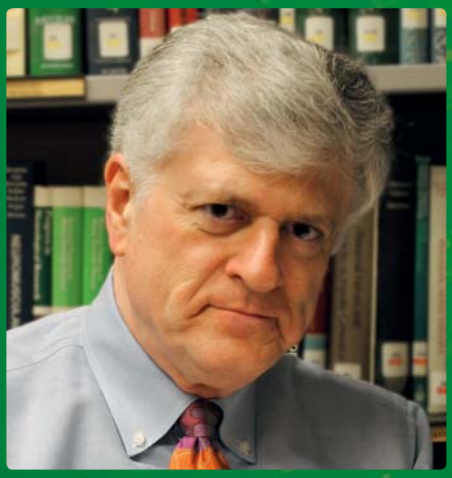
Global health in changing environments

The ever-evolving world in which we live presents equally adaptive challenges to human health, from climate change to chemical pollution to new viruses. **Professor Peter Spencer** and his team at **Oregon Health & Science University** are undertaking broad-reaching research which seeks to address these issues



Could you begin by providing an overview of your research and its primary aims and objectives? What inspired you to work in this field?

Chemicals of all types have been the subjects of my research scrutiny, including those of natural occurrence in bacteria, plants and animals used as food or medicine by humans, or those that are concentrated, utilised and disposed of in the course of human activity. I specialise in experimental and clinical neurotoxicology because, firstly, if chemicals cause or contribute to certain types of disease, these conditions can be prevented through exposure reduction. Secondly, the same chemicals are powerful laboratory tools to probe the molecular vulnerabilities of the nervous system.

Searching for the cause of an environmental disease is comparable to 'looking for a needle in a haystack', so my field-based research has often focused on little-known clusters of disease among desperately poor people in regions remote from the Western world; discoveries made there can lead to local disease prevention and contribute valuable insights into the cause (etiology) and development (pathogenesis) of comparable disorders around the world.

Can you describe what the Fogarty grant is and how it has helped your studies?

Awarded in 2008, this grant from the U.S. National Institutes of Health placed the Oregon Health & Science University (OHSU) Global Health Center (GHC) in a highly prestigious group of institutions both at home, including Harvard, Duke, Yale and University of California institutions, and abroad, such as Fudan University in Shanghai.

Receipt of this grant to OHSU has been instrumental in:

- Raising the profile of the GHC in advancing research, education, service and advocacy for global health across the OHSU campus
- Building a dedicated team of physicians, scientists, students and volunteers
- Winning base support and modest physical space for the GHC
- Creating innovative interdisciplinary global health educational programmes for students and late-career and retired community health professionals
- Attracting funds to create scholarships for OHSU students to travel abroad and learn about the realities of life and health in low-income settings
- Supporting colleagues to win grants for research abroad (eg. nutritional neurotoxic disease in Africa and India) and research training at home

Could natural, regularly consumed foodstuffs that are not known to be toxic actually instigate progressive and fatal brain degenerative diseases in later life?

The answer is not yet known. However, it is clear that while humans can link food or other exposures to illness that follows within minutes to days, they are unable – without scientific investigation – to link exposures to disease that follows in months to decades.

Witness, for example, the failure to link the onset of clinical parkinsonism a year or more after exposure to a presumed virus that triggered von Economo encephalitis early in the 20th century. In the case of exposure to chemicals, they might act in the short term by reducing the normal anatomical reserve of brain cells that are subject to age-associated attrition, such that years after exposure, the brain disease appears clinically as if the trigger was recent. However, certain chemicals might also initiate a slow-burning, irreversible pathological process that results in the slow, progressive demise of nerve cells. This hypothesis is central to a collaborative paper showing how cycasin, the major genotoxin in cycad plants, damages DNA and opens molecular pathways that lead to degeneration of nerve cells (Kisby, G E et al, PLoS One, in press).

Have you managed to identify any common and prolific lookalike diseases which occur on a global scale?

We have identified two types. Cycad-associated neurological disease is a tauopathy, which refers to a class of progressive neurodegenerative disorders (such as Alzheimer's disease) with a characteristic neuropathology; they include diseases that are inherited and others that may have environmental origins, or a mixture of both. Second, self-limiting crippling disorders in low-income countries, such as lathyrism and cassavism, have strong clinical similarities to inherited disorders characterised by spasticity.

While prevention is a viable approach for environmental disease, it is most unlikely that a cure for one could work for all – rather, the chemical triggers of neurological diseases can instead serve as powerful tools to probe vulnerabilities of the nervous system that result in common patterns of disease. Confounding this approach is recognition that the nervous system has a limited repertoire of clinical expressions of dysfunction, such that multiple causes acting at different critical steps in nervous system function may mislead the researcher because they surface clinically in similar neurological patterns.

Global health research

The pressures of increased food scarcity and climate change have a direct correlation with the incidence of neurodegenerative diseases, and research into these connections is essential for a stable and healthy future

GLOBAL HEALTH ADDRESSES physical and mental health worldwide. It transcends social, economic and political borders and seeks to address disparities in the quality of life through the prevention and treatment of disease. Research on the causes of diseases that unequally affect populations lays the foundation for knowledge and understanding, and can lead to sustainable interventions. Study of geographic isolates of disease can offer solutions both for affected communities and provide insight into lookalike diseases across the planet.

Dr Peter Spencer, of Oregon Health & Science University in Portland, has dedicated his life to understanding mechanisms behind the adverse effects of chemical substances on the human nervous system, and the relationship between chemical exposure and neurological diseases. His research has highlighted the plight of remote populations at high risk for neglected diseases, and is helping to confront these issues. The added threat posed by climate change has had a considerable impact on already vulnerable communities and their quality of life, requiring immediate action.

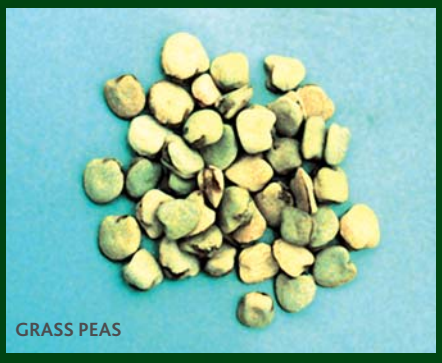
IMPACT OF CLIMATE CHANGE

Humans use plants to sustain life, but environmentally tolerant plants can also be health hazards. As climate change is set to increase, environmental extremes, such as drought, and flood, will force a growing number of impoverished humans to consume plants that can survive these events. This may lead to an increased consumption of hardy but potentially neurotoxic plants, raising the chances these populations will suffer from neurological diseases in the short- or long-term. Three such conditions studied by Spencer are the brain diseases caused by protein-rich grass pea (upper right) or protein-poor cassava (lower right), both of which can permanently cripple the heavy consumer, and a remarkable neurodegenerative disease linked to use of cycad seed (lower left) for food and medicine.


CYCAD PLANT

The cycad is a good example of a highly poisonous plant that has been used as a subsistence and emergency food because it resists hurricane, drought and fire. These attributes present obvious benefits to people who face such events and who must rely on whatever is available to eat. With adequate processing to remove toxic principles, as exemplified by Australian aborigines, the cycad is edible, but exposure to raw or incompletely detoxified seed is directly linked with neurodegenerative diseases that have plagued isolated communities in Guam (Mariana Islands), West Papua (Indonesia) and Honshu Island (Japan). Spencer's research into the connection between cycad consumption and the development of neurodegenerative diseases was the subject of the BBC documentary *The Poison That Waits*: "I have focused a considerable amount of research on neurodegenerative diseases associated with the ingestion of plant materials containing chemicals likely deployed in defence against predators," he confirms. "Those in cycad are linked experimentally with arrest of brain development and cancers in laboratory animals, with neuromuscular weakness in grazing cattle, and epidemiologically in humans with progressive brain degeneration reminiscent of motor neuron disease, parkinsonism and Alzheimer's disease. Thus identifying the environmental trigger of this prototypical neurodegenerative disorder will profoundly impact understanding of related diseases worldwide."

With a projected global population of 11 billion by 2100 and more extreme climatic events, the number of people who must rely on plants with toxic and neurotoxic potential is set to grow exponentially. While environmentally tolerant plants like cassava, sorghum and grass pea are valuable sources of food, new less-hazardous varieties with high nutritional value are sorely needed. "Such varieties must be tested experimentally to prove absence of significant toxic potential," Spencer remarks.


GRASS PEAS

THE IMPORTANCE OF LOCAL KNOWLEDGE

Furthermore, it is essential such plants are developed in partnership with affected populations to ensure they can be grown under local conditions, are palatable, and do not cause unanticipated problems. "A cardinal component of research in remote communities is investigational humility, sensitivity to socio-cultural heritage, and acceptance of the fact that critical knowledge can be acquired by understanding the ideas of disease-affected populations," states Spencer. Research projects of this kind are most productive where such diseases are highly prevalent, can be modelled in the laboratory, and subjected to cellular and molecular scrutiny. "When these studies link disease to plant chemicals, affected people may not understand how a food that is tasty and nourishing, and essential to life, could possibly be the cause of the medical disaster that has befallen them".

This research is fundamental to creating equality in global health and addressing the growing issue of food provision in the face of both climate change and population expansion. There is both a special opportunity to discover the causes, mechanisms and prevention of brain diseases that plague the human species and for the development of safe, climate-resistant crops that can protect and extend life of those who live in rain-fed areas of the world.


CASSAVA ROOTS

Education: the power of knowledge

Research into environmental hazards may identify their dangers, but this is only half of the battle. Education is essential in addressing the diseases they cause and improving the quality of life in developing nations

THE OREGON HEALTH & SCIENCE UNIVERSITY Global Health Center (OHSU GHC) offers interdisciplinary educational courses for tomorrow's healthcare professionals and research scientists. The various courses are designed to cover a wide range of socioeconomic and environmental factors that influence global public health, alongside the application of medical, surgical and nursing skills in low-resource settings.

With the aid of the Fogarty grant, Professor Peter Spencer teaches an elective course on Global Health in Changing Environments, which examines the major forces shaping population health worldwide and includes Oxford-style debates on ethically sensitive questions. "The goal is to challenge the health profession students to think, analyse and to expose and challenge pre-conceived ideas," he elucidates. Spencer's colleague, public health specialist Dr Jay Kravitz has for many years taught global health to OHSU's MPH students and recently developed a MPH Concentration in Global Health. He also organises weekly 'Conversations in Global Health' that expose students to a wide range of topics relating to health and disease in low-income settings.

INTERDISCIPLINARY COMMUNITY HEALTH & EDUCATION EXCHANGE (ICHEE)

Best-loved by OHSU's global health students is an innovative GHC elective that harnesses the teaching power of Portland's refugees and immigrants who in turn are offered health checks and, if needed, referrals to low-cost and mobile health clinics run by OHSU and other healthcare organisations. Spencer's long-time research associate and iCHEE director Valerie Palmer, together with Dr Isabel Soule and Cate Bishop, developed this popular elective to improve cross-cultural understanding and minority health. Under faculty supervision, students of dentistry, medicine, nursing and pharmacy work in teams in community settings in an educational exchange with people from all continents. The students develop an understanding of their clients' diverse cultures and experiences while also gaining an appreciation and respect for their health profession colleagues in the iCHEE programmes.

PROFESSIONALS' TRAINING IN GLOBAL HEALTH (PTGH)

Dr Andy Harris, an ophthalmologist by training with considerable experience in low-income settings, organises another highly innovative educational programme aimed at late-career and retired health professionals and available through the OHSU GHC. PTGH provides comprehensive training in global medicine for physicians, physician assistants and nurses who wish to volunteer for medical work in low-income countries or provide disaster relief. While offering essential education in primary care, such as family medicine, the PTGH also offers training in pertinent issues of public health in developing nations, including infectious diseases and tropical medicine.

Since its creation, 15 trainees have participated in 37 trips to over 19 countries, predominantly in Africa and Central America, while 89 per cent of all trainees have worked in free medical clinics in Oregon, providing much needed healthcare to those without provision or who are unable to afford medical treatments elsewhere.

RECEPTION

The interdisciplinary nature of the programmes offered by OHSC GHC has been highly praised for the range of skills and the preparedness that they provide to students who have worked in developing nations. However, Spencer believes that the truly innovative aspect of the training goes beyond the mere education provided: "They enjoy learning across disciplines in addition to their exposure to foreign cultures and attendant illness that may be seen rarely in their own home community. Cultural understanding and sensitivity are paramount components of these courses. Social determinants of health are key in understanding health and wellness," he explains. Funds permitting, the goal is to extend this interdisciplinary global health education to all OHSU students.

INCENTIVES

The GHC offers Summer Travel Scholarships to selected students to aid them in their studies abroad. To win one of these coveted scholarships, students must complete a semester-long global health course and submit a written application with an outline of the research project or anthropological study they wish to conduct. Applications are scored without knowledge of the applicant by a faculty-student award selection committee.

Over 50 per cent of all applications have received funding for a wide range of research projects that encompass the fields of dentistry, medicine, nursing and pharmacy. Students must submit progress reports based on what they have learnt and give oral presentations of their experience once it has concluded. This work is fundamental in encouraging trainees to develop their own knowledge and to explore common health problems in developing countries in the hope of finding innovative solutions.

VILLAGE GROUP IN PAPUA NEW GUINEA, S. FORE REGION NEAR KURU HOSPITAL (VALERIE PALMER, CENTRE)

Advocacy: progression through collaboration

Without effective communication, research remains purely conceptual and cannot be utilised to its full potential. The **OHSU** has employed a number of methods to disseminate its latest studies

ADVOCACY IS AN essential aspect of any modern research initative, and plays a particularly fundamental role in influencing public policy and resource allocation for medical care in emerging economies. Professor Spencer and his colleagues at the GHC, including business-trained Dr Jennifer Boyd, have taken advocacy one large step further in Oregon by calling for state-wide academic institutions, businesses, NGOs and government to collaborate in a synergistic, non-profit enterprise focused on education, health and sustainability.

The goal of GlobalOregon, as this initiative is called, is to develop innovative solutions that employ Oregon-pioneered technologies and expertise to promote development and improve health and wellness in populations at home and abroad. This will be achieved through the fusion of ideas drawn from multiple disciplines and across societal sectors.

According to Spencer: "Long-term, the combination of development and health projects could evolve into a significant specialisation of the U.S. Pacific Northwest, particularly here in Oregon and Washington," he states. "Brainpower-sharing and synergy across Oregon-based organisations is starting to open up exciting new research and capacity-building opportunities." One recently announced example is the Oregon African Stuies Consortium, a collaboration of key African specialists across five universities, including the OHSU GHC.

A particularly innovative local programme for which funding is sought by GlobalOregon is Smart Harnessing of Expertise of Refugee Professional Abilities (SHERPA). It seeks to identify and harness the expertise of professionals, such as doctors or nurses, among refugee populations who are not able to practice their skills in the U.S. These people can act as important figures between ethnic communities and licensed professionals, helping to overcome common socio-cultural obstacles and providing these fragile communities with a better quality of life.

RAISING AWARENESS

GlobalOregon has employed a number of tools to disseminate their work and to raise awareness of global health issues, including its website, a number of symposia, educational classes and public fundraisers. Foremost amongst their advocacy efforts is the need to raise awareness of the rapidity by which infectious diseases such as SARS and HIV can spread across the globe, and of the value in promoting education, health and environmental sustainability for fast developing countries. "Educational topics include the health of foreign populations employed in Oregon-owned industries that manufacture abroad, and the challenges and opportunities posed by the rise of China – Oregon's number one trading partner – and the possibility of a shared role in promoting public health in Africa.

EMPOWERING YOUTH FOR GLOBAL HEALTH

The GlobalOregon initiative received strong support from Dr Anne-Marie Slaughter, the 2011 inaugural Kathryn Robertson Annual Lecturer in Global Health, which was established in memory of the late daughter of OHSU President Joseph Robertson. Slaughter, a distinguished professor of International Politics at Princeton University. currently advises U.S. Secretary of State Hillary Clinton and co-developed her 2010 Quadrennial Diplomacy and Development Review. This review identifies the empowerment of girls and women as crucial determinants of future planetary development, health and security.

The education and empowerment of youth in developing countries is a fundamental basis for bottom-up development. GlobalOregon is seeking to incentivise young women to promote health and reduce disease and injury in vulnerable populations in the hope they can serve as collectors and distributors of health information, especially for areas where health professionals are scarce.

In many resource poor regions, 50 per cent of the population is under 20 due to the prevalence of disease and shorter life expectancy. By providing youths with education on health issues, GPS equipped cell phones and appropriate software, GlobalOregon seeks to empower these youths within their communities, providing them with the ability to improve their own social standing, and the health of their fellow citizens.

GLOBAL IMPACT ON HEALTH

In its three years, the OSHU GHC has had a significant impact on the world of global health, not only conducting fundamental research into neglected public health problems, but also in educating vulnerable populations to the dangers that they face, and the sustainable choices that they can make, all the while ensuring that these issues are known by the people who can help to make a difference. Their approach is truly holistic and is a perfect example of how to address disparities in disease burden and medical care worldwide and prepare for the future that we all face together.

INTELLIGENCE

GLOBAL HEALTH IN CHANGING ENVIRONMENTS

OBJECTIVES

Professor Peter Spencer seeks to address the issue of global health on three fronts: research, education and advocacy. His team implements this goal by creating innovative educational programmes, enacting an advocacy initative and conducting pioneering research.

KEY COLLABORATORS

Professor Spencer acknowledges the many contributions of numerous colleagues with whom he has been privileged to collaborate. This includes 27 years of collaboration with Valerie Palmer, GHC iCHEE director, and founder and President of Third World Medical Research Foundation.

FUNDING

40 years of continuous research funding, notably the U.S. National Institutes of Health

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PROFESSOR PETER SPENCER has dedicated his life to the causes and solutions of neglected human diseases of disadvantaged people in low-income countries. He received his doctoral degree from the University of London, Faculty of Medicine (Pathology), before commencing postdoctoral training in neuroscience at the Albert Einstein College of Medicine, where he became Professor of Neuroscience, Neurology and Pathology (Neuropathology), and Director, Institute of Neurotoxicology.

He joined Oregon Health Sciences University in 1988 and founded the Center for Research on Occupational and Environmental Toxicology, which he directed for 21 years. In 2007, Professor Spencer was invited to found and lead the OHSU Global Health Center.