



Twin Research &

Genetic Epidemiology Unit

St Thomas' Hospital TwinsUK

Newsletter Winter 2003/04

The Twin Research Unit is supported by the Arthritis Research Campaign, Medical Research Council, National Osteoporosis Society, Wellcome Trust, British Heart Foundation, Psoriasis Association, Chronic Disease Research Foundation (CDRF) and the European Union GenomEUtwin project.

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Welcome

Dear Twin Volunteers,

A big Welcome to 2004 and our 12th year of twin research!

Many of you won't have heard from us for a while. With around 10,000 of you on our register it is - as you can imagine - hard to keep up with everyone. There have been many changes to our unit over the past twelve years. We initially started with three staff and about 400 twins, and we reached our peak 2-3 years ago with around 50 staff when we were seeing hundreds of twins every month. Our staffing and what we can achieve at the unit depends on our level of research funding, which is very variable from year to year. We are totally reliant on charity funds and receive no money from the government or industry at present - so please bear with us.

Breaking news! We have just been awarded a £1.6 million grant from the Wellcome Trust. This grant will fund a study called 'TwinsUK', which will involve all of you and will include a visit either at St Thomas' hospital or a satellite centre nearer to your home.

Throughout the years we have had some remarkable research successes and breakthroughs, often in unusual areas. The St Thomas' twin registry has been responsible for changing the way doctors and the public think about a number of diseases. These include diseases that were previously thought

to be due to bad luck or old age, but which we have shown to be mainly genetic, such as back pain, neck pain, short-sightedness, varicose veins, arthritis of the hip and knee, travel sickness, cataracts, blood clotting, obesity, acne, depression and eczema. Some of this information comes from questionnaires and other data come from examining you in person, but both are equally valuable. We have also located the position of several important genes for osteoporosis and short-sightedness which will be used for new diagnostic tests and treatments.

As well as the new Wellcome Trust grant, we are forming collaborations with other European and Australian twin registers and 60,000 other twins as part of the GenomEUtwin project. We would like to see all 10,000 twins from the register in person and take greater DNA stores so more scientists can work with us. We are also plan

ning new studies such as the genetics of pain, the genetics of smell and attraction, skin ageing, and many other projects, such as our different responses to medicines and our never-ending search to find out whether your sense of humour is genetic or not (we still don't know!).

Finally I'd like to thank all of you for the sacrifices you make to help our world-beating research - being a twin isn't always easy and we appreciate your efforts, which have led to so many discoveries about ourselves. We still need more twins to join our register, so keep spreading the word as well as continuing to help us with our research by agreeing to visit us for tests and keep filling in those EXCITING questionnaires!

Best Wishes
Prof Tim Spector,
Director



YOUR QUESTIONS & OUR ANSWERS

We frequently get asked questions from twins about the research we are doing and what it means. Here we try and answer a few of the most common questions.

Can you tell us if we are identical or non-identical?

The only 100% certain way of determining whether twins are identical or not is by full-scale genotyping. However, this is a very expensive process, so the next most reliable test is genetic finger-printing, a DNA test, which looks at 6-10 different gene markers and is over 99% accurate in determining zygosity. This still requires blood to be taken, so for those twins who have not yet visited the Unit, we rely on the 'peas-in-the-pod' zygosity questionnaire – 5 short questions – that has been shown to give a 95% level of accuracy. The number of placentas at birth is not an accurate method as non-identical twins can have a single placenta.

Why do we receive so many questionnaires and never get asked to come in for a visit?

We have over 10,000 twins on our register. This includes all types of twin pairs – identical and non-identical, male and female twin pairs as well as a few opposite sex twin pairs. In the past we have only asked those twins who fit the requirements for a specific funded study up to the Unit e.g. the alcohol study involved carrying out body scans of female identical twin pairs where one twin drank alcohol and the other did not. However we have always been interested in collecting data from a large number of twins so that we have sufficient numbers to enable us to obtain significant results. In the past we have been able to collect this information more easily (and cheaply!) by postal questionnaire, which has not necessitated a visit to the Unit. The recently awarded Wellcome Trust grant 'TwinsUK' will enable us to collect blood samples and other clinically relevant data from ALL of you (and some parents and siblings) who are

registered. There is more information about this study on pages 3 and 4.

Why is it important for the Unit to get information from both twins and not just one?

In order to determine the relative importance of genetic and environmental factors, we need to compare the similarity of identical twins with the similarity of non-identical twins for the trait of interest. If we only have information from one twin within a pair, we do not know how similar their co-twin is to them and therefore the information cannot be used in the analysis.

If a disease is found to be highly heritable and my identical twin has been diagnosed with this disease will I automatically get it?

Not necessarily – heritability does not directly reflect the genetic risk to an individual, which also depends on how common the disease is in the population. It does NOT represent the percentage of a disease caused by genetic factors, but is the proportion of disease variability in the population that is due to genetic factors. Furthermore, few diseases are 100% genetic; environmental triggers due to lifestyle usually cause expression of most common diseases for which you may have a genetic propensity and many identical twins do not share all diseases.

What is my blood group?

At the moment we do not routinely test this for twins who visit. However, we are looking into the possibilities of testing for blood type together with cholesterol and zygosity during 2004 and beyond.

TWIN SURVEY ON THE TRU

From time to time we ask our twins to tell us what they think of the Unit. We asked 126 twins attending the Unit in April/May 2003 to complete a brief questionnaire. We had a fantastic response with 92% of you returning the questionnaire. Here are the results.

We were interested in why twins volunteered to take part in the study.

More than half said they volunteered for altruistic reasons, that is, in order to help others. The other half took part for various reasons, such as a free medical check up, as a result of an advert or media information and to be with their twin. Just over 90% continue to participate for the same reason they volunteered in the first place.

The vast majority believed that the visit was worthwhile and informative and 95% said they would attend for another visit again in the future. The majority of twins said that they were generally happy with the TRU and found our staff helpful, pleasant and kind. However, 25% of you are still waiting for the medical results of tests you had whilst on a visit. We are making every effort to improve on this and get the results to your GP as soon as possible.

80% agreed that the questionnaires were essential for the research. A small percentage, 10% found them too time consuming and said that some questions were repetitive. 15% stated that certain questions were rather embarrassing and personal. We do understand this and always try to ask such questions as sensitively as possible.

When asked whether you would appreciate a follow up call after the visit, Christmas cards, birthday cards, almost half of you said that you would prefer the money to be spent on research rather than on these tokens of appreciation.

Some of you came up with interesting ideas, such as, small twin parties in different parts of the UK (as opposed to large events based in London) and we will look into this in 2004.

We would like to take this opportunity to say a big **'thank you'** for all twin participants in this and all our surveys.

Gabriela Surdulescu,
Lab Manager, Twin Research Unit

TWIN UNIT FINDINGS

Alcohol and Bone Study

The data collected from the MZ discordant alcohol study was recently analysed. We found that identical twins who drink within the recommended UK limits have, on average, slightly higher bone mineral density at both the spine and the hip than their non-drinking co-twins. This work has been submitted for publication.

Vasospastic Syndrome

We have recently performed a study of twins looking at migraine, high blood pressure, coronary artery disease and Raynaud's phenomenon, a condition affecting the peripheral circulation. Comparing MZ and DZ twins shows that each condition has a significant genetic basis and further, there seem to be a single genetic factor underlying the 4 conditions. This paper has also been submitted for publication.

Statistical Work

In the last year we have been busy tidying up data and developing new statistical methods to correlate traits with 737 genetic markers placed across the genome (referred to here as a "genome scan"). Based on these analyses we aim to identify new genes involved in regulating a number of common traits. We have already conducted genome scans on bone at multiple body sites, qualitative ultra-sound (QUS) bone measures, markers of bone turnover and short-sight in eyes. Finally, we have successfully confirmed the existence of a candidate gene for bone on chromosome 1. Six papers have been published as a result of this hard work!

GORD – Gastro-oesophageal reflux disease (Hiatus Hernia)

A twin study of gastro-oesophageal reflux disease (GORD) showed approximately half the liability to the disease is due to our genes. Further work with specific twin pairs aims to look at the environmental factors, such as diet and exercise that may have an important influence.

Sleep disorders

Obstructive sleep apnoea is quite a common problem in middle age. Our twin study revealed a substantial genetic contribution to the aetiology of disruptive snoring, restless legs and involuntary leg jerking during sleep (between 52-60%).

CURRENT STUDIES

The Genetic Epidemiology of Pain Perception

This new twin study, funded by the Arthritis Research Campaign, is due to begin in the New Year. Twin pairs will come to the Twin Unit for a half day.

The visit includes a series of tests, which measure perceptions of heat, cold, pressure and mechanical pain sensations. These cause minimal discomfort yet will provide enormous insight into the biological mechanisms that lead to a person feeling different types of pain. There are also questionnaires covering issues that may affect how we respond to these painful stimuli.

If you have not received any information about this study, are interested in taking part and live within easy travelling distance from St Thomas' Hospital then please contact:

Jane Urwin 020 7 928 9292 ext 1575
or jane.urwin@gstt.sthames.nhs.uk

Macular Pigment Eye Study

A new Wellcome Trust funded eye study has now begun at the Twin Unit. We are looking at macular pigments, which are similar to vitamins and concentrated in the eye.

There is growing evidence that macular pigment - found in various fruits and green leafy vegetables - protects against age related macular degeneration (ARMD) by absorbing harmful wavelengths of light and acting as an antioxidant.

ARMD is a form of blindness where the macula develops wear and tear changes resulting in visual loss varying from mild distortion to severe central loss with inability to read or recognize faces.

This study will involve taking a daily vitamin supplement, which is safe and normally found in the diet and 3 visits to the Twin Unit over a 6 months period. This study will be important in identifying how heritable macular pigment is and also if we can modify the concentration of these pigments in our eyes, and possibly reduce the risk of macular degeneration, which increases with age. In other words, does 'eating your greens' really protect your eyes? We are still recruiting twins aged 18 to 50 years old for the study.

If you are interested, please telephone **Melissa or Hanske on 0207 9289292 ext. 1574.**

Myopia Study

A big thank you to all the twins who



have kindly sent in their spectacle prescriptions. As many of you will know, we found that short-sight (myopia) is highly heritable, and needed more twins to confirm our first genetic linkage findings which are very exciting. There seem to be 4 areas on the human genome that are of interest, and the next step is to look at these areas in more detail.

We will be asking some of you who sent in details for a blood sample so that we can extract some DNA (genetic material) to further the research, and (apologies!) will be chasing a few of you who have not sent us details yet!

Dr Chris Hammond, who is conducting the eye research, says that we are at the forefront of research in this area. He has been invited to talk on the genetics of myopia at the biggest eye research meeting in the world. We hope to take the lead in an international consortium of scientists studying myopia, and it is your support that makes this possible. Myopia is becoming more common therefore if we could find an important gene involved, we might go some way to preventing this happening.

Wellcome Trust 'TwinsUK' Study

This new grant is a very important one for us. Over the next 3 years we will see every single twin (and parent and sibling) on our database. This will enable us to set up a 'twin bank' of DNA that will allow us to perform extensive genetic analyses of a wide range of common diseases. You will be receiving an invitation for a visit over the next few years, which will explain further the scope of this study.

FUTURE WORK

Back & Neck Pain: Follow-up Study

We are planning a further study of those twins who had MRI scans of the neck and low back in 1995/8 to investigate changes that have taken place in their spine over the intervening 8 or so years. We are so grateful to twins who have taken part in the past and realise that this represents a considerable contribution of your time. However, this study will answer an important question of how wear-and-tear disease (osteoarthritis) of the spine progresses. Only those who have been scanned previously can help in this study. So, if you were scanned last decade, please consider agreeing to be re-scanned when we contact you next year!

FUNDRAISING

Research Grants

We were awarded 8 research grants during 2003. These grants fund research into areas such as the genetics of pain perception, eye disease and height and weight. We are also one of twelve European Countries to receive funding from the European Commission for a project called GenomEUtwin which aims to identify critical genetic and lifestyle risk factors for common diseases using European strength in genetics, epidemiology and bio-computing.

Chronic Disease Research Foundation (C.D.R.F.)

It has also been a very successful year for our Twins' charity! The CDRF has raised over £85,000 in the last year. The money raised has been used towards the funding of 2 projects; a PhD fellowship and a project grant, carried out at the Twin Research Unit. The PhD project will look at the Genetic Epidemiology of Cognitive Behaviour and the project grant will study the Genetics of Migraine. The CDRF is actively working on getting support from major UK Trusts. The charity just hosted a charity cocktail party at the BT Tower which was very successful and raised over £4,000.

The charity is now preparing its 4th charity dinner at the House of Lords in July 2004. We will give you an update of how successful the CDRF work has been in our next newsletter. If you are interested in attending please contact Christel on

020 7633 9790 or christel.barnetson@kcl.ac.uk. The House of Lords ticket price will be £200.



MEDIA UPDATE *BBC City Hospital*

Guy's and St Thomas' NHS Trust was once again the BBC's choice for the filming of City Hospital's 4th series. As always they were keen to do a piece on the Twin Research Unit. This time our "eye doctor", Dr Chris Hammond (Consultant Ophthalmologist) and his colleague Dr Melissa Lieu were in the limelight. There are more details on page 2. Many thanks to all of the twins who kindly agreed to help us with this programme and came along to St Thomas' to undergo an eye examination in front of the cameras!

TWIN UNIT APPEALS

Media Appeal

We are always in need of twins who would be willing to help with media campaigns (i.e. appear on a TV programme such as City Hospital, or attend a press conference etc.). When the unit does get involved in media events it is usually very hectic and we have very little time to organise ourselves which is why we are always keen to keep names and contact numbers of twins who are willing to be contacted at very short notice to support us in our media campaigns. If you live in the London area or its suburbs and are willing to help please contact **Tara or Pauline** on **020 7922 8149 / 8137** or email **tara.chalk@gstt.sthames.nhs.uk** or **pauline.rook@gstt.sthames.nhs.uk**

Electronic Appeal

As you know we very often contact you and ask you to fill in a questionnaire and take part in pilot postal studies. This type of exercise is extremely costly to us and we would very much like to contact you via email as often as possible. This will be a fast and cost effective way of running some of our projects. Could all twins with an email address contact **Tara or Pauline** on **020 7922 8149/8137** or email **tara.chalk@gstt.sthames.nhs.uk** or **pauline.rook@gstt.sthames.nhs.uk** Thank you for your co-operation in this matter.

Change of address

It is vital for us to always be kept informed of any change of circumstances that might occur, so please, when moving house, let us have your new contact address as well as your new telephone number and new GP details (if appropriate). Please contact Pauline on **020 7922 8149** or email **pauline.rook@gstt.sthames.nhs.uk**

Australian Appeal

Do you and your sister have Non-Identical Twins?

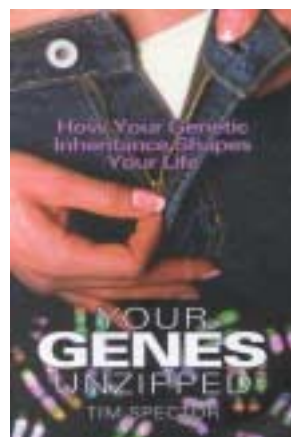
A major Australian medical research centre we work with is looking for sisters who have both given birth to non-identical twins (without the assistance of hormone or invitro-fertilisation treatment). The purpose of the research is to find the gene(s) responsible for the tendency to conceive non-identical twins, which will lead to a better understanding of the mechanisms of female fertility and infertility.

All requirements of this study can be met by telephone and mail at no cost to the participant.

To register your interest to participate in this study please call Pauline or Tara on 020 7922 8149/8137

INTERESTING READ

Your Genes Unzipped by Tim Spector



After a year's hard toil Tim wrote a paperback 'birth to death' guide for the public on how your genes shape your life entitled 'Your Genes Unzipped'

which is now released. Much of the book refers to twin studies from our work together –but also other twin work from around the world. We think many of you would find it interesting. The book retails at £8.99 (published by Robson Books—ISBN 1-86105-662-1) or can be purchased online at amazon.co.uk