HDSA CALIFORNIA CHAPTERS

HDSA Greater LA Chapter
9903 Santa Monica Blvd
Beverly Hills, CA 90212
(310) 461-8335
(213) 294-7250 (HELPLINE)

HDSA Northern California
1212 Broadway Suite 830
Oakland, CA 94612
(415) 823-3226
(510) 526-3137 (HELPLINE)

HDSA San Diego Chapter
P.O. Box 152263
San Diego, CA 92176
(619) 447-7445
(619) 552-8585 (ext. 3431) (HELPLINE)
HD RESEARCH ROSTER AND DNA BANK

National HD Research Roster

The HD Research Roster is a national data bank which links scientists with HD families to facilitate research. All information is kept strictly confidential.

Dept. of Medical and Molecular Genetics
Medical Research and Library Building
Indiana University Medical Center
975 West Walnut Street
Indianapolis, IN 46202-5251
(317) 274-5744

To bank blood samples:

Bank by Mail Program
Dept. of Medical and Molecular Genetics
Medical Research and Library Building
Indiana University Medical Center
975 West Walnut Street
Indianapolis, IN 46202-5251
(317) 274-5745

BRAIN TISSUE BANKS

Brain tissue, from people who had Huntington's Disease or were at risk for HD, is a vital resource for scientists investigating
the cause, effects, and possible treatment of HD. Contact:

The Brain Tissue Resource Center
McLean Hospital
115 Mill Street
Belmont, MA 02178-9106
(800) BRAIN-BANK
(617) 855-2400

National Neurological Research Specimen Bank
VA Wadsworth Medical Center
Neurology Research
Wilshire & Sawtelle Blvds.
Los Angeles, CA 90073
(310) 824-4307 or (310) 478-3711

INTERNATIONAL HUNTINGTON ASSOCIATION

Voluntary HD organizations exist in many countries throughout the world. They offer a range of services and care programs to
benefit people with HD and their families, and are a useful source of information and referrals for both families and health care
professionals.

In North America:

HUNTINGTON'S DISEASE SOCIETY OF AMERICA
140 West 22nd Street, 6th Floor
New York, NY 10011-2420
Phone: (212) 242-1968 or (800) 345-HDSA
Fax: (212) 243-2443

HUNTINGTON SOCIETY OF CANADA
13 Water Street North, Suite 3 P.O. Box 1269
Cambridge, Ontario N1R 7G6
Phone: (519) 622-1002
Fax: (519) 622-737
For information on, or referral to, lay organizations in other countries, contact either of the above, or:

INTERNATIONAL HUNTINGTON ASSOCIATION
c/o Gerrit Dommerholt
Callunahof 8
7217 ST Harfsen
Netherlands
Phone: 31-5733-1595

Spring 1997

A: General Information
B: The Huntington's Disease Gene and Genetic Testing
C: Caregiving and Nursing
D: Clinical Care
E: Physical and Occupational Therapy
F: Juvenile Huntington's Disease
G: Behavioral Issues
H: Nutrition, Communication and Swallowing
I: Individual and Family Issues
J: Counseling, Psychosocial Issues, Support Groups
K: Research
L: Financial/Legal Issues
M: Foreign Language Publications
Suggested Reading (not available from HDSA)

Videotapes

A: GENERAL INFORMATION

101

Huntington's Disease: A Disease of Both Mind and Body
HDSA, 1987, revised 1993. Folded brochure.

FREE*

102

Huntington's Disease: Facts at a Glance
HDSA, 1994, 2 pages.

FREE*

103

So You Got The News: What Happens Now?
HDSA, 1988, revised 1993. Folded brochure. For the newly diagnosed.

FREE*

A Neurologist Speaks About Huntington's Disease
Dr. Anne B. Young, 1986, 24 pages.
Unavailable pending revision.

105

Understanding Huntington's Disease: A Resource for Families
Huntington Society of Canada, 1995, 55 pages.
This informative booklet is divided into three sections: Facts About HD, which covers symptoms, diagnosis, prevalence, treatment, and genetic testing; Experiences of Family Members; and Living With HD, which includes coping with being at risk, marriage and parenthood, counseling, and therapeutic interventions.

$2.00

106

Huntington's Disease: A Guide for Families
HDSA, 1996, 21-page booklet.
This short booklet offers an overview of Huntington's Disease.

FREE*

See Suggested Reading" for additional publications of a general nature.

B: THE HUNTINGTON'S DISEASE GENE AND GENETIC TESTING

200

Genetic Testing for Huntington's Disease: A Guide for Families
HDSA, 1996, 18-page booklet.
An introductory guide to genetic testing for HD in question and answer format.

FREE*

201

GENETIC TESTING PACKET (includes the following):

Genetic Testing for Huntington's Disease - What's New?
Dr. Randi Jones, The Marker, Vol. 7, No. 1, 1994. 2 pages

Testing For The Huntington's Disease Gene
HDSA, 6 pages.
List of HD testing centers.

Experiences of Predictive Testing for HD
Collected from The Marker, 6 pages.
Perspectives on predictive testing from people who have taken the test -- or decided against it.

$1.00

202

Team Pinpoints Genetic Cause of Huntington's
Natalie Angier, The New York Times, March 24, 1993, 1 page.

FREE*

203

We've Got the Gene! But What Does It Mean?
Dr. Nancy Wexler, The Marker, Vol. 6 No. 2, 1993, 1 page.

FREE*

204

Guidelines for Genetic Testing for Huntington's Disease
Summary of Recommendations, HDSA, 1994, 1 page.

FREE*

205

Genetic Testing for Huntington's Disease--A Family Issue
Catherine Hayes, The New England Journal Of Medicine, 327:20, 1992, 1 page.

FREE*

206

Genetic Clairvoyance
Richard Saltus,The Boston Globe Magazine, 1995, 9 pages.
The impact of a negative test result on a woman undergoing testing and her family.

$1.00

207

The Neurogenetics Genie: Testing for the HD Mutation
Steven Hersch, MD, PhD; Randi Jones, PhD; Walter Koroshetz, MD; and Kimberly Quaid, PhD., Neurology, Vol. 44, No. 8, August 1994. 5 pages.
Explanation of the testing guidelines written for health professionals.

FREE*

208

The Verdict
Susan Ager, Detroit Free Press Magazine, 1988, 10 pages.
An in-depth look at one person's experience of predictive testing.

$1.00

C: CAREGIVING AND NURSING

301

CAREGIVING PACKET (includes the following):

Practical Hints for Care Givers
HDSA, 1988, 9 pages.
Covers eating, swallowing, clothing, cleanliness, communication, smoking, recreation and attitudes.

Nursing Tips: A Collection of Caregiving Hints
Beryl Westphal, 1995, HDSA, 9 pages.
A compilation of professional caregivers' suggestions on feeding, communication, behavior and other daily concerns.

Huntington's Disease Management
Edward Bird, et al., Middlesex County Hospital, MA, 1984, 6 pages.
Dressing aids, relaxation, nutrition, communication, physical fitness.

$2.00

302

Toward A Fuller Life: A Guide To Everyday Living With Huntington's Disease
19.95 Eileen Werbel, HDSA, New York, 1990, 98 pages.
A useful reference guide for people with HD, families and caregivers, in a convenient loose-leaf format. Divided into three sections: Meeting Challenges offers advice on safety, personal care, clothing, communication, sleep, etc.; Getting Help focuses on legal and financial planning; and How To Cope addresses the social and psychological issues encountered by HD families.

$19.95

303

Caring For Persons with Huntington's Disease: A Handbook for Health Care Professionals

Second Edition. Dr. Edmond Chiu, HDSA, 1991, 150 pages.

This book promotes an interdisciplinary approach to residential care. Includes chapters on: management of emotional and behavioral aspects of HD; nursing care; physiotherapy; occupational therapy; music therapy; swallowing; speech; and dental care.

$18.00

304

Huntington's Disease Manual for Care

Patricia A. Prentice, Huntington Society of Canada, 1986, 110 pages.

Includes information for caregivers in the home and in long-term care facilities on behavior, nutrition, stress, communication and many other areas of care.

$20.00

305

Nursing Approaches for Clients with Huntington's Disease

Winkie Simpson, Horizon, No. 76, Spring 1995, Huntington Society of Canada, 3 pages.

Discussion of nursing strategies used at Runnymede Chronic Care Hospital, Toronto, Ontario.

$0.50

306

Understanding Huntington's Disease: An Overview of Symptomology and Nursing Care Christine Kovach and Sandra Stearns, Geriatric Nursing, 1993, 4 pages.

$0.50

307

The 36 Hour Day

Nancy Mace & Peter Rabins, Johns Hopkins University Press, 1981, 251 pages.

Comprehensive guide to home care for persons with degenerative disorders. Combining practical advice with specific examples, it covers medical issues, daily care, and legal and emotional aspects of caring for a relative affected by degenerative brain disease.

$11.00

308

How To Choose A Nursing Home

Jeanne Farrell, HDSA, 5 pages.

$0.50

D: CLINICAL CARE

401

A Physician's Guide to the Management of Huntington's Disease: Pharmacologic and Non-Pharmacologic Interventions

Neal G. Ranen, MD, Carol E. Peyser, MD, Susan E. Folstein, MD. HDSA, New York, 1993. 47 pages.

This valuable resource for the clinician includes in-depth information on: the general principles of treatment; management of specific symptoms; medication guidelines, including dosage; adaptive equipment and products.

$6.00
(reduced rates for
bulk orders)

402

Correlates of Early Disability in Huntington's Disease Richard Mayeux et al., 1986, 5 pages.

Focuses on intellectual impairment as a major factor in reducing functional capacity in early stages of HD.

$0.50

403

Evaluating Driving Capacity in HD

Allen J. Rubin, MD, University of Medicine and Dentistry of New Jersey, 1994, 11 pages.

Practical guidelines to assist physicians and other professionals in making this difficult determination.

$1.00

E: PHYSICAL AND OCCUPATIONAL THERAPY

501

Huntington's Disease at Mid-Stage

Suzanne Imbriglio, PT, Clinical Management, Vol. 12 No. 5, Sep/Oct 1992, American Physical Therapy Association, 11 pages.

Explanation of how physical and occupational therapies benefit people with HD. Practical advice on designing a plan that combines maximum independence with minimal risk.

$1.00

502

Physiotherapy for Huntington's Disease Patients

Anne Hoy, 5 pages, 1991.

Discusses treatment and exercises.

$0.50

503

A Physical Therapy Program for HD Patients

Inez Peacock, Clinical Management in Physical Therapy, Vol. 7, 1987, 7 pages.

Collection of information about her physical therapy program. Includes actual exercises.

$0.50

504

Huntington's Disease: Delivery of Physical Therapy Services in a Group Setting

Inez Peacock, Proceedings, Book II, World Conference for Physical Therapy, 1991, 3 pages.

Overview of physical symptoms and how a physical therapist can help to mitigate them.

FREE*

505

Occupational Therapy in Huntington's Disease

Cheryl Hicks, 5 pages.

Describes group activities to help with physical, intellectual and psychological problems.

$0.50

F: JUVENILE HUNTINGTON'S DISEASE

601

Living with Juvenile Huntington's Disease

Wendy Elliott, Huntington Society of Canada, 1993, 67 pages.

Written for family members, health professionals and care providers, this book interweaves first person accounts with information on the diagnosis, management, and stages of the juvenile form of HD.

$4.00

G: BEHAVIORAL ISSUES

701

Behavioral and Sexual Problems in Huntington's Disease

Shirley Dalby, from Horizon, No. 64, 1992, Huntington Society of Canada, 4 pages.

This article by veteran British social worker Shirley Dalby, discusses in everyday language the kinds of changes in mood and behavior that can be experienced by people with HD.

$0.50

702

Understanding Behavioral Changes in Huntington's Disease

Edmond Chiu, HDSA, 1989, 28 pages.

Comprehensive, readable explanation of the causes of behavioral difficulties associated with HD. Practical advice for the home and professional caregiver is provided with emphasis on enabling the person with HD to obtain the best possible quality of life.

$2.00

H: NUTRITION, COMMUNICATION AND SWALLOWING

801

Coping with Speech and Swallowing Difficulties in Huntington's Disease: A Guide for Families
Lynn Rhoades, MS, CCC-SLP, HDSA, 1996, 26-page booklet.
FREE*

802
Mealtime Manual for Huntington's Disease Patients
Folstein et al., Baltimore HD Research Center Without Walls, 1983, 11 pages.
A guide to feeding. Includes recipes.
$1.00

803
Managing Swallowing Difficulties Associated with HD
Estelle R. Klasner, M.A., CCC-sp, Reg. OSLA, Huntington Society of Canada, 1990, 13 pages.
This booklet offers explanations, diagrams and strategies for the family member and professional.
$0.50

804
Managing the Communication and Speech Difficulties Associated with Huntington's Disease
Estelle R. Klasner, M.A., CCC-sp, Reg. OSLA, Huntington Society of Canada, 1990, 9 pages.
This booklet explains the causes of speech and communication difficulties in HD, and offers practical advice on how to maintain communication skills for as long as possible. HD family members, nursing home staff and other caregivers will benefit from it.
$0.50

See "Suggested Reading" for other publications on this topic.

I: INDIVIDUAL AND FAMILY ISSUES

901
A Family Member Speaks About Huntington's Disease
(Formerly A Personal View of Genetic Counseling)
Marjorie Guthrie, 1979, 21 pages.
Early recollections, doctors & hospitals, difficult decisions, coping, professional support.
$1.50

902
Telling the Children
Shirley Dalby, 2 pages.
How, why, when to tell children about HD.
$FREE*

903
Teens and HD and Adolescent Reaction to HD
From Horizon, No. 77, Huntington Society of Canada, Fall 1993
Two teens discuss how HD has affected their lives; Sandra L. Funk, HD Resource Centre Director, Winnepeg, Manitoba, offers a professional viewpoint.
$0.50

905
Living Through Grief
Denis Boyd, Horizon, No. 55, 1989, Huntington Society of Canada, 3 pages.
Discusses the grief which family members experience and how to cope with it.
$0.50

906
Suicide and Huntington's Disease
Allen J. Rubin, Horizon, No. 68, 1993, Huntington Society of Canada, 6 pages.
Personal perspectives of three HD family members, followed by a psychiatrist's thoughts on the subject.
$0.50

907

The Experience of Being "At Risk" for Huntington's Disease
Nancy Wexler, 1979, 23 pages.
Reactions, probability, family planning, psychotherapeutic suggestions.
$1.50

908
Huntington's Chorea: Its Impact on the Spouse
Hans & Koeppan, 1980, 6 pages.
Case reports.
$0.50

909
Experiences of a Huntington's Disease Patient
Nee and a Patient, 1977, 7 pages.
Anonymous recollections of a person with HD.
$0.50

J: COUNSELING, PSYCHOSOCIAL ISSUES, SUPPORT GROUPS

1001
Families with Huntington's Disease: Psychologic and Social Treatment
Mary Louise Franz & Susan Folstein, 1985, 9 pages.
Information for social workers and other health professionals on: diagnosis; financial, behavioral, social and household management; communication; nutrition;institutional placement; effects on community.
$0.50

1002
Psychosocial Aspects of Genetic Disorders: Implications for Practice
Kathleen Kirk Bishop, The Journal of Contemporary Human Services, April 1993, 5 pages.
This article explores some of the issues which arise for families following the diagnosis of a genetic disease.
$.50

1003
Living with the Characterologically Altered Brain-injured Patient
Muriel Lezak, Clinical Psychiatry, 1978, 6 pages.
Common family and spousal problems, family expectations, counseling.
$0.50

1004
The Adolescent's Reaction to Chronic Illness of a Parent:
Some Implications for Family CounselingPaul Power, Boston University, 1975, 9 pages.
Adolescents' reactions to their parents' illness based on a study of children in 15 HD families. Last section includes implications and suggestions for family counselors.
$0.50

1005
Social Work with Victims of Huntington's Disease
Roberta Sands, Social Work in Health Care, Vol. 9(4), Summer 1984, 9 pages.
Problems of diagnosis, impact of HD on family, services.
$0.50

1006
You Are Not Alone: A Guide to Establishing Huntington's Disease Support Groups
Rickey Greene, HDSA, New York, 1992, 56 pages.
A how-to guide for starting a group in your area.
$6.00

K: RESEARCH

1101
Research Roundup
Research reports collected from The Marker, 1994/95. HDSA. 6 Pages.
FREE*

L: FINANCIAL/LEGAL ISSUES

1201

The ABC's of Government Disability Programs: SSD & SSI
Eileen Werbel, HDSA, 1991, 4 pages.
Describes Social Security Disability & Supplemetal Security Income, eligibility, and how to obtain these benefits.

FREE*

See "Suggested Reading" for other publications on this topic.

M: FOREIGN LANGUAGE PUBLICATIONS

1301

Una Guía Médica para el Manejo de la Enfermedad de Huntington:
Intervenciones Farmacológicas y No Farmacológicas.
Neal Ranen, Carol Peyser, Susan Folstein, HDSA, 1993, 47 pages.
Spanish translation of A Physician's Guide to the Management of HD (#401).
This valuable resource for the clinician includes in-depth information on the general principles of treatment, management of specific symptoms, medication guidelines, including dosage, adaptive equipment and products.

$6.00

SUGGESTED READING (not available from HDSA)

Huntington's Disease: A Disorder of Families
Susan E. Folstein, M.D., Johns Hopkins University Press, Baltimore, 1989. 251 pages.
A detailed overview of symptoms, diagnosis, clinical care, and research. The author is formerly director of the Baltimore Huntington's Disease Project at Johns Hopkins.
To order, call Johns Hopkins University Press at 1-800-537-5487.

$45.00 (A 30% discount is offered to HDSA members)

Mapping Fate: A Memoir of Family, Risk, and Genetic Research
Alice Wexler, Random House, 1995, 294 pages.
Acclaimed autobiographical account of the Wexler family's personal battle with HD, and their efforts to conquer it by spearheading the research effort.

$20.00

Non-Chew Cookbook
J. Randi Wilson, 1985, 188 pages.
Easy recipes complete with caloric intake tables.
To order, write: Wilson Publishing Inc., P.O. Box 2190, Glenwood Springs, CO 81602-2190, or call 800-843-2409.

$23.95

Genes and Generations: Living with Huntington's Disease
Alison Gray, Wellington Huntington's Disease Association, 1995, 195 pages.
A series of interviews in which people with HD, family members, and professionals recount with honesty, hopefulness and humor their varied experiences of HD.
Send check for US$15.00 to: Wellington Huntington's Disease Association, Social Work Dept. (Res 2), Wellington Hospital, Private Bag 7902, Wellington South, New Zealand.

$15.00

A Shopper's Guide to Long-Term Care Insurance
National Association of Insurance Commissioners, 1993.
A guide to understanding how these policies work, who should obtain long-term care insurance, and what to be aware of when buying.
To order, write: NAIC Publications, 120 W. 12th St., Suite 1100, Kansas City, MO 64193-0042, or call 816-374-7259.

FREE

The American Association of Retired Persons (AARP) publishes the following booklets. To order, call 800-424-3410

or write to AARP Fulfillment, 601 "E" Street NW, Washington, DC 20049.

Before You Buy: A Guide to Long Term Care Insurance
AARP, 1991, 45 pages
Need for long-term care insurance, costs, what it includes, guide for evaluating policies.
(Request publication #D12893)

FREE

A Handbook About Care in the Home: Information on Home Care Services
AARP, 1982 (revised 1992)
(Request publication #D955)

FREE

MEDIGAP: Medicare Supplement Insurance
AARP, 1994.
A guide to Medigap insurance: is it suitable for your needs, and how do you obtain it?

FREE

Medicare's Prospective Payment System: Knowing your Rights
AARP, 1995.
A complete description of Medicare's Prospective Payment System for hospitals from the consumer point of view.
(Request publication #D12330)

FREE

A MATTER OF CHOICE: Planning Ahead For Health Care Decisions
AARP, 1992.
Planning for the difficult times in life, for individuals and families.
(Request publication #D12776)

FREE

VIDEOTAPES

NANNY'S BIRTHDAY
HDSA, 1990. 38 minutes
Presentation by Australian psychiatrist Dr. Edmond Chiu, a leader in caring for people with HD for over 20 years. Includes demonstration of caring techniques to enhance the quality of life for people with HD and footage from the HD unit at the Terence Cardinal Cooke Health Care Center in New York City.

$10.00**

LIVING WITH HD: A NURSE'S PERSPECTIVE
Middlesex County Hospital, 1989, 30 minutes.
Deals with a variety of care issues for patients with HD in a long-term care facility.

$10.00**

CARING VIDEO
Huntington Society of Canada, 1985. 110 minutes
Four Segments:

1.How To Deal With Difficult Behavior
2.Mobility
3.Speech and Communication
4.Nutrition and Swallowing

$20.00**

THE GIFT OF CARING: A PRACTICAL GUIDE TO MANAGING FEEDING AND SWALLOWING DIFFICULTIES ASSOCIATED WITH HD
Huntington Society of Canada, 1991. 13 minutes.

$10.00**

CLAUDIA'S CHALLENGE
HDSA, Massachusetts Chapter
Profile of Claudia Frank, who confronts the challenge of HD and leads an active and fulfilling

life by making good use of available community resources.

$10.00**

COMMUNICATION STRATEGIES FOR PEOPLE WITH HD
Huntington Society of Canada, 1993. 20 minutes.
Addresses the speech and language difficulties associated with HD and offers suggestions for improving communication.

$10.00**

WITHIN REACH: CLOSING IN ON A CURE
HDSA, 1993. 12 minutes.
In interviews with HD researchers and family members, this video captures the optimism generated by the HD gene discovery and looks forward to future breakthroughs. Introduced and narrated by Spencer Christian.

$10.00**

HUNTINGTON'S DISEASE: LIVING WITH HOPE
HDSA, Sioux Valley Chapter, 1992. 34 minutes.
General overview of HD and interviews with family members and professionals.

May be purchased from: HDSA, Sioux Valley Chapter, P.O. Box 1311, Sioux Falls, SD 57101-1311

$16.50**

* Only ONE copy of any item marked * will be sent free. A nominal fee will be charged for quantity orders to
offset the cost of duplication.

** Prices include shipping and handling

[Huntington's Disease Society of America Main Menu]

HDSA Order Form

Huntington's Disease Society of America
140 West 22nd Street, 6th Floor
New York, NY 10011-2420

1-800-345-HDSA
212-242-1968
curehd@hdsa.ttisms.com

Please print out this order form, fill it out, and mail to the above address. We hope to have online ordering as an alternative option in the near future. Thanks!

Send to:

Name: _____
Affiliation: _____
Address:_____
_____
Phone number: (_____)_____

PLEASE NOTE: We are able to send only one copy of any free publication (excluding brochures for chapter and affiliate use). These items may be reproduced but please credit HDSA as the source.

ITEM NO.	NO. COPIES	COST	TOTAL COST

Subtotal
$
*Shipping Cost (see below)
$
Total
$

SHIPPING COSTS: (For overseas shipments please contact HDSA)

For subtotals:

up to $4.99 --------- add $2.00
$5.00 to 9.99 ------ add $3.00
$10.00 to19.99 ----- add $4.00
$20.00 to 39.99 ---- add $6.00
$40.00 to 59.99 ---- add $10.00
$60.00 and over ---- add $15.00

Do you wish to be added to the mailing list ?
_____Yes _____No

The contents of this order will be used by:
_____ HDSA chapter/affiliate
_____ Person with HD/Family member
_____ HD support group
_____ HD area contact
_____ Friend of person with HD
_____ Library
_____ Health professional (please specify_____)
_____ Other (please specify_____)

Please make check payable to:
Huntington's Disease Society of America, Inc.

Credit card payment(minimum order $25):

Name as it appears on credit card: _____
___ Visa ___ MasterCard ___ American Express
Account number:_____
Expiration Date ____/____

[Huntington's Disease Society of America Main Menu]

No Ordinary Mouse: Researchers Take Big Step Forward With Help of HD Mouse Model

By Gillian Bates, Ph.D., Guy's Hospital, London (September 1997)

Two papers published in the scientific journal Cell in August have been heralded as a major breakthrough in research into the
cause of Huntington's disease (HD). They were the result of work carried out by research groups at Guy's Hospital in London
and those of Stephen Davies at University College London and Hans Lehrach and Erich Wanker at the Max Planck Institute in
Berlin.

In London we have made a transgenic mouse model of Huntington's Disease. As you may know, the HD gene contains a
CAG repeat very close to its beginning. The gene makes a protein called huntingtin and the CAG repeat codes for `glutamine,'
a standard protein building block.

The model was made by putting the first part of the HD gene, containing very long CAG repeats, into the mouse. This human
`transgene' then gets inherited from one mouse generation to the next along with all of the mouse genes. The mouse cells
contain a small protein made from the human transgene that has an extremely long polyglutamine tract.

These mice show a progressive, late onset movement disorder with similarities to HD. We have generated three different

mouse lines that make the same small human protein each with different numbers of glutamines. One of these lines has an age
of onset of approximately two months, which means that we can study the disease in these mice very rapidly.

Steve Davies has been looking at the brains of these mice very carefully to see if he can find any differences between the brains
from transgenic mice with symptoms and those from normal mice. Steve used antibodies to the huntingtin protein (kindly
provided by the Berlin group, Marian DiFiglia at Massachusetts General Hospital in Boston, and Christopher Ross at Johns
Hopkins in Baltimore) to find out where the small human transgene protein was located in the brain cells.

He found that in mice with symptoms, the polyglutamine containing human protein had moved to the nucleus. This is a different
part of the brain cell from where it is found in normal mice or those that have not yet developed symptoms. He used an
electron microscope (EM) to look at the brain cells in great detail and found that the human protein had clumped together to
form a structure which he has called a neuronal intranuclear inclusion (NII). At first we did not understand the significance of
this. It had always been stated that there are no deposits in the brain cells of HD patients.

Steve started to search through the literature to see what EM studies of HD patient brain material had previously shown. Then,
one Saturday lunchtime, he appeared at my house clutching a book from 1979 and saying that it was just too exciting to tell me
over the phone!

In this book there was a paper showing an EM photograph from an HD patient. It contained a structure identical to the NII
seen in the mouse brains. Since then, the presence of these structures in HD patient brains has been confirmed.

One of the major advantages of the HD transgenic mice is that they allow us to study all stages of the disease. Steve was able
to show that the formation of these clumps of protein in the mouse brains occurs before we see any other changes and well
before we see any signs of the movement disorder.

This suggests that the formation of the protein clumps may be the primary event that causes HD.

When the mice first started to show symptoms, Erich and Hans decided to make the same human protein that was introduced
into the mice in the test tube. They made several versions of this protein containing different CAG repeat sizes.

They were very surprised to find that when the protein contains repeats of a size that cause HD, the polyglutamines allow the
protein to stick together forming fibers. This did not happen when the repeats were in the unaffected size range. This suggests
that when the repeats reach a certain size, the HD protein molecules gain this new ability to stick together.

It is important to emphasize that these are research breakthroughs and that at this time they have not changed the way in which

HD can be treated. However, until the publication of this work, people had no idea that these protein clumps were present in
HD brains. The fact that we see them so early in the mice might suggest that they are important in the first stages of the disease.

A major research focus will be to see if we can develop methods to stop the protein clumps from forming. In Berlin, Hans and
Erich are working on an automated method of screening more than a hundred thousand potential drug compounds to see if any
of them will keep the proteins apart. We don't know if this will work but it is an approach that can be started now and there is
only one way to find out.

There is an enormous amount that we still don't know. However, the pace of research is picking up and the technologies
required to find a cure for HD are all in place. It is not possible to predict how long this will take but there is good reason to be
optimistic.

Scientists Report New Understanding of Cell Death in HD

As reported in The Marker, Summer 1997

An important new HD research finding made the headlines this past August. In what The New York Times called "a major
medical advance," scientists have found that brain cell death in HD may be caused by a ball of protein that forms in the nucleus
of cells. The same phenomenon is also seen in six other disorders caused by a similar genetic mutation.

Three articles on the subject were published in scientific journals by researchers in Britain, Germany and the U.S. Dr. Gillian
Bates of Guy's Hospital, London, had previously reported her development of a genetic mouse model of HD. By inserting a
portion of the human HD gene into fertilized mouse eggs, Dr. Bates was able to create a mouse that developed symptoms of
HD.

It was in this mouse model that Dr. Stephen Davies, of University College, London, working with Dr. Bates, discovered balls
of protein, or `neuronal intranuclear inclusions,' in brain regions known to be affected in HD. These inclusions contain high
levels of a piece of the huntingtin protein, including the protein encoded by the expanded `CAG repeat' in the HD gene.
Working with Eric Wanker and Hans Lehrach in Germany, Dr. Bates and Dr. Davies showed that this portion of huntingtin
could also precipitate or "clot up" in a test tube.

Back in May, both Dr. Bates and Dr. Davies had presented their research at the inaugural meeting of the HDSA Coalition for
the Cure in Baltimore, MD. Dr. Bates heads one of the 6 HDSA-funded labs in the Coalition.

Explaining the significance of the studies for the Jim Lehrer News Hour on PBS, HDSA National Science Council Chairman
Dr. Christopher Ross said, "What this really gives us is a better understanding of the disease."

Dr. Ross, a co-author of Dr. Bates' study, explained that "the Huntington's Disease protein abnormally changes its location within the cell and it accumulates in kind of a dense mass that, we hypothesize, gums up how nerve cells work." Dr. Marian DiFiglia, a member of the Coalition, and Dr. Ross also have preliminary data indicating that these inclusions are present in brains from HD patients.

Cautioning that the finding would not lead immediately to a treatment for HD, Dr. Ross said he was hopeful that newly-developed animal and cell models could be used to test drugs that might prevent the accumulation of the protein in cells. "That would be the hope for developing treatments," he said.

National Institutes of Health Grants $6.5 Million for HD Drug Study

As reported in The Marker, Summer 1997

The National Institute of Neurological Disorders and Stroke (NINDS) is funding a $6.5 million clinical drug trial for Huntington's Disease, it was announced in June.

The four-year trial involves 22 medical centers -- Huntington Study Group sites -- across the United States and Canada. Subject enrollment began July 7 and recruitment has progressed very rapidly and successfully. It is being coordinated at the University of Rochester.

In the study, titled CARE-HD, the drug Remacemide and the nutritional supplement Coenzyme Q10 are being tested both individually and in combination. The drugs are not expected to reverse or eliminate the symptoms of HD, but it is hoped that one or both of them will prove effective in slowing the progression of the disease.

Dr. Karl Kieburtz, a neurologist at the University of Rochester, is the study's principal investigator, and Dr. Walter Koroshetz, of Massachusetts General Hospital, Boston, is co-principal investigator. Dr. Kieburtz talked about CARE-HD at the HDSA convention in June.

Remacemide, he said, "is a glutamate receptor antagonist, which means it blocks the effect of glutamate in the human brain." Studies have shown that toxic levels of glutamate, a substance that occurs normally in the brain, plays a role in the development of HD.

Coenzyme Q10, or CoQ10, helps buttress energy production in the brain. "There is increased lactate in patients with HD...which indicates a problem with energy," said Dr. Kieburtz. "[CoQ10] can reduce this elevated lactate. In addition, it's a free radical scavenging agent. That is, it can soak up some of the natural byproducts of chemical reactions which may ultimately do damage in the brain and other structures."

In preliminary short-term studies, both agents have been shown to be well tolerated in people with HD.

The study will be double-blind and placebo-controlled, in a `two-by-two factorial' design. This means that a quarter of the
people will receive Remacemide, a quarter will receive Coenzyme Q10, a quarter will get both, and a quarter will get placebo.
Participants and investigators will not know which they have received until the very end of the study.

In a significant departure from other clinical trials, the minimum age for enrollment in the study will be reduced from 18 to 14.
"We're trying to address younger onset HD," explained Dr. Kieburtz. "Making a movement from 18 down to 14 is difficult --
going lower than that is even more difficult - -but in the future we're committed to including younger patients with HD."

"We plan on enrolling 340 patients [altogether]. The primary outcome measure is to look at functional capacity, rather than just
motor [symptoms] or cognition, 30 months after starting these treatments.

"340 patients, two and a half years -- that's a big commitment on the part of the HD community... and it's a big commitment on
the part of the investigators. And I must say that the response on all sides has been overwhelmingly enthusiastic to go and do
this...to make this commitment."

Given the enthusiasm of the large number of HD patients currently available to the sites participating in CARE-HD, it is not
anticipated at this time that additional sites or patients will be needed for this study.

Coalition for the Cure gives New Impetus to HD Research: HDSA Awards $570,000 in Start-up Funding

(As reported in The Marker, Summer 1997)

Forty scientists from leading institutions in North America and Europe gathered in Baltimore, May 29, to launch an important
new research collaboration aimed at developing treatments for HD.

"We are very excited about this new initiative," said Dr. Christopher A. Ross, Professor of Psychiatry and Neuroscience at the
Johns Hopkins University School of Medicine and HDSA National Science Council Chairman, who heads up the Coalition.
"We hope it will unlock many of the mysteries surrounding HD."

The HDSA Coalition for the Cure pools the skills and resources of scientists from leading laboratories in the United States,
Canada, Britain and Italy. In March, the HDSA Board of Trustees allocated $570,000 for the Coalition over two years.
Additional allocations will be considered when the Board convenes next spring. Funding for the Coalition is separate from, and
supplementary to, the Society's existing grant and fellowship program.

Huntington's Disease research has a history of successful collaboration. In 1993 the gene that causes HD was discovered by a
Collaborative Research Group, also involving labs from North America and Europe. And while concentrating on basic
research, the new Coalition will work closely with the Huntington Study Group. "The Coalition is a kind of conduit for...basic
science to develop treatments that will then be given to the Huntington Study Group to be tried out in patients," said Dr. Ross.

The Coalition for the Cure involves investigators from: The Johns Hopkins University, Baltimore, MD; Emory University,
Atlanta, GA; Massachusetts General Hospital, Boston, MA; University of British Columbia, Vancouver, Canada; Guy's
Hospital, London, England; and University of Milan, Italy. Additional labs may be invited to participate as time goes on.

"We're fortunate to be working in partnership with some very talented and motivated scientists," said HDSA's National
Executive Director, Barbara Boyle, who collaborated with Dr. Ross in setting up the Coalition. "We believe this new group will
be the catalyst for further breakthroughs -- and a cure for Huntington's Disease."

The Coalition will focus on four key areas of study: biochemistry, cell biology, cell models, and animal models. Working
collaboratively, as well as independently, the scientists in the group will study the function and interactions of huntingtin, the
protein product of the HD gene, in an effort to determine how it causes selective nerve cell death in a part of the brain called
the striatum. Cell and animal models will be constructed to examine the mechanisms of pathogenesis in HD and to screen
possible treatments.

"An additional goal of the organization is to share information," said Dr. Ross. The aim is "to get all those people who are
already working independently to talk more together and to speed the way information can jump from one lab to another so
that new results can be disseminated."

Oversight for the Coalition comes from a Steering Committee comprising leaders in the field of neurodegenerative disorders:
Kevin Campbell, Ph.D., University of Iowa; Kenneth Fischbeck, M.D., University of Pennsylvania; Harry T. Orr, Ph.D.,
University of Minnesota; Jeffrey Rothstein, M.D., Ph.D., The Johns Hopkins University; and Anne B. Young, M.D., Ph.D.,
Massachusetts General Hospital and Harvard University. The Steering Committee will give guidance to the Coalition and make
decisions on funding.

"There was a great deal of excitement and energy generated at the Coalition meeting in Baltimore," said John Madden, Ph.D.,
an Emory University scientist who is the research liaison for the national HDSA Board of Trustees. "It was wonderful to see so
many scientists getting up to share and discuss brand new data from their labs."

Interviewed on WMAR-TV, the Baltimore ABC News affiliate, Dr. Ross said, "We now have...animal models in which the

abnormal gene is put into a mouse and you can actually see symptoms that look very much like HD. Hopefully we can develop
treatments using these mice as models."

While several labs are developing animal models, Dr. Gillian Bates' transgenic mouse is generating the most excitement among
scientists. "It is clear that we are now entering a new understanding of the molecular basis of HD," said Dr. Bates, of Guy's
Hospital, London. "HDSA has done an absolutely fantastic job in a very short time in establishing such an impressive research
fund. I hope that the families who have contributed so generously realize how much they are going to make a difference."

Huntington's Disease Coalition for the Cure

Institutions and Investigators	Focus
EMORY UNIVERSITY, Atlanta, GA	
J. Timothy Greenamyre, MD, PhD	Cell and animal models
Steven M. Hersch, MD, PhD	Biochemistry and cell biology
THE JOHNS HOPKINS UNIVERSITY, Baltimore, MD	
David Borschelt, PhD	Animal models
Christopher A. Ross, MD, PhD	Biochemistry, cell and animal models
Alan Sharp, PhD	Cell biology
MASSACHUSETTS GENERAL HOSPITAL / HARVARD UNIVERSITY, Boston, MA	
M. Flint Beal, MD	Animal models
Marian DiFiglia, PhD	Cell biology and cell models
Marcy MacDonald, PhD	Biochemistry, cell and animal models
UNIVERSITY OF BRITISH COLUMBIA, Vancouver, Canada	
Michael Hayden, MB, PhD	Biochemistry, animal models
GUY'S HOSPITAL, London, England	
Gillian Bates, PhD	Animal models
UNIVERSITY OF MILAN, Milan, Italy	
Elena Cattaneo, PhD	Cell biology and cell models

Huntington Study Group Position Statement on Experimental Surgical Treatments in HD

January 1997

Patients and families with Huntington's Disease (HD) as well as HD clinicians and researchers worldwide have been extremely interested in the recent exploration of potential surgical treatments for HD. Various surgical procedures have been proposed, and in some cases performed, including transplantation of human or pig fetal cells, and permanent destructive lesions of the brain (pallidotomy). The Huntington Study Group (HSG), a group of academically-based HD clinicians and researchers, has carefully and extensively monitored these developments with both hope and growing concern.

Based on a careful evaluation of all available information, we conclude that all potential surgical treatments are experimental and unproven regarding both safety and efficacy. We believe that the only responsible way for HD patients to receive any potential surgical treatment is in a well planned, well executed, carefully monitored controlled clinical trial designed to initially assess safety and, eventually, efficacy. Patients and families entering these trials must be informed of all available current information and should understand that no potential surgical treatment is known to be safe or effective.

Participation in surgical clinical trials will carry the risk of harm, potentially irreversible, as well as the possibility of improvement. Patients and families with HD should carefully consider participation in such trials and would benefit from consultation with HD caregivers knowledgeable about currently available experimental protocols. The following are a series of questions and answers that many HD patients and families may find useful in considering these decisions.

Why have clinical trials of surgery started if we do not know if the surgery is safe or effective?

For both experimental drug and surgical therapy trials, we rely on results from studies in animals, and from human experience with similar therapies to decide if there are enough reasons to try a new therapy. In the case of both transplantation and destructive brain lesions, many HD investigators and researchers believe there is enough reason to begin trials; however, some researchers do not agree. Further experiments continue in animals to help refine and guide new experimental surgical therapies.

How can patients and families tell if a clinical trial study is well designed?

The HD research community has not identified any single study design as preferred; however, there are essential elements in all well designed HD studies. One is that patients need to be informed about the study and the experimental nature of the surgery. A written informed consent document reviewed by an Institutional Review Board should be available for review and discussion. Also, patients must be evaluated in a structured manner by experienced HD clinicians for at least six months before surgery to adequately define HD symptoms. The same structured evaluations should continue for at least two years after

surgery. The structured testing should include measures of movement, thinking and behavior. The study should allow for direct
comparisons to patients who do not receive surgery or receive a different kind of surgery. Some patients involved in the trial
may not initially get any surgery. This is the only well accepted way to measure the safety and efficacy of a new experimental
treatment. The federal government prohibits charging patients for experimental drugs, and patients are usually not charged for
the costs of experimental surgery.

How many studies have shown that the experimental surgery may help?

There are no published reports of well designed trials of surgery in HD. The few published reports of patients who have had
surgery have received it in a setting that did not allow the safety or efficacy to be measured. We strongly recommend that HD
patients participate only in well designed and conducted clinical trials of any experimental treatment, surgery or drug. Patients
and families with HD should understand that all current trials of potential surgical treatments are designed to measure safety,
and that clinical trials designed to measure benefit are not currently available.

Neural Transplantation for Huntington's Disease

May 16, 1996

(By Steven M. Hersch, MD., Ph.D., Department of Neurology, Emory University Member, HDSA National Science Council)

The wealth of experimental studies using animal models of Huntington's Disease and the growing success in neural
transplantation in Parkinson's disease patients has made it almost inevitable that this new experimental technique will be applied
in HD.

The goal is to replace lost striatal neurons with fetal neurons that can take their place in the circuitry of the basal ganglia and
ameliorate the symptoms of HD that are due to striatal pathology. While there is certainly a great deal of neuropathology
outside the basal ganglia that this approach would not be expected to impact on, improving basal ganglia function would be
extremely worthwhile since many of the motor and behavioral symptoms of HD originate there.

A number of investigator groups around the world have been working towards initiating clinical trials of neural transplantation in
HD. Perhaps the first such case was done in Mexico several years ago, although the method and measures used were dubious
at best.

A group of investigators, led by neurosurgeon Oleg Kopyov of the Good Samaritan Hospital in Los Angeles and

neurologist Matthias Kurth of the Barrow Neurological Institute in Phoenix, has recently begun performing neural
transplantation in HD patients, and this spring they have reported on the results from one patient at meetings of the American
Academy of Neurology and the American Society of Neural Transplantation.

The method these investigators have been using consists of isolating brain tissue containing the precursor cells for the adult
basal ganglia from four aborted 7-8-week-old human fetuses and then placing multiple plugs of this tissue into the caudate
nucleus and putamen of their patients. They are following the patients using a variety of measures, including videotape, a
modified version of the Unified Huntington's Disease Rating Scale (UHDRS), PET scanning, and neuropsychological testing.

As of April 1996, three transplantations had been performed. However, the investigators felt that only one of them had had a
long enough follow-up period to be reported on. This patient was unusual for several reasons. First, he had juvenile onset of
symptoms and had the rigid, parkinsonian variant of HD. Second, his pre-surgical disease course included an astoundingly
rapid six months of decline -- something generally not seen in the absence of factors beyond the disease itself.

The results in this case are also somewhat difficult to interpret. The patient experienced significant improvement in his motor
disability, particularly in his parkinsonian symptoms. This improvement, however, was essentially immediate and was sustained
for some months before declining again, though not back to baseline, by six months after the surgery. What is not clear is why
this patient improved. The natural history of improvement due to the transplanted neurons should be a gradual one over many
months as the graft takes hold and forms functional neuronal connections. The immediate improvement seen in this first case
raises the possibility that something other than the grafted neurons are responsible for his improvement. Furthermore, a
follow-up functional brain scan indicated only one region of viable graft in only one side of the brain. An analagous
improvement, despite nonviable grafts, was seen in some of the early efforts at neural transplantation for Parkinson's disease.
Also difficult to explain is the improvement experienced in the patient's neuropsychological testing. He experienced significant
performance improvements and, in fact, improved in almost every test -- including many for which the improvement cannot
easily be explained by the transplanted circuit.

The results of this one case thus raise so many questions that, by itself, it cannot be used to judge the efficacy or advisability of
the procedure. As Dr. Kurth readily states, the only really clear result from this case is that the procedure itself was well
tolerated and did not make the patient worse.

According to Dr. Kurth, the investigators do plan to perform additional transplantations and to follow their progress for a time
before deciding whether to continue their current procedure. These investigators seem to be responsible, have a genuine

background in patient care and neural transplantation, and have been very open about their procedures and results. It remains
to be seen whether this procedure has any potential benefit for HD patients.

NOTE: The Huntington's Disease Society of America has not funded any research involving the transplantation of fetal tissue.

New Theory on Cause of Huntington's Disease

March 1996

(from "The Marker," newsletter of the Huntington's Disease Society of America, Spring 1996)

Scientists at Duke University Medical Center have reported findings that could explain how the mutant HD gene destroys
brain cells and causes Huntington's Disease.

Their research suggests that the expanded protein produced by the HD gene binds with an important enzyme called GAPDH,
interfering with its crucial ability to produce energy in the brain. The result is brain cell death -- and HD.

While the scientists cautioned that many questions remain, the findings, published in the March issue of the journal Nature
Medicine, point to the possibility of some form of treatment based on the idea of blocking the interaction between protein and
enzyme.

"We are beginning to cross the difficult area between gene discovery and abnormal functions of the brain, and to open the door
to target drugs," said Dr. Allen Roses, scientific director of the Deane Laboratory at Duke, where the studies were done.

A team of scientists headed by neurologist Dr. Warren Strittmatter became interested in "triplet repeat" diseases, like HD,
two years ago when they discovered Haw River Syndrome, an inherited brain disorder that affects residents of a rural North
Carolina community.

They found that, as in HD, the syndrome was caused by a gene containing an expanded CAG nucleotide sequence.

HD and Haw River are among a small family of triplet repeat disorders all caused by a similar genetic flaw. Without knowing
the precise roles of the proteins produced by any of these disorders, the Duke team hypothesized that "these different proteins
are all doing something similar, which is binding to the same protein," according to Dr. Jeffery Vance, another member of the
team.

In other words, the abnormal repeat in the DNA is adding a "docking area" in the protein, allowing substances that bind
loosely to the normal protein to stick more tightly to the enlarged disease protein.

To test the theory, the scientists made artificial strings of glutamines -- either 20 glutamines, found in normal proteins, or 60
glutamines, found in mutant proteins. They then mixed the glutamine strings with brain proteins to see what interactions took
place.

They found that one brain protein, GAPDH, bound to the long glutamine string better than to the short one. GAPDH, found in
all cells, is known to produce energy, along with a number of other important functions.

Said Dr. Strittmatter, "The brain is entirely dependent on glucose metabolism, and this is a protein that is important in that
pathway. But because GAPDH is expressed in every cell, not just in brain cells, there has to be another level of complexity
that we don't understand."

Hopkins Scientists Find New Piece of HD Puzzle

March 1996

(From "The Marker," newsletter of the Huntington's Disease Society of America, Spring 1996, by Christopher Ross, M.D.,
Ph.D.)

While the discovery of the HD gene has clarified the genetics of HD and permitted more accurate diagnosis, a number of
questions remain about what causes Huntington's Disease and how to search for treatments.

Remember that all people carry the "HD gene," which produces a protein product called huntingtin. Huntington's Disease
results when this gene has mutated, or changed, producing an altered form of huntingtin.

One major question arises from the fact that the HD gene is active, meaning that it is converted into huntingtin everywhere in
the body. How then can the HD mutation cause disease only in the brain?

This puzzle was deepened during the past year when several groups reported that in HD, the altered huntingtin is also made
everywhere in the body.

One approach to solving this puzzle is to find other proteins with which the mutated huntingtin might associate. Several groups
are engaged in a search for such proteins.

A research group working in my lab at Johns Hopkins has recently found one, and has suggested that it might help explain
some of the features of HD.

The researchers, Shi-Hua Li and Xia-Jiang Li, used a technique newly developed by geneticists at SUNY Stoneybrook,
called the yeast two-hybrid screen, to search for proteins interacting with the HD protein. They called this new protein
"huntingtin associated protein 1," or HAP1.

With antibodies made in the lab by Alan Sharp, they used several different kinds of biochemical techniques to confirm that a
specific interaction between huntingtin and HAP1 indeed does take place.

Two features of the interaction are especially significant. First, the interaction takes place at the region of huntingtin containing
expanded glutamine repeat (the mutation that causes HD). Furthermore, the interaction is stronger when huntingtin has the
expanded repeat, and the longer the repeat, the stronger the interaction.

Second and most striking, unlike huntingtin, HAP1 is expressed selectively in the brain and not in other tissues in the body.

We believe that the abnormally strong interaction between huntingtin and HAP1 might be related to the initiation of the disease
process and might help explain why HD is a brain-specific disease. We are currently attempting to find out whether HAP1 is
involved with any of the known pathways that can cause neuronal cell death. If so, this will point the direction for therapeutic
(drug) intervention.

An attractive feature of the research is that the same assay that was used to find the interaction, the yeast two-hybrid screen,
can be used to screen for compounds that reduce the strength of the interaction. It's a relatively simple assay that can be used
to screen many compounds. A compound which could reduce the strength of the interaction between huntingtin and HAP1
might, potentially, be used to treat HD. Presumably, it would just have to bring the strength of the interaction back down to the
level seen with normal huntingtin to be effective.

Dr. Ross is associate professor of psychiatry and neuroscience at the Johns Hopkins University School of Medicine,
Baltimore, and is the newly appointed chairman of the HDSA National Science Council.

Research Progress Continues on Several Fronts (Animal Models, Clinical Trials, and Pallidotomy)

February 1996

Outgoing HDSA Science Council Chairman Dr. Roger Albin, of the University of Michigan, summarizes some of the main
areas of HD research.

ANIMAL MODELS

Two different strategies are being applied to the development of a useful animal model of Huntington's Disease:

A) Genetically Manipulated Mice Molecular biology techniques permit remarkable manipulation of mouse genes to create
rodent models of human diseases.

Techniques exist to eliminate the function of a particular gene (so-called knock-out mice), to insert a human or other foreign

gene into the DNA of mice (transgenic mice), and to alter the structure of a native mouse gene (knock-in mice).

All of these approaches have been, or are being, pursued by scientists trying to produce a mouse model of HD. This technology takes advantage of the fact that the human HD gene and its mouse equivalent are very similar in structure and presumably similar in function.

At least three labs have disrupted the function of the mouse HD gene. In these knock-out animals, death occurs in early embryonic life, suggesting a role for the `normal' (non-mutated) HD gene in normal development. Though these knock-outs are not models of HD, they may give valuable clues to the function of the HD gene.

Several labs are trying to introduce the human HD gene into mouse DNA. The hoped-for result is for expression of the "abnormal" human HD gene to cause nerve cell degeneration similar to that seen in HD.

This approach has been used with some success in producing mouse models of genetic Alzheimer's disease and Amyotrophic Lateral Sclerosis (ALS, or Lou Gehrig's Disease).

A parallel approach is to take advantage of the fact that the mouse equivalent of the human HD gene is very similar to the human gene. Some labs are attempting to introduce an expanded CAG repeat into the appropriate portion of the mouse HD gene equivalent, a knock in, in the hope of producing nerve cell degeneration.

If either the transgenic or knock-in mice produced a model of HD, then these animals would be used to investigate the mechanisms of nerve cell degeneration and to test potential therapies. Successful development of a mouse model could revolutionize research on HD.

B) Exploitation of Existing Models There are presently some rat models that mimic many features of the pathology of HD. These models are based on either the concept of excitotoxicity, in which normal methods of nerve cell communication have become toxic to nerve cells, or impairment of energy metabolism of nerve cells. These models have provided some excellent clues about the mechanisms of nerve cell death in HD.

Use of these models is proceeding in two directions. They are being studied to derive a complete description of the sequence of nerve cell death, possibly identifying additional points in the sequence for intervention. Secondly, they are also being used to evaluate potential therapies for HD.

CLINICAL TRIALS

The Huntington Study Group (HSG) is attempting to mount a major clinical trial of drugs we hope will slow the progression of HD.

This trial, which would evaluate the effects of remacemide (an anti-excitotixicity agent) and co-enzyme Q10 (an agent to boost
nerve cell metabolism) on the progression of HD, would involve 20 centers and about 350 patients in the USA and Canada.

An application to obtain funds to support the trial was submitted this past year to the National Institutes of Health (NIH). The
application did not receive funding but is being modified and will be submitted again. HSG investigators are optimistic about the
chances of funding with the revised application. The HSG is exploring other possible pilot clinical trials with other agents.

The HSG is now a substantial organization that contains almost all the clinicians interested in HD in the US and Canada and
several non-North American collaborators. It's a dynamic group with excellent leadership that is making real progress in
implementing clinical trials.

PALLIDOTOMY

Pallidotomy is a procedure, developed decades ago for treatment of Parkinson's disease, that is undergoing a renaissance. In
pallidotomy, a small portion of the brain is destroyed in an effort to control some of the movement problems that occur with
Parkinson's disease.

There appears to be a real role for pallidotomy in the treatment of advanced Parkinson's Disease. It has been suggested that
pallidotomy might be useful in treating HD patients with very violent chorea. This is plausible, but pallidotomy will not alter the
progression, nor alleviate the psychiatric/behavioral manifestations, of HD.

It is conceivable that pallidotomy might be useful for treating a small number of patients with very violent chorea but
pallidotomy will probably not be appropriate for the great majority of patients.

[Huntington's Disease Society of America Main Menu]