GENETICS IN YOUR PRACTICE

Introducing the Human Microbiome Project

You are never alone as you travel through this life; in fact, each of us is outnumbered on a cellular level by the microflora that travel with us. Estimates place the total number of microbial cells that we carry at a 10:1 ratio to the number of human cells.

BY MICHAEL F. MURRAY, M.D.

The Human Microbiome Project has been launched in an effort to better understand these fellow travelers. The net contribution of this research effort to our understanding of human health and disease will rival that of the Human Genome Project. In the future, the eventual integration of the microbiome project with the genome project will provide unprecedented opportunities to understand the interplay of "nature and nurture." The National Institutes of Health and other organizations around the world are funding microbiome research aimed at better understanding our commensal flora.

The five different "microbial communities" targeted by the current research agenda are the gastrointestinal tract, the female urogenital tract, the oral cavity, the nasopharyngeal tract, and the skin.

As the NIH Web site for the project states, the Human Microbiome Project has set the following goals: determining whether individuals share a core human microbiome, understanding whether changes in the human microbiome can be correlated with changes in human health, developing the new technological and bioinformatic tools needed to support these goals, and addressing the ethical, legal, and social implications raised by human microbiome research (http://nihroadmap.nih.gov/hmp).

Currently, we have relatively few practical clinical insights into how and why this exciting area of research matters. But *Clostridium difficile* colitis and vaginal candidiasis are two examples that provide simple but important lessons about the function of our microbiome as a protective mucosal barrier. As every clinician knows, when antibiotics are used to treat infection, the critical balance within these communities of flora can become altered in a way that allows a minor member of the community to overrun the anatomical space and create symptomatic disease. In these two examples, the effects of an altered community are usually relatively short term and treatable.

But a study published last year points to a new paradigm of longer-term and perhaps lifelong consequences of altered microbiomes. The research showed that the pathogenic potential of *Helicobacter hepaticus* in a mammalian colitis model is altered by the presence of different strains of *Bacteroides fragilis*.

The presence or absence of a particular bacterial polysaccharide expressed on the microbial cell surface of *B. fragilis* controls whether there is an inflammatory response to *H. hepaticus* (Nature 2008;453:620-5).

Among the implications of this research is the proof of concept that a staged exposure to microbes can lead to an inflammatory on-off switch in the colon. It is conceivable that within the practice life of many of the readers of this column, we could be engineering the gastrointestinal microbiome to induce the regression of colonic polyps or to treat inflammatory bowel disease.

Some other general areas of clinical interest to watch for as microbiome research progresses include the following:

- ► Routine manipulation of human mucosal microbiomes to improve barrier defenses.
- ► Optimization of human immune responses through altered microbial communities.
- ► Use of microbes as on-off switches for human cellular pathways.
- ► Targeted human gene regulation via microbial signaling.
- ► The discovery of new microbes.

Regarding new microbe discovery, the Human Microbiome Project promises a fascinating opportunity to discover and ultimately understand whole classes of human commensal microbes that have not yet yielded any of their secrets simply because they cannot be cultured via any currently available technique.

The study of the microbiome and its interaction with the human genome is sure to reveal much about human health and disease. ■

DR. MURRAY *is the clinical chief of genetics at Brigham and Women's Hospital and an instructor at Harvard Medical School, Boston.*

Feds Issue Rules for Use of Genetic Information by Insurers

BY MARY ELLEN SCHNEIDER

The federal government has issued rules spelling out how it intends to police the use of genetic information by health plans.

The regulations bar health insurers from increasing premiums or denying enrollment based on genetic information. The regulations implement certain provisions in the Genetic Information Nondiscrimination Act (GINA), which was signed into law by President Bush in May 2008.

Beefing up consumer protections for genetic information should help accelerate progress in genetic testing and research, said Health and Human Services secretary Kathleen Sebelius. "Consumer confidence in genetic testing can now grow and help researchers get a better handle on the genetic basis of diseases," Ms. Sebelius said in a statement. "Genetic testing will encourage the early diagnosis and treatment of certain diseases while allowing scientists to develop new medicines, treatments, and therapies."

In an interim final rule, federal officials provide details on how health plans can obtain and use genetic information. The regulation generally bars health plans from increasing premiums based on genetic information. They also cannot require, or even request, that individuals or family members undergo genetic testing. And health plans cannot request, require, or purchase genetic information at any time for underwriting purposes, or prior to or in connection with enrollment.

Although the rule bars insurers from charging its members more based on genetic information, it doesn't limit them from doing so because of the manifestation of a disease. However, a health plan can't use the manifestation of a disease in one of its members as genetic information for a family member and raise their premiums, according to the interim final rule.

The rule does allow plans to request limited genetic information if it's necessary to determine the "medical appropriateness" of a certain treatment.

Plans also can request that individuals participate in research in which genetic testing will be conducted. However, none of the genetic information collected during that research can be used for underwriting purposes.

The interim final rule goes into effect 60 days after publication in the Federal Register.

HHS officials also issued a proposed rule that would modify the Health Insurance Portability and Accountability Act (HIPAA) to comply with the provisions of GINA.

Like the GINA rule, the HIPAA rule bars health plans from using and disclosing genetic information for underwriting purposes. However, because HIPAA applies more broadly, the prohibition in the proposed rule also affects employee welfare benefit plans and long-term care policies. It would exclude nursing home fixed indemnity policies.

If the proposed rule is finalized, then plans would have 180 days to comply with the provisions. ■

Most Board Exams Fail to Make the Grade on Genetics

BY JEFF EVANS

BETHESDA, MD. — Few board certification examinations require physicians to understand concepts related to genetic testing and counseling or how to take or interpret family history, according to an analysis of the content outlines of such exams for 43 medical specialties.

"The lack of genetics and genomics knowledge by our current physicians is based in part on the competing priorities among the certifying specialty boards. … Few physicians are expected to know the practical applications of genetics to become certified; thus, the curriculum does not make genetics content a priority," Carrie A. Zabel said at the annual meeting of the National Coalition for Health Professional Education in Genetics.

In an analysis of the exam outlines for 24 specialties certified by the American Board of Medical Specialties and 19 subspecialties certified by the American Board of Internal Medicine (ABIM), 11 did not mention genetics or genomics in their certification exam content outline, or had no outline, according to a review done by Ms. Zabel and her colleague at the Mayo Clinic in Rochester, Minn., Dr. Paul V. Targonski.

Fifteen exam outlines referred only to syndromes that were specific to the practice of a particular specialty and for which an underlying genetic etiology was known. These outlines did not otherwise specify basic genetics knowledge within their content, said Ms. Zabel, a certified genetics counselor at the Mayo Clinic.

A total of seven content outlines made reference to having an understanding of basic genetics. Another 10 content outlines provided a detailed listing of specific genetics content and concepts, but only two of them—the exams for the American Board of Medical Genetics and the American Board of Obstetrics and Gynecology—mentioned family history. This "may be due to a lack of evidence of the utility of family history," said Ms. Zabel, who had no relevant financial disclosures to make.

Even though 8 of the 10 detailed content outlines included genetic testing, only 4 also mentioned genetic counseling, "which is more than just services provided by a genetic counselor. It's the informed consent process and the discussion of the implications of results," Ms. Zabel said. "I think this is potentially doing a disservice to those patients."

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