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A PHYSIOLOGICAL RULE-BASED SYSTEM FOR INTERPRETING PULMONARY FUNCTION TEST RESULTS

by

J.C. Kunz, R.J. Fallat, D.H. McClung, J.J. Osborn
The Institutes of Medical Sciences
Pacific Medical Center
2200 Webster Street
San Francisco, California 94115

B.A. Votteri
Sequoia District Hospital
Alameda & Whipple Streets
Redwood City, California 94062

H.P. Nii, J.S. Aikins, L.M. Fagan, E.A. Feigenbaum
Heuristic Programming Project
Computer Science Department
Stanford University
Stanford, California 94305

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J.C. Kunz*, R.J. Fallat, D.H. McClung, J.J. Osborn

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H.P. Nii, J.S. Aikins, L.M. Fagan, E.A. Feigenbaum

Heuristic Programming Project
Department of Computer Science
Stanford University
Stanford, California 94305

Running Head: Rule-Based Pulmonary Function Test Interpretation

*To whom correspondence should be addressed.

ABSTRACT

We present results of using a computerized system (PUFF) for the interpretation of standard laboratory measures of pulmomary function. PUFF is now in routine use in Presbyterian Hospital, Pacific Medical Center (PMC), in San Francisco. The program produces a report, intended for patient records, that explains the clinical significance of measured quantitative test results and gives a diagnosis of the presence and severity of pulmonary disease in terms of the measured data, referral diagnosis, and patient history. "Rules", or statements of the form "IF <condition> THEN <conclusion>", are used by the physiologist and the computer system to specify the system operation. The sequence of rules used to interpret the case also specifies a line of reasoning about the case, or the detailed explanation of the interpretation of the case. The use of rules for this type of knowledge based system is taken from the results of applied Artificial Intelligence research. In a 144 case prospective evaluation, there was a 91% overall rate of agreement between the rule based system diagnoses and the diagnoses of the designing physiologist; there was a 89% rate of agreement between the system diagnoses and diagnoses of a second independent physiologist.

INTRODUCTION

PUFF was designed to model explicitly and consistently the interpretive process used by the physician. Accordingly, PUFF uses measured and predicted normal parameters, patient history, and referral diagnosis to diagnose the presence and severity of pulmonary disease. PUFF includes knowledge about pulmonary function test interpretation represented as a set of physiologically based interpretation "rules." PUFF also includes a program to execute the rules. PUFF is supported by a set of computer programs that allow on-line data entry by laboratory technicians, compute flow rates and volumes from the electrical output of the spirometer, compute predicted normal values from standard regressions equations, execute the rules and produce the reports. The support functions are not discussed further in this paper.

The medical specification of the system lies in the interpretation rules. These rules use medical terminology and a syntax similar to English. The rules include statements about physiology and medicine and the practitioner's "rules of thumb" [6]--those statements about the partly public, partly private knowledge of an expert pulmonary physiologist. Each rule is a production rule [7] of the form "IF <condition> THEN <conclusion>." The <condition> specifies physiological measurements or states, and the <conclusion> contains the corresponding physiological significance or interpretations of the measurements or states. Additional rules relate measured and derived parameters to diagnoses and recommended therapies. Rules are related so that the sequence of rules used for interpreting a case will characterize a "line of reasoning" for interpreting the particular case.

Initially the rules were proposed by our pulmonary physiologist, RJF. The process of rule development involved an iterative refinement of the proposed rules to make the rule interpretations arbitrarily close to those of the physiologist for a set of test cases. A set of 107 representative case results was selected from the files of our laboratory for retrospective analysis during rule development. Then the prospective analysis of 144 new cases was used to evaluate the consistency of the interpretations of the original physiologist, a second independent physiologist (BV), and the rules.

CHARACTERIZATION OF THE MEDICAL DOMAIN

This section presents an overview of the pulmonary physiology and the diagnostic concepts represented in the PUFF system.

Pulmonary function testing routinely involves measurement of flows and volumes during a breathing maneuver in which the patient makes a maximal inspiration and a forced exhalation. This procedure indicates the capacity of the patient to take in a large inspired volume (Inspired Vital Capacity), the rates at which air can be forcibly exhaled (forced expired volume in 1 second; maximum mid-expiratory flow), and the volume of air which can be forcibly exhaled (forced vital capacity). From this maneuver, the airway flow and the integral of flow are routinely plotted as the "flow-volume loop". Measures of lung volumes by plethysmography yield residual volume and total lung capacity. In addition, there is a test to determine the diffusivity of small amounts of inhaled CO into the blood.

Interpretation of standard pulmonary function tests involves identifying the presence of disease and determining its severity [10,11]. Initially, we limited our efforts to identifying Obstructive Airways Disease (OAD: indicated by reduced flow rates during forced exhalation), Restrictive Lung Disease (RLD: indicated by reduced lung volumes), and alveolar-capillary Diffusion Defect (DD: indicated by reduced diffusivity of inhaled CO into the blood). We define four levels of severity for each disease type. Obstruction and restriction may exist concurrently, and the presence of one mediates some indications of the other. The system recognizes three subtypes of airway obstruction: asthma, bronchitis, and emphysema. In the Pulmonary Function Laboratory at PMC, about 50 quantitative results are calculated from measurements of lung volumes, flow rates, and diffusion capacities. In addition to these measurements, the physician uses graphs of patient volume and flow measurements during test breathing maneuvers ("flow volume loop"), patient history, and referral diagnosis, in interpreting the test results and diagnosing the presence and severity of pulmonary disease. Future work includes implementing interpretation of blood gas measurements, analysis of neuromuscular disease, and comparison of previous with current test results.

Predicted Normal Values

Diagnosis of pulmonary function test results is routinely done by comparing measured values and predicted normal values. Predicted normal values for a patient are calculated from regression equations based on patient height, age, and sex [5,10,11]. Figure 1 lists the predicted normal parameters used by the interpretation system. In general, PUFF uses the standard convention of expressing a measured parameter value as a percent of the predicted normal value.

Physiological Interpretation of Measured Values

This section gives an overview of the physiologic knowledge incorporated in PUFF, and it discusses how the program makes conclusions. TLC, RV, and FVC are compared with predicted normal values to determine whether lung volumes are normal. If measured TLC, RV, and FVC are near predicted values for the patient, then lung volumes are normal. If RV exceeds 140% of normal and if TLC is normal or elevated, then overinflation, possibly caused by OAD, is recognized. Air trapping is indicated if the observed RV/TLC ratio is greater than the predicted by more than 5%.

Evidence of reduced expiratory flows in the presence of normal or reduced FVC indicates airway obstruction. In addition, the severity of any obstruction is assessed in terms of the reduction of peak flow, or the degree to which the FEV1/FVC ratio differs from the prediction. The mid-flow of the expiration is evaluated by comparing MMF with its predicted value. The FEV1/FVC ratio and MMF parameters are dependent on the FVC, since patients with a low FVC will normally have lower flows. For this reason, less stringent criteria are used for judging flows accompanying lower forced vital capacities. Finally, a measure of the slope of the flow-volume loop is also used to indicate obstruction. Physiologists routinely use a somewhat subjective measure of slope of the flow-volume curve late in the forced exhalation as an indicator for OAD. Low slope, or comparatively low flows at the end of exhalation, indicates the presence of obstruction. The slope measure (F50-F25)/FVC, where F25 is the flow when 25% of the FVC is still to be exhaled and similarly for F50, was chosen as the most useful indicator of the slope perceived by the physiologist and a useful quantitative indicator of OAD. A conflict resolution procedure determines the concluding degree of OAD, i.e. the severity of obstruction, from the three indications.

Values taken after bronchodilation are interpreted to assess the degree of reversibility in the airway obstruction. Bronchodilation will increase exhaled flow rates if OAD is reversible. Decrease in airway resistance is taken as independent confirming evidence for significant reversibility, and the degree of reversibility is confirmed or adjusted depending upon the change in resistance following bronchodilation.

Bronchitis is typically diagnosed from presence of cough, sputum production, and obstruction. Asthma is diagnosed by the physician using patient history, and possibly laboratory tests. PUFF uses patient history, presence of OAD, and response to bronchodilation to make its diagnosis. Continued use of bronchodilating agents is suggested when the patient with a history of asthma and the presence of OAD shows good response to bronchodilation. Asthma is in a refractory state if there is a history of asthma but bronchodilators have little or no effect.

Restrictive lung disease is characterized by reduced lung volumes. Simple restriction is defined by the reduction of TLC by 20% or more (below predicted). Since obstruction tends to cause elevation of lung volume, restriction is considered to have increased severity if lung volume is reduced in the presence of obstruction.

The diffusion capacity (single breath test) is used to diagnose the presence of a diffusion defect and emphysema. Emphysema is diagnosed by the presence of OAD, diffusion defect, and elevated TLC or elevated RV/TLC ratio. In the case of marginally reduced TLC measurement by the somewhat unreliable CO diffusion test method, a comment is made about the possible likelihood of emphysema. A measurement of TLC by a more accurate method (body plethysmography) is recommended in order to make a definitive diagnosis.

Diagnosis and referral diagnosis are compared to make conclusions about: the effect of smoking on OAD, the likelihood of emphysema, the sufficiency of pulmonary causes for reported dyspnea, and the need for trial or continued use of bronchodilating drugs.

METHODS

1. Methods of the study

Instrumentation

The measurement system includes an Ohio 840 Rolling Drum Spirometer, a Warren-Collins whole body plethysmograph, and a Varian P3 gas chromatography system for use in measurement of diffusion capacity for carbon monoxide (CO).

The lab technician uses an on-line computer system for automatic collection and analysis of flow-volume spirometry data. The technician manually enters patient history (name, age, sex, height, smoking history, sputum production, referral diagnosis) and hand-calculated plethysmography and diffusion capacity data. The computer collects data during the forced vital capacity maneuver, and it then calculates the spirometry results. It presents a display (to the technician) with a plot of the flow-volume loop and a table with all of the entered, calculated, and predicted data. The technician accepts the data if the maneuver was properly performed; otherwise the maneuver is repeated.

Patient Material

Patient records were selected from the files of our pulmonary function test laboratory. Cases were selected to be representative, but excluding those of known severe neuromuscular disease and those made with poor patient effort. A total of 107 cases were included in the data set for rule development. Prospective evaluation of the interpretation rules was performed on a second set of 144 cases, 56 of which were female and 88 of which were male. Figure 2 summarizes the referral diagnoses of this group.

2. Rule Validation and Evaluation

The rule set was developed and validated through an iterative process in which the first MD-physiologist (RJF) proposed rules which were then applied to the patient data and successively changed following evaluation of interpretations by the rules. For this development process, the physiologist first reinterpreted the 107 cases. He assigned to each case the presence and severity (none, mild, moderate, moderately severe, severe) of OAD, RLD, and DD, carefully reexamining his original diagnosis prior to entering the case into the retrospective data test set, modifying the original diagnosis if he considered it appropriate. If OAD was diagnosed and if indications for one or more subtypes (asthma, bronchitis, emphysema) were also present, OAD subtypes were also reported.

Having reached arbitrarily good agreement in the retrospective comparison of MD and rule interpretations, we then prospectively compared the diagnoses of the physiologist with diagnoses by a second pulmonary physiologist (BV) and by the rules. With the exception that BV never saw the PUFF interpretation rules, both physiologists had the same information available to them to make interpretations--the quantitative results of the pulmonary function tests, the flow-volume plot from the forced vital capacity maneuver, and an abbreviated summary of each patient history. At a later date, they reviewed their diagnoses with systems staff to eliminate obvious clerical errors.

3. Implementation (PUFF)

The PUFF interpretation rules used the following information (see Fig. 2):

1. Abbreviated patient history.

2. Referral diagnosis: Normal, Asthma, Emphysema, Chronic Obstructive Pulmonary Disease (COPD), Obstructive Airways Disease (OAD), Restrictive Lung Disease (RLD), cardiac abnormality, bronchitis, dyspnea, carcinoma, fibrosis, neuromuscular disease.

3. Measured and predicted normal flow-volume curve parameters. Measurements following inhalation of bronchodilators may also be available.

4. Body plethysmograph measurements and predicted normal values, including lung volumes and resistance. Measurements following bronchodilation may also be available.

5. Measurement of CO diffusion capacity (single breath test).

The interpretation report included:

1) Interpretation of the physiological meaning of the test results including:

   a.) consistency of multiple indications for airway obstruction;

   b.) response to bronchodilators if used;

   c.) limitation on the interpretation because of bad or missing data.

2) Summary of clinical findings including:

   a.) applicability of the use of bronchodilators:

   b.) relation between test results;

   c.) consistency of the findings and referral diagnosis.

3) Interpretation summary: Diagnosis of the presence and severity of abnormality of pulmonary function.

PUFF was implemented on the PDP-10 in a version of the MYCIN system [1] that was designed to accept a new rule set. After demonstrating the clinical promise of the rule-based interpretation system, we implemented PUFF on the PDP-11 in BASIC. In the PDP-10 implementation, rules were processed in a "goal-directed" fashion. Thus, to initiate system operation, a rule had to be written in the general form "IF degree of OAD is known and... THEN print an interpretation." Starting with this initiating rule, the system processed rules that defined the presence and severity of OAD; these rules in turn invoked rules to interpret actual physiological measurements. Once degree of OAD was finally determined, the system processed succeeding clauses of the initiating rule to diagnose the presence and severity of other diseases such as RLD. In the PDP-11 implementation, rules are processed in a "data-directed" fashion. Thus, the system obtains test measurement data, makes direct interpretations about the diagnostic significance of the data, and then interprets the individual disease diagnoses to make a summary diagnosis. In the MYCIN-based implementation, rules were entered into the system and interpreted by a version of the MYCIN interpreter. These rules were recoded into executable BASIC statements for the PDP-11 implementation.

RESULTS

1. Rule Set

Two typical rules are shown in Figure 3. The first example rule gives a simple physiological interpretation of a measured test result. The measured diffusion capacity of CO is normalized by the predicted capacity for a normal patient to determine the "DLCO" of the rule. If this computed parameter is less than 80%, the rule indicates that there is a diffusion defect of a severity determined by the actual value of the normalized parameter. If the value of the measurement is abnormal, i.e. if the concluded degree of the disease is 'mild' or greater, then the interpretation of the conclusion is included in the output report. A statement about the concluded severity of the disease is also included in the interpretation summary. Conclusions about presence and severity of disease are maintained for internal system use. The second example rule relates the interaction between conclusions about two disease states and a measurement. Degree of obstruction, degree of diffusion defect, and measured TLC by body plethysmography (TLCB) are compared to identify the possible presence of emphysema. Similar rules interpret the physiological significance of other measured test results, explain findings about the relation of diagnosis to patient history, and recommend additional tests or therapy.

2. Retrospective Data Analysis

During the process of characterizing the data base statistically and developing the rule set for interpretation, the director of our pulmonary laboratory modified his diagnosis on some of the 107 retrospective cases. The largest number (14) of changes in diagnosis were changes from an original diagnosis of pulmonary function "Within Wide Limits of Normal" to a diagnosis of obstruction or restriction of a mild degree. Explanations for the original normal diagnoses were either that he had felt that nothing was to be gained by confronting the patient with a slightly abnormal diagnosis, or he had known the patient and had made the diagnosis on background information rather than on measured data. In other cases, he made explicit his previously implicit diagnosis of diffusion defect. In five cases, a mild restriction diagnosis was added for patients with OAD. Three data errors were found, and three OAD subtype changes were made. The remainder of the changed diagnoses were changes of degree of severity by one degree--e.g., from mild to moderate. The changes in severity were made because systematic analysis of data permitted different conclusions than did the analysis of individual cases in isolation.

3. Prospective Data Analysis

The results of the comparison of the interpretation rules with the physiologists' interpretations are summarized in Tables 1-2. The rate of agreement of diagnosis between MD-2 and MD-1 is defined as the number of cases in which the diagnoses are the same divided by the total number of cases for which diagnoses were made. Table 1 shows agreement between independent diagnoses made by the MD-pulmonary physiologists, and by the rules. Diagnoses are "the same" in the comparisons (Tables 1-2) if both report the presence of the disease or if both report the absence of the disease. Comparison is made independent of the degree of severity of the disease reported in the diagnosis. Results show that the overall rate of agreement between the two physiologists on four diagnoses (Normal, OAD, RLD, DD) for 144 cases was 89%. The first physiologist agreed with the diagnoses by the rule set (which he created) in 91% of the cases.

Table 2 compares "close" agreement in severity of the disease in the diagnoses made by the two MDs and by the rules. "Close" is defined as differing by at most one degree of severity. Thus, two diagnoses of severity, mild (degree=1) and moderately-severe (degree=3) are not close, while normal (0) and mild (1) are close. In 94% of the 144 cases, the second MD diagnosed the severity of OAD within one degree of the severity diagnosed by the first MD. The rules were "close" in diagnosis of severity of OAD in 99% of these cases. The severity of OAD diagnosed by the rules was "close" to that diagnosed by MD-2 in 94% of the cases.

2. Example PUFF report

A representative PUFF report, including summary patient history, measured results, and the PUFF interpretation, is shown in Figure 4.

Diagnosis (Dx)	Number of Cases		Percent Agreement in Diagnoses		
	Dx by MD-1	Dx by MD-2	MD-2: MD-1	Rules: MD-1	Rules: MD-2
NORMAL	31	26	0.92	0.95	0.92
OAD	79	85	0.86	0.89	0.89
RLD	52	45	0.92	0.94	0.89
DD	53	35	0.83	0.87	0.79
TOTAL	144	144	0.89	0.91	0.87

Table 1. Percentage agreement in independent diagnoses by two MD-physiologists with each other and with the rules. A total of 144 cases were interpreted prospectively for each of the four diagnoses. Some abnormal cases had more than one pathological condition.

Diagnosis (Dx)	Number of Cases		Percent Agreement in Diagnoses within 1 degree of severity		
	Dx by MD-1	Dx by MD-2	MD-2: MD-1	Rules: MD-1	Rules: MD-2
OAD	79	85	0.94	0.99	0.94
RLD	52	45	0.92	0.97	0.85
DD	53	35	0.90	0.91	0.85
TOTAL	144	144	0.92	0.95	0.88

Table 2. Percent agreement within 1 degree of severity of diagnoses by two MDs. Tables 1-2 are taken from prospective analysis of the same 144 cases.

DISCUSSION

Newell and Simon [8] suggest the possibility of a close and perhaps basic resemblance between human program organization and production system organization. Our experience was that the production rule formalism provided an extremely powerful technique for developing the pulmonary function interpretation system. The set of interpretation rules was used both by the physiologist during rule development and by the computer scientists for system implementation. The initial system was developed during an eight-week period. The single-rule specification allowed for far more rapid and amicable system development than any that the participants had previously experienced.

Ellis [3] describes a computer program to interpret pulmonary function test studies. Our work extends his representation of the clinical problem in ways we have found to be important and useful, including the comparison of diagnosis with referral diagnosis and patient history; analysis of early, middle, and late portions of the flow-volume loop; consideration of the interaction between OAD and RLD; and dependence of FEV1 upon FVC. In addition, use of production rules provides a mechanism for defining the interpretation system that is equally valuable to both clinicians and implementing computer scientists. Finally, since the system was designed with both the sophisticated flexibility of the PDP-10 implementation and the economy of the straightforward PDP-11 implementation, PUFF researchers and clinical users can continue to have fruitful interactions.

The PUFF system is now in routine use at the PMC hospital. Each report is read by an MD. The staff physicians are free to accept, modify or reject the PUFF interpretations. More than half of the reports are accepted without change; they are signed and entered into the patient record. Most of the remaining reports require simple additional comments about tests that are not yet part of the PUFF interpretation system (e.g., arterial blood gases), the interpretation of measurements from patients with neuromuscular disease, or comments about the relation of current to previous test results. A few reports require correction of some point in the PUFF interpretation. The consistency and detail of the explanation of results has proved to be an attractive service to the staff.

The use and implementation of production rules for this domain were achieved using techniques of applied artificial intelligence research [9,1,2]. These techniques provided the possibility of direct computer manipulation of the clinical knowledge represented symbolically by the physiologist. In addition, the symbolic manipulation allows elucidation of a line of reasoning, or the sequence of judgments used to interpret individual measurements and to form diagnoses based on these judgments. This explainable reasoning process is appropriate for analysis of individual patient cases, whereas an analytical approach, such as linear discriminant analysis, is more useful for groups of cases. The clinician need not simply accept or reject the conclusion of an analytical manipulation but can examine the components; wherein lies the credibility of the system.

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Airway resistance	(RAW)
Diffusion capacity for CO	(DLCO)
Forced expired volume in 1 second	(FEV1)
Forced vital capacity	(FVC)
Inspired vital capacity	(IVC)
Maximum mid-expiratory flow	(MMF)
Residual volume	(RV)
Total lung capacity	(TLC)

Figure 1. Parameters whose predicted normal values are used in PUFF.

Referral Diagnosis	Number
Normal	21
OAD	20
Cardiac case	20
COPD*	11
Tumerous growth	10
None	7
RLD	5
neuromuscular	3
Miscellaneous	47
TOTAL	144

Figure 2. Distribution of referral diagnoses in the pulmonary function test results used for prospective evaluation.

* COPD is chronic obstructive pulmonary disease.

```
IF  (0 < DLCO < 80)
THEN "Low diffusing capacity indicates loss of alveolar
capillary surface which is "
        IF (70 <= DLCO < 80) "mild"
        IF (60 <= DLCO < 70) "moderate"
        IF (      DLCO < 60) "severe"


IF [(degree(OAD)>=mild) and (degree(Diffusion Defect)>=mild) and
        (TLCB>=110)]
THEN "The low diffusing capacity, in combination with obstruction and
a high Total Lung Capacity, would be consistent with a diagnosis of
emphysema."
```

Figure 3. Typical PUFF interpretation rules. Conclusions are made for internal system use and for inclusion in the summary. The first rule would conclude Degree(diffusion defect)=mild if DLCO = DLCO-measured/DLCO-predicted = 75%. TLCB is the measured TLC by body plethysmography, normalized by normal predicted TLC for the patient.

PRESBYTERIAN HOSPITAL OF PMC
CLAY AND BUCHANAN, BOX 7999
SAN FRANCISCO, CA. 94120
PULMONARY FUNCTION LAB

DOE JANE
P336666.
DR. SMITH, JOHN

5S2

WT 56.7 KG, HT 166 CM, AGE 58 SEX F
SMOKING 40 PK YRS,CIG 1.0 PK QUIT 0,PIPE 0 QUIT 0,CIGAR 0 QUIT 0
DYSPNEA-W/MILD-MOD. EXER, COUGH-NO , SPUTUM-LT 1 TBS, MEDS-YES
REFERRAL DX-CORONARY ARTERY DISEASE , PRE OP
**TEST DATE 10-26-78

		PREDICTED (+/-SD)	OBSER	(%PRED)	POST DILATION OBSER	(%PRED)
INSPIR VITAL CAP (IVC)	L	3.1(0.4)	3.0	(98)		
RESIDUAL VOL (RV)	L	2.1(0.3)	3.0	(140)	3.5	(166)
TOTAL LUNG CAP (TLC)	L	5.2(0.7)	6.0	(116)	6.5	(125)
RV/TLC	%	40.	49.		53.	
FORCED EXPIR VOL(FEV1)	L	2.6(0.3)	2.1	(81)	2.1	(84)
FORCED VITAL CAP (FVC)	L	3.1(0.4)	2.9	(96)	3.0	(98)
FEV1/FVC	%	83.	70.		71.	
FORCED EXP FLOW 200-1200	L/S	4.2(0.8)	4.5		4.4	
FORCED EXP FLOW 25-75%	L/S	2.9(0.7)	1.5		1.5	
FORCED INS FLOW 200-1200	L/S	2.9(0.6)	2.9		2.9	
AIRWAY RESIST(RAW)	(TLC= 6.0)	1.1(0.5)	1.6	(HIGH)	1.4	
DF CAP-HGB=14.4	(TLC= 5.3)	25.	17.2	(68)	(69%IF TLC= 5.2)	

****

INTERPRETATION: Elevated lung volumes indicate overinflation. In addition, the RV/TLC ratio is increased, suggesting a mild degree of air trapping. Forced vital capacity is normal but the FEV1/FVC ratio is reduced, suggesting airway obstruction of a mild degree. Reduced mid-expiratory flow indicates mild airway obstruction. Obstruction is indicated by curvature in the flow-volume loop of a small degree. Following bronchodilation, the expired flow shows slight improvement. This is confirmed by the lack of change in airway resistance. The low diffusing capacity indicates a loss of alveolar capillary surface, which is moderate.

CONCLUSIONS: The low diffusing capacity, in combination with obstruction and a high total lung capacity would be consistent with a diagnosis of emphysema. The patient's airway obstruction may be caused by smoking. Discontinuation of smoking should help relieve the symptoms.

PULMONARY FUNCTION DIAGNOSIS:
1. Mild Obstructive Airways Disease.
   Emphysematous type.

Robert Fallat, M.D.

Figure 4. Sample PUFF report.

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