American Thoracic Society Pulmonary Function Laboratory Registry Newsletter

Edited by Neil MacIntyre, MD

CLSI Guidelines

The Clinical and Laboratory Standards Institute (CLSI – formerly NCCLS, The National Committee for Clinical Laboratory Standards) is a nationally recognized laboratory standards setting organization. They have recently published standards for respiratory service operations that are designed to improve processes and help laboratories meet regulatory and accreditation requirements. The document, “Application of a Quality Management System Model for Respiratory Services; Approved Guideline – Second Edition”, is available through the CLSI website www.clsi.org.

The Foreword to the document is as follows: “In the present environment of limited resources, it is expected by those who fund, receive, and provide healthcare services that quality is integral. This CLSI document (HS4-A2) introduces the path of workflow that is, the processes that transform a request for a respiratory-related service or patient assessment, performing the requested intervention or test, evaluating the outcome of the intervention or interpreting the results, and providing the information to the clinician or practitioner coordinating the patient care.”

Much of the Guideline is based upon the current editions of GP26, HS10, American Association for Respiratory Care (AARC) clinical practice guidelines, and American Thoracic Society (ATS)/European Respiratory Society (ERS) statements. The documents are consistent with the International Organization for Standardization (ISO) and The Joint Commission (formerly JCAHO) requirements as well.

With regard to Pulmonary Function Laboratories, a review of the Guideline in AARC Times (August 2007) reports: “Based on the current literature, it appears that a large number of pulmonary function laboratories need to establish quality control (QC) programs as an initial step and then gradually move toward a quality system. The 2005 ATS/ERS documents (www.thoracic.org) should serve as primary resources along with the 2005 ATS Pulmonary Function Laboratory Management and Procedure Manual. The 2005 Guideline clearly outlines the technologist’s role in QC and the need for a manual of procedures containing: calibration procedures, test per-

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**DLCO Quiz**

A patient is having the lung diffusing capacity for CO (DLCO) measured and the test volume and gas concentrations tracings are depicted in the figure. The CO and tracer gas measurements are made between the two dashed lines (“sample volume”).

What can be said about the resulting DLCO calculation in this patient:

A. It will be accurate         C. It will be spuriously high
B. It will be spuriously low    D. It will be in proportion to a spuriously high alveolar volume

For answer and discussion, go to the end of the newsletter.

**Spirometry and DLCO Reproducibility**
(adapted from MacIntyre NR, Chest 2007;132:367)

The American Thoracic Society – European Respiratory Society (ATS/ERS) pulmonary function task force has addressed interpretation standards (Pellegrino R et al. Eur Resp J 2005;26:948) and their recommendations are based upon the coefficient of variation (CV – the standard deviation divided by the mean of multiple measurements) of the reference or baseline value. Two times the CV gives a range that encompasses 95% of those measurements (95% confidence interval or 95% CI). For a single determination of normal-
A Standard Pulmonary Function Report?
Robert Crapo, MD

At their next meeting, the Lab Proficiency Standard Committee will consider whether to develop a standard report format for pulmonary function testing. Our interest was stimulated by two papers looking at how data are displayed and how the display may influence interpretation. Elling reported that clinical investigator decisions were affected by how the data were displayed. Other authors have emphasized the importance of design on medical record data. For example Wyatt and Wright emphasized the importance of organizing medical records so data are displayed in a way that helps rather than hinders physicians making decisions.

In our laboratory, Robert Jensen, PhD and I have evaluated thousands of pulmonary function tests from laboratories around the world. Some of the reports we’ve seen have displays that make it very easy for us to establish test quality and interpret the data; some do not.

The ATS Laboratory committee has been focused for some time on assuring the quality of test instrument and the procedural aspects of the tests. We think those are now more settled and we can now turn our attention to assuring the displays minimize interpretative errors.

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formance procedures, calculations, criteria, and reference values source. There should be defined actions to be taken when "panic" values are observed. Logbooks should be in place for daily calibration, corrective action, system hardware, or software upgrades. The Guideline also defines the role of mechanical and/or biological controls for each test modality. Biologic QC incorporates the testing of healthy laboratory personnel to establish mean and standard deviation for that individual on a given piece of equipment. In addition, the Guideline makes recommendations for technologist competency and feedback. Feedback should be available that addresses:

- Information concerning the nature and extent of unacceptable maneuvers and non-reproducible tests

- Corrective action the technologist can take to improve the quality and number of acceptable maneuvers

- Positive feedback to technologists for good performance

- Comments regarding system set-up and reporting results.”

AARC Times concludes: “Pulmonary function laborato-

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Spirometry and DLCO reproducibility
(adapted from MacIntyre NR, Chest 2007;132:367)

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abnormal in an individual patient, an abnormal test is defined as being outside of the 95% CI from a reference population. For a change in a measurement either over time or as a response to an intervention, the ATS/ERS task force has made recommendations based upon published week to week CVs for various tests. In an individual, the ATS/ERS task force states that the FEV1 would have to change 12%-15% to be considered a “signal” outside the range of “noise”. For the DLCO, they state that a change would have to exceed 6 ml/min/mmHg to be considered significant. Importantly, smaller signals than these can be detected in clinical trials or population studies by making measurements on multiple patients (sample size) to create a 95% CI around the signal.

In the August issue of Chest, Jensen and colleagues assessed instrument and patient variability and significantly added to our understanding of pulmonary function testing variability and went on to demonstrate how this variability can have profound effect on clinical trial design (Jensen et al. Chest 2007; 132:388 and 132:396). In general, they found that technical performance of modern PFT instruments was quite good with FEV1 (and vital capacity) performance well within ATS/ERS guidelines. They also found that the CVs for the FEV1 and DLCO with repeated patient testing (5.12%-8.48% for FEV1; 9.86%-19.66% for DLCO) were lower than the week to week variability cited by the ATS/ERS review noted above.

There are implications from these studies for clinicians who are usually asking one of two questions from pulmonary function testing: Is the patient outside the normal range? Has function changed? The Jensen results suggest that the current generation of pulmonary function devices have as good or better instrument variability as the earlier devices that were used to generate the commonly used reference equations. Importantly, the lower variability for FEV1 and DLCO over multiple weeks observed by Jensen et al. as compared to the ATS/ERS review suggests that smaller changes over time than those recommended by the ATS/ERS might be considered significant in carefully controlled laboratories such as the one in this study.

There are implications from these studies for clinical researchers and trial designers as well. Researchers are usually asking one question: Does the intervention being studied affect pulmonary function? An important signal in an individual, however, may not be outside the testing variability or noise. To address this, multiple, repeated measurements are required to characterize the signal variability and statistically compare it to the baseline. In a clinical trial, these repeated measurements, usually in multiple patients, are termed the sample size. In general, the smaller the signal or the larger the noise, the more repeated measurements are needed and the larger the sample size required to detect the signal. The Jensen analysis puts this into context for studies using FEV1 and DLCO. Specifically, the data show that several fold changes in sample size may be required to detect a signal if there if using instruments and procedures with large variability characteristics. The Jensen results also emphasize that standardizing equipment and procedures in a clinical trial can also help reduce inter-device and inter laboratory sources of variability.
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ries are ultimately responsible for the quality of data released for each individual tested regardless of the current regulatory environments. Poor quality testing leads to misdiagnosis, misclassification of disease severity, and treatment errors—all of which can potentially increase health care costs and patient anxiety. Achieving quality standards yields consistent, accurate, and reliable results. It also reduces medical errors while meeting customer requirements. In some countries, it has proven to be the method for successful governmental and accreditation assessment.”

PFTs and the ACCP Meeting

The annual meeting of the American College of Chest Physicians will take place in Chicago from Oct 20-25 2007. Included in the program are sessions on pulmonary function testing methods, pulmonary function testing interpretation, pulmonary physiology, exercise testing, and PFT coding. A special highlight is a series of simulator labs on pulmonary function testing. For more details, go to www.chestnet.org.

DLCO Quiz answer

B. It will be spuriously low

but as can be seen from the tracer gas concentrations in this patient, the sample gas volume is contaminated by dead space gas (i.e. the tracer gas has not yet reached a plateau during gas sampling). As a consequence the measured CO will be an overestimate of alveolar CO because it is contaminated with the inhaled CO in the dead space. CO uptake (DLCO) will thus be underestimated (Choice B is correct and Choices A and C are incorrect). Tracer gas measurements will also have dead space contamination in this patient and be spuriously high. This will result in an underestimation of alveolar volume and thus Choice D is incorrect. Moreover, because alveolar volume is used in the calculation of DLCO, the spuriously low alveolar volume will further inappropriately lower the DLCO.

Most modern DLCO devices can provide a graphical display of exhaled gas concentrations to assure that dead space gas is not present in the alveolar sample. The most recent ATS/ERS guidelines have suggested that if these graphical displays are available, the technicians should adjust washout volume to assure adequate dead space clearance and accurate alveolar gas sampling. Physician interpreters should be aware of this potential problem in their interpretations.

In most patients, this 750 ml recommendation is reasonable but as can be seen from the tracer gas concentrations in this patient, the sample gas volume is contaminated by dead space gas (i.e. the tracer gas has not yet reached a plateau during gas sampling). As a consequence the measured CO will be an overestimate of alveolar CO because it is contaminated with the inhaled CO in the dead space. CO uptake (DLCO) will thus be underestimated (Choice B is correct and Choices A and C are incorrect). Tracer gas measurements will also have dead space contamination in this patient and be spuriously high. This will result in an underestimation of alveolar volume and thus Choice D is incorrect. Moreover, because alveolar volume is used in the calculation of DLCO, the spuriously low alveolar volume will further inappropriately lower the DLCO.

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