

Kent Thornburg, Ph.D.

Message from the Director

Greetings from the Center for Developmental Health.

Many of you will remember the 20 year period during which the Heart Research Center was the primary agent for heart and blood vessel research at OHSU. In 2013, things changed in an exciting way. Sanjiv Kaul, M.D. and his team, along with Albert Starr, M.D., established the Knight Cardiovascular

Institute funded by Phil and Penny Knight. The Heart Research Center, whose focus had been on developmental heart disease, was given the opportunity to become a new center in the Knight Cardiovascular Institute. The Heart Research Center is now appropriately called the Center for Developmental Health and is devoted to discovering the early life roots of heart and blood vessel disease. Why, you might ask, is this work so important?

About 10 percent of people in Oregon are diabetic; that is twice the prevalence of 1990. People with diabetes are prone to have heart attacks or strokes as they age. In order to halt this dramatic increase in people who get these diseases, we must examine the origins of these diseases.

Research from Oregon and around the world has now shown that chronic diseases like diabetes, heart disease and obesity are developmental diseases. That means that people acquire these diseases because they were exposed to poor nutrition

before or soon after birth or from high stress levels in the mother before birth.

You will notice that the center continues its efforts to bring good nutrition to those minority communities that suffer most from the diseases that we are trying to cure. One of the culprits is the poor diets of men and women before they bear children.

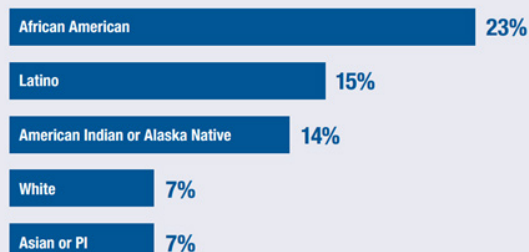
We care about nutrition in schools too. Changing the way we Oregonians eat is an uphill battle, but we are up for it. Remember three facts about our food culture:

- 1) Calories are cheap, but nutrients are expensive. It is cheaper to consume plenty of calories that contain few nutrients. Thus, Oregonians of all social strata suffer from high calorie malnutrition.
- 2) If everyone ate a nutritious diet, together we would reduce the rates of chronic diseases dramatically.
- 3) Stress and poor diets among people without means work together to make them especially vulnerable for chronic disease. We need to find ways to alleviate these problems.

The 60 some scientists in the Center for Developmental Health care about finding answers to one big question. How does poor nutrition and stress in early life lead to heart and blood vessel disease? Within the pages of this newsletter, you will see that six groups of world class scientists

are working around the clock to find answers to this question. We offer warm thanks to those of you who have supported this research for more than 20 years. Let's work together to change the health of Oregon.

Diabetes among African Americans is three times that of non-Latino whites in Oregon



Estimates are age-adjusted. Source: 2010–2011 Oregon Behavioral Risk Factor Surveillance System Race Oversample

Note: Race categories refer to non-Latino; PI=Pacific Islander

Oregon Diabetes Report 2015 public.health.oregon.gov/DiseasesConditions/ChronicDisease/Diabetes/Documents/OregonDiabetesReport.pdf



Partnership brings heart program to Astoria

OHSU started a cardiology clinic in Astoria five years ago as part of a partnership with the local hospital, Columbia Memorial Hospital, to bring medical specialists to the Northern Oregon Coast. Diana Rinkevich, M.D., associate professor of medicine, OHSU School of Medicine, became the director of the new service.



Diana Rinkevich, M.D.

The venture came about when the community raised concerns over heart health. Clatsop County has the third highest death rate from heart disease in Oregon. Over time, more and more community members have added their voices to this conversation. Schools, the community college, city government and many others are working together to improve heart health.

As a result, Rinkevich says the community is very invested in understanding and improving its health and being involved in research. “The community wants our presence, which gives access to pioneering research, health and health care,” she says.

The joint program between Columbia Memorial Hospital and OHSU includes increased local

diagnostic capabilities, new wellness and prevention programs (see accompanying stories on WomenHeart of North Oregon Coast and the study on pregnant women), and seamless coordination of clinical services for patients. “Before, people who had a cardiovascular problem were anonymous when they were sent to OHSU. Now they know who will meet them and that the care will continue at the same high level of quality at OHSU and in Clatsop County,” Rinkevich says.

Heart disease is the number one cause of death and disability among women in the United States. “In the 1990s we began to recognize that women had not been represented in cardiovascular research studies anywhere near what men had,” she said. Heart and blood vessel diseases do not affect men and women exactly the same way, so women’s studies are important.

To contribute to that knowledge, Rinkevich is preparing a Clatsop County study on blood markers that may help identify women at risk of heart disease. After menopause the rate of heart disease in women increases significantly. Early detection and possible aggressive treatment/lifestyle modification for those at higher risk may decrease the risk of heart attacks and strokes.

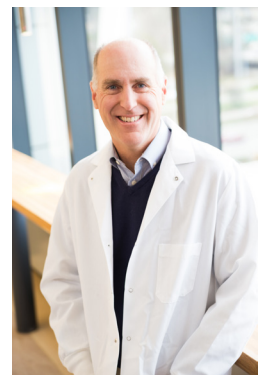
Rinkevich also feels that this research is a chance for the community in Astoria to be part of the research performed at OHSU, and that the results of this study will add to the body of knowledge about woman and heart disease.

“Heart disease is the number one cause of death and disability among women in the U.S.”

Improving Maternal Nutrition in Astoria

How can we improve the nutrition of women who are pregnant and improve their babies’ chances to live a healthful life even before they are born? The Center for Developmental Health is starting the Clatsop/Astorial Maternal Partnership Study, a community-based study of women in their childbearing years to try to answer this question. Led by Jonathan Purnell, M.D. and teaming up with Columbia Memorial Hospital and clinics in Astoria, one hundred women in the first trimester of pregnancy will be enrolled and assigned to either their usual care or to receive instruction on a heart-healthy diet based on a curriculum designed in consultation with the Heart’s Kitchen. During this twelve week course, women in their first trimester will attend cooking classes and group learning sessions where emphasis will be on making healthy food choices. The women will also participate in group sessions that will reinforce their learning, provide group support, and identify barriers they face in their daily lives that may prevent them from making these choices. Both groups will be followed through their deliveries and the first six months of their babies’ lives to study the impact of diet changes on the health of their pregnancy and babies’ growth.

Lesson’s learned from this study will be combined with the results of a recently published study led by Melinda Davis, Ph.D., of the Oregon Rural Practice-based Research Network and the Bob and Charlee Moore Institute for Nutrition & Wellness that describes the challenges that a cohort of women from the North Clatsop region faced when trying to find, afford, and prepare healthy food choices for themselves and their families. These findings will be fed back to the communities so that they can become part of local solution making and will be incorporated into designs of future community-based interventions in other Oregon regions.



Jonathan Purnell, M.D.

Michele Abrahams and WomenHeart not alone with heart disease

Astoria native Michele Abrahams has a very personal reason for becoming a local leader of women who experience heart disease: She wants women with heart disease to support each other.

“My congenital heart condition is rare. All my medical care has been in Portland. I never had this type of support and sharing until this group started,” Abrahams says of the WomenHeart of North Oregon Coast group she helped form and now facilitates.

WomenHeart is a program of the National Coalition for Women with Heart Disease. Astoria cardiologist Diana Rinkevich, M.D., asked Abrahams to train as a leader (referred to as a WomenHeart champion) at the Mayo Clinic.

WomenHeart’s goal in Clatsop County is to educate women experiencing cardiovascular disease by going to hospitals after surgery, attending community education events, etc. WomenHeart also provides a network support group for Clatsop County women with heart disease or who are at risk of heart disease. Abrahams serves as local Support Network Coordinator.

Between 12 and 18 women come regularly to the support group. Topics range from pacemakers to broken heart syndrome to diabetes to preparing healthy meals. “The group members are excited to be learning and in the same room with women who, though they may not have the same problem, experience cardiovascular disease. It makes them feel they are not alone.”



Michele Abrahams

“Women put everyone else before themselves. For example, you don’t tell your husband you haven’t been feeling well,” she says. “We are nurturers, but we are putting ourselves at risk by taking care of everybody but ourselves.” The support group helps Clatsop County women experiencing heart disease and its risk factors to feel empowered to make changes and educate themselves.

Michele was born with a congenital heart defect. In her case, the great vessels were transposed. Here’s her story: My family had no idea I had a heart problem when I was born. Two weeks later, my grandma noticed the bottom of my feet were bluish. When my parents took me to the doctor, he sent us with an oxygen tank in the car to OHSU. He told my parents to stop at the St. Helens hospital if we ran out of oxygen!

I was born Dec. 26, 1966 and had my first surgery Jan. 19. When I was almost 4, I had my major repair surgery, the Mustard Procedure. Now, babies with my condition have corrective surgery within a month of their birth. The Mustard Procedure is no longer used; doctors now do a full atrial switch.

I started wearing a Medic Alert bracelet after my oldest daughter was born. I would encourage all women with heart conditions to wear one. It’s a very valuable tool that tells all my medical information if I have an

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Partnership with the Heart’s Kitchen

The Heart’s Kitchen is working with the Center for Developmental Health and the Moore Institute to bring education to groups in communities. They have designed a 12-week class as one of the cornerstones of the Clatsop/Astoria Maternal Partnership Study. Pregnant women will participate in hands-on demonstrations of how to prepare food designed to help them cook more at home using locally produced foods as much as possible. They will learn about epigenetics and the importance of good nutrition during pregnancy to their child’s long-term health.

“The classes will both emphasize why healthy cooking is important [to their unborn children’s lifetime health profile] and a love for cooking,” says The Heart’s Kitchen CEO and Education Director, Mollie Harris, M.S.

The Heart’s Kitchen is a group of doctors, dietitians, chefs and educators working together to create marketing solutions for the culinary and medical worlds. Their message is inspired by epigenetics principles. Harris says, “Dr. Thornburg’s research is what inspired us to launch The Heart’s Kitchen. We realized how critical it was to get this science publicized in a way that mainstream Americans would understand the message, recognize the urgency, and be motivated to change. To this day, we continue to look to Dr. Thornburg for research updates and advice as we help to deliver the message of epigenetics and developmental origins of health and disease to the public.” You can learn more about The Heart’s Kitchen at www.theheartskitchen.com.



Mollie Harris and Jennifer Bryman

Latino Outreach Committee turns concern to action

Natasha Holstein is alarmed by the following statistics and wants to do something about them.



Natasha Holstein

A Robert Wood Johnson Foundation-funded study through Salud America, found:

- More than 39 percent of Latino children ages 2-19 are overweight or obese, compared to almost 32 percent of all U.S. children.

- These rates are especially alarming because Latino youth are

the fastest growing minority group in the U.S. They comprise 22 percent of all U.S. youth.

Holstein and the Center for Developmental Health's Latino Outreach Committee, which she chairs, has turned this concern to prevention actions – reaching out to the Latino community to prevent heart disease. "Our committee's mission is to reverse the trend of deteriorating health in Latinos using the developmental origins model," she says.

Holstein notes that there used to be a healthier lifestyle and food in Mexico and other Latin cultures. "Diabetes was not prevalent in the 1930s and '40s," she says. Grandma prepared a good meal from local food for the extended family. In the 1950s, processed food was introduced. According to Kent Thornburg, Ph.D., director of the Center for Developmental Health, "The rise in the availability

of processed foods has made it cheaper and easier to eat diets that lack nutrients. Among Hispanics, first generation Mexican-Americans, for example, have low obesity and diabetes rates, but people in the next generation have high rates. Third generation Mexican-Americans are also acquiring heart disease, which is much less common in Mexico."

To avert these problems, the Latino Outreach Committee, formed in 2014, works in partnership with community organizations such as the Wallace Medical Group, Multnomah County Health Department, Familias en Acción and the Mexican Consulate. They collaborate to highlight health challenges that are especially prevalent in Latinos, develop culturally relevant Spanish language materials, conduct developmental origins trainings for community health workers and attend events such as farmers' markets and health fairs to help Latinos feel empowered to improve their health.

"Many people are hungry for this information,"

she says. Holstein stresses that being effective in the Latino community is

"all about creating and building trust." The committee focuses on

one-on-one opportunities to create awareness and educate in a culturally sensitive

manor. She cites the example of a Latina learning she has diabetes and being handed

material that, though translated, is not at all culturally relevant to

her. "We have to communicate in a way Latinos can understand and trust,"

Holstein emphasizes. "If materials are not presented in a culturally relevant manner, we lose that connection."

"The rise in the availability of processed foods has made it cheaper and easier to eat diets that lack nutrients."

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Michele Abrahams and WomenHeart

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emergency. When I gave birth to my second daughter, I developed atrial fibrillation. Atrial fib can cause blood to not be pushed efficiently through the ventricles. Doctors inserted a dual pacemaker that delivers therapies and will pace my heart into a normal rhythm. I am now on my fifth pacemaker.

Living my entire life with heart disease could at times be isolating, but with WomenHeart of North Oregon Coast I am no longer alone. The women we help through the support group and education are now my HEART SISTERS along with the other women who, like me, are volunteering to help support and educate women all across the nation through WomenHeart. To hear, "Thank you, you have made a difference in my heart journey," makes the time and energy I put into WomenHeart more than well worth it!

Knight Cardiovascular Institute emphasizes nutrition & prevention

Survival rates from heart attacks and strokes have significantly improved in the United States over the last 30 years – from 20 percent mortality to approximately 5 percent after a cardiovascular event. That's good news. But Joaquin Cigarroa, M.D. clinical professor of medicine, OHSU School of Medicine, sees a missing link.

Cigarroa, OHSU's clinical chief of cardiology and an interventional cardiologist, says, "The missing connection that we need to emphasize is prevention – focusing on who is at risk early on in people's lives." A healthy investment in prevention pays off. For example, Cigarroa says better nutrition for those at risk for cardiovascular disease lowers their risk by one-third, which is approximately the same as the effect of prescribing statins for that population.

"The connection between nutrition, activity and the onset of disease is critical for our area and the U.S.," he says. Cigarroa and OHSU have embraced the responsibility for prevention both within the hospital system's walls and in outreach to the community. "One of OHSU's goals is to prevent the development of cardiovascular disease. We can't do that without community engagement."

He participates in one of the many outreach efforts – a partnership between OHSU clinical cardiology, cardiac rehabilitation, and food and nutrition to provide monthly heart-healthy cooking demonstrations for OHSU patients. These pilot events, called "Cooking Your Way to a Healthier Heart," will soon expand to other communities outside OHSU. "Now that we've developed our rhythm here, we will create opportunities in the Latino culture."

During the demos, Cigarroa works with OHSU Executive Chef Fernando Divina. While Divina cooks, Cigarroa discusses how heart healthy and tasty foods can be made at home in the context of people's busy lives. "Almost half of the people participating didn't know how to make these items themselves and were afraid their family wouldn't eat them," he says. "They learned they could be successful."

One of Cigarroa's goals is to tailor these events to the Latino community. "It is very important to engage and collaborate with Latinos," he says. He participates as a member of the Center for Developmental Health's

Latino Outreach Committee and believes that when Latinos know their risk factors and how to correct them, diabetes and obesity rates will dramatically decrease in that population. He says Latinos need access to healthy foods and education on how to substitute

healthy options in traditional cultural foods without compromising taste. "We can use simple techniques to cook healthier, save time and make food that will last for several meals," he says. "This will help people begin to succeed in maintaining their culture while lowering their risks for heart disease."



Joaquin Cigarroa, M.D.

"better nutrition for those at risk for cardiovascular disease lowers their risk by one-third, which is approximately the same as the effect of prescribing statins for that population."

Cigarroa recommends that you follow the heart healthy plate at www.ohsuheart.com/plate when preparing meals. Fill one-fourth of your plate

with lean proteins (seafood, poultry, ground turkey, beans), one-half with non-starchy vegetables and fruit (peppers, onions, salsa) and one-fourth with whole grains, starchy vegetables and legumes.

In addition, Cigarroa suggests the following:

- Make brown or wild rice instead of white rice. They are whole grains and have more nutrients.
- Use corn or whole wheat tortillas. White flour tortillas lack nutrients.
- Dried beans have less sodium than canned beans. If using canned beans, purchase fat free beans and rinse to remove sodium.
- Make fresh salsa or read labels carefully. Commercial salsa is often full of sodium and sugar.
- Reduce the fat and avoid lard and butter. Use small amounts of olive oil, vegetable oil and cooking spray.
- Cheese is high in saturated fat and sodium so use small amounts.
- Substitute non-fat plain or Greek-style yogurt for sour cream. It has fewer calories and fat than sour cream.

CDH scientists form collaborative research teams

Scientists from the OHSU Center for Developmental Health have organized themselves into six teams to understand the development of cardiovascular disease. The teams meet monthly to develop research projects and the entire group meets quarterly to further collaborate and provide feedback.



Christopher Kroenke, Ph.D.

Brain and Behavioral Development: Chairs: **Christopher Kroenke, Ph.D.**, associate professor of behavioral neuroscience, OHSU School of Medicine, and **Joel Nigg, Ph.D.**, professor of psychiatry, OHSU School of Medicine

CDH researchers in this group are investigating how the maternal/intrauterine environment affects brain development in the fetus and in subsequent offspring. Environmental insults include fetal exposure to alcohol and anesthetics during pregnancy. Research investigates the effects of maternal diet on fetal central nervous system development, such as protein restriction, manipulation of dietary fatty acid composition, and examination of the effects of a high-fat (western style) diet. The team uses state-of-the-art magnetic resonance imaging (MRI) brain imaging to map the fetal central nervous system's development over time. They frequently observe inflammation in the developing central nervous system in response to the experimental conditions of unhealthy diet and other negative conditions. This can lead to later behavioral abnormalities or even a propensity for a stroke.

OHSU researchers within this group aim to build the interface between studies focused on human patient populations and animal models of neurodevelopmental disorders and apply them to human neurodevelopmental disorders such as attention deficit hyperactivity disorder or autism spectrum disorders. Findings will be applied to the way that the vascular tree develops in the brain.



Joel Nigg, Ph.D.

Endothelium and Developmental Origins: Chair: **Monica Hinds, Ph.D.**, associate professor of biomedical engineering, OHSU School of Medicine

The endothelium is a single cell thick layer that lines the entire vascular system. It controls transportation of molecules between blood and tissue. Thus the endothelium is the first responder to anything wrong in the blood. It is important to understand how a mother's diet or diabetes, will affect the endothelium's ability to sense changes in disease states. The group speculates that the environment in the womb will hamper the cells' ability to respond to disease states later in the child's life and will lead to cardiovascular disease.



Monica Hinds, Ph.D.

Heart & Blood Vessel Development: Chair: **George Giraud, M.D., Ph.D.**, professor of medicine, OHSU School of Medicine

This research team is determined to find the mechanisms in the fetus that lead to adult cardiovascular disease. They want to know why people who have very high and very low birthweights are likely to get heart disease. They will study how a person's blood cholesterol interacts with the endothelium in the blood vessels in the heart to cause a heart attack.



George Giraud, M.D., Ph.D.

Inflammation, Immunology and Second Hit: Chair: **Nancy Haigwood, Ph.D.**, director and senior scientist, Oregon National Primate Research Center; adjunct professor of molecular microbiology and immunology, OHSU School of Medicine

This group's major goal is to support other groups by providing expertise on inflammation. Inflammation is not a well understood process. It is important in fighting infectious organisms, and to eliminate them. Many disease conditions—including obesity, arthritis and heart disease-- are affected by an ongoing inflammation even when there is no infection. The group is also looking at how prenatal nutrition regulates the inflammatory state in newborns, and whether chronic inflammation during pregnancy predisposes the offspring to obesity and diabetes.



Nancy Haigwood, Ph.D.

Metabolism and Development: Co-chairs: **Jon Hennebold, Ph.D.**, associate scientist, Oregon National Primate Research Center; assistant professor of obstetrics and gynecology, OHSU School of Medicine, and **Jonathan Purnell, M.D.**, professor of medicine, OHSU School of Medicine; associate director, OHSU Bob and Charlee Moore Institute for Nutrition & Wellness

During fetal development, maternal under-nutrition and over-nutrition are associated with an

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CDH scientists form collaborative research teams

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Jon Hennebold,
Ph.D.



Jonathan
Purnell, M.D.

elevated risk of chronic diseases later in life. Thus, the overall objective of this group includes defining how abnormalities in maternal nutrition and metabolism affect critical developmental processes that lead to later disease. This will include studies of 1) germ cell development and epigenetic effects that persist following fertilization, 2) the uterine environment during implantation, as well as 3) placental and organ formation and function and related development of chronic diseases after birth.

Placental Origin of Disease: Co-chairs: Leslie Myatt, Ph.D. professor of obstetrics and gynecology, OHSU School of Medicine, and Antonio Frias, M.D., associate professor of obstetrics and gynecology, OHSU School of Medicine



Leslie Myatt,
Ph.D.



Antonio Frias,
M.D.

This group's goal is to better understand how the growth of the placenta affects fetal development and long-term disease risk. "The placenta is the least understood human organ," says Antonio Frias, M.D. The placenta functions as the fetal respiratory, renal, hepatic, endocrine and immune system. Placental research is currently limited by inadequate imaging modalities to understand its function in real time. It is hard to do biopsies on the placenta except after birth, making it difficult to understand its development in-utero. Dr. Frias has recently been funded to carry out work on imaging the placenta through the National Institutes of Health Human Placenta Project. Frias was quick to point out, "We're a very collaborative group representing genetics, epigenetics, radiology, cardiology and other disciplines that are central to fetal development."

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Andrew Adey's research is focused on one single cell

Andrew Adey, an assistant professor in the OHSU Molecular and Medical Genetics Department, found a fit for his collaborative style when he came here a year ago. Adey's work on single-cell dynamics is broadly applicable to cardiovascular and other diseases. He came to OHSU because he saw the chance to work with scientists across disciplines. "There are so many applications of this work to different areas. Being able to nurture that was my biggest draw to OHSU."

In his research, Adey uses technology to push the limits of knowledge of a single cell's inner workings. Ultimately, his goal is to learn which of the cell's developmental steps are more susceptible to either genetic or environmental insults such as poor nutrition and exposure to chemicals. "First, it's crucial to understand a healthy cell's trajectory before we can start to identify where the developmental program can go wrong," he says. "Understanding a healthy single cell using very high-resolution technology will help target specific events in the cell program that may lead to disease. We can learn how a cell is supposed to progress and, if some cells don't follow a healthy pattern, we will be able to identify where and how the disease state occurred," Adey says.

His work is key to the new field of epigenetics—how the environment changes how genes work. "Cells follow a program of epigenetic changes as they mature in development. If some of these steps are missed, or carried out inefficiently early on in development, it may affect that person's lifetime disease profile. We are now building this map so we can, eventually, change the progression when needed."

He has found many kindred scientists at OHSU. "Everyone I've talked to is very open to discussing ideas," Adey says.



Andrew Adey, Ph.D.