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COMMENTARY

Significance of Biodiversity to Health

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ABSTRACT

The United Nations declared 2010 the International Year of Biodiversity. Despite the magnitude of the global crisis of biodiversity loss, its far-reaching consequences to human health remain largely unappreciated. The legacy of the natural world to medicine is profound and its potential to yield new therapeutics and advancements in biomedical science undervalued. The enormity of the global crisis underscores a fundamental truth, one that is seemingly obvious but has been tragically overlooked: Our species does not exist in isolation from the biosphere. Rather, our fate depends on it.

Key words: biodiversity; conservation; extinction; rain forest; health; medicine; natural products.

DEEP IN THE ANCIENT FORESTS OF SARAWAK, on the island of Borneo, a tree of unassuming appearance held a powerful secret. That secret was unlocked by chance in 1987 when researchers collected specimens of its bark as part of a screening initiative by the National Cancer Institute. To their surprise, *Calophyllum lanigerum* var. *austrocoriaceum* yielded an extract with potent anti-HIV activity. Returning to the site to collect more material for analysis, the scientists were shocked to find the tree, and its promise, gone. Its disappearance triggered a frantic search to locate further specimens. Forests were surveyed, biological inventories scanned, and garden collections scoured. Finally trees, collected a full century earlier, were located in Singapore's Botanic Garden (Pick & Sloan 2004). Subsequent studies revealed its bioactive compound, calanolide A, to be an inhibitor of HIV with low potential for cross-resistance with other therapies (Currens *et al*. 1996).

No one knows how many species have disappeared in the past 40 years. Estimates range widely from the tens to hundreds of thousands, the vast majority of which have never been catalogued, let alone investigated for their potential benefit to mankind. These organisms are being extinguished as a direct consequence of human action: clear-cutting forests for timber and palm oil, bulldozing deserts for housing and infrastructure development, processing of coral reefs for cement, and the damming and polluting of rivers. While species loss may not be apparent in the course of our everyday lives, Earth's biological endowment—millions of species evolved over a time course of millions of years—is being irretrievably lost at a scale unprecedented in human existence.

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The United Nations has declared 2010 the International Year of Biodiversity. So how is the loss of biological diversity relevant to health and biomedical science? Over half of all pharmaceuticals developed over the past quarter century are directly derived from or modeled after compounds from nature (Newman & Cragg 2007). Some of our most important pharmaceuticals, including aspirin, quinine, and morphine, have been discovered from plants with a long history of use by mankind. Globally, the World Health Organization (2002) estimates that in many developing countries as much as 80 percent of the population relies on traditional therapeutics from nature as a primary or major source of health care.

In an era of recombinant hormones and emerging stem cell therapies, the medical potential of the natural world is undervalued and remains largely unexplored (Plotkin 2000). A phytochemical survey of old growth forest in the Pacific Northwest region of the United States in the 1960s yielded paclitaxel (Taxol), a chemotherapeutic agent with a novel mechanism of action that has enhanced the lives of uncounted thousands of women with breast and ovarian cancer. Its source, the slow-growing and uncommon Pacific yew tree, had been previously discarded by logging operations in the region. As is the case with many naturally-occurring bioactive compounds, the highly complex molecular structure of paclitaxel would have been virtually impossible to discover through even the most advanced synthetic approaches available today (Chivian & Bernstein 2008).

In tropical rain forests, the world's greatest repository of botanical diversity, less than one percent of plant species has been screened for bioactivity (Balick *et al*. 1996). An even smaller fraction of their vast and scarcely described myriad of fungi and soil microbes has been evaluated for medical potential. Yet over the last 20 years, more than 33 million hectares (338,000 km^2) of

Amazonian rain forest in Brazil alone have been cleared (Ministério da Ciênca e Tecnologia Brasil 2009). Only fragments of forest remain in Madagascar, a country of extraordinary biological richness whose legacy to medicine includes the *Vinca* alkaloids which helped to make pediatric leukemia and Hodgkin's lymphoma curable.

Rain forests have received the greatest public attention, but other biologically diverse and complex ecosystems, such as coral reefs, are as threatened and less appreciated as a source of new medicines. Few physicians realize that the synthesis of the first effective antiretroviral drug AZT was guided by compounds isolated from a Caribbean sponge (Newman *et al*. 2000). Reef-dwelling cone snails, unable to chase down anything but the slowest prey, have evolved novel and potent neurotoxins in the form of peptides that they inject through a harpoon-like tooth to instantaneously immobilize their targets. Each of the 700 living species of *Conus* produces a venom that is a cocktail of 100 or more distinct toxins (Olivera 2006). Astoundingly, nearly every toxin appears to be unique to the single species of cone snail that produces it. Only about 100 of the estimated 70,000 cone snail toxins have been characterized; from these few, several drugs have entered clinical trials (Chivian & Bernstein 2008). In 2004, ziconotide, a medication modeled after a toxin from a Philippine cone snail, received approval in the United States as a non-addictive therapeutic option for patients with severe pain refractory to narcotics.

Paracelsus (1493–1541), the Father of Pharmacology, recognized that the difference between a deadly poison and a life-saving remedy can be a question of dose. In the Neotropics, among the most conspicuous advertisements of toxicity—and of potential therapeutics—are the tiny but flamboyantly colored poison dart frogs. One golden yellow species contains sufficient toxin in its skin to kill ten adult humans. To date, over 500 alkaloids have been extracted from frogs of the family Dendrobatidae, many structurally-complex compounds new to science and difficult to synthesize in the laboratory (Daly *et al*. 2002). One drug investigated in clinical trials, ABT-594, was almost lost when one of the two sites of Ecuadorian forest from which the frog was originally collected was cleared for a banana plantation (Plotkin 2000).

The biomedical promise of these celebrated frogs is more inextricably tied to the fate of their ever-dwindling habitats than commonly appreciated. Once removed, the frogs lose their toxicity, becoming inert in captivity. The secret of their chemistry, much like the cancer cure in the 1992 Hollywood film *Medicine Man*, is in the 'bugs'. In their natural ecosystems, the frogs sequester poisons through the selective ingestion of species of ants, beetles, millipedes, and mites which contain the toxins. The exact identity of the arthropods remains largely undiscovered among the immense diversity of invertebrate life teeming within Neotropical forests. To give perspective, a single tree in the Peruvian Amazon was found to harbor 43 species of ant, a greater variety than exists within the British Isles (Wilson 1987).

Insects and other microfauna lack the conservation appeal of an orangutan, but these extraordinary expressions of life are a medical treasury for mankind (Eisner 1972, Plotkin 2000). Their potential to ameliorate human suffering is yet realized but is depleted with each parcel of forest that is burned. Global estimates of the number of species that disappear each year are staggering, but scarcely convey the full accounting of our loss, which is unfathomable. From a medical perspective, we squander not only novel bioactive compounds, but also the scientific advances that would be gained from the study of the singular adaptations and complex interactions species have within their ecosystems. What marvels await discovery in the microcosm that exists within the leaf litter of a rain forest floor?

One such denizen is the predatory fungus *Cordyceps*, whose life seems extracted from the pages of science fiction. *Cordyceps*' lifecycle begins as spores which adhere to the body of an ant meandering through the detritus of the rain forest floor (Evans 1982). From there, *Cordyceps* infiltrates the ant's exoskeleton and is somehow able to evade its immune system. The fungus begins to selectively devour its host's non-vital tissues. When ready to reproduce, fungal filaments take control of the ant's brain, directing its hapless victim to climb upwards on the vegetation. Once it reaches a desired height, the zombie-like ant is induced to bite down on a stem, anchoring itself firmly in place before being killed by the fungus. A few days later, a wiry stalk starts to emerge like an elongated antenna from the dead ant's head. This fruiting body disperses fungal spores widely onto the forest floor below, setting the stage for the cycle to repeat itself with other unsuspecting ants.

Scientists do not yet understand how *Cordyceps* is able to manipulate its host's behavior but its elucidation may yield important neurobiological insights. Hundreds, if not thousands, of *Cordyceps* species exist in both tropical and temperate zones worldwide, remarkably each targeting a particular insect host (Sung *et al*. 2007). From a Chinese species of *Cordyceps*, scientists have isolated an antibiotic secreted by the fungus to discourage competition (Ahn *et al*. 2000, Lee *et al*. 2005). Only about 70,000 of the 1.5 million species of fungi conservatively estimated to exist have been named by science (Hawksworth & Rossman 1997). Although fungi have contributed to mankind several breakthrough drugs including penicillin and lovastatin, we know comparatively little about their natural history. The Norwegian soil mold that yielded cyclosporine, the immunosuppressive which changed the field of human organ transplantation in 1979, was only realized in 1996 to be the asexual life stage of a scarab beetle-eating species of *Cordyceps* (Hodge *et al*. 1996).

Advancements in biomedical science depend on the study of other species. At a fundamental level, biodiversity serves as mankind's resource bank for the biological sciences. Toxins too potent for direct medical application have helped scientists as research tools to determine the function of cellular proteins and elucidate physiologic pathways. Even the most esoteric species without pharmaceutical potential can benefit medicine in the most unexpected and significant ways. The 2008 Nobel Prize in Chemistry, for example, was awarded for the isolation and development of the biomarker green fluorescent protein from a bioluminescent species of Pacific jellyfish. Polymerase chain reaction (PCR), the methodological invention that revolutionized the field of molecular biology, was achieved through isolation of a thermostable DNA polymerase from a bacterium collected out of a Yellowstone hot spring.

Innumerable scientific breakthroughs, such as these, were made possible by the extraordinary adaptations organisms have evolved over millions of years to enable survival within a diversity of ecosystems and often harsh physical environments. Wood frogs can survive North American winters frozen for weeks without cardiac activity, circulation, or respiration. Research is ongoing to understand the vertebrate's mechanisms of freeze tolerance at molecular, cellular, and physiologic levels. The two species of Australian gastric brooding frog were able to protect their young through a unique adaptation. The mother frog raised her offspring, from fertilized eggs to tadpoles, within the shelter of her stomach. No hope remains to gain therapeutic insights on their mechanism of gastric acid suppression: both species went extinct in the 1980s.

The fallout of the modern world's assault on nature extends beyond loss of biological diversity. Ecosystem alteration and introduction of alien species can compromise human health in a myriad of ways (Grifo & Rosenthal 1997, Chivian & Bernstein 2008). Deforestation favors proliferation of *Anopheles* species that are more efficient vectors for malaria than native mosquitoes (Walsh *et al*. 1993). As roads are carved into remote forests, human exposure to pathogens increases (Eisenberg *et al*. 2006). Sixty percent of infectious diseases emerging between 1940 and 2004 came from animals; 72 percent of these originated from wildlife (Jones *et al*. 2008). Indeed, some of our most devastating infectious diseases, including HIV and Ebola, have arisen through crossover from animals in the process of forest encroachment by man.

A view of our blue and green planet from space only hints at the amazing expression of life that abounds within its landscapes and oceans. Yet, entire ecosystems are being destroyed and uncounted species lost forever despite compelling scientific evidence and common sense reinforcing the critical importance of their conservation. Life, in all of its forms, is sacred and worthy of preservation. Despite a prevailing mindset that the fate of mankind is somehow separate from that of the natural world, the human condition is in fact profoundly dependent on the biosphere of which we are inextricably a part. Conservation is not the exclusive domain of ecologists and policy-makers, but rather a shared responsibility for all of us. Physicians and other health professionals have a critical role as advocates to ensure that the extraordinary diversity of life on our planet—its greatest resource—is available for the benefit of future generations.

LITERATURE CITED

AHN, Y., S. PARK, S. LEE, S. SHIN, AND D. CHOI. 2000. Cordycepin: Selective growth inhibitor derived from liquid culture of *Cordyceps militaris* against *Clostridium* spp. J. Agric. Food Chem. 48: 2744–2748.

BALICK, M., E. ELISABETSKY, AND S. LAIRD (Eds.). 1996. Medicinal resources of the tropical forest. Columbia, New York, New York.

CHIVIAN, E., AND A. BERNSTEIN (Eds.). 2008. Sustaining life: How human health depends on biodiversity. Oxford University Press, New York, New York.

CURRENS, M., R. GULAKOWSKI, J. MARINER, R. MORAN, R. J. BUCKHEIT, K. GUSTAFSON, J. MCMAHON, AND M. BOYD. 1996. Antiviral activity and mechanism of action of calanolide A against the human immunodeficiency virus type-1. J. Pharmacol. Exp. Ther. 279: 645–651.

DALY, J., T. KANEKO, J. WILHAM, H. GARRAFFO, T. SPANDE, A. ESPINOSA, AND M. DONNELLY. 2002. Bioactive alkaloids of frog skin: Combinatorial bioprospecting reveals that pumiliotoxins have an arthropod source. Proc. Natl. Acad. Sci. USA 99: 13996–14001.

EISENBERG, J., W. CEVALLOS, K. PONCE, K. LEVY, S. BATES, J. SCOTT, A. HUBBARD, N. VIEIRA, P. ENDARA, M. ESPINEL, G. TRUEBA, L. RILEY, AND J. TROSTLE. 2006. Environmental change and infectious disease: How new roads affect the transmission of diarrheal pathogens in rural Ecuador. Proc. Natl. Acad. Sci. USA 103: 19460–19465.

EISNER, T. 1972. Chemical defense against predation in arthropods. *In* E. Sondheimer and K. Simeone (Eds.). Chemical ecology, pp. 157–217. Academic Press, New York, New York.

EVANS, H. 1982. Entomogenous fungi in tropical forest ecosystems: An appraisal. Ecol. Entomol. 7: 47–60.

GRIFO, F., AND J. ROSENTHAL (Eds.). 1997. Biodiversity and human health. Island Press, Washington, DC.

HAWKSWORTH, D., AND A. ROSSMAN. 1997. Where are all the undescribed fungi? Phytopathology 87: 888–891.

HODGE, K., S. KRASNOFF, AND R. HUMBER. 1996. *Tolypocladium inflatum* is the anamorph of *Cordyceps subsessilis*. Mycologia 88: 715–719.

JONES, K., N. PATEL, M. LEVY, A. STOREYGARD, D. BALK, J. GITTLEMAN, AND P. DASZAK. 2008. Global trends in emerging infectious diseases. Nature 451: 990–993.

LEE, S., I. NAKAJIMA, F. IHARA, H. KINOSHITA, AND T. NIHIRA. 2005. Cultivation of entomopathogenic fungi for the search of antibacterial compounds. Mycopathologia 160: 321–325.

MINISTÉRIO DA CIÊNCA E TECNOLOGIA BRASIL. 2009. Estimativas anuais desde 1988 até 2008. *Coordenação-geral de observação da terra (OBT)*, 3/1/2010, Ministério da Ciênca e Tecnologia, São José dos Campos, Brazil.

NEWMAN, D., AND G. CRAGG. 2007. Natural products as sources of new drugs over the last 25 years. J. Nat. Prod. 70: 461–477.

NEWMAN, D., G. CRAGG, AND K. SNADER. 2000. The influence of natural products upon drug discovery. Nat. Prod. Rep. 17: 215–234.

OLIVERA, B. 2006. *Conus* peptides: Biodiversity-based discovery and exogenomics. J. Biol. Chem. 281: 31173–31177.

PICK, N., AND M. SLOAN. 2004. The rarest of the rare: Stories behind the treasures at the Harvard Botanical Museum of Natural History. HarperCollins, New York, New York.

PLOTKIN, M. 2000. Medicine quest: In search of nature's healing secrets. Viking, New York, New York.

SUNG, G., N. HYWEL-JONES, J. SUNG, J. LUANGSA-ARD, B. SHRESTHA, AND J. SPATAFORA. 2007. Phylogenetic classification of *Cordyceps* and the clavicipitaceous fungi. Stud. Mycol. 57: 5–59.

WALSH, J., D. MOLYNEUX, AND M. BIRLEY. 1993. Deforestation: Effects on vector-borne disease. Parasitology 106: S55–S75.

WILSON, E. 1987. The arboreal ant fauna of Peruvian Amazon forests: A first assessment. Biotropica 19: 245–251.

WORLD HEALTH ORGANIZATION. 2002. WHO traditional medicine strategy: 2002–2005. World Health Organization, Geneva, Switzerland.