Genetic Disorders: Implications for Allied Health Professionals: Two Case Studies

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ABSTRACT
With advances in study of the human genome, increasingly accurate genetic testing has become available. Genetic-based birth defects may result in progressive dysfunction. Consequently, because of the negative associations, many people do not want to consider prognostication testing or accept the most appropriate treatments. The allied health practitioner may see this as counter to the goal of optimal health care. However, consideration must be given to the patient’s comfort with advanced knowledge. In this paper we discuss ethical, legal, and social implications of genetic testing and how these relate to patients seen in an allied health environment. First, background on genetic disorders, their causes, and how they are characterized is presented. Then two case studies are described. One is a 50-year female with Huntington’s disease (chorea), an inherited autosomal dominant condition leading to central nervous system deterioration. The second is a 5-year boy with Stickler syndrome, a hereditary autosomal dominant connective tissue disorder affecting Type II collagen. Symptoms, therapeutic approaches, and long term prognoses are discussed. Working with patients having genetic disorders presents unique challenges for allied health professionals because of the social and political implications of these maladies. Suggestions are provided on how allied health professionals may respond to these issues.

INTRODUCTION
Following the initiation of the Human Genome Project in 1990 the amount of information related to human genes and their contribution to disease has grown substantially. In addition to the understanding of rare genetic disorders, the documentation of genetic variation is also contributing to the understanding of the genetic component of more common conditions such as mental illnesses, heart disease, certain forms of cancer, mental retardation, and developmental disabilities. Genetic advances have had a significant impact on health care delivery. The information emerging from the Human Genome Project indicates that all health professionals who serve individuals with genetic conditions (overt or potential) would benefit by being informed of the new genetic advances and their ethical, legal and social implications.
Unfortunately, US society has the potential for serious prejudicial restrictions on individuals who have been identified with genetic disorders. Employers may be unwilling to hire workers with identified genetic disorders, and insurance coverage could be denied based solely on diagnosis. In general, opportunities for education, recreation, or vocation could be curtailed. For these reasons, as well as the natural inclination of an individual to not want to know his or her fate, many people are unwilling to undergo genetic testing. This paper will demonstrate the importance of fore-knowledge related to two genetic conditions and how appropriate care can improve the lives of these patients.

Genetic disorders and birth defects are among the leading causes of infant morbidity and mortality. Two to three percent of all newborns are born with some type of birth defect and one-third of infant mortality in the United States is due to birth defects associated with a genetic component. Additionally, genetic disorders account for about 30-50% of all pediatric hospital admissions.

Although the study of genetics has clear implications for children, there is growing evidence of genetic implications for adult onset disorders, and the Human Genome Project may help in the identification of patients who are predisposed to a disease. Progress in the identification of genes has included markers for more than 1200 disorders, including cancer, metabolic disorders, cardiovascular disorders, neurological and psychiatric disorders. Many of these advances have been due to the ability of the Human Genome Project to unravel the mysteries of the cells in our bodies by locating and identifying the estimated 100,000 genes within 23 pairs of chromosomes. The nucleotides of the DNA combined can encode an estimated 3 billion bits of information by arranging four amines in varying orders: adenine, cytosine, thymine, guanine. (These amines are usually represented by four letters: A, C, T, and G, respectively.) Gene location and identification has been based on sequencing and mapping the bits of DNA information, which has allowed determination of the function of each gene and its relationship to disease and other human characteristics.

Allied health professionals are often the first contact many people have with the health care system. In addition, the nature of allied health care may involve extensive and prolonged interaction with a patient, resulting in a level of rapport rarely attained with other members of the medical team. This can provide the allied health practitioner with the opportunity to gain insight, not only into a patient's physical condition, but also their psychological state. Patients should first be counseled on the value of learning the long term prognosis of a genetic disorder. Then adaptive mechanisms can be brought into play. These might include appropriate vocational adaptations and career adjustments, in addition to rehabilitative approaches to ameliorate, retard, or reverse physical limitations.

Knowledge of genetic conditions and the impact these conditions may have on client treatments and their emotional responses should be important to allied health professionals because of the unique position in the health care hierarchy which allied health occupies. Physical, occupational, and speech therapists may be the first health care practitioners to 1) suspect that clients have a genetic condition, 2) label or diagnose behavioral symptoms that have a genetic component, 3) recommend further evaluations including genetic testing, 4) interpret and discuss results of testing and diagnosis, 5) influence attitudes and decisions of clients about participating in genetic testing or research, 6) provide referrals to other resources including genetic counselors or support groups, and 7) provide suggestions and education related to coping with and adjusting to a genetic condition.

TYPES OF GENETIC DISORDERS
Genetic disorders can be divided into four categories: single gene disorders, mitochondrial disorders (a special subclass of single gene disorders), chromosomal disorders, and multifactorial conditions.

Single Gene Disorders
Health care professionals are most familiar with the concept of single gene disorders. These disorders, also known as Mendelian disorders, are rare, occurring in approximately 1% of the population. Single gene disorders are caused by an error in a single unit of the genetic information.

One category of single gene disorders is autosomal dominant, which includes Huntington’s disease, achondroplasia, neurofibromatosis, Marfan’s syndrome, and certain types of breast and colon cancer. In these conditions, a parent will have the defective gene, and there is a 50% chance of the child being affected. Men and women are affected equally. Although autosomal dominant conditions are usually inherited, they can occur as a result of a fresh mutation (a change in the sperm or egg at the time of fertilization).

Autosomal recessive disorders, another category of single gene disorders, only occur when both parents are carriers of the gene mutation. A carrier of a gene mutation has no symptoms and is usually unaware of his or her status until a child is born affected.
As with autosomal dominant disorders, males and females are equally affected by autosomal recessive disorders. Autosomal recessive disorders are typically metabolic disorders resulting in enzyme deficiencies. Although rare in the general population, they occur more frequently among certain ethnic or racial populations. Cystic fibrosis, sickle cell anemia, and Tay Sachs disease are commonly known forms of autosomal recessive disorders. Cystic fibrosis is the most common autosomal recessive disorder in Caucasian children with an incidence of 1/2500 (0.04%) of newborns. Sickle cell anemia is the most common genetic disorder affecting African-Americans, occurring in 1/500 African-Americans, and it is estimated that 10% of the African-American population are carriers of the sickle cell gene. Extremely rare in most populations, Tay Sachs disease has an estimated incidence of 1/3600 (0.03%) births from parents in the Ashkenazi Jewish population.  

X-linked disorders such as Duchenne’s muscular dystrophy, fragile X syndrome, and hemophilia are single gene disorders. X-linked disorders involve mutant genes on the X (female) sex chromosome. Genetic testing is available for many X-linked disorders. Female carriers have a 50% chance of passing on the defective gene. Males are primarily affected because males have no normal second X gene to compensate for the defective gene.  

Mitochondrial Disorders  
Because of the presence of a few genes within the cytoplasm of the mitochondria, a special subcategory of single-gene disorders has been identified. At birth some infants with these conditions may be severely affected, but in general, only 25% display symptoms. By puberty, 90% will be symptomatic. This may be because muscle function and energy management become progressively more important as the child grows larger. Empiric recurrence risk for true mitochondrial diseases are about 3% for siblings and 6% for offspring. The affected genes are structurally altered and result in defective energy production and severe adult onset disorders. Dysfunction is especially noticeable in tissues requiring a high utilization of ATP, such as nerve, muscle, kidney, and liver. Mitochondrial disorders include certain types of blindness such as Leber’s optic neuropathy, muscle disease, epilepsy, and dementias associated with aging. Mitochondrial encephalo-myopathy and lactic acidosis (MELA) is an adult onset progressive neurological disorder marked by episodes of strokes and dementia. Mitochondrial disorders can only be inherited from the mother.  

Chromosomal Disorders  
Chromosomal disorders occur when a fertilized egg has too few or too many chromosomes. These occur in 0.7% of all newborns, but account for 50% of all first trimester spontaneous abortions and 10-15% of individuals with severe mental disorders and/or congenital malformations. Most chromosome disorders, such as Down syndrome, trisomy 18, trisomy 13, and Cri du chat, are characterized by mental retardation, unique physical features, and an increased incidence of congenital anomalies. Chromosome disorders on the sex chromosomes (Klinefelter syndrome and Turner syndrome) are usually characterized by learning disabilities and short or tall stature. In general, chromosomal abnormalities represent independent events with a low risk for occurrence in other family members.  

Multifactorial Disorders  
Multifactorial disorders are the most common form of genetic disorders in the general population and account for visible birth defects (cleft lip, cleft palate, spina bifida), chronic conditions (diabetes), and adult onset disorders (schizophrenia, coronary artery disease). Incidence varies among different populations, but overall, of the 3% of births having some level of birth defects, 20% are believed to be multifactorial disorders. Risk to siblings or offspring are estimated to be between 2 to 6% when there is one affected individual in the family. In multifactorial disorders, there is no single error in genetic information but rather a combination of environmental factors with one or more small variations in genetic material that together produce a serious defect. Environmental factors may include psychological and emotional stress, environmental toxins, allergens and diet.  

**ETHICAL, LEGAL AND SOCIAL IMPLICATIONS OF GENOME MAPPING**  
Enormous progress has been made over the last 20 years in the isolation of specific genes and the mapping of those genes to a precise location on particular chromosomes. Implications of this progress are far reaching. In addition to identifying causal factors of specific conditions, medical services can be developed and targeted to groups or individuals. Some of the more common services that have been developed to screen individuals at high risk for genetic conditions are listed in Table 1.
Table 1. Screening for High Risk Genetic Conditions

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<td>1</td>
<td>Newborn screening for inborn errors of metabolism</td>
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<td>2</td>
<td>Blood typing of pregnant women with emphasis on the Rh response</td>
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<tr>
<td>3</td>
<td>Prenatal triple screening for fetal markers</td>
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<td>4</td>
<td>Prenatal diagnosis in advanced maternal age and in selected families</td>
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<tr>
<td>5</td>
<td>Heterozygote screening of certain ethnic populations for detection of carriers</td>
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Because of this ability to now identify genetic risks, ethical, legal and social questions may be raised pertaining to these individuals and their families. Specifically, the Human Genome Project has identified four areas that require discussion and reflection among health care practitioners and their patients. These areas include:

- Privacy and fair use of genetic information
- Responsible clinical integration of genetic information
- Stigmatization and discrimination based on genetic traits
- Professional and public education.

Questions that therapists may consider regarding these issues are presented in Table 2.

Table 2. Questions Pertaining to Genetic Screening Information.

<table>
<thead>
<tr>
<th>Privacy and fair use of genetic information</th>
<th>Should genetic information be treated differently from other medical information in reports, charts, or other medical records?</th>
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<td>Should written informed consent be obtained from clients before their genetic information is shared with third parties?</td>
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<td>After taking a genetic test, should clients have the right not to be told the results?</td>
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<td>Responsible integration of genetic information</td>
<td>Should health care professionals provide patients and families with developmental prognoses based on genetic screening results?</td>
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<td>Should parents be able to have their children tested for genetic conditions that do not show symptoms until adulthood if the conditions are neither treatable nor preventable?</td>
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<td>If a health care professional suspects that a patient has a genetic condition that is not diagnosed, does he or she have a professional obligation to share this information? If so, with whom?</td>
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<tr>
<td>Preventing stigmatization and discrimination based on genetic traits</td>
<td>What role should society have to ensure fairness in the use of genetic information by health insurers and employers?</td>
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<td></td>
<td>What role should professionals have in helping to prevent stigmatization of people with genetic conditions?</td>
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<td></td>
<td>What are some of the racial/ethnic issues in genetics that professionals should consider?</td>
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<tr>
<td>Professional and public education</td>
<td>What should professional associations do to help ensure their members’ professional competence in the new genetics?</td>
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<td></td>
<td>What role should health care professionals have in educating their patients about the implications of the genetics?</td>
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CASE STUDIES

The following two case studies have been chosen to illustrate the factors a therapist should consider when working with individuals having conditions of genetic origin. One of these cases demonstrates the ELSI issues for conditions that are present in adulthood (Huntington’s disease), and one, in childhood (Stickler syndrome).
Genetic Disorders: Implications for Allied Health Professionals: Two Case Studies.

Case 1: Huntington’s Disease
Huntington’s disease (HD), first described in 1872, has three hallmark features: chorea, clear hereditary link, and the tendency for individuals with HD to have mental illness and commit suicide.11 Huntington's disease is an inherited autosomal dominant condition leading to central nervous system cell death. This nervous system disorder is related to degeneration in the basal ganglia including the caudate nucleus, striatal neurons, and the putamen. The dementia is associated with atrophy of the cortex.14 HD is a relatively rare condition affecting 6.5 persons per 100,000 (0.0065 %).11

Persons at risk may now be identified because of the specificity of the gene responsible for the condition. The condition is a single gene disorder associated with increased length of a CAG protein in the gene called “huntington” located on the short arm of chromosome 4p16.3.12-14 The mutation has a high penetrance (individuals who test positive for the mutation will eventually display symptoms of the condition). Children of fathers affected by HD are more likely to display an early onset of the condition as compared to children of affected mothers. This phenomenon is a consequence of genomic imprinting.14-17

Diagnosis is made primarily through family history and/or genetic testing and magnetic resonance imaging studies. The MRI reveals the characteristic atrophy of the basal ganglia.14 Onset is generally in early middle age (mid 30’s to 40’s), but can occur in childhood (juvenile HD). Individuals may display early psychotic and behavioral symptoms (memory loss, intellectual decline, hallucinations, lack of motivation, paranoia) up to 10 years prior to symptoms of chorea.12-14 Individuals with HD survive 1-40 years following onset, with a median of 21 years. Early onset of HD usually leads to rapid progression and early death. Death is usually related to pneumonia and cardiovascular complications.18

As shown in Table 3, symptoms can be categorized as either neuromotor or psychiatric in nature.12,14,18

<table>
<thead>
<tr>
<th>Category</th>
<th>Symptoms</th>
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<tr>
<td>Neuromotor</td>
<td>Chorea, dystonic movements, eye movement abnormalities, rigidity, bradykinesia, cerebellar dysfunction, upper motor neuron abnormalities, epilepsy, myoclonus.</td>
</tr>
<tr>
<td>Psychiatric</td>
<td>Schizophrenia, paranoia, depression, dementia</td>
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Progression of the condition takes place over a number of years.20 The Huntington’s Disease Functional Capacity Scale24 categorizes an individual’s functional performance in five areas: occupation, financial affairs, domestic responsibilities, activities of daily living, and living situation. The stages describe the capacity of the individual to perform tasks in each area ranging from stage 1 indicating full participation to stage 5 indicating complete inability.

Currently there is no treatment for HD. While attempts at pharmacological intervention to slow the progression of motor symptoms have been made, there has been very little success. The medications used to control the choreiform movements (halopenital, perpherazine, resperpine) often lead to side effects including decreased alertness, depression, and drowsiness.19 The psychiatric disorders have been treated with psychotropic medications to alleviate symptoms again leading to side effects such as tardive dyskinesia.14

Implications for Physical and Occupational Therapy
An individual with HD is likely to seek physical or occupational therapy treatment when gait abnormalities and difficulty with activities of daily living (ADL’s) become apparent.20,21 The motor impairments such as chorea, dystonic movements, eye movement abnormalities, rigidity, and bradykinesia will eventually lead to the individual’s inability to perform ADL’s independently. Physical and occupational therapy efforts may reasonably focus on optimizing the individual’s quality of life although the condition will inevitably progress to complete dependence on others for mobility and self care.28 Therefore health care professionals should also provide anticipatory guidance and education to the family or other caregivers so they will know what to expect. Assistive technology may also be prescribed as needed.14

The Huntington’s Disease Total Functional Capacity Scale (TFC) can be used longitudinally to follow the progression of the condition and track its impact on functional skills.22 This scale specifically focuses on the individual’s functional capabilities. Unfortunately there is a dearth of information on how therapeutic interventions can be specifically used to address the needs of individuals with HD.
The following case presents an example of how a physical therapist may approach the management of an individual with Huntington’s Disease (HD). Other allied health practitioners may be similarly involved.

Examination

History and Systems Review: Ms. J was a 50-year woman, referred to outpatient physical therapy because of mild clumsiness and balance problems. Although she had not fallen, her physician felt she was at increased risk for falling. Ms. J had not been formally diagnosed with Huntington’s disease. However, her father died from complications of the disease five years previously. She chose not to be tested for the Huntington gene mutation. Through MRI examination, mild degeneration of the caudate and putamen was identified. Past medical history included treatment for depression. The physician felt that there was sufficient cause to establish suspicion of HD.

Ms. J was an active woman and avid bike rider. She regularly rode to work a distance of about 7 miles and had participated in many bike adventure trips. She was employed by a large company as an administrative assistant. She was married and had a 15-year son at the time of referral.

Tests and Measures

Aerobic capacity and endurance: This patient’s resting heart rate was 80 bpm, with blood pressure of 100/70.

Arousal, attention and cognition: Ms. J was oriented to person, place and time. She did not feel that her memory or attention had diminished, nor did her family report any personality changes.

Sensation, integrity and reflex integrity: Sensation to light touch, pinprick and proprioception was intact. Deep tendon reflexes were brisk without clonus.

Motor function: Ms. J demonstrated mild, low amplitude, increasing to high amplitude (under stress), choreiform movement. Finger to thumb tapping and diadochokinesia was arrhythmic and slow. She displayed mild bilateral in coordination with finger-to-nose and finger-to-finger tests. Her ability to bike to work was only minimally affected at the time of referral. She rode slowly and cautiously. Some days she had to convince herself to bike because she felt so tired.

Range of motion and muscle performance: Passive and active range of motion were within normal limits. Muscle strength was generally 4/5.

Gait, locomotion, and balance: This patient could sit independently without any back support for an indefinite period of time. She could stand up from a sitting position without assistance, but slowly. She stood independently without support. Although she could stand with her feet together, her gait was wide-based. Walking on a flat surface, ascending and descending stairs, and on uneven terrain were all within normal limits. She had difficulty with tandem walking and heel-to-toe walking.

Self-care and home management: She planed and made all family meals and completed all household tasks. Ms. J complained that she was slower performing these tasks, and she felt disorganized. She was independent with all her self help skills. Her home was a large two-story house where most of the flooring was wood with a variety of floor coverings.

Evaluation, Diagnosis, Prognosis

Ms. J scored 11/13 on the Huntington’s Disease Functional Capacity Scale. She did not report difficulty performing her job related tasks. She did require some assistance with domestic and financial affairs due to her lack of organization. She was living at home and was independent with all self care and home management. Due to the choreiform movements, Ms. J was beginning to experience difficulty with driving, especially at night. This impacted her ability to drive her son to his sporting events. She had been actively involved in organizing fundraisers, practices and other team related events for her son, but was considering dropping these activities.

At the time of this writing Ms. J’s deficits were very minimal. According to the Huntington’s Disease Functional Capacity Scale, she was at Stage 1 of the condition. She was independent with all of her ADL’s. She was continuing her work as a secretary and was able to carry out her household responsibilities with minimal assistance. On some days she did not feel comfortable biking or driving to work, so she would take the bus, which required additional planning. She was especially concerned about being able to maintain her biking ability.
Our therapeutic goals for this individual focused on maintaining her ability to complete all ADL's independently, preservation of present range of motion and strength, and overall preservation of her ability to move independently. To accomplish these goals, we recommended an exercise program to help maintain her range of motion and strength. In addition, anticipatory guidance was provided to her and her family about the consequences of HD and the need to plan for eventual movement limitations. She was instructed in relaxation strategies to decrease her stress and minimize her chorea movements. We also recommended that she take mini-breaks at work, which we believe would help her to stay focused and organized.

**Intervention**

Due to her status, ongoing intervention was not currently necessary. One to two sessions of education and anticipatory guidance were considered adequate as Ms. J and her family were knowledgeable about the consequences of the condition. Ms. J was encouraged to become involved in a 3-5 times per week community-based exercise program. This program consisted of a variety of aerobic activities such as stationary bike, treadmill, elliptical training, and aerobic exercise classes. Additionally, a comprehensive strength training program was designed. To maintain flexibility, Ms. J chose to participate in a flexibility and strength class and planned also to participate in a yoga program. Because biking was of particular concern to Ms. J, she engaged a trainer who was knowledgeable in biking exercises.

A variety of referral sources that she might benefit from over the course of the next 6 months were presented to Ms. J. These were intended to help her maintain an organized environment at home, continue with the performance of her household duties, and structure management of her financial affairs. The referrals included an organization specialist, a HD support group, a physical therapist who specialized in office ergonomics, and an occupational therapist who specialized in assistive technology.

**Re-examination and Goal Modification**

The median survival after diagnosis of Huntington’s disease is approximately 21 years; therefore, re-examination and follow-up for supportive needs may be needed. Because Ms. J indicated that she would like to maintain an active role in decision making regarding her condition for as long as possible, she will need to establish collaborative relationships with a variety of professionals. A 6-month re-examination with the physical therapist is appropriate. In addition to re-examining physical status and maintaining functional status, the therapist and Ms. J would be expected to discuss the need for any additional resources.

Understanding the progressive nature of the condition is imperative for the family to prepare themselves for future situations, physically and psychologically. As Ms. J’s condition deteriorates, physical therapy will modulate from a consultative role to a direct service provider. As the limitations become more severe, physical therapy goals will evolve from prevention to restoration to maintenance - with an increased emphasis on management of impairments. Comprehensive care for Ms. J would entail collaboration among a variety of professionals. Occupational therapy will be needed to address self-care issues; and speech pathology, to address communication, feeding and swallowing issues. Having the family maintain a link to rehabilitation services as the condition progresses may minimize feelings of isolation.

**Outcome**

This patient was provided with a variety of strategies to maintain safe ambulation, strength, and flexibility. Over the next decade, it is probable that she will become increasingly dependent on others for assistance with activities of daily living, home management, and professional responsibilities. Future issues for her will include dependence related to ADL’s, domestic management, and inability to work. Prior to her inability to continue working, her employer may need to make adaptations to her work environment in order to comply with ADA regulations. The adaptations may include changing her workstation, providing her with a time management device, and project management software to help her stay organized.

Although she had chosen not to get tested for the genetic mutation, we believe she should consider having her son tested. We have encouraged her to meet with a genetics counselor to discuss this. Ms. J’s decision to avoid genetic testing was based on the knowledge that there is currently no cure or specific effective treatment for HD, and she would not be able to change the eventuality of having HD. However, when her son reaches the age of maturity, he may choose to be tested. Knowing that he has the genetic mutation may help him to prepare for its eventual presentation. Unfortunately, this information also may lead to stigmatization and discrimination. There have been cases in which both health and life insurers have denied coverage to those with a genetic disease although the individuals were currently healthy. Additionally, when Ms. J’s son enters the workforce, he could experience workplace discrimination. Because there is an increased risk for suicide in this population, psychological counseling is an important service to which Ms. J’s son may desire access. Thus, any health insurance should include behavioral care.
**HD Summary**

Huntington’s disease is an autosomal dominant disease affecting the CNS system. The three hallmark features of the disease are choreiform movement, hereditary linkage, and dementia. The specific gene mutation has been localized, making it possible for family members of affected individuals to be tested pre-symptomatically. Before testing, the ethical, legal and social implications need to be identified, and the person undergoing the test should be made fully aware of the consequences of the outcome of those tests. A variety of support systems must be available for individuals and families. To date, there is no cure for the condition nor has there been any pharmacological intervention successful in slowing down the progression of the condition. Allied health professionals working in concert with the family may be able to establish a treatment plan that will address the physical, psychological, ethical, legal, and social parameters of a complex condition such as Huntington’s disease. Treatment plans should be coordinated among health care professionals because psychological support is as important as physical support for these patients.

Recent advances in genetic testing have the potential to change the management of HD as the family and individual now are able to choose to have additional testing. This would give them the opportunity to plan for future health care needs of the individual as well as supportive services for other family members. Therapeutic intervention can be specifically tailored to the provision of timely services while the patient is less affected, and additional therapy and equipment can be employed as the condition progresses. Allied Health professionals may also assist in providing resources should the family choose to think about future plans.

**Case 2: Stickler Syndrome**

Stickler syndrome (SS), or arthro-ophthal-myopathy, was identified in 1965 as a hereditary autosomal dominant connective tissue disorder affecting Type II collagen. One in 10,000 (.01%) persons are affected by this disorder. Malformations in ocular, orofacial, and musculoskeletal tissues are primarily seen in SS due to structural deficits of the collagen matrix. These tissues are affected because Type II collagen is the principal collagen in cartilage, the nucleus pulposus of the spine, the inner ear, and the vitreous humour of the eye. Some symptoms are initially recognized at birth. However, other symptoms are not easily recognized, and individuals may be diagnosed later in childhood or, although rarely, in adulthood. Mitral valve prolapse is seen in 46% of all persons affected, and sensorineural hearing loss can also occur. Although cognitive problems have been documented in one family, intelligence is usually normal.

The spectrum of impairments seen in persons with SS is due to mutations of the COL2A1 gene. Mutations in COL11A1, and COL11A2 have also been identified in families with SS. Those family members with evidence of abnormal COL2A1 and COL11A1 genes demonstrate a vitreo-retinal disorder and clinically present with ocular symptoms. Skeletal manifestations are displayed in persons with abnormalities in the COL11A1 and COL11A2 genes. Clinical symptoms without ocular involvement are found when only the COL11A2 gene is involved.

Specific physical characteristics found within families after clinical evaluation are referred to as phenotypic traits. These physical characteristics, along with numerous laboratory tests are used to group families and assist in making a diagnosis. However, depending on the gene found during testing, an individual can present with all of the manifestations of SS or just a few of the symptoms. Therefore, phenotypic variation among SS families is high, and a wide spectrum exists in the symptoms often reported in this population. This variability in phenotypic expression makes it difficult for the diagnosis of SS to be definitively made. Genetic familial linking is usually needed to determine the diagnosis and sub-classifications of these genes.

**Ocular**

Ocular dysfunctions are not unusual in persons with SS. These conditions are usually congenital and non-progressive. Moderate to severe myopia may occur as early as 1.5 years of age in children. Individuals may also have vitreo-retinal degeneration, retinal detachments, astigmatism, cataracts, strabismus, and glaucoma.

**Orofacial Structures**

Facial anomalies such as clefts of the soft or hard palate, micrognathia, mild facial hypoplasia, flat facies with depressed nasal bridge, and anteverted nares are all consistent with the diagnosis of Stickler syndrome. Children diagnosed with Pierre Robin (micrognathia, U-shaped palate, glossoptosis, respiratory difficulties and choking) are highly likely to have SS. The facial anomalies of micrognathia, mid facial hypoplasia, flat faces with depressed nasal bridge, anteverted nares, epicanthal folds, and prominent eyes seen in the infants and children are less apparent in adults.
Musculoskeletal
Eighth percent of persons with SS develop joint and musculoskeletal abnormalities secondary to the suspected collagen defect. At birth, the child may present with hypotonia, extremely large joints (specifically of the wrist, knees, and ankles), hypermobility, and talipes equinovarus. Degenerative changes during infancy are only detected on radiological findings. However, severe arthropathy may occur in childhood. Because of the connective tissue problems and associated joint defects, some children have been mistakenly diagnosed with juvenile rheumatoid arthritis while the diagnosis has been completely missed in others. Bony abnormalities continue throughout childhood. By the second decade, the child may develop flat vertebrae with anterior wedging, underdevelopment of the distal tibial epiphyses, and a flat irregular femoral epiphysis (spondyloepiphyseal dysplasia). These changes gradually lead to avascular necrosis, subluxation, chondrolysis, or slipped capital epiphysis. Osteoarthritis occurs in the third and fourth decades. Arthritic symptoms such as joint stiffness, pain, and discomfort in the weight bearing joints of the hips and knees often develop as persons approach middle age.

Strenuous exercise aggravates the joints and is followed by redness or warmth if the activity persists. Rest, modalities and non-weight bearing activities may alleviate these symptoms. Recommendations for total hip or knee replacements are made as degenerative changes advance. Skeletal abnormalities of scoliosis, kyphosis, lumbar lordosis, pectus excavatum, thoracic disc herniation, pes planus, genu valgus, and arachnodactyly occur less frequently but have also been documented in the literature.

Developmental Delay
There is some indication that developmental delay is caused by generalized hypotonia, muscular weakness, and the presence of small pharyngeal airways, which may lead to hypoxia. Sensorineural and conductive deafness are often present, and hearing loss contributes to speech and language delays.

Implications for Physical and Occupational Therapy
Due to the widespread physiological involvement of the Type II collagen pathology, there are several potential approaches for physical therapy intervention. The musculoskeletal abnormalities seen in individuals with SS can lead to a variety of impairments and functional limitations that might benefit from physical therapy. Paraplegia or severe lower extremity muscular weakness may occur due to thoracic spinal cord stenosis, disc herniation, or narrowing of the cervical intervertebral foramina. Because joint dislocation in the extremities can result from ligamentous laxity, external protection of the joints and strengthening of the associated muscles may be required to perform routine activities. Occupational therapy may be needed to provide protective devices and coping strategies. Orofacial anomalies restrict the airways during infancy, which might result in problems of respiration and swallowing and various feeding disorders. Delayed ambulation, lack of strength, and decreased endurance result from low tone or hypotonia. Individuals with Stickler syndrome often require vision training or adaptive devices to increase independence. Therefore, collaboration with an ophthalmologist is critical. Ocular manifestations may occur early in life, may only be associated with a few symptoms, or may even be asymptomatic initially.

Therapists routinely address the impairments identified during initial examination. Because of the abnormal structure or function of connective tissue, individuals with SS are at risk for continuous problems that will require physical therapy throughout their lives. Intervention to improve function must be approached conservatively due to the fragility of the musculoskeletal system. Table 4 lists guidelines to prevent excessive joint aggravation that can lead to joint pain, discomfort and limitations:

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<th>Table 4. Guidelines to Minimize Joint Problems in Stickler Syndrome Patients</th>
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<tr>
<td>Have patient/client wear proper well fitting shoes</td>
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<td>Teach isometrics and joint stabilization exercises</td>
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<tr>
<td>Use fewer repetitions to prevent joint discomfort during exercises</td>
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<tr>
<td>Teach joint protection activities</td>
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<td>Minimize high impact joint activities</td>
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Examination
**History and Systems Review:** John was a 5 ½-year boy with developmental delay when he was referred to physical therapy. He was born at 39 weeks gestation, following an uncomplicated vaginal delivery. He was diagnosed with Pierre Robin and Stickler syndrome at four days of life. He previously received physical therapy at 13 months because of scapular elevation and...
protraction during reaching in sitting. Delayed protective extension to the right, left, and backwards; inability to lower self to the floor; and wide based ambulation were noted at that time.

John was pleasant and alert during the examination. He was curious and explored his surroundings spontaneously. John's mother reported that he was clumsy, falling easily and that he had a history of glenohumeral subluxation.

**Tests and Measures**

**Aerobic Capacity and Endurance:** These were within normal limits for his age.

**Joint Integrity and Mobility:** Positive findings included excessive mobility at knees and ankles, ten degrees knee hyperextension bilaterally, bilateral pes planus, bilateral glenohumoral laxity, and generalized hypotonia. On passive movement, excessive mobility was found at the knees and feet and shoulders. No evidence of hip or shoulder subluxation was found.

**Arousal, Attention, Cognition:** John was alert and oriented to his environment. He explored the physical therapy setting and interacted with the therapist appropriately.

**Gait, Locomotion, Balance:** John could walk independently, but he had difficulty ascending/descending stairs and stepping on/off uneven surfaces. Static sitting balance was adequate to maintain position. Dynamic balance on the balance beam was poor because he had difficulty with tandem walking. He was unable to perform static single limb support without assistance, and he required moderate assistance to maintain an erect posture. His mother reported that John fell easily, mostly during ambulation on grass or uneven terrain.

**Posture:** Excessive trunk flexion was observed during sitting, but this was easily corrected with verbal cues.

**Self Care and Home Management:** This patient was independent in self care, transfers, walking (except for occasional falls), communication and social cognition. He was independent in toileting during the day. However, at night he required frequent assistance. He had not yet learned to tie his own shoes.

**Community and Work (Job, School, Play):** John had begun pre-kindergarten at the time of his examination. His teacher (reported via John's mother) had commented that he was a hard worker, but required additional assistance with the use of scissors and handwriting. His teacher was concerned about his safety as he had been noted to fall at least weekly on the playground.

**Motor Function:** Postural, equilibrium, and righting reactions were intact; equilibrium reactions were slightly delayed. Hopping, skipping, running, and jumping skills were difficult for him to perform. Some motor coordination was observed during these activities, but the timing and sequence of movements was poor.

On the Peabody Developmental Motor Scales, John achieved a mean motor age equivalent of 44.5 months (note that his actual age was 66 months), falling at the 1st percentile on the fine motor scale and the 2nd percentile on the gross motor scale. He looked very closely at the objects during the fine motor tasks. Difficulty with the use of scissors, blocks, buttons, and poor visual spatial perception, balance and coordination were observed. Mild muscle weakness was found in the proximal hip muscles, especially gluteus maximus and iliopsoas.

**Muscle Performance (Strength, Endurance):** Generalized hypotonia was present. Antigravity strength of the lower extremities was functional. He could climb stairs with support, but he was unable to leap frog or crab walk independently. Direct manual muscle testing revealed strength of 3/5 in lower extremity function.

**Evaluation, Diagnosis, Prognosis**

Based on the physical therapy examination we concluded that John had deficits in the areas of balance, coordination, strength, and visual spatial orientation. His score on the Peabody Developmental Motor Scale indicated a significant delay in the acquisition of developmental motor skills. His difficulties with upper extremity motor skills would be likely to increase his risk for motor/performance-based learning problems such as math, handwriting, and production work such as long written assignments. Additionally, because of lower extremity weakness, safety on the playground would be a concern and might limit his integration into school activities.
**Intervention**

John had been receiving school-based therapy services to enhance motor skill development, and to prevent falls. The PT treating John in school was collaborating with John’s regular therapist to increase lower extremity and trunk strength. In our clinic commercially–available orthotics with medial scaphoid pads to control excessive pronation were fitted for John. After eight weeks John’s function improved, and he began to independently ascend and descend stairs, climb on and off surfaces, pedal a large tricycle or bicycle with training wheels, and walk on uneven terrains. His frequency of falling was reduced to less than once/week.

Because he complained of pain with high impact activities requiring excessive movements (e.g. tennis, basketball, football), we recommended that his activities be limited to participation in low impact activities, which would be less stressful on his joints. Collaboration among interdisciplinary team members is important for early detection of any joint problems and the minimization of complications. John’s prognosis means that in the future he will likely require services from occupational therapy, audiology, speech-language pathology, as well as medical services from genetics, orthopedics rheumatology, and ophthalmology.

**Re-examination and Goal Modification**

Additional musculoskeletal problems may affect John during early adolescence. Around 10 years of age, joints in children with SS begin to take on irregular shapes. John will then run an increased risk of irregularities in his joints including the possibility of developing a slipped capital epiphysis. His musculoskeletal status will continue to deteriorate (including arthritic changes) as he reaches adulthood. Assistive devices for community ambulation or a brace for external joint support may be necessary. He may eventually require one or more total joint replacements. Other professionals such as an occupational therapist may be needed to monitor him for joint protection, visual spatial awareness, and sensory integration. Because of the progressive hearing loss that is common with SS, a speech-language pathologist may be needed as a major collaborator to design appropriate communication strategies. Consultation with members of a health team including a geneticist, orthopedist, rheumatologist, and ophthalmologist is advised for when John considers marriage so that he will be fully aware of all implications of his condition and how these would relate to producing and raising children.

**Expected Outcomes**

This patient can be expected to maintain functional ambulation skills and the ability to participate in non-contact, low risk physical activities throughout his childhood. However, participation in school sports will be limited. He may need therapeutic intervention intermittently throughout his lifetime. Because of physical safety concerns, career choices may be limited. For example, John should avoid physically demanding jobs. Additionally, because SS is genetic and is characterized by physical findings, insurance underwriters may deny coverage, and potential employers may be wary of hiring John.

**Stickler Syndrome Summary**

Children with SS have musculoskeletal, visual, and performance changes that will progressively worsen across their lifespans. Therapists should be aware of, not only, physical issues with SS, but also psychological issues related to this diagnosis and how these will influence both motor and social development. Successful intervention for patients will include muscle strengthening, joint protection, and integration into lifetime activities at appropriate levels. Ophthalmological, speech and occupational evaluation and therapeutic intervention will also be of great value for these children. Appropriate management and frequent re-examinations will contribute to optimal function for children growing up with this condition.

**OVERALL SUMMARY**

General issues of genetic testing including ethical considerations of the interaction between society and the individual have been raised in this paper. Whether an individual is better off knowing his or her long-term prognosis and whether this information should be available to future partners, employers, and insurance carriers is an arguable issue.

Case studies of an employed adult woman with Huntington’s disease and a pre-kindergartner with Stickler syndrome have been presented. In the first case, diagnosis was via symptoms rather than genetic testing, and the woman did not want her employer to know of her long-term prospects. She also did not want her son to be tested. In the second case, diagnosis was achieved via testing shortly after birth. The decision had not yet been considered about notification of employers and others, since this was a young child.

Appropriate physical therapy approaches can enhance function and minimize the inevitable deterioration associated with these genetic disorders. We believe that all allied health professionals should be fully aware of the course these disorders follow, and that long-term planning should be in place to optimally support the functions of these (and similar patients). In addition, the patients with known genetic disorders should be made fully aware of their long-term prognoses. Health care professionals such
as occupational therapists, speech and language therapists, and psychological counselors will be needed to contribute to the support of these patients.

Allied health professionals often have long term relationships with patients who have complex musculoskeletal conditions and with their families. Because of this close working relationship, these practitioners may be in a position to assist families with referrals for social assistance. Given the irreversible nature of genetic conditions such as Huntington’s disease and Stickler syndrome, many societal restrictions may be present that could interfere with integration into the community, especially involving participation in physical activities. Allied health professionals may suggest strategies to families to enhance participation in community based activities at appropriate levels, to assist with the development of a legal basis for inclusion into activities, and to ensure appropriate accommodations for the persons involved.

We believe allied health professionals should encourage the patient to receive genetic testing and appropriate counseling and to begin preparation for long-term intervention. Appropriate strategies for therapy and other health care can contribute to a better, more productive life than if the condition is ignored. Most likely, some political intervention in US society will be necessary to provide safeguards for individuals who are resisting knowledge of genetic-based defects because of potential prejudicial treatment. Other personal reasons may influence the patient’s hesitancy to undergo genetic testing, so these issues should be addressed with great sensitivity. We encourage all allied health professionals to support the concept of genetic testing and the need for legal protection of individuals with genetic-based health issues.

GLOSSARY*

- **Cell.** The smallest living structural unit in the body composed of a nucleus (present in the center) containing the chromosomes, an outer volume, containing the cytoplasm (where most metabolic functions are carried out), and a surrounding membrane.

- **Chromosomes.** These are strands inside cells that contain the genes. Humans have 46 chromosomes or 23 pairs. Half of each pair is derived from each parent. One of the pairs is the sex chromosome. Males have an X and Y chromosome, females have two X chromosomes. Eggs and sperms each contain 23 chromosomes.

- **Gene.** This is a package of DNA containing information for a particular function. It is estimated that there are 100,000 genes located on the chromosomes.

- **Gene Mapping.** Finding the exact location of a gene on a chromosome.

- **Gene Sequencing.** Reading the letters of DNA in the human model.


REFERENCES


