Clinical descriptions of previously unpublished patients

Patient 78 was first seen in the genetics clinic at age 15 months, with mild to moderate developmental delay. Karyotype was 46,XX,del(2)(q37.1). Investigation of a heart murmur had revealed an ASD and PDA. Length, weight and head circumference were all just below the 50th centile. She was dysmorphic with brachycephaly, frontal bossing, upslanting palpebral fissures, fine hair, round face and small nose. Generalized eczema was present from birth and has remained moderate to severe. Hands and feet appeared normal; no metacarpal or metatarsal shortening was noted. There was generalized joint laxity and hypotonia. She walked alone aged 3 years 10 months. A congenital lung abnormality was queried due to recurrent respiratory infections. By 7 years 5 months, her height and weight had fallen to 2nd and 0.4-2nd centile respectively. Developmentally she was said to be like a 3 year old, with controlling and attention-seeking behaviour and conversation confined to 2-3 word statements.

Patient 8490 is the first child of a healthy unrelated couple with no family history of note. She was born by emergency LSCS for failure to progress and fetal distress following a pregnancy in which the baby had been considered small for dates although had a birth weight of 8lb3oz close to term. There were no immediate neonatal concerns but following an episode of cyanosis the baby was transferred briefly to the special care baby unit. She was hypotonic, had an umbilical hernia (later repaired), excess nuchal skin and feeding difficulties from birth for which she required tube feeding overnight for over 3 months. At 2 months of age she was readmitted having had seizures following her first immunisations which were treated with phenytoin and carbamazepine. She failed to thrive in infancy and was prone to recurrent chest infections. Her early developmental progress was mildly delayed, she walked independently at 23 months of age. At 2 years of age all of her growth parameters lay below 3rd centile and she had no speech. When reviewed aged 6 years she was talking in short sentences but her speech was repetitive and often unclear. She was clumsy with poor coordination and had developed a kyphoscoliosis. She had an episode of sudden hair loss.
and her hair, which had previously been thick and dark, regrew sparse blonde and wispy
with patchy alopecia. By 10 years of age she had developed autoimmune thyroiditis and
Raynaud's phenomenon. She was having increasing difficulties with her balance and
walking. She has some problems with urinary continence although this is improving. She is
intermittently constipated and has recurrent rectal prolapse. She is mildly asthmatic and has
been seizure free since the age of 2 years. On examination she is dysmorphic with a flat
nasal bridge, epicanthic folds, upslanting palpebral fissures and a high palate. She has wiry
hair and patchy alopecia. There is a mild kyphoscoliosis, short distal phalanges of the first
fingers, shortening of the 3rd to 5th metacarpals bilaterally (confirmed radiologically) and
broad toes. She is very routine bound but mixes well. Her karyotype is 46,XX,del(2)(q37.2).

Patient 12410 was ascertained to have a cytogenetic abnormality, 46,XY,del(2)(q37.1), at
the age of 32 years. Maternal karyotype was normal, but his father had died of a myocardial
infarction. The patient's early motor milestones were normal but severe delay in speech and
intellectual development necessitated special education and later institutionalized care.
Seizures commenced aged 25 years, initially of grand mal type but subsequently partial with
myoclonic jerks, and his behaviour is sometimes difficult. Since age 27, he has sustained
ten fractures involving the lower limbs caused by minor trauma and a dislocated hip. X-ray
revealed generalized osteoporosis that may result from relative inactivity or long-term
anticonvulsant medication. On examination at the age of 32, height, weight and head
circumference were on the 3rd, 90th and 75th centiles respectively, with central obesity.
Speech was limited with marked echolalia. He was brachycephalic with low anterior and
posterior hair lines. Dysmorphic features included short, upslanting palpebral fissures,
strabismus and high arched eyebrows. The philtrum was flat and the upper lip thin. There
was mild prognathism and the ears were long, with a poorly developed tragus, thickened
lobes and mild posterior rotation. His hands were small, with tapering fingers and thumb,
and bilateral single transverse palmar creases. Examination of the lower limbs revealed
genu valgum, small flat feet, pitting oedema of the lower limbs and ulcerative skin lesions.
Gait was rigid, unsteady and wide based, requiring assistance. General examination was otherwise normal.

Patient 315 is a four-year-old boy born to unrelated parents at 42 weeks gestation weighing 3.6kg. He had an Apgar of 5 at 1 minute and 6 at 8 minutes and, although requiring no resuscitation, was initially irritable and floppy. He has one younger male sibling who is well and there is no contributory family history of note. Early milestones were normal but he presented at two years of age with delay in walking, poor speech and hyperactivity. Initial investigation revealed no underlying cause for developmental delay but subsequently an abnormal karyotype was found, 46,XY,del(2)(q37.1). Parental chromosomes were normal. On examination at 4 years, height and weight were on the 10th centile but head circumference was below the 3rd centile. He was mildly dysmorphic with short upslanting palpebral fissures and high arched eyebrows. The nose was short and upturned and the philtrum flat and long with a thin upper lip. The ears were simple and cupped with thickened outer helices. The hands revealed a left sided single transverse palmar crease with tapering fingers. He had genu valgum with poorly developed calf musculature. General examination revealed no other abnormality. The patient had little speech and showed echolalia. He is moderately myopic and has good hearing. He engaged in little social interaction but manipulated toys well. He had a wide based, flat-footed gait.

Patient 8491 was born following a normal pregnancy between 34-37 weeks gestation weighing 2.08kg. She required intubation for about 5 minutes and subsequently went to special care. She had micrognathia and required nasogastric top-up feeds. There is a history of bilateral congenital hip dislocation, Perthes disease of the right hip, hydrocephalus requiring a VP shunt, fits at age 2¼ mainly associated with fever and marked excess delta activity on EEG. All motor and language skills have been delayed and she attends a special school, but is sociable and not aggressive. On examination, she was small with weight on the 25th centile and head circumference between the 25th and 50th. She had a round face
and short neck, mid-face hypoplasia with a low nasal bridge and mandibular prognathism. Her left ear appeared rather simple and cupped. She has a mild pectus excavatum and quite a pronounced lumber lordosis. She had short 4th and 5th metacarpals on the right hand and 3rd, 4th and 5th on the left with knuckle dimples and short distal phalanges, particularly of the thumb. In the feet, she had first ray hypoplasia with short 2nd to 5th metatarsals and distal phalanges. There was no cutaneous ossification or abnormal pigmentation. Initial cytogenetic analysis was normal, but a 2q37.3 deletion was subsequently detected by subtelomeric FISH analysis and was just discernible on G-banded karyotype.

Patient 63 is a female born weighing 6lb 6oz at 41 weeks gestation. She had a small head from birth and required tube feeding for 2 days. At 9 months she was nearly sitting alone and starting to reach out. She walked at 23 months. Length, weight and head circumference were all around 3rd centile. Dysmorphic features included trigonocephaly, a high forehead, wide lower face, hooded eyes, bilateral ptosis, flat nasal bridge, anteverted nares, wide mouth, small ears and clinodactyly of the 5th fingers. Cytogenetic analysis showed an inverted duplication of the long arm of chromosome 2, karyotype 46,XX,inv dup(2)(q36.2q37.3). Renal and cardiac echo were normal. There is a history of squint, unilateral glaucoma that required goniotomy, recurrent chest infections, meningitis at age five and also two febrile convulsions by this age, but no other seizures. At 9 years she remained small, was able to read and was fond of puzzles and computers but was still not continent at night. There was mild camptodactyly of the little fingers but no clinical evidence of metacarpal or metatarsal shortening.

Patient 80 was born prematurely at 34 weeks weighing 2.44kg and had severe hyaline membrane disease and pneumothorax. On examination at 11 months, there was mild hypotonia, facial dysmorphism and bilateral single palmar creases. Head circumference was on the 50th centile, weight on the 10th centile and length on the 50th centile. Chromosome analysis revealed a 2q37 deletion, karyotype 46,XX,del(2)(q37.3). At 2 years, head
circumference had fallen to the 10\textsuperscript{th} centile. At 8 years, the patient had one fit, accompanied by repeated absences at school. EEG was normal. A horseshoe kidney was discovered on scan following a urinary tract infection. She also required a squint operation. On examination at 9 years there was frontal bossing, upslanting palpebral fissures, narrow pinched nose with hypoplastic alae, slightly small ears, mild little finger clinodactyly, short tapering fingers, possible shortening of 4\textsuperscript{th} and 5\textsuperscript{th} metacarpals, shortening of 4\textsuperscript{th} and 5\textsuperscript{th} metatarsals and mild proximal 2-3 toe syndactyly. She has moderate to severe delay, uses short sentences and attends a school for the learning disabled. She is shy with a short attention span and has behavioural problems with aggression.

Patient 106 is a female born at 38 weeks weighing 5lb 6oz, after a pregnancy complicated by severe vomiting. Early feeding was difficult, with a brief period of tube feeding. A heart murmur was noted and follow-up identified aortic stenosis and a ventricular septal defect. On examination at 3 months the head circumference was on the 50\textsuperscript{th} centile, while weight and height were on the 10\textsuperscript{th} centile. Karyotype was 46,XX,del(2)(q37.3). At 16 months, she was cruising and pulling to stand and spoke more than 6 words. There was possible mild motor delay, small hands and feet, possible asymmetry in the length of the legs, plagiocephaly, frontal bossing, but otherwise no dysmorphism.

Patient 127 is a male born by Ventouse delivery after a normal pregnancy. He was slow in feeding, which persisted through much of the first year. He underwent bilateral inguinal hernia operations as a baby and walked at 2 years. There is a history of recurrent respiratory infections. At age five, he is described as always active, noisy, with a short attention span and obsessional behavior. He is behind at school. On examination he had thick blond hair, prominent philtrum, prominent cheeks, thin lips, high palate, small chin, short 4\textsuperscript{th} and 5\textsuperscript{th} metacarpals and short thumbs. Height was just below the 9\textsuperscript{th} centile and weight 9-25\textsuperscript{th} centile. Cytogenetic analysis revealed a 46,XY,del(2)(q37.3) karyotype. An abdominal scan to exclude situs inversus was normal.
Patient 128 was born at 38 weeks gestation, weighing under 5lb. She was hypotonic in the newborn period. At 3 months she had an operation for a lump in the groin, possibly an inguinal hernia. Subsequently she underwent a squint correction operation. Weight gain was noted from age 4, associated with increased appetite. Aged 11, she had learning difficulties and a short temper. She attends a special school, has simple reading skills and uses a computer. Height was on the 25th centile, weight 98th centile, head circumference 55cm. She had truncal obesity, a round face, narrow palpebral fissures, prominent cheeks and anteverted nose, but no eczema. There is shortening of the 3rd, 4th and 5th metacarpals, confirmed on X-ray, together with cone epiphysis of the little finger middle phalanx and shortening of distal phalanx of thumb. The 3rd, 4th and 5th toes are proximally placed, with very short 4th metatarsals. The heart is clinically normal. Testing for Prader-Willi syndrome was normal. Karyotype was determined to be 46,XX,del(2)(q37.3) with deletion of subtelomeric FISH probe 210e4.

Patient 389 was ascertained at the age of 22 years. She has mild learning difficulties but attended mainstream school with additional help. Her height was on the 25th centile, with normal weight for height and she does not have an AHO-like body habitus. She has upslanting palpebral fissures and epicanthic folds, but is not otherwise facially dysmorphic. She has short 4th and 5th metacarpals, slightly short toes and short terminal phalanges of the thumbs and great toes. Serum calcium and phosphate levels were normal. Her karyotype is 46,XX,del(2)(q37.3), confirmed by deletion of FISH probe D2S90.

Patient 122 was seen in the genetics clinic aged 6 years 7 months. She was born at term weighing 7lb, fed well and gained weight rapidly. She crawled at 11 months and walked at 18 months. Speech was delayed, with only 5 words at 18 months then improved rapidly to sentences by 2 years. At age 6, she is one year behind at school and was recently thought to have receptive language and social communication disorders. Original chromosome
analysis was normal but on repeat analysis, a subtelomeric 2q deletion was identified by FISH, 46,XX,del(2)(q37.3). On examination, she had a round face with full cheeks and slight downward slant to palpebral fissures. Head circumference was 51.7cm (50th-75th centile), height 9th centile and weight 50th centile. There was generalized joint laxity and reduced muscle tone. The liver edge was palpable. Slight shortening of 5th metacarpals was noted bilaterally with shortening of 4th and 5th metatarsals and mild 2-3 toe syndactyly.

Patient 53 was born at 37 weeks weighing 2.1 kg. He was slow to feed initially and was noted to have a small head at 3 months. At 7 months he was smiling, sitting alone briefly and starting to reach out. He had eczema and absences but normal EEG. Length and weight were below the 0.4 centile but growth was parallel to the centile line. On examination there was a slight upslant to palpebral fissures and clinodactyly of the 5th fingers. No other dysmorphic features were noted. Cytogenetic analysis revealed a ring chromosome 2, karyotype 46,XY,r(2)(p25.3q37.3). There is virtually no loss of 2p material and the phenotype is therefore presumed to be due solely to the 2q37 deletion.