

# **Appendix A**

## **Database I**

**One page description of genetic tests for non-cancer conditions  
with high likelihood applicability to the Medicare population**

1. Gene Symbol: SERPINA1 Chromosomal Locus: 14q32.1
2. Protein Name: Alpha-1-antitrypsin
3. Disease: Alpha-1-antitrypsin deficiency
4. Description: Alpha-1-antitrypsin (AAT) deficiency affects the lung, and occasionally the liver, vulnerable to injury. AAT inhibits elastase around normal tissue. Deficiency is caused by mutations in the SERPINA1 gene, located on chromosome 14.
5. Purpose: Diagnostics
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Targeted mutation analysis, sequence analysis, linkage analysis (mutation panel includes M, Z, S alleles)
9. Other Diseases: ND
10. Clinical use(s) for the Medicare: May be useful for diagnostic and identification of at risk individuals especially who inherit at least one normal allele..
11. Source of Information: GeneTests.org, OMIM
12. Exploratory Medline Search (10/30/06):
  - a) "Alpha-1- antitrypsin deficiency" = 2805 citations
  - b) "SERPINA1" = 79 citations
  - c) "Alpha-1- antitrypsin deficiency" and "SERPINA1" = 25 citations (limit to human)

1. Gene Symbol: COL4A5 Chromosomal Locus: Xq22.3
2. Protein Name: Collagen alpha 5(IV) chain
3. Disease: Alport Syndrome
4. Description: The type IV collagen genes (*COL4A3* and *COL4A4*) implicated in autosomal recessive Alport syndrome Alport syndrome is characterized by renal, cochlear, and ocular involvement. About 80% of Alport syndrome is X-linked; about 15% is autosomal recessive. The hallmark of Alport syndrome is microscopic hematuria (microhematuria). Males with X-linked Alport syndrome (XLAS) have persistent microhematuria from early in life. Over 90% of females with XLAS have microscopic hematuria. Overall, about 60% reach ESRD by age 30 years, and 90% by age 40 years. About 10% of females with XLAS develop ESRD by age 40, and about 30% by age 60.
5. Purpose: Diagnostics
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis, Preimplantation genetic diagnosis
9. Other Diseases: ND
10. Clinical use(s) for the Medicare: Useful for the diagnosis and confirmation
11. Source of Information: GeneTests.org,
12. Exploratory Medline Search (10/31/06):
  - a) "Alport Syndrome" = 543 citations
  - b) "COL4A5" = 236 citations
  - c) "Alport Syndrome" and "COL4A5" = 176 citations (limit to human)

1. Test Name: ADmark<sup>®</sup> Phospho-Tau/Total-Tau/Ab42 CSF Analysis & Interpretation (Symptomatic)
2. Protein name: Phosphorylated-Tau protein, Total-Tau protein and A $\beta$ 42 peptide
3. Disease: Alzheimer's Disease
4. Description: Test detects for dementia. Test correlates levels of Phosphorylated-Tau protein, Total-Tau protein, and Ab42 peptide in CSF.
5. Purpose: Diagnostic
6. Availability: Athena Diagnostics
7. Specimen: Cerebrospinal fluid (CSF)
8. Methodology: ELISA
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population:
  - a) Detection of dementia
11. Source of Information: Athena Diagnostics
12. Exploratory Medline Search: (10/20/06)
  - a. "Alzheimer Disease/ or Alzheimers disease.mp."=40492
  - b. "Tau protein.mp. or exp tau Proteins"=4474
  - c. a and b (limit to humans) = 330

1. Test Name: ADmark<sup>®</sup> ApoE Genotype Analysis (Symptomatic)
2. Gene Symbol: ApoE2, E3, E4 alleles
3. Disease: Alzheimer's Disease Late onset disease
4. Description: Late-onset AD is a complex disorder that may involve multiple susceptibility genes. There has been well-documented association of late-onset FAD with the *APOE* e4 allele.
5. Purpose: Diagnostic
6. Availability: Athena diagnostics and Clinical laboratories outside US
7. Specimen: Blood; Buccal swab
8. Methodology: Serial Invasive Signal Amplification Reaction (SISAR)
9. Other Diseases: Cardiovascular disease risk factor
10. Clinical use(s) for the Medicare population: Applicable
  - a) Detection of dementia
11. Source of Information: Athena Diagnostics
12. Exploratory Medline Search: (10/20/06)
  - a. "Alzheimer Disease/ or Alzheimers disease.mp."=32654
  - b. "ApoE.mp. or exp Apolipoproteins E" = 7685
  - c. a and b (limit to humans) = 2837

1. Gene Symbol: SERPINC1 Chromosomal Locus: 1q23-q25
2. Protein Name: Antithrombin-III
3. Disease: Antithrombin-III Deficiency
4. Description: An absence or reduced level of Antithrombin III leading to an increased risk for thrombosis. Antithrombin gene (SERPINC1) mutations have been found to be associated with antithrombin deficiency or Inherited thrombophilia, which has a genetic tendency to venous thromboembolism.
5. Purpose: Diagnostic
6. Availability: Clinical Laboratories
7. Specimen: ND
8. Methodology: Sequence analysis, Deletion/duplication analysis
9. Other Diseases: ND
10. Clinical use(s) for the Medicare: May be useful for diagnostic purposes
11. Source of Information: GeneTests.org, Center for Nephrology and Metabolic Disorders  
Laboratory for Molecular Diagnostics
12. Exploratory Medline Search (11-06-06):
  - a) "Antithrombin-III Deficiency" = 986 citations
  - b) "SERPINC1" = 5 citations
  - c) "Antithrombin-III Deficiency" and "SERPINC1" = 2 citations (limit to human)

1. Gene Symbol: ARVD 1 to 9; RYR2, DSP, and PKP2
2. Protein Names: Ryanodine receptor 2; Desmoplakin; Plakophilin-2
3. Disease: Arrhythmogenic Right Ventricular Dysplasia/Cardiomyopathy
4. Description: Mutations in the RYR2, DSP and PKP2 genes are associated with Arrhythmogenic Right Ventricular Dysplasia/Cardiomyopathy. Autosomal dominant arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVD/C) is a progressive disorder characterized by fibrofatty replacement of the myocardium that predisposes to ventricular tachycardia and sudden death in young individuals and athletes.
5. Purpose: Diagnostic
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Direct mutation analysis; Sequence analysis; mutation scanning; Linkage analysis; Deletion/Duplication analysis.
9. Other Diseases: Catecholaminergic polymorphic ventricular tachycardia; Palmoplantar keratoderma with left ventricular cardiomyopathy and woolly hair/Carvajal syndrome.
10. Clinical use(s) for the Medicare population: Diagnostic for late onset disease
11. Source of Information: Genetests.org
12. Exploratory Medline Search: (10/20/06)
  - a. "Arrhythmogenic Right Ventricular Dysplasia" = 608
  - b. "RYR2 or DSP or PKP2" = 3393
  - c. a and b (limit to humans) = 33

1. Gene Symbol: CHRNA4 Chromosomal Locus: 20q13.2-q13.3  
Gene Symbol: CHRNB2 Chromosomal Locus: 1q21
2. Protein Name: Neuronal acetylcholine receptor protein, alpha-4 subunit; Neuronal acetylcholine receptor protein, beta-2 subunit
3. Disease: Autosomal Dominant Nocturnal Frontal Lobe Epilepsy (ADNFLE)
4. Description: Autosomal dominant nocturnal frontal lobe epilepsy (ADNFLE) is characterized by clusters of nocturnal motor seizures, which are often stereotyped and brief. Mutations in the CHRNA4 and CHRNB2 genes are associated with Autosomal Dominant Nocturnal Frontal Lobe Epilepsy (ADNFLE) and the test identifies mutations in approximately 20-30% of individuals with a positive family history and fewer than 5% of individuals who have no other family members with ADNFLE
5. Purpose: Diagnostic
6. Availability: Clinical laboratory (Institute of Human Genetics, Munich, Germany)
7. Specimen: Serum
8. Methodology: Sequence Analysis of select exons
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Unclear (early onset)
11. Source of Information: Gene Tests
12. Exploratory Medline Search: (10/22/06)
  - a. "exp Epilepsy, Frontal Lobe/ or Autosomal Dominant Nocturnal Frontal Lobe Epilepsy.mp."=472
  - b. "CHRNA4.mp."=76
  - c. "CHRNB2.mp."=55
  - d. a and (b or c)=36

1. Gene Symbol: BBS10 Chromosomal Locus: 12q21.2  
Gene Symbol: BBS2 Chromosomal Locus: 16q21
2. Protein Name: Bardet-Biedl syndrome 10 protein, Bardet-Biedl syndrome 2 protein
3. Description: Bardet-Biedl syndrome (BBS) is characterized by cone-rod dystrophy, truncal obesity, postaxial polydactyly, cognitive impairment, male hypogonadotropic hypogonadism, complex female genitourinary malformations, and renal dysfunction. Eleven genes are known to be associated with Bardet-Biedl syndrome: *BBS1*, *BBS2*, *ARL6/BBS3*, *BBS4*, *BBS5*, *MKKS/BBS6*, *BBS7*, *TTC8/BBS8*, *B1/BBS9*, *BBS10*, and *TRIM32/BBS11*
4. Purpose: Diagnostics
5. Availability: Clinical Laboratories
6. Specimen: Blood
7. Methodology: Sequence analysis, Sequence analysis of select exons, linkage analysis, targeted mutation analysis
8. Disease: Bardet-Biedl Syndrome
9. Other Diseases: Meckel-Gruber syndrome
10. Clinical use(s) for the Medicare: Useful for diagnostic and prevention of renal disease.
11. Source of Information: GeneTests.org, Centro Genetica Clinica
12. Exploratory Medline Search (11-08-06):
  - a) "Bardet-Biedl Syndrome" = 375 citations
  - b) "BBS10" or "BBS2" = 45 citations
  - c) "Bardet-Biedl Syndrome" and "b" = 41 citations (limit to human)

1. Gene Symbol: NOTCH3 Chromosomal Locus: 19p13.2-p13.1
2. Protein Name: Neurogenic locus notch homolog protein 3
3. Disease: Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy (CADASIL)
4. Description: The NOTCH3 gene is associated with Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy (CADASIL). More than 90% of individuals with CADASIL have mutations in NOTCH3. CADASIL, cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy, is characterized by a history of migraine headaches (30-40% of individuals), mid-adult (30s-60s) onset of cerebrovascular disease progressing to dementia, and diffuse white matter lesions and subcortical infarcts on neuroimaging.
5. Purpose: Diagnostic and Prognostic
6. Availability: Clinical laboratories
7. Specimen: Blood
8. Methodology: Sequence Analysis, PCR
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population:
  - a) Confirmatory diagnostic testing
  - b) Predictive testing
11. Source of Information: GeneTests.org
12. Exploratory Medline Search: (10/22/06)
  - a. "CADASIL.mp. or exp CADASIL"=401
  - b. "NOTCH3.mp."=245
  - c. a and b (limit to humans)=55

1. Gene symbol: ACE Chromosomal Locus: 17q23
2. Protein Names: Angiotensin-converting enzyme
3. Disease: Cardiovascular Disease Risk Factor or Coronary Artery Disease Risk Factor
4. Description: Plasma and tissue concentrations of ACE, and therefore levels of angiotensin II, are determined in part by the ACE gene, which is located on chromosome 17. This gene may manifest insertion (I) or deletion (D) polymorphisms and therefore three genotypes (DD, II, and ID). The DD genotype has been associated with a variety of adverse cardiovascular effects including progressive ventricular dilatation after acute myocardial infarction, left ventricular hypertrophy in hypertension, reduced survival and increased left ventricular mass in patients with heart failure due to idiopathic dilated cardiomyopathy, and an increased risk of cardiomyopathy induced by excess alcohol intake.
5. Purpose: Diagnostic and secondary prevention
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Targeted mutation analysis; Deletion/duplication analysis
9. Other Diseases: nd
10. Clinical use(s) for the Medicare population: Useful for cardiovascular risk assessment
11. Source of Information: Genetests.org; UptoDate; Quest diagnostics
12. Exploratory Medline Search: 10/27/06
  - a. "cardiovascular disease risk.mp or exp" = 92189
  - b. "ACE gene polymorphism" = 1573
  - c. a and b (limit to humans) = 1354

1. Gene Symbol: CCM2 Chromosomal Locus: 7p13
2. Protein Name: CCM2 protein
3. Disease: Cerebral Cavernous Malformations
4. Description: The second gene detected that can cause Cerebral Cavernous Malformations (CCMs) was identified as CCM2 (aka MGC4607). The first gene that can cause CCMs is KRIT1 (see separate gene test profile). It is thought that the CCM2 gene accounts for approximately 20% of familial CCM cases. Cerebral cavernous malformations (CCMs) are vascular malformations consisting of closely clustered enlarged capillary channels (caverns) and inherited autosomal dominant. Symptoms onset between 2<sup>nd</sup> and 5<sup>th</sup> decade.
5. Purpose: Diagnostic, prognostic
6. Availability: Clinical laboratory (PreventionGenetics, WI, US)
7. Specimen: Blood or extracted DNA
8. Methodology: Sequence Analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population:
  - a) Confirmatory diagnostic testing
  - b) Predictive testing
11. Source of Information: GeneTests.org, Prevention Genetics
12. Exploratory Medline Search: (10/22/06)
  - a. "Cerebral cavernous malformation.mp."=41
  - b. "CCM3.mp"=17
  - c. a and b (limit to humans)=6

1. Gene Symbol: PDCD10 Chromosomal Locus: 3q26.1
2. Protein Name: CCM3 protein; PDC10 Gene Testing
3. Disease: Cerebral Cavernous Malformations
4. Description: Cerebral cavernous malformations (CCMs) are vascular malformations consisting of closely clustered enlarged capillary channels (caverns) with a single layer of endothelium without normal intervening brain parenchyma or mature vessel wall elements. CCMs are inherited autosomal dominant and 40% of individuals with familial CCM may be linked to *PDCD10*
5. Purpose: Diagnostic, prognostic
6. Availability: Clinical laboratories
7. Specimen: Blood
8. Methodology: Sequence Analysis; Linkage analysis; Targeted mutation analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population:
  - a) Confirmatory diagnostic testing
  - b) Predictive testing
11. Source of Information: GeneTests.org, Prevention Genetics
12. Exploratory Medline Search: (10/22/06)
  - a. "Cerebral cavernous malformation.mp."=41
  - b. "CCM2.mp"=26
  - c. a and b (limit to humans)=7

1. Gene Symbol: KRIT1 (CCM1) Chromosomal Locus: 7q11.2-q21
2. Protein Name: Krev interaction trapped 1.
3. Disease: Familial Cerebral Cavemous Malformation 1 (CCM1)
4. Description: Mutations in the KRIT1 gene are associated with Familial Cerebral Cavemous Malformation 1 (CCM1). CCMs are congenital vascular abnormalities of the brain that can cause neurological disabilities (i.e. hemorrhagic stroke, seizures). Mutation analysis is done for “common Hispanic mutation.” A single mutation in the KRIT1 gene has been identified in about 70% of Hispanic families.
5. Purpose: Diagnostic, prognostic
6. Availability: Clinical laboratories
7. Specimen: Serum
8. Methodology: Sequence Analysis; Linkage analysis; Targeted mutation analysis
9. Other Diseases:
10. Clinical use(s) for the Medicare population:
  - a) Confirmatory diagnostic testing
  - b) Predictive testing
11. Source of Information: GeneTests.org, Prevention Genetics
12. Exploratory Medline Search: (10/22/06)
  - a. “Familial Cerebral Cavemous Malformation.mp.”= 274
  - b. “KRIT1” = 57
  - c. a and b (limit to humans) = 21

1. Gene Symbol: UGT1A1 Chromosomal Locus: 2q37
2. Protein Name: UDP-glucuronosyltransferase 1-1
3. Description: Crigler-Najjar syndrome, also referred to as congenital nonhemolytic jaundice with glucuronosyltransferase deficiency, is a rare, autosomal recessive disorder of bilirubin metabolism. It has been divided into two distinct forms (types I and II) based upon the severity of the disease. The phenotype of Crigler-Najjar syndrome type I can be caused by a variety of alterations in the coding sequences of the bilirubin-uridine diphosphate glucuronosyltransferase (UGT1A1) gene which is responsible for the conjugation of bilirubin. These mutations lead to the production of an abnormal protein, resulting in complete loss or very low levels of hepatic bilirubin-UGT (UGT1A1) activity. Crigler-Najjar syndrome type II (also known as Arias syndrome) is phenotypically similar to type I disease but the unconjugated hyperbilirubinemia is usually less marked (serum bilirubin <20 mg/dL). The clinical manifestations of this disorder can be between 14 and 52 years of age
4. Purpose: Diagnostic
5. Availability: Clinical Laboratories
6. Specimen: Blood
7. Methodology: Mutation scanning, Targeted mutation scanning, Sequence analysis, Sequence analysis of select exons
8. Disease: Crigler-Najjar Syndrome
9. Other Diseases: n/d
10. Clinical use(s) for the Medicare: Useful for diagnostic of late onset type
11. Source of Information: GeneTests.org, Children's University Hospital G2/811 Human Molecular Genetics
12. Exploratory Medline Search (11-13-06):
  - a) "Crigler-Najjar Syndrome" = 392 citations
  - b) "UGT1A1" = 514 citations
  - c) "Crigler-Najjar Syndrome" and "UGT1A1" = 52 citations (limit to human)

1. Gene Symbol: CARD15 Chromosomal Locus: 16q12
2. Protein Name: Caspase recruitment domain protein 15
3. Disease: Crohn Disease
4. Description: Crohn's disease is a common, progressive debilitating disease of the bowel that affects about 1 in 500 individuals in the western population. The pathogenesis of Crohn's disease appears to involve both environmental and genetic factors. The identification of predictive genetic risk factors in individuals with a family history can be an important component of detection and therapy. Within the *NOD2/CARD15* gene (chromosome16q12), 4 autosomal dominant susceptibility loci (R702W, G908R, 3020insC(1007fs) and IVS8+158) have been identified that predispose an individual to Crohn's disease (but not ulcerative colitis).
5. Purpose: Diagnostic
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Sequence analysis, Sequence analysis of select exons, Mutation scanning
9. Other Diseases: Blau syndrome
10. Clinical use(s) for the Medicare: useful for diagnostic and management purposes
11. Source of Information: GeneTests.org, Chapman Institute/Center for Genetic Testing at Saint Francis, Genetics Laboratory
12. Exploratory Medline Search:
  - a) "Crohn's Disease" or "Crohn Disease" = 24422 citations
  - b) "CARD15" = 592 citations
  - c) "a" and "CARD15" = 443 citations (limit to human)

1. Gene Symbol: CTNS Chromosomal Locus: 17p13
2. Protein Name: Cystinosis
3. Disease: Cystinosis
4. Description: Nephropathic cystinosis is characterized by poor growth, renal tubular Fanconi syndrome, hypophosphatemic rickets, impaired glomerular function, and involvement of other tissues and organ systems. In untreated individuals, growth failure is generally noticed at six to nine months of age. Signs of renal tubular Fanconi syndrome appear as early as six months of age and include polyuria, polydipsia, dehydration, and acidosis. Corneal crystals can be present before one year of age, and are always present after 16 months of age, at least in untreated individuals with nephropathic cystinosis. Intermediate cystinosis is characterized by all the typical early manifestations of nephropathic cystinosis, but at a later age. Renal glomerular failure occurs in all affected individuals, usually between 15 and 25 years of age. Non-nephropathic cystinosis is characterized by photophobia only. Mutations in *CTNS* cause all three types of cystinosis.
5. Purpose: Diagnostic
6. Availability: Clinical Laboratories
7. Specimen: Cultured cells or skin biopsy
8. Methodology: Targeted mutation analysis, Analyte
9. Other Diseases: None
10. Clinical use(s) for the Medicare population: Useful for diagnostic because of onset of end stage kidney disease
11. Source of Information: GeneTests.org, Children's Hospital of Eastern Ontario Molecular Genetics Diagnostic Laboratory
12. Exploratory Medline Search (11-13-06):
  - a) "Cystinosis" = 1845 citations
  - b) "CTNS" = 96 citations
  - c) "Cystinosis" and "CTNS" = 48 citations (limit to human)

1. Gene Symbol: SLC3A1 Chromosomal Locus: 2p16.3  
Gene Symbol: SLC7A9 Chromosomal Locus: 19q13.1
2. Protein Name: Neutral and basic amino acid transport protein rBAT, B(o,+)-type amino acid transporter 1
3. Disease: Cystinuria
4. Description: Cystinuria is a heritable disorder of amino acid transport, transmitted as an autosomal recessive trait and is one of the most common genetic disorders. It is due to the defective transport of cystine and dibasic amino acids through the epithelial cells of the renal tubule and intestinal tract. Cystine has a low solubility, and its precipitation results in the formation of calculi in the urinary tract, which leads to obstruction, infections, and ultimately renal insufficiency. Cystinuria can be caused by mutation in the SLC3A1 amino acid transporter gene, which encodes the heavy subunit of the renal amino acid transporter and is located on chromosome 2p, and by mutation in the SLC7A9 gene, which encodes the light subunit and is located on chromosome 19.
5. Purpose: Diagnostics
6. Availability: Clinical Laboratories
7. Specimen: Blood or urine
8. Methodology: Sequence analysis, Deletion/duplication analysis, Analyte
9. Other Diseases: ND
10. Clinical use(s) for the Medicare population: Useful for diagnostic purposes because of onset of end stage renal disease.
11. Source of Information: GeneTests.org, Center for Nephrology and Metabolic Disorders  
Laboratory for Molecular Diagnostics
12. Exploratory Medline Search (11-13-06):
  - a) "Cystinuria" = 1288 citations
  - b) "SLC3A1" or "SLC7A9" = 192 citations
  - c) "Cystinuria" and "b" = 156 citations (limit to human)

1. Gene Symbol: CLCN5 Chromosomal Locus: Xp11.22  
Gene Symbol: OCRL Chromosomal Locus: Xq26.1
2. Protein Name: Chloride channel protein 5; Inositol polyphosphate 5-phosphatase OCRL-1
3. Disease: Dent disease (Low-Molecular Weight Proteinuria with Nephrocalcinosis, X-Linked Recessive Hypophosphatemic Rickets +/-Hypercalciuria, X-Linked Recessive Nephrolithiasis)
4. Description: The term 'X-linked hypercalciuric nephrolithiasis' comprises several related forms of hereditary renal tubular disorders caused by mutations in the CLCN5 gene, including Dent disease, X-linked recessive nephrolithiasis, X-linked recessive hypophosphatemic rickets, and low molecular weight proteinuria. Although these disorders are allelic and are all characterized by progressive proximal renal tubulopathy with hypercalciuria, low-molecular-weight proteinuria, and nephrocalcinosis, they vary in degree of severity and were originally reported as separate disorders. Some have considered these disorders as phenotypic variants of a single disease, referred to as the 'Dent disease complex'.
5. Purpose: Diagnostic
6. Availability: Clinical laboratories
7. Specimen: Blood or buccal swab
8. Methodology: Mutation scanning, Sequence analysis, Linkage analysis; Enzyme assay, Deletion/duplication analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Useful for the diagnosis as it may cause end-stage renal disease
11. Source of Information: GeneTests.org
12. Exploratory Medline Search: (11/13/06)
  - a) "Dent Disease" = 22 citations
  - b) "OCRL" or "CLCN5" = 219 citations
  - c) "Dent Disease" and "OCRL" or "CLCN5" = 12 citations (limit to human)

1. Gene Symbol: ATN1 Chromosomal Locus: 12p13.3
2. Protein Name: Protein Name: Atrophin-1
3. Disease: Dentatorubral-Pallidolusian Atrophy (Naito-Oyanagi Disease)
4. Description: DRPLA is a progressive disorder of ataxia, choreoathetosis, and dementia or character changes in adults, and ataxia, myoclonus, epilepsy, and progressive intellectual deterioration in children. The age of onset is from one to 62 years with a mean age of onset of 30 years.
5. Purpose: Diagnosis
6. Availability: Clinical Laboratories
7. Specimen: Blood
8. Methodology: Targeted mutation analysis
9. Other Diseases: None
10. Clinical use(s): Confirmation of clinically symptomatic; predictive testing; prenatal testing
11. Source of Information: Genetests.org
12. Exploratory Medline Search: (8/14/06)
  - a) "Dentatorubral-Pallidolusian Atrophy.mp. or exp Myoclonic Epilepsies, Progressive"= 672 citations
  - b) "DRPLA gene.mp"=70 citations
  - c) 1 and 2 = 50 citations (limit to humans)

1. Gene Symbol: CIAS1 Chromosomal Locus: 1q44
2. Protein Name: Cold autoinflammatory syndrome 1 protein; Muckle Wells Syndrome
3. Description: Mutations in the CIAS1 gene are associated with familial cold urticaria.
4. Purpose: Diagnostic, Treatment
5. Availability: Clinical laboratories
6. Specimen: Blood, buccal swab
7. Methodology: Bi-directional sequence analysis
8. Disease: Familial Cold Urticaria
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population:
  - a) Confirmation of diagnosis in patient with episodic fever syndrome
  - b) To differentiate between Familial Cold Urticaria/Muckle Wells Syndrome and other familial periodic fever syndromes
  - c) Genetic counseling
  - d) Choosing of appropriate therapy
11. Source of Information: GeneTests.org, GeneDx
12. Exploratory Medline Search: (10/24/06)
  - a. "exp Urticaria/ or Cold autoinflammatory syndrome.mp."=3096
  - b. "CIAS1.mp."=84
  - c. a and b (limit to humans)=30

1. Test Name: Mutation Testing of the Microtubule Associated Protein Tau (MAPT) Gene
2. Other Names:
3. Description: In studies, 25-40% of patients with autosomal dominant frontotemporal dementia show mutations in MAPT. Frontotemporal dementia with parkinsonism-17 (FTDP-17) is a presenile dementia affecting the frontal and temporal cortex and some subcortical nuclei. Symptoms usually start between 40 and 60 years of age, but may occur earlier or later.
4. Purpose: Diagnostic
5. Availability: Clinical laboratories
6. Specimen: Blood
7. Methodology: Sequence analysis, PCR
8. Disease: Autosomal dominant frontotemporal dementia.
9. Other Diseases: Progressive supranuclear palsy (PSP), corticobasal degeneration (CBD) and dementia with epilepsy.
10. Clinical use(s) for the Medicare population: Diagnostic testing
11. Source of Information: GeneTests.org
12. Exploratory Medline Search: (10/24/06)
  - a. "frontotemporal dementia.mp."=1086
  - b. "MAPT.mp. or exp tau Proteins"=3083
  - c. a and b (limit to humans)=383

1. Gene Symbol: UGT1A1 Chromosomal Locus: 2q37
2. Protein Name: UDP-glucuronosyltransferase 1-1
3. Description: Considered in the differential diagnosis of jaundice. The liver function tests of the usual type are normal, and so is the liver histology. There is delayed clearance of bilirubin from the blood, and mild jaundice that tends to fluctuate in severity, particularly after fasting. This disorder is difficult to distinguish from prolonged posthepatic hyperbilirubinemia. This is a benign disorder.
4. Purpose: Diagnostics
5. Availability: Clinical Laboratories (outside the USA)
6. Specimen: Blood
7. Methodology: Targeted mutation analysis
8. Disease: Gilbert syndrome, or Type I of Hyperbilirubinemia
9. Other Diseases: n/d
10. Clinical use(s): Potentially eligible for the Medicare population.
11. Source of Information: GeneTests.org, BioLab spol. s.r.o.  
Molecular Biology Laboratory; OMIM
12. Exploratory Medline Search (11/09/2006):
  - a) "exp Gilbert Disease/ or Gilbert Syndrome.mp."=632
  - b) "UGT1A1.mp."=514
  - c) a and b = 70

1. Gene Symbol: Hemoglobin E
2. Other Names: HbE
3. Disease: rare forms of thalassemia
4. Description: Formation of HbE is due to a single base substitution that alters the coding property of codon 27 in the beta globin gene (Lys instead of Glu). This globin forms an  $(\alpha(2)/\beta(2)E$  hemoglobin with an altered mobility, called HbE. Homozygotes and heterozygotes have reduced RBC life but only mild symptoms.
5. Purpose: Diagnostics
6. Availability: Clinical laboratory
7. Specimen: Blood sample
8. Methodology: Sequence analysis of selected exons; Targeted mutation analysis
9. Other Diseases: ND
10. Clinical use(s): May be applicable to the Medicare population People with the disease have normal life expectancy.
11. Source of Information: GeneTests.org; UptoDate
12. Exploratory Medline Search:
  - a) "exp beta-Thalassemia/ or exp Thalassemia/"=14323
  - b) "hemoglobin E.mp. or exp Hemoglobin E/"=648
  - c) a and b limited to humans = 425

1. Gene Symbol: GNE gene
2. Protein name: UDP-N-acetylglucosamine 2-epimerase/N-acetylmannosamine kinase). Inclusion Body Myopathy 2 (IBM2), Inclusion Body Myopathy, Autosomal Recessive, Quadriceps Sparing Myopathy, Nonaka Myopathy (Allelic disorder).
3. Disease: Hereditary Inclusion Body Myopathy
4. Description: Mutations in the GNE gene cause Hereditary Inclusion Body Myopathy (HIBM), a disease characterized by progressive muscle weakness. Analysis is done for the M712T mutation in the GNE gene. HIBM is an adult-onset, autosomal recessive disorder, characterized by slow progression of muscle weakness, both distal and proximal, but with the unusual feature of relative sparing of the quadriceps even in the advanced stages of the disease.
5. Purpose: Diagnostic, prognostic
6. Availability: Clinical laboratories
7. Specimen: Blood, buccal swab
8. Methodology: PCR, sequence analysis, mutation analysis
9. Other Diseases: ND
10. Clinical use(s) for the Medicare population: Useful (late onset)
  - a) Confirmation of a clinical diagnosis
11. Source of Information: GeneDx; Genetests.org
12. Exploratory Medline Search: (10/24/06)
  - a. "exp Myositis, Inclusion Body/ or Hereditary Inclusion Body Myopathy.mp."=446
  - b. "GNE.mp."=46
  - c. a and b (limit to humans)=29

1. Gene Symbol: ACVRL1 (ALK1)
2. Protein Name: Serine/threonine-protein kinase receptor R3
3. Disease: ACVRL1-Related Hereditary Hemorrhagic Telangiectasia
4. Description: Hereditary hemorrhagic telangiectasia is characterized by the presence of multiple arteriovenous malformations, direct connections between arteries and veins. These often rupture and bleed after slight trauma. Large malformations in the brain, lungs or gastrointestinal tract may result in shunting on bleeding complications. It is caused by mutations in either the gene encoding endoglin (ENG) or ACVRL1 (ALK1), the gene encoding the activin receptor.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory testing
7. Specimen: Blood
8. Methodology: Sequence analysis; Sequence analysis of select exons; Mutation scanning; Linkage analysis; Deletion/duplication analysis; Sequence analysis of RNA
9. Other Diseases: No
10. Clinical use(s): The condition may present throughout lifetime, so it may be applicable to Medicare population
11. Source of Information: GeneTests.org; OMIM
12. Exploratory Medline Search (20/10/2006):
  - a) "hereditary hemorrhagic telangiectasia.mp. or exp Telangiectasia, Hereditary Hemorrhagic/"= 1,804
  - b) "(ACVRL1 or alk1).mp."=232
  - c) a and b limited to humans =99

1. Gene Symbol: ENG
2. Protein Name: Endoglin
3. Disease: ENG-Related Hereditary Hemorrhagic Telangiectasia (Osler Rendu Weber Syndrome)
4. Description: Hereditary hemorrhagic telangiectasia is characterized by the presence of multiple arteriovenous malformations, direct connections between arteries and veins. These often rupture and bleed after slight trauma. Large malformations in the brain, lungs or gastrointestinal tract may result in shunting on bleeding complications. It is caused by mutations in either the gene encoding endoglin (ENG) or ACVRL1 (ALK1), the gene encoding the activin receptor.
5. Purpose: Diagnostic.
6. Availability: Clinical laboratory testing
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; Sequence analysis of select exons; Analysis of the entire coding region: Mutation scanning; Linkage analysis; Deletion/duplication analysis; Sequence analysis of RNA
9. Other Diseases: No
10. Clinical use(s): The condition may present throughout lifetime, so it might applicable to Medicare population
11. Source of Information: GeneTests.org; OMIM
12. Exploratory Medline Search (20/10/2006):
  - a) "hereditary hemorrhagic telangiectasia.mp. or exp Telangiectasia, Hereditary Hemorrhagic/"= 1,804
  - b) "(endoglin or eng).mp."=3119
  - c) a and b limited to humans =149

1. Gene Symbol: SPTLC1
2. Protein Name: Serine palmitoyltransferase 1
3. Disease: Hereditary Sensory Radicular Neuropathy Type I, HSN1
4. Description: Sensory loss secondary to distal axonal degeneration. First noticed when painless injuries are encountered. Onset may be from teens to the 6<sup>th</sup> decade. Autosomal dominant trait.
5. Purpose: Aid in the differential diagnosis of radicular sensory neuropathy
6. Availability: Clinical research laboratory.
7. Specimen: Blood
8. Methodology: Sequence analysis of select exons
9. Other Diseases: No
10. Clinical use(s): May be pertinent to the Medicare population, disease may have late onset
11. Source of Information: geneTests.org; OMIM
12. Exploratory Medline Search:
  - a) "exp "Hereditary Sensory and Autonomic Neuropathies"/"=492
  - b) "SPTLC1.mp. or exp Serine C-Palmitoyltransferase/"=194
  - c) a and b = 19

1. Gene Symbol: HEXA Chromosomal Locus: 15q23-q24
2. Protein name: Beta-hexosaminidase alpha chain
3. Disease: GM2 Gangliosidoses (Hexosaminidase A-Deficient)
4. Description: HEXA deficiency results in a group of neurodegenerative disorders - GM2 Gangliosidoses (Hexosaminidase A-Deficient). The juvenile (subacute), chronic, and adult-onset variants of the hexosaminidase A deficiencies have later onsets, slower progression, and more variable neurologic findings, including progressive dystonia, spinocerebellar degeneration, motor neuron disease, and, in some individuals with adult-onset disease, a bipolar form of psychosis.
5. Purpose: Counseling, Diagnostic
6. Availability: Clinical laboratories
7. Specimen: Blood, serum
8. Methodology: Sequence analysis, mutation screening
9. Other Diseases: Chronic and Adult-Onset Hexosaminidase A Deficiency
10. Clinical use(s) for the Medicare population: Useful for the late onset type
  - a) Confirmatory diagnosis
11. Source of Information: GeneTests.org
12. Exploratory Medline Search: (10/22/06)
  - a. "exp Gangliosidoses GM2/ or exp Gangliosidoses/ or Gangliosidoses.mp." = 481
  - b. "HEXA.mp." = 792
  - c. a and b (limit to humans) = 49

1. Gene Symbol: HEXA
2. Protein Name: Beta-hexosaminidase alpha chain
3. Disease: Hexosaminidase A Deficiency or GM2 Gangliosidoses (Hexosaminidase A-Deficient)
4. Description: The condition results in neurodegenerative disorders caused by intralysosomal storage of the specific glycosphingolipid GM2 ganglioside. Apart from the infantile and acute-onset Tay-Sachs disease, other phenotypic expressions of the disease have later onset and variable clinical course.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: blood, serum
8. Methodology: Sequence analysis; Mutation scanning; Targeted mutation analysis; Analyte; Enzyme assay; Protein analysis
9. Other Diseases: NA
10. Clinical use(s): Potentially relevant to the Medicare population
11. Source of Information: geneTests.org; OMIM
12. Exploratory Medline Search:
  - a) "exp Gangliosidoses GM2/ or exp Tay-Sachs Disease/ or Hexosaminidase A Deficiency.mp."=1077
  - b) "exp Hexosaminidases/ or exp beta-N-Acetylhexosaminidase/ or Beta-hexosaminidase alpha chain.mp. or HEXA.mp. "=10497
  - c) a and b = 549

1. Gene Symbol: HFE
2. Protein Name: Hereditary hemochromatosis protein
3. Disease: HFE-Associated Hereditary Hemochromatosis
4. Description: Hereditary hemochromatosis is an autosomal recessive disorder of iron metabolism that varies in clinical severity. Three mutations (C282Y, H63D, and S65C) have been described in the majority of patients with hemochromatosis. Their penetrance is variable. Onset (or diagnosis) may occur at all ages, and the clinical course is variable.
5. Purpose: Diagnostics
6. Availability: Clinical Laboratory
7. Specimen: blood
8. Methodology: Sequence analysis; Sequence analysis of select exons; Mutation scanning; Targeted mutation analysis
9. Other Diseases: NA
10. Clinical use(s): Potentially applicable to the Medicare population
11. Source of Information: geneTests.org; OMIM; UptoDate
12. Exploratory Medline Search (11/04/2006):
  - a) "exp Hemochromatosis/ or hereditary hemochromatosis.mp."=5385
  - b) "HFE.mp."=1692
  - c) a and b =1297

1. Gene Symbol: HD Chromosomal Locus: 4p16.3
2. Protein Name: Huntington
3. Disease: Huntington Disease
4. Description: The HD gene is the only gene that is associated with Huntington disease. A trinucleotide CAG repeat expansion is the only mutation that has been observed. Huntington disease (HD) is a inherited autosomal dominant disease progressive disorder of motor, cognitive, and psychiatric disturbances. The mean age of onset is 35 to 44 years and the median survival time is 15 to 18 years after onset.
5. Purpose: Diagnostic, Prognostic
6. Availability: Clinical laboratories
7. Specimen: Blood
8. Methodology: Mutation analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Useful for late onset
  - a) Diagnosis
11. Source of Information: Genzyme Genetics, GeneTests.org
12. Exploratory Medline Search: (10/24/06)
  - a. "Huntington disease.mp. or exp Huntington Disease" = 2851
  - b. "HD gene.mp"= 196
  - c. a and b (limit to humans) = 139

1. Gene Symbol: JPH3
2. Protein Name: Juncophilin-3
3. Disease: Huntington disease-like 2, HDL2
4. Description: The disease typically presents in midlife with a relentless progressive triad of movement, emotional, and cognitive abnormalities progressing to death over ten to 20 years. The diagnosis requires molecular genetic testing. JPH3 is the only gene known to be associated with HDL2.
5. Purpose: Diagnostics
6. Availability: Clinical laboratory
7. Specimen: blood
8. Methodology: Targeted Mutation Analysis
9. Other Diseases: No
10. Clinical use(s): Potentially applicable to the Medicare population, may have late onset.
11. Source of Information: geneTests.org; OMIM
12. Exploratory Medline Search:
  - a) "exp Huntington Disease/ or hUNTINGTON DISEASE LIKE 2.mp."=6431
  - b) "Juncophilin 3.mp. or jph3.mp"=11
  - c) a nd b = 10

1. Test Name: Conjugated bilirubin in blood - Urinary coproporphyrin excretion
2. Other Names: No
3. Description: This is a conjugated hyperbilirubinemia, and a recessive inheritance is suggested. (Resembles the Dubin-Johnson syndrome) Has increased coproporphyrin excretion in the urine, and is a disorder of Hepatic storage. Mild disorder, does not require treatment.
4. Purpose: Diagnostic.
5. Availability: Clinical Laboatory
6. Specimen: Blood; Urine
7. Methodology: High-Performance Liquid Chromatography (HPLC)
8. Disease: Hyperbilirubinemia, rotor type
9. Other Diseases: NA
10. Clinical use(s): Potentially useful for the Medicare population.
11. Source of Information: geneTests.org; OMIM; Uptodate; PubMed
12. Exploratory Medline Search:
  - a) "Hyperbilirubinemia, Rotor type"=1498
  - b) "exp Bilirubin/ or Conjugated bilirubin.mp. or coproporphyrin.mp. or exp Coproporphyrins/"=17996
  - c) a and b = 639

1. Test Name: Apolipoprotein E
2. Other Names: APOE
3. Description: of the 4 alleles (e1 to e4, codominant inheritance) those who are homozygotes for e2 have higher probability for type III hyperlipoproteinemia, a risk factor for cardiovascular disease.
4. Purpose: Diagnostics
5. Availability: Clinical Laboratory
6. Specimen: Blood
7. Methodology: Targeted mutation analysis
8. Disease: Hyperlipoproteinemia Type III Risk Factor (APOE)
9. Other Diseases: NA [Alzheimer's disease but no genetests.org entry]
10. Clinical use(s): Perhaps applicable to the Medicare population
11. Source of Information: Genetests.org; OMIM
12. Exploratory Medline Search (11/06/2006):
  - a) "Hyperlipoproteinemia Type III.mp. or exp Hyperlipoproteinemia Type III/" = 495
  - b) "apoe.mp. or exp Apolipoproteins E/"=10704
  - c) a and b = 230

1. Gene Symbol: CACNA1S
2. Protein Name: Voltage-dependent L-type calcium channel alpha-1S subunit
3. Disease: Hypokalemic Periodic Paralysis Type 1
4. Description: the disease has two different forms: a paralytic form and a myopathic form. The age of onset of the first attack ranges from age one to 20 years; the frequency of attacks is highest between ages 15 and 35 and then decreases with age. The myopathic form results in a progressive fixed muscle weakness that begins at extremely variable ages as exercise intolerance predominantly in the lower limbs. It occurs independent of paralytic symptoms and may be the sole manifestation of HOKPP.
5. Purpose: Diagnosis
6. Availability: Clinical Laboratory
7. Specimen: Blood
8. Methodology: Sequence analysis of select exons; Analysis of the entire coding region: Mutation scanning; Targeted mutation analysis; Linkage analysis
9. Other Diseases: Hyperkalemic periodic paralysis and Paramyotonia Congenita
10. Clinical use(s): Probably useful for the Medicare population
11. Source of Information: genetests.org
12. Exploratory Medline Search:
  - a) "Hypokalemic Periodic Paralysis.mp. or exp Hypokalemic Periodic Paralysis/"=442
  - b) "exp Calcium Channels, L-Type/ or CACNA1S.mp."=3440
  - c) a and b=36

1. Gene Symbol: SCN4A
2. Protein Name: Sodium channel protein type 4 subunit alpha
3. Disease: Hypokalemic Periodic Paralysis Type 2
4. Description: the disease has two different forms: a paralytic form and a myopathic form. The age of onset of the first attack ranges from age one to 20 years; the frequency of attacks is highest between ages 15 and 35 and then decreases with age. The myopathic form results in a progressive fixed muscle weakness that begins at extremely variable ages as exercise intolerance predominantly in the lower limbs. It occurs independent of paralytic symptoms and may be the sole manifestation of HOKPP.
5. Purpose: Diagnosis
6. Availability: Clinical Laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; Sequence analysis of select exons; Analysis of the entire coding region: Mutation scanning; Targeted mutation analysis; Linkage analysis
9. Other Diseases: Hyperkalemic periodic paralysis and paramyotonia congenita
10. Clinical use(s): Probably useful for the Medicare population
11. Source of Information: genetests.org
12. Exploratory Medline Search:
  - a) "Hypokalemic Periodic Paralysis.mp. or exp Hypokalemic Periodic Paralysis/"=442
  - b) "SCN4A.mp."=126
  - c) a and b=23

1. Gene Symbol: GALC Chromosomal Locus: 14q31
2. Protein Name: Galactocerebrosidase
3. Disease: Krabbe Disease
4. Description: The disease has infantile or late adulthood onset. In the late-onset forms, individuals can be clinically normal until symptoms of weakness, vision loss, and intellectual regression become evident. The clinical course in these individuals is variable even between those with the same genotype.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical laboratory
7. Specimen: blood
8. Methodology: Targeted mutation analysis; Analyte; Enzyme assay
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Potentially applicable to the Medicare population
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/31/06):
  - a) "Krabbe Disease" or "Galactocerebrosidase Deficiency" or "Galactosylceramidase Deficiency" or "Globoid Cell Leukodystrophy" = 479 citations
  - b) "GALC" = 303 citations
  - c) "a" or "GALC" = 49 citations (limit to humans)

1. Gene Symbol: LCAT Chromosomal Locus: 16q22
2. Protein Name: Phosphatidylcholine-sterol acyltransferase (Lecithin-cholesterol acyltransferase)
3. Disease: Lecithin Cholesterol Acyltransferase Deficiency or Fish-Eye Disease or LCAT Deficiency or Norum Disease
4. Description: Rare condition characterized by severe high density lipoprotein deficiency, in which the predicted increased cardiovascular risk is not clearly apparent. The alternative name “fish eye disease” reflects the massive corneal opacification seen in these patients.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: ND
8. Methodology: Enzymatic Calorimetric
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Potentially relevant to the Medicare population
11. Source of Information: Genetests.org; PubMed
12. Exploratory Medline Search (8/30/06):
  - a) “Lecithin Acyltransferase Deficiency” or “Cholesterol Acyltransferase Deficiency” or “Fish-Eye Disease” = 335 citations
  - b) “LCAT” = 1469 citations
  - c) “a” and “LCAT” = 204 citations (limit to humans)

1. Gene Symbol: FBN1 Chromosomal Locus: 15q21.1
2. Protein Name: Fibrillin-1
3. Disease: Marfan Syndrome
4. Description: Mutations in the FBN1 gene have been associated with Marfan Syndrome. Molecular genetic testing detects 70-93% of mutations. Marfan syndrome is a systemic disorder of connective tissue with a high degree of clinical variability. Cardinal manifestations involve the ocular, skeletal, and cardiovascular systems.
5. Purpose: Diagnostic, prognostic
6. Availability: Clinical laboratories
7. Specimen: Whole blood
8. Methodology: Sequence analysis and mutation scanning
9. Other Diseases: Mitral valve prolapse syndrome; MASS phenotype; Familial ectopia lentis; Shprintzen-Goldberg syndrome; Weill-Marchesani syndrome
10. Clinical use(s) for the Medicare population: Useful since late diagnosis is a possibility
  - a) Confirmatory diagnostic testing
  - b) Predictive testing
11. Source of Information: Gene Tests
12. Exploratory Medline Search: (10/24/06)
  - a. "Marfan Syndrome.mp. or exp Marfan Syndrome" = 1390
  - b. "FBN1.mp." = 171
  - c. a and b (limit to humans) = 138

1. Gene Symbol: FBN1 Chromosomal Locus: 15q21.1
2. Protein Name: Fibrillin-1
3. Disease: MASS Syndrome
4. Description: In rare instances, the addition of a small amount of DNA to the FBN1 gene can cause MASS syndrome. MASS syndrome involves abnormalities in several structures, including the mitral valve (one of the valves that controls blood flow through the heart), the aorta (a large blood vessel that distributes blood from the heart to the rest of the body), the skeleton, and the skin.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Diagnosis of the syndrome secondary to complications at a later age.
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/29/06):
  - a) "MASS Syndrome" = 36 citations
  - b) "FBN1" = 226 citations
  - c) "MASS Syndrome" and "FBN1" = 1 citation (limit to human)

1. Gene Symbol: UMOD Chromosomal Locus: 16p12.3
2. Protein Name: Uromodulin
3. Disease: Medullary Cystic Kidney Disease
4. Description: Medullary cystic kidney disease (MCKD) is an autosomal dominant disorder. Mutations in the gene for uromodulin (also called Tamm-Horsfall mucoprotein) are responsible for type 2 medullary cystic kidney disease (MCKD2). MCKD2 and familial juvenile hyperuricemic nephropathy appear to be allelic disorders that arise from mutations in the UMOD gene
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Sequence analysis of select exons
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Useful as it can lead to endstage kidney disease.
11. Source of Information: Genetests.org; Uptodate
12. Exploratory Medline Search (8/29/06):
  - a) (“Cystic Kidney Disease” and “Medullary”) or “MCKD2” = 570 citations
  - b) “UMOD” = 24 citations
  - c) “a” and “UMOD” = 9 citations (limit to humans)

1. Gene Symbol: CFH Chromosomal Locus: 1q32
2. Test Name: Complement factor H
3. Disease: Membranoproliferative Glomerulonephritis, Type II
4. Description: Membranoproliferative Glomerulonephritis, Type II is also called dense deposit disease, because it is characterized by continuous, dense ribbon-like deposits along the basement membranes of the glomeruli, tubules, and Bowman's capsule. Associated with primary complement activation. Age of onset between 8 and 30 years.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Useful for diagnostic as it can lead to end-stage renal disease.
11. Source of Information: Genetests.org; UptoDate
12. Exploratory Medline Search (8/29/06):
  - a) "Membranoproliferative Glomerulonephritis" or "Dense Deposit Disease" = 2323 citations
  - b) "CFH" = 86 citations
  - c) "a" and "CFH" = 1 (limit to humans)

1. Gene Symbol: ARSA Chromosomal Locus: 22q13.3-qter
2. Protein Name: Arylsulfatase A
3. Disease: Metachromatic leukodystrophy
4. Description: ARSA is the gene associated with metachromatic leukodystrophy, an autosomal recessive inheritance disease condition. Adult MLD: Onset occurs after sexual maturity, sometimes not until the fourth or fifth decade. Initial signs include problems in school or job performance, personality changes, alcohol or drug abuse, poor money management, and emotional lability in some individuals; in others, neurological symptoms (weakness and loss of coordination progressing to spasticity and incontinence) or seizures predominate initially. Peripheral neuropathy occurs frequently.
5. Purpose: Diagnostic, Prognostic
6. Availability: Clinical laboratories
7. Specimen: Blood
8. Methodology: Determination of enzymatic activity with p-nitrocatechol sulfate
9. Other Diseases: 22q13.3 deletion syndrome; Ring 22
10. Clinical use(s) for the Medicare population: Useful for the late onset adult MLD
  - a) Confirmatory diagnostic testing
  - b) Prognostication
11. Source of Information: GeneTests.org, LabCorp
12. Exploratory Medline Search:
  - a. "Metachromatic leukodystrophy.mp. or exp Leukodystrophy, Metachromatic" = 274
  - b. "ARSA.mp." = 116
  - c. a and b (limit to humans) = 31

1. Test Name: Motor Neuropathy Profile-Complete
2. Other Names: Anti-GM1 motor neuropathy, Anti-MAG motor neuropathy, motor neuropathy
3. Disease: Motor neuropathy
4. Description: Test includes Co-GM1 Triad and MAG 'Dual Antigen'® Autoantibody tests.
5. Purpose: Diagnostic
6. Availability: Clinical laboratories
7. Specimen: Serum
8. Methodology: Western Blot, ELISA
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population:
  - a) Tests for motor neuropathy
11. Source of Information: Athena Diagnostics
12. Exploratory Medline Search: (10/24/06)
  - a. "exp Motor Neuron Disease/ or Motor neuropathy.mp." = 8975
  - b. "Anti-GM1.mp. or Anti-MAG.mp" = 1102
  - c. a and b (limit to humans) = 95

1. Gene Symbol: MYBPC3 Chromosomal Locus: 11p11.2
2. Protein Name: Myosin-binding protein C, cardiac-type
3. Disease: Dilated cardiomyopathy
4. Description: Mutations in the MYBPC3 gene are associated with MYBPC3 Related Dilated Cardiomyopathy.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory (Outside US)
7. Specimen: Blood
8. Methodology: Sequence analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Useful for late onset
11. Source of Information: GeneTests.org,
12. Exploratory Medline Search:
  - a. "Dilated Cardiomyopathy.mp. or exp Cardiomyopathy, Dilated" = 6427
  - b. "MYBPC3.mp." = 32
  - c. a and b (limit to humans) = 4

1. Gene Symbol: MYH7 Chromosomal Locus: 14q12
2. Protein Name: Myosin heavy chain, cardiac muscle beta isoform
3. Disease: Dilated cardiomyopathy
4. Description: Mutations in the MYH7 gene are associated with MYH7 Related Dilated Cardiomyopathy.
5. Purpose: Diagnostic
6. Availability: Clinical laboratories
7. Specimen: Blood
8. Methodology: Sequence analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Useful for late onset type
11. Source of Information: GeneTests.org
12. Exploratory Medline Search:
  - a. "Dilated Cardiomyopathy.mp. or exp Cardiomyopathy, Dilated" = 6427
  - b. "MYH7.mp." = 65
  - c. a and b (limit to humans) = 5

1. Gene Symbol: SGCE Chromosomal Locus: 7q21
2. Protein Name: Epsilon-sarcoglycan
3. Disease: Myoclonus-Dystonia
4. Description: Mutations in the *SGCE* gene are associated with familial Myoclonus-dystonia (M-D), a movement disorder characterized by a combination of rapid, brief muscle contractions (myoclonus) and/or sustained twisting and repetitive movements that result in abnormal postures (dystonia). The most prominent non-motor features have been psychiatric problems including depression, anxiety, obsessive-compulsive disorder (OCD), personality disorders, addiction, and panic attacks. Symptom onset is usually in childhood or early adolescence but ranges from six months to 38 years.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; Deletion/duplication analysis; Sequence analysis of select exons
9. Other Diseases: None
10. Clinical use(s) for the Medicare population: Useful as this disease is compatible with an active life of normal span
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/25/06):
  - a) "Myoclonus-Dystonia" or "Dystonia 11" or "Essential Myoclonus" or "Myoclonic Dystonia" = 160 citations
  - b) "SGCE" = 32 citations
  - c) "a" and "SGCE" = 25 citations (limited to humans)

1. Gene Symbol: DMPK Chromosomal Locus: 19q13.2-q13.3
2. Protein Name: Myotonin-protein kinase
3. Disease: Myotonic dystrophy type 1
4. Description: Myotonic dystrophy type 1 (DM1) span a continuum from mild to severe. Myotonic dystrophy type 1 (DM1) is suspected in adults with muscle weakness, especially of the distal leg, hand, neck, and face; myotonia (sustained muscle contraction); posterior subcapsular cataracts
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Targeted mutation analysis; linkage analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Applicable for the mild type of disease that occurs between the ages 20 to 70 yrs who also have 60 to normal years of life span
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/25/06):
  - a) "Myotonic Dystrophy" or "Steinert's Disease" = 3874 citations
  - b) "DMPK" = 242 citations
  - c) "a" and "DMPK" = 179 citations (limited to humans)

1. Gene Symbol: ZNF9 Chromosomal Locus: 3q13.3-q24
2. Protein Name: Cellular nucleic acid binding protein
3. Disease: Myotonic dystrophy type 2
4. Description: Myotonic dystrophy type 2 presents with a range of symptoms from cataracts to significant muscle wasting, cardiac complications, ptosis and myotonia. The DM2 locus maps to chromosome 3q21; the change at the DM2 locus is an expansion of a CCGT repeat in an intron of the zinc finger protein 9 gene (ZNF9).
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Targeted mutation analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Useful since most affected patients have onset of symptoms in their 30s or 40s
11. Source of Information: Genetests.org; UptoDate
12. Exploratory Medline Search (8/25/06):
  - a) "Myotonic Dystrophy" or "Proximal Myotonic Myopathy" = 3876 citations
  - b) "ZNF9" = 52 citations
  - c) "a" and "ZNF9" = 31 citations (limited to humans)

1. Gene Symbol: NEB Chromosomal Locus: 2q22
2. Protein name: Nebulin
3. Disease: Nemaline myopathy
4. Description: Mutations in the NEB gene have been associated with nemaline myopathy. The most frequent known occurring mutation observed in the NEB gene is a 2,502 bp inframe deletion of exon 55. Adult-onset (late-onset) NM varies in clinical presentation and disease progression with onset between age 20 and 50 years. Myalgia may be prominent, and weakness may progress rapidly.
5. Purpose: Diagnostic, Counseling
6. Availability: Clinical laboratories
7. Specimen: Blood, buccal cheek swabs
8. Methodology: Mutation analysis
9. Other Diseases: ACTA1 myopathy
10. Clinical use(s) for the Medicare population: Useful for adult onset type
11. Source of Information: GeneDx, GeneTests.org
12. Exploratory Medline Search: (10/25/06)
  - a. "nemaline myopathy.mp. or exp Myopathies, Nemaline" = 204
  - b. "NEB gene.mp"=182
  - c. a and b (limit to humans) = 9

1. Gene Symbol: PABPN1 Chromosomal Locus: 14q11.2-q13
2. Protein Name: Polyadenylate-binding protein 2
3. Disease: Oculopharyngeal Muscular Dystrophy
4. Description: PABPN1, encoding the polyadenylate binding protein nuclear 1, is the only gene known to be associated with Oculopharyngeal muscular dystrophy (OPMD) that is characterized by late-onset (usually after the age of 45 years) eyelid drooping (ptosis, defined as either vertical separation of at least one palpebral fissure that measures less than 8 mm at rest), swallowing difficulty (dysphagia, defined as swallowing time greater than seven seconds when drinking 80 mL of ice-cold water), and a positive family history with involvement of two or more generations.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Targeted mutation analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Applicable for diagnosis as symptoms are late onset
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/24/06):
  - a) "Oculopharyngeal Muscular Dystrophy" = 239 citations
  - b) "PABPN1" = 39 citations
  - c) "Oculopharyngeal Muscular Dystrophy" and "PABPN1" = 26 citations (limit to humans)

1. Gene Symbol: VDR Chromosomal Locus: 12q12-q14
2. Protein Name: Vitamin D3 receptor
3. Disease: Osteoporosis
4. Description: VDR genotypes are associated with the risk of fracture in postmenopausal women independently of BMD, rate of postmenopausal forearm BMD loss, bone turnover, and endogenous hormones.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory (outside US)
7. Specimen: ND
8. Methodology: Targeted mutation analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: May be useful (clear association between gene and fracture risk is not completely established)
11. Source of Information: Genetests.org; OMIM
12. Exploratory Medline Search (8/23/06):
  - a) "Osteoporosis" = 35470 citations
  - b) "VDR" = 2133 citations
  - c) "Osteoporosis" and "VDR" = 216 citations

1. Gene Symbol: PDB1 Chromosomal Locus: 6p21  
Gene Symbol: PDB2 Chromosomal Locus: 18q21-q22
2. Protein name: ND
3. Disease: Paget Disease of Bone
4. Description: Mutations in the PDB1/PDB2 genes are associated with Paget Disease of Bone 1 and 2, respectively. Paget's disease is a chronic bone disorder, in which bones become enlarged and deformed. This is the most common bone disorder after osteoarthritis in people over age 50.
5. Purpose: Confirmation of diagnosis
6. Availability: Clinical laboratory (outside US)
7. Specimen: Blood
8. Methodology: Mutation analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population:
11. Source of Information: GeneTests.org
12. Exploratory Medline Search: (10/26/06)
  - a. "exp Osteitis Deformans/ or Paget Disease.mp" = 874
  - b. "PDB1 or PDB2" = 8
  - c. a and b (limit to humans" = 5

1. Gene Symbol: LRRK2 Chromosomal Locus: 12q12
2. Protein Name: Leucine-rich repeat serine/threonine-protein kinase 2
3. Disease: LRRK2-Related Parkinson Disease
4. Description: The disease is characterized by tremor, muscle rigidity, bradykinesia and postural instability. This is the leading cause of neurologic disease in the Medicare population.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical laboratory
7. Specimen: blood
8. Methodology: Targeted mutation analysis; Analysis of the entire coding region: Sequence analysis; Sequence analysis of select exons
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Applicable to the Medicare population
11. Source of Information: Genetests.org; OMIM; UptoDate
12. Exploratory Medline Search (8/23/06):
  - a) "Parkinson\$ Disease" = 37742 citations
  - b) "LRRK2" = 79 citations
  - c) "Parkinson\$ Disease" and "LRRK2" = 75 citations (limit to humans)

1. Gene Symbol: PINK1 Chromosomal Locus: 1p36
2. Protein Name: Serine/threonine-protein kinase PINK1
3. Disease: Pink1-Related Parkinson Disease
4. Description: The disease is characterized by tremor, muscle rigidity, bradykinesia and postural instability. This is the leading cause of neurologic disease in the Medicare population.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: blood
8. Methodology: Analysis of the entire coding region: Sequence analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Applicable to the Medicare population
11. Source of Information: Genetests.org; OMIM; UpToDate
12. Exploratory Medline Search (8/23/06):
  - a) "Parkinson\$ Disease" = 37742 citations
  - b) "PINK1" = 51 citations
  - c) "Parkinson\$ Disease" and "PINK1" = 42 citations (limit to humans)

1. Gene Symbol: RDS Chromosomal Locus: 6p21.1-cen
2. Protein Name: Peripherin
3. Disease: Patterned Dystrophy of Retinal Pigment Epithelium or Butterfly-Shaped Pigmentary Macular Dystrophy
4. Description: Patterned dystrophies of the retinal pigment epithelium refer to a heterogeneous group of macular disorders. Three main varieties of patterned dystrophy of the RPE have been described: reticular ('fishnet-like') dystrophy, macroreticular ('spider-shaped') dystrophy, and butterfly-shaped pigment dystrophy of the fovea, which is the target of the test. The may occur later in life and may be mistaken for age-related macular degeneration.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Mutation scanning; Analysis of the entire coding region: Sequence analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: May be applicable to the Medicare population.
11. Source of Information: Genetests.org; OMIM; PubMed
12. Exploratory Medline Search (8/23/06):
  - a) "Retinal Pigment Epithelium" = 5458 citations
  - b) "Pattern\$ Dystroph\$" = 89 citations
  - c) "Retinal Pigment Epithelium" and "Pattern\$ Dystroph\$" = 46 citations
  - d) "RDS" = 2726 citations
  - e) "c" and "RDS" = 6 citations (limit to humans)

1. Gene Symbol: PKD1 and PKD2 Genes
2. Protein Names: Polycystin-1, Polycystin-2
3. Disease: Polycystic Kidney Disease
4. Description: Two genes are associated with polycystic kidney disease: PKD1 and PKD2 and these account for 85% and 15% of affected individuals, respectively. It is hypothesized that there is one other locus representing a small fraction of affected individuals not linked to either the PKD1 or PKD2 genes. Autosomal dominant polycystic kidney disease (ADPKD) is generally a late-onset, multisystem disorder characterized by bilateral renal cysts; cysts in other organs, such as the liver, seminal vesicles, pancreas, and arachnoid membrane; vascular abnormalities, such as intracranial aneurysms, dilatation of the aortic root, and dissection of the thoracic aorta; mitral valve prolapse; and abdominal wall hernias.
5. Purpose: Diagnostic
6. Availability: Clinical laboratories
7. Specimen: Blood
8. Methodology: Linkage analysis, sequence analysis, FISH/microarray analysis
9. Other Diseases: None
10. Clinical use(s) for the Medicare population: Applicable
  - a) Confirmation of diagnosis
  - b) Presymptomatic diagnosis
11. Source of Information: Gene Tests
12. Exploratory Medline Search:
  - a. "Polycystic Kidney Disease.mp. or exp Polycystic Kidney Diseases"
  - b. "PKD1.mp. or PKD2.mp." = 575
  - c. a and b (limit to humans) = 432

1. Gene Symbol: PRKCSH Chromosomal Locus: 19p13.2-p13.1;  
Gene Symbol: SEC63 Chromosomal Locus: 6q21
2. Protein Name: Glucosidase II beta subunit ; Translocation protein SEC63 homologue
3. Disease: Polycystic liver disease
4. Description: Autosomal dominant polycystic liver disease is a disorder that is not common and is distinct from polycystic kidney disease, since it is not associated with kidney involvement or cerebral aneurysms. Mutations in the PRKCSH and SEC63 genes have been associated with the disorder.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: blood
8. Methodology: Analysis of the entire coding region: Mutation scanning; Analysis of the entire coding region: sequence analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Potentially applicable to the Medicare population
11. Source of Information: Genetests.org; Uptodate
12. Exploratory Medline Search (8/22/06):
  - a) "Polycystic liver disease" = 1010 citations
  - b) "PRKCSH" = 63 citations
  - c) "SEC63" = 81 citations
  - d) "Polycystic liver disease" and ("PRKCSH" or "SEC63") = 16 citations (limit to humans)

1. Gene Symbol: GAA Chromosomal Locus: 17q25.2-q25.3
2. Protein Name: Lysosomal alpha-glucosidase
3. Disease: Pompe Disease
4. Description: Pompe disease is an inborn error of glycogen metabolism, resulting from an acid alpha glucosidase enzyme deficiency. The late onset form can present from childhood through adulthood with progressive muscle weakness and respiratory dysfunction.
5. Purpose: Diagnostic
6. Availability: Clinical laboratories
7. Specimen: skin fibroblasts, tissue samples
8. Methodology: DNA sequencing, mutation analysis; analyte, enzyme assay, protein analysis
9. Other Diseases:
10. Clinical use(s) for the Medicare population: Useful for late onset form
  - a) Diagnosis of Pompe disease
11. Source of Information: Genzyme Genetics, Thomas Jefferson University Lysosomal Diseases Testing Laboratory
12. Exploratory Medline Search:
  - a. "Pompe disease.mp. or exp Glycogen Storage Disease Type II" = 262
  - b. "Acid Alpha Glucosidase.mp." = 137
  - c. a and b (limit to humans) = 95

1. Gene Symbol: UROD Chromosomal Locus: 1p34
2. Protein Name: Uroporphyrinogen Decarboxylase
3. Disease: Porphyria cutanea tarda or symptomatic porphyria, or porphyria cutanea tarda symptomatica, or idiosyncratic porphyria (and Hepatoerythropoietic porphyria)
4. Description: Errors in the metabolism of heme. Porphyria cutanea tarda is cause by the heterozygous mutation status and Hepatoerythropoietic porphyria by the homozygous status. In the former there is a predominance of cutaneous manifestations and an onset usually in adult life. In the latter there is a large accumulation of porphyrins in the liver and in blood.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: blood
8. Methodology: analyte; enzyme assay; Analysis of the entire coding region: Mutation scanning; Analysis of the entire coding region: sequence analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Potentially applicable to the Medicare population
11. Source of Information: Genetests.org; Uptodate
12. Exploratory Medline Search (8/22/06):
  - a) "Porphyria cutanea tarda" = 1689 citations
  - b) "UROD" = 78 citations
  - c) "Porphyria cutanea tarda" and "UROD" = 33 (limit to humans)

1. Gene Symbol: GLC1B Chromosomal Locus: 2cen-q13;  
Gene Symbol: OPTN Chromosomal Locus: 10p15-p14;  
Gene Symbol: MYOC Chromosomal Locus: 1q24.3-q25.2
2. Protein Name: Optineurin; Myocilin
3. Disease: Primary open angle glaucoma
4. Description: The disease is characterized by elevated intraocular pressure. There are no anatomic factors that identify eyes that are at risk. There are no symptoms; the disease must be screened for and confirmed on comprehensive ophthalmic examination. Visual field loss cannot be recovered once it has occurred. The disease is common in older populations.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: blood
8. Methodology: Analysis of the entire coding region: Mutation scanning; Analysis of the entire coding region: Sequence analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Potentially eligible to the Medicare population.
11. Source of Information: Genetests.org; Uptodate
12. Exploratory Medline Search (8/22/06):
  - a) "open angle glaucoma" = 7890 citations
  - b) "OPTN" = 119 citations
  - c) "MYOC" = 151 citations
  - d) "open angle glaucoma" and ("OPTN" or "MYOC") = 131 citations

1. Gene Symbol: BMP2 Chromosomal Locus: 2q33
2. Protein Name: Bone morphogenetic protein receptor type II
3. Disease: Primary pulmonary hypertension
4. Description: The disease appears to be genetically transmitted as an autosomal dominant trait with incomplete penetrance. A responsible gene (BMP2) has been localized to chromosome 2 at locus 2q33, which results in defective function of the bone morphogenetic protein receptor type II (BMP2). High mean pulmonary arterial pressure at rest. Usually manifests as exertional dyspnea. Exertional chest pain, syncope, and edema are indications of more severe pulmonary hypertension and impaired right heart function.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; Deletion/duplication analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Potentially useful for the Medicare population.
11. Source of Information: Genetests.org; uptodate
12. Exploratory Medline Search (8/22/06):
  - a) "pulmonary hypertension" = 16398 citations
  - b) "BMP2" = 210 citations
  - c) "pulmonary hypertension" and "BMP2" = 111 citations (limit to humans)

1. Gene Symbol: FY Chromosomal Locus: 1q21-q22
2. Protein Name: Duffy antigen
3. Disease: NA
4. Description: Those with Duffy antigen are resistant to infection with Plasmodium vivax. The antibodies to Duffy antigen hemolytic transfusion reaction
5. Purpose: Prenatal diagnosis
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: NA
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Potentially applicable to the Medicare population
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/16/06):
  - a) "Red cell antigen\$" = 393 citations
  - b) "Duffy" = 978 citations
  - c) "FY" = 809 citations
  - d) ("Red cell antigen\$" or "Duffy") and "FY" = 177 citations (limit to humans)

1. Gene Symbol: SLC14A1 Chromosomal Locus: 18q11-q12
2. Protein Name: Urea Transporter, Erythrocyte (Solute Carrier Family 14, Member 1)
3. Disease: NA
4. Description: The Kidd blood group system is thought to be responsible for transporting urea across the red cell membrane and individuals are unable to concentrate their urine. Kidd blood group antibodies such as Anti-Jka, and to a lesser extent anti-Jkb, are responsible for a great percentage of serious hemolytic transfusion reactions
5. Purpose: Diagnostics
6. Availability: Clinical laboratory
7. Specimen: blood
8. Methodology: NA
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Potentially applicable to the Medicare population
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/16/06):
  - a) "Red cell antigen\$" = 393 citations
  - b) "Kidd" = 463 citations
  - c) "SLC14A1" = 11 citations
  - d) ("Red cell antigen\$" or "Kidd") and "SLC14A1" = 1 citation (limit to humans)

1. Gene Symbol: RHCE Chromosomal Locus: 1p36.2-p34
2. Protein Name: Blood group Rh(CE) polypeptide
3. Disease: NA
4. Description: Anti-e, which reacts with 98 percent of random donors, presents a problem with availability of compatible units, particularly in patients needing chronic transfusions. In autoimmune hemolytic anemia, a high percentage of autoantibodies demonstrate Rh system specificity, with anti-e being most commonly seen.
5. Purpose: Diagnostics
6. Availability: Clinical laboratory
7. Specimen: blood
8. Methodology: Targeted mutation analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Potentially applicable to the Medicare population.
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/16/06):
  - a) "Red cell antigen\$" = 393 citations
  - b) "Rh E" = 57 citations
  - c) "RHCE " = 159 citations
  - d) ("Red cell antigen\$" or "Rh E") and "RHCE" = 5 citations (limit to humans)

1. Gene Symbol: SLC4A1 Chromosomal Locus: 17q21-q22
2. Protein Name: Band 3 anion transport protein
3. Disease: Renal Tubular Acidosis, Distal, Autosomal Dominant
4. Description: Renal tubular acidosis refers to the development of metabolic acidosis because of a defect in the ability of the renal tubules to function properly. The impairment of the basolateral band III  $\text{Cl}^- / \text{HCO}_3^-$  exchanger in the alpha intercalated cells of the distal nephron results in the acidosis.
5. Purpose: Diagnostics
6. Availability: Clinical laboratory
7. Specimen: blood
8. Methodology: Sequence analysis; Deletion/duplication analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Potentially applicable to the Medicare population due to onset of end-stage renal disease.
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/16/06):
  - a) "Renal Tubular Acidosis" = 2478 citations
  - b) "SLC4A1" = 47 citations
  - c) "Renal Tubular Acidosis" and "SLC4A1" = 24 citations (limit to humans)

1. Gene Symbol: ATP6V0A4 Chromosomal Locus: 7q33-q34
2. Protein Name: Vacuolar proton translocating ATPase 116kDa subunit isoform 4
3. Disease: Renal Tubular Acidosis, Distal, Autosomal Recessive
4. Description: Renal tubular acidosis refers to the development of metabolic acidosis because of a defect in the ability of the renal tubules to function properly. The proton pump (ATP-ase) in the cells of the outer medullary collecting duct is affected, resulting in the acidosis.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; Deletion/duplication analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: potentially applicable due to the end stage renal disease.
11. Source of Information: Genetests.org; OMIM
12. Exploratory Medline Search (8/16/06):
  - a) "Renal Tubular Acidosis" = 2478 citations
  - b) "ATP6V0A4" = 13 citations
  - c) "Renal Tubular Acidosis" and "ATP6V0A4" = 8 citations (limit to humans)

1. Gene Symbol: PRPF3 Chromosomal Locus: 1q21.2
2. Protein Name: U4/U6 small nuclear ribonucleoprotein Prp3
3. Disease: Retinitis pigmentosa - PRPF3-Related Retinitis Pigmentosa
4. Description: Retinitis pigmentosa refers to a group of inherited disorders in which abnormalities of the photoreceptors (rods and cones) of the retina lead to progressive visual loss. The manner of inheritance is autosomal dominant. The loss of visual acuity is more pronounced in older individuals.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: blood
8. Methodology: linkage analysis; Sequence analysis of select exons
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Potentially applicable to the Medicare population.
11. Source of Information: Genetests.org; OMIM
12. Exploratory Medline Search (8/18/06):
  - a) "Retinitis pigmentosa" = 4847 citations
  - b) "PRPF3" = 14 citations
  - c) "Retinitis pigmentosa" and "PRPF3" = 6 citations (limit to humans)

1. Test Name: GNE Gene Mutation Testing
2. Protein Name: Bifunctional UDP-N-acetylglucosamine 2-epimerase/N-acetylmannosamine kinase
3. Disease: Sialuria
4. Description: Sialuria has been detected retrospectively in adults without any subjective signs or complaints of disease. Some signs and symptoms of sialuria include slightly flat and coarse faces, equivocal or mild hepatomegaly, microcytic anemia, frequent upper respiratory infections, episodes of gastroenteritis and dehydration, learning difficulties and seizures. GNE is the only gene known to be associated with sialuria.
5. Purpose: Diagnostic
6. Availability: Clinical laboratories
7. Specimen: Blood
8. Methodology: DNA sequence analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population:
  - a) Confirmation of the diagnosis
11. Source of Information: GeneTests.org
12. Exploratory Medline Search: (10/26/06)
  - a. "Sialuria.mp. or exp Sialic Acid Storage Disease" = 49
  - b. "GNE.mp" = 60
  - c. a and b (limit to humans) = 4

1. Gene Symbol: SOD1 Chromosomal Locus: 21q22.1
2. Protein Name: Superoxide dismutase (Cu-Zn)
3. Disease: SOD1-Related Amyotrophic Lateral Sclerosis
4. Description: Mutations in the SOD1 gene are associated with SOD1-Related Amyotrophic Lateral Sclerosis, a progressive neurodegenerative disease. This test is appropriate for any individual with ALS who has another affected family member or an incomplete family history, including the early death of a close relative from any cause, or to an affected individual with no family history of ALS. Approximately 20% of individuals with familial ALS have an identified disease causing mutation in SOD1. Molecular genetic testing for the other genetic forms of ALS are currently not clinically available.
5. Purpose: Diagnostic, Prognostic, Counseling
6. Availability: Clinical laboratories
7. Specimen: Blood
8. Methodology: Sequence analysis, Mutation analysis
9. Other Diseases: SBMA, SMA, hereditary spastic paraplegia
10. Clinical use(s) for the Medicare population: Useful (late onset)
  - a) Clarifying mode of inheritance
11. Source of Information: GeneTests.org
12. Exploratory Medline Search:(10/26/06)
  - a. "Amyotrophic Lateral Sclerosis"=9169
  - b. "SOD1-Related Amyotrophic Lateral Sclerosis"=14
  - c. a and b (limit to humans)=13

1. Gene Symbol: AR Chromosomal Locus: Xq11-q12
2. Protein Name: Androgen receptor
3. Disease: Spinal and Bulbar Muscular Atrophy
4. Description: Spinal and bulbar muscular atrophy (SBMA) is a gradually progressive neuromuscular disorder in which degeneration of lower motor neurons results in proximal muscle weakness, muscle atrophy, and fasciculations. SBMA is inherited in an X-linked manner. AR, the gene encoding the androgen receptor, is the only gene currently known to be associated with spinal and bulbar muscular atrophy.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Targeted mutation analysis
9. Other Diseases: Androgen insensitivity syndrome
10. Clinical use(s) for the Medicare population: Applicable as neurologic symptoms can be late onset
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/15/06):
  - a) "Spinal Muscular Atrophy" or "Bulbar Muscular Atrophy" or "Kennedy's Disease" or "SMBA" = 2063 citations
  - b) "AR" = 123 citations
  - c) "a" and "AR" = 107 citations (limit to humans)

1. Gene Symbol: ATXN2 Chromosomal Locus: 12q24
2. Protein Name: Ataxin-2
3. Disease: Spinocerebellar Ataxia Type 2
4. Description: Spinocerebellar ataxia type 2 (SCA2) is autosomal dominant inheritance characterized by progressive cerebellar ataxia, including nystagmus, slow saccadic eye movements and are associated with mutations in the *ATXN2* gene.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Targeted mutation analysis; linkage analysis; Mutation scanning
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Applicable as late onset is possible
11. Source of Information: Genetests.org
12. Exploratory Medline Search(8/14/06):
  - a) "Spinocerebellar Ataxia" or "SCA 2" = 4433 citations
  - b) "ATXN2" = 1 citations
  - c) "a" and "ATXN2" = 1 citations

1. Gene Symbol: ATXN3 Chromosomal Locus: 14q24.3-q31
2. Protein Name: Machado-Joseph disease protein 1
3. Disease: Spinocerebellar Ataxia Type 3
4. Description: SCA3 is characterized by progressive cerebellar ataxia and variable findings including a dystonic-rigid syndrome, a Parkinsonian syndrome, or a combined syndrome of dystonia and peripheral neuropathy. SCA3 is inherited in an autosomal dominant. The diagnosis of SCA3 rests upon the use of DNA-based testing to detect an abnormal CAG trinucleotide repeat expansion of the *MJD* gene.
5. Purpose: Diagnostic and prenatal diagnosis
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Targeted mutation analysis; Mutation scanning
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: May be useful as the disease onset is around 4<sup>th</sup> decade
11. Source of Information: Genetests.org
12. Exploratory Medline Search(8/14/06):
  - a) "Spinocerebellar Ataxia" or "SCA 3" or "Machado-Joseph Disease" or "MJD" or "Azorean Ataxia" = 4493 citations
  - b) "ATXN3" = 83 citations
  - c) "a" and "ATXN2" = 124 citations (limit to humans)

1. Gene Symbol: CACNA1A Chromosomal Locus: 19p13
2. Protein Name: Voltage-dependent P/Q-type calcium channel subunit alpha-1A
3. Disease: Spinocerebellar Ataxia Type 6
4. Description: Spinocerebellar ataxia type 6 (SCA6) is characterized by adult-onset, slowly progressive cerebellar ataxia, dysarthria, and nystagmus. *CACNA1A* is the only gene known to be associated with SCA6.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Targeted mutation analysis; Mutation scanning
9. Other Diseases: Episodic ataxia type 2; Familial hemiplegic migraine
10. Clinical use(s) for the Medicare population: Useful for diagnostic and management of late onset
11. Source of Information: Genetests.org
12. Exploratory Medline Search(8/15/06):
  - a) "Spinocerebellar Ataxia 6" or "SCA 6" = 3540 citations
  - b) "CACNA1A" = 299 citations
  - c) a and b = 71 citations (limit to humans)

1. Gene Symbol: ATXN7 Chromosomal Locus: 3p21.1-p12
2. Protein Name: Ataxin-7
3. Disease: Spinocerebellar Ataxia Type 7
4. Description: SCA7 in adults is characterized by abnormalities in color vision and central visual acuity, often presenting in the late teens or early 20's before the onset of cerebellar findings. The phenotype ranges from onset in infancy with an accelerated course and early death to onset in the fifth or occasionally sixth decade with slower disease progression. The disease is inherited autosomal dominant by the disease causing SAC7 allele.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Targeted mutation analysis; Mutation scanning; linkage analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: May be useful for the late onset type.
11. Source of Information: Genetests.org
12. Exploratory Medline Search(8/15/06):
  - a) "Spinocerebellar Ataxia" or "SCA 7" or "Hereditary Ataxia with Retinal Degeneration" = 4446 citations
  - b) "ATXN7" = 2 citations
  - c) "a" and "ATXN7" = 0 citations

1. Gene Symbol: ATXN8OS Chromosomal Locus: 13q21
2. Protein Name: ND
3. Disease: Spinocerebellar Ataxia Type 8
4. Description: SCA8 is a slowly progressive ataxia with disease onset typically occurring in adulthood. Onset has been reported from age one year to age 65 years. The progression is typically over decades regardless of the age of onset. Common initial symptoms are scanning dysarthria with a characteristic drawn-out slowness of speech and gait instability. The diagnosis of SCA8 must be confirmed by the presence of a CTA/CTG expansion in the *SCA8* gene.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Targeted mutation analysis; Mutation scanning
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Useful for diagnostic and management of late onset
11. Source of Information: Genetests.org
12. Exploratory Medline Search(8/15/06):
  - a) "Spinocerebellar Ataxia 8" or "SCA 8" = 3540 citations
  - b) "CTA/CTG" = 12 citations
  - c) a and b = 11 citations (limit to humans)

1. Gene Symbol: ATXN10 Chromosomal Locus: 22q13
2. Protein Name: Ataxin-10
3. Disease: Spinocerebellar Ataxia Type 10
4. Description: Spinocerebellar ataxia type 10 (SCA10) is an autosomal dominant disorder characterized by cerebellar ataxia and seizures. Most patients develop unsteady gait as the first symptom, while others may present with seizures. The age of onset is usually the third or fourth decade. The mutation associated with SCA10 was recently identified as a pentanucleotide repeat expansion in the SCA10 (also known as E46) gene that maps to chromosome 22q13-qter.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Targeted mutation analysis; Mutation scanning
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: May be useful for diagnostic in late onset disease type.
11. Source of Information: Genetests.org
12. Exploratory Medline Search(8/15/06):
  - a) "Spinocerebellar Ataxia" or "SCA 10" = 4314 citations
  - b) "ATXN10" = 1 citations
  - c) "a" and "ATXN10" = 0 citations

1. Gene Symbol: TBP Chromosomal Locus: 6q27
2. Protein Name: TATA-box binding protein
3. Disease: Spinocerebellar Ataxia Type 17
4. Description: SCA17 is characterized by ataxia, dementia, and involuntary movements, including chorea and dystonia. Psychiatric symptoms, pyramidal signs, and rigidity are common. The range of onset is 3-55 years of age. The diagnosis of SCA17 relies upon the use of molecular genetic testing to detect an abnormal CAA/CAG repeat expansion in the *TBP* gene.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Targeted mutation analysis; Mutation scanning
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Useful for diagnostic and management of late onset
11. Source of Information: Genetests.org
12. Exploratory Medline Search(8/15/06):
  - a) "Spinocerebellar Ataxia" or "SCA 17" = 4317 citations
  - b) "TBP" = 2108 citations
  - c) "a" and "TBP" = 27 citations (limit to humans)

1. Gene Symbol: SPG3A Chromosomal Locus: 14q11- q21
2. Protein Name: Atlastin
3. Disease: Spastic Paraplegia 3
4. Description: Hereditary Spastic Paraplegia is a slowly progressive lower extremity weakness and spasticity with autosomal dominant inheritance and mutations in the *SPG3A* gene
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Mutation scanning; Sequence analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Applicable for late onset
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/15/06):
  - a) "Spastic Paraplegia" or "SPG3" = 988 citations
  - b) "SPG3A" = 31 citations
  - c) "a" and "SPG3A" = 29 citations (limit to humans)

1. Gene Symbol: SPAST Chromosomal Locus: 2p22-p21
2. Protein Name: Spastin; Hereditary Spastic Paraplegia, Spastin Type; SPG4; Spastic Paraplegia 4
3. Disease: Spastic Paraplegia Type 4
4. Description: Mutations in SPG4 are responsible for the SPG4 type of spastic paraplegia, which is characterized by progressive bilateral lower limb spasticity. Onset of Spastic paraplegia type 4 (SPG4) is mostly in young adulthood, although symptoms may start as early as one year of age and as late as 76 years of age.
5. Purpose: Diagnostic, prognostic
6. Availability: Clinical laboratories
7. Specimen: Blood
8. Methodology: DNA sequence analysis, mutation scanning
9. Other Diseases: ND
10. Clinical use(s) for the Medicare population: Useful for late onset
  - a) Diagnostic testing
  - b) Predictive testing
11. Source of Information: GeneTests.org
12. Exploratory Medline Search: (10/27/06)
  - a. "spastic paraplegia Type 4" = 146
  - b. "SPAST" = 96
  - c. a and b (limit to humans) = 3

1. Gene Symbol: SPG7 Chromosomal Locus: 16q24.3
2. Protein Name: Paraplegin
3. Disease: Spastic Paraplegia 7
4. Description: Spastic paraplegia 7 (SPG7) is characterized by insidiously progressive bilateral lower limb weakness and spasticity. Most affected individuals have proximal or generalized weakness in the legs and impaired vibration sense. Onset is mostly in adulthood, although symptoms may start as early as age 11 years and as late as age 72 years. *SPG7* is the only gene known to be associated with SPG7
5. Purpose: Diagnostic
6. Availability: Clinical laboratory (Outside US)
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Applicable for diagnosis in late onset.
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/15/06):
  - a) "Spastic Paraplegia" or "Paraplegin" = 989 citations
  - b) "SPG7" = 45 citations
  - c) "a" and "SPG7" = 31 citations (limit to humans)

1. Gene Symbol: SMN1 (SMNt) Chromosomal Locus: 5q12.2-q13.3
2. Protein Name: Survival Motor Neuron Protein
3. Disease: Spinal Muscular Atrophy 4
4. Description: The SMN1 gene is believed to be the primary disease-causing gene in Spinal Muscular Atrophy (SMA) 4, which is characterized by progressive muscle weakness resulting from degeneration and loss of motor neuron cells in the spinal cord and brain stem nuclei. SMA Type 4 is the adult onset of the disease.
5. Purpose: Diagnostic, Prognostic
6. Availability: Clinical laboratories
7. Specimen: Blood
8. Methodology: Targeted sequence analysis, mutation analysis
9. Other Diseases: Amyotrophic lateral sclerosis
10. Clinical use(s) for the Medicare population: Useful for SMA 4 which is adult onset type
  - a) Diagnostic testing
11. Source of Information: GeneTests.org
12. Exploratory Medline Search: (10/26/06)
  - a. "Spinal muscular atrophy type 4" = 603
  - b. "SMN1" = 210
  - c. a and b (limit to humans) = 63

1. Gene Symbol: PPP2R2B Chromosomal Locus: 5q31-q33
2. Protein Name: Serine/threonine protein phosphatase 2A, 55 kDa regulatory subunit B beta isoform
3. Disease: Spinocerebellar Ataxia Type 12 (SCA12)
4. Description: In the presence of a clinical syndrome consistent with Spinocerebellar Ataxia Type 12 (SCA12), an expansion of 51 or more CAG triplets in the PPP2R2B gene is diagnostic of SCA12. Onset of disease is in the fourth decade, slowly progressing to ataxia. Spinocerebellar ataxia type 12 (SCA12) is characterized by onset of tremor in the fourth decade, slowly progressing to include ataxia and other cerebellar and cortical signs.
5. Purpose: Diagnostic
6. Availability: Clinical laboratories
7. Specimen: Blood
8. Methodology: Targeted mutation analysis
9. Other Diseases: ND
10. Clinical use(s) for the Medicare population: Useful for diagnostic purposes (late onset)
11. Source of Information: GeneTests.org
12. Exploratory Medline Search: (10/26/06)
  - a. "Spinocerebellar ataxia" = 432
  - b. "PPP2R2B" = 13
  - c. a and b (limit to humans) = 8

1. Gene Symbol: PRKCG Chromosomal Locus: 19q13.4
2. Protein Name: Protein kinase C, gamma type
3. Disease: Spinocerebellar ataxia type 14 (SCA14)
4. Description: Onset of spinocerebellar ataxia type 14 (SCA14) ranges from childhood to the sixth decade. A mutation in the PRKCG gene is associated with SCA14. Spinocerebellar ataxia type 14 (SCA14) is characterized by a slowly progressive cerebellar ataxia, dysarthria, and nystagmus. Subjects with SCA14 have normal life span. Axial myoclonus, cognitive impairment, tremor, and sensory loss may also be observed.
5. Purpose: Diagnostic, prognostic
6. Availability: Clinical laboratories
7. Specimen: blood
8. Methodology: PCR – direct sequencing
9. Other Diseases: retinitis pigmentosa type 11 maps to the same chromosome
10. Clinical use(s) for the Medicare population: Late onset and useful for diagnostic testing.
11. Source of Information: GeneTests.org
12. Exploratory Medline Search: (10/26/06)
  - a. “Spinocerebellar ataxia type 14”= 396
  - b. “PRKCG” = 340
  - c. a and b (limit to humans) = 14

1. Gene Symbol: MTHFR; Chromosomal Locus: 1p36.3
2. Protein Name: Methylene tetrahydrofolate reductase
3. Disease: Thrombophilia
4. Description: Increased plasma homocysteine levels, which is associated with homozygosity for a nucleotide variant in the methylene tetrahydrofolate reductase (MTHFR) gene. The MTHFR 677 C-T variant (leading to an alanine to valine substitution) results in a thermolabile enzyme and decreased production of folate, which is a cofactor required for homocysteine remethylation. Homozygosity for the MTHFR 677 C-T variant is associated with mild to moderate hyperhomocysteinemia.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Targeted mutation analysis, Analyte
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Applicable to elderly and for folate supplementation
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/11/06):
  - a) "Thrombophilia"=17,300
  - b) "MTHFR"=2500
  - c) "Thrombophilia" and "MTHFR"=320

1. Gene Symbol: *PROS1* Chromosomal Locus: 3p11.1-q11.2
2. Protein Name: Vitamin K-dependent protein S
3. Description: Deficiencies of protein S increase the risk of thrombosis about 10-fold in heterozygotes, with the highest risk for antithrombin deficiency. Major structural defects in the *PROS1* gene is associated with thrombotic event and had significantly lower total and free protein S levels than those relatives having missense mutations
4. Purpose: Diagnostic
5. Availability: Clinical laboratory
6. Specimen: Blood
7. Methodology: Analysis of the entire coding region: Sequence analysis, Targeted mutation analysis
8. Disease: Thrombophilia
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Applicable for those with late onset thrombosis
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/11/06):
  - a) "Protein S deficiency" = 1140
  - b) "PROS1"=40
  - c) "Protein S deficiency" and "PROS1"=28

1. Gene Symbol: F5 Chromosomal Locus: 1q23
2. Protein Name: Coagulation factor V
3. Disease: Thrombophilia
4. Description: The presence of the R2 polymorphism in the factor V gene increases the likelihood of thrombosis in factor V Leiden heterozygotes. The R2 polymorphism is very common, occurring in 1 in 10 individuals.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Targeted mutation analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Applicable to those diagnosed later ages.
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/11/06):
  - a) "Factor V R2 Mutation Thrombophilia"=6

1. Gene Symbol: F5 Chromosomal Locus: 1q23
2. Protein Name: Coagulation factor V
3. Disease: Thrombophilia
4. Description: Factor V Leiden Thrombophilia / Factor V Leiden Mutation / Hereditary Resistance to Activated Protein C is characterized by a poor anticoagulant response to activated protein C (APC) and an increased risk of venous thromboembolism. *F5* is the only gene associated with factor V Leiden thrombophilia.
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Targeted mutation analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Applicable to those with recurrent venous thromboembolism
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/11/06):
  - a) "Factor V Leiden Thrombophilia"=1280
  - b) "F5 gene" = 220
  - c) "Factor V Leiden Thrombophilia" and "F5 gene"=25

1. Gene Symbol: TTR Chromosomal Locus: 18q11.2-q12.1
2. Protein Name: Transthyretin
3. Disease: Transthyretin amyloidosis
4. Description: Transthyretin amyloidosis is inherited autosomal dominant disease and characterized by a slowly progressive peripheral sensorimotor neuropathy and autonomic neuropathy as well as non-neuropathic changes of nephropathy, cardiomyopathy, vitreous opacities, and CNS amyloidosis. Onset is usually in the third or fourth decade, but may be later
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; Sequence analysis of select exons; Targeted mutation analysis; Protein analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Applicable as the disease is late onset
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/11/06):
  - a) “transthyretin” = 1831 citations
  - b) “Familial Amyloid Cardiomyopathy” = 16 citations
  - c) “Familial Amyloid Polyneuropathy” = 371 citations
  - d) “Familial Oculoleptomeningeal Amyloidosis” = 3 citations
  - e) “Leptomeningeal Amyloidosis” = 7 citations
  - f) “a-e” = 2052 citations
  - g) “TTR” = 1031 citations
  - h) “F” and “TTR” = 659 citations (limit to humans)

1. Gene Symbol: TSC1 Chromosomal Locus: 9q34
2. Protein Name: Hamartin
3. Disease: Tuberous sclerosis I
4. Description: Tuberous sclerosis complex (TSC) involves abnormalities of the skin (hypomelanotic macules, facial angiofibromas, shagreen patches, fibrous facial plaques, unguual fibromas), brain (cortical tubers, subependymal nodules, seizures, mental retardation/developmental delay), kidney (angiomyolipomas, cysts), and heart (rhabdomyomas, arrhythmias). CNS tumors are the leading cause of morbidity and mortality, while renal disease is the second leading cause of early death. Two causative genes, TSC1 and TSC2, have been identified of which TSC1 is associated with tuberous sclerosis I
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis; Sequence analysis of select exons, Targeted mutation analysis
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Diagnostic for the category of mild form of disease
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/11/06):
  - a) "Tuberous sclerosis" = 3265 citations
  - b) "TSC1" = 416 citations
  - c) "Tuberous sclerosis" and "TSC1" = 260 citations (limit to humans)

1. Gene Symbol: TSC2 Chromosomal Locus: 16p13.3
2. Protein Name: Tuberin
3. Disease: Tuberous sclerosis 2
4. Description: Tuberous sclerosis complex (TSC) involves abnormalities of the skin (hypomelanotic macules, facial angiofibromas, shagreen patches, fibrous facial plaques, unguinal fibromas), brain (cortical tubers, subependymal nodules, seizures, mental retardation/developmental delay), kidney (angiomyolipomas, cysts), and heart (rhabdomyomas, arrhythmias). CNS tumors are the leading cause of morbidity and mortality, while renal disease is the second leading cause of early death. Two causative genes, TSC1 and TSC2, have been identified of which TSC2 is associated with tuberous sclerosis II
5. Purpose: Diagnostic
6. Availability: Clinical laboratory
7. Specimen: Blood
8. Methodology: Analysis of the entire coding region: Sequence analysis, Deletion/duplication analysis; Sequence analysis of select exons
9. Other Diseases: NA
10. Clinical use(s) for the Medicare population: Diagnostic for the mild category of disease
11. Source of Information: Genetests.org
12. Exploratory Medline Search (8/11/06):
  - a) "Tuberous sclerosis" = 3488 citations
  - b) "TSC2" = 593 citations
  - c) "Tuberous sclerosis" and "TSC2" = 430 citations

1. Test Name: Xdx Allomap Molecular expression testing
2. Other Names: Allomap testing
3. Description: The expression level of 20 genes is measured and translated using a mathematical algorithm into a clinically actionable AlloMap score.
4. Purpose: The assay measures signals from multiple immune system genes and pathways correlated with acute cellular rejection. Identifies non-invasively patients who are at low risk for acute cellular rejection.
5. Availability: Xdx expression diagnostics
6. Specimen: Blood
7. Methodology: Messenger RNA expression using quantitative real-time polymerase chain reaction (qRT-PCR)
8. Disease: Transplant recipients
9. Other Diseases: none
10. Clinical use(s): Non invasive method of identifying acute cellular rejection
11. Source of Information: [www.allomap.com](http://www.allomap.com)
12. Exploratory Medline Search:
  - a) allomap gene expression = 2 studies