Ecology of Infectious Disease: Forging an Alliance

Samuel M. Scheiner and Joshua P. Rosenthal

Abstract: The Ecology of Infectious Diseases (EID) program is a joint National Science Foundation–National Institutes of Health initiative to produce predictive understanding of disease dynamics, with a focus on diseases with an environmental component. The interdisciplinary research projects funded by this program take advantage of the wide range of theoretical and methodological advances developed over the past 30 years. The challenge for disease ecology is to unravel these systems, discover how complex they truly are, and to determine if they can be predicted and controlled using targeted environmental, public health, or medical interventions. Between 1999 and 2005, a total of 42 research awards were made under the EID program. EID projects have had affects on policy in two areas: adoption of novel interventions on a local scale and use of models by government agencies for the purpose of allocating public health resources. The past 6 years have been an exciting time for the field of disease ecology; we expect the coming years to be even more exciting and productive.

Key words: ecology, infectious disease, National Institutes of Health, National Science Foundation

INTRODUCTION

Over the past several years, at nearly every meeting on emerging infectious diseases, speakers have said that we need a greater understanding of the biology and environmental context of disease emergence and pathogen transmission. Without such an understanding, it will be difficult to anticipate and respond quickly to the effects of environmental changes on the health of humans, other animals, and plants. As the pace of anthropogenic change continues to accelerate, basic research will be essential to anticipating impacts and potential management or policy interventions. Whether the relevant questions concern long-range impacts of global climate change, more effective control of familiar pandemic diseases with animal vectors and reservoirs, or securing our food supply against the increasing threat of bioterrorism, the ecological dimensions of infectious disease are fundamental and poorly understood.

The Ecology of Infectious Diseases (EID) program was conceived in 1999 by program officers from the National Institutes of Health (NIH) and the National Science Foundation (NSF). The program focuses on interdisciplinary research projects that take advantage of the wide range of theoretical and methodological advances developed over the past 30 years by ecologists, physicians, veterinarians, mi-
crobiologists, disease specialists, and others such as geospatial and computational experts. It is a multiagency initiative because of the interdisciplinary nature of the questions being addressed, and because of the funding challenges facing truly ecological studies of disease transmission. While a handful of such studies had been funded, such as those of Terry Yates and colleagues in deciphering the cause of outbreaks of hantavirus (Yates et al., 2002) and Richard Ostfeld and colleagues in uncovering the complex story behind Lyme disease (Schauber et al., 2005), funding for disease ecology was scarce. At NSF, such projects were seen as too applied and too human-centric for an agency whose primary mission was support of basic research. At NIH, this type of research was considered, with occasional exceptions in vector biology, too field-oriented and far removed from biomedical research. Something was needed to fill this gap.

At NIH, the lead institute is the Fogarty International Center (FIC), with additional participation in the initial years by the National Institute of Allergy and Infectious Diseases (NIAID) and the National Institute for Environmental Health Sciences (NIEHS). At NSF, the program started in the Directorate for Biological Sciences, and later was joined by the Directorate for Geosciences. In addition, a number of other federal agencies have been involved in individual projects, including the Centers for Disease Control and Prevention (CDC), the U.S. Geological Survey (USGS), and the National Aeronautics and Space Agency (NASA).

The primary mission of the EID program is to produce predictive understanding of disease dynamics, with a focus on diseases with an environmental component (i.e., vector-borne diseases, diseases with nonhuman hosts, water- or long-distance airborne diseases, and diseases of nonhuman animals and plants). By predictive understanding, we mean that at the heart of any EID project must be a model that can be used to pull together the pieces of the disease puzzle so that we might be able to predict and control disease spread and effects. That model might be conceptual, but more often it is analytical or statistical. The challenge for disease ecology is to unravel these systems, discover how complex they truly are, and to determine if they can be predicted and controlled using targeted environmental, public health, or medical interventions.

**OVERVIEW OF THE EID PROGRAM**

**Range of Projects**

Between 1999 and 2005, a total of 42 research awards were made under the EID program. Of these, 13 (31%) were funded by NIH and 29 (69%) were funded by NSF. A number of the awards involve co-funding among one or more of these organizations and their components. The EID program has supported a broad array of studies on a variety of infectious diseases. The majority of the projects involve potential human pathogens, although they do not necessarily include a human component to the study. Projects also focus on diseases of other animals or plants. The range of host species includes: humans, primates, sea lions, cape buffalos, mule deer, wild dogs, raccoons, fruit bats, deer mice, prairie dogs, rainforest birds, tortoises, frogs, honey bees, shellfish, sea fans, grasses, and soybeans. The list of pathogens/diseases is equally long and include: echinococcosis, schistosomiasis, malaria, chagas, Hantavirus, rabies, dengue, West Nile virus, chronic wasting disease, plague, cholera, and chitrid fungi. Overall, the projects are divided roughly one-third each among viral pathogens, pathogenic bacteria, and protists or multicellular parasites (Table 1). The projects range among terrestrial, freshwater, and marine habitats (Table 2). Research topics range from the abstract (e.g., investigations of the impact of social behavior on spheroid transfer processes among honeybees) to environmental interven-

**Table 1. Number of EID Awards by Focal Pathogen Type, 2000–2005**

| Pathogen type                  | NIH | NSF | Total |
|-------------------------------|-----|-----|-------|
| Viral (including prions)      | 4   | 9   | 13    |
| Bacterial                     | 2   | 10  | 12    |
| Parasitic (protozoa and multicellular) | 7 | 3 | 10 |
| Not specified                 | 0   | 2   | 2     |
| Viral and fungal              | 0   | 1   | 1     |
| Bacterial and viral           | 0   | 1   | 1     |
| Parasitic and bacterial       | 0   | 3   | 3     |
| Total                         | 13  | 29  | 42    |

**Table 2. Number of EID Awards by Ecosystem Type, 2000–2005**

| Ecosystem type                  | NIH | NSF | Total |
|-------------------------------|-----|-----|-------|
| Terrestrial                   | 11  | 22  | 33    |
| Wetland, coastal or freshwater | 2  | 5   | 7     |
| Marine                        | 0   | 2   | 2     |
| Total                         | 13  | 29  | 42    |
tion and human epidemiology studies. Nearly all projects are both interdisciplinary and targeted at the development of new concepts and methods to predict and prevent infectious diseases.

Scientific and Public Health Impacts to Date

The EID program was recently reviewed by an external group of experts who assessed its achievements and impacts (Burke et al., 2005). The 27 projects for which publication information was available as of June 2005 have resulted in publication of a total of 228 journal articles, 95 abstracts, and 11 book chapters. Papers appeared in a total of 113 different international, peer-reviewed journals. Among them are journals of broad scientific interest (e.g., Nature, PNAS), medical and public health journals (e.g., The Lancet, Infectious Diseases, Emerging Infectious Disease, Environmental Health Perspectives), and ecology journals (e.g., Ecology, Ecological Applications, Behavioral Ecology). Recently, a book was published that collects the results of several of the EID projects (Collinge and Ray, 2006).

EID project have had effects on policy in two areas: adoption of novel interventions on a local scale, and use of models by government agencies for the purpose of allocating public health resources. Examples of new interventions include:

- In Belize, researchers have been working with public health officials to alter agricultural practices and local vegetation in order to limit the spread of malaria (Pope et al., 2005; Achee et al., 2006).
- In Malaysia, researchers demonstrated that elimination of fruit trees from certain areas of land used for pig farming can limit exposure to Nipah virus (Field et al., 2004).
- On Lake Malawi, Africa, researchers have been working with public health officials and directly with local fishermen to alter fishing practices in order to reduce exposure to schistosomes (Evers et al., 2006).

One example of direct policy impact emerged from an interview by the review committee (Burke et al., 2005) with a CDC employee involved in three EID awards. When asked about the effect of the research, he told of how a model of Hantavirus ecology developed through an EID program project had been adopted directly by the CDC to help in allocating scarce surveillance resources.

Personnel and Training

As of June 2005, at least 566 individuals have been listed as key personnel on EID projects. This is likely to be a drastic underestimate of the total number of people involved in the 42 projects because of incomplete records and inconsistent definitions of “key personnel” between NIH and NSF. These people are at 123 different institutions in 23 countries. Of the 31 projects for which full or partial key personnel information was available, only 9 had key personnel only from US-based academic institutions; all others had at least one participant from a nonprofit organization, government agency, or an academic institution located outside of the US.

Although EID is not a training program, it has resulted in substantial education efforts. EID projects already have helped to train at least 208 students at the undergraduate, graduate, and postdoctoral levels (Table 3). Importantly, the interdisciplinary nature of the research exposes participants to fields of research in which they do not already have expertise, and will likely result in people trained to work in, and span, diverse research areas.

| Agency | Postdoctoral researcher | Graduate student | Undergraduate student | Total |
|--------|-------------------------|------------------|-----------------------|-------|
| NIH    | 12                      | 8                | 7                     | 27    |
| NSF    | 30                      | 82               | 69                    | 181   |
| Total  | 42                      | 90               | 76                    | 208   |

*These counts were derived exclusively from data available in annual progress reports, which are not complete for all years and all projects. Data on students were available for only 28 of 42 projects, and the degree of completeness for these 28 projects is unknown. Reporting requirements are also inconsistent between NIH and NSF. Accordingly, these counts underestimate the true number of students who have been involved with EID grants.
The total annual budget for the EID program has increased from $4 to $5 million per year in 2000–2001 to $14 to $15 million per year today. Overall, about two-thirds (63%) of the total funding contributions came from NSF and the remainder from NIH, with FIC contributing 24% of the total, NIAID contributing 9%, and NIEHS contributing 4% (Table 4).

**Funding**

The total annual budget for the EID program has increased from $4 to $5 million per year in 2000–2001 to $14 to $15 million per year today. Overall, about two-thirds (63%) of the total funding contributions came from NSF and the remainder from NIH, with FIC contributing 24% of the total, NIAID contributing 9%, and NIEHS contributing 4% (Table 4).

**CHALLENGES: THE SOCIOLOGY OF SCIENCE**

Despite increasing recognition of the need for a robust understanding of the ecology of infectious diseases, research funding in this area is still primarily through special competitions such as the EID program. In part, the lack of funding opportunities is due to the inherently interdisciplinary nature of the research. Many of the relevant questions simply do not fall neatly under traditional research areas of basic ecology, classical epidemiology, or vector biology (Parkes et al., 2005), and tend to fare poorly in unsolicited grant applications at either of the supporting agencies.

Both disease management and long-term predictive research use ecological information. Among ecologists, the rapid rise in this area of study has been nothing short of astounding. When the EID program began, at the annual meeting of the Ecological Society of America, one might find a handful of talks on the subject of disease ecology. Now, there are multiple contributed-paper sessions and symposia. A stand-alone conference—Ecology and Evolution of Infectious Disease—is now in its fourth year with an annual attendance of several hundred. Recent reports by the National Academy of Sciences on needs in veterinary science highlights disease ecology as an important area for study (National Research Council, 2005).

However, the biomedical community has been slower to appreciate the potential of field-oriented ecological and epidemiology studies for public health. This lack of appreciation is due, in part, to a tendency to confuse such research with descriptive natural history and surveillance monitoring. However, increased recognition of the role of nonmedical events in influencing outbreaks of diseases such as SARS, the potential for bioterrorism, and the current global spread of avian influenza has added new urgency and made this a front-page issue. Recent trends in grant applications, government sponsored reports (e.g., Smolinski et al., 2003; Knobler et al., 2006), and a talks at various conferences suggest that there is growing recognition of the potential power of predictive ecological research that involves multiple disciplines and may span multiple spatial scales in order to achieve a quantitative understanding of disease transmission mechanisms. We believe that such research can help develop better predictive tools and the knowledge to minimize the prevalence of disease or even to prevent outbreaks before they occur. When integrated with research on vaccines, therapeutics, and other public health and environmental interventions, ecological studies may yield very powerful disease prevention and management tools.

**FUTURE DIRECTIONS**

There remain many major unanswered questions and challenges. How do ecological and evolutionary processes...
interact in determining disease dynamics? While substantial research exists on both the ecology and evolution of disease, almost none looks at the interaction of these processes, even though disease dynamics are happening in evolutionary time for microorganisms. What is the role of within-host ecology, including host–pathogen interactions and interactions among multiple pathogens? While disease ecology research is teasing apart the complexities of multiple hosts and vectors, nearly all focuses on just a single disease organism at a time. Can we develop truly useful predictive models for these complex ecological processes that are spatially and temporally explicit? This last is the ultimate question. While understanding is important, especially for long-term management, we desire accurate predictions if we are to be able to control or prevent disease outbreaks.

The science of disease ecology will continue to evolve in response to both internal developments and the exigencies of the world, and the EID program will continue to develop along with it in response to those changes and program evaluations (e.g., Burke et al., 2005). Addressing infectious disease requires a very wide approach that incorporates social scientists, clinical scientists, and public health researchers, and the EID program needs to be receptive to such projects. The questions posed above will likely result in a shift in the focus of proposals submitted to the EID program, for example, more projects that examine pathogen evolution. Our goal is to maintain the EID program as a broad, interdisciplinary program that will not only produce predictive understanding of disease dynamics, but also take that understanding, where possible, to the next level and translate knowledge into specific testable interventions. The past 6 years have been an exciting time for the field of disease ecology; we expect the coming years to be even more exciting and more productive.

References

Achee NL, Grieco JP, Masuoka P, Andre RG, Roberts DR, Thomas J, et al. (2006) Use of remote sensing and geographic information systems to predict locations of *Anopheles darlingi*-positive breeding sites within the Sibun River in Belize, Central America. *Journal of Medical Entomology* 43:382–392

Burke D, Bunnell J, Collins J, Morse S, Riley L, Russek-Cohen E, et al. (2005) Review of the Joint National Institutes of Health/National Science Foundation Ecology of Infectious Disease Program, Final Report. Available: http://www.fic.nih.gov/about/plan/eid_review2005.pdf [accessed July 19, 2006]

Collinge SK, Ray C (2006) *Disease Ecology: Community Structure and Pathogen Dynamics*. Oxford, UK: Oxford University Press

Evers BN, Madsen H, McKay KM, Stauuffer JR (2006) The schistosome intermediate host, *Bulinus nyassanus*, is a 'preferred' food for the cichlid fish, *Trematocranus placodon*, at Cape Maclear, Lake Malawi. *Annals of Tropical Medicine and Parasitology* 100:75–85

Field H, Mackenzie J, Daszak P (2004) Novel viral encephalitides associated with bats (Chiroptera)—host management strategies. *Archives of Virology* 18(Suppl):113–121

Knobler S, Mahmoud A, Leman S, Pray L (editors) (2006) *The Impact of Globalization on Infectious Disease Emergence and Control*. Washington, DC: National Academies Press

National Research Council (2005) *Critical Needs for Research in Veterinary Science*. Washington, DC: National Academies Press

Parkes MW, Bienen L, Breilh J, Hsu L-N, McDonald M, Patz JA, et al. (2005) All hands on deck: transdisciplinary approaches to emerging infectious disease. *EcoHealth* 2:258–272

Pope K, Masuoka P, Rejmankova E, Grieco J, Johnson S, Roberts D (2005) Mosquito habitats, land use, and malaria risk in Belize from satellite imagery. *Ecological Applications* 15:1223–1232

Schauber EM, Ostfeld RS, Evans AS (2005) What is the best predictor of annual Lyme disease incidence: weather, mice, or acorns? *Ecological Applications* 15:1223–1232

Smolinski MS, Hamburg MA, Lederberg JS (editors) (2003) *Microbial Threats to Health*. Washington, DC: National Academies Press

Yates TL, Mills JN, Parmenter CA, Ksiazek TG, Parmenter RR, Vande Castle JR, et al. (2002) The ecology and evolutionary history of an emergent disease: Hantavirus pulmonary syndrome. *Bioscience* 52:989–998