community partnerships prevention environmental hazards burden of illness managed care culture fertility beliefs and values barriers to access diversity innovative research women's health disability health policy homelessness communication quality improvement violence aging outcomes substance abuse ethics technology stress placebo youth genetic testing information and decision making morbidity and mortality poverty patient satisfaction cost families work conditions caregivers risk factors population health

exchange

the Center for Health *and* Community

at The University of California, San Francisco

From the Director

Obesity is the topic of the hour. Discussions about this epidemic appear regularly in books, mainstream publications, scientific and medical journals, government reports, and on television. Drug companies invest millions trying to find obesity's silver bullet.

Yet in the face of all this sturm and drang, the epidemic continues to gather force. We know that obesity is a critical problem but do not know how to address it effectively for individuals or for the population as a whole. Well over a quarter of US adults are obese, as are 15 percent of children and adolescents. Obesity places people at significantly higher risk for heart disease, type 2 diabetes, high blood pressure, kidney problems, arthritis, and some types of cancer. A recent article in JAMA projects that morbidly obese individuals will die 13 years prematurely.

For years, UCSF faculty members have been conducting cutting-edge research on the prevention and treatment of obesity, but until recently they were largely working in isolation. Clinicians had limited contact with basic scientists studying the underlying genetic and biochemical causes of obesity. Few of those in the basic science community engaged with the social and behavioral scientists studying the role of the family, community, and behavioral patterns in eating and exercise.

When The Center for Health and Community put out a call to bring these faculty together in an interdisciplinary group, the response was both exciting and instructive. It made clear that these leaders in the obesity field believe that interdisciplinary work is vital to battling the epidemic.

Together, they will have to address many critical questions.

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Tackling Obesity

Late Thursday afternoon, San Francisco General Hospital's (SFGH) pediatric waiting room fills with families. Many of the children are obese, here for the hospital's Healthy Lifestyle Clinic.

Down the hall, eleven year-old "Gilberto" listens as an occupational therapist talks gently to him about his love of basketball, encouraging the obese young man to continue playing when he can find safe places to do so. The therapist turns to Gilberto's mother and in halting Spanish explains that there is a program in their neighborhood with organized sports activities. The therapist also suggests that Gilberto cut down from his average of four sodas per day. From the boy's one-word answers and the mother's silent nods, it's difficult to tell if they will follow through.

Yet amongst the many difficult cases clinic staff has seen today, Gilberto offers hope. A year ago, he made a dangerous leap in weight, but on this visit, his weight is down. Though he is still obese, the mark on the graph that charts his weight causes visible elation in the staff's cramped office.

A Complex Epidemic

Despite this elation, in many ways Gilberto personifies the difficulty of addressing an epidemic that reportedly claims 300,000 lives per year and costs $100 billion in direct medical costs.

Surrounded by societal influences that tell him to drink soda and eat processed foods, with poor access to health services, with adult supervision limited by his parents' job options, Gilberto is fighting an uphill struggle. Dr. Cam-Tu Tran, the director of the Healthy Lifestyle Clinic and Chief of Pediatrics at SF General says that if she's lucky, she'll see Gilberto once a year. She has no resources to follow up, to make sure he's staying with a program. She and her staff have to hope that an hour or so of discussion and education will make a significant mark. Too often, she says, it doesn't.

And Gilberto made it through the door of the clinic. Not many even take that first step.

The members of the CHC's Obesity Center came together because they recognize that individually their ability to help the Gilbertos of the world is limited. But by bringing together their considerable accomplishments in this field—and creating something new out of their experience—they may be able to strengthen their attacks on the many forces that sustain the obesity epidemic.

Below, we highlight some of their work to date, and discuss their hopes for what can emerge from a coordinated effort.

Genetics Provides Clues, Not All the Answers

As he hunts for genetic clues to obesity, Christian Vaisse works from the basic observation that weight maintenance is about creating a balance between food intake and energy expenditure. Over a period of 25 years, it only takes an imbalance of 16 calories a day to move from normal BMI to extreme obesity. Vaisse's particular interest is in determining when and how such imbalances are tied to genetic mutations.

We know that such mutations exist. Researchers discovered the first one by studying overweight mice that failed to secrete leptin, a hormone secreted by fat cells to tell the brain how much fat remains in the body. Without the leptin signal, the body assumes it does not have enough fat and must continue to eat. Subsequently, researchers (including Vaisse) confirmed leptin's role in human weight regulation.

A few years later, Vaisse and others identified a mutation in the melanocortin-4 receptor (MC-4R) in the brain's hypothalamus, a receptor that also works to suppress appetite. Mutations in this receptor account

> "Gilberto personifies the difficulty of addressing an epidemic that **claims 300,000 lives** per year and **costs $100 billion** in direct medical costs."

for up to 4 percent of cases of extreme obesity, making it the most common obesity gene mutation identified to date.

It's an important finding, but it's also notable that mutations that are the primary cause of obesity occur in a very small percentage of people. That's why other genetic research looks at mutations that are not the primary factor, but which indicate a predisposition for obesity in a much larger percentage of obese people.

Laurel Mellin and Michele Mietus-Snyder

"The additive effect of genes on obesity is about 40 percent," says genetic researcher Wen-Chi Hsueh, who has studied what are known as founder populations, isolated groups that allow researchers to estimate the degree to which genetics affect obesity. Her work is geared towards understanding the gene-environment interaction—essential knowledge for addressing the epidemic.

Hsueh believes that further exploration will eventually lead to important advances in treatment and prevention. "In my lifetime, we will do genetic profiles, in much the same way that we do lipid profiles today," she says.

"Our Biology Is a Mismatch for Our Environment"

Genetic profiles, however, are at least a few years off. In their absence, a number of biochemical insights have led to some promising screening techniques that can lead to better prevention.

For example, Michele Mietus-Snyder, MD, a cardiologist who is associate director of UCSF Weight Assessment for Teen and Child Health (WATCH) program, speaks of "checking for clinical biomarkers, such as early indicators of chronic disease that we already know are associated with obesity."

The WATCH clinic's Andrea Garber, a dietitian and researcher, mentions using early adiposity rebound to screen for at-risk children. Adiposity rebound is when the body's fat declines to a minimum before increasing again into adulthood. Typically it occurs between five and six years of age, but some studies have indicated that children who experience that rebound earlier (at age two or three), are more likely to become obese as an adult.

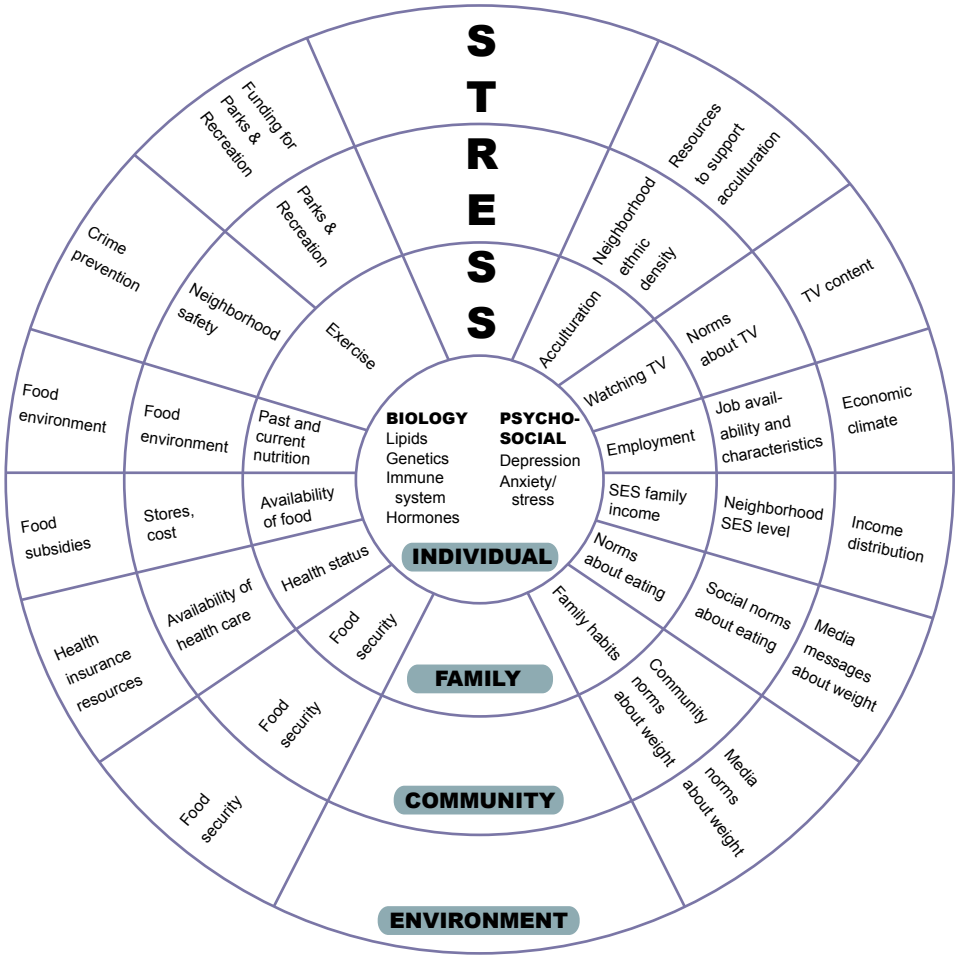
Bobby Baron

Unfortunately, screening and prevention efforts must wrestle against a simple biological fact. "Our biology is a mismatch for our environment," says Bobby Baron, MD and program director of the UC Primary Care Program. "We're programmed to preserve weight, because we evolved in a time of limited food resources, and hard physical work. This has to be explicitly acknowledged." Because our bodies have not yet evolved to meet the way our daily routines have changed over the previous century, our biology works against creating the precarious balance between food intake and energy expenditure.

Pediatric endocrinologist Robert Lustig, MD believes that the mismatch has translated into a critical problem with the hormone insulin, which he calls "the proximate (biochemical) cause of obesity."

Lustig's research has focused largely on hypothalmic obesity in children. While the condition occurs in only a small minority of cases, Lustig believes it provides an important window into the insulin problem.

"Virtually every single one of these patients is hyperinsulemic," says



Conceptual Multi-level Model of Obesity

Lustig, meaning that a disruption in the energy-balance pathway causes these patients to produce too much insulin. Or if the pathway isn't disrupted, the patients are what is known as insulin resistant—their body does not respond to insulin properly—and so they create excess insulin in response. In both cases, the body stores the excess insulin as fat.

Lustig works with many such patients —and many others struggling with obesity—as director of the UCSF WATCH clinic. There he and his colleagues use something called an oral glucose tolerance test (blood tests after drinking a sugary beverage) as a screening tool for insulin response. Using the results, clinic staff then help these patients to reduce their insulin levels. Successes and insights gleaned in both his clinic and his research are what have led Lustig to his belief in the centrality of insulin in obesity.

Exploring the Intersection Between Body and Mind

Whatever the biochemical and genetic causes, few doubt that psychosocial factors also play a role in proper regulation of the body's energy-food balance. The interaction of behavior and psychology within an individual occurs in the context of family, community and environmental factors (see diagram). Among those factors, stress is rapidly emerging as a significant concern.

In fact, there are some intriguing links between stress and eating habits in animals and biochemical factors. Recent research by UCSF's Mary Dallman supports the idea that stress and fat metabolism are regulated by the same biological mechanisms. Dallman's study found that animals subjected to greater chronic stress increased their consumption of sweet or fatty food and developed greater visceral fat deposition. Visceral fat is buried beneath the muscles and is stored centrally, in the abdomen. It is the type of fat associated with heart disease and other serious health problems.

Consequently, it is not only how fat you are that is important, but where that fat is stored. Psychologist Elissa

"There are some intriguing links between **stress and eating habits** in animals and **biochemical** factors."

Elissa Epel

Epel has long studied the links between stress, as measured by the release of cortisol, and where and how fat appears in the body. "We know that stress is a pathogenic factor in weight control and we believe that cortisol and insulin are each half of the picture of stress-induced obesity," she says. "Insulin alone promotes obesity; cortisol and insulin together promote visceral obesity."

Epel's current project examines in humans what Dallman has found in rats. "In looking at the eating habits of chronically stressed caregivers, we are trying to see if we can replicate the stress reaction in humans. Will the stress eaters (those who eat more under stress) show an increase in cortisol, insulin, and visceral fat over time? Our theory is that they will." In another recent study of medical students, Epel did find that stress eaters develop higher cortisol, insulin, and adiposity during exam times, as compared to those who report they eat less during stress.

Laurel Mellin has found similar links. Mellin, a nutritionist who has written numerous books on weight loss and who directs the Institute for Health Solutions, has observed a vicious emotional cycle wherein stress and depression lead to hormonal changes that then lead to decreased energy needs, increased appetite and increased fat storage.

"The people I work with eat for the same reasons we smoke or drink," says Mellin, "because we have emotional needs that are not fulfilled. We feel something missing, we can't identify it, and so we eat ice cream. We've found that the eating response is tied to parenting that fails to nurture or to provide limits. It is the absence of those two skills —nurturing and limit setting—that sustain our compulsion to overeat."

Mellin offers workshops and programs that teach nurturing and limit setting skills. She has surveyed people who have used her method and found a large percentage resolved their overeating problem, with many sustaining their improvement six years later.

She has also served as the Director of UCSF's Pediatric Obesity Clinic. In doing so, she created something called the Youth Evaluation Scale (YES), a computerized questionnaire that creates a bio-psychosocial profile that identifies the contributors to obesity and recommends reasonable care options.

A "Toxic" Environment

Regardless of their individual research or practice area, every member of the Obesity Center recognizes that today's "toxic environment" is a significant driver of the epidemic.

People variously describe this environment as a range of societal concerns that have clear links to obesity. Stressors, such as long work weeks, unsafe neighborhoods, even fears of terrorism press on people. In turn, these factors have a hand in a rash of psychological problems, especially the stress and depression associated with overeating. Researchers also refer to sedentary lifestyles, poor diets, the spotty availability of healthy food, and the political and economic influence of the fast food industry.

"This is a socially-driven epidemic," says Joaquin Barnoya, MD, who has been deeply involved in public health efforts to reduce smoking and who has now turned his attention to the obesity problem. "The food industry is marketing products that they know are damaging to people's health. One study revealed that something like 60 percent of the commercials aired during children's weekend television were for unhealthy foods like sugar-sweetened cereals."

Barnoya also notes that people in poor communities are particularly susceptible to the marketing of processed, rather than healthy

foods. He offers the example of poorer Latino communities that have limited access to affordable produce, and whose communities are inundated with McDonald's billboards in Spanish.

Another factor, says Barnoya, is that food in this country is relatively cheap and abundant compared to the rest of the world, thus encouraging people to eat more than is healthy. Historian Dorothy Porter, who is studying the history of obesity in her native England, says, "Wealthy economies do tend to show increasing levels of obesity." She points out that obesity grew among the working class during the late '50's in England, a time known as the age of "the affluent worker" that was accompanied by better access to food, the growth of television, and the move to less hard labor and more sedentary jobs.

Finally, this country's insurance system complicates the ability to address obesity in the physician's office. Andrea Garber points out that reimbursements for obesity treatments are virtually non-existent. Psychologist Joan Orell-Valente says that despite the lip service given to the need obese patients have for counseling, reimbursement is rare; in turn many counseling services simply disappear.

Barnoya has begun to explore ways that an anti-obesity public health effort can build on the success of anti-smoking programs. Yet he acknowledges the one significant difference between obesity and tobacco: everybody needs to eat.

Because of this, some worry that too much hope can rest on the public health approach. Historian Porter, who has spent much of her career examining the history of public health, says that the anti-smoking campaign has achieved its goals through social and political coercion. Smoking has been banned from many public buildings. Taxes were piled on to tobacco, without much complaint from anyone but smokers themselves. "Without structural transformation like that, behavioral change is nearly impossible to effect," she says.

She warns that such structural transformation will be more difficult with obesity. How will the lines be drawn between acceptable and non-acceptable food? How will the politicians be convinced? How will people react to seeing food prices increase dramatically? These are questions that have not yet been answered.

Barnoya, however, remains optimistic. "The word is getting out there," he says.

Andrea Garber

One Size Does Not Fit All

Despite the greater attention to obesity, the epidemic continues to grow.

A number of treatments—usually some combination of diet, exercise, counseling, and drugs or surgery—have already been proven quite effective, but even the good programs seem to generate results in only about 15 percent of their patients. When groups do better than that, they tend to be self-selected and motivated, and not those hit hardest by the obesity epidemic—ethnic minorities in disadvantaged communities.

Members of the CHC Obesity Center believe that the isolated nature of most obesity research and treatment contributes to the low success rate and the failure of today's prevention efforts. Certainly, all see the limits to their own particular discipline.

Vaisse, for example, is leery of the way people associate miracle promises with genetics. "The epidemic in this country has occurred over the last thirty years," he says. "There cannot have been a lot of gene mutation over that period of

"If we could **individualize** the treatment, can we **double our success** rate?"

time. In addition, genetic mutations that are solely or primarily responsible for an individual's obesity are extremely rare. That means the cause of the present epidemic lies elsewhere." Consequently, he believes that ultimately, success hinges on individuals and society doing the hard work of breaking old habits and changing the ways they approach diet and exercise.

Robert Lustig

Lustig feels that as important as the role of insulin is, "We have to figure out what in our environment has changed and led to our insulin levels being overhyped."

Unsurprisingly, then, one of the clear, early conclusions that the group has drawn is that there is no single solution for either prevention or treatment. "One size does not fit all" is a common theme.

Consequently, "The first research question on the table is: if we could individualize the treatment, can we double our success rate?" says Baron.

The group will strive to create what Andrea Garber calls "a treatment algorithm" for working with an obese patient. For example, patients with a genetic mutation that contributes directly to their obesity might move immediately to a drug treatment combined with a tailored diet and exercise regime. Those treatments might be supported by psychological and cultural insights that would help ensure compliance.

In contrast, obese individuals for whom genetics and biology are not the primary contributors would undergo intensive counseling accompanied by a diet and exercise regime that accounts for familial and cultural patterns around food, as well as the surrounding community factors. In the case of a child, parents might receive culturally sensitive training in nurturing and limit setting.

While creating and implementing such an algorithm is a complex challenge, "I feel tremendous cohesion across many disciplines" says Mietus-Snyder. "The attention we are all focusing on this may make it less of a David vs. Goliath proposition than it's been to date."

Longer-term, the group intends to add its voice to the public health effort that is gathering steam in pockets across the country. Valente, who works with families whose children are chronically ill, says that such an effort might be helped by research into the differences from culture to culture in parent-child mealtime interactions. Mellin argues that public health efforts must aim, at least in part, to provide education about nurturing and limits. Tran talks about working with young mothers to encourage breast feeding, since there are suspicions that the excessive use of formula creates a metabolic set point that encourages obesity and which is very difficult to alter.

Tools for the Here and Now

Still others suggest that a large national effort could be supported by smaller, pilot-type efforts in the Bay Area that would have a more immediate impact. Bobby Baron, for example, would like to see the CHC group begin by transforming UCSF into an obesity prevention environment that could be used as a model for programs around the country.

It is exactly that kind of short-term, grassroots effort that Tran would also like to see emerge. "At least 30 percent of our kids at SFGH are obese," she says. "Over the last few years, we've seen more Type II diabetes in younger people. Higher blood pressure. Higher cholesterol and triglycerides, even some hip and knee problems. We already know an

continued on back page

From the Director *continued from front page*

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awful lot and I want solutions that can work today."

For her patients, kids like "Gilberto," the solutions cannot arrive too soon. On the face of it, of course, Gilberto should simply stop drinking soda and play basketball at the local park. But it is in understanding how to achieve and sustain such behavior change among large groups of people that the key to the epidemic lies. If groups like the CHC can begin to make progress in this area, then the downward curve on Gilberto's chart will no longer be an isolated case. That's when the providers who care for him will have a lot more reason to cheer. ■

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