American College of Chest Physicians Evidence-Based Guidelines—the Next Generation

Considering Resource Use and Evolution to a Single Grading System

The American College of Chest Physicians (ACCP) has successfully provided high-quality clinical practice guidelines for over 10 years. Over the last 6 years, a concerted effort has been super-

vised by the ACCP Health and Science Policy Committee to ensure that these documents move as close as possible to an evidence-based platform. The reader is invited to visit the Health and Science Policy Committee Web site to learn more about the process of the ACCP in developing evidence-based guidelines. Some evidence-based guideline publication topics include lung cancer, pulmonary arterial hypertension, antithrombotic and thrombolytic therapy, aerosol therapy, atrial fibrillation after coronary arterial bypass grafting, and cough. A forthcoming evidence-based guideline will highlight occupational asthma.

All of these documents provide the best available evidence-based recommendations for the particular clinical topics at hand. However, perusal of the guidelines reveals the use of varying custom-derived grading systems on which the recommendations are based. This variability reflects the specific needs of each writing panel, but as a result the repertoire of the different grading systems can be bewildering and confusing to clinicians often wishing to compare the level of recommendations between different documents. Recognizing this problem, the ACCP financed a thorough review of our evidence grading system with the goal of developing and adopting a single grading system for all future ACCP evidence-based guidelines. In March 2005, a comprehensive review occurred at ACCP headquarters and continued off-site for several months. A new grading system was developed and was subsequently approved by the ACCP Board of Regents. This grading system arose as an adaptation of a preexisting grading methodology, but this adaptation is not an ACCP endorsement of that or any other existing grading system. The newly adopted ACCP system is found in this month’s issue of CHEST (pages 174). The consistent utilization of this grading system across all future ACCP evidence-based guidelines will provide consistency and clarity from one evidence-based guideline to another, thereby minimizing the confusion among clinicians adopting the recommendations.

The newly adopted grading system has several advantages. First, it is less complex than our previous system. As a result it is easier to use and understand by the practicing clinician. The simplicity results in part from a more comprehensive view of what constitutes evidence. In the past, there was an arbitrary threshold that separated “quality evidence” from “expert opinion,” with the former derived from randomized controlled trials and the latter from small observational studies or even case reports. In

References
the new grading system, all relevant published data are considered to be evidence. As a result, the definition of weak evidence has been extended. Another advantage of the new system is the emphasis on benefits vs risks and the burdens imposed by recommendations. This allows a greater focus when crafting recommendations on patient-centered outcomes, and the preferences and values of patients.

In addition to adopting a uniform grading system for evidence-based guidelines, the ACCP also began a systematic evaluation of how recommendations might impact resource utilization. To date, no evidence-based guideline, regardless of its sponsoring organization, has provided a consistent and transparent approach to resource/cost considerations in its recommendations. In part, this is due to the widespread differences in resource utilization internationally, the rapidly changing or variable costs from region to region, and the complexity of the resource issue impacting patients, caregivers, insurance providers, and others. It is important to note that resource/cost considerations involve not simply assessing the easily recognized immediate dollars consumed, but all surrounding and downstream resource effects of implementing a particular evidence-based guideline recommendation. One ideally must consider all consumed resources.

Recognizing the importance of resource considerations in ACCP evidence-based guidelines, the ACCP financed an in-depth evaluation of this topic, which also occurred in March 2005 concurrent with the convening evidence-based guideline grading system task force described above. The resulting document was critiqued and edited by all participants for several months, with the final outcome of the working group also found in this issue of CHEST\textsuperscript{10} (pages 182). This document represents what we think is the first published document providing a rational framework for considering resource consumption during the creation of an evidence-based guideline. Although evidence-based guideline grading systems have been evolving for over 10 years, the incorporation of resource utilization into evidence-based recommendations is very much in its infancy. Notably, the newly adopted ACCP evidence grading system considers resource consumption in developing evidence-based recommendations.

The resource document provides a framework for those considerations with nine specific recommendations. A central theme within these nine recommendations is that only a limited number of the recommendations within any evidence-based guideline can be selected for resource assessment. This has primarily evolved from the costly nature of incorporating resource considerations into evidence-based guidelines, in terms of both dollars and experience. A framework for selecting evidence-based guideline recommendations for resource consideration is provided. Those selected should be ones in which the incorporation of resource considerations will most likely influence the direction or strength of a recommendation.

The resulting evidence-grading and resource-utilization documents are not stand-alone products, but are meant to be used in concert. As experience is gained in using these documents, refinements and improvements will occur, especially with resource utilization, given the current nascent stage of development. However, the ultimate goal is that when used together, these documents will generate higher quality evidence-based guidelines with more sophisticated evidence grading producing higher quality evidence-based recommendations that thoughtfully consider the impact of resource consumption. Such a unified approach will lead to a more comprehensive consideration of patient values and preferences, and, ultimately, to a more focused approach to patient-centered, evidence-based recommendations. In the end, this guideline development approach aligns with the mission of the ACCP of providing tools enabling the practicing clinician to provide the best possible patient-centered care.

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Nasopharyngeal Detection of Severe Acute Respiratory Syndrome-Associated Coronavirus RNA in Health-Care Workers

The risk of developing severe acute respiratory syndrome (SARS) after exposure was conventionally determined by the prospective follow-up for symptomatic disease or the retrospective seroprevalence study of the exposed population. The average number of secondary cases resulting from a single case of SARS ranged from two to four.1 Transmission mostly resulted from contacts with patients with overt disease rather than from asymptomatic or mildly symptomatic patients. Seroprevalence appeared to be low (0%, 0.43%, and 1.2%) for healthy individuals, and about 1% for health-care workers, approximately 1% for asymptomatic family contacts under quarantine, and 0.19% for asymptomatic contacts overall.2–7 Systematic use of reverse transcriptase polymerase chain reaction (RT-PCR) in the early identification of patients with higher risk for developing SARS has not been reported. In this issue of CHEST (page 95), Ho et al8 report on the nasopharyngeal shedding of SARS-coronavirus (CoV) RNA from 27 of 217 frontline health-care workers (12.4%) after encountering SARS patients for 1 week. Twenty-five of those health-care workers were characterized by low mean (± SD) viral loads (312 ± 204 to 386 ± 203 copies per milliliter), a lack of or paucity of symptoms, and the absence of seroconversion during follow-up. This is in contrast to the two subsequently symptomatic health-care workers with significantly higher mean viral loads (16,900 ± 7,920 copies per milliliter) and subsequent seroconversion. The authors excluded contamination with PCR amplicon carryover by using 13 nonfrontline health-care workers as negative control subjects in addition to the usual PCR-negative control subjects. Since the word colonization is used to describe the establishment of a microbial agent in the host without inducing a specific immune response or invasion, as manifested by disease or distant dissemination, the authors concluded that SARS-CoV can “colonize” a significant proportion of exposed individuals, with disease manifestation occurring in only 2 of 27 initially colonized individuals (7.4%).

However, using the term colonization to describe this interesting phenomenon is premature, because the viral culture and virus-specific cell-mediated immune response of these colonized individuals were not performed as part of the workup. The amount of viral shedding is the end result of the interaction between a replication-competent virus in susceptible host cells at the nasopharynx and the innate immune system of the host defense. Populations of virus often contain particles that are not capable of completing an infectious cycle. Though a single virus particle can theoretically initiate an infection, many perfectly competent virions fail because of nonproductive interactions with the extracellular matrix at the cell surface. Even virions that have successfully entered the cell may be delivered to a wrong compartment, thereby resulting in an abortive infection. Thus, viral RNA can be detected by RT-PCR with no viable viruses isolated on a cell culture. Only a sufficient amount of viral replication occurs and results in cytolysis with the induction of host proinflammatory damage will lead to symptomatic disease and subsequent seroconversion.9

In these patients with more severe disease, a higher level of viral shedding is expected, and is manifested as a higher viral load on quantitative RT-PCR and even as a positive viral culture finding. Only 40.4% of those RT-PCR-positive respiratory secretions have a positive viral culture finding.10 A lower amount of viral replication may result in low-level viral shedding with a negative cell culture and asymptomatic or mildly symptomatic infection with or without seroconversion.11 It is important to remember that some commercial sex workers employed in areas that are highly endemic for HIV do not seroconvert despite repeated sexual exposure to HIV-1; they did, however, have local HIV-specific immune responses in the genital tract.12 It would be interesting if we can determine whether these RT-PCR-positive health-care workers have similar local