hat’s on my mind this month are the major transitions occurring across the School of Medicine and how necessary change is for the advancement—of our students, our academic units, our educational curriculum and our leadership team.

Students: This month we celebrate convocation and graduation for our remarkable medical, graduate and allied-health students in the Class of 2014. Graduation is a time for reflection, celebration and a preview of what lies ahead. You have been tested, inspired and motivated to reach your full potential, while maintaining an incredible standard of excellence as you balanced the intense desire to achieve your personal and professional goals. This passion and determination that brought you to the University of Maryland School of Medicine will be the fuel that advances you throughout your life and career. You join your brilliant predecessors and fellow alumni who have led exceptional careers, transformed medicine and science in profound ways throughout the state and the nation through discoveries, clinical care, and education. I strongly encourage you to accept the challenges that lie ahead with determination and integrity—always aspiring for excellence. As part of the next generation of physicians and scientists, you must be committed to improving the health and well-being of the people of Maryland and beyond.

Academic Units: In this special issue of SOMnews, we celebrate the history and major research and medical contributions of the School of Medicine’s Center for Vaccine Development (CVD). As the CVD marks its 40th anniversary, we take this opportunity to look back on the numerous milestones made by our faculty. The outstanding investigators of the CVD have devoted their careers to developing new therapeutics for infectious diseases that affect the world’s citizens.

In addition to the enormous accomplishments of the CVD investigators, we also celebrate the life work of one of the CVD’s founders and its current director, Dr. Myron “Mike” Levine, MD, DTPH. Dr. Levine is a true luminary, recognized nationally and internationally as an eminent scholar and expert in the field of vaccinology, and boasts an amazing track record for research funding that has supported the mission of the CVD over these four decades. We are indebted to Dr. Levine for his ambitious vision, passion for research, incredible discoveries, dedication to improving medical care for all people, and his consummate and extraordinary leadership over the years.

Curriculum: Many of you are aware that a major component of our Shared Vision 2020 is the Accelerating Innovation and Discovery in Medicine (ACCEL-Med) Initiative. We have considered how to more actively involve all our students in a scholar’s research continuum—beginning when each student enters the School of Medicine, either in the medical, graduate or allied-health programs, and is first exposed to—and becomes an active participant in—aucademic biomedical research. To crystallize the goals of the individual research programs and begin to recognize and award students who demonstrate extraordinary acuity and productivity in their research projects, we are bringing those collective efforts under one new program: the Young Brain Initiative (YBI).

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The Center for Vaccine Development Celebrates 40 years

This year the School of Medicine’s Center for Vaccine Development (CVD) is celebrating its 40th anniversary. What started as the Clinical Research Center for Vaccine Development (CRCVD), a clinical vaccine testing unit pilot project with $250,000 in funding and nine staff members, is now a multidisciplinary academic vaccine development enterprise with scores of millions of dollars in annual funding and facilities and hundreds of staff in several field sites around the globe. Myron “Mike” Levine, MD, DTPH, has been the Director of the CVD from its inception and has overseen this growth and transformation.

CRCVD was initially a one-year pilot project supported by a NUI research contract, with an option for an extension,” Dr. Levine explains. “The extension was dependent on us demonstrating that a functioning Research Isolation Ward could be established wherein clinical trials of vaccines that included live vaccines and experimental challenges (e.g., with influenza viruses) could be undertaken in community volunteers under physical containment.”

The CRCVD project was a resounding success, setting the groundwork for the establishment of the CVD as it exists today beginning in 1976. Dr. Levine’s vision when writing the first grant application for CVD was to merge research in vaccinology and global health. An important difference between CRCVD and CVD was that the latter could support clinical trials of enteric vaccine candidates designed and constructed at CVD, as well as studies of the pathogenesis of bacterial enteric infections, and there was core funding from the NIH to support related microbiology and immunology laboratory activities. With separate sources of funding, Dr. Levine and his colleagues could also begin to undertake various field epidemiologic studies of diarrheal disease and clinical trials of therapeutic and preventive measures in populations in developing countries, such as Latin America.

CVD Chile was a harbored for research during the last quarter of the 20th century, but it has diminished greatly in size as Chile has evolved from the developing country it was when Dr. Levine first started working there in the mid-1970s to the industrialized country it is now. “Plummeting young child mortality, extending life expectancy, and increasing gross national income per capita enabled Chile not only to achieve status as an industrialized country but to become the only South American country to be invited into the Organization for Economic Co-

CVD Timeline 1974 - 2013

July, 1974: Myron “Mike” M. Levine, MD, DTPH, and the late Richard B. Hamrick, MD, MACP, establish the Clinical Research Center for Vaccine Development (CRCVD), the precursor of the Center for Vaccine Development (CVD).

October, 1974: The CRCVD undertakes its first vaccine study, a clinical trial to assess the safety and immunogenicity of a candidate live Mycoplasma pneumoniae vaccine.

Early 1976: CRCVD is restructured by Mike Levine and becomes what is now known as CVD.

Summer 1976: CVD is designated as a Vaccine and Treatment Evaluation Unit (VTEU) for the first time. With fear of a swine flu pandemic spreading in the U.S., CVD is assigned by NIH to perform safety/immunogenicity studies of pandemic swine influenza vaccines in both adults and children, with the ambitious goal to produce sufficient vaccine to immunize more than 100 million people.

1978-1989: Dr. Levine, in conjunction with the late Dr. José Manuel Boggio, establishes a Typhoid Fever Control Program within the Ministry of Health of Santiago, Chile, and paves the way for

Late 1970s: CVD’s first oral cholera vaccine, a non-replacing vaccine consisting of alcohol-inactivated V. cholerae 01 administered in combination with glutaraldehyde-treated cholera toxin (i.e., a cholera toxoid) is tested. Also, CVD studies of bacterial pathogenesis in volunteers establish that enteroaggregative E. coli (EAggEC) strains that elaborate only heat-stable enterotoxins are capable of causing diarrhea. This result is contrary to the dogma prevalent at the time. Even more momentous is the discovery that volunteers who ingested classical serotype enteropathogenic E. coli (EPEC) strains that elaborated only heat-stable enterotoxins were not linked to tetanus toxin. To carry out malaria challenge studies in volunteers, CVD establishes an insectary, as well as a system to culture Plasmodium falciparum in vitro and purify the CVD-1 clone of P. falciparum (derived from the MSF strain).

1980s: CVD expands research on vaccines, including tetanus, pertussis, and cholera.

1985-1986: CVD gets deeply involved in studies of one of the first two early malaria vaccines, the Ruth and Victor Nussenzweig vaccine, which consists of 12 amino acid residues (14SP) covalently linked to tetanus toxoid. To carry out malaria challenge studies in volunteers, CVD establishes an insectary, as well as a system to culture Plasmodium falciparum in vitro and purify the CVD-1 clone of P. falciparum. The result is contrary to the dogma prevalent at the time. Even more momentous is the discovery that volunteers who ingested classical serotype enteropathogenic E. coli (EPEC) strains that elaborated only heat-stable enterotoxins were not linked to tetanus toxin. To carry out malaria challenge studies in volunteers, CVD establishes an insectary, as well as a system to culture Plasmodium falciparum in vitro and purify the CVD-1 clone of P. falciparum (derived from the MSF strain).

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operation and Development (OECD),” says Dr. Levine, who credits, in part, a series of collaborative public health research programs carried out by CVD and the Ministry of Health of Chile for this change.

Today, the Republic of Mali in West Africa is an important area of focus for the Center. “CVD-Mali has two components,” Dr. Levine explains. “One focuses on endemic and epidemic infectious diseases, mainly affecting young children. This component, under Dr. Malo, represents a partnership between the Ministry of Health of Mali and the University of Maryland, Baltimore. The other component is the Bandiagra Malaria Project, run by CVD’s Malari Group, which works in a hyper-endemic area of Mali around Bandiagara.”

Malaria and other diseases that mainly affect populations in the developing world and for which there do not exist substantial markets in industrialized countries have historically not been a priority for “Big Pharma” vaccine manufacturers. CVD has helped to fill this void, focusing on endemic diseases (cholera, typhoid & paratyphoid fever, Shigellosis, YETEC) malaria and Group A Streptococcal pneumonia. CVD also worked on ways to administer vaccines without injection (mucosal vaccines) or with fewer injections (combination vaccines and single-dose vaccines) and extending the targets (vaccines for early infancy, the elderly and pregnant women).

CVD has been a leader in introducing pneumococcal influenza type b and influenza vaccines in West Africa. Bio-defense vaccines were a major focus during the decade after 9/11/2001.

The Center is particularly devoted to infectious diseases that affect children in less-developed countries. To gather information on the burden of diarrheal diseases, CVD oversaw the Global Enteric Multicenter Study (GEMS), the largest, most comprehensive study of the burden and etiology of childhood diarrheal diseases ever conducted in developing country settings. The first CVD, Melinda Gates Foundation funded that historical effort. CVD faculty and staff also consult with international agencies such as the World Health Organization, the Agency for International Development, The World Bank, and the GAVI Alliance (the Global Alliance for Vaccines and Immunization), as well as with individual governments and industry.

A considerable portion of funding for the CVD comes from federal agencies, particularly the National Institute of Allergy and Infectious Diseases (NIAID). Recent major grants from NIH include: competitive renewals of the Vaccine and Treatment Evaluation Unit (VTEU) (Karen Koffert, PI), a 10-year N01 contract with potential funding up to $135 million, and of the Cooperative Center for Human Immunology (CCHI), a 5-year $13.5 million U19 grant (Marcelo Sztein, PI); and an award for a Center of Excellence for Translational Research (CETR), a 5-year $25 million U19 grant (Mike Levine, PI).

Funding for training also comes from federal sources. The CVD has trained generations of scientists in the field of vaccinology, a term that was rarely used when CVD started. CVD was the first to receive a $100 million support an array of funding up to $135 million, and of the CETR (CVD-Mali) is established as a Vaccine Research Unit (VTeU) (Karen Kotloff, PI), an award for a Center of Excellence for Translational Research (CETR), a 5-year $25 million U19 grant (Mike Levine, PI). Funding for training also comes from federal sources. The CVD has trained generations of scientists in the field of vaccinology, a term that was rarely used when CVD started. CVD was the first to receive a $100 million support an array of funding up to $135 million, and of the CETR (CVD-Mali) is established as a Vaccine Research Unit (VTeU) (Karen Kotloff, PI), an award for a Center of Excellence for Translational Research (CETR), a 5-year $25 million U19 grant (Mike Levine, PI). 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Lessons in Life and Medicine Garnered by Medical Students While Abroad

Through a variety of global projects, medical students at the University of Maryland are already becoming practitioners in the advancement of international medicine.

While in Burma studying drug-resistant malaria, third-year medical student Christian Larsen would take a cab to the Department of Medical Research and begin work. Then the power would go out. When it eventually flickered back to life, he would begin again. “It required you to be resilient and adaptable,” Larsen says. “It teaches you to learn to work with circumstances you have.”

This was a good lesson when working with a disease as unpredictable as malaria. “You take a virus, and a quadrivalent vaccine is good enough, it’s going to cover four of the most prevalent strains, and the virus won’t change quickly enough since it has a limited repertoire of genes,” Larsen explains. “If you take a protozoan parasite like malaria, it is complex, multicellular, and can make a lot of broad changes to its genome and continue to thrive. Malaria required us to use novel strategies in vaccine development.”

Kristin Lohr, a third-year medical student who spent six weeks in Malawi surveying rural health centers’ capability of providing care for expectant mothers, was as impressed as Larsen by the resourcefulness of clinicians practicing with limited means. “They really have to listen to what patients are saying. ‘They have a better grasp of clinical medicine than we do here,’” she said. “It’s something you hear a lot about but you don’t really grasp the extent of it until you’re there and actually see what it means.”

The Global Health Interest Group (GHIG) is a student-run program that serves as a forum for medical students to connect with mentors working internationally, to increase awareness of global health issues.

This year GHIG has worked with other professional schools to develop a new scholarship promoting interprofessional work abroad and has created a panel on international work being done locally. Crystal Bae, a second-year medical student and president of GHIG, has spearheaded these efforts. She also volunteers for the International Rescue Committee, where she teaches health workshops to English proficient refugees. “We talk about preventative health issues, like how to read a nutrition label,” Bae said. In the future, she plans to start home visits to refugees struggling with multiple medications that require close monitoring or have complex administration schedules. “Everyone has the right to a lead a healthy life and have access to care in medicine,” she said. “No matter what country or city you’re in.”

Students who have gone abroad emphasise that lessons learned working in international medicine continue to influence their training at home. “It makes me think, ‘How I am learning clinically?’” Lohr said. “In my third year, I rely so much on tests and things I can order. But would I do for this patient if I were in Malawi?”