Eunice Kennedy Shriver National Institute of Child Health and Human Development

NATIONAL ADVISORY CHILD HEALTH AND HUMAN DEVELOPMENT COUNCIL

MEETING MINUTES

September 9–10, 2020

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
***EUNICE KENNEDY SHRIVER* NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT**
NATIONAL ADVISORY CHILD HEALTH AND HUMAN DEVELOPMENT COUNCIL
MEETING SUMMARY
September 9–10, 2020[1]

The National Advisory Child Health and Human Development (NACHHD) Council convened its 174th meeting at 12:30 p.m. on Wednesday, September 9, by National Institutes of Health (NIH) videocast. The meeting was open to the public on September 9 from 12:30 to 5:06 p.m. and on September 10 from 12:30 to 1:30 p.m. As provided in Sections 552b(c)(4) and 552b(c)(6), Title 5, U.S.C., and Section 10(d) of Public Law 92-463, for the review, discussion, and evaluation of grant applications and related information, the meeting was closed to the public on September 10, 2020, from 1:45p.m. until 5:00 p.m.

Dr. Diana W. Bianchi, Director, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), presided.

Council members present:
Diana W. Bianchi, M.D. (Chair)
Michael Boninger, M.D.
Susan Bookheimer, Ph.D.
Michele Caggana, Sc.D.
John P. Coughlin, M.D.
Kathleen B. Egan, Ph.D.
Catherine Gordon, M.D., M.Sc.
Lucky Jain, M.D.
Missy Lavender, M.B.A.
Martin Matzuk, M.D., Ph.D.
Carmen L. Neuberger, J.D.
Adam C. Resnick, Ph.D.
Annette Sohn, M.D.
Alyce Thomas, RD
Alan Thevenet N. Tita, M.D., Ph.D., M.P.H.
Anthony J. Wynshaw-Boris, M.D., Ph.D.

Council members absent:
Clifford Tabin, Ph.D.
Rebeca Wong, Ph.D.

National Advisory Board on Medical Rehabilitation Research Council Liaison:
Art English, Ph.D.

***Ex officio* members present:**
Patricia Dorn, Ph.D.
Aaron M. Lopata, M.D., M.P.P.

Department of Defense:
MAJ Barbara K. Bujak, Ph.D., PT, DPT

[1] Members absent themselves from the meeting when the Council discusses applications from their own institutions or when a conflict of interest might occur. The procedure applies only to individual applications discussed, not to en bloc actions.

Executive secretary:
Eugene G. Hayunga, Ph.D.

Others present:
Members of NICHD staff
Members of NIH staff
Members of the public

Day 1: Wednesday, September 9, 2020

I. CALL TO ORDER AND INTRODUCTORY REMARKS

Dr. Bianchi welcomed members of the NACHHD Council and other participants to this meeting. She expressed the hope that those in attendance and their loved ones were in good health during the COVID-19 pandemic.

Review of Confidentiality and Conflicts of Interest

Dr. Hayunga reminded Council members that all members were required to read, agree to, and sign the confidentiality and nondisclosure rules for special government employees on the Council member website before evaluating any NIH grant applications. Before the meeting, Council members had received a conflict-of-interest certification form, which they were required to sign. Dr. Hayunga also reminded Council members that they are required to recuse themselves and leave the virtual meeting before any discussion involving any organizations or universities for which they are in conflict, in addition to those listed in the Council Action document. Council members are not allowed to serve on the NIH peer review panel while serving as Council members because NIH policy indicates that individuals may not serve on both the first and second levels of peer review.

Council Minutes

A motion to approve the June 11, 2020, NACHHD Council meeting minutes carried.

Future Meeting Dates

Dr. Hayunga reviewed the future Council meeting dates:

Tuesday, February 2, and Wednesday, February 3, 2021
Tuesday, June 8, 2021
Friday, September 10, 2021

II. NICHD DIRECTOR'S REPORT AND COVID-19 RESPONSE

Dr. Bianchi delivered the director's report.

Budget

The Coronavirus Aid, Relief, and Economic Security (CARES) Act provided $945.4 million to NIH to "prevent, prepare for, or respond to coronavirus, domestically or internationally." This funding went to the NIH Office of the Director and to five NIH Institutes and Centers (ICs) that

did not include NICHD. However, the Office of the Director made some CARES Act funds available to other ICs, and NICHD successfully competed for funding for several COVID-19–related initiatives.

House Speaker Nancy Pelosi and Secretary of the Treasury Steven Mnuchin have been negotiating about the fiscal year (FY) 2021 federal budget, and the likely result will be a continuing resolution. This resolution will probably keep NICHD's 2021 funding at the same level as in FY 2020, which could make it challenging to fund new initiatives. The House of Representatives and Senate have not reached agreement on a new COVID-19 relief package.

Trans-NIH COVID-19 Activities

NIH has used its CARES Act funding for several COVID-19 efforts, including:

- Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV), a public–private partnership to develop a coordinated research strategy for prioritizing and speeding development of promising treatments and vaccines
- Rapid Acceleration of Diagnostics (RADx), a fast-track technology development program that supports solutions to increase the U.S. capacity for SARS-CoV-2 testing
- Predicting Viral-Associated Inflammatory Disease Severity in Children with Laboratory Diagnostics (PreVAIL kIds), a large cohort study with $20 million of RADx funding to advance understanding of the pediatric SARS-CoV-2 spectrum of illness

Of those in the United States infected with SARS-CoV-2, 9.5% have been children, and approximately 0.5% of these children have developed multisystem inflammatory syndrome in children (MIS-C). NIH COVID-19 research goals for pediatric populations are to determine the following:

- Range of clinical manifestations of SARS-CoV-2 and COVID-19
- Etiology and clinical manifestations of MIS-C
- Risk profile for patients who develop MIS-C or severe COVID-19
- Variations in immune response underlying clinical manifestations in children infected with SARS-CoV-2 along with predictive and prognostic immune biomarkers
- Long-term consequences of SARS-CoV-2, COVID-19, and MIS-C

NICHD has worked with the National Heart, Lung, and Blood Institute and the National Institute of Allergy and Infectious Diseases (NIAID) to create a centralized cohort of hospitalized children with COVID-19 for MIS-C research. NICHD is also supporting MIS-C research through its Pediatric Trials Network, whose protocol has been expanded to include 12 drugs used to treat COVID-19 in children and to collect data on children with COVID-19.

A valuable resource for this research consists of state-level COVID-19 data (including data on cases, tests, hospitalizations, and deaths) reported every other week by the American Academy of Pediatrics. Approximately 100 children have died as a result of COVID-19.

The Global Network for Women's and Children's Research is tracking the prevalence and impact of SARS-CoV-2 infection among approximately 16,000 pregnant women in seven low-

and middle-income countries in Asia, Africa, and Central America. The study will compare maternal, fetal, and neonatal outcomes of infected women to those of noninfected women.

NICHD Efforts to Increase Diversity and Combat Health Disparities

NICHD leaders are committed to diversifying the scientific workforce, both within the Institute and in the broader extramural community. Ongoing activities led by NICHD's Office on Health Equity include:

- Development of plans to diversify the internal workforce
- Efforts to increase the diversity of the extramural workforce and encourage applications from investigators and trainees who are underrepresented in biomedical research
- Examination of the Institute's health disparities portfolio and the best way to address health disparity/health inequity with respect to the Institute's research populations

NICHD Strategic Plan Implementation

A few examples of activities to implement NICHD's 2020 strategic plan and recent advances are as follows:

- Theme 1: Understanding the molecular, cellular, and structural basis of development
    - Activities: Support for bioinformatics resource centers for developmental biology, leadership of the pediatric component of the NIH-wide Developmental Genotype-Tissue Expression Project
    - Advances: Identification of eight rare and damaging genetic variants associated with spina bifida and of a genetic mutation that enhances cognitive flexibility in mice
- Theme 2: Promoting gynecologic, andrologic, and reproductive health
    - Activities: The Centers to Advance Research in Endometriosis, a request for applications (RFA) on genomic predictors of pregnancy loss
    - Advances: U.S. Food and Drug Administration (FDA) approval of a drug for heavy menstrual bleeding due to fibroids, evidence that vitamin and mineral supplements do not increase male fertility
- Theme 3: Setting the foundation for healthy pregnancies and lifelong wellness
    - Activities: Tracking of COVID-19 in pregnant and lactating women, an RFA on the role of nutrition in the care and development of preterm infants
    - Advances: Evidence that low-dose aspirin might reduce the risk of preterm birth among first-term mothers and that adverse pregnancy outcomes are more common in women who are deaf or hard of hearing
- Theme 4: Improving child and adolescent health and the transition to adulthood
    - Activities: Identifying children at risk of MIS-C, an adolescent transition workshop on September 30 and October 1, 2020
    - Advances: A technology platform to maximize diagnostic tests while minimizing volumes of test samples collected from the youngest patients
- Theme 5: Advancing safe and effective therapeutic devices for pregnant and lactating women, children, and people with disabilities
    - Activities: Maternal and Pediatric Precision in Therapeutics, Rehabilitation Research Infrastructure Centers

- Advances: Seven pediatric label changes under the Best Pharmaceuticals for Children Act, evidence showing that use of personal protective equipment does not affect the quality of compression in pediatric cardiopulmonary resuscitation

The NICHD website soon will feature progress reporting on strategic plan implementation.

Task Force on Research Specific to Pregnant Women and Lactating Women (PRGLAC)

PRGLAC was created by the 21st Century Cures Act, and NICHD recently submitted an implementation plan to the Secretary of Health and Human Services (HHS). As soon as NICHD receives the secretary's response, it will post the recommendations.

Staff Updates

Theresa H. Cruz, Ph.D., is the new director of the National Center for Medical Rehabilitation Research (NCMRR). NICHD is in the midst of a search process for a new scientific director and a new director of the Division of Population Health Research. Acting directors who have been in place since February are Rohan Hazra, M.D., Division of Extramural Research; Gene Hayunga, Ph.D., Division of Extramural Research; and Sonia S. Lee, Ph.D., Maternal and Pediatric Infectious Disease Branch.

Dr. Bianchi also welcomed several new staff members of the Division of Extramural Research.

Council Discussion

Dr. Caggana asked whether PreVAIL kIds will only enroll children who are hospitalized or whether the study will include all children diagnosed with COVID-19. Dr. Bianchi explained that the study has not yet started, and grant applications are due on September 30. The study will include children with COVID-19 who are and are not hospitalized. Most of these children will be outpatients and will have mild effects or no effects. The goal is to predict which children will later develop MIS-C or become severely or chronically ill following a COVID-19 infection.

III. PRGLAC IMPLEMENTATION PLAN

Lisa Kaeser, J.D., provided an update on the implementation plan for the Task Force on Research Specific to Pregnant Women and Lactating Women (PRGLAC).

Background

In the past, clinical studies did not routinely include women (even those who were not pregnant), children, older adults, or individuals with intellectual and physical disabilities. As a result, the majority of people in the United States were not routinely represented in clinical studies. Consequently, many medications are prescribed for populations in which these medications have never been tested. Several populations that are underrepresented in clinical research are priority populations for NICHD.

The reasons for excluding pregnant women and lactating women from research include concerns about liability and the complexity of research during pregnancy (e.g., because the fetus and placenta change over time and pregnancy produces physiologic changes in women). More than

90% of the 6.3 million women in the United States who become pregnant each year take at least one medication, and 70% take at least one prescription medication.

The default position of clinical providers is that women who are preparing for pregnancy or are pregnant should stop taking all medications, even if they need them for a serious medical condition. In some cases, this position has worsened women's health and had severe consequences for their offspring.

These issues have come into particularly stark focus during the COVID-19 pandemic. The NIH Strategic Plan for COVID-19 Research calls for research to understand and address COVID-19 maternal health and pregnancy outcomes. However, this plan has not increased inclusion of pregnant women or lactating women in clinical COVID-19 studies.

History of PRGLAC

The 21st Century Cures Act of 2016 established PRGLAC to identify and address knowledge gaps pertaining to safe and effective therapies for pregnant women and lactating women. In 2018, PRGLAC submitted a report to the Secretary of HHS and Congress describing research gaps and made 15 recommendations for addressing these gaps.

As a result of PRGLAC activities, NIH began collecting and publishing data by category on NIH funding for research on pregnancy, maternal health, and breastfeeding, lactation, and breast milk. NICHD will publish a new category on maternal morbidity and mortality later this year. PRGLAC also established the PregSource® medications tracker to gather information on the medications and supplements used by pregnant women.

Implementation Plan

PRGLAC recently developed a plan to implement its recommendations with support from four working groups that addressed research and training, regulatory issues, communications, and discovery. Although the working groups met separately, they came up with several important, overlapping recommendations. The plan was recently submitted to the Secretary of HHS.

IV. SARS-CoV-2 VACCINES IN PREGNANT WOMEN

Emily Erbelding, M.D., M.P.H., director of the Division of Microbiology and Infectious Diseases at NIAID, provided a status report on considerations for SARS-CoV-2 vaccine research in pregnant women.

Background

Operation Warp Speed aims to deliver 300 million doses of a safe, effective vaccine for COVID-19 by January 2021 as part of a broader strategy to accelerate the development, manufacturing, and distribution of COVID-19 vaccines, therapeutics, and diagnostics. NIAID is primarily involved in the vaccine component of this program, which is leading simultaneous activities that are usually conducted sequentially.

Dr. Erbelding coordinates clinical trials in special populations, defined as populations associated with special regulatory or ethical considerations. Special populations include pregnant women because preclinical packages typically require developmental and reproductive toxicity testing for FDA approval, and children and adolescents younger than 18 years because parental consent is usually required. Other special populations are older adults, who have a high risk of poor outcomes from COVID-19, and individuals with HIV, whose exclusion from clinical trials has no valid justification.

Paradigm Shift

The traditional approach to vaccine research in pregnant women is to start with efficacy trials in nonpregnant adults. Participants who become pregnant during these trials are followed carefully. If the trials show that the vaccine has efficacy, bridging studies are conducted in pregnant volunteers to bridge the gap between efficacy and immunogenicity. This approach makes it possible to identify correlates of protection and protects women and their offspring from vaccine-related risks. However, the traditional approach would delay the administration of a new COVID-19 vaccine to women of childbearing age for more than a year, and a large proportion of first responders and essential workers would not be vaccinated.

A paradigm shift has occurred in the published literature on vaccine development toward the presumption that pregnant women will be included in efficacy trials if no reason exists to exclude them. Proponents of this view argue that it normalizes the inclusion of pregnant women in vaccine deployment and in vaccine research and development. Furthermore, pregnant women can give voluntary and informed consent, and the burden of proof falls on those who argue for excluding this population. Vaccine studies that include women of childbearing age should have plans to systematically collect data on immunogenicity and pregnancy-specific factors.

COVID-19 in Pregnancy

Pregnant women might have a higher risk of SARS-CoV-2 infection than other women, and they might have a greater risk of severe outcomes. The impact of the virus on the fetus and infant are unknown, as is whether pregnancy alters the immune response to the virus. A concern is that maternal vaccination might interfere with the ability to administer other vaccines in very young infants.

According to a report published on June 26, 2020, by the Centers for Disease Control and Prevention, the hospitalization rate for pregnant women with COVID-19 is approximately five times higher than in nonpregnant women. Similarly, rates of intensive care unit (ICU) admission are 1.6 times higher, and rates of mechanical ventilation are almost twice as high. Although some of the higher rates in pregnant women might be due to conservative management because of their pregnant status, this rationale does not explain the higher rates of mechanical ventilation. A report from Sweden had similar findings.

COVID-19 Vaccine Testing in Pregnant Women

FDA has issued guidance on the development and licensure of a vaccine to prevent COVID-19 in pregnant women. For example, FDA encourages sponsors to conduct developmental and

reproductive toxicity studies before enrolling pregnant women and women of childbearing potential who are not actively avoiding pregnancy into clinical trials.

In preparation for clinical trials in pregnant women, NIAID has convened a group of investigators and obstetrician/gynecologists with vaccine experience to draft a generic plan for a Phase 2 bridging study in pregnant women and lactating women to be conducted in parallel with ongoing efficacy trials. The plan, which is based on one that was never implemented for an H7N9 influenza vaccine, would assess the vaccine's safety and immunogenicity in the second and third trimesters in 130 to 150 women. The mothers would be followed for 12 months, and their infants would be followed for 3 months.

Early in the pandemic, children were believed to have a low risk of infection or serious COVID-19 if they were infected, but emerging data challenge these assumptions. Many children have now been hospitalized with COVID-19, and most have been admitted to the ICU. Children might need to be vaccinated for their own health and not only to prevent transmission to adults. The traditional approach to vaccine development in children is similar to that in pregnant women, except that the bridging studies start in older adolescents aged 17 to 18 and are followed by studies in younger and younger children. NIAID is developing template protocols for trials in children.

Discussion

Dr. Bookheimer recommended that children exposed to a COVID-19 vaccine *in utero* and those who develop COVID-19 be followed longer because the effects of medications given to pregnant women often do not show up in their children until the children start school and are identified as having learning disabilities. Dr. Erbelding reported that the Phase 2 trial plans will not follow children for these late effects, but such studies might be done as part of post-license surveillance by FDA.

V. ANNUAL DIVISION OF INTRAMURAL RESEARCH REPORT

Mary Dasso, Ph.D., Acting Scientific Director of the Division of Intramural Research (DIR), described DIR activities over the past year. DIR has approximately 880 employees, including 59 principal investigators, 48 staff scientists, and 293 trainees. The division has 12 scientifically based affinity groups, 66 clinical protocols, and six accredited medical training programs.

The Intramural Research Program, comprised of the DIR and the Division of Intramural Population Health Research (DIPHR), are supported by about 14% of NICHD's annual budget. Approximately one-third of the DIR's $200 million budget goes to salaries, and most of the rest is spent on the Clinical Center "school tax" (a fee paid by each IC's intramural research program to support the Clinical Center), overhead, and about one-fifth of the budget supports laboratory consumables.

The NIH Earl Stadtman Tenure-Track Investigator Program aims to recruit a diverse group of scientists studying important problems in innovative ways. The DIR has recruited two new Stadtman investigators: Jeffrey Farrell, Ph.D., Unit on Cell Specification and Differentiation, and Doreen Matthies, Ph.D., Unit on Structural Biology, who is expected to start soon. In 2020–

2021, DIR plans to hire a physician-scientist and a developmental biologist through this program. The DIR has also developed a Physician Scientist Development Program with the goal to improve recruitment and training of tenure-track physician scientists, using a series of programs at different career levels.

NICHD has ongoing clinical fellowship programs in endocrinology (the NIH Inter-Institute Endocrine Training Program and NICHD Pediatric Endocrinology Inter-Institute Training Program), gynecology and reproductive endocrinology (Combined NICHD/Federal Reproductive Endocrinology and Infertility Training Program and NICHD Pediatric and Adolescent Gynecology Training Program), and maternal-fetal medicine.

Two NICHD intramural researchers recently received important honors. Peter Basser, Ph.D., was elected to the National Academy of Engineering, and Douglas Fields, Ph.D., was elected to the American Association for the Advancement of Science.

Many NICHD DIR education programs are led by the NICHD Office of Education. Key office activities include workshops for trainees in public speaking and teaching, grantsmanship and publishing, and career development.

NICHD intramural diversity initiatives to train, support, and sustain a diverse cohort of individuals traditionally underrepresented in science include the NICHD Scholars Developing Talent Program at the postbaccalaureate/graduate student level and Fellows Recruitment Incentive Award at the postdoctoral level. In addition, the NICHD summer internship program supports a number of positions for students from groups traditionally underrepresented in science or from disadvantaged backgrounds. Graduates of NICHD's postbaccalaureate program have been accepted to numerous medical schools as well as to several M.D./Ph.D., Ph.D., and M.S. programs. In addition, NICHD fellows have received research funding from both NIH and professional societies.

Funding opportunities for intramural research at NICHD include the following:

- Opportunities for Collaborations at the NIH Clinical Center (U01) which supports collaborative research projects aligned with NIH efforts to enhance the translation of basic biological discoveries into clinical applications that improve health through collaboration between extramural and intramural investigators.
- Office of AIDS Research Strategic Funding
- NICHD Scientific Director's Awards, which support collaborations among investigators and support new research ideas
- NICHD Office of the Director Strategic Planning Awards, which support research to address objectives and aspirational goals in the plan

VI. GENETIC EPIDEMIOLOGY OF EARLY GROWTH AND CARDIOMETABOLIC LINKS

Fasil Tekola-Ayele, Ph.D., M.P.H., Earl Stadtman Investigator, Epidemiology Branch, Division of Intramural Population Health Research, NICHD, described his research on the genetic epidemiology of cardiometabolic diseases in early life. His work is motivated by the consistent

finding that both extremes of birth weight are associated with an increased risk of cardiovascular disease later in life.

Impact of Accelerated Placental Aging on Fetal Growth

Some placentas show signs of accelerated aging, which can lead to pregnancy complications, including fetal growth arrest. The epigenetic clock, which uses DNA methylation and selected markers, is a promising molecular marker of biological age that has high prediction accuracy. Placental epigenetic aging might be one of the functional links between genetic influences and fetal growth. Fetal growth is dynamic throughout gestation, and its genetic contributions might not be adequately captured by studying birth size.

Dr. Tekola-Ayele studied sex-specific associations of placental age acceleration with fetal growth, neonatal anthropometry measures, and risk of low birth weight using 301 placental samples provided at delivery from the NICHD Fetal Growth Studies. Placental age acceleration was defined as the difference between DNA methylation age and gestational age.

The findings showed no fetal sex differences in the correlations between epigenetic age and gestational age. In males, greater age acceleration was associated with decreases in all fetal growth measures in the last 8 weeks of gestation. In females, greater age acceleration had positive associations with fetal weight and all growth measures between 13 and 40 weeks of gestation. This work shows that the placental epigenetic aging clock might be a useful marker of pathophysiological processes that could lead to adverse fetal growth outcomes.

In a study of twins, the genetic contributions to fetal growth varied by gestational age. The influence of genetics compared to environmental factors, increased throughout gestation and peaked toward the end of the second trimester.

Causes of Accelerated Placental Aging

Dr. Tekola-Ayele investigated whether placental age acceleration is related to maternal cardiometabolic measures, including blood pressure, prepregnancy obesity, dyslipidemia, and gestational weight gain. The findings showed an inverse relationship between gestational weight gain in each trimester and age acceleration and between maternal dyslipidemia and age acceleration only in lean women. The findings did not show a strong relationship between genetic ancestry and age acceleration, but they did show an inverse correlation with African and East Asian ancestry and a positive correlation between age acceleration and Amerindigenous ancestry. Therefore, in additional to maternal dyslipidemia and higher gestational weight gain, genetic ancestry might drive placental aging.

Novel Biomarkers

A trans-ethnic genomewide association study of fetal growth identified and validated a novel locus in the *ITPR1* gene that is associated with lower fetal weight at 27 to 32 weeks of gestation. The *ITPR1* genetic locus might therefore reduce fetal weight through a functional impact on placental aging; identifying the *in utero* mechanism could help identify and inform molecular and clinical intervention targets.

Maternal cardiometabolic phenotypes are known to be associated with birth weight and future cardiovascular disease (CVD) risk. Understanding the mechanisms that underlie these links could be useful for developing early interventions. Studies show that maternal cardiometabolic traits are relevant to biological processes involved in early development, and several placental methylated and expressed genes that Dr. Tekola-Ayele has identified are well-known cardiovascular disease loci in adults. Epigenetic biomarkers relevant to CVD might be apparent in the placenta at birth.

The NICHD Study of Pregnancy and Neonatal Health is integrating genetic, epigenetic, and transcriptomic markers, as well as environmental factors, in a large cohort of pregnant women who will be followed through delivery. Dr. Tekola-Ayele's goal in this study is to identify genetic factors that regulate fetal growth and aging of the placenta through discovery in African Americans.

Discussion

Dr. Resnick asked whether myoinositol, inositol 1,4,5-trisphosphate (IP3) production, or calcium homeostasis could produce similar outcomes independently of the receptor level. Dr. Tekola-Ayele has not investigated these factors. However, he noted that *ITPR1* and *ITPR2* have been linked with fetal growth and several *in utero* exposures, including the products of smoking, that influence fetal growth.

Dr. Jain asked about the placental biopsies that Dr. Tekola-Ayele used in his studies and how, given the inverse correlation between fetal weight gain and placental aging, Dr. Tekola-Ayele might explain intrauterine growth restriction pregnancies. Dr. Tekola-Ayele replied that all of the placental biopsies were collected at birth from normal deliveries. He added that placental age acceleration is inversely linked to maternal gestational weight gain but not to fetal weight gain. For example, the placentas of obese mothers at delivery seem to be less mature than those of normal-weight mothers. Therefore, accelerated aging of the placenta might slow fetal maturity.

Dr. Tita is studying the impact of maternal hypertension on infant outcomes, and he asked about Dr. Tekola-Ayele's studies of hypertension in pregnancy. Dr. Tekola-Ayele explained that most of the women he had studied had blood pressure within the normal range, and the signals he had discussed are related to elevated blood pressure and not clinically defined hypertension.

VII. 30TH ANNIVERSARY OF THE NATIONAL CENTER FOR MEDICAL REHABILITATION RESEARCH

Theresa Cruz, Ph.D., the new director of NCMRR, explained that July 26, 2020, marked the 30th anniversary of the Americans with Disabilities Act. This landmark civil rights legislation prohibits discrimination against people with disabilities. Soon after President George H.W. Bush signed this bill into law, Congress passed an amendment to the Public Health Service Act establishing NCMRR at NICHD to address the need for biomedical research on disability and rehabilitation.

NCMRR History

NCMRR has its own advisory board, which meets twice a year. Dr. Cruz described some of the members of the first NCMRR Advisory Board, including Judy Heumann, a leader in the civil rights movement for people with disabilities, and Henry Betts, M.D., a physiatrist who helped advance the field of rehabilitation medicine. NCMRR's first permanent director was Marcus Fuhrer, Ph.D., who helped lead the development of the first NCMRR research plan in 1993.

Major advances in the 1990s in rehabilitation science included the application of neuroplasticity to rehabilitation and the development of new assistive technologies, including microprocessor prosthetic legs and a wheelchair that could climb stairs.

Other NCMRR directors were Yvonne Maddox, Ph.D., from 1998 to 2000, and Michael Weinrich, M.D., from 2000 to 2012. During this period, as the NIH budget doubled, NCMRR grew. The Center established training and infrastructure programs, and its mission expanded to include pediatric critical care and pediatric rehabilitation, although pediatric critical care was subsequently moved to the Pediatric Trauma and Critical Illness Branch. Scientific advances in the first decade of the 2000s included the development of new exoskeletons, several of which now have FDA approval, to improve balance, mobility, and bladder and bowel control in people with spinal cord injury, stroke, and other neurological disorders.

When NCMRR turned 20 in 2010, Ralph Nitkin, Ph.D., currently NCMRR's deputy director, was the Center's acting director and led a scientific symposium in honor of the anniversary. In 2012, Francis Collins, M.D., Ph.D., Director of NIH, initiated the Blue Ribbon Panel on Rehabilitation Research at the NIH to assess medical rehabilitation research across NIH. The panel concluded in 2014 that NCMRR was functioning but not thriving.

Recent NCMRR Activities

NICHD therefore took action. It organized a rehabilitation conference in 2016 to develop a research plan, which had not been done since 1993. In addition, NCMRR created the NIH-Department of Defense Limb Loss and Preservation Registry and engaged in efforts to develop common data elements for limb loss and neurorehabilitation.

NCMRR established its Research Infrastructure Network, which has co-funding from four other ICs, in the 2000s. The six Rehabilitation Research Resource Centers provide infrastructure and access to expertise, technologies, and resources to foster clinical and translational research in medical rehabilitation. The program also provides state-of-the-art facilities, webinars, courses, sabbatical programs, and pilot grants.

Upcoming Activities

The next rehabilitation research conference, Rehabilitation Research 2020: Envisioning a Functional Future, will take place on October 15–16, 2020. On December 1–3, 2020, the Office of Disease Prevention will host a virtual Pathways to Prevention Workshop, Can Physical Activity Improve the Health of Wheelchair Users? The workshop will inform physical activity guidelines for people with disabilities and address health and wellness in this population.

Although some studies have been conducted on the rehabilitation needs of people with COVID-19, clinical trials are needed to assess the efficacy of different interventions. In addition, more

research is needed on the pandemic's long-term effects on people with disabilities and the future of rehabilitation.

Discussion

In response to a question from Dr. Egan, Dr. Cruz confirmed that NCMRR has worked with the Defense Advanced Research Projects Agency, including on research on prosthetic devices. Dr. Boninger asked about upcoming projects that excite Dr. Cruz. Dr. Cruz looks forward to developing partnerships with agencies that have not worked with NCMRR in the past.

VIII. ADOLESCENT MEDICINE FELLOWSHIPS AND T32 POSTDOCTORAL TRIANING PROGRAM

Maria Trent, M.D., M.P.H., Adolescent Medicine Fellowship and T32 training director, professor of pediatrics, and Bloomberg Professor of American Health at Johns Hopkins University (JHU) School of Medicine, used the training program she leads as a case study of the impact of the COVID-19 pandemic on postdoctoral training programs in the United States.

Dr. Trent sought summaries of the pandemic's impact on medical fellowships and postdoctoral training programs from directors of these types of training programs. The 31 responses mentioned the reduced time spent by trainees in adolescent medicine clinical work, their shift to virtual clinical care, pauses in research and transitions to other types of research or training activities, personal and family stress, and limited professional development opportunities (including fewer opportunities to give presentations at conferences and fewer job openings).

The JHU Adolescent Medicine Training Program gives physicians the skills, knowledge, and experience necessary to build on scientific advancements across related disciplines and begin careers as clinician-scientists.

In past years, Dr. Trent has led bonding activities for fellows, such as joining a sailing race to practice working as a team. This year, Dr. Trent has not been able to conduct this type of bonding activity to build relationships. Instead, Dr. Trent planned to hold a virtual retreat.

Challenges for fellows during the pandemic include finding housing when they move to Baltimore and finding child care. Human subjects research at JHU has stopped, new processes have been implemented for approved studies, and the number of staff who can work in a given space has been limited. Some core rotations have been canceled, and clinic volume is less than half its usual level. The inpatients who do come to the clinic tend to have higher-acuity needs. Like other healthcare providers, fellows had to quickly gain the skills needed to offer telemedicine. Another challenge is that some fellows learn better in person, but most training is now virtual.

The only research that is continuing is related to oncology or COVID-19, and many people are not seeking needed care. Dr. Trent and her colleagues have therefore initiated studies to assess the effects of COVID-19 on adolescents and innovative ways to provide services to these patients.

One fellow was working to improve access to health services for adolescents. Because of the pandemic, she had to shift her plans to focus on service utilization before and during the COVID-19 pandemic. Another fellow had to change her research plan and will now conduct secondary data analyses on receipt of HIV and sexually transmitted infection testing among sexually active female adolescents of color who have sex with women.

Dr. Trent and trainees are working to support adolescents and young adults during the pandemic through town halls and podcasts.

Discussion

Dr. Gordon asked about the training provided through Dr. Trent's T32 program in leadership and professionalism. Dr. Trent explained that speakers come to adolescent grand rounds to discuss professional development issues, and speakers for the general pediatrics and adolescent medicine seminar discuss such issues as mentorship and negotiation. Many fellows participate in a School of Public Health seminar on leadership.

Dr. Bianchi suggested that Dr. Trent's trainees and colleagues might be interested in a workshop co-sponsored by NICHD on September 30 and October 1 that will address gaps in healthcare from childhood to adolescence and from adolescence to adulthood.

IX. CONCEPT CLEARANCE

The Council reviewed the following seven concepts and voted to approve each one:

- **NICHD Maternal Morbidity and Mortality Data Analysis Project** (Maurice Davis, D.H.A., M.P.A., M.H.S.A., Pregnancy and Perinatology Branch)
- **Pediatric Scientist Development Program** (Karen Winer, M.D., Pediatric Growth and Nutrition Branch)
- **Autism Centers of Excellence** (Alice, Kau, Ph.D., Intellectual and Developmental Disabilities Branch)
- **Screening and Functional Validation of Human Genomic Variants** (Mahua Mukhopadhyay, Ph.D., Developmental Biology and Structural Variation Branch)
- **Multipurpose Prevention Technologies – Contraceptive and HIV Prevention Dual Protection Technology** (Nahida Chakhtoura, M.D., Maternal and Pediatric Infectious Disease Branch)
- **Learning Disabilities Innovation Hubs** (Brett Miller, Ph.D., Child Development and Behavior Branch)
- **NICHD Data and Specimen Hub** (Regina Bures, Ph.D., Population Dynamics Branch)

Dr. Wynshaw-Boris commented that the Screening and Functional Validation of Human Genomic Variants concept addresses a critical problem because the signatures of many variants are unknown. Dr. Caggana added that structural birth defects are probably multifactorial. Dr. Mukhopadhyay confirmed that this concept will be broad and could include studies of structural rearrangements and sequence-based variants.

During the discussion of the Multipurpose Prevention Technologies – Contraceptive and HIV Prevention Dual Protection Technology concept, Dr. Sohn said that previous studies have assessed the potential link between contraceptive use and increased HIV risk. Dr. Chakhtoura confirmed that this link will be taken into consideration as part of human subjects protection.

Dr. Bookheimer described the Learning Disabilities Innovation Hubs concept as timely and important. Children, especially those with attention deficit/hyperactivity disorder, have had difficulty with distance learning. Dr. Sohn asked how the program has addressed the challenges of recruitment and retention of families who are difficult to reach. Dr. Miller replied that applicants are expected to include detailed recruitment plans for diverse research scholars and families. Several grant recipients have recruited very challenging populations, including incarcerated youth, young people with severe learning challenges, and underrepresented minorities.

In response to a question from Dr. Jain, Dr. Bures explained that the NICHD Data and Specimen Hub concept is a continuation of the current program.

Dr. Jain suggested that a future NACHHD Council meeting feature a presentation on the process NICHD uses to translate concepts that receive Council approval into requests for applications and how NICHD forms partnerships with other NIH ICs to further the scope and impact of NICHD's activities. Alison Cernich, Ph.D., explained that NICHD monitors the initiatives of other ICs and offered to give a presentation on this topic at the next NACHHD Council meeting.

Day 2: Thursday, September 10, 2020

X. NIH's SCIENTIFIC APPROACH TO INCLUSIVE EXCELLENCE: BRIDGING THE RACIAL GAP IN FUNDING

Background

Dr. Hannah A. Valantine, M.B.B.S., D.Sc., chief officer for scientific workforce diversity at NIH, explained that more diverse groups are more likely to come up with creative solutions to complex problems, including health disparities. The inclusion of more women in cardiology, for example, has led to a new understanding of heart disease in women and, consequently, to a better understanding of cardiovascular biology that can improve cardiovascular disease management for women and men. NIH can only meet its goal of recruiting the most talented scientists in the world if it pulls from the entire intellectual capital.

Women and men from underrepresented groups and women from well-represented groups account for decreasing proportions of adults in the United States who obtain graduate training and academic leadership positions. In addition, fewer than 20% of academic department chairs at top research institutions are women.

To address these gaps, institutional approaches must address transparency and accountability by, for example, conducting systematic reviews of hiring and promotion policies and procedures, collecting and publicizing aggregate diversity metrics, and giving divisions tools to enhance recruitment and retention of individuals from underrepresented groups.

Workforce Diversity Initiatives

NIH addresses the need to increase workforce diversity through several initiatives (including the Distinguished Scholars Program and Faculty Institutional Recruitment for Sustainable Transformation), trans-NIH searches to fill tenure-track positions, activities to mitigate implicit bias, the National Research Mentoring Network, and the NIH Equity Committee. Since the Distinguished Scholars Program began, the representation of women, Hispanics, and African Americans in the NIH Intramural Research Program has increased dramatically, and NIH plans to implement a similar program for its extramural research programs.

Grants to African American Applicants

An NIH working group reviewed the entire research funding continuum, from application submission to funding decisions. The number of R01-equivalent applications from African Americans has consistently been lower than from whites, and the proportion of African Americans drops at each step in the process. The reasons for these funding gaps include the fact that more African American investigators submit applications from institutions with fewer resources; more are at an early career stage; their submission rates, discussion rates, and impact scores are lower; and the topics they address contribute to 21% of the funding gap. Ultimately, the R01-equivalent grant funding rate for African Americans is about half that for whites.

A recent analysis found that the ICs have widely varying R01 award rates of 9.1% to 26.9%. Five of six ICs that received a higher than average proportion of applications from African Americans had a lower R01 award rate than the NIH average. In addition, ICs that received a greater proportion of applications on topics reflected in disproportionate numbers of applications from African American applications had lower award rates.

In FY 2019, NIH received 19,144 applications for R01-equivalent grants from white applicants and only 515 applications for such grants from African American applicants. NIH issued 4,500 awards to white applicants (24% success rate) and 62 (12% success rate) to African American applicants.

How to Address These Gaps

Dr. Valantine closed her session by offering some suggestions to address the impact of social injustice on biomedical research:

- Openly acknowledge the problem of anti-Black racism in science.
- Promote community-based research focused on external validity.
- Support Black peers during this time of emotional turmoil and feelings of hopelessness.
- Adjust the factors valued by admissions and other selection committees.
- Monitor and report acts of racial bias and hold perpetrators accountable.
- Empower allies to be actively antiracist.

Discussion

Dr. Matzuk reported that Baylor University has the Office of Institutional Diversity, Inclusion and Equity, and each department and center has ambassadors who serve on committees. Dr.

Matzuk wondered whether NIH also used ambassadors from throughout the agency to work on the issues Dr. Valantine had described. Dr. Valantine replied that when she came to NIH, she asked all IC directors to nominate two people to serve as diversity catalysts. The diversity catalysts provide input into Scientific Workforce Diversity Office activities and reported on the office's activities to their ICs. Most of the diversity catalysts are not faculty members, although the NIH Equity Committee, which reviews the diversity of each IC's intramural research program, is composed primarily of faculty members. Dr. Valantine is about to ask every IC to appoint an associate director for diversity and inclusion.

When asked about the proportion of NIH grant applicants who provide information on their race and ethnicity, Dr. Valantine replied that virtually all R01 applicants provide this information.

Dr. Bookheimer asked why a higher proportion of department chairs at Stanford University School of Medicine are female than are department chairs at other top-tier research institutions. Dr. Valantine explained that the dean established a committee to ensure that department leaders are diverse, and the search committees for these positions have also been diverse.

Dr. Bookheimer noted that although Dr. Valantine had focused much of her presentation on African Americans, Hispanic applicants also have difficulty obtaining research awards, especially for studies of issues in under resourced communities. Dr. Valantine explained that the gap for Hispanic researchers is smaller than for African Americans, but Hispanics are less likely than whites to obtain various types of NIH awards.

Dr. Bianchi noted that three of five NIH IC directors named in the past few months are women.

XI. COMMENTS FROM RETIRING NACHHD COUNCIL MEMBERS

Dr. Bianchi thanked Drs. Boninger, Gordon, and Tabin and Ms. Thomas, whose NACHHD Council terms end on November 30, 2020, for their service to NICHD. She asked the three retiring members in attendance to comment on their experiences as Council members.

Dr. Boninger said that the NICHD staff make Council members' experiences wonderful, and he had appreciated the opportunity to work with some of the best researchers in the United States. He plans to continue advocating for NCMRR and rehabilitation as core to NICHD's mission.

Dr. Gordon has been inspired by her experience that NIH in general, and NICHD in particular, is made up of special people working to help young people, mothers, and children with disabilities. She had been particularly honored to serve on a team that helped NICHD develop its vision statement: Healthy pregnancies. Healthy children. Healthy and optimal lives.

Ms. Thomas was pleased that nutrition was woven into NICHD's Strategic Plan, because diet plays a critical role in every phase of the life cycle. She was excited by the NICHD position that pregnant women, lactating women, and children should not be automatically excluded from research. She suggested that researchers visit high schools and participate in science fairs to encourage more people of color to enter scientific research careers. What Ms. Thomas will miss most about her time as an NACHHD Council member is hearing from those who benefit from

NICHD research. She hoped that NICHD will form another consumer panel on standardizing the diagnosis of gestational diabetes.

XII. CLOSED SESSION:

This portion of the meeting is closed to the public in accordance with the provisions set forth in Section 552b(c)(4) and 552b(c)(6), Title 5, U.S.C., and Section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2).

XIII. REVIEW OF APPLICATIONS

The session included a discussion of procedures and policies regarding voting and confidentiality of application materials, committee discussions, and recommendations. Members absented themselves from the meeting during discussion of and voting on applications from their own institutions or other applications in which there was a potential conflict of interest, real or apparent. Members were asked to sign a statement to this effect. The Council considered and approved 432 HD-primary applications requesting $111,122,327 in direct costs and $201,608,254in total costs.

XIV. Adjournment

There being no further business, the meeting adjourned at 5:00 p.m. on Thursday, September 10, 2020. The next meeting is scheduled for February 2–3, 2021.

I hereby certify that, to the best of my knowledge, the foregoing minutes and attachments are accurate and complete.[2]

_____ _____

Diana W. Bianchi, M.D. Date
Chair, National Advisory Child Health and Human Development Council
Director, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development

_____ _____

Eugene G. Hayunga, Ph.D. Date
Acting Committee Management Officer, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development

[2] These minutes will be formally considered by the Council at its next meeting, and any corrections or notations will be incorporated in the minutes of that meeting.