



## EDITORIAL

To PT or not to PT...

The availability of prenatal testing for many ataxias has raised numerous ethical, legal, social and even philosophical problems. The technology may well be there, but we're still unsure of its applications. This issue of *Euro-Ataxia* contains articles on PT from differing standpoints. From Italy Dr. Sergio Coccozza gives the scientific background of PT in the ataxias. This is followed by Dresdener Dr. med. Friedmar Kreuz's article on the psychosocial aspects of genetic counselling, written from a more clinical standpoint. Third, Shirley Dalby of the UK looks at the implications of recent research into Autosomal Dominant Cerebellar Ataxia. The Patient's View is an attempt to see things from the 'end-user's' perspective – often very different from that of scientists and clinicians.

Many people, it must be said, view genetics with suspicion. Their first thought is of the Nazis and eugenics. Genetics will need to confront this particular demon to regain public confidence. A new book examining what went on is reviewed inside. It marks a start in breaking down the taboo which has grown up around this subject.

PT and related issues cannot simply be approached from within a Medical Model alone, but raise broader, more fundamental questions concerning human life. From a different philosophical perspective comes Carolien Koopmans' article, 'Feedback'.

Also included in this issue is a report on last years 3rd International Workshop on Machado-Joseph Disease.

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## PRENATAL TESTING IN ATAXIAS

Every person has a risk of transmitting a genetic disease to the offspring.

In a family in which a mendelian disorder, as inherited ataxia, is present, the risk of transmitting it with every pregnancy can be exactly estimated for each member of the pedigree. In several cases it is also possible to predict the onset of the disease in a foetus, before born. This prediction is called Prenatal Testing (PT). Formally PT is also a risk calculation, but it concerns a specific pregnancy and uses DNA analysis tools. In other words, using molecular genetic tools it is possible, in several cases, to modify the theoretically estimated 'a priori' risk (calculated by mendelian inheritance). The result is to obtain higher values of probability referred to the risk of a specific pregnancy. The possibility to perform PT depends on the molecular knowledge on the disease. Concerning ataxias, three different situations could be defined:

1) The mutation/s in the gene that causes the disease is/are known (as in

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the cases of dominant spino-cerebellar ataxia type 1 and 3; SCA1, SCA3).

2) The causing disease gene has been located on a chromosome, but not yet cloned and identified (as in the cases of dominant spino-cerebellar ataxia type 2, 4, 5; SCA2, SCA4, SCA5 and recessive Friedreich's disease; FD).

3) Mutation and localisation are unknown (other ataxias).

In the last case, where nothing is known about the molecular genetics of the disease, prenatal testing can not be performed. In these situations clinical geneticists can only evaluate in term of probability the risk of transmitting the abnormal gene to the offspring. This risk is different in dominant ataxias and recessive forms. In autosomal dominant disorders the presence of the mutation on one chromosome results in the abnormal phenotype. In autosomal recessive forms both chromosomes must be mutated. In dominant ataxias an affected individual has 50% chance of transmitting the disease to the offspring with every pregnancy. In recessive forms the healthy parents of affected children have 25% risk of having an affected child. Risks can also be calculated for all the family members. These risks usually range from 0 to 50% (dominant forms) and 0 to 25% (recessive forms).

In conclusion, when no molecular information is available:

- 1) No Prenatal Test is possible.
- 2) An exact probabilistic estimate of the risk of transmitting the disease is possible for each family member. Genetic counselling should be provided to family members to inform them on their procreative risks.

In two forms of dominant spino-cerebellar ataxia, called SCA1 and SCA3, the disease causing genetic alterations have been identified. In both cases they consist of an expansion of a CAG repeat. Mutated alleles contain a higher number of this trinucleotide repeat in comparison with the normal alleles. So mutated alleles are called 'expanded' alleles.

The two genes are localised on chromosome 6 (SCA1) and on chromosome 14 (SCA3). In these cases a direct Prenatal Test is possible. The test allows the exact identification of a foetus who will (or will not) develop the disease. The analysis is performed by a Polymerase Chain Reaction (PCR) that allows the amplification of the DNA region containing the CAG repeat. The size of the PCR product, estimated by gel electrophoresis, will identify an 'expanded' allele. The presence of this 'expanded' allele predicts the disease. To perform this test, fetal DNA is needed.

Two techniques are available. The first is chorion villus biopsy (CVS). By transcervical or trans-abdominal aspiration, chorion villi containing fetal DNA are isolated. Good expertise is needed to separate fetal material from maternal tissues. CVS is performed at 10 to 12 weeks of pregnancy. DNA has to be checked for maternal contamination to avoid false positives or negatives.

The second method is amniocentesis. It is performed at 15 weeks of pregnancy. Analysis is performed on fetal cell present in the transabdominally aspirated amniotic fluid. Minor problems concerning maternal contamination are present. In several cases of Huntington's Chorea, another CAG repeat disease, 'intermediate' alleles have been observed. 'Intermediate' alleles' size ranges between normal and 'expanded'. The presence of these alleles makes the molecular diagnosis in these cases of Huntington's Chorea difficult. It is possible that this problem could concern also dominant ataxias, when more mutated alleles will be studied

In conclusion, when the causing disease gene is known (SCA1 and SCA3):

- 1) Prenatal test gives exact results in most cases.
- 2) Prenatal test needs CVS or amniocentesis.
- 3) Since, up to now, no clinical methods have been developed to discriminate between these forms and the other dominant ataxias, the presence of expansion has to be demonstrated at least in one affected member of the family.
- 4) The finding of an 'expanded' allele in a foetus will make the diagnosis also in the affected, still clinically normal parent. This topic, of course, is very hot if a 50% at risk asymptomatic individual (e.g. a sister of an affected individual) asks for information about her offspring but not on herself.

The last situation occurs when the disease gene is yet unknown, but it has been localised on a specific chromosome. This is the case for SCA2, SCA4, SCA5 and Friedreich's Ataxia. Also in these cases Prenatal Testing is possible, with several limitations. Since it is not possible to directly 'see' the mutated gene, we can track that gene analysing 'linked' genetic markers.

A linked genetic marker is a DNA polymorphism very close to the disease gene. By studying these markers in each family member (affected and unaffected) we could identify the form of the marker that cosegregates with the disease (they are jointly inherited). By studying the form of the marker in fetal DNA we can predict the phenotype. The result of this study has to be corrected for the genetic distance between marker and disease gene. The genetic distance represents the possibility that markers did not

segregate with the disease gene. However in most cases risk can be estimated with high values of probability (95%-100%). The source of fetal DNA is as previously described for direct analysis. Prenatal Testing is a little bit more complicated in recessive forms, as Friedreich's ataxia. In this case we have to track two altered genes (like in all recessive diseases). This goal can be easily achieved if parents had previous affected children or if they are consanguineous (and the common pedigree can be analysed). In these cases we are able to identify both the affected alleles. Otherwise, if we have asked to ascertain the true risk by, for example, a sister of an affected individual and her spouse (from unrelated unaffected family), our ability to predict is very low. We can easily establish if she carries the abnormal gene but we have no tools to investigate the spouse's allele. In these cases no Prenatal test is possible. A theoretical risk calculation can be performed. Also considering these limits, prenatal diagnosis of Friedreich's ataxia has been successfully performed in several cases.

In conclusion, concerning ataxias in which the genetic defect has been mapped but not yet fully identified:

- 1) It is possible to perform Prenatal Test, at least in many cases.
- 2) Many closely linked markers are necessary (this condition is now well satisfied in FD and SCA2, less in SCA4 and SCA5).
- 3) It is necessary to study many family members including affected and unaffected. The possibility to achieve informative results depends on the size of the pedigree and the informativity of the genetic markers.

The ethical problems concerning prenatal test represent, in my opinion, a very important topic that needs a different, specific space. Here I would like only to underline the necessity, as in the case of Huntington's Chorea, of strict guidelines from ethical committee. The above described is a flash of the 'up to date' possibilities about prenatal diagnosis in ataxias. It is hopeful that, in the next future, molecular advances (mapping of other ataxia forms, identification of new genes) will allow us to implement prenatal diagnostic tools.

*Dr. Sergio Coccozza*

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## GENETIC COUNSELLING AND PSYCHOSOCIAL ASPECTS OF PREDICTIVE AND PRENATAL DNA ANALYSIS

An international definition of genetic counselling was agreed by the Ad Hoc Committee on Genetic Counselling in 1975. In the U.S.A. and Europe, most of the genetic counsellors agree with this definition:

Genetic counselling is a communication process which deals with the human problems associated with the occurrence or the risk of occurrence, of a genetic disorder in a family. This process involves an attempt by one or more appropriately trained persons to help the individual or family to

[1] comprehend the medical facts, including the diagnosis, probable course of the disorder, and the available management;

[2] appreciate the way heredity contributes to the disorder, and the risk of recurrence in specified relatives;

[3] understand the alternatives for dealing with the risk of recurrence;

[4] choose the course of action which seems to them appropriate in view of their risk, their family goals, and their ethical and religious standards, and to act in accordance with that decision; and

[5] to make the best possible adjustment to the disorder in affected family member and/or to the risk of recurrence of that disorder.

Indeed, the rapid development in genetics has not only increased our knowledge of heredity, it has also produced new kinds of diagnostic methods. This development has had and will have far-reaching consequences both of the users of these diagnostic methods and for society at large. With respect to genetic counselling, the value of new diagnostic methods means more precise predictions. Additional and earlier knowledge about genetic diseases means more decisions for the individual regarding the planning of life and founding a family. The responsibility of the individual and the society has therefore increased.

On the other hand, few individuals, other than specialists, understand the new techniques of genetic analysis. DNA is of great interest to researchers but the general public remains in the dark with respect to the ways in which DNA is studied. However, the genetic counsellors are faced with an individual of the general public, the client asking for advice, an individual who needs help solving the difficult problems stemming from genetic diseases and anomalies. It is not possible to give figures for the

distress, difficulties, grief, harm, and ethical problems faced by a client: these things cannot be measured. Here is an individual in his own situation, possibly with his own family and society: an individual in a psychological and social network.

The object of genetic counselling is to inform single people or couples, who are confronted with a hereditary disease or (possible) congenital anomaly. On this basis, the client will be offered alternative possibilities in order for him to make decisions regarding his future life. Because genetic counselling sees the individual, the couple or the family and the background to the relevant problems as the focal point the decision of the client will be supported by the counsellor. The risk of having a handicapped child because of a lack of information should therefore be decreased by genetic counselling. Nevertheless, it must clear for both the counsellor and his client that genetic counselling does not involve any criticism of handicapped life and it is not the role of the counsellor to advise an abortion in a directed manner. The counsellor should inform the counselled. The efforts in these situations are directed at achieving the birth of a healthy child, not to avoid the existence of handicapped people.

Progress in biology involves new techniques and new problems. Now it is possible not only to diagnose a disorder by chromosomal analysis but also to predict a genetic disease by indirect and/or direct molecular or DNA analysis.

In 1989, the International Huntington's Association and the world Federation of Neurologists published guidelines for predictive and prenatal DNA diagnosis of Huntington's disease, as elaborated by both professionals and members of the national lay organisations. Most countries adapted the guidelines to their own national specifications and so these International Guidelines became one of the main instruments for daily work in predictive diagnostics and provided a pattern for ethics in human genetics. The guidelines were revised again recently, because the situation in diagnostics has changed from indirect to direct analysis. The main topics of the guidelines are the following:

- The predictive or prenatal diagnostic should be carried out at a genetic counselling unit that has experience in this kind of diagnostics.
- The persons at risk must be fully informed about the diagnostics, prognosis, and therapy of the disease, and about self-help organisations by the geneticist.
- The person at risk must be of age when he can take part in predictive DNA analysis.

The decision for taking the analysis must be a free decision of the client without pressure from other people (for instance, partners, parents, friends,

insurance companies, employers etc.)

- There must be more than one talk, and more than one month has to pass between the first information-giving talk and the decision to take the test.
- At any time, it must be possible for the person at risk to interrupt or to stop the procedure of the test programme.
- The person at risk shall nominate a companion person who will become a confidant during all phases of the test programme, especially when the test result (good or bad) is given. This confidant may be the partner, a close friend, a social worker or better a psychologist.
- The test result has to be given personally, and not by phone or letter.
- The genetic counsellor has to contact the tested person after advising the result.
- With respect to prenatal diagnostic, it has to be said that one parent is a carrier.
- Prenatal diagnostic testing will be carried out only if the parents are prepared to terminate the pregnancy. The motive behind this is to prevent parents knowing the gene carrier status of a child; later the child can decide for itself whether it wants to know this status.
- There could be a case in which a 50% at risk parent does not want to know its gene status, whereas the 25% at risk child wants to know its status. After testing, if the child has an unfavourable outcome, the parent knows automatically that it is also a gene carrier. In this complicated situation, both sides shall talk together. If there is no consensus, the right of the child has to be considered more highly than that of the parent.

A few weeks ago, the 4th European Meeting of 'Psychosocial Aspects Of Genetics' was held in Heidelberg, Germany. At this meeting, the international trend was in agreement with the Huntington guidelines. Genetic diagnostics have to be part of genetic counselling. There have to be more contacts between the counsellor and the clients, and people from the counselling unit have to deal with the psychosocial problems of the Counsellor and who have more contact to the partners, the families or the lay organisation than the doctor can have. In Germany, only five genetic institutes can afford a social worker or psychologist.

In September 1993 a working group of the German Federal Assembly gave the final report of 'Chances and Risks of Genetic Diagnostics'. It concluded that there have to be changes in the fundamental law regarding genetic testing in Man. Regarding the point 'Genetic counselling and prenatal diagnostics', the working group pointed out that an increasing number of people are willing to take part in genetic testing

but that the genetic counselling units are not able to offer a sufficient number of qualified consultations. With increasing numbers and with the simplifying of DNA diagnostic methods. The central problem will be seen in the commercial use of DNA analysis by private doctors and laboratories.

There are two consequences in the use of genetic tests. On the one hand, our knowledge will increase certainty with respect to decisions concerning the future life of the counselled, especially regarding the wish for a child. On the other hand, this knowledge is a burden for the counselled and makes them uncertain. For example, this burden results in nearly all counselled pregnant women thinking that their pregnancy must be an at risk pregnancy. The valuation of illness and handicap could change into stigmatisation of people carrying determined genetic signs.

The uppermost object of all procedures has to qualify the counselled to make voluntary individual, and informed decisions for or against genetic testing. To do this, there must be a greater opportunity for qualified, non-directive, non-commercial genetic counselling. The 'right of non-knowledge' has to be accepted and more attention has to be directed to the psychosocial problems of the persons at risk and the women taking the prenatal diagnostic tests.

These opinions of the working group of the German Federal Assembly agree well with the recommendations of the German Society of Human Genetics. It is unethical to deny predictive testing, because the person at risk has a right to know its own risk and to make decisions for its future life. Nevertheless, the offer of predictive testing has to be given carefully. There must be:

- an extensive offer with respect to information about testing and alternative possibilities;
- the security of the voluntary principle and of accepting the individuals right of non-knowledge;
- the security of non-directiveness in counselling;
- the ownership of all material and data by the tested individual;
- no routine predictive diagnostics, and an individual programme with time for reflection of the meaning of the test, and the possibility to stop the process.

In Germany, to my knowledge, no other lay organisation has guidelines for predictive and prenatal DNA analysis other than Huntington's Association (Deutsche Huntington-Hilfe e. V.) Two years ago, we in our association, the DHAG, began a discussion about these problems. In our newspaper, all members could read about preliminary guidelines for testing and were called to give their own opinions. The German Association Of Retinopathia Pigmentosa

was very interested in our guidelines and asked to have a reprint. A letter of the DHAG committee regarding guidelines as for Huntington's disease was addressed to the Professional Association Of Medical Genetics; it obtained great support and was printed in the newspaper *Fundus* at the present time. In November, in Münster, we will hold a weekend workshop and elaborate the final guidelines on which the assembly of the members will vote next spring.

I think the EURO-ATAXIA association must also evaluate new considerations, in the same way as the national associations. Because of the rapid progress in genetic methods, the EURO-ATAXIA must also become a refuge for people at a risk for ataxia. Where is the forum for discussing psychosocial problems in predictive and prenatal testing if not at the ataxia associations? Who will control genetic developments and their application to affected and unaffected people if not the ataxia association? How should national management in genetic laboratories and counselling units be organised if there are no guidelines worked out by the EURO-ATAXIA association and adapted by the national associations? I think guidelines are absolutely essential: guidelines for predictive, prenatal and differential diagnostics in dominant and recessive ataxias. The time is overripe, especially since direct predictive DNA analysis became possible last year.

*Dr. med. Friedmar R. Kreuz*

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## AUTOSOMAL DOMINANT CEREBELLAR ATAXIA

We now know that alteration in any one of at least six different genes can give rise to ADCA. Five of these genes have been located or mapped to specific chromosomes – 6, 11, 12, 14 and 16 – and there may be more to come! The number of genes involved may seem surprising, but the nervous system is extremely complex. The normal functioning of a nerve cell will require contribution from a large number of proteins. Breakdown in the structure or efficiency of any one of a number of these proteins could produce the same end result – the premature loss of a set of neurons giving rise to ADCA.

The most significant advances must include the isolation of the genes causing the forms of ADCA mapping to chromosome 6 (reported by Drs Zoghbi and Orr in the summer of 1993) and chromosome 14 (reported late last year). Although these genes are not related, the mutation mechanism of each is identical and involves an expansion in the number of normally occurring repeat units present in the coding

sequences of some neurologically important genes. Such mutations appear to affect the normal functioning of the protein produced by that gene.

Each offspring of a parent with ADCA has a 50% risk of inheriting the disorder. The expansion is transmitted to those who have inherited the CA gene but the number of repeat units in the expanded region may vary between individuals. It is this latter phenomenon that explains why age of onset and therefore, severity of symptoms may vary between affected members of the same family.

These advances offer hope for the future treatment of this group of disorders. However, there are more immediate implications for families affected by ADCA in terms of genetic counselling. Direct testing of 'at risk' individuals is already available for families known to carry the mutation in the chromosome 6 gene and will soon be on line for families shown to carry the mutation on chromosome 14. What does this mean for a family requesting counselling and how likely is it that the analysis will provide information?

At the moment, individuals and their families have to be checked to see whether their particular form of CA is on chromosome 6 or 14 – if so, diagnosis of the presence or absence of an abnormal expansion can be made accurately.

The information which we are currently lacking is the exact proportion of families where the cerebellar ataxia can be attributed to either of these two gene loci – for instance, the team at the Institute of Neurology in UK has so far identified five British families with the chromosome 14 variation. Consequently, when a new family requests information, we cannot predict the chance that they will be carrying the mutation in either of these genes, although the situation is expected to improve in the short term as more and more families are studied throughout the world and the true incidence of each gene disorder can be estimated.

If both these genes are excluded from causing the cerebellar ataxia in a specific family, analysis for linkage to one of the other three loci will be attempted. These tests can only give an alteration in risk status, either up or down, rather than a clear diagnosis, and that information will largely depend on the position of that particular gene – the smaller the area involved in testing, the more accurate it is likely to be.

For some families, therefore, it may be that no additional information (other than the inherent 50% risk) can be given until the other genes are finally isolated. It is highly likely that such families will be approached for their participation in the ongoing

research projects to clone the genes on chromosomes 11, 12 and 16, which should involve little more than giving permission for the DNA isolated for the above tests to be used for research purposes.

How do you obtain genetic counselling? A referral can be made by your GP or neurologist. It is likely that the first visit would concentrate on the explanation of the procedures, the implications of testing and the likelihood that definitive information could be generated for your family.

We are expecting that the dominant genes mapping to 11, 12, and 16 will also share the mutation mechanism outlined above and this could shorten the search for these additional genes quite considerably. Perhaps 1995 will prove to be a very eventful year!

The developments in CA research are very exciting. Genetic testing, though, before treatment is available, needs a lot of thought – the hope of good news has to be balanced with how you might cope with bad news. I would certainly like to hear from people who have been through the testing procedure, whether the results were negative, or positive, or non – informative. Maybe you could contact the FAG office in UK to let us know about your experiences and feelings, and those of your family. Please let me know whether you will be willing to have extracts printed, and/or whether you wish to remain anonymous.

*Shirley Dalby*

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## THE PATIENT'S VIEW

When I was first diagnosed as having Friedreich's ataxia, I or rather my parents must have been truly baffled by the exoticism of the thing, an unheard of disease with a funny German name. We knew it was 'genetic' in origin but that was all. I daresay as well that my experience would have been similar to many ataxic people in Europe.

Then, in the 1980s, the development of New Genetic technology offered scientists an invaluable research tool into unlocking the secrets of many genetic diseases, the ataxias among them.

But it was in 1988 and the location of the FRDA locus on chromosome 9 by Sue Chamberlain and her team at St. Mary's, London, that the great stimulus to ataxic people's involvement became apparent. The formation of EURO-ATAXIA a year later was in large part due to this renewal of interest.

Since then the pace of research has accelerated. Now we know the locations of SCA 1, SCA 2, SCA 4 and

DRPLA. SCA 1 has since been cloned and its protein identified. The Friedreich's Ataxia gene itself may well be the next to fall.

Hence genetics continues to keep us on a 'high' of excitement, expectation – and hope.

There is – of course – a downside to all of this. The New Genetics has become one of the most hyped areas of medicine. Hardly a month passes without somebody announcing the discovery of the 'gene for' oh, just about everything you can think of, from alcoholism to homosexuality to criminality. Long discredited theories, such as Lombroso's 19th Century attempt to relate deviance to cranial dimension, have resurfaced under a new guise. Genetics is increasingly seen as providing the answer to everything – a position more akin to magic than medicine.

This is why ataxia research in particular needs absolutely to maintain a realist position in regard to its applications, to carefully, and repeatedly, explain just what these scientific breakthroughs can do and what they can't.

Genetics is about prevention: prevention is about abortion. I personally find it a little disappointing that the most concrete application of new scientific discoveries in ataxia so far should have such a negative aspect. In saying this I'm not coming down one way or the other on the legitimacy of such a course, merely expressing a wish that there was something more. Gene therapy was for a time looked on as a positive application of genetics, but as the difficulties involved have become more obvious so too the original interest has slackened off. In the long term the best hope for treatment may lie with reverse genetics – first, find your gene, clone it, then plonk it into a yeast to find out what it does or doesn't do; hopefully we may then grasp the underlying chemistry involved in ataxia, from which an effective treatment may result. It all sounds so boringly conventional, but in this race my money's on the tortoise not the hare.

For the present, however, all we have are Prenatal Testing of various kinds, the availability and desirability of which is usually taken for granted. Hence an initial, disconcerting point may well be made that it's irrelevant for most Friedreich's Ataxia families anyway. Friedreich's Ataxia is recessive, so the first sign of its presence is when a child develops symptoms. But as age of onset for Friedreich's Ataxia averages at 10 years the family may already be complete before anybody's aware the condition's present. Without universal screening for Friedreich's Ataxia (and that's not going to happen) genetic

counselling is not really an option. Of course you can still have a predictive test done, find out who else has it once the first child develops symptoms, but *why?*

With Dominant Cerebellar Ataxia the situation seems more definite, but we're still dealing with percentages and chance. It's by no means cut and dried.

Genetic counselling refers to a process of information exchange between a professional counsellor and an at risk individual or couple. Elaborate steps are built-in to the process to ensure all adhere to the principle of individual choice, and rightly so. All counselling must be 'non-intrusive'. But this model of voluntary decision-making is an abstract one and makes little allowance for the social context in which such decisions are made. Coercion may take many forms – economic, moral, social, authoritarian. In reality many variables such as social class, cultural and religious background would play a major, perhaps a decisive, role in influencing choice. This unfortunately is often ignored in the highly simplistic, positivist, model which is currently employed. To take an example I can't see *any* Health Care system – whether state-funded or reliant on Private Insurance – setting up a highly expensive system for genetic screening and counselling without a prior commitment from those tested in favour of termination should the test prove positive. A supposedly 'free' choice would, in practice, be compromised, and being compromised would be negated.

*Michael Morgan*

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## BOOKREVIEW

To the popular imagination Genetics brings to mind one particular subject: the Nazis. Unjustly or not Genetics is now linked forever in the public mind with the mass 'euthanasia' programmes of Nazi Germany when hundreds of thousands of people were murdered. As a leading Geneticist, Steve Jones, has observed: 'its blemished past means that human Genetics is marked by the fingerprints of its own history.'

However current developments in Genetics offers unprecedented opportunities for the accurate screening of populations for defective genes that can cause appalling disabilities. Does allowing the possible prevention of handicapped births through selective abortion lead inexorably to the 'slippery-slope' at the bottom of which lies the wholesale slaughter of people on completely spurious medico-social grounds?

One problem is that, while the spectre of the Nazis is often raised as a bogeyman, relatively little serious historical research has been undertaken into precisely what went on. Until now, that is. Michael Burleigh's, *Death and Deliverance: 'Euthanasia' in Germany 1900 - 1945*, represents the first major study in English on this critical period, and will doubtless become the definitive text, at least in the English-speaking world. It's a grisly story, well told, and should become required reading for Geneticists and other health scientists. Between 1939 and 1945 over 200,000 people – mostly psychiatric patients – were systematically murdered in selected asylums throughout Germany, notably at Hadamar, Sonnenstein and Eichberg. A secret bureaucracy – Aktion T-4 – was established to organise the task under Karl's Bouhler, Brandt and the appropriately named Professor Heyde. Hence Hitler's personal involvement was carefully camouflaged: it was always a 'deniable' operation. In this it closely resembles the 'Final Solution' against the Jews, for which indeed it served as role model.

Few public protests were made, certainly not from the main institutional body of German Psychiatrists, as opposed to a few isolated individuals. Psychiatric Schindlers there were, such as Dr. med. John in Stuttgart, but they were few and far between. The main protest came, a little late in the day according to Burleigh, from Von Galen, Catholic Bishop of Münster.

Galen's intervention, in August 1941, forced Hitler to halt the programmes but this proved only a temporary respite as a more refined system was put into operation in 1942. Mass-gassing was discarded in favour of the more discreet method of slow starvation, aided in particularly difficult cases by lethal injection. Eugenics was only in part to blame, and that indirect. The Eugenics Movement promoted Genetic hygiene through selective breeding or, in the case of Genetic handicap, through enforced non-breeding. Basically an offshoot of 19th century Social Darwinism – 'Survival of the fittest' – Eugenics was a widespread, eminently respectable, intellectual movement throughout Europe and America in the early years of the 20th century. Its appeal was that it gave a spurious medico-scientific legitimacy to what were really *social* anxieties. At root Eugenics reflected *petit-bourgeois* prejudices and fears of sinking into 'the masses'. Thus fears of a growing, dark mass of Genetic handicaps was the nightmare scenario behind Eugenics, and prompted the habitually cruel and racist outlook that is associated with the movement. Its real damage, however, lay at a deeper ideological and cultural level, for it introduced ways of thinking into general discourse that represented a return to pre-modern barbarism. Many leading figures,

Winston Churchill and H.G.Wells amongst them, made fairly blood-curdling speeches on eugenic themes, but it was only in Germany that an entire *system* of mass-murder was put into operation.

The precedent had been set down already in the first world war when thousands of inmates of psychiatric asylums starved to death when their food supplies were re-directed to the army. But this was due to a unique combination of events – a case of wartime exigency when *everybody* in Germany faced starvation and 'sacrifices' had to be made. Nevertheless it betokened a sort of contempt towards the mentally ill and physically disabled – especially those whose disabilities were Genetic in origin. This view was to re-emerge in debates within German Psychiatry in the 1920s in the pseudo-intellectual concept of *vita non jam vitalis* – 'life unworthy of life'. Paradoxically it was the success of then modern therapies in a wide range of hitherto untreatable psychiatric disorders that helped create a highly visible, and professionally embarrassing, residue of incurables, 'total idiots' as they were contemptuously referred to. It was against this category of patient initially that the doctrine of 'life unworthy of life' was first developed. The seminal text was that by Karl Binding and Alfred Hoche, *Permission For The Destruction Of Life Unworthy Of Life*, published in 1920. But this view, although fast gaining ground, was not yet orthodox. Criticism centred on the 'slippery-slope' danger many saw inherent in the new doctrine. Once established in principle, the category of those deemed as 'life unworthy of life' could widen to include all those mentally and physically disabled and, ultimately, against those minority groups who were simply disliked – the gypsies and Jews for example. And, of course, this is precisely what happened.

Even at this stage it's entirely possible that this debate would have remained inert – a combination of intellectual arrogance, professional uncertainty and too much reading of Nietzsche – but for the rise to power of Adolf Hitler in 1933.

Hitler, *petit-bourgeois* to the last, had of course imbibed eugenic thought – then a widespread part of 20th Century cultural life. No doubt he was attracted by the *principle* of inequity he saw as inherent within it. Indeed, in a rare moment of originality, he had gone far beyond eugenic thinking to develop his own, particularly brutal, racist ideology, the lineaments of which are found in *Mein Kampf*. Thus he came to power with an extermination complex already well established towards anyone he felt to be 'inferior'.

The Nazi revolution was built around the idea of homage to the state – *Staatsabsolutismus* – were the collective life was all and that of individuals irrelevant. Most people, then as now, are sympathetic

to the idea of *voluntary* euthanasia – as being entirely a matter of individual choice with no external influence whatsoever. By contrast what the Nazis planned was a programme of *involuntary* euthanasia – carried out in the name of the collective: *Volk, Reich* etc., against the individual.

In effect the Nazis created a savage ethos based on a crude Social Darwinism that was, in reality, never more than a pretext for murder.

Apart from a small (critical) section on Peter Singer and 'Bio-ethics' Burleigh doesn't discuss the question that lies behind most contemporary worries on the new Genetics: *could such a thing happen again?*

For it is this, largely unspoken, fear that continues to blight Genetic research in Europe, to tarnish the tremendous advances being made into all Genetic diseases, including the ataxias. Like a ghost from the past it will continue to haunt us until we summon up the courage to face it, to understand it – and to make sure it can *never* happen again.

Michael Burleigh, *Death and Deliverance: 'Euthanasia' in Germany 1900 - 1945*, is published by Cambridge University Press.

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*Michael Morgan*

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## FEEDBACK

More than a century ago Charles Darwin introduced a theory of the history of life on earth, known as the evolution-theory. He stated that through a constant and continuing process of selection and variation – a process that is still going on – a lot of species came into existence, adapted to ever-changing circumstances or extinguished. A lot of species couldn't stand the struggle for life and only the fittest survived.

In very recent times – only some 5 million years ago – *homo sapiens* appeared on earth. In the last 100.000 years his brain developed in an extraordinary rapid way. The most remarkable feature of this rapid development is that the *homo sapiens* was equipped with a consciousness. As a result of this consciousness man has the desire – or the need – to see how things are connected, to give coherence to his thoughts and experiences. Man wants to relate his experiences to a higher stream of thought. In order to deal with this need of mental synthesis religions emerged. There are a lot of central issues that exist in the religion of every people that ever lived. For instance stories about the creation of the world, the connectedness of

life and death and of the existence of good and evil. You could say that religion was created as a system of feedback and served as a guide in life; it offered people a possibility to give meaning and direction to their acts and thoughts.

The religion of the Western world was christianity. During the Renaissance (15th, 16th century) a lot of scientific ideas were developed that were in direct contradiction with the bible. The christian church had no answer, simply stated that what was in the bible was the one and only truth. Someone who supported the new ideas risked excommunication or the burning-stake. But the ideas of people like Copernicus, Galileo, Descartes and Newton couldn't be stopped. Science went on with the detailed analysis of the universe and forgot to care about the overall point of view, about how things fitted together. With rational arguments the bible was pushed aside and the ground on which the christian belief stood disappeared. But what did science bring in return? Nothing. A huge vacuum.

The great problem of today is the lack of religion or feedback. This is especially true for those who are confronted with the diagnosis of a progressive handicap: they usually fall into great emptiness, a big black hole. The analytical, materialist way of thinking and the idea that science can solve all misery, offers no solution to people who have to cope with serious trouble.

I only have to look at myself to know that this abstract way of thinking has a lot to do with daily life. For years I thought I was a convinced atheist. But in recent times I have realized how deeply rooted my catholic upbringing is. And I realize how valuable that catholic background has been for the ease with which I accepted my FA. When you are brought up with the philosophy that money and good looks are the most important things in the world, what is left of life if you get an ataxia? Not much, I guess. But when you grow up with the idea that the love between people is the most precious thing in life, it is much simpler to accept a disease like FA or other forms of bad luck. That the love between human beings can last throughout a lot of misery, is a thought that makes coping with a progressive handicap less difficult.

Now catholicism is not the only religion. One can discover a lot of similarities between religions. And a lot of differences too. For instance the catholics, at least in my country (the Netherlands) put more emphasis on the New Testament, while the calvinist protestants have always emphasized the Old Testament more. Because I was raised a catholic, I have great sympathy for the ideas of Jesus. When I read about buddhism, some ideas seemed very

familiar to me. It didn't surprise me that in the Thomas' gospel, which they have found in 1945 or 1946 in Egypt, Jesus comes forward like a person who has a lot in common with Buddha.

One of the wonderful ideas of buddhism is that you can look at the body of a human being as a vehicle in which life's traveller has to make life's journey. The more I think about it, the wiser that idea seems to me. Regarded from this point of view, the body of a young, strong, healthy, athletic and beautiful person is just a vehicle of life, no more or less than the body of an ataxic individual is. That is a very comforting and relaxing idea. It makes ataxia much easier to cope with: a physical disorder is nasty but doesn't imply that the passenger is damaged too. It just means that the driver has problems with his car.

Buddhism has taken a lot of ideas from the much older Taoism, which already existed in China in the mythical times. The writer of the eldest and most famous Taoist book, the *I Ching*, was probably born in 3322 BC. The Chinese word Tao can be translated as the Way, the Meaning, the Word, God, but I prefer the translation into the Emptiness. The old Chinese had the point of view that the emptiness was the most basic essence of everything. At first sight this may seem a very threatening idea; it seems as though there is no certainty left in life. But if you look closer, you may see that the contrary is true: the emptiness is the most stable state there is. The emptiness exists of and contains nothing that *can* change.



Tao is the single Whole and being the single Whole can't manifest itself. Therefore Tao is split up into Yin and Yang, two opposites that can't exist without each other. For instance, male and female, light and dark, good and evil, misery and happiness. Yin and Yang, the two complementary counterparts, interact in harmony. The contrary forces succeed each other in a rhythmic sequence. The Yin and Yang-symbol symbolizes that when one complement is at its highest level, it already contains the full node of the opposite complement.

The relations in the Eastern religion or philosophy are characterized by the principle of synchronicity, not by the principle of causality. That means that things aren't related in a sense of cause and effect, but just are there at the same time. Because things are there at the same time (coincide or synchronize), they have a certain influence on each other. Because everything is part of the same Whole, nothing that happens stands alone. Although we, human beings, can't always point out or understand the relationships. So pure coincidence – in the meaning of things happening without relation to something else – doesn't exist in the Eastern way of thinking. But

coincidence in an other sense – the sense of things happening on which an individual doesn't have any influence and which we can't forecast – does exist.

One of the enchanting implications of this kind of feedback is that coincidence and fate can go hand in hand. Bad luck or coincidence can cross your way without any reason or any reason that you can see. But at the same time nothing does happen completely out of the blue. Combining those two features, you could look at that coincidence as destined for you. It may be nonsense, but if you take bad luck *as though* it is your destiny or fate, it's much easier to have peace with bad luck.

That is not only a nice thought in theory, but is real practical wisdom. It is the way I have always felt about my FA – although I only recently can express it in this way. I was never worried by the questions: Why and why me? I somehow knew that there were no answers to those questions. The only answer is emptiness. Well, having to make my life's journey in a rotten vehicle still means that I have to make that journey. So let that difficult journey be as good and nice as possible. And don't make too much fuss about the damaged car and other nasty things which no individual can change.

These are only some conclusions from *The emotional vacuum; on life and science*, for which I am still looking to find a publisher. For the original Dutch version, of course. Maybe I have tried in this article to tell too much in too few words; therefore my statements might seem to float in the air. In my book I have worked out serious arguments for these statements.

*Dr. Carolien Koopmans*

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**CLOSING DATE FOR THE  
NEXT ISSUE**

**1 OCTOBER 1995**

## FORTHCOMING EVENTS

### National Ataxia Foundation (USA)

The National Ataxia Foundation (NAF) are holding their 1996 Convention in Little Rock, Arkansas over the weekend of 29-31 March. It's being organised by Judy B. Cox, the President of the Arkansas Chapter of the NAF. She plans a special session on Physical Therapies. For further details contact her at:  
129 Live Oak Dr.  
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USA  
Tel: +1 501 767 4878  
or  
e-mail YXXD97A@prodigy.com.us

Alternatively contact National Ataxia Foundation Headquarters direct:  
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Fax: +1 612 473 9289

### The Internet is coming

Members of the NAF are already there and have formed E-NAF. If you've got Internet access, try reaching Americans with Ataxias at:  
YXXD97A@prodigy.com.us

### European National Ataxia Group AGMs for 1995

Germany, DHAG, 6-8 March, Wiesbaden  
Spain, AEAH, 24-26 March, Madrid  
Ireland, FASI, 25 March, Dublin  
Italy, AISA, 27-28 April, Sulmona  
Belgium, ABAF, 28 May, Melsbroek  
Belgium, VLAF, 23 September, AZ Middelheim  
UK, FAG, 7 October, Newcastle-Upon-Tyne  
Netherlands, VSN-WAF, 21 October, Baarn

Netherlands, EURO-ATAXIA, 27-29 October, Lunteren

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### 3RD INTERNATIONAL WORKSHOP ON MACHADO-JOSEPH DISEASE, FURNAS, SAO MIGUEL, AZORES (PORTUGAL), APRIL 7-9, 1994

The third workshop on Machado-Joseph disease (MJD), was held in the Azores, April 1994, after the ones held in Lisbon (organized by the International Joseph Diseases Foundation, June 1980) and Bethesda, Maryland (organized by the National Institutes of Health, June 1991). This workshop was

a turning point both in terms both of these meetings and of the research of MJD. Professor Corino Andrade (from Porto, Portugal), who could not travel to the Azores, was the honorary chairman. The scientific committee was formed by Patrick MacLeod (Canada), Roger Rosenberg (USA) and Tetsuo Sakai (Japan), in addition to ourselves, the main organizers.

The workshop brought together the vast majority of scientists currently working on MJD, as well as researchers from similar genetic disorders (other inherited ataxias, Huntington's disease, Myotonic Dystrophy and Alzheimer's disease) and from related fields (Neurosciences, Gene Therapy, Epidemiology, Cultural and Physical Anthropology, History), and the representatives of three lay associations (Azorean Machado-Joseph Association, International Joseph Diseases Foundation and the European Federation of Hereditary Ataxias). Seventy active participants from 14 countries (four continents) were present, in addition to forty other participants (mainly Azorean physicians and other health professionals, and local health authorities).

The program included sections on epidemiology of MJD and historical genetics, genetic registers, clinical and pathological presentation and differential diagnosis, molecular genetics and perspectives for treatment, psychosocial genetics and ethical aspects, and a panel discussion on lay associations. The specific aims of this workshop, which were largely met, included (1) to define the world distribution of MJD and the origins and dissemination of the MJD mutation(s), (2) to establish protocols for an international register of MJD, and to compare and pool pedigrees and other relevant information, (3) to define the clinical and neuropathological patterns of MJD, to define the criteria for differential diagnosis, and to ascertain older descriptions of MJD from the literature, (4) to reinforce the need for international cooperation for molecular genetics studies, to establish cooperative studies for symptomatic treatment of MJD patients and to define future issues in the treatment of MJD, (5) to assess the needs of patients and families, and to compare experiences and discuss different strategies for their organization, to converge efforts from lay associations dealing with dominant ataxias and to help organizing the lay association in the Azores.

Next workshop on MJD will be organized by Dr. Wang Guo-Xiang and held in Beijing, May 1996.

*Jorge Sequeiros and Paula Coutinho*  
Porto, Portugal

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