What doctors wish patients knew about precision medicine

JUL 21, 2023

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In the rapidly evolving health care landscape, precision medicine—also referred to as personalized medicine—has emerged as a revolutionary approach that tailors medical treatments to individual patients. By harnessing the power of advanced technologies and genetic insights, precision medicine is transforming the way we understand and treat diseases.

For patients, though, navigating this complex and cutting-edge field can be overwhelming. Understanding the basics and potential benefits of precision medicine is crucial for informed decision-making and active participation in one's own health care journey.

The AMA's What Doctors Wish Patients Knew™ series provides physicians with a platform to share what they want patients to understand about today's health care headlines.

For this installment, two physicians took time to discuss what patients need to know about precision medicine. They are:

- Mira Irons, MD, a pediatrician and medical geneticist and president and CEO of the College of Physicians of Philadelphia. In a prior role, Dr. Irons served as chief health and science officer at the AMA.
- Jordan Laser, MD, an anatomic, clinical and molecular genetic pathologist, and chair of the Personalized Medicine Committee for the College of American Pathologists.

We're in exciting times

"The take-home message is that we are really in an exciting time now," Dr. Laser said. "We've been talking about precision and personalized medicine for quite some time, and I'm really amazed to see

how far we've come in the past 10 years.

"We're really well on our journey to leverage this genetic knowledge in order to maximize benefit while minimizing risk for individuals," he added. "This could be more for oncology diseases and diseases more broadly ranging from the super common hypertension to rare genetic diseases."

Terms are used interchangeably

"Precision medicine and personalized medicine are two terms that are used pretty interchangeably and for good reasons," Dr. Laser said. "It actually represents the history of our thought process around it. Originally personalized medicine came out first and it's really rooted in the fact that we can test an individual for particular attributes—usually genetic attributes—that enable us to tailor a treatment plan to them.

"While we used to call it personalized medicine, we're actually starting to move away from that terminology because it gives the implication that the therapy is really uniquely tailored for that person, which is probably a bit of an overstatement," he said. Instead, "we are identifying genetic differences to help us tailor the therapy to the entire group with the same genetic differences, and we would treat them differently as we would another group with a different set of genetics.

"That's why we now prefer the term of precision medicine instead just to alleviate that real strict individual, unique nature implied by personalized medicine," Dr. Laser noted.

A person's genetic makeup plays a role

"People use the terms precision medicine and personalized medicine interchangeably," said Dr. Irons. "But the way I look at it as a geneticist is that personalized medicine is based on the concept that each individual has a unique genetic makeup and that can be used in many circumstances as additional information when evaluating them for illness or for new symptoms.

"We have to divide things up in this context into patients who come in with symptoms of illness versus identifying asymptomatic individuals who may be at increased risk for disease due to their specific genetic makeup," she said. "So, precision medicine is an emerging concept that is important both for disease diagnosis and treatment and in some instances for risk reduction and prevention.

"The main concept is that you're trying to use as much information about that particular person as you can get for their evaluation or treatment," Dr. Irons added. "If you are looking at it at from the preventive side, the question we ask is what genetic markers does a person have that may place them

at increased risk for a specific condition and how knowing that would that impact their care."

It's overcoming limitations

"Personalized medicine, because it's based on each patient's unique genetic makeup, is beginning to overcome the limitations of traditional medicine," Dr. Irons said. "So, it's allowing health professionals to shift the emphasis from reaction—people come in with symptoms of a disease—to prevention by predicting susceptibility."

Pharmacogenomics informs therapy

"Typically, in precision or personalized medicine, we are looking for genetic changes in a person to inform their therapy," Dr. Laser said. "So, pharmacogenetics or pharmacogenomics is a way in which we can test a patient's DNA to see if they have changes in their DNA that would make them more likely to benefit or experience adverse effects from a particular therapy. Armed with this information, we can tailor the therapy to maximize benefit while minimizing risk.

"And these changes are not necessarily mutations. They don't necessarily cause any problems. It can be simply normal human variation. But what's interesting is that some of those changes in the DNA can cause you to react differently to certain therapeutic drugs," he added. "By understanding how your DNA predicts how you're going to respond to a drug, we can tailor your treatments based upon your genes."

"We know that there are variations in certain genes that are involved in drug metabolism and that people can have changes in those genes that actually make them metabolize medication in different ways," Dr. Irons said. For example, "variations in pharmacogenomic genes have been identified that affect the metabolism of Warfarin, which is a blood thinner, and also clopidogrel which is a drug that works on platelets to keep them from forming clots, so it helps prevent heart attacks, in addition to others.

"There are people based on their genetic profile who may be either fast metabolizers or slow metabolizers. So, a fast metabolizer of a certain drug would not react as expected to a drug because they're metabolizing it too quickly," she added. "You're giving them a medication and it's not doing what you intended it to do. Slow metabolizers may actually become toxic because they would build up the drug."

"Knowing that upfront is really helpful otherwise I'm going to be trying the first drug and there's going to be some period of time where the patient may not get better," Dr. Laser said. "But if I have that

information upfront, I could skip that first trial drug and go straight to a drug that I know or predict will work."

Precision medicine "really impacts both sides of the spectrum, namely we can use it to identify those who may not respond or be hypersensitive to the drug, even to the point of causing adverse effects," he said.

The biggest use is for cancer

"Pharmacogenetics and pharmacogenomics are underutilized in the United States. That said, a subset of pharmacogenetics and pharmacogenomics that is really moving forward quite a bit is in the space of oncology," Dr. Laser said. "In the oncology space, we're really seeing that genetic variants or mutations in the tumor itself are being used to select specific treatments designed to specifically target the tumor as opposed to the healthy cells throughout the rest of the body."

"Cancer is the best example of personalized or precision medicine in practice because what's happening is that certain cancer types are actually now being based on the genetics of the cancer cells themselves," Dr. Irons said. "In the past, if there was a specific type of cancer, we might have just thought of it by that broader condition name.

"But now we know that even certain cancers that looked the same clinically and pathologically, if you look at the genetics of the cancer cells themselves, they are actually different," she added. "So, physicians are defining specific cancers based on the genetics of the cells themselves and that's actually helping direct personalized therapies because certain medications are being developed that target those specific genetic changes so that it's more effective in treating the specific type of cancer that person has."

It identifies genetic predispositions

"Cancer is actually a good example of using genetic testing in two different ways. Genetic testing is being done to define the cancer and to direct therapy and it can also help identify asymptomatic people who are at increased risk for certain types of cancers," Dr. Irons said. "Examples of this are people with BRCA1 or BRCA2 mutations for breast and ovarian cancer or people with mutations seen in Lynch Syndrome that is associated with GI and other cancers.

"Identifying those people before they present with cancer is what some may also call personalized medicine," she added, noting "the goal is to ultimately detect something at a much earlier stage or provide risk reduction strategies that can be done to prevent the cancer in individuals at increased risk

due to their genetic makeup."

Not all cancers are the same

"I would go as far as saying not every cancer is the same, but there are common patterns that we see within subsets of types of cancer," Dr. Laser said. "For example, within lung cancer, there are particular genes that are known to have variations or mutations in them that we can therefore have drugs to target and treat that lung cancer."

The HER2 gene in breast cancer is another example. "That's one gene in breast cancer that the major kind of variant is that it's overamplified. In other words, there are too many copies of that gene," he said. "So, if you were able to shut down HER2, you can shut down the tumor and that's exactly what those targeted therapies do."

The environment can impact genes

While "genetics is focused on single genes … genomics is different because it addresses multiple genes, and how they work together and their confined influence on the growth and development of the person," Dr. Irons said. "It basically means going from a single gene to how do these multiple genes work together because we do know that genes interact with each other.

"We are also learning that an individual's environment can cause epigenetic changes that also impact how genes function. And that can include stress, by childhood stress, by psychological stress, by people's living conditions," she said. "It's an evolving body of knowledge, but we know that there are things that occur during people's lifespans that actually can impact how their genes function and that's genomics."

Microbiomes also play a role

"That's another big topic that we're seeing in medicine these days and it's really our interaction with our body and the microorganisms that live on or in us," Dr. Laser said. "Different microbiome patterns in patients can be associated with certain diseases. For example, we now know there is an association with a microbial imbalance in the colon that contributes to colon cancer, most likely via an overabundance of a bacterium known as Fusobacterium.

“It really demonstrates the variability in all species and it’s just incredible how our knowledge base just continues to grow, and we learn so much more about us as humans,” he said. “We're not on an island. It's our interaction with our environment and the organisms around us that promote or prevent disease.”

Ask about genetic testing

“We have many tools in our toolbox for assessing genetic variation and gene sequencing is one of those tools, probably one of the most powerful and most widely used ones,” Dr. Laser said, noting “we can sequence individual genes, or we can sequence the entire genome. That would be one simple way of differentiating genetics and genomics respectively.

“The field is constantly expanding as to where the appropriate clinical application of genetic testing exists, so I would always encourage someone to ask about genetic and genomic testing for any disease,” he said. “The answer may be there isn’t anything available—depending on the clinical situation—but it’s forever growing and will likely change over time.”

“If you have a child or a family member with an unusual physical or developmental problem that you haven’t found an answer to, it’s important to ask about the role of exome sequencing or genome sequencing because there’s more and more information being generated in this area,” Dr. Irons said. “Over the last few years—especially if you consider children with physical or developmental abnormalities who don’t fit in a specific pattern—the diagnostic rate may be somewhere in that 30 to 40 to 50% range depending on the symptoms that the child has.

“In that sense, if you haven’t seen a geneticist or a neurologist or if you have an unusual presentation of a common disease, then genetic testing is worth discussing,” she said. “If you’re doing the testing because you have an affected family member, having the results of the family member is really important because then you can look for the specific genetic change the family member has.”