

XXX study day report

Families with a daughter with Triple X syndrome – a single extra X chromosome – met experts and researchers at a study day in Oxford, UK in September 2007. They heard what is already known from research conducted on girls and women with Triple X who were recruited in the 1960s and they were invited to tell researchers from the Sex Chromosome Trisomy study group what they would like the new study, launched this summer in the UK, to focus on. The findings from the study day will help to sharpen the focus of the study, which is looking at behaviour and learning in girls and boys aged between 4 and 16 with Triple X, XYY and XXY (Klinefelter syndrome).

Genetics of Sex Chromosome Trisomy: Professor Pat Jacobs



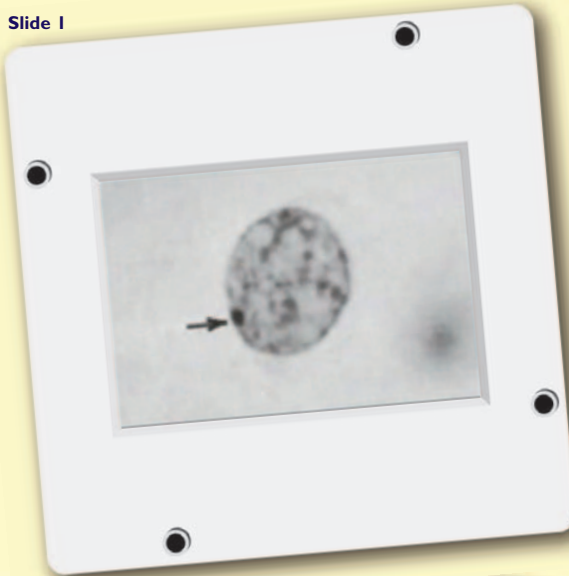
Pat Jacobs, Professor of Human Genetics at the Wessex Regional Genetics Laboratory, told families that they owed both the study day and the Sex Chromosome Trisomy study to the fact that she had shared a long taxi ride with Helen Clements, who runs the UK Triple X support group, and her daughter Megan and realised

how little we in Britain were doing for both girls with Triple X and boys with XYY (an extra Y chromosome).

What is that blob?

Professor Jacobs then took families back to the 1950s, before chromosomes were identified, when an astute microscopist noticed a blob in the nucleus of cells in females but not in males

Slide 1



(Slide 1). By analogy with the fly *Drosophila*, scientists assumed that the blob was two X chromosomes. However, in the early 1960s, Professor Jacobs looked at the chromosomes of a woman with Triple X and saw not one, but two blobs. What was then to be revealed was that when humans have two X chromosomes only one is fully working and the second one curls up on the edge of the cell to form a blob. That is true however many extra X chromosomes a person has. So a single blob was the second of two X chromosomes and a nucleus without a blob had only one X chromosome. To discover how many X chromosomes someone has, you count the blobs and add one.

Professor Jacobs then moved on to the six newborn studies that form the basis of almost everything that is known about children and

adults with a sex chromosome trisomy. In the early 1960s, all babies born at six centres worldwide – in Denmark, Scotland, two centres in Canada and two in the US – had a blood sample taken and their chromosomes analysed. From a total of some 60,000 babies it was found that each of the three sex chromosome trisomies – Triple X syndrome, XYY and XXY – occurs at a rate of around 1:1000 sex matched newborn babies. But what has happened before birth? She reminded families that not all babies are born alive, some miscarry (15-25 per cent of clinically recognisable pregnancies) and a very much smaller number (around one per cent) are stillborn. Looking at the three groups of babies with





Sex chromosome trisomies: Proportion ascertained

Ascertainment	XXY No. (%)	XXX No. (%)	YYY No. (%)
Developmental delay	58 (13)	35 (37)	33 (29)
Behaviour	-	-	25 (22)
Reproductive problems	277 (64)	6 (6)	13 (12)
Prenatal	72 (17)	40 (46)	33 (29)
Miscellaneous	25 (6)	13 (14)	9 (8)
TOTAL	432 (100)	94 (100)	113 (100)
Proportion Ascertained	20-33%	7%	18%

population – those babies whose mothers are offered prenatal diagnosis due to increased maternal age, because they are older mothers.

As 95 per cent of babies with Triple X get their extra X chromosome from their mother; you would expect to see many more Triple Xs in this group, and a rather smaller increase in boys with XXY, as only half of them get their extra X chromosome from their mother; while the others get it from their father. Looking at recent reports of babies with an extra sex

chromosome, Professor Jacobs found the increase she expected in babies with Triple X but a startling rise of 60 per cent since the 1960s in babies with Klinefelter syndrome. This remains unexplained but it is possible to test the hypothesis that the rise is due to an increase in babies with Klinefelter caused by an extra X chromosome from their father; which in turn could be linked with the well-publicised fall in the sperm count and rise in abnormal sperm.

How many girls with Triple X are diagnosed?

Professor Jacobs' Wessex genetics laboratory serves a population of almost 3 million, and Triple X occurs at a rate of 1:1,000 girls. Yet in Wessex only 94 girls with Triple X are known, about seven per cent of the expected total (Slide 2). Most of these girls with Triple X – 43 per cent in the Wessex sample – were diagnosed prenatally because they had an older mother and others – 37 per cent – after they showed some degree of developmental delay. Very few – just 6 per cent – are diagnosed because of reproductive problems. What is not known is how typical these 94 girls are and

why so few of them have been picked up and diagnosed. This is one thing a new study of XXX girls recognised at prenatal diagnosis should be able to show.

Growth and Development, Puberty and Fertility: Professor Gary Butler



Gary Butler, now Professor of Paediatrics (Growth and Development) at the University of Reading, explained the origins of his interest in children's growth as a young paediatrician and his pleasure at the opportunity to work with Dr Shirley Ratcliffe on following up the Edinburgh newborn study, which included 16 girls with Triple X (slide 3). The study showed that chromosome variations are far from rare, affecting one person in 150 and sex chromosome variations affecting one in 250. Professor Butler pointed out that baby girls with Triple X have no distinctive features or necessary health problems that would prompt diagnosis at birth. 'There is no particular regularly occurring problem that would mean

Slide 2

a sex chromosome trisomy, she found quite different rates of pregnancy loss – of babies with XXY (Klinefelter syndrome), half are lost; of those with XYY, none are lost; and of those with Triple X, 75-80 per cent are born, while 15-20 per cent are lost. No-one knows why these differences occur but one might wonder whether the extra Y chromosome in babies with XYY is in some way protective in pregnancy.

Need for new studies

Professor Jacobs admitted that she was seriously concerned about how little we know about children and adults with an extra sex chromosome. It is vital to start with an unselected population, not those who have had their chromosomes studied after birth because they have shown some problem of health or development. Yet it would not be possible to repeat the newborn study method of the 1960s, as it is no longer ethically acceptable to analyse the chromosomes of babies who appear entirely healthy. Instead, it would be possible today to capture a new unselected





Slide 3

The Edinburgh Study

- 1967-79 34,380 infants screened
- 1 in 150 any chromosome variation
- 1 in 250 sex chromosome variation
- 16 XXX girls 1 in 1000
- 23 XXY boys 1 in 700
- 18 XYY boys 1 in 1000
- 200 control girls and boys

that a paediatrician would automatically check the chromosomes. Usually there are no problems and this may be one reason why Triple X is rarely picked up at birth,' he said.

Growth

Differences in growth were subtle and only showed up when you observed groups, rather than individuals, Professor Butler pointed out. The Edinburgh study showed that at birth, baby girls with Triple X were slightly lighter (3.04kg compared with 3.36kg for girls with XX) and two centimetres shorter than the average for the population. However, their mothers were on average more than four centimetres shorter than the mothers of the girls with XX chromosomes and this could account for their size at birth, although it was also possible that the extra X chromosome did have some effect on growth within the womb. In one of the US studies (Denver, Colorado), the Triple X girls grew to be slightly taller than average but this was not seen in the Edinburgh study, where

most girls grew entirely normally although one or two were unusually tall. The pattern of growth was the same for girls with XX and those with Triple X, with lots of small growth spurts before a large growth spurt at puberty. However, in girls with Triple X the growth spurts occur slightly later than in girls with XX and the puberty growth spurt seems to occur about six months later.

'There is a very slight and subtle delay in the growth process in girls with Triple X,' Professor Butler said.

Measurements at ages 3, 5, 7 and 9 showed that throughout childhood girls' legs grow disproportionately to their backs, so they have subtly longer legs, he said. Their head circumference was also smaller than average overall, but 'we are looking at very, very subtle variations in growth,' he said.

Surprising

One family was surprised to hear that the study showed Triple X girls might be short and had been told that they were more likely to be tall.

Professor Butler agreed that the Denver study showed increased height and that two girls in the Edinburgh study were surprisingly tall but he suggested that information about height may be confused with Klinefelter syndrome, where boys with an extra X chromosome may have increased height. 'An extra X doesn't necessarily mean tallness,' he stressed. He suggested that differences may depend on which one of the three X chromosomes is not switched off. If the fully active X chromosome comes from the mother and the father's growth genes are switched off, the girl might be shorter, but if the mother's growth genes are switched off, the girl might be taller. Professor Butler admitted that the number of girls followed up from the worldwide newborn studies – 20-30 in all – is so tiny that it is not

possible to make universal statements. He also accepted that the Edinburgh girls showed greater variability in height than the population they were compared with.

Learning

The tests used to assess learning and intelligence thirty years ago were fairly crude, Professor Butler told families. One test that is admittedly crude but has stood the test of time is the Wechsler Intelligence Score for Children (WISC), used to assess IQ. The range of individual girls' scores on this test in the Edinburgh study was very wide but their average was 93, compared with 111 for the comparison population. WISC scores separate language from 'performance' – problem-solving and practical things – and the Edinburgh girls showed slightly more delay on the verbal side than in performance. All the girls in the Edinburgh study bar one had an IQ well within the normal range so what was showing here was certainly not a learning disability but a difference in the learning process.

Schools

But how useful are intelligence tests and psychology measures in terms of real life, Professor Butler wondered. All bar one girls in the Edinburgh study went to a mainstream school, the other attended a special school. In half the girls in mainstream education, schools picked up on their need for learning support with reading and/or maths and as the schools had not been alerted to the girls' Triple X, Professor Butler saw this as evidence that schools are doing their job and providing support on the basis of need. 'This gives us faith that even when it's stretched, the education system can and does recognise when children have learning problems and can put in place the necessary help,' he maintained.

Nonetheless, he said that most girls expressed relief when they could leave school. Perhaps





because of the differences in the learning process, they felt under pressure there. Three went on to college to study mainly arts-related subjects; others moved into practical careers including cooking, hairdressing and waitressing while others decided to be housewives. 'It was very positive – all of them were able to move on in ways they wanted to and contribute to society in very different ways,' he concluded.

Behaviour

In terms of behaviour, girls did seem to have somewhat more problems but the sorts of difficulties they experienced are found as well in girls without any sex chromosome variation. So for example at the age of three, slightly more girls had a difficulty with food or eating, some with soiling, others with being slightly underactive rather than hyperactive, some had difficulties with concentration, others had found problems with making and keeping friends, others had issues with being unusually dependent and in others tempers were more frequent, perhaps because of frustration at not being able to understand. At a later age, more girls had a referral to the child and adolescent psychiatry team than the comparison population, but the referrals (depression, due largely to family circumstances; drug abuse; obsessive-compulsive disorder) were not for unusual problems and whether they were related to the extra chromosome or not, no-one really knows.

Puberty and fertility

Professor Butler was upbeat about puberty. Puberty occurs entirely normally, though the first signs of puberty (breast development), he said, might occur around 11 years, perhaps six months later than the population norm and first periods at 13 to 14 years, a year or so later than in comparison girls.

Quote

“When looking at girls with Triple X, there’s nothing to say that this is something that always occurs in all of them. The children don’t look different, their physique and mind functioning is within the normal range. Given as you look under the microscope and see a whole extra chromosome, a huge extra package of genetic material, if it was one of the other sets of chromosomes 1 to 22 there would be a massive effect and the vast majority would not even see the light of day. Even a little chromosome like 21 which causes Down syndrome doesn’t have as much genetic information on it as the X chromosome and look at the big difference it has on the child and its functioning compared with the X chromosome.” GB

The evidence around girls going on to have healthy babies themselves is very thin, he said, in part because the girls in the original newborn studies are of an age when they might still have children and in part because it is not considered ethical to examine the chromosomes of an apparently healthy, normal baby. Certainly, the great majority of women with Triple X appear to have normal healthy babies but there is the possible suggestion from a review of the literature that 16 per cent may have a baby with a chromosome abnormality although this figure is heightened by the tendency of doctors to report abnormal rather than normal findings. Overall, there have not yet been enough studies looking at pregnancy outcomes for women with Triple X.

See also **Is Triple X hereditary?**

Getting the message out

Professor Butler ended with a plea to families and support groups to get out to the wider world the overall very positive and upbeat message about outcomes for girls with Triple X. When a couple is given a Triple X diagnosis in pregnancy they may be counselled by a geneticist, a paediatrician or an obstetrician. Health professionals such as geneticists and paediatricians who see families with a daughter with Triple X are much more likely to be positive in their counselling and present an

image of a child with whom there might be a few problems that can be coped with but otherwise is going to manage and contribute to society. Health professionals who have no personal experience of Triple X are more likely to present an unnecessarily bleak picture and this affects the termination rate.

Questions

When do we tell our 10-year-old daughter that she has Triple X and how?

This is a very important point that a lot of parents ask about. With each child it's different and it depends on your circumstances. I suggest to families with a son with Klinefelter syndrome that they explain bit by bit according to the child's level of understanding. If a girl who is asking why she has had difficulty with speech, or why she needed help in school or perhaps why she has seen a developmental paediatrician or an educational psychologist, you might tell her that since a test can help to explain the reasons, one was carried out and Triple X was found. One point not to forget is that every single one of us carries genetic variations, some of which are identifiable and known about while others are not.

One family pointed out that as the Triple X diagnosis is on their daughter's medical records, if they take her to the doctor with something





incidental like a cold, the doctor mentions the Triple X. As soon as she's old enough to go to the doctor's alone, she will discover about it.

At the age of 5, our daughter with Triple X has many holes in her teeth, quite unlike her three brothers and sisters. Is this part of Triple X or not?

This question led to a show of hands: 14 out of 20 families had noted some sort of dental problem. One mother; the wife of a dentist, said her husband had noticed that her daughter's teeth have a formation that is not hereditary. Helen Clements said that this was the subject of a thread on the Yahoo group (groups.yahoo.com/group/raregeneticdisorders) and other problems described there included pitting, poor enamel formation and the need for fluoride coating to stop disintegration. Victoria Leggett said that in her literature review she had come across a paper which suggested that girls with Triple X have a different tooth structure with thicker but less robust enamel.

See **Features of Triple X syndrome in Unique families**

Are the nails also affected?

A small number of families reported that their daughters have flaky nails and other nail problems such as biting.

Is Triple X hereditary?

Not as far as we know. In principle it should be because if you have an extra X chromosome, then in theory half your eggs will have 23 chromosomes and half will have 24 chromosomes. You would expect then that half the children would have Triple X or Klinefelter, depending on whether the egg is fertilised with an X-bearing or a Y-bearing sperm. But this does not appear to be the case and we don't know why, unless it is that an egg that gets an extra X by this mechanism may not be viable.

We do not have good data on the children of women with Triple X but the data we do have suggest that it is not hereditary.

Helen Clements suggested that there is anecdotal evidence of a higher miscarriage rate among women with Triple X, particularly those who have a mosaic form (some cell lines have an extra X chromosome while others do not) but Professor Jacobs said there is no hard evidence for this.

Should a woman with Triple X who is planning a pregnancy have genetic counselling beforehand or amniocentesis in the pregnancy?

Genetic counselling should be available and families can refer themselves direct to clinical genetics or ask for a GP referral. Most people would also say yes to an amniocentesis and if a woman with Triple X asked for amniocentesis, she should get it. The results of the triple test or other early pregnancy blood tests to assess the risk of certain abnormalities in the baby do not help with sex chromosomes.

My daughter with Triple X was also exposed to sodium valproate before birth and also has hypermobility, bendy joints.

Bendy joints are quite common in children. There might be a subtly increased chance of bendy joints but one difficulty when trying to compile lists of features associated with a genetic condition is that many of the features occur by chance and may not actually be caused by the condition. There are two main reasons for bendy joints – one is that the joints themselves can be a bit loose or the muscles and tendons are stretchier or not so strong. Usually there is no one particular cause.

Do women with Triple X have an early menopause?

The questions to ask are if there is likely to be an early menopause, by how much and is it significant? If there are reduced numbers of

eggs in the ovary of a woman with Triple X or if there are more eggs that are likely to have the extra X chromosome, then are some of those extra X eggs being sidelined? Is that a reason for an early menopause?

And what do you mean by an early menopause? If the average age of the menopause in this country is 52 years, if it were five years younger at 47, would that make a significant difference? It might make a difference if women are leaving it until later to have children. Also, we know that after the age of 37 in women with XX chromosomes, the number of eggs in the ovaries is reduced and that's one of the reasons why it's more difficult to conceive after the age of 37. It might be that that age in women with Triple X may be earlier because of the reduced number of normal eggs in the ovaries. But we don't know that and it would have to be looked at in further studies.

Families' questions were answered by Gary Butler and Pat Jacobs

Family concerns

Families formed two groups according to their daughter's age with families with a primary school age or younger daughter in one group and those with a daughter of secondary school age or older in the second group. Each group discussed issues around behaviour, social skills, learning and communication including speech but as you will see, their discussions ranged far wider. Here are the main issues that emerged.

Younger group: Everyone felt that their daughter had something in common with other girls with Triple X. Some had slightly emotionally immature behaviour or other behaviour issues relating to emotional immaturity, such as fighting or pinching. Girls might stand too close to other children who might find that difficult. A low pain threshold was mentioned by many families as well as growing pains; many girls were woken at night





with leg and growing pains. Some children displayed very different behaviour depending on their environment: children who behaved badly at school were good at home and vice versa. Some children got very tired and this affected their behaviour. Some had inappropriate or sexualised behaviour. Generally girls were felt to be quite naïve, trusting, impressionable and easily-led; younger girls got upset easily but older children grew out of this. Almost all girls had some degree of hypermobility or bendiness. Some had a degree of clumsiness, with some difficulties with coordination and balance; some families suggested horse-riding and ballet to help with balance and coordination. Many children had speech therapy, experiences both good and bad; other therapies were physiotherapy and occupational therapy. For speech, people recommended that singing, repetition and things with a beat worked well. Many parents said their girls didn't like loud noises such as planes going overhead or motorbikes.

A lot of families talked about their children being good with adults and younger or older children but perhaps sometimes struggling with their own age group. Many families found that time out was helpful for behaviour. On a statement of special needs: only one family got one, most were turned down because their child's special needs were not thought to merit a statement so they did not get extra help at school. On memory: some parents thought that their child had a poor short-term memory but an excellent long-term memory. A lot of the girls were very good at reading but less good at understanding what they had read. On life skills – crossing roads, going to shops alone – girls were able to do this but they did sometimes struggle to make decisions. On teeth: a lot had dental problems in common although this was a surprise to some families; lots had holes and fillings; a number had crossbite and other dental problems. On sources of information and what people found on the internet: the Yahoo support group

(groups.yahoo.com/group/raregeneticdisorders) was found to be very helpful as the information came from other parents, and was generally very positive and realistic while some other information was quite scary and horrifying. On girls' strengths – some were very good at accents or mimicry, others at art or music, and they were also very interested in how things worked and in engineering.

Reported by Sarah Wynn, Unique

Older group: On school – some girls were quiet in school but chattier outside and at home. Most children were in mainstream school with support. Parents were concerned to make teachers more aware; they discussed how good SENCOs (special educational needs coordinators) are and how good the routine is at school; one parent said her daughter's school was very organised, all the teachers knew about the Triple X and that was a big help as all teachers could support her daughter. The lack of printed information makes it very difficult to go into school and explain, as girls may only show the typical characteristics of Triple X outside school; sometimes teachers and authorities don't believe what parents tell them unless they have seen the behaviour themselves. A few parents were turned down for statements of special educational need; one was approved. Generally there was not a lot of support in school; one family lost their support between two school years. One concern was that school statements are not being administered by the authorities.

On behaviour: girls didn't like attention focused on themselves; some children had a temper and families used time out. Girls were sensitive and needed a sensitive approach. On personal hygiene, some girls had to be reminded to carry out daily personal care routines. However, this was not consistent throughout the group. Some girls were quite conscious of their appearance.

On social communication and skills: girls could make friends but might not understand the

complexities of relationships. They might take statements like 'You're not my best friend any more' literally and find it difficult to cope. Parents might have to keep their daughters on a short leash where friendships were concerned, explaining the dangers of being overfriendly with other children, especially boys. Building confidence: there was a general consensus that girls with Triple X are slow to mature emotionally. Their confidence may be undermined if they can't keep up with their friends. Children compared themselves with their siblings and where the siblings were brighter, their daughter struggled to reach the same level and that dented their confidence. In one case, a child with no siblings did well.

On communicating: it was important to use small pieces of information and to break instructions down into small bits. Singing and repetition were helpful. One girl picked up playing the piano very well because it was broken down into small pieces, each practised separately.

On coordination: a lot of the children were OK with gross motor skills but fine motor skills could be a problem; occupational therapy helped some; music helped too, as well as with frustration.

On memory: a lot of girls had a very good memory for fine detail; some could remember directions when they had only visited a place once. There was a general interest in music. Short term memory could be slightly difficult.

Girls generally showed a sensitivity to loud noises and strong smells and hypersensitivity to different textures. Children were used to routine and struggled more with novelty or breaking out of their routine.

From a show of hands to determine how the girls were diagnosed, seven were diagnosed prenatally, of whom six mothers had an amniocentesis due to advanced maternal age. Three girls were diagnosed after birth.

Reported by Satnam Juttla, Unique





After finding that many girls had features in common, families had a 'show of hands' to determine how commonly certain features occurred in their daughters with Triple X

Frequency of some features of Triple X Syndrome in *Unique* families

Feature	Number of girls (total 20)
■ Co-ordination/Balance	14
■ Leg pains	12
■ Stomach pains	12
■ Dental problems	14
■ Small hands/feet	5
■ Hypermobility/Bendiness	13
■ Hypotonia/floppiness in trunk	10
■ Stress reactions/Anxiety	13
■ Sensitivity to external stimuli (<i>noises, smells, textures, etc</i>)	16
■ Temper tantrums (<i>not age appropriate</i>)	7
■ Naivety (<i>emotionally immature behaviour</i>)	15
■ Low self esteem	10
■ Speech/Language problems	15
■ Word retention problem	15
■ Poor short-term memory	17
■ Good long-term memory	11
■ Good attention to detail	5
■ Poor personal hygiene (<i>those aged 10 and over</i>)	7/11
■ Good at directions	5
■ Good at music	13
■ Good at art	10
■ Good with younger children (<i>those old enough to be able to determine</i>)	14/14



Professor Kate Nation, Sarah Wynn (*Unique*) and Victoria Leggett.

The Sex Chromosome Trisomy study wants to look at any difficulties that girls may have and what kind of effect they have on their childhood. They want to look at what information is available on Triple X, what is needed and how they can improve it.

The study is recruiting families with a daughter aged between 4 and 16 years, where possible with a sibling for comparison. 150 children will have been prenatally diagnosed – 50 girls with XXX, 50 boys with XXY and 50 boys with XYY. In addition, from *Unique*, there will be 50 girls with XXX and 50 boys with XYY. The researchers will ask parents in a semi-structured interview questions about their child's responses in different situations. They will ask about the environment and about the impact of any difficulties the child may have on others, such as on the mother. They will ask parents to fill in questionnaires on social interactions, looking at emotional and behavioural development, on difficulties with attention including hyperactivity, on communication skills (social communication and language development), on fine and gross motor skills and on health, as well as birth and diagnosis. At this stage, the range of questions is very broad because the researchers are not yet sure what they are going to find.

From reading research papers published already, the researchers expect they may find

Sex chromosome trisomy study

Victoria Leggett, a researcher at the Department of Experimental Psychology in Oxford, explained the background to the current sex chromosome trisomy study. Many published studies are quite old. Some studies

contradict each other and many include only very small numbers of girls with three X chromosomes. Most studies focus on areas that are problematic and fail to highlight the strengths of girls with an extra X chromosome.





particular difficulties in learning and in movement (such as the flexibility mentioned by families), and possibly some difficulties with inattention and behaviours. The environment may be particularly important with different individuals responding differently in different environments.

Victoria explained that in this preliminary study the parents will be interviewed but the children will not be tested directly. This is because the 150 children with a prenatal diagnosis may not even know about their extra sex chromosome yet. Any parents who want to know more can email Victoria at victoria.leggett@psy.ox.ac.uk or telephone 01865 271381.



Ivan Foster with Gaia Scerif.

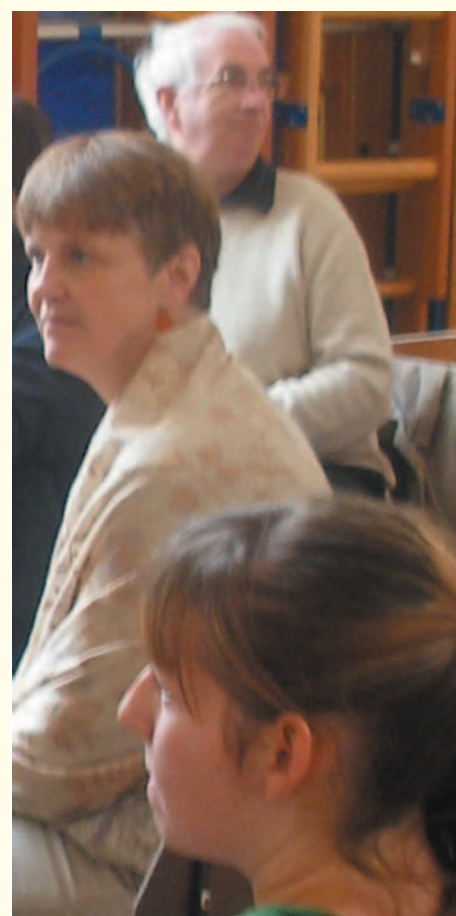
Gaia Scerif, a lecturer in the Department of Experimental Psychology in Oxford, is a developmental psychologist interested in attention and behaviour and memory in the classroom. Together with all the members of the study team, she pointed out that although the Sex Chromosome Trisomy study is a preliminary one and will hopefully lead on to a much larger study, it is likely to be larger than any other study of the sex chromosome trisomies published so far. The studies conducted so far have been very general and looked at differences in measures such as IQ rather than the processes that might underlie these differences. Some evidence has suggested that some girls have difficulties with paying attention, with memory or in understanding complex language. Teasing those differences apart may help in understanding why girls might have difficulties in understanding and following complex instructions and planning complicated behaviour.

The study team would also like to tease apart any differences in speaking, understanding and attention and to identify any strengths that girls with Triple X have. The researchers need to know about girls' strengths and weaknesses and Dr Scerif stressed that parents should let them know if there are particular types of memory and attention that they feel their girls are good at or less good at. The team will be able to tease different types of attention and memory apart – such as sustained attention versus selective attention, long term versus short term memory, visual memory in the environment, spatial memories, memorising routes, auditory memories. These types of attention and memory don't always hang together in the same child and the team will be able to examine this in girls with Triple X.

In the first instance, the study team will only be asking parents about their experience but if at a later stage they do test the children, there are many tests now available that can be used with very young children who may not even be talking yet.

Dorothy Bishop, Professor of Developmental Neuropsychology in the Department of Experimental Psychology at Oxford, has an expert interest in language. Her particular expertise is in children who have known learning difficulties and a Specific Language Impairment where everything has developed normally except language. If a child does have problems with language, she is interested in which aspects are affected and whether anything can be gained from looking at it in the same sort of way as Specific Language Impairment and related disorders such as autistic disorders are looked at.

Professor Bishop explained briefly some of the complexities of language. The production of speech sounds can be a difficulty – it may be normal for a toddler to say *pit* instead of *fish* or *dado* instead of *table* but not for a 4-5-year-old child. It is not yet known whether this is a particular problem for girls with Triple X. Similarly, some children have difficulty discriminating between speech sounds. Young babies tend to discriminate better than older babies, children and adults who lose the ability quite early on to distinguish between speech sounds that are not relevant to their own language. Again, it isn't known whether this is a particular problem for girls with Triple X. Typically developing children produce their first words around 12 months and from around 18 months to 6 years acquire vocabulary at the phenomenal rate of nine new words a day, acquiring a vocabulary of around 16,000 words between age 1 and age 6. It's not known whether this is a problem area in girls with Triple X or whether they acquire the same sort of words as other children. Putting words together to form short phrases and adding endings to words (grammatical inflections) so that events can be described (I walked) rather



Ivan Foster, Professor Dorothy Bishop and Rosie Van Moppes.

than objects being labelled (fish, table) can be the source of great difficulty for children with a specific language impairment but again it isn't known if this is an area where girls with Triple X have particular difficulties. Some children have difficulties because they understand language literally or fail to take the context into account. An example is a child being tested who was asked by the researcher 'Could you stand to do some more?' and promptly stood up. These are known as higher level comprehension skills or pragmatic language skills and the researchers hope that the questionnaires parents complete will show them how far this type of comprehension is a problem with their daughter.

'Talking to parents about the sorts of things that they have observed will give us a feel that we can then home in on and get a much more precise picture of the nature of the problems children have and indeed their strengths also. We want to get a better picture before we rush in with tests that might not be totally relevant to the problems children have,' Professor Bishop concluded.

Photographs: HELEN CLEMENTS