Comorbidity: Preventable Premature Morbidity and Mortality Due to Skin Disease

During *JID*'s year of the patient, comorbidity is an important and appropriate subject for consideration. In its simplest form, comorbidity refers to the prevalence of two conditions in the same patient at frequencies that are higher than would be expected by chance alone. In 2002, some 15,000 deaths were considered to be directly attributable to skin diseases (Weinstock and Chren, 2008). If skin diseases have significant comorbidities and fatalities, the numbers of deaths associated with such diseases may be even higher, pointing to an increased role for the dermatologist in the overall health of his or her patients. Forty years ago, Shuster and Marks (1970) delineated many of the systemic metabolic effects associated with extensive skin conditions, especially erythroderma. Seventy years ago, John H. Stokes, in his presidential address at the third annual meeting of the Society for Investigative Dermatology (SID), discussed the complexity of casual concepts (Stokes, 1940). Contemporary investigators are defining and struggling with these complexities. Geriatricians are interested in comorbidity because of the higher-than-expected concurrence of diseases in the aging population (Guralnik and Ferrucci, 2009).

Access to large administrative databases has enabled epidemiologists and dermatoepidemiologists to identify severe long-term vascular and cardiovascular consequences of psoriasis, the most widely studied disease for potential comorbidities (e.g., Gelfand *et al.*, 2006; Gelfand *et al.*, 2010). In approaching the study of any condition and its comorbidities in order to establish comorbidity associations, there are several common steps:

- Repeating epidemiological studies in many population groups.
- Confirming studies with data in prospectively studied populations. This process is not trivial, considering the number of patients and the duration of study necessary to establish comorbidities.
- Ensuring that cause, effect, and confounding variables are all considered in the analyses.
- Considering cause and effect and "reverse causation," using a Mendelian randomization approach when appropriate (Ebrahim and Smith, 2008; Thanassoulis and O'Donnell, 2009).
- Having a plausible biological mechanism(s).
- Presenting the data in a meaningful fashion for physicians (such as numbers needed to treat formulations to reduce one death).
- Determining, with randomly controlled intervention (prevention) studies, whether comorbidities can be decreased (this is the ultimate goal following the analytical studies).

The SID has been interested in comorbidity for several years and has made tangible commitments to increasing awareness of comorbidity of skin diseases and encouraging comorbidity research through the following activities:

- The first free-standing SID comorbidity conference in 2008 brought together researchers in dermatology, epidemiology, cardiology, and pharmacology to present data and discuss skin diseases and comorbidities associated with psychiatric diseases, cardiac diseases, and chemotherapeutic drugs (Schultz, 2009).
- The second SID comorbidity session at the SID's 2009 annual meeting in Montreal emphasized the detailed epidemiological processes required for outstanding comorbidity research.
- The third SID and American Academy of Dermatology comorbidity session at the SID 2010 annual meeting in Atlanta emphasized the role that genome-wide association studies may have in defining risk factors for comorbidity, newer ways of collecting data directly from patients online, therapies for addressing comorbidities, and progress in defining the systemic nature of many skin diseases. Using input from patients

Journal of Investigative Dermatology (2010) **130**, 2155–2156. doi:10.1038/jid.2010.134

and their families, new ways of delivering medical and dermatology care and enhancing physician and patient education were considered, as were the changes necessary to define optimal and complete patient care.

The April 2010 issue of *JID* featured articles addressing whether psoriasis is an independent risk factor in acute ischemic heart disease; a study from the Netherlands is accompanied by two commentaries discussing the methodological issues involved when considering psoriasis as a risk factor for cardiovascular disease (Wakkee *et al.*, 2010; Gelfand *et al.*, 2010; Stern, 2010). A related article shows the challenges in determining the clinical severity of psoriasis that may be important in stratifying cardiovascular risk studies (Spuls *et al.*, 2010).

These recent articles indicate that concern about comorbidity will not be going away; instead, it will be defined with higher degrees of precision, and preventive protocols will have to be developed by investigators who are aware of the complexity of the issues involved. Mendelian randomization studies may be an important methodology to approach questions of cause and effect when applied to comorbidity studies.

Concluding thoughts

Is comorbidity a fad, or will it be an important component of patient-oriented medicine? I think the latter. PubMed lists more than 53,000 citations related to comorbidity (as of 15 April 2010). More pragmatically, 990 funded grants in the National Institutes of Health (NIH) RePORT system include comorbidity as a key word (15 April 2010). Forty-four funded NIH grants have the word "comorbidity" in their titles, indicating a serious commitment of investigators to the topic. Most interestingly, almost three-quarters of those grants were from institutes in which behavior is a major component of study (the National Institute of Mental Health, the National Institute on Drug Abuse, and the National Institute on Alcohol Abuse and Alcoholism); historically, comorbidity studies came out of the psychiatry and mental health fields, and these disciplines show both the most interest and the most success in securing NIH funding for comorbidity studies. Studying comorbidity requires diverse talents, including knowledge of epidemiology, clinical diseases, and biology, the exact talents necessary to improve human health based on robust data and to guide the direction of future health sciences studies.

Lowell A. Goldsmith
Editor Emeritus

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