A Laboratorians' Perspective on Reimbursement of Genetic Technologies and Services
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DR. McCABE: So next, the next two presentations will discuss the perspectives of the providers. First we're going to hear from Dr. Andrea Ferreira-Gonzalez, Associate Professor and Director of the Molecular Diagnostic Laboratory at Virginia Commonwealth University, who we heard before during the public commentary. Dr. Ferreira-Gonzalez will give us the laboratorian's perspective.

DR. FERREIRA-GONZALEZ: Thank you, Dr. McCabe.

I would like to thank Dr. McCabe and members of the committee for inviting me here today to share providers' perspective on reimbursement for genetic testing.

As has already been alluded to today, codes are the language of reimbursement. They hold the key for laboratorians to get reimbursed or pay for the services that we provide, either by performing the laboratory testing, interpretation or report on that. The current two levels of codes are mostly used by many providers, insurance companies. These procedure codes are, first, Level I. They're called the Current Procedural Terminology, or what we call CPT codes that were developed by the American Medical Association.

For laboratories, they usually are five-digit numbers that identify specific analytes, either methodology-specific analytes, assay stains, interpretations, even consultation. There is also another set of codes that could be added to the CPT codes. They're usually called code modifiers, two-digit coded, that are added to the five-digit number that further give a little bit more information about what the depth of the procedure or the interpretation.

The second level of coding, the HCPCS codes that were previously mentioned by Dr. Schoonmaker, is the ones that have been developed by the Center for Medicaid and Medicare that allow to deal with testing or interpretation and reports that don't have currently a CPT code approved, or for those newer technologies as they start gathering information to determine what will be the best level for reimbursement.

So the use of these CPT codes are the means by which the payers match the service with the appropriate limit of the payment. A majority of the payers, Medicare and Medicaid, all of the private payers, actually recognize the CPT codes to identify the services. In addition to the CPT code, we provide billing or filling out claim forms, we also have to add another specific code that identified the diagnosis or the set of symptoms or signs that are required or triggered the physician to order the different testing, and allows us also to determine what is the diagnosis for that particular patient.

For molecular diagnostic testing, there are actually 14 different CPT codes. These 14 CPT codes are used to reimburse for all the genetic testing that is currently used in this country. As you can see here, these 14 codes are procedure specific CPT codes. Here you can see that the numbers are associated with a code from 83890 down to 83912. Each of these different CPT codes has a description associated that allows the third party to identify what part of the procedure, what methodology was used to come up to the diagnosis that we're rendering.

As you can see, for example, CPT code 83890 is for molecular isolation or extraction, and 83891 is also isolation and extraction but for highly purified nucleic acid. So it seems that there might

be a little bit of flexibility in some of the CPT code they would currently use, but as I'll show you as we go through the different slides, this is not the case.

So we have 14 codes to allow us to bill for a large amount of different kinds of services. In addition, all these different services, when they require interpretation and report, we have at different levels. This also is represented by the single CPT code.

In here I have provided you the Medicare laboratory fee schedule for 2004. This is the current fee schedule that we use when somebody claims reimbursement for our testing. I'll walk you through this table. In the far corner here, we have the number of the CPT code. Remember the first one I mentioned, 83890 for nucleic acid isolation. As you can see, the first list here is the national limit allowed that Medicare sets for the payment of that particular code. What I don't have here is the lower limit that is allowed, and that is zero. So the national limit goes from $5.60 down to zero.

After the national limit has determined each of the different states, take the code and determine what actually is going to be the level of reimbursement for each of the different states. I have provided you here CPT code and reimbursement with the Medicare fee schedule for different states. In here, this is Georgia, this is Virginia State, and this is Tennessee, North Carolina, and California. What I want to point out here is that even though there is a national limit allowed for all these different tests, there are particular states that reimburse at very low levels for every single CPT code that we use for genetic testing. There are other states that aren't the same.

But the other states -- for example, the State of Virginia, where there is a very similar reimbursement level or the national limit allowed, except for one particular CPT code for reverse transcriptase. That is $17.47.

I want you to look at these levels of reimbursement for a couple of specific CPT codes, for the 83890, nucleic acid isolation, and also for the 83891, isolation for highly purified. What you see is a short description of that CPT code, it's implied that it requires further manipulation of the nucleic acid to obtain the more purified that is required for the testing. As you can assume, there is more work, label and reagents that are required to perform this highly purified nucleic acid isolation, but the limit is set to the same level. Please keep that dollar amount in mind as I go through.

Before we go through the financial analysis, I think you need to know what kind of services are provided. The Virginia Commonwealth University Medical Center is comprised of three different entities: the Medical College of Virginia Hospitals, MCV Associate of Physicians in private practice, and the VCU Medical School. These are three independent organizations. The Medical College of Virginia Hospital is a 350-bed hospital. It's actually three different hospitals. They are combined under the umbrella of MCV Hospital. We're located downtown Richmond across from the governor's house, so we are downtown in a very large metropolitan city. We serve the central Virginia area of about 850,000 individuals.

We are one of the sole tertiary care centers in that central Virginia area. Our laboratory, the molecular diagnostic laboratory, is what's called a comprehensive laboratory. We provide molecular diagnostic testing for infectious disease, oncology, hematology, and inherited disorders. Just to give you an idea of the volume of testing that we handle in the laboratory, in calendar year 2003, meaning January to December last year, we did 13,200 tests.

Just to give you examples of the levels of reimbursement, I have chosen three example. One

example that is highly complex testing and requires highly interpretation is second one, intermediate, and the third one is considered more simple within our standard of high complexity testing. I'm not going to go into detail on Fragile X syndrome because that's not the purpose of this lecture. I'm only going to point out some issues here.

Fragile X syndrome is the most common cause of inherited mental retardation, with a prevalence of 1 in 1,200 for males and about 1 in 2,500 for females. The cause of Fragile X syndrome, it's an expansion of the tri-nucleotide repeat sequence comprised of CGG near the 5 prime M of the FMR1 gene. One of the major issues of the diagnosis or trying to identify individuals with Fragile X syndrome is trying to measure the amount of repeats that are located in this area of the 5 prime M of the gene. The number of repeats with allocate the individual within certain categories or areas. If you have 6 to 50 repeats of that particular trinucleotide, you're considered part of the normal population. Individuals with a mutation will have 50 to 200 repeats. These individuals might not necessarily have any phenotype of the disease but are carriers that can pass it along through different offsprings, and actually that mutation can expand to the full mutation that will produce the full phenotype.

Full mutations contain about 200 repeats or even higher number of repeats. So there is an area that needs to be very accurate in the amount of quantification of the nucleotide repeats to be able to put individuals within normal populations and at risk or having mutation, and it's about 45 to 55 copies. Due to the fact of the complexity of the sequence and the complexity of the measurement of the repeats, we require the use of two techniques in our laboratory, the polymerase chain reaction and southern blotting analysis.

The polymerase reaction allows us to size very good trinucleotide repeats up to 110 repeats. So the normal range plus the mutation. Individuals with larger mutations will not amplify with a PCR reaction. So southern blotting analysis also comes in handy in trying to identify larger permutations and also give us information about the methylation status.

So we perform the test, and then we provide the series of CPT codes to the provider to get reimbursed for our test. I have provided here the description and the CPT codes that we currently use for the reimbursement of southern blotting analysis and PCR. As you can see here, sometimes, due to the fact of the way we perform the assays, some of the CPT codes are used more than once. The cost of providing it here is actually the direct cost. It is the cost of the reagent plus personnel. I have not added indirect costs because these will vary from institution to institution. So these will allow you to translate more into different institutions.

As you can see here, the total reimbursement for our cost of the testing is $266.34, and what the Virginia Medicare expects is $62.30. Remember from that slide where I pointed out to you that the Virginia Medicare expect was only different from the national limit allowed in a single CPT code that we don't use here. So this is very similar to the national limit allowed for this particular testing.

For the PCR analysis here, we also have different CPT codes. We do not have a code for nucleic acid isolation because it was already extracted when we performed the southern hybridization analysis. There's a clean-up of the PCR product that is required before capillary electrophoresis, so we needed to add nucleic acid isolation. As you can see here, our cost of performing the test is $116.06, versus $17.85. That's what Virginia Medical expect.

What I pointed out to you here is that our cost to perform nucleic acid isolation highly purified is $15.06, and it's about $55.47 for reimbursement. I also want to point out interpretation and

report, our cost is $40.00 for this other hybridization analysis, and about $35.00 for that. I want to show you for genetic interpretation, the national limit allowed for all the testing is $5.60.

Now, let's move on to intermediate complexity testing, and I've specifically chosen the immunoglobulin gene rearrangement by PCR because it's also a somatic change. It's not inherited disorder but it's a somatic change, and actually it's intermediate complexity, what we consider complexity in molecular genetic testing.

This actually is extremely important in the diagnosis of lymphoma and leukemia because it allows us to identify the proliferation of lymphoid cells, central to the diagnosis of these two entities, because it allows us to differentiate a diagnosis of reactive lymphoidopathy versus lymphoma or lymphoid malignancy.

Here again we have a description of the codes that we currently use for seeking reimbursement. As you can see here, we have a nucleic acid extraction of 83891, a highly purified nucleic acid extraction. In the previous slide I showed you that the cost was significantly lower than this one. The reason why this one is so high compared to the highly purified for hybridization analysis is because most of the testing is done on tissue that has been paraffin embedded that needs to be further processed to remove the paraffin and then get washed and get ready for the nucleic acid isolation.

What I'm trying to point out to you is that we have two codes for nucleic acid isolation, and I've already described to you at least three different ways to extract the DNA or nucleic acid using different procedures. So there's not much flexibility in the current coding to allow us to account for those differences. In here you will see the particular CPT code we used three times due to the fact that we amplify three areas of the gene or family regions that increase the sensitivity and specificity of our particular assay. Again, interpretation is $40, and we will get reimbursed $18.54 because we submit the interpretational report with the 26 modifier.

But you can see that there's a discrepancy in what it's actually costing us to do the interpretational report and what we were actually reimbursed, and for that matter for the entire procedure.

The third example I chose is one of the most simple assays we have in the laboratory and that is widely used and performed in many laboratories. Factor V Leiden is the most common hereditary blood coagulation disorder in the United States. We have a prevalence in the general population of 5 percent for Caucasians and 1.2 percent for the African American population. The reason why it's so important to do genotyping for the Factor V Leiden is that we need to identify individuals that are heterozygous, but mostly homozygous individuals, because we have different consequences of treatment for these particular patients.

Being heterozygous for the Factor V Leiden increases your risk of venous thrombosis about five-fold. On the other hand, homozygous it's about 100-fold increase. Individuals homozygous for the Factor V Leiden might be required to place on anticoagulant therapy for the rest of their lives.

I have listed here the number of different coagulopathies where Factor V has been associated with. Here again we have the description of a technology and we have nucleic acid isolation, 83890. That's the lowest level of nucleic acid extraction, and you can see the cost is lower too, at $9.69. This is one of the assays that we perform that has a single amplification technology, currently used in commercially available ASARs have been validated and put together in our laboratory.

Again, here we can see that we have to use the same CPT code several times to reflect the procedure that we're currently using. Here, the more simple genetic testing is a lot closer in reimbursement to what it's actually costing us to perform the test.

Now, this is how the level of reimbursement. What do we actually get reimbursed? I've showed you Medicare will not be able to provide you specific reimbursement percentage for all the third-party payers of private insurance due to contract agreements and non-disclosure issues that we have with them. But I can tell you that we have submitted a number of claims for all the testing that we did, and we get reimbursement from Medicare about 89 percent of the time, 72 percent for Medicaid, and there's a range for the other third-party payers, from 61 percent up to 85 percent.

What it was striking for me to realize that the Medicaid/Medicare reimbursement were getting the national limit allowed. But actually, the third-party payers are paying us almost the identical amount, all of them. So this is something that is across the board for all the different payers.

I think also we need to spend some time in the very crucially important code interpretation and report. As we know, interpretation of genetic testing requires the analysis of the testing plus putting information, clinical history, family history, clear pathological correlation, all together to be able to come up with the right result.

When we looked at our level of reimbursement for the CPT code 83912, with modifier 26, we see that we get reimbursed, and it's the same level that we get reimbursed for the procedure component of the test that we do, again from 93 percent down to 61 percent. But what we get here, the Medicare/Medicaid gives us the national limit allowed for the 83912 with the 26 modifier, but the third-party payers or commercial payers have not recognized the 26 modifier and actually reimburse the national limit allowed for the code without the modifier.

So what are the factors that affecting access of genetic testing? I have shown you a little bit about the level of reimbursement for the testing that we do, and that has to be crucial to understanding. But also, genetic testing utilization is increasing, and another factor that will dramatically affect access to genetic testing is that the laboratory fee schedule was frozen for five years, from '98 to 2002. After that time, we got a 1.1 increase, and then it was frozen again, and it's going to remain frozen from 2004 to 2008. So we have already lower level of reimbursement, genetic testing will increase, and the fees have been frozen.

Now, our costs will continue to increase. Even if reagents don't increase in cost, we're going to have to adjust the cost of living of our personnel, rent, and other expenses. So our ability to cost shift is extremely limited. I'm showing you some examples of this. I think we need to spend some time in this diagram because it gives a very nice example of what is happening in the field of genetic testing and what is to come.

The molecular diagnostic laboratory of Virginia Commonwealth University started operation in fiscal year '95. We were doing very little genetic testing. This is a diagram of the different molecular genetic testing that is currently performed in our laboratory, and I have done percent increase through the different years. In 1995, we had barely any genetic testing performed in the laboratory, but you can see that there's a little bit of increase in that particular testing or utilization of that testing. In 1999 and 2000, we've seen an explosion in the utilization of that particular testing. We have gone up to over 100-fold increase in about 10 years of service of the laboratory. I haven't put 2004, but I could tell you that it's going to be even higher.

So far we have been able to cope with the genetic testing because we've been cost shifting within the laboratory. With the freezing of the Medicare fees, that will put a hamper on our ability to be able to cost shift. What we see specifically is what happened to the molecular CPT codes. When we look at other molecular testing that is currently done in our laboratory and other laboratories, one can see that our ability to cost shift will be diminished.

I have given an example here of three different tests. All these tests have to extract RNA, nucleic acid, perform a reverse transcriptase reaction, PCR, and then quantification to quantify the chimeric messenger RNA that is a result of the T922 translocation. This is a chronic myelogenous leukemia patient, and this test is crucial for the detection of minimal disease for these particular patients. HIV viral load is crucial for the quantification of HIV in circulation, mostly for patients that are undergoing antiretroviral therapy. More recently, HCV viral load is starting to increase in utilization.

As you can see here, we have a little bit higher cost of performing these laboratory-developed assays, and we have a Medicare reimbursement of $51.65. On the other hand, in the past, the molecular infectious disease CPT code had been reimbursed a little bit better than the other procedure CPT codes. $99.18 is actually the mean value of cost among 25 different laboratories across the country, and you can see the Medicare reimbursement is $114.36. So we recuperating some of the cost and actually making a little bit. But with the increase in use of hepatitis C viral load and other testing that are not fairly reimbursed currently, these are going to put extra strength in the laboratory and our ability to cost shift will be reduced to almost none.

The other factor affecting access to genetic testing that will increase the cost of testing will be royalty payments. Currently we deal with different royalty payments for patented procedures, or even patent genes or sequences. The most common royalty payment for patent procedures is having a percentage fee of the receipts or the reimbursement that we get for the testing that we do, and it can vary depending upon your royalty agreement fee schedule between 9 percent of what you recover to 15 percent of what you recover.

On the other hand, royalty payment for patented genes and sequences can have different ways to be performed or different fees, an upfront fee plus a flat fee per test, or a one-time payment plus percentage of the charges. I think it's interesting to see what has actually happened with hemochromatosis in this country. There was a requirement of the patent by SmithKlineBeecham Laboratory, which was acquired by Quest Laboratories, to perform exclusive licensing to perform hereditary hemochromatosis, pretty much testing the 12 most common mutations of this particular gene.

Quest entered into an agreement with BioRad by which BioRad Laboratory acquired the rights to the patent and developed commercial kits, and it will further sublicense that to laboratories. So you have two options if you want to perform hemochromatosis. You can either buy a reagent from BioRad at a set level or you can license, develop your test by your laboratory, but we have to provide an upfront fee, which is extremely high, plus $20 per test. You can see what this can do to performing the test for the current cost of performing all the other Factor V Leiden. Also, we can have a one-time payment plus percentage of the charges.

The last issue I would like to point out is access to genetic testing, and also our ability to continue to perform testing. It's from work performed by Cho and collaborators that was published last year in the Journal of Molecular Diagnostics, where they did a survey of 122 laboratories. The main objective of the study was to try to identify current practices by patent holders and the ability of the laboratories to perform genetic testing.

The 122 laboratories were recruited from GeneTests' list and from the directory of the Association for Molecular Pathology. As you can see here, there's a description of the different kinds of laboratories that were enrolled in the survey. It's a little tilted toward university, non-profit private hospital, again because the majority of the genetic tests is currently provided by academic institutions. The companies or commercial laboratories were less represented here.

I think what was striking to see from this study is that there was a number of laboratories that received letters from patent holders requesting to stop, cease and desist performing certain testing. There were nine laboratories that received that notice and decided to stop the testing, performing apolipoprotein genetic testing for Alzheimer's disease, and nine laboratories also for breast cancer.

I think what was also striking from this study was that 25 percent of the laboratories had to stop testing that they were currently offering. But also, 55 percent of the laboratories expressed that they had not developed a test due to the fact of licensing or patent issues.

I hope I've been able to convey to you what is currently happening in the clinical practice of laboratory testing and what some of the major factors are that are going to affect access of this testing to the population.

Thank you.

DR. McCABE: Thank you, Dr. Ferreira-Gonzalez.