Published in final edited form as:

JAMA. 2009 April 22; 301(16): 1708–1709. doi:10.1001/jama.2009.506.

Management of Diseases Without Current Treatment Options Something Can Be Done

Ava K. Kiser, OD and Peter J. Pronovost, MD, PhD

Department of Ophthalmology, Wilmer Eye Institute (Dr Kiser); and Departments of Anesthesiology and Critical Care, Surgery, and Health Policy and Management (Dr Pronovost), Johns Hopkins University, Baltimore, Maryland.

After being diagnosed with a disabling, chronic disease, such as some retinal diseases and neurodegenerative diseases, there is nothing more disheartening than for the patient to hear that nothing can be done to treat it. Tragically, some diseases still lack a medical treatment to slow, stop, or reverse their course. In addition, even when therapy is available to treat a chronic disease, some patients are often left with distressing symptoms. Research to alleviate these symptoms has received relatively little attention, and physicians struggle with how to provide care for these patients. Studies are needed to understand and mitigate patients' disease-related symptoms that often result in significant distress, morbidity, and reduced quality of life. In this Commentary, we discuss research that is based on patient feedback and focused on investigating the concerns pertinent to patients.

The traditional model for translational research involves identifying and applying knowledge from the bench to the bedside, as discoveries are transferred from the laboratory to the clinical study and to the patient. However, this model also can proceed in the opposite direction, with research that is conceived from patient interactions leading to clinical and laboratory-based investigations. Both approaches are needed, although the traditional model predominates. Practice-based research identifies new clinical questions and gaps in care through observational studies, survey research, and phase 3 and 4 clinical trials.¹ Currently, there is a paucity of research efforts to address the needs identified by patients, as would originate from clinical practice.² The medical and scientific communities need a stronger commitment to find practical, relevant answers to the challenges encountered by patients coping with disease or distressing symptoms.

Research to better understand the day-to-day intricacies of how disease affects patients will allow physicians to gain a better appreciation of what patients experience, thus leading to interventions that meet patients' needs. Such research will help physicians attempt to assuage the disease-related symptoms that interfere with patients' daily functioning. For example, patients who are gradually losing their sight due to retinitis pigmentosa, a slowly progressive retinal degeneration, experience day-to-day fluctuations in their vision. This manifests as periodic reductions in central acuity, decreased sensitivity to detect various contrasts, or changes to the size of the visual field. Even though the factors and causes for this variability have not been defined through scientific study, patients report that stress, fatigue, time of day, and changes in illumination may play a role.³ If relationships between

©2009 American Medical Association. All rights reserved.

Corresponding Author: Ava K. Kiser, OD, 550 N Broadway, Sixth Floor, Baltimore, MD 21205 (abittne1@jhmi.edu).

Financial Disclosures: Dr Kiser reported receiving funding (K23 EY018356) from the National Eye Institute to investigate the factors potentially associated with daily fluctuations in vision among visually impaired retinitis pigmentosa patients. Dr Pronovost reported no disclosures.

such factors and short-term fluctuations in vision can be verified, recommendations could be made to alleviate those factors and reduce the uncertainties that accompany such visual fluctuations. Periodic shifts or changes in the way disease affects patients' ability to function and accomplish important tasks leads to experiences of increased disability at potentially critical times. Attempts to understand and manage these aspects of disease processes may improve patients' quality of life, help identify therapies, and improve the reliability of outcome measures in clinical trials.

Neurodegenerative diseases, such as Alzheimer disease, also exhibit striking within-day fluctuations in functional and cognitive abilities⁴ and also may benefit from this type of approach. There have been few systematic studies of this phenomenon in chronic disease, especially retinal and neurodegenerative diseases. Research to understand the mechanisms involved with these fluctuations may lead to management strategies or treatments to optimize performance, reduce disability, and potentially lead to new therapies and understanding of disease mechanisms.

In addition to research that focuses initially on understanding disease biology and then finding effective treatments for the patient's disease state, the federal government should also fund research to evaluate the daily problems patients face as they live with certain diseases. Many disabling diseases, including retinitis pigmentosa, are not likely reversible with the potential treatments currently being studied, and these patients will never fully regain the functional ready lost. Therefore, research efforts should also aim to help patients better survive with the consequences of the disease. However, this type of research needs to be informed by patients to address the issues that are truly critical to maintaining a high quality of life.

In addition to patient-physician interactions, a novel and potentially useful approach for obtaining the patient's perspective is through social networking such as online message-boards and forums. These types of sites are gaining in popularity and offer a vast variety of resources and opportunities to help patients and clinician researchers. An example of this concept to help assist research, improve education, and connect communities is the Interactive Autism Network (<http://www.ianproject.org/>). This online project was designed to accelerate the pace of autism research by linking researchers and families.⁵ In this forum, patients provide information about their symptoms, researchers provide information about clinical studies, and patients provide comments about research. Patients with retinal degeneration also have an online message board forum (the RPlist) on which they discuss disease and research. This forum has been used in previous online survey research to obtain responses from patients with the blinding eye disease retinitis pigmentosa, regarding their use of nontraditional therapies⁶ and experiences of visual phenomena such as photopsias or flashes of light.

When patients lose the ability to perform valued activities, as well as their sense of control and self-confidence, it can cause them to view themselves and their future negatively. Greater severity of disability and loss of psychosocial resources associated with the chronic medical condition may lead to psychological disturbances including depression, anxiety, and stress.⁷ Stress may begin when an objective event or threat, such as the diagnosis of disease or its progression, requires an adaptation. If the demands and burden of the disease exceed the patient's ability to cope, this results in a biological activation, as well as negative mental and emotional responses. These issues must be managed to improve patients' overall wellbeing. Moreover, several chronic diseases have been shown to worsen with stress, such as diseases with immune or inflammatory processes, some cardiovascular disease, human immunodeficiency virus/AIDS, and cancer.⁸ Therefore, caring for patients' psychological well-being has multiple implications.

Such distressing systems are also common in patients who survive acute illness.⁹ Increasing evidence suggests that patients who survive acute lung injury and acute respiratory distress syndrome experience chronic morbidity, including posttraumatic stress disorder, depression, and reduced physical functioning.¹⁰ Only by understanding these symptoms can physicians design interventions to reduce them.

Multiple repercussions exist when physicians communicate to their patients that nothing can be done for their disease and fail to address their symptoms. Patients may be unlikely to return for care in the future when clinical trials and new treatments or developments do become available. Patients who do not return for regular follow-up care are less likely to be informed of new trials and may miss the opportunity to participate or receive the most current medical care. Moreover, other medical problems may develop that contribute to further declines in function although they may be potentially treatable, but remain undetected among patients who do not return for care.

The traditional research model that progresses from understanding disease biology to identifying effective therapies and ensuring patients receive those therapies is a long and laborious journey that often may do little to relieve patient distress and morbidity. The traditional translational research model could be coupled with a model that begins with patient systems, ensures that patients receive known effective therapies for their symptoms, conducts clinical research to find new therapies, and investigates disease biology. This model might begin with the development of systems to monitor and report patient symptoms, which could elicit patients' experiences via the Internet, electronic databases, or through the use of other technologies. This approach could lead to several areas of research including the design of interventions from known therapies to ameliorate those symptoms, the induction of clinical studies to fill knowledge gaps regarding effective therapies, and conduction of basic science research to fill knowledge gaps regarding disease biology as it relates to patient symptoms.

When a particular disease is inexorable and forms a continuous threat to a patient's independence and quality of life, clinicians and researchers should seek ways to help the patient cope with the psychological and functional difficulties experienced as a result of the disease. The medical and scientific communities should strive to achieve better understanding and mitigation of these symptoms, in addition to finding treatments and cures for the disease process. Improving health goes beyond finding the treatments and cures for diseases, and also involves improving patients' current functioning with their disease and overall well-being.

REFERENCES

1. Westfall JM, Mold J, Fagnan L. Practice-based research—"Blue Highways" on the NIH roadmap. *JAMA*. 2007; 297(4):403–406. [PubMed: 17244837]
2. Woolf SH. The meaning of translational research and why it matters. *JAMA*. 2008; 299(2):211–213. [PubMed: 18182604]
3. Heckenlively JR, Yoser SL, Friedman LH, Oversier JJ. Clinical findings and common symptoms in retinitis pigmentosa. *Am J Ophthalmol*. 1988; 105(5):504–511. [PubMed: 3259404]
4. Palop JJ, Chin J, Mucke L. A network dysfunction perspective on neurodegenerative diseases. *Nature*. 2006; 443(7113):768–773. [PubMed: 17051202]
5. Zhao X, Leotta A, Kustanovich V, et al. A unified genetic theory for sporadic and inherited autism. *Proc Natl Acad Sci U S A*. 2007; 104(31):12831–12836. [PubMed: 17652511]
6. Kiser AK, Dagnelie G. Reported benefits of non-traditional treatments and complementary and alternative medicine by retinitis pigmentosa patients. *Clin Exp Optom*. 2008; 91(2):166–176. [PubMed: 18271780]

7. Ormel J, Kempen GI, Penninx BW, Brilman EI, Beekman AT, van Sonderen E. Chronic medical conditions and mental health in older people: disability and psychosocial resources mediate specific mental health effects. *Psychol Med*. 1997; 27(5):1065–1077. [PubMed: 9300512]
8. Cohen S, Janicki-Deverts D, Miller GE. Psychological stress and disease. *JAMA*. 2007; 298(14): 1685–1687. [PubMed: 17925521]
9. Herridge MS, Cheung AM, Tansey CM, et al. Canadian Critical Care Trials Group. One-year outcomes in survivors of the acute respiratory distress syndrome. *N Engl J Med*. 2003; 348(8):683–693. [PubMed: 12594312]
10. Davydow DS, Desai SV, Needham DM, Bienvenu OJ. Psychiatric morbidity in survivors of the acute respiratory distress syndrome: a systematic review. *Psychosom Med*. 2008; 70(4):512–519. [PubMed: 18434495]