



The X Factor

Few people have heard of fragile X syndrome and yet it's the most common cause of inherited mental retardation. Pamela Fleming reports.

For five years Anita Nicholls and Chris Hollis watched with sinking hearts as their first baby, then his brother, grew into toddlers who were unable to walk, talk, socialise or even eat normally.

When Ben began missing normal developmental milestones they clung to the old maxim that all babies are different. Give him time, they thought, he'll come right. But he didn't, and when James was born three years later and began to display even more serious symptoms of intellectual disability, they looked desperately for answers. By then they were exhausted and close to breaking point.

"When your child isn't walking and talking and you can't find a logical reason, invariably you blame yourself," says Hollis. "We thought it might be birth trauma or, heaven forbid, bad parenting."

They now know Ben and James have fragile X syndrome, an inherited condition in which a gene sequence in the X chromosome expands, then switches off, failing to make a protein needed for the development of normal brain function.



Opposite: James Hollis. After his early diagnosis James received seven years of focussed help. He is now a passionate learner.

Above: Ben Hollis and his mother Anita.

The very conservative estimate – given that some symptoms go undiagnosed – is 1000 New Zealanders have the condition. In comparison, the much higher profile and fundraiser-friendly disease cystic fibrosis afflicts 300 New Zealand children and adults. Fragile X is also the most common cause of

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Danielle Spier and friend James Hollis, who both have fragile X syndrome. Danielle has two X chromosomes — only one has the fragile X gene change. James, being male, has one affected chromosome, with no “backup”. This may be why James is more severely affected.

inherited mental retardation.

Nicholls is chairwoman and Hollis national co-ordinator of the Fragile X Trust NZ, a family-based initiative to raise awareness of the condition and support people affected by it. They’re considered experts in their field. But it’s hard-won expertise: it took them more than five years knocking through the medical system to get their boys’ conditions correctly diagnosed; they then fought a long battle with the Ministry of Education for teacher aid funding (fragile X didn’t “fit the funding boxes”, says Nicholls); they had to educate themselves about the condition and learn to manage their sons’ behaviour through a tortuous process of trial, error and observation.

Hollis believes the condition is grossly under-diagnosed because less obvious symptoms are sometimes missed. “Doctors are becoming better at picking up children whose fragile X symptoms are more obvious, but they tend to miss the more able ones.”

In fact, fragile X symptoms manifest early, but babies and toddlers’ “failure to develop” markers can fit a variety of conditions. “Ben had been diagnosed as having a ‘global

learning delay’, which I understood to mean, ‘He’ll be right with a little extra help’,” says Nicholls.

“With James the problems were more obvious. He had no speech, and even with a big appetite was unable to eat solid food; the slightest lump made him throw up his entire specially prepared meal.”

James was constantly demanding, his sleep patterns were horrible and he often cried or hit out for no understandable reason, but Nicholls says she’d convinced herself it wasn’t too serious. “It just seemed unbelievable to have two children with a disability.”

A constant round of appointments with medical and educational professionals left Nicholls and Hollis feeling as though they were running in circles. “Ben was attending an early intervention centre,” says Nicholls, “and although they were helping with his learning needs, there was no help or advice on our wider family needs — like toilet training or advice on James’s sleep patterns and behaviour.”

The couple were severely sleep-deprived, there was no carer to provide regular relief for them; the family were isolated. Although they

didn’t know it then, their naturally sweet-natured boys had a condition that made them acutely fearful of change. As a result, they were often aggressive in social situations; they were never invited to play with other children and it was almost impossible for the family to invite people over.

With Ben a preschooler and four-month-old James, the family embarked on what should have been a wonderful opportunity. Hollis, a palaeontologist specialising in evidence of ancient greenhouse gas events, took up a post-doctoral fellowship in Japan.

His face clouds as he describes “a completely traumatising year” during which the boys’ behaviour deteriorated markedly. “Easy, enjoyable events for other host or expat families were an absolute nightmare for ours,” he says.

Back in New Zealand, Ben was five and a half and James 18 months when, on their paediatrician’s advice, the boys, their parents and extended families took a simple genetic test that confirmed they had inherited fragile X from Nicholls, despite there being no history of intellectual disability in her family.

“For the first time,” says Nicholls, “we understood both boys had a condition and a degree of mental retardation that wouldn’t come right in a few years. My whole body ached. I felt like we’d been hit by a train.”

Ironically, naming their children’s condition proved to be the end of their nightmare and the beginning of a new and much more positive chapter in their lives.

“I suddenly understood that James, in particular, was at the high-needs end of the fragile X spectrum and other people around the world were coping with the same problems. We jumped on the internet and began learning.”

These days 10-year-old James, with the flaming red hair and infectious grin, is passionate about and exceptionally good at making pottery and playing pool. Ben, his much shyer 13-year-old brother, is equally excited by music, stories, rugby and — here’s the unusual bit — helping around the family’s sunny two-storey ex-state house in the Hutt Valley, and mowing the lawn. Ben also loves visiting his grandfather’s Taranaki farm, where with gentle tuition he’s learned to milk the house cow, build fences, round up stock and stack firewood.

Both boys were mainstreamed at Dyer St School around the corner from home; Ben moved on to Naenae Intermediate and this year starts at Hutt Valley High School. “It has a special unit and a good ‘transition



Liam Spier and James Hollis, who both have fragile X, indulge a mutual fascination for YouTube haka videos. Below right: Fragile X children love to play along with music videos.

to work’ programme,” says Nicholls. Their maternal grandmother moved to Lower Hutt to help the family, often caring for the boys after school and teaching James pottery at weekends.

When in primary school Ben repeatedly missed out on teacher aid funding, Gwyneth Nonweiler spent long, unpaid hours sitting next to her grandson in the classroom, helping him to learn and interpret a loud, confusing world.

At first glance they’re just like other kids their age, but both are prone to anxiety and hyperactivity and are obsessive about

routine; they’re also years behind their peers academically.

Nicholls says Ben’s biggest challenge is anxiety. “Recently his beloved granddad came to visit. As Dad got out of the car, Ben put his hands around my neck and squeezed. I know that Ben acted like this because even a visit from my Dad, someone he loves very much, triggers a feeling of overwhelming anxiety.

“James has had more difficulty with verbal dyspraxia, which affects the motor function of his lower face and leads to speech difficulties. He’s also sensitive to





Three generations with fragile X: Gwyneth, her grandson Ben, and daughter Anita. Ben's symptoms led to testing and the recognition of more subtle symptoms in the two women and their extended family.

Fragile X, Autism and Family Links

Chances are you've heard of autism and Asperger syndrome – developmental disorders popularised in film and fiction (*Rain Man*, *The Curious Incident of the Dog in the Night Time*), and reality (the claim by the mother of a Whitianga teenage hacker at the centre of an FBI investigation that her son has Asperger's made front page news late last year).

Unfortunately, the fascinating mega-memory and mathematical abilities highlighted by such cases have contributed to a widespread, albeit mistaken, belief that to be autistic is also to be curiously gifted. Actually, autistic savants – those who have a blend of autism and savant syndrome, marked by high ability in a specialised area – are rare. (Exactly how rare is a topic of contention due to classification disparity, says Ministry of Education special education researcher Joanna Curzon; various studies suggest anywhere from 0.5 to 10 per cent of autistic individuals are autistic savants). Around six per cent of people with autism have fragile X syndrome, although many fragile X sufferers display autistic-like symptoms: a dislike of eye contact, anxiety in social situations often leading to tantrums, insistence on familiar routines and hand-flapping. Fragile X is typically more severe in

males, whose symptoms may also include intellectual disability, attention deficit, hyperactivity and epileptic seizures. The genetic disorder affects about one in 4000 people; Autistic Spectrum Disorders (ASD), of which autism, high-functioning autism and Asperger's are the main forms, affect about 115 per 10,000. However, unlike ASD, fragile X can be identified by a simple blood test. The genetic error is carried on the X chromosome, so it can be passed on by one parent. When Anita Nicholls' two boys were diagnosed with fragile X, and she learned she was the carrier – she immediately informed her extended family, suggesting they be tested. Most did; some refused. “A somewhat distantly related family has four children, three of whom have fragile X,” says Nicholls. Other clues to fragile X-carrying families: higher incidence of women with premature ovarian failure, manifesting in very early menopause (before 40). Male carriers, who make up around one in 500 of the general population, have a high chance of developing a Parkinson's-like dementia in their old age (which is unlikely to be correctly diagnosed if it isn't known that the men are carriers). And, of course, family histories sprinkled with individuals with undiagnosed intellectual disabilities.

sensory input.” His parents know that too much TV, for example, can produce anxiety, so they'll calm him down with a game in the park, a bike ride or encourage him to bounce on an oversized exercise ball.

Understanding the children's needs opens the door to more and more normal family activities. With a lot of planning they're now able to go on family holidays. Nicholls builds a detailed itinerary including maps, downloaded pictures of accommodation, activities and scenery and continually tells the boys what's coming up around the corner or in the next town, giving them time to adjust to change.

Since her children's diagnosis, Nicholls has become an enthusiastic educational adviser for the Fragile X Trust. Under its auspices she and another fragile X mother, Jodi Heenan, travel the country delivering a comprehensive programme introducing fragile X-specific teaching and behavioural strategies into New Zealand homes, preschools and schools. The trust also fundraises to bring speakers to New Zealand – most recently American fragile X expert Dr Marcia Braden, adjunct professor at the Colorado School for Professional Psychology.

Nicholls is also a facilitator for the Special Education Service's Tips for Autism programme, a professional learning and development scheme that wraps teams, including family members and teachers, around young people with autism spectrum disorder (ASD).

Joanna Curzon, team leader (research) at the Ministry of Education-based service, is full of praise for the work of Nicholls and Heenan. “Many teachers may never meet a child with fragile X. The rich in-depth knowledge collected by family, friends, teachers and everyone else involved in their care and development is absolutely crucial.”

Some children with fragile X qualify for special funding under the ministry's Ongoing and Reviewable Resourcing Schemes (ORRS). This is available to a small group of students with the highest need for extra support. James qualified early but Ben received ORRS assistance only a year ago, a decision that both Nicholls and Hollis believe had a huge effect on his development.

“Ben is naturally more able but James had overtaken him socially and academically, because he has received more intense intervention,” says Nicholls.

That intervention came in the form of special needs teacher Andrea Scanlan, who was able to spend two and a half hours a week co-ordinating a programme delivered



Danielle Spier's symptoms include high levels of anxiety.

by teacher aid Sue Plumb and James's class teacher, Kelly Layton.

All three agree that James, who wouldn't speak or make eye contact when he started at Dyer St School, has made huge strides. Scanlan says he's very astute, relates well to people and, like his classmates, chats all the time – an extraordinary achievement for a boy who didn't start talking at all until he was six. James still gets anxious but can manage it himself, by bouncing on another big plastic ball in the corner of the classroom or by biting down on a tiny, bright yellow

plastic mallet – a calming technique widely used by autistic children. The chewing response to anxiety is typical of his verbal dyspraxia and sensory difficulties.

Adamant they were able to access the correct interventions only once they knew what they were up against, Nicholls and Hollis believe family-wide testing should be strongly encouraged when symptoms of fragile X are present in a relative.

Dr Joanne Dixon is clinical leader at Wellington's genetic services laboratory, where tests for all kinds of genetic disorders

are carried out. She says many members of families with known genetic diseases simply don't want to know if they're at risk. Over half choose not to have testing when it's available. “If they feel the information is not appropriate for them at that point in their lives, we respect that decision,” she says.

Typically, she says, families are tested for fragile X on referral from their paediatrician, who will have considered all causes of learning disability in the child. If the results are positive the family are referred to counselling.



Although some males transmit small mutations that don't cause symptoms, fragile X is almost always carried by the mother — so Dixon's team usually arranges further testing to confirm she is the carrier.

"We discuss implications for both parents and children, including siblings without symptoms, and for future children.

"When it comes to healthy normal siblings, we take the internationally recommended approach of not testing them until they're above the age of consent. Then they can make the choice for themselves."

Sounds reasonable? Nicholls and Hollis point out that, in practice, the Wellington Genetic Services Laboratory will refuse to test the siblings (under 18) of diagnosed children, even if their parents detect symptoms and have asked for a test.

"This is about Genetic Services in New Zealand saying we know best, but they are wrong," says Nicholls. "They do not know better than families, or the M.I.N.D. Institute [UC Davis, California] — the world's leading research centre for fragile X, where siblings are routinely tested."

Nicholls and Hollis say early diagnosis means early intervention and that can make a

world of difference to a child's development and peace of mind. The extreme anxiety levels which may come with a fragile X adolescence, for instance, can be planned for, and made intelligible. Also, they say, siblings of fragile X children want to know how fragile X will affect them. Parents want to support their child with the right information at the right time and, in their experience, overwhelmingly seek an early diagnosis.

There is another dimension to this issue, which may affect an unsuspecting grandparent. Seventy-five per cent of male carriers (who may have few symptoms) will be affected by "fragile X-associated tremor-ataxia syndrome", a newly identified neurological disorder that crops up in later life. Most neurologists are unaware of the relationship between fragile X and this severe tremor, so it is generally misdiagnosed.

New Zealand Genetic Services is not the only battlefield for Nicholls and Hollis.

Joanna Curzon says the MOE takes "a functional approach" to special needs funding. "If a child isn't learning academically or socially, parents can apply for ORRS funding assistance, which we will consider

on the basis of a whole range of abilities, needs, symptoms and behaviours, including medical information."

She claims funds are available for fragile X children who are less affected. Nicholls and Hollis say they had a huge struggle to get help for Ben.

Their main focus now is mutual support from other fragile X Trust families throughout the country, but Nicholls is concerned only 85 families belong to an official support group. "We know there are at least 1000 people with fragile X — and our trust member-parents are overwhelmingly white and well-educated. We have one Tongan family and one Indian family. We should be multi-ethnic and cross all socio-economic groups — and we don't. It suggests there are many families with fragile X kids who are struggling in silence."

Nicholls and Hollis say the disorder has defined their lives, yet it's something they're incredibly positive about, and they've become sophisticated lobbyists for the cause. Grinning broadly, Nicholls reckons they make a good pair. "I've got a passion for education [until last year she worked part time as an early education teacher] and Chris is very organised and skilled at writing position papers in the language professional agencies understand."

Although there is currently no cure for fragile X, Hollis — ever the scientist — talks of exciting overseas research. "Unlike other genetic disorders, fragile X is the result of a single gene mutation. In theory this makes it easier for researchers looking for answers to autism-associated disorders to identify the missing protein in fragile X cases. One day we may see a cure."

This blue-sky outcome is unlikely to help Ben and James, but their parents are optimistic about their future. When asked how she sees her children living in adulthood, Nicholls is upbeat, contemplating the prospect with the same confidence as any other parent. "Ben is more able, so with support he could get a job in something practical. While James is a guy who will indulge his passions, if he too is supported I can see him living in a flat with some of the other fragile X kids he's growing up with.

"Maybe he'll end up making and selling pottery. He loves that already and he's good at it — so why not?" +

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