed as a percent of VC. In addition, $V_{max\ 50}$ is measured both on room air and helium.



$$\Delta\dot{V}_{Max}\ He\ air = \frac{\dot{V}_{Max50}\ He - \dot{V}_{Max50}\ air}{\dot{V}_{Max}\ air} \times 100 =$$

%

Ranges: $\dot{V}iso\ V$ range 3-40% VC air

$\Delta\dot{V}_{Max50}$ He = 0-120%

Fig. 7 Maximal expiratory flow-volume curves breathing air and air He + O_2. The response to He + O_2 is expressed as the percentage of increase in flow compared to flow in air at 25 percent of VC; i.e., BC/AB x 100 = $\Delta\dot{V}_{25}$. The point where flows breathing air and He + O_2 are the same as identified and Viso $\dot{V}$ is measured from this point to RV.

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