

# EUR - ATAXIA

EUROPEAN FEDERATION OF HEREDITARY ATAXIAS

## EDITORIAL

The 4th AGM of EURO-ATAXIA was recently held in the Holiday Inn Gatwick, England. The meeting lasted over two days from 26th to 27th September and was hosted by the F.A. Group of the U.K. who did their customary excellent work in organising the conference.

In his opening speech President Manfred Van den Kerchove again stressed the vital importance of molecular genetics in the fight against all forms of ataxia.

He stated that the placing of genes on correct chromosomes may have begun as an intellectual exercise, but which has gained greatly in importance over the years. Now that molecular genetics have become widely established, it is vital that clinicians and scientists should continuously exchange information, and EURO-ATAXIA, although only a small group, is privileged to play a part in the distribution and exchange of this information.

Dr. Manfred Van den Kerchove also introduced Dr. Eric Legius, a clinical geneticist from Leuven, working closely with him.

A special welcome was made to Dr. Sue Chamberlain who combines in one person the qualities of accomplished scientist and a caring and sympathetic person.

The line-up of the present board has changed with the resignation of Sian Williams as vice-president owing to pressure of other commitments. We thank her for her enthusiasm. Her place as vice-president will be taken by Michael Morgan (Ireland).

During the coming year EURO-ATAXIA plans to produce a book on all aspects of ataxia and ataxia research in Europe. Hopefully it should be available by the end of 1993.

The thorny problem of subscription was again debated. After much discussion it was decided to base this on a rate of 1 ECU per voting member of each national group.

## ESHG AT HELSINGØR

The European Society of Human Genetics (ESHG) chose the historic location of Helsingør in Denmark as the venue for its 24th Annual Meeting, which was held earlier this year, over the elongated weekend of 27-31 May.

A number of papers dealing specifically with the ataxias were presented, as were a number of wider workshops and discussions in which ataxia researchers (as well as ataxia groups) could be expected to be keenly interested. An early session on the 27th discussed *Genetic Services in Europe: Who provides them?*, chaired by Rodney Harris of St. Mary's Hospital, Manchester, England. Participants included Lucien Koulischer of the University of Liège in Belgium and Gert-Jan van Ommen, from the University of Leiden in Holland. Discussion centred on the teaching of genetics to medical students as well as the training of laboratory geneticists.

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These general themes were continued in a number of sessions held on 30th May. In a discussion organised by the Lay associations of ESHG (EAMDA, VSOP, GIG and others), Terkel Andersen, of Copenhagen, Denmark, reported on a *New information and counselling service on rare diseases in Denmark*, while at a scientific session held the same day Gerry Evers-Kiebooms, of the University of Leuven in Belgium, presented a paper entitled, *Genetic counselling and genetic testing: Psychological aspects and psychosocial studies*. Both are surely very important areas, both for medical personnel, especially clinicians who deal with ataxia on a daily basis, and of course, for ataxic people themselves – the potential 'clients' of any new service. Ineke L.L.E. Bolt followed with a paper on *Ethical aspects of predictive diagnostics for late onset diseases*, again, an area as yet little developed by medical authorities, yet of course, of major, daily importance to people with ataxia.

Papers dealing specifically with ataxias of one sort or another were also presented in the conference. At a workshop on 28th May, Eva Nelis, of Wilrijk, Belgium, delivered a report on a *Genetic heterogeneity study in nine families with Charcot-Marie-Tooth type 1 (CMT 1) disease*. At the same session Michael Koenig, of Strasbourg, France, presented *Mapping the Friedreich's Ataxia locus by recombinant microsatellite haplotype in a population with founder effect*.

Some of the abstracts presented to the conference also dealt with ataxia research. A list of titles are set out below, while copies of the abstracts themselves can be obtained from either the EURO-ATAXIA editor or secretary:

*DNA Extraction from Fmol preserved samples of Liver and Brain: Molecular study of Olivopontocerebellar Atrophy 1 (OPCA 1)*; Matilla, T; Rosell, J; Estivill, X; Volpini, V. Molecular Genetics Department, I.R.O., Hospital Duran i Reynals, Barcelona, Spain.

*Molecular Genetic Analysis of a Friedreich's Ataxia Founder effect in South-Eastern Spain*; Monros, E; Prieto, F; Lopez-Arlandis, J; Vilchez, J; Sevilla, T. Genetics and Neurology Services, Hospital La Fe, Valencia, Spain.

*Friedreich's Ataxia in the Spanish Population: Linkage Disequilibrium and Recombinations which orientate the location of the Disease Locus*; Monros, E; Lopez-Arlandis, J; Vilchez, J; Prieto, F; Palua, F. Genetics and Neurology Services, Hospital La Fe, Valencia, Spain.

*Genetic Heterogeneity study in nine families with Charcot-Marie-Tooth Type 1 (CMT 1) Disease*; Nelis, E; Timmerman, V; Raeymaekers, P; De Jonghe, P; Martin, J-J; Van Broekhaven, C. Laboratories for Neurogenetics and Neuropathology, Born Bunge Foundation, University of Antwerp, Belgium.

## CUBAN SYMPOSIUM ON DOMINANT ATAXIA

An International Symposium on Dominant Hereditary Ataxia will be held in Havana, Cuba at the end of this year, on 11th December to be precise. The Symposium will be held as part of the International Congress of Neurology and Neurosurgery, which runs from 7th to 11th December.

The Symposium on Ataxia will discuss a wide range of topics including; clinical features, classification and nomenclature, molecular genetics, neuropathology and clinical neurophysiology. Invited speakers will discuss recent developments in research into dominant hereditary ataxia, and those wishing to submit abstracts and poster presentations should do so before August 31st.

If you are interested in attending the Symposium, please contact either Dr. Alberto Nodarse, the Symposium convenor, or the Congress and Symposium organizing agency for 'Neurology and Neurosurgery 92, Ataxia Symposium' (addresses below).

Attendance fee for the Symposium is set at \$100 (US). Travel arrangements, hotel reservations and visa requirements may be made through any Havana International Conference Centre representative in your home country, as well as through the Congress and Symposium organizing agency in Cuba itself.

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## SPAIN: THE AEAH

The Asociacion Española de Ataxias Hereditarias is a national organization trying to meet the needs of ataxic people in Spain. It sees EURO-ATAXIA as an ideal forum for the interchange of fresh ideas to meet the needs of ataxic people everywhere.

In Spain, as elsewhere, the medical aspects of ataxia take first place. A major problem arises with initial diagnosis. There is a need to establish fixed diagnostic criteria agreed to by all doctors, for correct diagnosis of the different types of ataxia. Secondly there is a need for treatment and the increased development of research, information and prevention programmes. While these objectives gather most effort in the fight against ataxia, the question of what

to do until a medical solution is available remains unanswered.

Ataxic people everywhere face many problems in living: education, psycho-social, psycho-sexual development, coping with emotional pressures. The Family appears, on this basis, to be an important site of these 'problems in living' but also the space where some of the principal problems can be met. There is of course its influence on children through education, socialization, etc. As well, the family itself suffers from the disease too: frustration, guilt, culpability, etc. This is especially so in the case of hereditary diseases, often affecting several members of the same family.

Our aim is therefore to supply skills to the families to enable them to know what to do, to see the crucial importance of a good education, the path to social integration and personal autonomy.

Ataxia very often leads to personal isolation and depression, especially as the first signs of disability come during adolescence. This is where the Asociación has proved itself of great value, as a means of sustaining relationships. Psychotherapy groups as well as a personal approach (especially when performed by other ataxic people) have also proved their worth.

The lack of general rehabilitation and logotherapy programmes is another serious problem, deepened by the difficulty to find suitable places to develop them. Employment, leisure, personal autonomy also deserve a detailed study. We believe that EURO-ATAXIA offers a unique opportunity for this, which should be firmly grasped.

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## SPAIN: RESEARCH IN VALENCIA

The genetics unit of the hospital La Fe in Valencia, Spain, is a cytogenetic and molecular genetic department working in both diagnosis and research into hereditary diseases. The genetics and counselling of Friedreich's ataxia is one of our research projects. At present a research team of three (two Doctors and a Ph.D. student) are working on the project, supported by a grant from the Fondo de Investigación Sanitaria (a research agency within the Spanish Ministry of Health). Another project at Valencia, on neurogenetics, also includes work on Friedreich's ataxia.

Altogether, we can distinguish between three aims:

- 1) Clinical diagnosis, together with epidemiological and prevalence studies, performed by a team of neurologists from the Neurology Department at

La Fe.

- 2) Genetic analysis, looking for the following: Research into linkage disequilibrium studies in the Spanish population using probes from the FA linked marker loci D9S5 and D9S15, and to find recombinant families that will allow us a correct gene location (we already have two of this specific type of family identified).

Investigating new probes in order to see if FA gene could be located in a smaller genomic region. Later our purpose will be to isolate and characterize a candidate gene for the disease.

- 3) Offering a prenatal and predictive diagnostic service to families if so requested.

Currently we have determined the incidence (6.18/100,000) of Friedreich's ataxia in Valencia. Also molecular genetic studies have been performed in 23 Spanish families with samples available from a further six. Up to the present moment no prenatal diagnosis has been requested.

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## AMERICAN REPORT: THE NAF

The National Ataxia Foundation (NAF) is the main organization fighting ataxia in the USA. As well as a central office, based in Wayzata, Minnesota, the NAF is composed of thirty 'Chapters' and Support Groups. A Chapter is simply an Americanism for a local, or regional, branch of a national organization. In the case of the USA these are usually state-wide groups, with a high proportion (21 out of 30, or 70%) located in a broad swathe linking the Great Lakes in the north to the Gulf of Mexico in the south. The Mid-Western states are especially well represented.

The NAF puts a tremendous input into ataxia research at various centres throughout the USA. It's currently running a campaign to raise \$1 million for research, under the title: 'Stop Ataxia'. Funds raised are well-spent. Hence in the eighteen months up to January 1992 NAF funded the following six research projects:

*Linkage studies of a Large Spinocerebellar Ataxia Pedigree*, Dr. Bronya JB Keats, Ph.D., Dept. of Biometry & Genetics, Louisiana State University Medical Center, New Orleans.

*Locating the Gene(s) for Episodic Ataxia*, Dr. Michael Litt, Ph.D., Professor of Biochemistry & Molecular

Biology, Oregon Health Sciences University.

*Isolation & Molecular Cloning of an Ataxia-Telangiectasis Gene*, Gary Braedt, Ph.D., Assistant Professor, Dept. of Biological Sciences, University of New Orleans.

*The Brain Polyamine System in Dominantly Inherited Olivopontocerebellar Atrophy*, Stephen Kish, Ph.D., Clarke Institute of Psychiatry, Toronto.

*Genetic Mapping of Inherited Murine Cerebellar Ataxias*, Dr. Daniel Goldowitz, Ph.D., Associate Professor of Anatomy & Neurology, University of Tennessee.

*Localization & Isolation of the Gene for an autosomal dominant, HLA-linked form of Spinocerebellar Ataxia (SCA1)*, Harry T. Orr, Ph.D., University of Minnesota, Minneapolis.

Photocopies of all six research reports are available from the EURO-ATAXIA editor on request, or, indeed, from the NAF itself.

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## GENETIC INTEREST GROUP

The Genetic Interest Group (GIG) was founded in May 1989 as an umbrella group to represent the common interests of voluntary organisations concerned with genetic disorders. It believes that it can achieve much more than groups working separately. Specifically it wants genetic services to be as coordinated as possible (clinical investigation, laboratory tests & specialised counselling provided by trained doctors, nurses and social workers.)

Last year, November 15th, 1991, the second GIG Interface meeting took place at Baden Powell House in London. Many professionals and members of voluntary bodies attended the meeting which looked at *CHOICES: Transition to Adult Life for People with Genetic Disorders*, and examined some of the social, psychological and sexual issues that are important to people growing up with genetic conditions. Professor David Taylor (Professor of Child & Adolescent Psychiatry, Royal Manchester Children's Hospital) spoke about the problems facing all young people during adolescence, such as the desire to be physically attractive, independent and sexually competent.

Medication may successfully combat a particular symptom, but the need for psychological help, the opportunity to share feelings of isolation, anxiety or fear, for example, is equally important. As in many situations, denial of the particular problem may well cause even more distress. Other subjects discussed included *Transition of Esteem, Awareness of Mortality and Psychological problems that affect Sexuality*. Dr. I.K. Temple (Wessex Regional Genetics Centre, Southampton) spoke on the subject of *Reproductive choices for someone with a genetic disorder*, recognising that the genetic risks involved, when deciding whether or not to have children, can create much anxiety, guilt and confusion. The different choices available clearly demonstrate that there can be no right or wrong decision, a fact which emphasises the importance of having access to genetic counselling services which can offer information and support. At the end of the GIG meeting, a panel of people with genetic disorders (which included myself and Shirley Connell, also from FAG) talked about our own experiences and answered some questions from the audience. The conference highlighted several important issues, such as the vital importance of counselling services for those affected by genetic disorders.

During 1992 GIG aims to campaign for better services for people affected by genetic disorders, particularly for the provision of many new diagnostic tests, treatments and therapies currently being developed through research.

GIG held its third interface meeting on April 10th last, at the Institute of Child Health in London. Entitled *Biotechnology – The Way Forward*. The meeting was called to discuss reactions to the recent UK Government Report of the Committee on the Ethics of Gene Therapy (The Clothier Report), published in January 1992. A series of speakers outlined their researches to the day-long meeting, chaired by Professor Bob Williamson of St. Mary's Hospital Medical School, London. Bob Williamson himself gave the first talk, on Gene Therapy, followed by Dr. Gareth Morgan of the Institute of Child Health on Bone Marrow Transplant techniques, Dr. Elaine Dzierzak of the National Institute for Medical Research, on Transgenic animals and, concluding the morning session, Dr. Bernadette Modell of the University College Medical School, London, talked on the Ethical implications of genetic testing. Each paper delivered was followed by an open discussion of the points raised. Leading in the afternoon was Professor Martin Bobrow of Guy's Hospital Medical School, London, who gave a talk on Development and availability of Diagnostic Tests, which looked at the realities behind genetic testing, a theme taken up by the last speaker of the day, Dr. Roger Beech of St. Thomas's Hospital Medical School, London, who discussed Resource Implications to the NHS of the new techniques. These

latter were a timely reminder that the main business of the day was not simply the reporting of research findings, but in making an organized response to the challenges presented by the Clothier report.

Clothier drew a clear distinction between Somatic cell gene therapy (affecting only the individual concerned) and Germ line gene therapy (affecting future generations as well). Whilst gene therapy as a whole raised no new ethical principle as such it did heighten older, familiar ones on the efficacy and safety of any new medical research and practice. Only Somatic cell gene therapy should be attempted at present, he argued, simply because there was insufficient knowledge to estimate the risk to future generations which might be posed by Germ line gene therapy. It's important, however, to recognize that this opposition was subject to the following qualification: "genetic modification of reproductive cells ... should not at present be attempted." In other words this rejection is not a final one but is subject to the (rapidly developing) state of knowledge concerning the potentialities of Germ line gene therapy. Also, because gene therapy is in its infancy as yet, and because it entails research on human subjects, it has to be subject to the strictest of controls, and Clothier recommends the setting up of a central supervisory body, composed of experts, who would adjudicate on every individual gene therapy proposal made in the UK.

GIG's response was, after extended discussion, to launch a 1992 campaign, centred on the following policy statement:

To meet the needs of people in the community whose lives are affected by genetic disorders, the member organizations of the Genetic Interest Group call for improvement of services to provide, irrespective of place of residence, equal access through the NHS to all available tests and treatments.

GIG then outlined a number of goals, services required now as well as needs for the future. Early diagnosis of genetic disorders at accredited testing centres to which full information and access are widely available is required now, as also is the provision (and funding) of specialized clinical management and treatment centres. For the future a commitment to Government funded research and development into human genetics was needed, as was the early adoption of new techniques of diagnosis, management and treatment of genetic diseases, as revealed by ongoing research programmes. Finally, close attention should be given to the ethical debate surrounding human genetics, also an ongoing area requiring continual monitoring.

GIG's aims, it seems to me, could be reproduced at the European level (which is why I've devoted so much space to them) and it's very interesting to see that an attempt by GIG to initiate action on the European front has already been made.

Full documentation of all GIG 'Interface' meetings are

available now, either from the EURO-ATAXIA editor or direct from GIG itself (address below). A fourth Interface meeting, on the problems faced by young adults with genetic disorders, is scheduled for November 6th at the headquarters of the Wellcome Foundation in London.

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## ATAXIA IN IRELAND

There are two organizations for Friedreich's and other ataxia sufferers on the island of Ireland, paralleling the political and administrative divisions in the Country laid down in the 1920s. Ireland is partitioned into two states, Northern Ireland in the North-East and the Republic of Ireland in the South and West. Northern Ireland is much smaller than the Republic of Ireland, covering just six counties, against twenty six counties in the Republic. People usually refer to 'the North' and 'the South' in daily speech, but this is not strictly accurate, as there are parts of the Republic of Ireland ('the South') which are geographically more northerly than Northern Ireland ('the North'). This is not the only confusing aspect of the situation either, but I shall pass...

Northern Ireland is part of the UK and shares in all the major post-war British Social Institutions – the Welfare state, the NHS etc. The Republic of Ireland is independent of the British system and is responsible for its own welfare and Health services. Consequently there are differences in how disabled people are treated depending on where they live in Ireland. In Northern Ireland the emphasis is on state provision, whilst in the Republic of Ireland the voluntary sector plays the leading role. This affects the role and range of activities of disabled organisations – including Ataxia groups. The Northern Ireland Friedreich's Ataxia Group (NIFAG) was set up in 1985 and has about 40 members scattered throughout 'the North'. As we are a very small group we are directly affiliated with the FAG in the UK. The Friedreich's Ataxia Society of Ireland (FASI) is based in Dublin and is a much larger group, with over 100 members spread throughout 'the South'.

Both FASI and NIFAG are primarily social support groups for ataxic people – mostly Friedreich's but with some Cerebellar and others as well – in Ireland. We try to alleviate some of the distress caused by creating a network of social support, as well as or-

ganizing holidays (we try to participate in a joint 'official' holiday each year), swimming clubs and social activities for our members. There are, however, major differences between us in what services we can provide to our members. State provision being greater in Northern Ireland means that NIFAG doesn't have to undertake many of the things that FASI in the Republic of Ireland does. NIFAG is, as well, very small. Much of our effort goes into raising funds for the medical research programme, especially that of Dr. Sue Chamberlain and her research team based at St. Mary's in London. FASI is, however, in a different position. Again, because voluntary organizations in the Republic of Ireland are more central and because FASI is a much larger group, it has more responsibilities as a result. It is much more involved in the daily life of ataxic members, running a counselling service for ataxics and their families, helping with housing adaptations etc. In terms of research Ireland played a key role in an earlier phase of the search for the rogue gene causing FA, a research project based in St. Mary's Hospital Medical School in London. It's a well-known fact that Irish family-size tends to be large, and this, naturally, extends to ataxic families as well. This meant that a large sample population was available to researchers who specifically needed blood samples from large-size FA families.

*Contact:**NIFAG:**Ida Walker**4 Kingsway Close**Cherryvalley**Belfast BT5 7HA**NORTHERN IRELAND**Tel: +44 232 484046**FASI:**Claire Creedon**San Martino**11 Mart Lane**Foxrock**Dublin 18**REPUBLIC OF IRELAND**Tel: +353 1 894788***NETHERLANDS: THE VSN**

The Werkgroep Ataxie van Friedreich is an integral part of the VSN – Vereniging Spierziekten Nederland (or Dutch National Neuromuscular Disease Association). The VSN is the leading organization in the Netherlands for all neuro-muscular diseases and is very active on many fronts. It has almost 3,500 members (about 65 with Friedreich's ataxia) and runs a professional office in Baarn with a maximum staff of 20. It is a complex, well-run organisation catering for all people with neuro-muscular disabilities through-

out the Netherlands – there are as well ten regional groups, fourteen diagnosis groups and a youth group. All these levels are staffed by volunteers. VSN deals on a common basis with many areas of need: psychosocial counselling, social security, insurance and taxation advice (the much-vaunted social security system in the Netherlands is in fact quite complicated), while a technical section provides advice on new equipment. On the Medical and Scientific front VSN continually tries to support new initiatives, particularly in the University hospitals. In 1990 it helped support 'patients and parents', a project which led to the creation of three new professorships.

The VSN is also very active internationally. It has taken the initiative in forming EAMDA (European Alliance of Muscular Dystrophy Associations), ENMC (the European Neuro-Muscular Centre), WAMDA (World Alliance of Muscular Dystrophy Associations) and Stichting Onderzoek Neuromusculaire Ziekten (Dutch Foundation for Research into Neuromuscular Diseases).

*Contact:**Vereniging Spierziekten Nederland (VSN)**Ysbrand Poortman, Director**Lt.-Gen. van Heutszlaan 6**NL-3743 JN Baarn**NETHERLANDS**Tel: +31 2154 18400**Fax: +31 2154 21616**VSN – Werkgroep Ataxie van Friedreich**Carolien Koopmans**Mina Krüseman-erf 131**NL-3315 GE Dordrecht**NETHERLANDS**Tel: +31 78 212110***ITALY: RESEARCH IN MILAN**

Our knowledge of the causes of hereditary ataxia is developing at an ever faster rate, and perhaps the most exciting area for research at the present time is that of molecular genetics. However, it would be quite wrong to create false hopes of revolutionary results among the wider ataxic community, inflated and unrealistic expectations which can give way to unjustified mistrust or even outright rejection of the whole enterprise. Scientific research is, by its very nature, a slow and careful business – sometimes infuriatingly so.

While the general picture is without doubt getting clearer, we still have not discovered the genetic alterations that produce ataxia. The big problem found by researchers is that, in the relatively more common forms of ataxia, such as Friedreich's ataxia, Olivopontocerebellar atrophy and other Cerebellar atrophies, no particular alteration in the metabolism

of the damaged nerve cells was discovered, nor indeed throughout the organism. Utilising techniques developed by biochemistry, our researchers could not find a metabolic alteration common to all ataxia patients (but only to them) which could reasonably explain the atrophy of the same subset of nerve cells, which in turn gives rise to the onset of characteristic ataxic symptoms: poor co-ordination, loss of balance, etc.

Up until recently this has been a major impasse to research, blocking and impeding further understanding of the causes of ataxia. However, we now have the means to break through this barrier.

First, let us return to the fundamental principles behind classical and molecular genetics. Proteins are the basis of our search, the most important components for the normal development of our organism as a whole and its functions. Structural proteins are those which hold cells together in a mass to form tissues and organs, also to control their movement. Proteins which operate as catalysts are called enzymes, and make all chemical reactions within the body work, such as the transfer of energy from cell to cell.

Proteins have a very complex composition as they are composed of long chains of simple acids, called amino-acids. There are about twenty different kinds of amino-acids in all. Each protein is made up, not only of specific amino-acids, but also of accurate sequences of them – a sort of morse code if you like. Genetic knowledge, passed from generation to generation, is composed of the structural plan determining the production of all proteins in the organism, also the code that specifies the sequence of amino-acids that makes them up.

This sequence is preserved within the DNA molecule – the 'master-plan' that governs all genetic information. DNA is composed of four elements, called nucleotides. Try imagining the nucleotides as four individual letters making up a simple alphabet (a computer language is a good example). Letters are grouped into words and words into sentences, to emerge, finally, as coherent text. Now, if we think of the nucleotides as the letters, then genes – sequences of nucleotides – are the words. Genes are the coded instructions that govern the production of proteins (the 'sentences' in our metaphor) and, of course, proteins are the basic building-blocks of the organism as a whole (the finished 'text'). DNA is divided into twenty-three chromosomes, each composed of an exact number of genes, all laid out in accurate sequence.

Ataxias and other hereditary diseases are caused by an altered gene, found in a precise location on a particular chromosome. The molecular genetic approach first attempts to isolate the 'rogue' gene within the chromosomal maze, and then, armed with this information, it becomes possible to discover the protein responsible for the alteration causing the disease.

'Polymorphism' is perhaps our most important tool in conducting this search. Polymorphism is the scientific name given to differences in the DNA sequence at the

same place in a chromosome between different people, and passed on from generation to generation in the population. Most importantly for us, they are observable in the laboratory and so offer a vital clue as to the location of the 'rogue' gene itself. This is why the DNA of large numbers of patients and their families are so closely studied: to check if there are polymorphisms which are inherited along with the disease gene. This will mean that both the affected gene and the polymorphism are located on the same chromosome – where the polymorphism is, so also is the affected gene.

Already this approach has yielded results for two types of ataxia. The gene responsible for Friedreich's ataxia has been localized to chromosome 9, while that causing Olivopontocerebellar atrophy has been traced to chromosome 6. The question is now to further define the exact point on the chromosome where the genes lie. For Olivopontocerebellar atrophy the identification of new probes on chromosome 6 has aided researchers greatly. As for Friedreich's ataxia the progress has been even more remarkable. Several probes are available (with more to come) which will recognize polymorphism next to the gene, and thus the location of the gene itself. Many laboratories have already isolated large fragments of chromosome 9 for analysis by this method, and the search is continuing all the while. Thus in both diseases we can find practical application of new research findings.

Even if our researches have not as yet led to an effective therapy or treatment for ataxia, our findings so far are nonetheless very important for the families, as it gives us the means to construct an efficient method of pre-natal analysis and pre-symptomatic diagnosis (although this of course raises a whole range of ethical questions). Progress does not go amiss and, even if we have not yet gained our desired ends from the research to date, even if the search may continue for many more years to come, things are definitely going the right way. Overall the Italian contribution to the molecular genetics of ataxia has been remarkable and much appreciated at international level. In particular I would like to thank all the individual participating families and Associazione Italiana per la lotta alle Sindromi Atassiche, without whose help and support none of the above research could have been completed.

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**CLOSING DATE FOR THE NEXT ISSUE:  
1 JANUARY 1993**

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