Sleep Tools

Ralph Waldo Emerson once wrote, “All the tools and engines on earth are only extensions of man’s limbs and senses.”1 Tools born from the marriage of health and computer sciences have tremendously extended both our reach and sight. In sleep medicine, computerization has long boasted great promise. That promise is at last long reaching fruition. Perhaps the greatest attraction of computerization in sleep medicine relates to data reduction. From the very beginning, sleep specialists had to devise rules in order to summarize the hours of data and miles of paper (now megabytes of disk files). On average, it takes a well-trained polysomnographic technologist and polysomnographer several hours to distill a sleep recording to the essence required for clinical purposes. As sleep medicine grows, so does the pressure to develop more efficient tools for recording and reducing data.

As with any tool, computerized sleep recording-analyzers present both advantages and disadvantages. Automation speeds the process, thereby creating efficiencies. However, automation often removes us further from the actual data. During development, these tools are, in engineering terms, “benchmarked.” This may be accomplished by using specific “test data sets” or specific, well-defined test sample problems. In evidence-based medicine lingo, these would represent the sample on which a system is validated. Furthermore, the sample composition and characteristics define the population to which the results may be generalized. For example, the sensitivity and specificity for detecting obstructive sleep apnea syndrome (OSAS) may differ when a system is tested on young adults compared to elderly, patients with heart disease compared to otherwise healthy individuals, or patients with insomnia compared to patients with excessive sleepiness. Often, differences are subtle, making little difference in outcome; however, in the clinic we do not play the odds. Accurate information is needed in each individual case to ensure that treatment decisions are made rationally. Thus, it is essential for the craftsman to understand the limitations of his or her tools.

In this issue of CHEST (see page 1387), Cirignotta and colleagues provide an example of a computerized sleep system shortfall. MESAM (MAP; Martinsried, Germany) is a widely used, well-engineered cardiopulmonary sleep recording-analyzer. It can detect, with relative accuracy, desaturation events in patients afflicted with OSAS who do not have clinically significant cardiopulmonary disease (ie, the “benchmark” is non-complicated OSAS). Cirignotta and colleagues provide examples where accuracy is compromised—specifically, when the device is used to evaluate what they call “complicated” OSAS. Furthermore, the authors probe the underlying polysomnographic features that interact with the detection algorithm producing this problem. It is precisely this type of approach that provides useful guidance to further develop the tool. It also highlights the need for benchmark test data sets to include “complicated” OSAS. This is especially the case for computerized polysomnographic and sleep cardiopulmonary recorder-analyzer validation because these tools are gaining popularity and becoming more widely used by individuals with less expertise.

In summary, computerized polysomnographic and sleep cardiopulmonary equipment can be a very effective tool and is extending the reach of sleep medicine. However, it has shortcomings. As with any tool, a skilled user must understand how that tool functions and be aware of its limitations. Recognizing the limitations of a tool is often the first step to developing a better tool. Not being aware of the limitations of a tool can lead to its misapplication, thereby posing a hazard. As Czech novelist Milan Kundera wrote, “A worker may be the hammer’s master, but the hammer still prevails. A tool knows exactly how it is meant to be handled, while the user of the tool can only have an approximate idea.”2

Max Hirshkowitz, PhD
Amir Sharafkhaneh, MD
Houston, TX

DR. HIRSHKO WITZ IS ASSOCIATE PROFESSOR, DEPARTMENT OF MEDICINE, DEPARTMENT OF PSYCHIATRY, AND DR. SHARAFKHANEH IS ASSISTANT PROFESSOR, DEPARTMENT OF MEDICINE, VETERANS AFFAIRS MEDICAL CENTER AND BAYLOR COLLEGE OF MEDICINE, SLEEP DISORDERS AND RESEARCH CENTER.

Correspondence to: Max Hirshkowitz, PhD, Sleep Disorders and Research Center, VA Medical Center 116A, 2002 Holcombe Bled, Houston, TX 77030-4298, e-mail: maxh@bcm.tmc.edu

REFERENCES


Asymptomatic Respiratory Infection With Chlamydia pneumoniae

What Does It Mean?

One of the distinguishing characteristics of members of the genus Chlamydia is the ability to cause prolonged, often subclinical infection. It has been recognized for years that the majority of genital
infections with Chlamydia trachomatis are asymptomatic, especially in women.\(^1\) It is also recognized that asymptomatic C trachomatis infections are not trivial; they can be associated with significant sequelae.\(^2\) In this issue of CHEST (see page 1416), Miyashita et al add to the growing number of studies that demonstrate that Chlamydia pneumoniae is also capable of causing asymptomatic infection, but in the respiratory tract. The data presented by Miyashita et al are not new but represent the largest prospective evaluation of asymptomatic infection presented thus far. They screened 1,028 healthy, asymptomatic adults over a 6-year period by obtaining nasopharyngeal swabs for C pneumoniae culture and polymerase chain reaction (PCR) testing, as well as obtaining sera for anti-C pneumoniae antibodies, using the microimmunofluorescence (MIF) method. The overall rate of C pneumoniae infection was 1.4%, ranging from 0 to 3.2% over the 6 years of the study. These numbers are very similar to the 2 to 5% rates of asymptomatic infection in adults and children reported in several studies\(^3,4\) from the United States. Of the 14 culture-positive and/or PCR-positive individuals reported by Miyashita et al, 3 of 10 patients from whom follow-up specimens were obtained remained positive for periods up to 12 weeks. The other patients appeared to have spontaneously cleared their infections. Persistent respiratory infection with C pneumoniae has been documented for periods up to 8 years.\(^5\)

Unlike C trachomatis, the complications or long-term sequelae of persistent asymptomatic respiratory infection are not really known. Persistent C pneumoniae infection has been hypothesized as being responsible or associated with several chronic diseases, most notably atherosclerosis.\(^6\) Asymptomatically infected individuals may also be a reservoir for transmission of infection in the community.

Very little is known about the natural course of C pneumoniae infection in general. When does infection first occur? Is it always associated with illness? How long can it persist? Seroepidemiologic studies\(^7,8\) suggested that C pneumoniae infection occurs primarily in school-aged children and the prevalence of infection increases with increasing age. Following the criteria proposed by Grayston et al,\(^9\) acute infections were defined by a fourfold rise in IgG titer between consecutive specimens or a single IgM titer of \(\geq 16\) or a single IgG of \(\geq 512\). An IgG titer \(\leq 256\) was considered to indicate past exposure. However, subsequent studies\(^4,10\) that have utilized culture and PCR for detection of C pneumoniae suggest that infection may occur at earlier ages than implied by MIF serology. The most interesting observation was the lack of correlation between positive culture results and serology; approximately 70% of culture-positive children in these studies were MIF negative, and <5% met the serologic criteria for acute infection.\(^10\) Hyman et al\(^3\) reported that 18% of a group of culture-negative, subjectively healthy adults met the serologic criteria for acute infection with a single serum sample, IgG \(\geq 512\) and/or IgM \(\geq 16\). Two subjects in this study\(^3\) had nasopharyngeal swab specimens that were culture positive and/or PCR positive; one subject was seronegative and one subject had an IgG titer of 256 in a single serum specimen. The results of other studies\(^11–13\) in adults suggest that some high anti-C pneumoniae IgG antibody detected by MIF may be heterotypic, either due to infection with other chlamydioid species or other organisms, including Bartonella and Bordetella pertussis. Chlamydia heat shock protein (HSP) 60 is almost identical to that of Escherichia coli,\(^14\) and a recent study\(^15\) found picornavirus proteins also share antigenic determinants with HSP60/HSP65, including C pneumoniae HSP60.

The major obstacle to understanding the natural history of C pneumoniae infection and its potential role in disease is the lack of standardized diagnostic methods, including serology and PCR. Because of the perceived difficulty in culturing C pneumoniae, serology using the MIF test was promoted as the diagnostic method of choice.\(^9\) Some of the limitations of MIF are illustrated by Miyashita et al in the present study. Of the 14 culture-positive and/or PCR-positive individuals in their study, none met the serologic criteria for acute infection.\(^9\) Five subjects had IgG titers believed to be indicative of past infection, and the remainder were seronegative. In addition to the issue of correlation with culture and/or PCR, the MIF assay is also not standardized. It has a significant subjective component, and performance can vary significantly from laboratory to laboratory, even when the same assay kits are used.\(^16\) Recently, the Centers for Disease Control and Prevention recommended that the serologic criteria using the MIF assay be made more stringent.\(^17\) Acute infection required demonstration of a fourfold increase in IgG or IgA, and/or an IgM \(\geq 16\). In addition, the panel believed that there were no reliable serologic markers for past or persistent infection.

Although at least 18 in-house PCR assays for detection of C pneumoniae in clinical specimens have been reported in the literature, none have been adequately validated compared to either culture or another PCR assay using a different target.\(^18\) There are no standardized, commercially available nucleic acid amplification assays (NAAs) for detection of C pneumoniae, whereas there are now four NAAs approved by the US Food and Drug Administration
for the detection of *C. trachomatis*. Data are emerging that suggest there is substantial variation in performance of in-house PCR assays for detection of *C. pneumoniae* in clinical specimens, even between laboratories using the same assay with the same specimens. In that study, identical sets of 15 human atheroma specimens and 5 spiked control specimens were analyzed by 16 PCR assays in nine laboratories. The number of atheroma specimen results reported as positive ranged from 0 to 60% from laboratory to laboratory, and the maximum concordant result for positivity was only 25% for one specimen. In addition, 3 of 16 negative control specimens (19%) were reported as positive in two of the laboratories. Of the 14 asymptptomatically infected individuals identified by Miyashita et al, 13 were PCR positive, 3 of whom were also culture positive and 1 was PCR negative and culture positive. Does this mean that PCR is superior to culture? Not necessarily; it may be that their culture methods were suboptimal. Other laboratories using culture have reported higher prevalences of asymptomatic infection. Use of NAAs has revolutionized the diagnosis and treatment of genital *C. trachomatis* infections; one would expect that such an assay would accomplish the same for *C. pneumoniae*.

Margaret R. Hammerschlag, MD
Brooklyn, NY

Dr. Hammerschlag is the Professor of Pediatrics and Medicine and the Director of Pediatric Infectious Diseases, Department of Pediatrics, SUNY Downstate Medical Center.

Correspondence to: Margaret R. Hammerschlag, MD, Department of Pediatrics, Box 49, SUNY Downstate Medical Center, 450 Clarkson Ave, Brooklyn, NY 11203-2908; e-mail: mhammerschlag@pol.net

**REFERENCES**

19. de Barbezay B, Geibaux M, Hocke C, et al. Detection of *Chlamydia trachomatis* in symptomatic and asymptomatic populations with urogenital specimens by AMP CT (Gen-Probe) compared to other commercially available amplification assays. Diagn Microbiol Infect Dis 2000; 37:181–185