

Genetics Services in NSW

2001–2004



NSW DEPARTMENT OF HEALTH

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Introduction

1

Genetics Services in NSW were recognised in their own right in 1987 with the establishment of the NSW Genetics Service Advisory Committee and enhancement funding over the next four years to boost service delivery. Since that time a coordinated network of services has grown across the state with major clinical units and laboratory services in the metropolitan area and links to outreach genetic counselling services in rural areas.

Rapid technological developments and expanding discoveries and knowledge about the human genome have led to a greater ability to diagnose, prevent, manage and treat genetic disorders. Genetics has expanded from its early focus on the paediatric and prenatal area into adult medicine, particularly in the neurogenetic, cancer and cardiac areas. As many more children with genetic conditions survive to adulthood, transitional services have become necessary. Six out of ten people are likely to develop a disease that is genetic or partly genetically determined by the age of 60.

The more that is understood about the human genome the greater will be the impact on health care. A greater number of diseases will be linked to particular genes or gene sequences. There will be new ways of diagnosing, predicting, preventing and managing ill health. There will be targeted gene therapies and gene-based drug treatments.

This report reviews developments in genetics services in NSW over the last four years and provides the basis for future planning. There has been growth in all aspects of service provision. The demand for general clinical genetics services continually increases. The number of genetic conditions amenable to laboratory testing has expanded. Newborn screening services test for a greater range of disorders. Cancer genetics services, non-existent ten years ago, are now a major service area. There is improved diagnostic ability and possible treatment for intellectual disability. The importance of information for individuals and the community, and education of health professionals, about genetic conditions and services creates a vital role for the Centre for Genetics Education. The Association for Genetic Support Community provides a valued support service for individuals and families affected by genetic disorders. The newest service in the genetics network, MotherSafe is an important service for pregnant and lactating women at potential risk from exposure to medications and other environmental hazards.

The cooperative, integrated approach adopted by all service providers has allowed a rational and networked approach to service development and delivery.

2 The NSW Genetics Service

The NSW Genetics Service is a network of service providers in all the genetics service disciplines in NSW Health. A cross-Area service is provided from clinical genetics units in metropolitan hospitals in conjunction with outreach services in all Area Health Services. Some services operate from one site as indicated below and provide a statewide service. Services include:

Clinical services:

- clinical genetics and counselling services (6 metropolitan sites)
- outreach genetic counselling services in conjunction with clinical services provided from metropolitan sites (14 sites)
- cancer genetics services (5 metropolitan sites)
- the genetic metabolic disease service (2 metropolitan sites)
- prenatal diagnosis services (clinical genetics and counselling services in conjunction with fetal medicine units and obstetricians)

- the Genetics of Learning Disability Service (GOLD) (1 site)
- the Connective Tissue Dysplasia Clinic (1 site)
- MotherSafe (1 site).

Laboratory services:

- cytogenetics services (4 laboratories)
- molecular genetics services (7 laboratories)
- The NSW Newborn Screening Programme (1 laboratory)
- The NSW Biochemical Genetics Service (1 laboratory).

Education and Liaison services:

- The Centre for Genetics Education (1 office)
- The Association of Genetic Support of Australasia (AGSA) (1 office).

Full address details are provided in Appendix 1.

Structure and locations 2001–2004 of NSW Genetics Services

Area Health Services	Area-Based Service Sites		Cross-Area Services Sites			Statewide Services Sites					
	Genetic Counselling	Clinical Genetics	Cancer Genetics	Prenatal Diagnosis	Cytogenetics	Molecular Genetics	Biochemical & Metabolic Genetics	Newborn Screening	Genetic Education	AGSA	MotherSafe
South Eastern Sydney	2	1	2	1	1	1				1	1
Central Sydney	1	1		1		2					
South West Sydney	1	1		1							
Western Sydney/CHW	1	1	1	1	1	2	1	1			
Wentworth	1	1		1							
Northern Sydney	1		1p/time	1	1	1			1		
Hunter	1	1	1	1	1	1					
Central Coast	1										
New England	1										
Illawarra	1										
Northern Rivers	2										
Mid North Coast	3										
Macquarie	1										
Mid Western	1										
Far West	1										
Southern	1										
Greater Murray	1										
Private				1	1	1					

All genetic counselling services are supported by visiting clinical geneticists

Structure and locations 2005 of NSW Genetics Services

Area Health Services	Area-Based Service Sites		Cross-Area Services Sites			Statewide Services Sites					
	Genetic Counselling	Clinical Genetics	Cancer Genetics	Prenatal Diagnosis	Cytogenetics	Molecular Genetics	Biochemical & Metabolic Genetics	Newborn Screening	Genetic Education	AGSA	MotherSafe
South Eastern/Illawarra	3	1	2	1	1	1				1	1
Sydney South West	2	2		2		2					
Sydney West	1	1	2	2		1					
CHW	1	1			1	1	1	1			
Northern Syd/Central Coast	2		1p/time	1	1	1			1		
Hunter/New England	2		1	1	1	1					
North Coast	5										
Greater Western	3										
Greater Southern	2										
Private				1	1	1					

Genetics services workforce

Services/Staff	1998 FTE	2001 FTE	2004 FTE
Clinical Genetics			
Clinical Geneticist	10.00	11.20	12.70
Clinical Academic	0.60	0.60	0.60
Clinical Geneticist Administration	0.50	0.50	0.50
Genetic Fellows	4.00	4.00	4.50
Genetic Counsellor (Certified)		6.50	7.00
Associate Genetic Counsellor	27.35	18.30	21.20
Social Worker		2.25	2.25
Administration	12.10	13.90	14.00
Total	54.55	57.25	62.75
Cancer Genetics			
Clinical Geneticists	1.00	1.80	1.60
Oncologist/Geneticist	1.00	1.00	1.80
Genetic Counsellor (Certified)	1.00	1.50	1.50
Associate Genetic Counsellor	1.00	3.00	5.30
Cancer Genetic Education	1.00	1.00	1.00
Administration	2.50	3.50	3.50
Other	1.50	1.00	1.00
Total	9.00	12.80	15.70
Additionally some oncologists spend a proportion of their work in cancer genetics consultations			
Cytogenetics Services (Public Hospital Labs)			
Staff Specialists/Registrars	1.6	1.50	1.50
Scientific Staff	57.5	61.00	61.00
Administration	1.9	1.73	1.73
Other			
Total	61	64.23	64.23
Molecular Genetics Services			
Staff Specialists/Registrars	1.30	3.30	3.30
Scientific Staff	24.20	38.10	38.10
Associate Genetic Counsellor	0.40	0.00	0.00
Administration	2.10	2.50	2.50
Other			
Total	28.00	43.90	43.90

Services/Staff	1998 FTE	2001 FTE	2004 FTE
Biochemical Genetics and Newborn Screening			
Staff Specialists/Registrars	0.50	0.50	0.50
Scientific Staff	21.50	20.50	20.50
Administration	3.00	2.50	2.50
Other	1.00	1.00	1.00
Total	26.00	24.50	24.50
Metabolic Service			
Metabolic Physician		1.30	0.70
Honorary Fellow		1.00	1.00
Dietician		0.90	0.90
Social Worker		0.20	0.20
Nurse		1.00	1.00
Total		4.40	3.80
MotherSafe			
Clinical Geneticist		0.50	0.50
Associate Genetic Counsellor		0.50	0.50
Total		1.00	1.00
Maternal Serum Testing	2.00	2.00	2.00
Genetics Education (excluding 1 Cancer Education)			
	3.70	3.40	3.40
DOH Genetics Services			
Administration	2.00	2.00	2.00
Total Staff	186.25	215.48	223.28

The NSW Genetics Service Advisory Committee

The NSW Genetics Service is coordinated by the NSW Genetics Service Advisory Committee (GSAC) which was established in 1987. The Committee's membership is drawn from all the genetics service disciplines. The charter of the GSAC is to provide policy and planning advice to the Director-General of the NSW Department of Health through the Statewide Services Development Branch (SSDB).

Committee membership

Genetics Service Discipline	Representative 2004
Clinical Genetics South Eastern Sydney and Illawarra	Dr Anne Turner
Clinical Genetics Sydney South West	Dr Alison Colley
Clinical Genetics Hunter New England	A/Prof Matt Edwards
Clinical Genetics CHW	Dr Meredith Wilson
Clinical Genetics Sydney South West	Dr Robert Ogle
Biochemical Genetics and Newborn Screening	Prof Bridget Wilcken, Chair
Molecular Genetics	Prof John Christodoulou
Cytogenetics Services	Kerry Fagan
Genetics Education Services	Dr Kristine Barlow-Stewart, Deputy Chair
Genetic Counselling	Carolyn Rogers
Prenatal Diagnosis Services	A/Prof Warwick Giles
Cancer Genetics Services	Professor Rodney Scott
Community Representative (AGSA)	Dianne Petrie
Academic Genetics	Prof David Sillence
Genetics Services/NSW Department of Health	Jennifer Blackwell

Rural services are represented by clinicians from major units who provide rural outreach services.

Terms of reference

To advise and make recommendations on:

- relevant policy issues
- the development of guidelines for the delivery of high quality clinical, counselling, laboratory and educational genetics services
- current and projected service requirements consistent with NSW Department of Health service delivery processes for equitable access
- evaluation of outcomes of genetics service provision.

Current working parties

- Cancer Genetics
- Data Storage and Computer Systems
- DNA/Molecular Genetics Laboratory Services
- Cytogenetics
- Genetics Education
- Newborn Screening
- Predictive and Presymptomatic Testing for Adult Onset Neurological Disorders
- Prenatal Diagnosis.

Highlights and achievements 2001–2004

3

The GSAC has successfully fostered the rational planning and coordination of services across the State. This has been documented in several earlier publications listed at the end of this report.

Business plan 2003–2006

Rapid advances in genetics have increased demands and created pressure on clinical and laboratory services. Waiting times for first appointments are steadily increasing as community and professional awareness and expectations grow. To guide the next phase of service planning, a three-year business plan has been developed. The plan incorporates key result areas and performance indicators. It was developed during several workshops, with active participation by members of the GSAC, service providers in genetics and related disciplines, and representatives from Area Health Services, NSW Health and Greater Metropolitan Transition Taskforce.

The Business Plan has enabled the NSW Genetics Service to set priorities. Its implementation will result in enhanced clinical, laboratory, education and patient care services that will improve care and outcomes for individuals and families with genetic conditions.

The areas in which the NSW Genetics Service will achieve significant results over the next three years are:

- **Building blocks** – so that there is the necessary infrastructure (people and resources) to provide a successful genetics service.
- **An effective service model** – so that optimal use is made of resources.
- **Strategic increase in capacity** – so that the genetics service can implement beneficial new technologies and services and manage patient needs.
- **Integration into mainstream medical practice** – so that all medical practitioners have a working understanding of the relevance of genetics in the management of their patients and know when to refer patients to genetics services.
- **Outcomes for high risk children and adults** – so that people at high risk are identified and gain effective care.

The aims of the NSW Genetics Service are that through specialist genetics knowledge and expertise:

- the incidence of genetic disorders will be decreased
- the onset of genetic disorders will be delayed
- the impact of genetic disorders will be lessened.

By pursuing these aims the NSW Genetics Service is also working towards achieving:

- considerable savings for the NSW Government and community
- increased prosperity for NSW through a healthier community.

New clinical and counselling services

The previous Report on Genetics Services 1996–2000 highlighted the establishment of new clinical and counselling services. The period of this report 2001–2004 has generally been a time of consolidation leading up to the new planning cycle. A new outreach genetic counselling service has been established at Tweed Heads, supported by clinical services from Hunter Genetics. Telehealth services between major metropolitan clinical genetics services and rural genetic counselling services have been established to improve access to services across the state. Services now operate between Liverpool and Goulburn, Hunter Genetics and Tamworth. Hunter Genetics has a telehealth grant to provide telegenetics clinics to Broken Hill, New England, Mudgee/Dubbo, Lismore, Coffs Harbour, Port Macquarie and Taree for one year.

New cancer genetics services

A part-time clinical geneticist and a part-time genetic counsellor have been established for cancer genetics services at Royal North Shore Hospital.

Policies and guidelines

Achievements in the policy area during 2001–2004 include:

- Implementation of a charging policy and cost recovery process for specialised genetics tests which are non Medicare Benefits Schedule Items. Circular 2003/86.
- Submission through NSW Health to the Australian Law Reform Commission Inquiry into the Protection of Human Genetic Information with many comments included in the final report 'Essentially Yours' 2003.
- Submission through NSW Health to the Australian Law Reform Commission Inquiry into Gene Patents and Human Health with many comments included in the final report 'Genes and Ingenuity' 2004.
- Submission through NSW Health to the National Pathology Accreditation Advisory Council review of Laboratory accreditation standards and guidelines for nucleic acid detection and analysis. Recommendations have been included in the final draft.

Current policies and guidelines are listed in Section 16.

Genetic disorders

4

What are genetic disorders?

Genetic disorders result from a change in the hereditary (genetic) material contributed by the parents at the time of conception of an individual. Symptoms may be apparent at birth or may occur later in life.

Genetic disorders can affect growth, development and all aspects of health. Amongst the many hundreds of genetic disorders are:

- cystic fibrosis
- muscular dystrophies
- Down syndrome
- fragile X syndrome
- haemochromatosis
- haemophilia
- Huntington disease
- neural tube defects
- Charcot-Marie-Tooth disease
- myotonic dystrophy
- neurofibromatosis
- phenylketonuria
- polycystic kidney disease
- spinal muscular atrophies
- thalassaemias

and some forms of:

- asthma
- cancer
- diabetes
- epilepsy
- heart disease
- hearing disorders
- hypothyroidism
- intellectual disability
- visual disorders
- short stature syndromes.

How common are genetic disorders?

Genetic factors make a substantial contribution to physical and intellectual disability, chronic ill-health, psychiatric illness and familial cancer:

- cystic fibrosis – incidence 1 in 2500¹
- Down syndrome – incidence 1 in 770 pregnancies²
- Duchenne muscular dystrophy – incidence 1 in 3300 males²
- Charcot-Marie-Tooth disease – incidence 1 in 2500²
- polycystic kidney disease – incidence 1 in 1000²
- fragile X syndrome – incidence 1 in 4000 males³
- haemophilia – incidence 1 in 10,000²
- neural tube defects (spina bifida, anencephaly, encephalocele) – incidence 1 in 500–1,000²
- phenylketonuria – incidence 1 in 10,000⁴
- approximately 5% of cancers are inherited⁵
- moderate to severe intellectual disability – incidence 1 in 400, 80% genetically determined
- 1 in 20 people experience gene related illness, impairment, or disability by age 25⁶
- during their lifetime 50% of people have a disorder with a genetic component
- about half of the admissions to paediatric hospitals and 12% of adult admissions to general hospitals are for genetic disorders
- many chronic disorders of middle and old age are due to a combination of genetic and non-genetic factors
- genetic factors are a major cause of psychiatric illness.

What can be done about genetic disorders?

Genetics services provide information, education, clinical, counselling and diagnostic services, management of some conditions, and support to individuals and families who are concerned about a disorder with a hereditary or genetic basis. The genetics service also provides clinical support and education and training to the professionals who care for these families.

Genetic disorders

Diagnosis – A key part of a genetics service is the establishment of an accurate diagnosis for people with clinical features suggesting a genetic disorder. Without an accurate diagnosis of what may often be rare disorders, little else can be provided to aid patients. Genetic testing is increasingly being used to confirm a clinical diagnosis. Diagnosis is therefore a major component of the clinical and laboratory services.

Genetic counselling for people with an established genetic disorder, or those at risk assists them to make informed choices about their health, lifestyle and reproductive options. It is essential before undertaking testing to ensure that tests are conducted on an informed basis.

Prenatal testing is the process of detecting and diagnosing fetal abnormalities before birth. It is available for women or couples at high risk for some disorders. Diagnostic tests include ultrasound, amniocentesis and chorionic villus sampling. Screening ultrasound and/or blood tests are also used.

Genetic carrier testing may be available for people who have a family history of an inherited condition to determine if they are carriers of the altered gene involved. This information may be useful in planning pregnancies. Carriers of autosomal recessive conditions usually do not show any signs or symptoms of the disorder. However, in the reproductive context, if both parents are mutation carriers, their offspring may be at risk of being affected.

Presymptomatic and predictive testing for individuals at high risk due to a family history of a condition can enable prevention of occurrence of some conditions, minimise their impact through close monitoring and early treatment intervention or assist with life planning where there is no treatment.

Newborn screening and subsequent appropriate early intervention achieves significantly improved outcomes for babies born with phenylketonuria, galactosaemia, hypothyroidism and cystic fibrosis.

Management – Ongoing patient management is a core activity of the genetic metabolic services and some clinical genetics services, and includes outpatient care and monitoring, care of patients with acute illness, and overseeing and delivering new curative therapies, such as enzyme replacement.

Further information

Further information on genetic disorders, patterns of inheritance and services is available from:

The Genetics Resource Book (2004/2005): an Australasian directory with facts and information about 140 conditions and support groups, as well as genetic services in Australia – A comprehensive resource for Australia and New Zealand, published biennially for the health, education and welfare professionals; and for the individuals and families affected by genetic conditions:

The NSW Centre for Genetics Education
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ST LEONARDS NSW 1590

Tel. (02) 9926 7324

Fax. (02) 9906 7529

Website www.genetics.com.au

Genetic health outcomes

5

A key area of services planning involves identifying high risk individuals and families and providing effective care. Following is an indication of progress on outcomes for selected genetic conditions.

Pregnancy and genetic disorders

Down syndrome and other chromosomal disorders

outcome

- Reduced impact of Down syndrome and other chromosomal disorders through improved awareness of, and access to a range of services including education, counselling, diagnosis and options to enable couples to arrive at informed decisions about pregnancy and genetic disorders.

Down syndrome has an incidence of 1 in 770 pregnancies. It results from the presence of an extra chromosome 21, usually in all cells. The extra chromosome usually results from an incorrect division which arises mostly from an egg cell and occasionally a sperm. It is usually a chance event but this chance increases as the mother grows older. Some other chromosomal disorders are similarly due to the baby's cells containing an extra copy of other chromosomes, most commonly chromosomes 13, 18, X or Y.

Risk of a live born affected with Down syndrome

Years of Age of, mother, at delivery	Risk
20	1:1530
25	1:1350
30	1:910
35	1:380
40	1:110
45	1:30
50	1:6

The number of women using prenatal diagnosis by cytogenetic testing almost doubled from 3869 in 1990 to a peak of 7172 in 1998 before declining to 6495 in 2003. The decline since 1998 is due to the increased availability and use of (non-invasive) prenatal screening tests. Between 1998 and 2003, the percentage of women using cytogenetic testing for reason of advanced maternal age dropped from 75% to 61%. In the same period the percentage of women using cytogenetic testing after indication of increased risk on prenatal screening tests, including abnormality on ultrasound, increased nuchal translucency or maternal serum testing rose from 15% to 28%. (See Section 6 on Clinical Genetics Services and Section 11 on Cytogenetics Services). Many of these women use genetic counselling services to help them make informed choices.

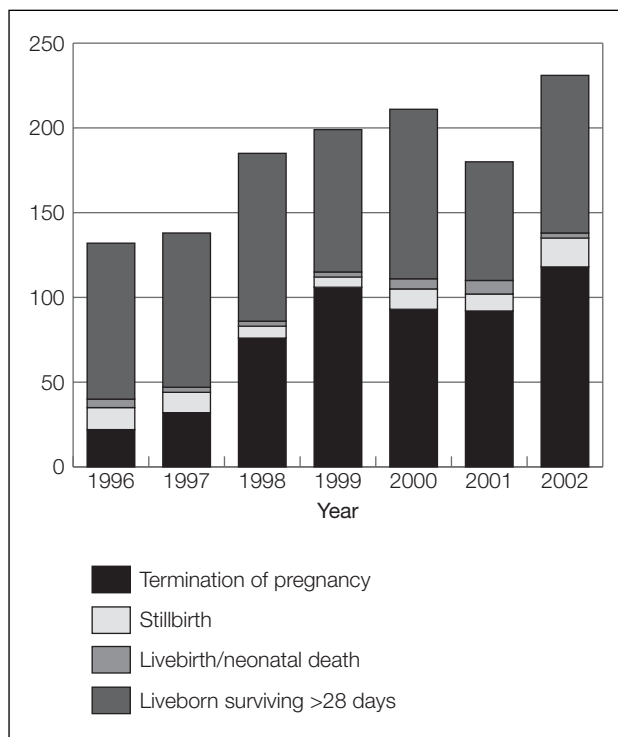
Confinements for women 35 years and over⁷

Confinements	1990		1998		2003	
	No	%	No	%	No	%
Maternal age 35+	8,974	10.4	13,839	16.3	16,477	19.3
Total all ages	86,499	100.0	85,072	100.0	85,032	100.0

Reproductive patterns are changing so that the percentage of women confined at 35 years of age and older has increased from 10.4% in 1990 to 19.3% in 2003. This has the potential to increase the number of babies born with Down syndrome, highlighting the

importance of genetic counselling, provision of information and prenatal testing. The following chart shows that the number of liveborn babies with Down syndrome does not appear to have increased during this time.

Down syndrome: cases by year and pregnancy outcome, 1996–2002



New South Wales Mothers and Babies 2003⁷ and NSW Genetics Service

See also Section 11.

Neural Tube Defects: Spina Bifida, Anencephaly and Encephalocele

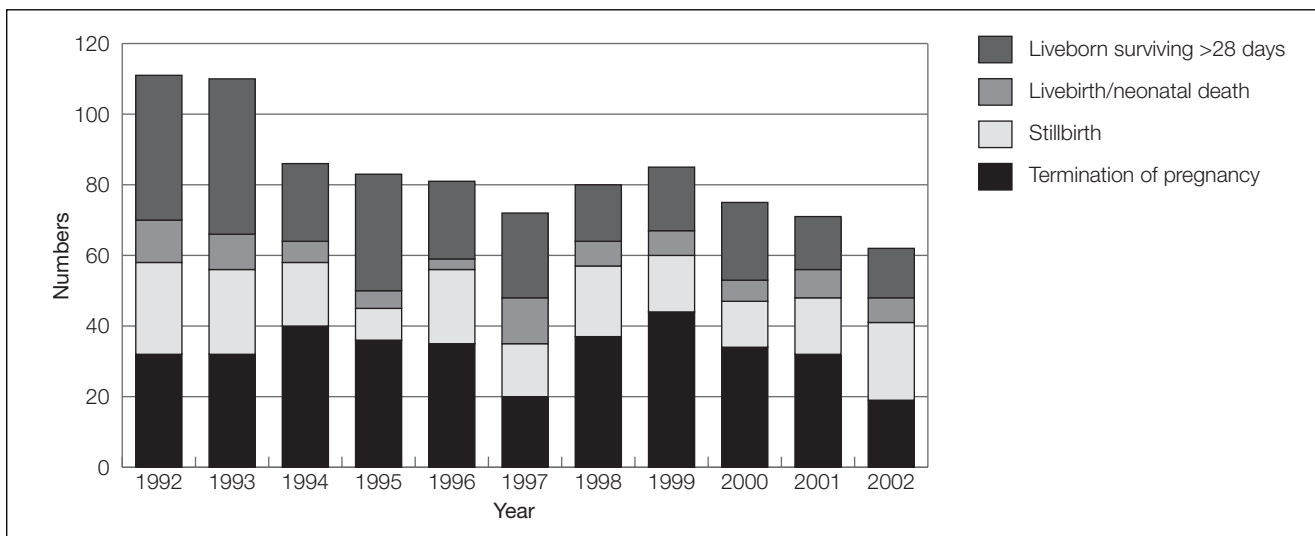
outcomes

- Increased intake of folate among women of childbearing age.
- Reduced incidence of neural tube defects: spina bifida, anencephaly and encephalocele.

In the early 1990s, in NSW, about 110 children were born each year affected by neural tube defects. Most infants are stillborn or die early in life. The remainder may have lifelong physical and sometimes also intellectual disability. At that time evidence from multicentre trials showed that increased intake of folic acid by women of childbearing age reduced the incidence of neural tube defects. A number of organisations including the NSW Department of Health, the Commonwealth Department of Health and Aged Care and the food industry undertook a range of health promotional initiatives, including encouraging improving dietary intake of folic acid rich foods, promoting tablet supplementation and folate fortification of a number of breakfast cereals.

Data from the NSW Birth Defects Register indicate a fall in reported cases from 111 in 1993 to 62 in 2002.

Neural tube defect: cases by year and pregnancy outcome 1992–2002



New South Wales Mothers and Babies 2003⁷

Newborn screening for genetic disorders

Cystic Fibrosis, Phenylketonuria, Galactosaemia, Hypothyroidism

outcome

- Early diagnosis and immediate treatment reduces severe mental and physical impairment and mortality.

The NSW Newborn Screening Programme tests about 90,000 babies born in NSW and ACT for several disorders, including phenylketonuria, cystic fibrosis, galactosaemia and hypothyroidism.

Each year about 90 babies are diagnosed with one of these conditions and more than 300 affected children and adults are monitored. Early detection and intervention results in significantly improved outcomes.

As an example, phenylketonuria has a frequency of 1 in 10,000 births. Each year the Programme diagnoses about 8–10 infants with this disorder. Early treatment with a special milk formula and diet prevents severe mental retardation and results in normal growth and development.

New Diagnoses 2001–2004

Disorder	Number Diagnosed
Cystic Fibrosis	96
Galactosaemia	8
Hypothyroidism – primary congenital	125
Phenylketonuria	31
Other rare disorders	101
Total	361

New South Wales Newborn Screening Program

See also Section 8.

X-linked disorders

X-linked disorders causing intellectual disability

Genetics of Learning Disability (GOLD)

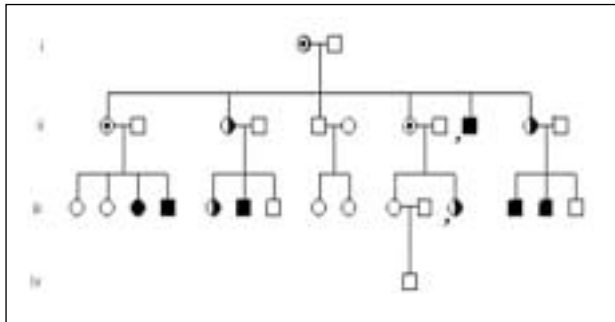
outcomes

- Counselling and testing in the extended families with the Fragile X syndrome has resulted in the incidence dropping from 1: 4,000 to 1: 10,000 births in NSW 3.
- Cost saving to the State from this reduction is estimated in 2005 to be \$12 million/year and is cumulative.
- 25% of NSW families with previously unknown mutations in genes coded on the X chromosome have had their mutations identified. Carrier testing is restoring reproductive confidence for some women in these families. One woman described this as ‘better than winning the lottery’
- Genetic testing using a tiling path microarray with 1500 specific DNA sequences designed to detect deletions and duplications on the X chromosome is being developed.

The Genetics of Learning Disability (GOLD) Service provides a service to individuals and families with inherited intellectual disability. This includes X-linked conditions such as fragile X syndrome and other X-linked conditions causing intellectual disability (referred to as XLMR). The gene mutation has been identified in an increasing number of these conditions.

The incidence of X-linked conditions causing intellectual disability in the male is estimated to be 1/650 births.

An example of a fragile X family



Fragile X syndrome causes moderate to severe intellectual disability and is due to a lack of FMR1 protein. Individuals affected by this condition require special education assistance and lifelong supervision. Both males and females can be unaffected carriers.

The pedigree illustrates four generations of a fragile X family. The great grand mother is an unaffected carrier (circle with dot). She had six children – two unaffected carrier daughters, two daughters with learning disabilities (circles half black and half white), one unaffected son (blank square) and one son with fragile X (black square).

The third generation has a number of normal and affected individuals. This generation have reproductive choices enabling the possibility of a child without fragile X.

The GOLD Service:

- Runs an expanding register of 299 extended families with fragile X syndrome and 315 families with XLMR or autism
- Offers testing to affected individuals and those at risk of being carriers
- Offers up to date information about prenatal testing and PGD (preimplantation genetic diagnosis) and supportive counselling to assist in decision-making appropriate to the individuals concerned
- Collaborates with researchers in Australia and overseas targeting the identification of new genes causing X linked mental retardation
- Participates in the NSW Chromarray Group for the development of microarrays to improve the rates of diagnosis in intellectual disability

Fragile X DNA testing is funded by Medicare, with the:

- Medicare Item 73300 (Nucleic Acid Amplification testing, Schedule fee \$103.10, 85% benefit \$87.65 in the following circumstances:
 - Detection of genetic mutation of the FMR1 gene by nucleic acid amplification (NAA) where:
 - (a) the patient exhibits one or more of the clinical features of fragile X (A) syndrome, including intellectual disabilities; or
 - (b) the patient has a relative with a fragile X (A) mutation
- Item 73305 (Schedule fee \$206.20, 85% benefit \$175.30): Detection of genetic mutation of the FMR1 gene by Southern Blot where the results in item 73300 are inconclusive.

Prior to ordering these tests (73300 and 73305) the ordering practitioner should ensure the patient has given informed consent. Appropriate genetic counselling should be provided to the patient either by the treating practitioner, a genetic counselling service or by a clinical geneticist on referral. Further counselling may be necessary upon receipt of the test results.

Duchenne Muscular Dystrophy

outcomes

- Improved carrier detection.
- Reduction in unnecessary terminations of pregnancy from >50% to 2–5%.
- Reduced incidence of Duchenne muscular dystrophy in NSW between the mid 1960s and 1980s from 1 in 3,500 to 1 in 5,0008.

In New South Wales there are at least 500 families for whom Duchenne muscular dystrophy (DMD) is an ongoing clinical problem. DMD is a progressive, profoundly disabling and terminal genetic disorder of muscles. Affected males are usually diagnosed between 3 and 5 years of age and are wheelchair dependent by 13 years of age. Average survival is to the third decade of life.

At present there is no cure. It is inherited in such a way that it affects only males, with rare exceptions. It is usual that when a boy is diagnosed with Duchenne muscular dystrophy several of his female relatives are recognised to be possible carriers, meaning that although

unaffected they may pass the disorder on and have affected sons and grandsons.

The decreased incidence from 1 in 3,500 male births in the mid 1960s to 1 in 5,000 in the 1980s reflects the effectiveness of genetic counselling and DNA diagnostic testing since 1986.

Before the availability of prenatal DNA diagnostic testing, women who were known to be or likely to be carriers had very limited reproductive options. They usually remained childless or opted for fetal sex determination with termination of pregnancy if the fetus was male. This almost certainly meant that more than 50% of the pregnancies terminated were unaffected.

Today, it is possible with recent advances in DNA testing to quickly and reliably screen the entire Dystrophin gene to determine the presence or absence of two of the common forms of mutation (exon deletions and exon duplications) which account for about 75% of cases of DMD. Recent technological changes have also made it possible to determine which females in a family are genetic carriers of these mutations. Thus possible carrier women and male fetuses can be tested to see if they are affected or carry the Dystrophin mutation and so the risk of terminating an unaffected pregnancy is very much diminished.

By the end of 2005 all NSW families where there is a DNA sample from an affected male or likely genetic carrier female will have been screened for mutations in the Dystrophin gene. It is expected that more than 90% of families will have a molecular diagnosis as a result.

Single gene disorders

Huntington Disease

presymptomatic and prenatal testing

outcome

- Knowledge of risk status in families with a history of Huntington disease allows informed choices to be made by individuals and couples regarding issues such as family, career and financial planning.

Huntington disease (HD) is an autosomal dominant neurodegenerative condition with age of onset usually between 35 and 45 years (range 2–80 years).

The incidence of HD in the population is 6–7 per

100,000 and NSW has about 400 affected people. The 'at risk' estimate is 1 in 4000 people). The HD mutation, identified in 1993, is a trinucleotide repeat expansion on chromosome 4.

Presymptomatic and prenatal testing for the HD mutation is available for persons at risk for HD aged 18 years and older. Because of the complexity of issues, HD testing is best accessed through an expert team, including a clinical geneticist, genetic counsellor, neurologist and neuropsychologist/psychiatrist who can provide detailed information about the test; its limitations, possible outcomes and supportive pre and post result counselling. Ongoing assessment and management by a neurologist and psychiatrist is recommended. HD DNA testing is very helpful in the neurological diagnosis of patients that have clinical features of HD. They and their relatives benefit from referral for genetic counselling as a positive test result indicates that relatives could have the HD genetic alteration.

Worldwide, the uptake of presymptomatic testing is 15–20%, and uptake of prenatal testing for HD is extremely low.

There are established Huntington Disease Services at Westmead Hospital and Hunter Genetics. Services are also available through genetic clinical and counselling units. The Huntington Disease Unit at Lottie Stewart Hospital in Sydney provides 18 beds and services. Residential and counselling services are also provided in the Hunter Area.

Predictive Testing Program Participation 1993–October 2004

	Female	Male	Total
No. enrolled for presymptomatic testing	586	515	1101

Results of testing 1993–October 2004

	Mutation +ve	Mutation -ve	Inter-mediate	Total
No. of presymptomatic test results	337	513	40	890
No. of prenatal test results	2	5		7

Hereditary Haemochromatosis

outcome

- Early diagnosis and treatment prevents organ damage and allows normal life expectancy.

Hereditary or genetic haemochromatosis (HH) is the commonest adult onset genetic disorder in Australia, affecting one in 200–300 people. One in eight to one in ten people is likely to be a carrier of the gene mutation. Carriers usually show no symptoms of the disorder but may develop it if they have diabetes, are alcohol dependent or have some other triggering factor. Couples who are both carriers of the faulty gene have a 1 in 4 chance in every pregnancy of having a child who is at risk of developing HH as an adult.

HH is characterised by accumulation of iron in various organs which leads to conditions such as cirrhosis, cardiomyopathy and diabetes. Early diagnosis and treatment is important to prevent organ damage and allow normal life expectancy. However, it is under-diagnosed because of its late onset (average age of onset of symptoms is late 40s) and multiple non-specific clinical presentations.

Treatment consists of regular blood collection from the patient to reduce excess body iron stores. The collected blood can potentially and very inexpensively be used for blood transfusion services.

Excess body iron is commonly due to HH. Patients exhibiting symptoms would usually undergo fasting iron studies in the first instance (preferably fasting transferrin saturation, ferritin and iron). Where indicated by iron studies, family history and other risk factors, gene mutation testing can be carried out. Mutation testing has been available since 1997. One mutation, C282Y is usually found in HH, so DNA testing can be done quickly and relatively cheaply by a PCR reaction performed by many pathology laboratories. The risk implications for other family members can then be ascertained and early diagnosis and monitoring can avoid development of more serious conditions. Screening can detect gene status, iron overload or both, either by screening of the population or 'cascade' screening of relatives of patients known to have genetic haemochromatosis. Both methods have advantages and

disadvantages, and population screening trials are presently determining the best approach.

DNA testing for HH is covered by Medicare (Item number 66794), scheduled fee \$37.10, 85% benefit under the following circumstances:

Detection of the C282Y genetic mutation of the HFE gene and, if performed, detection of other mutations for haemochromatosis where:

- the patient has an elevated transferrin saturation or elevated serum ferritin on testing of repeated specimens; or
- the patient has a first degree relative with haemochromatosis; or
- the patient has a first degree relative with homozygosity for the C282Y genetic mutation, or with compound heterozygosity for recognised genetic mutations for haemochromatosis.

Penetrance (development of disease during the lifetime of a person with two HH mutations) varies from 10–75% in different studies. This variability has been attributed to different epidemiological factors that modify the effect of the mutation, including ethnic origin, gender and environment of the group studied. Penetrance is higher when measured by serum indicators of iron overload.

As the early detection of HH can prevent serious disease, some life insurance companies have agreed to provide cover to homozygous patients on the condition that the patient undergoes regular surveillance for complications.

Genetically determined cancers

About 5–10% of certain cancers are caused by inheritance of a genetic susceptibility⁵. Where there is a strong family history genetic susceptibility may be considered. Genetic counselling and pedigree construction provides information to enable initial risk estimation. Decisions can then be made on the appropriateness of genetic testing for more accurate risk estimation on inheritance of mutations in cancer susceptibility genes.

People identified at high risk then have a basis for making informed choices about preventive and early detection strategies or prophylactic interventions.

Breast Cancer*outcome*

- Reduced impact of genetically determined and partly genetically determined cancers.

DNA test results for familial breast cancer for the year 2003 indicate that a pathogenic mutation is found in about 15% of cancer affected women tested. A positive result in the cancer affected woman, means that her asymptomatic first degree relatives have a 50% chance of also carrying the gene mutation and are therefore at potentially high risk for developing breast and ovarian cancer. They may wish to clarify their risk through predictive genetic testing to identify the family mutation so that they can take steps to minimise their risk of developing cancer. Where predictive testing is offered to blood relatives at potentially high risk, the detection rate is just over 40%, ie approaching the 50% theoretical risk. Those who test negative can avoid unnecessary intensive cancer screening, high concern and associated costs, and their cancer risk is the same as the rest of the population. For those who test negative, their offspring cannot have inherited the genetic cancer susceptibility and can be reassured they are also not at high risk.

Preliminary results from a survey show the effectiveness of genetic counselling in decreasing psychological distress in women at moderate or high risk of developing breast cancer. Genetic counselling was also shown to improve women's knowledge of breast cancer genetics and that this knowledge was retained in the long term.

Colorectal Cancer*outcomes*

- Improved detection of families at risk through increased registration of families with familial adenomatous polyposis (FAP), hereditary non polyposis colorectal cancer (HNPCC) and other polyposis syndromes at the NSW and ACT Hereditary Bowel Cancer Registers and at family cancer clinics statewide.
- Genetic testing introduced for these syndromes.

There has been a significant increase in registrations (families) since NSW & ACT Hereditary Bowel Cancer Registers were relaunched in 1998. Improved collaboration between the Registers and other state and international registers, as well as with family cancer clinics, has allowed multiple families, previously thought to be independent, to be linked. This can simplify the gene testing process, achieving savings in time with a concomitant reduction in anxiety, and also in costs.

See also Section 7.

Genetic education**Genetic Education***outcome*

- Raised awareness of genetic disorders and genetic technologies to reduce impact of genetic disorders.

The Centre for Genetics Education (CGE) develops and provides information, resources and educational programs. Activities of the Centre are targeted at all levels of the community: government, professionals, individuals and families affected by a genetic disorder and the general public.

The Centre's website (www.genetics.com.au) was established in 1996, now hosted by NSW Health, increasing accessibility to information and awareness of genetics services. The number of website 'hits' reached over 600,000 per month in 2004, increasing by more than 10-fold over a 12-month period.

Resource production

The CGE develops and produces resources that are fundamental tools for the NSW genetic counselling services as well as easy to read 'guides' providing direction and risk information to clinicians on array of prenatal screening and diagnostic options and disorder specific information. Some examples of new resource development and updates are:

- **The Genetics Resource Book**

The 2004/2005 (7th) edition was produced in May 2004. It is a compendium of Genetics Support Groups, Services and Information for Australia and New Zealand. The 54 Fact Sheets in the Book are also provided online.

Genetic health outcomes

■ PND booklet revision and printing

Although available online, hard copy is in strong demand by professionals for use with patients. A chapter on preimplantation genetic diagnosis has now been inserted in the latest edition (2003).

■ The Family Health Tree Guide

Now produced in two versions, one for the community and one for health professionals. These resources are also available in hard copy and online.

■ Disorder Information sheets

The Centre produces and keeps up-to-date over 700 Information Sheets on genetic disorders, many covering very rare conditions. These Sheets are used before, after or during genetic counselling.

Professional education

- A range of educational activities has been conducted for professionals including genetic counsellors, GPs and oncologists and other professional groups including teachers.
- The Centre is certified as an RACGP education provider through evaluation of GP bowel cancer workshops (video) and CME evaluation of bowel guidelines (500 GPs).

Public engagement and partnerships

The Centre's resources are also the foundations of public education. Using these tools, the Centre has conducted activities to engage the public in informed discussion to facilitate decision making regarding the utilisation of the new genetic technologies. The Centre recognises that partnerships with other relevant groups can lead to a more holistic approach to these challenges and will strengthen the breadth of genetics education within the community. Partners include professional and academic organisations, biotechnology and research facilities and scientific media.

See also Section 13.

Clinical genetics and genetic counselling services 6

Clinical genetics services

Diagnosis and management

Clinical genetics services are provided by a team which can include clinical geneticists, genetic counsellors and genetic social workers. Clinical geneticists bring specialised skills to the diagnosis, investigation and management of a genetic disorder, which may present in a pregnancy, after birth, in childhood or later in life. The diagnosis may be made on the basis of clinical features or laboratory analysis of tissue or blood, using cytogenetic, molecular genetic or biochemical genetic testing techniques. Genetic counsellors and social workers provide specialised counselling services relevant to genetic disorders. All members of the clinical genetics team may contribute to the genetic counselling or diagnostic process.

The genetic counselling process

Genetic counselling provides an individual or family with current information, available options and supportive counselling regarding problems in growth, development and health which may have a genetic basis. Counselling can assist families and individuals to understand and adjust to the diagnosis of a genetic disorder.

Informed consent for genetic testing

A key feature of genetic counselling is the provision of information to individuals, so that where genetic testing is an option, it can be undertaken on the basis of full information.

The shared nature of genetic inheritance means that a clinical diagnosis or genetic test result in one family member may have implications not only for that person but also for other family members. Because genetic disorders can be family health problems, this raises specific ethical issues about information-sharing, which are different from those associated with other medical interventions. Further information is available in the *Ethical Code Governing the Provision of Genetics Services, 1998*.

Issues for consideration prior to consenting to genetic testing include privacy, ownership of and access to information, responsibilities and obligations to family members and impact of a positive diagnosis on access to insurance and employment.

Data collection

A statewide genetics service database for clinical and genetic counselling services has allowed the gathering of non-identifying data on service activity. Three of the smaller outreach genetic counselling services (based in Far West, Macquarie and Greater Murray) do not have facilities to record their service activity data. Services provided by major genetics units to these outreach services are included in the major unit's database.

Data on service use to 2003 are summarised in the charts on the following pages. The data indicate venue of service provision, most common reasons for referral, major diagnostic categories, referral sources and types of services.

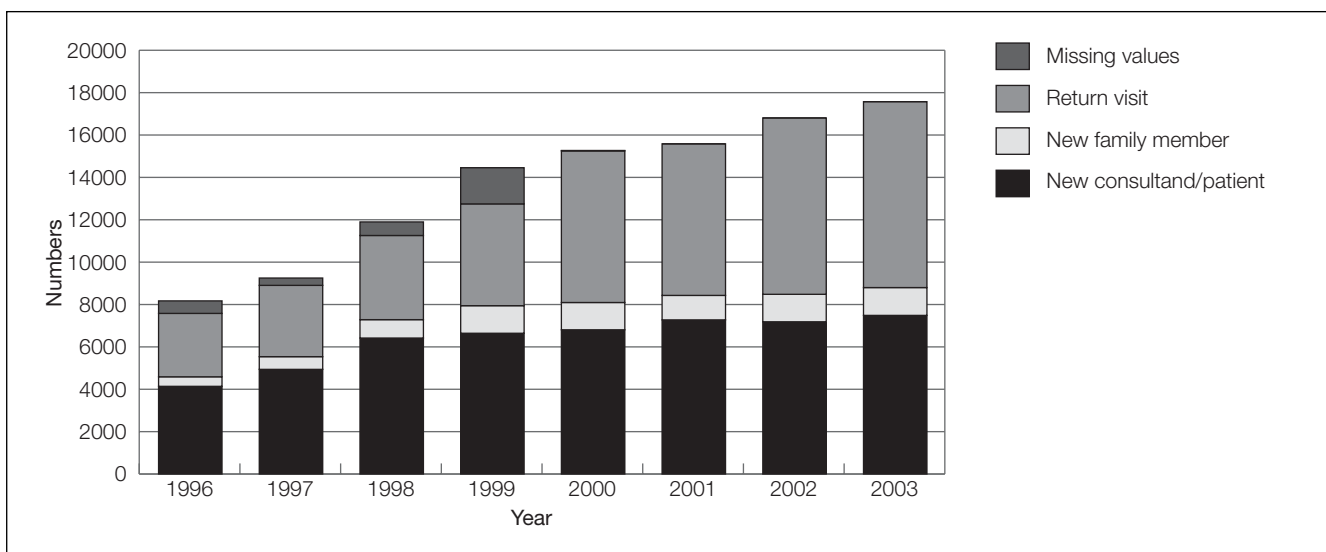
The majority of cancer genetics services are provided by specialised Familial Cancer Services and detailed data are included in Section 7.

Service use

- The chart below shows growth in demand for genetics services. Reported consultations have more than doubled from 8172 occasions of service in 1996 to 17574 in 2003.
- In 2003, 43% of patients were new referrals, 50% return visits and 7% new family members.

Patient occasions of service (consultations) 1996–2003

Occasions of service for 1996 = 8,172. Occasions of service for 2003 = 17,574



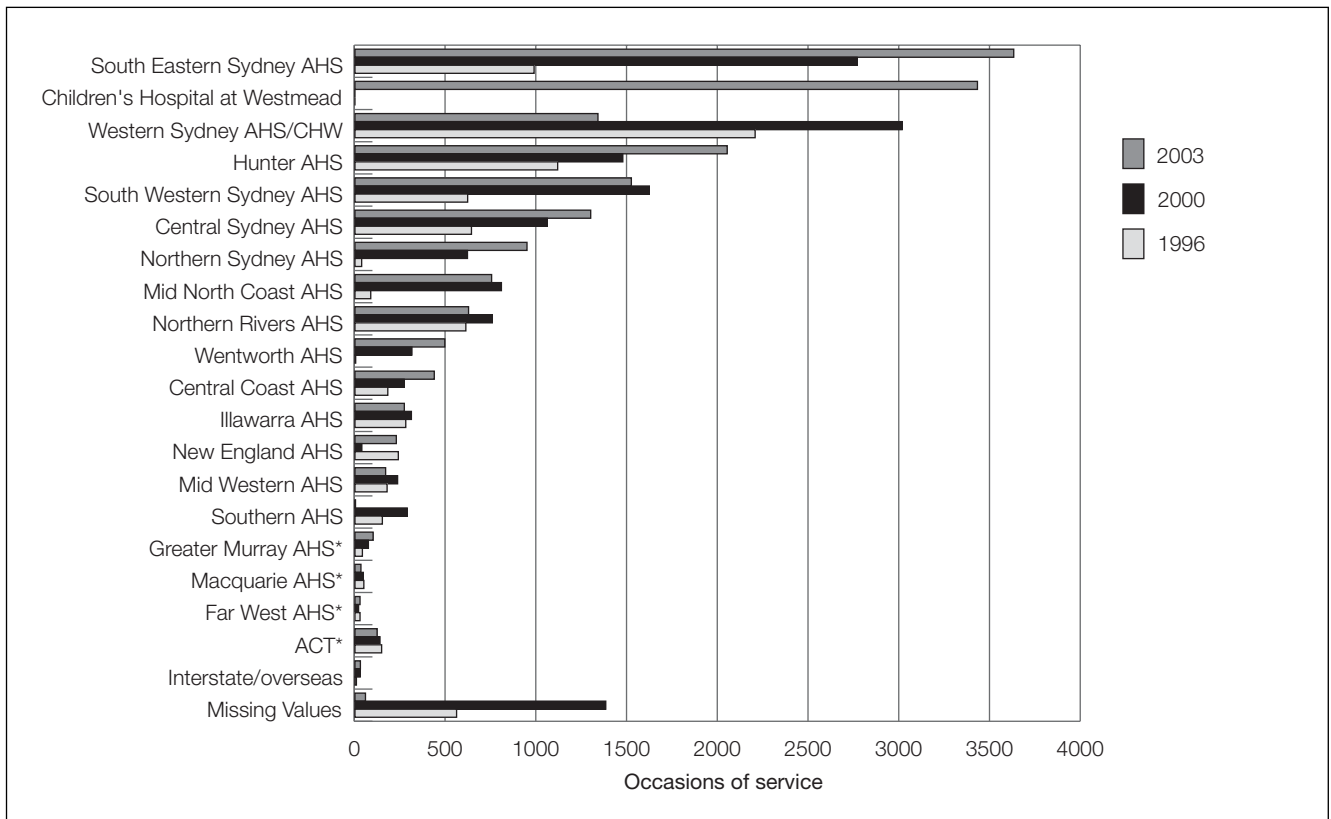
Venue of service provision

- As indicated in the chart below, growth is evident in all venues of service provision, particularly in the larger and more well-established units in Children’s Hospital at Westmead (CHW)/Western Sydney, South Eastern Sydney and Hunter.
- From 2001 occasions of service at the Children’s Hospital at Westmead have been counted separately from those provided to adults in Western Sydney AHS.

- Data for the ACT represent occasions of service provided by Clinical Geneticists from NSW. Genetics counselling services provided by ACT staff are not included here.
- Data have not been adjusted for staff variations between units
- Data for Far West, Macquarie, Southern and Greater Murray represent occasions of service provided by metropolitan Genetics Service staff. Occasions of service provided by local Associate Genetic Counsellors are not included.

Occasions of service by venue of service provision 1996–2003

Occasions of service for 1996 = 8172. Occasions of Service for 2003 = 17574



Most common reasons for referral

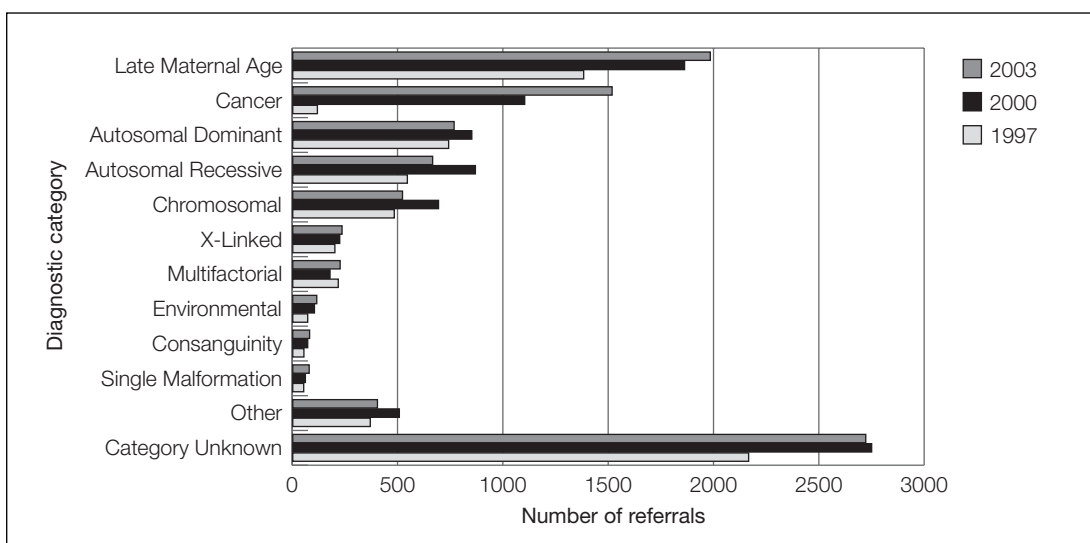
- Genetic conditions are classified according to standard genetic diagnostic categories listed below as well as by their syndrome or condition name.
- The following chart shows most common reasons for new referrals according to standard genetic diagnostic categories.

- Growth is apparent in most categories, particularly cancer and late maternal age.
- Cancer Genetics Services were introduced in the mid 1990s and new referrals have grown rapidly since that time. Detailed data are found in Section 7.

Diagnostic categories/reason for new referrals 1997, 2000 and 2003

Total new referrals for 1997= 6,388. Total new referrals for 2003 = 9258

Note: new referrals may have more than one diagnostic category

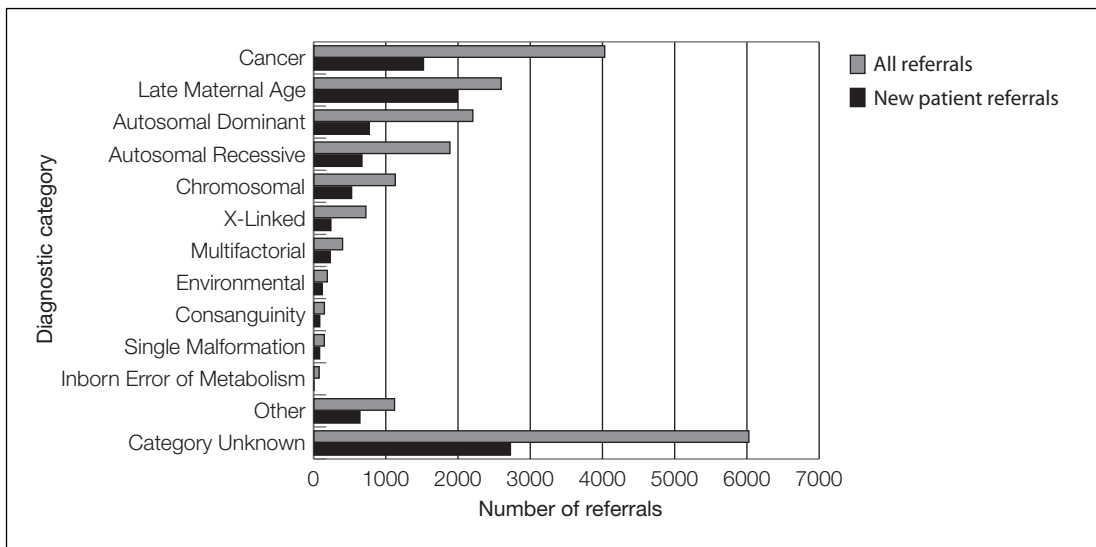


- The chart below shows most common reasons for new referrals compared with all referrals for 2003. It indicates that cancer is the most common reason for service consultation. The complexities of cancer genetics mean that two to three consultations per patient are often necessary.
- Many of the referrals included in the Category Unknown are for complex conditions where a clear diagnosis may be difficult. This occurs in a large number of dysmorphism, mental retardation and neurological phenotypes.
- Generally referrals for late maternal age require only one consultation.
- After referrals for advanced maternal age and cancer (see Section 7) the most common genetic conditions or syndromes amongst reasons for new referrals are:
 - Pregnancy at increased risk for Down syndrome and other chromosomal abnormalities
 - Down syndrome
 - Consanguinity
 - Teratogen exposure
 - Spontaneous Abortions, Recurrent
 - Dysmorphic features
 - Haemochromatosis
 - Marfan Syndrome
 - Huntington Disease
- Recent advances in antenatal ultrasound techniques, particularly the detection of increased nuchal translucency are reflected in the increasing number of referrals of women with increased risk pregnancies
- Genetic haemochromatosis is also attracting a growing number of referrals. Many more people with genetic haemochromatosis would be seen outside genetics units.

Diagnostic categories/reasons for new referrals and all referrals 2003

Total new referrals for 2003 = 9505. Total referrals for 2003 = 20483

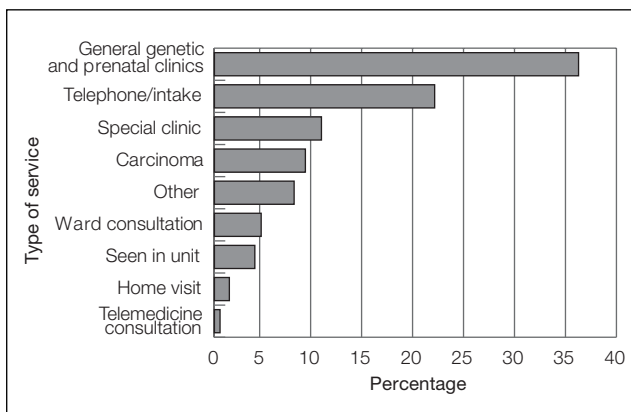
Note: referrals may have more than one diagnostic category



Types of services

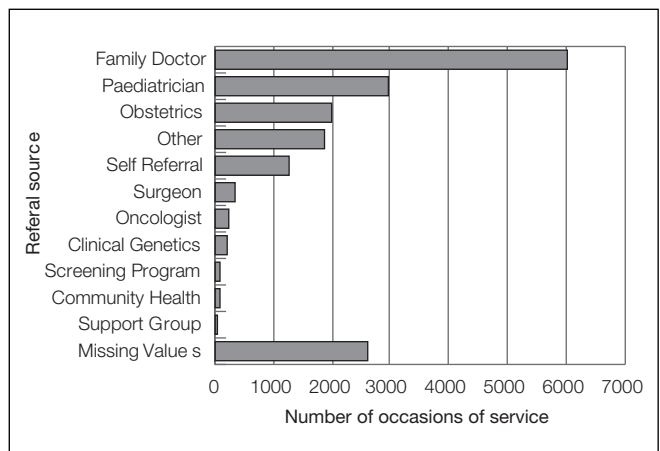
- 60% of consultations or occasions of service are held in clinics on a non-inpatient basis.
- 22% of consultations and most intake consultations are by telephone. Telephone consultations of therapeutic value are counted as occasions of service.
- Telephone consultations have an important role in eliciting relevant information prior to the clinic visit and for consultant follow up concerning the understanding, assimilation and management of complex information.
- Telemedicine is a growing part of service provision. A significant component of a genetics consultation can involve provision of information and counselling and this aspect is therefore well suited to telemedicine. It is particularly valuable in improving access to services for rural residents, where the patient and the outreach counsellor can have easier access to a metropolitan-based clinical geneticist. The outreach counsellor provides pre-consultation information and counselling and post-consultation follow-up.

Types of occasions of service 2003



Referral sources

Referral source 2003



Length of consultation

- Typically a genetics consultation lasts between 30 and 70 minutes with an average of 45 minutes. Routine screening, carrier testing advanced maternal age consultations are generally quite short (except where interpreters for non English speakers are used). General genetics/dysmorphism consultations are longer. Conditions are complex, possibly life threatening or emotionally devastating and may be difficult to diagnose.

Age and sex of consultands

- Women of reproductive age (25–44 years) are the most frequent users of services, largely due to advanced maternal age consultations. However, even excluding this group, women are more likely to access services. In most instances they are consulting for themselves, although frequently they are the parents of a child who is affected with a genetic disorder.
- The next most frequent patient age group is the 0–15 years group.

Interpreter use

- Data are incomplete but from data reported, the most commonly used languages excluding English, are Mandarin, Vietnamese, Cantonese and Arabic.

Cancer genetics services

7

Genetic susceptibility to cancer

Five to ten per cent of cancers are considered to be due to genetic susceptibility⁵. These include:

■ Inherited breast and/or ovarian cancer

About 5% of all individuals with breast or ovarian cancer are thought to have inherited, from a parent, a mutation in one copy of the genes controlling cell division and growth in breast and/or ovarian tissue. Key genes identified as important in the development of breast and/or ovarian cancer include: the Breast Cancer 1 gene (BRCA1) and the Breast Cancer 2 gene (BRCA2). Others have been identified but represent a small fraction of the inherited susceptibilities to breast cancer.

■ Inherited bowel cancer

Two types of hereditary bowel cancer familial adenomatous polyposis (FAP) and hereditary non-polyposis colorectal cancer (HNPCC) contribute to about 2–5% of all bowel cancers but are significantly over-represented in persons diagnosed at younger ages (ie under 50 years of age).

■ Rare inherited susceptibility to cancer

There are a number of other rare syndromes in which inherited gene mutations predispose to cancer. These include the multiple endocrine neoplasias (MEN), melanoma, retinoblastoma, von Hippel-Lindau disease, renal cancers and the Li-Fraumeni syndrome.

Familial cancer services

Familial Cancer Services, often in conjunction with specialist cancer services, are available to individuals concerned about their cancer risk because of a strong family history of disease.

Family history can be used to assess risk and guide appropriate screening to facilitate early detection. At the intake consultation, people determined to be at population risk can be reassured and referred back to their GP. Where there is a strong family history, genetic susceptibility may be considered. Genetic counselling and pedigree construction including first, second and third degree relatives, provides information to enable

initial risk estimation. Where appropriate, molecular genetic testing may be offered for more accurate determination of risk.

Molecular genetic testing:

Molecular genetic testing is usually only an option when the gene has been isolated or closely linked markers are known and the family structure is appropriate.

■ Mutation search

Usually the process of cancer associated genetic testing commences by searching for a disease-associated mutation in the relevant gene(s), by taking blood from an affected family member. This process is referred to as a mutation search or screening test. In breast cancer for example, a positive result from a mutation search in the cancer affected woman, means that asymptomatic first degree family members have a 50% risk of also carrying the gene mutation and are at potentially high risk for developing breast and ovarian cancer.

■ Predictive Testing

Once the causative gene mutation has been found, asymptomatic at-risk family members may wish to clarify their risk through predictive genetic testing. Those who test positive for the gene mutation can take steps to minimize their risk of developing cancer by making informed choices about preventive and early detection strategies or prophylactic interventions. Those who test negative can avoid unnecessary cancer screening, concern and associated costs. For those who test negative, their offspring cannot have inherited the genetic cancer susceptibility and can be reassured they are also not at high risk.

The benefits of new advances in cancer genetic technology have been made available through the establishment over the last 10 years, of specialised cancer genetics services (also known as Familial Cancer Services) at Westmead Hospital, Hunter Genetics and Prince of Wales Hospital, with a limited cancer genetic counselling service at St George Hospital. Limited services were set up in Northern Sydney in 2004. Metropolitan outreach clinics are held at Concord,

Nepean and Royal Prince Alfred Hospitals. Rural clinics are held in Central Coast, Far West, Greater Murray, Illawarra, Macquarie, Mid North Coast, Mid Western, New England, and Northern Rivers. Telehealth is increasingly used to make services more accessible, particularly for rural areas.

Familial cancer service use

The installation of a purpose built cancer genetics patient management system in all Familial Cancer Services has made it possible to produce non-identifying data as follows. The data refer to Familial Cancer Services only. General Clinical Genetics Services provided an additional 421 services, mostly in rural outreach services. The data are not included in this analysis as they were collected using a different system. They are recorded in Section 6.

In 2003, 2159 patients were seen. New patients and new family members numbered 1342. 3064 occasions of service were provided with 1469 to new referrals or new family members (40%) and 2135 return visits. A patient may receive more than one occasion of service where consulting with more than one service provider. Occasions of service include clinic visits, telephone calls of therapeutic value, telehealth consultations and intake consultations. Ninety percent of these services were provided in the Sydney metropolitan Area. The remaining 10% were in clinics in rural centres.

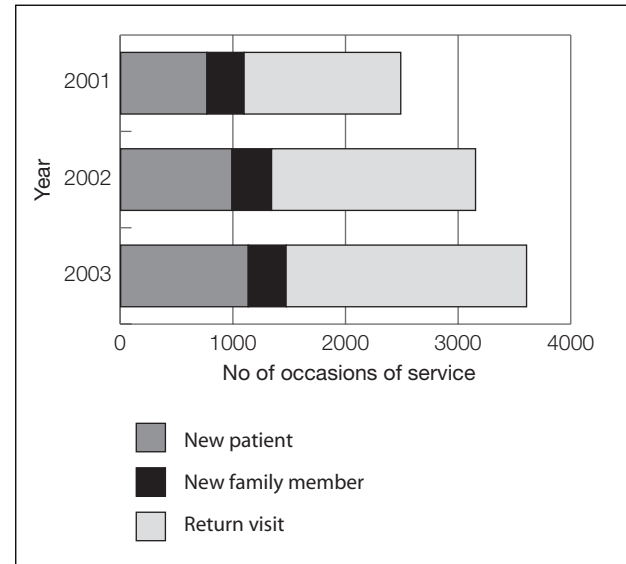
Numbers of patients and occasions of service – 2003

Patient Type	No of Patients	No of Occasions of Service
New patient	1024	1133
New family member	318	336
Total new patient and new family member	1342	1469
Return visit	817	2135
Total patient type	2159	3604

Occasions of service 2001–2003 in Familial Cancer Services

Total patient occasions of service in 2003 = 3604

Total new patient and new family member occasions of service in 2003 = 1469

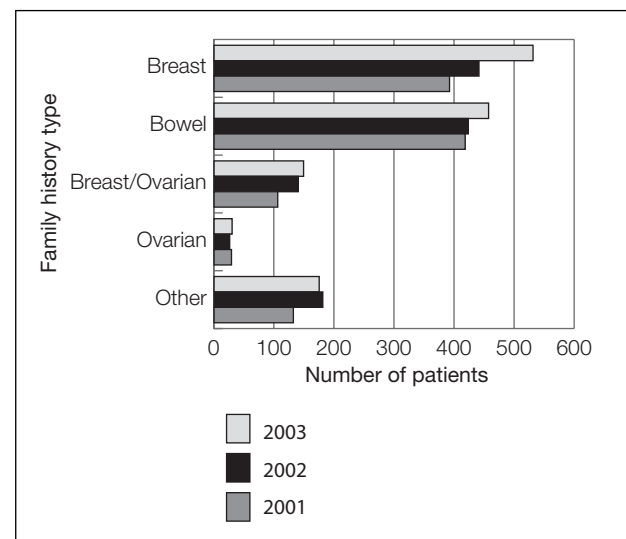


Most common reasons for referral

Family history of bowel or breast cancer are the most common reasons for referral, followed by breast/ovarian and ovarian cancer. Among the remaining cancer susceptibilities, the most frequently reported are hereditary paraganglioma, von Hippel-Lindau and Li-Fraumeni syndromes.

Familial cancer services by family history type

New patient and new family members
Number of patients for 2003 = 1342



Guidelines have been produced to help health professionals and consumers assess familial cancer risk, so that individuals at potentially high risk can be referred to Familial Cancer Services for further investigation and individuals at average or moderate risk can be managed by their family doctor.

Potentially high risk covers less than 1% of the population. Risk assessment criteria depend on the particular cancer. The potentially high-risk group may include having two or more first or second degree relatives on one side of the family diagnosed with the cancer, plus other features including diagnosis before age 40 or 50 (dependent on which disease) and related history of cancer within a family.

Full information is available in the following guidelines:

- Advice about familial aspects of breast cancer and ovarian cancer, National Breast Cancer Centre 2000, www.nbcc.org.au/bestpractice/resources/BOG_BreastOvarianGuideSimpl.pdf
- Familial Aspects of Bowel Cancer – a guide for health professionals, Australian Cancer Network 2002, www.cancer.org.au/documents/Familial%20aspects%20of%20bowel%20cancer.pdf

Reason for referral and risk categories

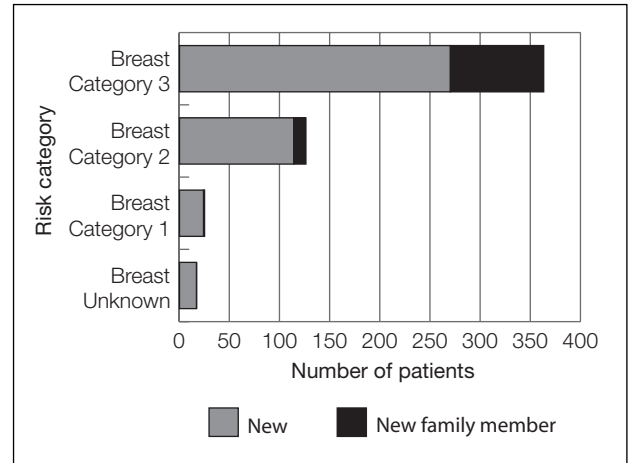
The following charts indicate the success of the guidelines, with most referrals to Familial Cancer Services being for individuals at potentially high risk (category 3) and significantly smaller numbers of referrals for individuals at moderate or average/population risk (category 2 and 1)

Note:

- Category 1 = At or only slightly above the population risk
- Category 2 = Moderate risk
- Category 3 = Potentially high risk (includes proven high risk)

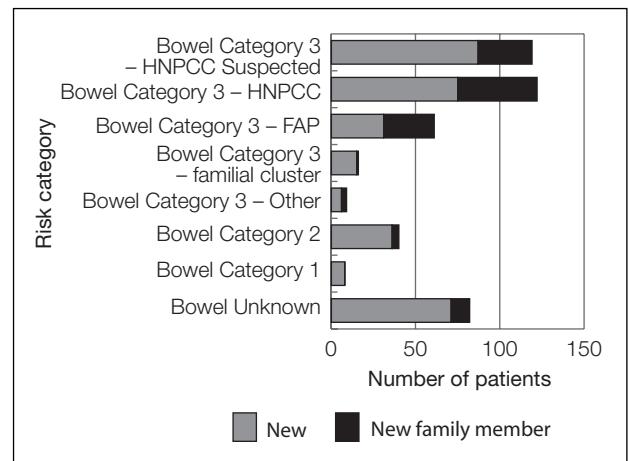
Breast Cancer Family History

New patient and new family members 2003
Reason for referral by risk category



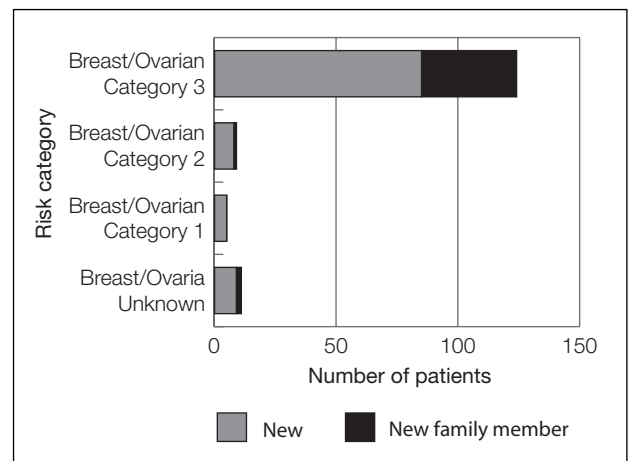
Bowel Cancer Family History

New patient and new family members 2003
Reason for referral by risk category



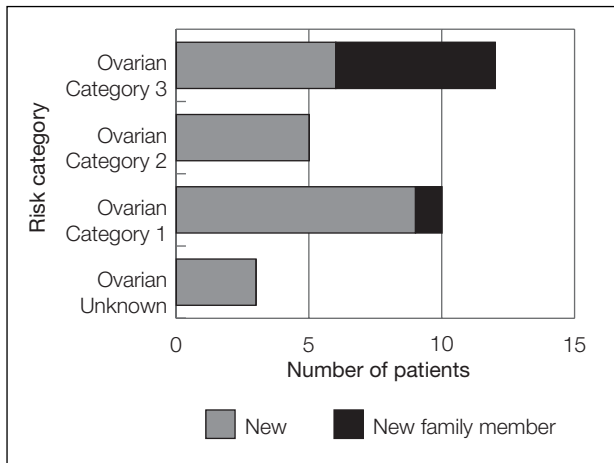
Breast/Ovarian Cancer Family History

New patient and new family members 2003
Reason for referral by risk category



Ovarian Cancer Family History

New patient and new family members 2003
Reason for referral by risk category



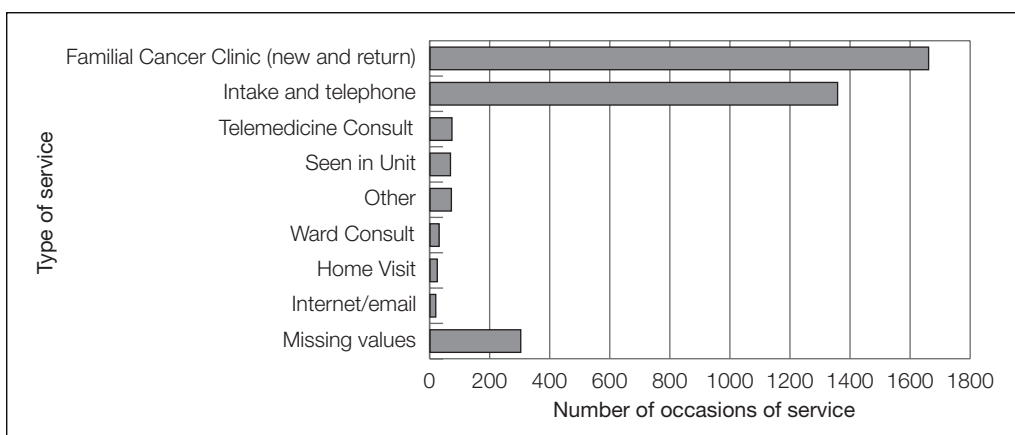
Note: Clinical Practice Guidelines for the management of women with epithelial ovarian cancer, published in 2004 have only two risk categories. www.ovariacancerprogram.org.au/pubs/cpguidelines.html

Types of services

Genetic Counselling is an important component of service provision. A great deal of pre-clinic information can be obtained by telephone consultation and telephone intake. Patients can be triaged at this point. Through discussion of their family history, patients identified at population risk can be referred back to their General Practitioner for standard monitoring and those at increased risk are offered a clinic appointment. Telephone consultations of greater than

Types of patient occasions of services

Total patient occasions of service = 3604



15 minutes and with therapeutic value are recorded. Telephone consultations lend themselves well to follow up discussions necessary when complex information needs to be given to the patient. Telehealth consultations are being introduced to improve access for rural patients and are a growing component of service provision.

Length of consultation

The nature of the information required in a consultation is quite complex. The average length of a consultation is 75 minutes.

Age and sex of patients

Half the patients are aged between 35 and 55 years of age and 20% are male and 80% female.

Laboratory testing results

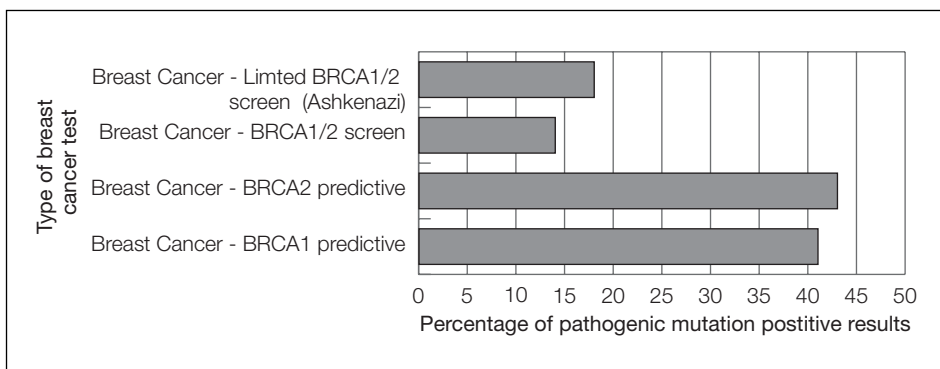
DNA/molecular genetic testing may be an option for individuals at potentially high risk of cancer where the gene has been identified or closely linked markers are known and the family structure is appropriate. Three public laboratories in NSW provide this testing.

The process usually requires first searching for a causative gene mutation in a family member who has already been diagnosed with the cancer. This process is referred to as a mutation search or screening test. The chart below refers to breast cancer testing and shows that a pathogenic mutation is found in about

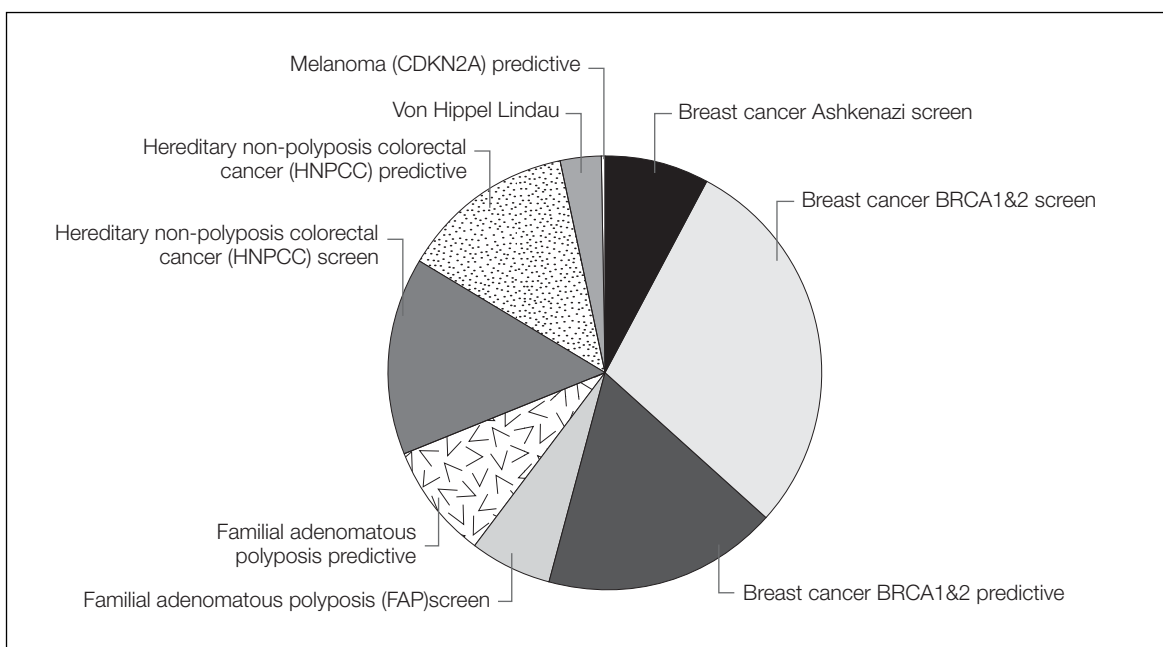
15% of cancer affected women tested. A positive result in the cancer affected woman, means that asymptomatic first degree family members have a 50% risk of also carrying the gene mutation and are at potentially high risk for developing breast and ovarian cancer. They may wish to clarify their risk through predictive genetic testing so that they can take steps to minimize their risk of developing cancer. The chart indicates that where

predictive testing is offered to relatives at potentially high risk, the detection rate is just over 40%, ie approaching the theoretical risk of 50%. Those who test negative can avoid unnecessary cancer screening, concern and associated costs. For those who test negative, their offspring cannot have inherited the genetic cancer susceptibility and can be reassured they are also not at high risk.

Mutation positive DNA test results for familial breast cancer 2003



Proportion of samples received by type of test 2003



8 The NSW Newborn Screening Programme

A few diseases that are severe, without specific early symptoms, and treatable, can be detected by tests carried out on dried blood samples obtained by heel-prick. The NSW Newborn Screening Programme tests all babies born in NSW and in ACT for a number of such disorders. Each year the Newborn Screening Programme tests over 90,000 babies and now detects about 90 per year who need urgent assessment and treatment.

The screening laboratory offers a monitoring service for patients with PKU, who have blood tests monthly, or, in the case of patients who are pregnant, weekly. Over 300 patients are monitored in this way.

Until 1998 the Programme tested for only five conditions:

Disorder	Testing Started	Analyte	Frequency
Phenylketonuria	1965	Phenylalanine	1:10,000
Hypothyroidism	1977	TSH	1:3,500
Cystic fibrosis	1981	IRT/DNA	1:2,500
Galactosaemia	1983	Gal metabolites	1:40,000
Homocystinuria	1994	Methionine	1:60,000

New technology – tandem mass spectrometry

In 1998 new technology was introduced, using tandem mass spectrometry to test for groups of compounds, so that a number of extremely rare disorders can be tested for in a single operation. The NSW programme was the first state-wide public laboratory in the world to adopt this screening. The experience during the first four years was recently reported⁹.

An Australia-wide study on the effectiveness of newborn screening

Worldwide, there have been very few formal studies of the clinical effectiveness of newborn screening. The only randomised controlled trials carried out have been of cystic fibrosis screening, in the USA and UK. The NSW Newborn Screening Programme is leading an Australia-wide study of the effectiveness of tandem mass spectrometry in newborn screening, and has obtained funding from the National Health and Medical Research

Council to do this. The study began in 2003 and will run until early 2006. It is studying the diagnostic performance, medical and neuropsychological outcomes for patients, and the costs incurred, comparing patients detected by screening with those detected clinically.

Website

A description of the activities of the programme and fact sheets for parents can be found on the website: www.chw.edu.au/prof/services/newborn

Service use

Patients diagnosed by newborn screening – four year period 2001–2004, NSW and ACT

Babies screened	358,000
Amino acid disorders	
PKU	31
Hyperphenylalaninaemia	11
Pterin defect	1
Homocystinuria	1
Maple syrup urine disease	2
Urea cycle disorders	4
Tyrosinaemia type II	1
Organic acidurias	
Various	15
Maternal defects	11
Fatty acid oxidation defects	
MCAD deficiency	26
Other fatty acid oxidation	14
Secondary	
B12 deficiency	7
Cystic Fibrosis	
Detected	96
Missed	8
Galactosaemia	
Transferase deficiency	7
Galactokinase deficiency	1
Hypothyroidism – primary congenital	125
TOTAL	361

The NSW Biochemical Genetics Programme

9

The NSW Biochemical Genetics Service is a National Association of Testing Authorities (NATA) accredited facility providing comprehensive diagnosis and biochemical management for patients with inborn errors of metabolism (IEM). The laboratory has experience in diagnosing approximately 200 different disorders and has recorded well over 1000 affected patients. Many need long-term monitoring by the laboratory.

The service works closely with the other statewide services: the NSW Newborn Screening Programme and the NSW Genetic Metabolic Service. In particular it is very much involved in the follow-up of newborns detected via the extended Newborn Screening Programme using tandem mass spectrometry (MS).

A range of services is provided, as detailed on the website: www.chw.edu.au/prof/services/biogen

A wide range of investigations is available including amino acid and organic acid profiles, quantitative assays of specific metabolites, diagnostic enzymology and molecular biology. The laboratory has had a long-standing interest in the disorders of fatty acid oxidation and carnitine transport and maintains an active program for developing assays in this area.

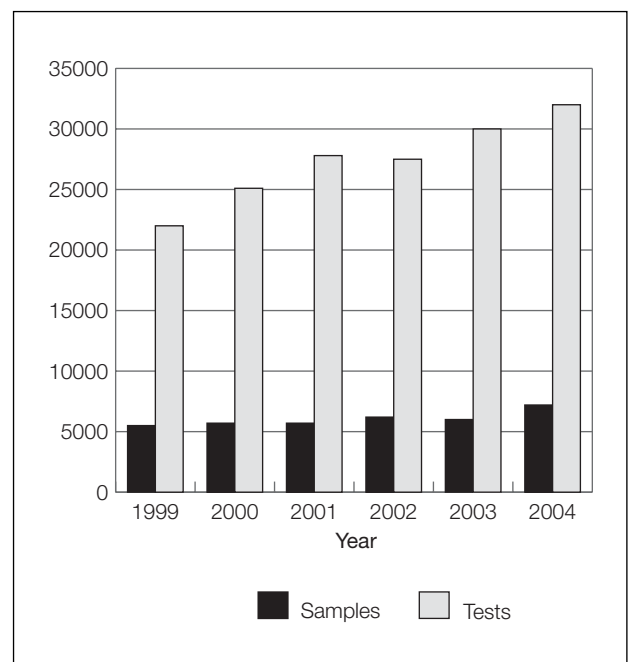
Samples are received from health care providers across the Asia-Pacific region; there are particularly strong ties with New Zealand. Functions also include:

- sending samples to other laboratories within Australia or overseas if appropriate tests are unavailable
- adding each new test to the website, as it becomes available
- a prenatal diagnostic service including arranging the transport of chorion villus or amniotic fluid to international centres when the analysis is not available locally
- an advisory service to clinicians and other laboratories about the investigation of suspected IEMs in sick babies, children and adults
- long-term storage of tissues, cultured cells and DNA from families with proven or suspected IEM.

Service use

The number of samples received has been increasing steadily.

NSW Biochemical Genetics sample numbers and tests performed 1999–2004



New tests introduced

Transferrin isoforms – A new test using capillary electrophoresis was introduced to diagnose a recently described class of disorders with multisystem effects – congenital disorders of glycosylation.

Creatine and guanidinoacetate – A test performed by tandem mass spectrometry will diagnose disorders of creatine biosynthesis – disorders which lead to developmental delay, seizures and other serious neurological abnormalities. Tests to screen for creatine transport disorders are being developed.

New diagnoses 2001–2004

Class of disorder	New diagnoses
Amino acid	22
Urea cycle	7
Organic acid	29
MCAD	36
Other fatty acid oxidation	18
Storage disorders	12
Peroxisomal disorders	13
Mitochondrial respiratory chain, other lactic acidoses	15
Congenital disorders of glycosylation	4
Other	14
Total	170

These figures include some patients whose samples were referred from interstate or overseas.

Many, though not all, fetal abnormalities can now be diagnosed prenatally. Prenatal diagnostic services are provided in conjunction with genetics services by fetal medicine units in South Eastern, Central, Western, Northern and South Western Sydney, Wentworth and Hunter, and some outreach areas.

Information and counselling

Screening ultrasound, nuchal translucency screening alone, and nuchal translucency screening combined with first trimester serum screening and second trimester maternal serum screening are used during pregnancy to determine risk of abnormalities such as Down syndrome. These tests are risk estimates, not definitive tests. This concept requires careful explanation because of the possibility of false positive and false negative results.

Ultrasound or maternal serum testing are not threatening to the pregnancy, but an increased risk result leads to the option of more definitive testing by amniocentesis or chorionic villus sampling (CVS).

Amniocentesis and CVS are invasive tests which carry a small procedure related risk. Before amniocentesis and CVS are offered, women should be advised about the risks to the pregnancy associated with these procedures, and the time lag between testing and receiving results.

The main reasons for prenatal diagnostic testing using amniocentesis or CVS are:

- where a woman is having a baby when she is in her mid thirties or older
- having a family history of a person with a serious disorder or of being a 'carrier' for a mutation
- where one of the partners in a couple has a serious disorder which may be passed on to a baby
- having a previous child affected by a serious problem in growth, development and/or health
- where the results of tests such as the maternal serum test have determined that the woman is at an increased risk for having a baby with a particular disorder
- having a previous child with a chromosomal abnormality.

Prenatal tests

Nuchal translucency measured by ultrasound

Nuchal translucency measurement is a targeted form of ultrasound. An increase in nuchal translucency between 11½ and 13½ weeks is known to be associated with babies at increased risk of a chromosomal abnormality such as trisomy 21 (Down syndrome), trisomy 13 and trisomy 18. This is a risk assessment rather than an absolute diagnosis. About 70–80% of babies with Down syndrome will be identified as being at 'increased risk' and about 20–30% of affected babies will be missed.

First trimester serum screening

The nuchal translucency screen may be combined with a biochemical first trimester screening test which improves the detection rate to 80–90%.

Maternal serum testing

The maternal serum test is available to women between 15 and 17 weeks of pregnancy to assist in the prenatal identification of several birth defects including Down syndrome and neural tube defects. This blood test, combined with age and other factors can provide an estimate of risk that the baby is affected. It is not a diagnostic test. Women identified at high risk usually follow up with more definitive diagnosis by amniocentesis or ultrasound. It is estimated that this process will lead to the detection of 60% of Down syndrome affected pregnancies. Results are not usually available until 17 to 19 weeks of pregnancy.

Ultrasound

Ultrasound or fetal imaging can be conducted at any time during the pregnancy. The optimal time for dating the pregnancy or determining the number of babies is between 8 and 12 weeks. A fetal anomalies scan to check the baby's physical development is best done between 18 and 20 weeks.

Chorionic villus sampling (CVS)

A small amount of the placental tissue is sampled either vaginally or abdominally guided by ultrasound scanning. The procedure is undertaken during the 11th to 14th week of pregnancy and sometimes later. Approximately 1% of the procedures are followed up by an

Prenatal Testing Services

amniocentesis when tissue is inadequate or the result is equivocal. The result is usually available within 18 days. There is about a 1% risk of loss of the pregnancy due to the procedure.

Amniocentesis

A sample of amniotic fluid is withdrawn by a needle through the abdomen during the 14th to 18th week of pregnancy. The result is available within 18 days. There is a less than 1% risk of loss of the pregnancy due to the procedure.

Prenatal testing results

Ultrasound, nuchal translucency scanning and maternal serum testing are a routine part of obstetric care and service data on these tests are not collected for inclusion in this report. However, increased risk on these tests is usually followed by amniocentesis or CVS for sample collection for further testing. Specimens collected by amniocentesis and CVS are most commonly subjected to cytogenetic testing for chromosomal disorders (see Section 11). A small number require molecular genetic testing (see Section 12).

Prenatal cytogenetic testing for chromosomal disorders

Cytogenetic testing is a process used to identify any change in the usual number or structure of an individual's chromosomes and may aid in the diagnosis of a genetic disorder. It has been available since the 1970s to women of advanced maternal age (35 years and over) who are at greater risk of having a child with Down syndrome or other cytogenetic abnormality (see Section 5). Other major reasons for referral include women whose pregnancies are found to be at increased risk on ultrasound, nuchal translucency scanning or maternal serum testing, and women with a previous child or family history of a chromosomal/genetic disorder.

Samples for cytogenetic testing are collected by chorionic villus sampling (CVS) or amniocentesis (see Section 10) and very rarely by fetal blood sampling.

Chromosomal disorders

The most commonly occurring chromosomal disorders are:

- **Trisomy 21/Down syndrome** – Incidence is about 1 in 770 births. Congenital heart disease is common and is a major cause of early death. Mild to moderate mental retardation is usual.
- **Trisomy 13** – Incidence is about 1 in 8000 births. All patients are profoundly retarded. Half the babies

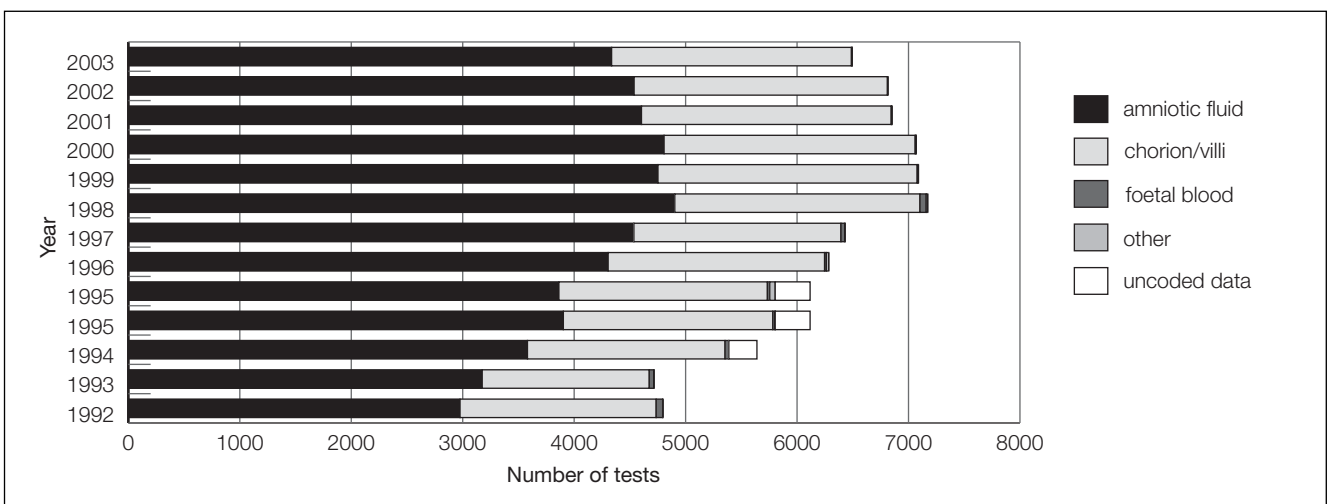
born die by one month of age and others rarely survive more than 3 years.

- **Trisomy 18** – Incidence is about 1 in 6600 births. All patients are profoundly retarded. 30% die by 1 month, 90% by 1 year and 99% by 10 years.
- **Klinefelter syndrome** – Incidence is about 1 in 500 males. Intelligence is usually normal. The majority of Klinefelter syndrome adults will be infertile and male hormone therapy may be required.
- **Turner syndrome** – Incidence is about 1 in 2000 females. Intelligence is usually normal but there may be specific learning difficulties. It is characterised by short stature, possible infertility, and lack of sexual maturation at puberty. There are a number of potential physical problems such as heart defects.

Prenatal cytogenetics test use

Non-identifying data for the State have been collected since 1992 from laboratories located in South Eastern Sydney (SEALS), Northern Sydney (PaLMS), Western Sydney Genetics Program (Children's Hospital, Westmead), Hunter Area (HAPS); and one private laboratory (Sydney Genetics). The data do not include tests for some residents of northern and southern NSW which are processed by cross border laboratories in Queensland and Victoria. Data have been evaluated to provide a comprehensive picture of service utilisation and outcomes of testing.

Prenatal cytogenetic tests 1992–2003



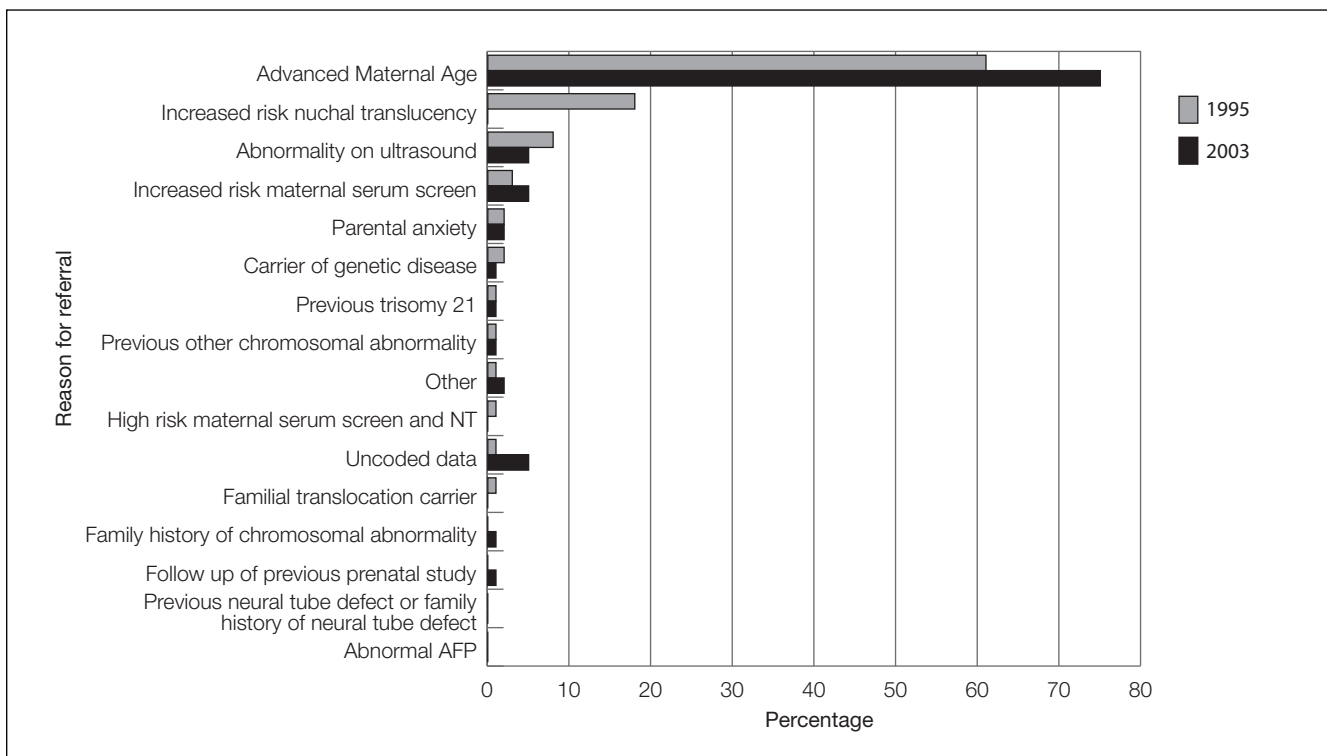
- The chart on page 35 shows that referrals grew at a rate of approximately 10% per annum until a peak of 7172 in 1998. There were 6495 referrals for testing in 2003.
- A leveling off in numbers of referrals between 1998 and 2000 coincided with the introduction in 1997/98 of nuchal translucency measurement in ultrasound to detect increased risk of chromosomal

abnormalities such as Down syndrome. Increased use of the non-invasive combined nuchal translucency measurement and first trimester serum screening since 2000 has further contributed to the decline in use of invasive tests, particularly amniocentesis.

- Amniocentesis is used twice as often as chorionic villus sampling (CVS).

Reason for referral for prenatal cytogenetic testing

Reasons for referral for prenatal cytogenetic testing 1995–2003



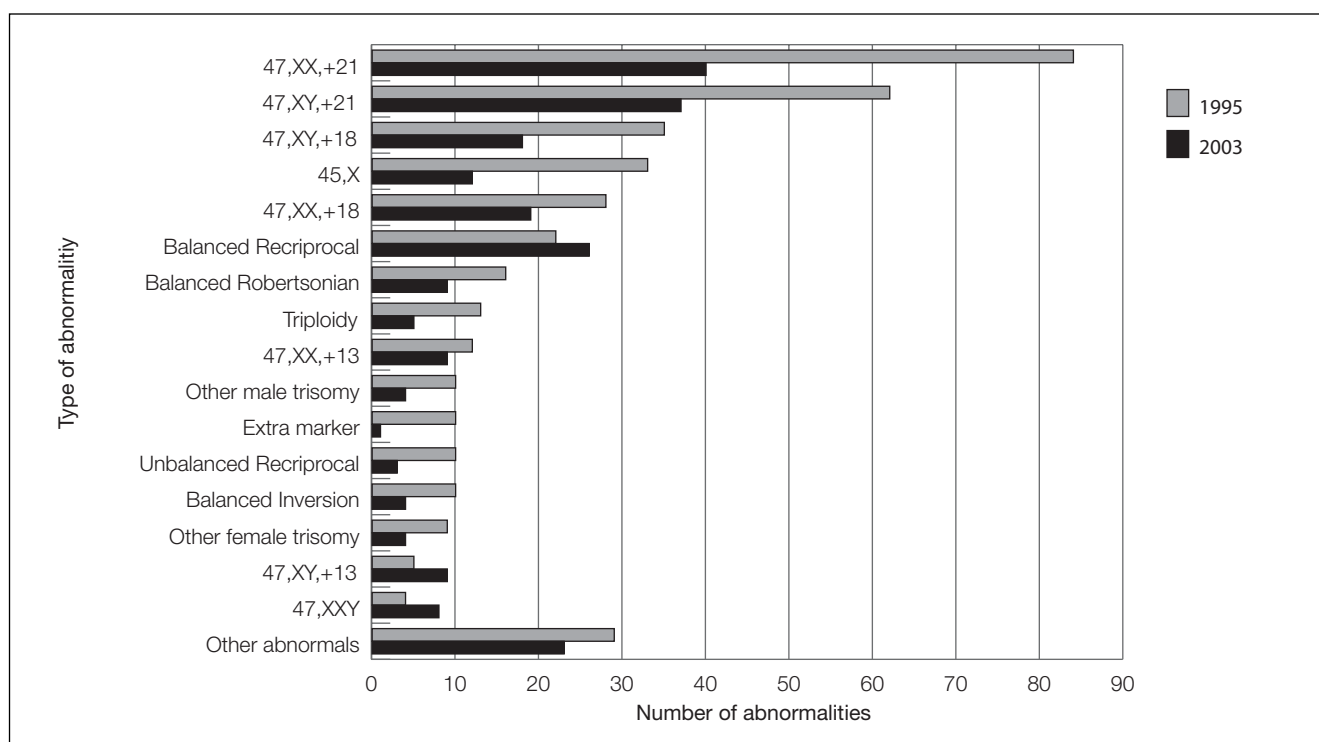
- *Advanced maternal age* is the most common reason for referral for cytogenetic testing. In 1996 referrals for *Advanced maternal age* reached a peak of 82%, compared with a 75% rate for 1995 and a decline to 61% in 2003.

- This decline has been offset by an increase in referrals for *abnormality on ultrasound* from 4.8% in 1995 to 8% in 2003 as well as a growing number of referrals for *increased nuchal translucency* measurement. Referrals for *increased nuchal translucency* have risen to 18% in 2003 since their introduction in 1997/98. These data may reflect women's preferences for ultrasound and nuchal translucency measurement over the more invasive procedures of amniocentesis and CVS.

Types of abnormalities detected by prenatal cytogenetic testing

- There has been a 69% increase in the number of abnormalities detected since 1995, rising from 231 abnormalities in 6117 referrals to 392 abnormalities in 6495 referrals in 2003.
- The number of trisomies detected has risen from 61% of all abnormalities in 1995 to 63% in 2003.
- In 2003, trisomy 21 or Down syndrome comprised 146 (37%) of the abnormalities detected compared with 33% in 1995. There were 62 male trisomy 21 (47,XY,+21) and 84 female trisomy 21 (47,XX,+21).

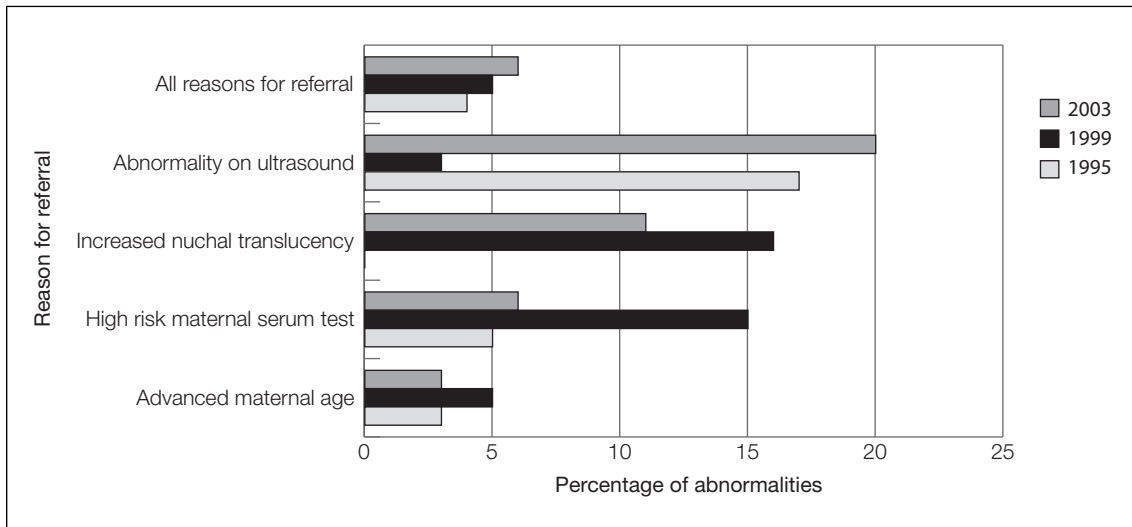
Numbers and types of abnormalities detected in 1995 and 2003



Abnormalities and reason for referral

- The chart and table below show that the detection rate for abnormalities for all *reasons for referral* has increased from 3.8% in 1995 to 6.0% in 2003. This is likely to be the result of growth in referrals for abnormality on ultrasound and increased risk on nuchal translucency measurement.
- In 2003 the highest abnormality detection rate was 19.7% for those patients referred because of *fetal abnormality on ultrasound* (96 abnormalities among 488 referrals in 2003). During 1998/99, laboratories began to record referrals for *increased nuchal translucency* separately from other ultrasound abnormalities. The detection rate in 2003 for abnormalities for patients referred for *increased nuchal translucency risk* was 10.9% (128 abnormalities among 1171 referrals).
- The most common reason for referral, ie *advanced maternal age* has the lowest detection rate at 2.9%. However, the number of referrals has declined along with the rise in increased nuchal translucency referrals.
- There has been a decline in referrals for *high risk maternal serum testing* from 327 in 1995 to 171 in 2003.

Abnormalities detected by most common reasons for referral 1995, 1999 and 2003



Normal and abnormal results according to reason for referral 1995, 1999 and 2003

	All reasons for referral		Abnormality on ultrasound		Increased nuchal translucency		Advanced maternal age		High risk maternal serum test	
	No.	%	No.	%	No.	%	No.	%	No.	%
1995										
Total normal	5447	89.05%	240	81.08%			4400	96.15%	308	94.19%
Total abnormal	231	3.8%	49	16.6%			132	2.9%	16	4.9%
Total other	439	7.2%	7	2.4%			44	1.0%	3	0.9%
Total	6117	100%	296	100%			4576	100%	327	100%
1999										
Total normal	6644	93.7%	428	82.1%	384	84.0%	5010	97.0%	231	94.3%
Total abnormal	353	5.0%	79	15.2%	72	15.8%	134	2.6%	12	4.9%
Total other	92	1.3%	14	2.7%	1	0.2%	22	0.4%	2	0.8%
Total	7089	100%	521	100%	457	100%	5166	100%	245	100%
2003										
Total normal	6044	93.1%	387	79.3%	1029	87.9%	3844	96.4%	158	92.4%
Total abnormal	392	6.0%	96	19.7%	128	10.9%	114	2.9%	10	5.8%
Total other	59	0.9%	5	1.0%	14	1.2%	28	0.7%	3	1.8%
Total	6495	100%	488	100%	1171	100%	3986	100%	171	100%

Maternal age and reason for referral

Advanced maternal age (over 35 years) and prenatal cytogenetic test use

- In 2003, among *all reasons for referral*, approximately 48% of prenatal cytogenetic referrals were for women aged between 35 and 39. This is a decline from 59% in 1999 and 55% in 1999.
- *Advanced Maternal Age* is the main reason for referral, although the proportion has declined from 64% in 1999 to 58% in 2003 with a corresponding increase in referrals for *Increased nuchal translucency* in the 35 to 39 year age group.

- Women 40 years and over are an increasing proportion of referrals in all categories. As women get older their preference for CVS over amniocentesis increases. Factors may include declining reproductive opportunities with advancing age, previous experience, availability of CVS earlier in the pregnancy or awareness of options.
- The 30–34 age group provides 15% of referrals and a significant proportion of referrals from *increased risk on ultrasound, nuchal translucency and maternal serum screening*.

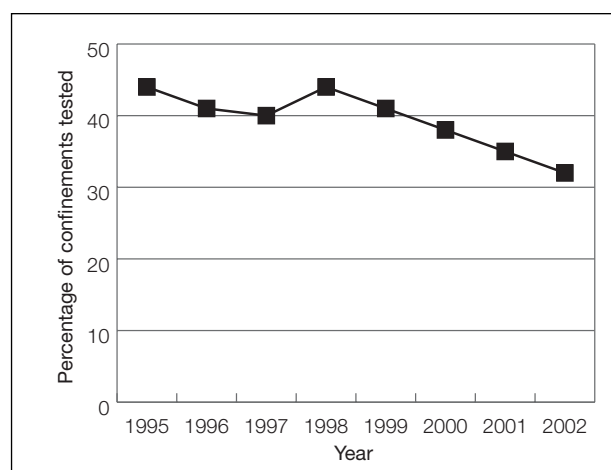
	All reasons for referral		Abnormality on ultrasound		Increased nuchal translucency		Advanced maternal age		High risk maternal serum test	
	1999	2003	1999	2003	1999	2003	1999	2003	1999	2003
<15	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
15–19	0%	0%	0%	0%	3%	4%	0%	0%	2%	1%
20–24	2%	2%	0%	0%	11%	10%	3%	2%	4%	4%
25–29	5%	6%	0%	0%	22%	21%	16%	12%	14%	9%
30–34	11%	15%	2%	3%	37%	35%	36%	31%	36%	43%
35–39	55%	48%	64%	58%	21%	21%	35%	39%	38%	35%
40–44	25%	27%	31%	36%	5%	7%	9%	14%	4%	7%
>45	1%	1%	2%	2%	1%	0%	0%	1%	0%	1%
unknown	1%	0%	0%	0%	0%	2%	1%	0%	2%	0%
uncoded data	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
Totals	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%

Confinements for women 35 years and over and test use

- The number of confinements has been relatively constant between 1990 and 2002 at around 85,000 to 86,500, but confinements to women aged 35 years and over have risen from 10.4% in 1990 to 16.3% in 1998 to 19.3% in 2003. (BDR Reference)
- The percentage of confinements subject to cytogenetic testing has declined with increased use of non-invasive testing.
- The following chart shows the percentage of confinements to women 35 years and over having cytogenetic testing. The data are from metropolitan Area Health Services only – Northern Sydney, South Eastern Sydney, Western Sydney, Wentworth, South Western Sydney, Central Coast, Hunter and Illawarra.

Percentage of confinements to women 35 years and over having cytogenetic testing

Sydney Metropolitan Area including Illawarra and Hunter
 No. of confinements to women 35+ years in 2003 = 13670
 No. of confinements to women 35+ years in 1995 = 9364



Maternal age and abnormalities

■ Of the total 392 abnormalities detected in 2003, the 35–39 year age group had the highest number of abnormalities at 130 or 33.2%.

■ Although the 35–39 age groups had the highest number of tests and the highest number of abnormalities detected, it had the lowest detection rate of abnormalities at 4.2%. The detection rate in all age groups has increased.

Tests and abnormalities by Maternal Age 1995, 1999 and 2003

Age	No of tests by age groups						No of abnormalities detected by age group						Abnormalities within age groups as a percentage of total abnormalities		
	1995		1999		2003		1995		1999		2003		1995	1999	2003
	No	%	No	%	No	%	No	%	No	%	No	%	%	%	%
<20	16	0.3%	34	0.5%	27	0.4%	2	0.9%	3	0.8%	4	1.0%	12.5%	8.8%	14.8%
20–24	89	1.5%	110	1.6%	111	1.7%	5	2.2%	9	2.5%	19	4.8%	5.6%	8.2%	17.1%
25–29	215	3.5%	345	4.9%	369	5.7%	15	6.5%	36	10.2%	37	9.4%	7.0%	10.4%	10.0%
30–34	568	9.3%	802	11.3%	1002	15.4%	42	18.2%	79	22.4%	70	17.9%	7.4%	9.9%	7.0%
35–39	3613	59.1%	3918	55.3%	3121	48.1%	96	41.6%	127	36.0%	130	33.2%	2.7%	3.2%	4.2%
40–44	1211	19.8%	1752	24.7%	1741	26.8%	63	27.3%	85	24.1%	113	28.8%	5.2%	4.9%	6.5%
>44	43	0.7%	89	1.3%	95	1.5%	6	2.6%	13	3.7%	15	3.8%	14.0%	14.6%	15.8%
Unknown	362	5.9%	38	0.5%	29	0.4%	2	0.9%	1	0.3%	4	1.0%	0.6%	2.6%	13.8%
Total	6117	100%	7088	100%	6495	100%	231	100%	353	100%	392	100%	3.8%	5.0%	6.0%

Other cytogenetic services

Cytogenetics laboratories also conduct tests for:

- The diagnosis of congenital cytogenetic abnormalities, as well as cytogenetic aberrations which lead to developmental delay in childhood and adolescence. Cytogenetic investigation of these syndromes is carried out by peripheral blood sampling.
- The investigation of infertility or repeated miscarriages in couples. Testing is carried out on peripheral blood samples of affected couples.
- The diagnosis of patients with haematological disorders such as leukaemia, myelodysplasia and lymphoma, as well as for the characterisation of solid tumours. Cytogenetics is carried out on a bone marrow aspirate sample, peripheral blood, lymph node or on tumour biopsy material.

A diagnostic karyotype may provide confirmation of specific haematological disorders and crucial prognostic information. Follow-up karyotypes are crucial for the detection of minimal residual disease, (MRD), following treatment regimens.

Currently, molecular cytogenetic techniques, such as fluorescent in situ hybridisation (FISH) techniques are being utilised in increasing numbers for the purposes of prenatal screening for autosome and sex chromosome aneuploidy. These techniques are also used widely for the detection of microdeletion syndromes, such as Williams or di George syndromes, and for the disease classification and detection of MRD in haematological malignancies.

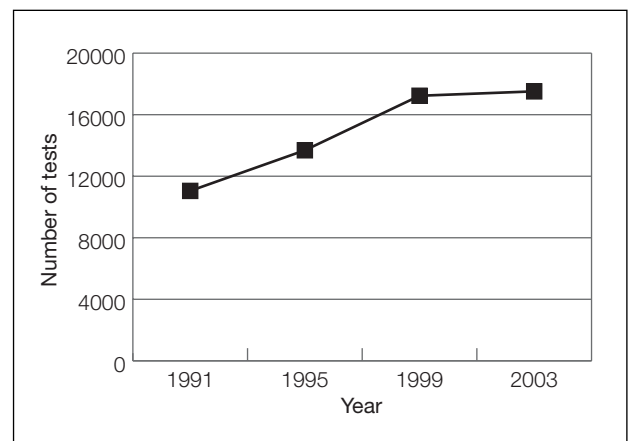
Cytogenetic testing data

Data presented below for all cytogenetic testing including prenatal tests have been collected since 1989 from the four public laboratories located in South Eastern Sydney, Northern Sydney, Children's Hospital at Westmead and Hunter Area; and one private laboratory (Sydney Genetics).

Test use

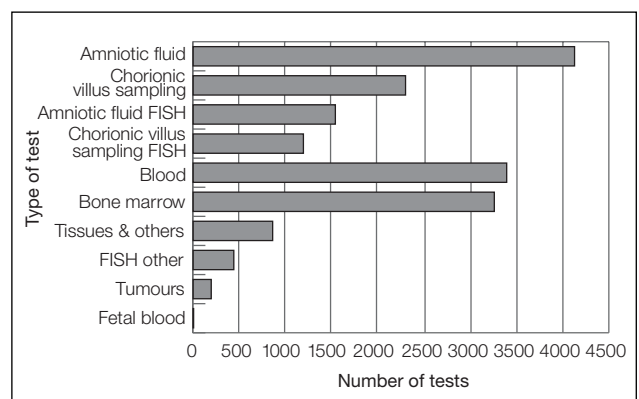
- The demand for cytogenetic testing has grown steadily over the past 10 years, from 11046 studies in 1991 to 17516 studies in 2003.

Cytogenetic testing in NSW 1991–2003



- A significant proportion of testing is for prenatal diagnosis. A total of 6495 samples was received in 2003. A number of samples are subjected to fluorescent in-situ hybridization (FISH) in addition to standard testing. FISH gives a rapid response which is usually confirmed by the standard long term test.

Types of cytogenetic testing in 2003



12 Molecular genetics services

This type of testing involves examination of the DNA (deoxyribonucleic acid) to look for changes (mutations) in genes which may indicate a specific genetic disorder. DNA is the chemical compound which makes up genes within chromosomes and is the basic material of heredity.

DNA diagnostic testing is provided by seven molecular genetics laboratories in the State in South Eastern Sydney, Central Sydney, Northern Sydney, Hunter, the Children's Hospital at Westmead and Western Sydney. In past years, each genetic disorder was tested in only one laboratory. This approach was adopted because the rarity of genetic disorders was such that individual laboratories would see too few cases to maintain proficiency of diagnosis and interpretation; and because low sample numbers together with high consumables and labour costs meant that costs could be minimised and duplication of services avoided through concentration of expertise. More recently some specific testing of genetic disorders is being undertaken in more than one laboratory. Several factors have contributed to this change, including improved testing techniques, wider application of DNA testing than for genetic disorders alone, introduction of new tests and increased demand for genetic testing. Furthermore, the networking of pathology services is influencing the way DNA testing is provided.

Test use

Technological developments have expanded the range of tests available and improved techniques. Since 1995, testing has been introduced for haemochromatosis and

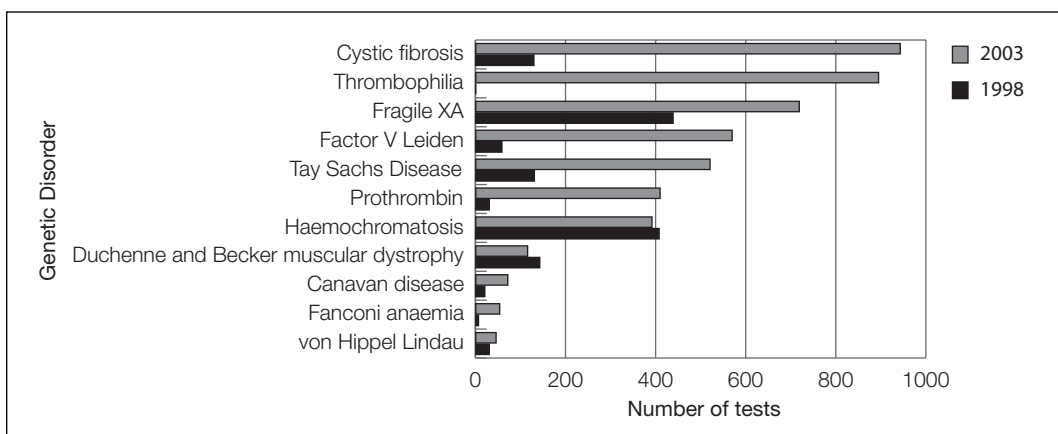
thrombophilia (Factor V Leiden, Prothrombin g.20210G>A). Testing has increased for cystic fibrosis, fragile X, hereditary cancers and Tay Sachs disease. In other cases, testing been in decline. This pattern is typical of DNA testing for many genetic disorders where there is an initial demand which tapers off after the identification of a significant number of people within the affected group. Additionally, there are many more instances of 'one-off' testing for extremely uncommon disorders, mainly for prenatal diagnosis, after the establishment of the mutation of the proband has been undertaken by an interstate or overseas laboratory.

The most commonly tested conditions include:

- Cystic Fibrosis
- Fragile X
- Haemochromatosis
- Factor V Leiden
- Prothrombin
- Genetic Cancers
- Duchenne/Becker Muscular Dystrophy
- Charcot Marie Tooth
- Tay Sachs Disease
- Spinocerebellar Ataxia
- Huntington Disease
- Thalassaemia
- Myotonic Dystrophy.

The following chart shows demand for testing in a sample from two laboratories

Demand for molecular genetic testing in a sample from two laboratories



A breakdown by mutation type for cystic fibrosis is shown in the table below

Cystic Fibrosis Mutations	Number of tests
CFTR 29 mutation screen	251
CFTR poly T	33
CFTR 508 only	643
CFTR single mutation (not 508)	15
Total Cystic Fibrosis	942

Cancer genetic testing

Between 5 and 10% of cancers are thought to be due to inheritance of genetic susceptibility. Key genes identified and types of tests include:

- Breast Cancer, BRCA1 and BRCA2 – predictive testing for a known mutation and mutation screens.
- Hereditary non-polyposis colorectal cancer – predictive testing for a known mutation and mutation screens.
- Familial adenomatous polyposis – predictive testing for a known mutation and mutation screens.
- Other rare inherited syndromes.

More detail on hereditary cancers can be found in the Cancer Genetics Services (Section 7).

Prenatal diagnostic testing

Where a mutation has been identified in one or both parents, the risk for their offspring can be estimated. For example, a parent with the Huntington disease gene mutation has a 1 in 2 risk of having an affected offspring. In the case of cystic fibrosis, if both parents are mutation carriers, the offspring has a 1 in 4 risk of being affected. Prenatal testing can be offered to determine if the fetus is affected. Prenatal diagnostic testing is available for a number of genetic disorders including:

- Cystic fibrosis
- Huntington disease
- Thalassaemia
- Haemophilia
- Duchenne & Becker Muscular Dystrophy

- Spinal Muscular Atrophy
- Fragile X
- Charcot Marie Tooth
- Uniparental disomy
- Myotonic dystrophy.

Carrier testing/ presymptomatic diagnosis

A parent who has inherited a mutation from his or her parents that makes the gene faulty has a chance of passing that faulty gene on to their children. The parent/consultand is known as a carrier when the gene has not manifested causing a disorder or a recognisable pattern trait. Carriers can be asymptomatic (recessive disorders) or presymptomatic, ie the disorder has yet to manifest itself eg breast/ovarian cancer.

Asymptomatic carriers

- Cystic fibrosis
- Duchenne & Becker Muscular Dystrophy
- Thalassaemia
- Haemophilia
- Kennedy disease.

Presymptomatic carriers

- Huntington disease
- Breast/Ovarian Cancer
- Myotonic dystrophy
- Charcot Marie Tooth
- Multiple Endocrine Neoplasia 2
- Familial Adenomatous Polyposis.

In asymptomatic carriers, the pattern of inheritance depends on the type of gene mutation. It may be X-linked or autosomal recessive. Presymptomatic carriers usually have disorders showing autosomal dominant inheritance.

13 The NSW Centre for Genetics Education

The Genetics Education Program of the NSW Genetics Service was established in 1987 and is based at Royal North Shore Hospital, St Leonards, Sydney, as part of the delivery of comprehensive genetic services to the people of NSW. In 2002, the Program became The Centre for Genetics Education (CGE), reflecting the diversity of its role as a Centre for genetics education and training in NSW.

The Centre develops and provides information, resources and educational programs. Activities of the Centre are targeted at all levels of the community: government, professionals, individuals and families affected by a genetic disorder and the general public. It is the central referral base for genetics services and information for NSW.

Accessing the Centre

The Centre's website (www.genetics.com.au) was established in late 1996.

In early 1996, prior to the establishment of the website, direct contacts (letter, telephone and fax) were made by students 24%, professionals 48% and individuals and families 28%. Now student needs are predominantly met via the website allowing the skills of staff to be better utilised in providing a more meaningful service to the increasing number of professionals and individuals contacting the Centre directly.

The online delivery of information and resources has meant that the CGE now has the ability to reach a wider audience. The number of website 'hits' has reached over 600,000 per month in 2004, increasing by more than 10-fold over a 12-month period. It provides information on genetics services, support groups and 54 Fact Sheets. The site is now hosted by NSW Health, increasing awareness of genetics services and accessibility.

Service use – Client contacts for the CGE

Target group	1996 No. of direct contacts	2002 No. of direct contacts	2002 No of contacts through website
Students	547 (24%)	476 (16%)	1993 (65%)
Professionals	1091 (48%)	5096 (65%)	488 (16%)
Individuals & Families	655 (28%)	2341 (19%)	571 (19%)
Total	2293	7913	3052

Resource production

The CGE has established itself as an integral part of a comprehensive clinical genetics service, developing and producing resources that are fundamental tools for the NSW genetic counselling services as well as easy to read 'guides' providing direction and risk information to clinicians on an array of prenatal screening and diagnostic options and disorder specific information.

Some examples of new resource development and updates are:

■ The Genetics Resource Book

The 2004/2005 (7th) edition was produced in May 2004. It is a compendium of Genetics Support Groups, Services and Information for Australia and New Zealand. It is marketed and sold throughout Australia and New Zealand to cover production costs. The 54 Fact Sheets in the Book are also provided online.

■ PND booklet revision and printing

Around 10,000 of these booklets that cover screening and diagnostic testing for fetal abnormalities are requested annually. They have been produced since 1992 with biennial updates. An evaluation of their usefulness and relevance to practice was conducted with GP's and genetic counsellors. Although available online, hard copy is in strong demand for use with patients. A chapter on preimplantation genetic diagnosis was considered warranted and that has now been inserted in the latest edition (2003).

■ The Family Health Tree Guide

First produced in 1992, the guide has been used extensively by professionals and the community for its value in the correct ascertainment of a family health history. Consultation has led to the production of two versions, one for the community and one for health professionals. These resources are also available in hard copy and online.

■ Disorder Information sheets

The Centre has produced, in conjunction with Clinical Genetics expertise, over 700 Information Sheets on genetic disorders since 1994, many covering very rare conditions. These sheets are used before, after or during genetic counselling and are the major source of information provided to the community by the Association of Genetic Support of Australasia. Given the rapid development in genetics testing and diagnosis, the sheets are not sent out if they are more than 6 months old so they are regularly updated. An evaluation of their clinical usefulness and need has proven their positive value to GP's, clinical geneticists, genetic counsellors and community recipients through AGSA. This activity is an essential part of the Centre's work.

■ Other resources

The CGE has recognised the need for developing up-to-date resources as a response to the changing nature of genetic technology and its potential uses. Other resources include:

- genetic information and life insurance products
- information on genetic counselling

- prenatal diagnosis testing information
- information sheets with Cancer Council (Bowel cancer)
- printing and dissemination of prophylactic mastectomy booklet for women at high risk of breast cancer
- printing and dissemination of prophylactic oophorectomy decision aid for women at high risk of ovarian cancer
- video of bowel cancer workshops for rural GPs and a cancer genetic counselling tool.

The CGE works with the multicultural Health Centre (NSW Health) to produce web-based translated versions of many of its resources.

Professional education

A range of educational activities has been conducted for health professionals and other professional groups including:

- high school science teachers seminars
- development of school web resources such as a Diabetes lesson plan in partnership with the Garvan Institute and the NSW Department of Education and Training
- workshops with the Cancer and Oncology Society of Australia (COSA) on cancer genetics
- communication skills for genetic counsellors
- the health Diversity Institute
- GP's through the RACGP
- continuing education with monthly education meetings with the Family Cancer Service
- certification as an RACGP education provider through evaluation of GP bowel cancer workshops (video) and CME evaluation of bowel guidelines (500 GPs).

Public engagement

The Centre resources are also the foundations of public education. Using these tools, the Centre has conducted activities to engage the public in informed discussion to facilitate decision-making regarding the utilisation of the new genetic technologies. Examples include:

- **The 'Helix of Humanity' campaign to celebrate the 50th anniversary of the discovery of the structure of DNA (May, 2003).** The anniversary was seen as an opportunity to enhance community awareness of genetics developments and services. Worksheets for Year 10 were designed and distributed to all secondary schools in NSW to coincide with the publication of a 4-page insert in the Body and Soul section of the Sunday Telegraph on Mother's Day 2003 – circulation 750,000). The insert included an article promoting the Family Health Tree Guide to aid in documenting a family health history (available from the Centre and online); an interview with a woman who had undergone predictive genetic testing for breast cancer; 'Facts and Myths'; a timeline of human genetic discoveries and developments in the last 50 years; a discussion of the freedoms, burdens and power associated with use of genetic technologies, and a promotion of the NSW Genetics Service and support groups. An outcome was an increase in visitors to the Family Health Tree Guide page on the website.
- **The Sulston Event – Who owns our genomes?** *Public science versus Private Science: The politics, the ethics and the insider's story on mapping human DNA (ABC Radio, ABC Science On-Line and British Council) – Australian Museum (July 2003).* A panel discussion and broadcast with Sir John Sulston: Winner of the Nobel Prize for Medicine 2002.
- **Cafe Scientific in Wodonga 'Too much information? Your family and the New Genetics'.** *ABC Radio, British Council and New Scientist as part of the Albury-Wodonga Festival of Learning. (August 2004) – A discussion in the Pub (and broadcast) with health professionals and the community.*

Partnerships

The phenomenal impact that genetic technology has on numerous aspects of life is a challenge faced by society. In 2003, the completion of The Human Genome Project steered genetics professionals into a new era. The challenges now lie in ensuring that the potential benefits from the new technology are recognised within the context of its limitations, possible harm and discrimination. The Centre recognises that partnerships with other relevant groups can lead to a more holistic approach to these challenges and will strengthen the breadth of genetics education within the community. Partners of the CGE include:

- Biotechnology Australia (on-line Information Sheets)
- Better Health Channel (Vic Health) (on-line Information Sheets)
- British Council (Montage, Sulston event)
- ABC (Science on-line, Café Scientific)
- CRC (Genethics high school competition)
- Garvan (Genethics, diabetes lesson plan)
- Hereditary Cancer Clinic POWCH (prophylactic oophorectomy decision aid)
- University of Sydney Dept of Psychological Medicine (cancer genetic counselling tool)
- Australian Cancer Network (GP Bowel Cancer Guidelines)
- National Breast Cancer Centre
- NSW Cancer Council (Information Sheets, seminars)
- Cancer Council of Victoria (Bowel guide development and evaluation)
- IFSA (Life Insurance policies)
- Institute of Actuaries of Australia (Reports for Genetic Discrimination).

MotherSafe provides telephone counselling for women and their healthcare providers throughout the State regarding agents of all types:

- prescription and over-the counter medications
- radiation
- chemicals
- infections
- occupational exposures.

The service aims to provide the most up-to-date information available to callers who are concerned about the potential risks of exposures during pregnancy and breastfeeding.

Apart from the telephone counselling service there is also a face-to-face counselling clinic for those women (around 5% of callers) who have been exposed to agents with increased risk or who wish to have further discussion about their concerns for other reasons.

Since the service commenced in January 2000, MotherSafe has handled over 20,000 calls. Currently approximately 1,000 calls are answered each month. Most calls have come from consumers (women and their partners) with around 40% of calls from health care professionals including general practitioners, obstetricians, clinical geneticists, genetic counsellors, pharmacists, midwives, lactation consultants and early childhood nurses.

MotherSafe is based in South Eastern Sydney/Illawarra Area Health Service but provides a service for women throughout the whole state of NSW. Approximately 70% of the calls have come from Sydney, with 27% from non-metropolitan NSW and the remainder from interstate, including the ACT, and overseas.

The majority of calls (62%) have been regarding exposures during pregnancy, while 25% have been questions about exposures during lactation. The remainder of the calls has been from women planning a pregnancy or questions about exposures during previous pregnancies.

MotherSafe has been involved in professional and public education as well as public health initiatives such as the promotion of pre-conceptual folic acid.

MotherSafe is also establishing follow-up studies to improve the information available to pregnant women and their health care providers on the outcomes of exposures to new or unusual medications during pregnancy and lactation.

15 The Association of Genetic Support of Australasia (AGSA)

AGSA is a registered charity that provides support and information for individuals and families affected by a genetic condition. It has been supported under the NSW Department of Health's Non-Government Organisation program since 1993 and recently by the Carers Statewide Grant Program (2005).

Since the service commenced, AGSA has assisted well over 100,000 people directly or indirectly. AGSA has a contact register of over 550 genetic conditions.

How AGSA helps

The diagnosis of a genetic condition in a family member, particularly a child, places enormous stress on a family. Families have a need for AGSA's personal support service offering a specialised understanding of their particular condition at a time of crisis. While there are support groups established for a number of genetic disorders, AGSA may provide the only contact point for families affected by a rare condition. AGSA will endeavour to facilitate contact with another family/individual affected by the same, or similar conditions, and/or provide information about relevant support groups.

AGSA also provides:

- telephone counselling
- a non-clinical support approach
- practical management information and support
- facilitation of ongoing support for families, health professionals and other interested groups
- quarterly newsletter
- resources relating to education, medical services, other helpful organisations, allowances and respite care
- genetic seminars throughout New South Wales
- annual Genetic Disorders Awareness Week
- the capability to establish new support groups and networks
- an annual Breast Cancer Information Day
- an annual Bowel Cancer Information Day.

AGSA is a consumer representative on:

- NSW Genetics Advisory Committee
- Congenital Malformation & Birth Defects National Data Collection Review Committee
- NSW Newborn Screening Advisory Committee
- Carers Coalition Working Party on Ageing Parents.

AGSA is a member of the following:

- Australasian Society of Genetic Counsellors.
- Human Genetics Society of Australasia
- Australasian Genetic Alliance (AGA) 2003
- The International Genetic Alliance 2003
- World Alliances of Organisations for the Prevention and treatment of Genetic and Congenital Conditions (WAO) 2004.

Contact details:

The Association of Genetic Support of Australasia Inc (AGSA)

66 Albion Street

Surry Hills NSW 2010

Tel. +61 02 9211 1462

Fax. +61 02 9211 8077

Email. agsa@ozemail.com.au

Website www.agsa-geneticsupport.org.au

Publications and resources **16**

NSW Genetics Service

Publications

- *Genetics Services in NSW 1996–2000*, July 2002
- *Specialised Testing for Genetic Disorders*, May 2000
- *Ethical Code Governing the Provision of Genetics Services*, June 1998
- *Report on the Impact of Cancer Genetic Technology and Recommendations for Cancer Genetics Service Provision*, April 1996
- *The Goal and Objectives of the NSW Genetics Service*, September 1995
- *Genetics Services in NSW Five Year Plan 1993–1998*, July 1993
- *Genetics Services in NSW 1987–1991*, August 1991
- *Report of the Genetics Services and Birth Defects Sub-Committee on Super-Specialty Genetics Services in NSW and ACT: Review and Planning for Future Development of Delivery, Distribution and Organisation*, March 1987.

Circulars and Information Bulletins relevant to Genetics, released by NSW Health

- *Charging Policy for Clinically Required Specialised Genetics Tests which are non Medicare Benefits Schedule Items*, Policy Directive PD2005_335 previously issued as Circular No. 2003/86
- *Guidelines for predictive and diagnostic DNA testing for serious adult onset neurogenetic disorders with predictive implications for other family members and which are likely to reduce normal life expectancy*, Policy Directive PD2005_303 previously issued as Circular No. 2003/25
- *Newborn Screening Guidelines*, Policy Directive PD2005_566
- *Haemochromatosis – Information for Health Care Providers on Diagnosis and Management*, Information Bulletin 2000/9

- *Guidelines for Diagnosis and Management of Haemoglobinopathies*, Information Bulletin 99/14
- *Guidelines for Testing for Genetic Disorders*, Policy Directive GL2005_012 previously issued as Circular No. 97/48
- *Folic Acid and Neural Tube Defects*, Policy Directive PD2005_066 previously issued as Circular No. 94/68
- *Genetics Services Policy Guidelines*, 1987

Other relevant NSW Health publications

- *NSW Health Privacy Manual*
www.health.nsw.gov.au/pubs/2004/privacymanual.html
- *NSW Health Mothers and Babies*
www.health.nsw.gov.au/public-health/phbsup/mcd03.html
- *Guidelines for Investigation of a Stillbirth*
Policy Directive GL2005_013 previously issued as Circular No. 97/107
- *Reporting and Submission Requirements of Data for the NSW Birth Defects Register (BDR)*
Policy Directive PD2005_217 previously issued as Circular No. 2001/85
- *Pregnancy – Framework for terminations in New South Wales public health organizations*.
Policy Directive PD2005_587

Research publications

Numerous research reports are published annually in peer-reviewed journals by the staff of the various genetics service units, but these are not included in this report.

NSW Centre for Genetics Education

Publications

Following is a comprehensive list of resources available from:

The NSW Centre for Genetics Education
PO Box 317
ST LEONARDS NSW 1590
Tel. 02 9926 7324
Fax. 02 9906 7529
Website www.genetics.com.au

General

- *The Importance of Your Family Health Information* – This guide for drawing a family health tree helps consumers complete family health information in a form they can then take to their doctor for assessment.
- *The Genetics Resource Book (2004/2005)*: an Australasian directory with facts and information about 140 conditions and support groups, as well as genetic services in Australia – A comprehensive resource for Australia and New Zealand, published biennially for the health, education and welfare professionals; and for the individuals and families affected by genetic conditions.
- *Genetic Information Fact Sheets* on over 700 genetic conditions – information is prepared concerning a particular condition utilising the most recent data available and existing support services. Each information sheet is dated and will not be distributed if more than 6 months has passed since its last update.
- *Genetic Information and Life Insurance Products in Australia* – This resource provides information for individuals and professionals about the implications personal genetic information may have on Australian insurance products. It contains information relevant both prior to and following any genetic testing that may be undertaken.
- *Autopsy Information for parents about the post-mortem examination* – pamphlet for parents whose baby has died before or after birth, or whose infant or older child has died.

Genetic Services and Counselling:

- *Why knowing about your genes is important to your future* – Pamphlet.
Available in Arabic, Armenian, Chinese, Croatian, Greek, Italian, Khmer/Cambodian, Lao, Macedonian, Maltese, Polish, Portuguese, Serbian, Spanish, Turkish, Vietnamese

Folate:

- *Facts Sheets for Professionals* – A simple vitamin called folate taken before pregnancy as well as in early pregnancy can help prevent spina bifida

Cystic Fibrosis:

- *Genes and Cystic Fibrosis – Basic Facts About Chromosomes, Genes and Cystic Fibrosis* – Information kit

Huntington Disease:

- *Predictive Testing For Huntington Disease Information Kit*
- *Predictive Testing – Information for Physicians* – Pamphlet

Screening In Pregnancy:

Ultrasound

- *Obstetric care for women* – pamphlet
- #### First Trimester Screening
- *Screening tests for your baby in early pregnancy* – brochure for consumers
 - *First trimester screening using nuchal translucency ultrasound and biochemical testing* – information for health professionals

Maternal Serum Testing:

- *A Blood Test to Determine the Risk of Certain Problems in your Pregnancy, The Maternal Serum Test* – Pamphlet
- *Some questions and answers when your test result shows an 'increased risk' of your baby having Down syndrome* – Pamphlet
- *Some questions and answers when your test result shows an 'increased risk' of your baby having a neural defect such as Spina Bifida* – Pamphlet

Prenatal Diagnosis:

- *Prenatal Diagnosis and Counselling – Importance of checking your baby’s health before birth* – Pamphlet. Available in Arabic, Chinese, Croatian, Khmer/Cambodian, Korean, Lao, Macedonian, Polish, Portuguese, Spanish, Turkish, Vietnamese.
- *Prenatal Testing – Special Tests For Your Baby During Pregnancy, Chorionic Villus Sampling (CVS), Amniocentesis, Ultrasound, Cordocentesis and Preimplantation Genetic Diagnosis (PGD)* – Prenatal Diagnosis Booklet
- *Prenatal Diagnosis – Towards an Informed Decision* – an educational video produced for use in the community

Support After Fetal Diagnosis of Abnormality (SAFDA)

- *Support After Fetal Diagnosis of Abnormality (Safda)* – Pamphlet.
- *Diagnosis Of Abnormality In An Unborn Baby, A Booklet for Parents.*
- *When your unborn baby has a problem: How to manage the weeks ahead* – booklet

Cancer Resources

- *What if I have a family history of cancer* – brochure for consumers
- *Cancer: the significance of family history* – brochure for health professionals
- *Information for women considering preventive mastectomy because of a strong family history of breast cancer* – booklet
- *Is breast cancer inherited?* – video for consumers
- *Understanding your breast cancer risk* – a communication aid to assist women during genetic counselling to discuss their risk of familial breast cancer
- *Risk Management Options for Women at Increased Risk of Developing Ovarian Cancer* – Part 1 Information Booklet – Part 2 Decision Aid

Glossary

ABNORMAL:

Any change from the 'correct' or 'usual'. It may not necessarily mean harmful or undesirable; it can equally mean atypical, unusual or uncommon. When used in reference to genes, an abnormal gene may result in a specific genetic condition.

ALPHAFETOPROTEIN (AFP):

A protein, which is made by the fetus, that can be found in the mother's blood circulation. The amount of the protein, both in the mother's blood and in the amniotic fluid, at particular periods during the pregnancy, may be associated with the presence of neural tube defects or chromosomal problems in the baby.

AMNIOCENTESIS:

A procedure for obtaining amniotic fluid for prenatal diagnosis. Using a sterile needle, a sample of amniotic fluid is removed from the uterus; the amniotic fluid contains cells from the fetus that can be analysed to determine if the fetus has a specific condition. The test is usually carried out in the 14th–18th week of pregnancy.

AMNIOTIC FLUID:

Fluid in which the fetus floats in the uterus; fetal cells are found suspended in this fluid.

AUTOSOMAL GENE:

Any gene which is located on an autosome.

AUTOSOMAL DOMINANT MUTATION:

A dominant mutation in a gene which is carried on an autosome.

AUTOSOMAL RECESSIVE MUTATION:

A recessive mutation in a gene which is carried on an autosome.

AUTOSOME:

Any chromosome that is not a sex chromosome (that is not an X or Y chromosome). In humans, the autosomes are the numbered chromosomes and are given the numbers 1–22. Chromosome 1 is the largest and 22 is the smallest.

BALANCED TRANSLOCATION

(RECIPROCAL TRANSLOCATION):

A rearrangement of the chromosomes with no apparent loss or gain of chromosomal material. A person with this rearrangement is not affected in any way. When a translocation chromosome results in the gain or loss of genetic material, it is said to be unbalanced and may cause a problem in health, growth or development.

CARRIER OF A CHROMOSOMAL REARRANGEMENT:

This definition applies to an individual who has a rearrangement of his/her chromosomes so that the normal genetic information is present (that is, it is 'balanced') but it is not in the usual 46 chromosome pattern.

CARRIER OF A MUTATED GENE:

Every cell contains two copies of each gene. One gene copy may be mutated and the other may be 'correct'. If the mutated gene is not expressed in the cells (resulting in a particular characteristic or a genetic condition), the mutated gene is said to be recessive to the other 'correct' copy of the gene. An individual who has one correct gene copy and one faulty (recessive) gene copy is said to be a 'carrier' for the mutation leading to a specific condition. The carriers of a recessive mutation in a gene are usually not affected but they are at risk for passing on the mutant gene to their offspring.

CARRIER SCREENING:

Testing populations of people to determine if individuals are genetic carriers of a mutated or faulty gene for a particular genetic condition.

CARRIER TESTING:

Testing an individual who is at risk due to a family history to determine if he or she is a carrier of a mutated or faulty gene for a particular genetic condition.

CELL:

The basic structural unit of all living organisms. While some organisms are made up of only one or several cells, humans are composed of millions of cells. Each cell is enclosed by a membrane and has a nucleus which contains the genetic material (DNA) in the form of chromosomes. Mitochondria are also found randomly scattered throughout the cell.

CHORION:

The chorion develops into the placenta. Chorionic cells have the same genetic composition as cells of the fetus. Cells of the chorion are sampled during a prenatal diagnostic test called CVS (chorionic villus sampling).

CHORIONIC VILLUS SAMPLING (CVS):

A procedure for obtaining cells of the chorion to enable testing of the fetus for specific abnormalities. Samples of the cells may be taken through the vagina or through the abdomen of the pregnant mother: it is usually carried out in the 10th – 12th week of pregnancy.

CHROMOSOME:

A threadlike structure found in the nucleus of all the body cells (except red blood cells) consisting of DNA and proteins. Each chromosome can be thought of as a string of beads where every bead represents a gene. (See Genetic Fact Sheet 1: Genes and Chromosomes)

CLINICAL GENETICS:

A specialty of medicine concerned with the diagnosis and discussion of risks of developing a genetic condition in individuals and families.

CLONE:

A clone is a cell or group of cells that are identical and are derived from an original source of genetic material.

CONGENITAL:

Present at birth, not necessarily inherited.

CONSANGUINITY:

Relationship between two individuals with a common ancestor, eg first cousins.

CONSULTAND:

The person seeking, or referred for, genetic counselling.

CVS:

See Chorionic villus sampling.

CYTOGENETICS:

The microscopic study of chromosomes and how changes in chromosome structure and number affect individuals.

DYSMORPHOLOGY:

Comes from the Greek DYS – meaning abnormal, disease, faulty, impaired and MORPHOLOGY – meaning structure or form. Refers to the changes in the usual structure of a person's cells.

DNA (DEOXYRIBONUCLEIC ACID):

The chemical compound that makes up genes within chromosomes and is the basic material of heredity. It is made up of chemicals called nucleotide bases, linked together in a chain. Two chains of nucleotides twist around each other to form a double helix.

DNA SEQUENCING:

Determining the pattern or order in which the nucleotide bases occur in a piece of DNA. This sequence is the genetic code.

DOMINANT:

Every cell contains two copies of each gene. Where only one of the gene copies or allele is mutated, and the other allele is 'correct', but the person is affected by a genetic condition due to that mutation, the mutation is described as dominant. The mutated gene is said to be dominant over the other 'correct' copy of the gene. A condition or characteristic caused by a dominant gene mutation only requires one of the genes to be mutated for the person to be affected.

ENVIRONMENTAL FACTORS:

Factors in the environment that may have an effect on our development or growth eg. diet, atmospheric pollutants, cigarette smoke, preservatives, X-rays etc.

ENZYME:

A protein molecule which promotes or enables a chemical reaction in the cells (a biochemical reaction) to take place. These biochemical reactions include breaking down food into the essential chemicals required by the body and breaking down toxic by-products of our bodies. Enzymes are essential for the correct function of the body's metabolism.

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ENZYME REPLACEMENT THERAPY:

A method of treating genetic conditions that are due to a deficiency of a particular enzyme. Overcoming the deficiency by providing the body with the enzyme enables the cells to function correctly and the symptoms of the condition may be decreased or eliminated.

ETHICS/ETHICAL BEHAVIOUR:

Code of behaviour considered correct; especially that of a particular group, profession or individual.

EUGENICS:

The practice of trying to influence human heredity by encouraging the transmission of 'desirable' characteristics and discouraging the transmission of 'undesirable' ones.

FAMILIAL:

A characteristic or condition that tends to run in families.

FETAL BLOOD SAMPLING:

A prenatal diagnosis technique where a blood sample is obtained from the fetus.

FETUS:

In humans, the product of conception after the end of the eighth week of pregnancy to the moment of birth.

FRAGILE SITE:

A small break or a constriction of a chromosome that can be visualised after special treatment of the chromosomes. In individuals affected with Fragile X syndrome, a fragile site can often be seen on their X chromosome.

GENE: The basic unit of heredity; a segment of DNA that contains the information for a specific characteristic or function.

GENE CLONING:

Isolating a gene and then making multiple copies of it by inserting it into a bacterial cell or another organism.

GENE MAPPING:

Determining the relative locations of different genes on chromosomes.

GENE THERAPY:

A method of treating genetic conditions by inserting a correct copy of the gene in question into the cells of individuals who have the mutated gene.

GENETIC CARRIER:

See Carrier of a mutated gene

GENETIC CODE:

The information contained in the DNA which is 'interpreted' by the cells to produce proteins. The chemicals (nucleotides) which make up the DNA can be described by the letters A (Adenine), T (Thymine), C (Cytosine) and G (Guanine). Thus the genetic code can be written as a series of letters (eg AAA CGT TTC).

GENETIC CONDITION:

A genetic condition is caused by a change in the genetic information. Genetic conditions may be caused by a mutation in a single gene or may be caused by a change in chromosome structure or number.

GENETIC COUNSELLING:

Diagnosis, information and support provided by health professionals with specialised training in genetics and counselling.

GENETIC COUNSELLOR:

A health professional with specialised training in genetics and counselling who can provide information and support to individuals or families with concerns about a genetic condition which may run in their family.

GENETIC ENGINEERING:

Laboratory techniques used to alter or manipulate the genetic makeup of cells by deliberately removing, changing or inserting individual genes.

GENETIC MAPPING:

Determination of the relative positions of genes on a chromosome and a measure of the distance between them.

GENOME:

The complete set of genes carried by an individual or a cell.

HEREDITARY:

The transfer of a gene from parent to child. In mothers, the gene is transferred via the DNA in the egg and in fathers, the gene is transferred on the DNA of the sperm.

INBORN ERROR OF METABOLISM:

A congenital condition which results from a change in a gene which causes a deficiency in the presence or activity of particular enzymes important for the functioning of the body's metabolism. (See Genetic Fact Sheet 18: Newborn Screening for Genetic Conditions)

INCIDENCE:

The number of new cases of a condition detected annually, per unit of the population. For genetic conditions, the incidence is quoted as the number of affected individuals per 1,000 births whether detected at birth or not.

INHERITED:

The transmission of genetic information from a parent to a child.

INVERSION:

Where there are two breaks in a chromosome, the segment may flip over and rejoin, that is, become inverted. This results in the genes being in the reverse order along the chromosome. This may cause the genetic code to be read or translated incorrectly.

KARYOTYPE:

The term used to describe an individual's chromosomes that have been photographed through the microscope and then arranged according to a standard classification based on their group and size. This is done by a specialised scientist trained in cytogenetics.

LINKAGE:

The tendency for genes or segments of DNA that are located close together on the same chromosome to be inherited together.

MATERNAL SERUM TESTING:

A test which assesses the risk of fetal abnormalities such as neural tube defects and Down syndrome by analysing a number of chemicals in the mother's blood during pregnancy.

MENDELIAN INHERITANCE:

This refers to the inheritance of single genes and follows specific patterns: autosomal dominant, autosomal recessive and X linked inheritance.

METABOLISM:

The physical and chemical processes by which energy is made available for essential body functioning, growth and development.

MISCARRIAGE:

Loss of a baby before the twentieth week of pregnancy.

MITOCHONDRIA:

These structures or organelles in the cell are the main energy source: they are often called the powerhouse of the cell. The mitochondria also contain their own DNA and therefore genes; mitochondrial genes follow maternal inheritance.

MOLECULAR GENETICS:

The branch of genetics that studies the function and structure of genes at the molecular level.

MULTIFACTORIAL INHERITANCE:

A pattern of inheritance which results from the interaction of one or more genes with environmental factor(s).

MUTATION:

A permanent change in a gene. If the mutation occurs in the egg or sperm (sex cells), it can then be inherited. Mutations in body (somatic) cells such as skin cells cannot be inherited. Mutations can occur naturally and spontaneously or they may be due to exposure to mutagens.

NEURAL TUBE:

The embryonic structure which forms into nervous system including the spinal cord and brain.

NEURAL TUBE DEFECT (NTD):

An abnormality which results when the neural tube in the fetus fails to close. Spina bifida and anencephaly are forms of NTD.

Glossary

NUCHAL TRANSLUCENCY

In early pregnancy the space between the skin and the subcutaneous tissue at the back of the fetal neck is filled with fluid. The fluid filled space is called the nuchal translucency. Its depth can be measured with high resolution ultrasound between 11 and 13 weeks gestation.

PEDIGREE:

A diagrammatic representation of a family health history or family health tree.

PENETRANCE:

The probability of detecting the presence or clinical expression of a gene or combination of genes when they are present. If the penetrance of a particular gene is less than 100%, not all individuals who carry a mutation in the gene will develop symptoms of the condition it causes. Such a genetic condition is said to have reduced or incomplete penetrance.

PHENOTYPE:

The physical and/or biochemical characteristics of a person, an animal or other organism which are determined by their genetic makeup and/or environment.

PREDICTIVE TESTING:

A form of genetic testing performed on a person with a family history of a particular genetic condition, but who does not have any symptoms of the condition at the time of testing. This testing determines whether that person has inherited the mutation (present in their family). If testing for this mutation reveals that it is present in the person, then they have an increased predisposition to developing the condition that was tested for. The detection of a specific mutation does not necessarily mean the individual will definitely develop the condition. Familial breast cancer is an example of a condition where predictive testing is used.

PREDISPOSITION:

A situation in which a person, due to their inherited genetic makeup, may have a particular susceptibility to a condition if exposed to the correct environmental triggers.

PRENATAL DIAGNOSIS:

The detection of fetal abnormalities during pregnancy.

PRESYMPTOMATIC TESTING:

A form of genetic testing performed on a person with a family history of a particular genetic condition, but who does not have any symptoms of the condition at the time of testing. This testing determines whether that person has inherited the mutation (present in their family). If testing for this mutation reveals that it is present in the person, then they will most likely develop symptoms of the genetic condition it causes at some stage of their life. Huntington disease is an example of a genetic condition where presymptomatic testing is used.

PREVALENCE:

Proportion of the whole population affected by a certain condition.

RECESSIVE:

Every somatic cell in our body contains two copies of each gene. Each gene contains the information for a particular gene product, such as a protein. If a gene is mutated, the gene no longer codes for the gene product. Where an individual has one gene copy or allele mutated and the other copy 'correct', the cell will only be producing half the amount of gene product. If this does not result in a genetic condition in the individual, the mutation is described as being hidden or 'recessive' to the correct copy of the gene. An individual with this genetic constitution is said to be a 'carrier' of a recessive gene mutation. For a recessive gene mutation to result in a particular characteristic or a genetic condition, both copies of the genes must be mutated.

RECURRENCE RISK:

The risk that a genetic condition will occur again in a family.

ROBERTSONIAN TRANSLOCATION:

A type of translocation exclusive to the acrocentric chromosomes (13, 14, 15, 21 and 22) in which two of these chromosomes join at or near their centromeres. This is effectively a fusion between two whole chromosomes.

SENSITIVITY:

The ability of a test to detect the presence of a genetic condition or a mutation when it is truly present.

SEX LINKED:

A genetic condition or characteristic which is determined by genes carried on the X chromosome.

SPECIFICITY:

The ability of a test to determine whether a genetic condition or mutation is absent when it is truly absent.

SYNDROME:

A group of characteristics or symptoms that occur together in a recognisable pattern.

TERATOGEN:

A substance that produces or increases the incidence of birth defects or congenital abnormalities by interfering with development of the fetus during pregnancy.

TERMINATION OF PREGNANCY:

Intervention to ensure a pregnancy does not continue.

TRANSLOCATION:

This occurs when a piece of one chromosome breaks off and attaches to another different chromosome. When no material is lost or gained the translocation is said to be 'balanced' and the individual may or may not be affected by it. An 'unbalanced' translocation results in the loss or gain of genetic material which may result in a genetic condition.

TRIPLOIDY:

Having three copies of every chromosome resulting in 69 chromosomes in a cell instead of the usual 46.

TRISOMY:

Three copies of a particular chromosome are present in a cell resulting in 47 chromosomes instead of the usual 46.

ULTRASOUND:

The use of sound waves for visualising body tissues and structures. In pregnancy, structural abnormalities in the fetus can be detected.

X LINKED GENE:

Any gene which is located on the X chromosome.

X LINKED RECESSIVE MUTATION:

A recessive mutation in a gene carried on the X chromosome.

X LINKED DOMINANT MUTATION:

A dominant mutation in a gene carried on the X chromosome.

References

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Appendix 1

Clinical and genetic counselling service locations

Clinical and counselling services

CAMPERDOWN

Department of Molecular and Clinical Genetics
Royal Prince Alfred Hospital
CAMPERDOWN NSW 2050
Tel. 02 9515 5080
Fax. 02 9515 7595

LIVERPOOL

Department of Clinical Genetics
Health Services Building
Cnr Campbell and Goulburn Sts
LIVERPOOL NSW 2170
Tel. 02 9828 4665
Fax. 02 9828 4650

PENRITH

Nepean Hospital
PENRITH NSW 2750
Tel. 02 4734 3362
Fax. 02 4734 2561

RANDWICK

Department of Medical Genetics
Sydney Children's Hospital
RANDWICK NSW 2031
Tel. 02 9382 1708
Fax. 02 9382 1711

WESTMEAD

Department of Clinical Genetics
Children's Hospital at Westmead
Department of Genetic Medicine
Westmead Hospital
WESTMEAD NSW 2145
Tel. 02 9845 3273
Fax. 02 9845 3204

NEWCASTLE

Hunter Genetics
Cnr Turton & Tinonee Sts
WARATAH NSW 2298
Tel. 02 4985 3100
Fax. 02 4985 3105

Genetic counselling services in conjunction with visiting clinical genetics services

KOGARAH

Women's and Children's Health
2nd Floor Prichard Wing
St George Hospital
Gray Street
KOGARAH NSW 2217
Tel. 02 9350 2315
Fax. 02 9350 3901

ST LEONARDS

Genetic Counselling Service
Royal North Shore Hospital
ST LEONARDS NSW 2065
Tel. 02 9926 6478
Fax. 02 9926 7880

BATHURST

Community Health Centre
Eric Sargeant Drive
Gorman's Hill
BATHURST NSW 2795
Tel. 02 6339 5677
Fax. 02 6339 5655

BROKEN HILL

Community Health Centre
BROKEN HILL NSW 2880
Tel. 08 8080 1556
Fax. 08 8080 1611

CANBERRA

The Antenatal Clinic
The Canberra Hospital
PO Box 11
CANBERRA ACT 2605
Tel. 02 6244 4042
Fax. 02 6282 2844

Appendix 1 Clinical and Genetic Counselling Service Locations

COFFS HARBOUR

Coffs Harbour Health Campus
Pacific Highway
COFFS HARBOUR 2450
Tel. 02 6656 7806
Fax. 02 6656 7203

GOSFORD

Genetic Counselling Service
Central Coast Health
Gateway Centre
PO Box 361
GOSFORD NSW 2250
Tel. 02 4328 7994
Fax. 02 4328 7925

GOULBURN

Child Development Unit
195 Faithful Street
GOULBURN NSW 2580
Tel. 02 4827 3951
Fax. 02 4827 3958

KINGSCLIFF

Kingscliff Community Health Centre
KINGSCLIFF NSW 2487
Tel. 02 6674 9500
Fax. 02 6674 9599

LISMORE

37 Oliver Avenue
GOONELLABAH NSW 2480
Tel. 02 6625 0111
Fax. 02 6625 0102

MUDGEE/DUBBO

Mudgee Community Health Centre
MUDGEE NSW 2850
Tel. 02 6378 6236
Fax. 02 6372 7341

PORT MACQUARIE

Community Health
Morton Street
PORT MACQUARIE 2444
Tel. 02 6588 2882
Fax. 02 6588 2800

TAMWORTH

Community Health Centre
Cnr Dean and Johnston Streets
TAMWORTH NSW 2340
Tel. 02 6767 8151 or 6767 8100
Fax. 02 6766 3967

TAREE/FORSTER

Community Health Centre
64 Putney Street
TAREE NSW 2430
Tel. 02 6592 9703
Fax. 02 6592 9607

WAGGA WAGGA

Wagga Base Hospital
WAGGA WAGGA NSW 2650
Tel. 02 6938 6443

WOLLONGONG

Maternal and Paediatric Services
Wollongong Hospital
Crown Street
WOLLONGONG NSW 2500
Tel. 02 4253 4267
Fax. 02 4253 4257

MotherSafe

Statewide Medications in Pregnancy and Lactation

Advisory Service

Royal Hospital for Women
RANDWICK NSW 2031
Tel. 02 9382 6539 (Sydney calls)
Tel. 1800 647 848 (Other calls)

AGSA

Association of Genetic Support of Australasia Inc.

66 Albion Street
SURRY HILLS NSW 2010
Tel. 02 9211 1462
Fax. 02 9211 8077
Email. agsa@ozemail.com.au
Website www.agsa-geneticssupport.org.au

GOLD Service (Genetics of Learning Disability)

Hunter Genetics
PO Box 84
WARATAH NSW 2298
Tel. 02 4985 3131
Fax. 02 4985 3133

Prenatal diagnosis and counselling

Specialised services:

CAMPERDOWN

Fetal Medicine Unit
King George V Hospital
CAMPERDOWN NSW 2050
Tel. 02 9515 8258
Fax. 02 9515 6579

LIVERPOOL

Fetal Medicine Unit
Liverpool Hospital
Elizabeth Drive
LIVERPOOL NSW 2170
Tel. 02 9828 5631
Fax. 02 9828 5570

RANDWICK

Prenatal Diagnosis
Royal Hospital for Women
RANDWICK NSW 2031
Tel. 02 9382 6098
Fax. 02 9382 6706

PENRITH

Fetal Medicine Unit
Nepean Hospital
PENRITH NSW 2750
Tel. 02 4734 3163
Fax. 02 4734 3764

ST LEONARDS

Fetal Medicine Unit
Royal North Shore Hospital
ST LEONARDS NSW 2065
Tel. 02 9926 7099
Fax. 02 9926 5590

WESTMEAD

Fetal Medicine Unit
Westmead Centre
WESTMEAD NSW 2145
Tel. 02 9845 6802
Fax. 02 9891 1216

NEWCASTLE

Prenatal Diagnosis Unit
John Hunter Hospital
NEWCASTLE NSW 2310
Tel. 02 4921 4694
Fax. 02 4921 3133

Cancer genetics

Specialised services:

DARLINGHURST

Family Cancer Clinic
Department of Medical Oncology
St Vincent's Hospital
Victoria Street
DARLINGHURST NSW 2010
Tel. 02 8382 3395
Fax. 02 8382 3386

KOGARAH

Cancer Care Centre
St George Hospital
Gray Street
KOGARAH NSW 2217
Tel. 02 9350 3815
Fax. 02 9350 3391

RANDWICK

Hereditary Cancer Clinic
Prince of Wales Hospital
RANDWICK NSW 2031
Tel. 02 9382 2587
Fax. 02 9382 2588

ST LEONARDS

Family Cancer Clinic
Royal North Shore Hospital
ST LEONARDS NSW 2065
Tel. 02 9926 6502
Fax. 02 9926 8930

WESTMEAD

Familial Cancer Services
Westmead Hospital
WESTMEAD NSW 2145
Tel. 02 9845 5079
Fax. 02 9687 2331

NEWCASTLE

Hunter Genetics
Cnr Turton & Tinonee Sts
WARATAH NSW 2298
Tel. 02 4985 3100
Fax. 02 4985 3105

Further Information:

on services in other areas and newly developed services:

NSW Genetic Education Program

PO Box 317

ST LEONARDS NSW 2065

Tel. 02 9926 7324

Fax. 02 9906 7529

Website www.genetics.com.au

