Understanding Molecular Pathology and the Recent Changes to CPT

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What We Should Discuss Today

General changes to CPT for 2012
Review of molecular diagnostics generally
The new molecular pathology codes in CPT 2012
Changes to anticipate for 2013
Challenges that remain in molecular diagnostics and related testing
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For 2012, Changes Were Made To CPT

- Two New Codes
  - 86386 Nuclear Matrix Protein 22 (NMP22), qualitative
  - 87389 HIV-1 antigen(s), with HIV-1 and HIV-2 antibodies, single result
- Five Revised Codes (basically language cleanup)
  - 86703 Antibody; HIV-1 and HIV-2, single result
  - Special stain including interpretation and report;
    - 88312 Group I for microorganisms
    - 88313 Group II, all other (eg, iron, trichrome), except stain for microorganisms, stains for enzyme constituents,
    - 88314 Histochemical stain on frozen tissue block (List separately in addition to code for primary procedure)
    - 88319 Group III, for enzyme constituents
For 2012, Changes Were Made To CPT

• Two Deleted Codes
  – 88107 Cytopathology, fluids, washings or brushings, except cervical or vaginal; simple filter method with interpretation
    (88107 has been deleted. To report smears and simple filter preparation, see 88104, 88106)
  – 88318 Determinative histochemistry to identify chemical components (eg, copper, zinc)
    (For determinative histochemistry to identify chemical components, use 88313)

• Addition of Two Category III Codes
  – 0279T Cell enumeration using immunologic selection and identification in fluid specimen (eg, circulating tumor cells in blood);
  – 0280T interpretation and report

• Revision of Modifier 92: Alternative Laboratory Platform Testing
NMP22 Was Added to Immunology

- **86386** Nuclear Matrix Protein 22 (NMP22), qualitative

Previously coded as:

- **86294** Immunoassay for tumor antigen, qualitative or semiquantitative (eg, bladder tumor antigen)

- NMP22 is found in human epithelial cells. In the urine of healthy individuals, the protein is present at low levels. The majority of patients with bladder cancer release large quantities of NMP22 into their urine.

- This test is used
  - Aid in diagnosing and monitoring of bladder cancer
  - Evaluating symptomatic patients (eg, hematuria)
  - Assessing patients with risk
    - Smokers
    - Workplace carcinogens
NMP22 marker is released from tumor cells into the urine by apoptosis. Elevated levels are detected by the NMP22 BladderChek Test.

*http://www.stellarpharma.com/bladdercheck.html
NMP22-lateral flow immunochromatographic strip*

*http://www.stellarpharma.com/bladderchek.html
There Were Changes in HIV Testing

A combined *single result assay* to identify HIV infected patients. Including:

- HIV-1 antigen (p24)
- HIV-1 antibodies (HIV-1 group M and group O)
- HIV-2 antibodies

- **87389** Infectious agent antigen detection by enzyme immunoassay technique, qualitative or semiquantitative, multiple-step method; HIV-1 antigen(s), with HIV-1 and HIV-2 antibodies, single result

- There previously was not an adequate way to code this service

- Code changes in several areas of CPT were required
  - Also used this opportunity to clarify other problematic wording
This Testing Strategy Shrinks The Diagnostic “Window”

Serologic Profile of HIV-1 Infection

- HIV Ag
- Anti-HIV IgM
- Anti-HIV Core
- Anti-HIV Env

Relative concentration over time:
- HIV-1 infection
- weeks
- months
- years
Here’s what has happened in the ability to detect HIV using common tests over the last few decades.

Frank H. Wians Jr., et al, September 2011 ■ Volume 42 ■ Number 9 LabMedicine
So Cross References Needed Cleanup and Modification

- 86703 Antibody; HIV-1 and HIV-2, single assay result

(For HIV-1 antigen(s) with HIV-1 and HIV-2 antibodies, single result, use 87389)

Alternate Laboratory Platform Testing -92 modifier:
(When HIV antibody immunoassay [HIV testing 86701-86703 or 87389] is performed using a kit or transportable instrument that wholly or in part consists of a single use, disposable analytical chamber, the service may be identified by adding modifier 92 to the usual code)
CPT Code 88107 Was Deleted

88104  Cytopathology, fluids, washings or brushings, except cervical or vaginal; smears with interpretation

88106  simple filter method with interpretation

88107  smears and simple filter preparation with interpretation

► (Do not report 88106 in conjunction with 88104) ◄
► (88107 has been deleted. To report smears and simple filter preparation, see 88104, 88106) ◄

(For nongynecological selective cellular enhancement including filter transfer techniques, use 88112)
What Happened To Poor Unfortunate 88107?

The AMA/Specialty Society RVS Update Committee (RUC) analyzes code usage

- Input solicited from specialty societies
- The service is no longer in widespread clinical use (used 7236 times in 2008)
- The code is likely a mistake with the intended code being 88112 (Cytopathology, selective cellular enhancement technique with interpretation (eg, liquid based slide preparation method), except cervical or vaginal)
- An exclusionary note was added restricting code 88106 in conjunction with code 88104. A cross-reference note was also added directing users to report codes 88104 and 88106 for smears and simple filter preparation services
Pathology Special Stains Underwent A Cleanup

• The codes (88312-88319) were revised to:
  – Came about as a result of the RUC process – hard to evaluate codes that were not clear
  – Better define special stain codes 88312-88319
  – Eliminate confusion concerning special stains where procedures overlap two code definitions
  – Delete code 88318
  – Revise existing and add new instructions and cross-reference parenthetical notes to create a defined hierarchy for codes 88314 and 88319
  – Defined units of service
# So Here’s How It Falls Out

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<td>II</td>
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<td>Yes</td>
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<td>Histochemistry for chemical components (eg, copper, zinc)</td>
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<tr>
<td>88319</td>
<td>Yes or Frozen</td>
<td>III</td>
<td>Enzyme constituents (non-IHC)</td>
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</table>
88312 Is The Microorganism Code (Editorial Revision)

▲ 88312 Special stain including interpretation and report; Group I for microorganisms (eg, Gridley, acid fast, methenamine silver)

► (Report one unit of 88312 for each special stain, on each surgical pathology block, cytologic specimen, or hematologic smear) ▼
88313 Was Also Clarified for 2012

▶ 88313  Special stain including interpretation and report; Group II, all other (eg, iron, trichrome), except immunocytochemistry and immunoperoxidase stain for microorganisms, stain for microorganisms, stains for enzyme constituents, or immunocytochemistry and immunohistochemistry

► (Report one unit of 88313 for each special stain, on each surgical pathology block, cytologic specimen, or hematologic smear) ◄
► (For immunocytochemistry and immunohistochemistry, use 88342) ◄
88313: Special stain **including interpretation and report**; Group II, all other (eg, iron, trichrome)

- Perl’s Iron Stain
- Masson Trichrome Stain
88314 Is An Add On Code Used For Histochemistry on A Frozen Tissue Block

88314 Special stain including interpretation and report; histochemical stain on frozen tissue block (List separately in addition to code for primary procedure)

(Use 88314 in conjunction with 17311-17315, 88302-88309, 88331, 88332)

► (Do not report 88314 with 17311-17315 for routine frozen section stain [eg, hematoxylin and eosin, toluidine blue], performed during Mohs surgery. When a nonroutine histochemical stain on frozen tissue during Mohs surgery is utilized, report 88314 with modifier 59)

► (Report one unit of 88314 for each special stain on each frozen surgical pathology block)

► (For a special stain performed on frozen tissue section material to identify enzyme constituents, use 88319)

Oil Red O Stain
**88319 Remains For Use In Detecting Enzyme Constituents**

▲ 88319 Special stain including interpretation and report; Group III, for enzyme constituents

► (For each stain on each surgical pathology block, cytologic specimen, or hematologic smear, use one unit of 88319)

► (For detection of enzyme constituents by immunohistochemical or immunocytochemical technique, use 88342)
New Category III Codes Were Created For Circulating Tumor Cells

- **0279T** Cell enumeration using immunologic selection and identification in fluid specimen (e.g., circulating tumor cells in blood);

- **0280T** interpretation and report

  - (Use 0280T in conjunction with 0279T)
  - (For flow cytometric immunophenotyping, see 88184-88189. For flow cytometric quantitation, see 86355-86357, 86359-86361, 86367)

The test determines disease prognosis in cancer patients and is used in determining the course of treatment.

0280T is a physician only service, if required. The service requires that the physician scans the entire image file, categorize the cells and provide a written interpretative report. The AMA CPT Changes provides additional details.

The CPT panel did not feel the evidence for 2012 was sufficiently mature to grant a Category I code. This will be reassessed for 2013.
Circulating Tumor Cells

Fluorescent antibody #1

Fluorescent antibody #2
What We Should Discuss Today

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The new molecular pathology codes in CPT 2012

Changes to anticipate for 2013

Challenges that remain in molecular diagnostics and related testing
Created the new Molecular Pathology Section in CPT!

- Guidelines and Introductory Notes
- Definitions
- Tier 1
  - 92 new codes
  - Human Leukocyte Antigen (HLA) typing
- Tier 2
  - 9 new codes/Levels
Let’s Review Molecular Biology

• DNA is deoxyribonucleic acid, a complex string of syllables found inside humans and other living things in tiny genes within chromosomes.

• The information in your DNA determines your unique biological characteristics, such as eye color, gender, skin color, and blood type
  • Most DNA in humans is pretty well conserved. The differences among people are quite small.
  • Contrary to public belief, there is no scientific difference between liberals and conservatives.
If You Drill Down On Life

- Whole organisms
- Organs
- Tissues
- Cells
- Intracellular organelles (e.g., mitochondria)
- Chemical components
  - Proteins
  - Lipids
  - Nucleic acids: DNA and RNA
So Molecular Biology Gets To The Root Of Life

• Molecular biology techniques use DNA, RNA, and enzymes that interact with nucleic acids to understand biology at a molecular level.

• Molecular Pathology
  – The pathology subspecialty that employs molecular biology techniques to:
    • Detect normal and disease states (diagnosis)
    • Predict disease progression (prognosis)
  – The field is quite diverse
Experts Specialize In Sub-disciplines of Molecular Pathology

- **Inherited disease (genetics)**
  - Cystic fibrosis
  - Sickle cell anemia
  - Predispositions to cancer

- **Infectious disease**
  - Bacteria
  - Viruses
  - Fungi

- **Forensics**

- **Identity testing**
  - HLA
  - Parentage

**Oncology**

- **Hematopathology**
  - Leukemias
  - Lymphomas

- **Solid oncology**
  - Breast cancer
  - Colon cancer
  - Brain cancer
CPT Defines Molecular Pathology

• Medical laboratory procedures involving the analyses of nucleic acid to detect variants in genes that may be indicative of germline (eg, constitutional disorders) or somatic (eg, neoplasia) conditions, or to test for histocompatibility antigens (eg, HLA).
So Let’s *Digress To Nucleic Acid Chemistry*

- Genetic material of all known organisms
- DNA: deoxyribonucleic acid
- RNA: ribonucleic acid (e.g., some viruses)
- Consist of chemically linked sequences of nucleotides
  - Nitrogenous base
  - Pentose- 5-carbon sugar (ribose or deoxyribose)
  - Phosphate group
- The sequence of bases provides the genetic information
There Are Two Types of Bases

• Purines are fused five- and six-membered rings
  • Adenine A DNA RNA
  • Guanine G DNA RNA

• Pyrimidines are six-membered rings
  • Cytosine C DNA RNA
  • Thymine T DNA
  • Uracil U RNA
Nucleic Acid Pairing Is Specific

- **Hydrogen bonds** are relatively weak bonds compared to covalent bonds.
- But with a large DNA molecule, it’s one of the strongest chemical associations known.
- Hydrogen bonds can form between a pyrimidine and a purine.
- The specificity of pairing formed the basis for the Nobel Prize.
Generally, DNA is double-stranded. Double-stranded (ds) DNA takes the form of a right-handed helix with approximately 10 base pairs per turn of the helix.
Base Pair Complementarity IS The Basis of Life

- In the DNA double helix, purines and pyrimidines face each other.
- The two chains in the double helix are connected by hydrogen bonds.
- Watson-Crick base-pairing rules:
  - Adenine always pairs with thymine (uracil).
  - Guanine always pairs with cytosine.
- GC base pairs (bps) have more energy than AT bps.
- Since one strand of DNA is complementary to the other, genetic material can be accurately reproduced; each strand serves as the template for the synthesis of the other.
Strands Have Specific Relationships And Carry Genetic Information

- Two strands of the DNA double helix are antiparallel and complementary to each other.

- Genes carry the information that codes for unique structural proteins, enzymes, etc.
Nucleases Cut DNA At Specific Points

5’ Exonuclease

3’ Exonuclease

Endonuclease
Restriction Enzymes Are Specific Endonucleases

• Recognize specific short sequences of DNA and cut the DNA at or near the recognition sequence
• Recognition sequences: usually 4 or 6 bases but some are longer
• Recognition sequences are palindromes
  – DNA sequences that are the same when one strand is read from left to right or the other strand is read from right to left – consists of adjacent inverted repeats, for example
    • GAATTC and CTTAAG
Restriction Enzymes Are Isolated From Bacteria

• Derive names from the bacteria
• Genus- first letter capitalized
• Species- second and third letters (small case)
• Additional letters from “strains”
• Roman numeral designates different enzymes from the same bacterial strain, in numerical order of discovery

• Example: EcoRI
  – E Escherichia
  – co coli
  – R R strain
  – I First enzyme discovered from
    Escherichia coli R
**Nucleic Acid Hybridization: Formation of a Duplex Between Two Complementary Sequences**

- Intermolecular hybridization: between two polynucleotide chains which have complementary bases (i.e., DNA-DNA, DNA-RNA, RNA-RNA)
- Annealing: hybridization of two complementary molecules
- Denaturation occurs when complementary sequences are separated (e.g., by chemicals, heat)

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**Diagram:**
- Double-stranded DNA
- Single-stranded DNA
- Initial Base pairing
- Renatured DNA

**Annotations:**
- Denaturation
- Renaturation
So How Do You Detect Molecular Changes? You Need Probes For Detection

- A probe is itself a nucleic acid
- Labeled with a marker to allow identification and quantitation
  - Radioactive ($^{32}$P, $^{35}$S, $^{14}$C, $^{3}$H)
  - Fluorescent
    - FISH: fluorescent in situ hybridization
      - chromosomes
    - Biotinylated (avidin-streptavidin)
- Hybridizes to another nucleic acid based on base complementarity
Solid Support Hybridization

• DNA or RNA is immobilized on an inert support so that self-annealing is prevented

• Bound sequences are available for hybridization with an added nucleic acid (probe)

• Filter hybridization is the most common application:
  – Southern Blots
  – Dot/Slot Blots
  – Northern Blots

• In-silica hybridization (glass slides)
  – in situ hybridization (tissue)
  – Chromosomal (FISH)
  – Microarrays
Southern Blots Are Commonly Used

- A procedure for transferring denatured DNA from a gel to a solid support filter where it can be hybridized with a complementary probe
- The DNA is separated by size so that specific fragments can be identified
  - Restriction digest to make different sized fragments
  - Gel electrophoresis to separate by size
  - Only single strands bind to the filter so the DNA must be denatured (NaOH)
  - Transfer to filter paper
  - Hybridize to probe
  - Detect the hybridization
Restriction enzyme

DNA of various sizes

Electrophorese on agarose gel

Denature - transfer to filter paper.

blot
Hybridize to probe

Visualize

Denature - transfer to filter paper.

blot
A Southern Blot Might Look Something Like This
Innovation Is Expediting The Process
User-Friendly, Faster, and Cost-Effective

This electronic microarray is an example of "Lab-on-a-Chip" technology. It is an electrophoresis device that produces results up to 1000 times faster than conventional techniques while using much less sample.
The chromosome banding technique performed 20 years ago missed the small deletion. High resolution banding developed more recently can elucidate the abnormality.

Fluorescence in situ Hybridization (FISH) is a powerful technique in that it can reveal submicroscopic abnormalities even in non-dividing cells.
Polymerase chain reaction has expanded the capabilities of molecular diagnostics

- PCR is the in vitro enzymatic synthesis and amplification of specific DNA sequences
- Can amplify one molecule of DNA into billions of copies in a few hours
- There are many uses
  - Detection of chromosomal translocations
  - Chromosome painting
  - Detection of residual disease
  - Infectious disease
  - Forensics
  - HLA typing
  - Detection of Loss of Suppressor Genes
    - Loss of Heterozygosity (LOH)
The Person Sitting Next To You Isn’t Exactly Like You: Genetic Variation

• Most genes have small sequence differences between individuals
  – Occur every 1350 bp on average
• Some of these polymorphisms may affect:
  – How well the protein works
  – How the protein interacts with another protein or substrate
• The different gene forms containing polymorphisms are called alleles
Restriction fragment length polymorphism

• RFLP is a polymorphic allele identified by the presence or absence of a specific restriction endonuclease recognition site:
  – GAATTC versus GATTTC

• RFLP is usually identified by digestion of genomic DNA with specific restriction enzymes followed by Southern blotting

• Regions of DNA with polymorphisms:
  – Introns
  – Flanking sequences
  – Exons
Mutation detection

- Sequence DNA
- Hybridization Methods
  - Blotting
  - Chips
- Restriction enzyme polymorphisms:
  - GAATTC versus GATTTC
- SNPs (single nucleotide polymorphisms)
  - DNA variation within the population, in which a single nucleotide differs between individuals or within an individual's paired chromosomes
  - Not considered mutations (pathologic variants)
  - SNPs in exons are called coding SNPs
  - SNPs in introns or regulatory regions may affect transcription, translation, RNA stability, RNA splicing
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The Evolution Of Molecular Pathology Coding Has Emerged Over A Decade

• The new section is the product of the Molecular Pathology CPT Workgroup, created in response to input at the October 2009 CPT Advisors meeting

• General findings included
  – Genetic Testing Modifiers (Appendix I) didn’t work
  – The methodologic stacking codes are nonspecific and not acceptable
  – Everyone had different options for how to solve the issue
  – Everyone agreed that it is mandatory that CPT address the issue ASAP!
Findings Ran Deep And Wide

• Problems with pricing and contracting
  – Current coding is inconsistent for a given analysis
  – Need a single code for a uniform payment for same analysis
  – Need to understand what test is being performed
  – If payers can identify a specific test, it could be processed without manual intervention (huge cost savings)

• Need for a system that addresses patient care, outcomes and benefits for the patient
  – How do you create a system that will continue to reward innovation and development?

• Need transparency and useful measurement of what is being done

• The field is perhaps the most rapidly advancing in medicine. Creating codes for today’s test menu may not be the solution for tomorrow
**What Makes This So Difficult?**

Top 12 tests comprise 85% of a large commercial lab’s volume

There are a lot of genes for different stuff in the human body!
There Is A Very Long Tail, But Most Actual Services Fall Into A Limited Number of Tests

Next 12 tests add only 7% to the lab’s total volume
The Association of Molecular Pathology Provided Some Direction To Start The Process

• **Tier 1:** Code the most common molecular genetic and molecular oncology services using a single specific CPT code. Even a relatively short list could encompass >80% of the total volume of molecular services performed.

• **Tier 2:** Since a code for every gene is not possible in the current structure of CPT, the large and growing number of ‘less common’ services could be coded by assigning single complexity level codes that have a relatively narrow range of variation in resources required to perform, analyze and interpret such services.
The Tier 1 Codes Are Specific For The Test Performed

• A Tier 1 workgroup met repeatedly to
  – Determine members of the Tier 1 group
  – Identify the structure for molecular and genetic codes
  – Write the accompanying directions for use
• Coding instructions clarify that Tier 1 codes are stand-alone and are not to be used with methodologic “stacking” codes (83890-83914 and 88384-88386 series)
  – The code set is based on the analyte (gene/gene variant), not the technology used to determine the result
So Here’s What The Codes Look Like

Prototype root descriptor format

- Gene name (typically HUGO, Human Genome Organization) abbreviation
- Full HUGO gene name (in parentheses)
- Example of disease being tested (in parentheses)
- “Gene analysis”
- What is being tested for (eg, common variant(s), full gene sequence)
- Examples of variants tested (listed as amino acid change)

Some examples

81200  **ASPA (aspartoacylase)** (eg, Canavan disease) gene analysis, common variants (eg, E285A, Y231X)

81211 **BRCA1, BRCA2 (breast cancer 1 and 2)** (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis and common duplication/deletion variants in BRCA1 (ie, exon 13 del 3.835kb, exon 13 dup 6kb, exon 14-20 del 26kb, exon 22 del 510bp, exon 8-9 del 7.1kb)
Tier 2 Codes Are A Work In Progress

• There are nine level codes
  – Escalating work and practice expense
  – Professional and technical components actually aligned nicely
• Assignment into a particular tier is determined by CPT, not by the test provider
• Each level code contains examples of technologies considered within that level
  – But, like Tier 1, because the code selection is determined by the analyte (gene/gene variant) and not the technology used, they are only examples (not mandatory for code use)
• Nomenclature for genes in Tier 2 parallel Tier 1
• The ≈80 analytes in the 2012 book are just the beginning
  – When mature, there may be over 1000 analytes in Tier 2
Here’s What Level 1 Looks Like

81400  Molecular pathology procedure, Level 1 (eg, identification of single germline variant [eg, SNP] by techniques such as restriction enzyme digestion or melt curve analysis)

ACADM (acyl-CoA dehydrogenase, C-4 to C-12 straight chain, MCAD) (eg, medium chain acyl dehydrogenase deficiency), K304E variant

ACE (angiotensin converting enzyme) (eg, hereditary blood pressure regulation), insertion/deletion variant

AGTR1 (angiotensin II receptor, type 1) (eg, essential hypertension), 1166A>C variant

CCR5 (chemokine C-C motif receptor 5) (eg, HIV resistance), 32-bp deletion mutation/794 825del32 deletion

...
Specific Tier Wording Is For Guidance But Code Use Depends On An Analyte Match

81401 Molecular pathology procedure, Level 2 (eg, 2-10 SNPs, 1 methylated variant, or 1 somatic variant [typically using nonsequencing target variant analysis], or detection of a dynamic mutation disorder/triplet repeat)

81402 Molecular pathology procedure, Level 3 (eg, >10 SNPs, 2-10 methylated variants, or 2-10 somatic variants [typically using non-sequencing target variant analysis], immunoglobulin and T-cell receptor gene rearrangements, duplication/deletion variants 1 exon)

81403 Molecular pathology procedure, Level 4 (eg, analysis of single exon by DNA sequence analysis, analysis of >10 amplicons using multiplex PCR in 2 or more independent reactions, mutation scanning or duplication/deletion variants of 2-5 exons)

81404 Molecular pathology procedure, Level 5 (eg, analysis of 2-5 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 6-10 exons, or characterization of a dynamic mutation disorder/triplet repeat by Southern blot analysis)
An The Rest, For The Sake of Completeness

81405 Molecular pathology procedure, Level 6 (eg, analysis of 6-10 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 11-25 exons)

81406 Molecular pathology procedure, Level 7 (eg, analysis of 11-25 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 26-50 exons, cytogenomic array analysis for neoplasia)

81407 Molecular pathology procedure, Level 8 (eg, analysis of 26-50 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of >50 exons, sequence analysis of multiple genes on one platform)

81408 Molecular pathology procedure, Level 9 (eg, analysis of >50 exons in a single gene by DNA sequence analysis)
There Are 14 New Codes for Human Leukocyte Antigen (HLA) Typing

- Assess compatibility of recipients and potential donors
- Identify HLA alleles and allele groups associated with specific diseases and responses to drug therapy
- Typically done with a set of multiple analyses but uncommonly are exactly the same set
- Coding separates low-resolution and high resolution, class I vs. class II typing, and complete analysis vs. single locus vs. “antigen equivalent”/allele
- If additional testing is required to resolve ambiguous allele combinations for high resolution typing, this is included in the base code (ie, not separately coded)
- More information will be contained in the introductory section
- Specialized use for histocompatibility experts
**HLA Code Descriptor Example**

**81372**  HLA Class I typing, low resolution (eg, antigen equivalents); complete *(ie, HLA-A, -B, and -C)*

▶ (When performing both Class I and II low resolution *HLA typing for HLA-A, -B, -C, -DRB1/3/4/5, and -DQB1*, use 81370)

**81373** one locus *(eg, HLA-A, -B, or -C)*, each

▶ (When performing a complete Class I *[HLA-A, -B, and -C]* low resolution HLA typing, use 81372)

▶ (When the presence or absence of a single antigen equivalent is reported using low resolution testing, use 81374)

**81374** one antigen equivalent *(eg, B*27)*, each

▶ (When testing for presence or absence of more than 2 antigen equivalents at a locus, use 81373 for each locus tested)
This Set Will Be Used By Histocompatibility Experts

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The Introductory Notes and Guidelines May Be Sufficient To Get a PhD

• Apply to both Tier 1 and Tier 2
• Code selection typically based on specific gene(s) analyzed
• Codes include all analytical services performed
• Procedures required prior to cell lysis are reported separately
• Append modifier 26, Professional Component, when only the interpretation and report are performed
• Analyses are qualitative unless otherwise noted
• For 2012, procedures not specified in Tier 1 or Tier 2 code set are reported using methodology codes (83890-83914 and 88384-88386)
There Are Many Definitions To Help Provide A Better Understanding

**Common variants**: variants (as defined elsewhere) that are associated with compromised gene function and are interrogated in a single round of laboratory testing (in a single, typically multiplex, assay format or using more than one assay to encompass all variants to be tested). These variants **typically fit the definition of a “mutation,”** and are **usually the predominant ones causing disease**. Testing for additional uncommon variants may provide additional limited value in assessment of a patient. Often there are professional society recommendations or guidelines for which variants are most appropriate to test.
What We Should Discuss Today

General changes to CPT for 2012
Review of molecular diagnostics generally
The new molecular pathology codes in CPT 2012
Changes to anticipate for 2013
Challenges that remain in molecular diagnostics and related testing
The Migration To The New World Of Molecular Pathology (MoPath) Continues

- While changes to CPT are not official until the new book is published, there are some things we can anticipate
  - We haven’t seen the end to new Tier 1 codes
  - Specific tests within the Tier 2 family of codes will increase rapidly

- Since the goal was to go to specific coding, once the build out of Tiers 1 and 2 is complete
  - The molecular stacking codes will go away
  - Appendix I will disappear
What We Should Discuss Today

General changes to CPT for 2012
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Challenges that remain in molecular diagnostics and related testing
There Remains Uncertainty Regarding How These Services Will Be Reimbursed by CMS

- Many professional societies recommend that the codes be placed on the Physician Fee Schedule
  - CAP provided information to value most MoPath services
- CMS was uncertain regarding the placement of the new MoPath codes
  - Services currently reside on the CLFS
  - CMS delayed valuation of the new codes for 2012
  - For 2012 Medicare reporting requires the stacking codes

- But payers differ in how they are using the codes in 2012
- To gather additional information CMS is requesting providers submit both the stacking codes and the new specific code along with the price of the procedure.
  - This is problematic for many providers and you should review your individual situation to determine how to address the request.
The New MoPath Codes Don’t Answer All Questions

• One of the main drivers for the new codes was provision of specificity to molecular services performed
  – Specificity does exist now for Tier 1 codes – that cover the majority of billed services
  – But Tier 2 codes still don’t convey the exact service provided
• Payers want to know exactly what test was performed so they can make decisions regarding medical necessity
  – Palmetto GBA has been particularly vocal in this request
CPT and Others Are Struggling With The Specificity

• Palmetto GBA has indicated they will request and then require supplemental codes when CPT does not provide sufficient specificity
  – Palmetto GBA Codes (Palmetto Test Identifier/PTI codes)
  – McKesson Codes (Z codes)
• Right now, Palmetto has published a table on their web site indicating which services will require these supplemental codes.
Here’s What Palmetto Says

• Purpose: To identify tests and determine coverage and determine reimbursement.

• For your own good: Once the required information is received and a short unique identifier (PTI/Z-Code) is assigned, Palmetto GBA can determine coverage and payment without documentation review. This process removes the need for the provider to submit large amounts of additional information with every claim and expedites claim payment.

• Who: All hospital, private and reference laboratories that perform molecular diagnostic testing and bill Medicare in J1 are affected by this program.
  – Although the MolDx Program covers J1 (CA, NV, HI), labs that bill J1 services performed by a lab that is not located in J1 will have to register MDTs to identify the service.
And A Bit More

• Effective May 1, 2012
  – Claims for MDTs will only be considered for adjudication when a Z-Code or a PTI has been assigned to the test and is entered in the comment/narrative field of the claim form.
  – If a PTI/Z-Code is pending or the laboratory provider is unable to update internal systems for claims submission, Palmetto GBA will accept a FAX and a completed Palmetto GBA Test Identifier Application form with each claim.

• May, 2012
  – Laboratory providers will submit coverage determination requests online via the McKesson Diagnostics Exchange Test Assessment Module.
  – Laboratories that do NOT apply for a Z-Code will receive coverage notification.
Here’s A List Of What Is Required When

<table>
<thead>
<tr>
<th>MolDx Exempt (no Z-Code or TA required)</th>
<th>Z-Code Required</th>
<th>Z-Code Required</th>
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</thead>
</table>
| **Tests specifically described by a single CPT/HCPCS code and submitted with one unit of service** | Any test that meets the following:  
• 101 New MDT CPT codes  
• FDA cleared/ approved (unmodified) tests  
• Current New York State (NYS) approved tests  
• Grandfathered NYS tests developed prior to 2003  
• National Institute of Health Genetic Testing Registry (GTR) | A laboratory developed test (LDT) producing a single result and billed with multiple CPT codes including any combination of the following:  
• methodology-based stacking CPT codes (83890-83914)  
• micro-array CPT codes (88384-88386)  
• microdissection CPT codes (88380-88371)  
• other pathology/laboratory codes |
| **Infectious disease molecular diagnostic testing described by CPT codes (87001-87905)** | Coverage Determination by Palmetto GBA LCD or Article, i.e.  
• Tumor of origin assays  
• OncotypeDx Breast™  
• OncotypeDx Colon™  
• Allomap™  
• HERmark™ | MDT/LDT that provides  
• diagnostic determination  
• prognostic/predictive determination  
• risk assessment  
• screening |
Here’s A List Of What Is Required When

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<tr>
<th>MolDx Exempt (no Z-Code or TA required)</th>
<th>Z-Code Required NO Tech Assessment Required</th>
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<tbody>
<tr>
<td>Cytogenetics – CPT codes 88230-88291</td>
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<td>Pathology and Laboratory Not Otherwise Classified (NOC) codes</td>
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</table>
| Surgical Pathology (CPT codes 88300-88372) including the following:  
  • Flow cytometry – CPT codes 88182-88189  
  • Immunohistochemistry (IHC) CPT code 88342  
  • *in situ* hybridization (ISH) testing CPT code 88365 |                                            | Modified FDA cleared/approved tests |
| Reagents  
  • Analyte Specific Reagents (ASR)  
  • Research Use Only Reagents (RUO) |                                            | |

AAPC 2012 Pg 79
**Z-Code/PTI Application**

- The application contains two main tabs:
  - **Organizational Tab**
    - Organization information
    - Contact information
    - Medical/Lab Director information
    - Credential information
  - **Lab Tests Tab**
    - General Test information
    - Procedure coding information
    - Algorithm
    - FDA
    - Instruction
    - Additional Test / Assay information
Z-Code/PTI Application Data

• The information required is extensive for each test.

• Total number of fields for each tab
  – Organizational Tab - 23 fields
    • includes facility name, contact information, CLIA #, etc.
  – Lab Test Tab – 25 fields
    • Includes test name, methodology, CPT codes, FDA status, specimen type(s), LDT, kit information, etc.
PTI/Z-code Tech Assessment

• TA purpose: to determine the coverage policy

• A Tech Assessment (TA) needs to be submitted if a test meets the criteria listed in the MolDx Exempt Tests table
  – See the Technical Assessment (TA) Process information on the Palmetto GBA website for detailed submission instructions

• TA includes a comprehensive set of documents that will be reviewed by Palmetto to determine if the test is reasonable and necessary and demonstrates improved patient outcomes.
The types of information requested by Palmetto for a TA includes:

- Demographics of the test
- Analytical validity evidence
- Clinical validity (sensitivity, specificity)
- Clinical utility
- Peer review articles addressing the various aspects of the test
Where does the PTI/Z-code live?

- PTI/Z-codes are public knowledge through the Palmetto web-site and/or the McKesson website.

- If a test is not listed you will need to contact the performing laboratory for updates.
So now you have a PTI/Z-code

• The claims submission process is outlined on the Palmetto website in the ModDx Claims Submission Guidelines document. Additional information is also in the FAQs.

• The guidelines provide instructions for:
  – Paper claim CMS 1500 form
  – electronic claims (5010)
  – 837 (Physician/Professional) PART B
  – 837I (Institutional) PART B of A
What if you don’t have a PTI/Z-code?

- Palmetto stated that if a unique identifier (PTI/Z-code) is required and not included that the claim would be rejected (front end rejection) for lack of sufficient information.

- Palmetto was requested to create a unique rejection code indicating that the PTI/Z-code was not submitted. Palmetto acknowledged the concern and will explore the possibility...stay tuned.

- Each facility will need to determine how to process this type of rejected claims.
CPT and Others Are Struggling With The Specificity

• More information is forthcoming on this issue

• There are questions whether alternate coding can be required since these would not be approved HIPAA code sets
Questions?