



Dear Friends,

the Year 2006 is almost over and, although the temperatures are more like springtime here in Hamburg, we are all hoping - as usual - for a White Christmas (at least in the northern parts of Europe). I have always dreamed of having lots of time before the festive season to deal with all the jobs which need to be done in advance, to enjoy the wonderful Christmas decorations in shops and houses, to feel the same excitement as the children waiting for this special day. But my dream hasn't come true yet! I always feel sentimental too, around this time of year - maybe because another twelve months have passed and I feel I have not managed to finish all the tasks I promised myself that I would complete. Dystonia has been one of the important tasks of my annual diary for many years and the future is full of inspiring and significant milestones for EDF. We are constantly working for you, for anyone affected by Dystonia, but it takes time and much effort and we are grateful for your continued support as we move forward together.

On behalf of the EDF Board I wish you and your families a Merry Christmas and a happy and peaceful New Year.

Didi Jackson, President



Annual Meeting 2006 in Brussels

The 13th General Assembly was again held in the Club de la Fondation Universitaire in Brussels with a record attendance of 22 delegates. The procedure is really the same every year: we start with scientific talks by members of our Medical Advisory Board and special guests and end with the General Assembly on Sunday morning.

This year, as well as welcoming Prof. Albanese, Prof. Relja, Prof. Ceballos-Baumann and Dr. Warner, we were delighted to have Jean-Pierre Bleton, who was a EDF Board Member for many years, Alexina Fantato from Oxford and Benedicte De Pauw, President of the Chilean Dystonia Society with us. We have published their interesting contributions in this Update.

Months before the Meeting we had also asked all the national groups to send in any questions on a Dystonia topic, as we thought this would be something new and interesting to everyone. A panel of experts answered altogether over 50 questions at the Meeting and a supplement with all

the answers is now attached to this Update.

Apart from talks on Dystonia we of course also enjoyed the social part of the Meeting – the traditional Welcome Dinner of Friday night and a surprise outing on Saturday late afternoon. This year it was a bus trip to Waterloo in bright sunshine, a most interesting talk on the amazing Battle of Waterloo and the more sporty delegates ventured up the 226 steps of 'Lion Hill', whilst others decided rather to sit in the sunshine and to have a good Belgian beer. This part of the Meeting is not only enjoyed by all, but it is an important element of any EDF Meeting, which allows delegates to get to know each other

better and introduces new delegates to the European Dystonia 'Family'.

Our EDF Meeting 2007 was planned to be in Hamburg in September, incorporating the first major Dystonia Medical Conference in Europe since 1994, with well-known speakers from Europe and North America. Such a meeting needs a lot of organising and planning well in advance and it will now be held in Autumn 2008, also in Hamburg.

We therefore have decided to hold the next EDF General Assembly in Vienna from the 21.–23. September 2007. Please keep the date free, more detailed information will follow soon.

A Systematic Review on the Diagnosis and Treatment of Primary (Idiopathic) Dystonia and Dystonia Plus Syndromes

Most well-known medical conditions have 'management guidelines' – basic rules, written and updated regularly by specialist medical committees which allow other doctors to be sure that they diagnose and treat patients in the best possible way, using the latest diagnostic techniques, medications and other therapies. These rules are written for each illness separately. In the case of less well-known (and, often, much more complicated) illnesses like dystonia, guidelines do not always exist and, therefore, fewer doctors have the information to give the best diagnosis and treatment. Until only a very few years ago, there were no guidelines for Parkinson's Disease!

In 2004, the European Federation of Neurological Societies (EFNS) and the Movement Disorder Society- European Section (MDS-ES) invited Prof. Alberto Albanese to create a task force of experts to write management guidelines for dystonia across Europe. The EDF Executive Director, Alistair Newton, was invited to become a member of this group and was very pleased to be able to represent dystonia patients' interests during the discussions. The final draft of the 'guidelines' was considered by the MDS – Europe committee and was published in the European Journal of Neurology in May 2006 as "A systematic review of the diagnosis and treatment of primary (idiopathic) dystonia and dystonia plus syndromes".

The following article is taken from the notes of a presentation made at the 2006 General Assembly by Prof. Alberto Albanese, Member of the EDF Medical Advisory Board. The full paper published in the European Journal of Neurology 2006, No. 13, Page 433-444 can be viewed and copied only by subscribers of the journal.

The Task Force

Alberto Albanese (Chairman) Milano, Italy; **Michael P. Barnes** (Neurorehabilitation) Newcastle Upon Tyne, UK; **Kailash P. Bhatia** (Clinical Neurology) London, UK; **Emilio Fernandez** (Paediatric Neurology) Barcelona, Spain; **Graziella Filippini** (Epidemiology and Systematic Reviews) Milano, Italy; **Thomas Gasser** (Neurogenetics) Tübingen, Germany; **Joachim K. Krauss** (Neurosurgery) Hannover, Germany; **Alistair Newton** (European Dystonia Federation) Brussels, Belgium; **Ivan Rektor** (Clinical Neurology) Brno, Czech Republic; **Mario Savoiardo** (Neuroimaging) Milano, Italy; **Josep Valls-Solè** (Neurophysiology) Barcelona, Spain.

Task Force Objective

The objective of the task force was to review the literature on diagnosis and treatment of primary dystonia and dystonia plus to provide evidence-based recommendations for diagnosis and treatment.

Background Diagnosis

- Dystonia is thought to be rare, but it is possibly underdiagnosed or misdiagnosed due to the lack of specific clinical criteria.
- A recent study evaluated the ability among neurologists with different expertise in movement disorders to recognise adult onset focal dystonia and found relevant disagreement, particularly among examiners with lesser expertise.

Prevalence

The prevalence of dystonia is difficult to ascertain. On the basis of the best available prevalence estimates, primary dystonia may be:

- 111 per million for early-onset cases in Ashkenazi Jews from New York area
- 600 per million for late-onset cases in Northern England
- 3000 per million for late-onset cases in the Italian population over age 50

Primary dystonia and dystonia plus are chronic and often disabling conditions with a widespread spectrum mainly in young people. Areas of specific concern include:

- Differential diagnosis with other movement disorders
- Etiological diagnosis
- Drug treatment
- Surgical interventions
- Genetic counselling

Search Strategy

- Computerised MEDLINE and EMBASE searches (1966-February 2005) were conducted using a combination of textwords and MeSH terms "dystonia", "blepharospasm", "torticollis", "writer's cramp", "Meige syndrome", "dysphonia" and "sensitivity and specificity" or "diagnosis", and "clinical trial" or "random allocation" or "therapeutic use" limited to human studies.
- The Cochrane Library and the reference lists of all known primary and review articles were searched for relevant ci-

tations.

- No language restrictions were applied.
- studies of diagnosis, diagnostic test, and various treatments for patients suffering from dystonia were considered and rated as class I to class IV according to the recommendations for EFNS scientific task forces.

Methods for Reaching Consensus

- The results of the literature searches were circulated by e-mail to the task force members for comments.
- The task force chairman prepared a first draft of the manuscript based on the results of the literature review, data synthesis and comments from the task force members.
- The draft and the recommendations were discussed during a conference held in Milan on February 11-12, 2005, until consensus was reached within the task force.

Diagnosis

- Literature search on the diagnosis of dystonia identified no existing guidelines or systematic reviews.
- Two consensus agreements, two reports of workshops or taskforces and 69 primary studies on diagnostic accuracy were found.
- Dealing with primary studies, there were 6 cohort studies, 23 case-control studies, 3 cross-sectional, and 37 clinical series.

Classification

The classification of dystonia is based on three axes:

- a) Aetiology
- b) Age at onset of symptoms
- c) Distribution of body regions affected

Aetiology (by Cause)

- **Primary (or idiopathic):** Dystonia is the only clinical sign and there is no identifiable exogenous cause or other inherited or degenerative disease.

Example: DYT1 dystonia

- **Dystonia plus:** Dystonia is a prominent sign, but is associated with another movement disorder. There is no evidence of neurodegeneration.

Example: Myoclonus-dystonia (DYT11)

- **Heredito-Degenerative:** Dystonia is a prominent sign, among other neurological features, of a heredito-degenerative disorders.

Example: Wilson's disease

- **Secondary:** Dystonia is a symptom of an identified neurological condition, such as a focal brain lesion, exposure to drugs or chemicals.

Examples: dystonia due to a brain tumour, off-period dystonia in Parkinson's disease.

- **Paroxysmal:** Dystonia occurs in brief episodes with normalcy in between. Idiopathic (often familial although sporadic cases also occur); symptomatic forms are due to a variety of causes.

- Paroxysmal kinesigenic dyskinesia (PKD; DYT-9): attacks are induced by sudden movement.

- Paroxysmal exercise induced dystonia (PED): attacks are induced by exercise, such as walking or swimming.

- Non-kinesigenic form (PNKD; DYT-8): attacks are in-

duced by alcohol, coffee, tea, etc.

- A complicated familial form with PNKD and spasticity (DYT-10) has also been described.

By Age at Onset

- **Early onset** (variably defined as £20-30 years)

Usually starts in a leg or arm and frequently progresses to involve other limbs and the trunk

- **Late onset**

Usually starts in the neck (including the larynx), the cranial muscles or one arm. Tends to remain localised with restricted progression to adjacent muscles.

By Distribution

- **Focal:** Single body region

Examples: writer's cramp, blepharospasm

- **Segmental:** Contiguous body regions

Examples: cranial and cervical, cervical and upper limb

- **Multifocal:** Non-contiguous body regions

Examples: upper and lower limb, cranial and upper limb

- **Generalised:** Both legs and at least one other body region (usually one or both arms)

- **Hemidystonia:** Half of the body (usually secondary to a structural lesion in the contralateral basal ganglia)

Description of Patients

The three axes should all be described in the clinical diagnosis of a patient with dystonia.

Examples:

- Early-onset primary generalised dystonia (DYT1 positive, DYT1 negative, etc.)
- Late-onset primary focal dystonia (cervical dystonia or "torticollis")
- Early-onset secondary multifocal dystonia (perinatal lesion, cerebral palsy, etc.)

Clinical Indicators

- Two articles have addressed the possibility of identifying clinical features to distinguish between primary and non-primary forms.

- The committee has evaluated that the evidence provided by these studies (both level IV) does not allow the use of their criteria as indicator for aetiological classification.

Diagnosis

Good Practice Points:

1. Diagnosis and classification of dystonia are highly relevant for providing appropriate management, prognostic information, genetic counselling and treatment.
2. Based on the lack of specific diagnostic tests, expert observation is recommended. Referral to a movement disorders expert increases the diagnostic accuracy.
3. Neurological examination alone allows the clinical identification of primary dystonia and dystonia plus, but not the distinction among different aetiological forms of heredito-degenerative and secondary dystonias.

Genetic Tests

- Diagnostic DYT-1 testing in conjunction with genetic counselling is recommended for patients with primary dystonia with onset before age 30 years (level B).

- Diagnostic DYT-1 testing in patients with onset after age 30 years may also be warranted in those having an affected relative with early onset (level B).
- Diagnostic DYT-1 testing is not recommended in patients with onset of symptoms after age 30 years who either have focal cranial-cervical dystonia or have no affected relative with early onset dystonia (level B).
- Diagnostic DYT-1 testing is not recommended in asymptomatic individuals, including those under the age of 18, who are relatives of familial dystonia patients. Positive genetic testing for dystonia (e.g. DYT-1) is not sufficient to make a diagnosis of dystonia unless clinical features show dystonia (level B).
- A diagnostic levodopa trial is warranted in every patient with early onset dystonia without an alternative diagnosis (good practice point).
- Individuals with myoclonus affecting the arms or neck, particularly if positive for autosomal dominant inheritance, should be tested for the DYT-11 gene (good practice point).
- Diagnostic testing for the PNKD gene (DYT- 8) is not widely available but this may become possible in the near future (good practice point).

Neurophysiology

- Neurophysiological tests are not routinely recommended for the diagnosis or classification of dystonia; however, the observation of abnormalities typical of dystonia is an additional diagnostic tool in cases where the clinical features are considered insufficient to the diagnosis (good practice point).

Brain Imaging

- Structural brain imaging is not routinely required when there is a confident diagnosis of primary dystonia in adult patients, because a normal study is expected in primary dystonia (good practice point).
- Structural brain imaging is necessary for screening of secondary forms of dystonia, particularly in the paediatric population due to the more widespread spectrum of dystonia at this age (good practice point).
- MRI is preferable to CT, except when brain calcifications are suspected (good practice point).
- There is no evidence that more sophisticated imaging techniques (e.g., voxel-based morphometry, DWI, fMRI) are currently of any value in either the diagnosis or the classification of dystonia (good practice point).

Treatment Recommendations

Botulinum Neurotoxins

1. BoNT-A (or Type B if there is resistance to Type A) can be regarded as first line treatment for primary cranial (excluding oromandibular) or cervical dystonia (level A).
2. Actual evidence is lacking on direct comparison of the clinical efficacy and safety of BoNT-A vs. BoNT-B.
3. Due to the large number of patients who require BoNT

injections, the burden of performing treatment could be shared with properly trained nurse specialists, except in complex dystonia or where EMG guidance is required (level B).

4. BoNT-A may be considered in patients with writing dystonia (level C).

Anticholinergic Drugs

The absolute and comparative efficacy and tolerability of anticholinergic agents in dystonia is poorly documented and no recommendations can be made to guide prescribing.

Antiepileptic Drugs

There is lack of evidence to give recommendations for this type of treatment.

Anti-dopaminergic Drugs

There is lack of evidence to give recommendations for this type of treatment.

Dopaminergic Drugs

Following a positive diagnostic trial with levodopa, a chronic treatment with levodopa should be initiated and adjusted according to the clinical response.

Surgery

Deep Brain Stimulation

- Pallidal DBS is considered a good option, particularly for generalised or cervical dystonia, after medication or BoNT have failed to provide adequate improvement.
- While it can be considered second-line treatment in patients with generalised dystonia, this is not the case in cervical dystonia since there are other surgical options available (see below).
- This procedure requires a specialised expertise, and is not without side effects.

Selective Peripheral Denervation and Myectomy

- Selective peripheral denervation is a safe procedure with infrequent and minimal side effects that is indicated exclusively in cervical dystonia (level C). This procedure requires a specialised expertise.

Intrathecal Baclofen (Consensus)

- There is insufficient evidence to use this treatment in primary dystonia; the procedure can be indicated in patients where secondary dystonia is combined with spasticity.

Radiofrequency Lesions (Consensus)

- This procedure is currently discouraged for bilateral surgery.

Diagnosis and Classification

Clinical observation is the key to diagnosis and classification. Genetic tests, neurophysiology and brain imaging provide supportive criteria.

Prof. Alberto Albanese
Istituto Neurologico Carlo Besta
Milano

The Genetic Survey of Dystonia in the North East of England

This is the script of the presentation made by Dr A. G. Butler, Vice-President of EDF, to the delegates at the EDF 2006 General Assembly in Brussels.



Good morning, ladies and gentlemen. If you remember I talked last year about the Epidemiological Survey of Dystonia (ESD) but this year I want to tell you about something that we started over three years ago. Those of you who were here last year should remember who I am, where I have been doing the research work for the past 13 years and why I have been doing it as the world's only full time Dystonia Epidemiologist.

All of the people I have been working with have given me tremendous assistance over the past 13 years in just finding the people with dystonia in this region (North East England). Remember my wife was the 97th person in the entire UK in 1972. When we started on 6th May 1993, there were only 143 people known to have dystonia within the North East of England. Today we have exactly 2,152 people registered within the ESD.

An important point is that no one has been paid anything since we first started. It has all been done entirely voluntarily. However we have now reached the point where we can no longer continue unfunded. Therefore we are about to put in a bid to the Medical Research Council in Great Britain in order to pay for a couple of phlebotomists to take the blood samples and a research worker to analyse the results.

However I like to tell you who I work with and where, before getting onto the important bit – **what** some of the results are and **what impact** they could have on your lives and **how** any of this research could alter the dystonia community in Europe.

So - who has helped me?

The Research Team

- Dr A.G. Butler – Dystonia Epidemiologist
- Dr Phil Duffey – Consultant Neurologist, York.
- Mr Maurice Hawthorne – Ear Nose and Throat (ENT) Consultant, James Cook Univ. Hospital in Middlesbrough

- Professor Mike Barnes – Neurological Rehabilitation Centre in Newcastle.
- Professor Patrick Chinnery – Professor of Neuro-genetics at Newcastle Medical School

with a lot of help from:

- John Whitaker - Outreach Nurse Practitioner
- Marjan Jahanshahi - Clinical Psychologist
- Jay Holland - Psychiatric Registrar
- Claire Gudex - Health Economist
- Peter Tilley - Consultant Neurologist
- Robert Allchin - Ophthalmic Surgeon

But mainly, the patients themselves !

The first four have been working together since the very beginning when we started officially on 6th May 1993 on the Epidemiology. Patrick Chinnery has come on board since 2002 as a specialist on the Genetics of Dystonia.

Map of the North of England and South of Scotland



This is **where** we are talking about. The North East of England includes the counties of Northumberland, Tyne & Wear, Co. Durham and Cleveland, with patients also taken from Cumbria and North Yorkshire but treated within just 8 dystonia clinics – Hunters Moor Regional Rehabilitation Centre and the Ophthalmology Unit at the Royal Victoria Infirmary in Newcastle, the James Cook University Hospital in Middlesbrough, the District Hospital in York, the Eye Infirmary in Sunderland and the Ophthalmology Department of Cumbria Infirmary in Carlisle. There are also two outreach clinics which operate from two of these hospitals at Whitehaven and Penrith in Cumbria.

Hunters Moor in Newcastle is the UK's largest user of

Botulinum Toxin and James Cook is No 4.

This area also has 11 dystonia nurse practitioners giving the injections once the patients have been seen and diagnosed by a consultant neurologist or ENT surgeon.

This area measures just 100 miles x 120 miles (160 km x 200 km) but it now has the world's largest regional database on dystonia.

The Genetic Survey of Dystonia (GSD)

- inclusive all types of dystonic movement
- inclusive Primary & Secondary Dystonia
- includes the whole of North East England
- each case clinically verified
- each person personally interviewed
- the research will be published in 2008
- the result of 15 years work

The GSD has been run as shown above, exactly the same as the ESD. In other words, the people in it are not exclusively registered at one clinic or another. Indeed importantly some are not registered at any clinic at all, thus making it totally inclusive. This has been one of the most important things about this epidemiology.

They are not just primary dystonias (although the majority are). All patients have been interviewed personally and have had a clinical diagnosis. We hope to have the results of the genetic survey completed and published in 2008

What are the Results?

- The numbers of people affected
- Their onset and diagnosis dates
- The genetic survey of dystonia
- The genes positively known
- The genes roughly known
- The future – where are we going?

So what are the results to date?

First I need to talk about the difference between onset and diagnosis – when their dystonia started and when it was first officially recognised. Then I will talk about the genetics of dystonia and how we are attempting to come

up with some definite answers to the questions that I am sure you all want to ask. Remember when I started we only knew of 147 people with dystonia in the North East of England. After the 1st year, we had nearly 250, and over 500 by the end of year 3. Today we have currently 2,152 people and the list is still growing at the rate of 168 new people each year or 3.2 every week.

Here are just the statistics of the 13 years work. Remember these are mostly new diagnoses, as can be seen next. I have deliberately not recruited anyone new since I gave the ESD talk a year ago, BUT we still have had 137 new people come into the epidemiology. In other words it is still growing day by day, week by week.

ONSET v DIAGNOSIS (1)

1992	74	73
1991	78	60
1990	90	54
1980's	411	168
1970's	152	27
1960's	70	11
1950's	18	2
1940's	13	2
1930's	8	0
1920's	3	0

The earliest onset date is 1924, but the earliest diagnosis date is 1942. The above figures just show those people up to 1992 before we started the research.

Remember the numbers of diagnoses. 355 (9 more than last year) people were diagnosed between 1980 and 1992, averaging just 29 per year or just over 0.5 persons per week. Prior to that, up to 1979 the figure was just 42 diagnoses within 37 years, ie 1.1 per year. This is the information on the 1,913 people whose data have been analysed to date, with 239 still to be completed. The average number of dystonia patients diagnosed for the past twelve years has been 2.3 people every week. The average number of cases of onset is just 1.58 per week. Deaths were only recorded since 6th May 1993 – no one has ever died directly from dystonia – these are all just natural deaths except two, and they were self-induced. The overall incidence of dystonia is far far higher than anyone has previously seen or even considered possible.

What is also surprising is the incidence of people with genetic forms of dystonia.

The human body contains 100 trillion cells (ie one million million). Each cell contains a black blob called a nucleus. Inside the nucleus are two sets of the genome. One set of the genome came from the mother of the patient, the other set came from the father. Each set contains 60,000 – 80,000 genes. Both sets are on 23 chromosomes. In practice there are often small and subtle differences between the two sets, thus causing blue eyes or red hair, etc. This is just to give you all an overview of how the human body relates to its DNA.

Remember I am the dystonia epidemiologist, but I will try to give you an overview of the genetics of dystonia as we know it to date.

The Genome (1)

- Twenty three **chromosomes**
- Each chromosome has several thousand **genes**
- Each gene has **exons**, interrupted by **introns**
- Each exon is made up of **codons**
- Each codon is made up of **bases**
- There are over one billion **codons** in the human body

The genome (the complete set of human genes) is “constructed” as above. 23 chromosomes – these are the bits that everyone knows about. But each chromosome has several thousand genes in it and so on and so on.

The Genome (2)

- Genomes are written in 3 letter sets
Using only four letters
- A = Adenine
- C = Cytosine
- G = Guanine
- T = Thymine

The way we understand these genomes in by using four letters. A, C, G and T. These are written entirely in three letter words. However there are some “rules”: A likes to pair with T and G with C. The usual state of DNA is the famous “Double Helix” with the original strand and its complementary pair intertwined. To make a copy of the

complementary strand it therefore brings back the original text, so the sequence ACGT becomes TGCA in the copy, which transcribes back to ACGT in the copy of the copy. This enables DNA to replicate indefinitely yet still contain the same information.

The Genome (3)

- These are “written” on long chains of sugar and phosphate called DNA molecules
- Each chromosome is one pair of (very) long DNA molecules

Let us now examine which DNA molecules are thought to cause dystonia in all its various forms. Each chromosome is one pair of very long DNA molecules. I am NOT an expert on DNA, but I hope that this so far gives you an oversight into the incredibly complex programme which constitutes the human body.

So what goes wrong to cause dystonia?

4 defined genes

- DYT1 = ITD = 9q34 Torsion A
- DYT5 = DRD = 14q22 GCH 1
- DYT11 = Myoclonic = 7q21 Sarcoglycan
- FTL = Neuroferritinopathy = 19q13

This last one has not been recognised as yet but was discovered in Newcastle and has a very large family in Cumbria.

All of the information given to you today is already ‘old news’, merely because things are moving so quickly. As far as I am aware, there are only 4 genes fully defined which cause various forms of dystonia.

Everyone has heard of the DYT1 gene, which causes early-onset dystonia, previously called Idiopathic Torsion Dystonia or more recently Oppenheim’s Dystonia. It may present initially as focal in the limbs, but often generalizes, especially if early onset.

The DYT5 symbol has now been officially withdrawn but I will continue to use it here. It is hereditary progressive dystonia such as Segawa’s Syndrome, which is usually Dopa Responsive.

DYT11 is the myoclonus gene which is also usually alco-

hol responsive. I have a small number of alcoholics in my study because they have become so after getting used to drinking in order to stop their shakes. So much so that they have become addicted to the "medication".

Finally Professor Chinnery in Newcastle has discovered the Neuroferritinopathy gene 19q13 which has been found to be causing a very large family in Cumbria various different forms of dystonia.

10 less defined genes

- DYT2 = Spanish Gypsies –
- DYT3 = Lubag Disease = Xq13.1
- DYT4 = Whispering dystonia =
- DYT6 = Mennonite = 8q21-p22
- DYT7 = German family = 18p
- DYT8 = Paroxysmal dystonia = 2q33-q35
- DYT9 = Choreoathetosis = 1p
- DYT10 = Choreoathetosis = 16q11.2-q12.1
- DYT12 = Rapid-onset dystonia = 19q13
- DYT13 = Cranio-cervical dystonia = 1p36.13-36.32

DYT2 was discovered within the group of Spanish Gypsies but no firm evidence has been produced.

DYT3 causes the famous Lubag Disease prevalent in the Philippines mainly in males. Incidentally my research has shown that dystonia is almost exactly twice as prevalent in females than males.

DYT4 was found in a single large Austrian (or Australian) family with mainly laryngeal or cervical dystonia

DYT6 found in two Mennonite families with cranial, cervical or limb dystonia

DYT7 was found in a single German family with focal or postural tremor from 28 to 70 years old

DYT8 is technically Paroxysmal Non-Kinesogenic Dyskinesia or Choreoathetosis.

DYT9 causes choreoathetosis, spasticity or episodic ataxia.

DYT10 is defined as causing Paroxysmal Kinesogenic Choreoathetosis

DYT12 causes Rapid Onset Dystonia with Parkinsonism
DYT13 has been found in a single Italian family with cranio-cervical features

The Future

- Dystonia is a **significant** movement disorder
- It is 2nd only to Parkinson's in prevalence
- It has remained unknown for far too long
- Treatment is better now than previously
- The genetics are giving significant results
- We are just at the beginning of a long road
- This is only one of the ways in which we will eventually discover the cure for the very debilitating disorder called **DYSTONIA**.

So, finally, what does the future hold for us all?

We have already started to collect blood from everyone in the ESD with any form of dystonia, even the HFS. Remember what I (and indeed John Whitaker, our Dystonia Nurse Practitioner) have said in the past. Not every HFS is caused by a blood vessel touching a nerve behind the ear, some definitely have dystonia.

We already have 37.5% of the people in the ESD with a family member (alive or dead) who has definitely been diagnosed or is greatly suspected of having dystonia. I estimate this will rise to over 50% of all people in the ESD when we have finished and analysed the results.

BUT this still leaves the other 50% with no genetic connection at all. Let us not get carried away with the genetics, although vitally important for us all understanding more about dystonia, it is not the answer for everyone. We need to continue in all possible ways to help everyone with dystonia. Even if we do not discover the cure immediately, the sense of relief that a correct diagnosis gives people can be visibly seen.

Dr. Anthony G. Butler, PhD

Dystonia Epidemiologist

EDF Vice-President

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A Mechanical Device to relieve Blepharospasmus

A new device to help patients with Benign Essential Blepharospasm is being developed at The Oxford Eye Hospital in the United Kingdom and Alexina Fantato, who is a Specialist Ophthalmic Nursing Sister there, was invited by EDF to talk about it at our recent General Assembly in Brussels in September. Alexina has sent the following summary of her presentation and has asked us to express her thanks to EDF for the warm welcome she received at the GA.



What is Blepharospasm?

Benign Essential Blepharospasm is a Focal Dystonia, which causes involuntary spasmodic eye closure due to over-activity of the orbicularis oculi muscle. This disabling condition can make the patient functionally blind, and can severely affect the quality of life. The increased frequency of blinking and fluttering of the eyelids is gradually replaced by the unpredictable and increasingly long periods of bilateral eye closure.

Blepharospasm can vary in severity, especially during the early stages. Characteristically, spasms can become worse in the bright light or when the patient is tired or feeling particularly anxious. Reading, or walking outside, especially among other people when the patient needs to see, often causes eye closure. Paradoxically, talking and eating seems to improve the condition.

Blepharospasm affects more females than males, and usually develops in the 5th to 7th decade of life. More than 4,000 individuals are known to have Blepharospasm in the U.K., and the total number of patients is more than 400,000 worldwide. The cause is still unknown, but it is thought to be a neurological disorder in the Basal Ganglia of the brain, which regulate muscle movement.

Small amounts of Botulinum Toxin injected into the eyelids are a safe and effective treatment for Blepharospasm, producing an overall weakening of the orbicularis oculi muscle. Relief from symptoms usually lasts between 6-12 weeks, so patients return for repeat treatment every 2, 3, or 4 months.

Mechanical device

There is an alternative method to allow eye opening for patients who have Blepharospasm. This is a pressure device, - attached to the arm of the spectacles -, which

stimulates the afferent nerve pathway with impulses and blocks that pathway to relieve the spasm. The pressure is applied quite gently to the side of the head, and is based on the "Geste Antagoniste" phenomenon. There is no known study so far into the "Geste Antagoniste", although it is acknowledged that Blepharospasm patients get relief from touch or pressure.

The study at the Oxford Eye Hospital is examining whether this device is effective in relieving the symptoms of Blepharospasm. The study is intended to show whether the patients who do not respond to Botulinum Toxin injections, or who need more therapy than injections alone, would benefit from wearing the device attached to their spectacles.

A number of patients have already been involved in trials of a prototype of this device with positive results. Some of these patients now rely on the device to be able to continue their jobs. It seems likely that the further research will show that many more patients will benefit from wearing this device. Many more people with Blepharospasm could have improved self-esteem and be more confident and independent in their activities of daily living.

The formalities of setting up a clinical trial are under way, with applications awaiting approval from the Ethics Committee and the Medicines and Health Regulatory Agency. A manufacturer is working on designing and producing a device which is practical, safe and cosmetically discreet. The trials are being scheduled for the spring of 2007 and we hope they will give positive results. We will then be able to make larger numbers of the devices, so that this aid can be introduced to the wider population of Blepharospasm patients. The study results can be published to inform other health care professionals, who can then introduce this new form of relief to their patients.

This project has also been made possible through the generous support and funding of The Dystonia Society of the United Kingdom, under the management of Philip Eckstein. We also look forward to working with EDF to make the device available to Blepharospasm patients in other European countries.

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Rehabilitation Programmes for Dystonia

One of our speakers at the 2006 General Assembly in Brussels was former EDF Board member Jean-Pierre Bleton from Paris. Jean-Pierre is well-known throughout the world of dystonia as an expert in applying physiotherapeutic techniques in rehabilitation of patients. He has written several books on the use of physiotherapy in dystonia rehabilitation, especially cervical dystonia and writer's cramp. The following is a transcript of his notes for his presentation in Brussels.



Writer's Cramp

Writer's cramp is an occupational dystonia which appears as soon as the person starts to write and leads to partial or complete inability to write.

The Rehabilitation programme for Writer's cramp is designed as a re-learning process, using a behaviourist approach. Each rehabilitation session is personalised to the patient and lasts for 30 to 40 minutes. A programme lasting between 6 and 18 months is required to correct writer's cramp, and stopping rehabilitation too soon can lead to a relapse. Should the treatment fail, there are palliative options which can be applied, such as orthoses, appropriate pens, information technology or the use of the other hand.

As demonstrated by a practitioner named Ajurriaguera, the application of and training in certain relaxation methods are very beneficial in preparing for the writer's cramp rehabilitation programme.

The first step is to perform exercises (not related to writing) to improve independence and precision of fingers and wrist movements before pre-writing exercises with a pencil are used to regain fluidity and comfort of holding the pen. Then the patient is helped to achieve an ergonomic grip on the pen. At the same time the muscles involved in the correction of dystonic postures are trained by drawing of loops, curves and arabesques.

During writing practice, the patient concentrates on breathing evenly and on keeping the arm, shoulder and torso relaxed. At this stage of learning it is recommended that certain movements should be over-emphasised, so that the patient becomes familiar with them and able to control them perfectly. Exercises and material which will not trigger the dystonic movement are selected.

An imaging study on patients after recovery has shown the changes of brain patterns. A reshaping of the sensory cortical hand representation appears to be associated with clinical improvement in dystonic patients after rehabilitation.

Rehabilitation of Cervical Dystonia

The abnormal head posture in cervical dystonia is due to repetitive pathological contractions (clonic form) or constant deformity (tonic form) of one or more neck muscles.

Specific rehabilitation of Cervical Dystonia has been commented on for a long time. Each Cervical Dystonia is singular so the approach of the physiotherapist has to be specific. There is not one single method but several strategies, which deal with the various clinical presentations. The exercise programme is selected in the light of the physiopathology of the dystonia:

- shortening reaction
- lack of balancing action among the main muscles
- difficulty to isolate individual muscle action

There are two main physiotherapy strategies according to clinical presentation:

- The first is the rehabilitation of 'tonic form' which tries to recover the balance between the actions of the different muscles that play a role in the position of the head.
- The second is the rehabilitation of 'myoclonic form' which tries to stop and replace involuntary and inappropriate head movements by conscious and co-ordinated movements.

Cervical Dystonia rehabilitation is essentially behavioural, combining resistance to spasm and muscle relaxation. Physiotherapy and the botulinum toxin injections mutually interact in order to reduce the symptoms and improve quality of life. The weeks following the course of botulinum toxin injections are the ideal time to carry out physiotherapy treatment. Given the weakness of the dystonic muscles after injection, the antagonistic muscles are more able to contract.

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FUNDACIÓN Dystonía (CHILE)



Benedicte De Pauw, who was founder of the Chilean Dystonia Society and has been President since 1995, attended the General Assembly in September in Brussels. Her talk on the enormous problems, but also achievements of the Chilean Group was most interesting and we like to congratulate her on her wonderful work.

The Chilean Dystonia Association was founded in 1997 on the initiative of a few patients, as until then, dystonia was totally unknown and any treatment was very expensive.

Our Mission is

- to establish Dystonia as a neurological disorder among the medical community, the patients, their families and the community in general, in order to improve the diagnosis process.
- to obtain improvement in the treatment of dystonia.
- to achieve a better quality of life for patients

Through our organization we want to generate a network of support and self-assistance among patients and their environment.

Our Main Activities for our 430 Members:

- Four meetings a year for patients and their families with medical presentations.
- Four issues a year of our Newsletter "DISTONÍA NEWS" for all foundation members and supporters.
- Special assistance for members with a low income.
- Celebration of the National Dystonia Day and an annual dinner.
- Medical meetings every second year inviting dystonia specialists from other countries.

CETRAM

We participate in a Movement Disorder Centre (CETRAM) where specialized treatment for patients is provided thanks to the generosity of Chilean neurologists, therapists and the support of the University of Santiago and the Friends of Parkinson.

The Importance of being Together

In CETRAM almost 100 patients with Parkinson's and Dystonia are participating in various rehabilitation programs including a Workshop amongst the hanging gardens, a Workshop for personal development and kinetic exercises. At the Centre we also share and organise parties to celebrate Chile's Independence Day, Christmas, and before the summer vacations we have a special meeting to end the activities for the year. An important part of our

social rehabilitation is formed by simple things like being an active member of a group, having a meal together and being there to share good and bad moments with Dystonia. One of our next activities will be to establish more selfhelp groups in other parts of the country.

Government Support on Botulinum Toxin Treatment for Dystonia



On the 1st of September 2006, - the National Day of Dystonia - after 6 years of meetings with the health authorities and public demonstrations by members of the Dystonia Foundation, the Health Ministry finally agreed to finance – subject to a limited amount of funds – a pilot program on botulinum toxin treatment for cervical dystonia and blepharospasm at public hospitals. The Health Ministry has now formed a Committee including a member of the Chilean Dystonia Foundation and a neurologist of our medical center to initiate the program. This program will improve lives of Dystonia patients in Chile considerably.

It was worthwhile fighting for this facility for over 6 years and we hope the support will continue in the coming years. As copper is the most important source of income in Chile and the price for copper is three times higher than 2 year ago, it seems fair that the government should increase its contribution to social projects.

Bénédicte De Pauw

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New EDF Secretary

At the General Assembly 2006 Barbara Gygli Dill resigned as Secretary from the EDF Board for personal reasons and we thank her for her very dedicated work for the last two years. As the election for this position is only due next year, the EDF Board co-opted **Philip Eckstein**, the delegate of The Dystonia Society, UK, (TDS) onto the Board as Secretary.

Philip Eckstein is Chief Executive of TDS and was appointed to this EDF position with the full agreement of the TDS Board. As a co-opted member of the Board, Philip will not have a vote but will be eligible for election to this position at the 2007 General Assembly.

The present Board members welcomed him to the usual short Board meeting immediately after the GA and look forward to working with him.



Merger of AMADYS and LFCD

Over a period of more than three years the Board of AMADYS and LFCD have worked on merging the two French Dystonia Groups, which was not an easy decision. After long and amicable discussions it was agreed at the General Assembly of LFCD on the 30th September 2006 to dissolve LFCD, in order to facilitate the necessary administrative procedures. The new Association is called 'Association de Malades atteints de DYStonie (AMADYS), but the acronym will be AMADYS/LFCD. This will be effective from January 1st 2007.

Board members from both Societies will work together in the newly formed group and Chantal Lecerf (formerly LFCD) and Françoise Prat (AMADYS) will both be contact persons to EDF member groups. EDF congratulates the new Society on their achievement and will give it every support.

Suomen Dystonia-Yhdistys ry

In January 2006 Marjut Vannainen, who attended the General Assembly in Brussels in September, was elected as the new Chairwoman of the Finnish Dystonia Society. She lives in Paimio – 30 km from Turku -, is married and worked in a Bank for 31 years. Because of her Cervical Dystonia, which started in 1988, she had to retire and now dedicates her time to helping people with Dystonia. Marjut will also be the contact person for EDF, as Liisi Niemi retired from the Board. We like to thank Liisi for all her support, which she has given EDF for many years and wish her all the best.

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