# DIAGNOSIS OF CEREBRAL PALSY
# A RESEARCH STATUS REPORT

**UCP Research and Educational Foundation**
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**THE UCP RESEARCH AND EDUCATIONAL FOUNDATION'S**
**RESEARCH PROGRAM**

# SUMMARY: RESEARCH ON DIAGNOSIS

- Cerebral palsy is a non-progressive disorder of the motor (muscle) control area of the developing brain.
- There are 550,000-764,000 persons in the USA with cerebral palsy; the number of new cases have increased 25% during the past decade; there are now 9,750 new cases/year.
- 70% of cerebral palsy occurs prior to birth (prenatal); 20% occurs during the birthing period (perinatal); 10% occurs during the first two years of life (postnatal)

The diagnosis of cerebral palsy is a clinical diagnosis consisting of the clinical history of the mother and infant and the pediatric and neurological examination of the infant. ***The diagnosis is dependent upon two key findings: evidence of non-progressive damage to the developing brain and the presence of a resulting impairment of the motor (neuro-muscular) control system of the body; the latter usually accompanied by a physiological impairment and functional disability.*** These clinical findings can be enriched by a number of laboratory evaluations.

THE RESEARCH TARGETS OF THE FOUNDATION'S ***DIAGNOSIS*** PROGRAM ARE:

IMPROVED CLINICAL EVALUATION

- Improving the diagnostic tools of the clinician to better recognize the criteria for the diagnosis of cerebral palsy.
- Developing new clinical evaluation methods which are more precise and more sensitive for documenting the health and functional status of the individual with cerebral palsy.
- Using the above diagnostic tools and measurement instruments to promote the establishment of prospective, community based studies to ascertain the occurrence of new cases of cerebral palsy (incidence), the presence of persons with disabilities due to cerebral palsy (prevalence) and the impact of new therapies.

MORE PRECISE LABORATORY EVALUATION

- Improving the present and developing new laboratory evaluation methods (e.g. brain imaging) for documenting and measuring damage to the developing brain in utero, at birth and during infancy.
- Improving the present and developing new laboratory methods for documenting and measuring impairment of neuro-muscular control and the resulting disability.

BETTER PUBLIC INFORMATION

- In collaboration with UCPA and its affiliates, tailoring the Foundation's public information programs so they are relevant, timely, user friendly, easily available and widely disseminated.

**THE UCP RESEARCH AND EDUCATIONAL FOUNDATION**
**RESEARCH PROGRAM**

# RESEARCH ON DIAGNOSIS: RESEARCH STATUS REPORT

Cerebral palsy is a disorder of the motor (muscle) control areas of the developing brain, injury to which occurred in intrauterine life thru the second year of postnatal life. The brain injury is a one-time event, although several different events can occur during brain development; each injury is non-progressive (does not get worse). The brain injury results in dysfunctions of muscle coordination often causing muscle spasticity, muscle weakness, dystonia (an abnormal posture of a body part) and/or abnormal body movements (dyskenesia, athetosis); these can change over time. Cerebral palsy is not a genetic disorder although it can sometimes "run in families"; this is probably due to a genetic susceptibility to an environmental factor or to the continuing presence in or near the family of an environmental risk factor. Cerebral palsy can be associated with other damage to the brain that can cause epilepsy, a visual or hearing disorder, mental retardation, a learning disability or a behavioral dysfunction. The presence and degree of associated problems is often related closely to the degree of lack of muscle control (e.g. the probability and degree of impaired vision is highest in those children with severe spasticity).

There are between 550,000-760,000 persons in the USA with disabilities due to cerebral palsy; a prevalence rate of 2.0-2.8 per 1000 population. The number is gradually increasing because of the growing number of new cases and the lengthened life expectancy of persons with cerebral palsy. There are now approximately 9,750 new cases of cerebral palsy occurring each year. The number of new cases has increased from 1.5-1.8 new cases per 1000 live births in 1990 to 2.0-2.5 new cases per 1000 live births in 2000, a 25% increase. Cerebral palsy is the second most common disorder of the developing brain, exceeded only by mental retardation.

The overall objectives of the Foundation's research program are (1) the prevention of cerebral palsy (damage to that part of the developing brain controlling muscle coordination) and (2) the development of more effective methods for diminishing disability in order to improve quality of life.

In 2002, the Foundation initiated a series of **Research Status Reports** that summarize the directions being taken to address the important but as yet unanswered questions for the prevention, diagnosis, treatment and management of cerebral palsy and the disabilities associated with it. The first Research Status Report was made available in July 2002; it addressed research on prevention. The following is the second report; it addresses research on diagnosis. A third report on research on treatment and management is in preparation.

## RESEARCH ON DIAGNOSIS

The diagnosis of cerebral palsy is a clinical diagnosis, one dependent upon the clinical history of the mother and infant and the pediatric and neurological examination of the infant. It includes the family history, the history of fetal and maternal health and illness during pregnancy, the health status of the newborn; the infant's postnatal development (reaching developmental milestones) and postnatal illnesses and dysfunctions during the child's early years of life. This information can be enriched by a number of other clinical and laboratory examinations including genetic testing (parents and child), prenatal intrauterine evaluations (e.g. ultrasound, amniocentesis), newborn screening evaluations (e.g. genetic screening), postnatal examinations (e.g. brain scans of the infant or child), and evaluations of the infant or child's impairments and disabilities (e.g. electromyography, gait analysis). The physician integrates this information and arrives at a clinical diagnosis of cerebral palsy; however, because a delay in development that occurs early in the child's life can later disappear (the child "catches-up"), in many cases the physician is hesitant to make a diagnosis of cerebral palsy until the child reaches 18-24 months of age.

### Research Targets

The diagnosis of cerebral palsy is dependent upon two key issues: evidence of non-progressive damage to the developing brain and the presence of a resulting impairment of the motor (neuro-muscular) control system of the body (e.g. muscle spasticity) --- the impairment is usually accompanied by a functional disability (e.g. toe walking). Thus, research on diagnosis focuses on improved methods for obtaining reliable **evidence of developmental brain damage** and on better **evaluation of the neuromuscular and muscular impairments** which result from it. Cerebral palsy can be accompanied by evidence of injury to other systems of the brain resulting in visual impairment, hearing loss, epilepsy, mental retardation, learning disorders and/or behavioral dysfunction. It is estimated that between 50-75% of persons with cerebral palsy have an associated injury to other areas of the brain; however, evidence of developmental brain injury and a resulting impairment of motor control must both be present for a diagnosis of cerebral palsy to be made irrespective of evidence of injury to other areas of brain function.

### CLINICAL EVALUATION

***One area of research emphasis on diagnosis has been improving the methods for obtaining reliable information about occurrences to the mother and infant that impact on the probability of developmental brain damage having occurred and the improvement and evaluation of clinical diagnostic methods to demonstrate damage to the brain's motor control system.*** This research includes the study of a series of case histories of children with cerebral palsy as compared to similar children who did not develop cerebral palsy (the "controls").

The most reliable evaluation studies are prospective—following the history of new pregnancies and the resulting offspring over time and developing correlations between one or more "events" during pregnancy and delivery with the subsequent health status of the infant and child. These studies are difficult to conduct because of the length of time required (often 5-7 years) and the loss of contact with families who move to other locations. Another problem is how representative of all pregnancies are the persons being studied. Are the mothers a special group (age; past history; exposure to risk factors)? Retrospective studies---examining past records---are more easily done, but suffer because of both a lack of inclusion in the records of reliable information about events that may have occurred and the identification of adequate controls in order to be able to evaluate the differences between groups. However, a great deal of information presently used in clinical diagnosis depends on these prospective and retrospective studies of clinical experience: evaluating the information from case series and correlating events in development with outcomes (impairments and disabilities) in the child.

In order to do the above research and to assist the physician in clinical diagnosis, a number of evaluation scales have been developed that assist in delineating and quantifying the specific status of the infant and child. A few examples of these are the Agar Score used at birth to evaluate the cardiac-pulmonary status of the newborn, the Gross Motor Function Classification System for Cerebral Palsy used during infancy and childhood to ascertain the achievement of developmental functional milestones, the Modified Ashworth Scale for measuring a muscular impairment (spasticity), the Pediatric Evaluation and Disability Inventory (PEDI) to evaluate health status and the Denver Developmental Screening Test to detect early developmental deviations in young children. ***On the basis of past and present experience using these evaluation scales, new examination methods and scales are being developed which are more precise and are more sensitive for identifying and quantifying the function being evaluated. The Foundation is giving special attention to the development of improved methods for the evaluation of disabilities and overall health status.***

## LABORATORY EVALUATION

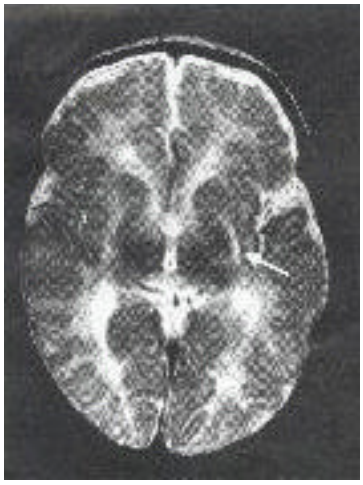
Research on diagnosis also attempts to reinforce the present reliance on the physician's clinical skills with objective laboratory methods that will demonstrate and quantify what the clinician observes and presumes. Research on laboratory information that assists in the diagnosis of cerebral palsy addresses two cardinal issues: (1) improved ability to ***recognize, locate and measure the damage to the developing brain*** and (2) increasing the ability to ***quantitatively evaluate the resulting neuro-muscular impairment(s) and functional disabilities.*** Examples include: the development of improved methods for imaging the structure, biochemistry and activity of the developing brain both in utero and after birth; more efficient methods of neonatal screening to ascertain jaundice, thyroid insufficiency, and metabolic disturbances in the newborn; and the development and evaluation of improved methods to measure the functional

performance of the infant, child and adult with a motor dysfunction (e.g. impaired walking, difficulty with finger control, communication difficulty, swallowing inadequacy). Increasingly, important laboratory tools are becoming available for assisting in describing events during and after pregnancy and their effect on the developing brain.

During the past decade, advances in brain imaging have been one of these. These include:

- the development and evaluation of instrumentation to visualize the anatomy of the developing brain and lesions in the brain; examples are ultrasound, CT scanning and magnetic resonance imaging (MRI). Ultrasound is also being explored to study the placenta and its abnormalities (site of attachment, inflammation, areas of injury);
- the development of instrumentation to evaluate the metabolism (functioning) of specific areas of the developing brain; examples are functional MRI (fMRI), NMR spectroscopy, and positron emission tomography (PET);
- improvement in electroencephalography (EEG) technology and analysis to better evaluate the electrical activity of the brain at rest and during activity;
- the development of sophisticated computer programs to construct three dimensional anatomic, electro-physiologic and metabolic images of whole brain and brain sections from data obtained from imaging techniques.

A major problem in the use of brain imaging continues to be the small size of the infant brain with a resulting loss of the instrument's ability to visualize very small details. Another problem is the restraint of the infant during the imaging procedures. Quieting and immobilizing the infant physically or by the use of a sedative will cause changes in brain activity, thus complicating the interpretation of the image. Ongoing research is addressing both these problems.



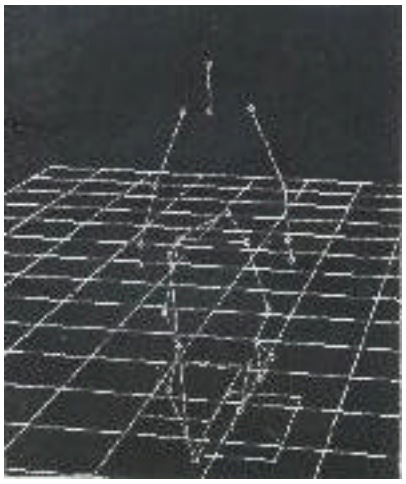
In the June 2002 issue of the medical journal *Neurology*, an expert committee documented its recommendations on "neonatal imaging strategies for evaluating both very low birth weight preterm infants and encephalopathic (brain damaged) term infants". These recommendations provide the clinical community with guidelines for the present role of brain imaging technologies to assist in the diagnosis of cerebral palsy. As new technologies are developed and evaluated, these guidelines will need to be reconsidered and revised.

Despite the sophistication of brain imaging technologies, a major problem that exists is the correlation of these images with functional deficits in the child's performance. The injury demonstrated in brain images often correlates well with evidence of impairments such as poor muscle control (spasticity, involuntary movements) --- and disturbed function in the child's performance, thus helping to confirm the clinical diagnosis. However, there are still occasions where the correlation is poor; the child's

impairments and disabilities clearly must be due to brain injury, yet the imaging fails to show any significant injury. On the other hand, sometimes there are demonstrated areas of injury or poor development in the motor control areas of the child's brain, yet the child's motor control appears to be "normal". ***Ongoing research in several areas of technology is aimed at developing even more precise methods to identify and document infant brain damage before, during and after birth and its association with disturbed neuro-muscular performance (cerebral palsy).***

Laboratory evaluations of impairment have been developed to assess the physiological status of the child's neurological and neuromuscular systems and to assist in differentiating cerebral palsy from direct injury to peripheral nerves and muscle. These include nerve conduction time evaluation, muscle electrical activity (electromyography) and muscle biopsy (microscopic study of muscle tissue). Studies are ongoing to place these evaluations in proper perspective and to ***develop better criteria for their more efficient use and appropriate interpretation.*** These measurements of nerve and muscle status and function are also valuable laboratory tools in evaluating the usefulness of therapy.

However, physiological impairment is not synonymous with disability. A person can have a modest impairment (e.g. muscle spasticity) and yet have no meaningful difficulty with activities of daily living; the person does not have a disability. In the past, the terms impairment and disability have often been used interchangeably. However, for the diagnosis of cerebral palsy and for the goals of treatment, they need to be differentiated. There are a number of precise methods available for the diagnosis and measurement of impairments. However, there are few methods available to assist in the measurement of disability; this latter requires better measurements of function.



One method that is now available and is under evaluation and refinement is gait analysis. Gait analysis is a method utilizing electronic imaging of a person who is walking. Sensors measure changes in joint angles while walking (e.g. at the knee), joint dynamics while moving and the timing and intensity of muscle contraction (dynamic electromyography). Thus, the present status of limb movement can be objectively measured and changes resulting from treatment evaluated. However, as objective as these methods are, the differences in the specific techniques used in the various gait analysis laboratories make it very difficult to pool the data from several laboratories to answer research questions. Also, the correlation between these objective measurements and actual performance (i.e. efficient walking) has yet to be determined and standardized. ***Research is being done to address these problems of instrumentation and data interpretation and to make performance measurement tools more useful both in clinical diagnosis and as an evaluation methodology in research.***

The products of past research on diagnosis have already enriched the armamentarium of the clinician. He/she can more precisely make a timely diagnosis of cerebral palsy, identify the specific areas of brain that have been injured and evaluate the resulting physiological impairments and functional disabilities. The methods and tools available to do these are being refined and new methods developed to acquire the information needed for increased certainty and preciseness of diagnosis. ***The research program of the UCP Research and Educational Foundation has contributed to these previous developments in diagnosis and are actively encouraging and supporting advances that are still needed to make diagnosis even more timely and accurate.***

## UCP FOUNDATION PROGRAM GOALS AND STRATEGY

***The goals of the Foundation are the prevention of cerebral palsy and improving the quality of life of persons with disabilities due to cerebral palsy***. In order to achieve these, it sponsors research and educational programs on the basic science and clinical research aspects of prevention, diagnosis and treatment. The Foundation program strategy includes:

STIMULATING NEEDED RESEARCH

- seeking the continuing advice and assistance of research leaders in the field, particularly the Foundation's Research Advisory Council.
- interacting with and sometimes being part of the research advisory structure of other organizations such as government research agencies (e.g. NIH, CDC, NIDRR), academic institutions, research institutes (e.g. Burke, Kessler, Salk, Kennedy Krieger), foundations (e.g. Hearst Foundation; Kirby Foundation; Dana Foundation), industry and other organizations.
- sponsoring research workshops in which scientific leaders address a critical research question, share findings and problems, and agree to cooperate in answering the question.

SUPPORTING RESEARCH AND CAREER DEVELOPMENT; PROVIDING PUBLIC INFORMATION

- providing risk venture financial support for pilot research projects exploring new approaches to the answer of important basic science and clinical research questions.
- funding the career development of young clinician-scientists to become the future academic leaders in cerebral palsy research, teaching and patient service.
- informing the public of the status of and continuing advances in research and clinical care relevant to cerebral palsy and the disabilities associated with it.

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