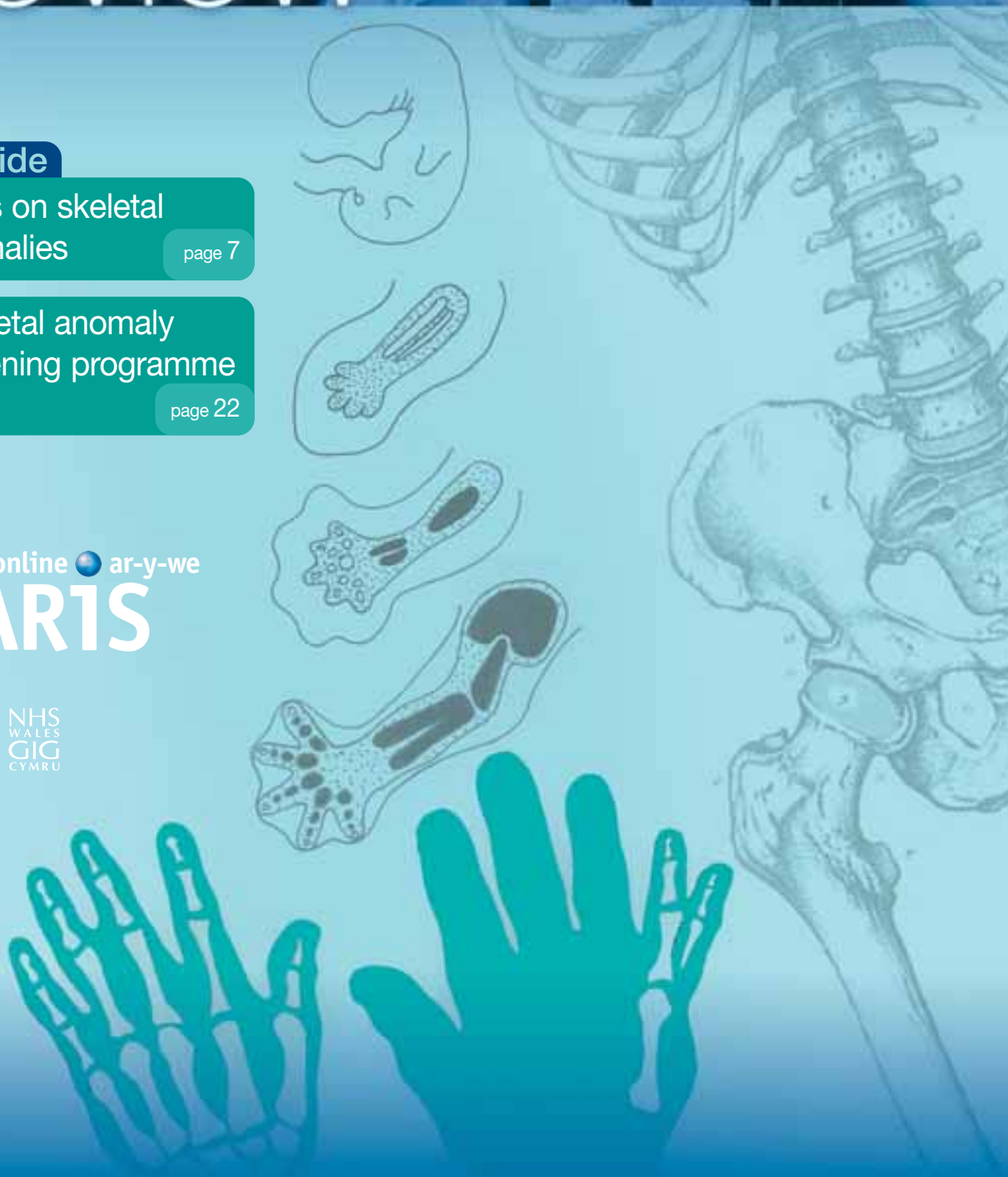
Congenital Anomaly Register & Information Service for Wales

caris review

inside

online ar-y-we CARIS

NHS WALES GIG CYMRU



Contents

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CARIS, the Congenital Anomaly Register and Information Service for Wales, is based at Singleton Hospital, Swansea. It is funded by the Welsh Assembly Government and is part of Public Health Wales[1].

Foreword

Welcome to the 2008 CARIS annual review.

This report includes a summary of congenital anomalies in Wales. More detailed information and data tables are available from the CARIS website www.wales.nhs.uk/caris[2]. This year we include a special focus on various skeletal anomalies. These will also be featured in our 2009 annual meetings, along with a discussion on a new rationale for antenatal ultrasound.

Once again thank you to all contributing health professionals for your ongoing support.

We would also like to thank Tracy Price, Hugo Cosh and other members of the Health Information and Analysis Team of the National Public Health Service for Wales who have undertaken the main annual data analyses.

Special thanks to Dr Colin Davies for his contribution on the way forward in antenatal ultrasound.

Bethan Thomson kindly provided several of the illustrations in this report.

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The CARIS team.

We are (left to right) David Tucker, Margery Morgan, Judith Greenacre, Val Vye and Helen Jenkins.

1 From October 1st 2009. Public Health Wales is the new public health NHS trust for Wales

2 also accessible through the HOWIS (NHS Wales) website at www.howis.wales.nhs.uk/caris

Summary

CARIS is the Welsh Congenital Anomaly Register and Information Service.

CARIS aims to provide reliable data on congenital anomalies in Wales. These data are used to assess:

- **Patterns of anomalies in Wales**
- **Possible clusters of birth defects and their causes**
- **Antenatal screening / interventions**
- **Health service provision for affected babies and children.**

We collect data on any baby or fetus born with a congenital anomaly and diagnosed within the first year of life where the mother was normally resident in Wales at the end of pregnancy.

Key Points (1998 – 2008)

The following key points are based on eleven years of data now available:

- **The gross[3] rate of congenital anomalies reported is 5.0%**
- **The rate of congenital anomalies in live born babies is 4.3%**
- **85.4% of cases are live born and 96% of these survive to the end of their first year. Increasing complexity of anomalies reduces the chance of survival**
- **Reported congenital anomaly rates in Wales are often higher than for other areas of Europe or Britain**
- **Variations in rates are again seen around Wales. In part this is due to differences in reporting**
- **Factors that can be shown to affect anomaly rates include maternal risk factors such as age and smoking. There is also an association with socioeconomic deprivation, particularly for non chromosomal anomalies**
- **Heart and circulatory defects are the largest group reported, followed by anomalies of the urinary and musculoskeletal systems**
- **For anomalies detected up to the first birthday, approximately one third of cases are detected antenatally, one third within the first week after end of pregnancy and the remaining third later in infancy**
- **Some specific anomalies continue to be investigated because of particularly high rates in Wales. These include gastroschisis and isolated cleft palate.**

Interventions and services for anomalies

- **rates of antenatal detection continue to improve in Wales, particularly for heart defects**
- **outcome data can be useful in planning services and for parent information.**

[3] The gross rate includes all cases of anomaly recorded as miscarriages, terminations of pregnancy, live and stillborn babies, per 10,000 live and still births.

CARIS activity 2008

The team continued to be involved with projects in Wales, the United Kingdom and internationally.

Wales

- The Welsh Paediatric Surveillance Unit completed data collection on craniosynostosis for CARIS, a condition for which there was potential for improved reporting in Wales.
- Annual meetings were held in Grand Theatre, Swansea and Wrexham Maelor Hospital. The special focus was on ten years of CARIS data and what this tells us about congenital anomalies in Wales.
- Presentation at the National Public Health Services Staff conference on public health aspects of congenital anomalies.

United Kingdom

- CARIS continues to contribute to the British Isles Network of Congenital Anomaly Registers (BINOCAR) executive group.
- David Tucker continued to chair the BINOCAR clinical coding working group and presented the work of the group to the UK BINOCAR annual meeting in Leicester.
- CARIS organised a CNS anomalies study day at the Norwegian Church, Cardiff, for clinicians and staff from other BINOCAR Registries. The day covered coding, anatomy and outcomes.
- David Tucker gave a presentation on antenatal detection and outcomes for heart defects in Wales at the Tiny Tickers workshop organised by the Royal College of Obstetrics and Gynaecology (RCOG).

International

- David Tucker presented an update on Gastroschisis in Wales and led a workshop on inpatient data at the European Collaboration of Congenital Anomaly Registers (EUROCAT) meeting in Helsinki conference in Italy.
- CARIS attended the International Clearing House of Birth Defects Surveillance and Research (ICBDSR) annual meeting in Padua, Italy and presented work by Dr Ciarán Humphreys (National Public Health Service for Wales) on the evaluation of a congenital anomaly register. CARIS also presented a poster on cystic fibrosis in Wales.

Websites

www.binocar.org.uk

www.eurocat.ulster.ac.uk

www.icbdsr.org

CARIS activity 2008

Publications in 2008 using CARIS data

- Barisic I, Tokic V, Loane M, Bianchi F, Calzolari E, Garne E, Wellesley D, Dolk H and EUROCAT Working Group (2008), "Descriptive epidemiology of Cornelia de Lange syndrome in Europe", *American Journal of Medical Genetics Part A*, Vol 146A, pp 51-59
- Boyd PA, de Vigan C, Khsohnood B, Loane M, Garne E, Dolk H and the EUROCAT Working Group (2008), "Survey of prenatal screening policies in Europe for structure malformations and chromosome anomalies, and their impact on detection and termination rates for neural tube defects and Down syndrome", BJOG, Vol 115, pp 689-696. [www.blackwell-synergy.com/doi/full/10.1111/j.1471-0528.2008.01700.x?prevSearch=allfield%3A%28Survey+of+Prenatal+Screening+Policies%29].
- Dolk H, Jentink J, Loane M, Morris J, de Jong-van den Berg LTW and the EUROCAT Antiepileptic Drug Working Group (2008), "Does lamotrigine use in pregnancy increase orofacial cleft risk relative to other malformations", *Neurology*, Vol 71, pp 714-722.
- Pedersen RN, Garne E, Loane M, Korsholm L, Husby S and a EUROCAT Working Group (2008), "Infantile hypertrophic pyloric stenosis: A comparative study of incidence and other epidemiological characteristics in seven European regions", *J Matern fetal Neonatal Med*, Vol 21, No 9, pp 599-604.
- Emanuele Leoncini, Giovannni Baranello, Ieda Orioli. Goran Anneren, Marian Bakker, Fabrizio Bianchi, Carol Bower, Mark Canfield, Eduado Castilla, Guido Cocchi, Adolfo Correa, Catherine De Vigan, Berenice Doray, Marcia Feldkemp, Mariam Gatt, Lorentz Irgens, R Brian Lowry, Alice Maraschini, Robert Mcdonnell, Margery Morgan, Ovsvaldo Mutchinick, Simone Poetzch, Merilyn Riley, Annukka Ritvanen, Elisabeth Robert-Gnansia, Gioacchino Scarano, Antonin Sipek, Romano Tenconi, and Pierpaolo Mastroiacovo."Frequency of holoprosencephaly in the International Clearinghouse Birth Defect Surveillance Systems: Searcing for population variations." *Birth Defects Research (PartA)* 82:585-591.

caris review

Focus on skeletal anomalies

Focus on skeletal anomalies

Development of the skeleton

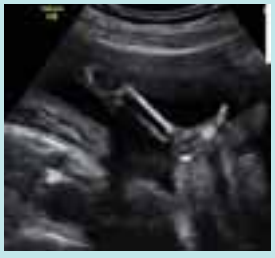
The formation of the skeleton involves the laying down of bone in two different ways.

1 ossification from cartilage – most of the skeleton

2 membranous ossification – clavicle and mandible

The complex development of the limbs is active between the 4th and 8th week of gestation (see figure 1). As we know from the thalidomide story the fetus is very susceptible at this time to the effect of adverse events.

The upper limb buds develop first, followed closely by the lower limb buds. Cartilage develops from mesenchyme and forms the skeleton by the 6th week.



Ultrasound scan showing a normal lower leg and foot

Ultrasound assessment

All women in Wales are offered a 18-20 week anomaly scan. This scan acts as a screen for any other problems which may require more detailed study.

Screening bone assessment

Head – measure biparietal diameter and head circumference

Femur – measure length, assess morphology

If a problem is found then a full survey of the fetal skeleton is necessary.

Full skeletal survey

Long bones –	measure all
	assess structure and texture
	assess ossification and look for fractures
	check hands and feet
Cranium –	look at vault bones and facial profile
Ribs and spine –	assess length, shape and any fractures

conception	upper limb buds begin to form	lower limb buds begin to form	rudimentary hand present	skeleton is cartilaginous digital rays present	limbs formed but not ossified
day 0	**day 26**	**day 28**	**day 32-34**	**day 40**	**day 56**

Figure 1: Timing of limb development (by day of gestation)

Skeletal Dysplasias

Problems with the skeleton can occur as a feature of over 500 conditions associated with congenital anomalies. Most of these are rare but overall they do make a significant impact on infant mortality and disability.

Skeletal dysplasias are a heterogenous group of over 100 disorders. These include:

- Osteochondrodysplasias –

a defective growth and development of tubular bones/spine eg achondrogenesis, thanatophoric dysplasia

b disorganised development of cartilage and fibrous parts

c density abnormalities of diaphyses /metaphyseal modelling eg osteogenesis imperfecta

- Dysostoses – defect in the normal ossification of fetal cartilage e.g. cleidocranial dysostosis
- Idiopathic osteolyses – dissolution of bone
- Dysplasias related to chromosomal aberrations
- Primary metabolic abnormalities eg hypophosphatasia
- Miscellaneous

Craniosynostosis

Craniosynostosis is the term used to describe various conditions in which there is premature fusion of the sutures between the bony plates of the skull (cranio – skull; syn – joining; ostosis – bone). The condition can affect different skull sutures (figure 2); may occur in isolation or as part of a wider syndrome and can be a primary or secondary defect.

The condition is therefore categorised in a number of different ways in the literature:

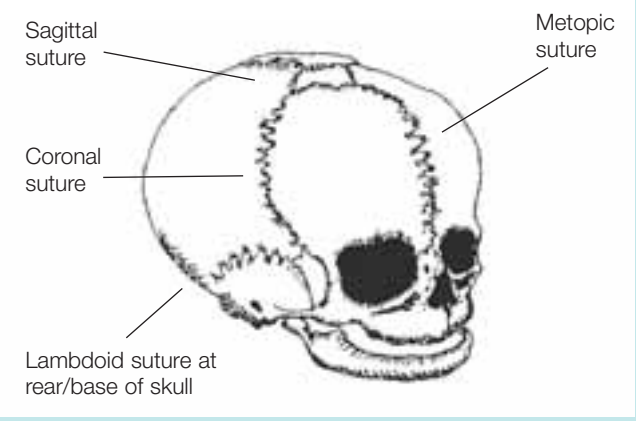
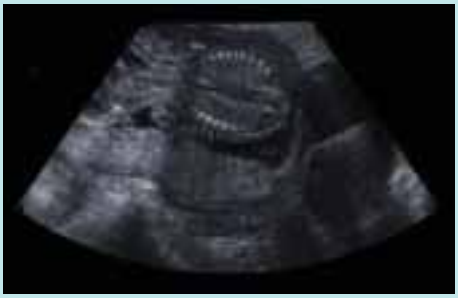


Figure 2: sutures of the fetal skull[4]

Commoner skeletal dysplasias

Condition	published rate	Welsh rate
Thanatophoric dysplasia	1 in 30,000	1 in 29,953
Osteogenesis imperfecta (type 2)	1 in 55,000	1 in 32,675
Achondrogenesis (all types)	1 in 75,000	1 in 179,715
Chondrodysplasia punctata	1in 85,000	1 in 59,905
Hypophosphatasia (severe form)	1 in 110,000	1 in 179,715
Camptomelic dysplasia	1 in 150.000	1 in 359,430



Ultrasound scan of hypophosphotasia showing echo poor vertebrae

4 http://www.headlines.org.uk/HL3%20Non-syndromic%20Craniosynostosis.pdf

Focus on skeletal anomalies

Ways of describing craniosynostosis

a) According to the suture and corresponding shape of skull

The particular type of craniosynostosis depends on which bones are affected (figure 3):

- *Scaphocephaly* - early fusion of the sagittal suture
- *Anterior plagiocephaly* - early fusion of 1 coronal suture
- *Brachycephaly* - early bilateral coronal suture fusion
- *Posterior plagiocephaly* - early closure of 1 lambdoid suture
- *Trigonocephaly* - early fusion of the metopic suture

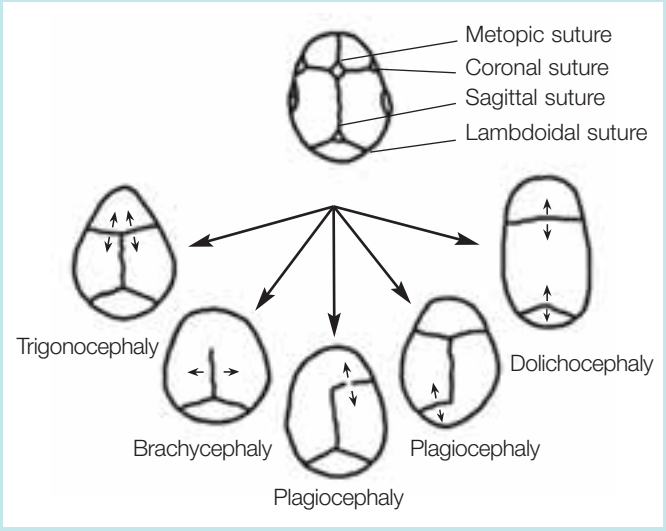


Figure 3: skull shape resulting from abnormal patterns of suture fusion

Moulding of the normal soft infant skull can occur when a baby lies on his back causing postural plagiocephaly. The supine position is recommended to reduce the risk of cot death. True synostotic plagiocephaly should be distinguished from this postural condition[5].

(A useful overview of the different types of craniosynostosis in layman's language can be found at www.headlines.org.uk[6])

b) Primary / Secondary

The growing brain in the fetus or young child forces the bony plates of the skull apart at the suture line, allowing the skull to grow.

Primary premature fusion of sutures may restrict brain growth and cause increased intracranial pressure. Surgery will be required to relieve pressure on the brain as well as to improve appearance.

Secondary premature fusion usually follows failure of brain growth (microcephaly) and is often associated with neuro-developmental delay.
In secondary cases, intracranial pressure will remain normal.

c) Simple / Complex

Simple craniosynostosis is a term used when only one suture fuses prematurely. In cases described as *complex or compound*, multiple sutures are affected. Raised intracranial pressure is rare in simple cases.

5 Jones BM, Hayward R, Evans R, Britto J. Occipital plagiocephaly: An epidemic of craniosynostosis? (editorial) BMJ 1997; 315:693-694 (20th September)

6 Headlines Website www.headlines.org.uk Accessed 16/5/04

d) Syndromic / Non-Syndromic

In syndromic cases, craniosynostosis represents one feature of a known pattern of anomalies forming recognised syndromes. Although many different syndromes are known, these tend to be extremely rare and include:

- Apert syndrome
- Carpenter syndrome
- Crouzon syndrome
- Pfeiffer syndrome
- Saethre Chotzen syndrome

Non-syndromic cases tend to involve simple craniosynostosis and do not have additional defects forming a recognised pattern.

Epidemiology and risk factors

There is a lack of published good quality studies describing the epidemiology of craniosynostosis.

The variable ways in which the condition is categorised further complicates comparisons of published rates. The overall prevalence is variable and is often quoted at around 5/10,000 live & stillbirths.

A recent rise in cases has been suggested although this may be secondary to changes in diagnostic patterns.

The Texas Birth Defects Monitoring Division of the Texas Department of Health has reviewed published literature to identify the following risk factors for craniosynostosis[7].

Demographic and Reproductive factors

- Increasing maternal age and increasing paternal age
- Possibly higher among non-black ethnic groups (reports vary)
- Male gender, especially for sagittal and lambdoidal craniosynostosis. Female gender for coronal craniosynostosis.

Lifestyle or environment

- Living in urban areas for coronal and lambdoidal craniosynostosis. Possibly living at high altitude (reports vary).
- Paternal occupation in agriculture/ forestry or mechanic/repairmen have been suggested (reports vary). No apparent link with maternal occupation.
- Maternal smoking
- Maternal use of nitrosatable drugs (some antibiotics, antihistamines and aspirin) has been suggested as a link to sagittal and lambdoidal craniosynostosis.

Genetic influences

- At least 100 syndromes with craniosynostosis are known and more than half of these follow Mendelian patterns of inheritance. There is considerable variation in how the genes are expressed. This had led to confusion between syndromic and non-syndromic cases.
- Most cases of isolated or non-syndromic craniosynostosis are sporadic, regardless of which sutures are involved[8]. A genetic basis for some of these cases (mutations or polymorphisms) is suggested by variable familial histories, unequal sex ratios and increased recurrence risk for siblings of affected children.

7 Texas Birth Defects Monitoring Division. Birth defect risk factor series: Craniosynostosis. March 2002. www.tdh.state.tx.us/tbdmd/risk/risk-craniosynostosis.pdf Accessed 22/6/04

8 Harper, PS. Practical Genetic Counselling 5th Ed Butterworth Heinmann 1998

Focus on skeletal anomalies

Treatment services

Surgical treatment for craniosynostosis is designated as a national, highly specialised service. It is funded centrally by the Department of Health. Arrangements for the provision of these services are overseen by the National Specialist Commissioning Advisory Group (NSCAG). Four centres currently undertake surgery for craniosynostosis:

- Birmingham Children's Hospital NHS Trust
- Great Ormond Street Hospital for Children NHS Trust (London)
- Oxford Radcliffe Hospitals NHS Trust (The John Radcliffe Hospital)
- Royal Liverpool Children's NHS Trust (Alder Hey Hospital)

Trigonocephaly

In 2004, concern was raised about a possible excess of cases of trigonocephaly in North Wales. Investigation at the time was inconclusive but it was noted that reporting across Wales was variable and incomplete.

Trigonocephaly occurs as a result of premature fusion of the metopic suture which separates the two frontal bones in the centre of the forehead. The condition is characterised by a triangular shaped head and a pointed forehead. The deformity can vary from mild to severe and may be syndromic. It can resolve with time so cosmetic surgery may not be necessary, although other sources describe the required surgical procedures. One review of unstated quality suggests the condition comprises 4-10% of all cases of craniosynostosis[9]. A recently obtained abstract of one published study based on hospitalised patients in France estimated the "population" prevalence of this condition as 1 in 15,000 or 0.67 / 10,000 "children"[10]

Craniosynostosis in Wales

Following concern on the completeness of reporting of craniosynostosis in Wales, The Welsh Paediatric Surveillance Unit agreed to facilitate enhanced reporting for the two year period 2007 to 2008. A full report of the data collected in this way is being prepared. The following analyses of craniosynostosis take account of cases identified from the WPSU as well as through routine reporting to CARIS. The WPSU notifications led to a notable rise in reporting and previously noted regional differences in rates were considerably reduced.

Reporting from the Welsh Paediatric Surveillance Unit (WPSU)

The WPSU looks at conditions in children in Wales, which are considered too common for a UK study or too uncommon for a local hospital to perform. The WPSU uses a similar system to the orange card of the British Paediatric Surveillance Unit (BPSU).

Monthly green cards listing the conditions currently being studied are distributed by post or by email to consultant paediatricians and senior doctors working in Wales and covering an approximate child population of 560,000. A tick box system is used to identify if one of the conditions has been

9 Sheth, Raj D. Craniosynostosis. e-medicine website. Accessed 21/6/04.

10 Lajeunie E, Le Merrer M, Marchac D, Renier D. Syndromal and nonsyndromal primary trigonocephaly: analysis of a series of 237 patients. Am J Med Genet. 75(2):211-5 (13/1/1998) (Abstract only)

encountered in the preceding month. If so, the number of patients is entered into the appropriate box, and the patients details are recorded separately as a reminder for the doctor. The green card or email card is then returned to the new Surveillance Office with Cardiff and Vale NHS Trust at the University Hospital of Wales in Cardiff.

226 cases of craniosynostosis have been reported to CARIS with pregnancy ending in 1998-2008. The rates are calculated as:

- *Gross rate* (all cases, including TOP and fetal losses -226 cases) = 6.3/10,000 total births
- *Liveborn rate* (207 cases) = 5.8/10,000 livebirths

This means that the overall rate for Wales now corresponds to overall rates from published literature of around 5/10,000 total births.

General rates for trigonocephaly do appear to be higher than those reported in the literature with this form accounting for 14.6% of all cases of craniosynostosis and a gross rate of 0.92/10,000 births (Table 1). There is no demonstrable excess of cases in North Wales as was previously suggested (Table 2).

Of 40 cases reported through the WPSU, 31 (74%) were reported as having surgery planned or carried out, predominantly at Birmingham or Liverpool.

Table 1: Cases of craniosynostosis reported to CARIS, showing type of craniosynostosis and syndromic status

Type of craniosynostosis	Sutures affected	Syndromic status			total	Approx gross rate/ 10,000 total births
		chromosomal	syndromic	non syndromic		
brachycephaly	coronal bilateral	24 (80%)	6 (30.0%)	33 (18.8%)	**63 (27.9%)**	1.76
scaphocephaly	sagittal	0	1 (5.0%)	48 (27.3%)	**49 (21.7%)**	1.37
trigonocephaly	metopic	1 (3.3%)	2 (10%)	30 (17.0%)	**33 (14.6%)**	0.92
lambdoid	lambdoid	1 (3.3%)	1 (5.0%)	3(1.7%)	**5 (2.2%)**	0.14
turricephaly	coronal	0	1 (5.0%)	0	**1 (0.4%)**	0.03
multiple types		1 (3.3%)	3 (15.0%)	6 (3.4%)	**10 (4.4%)**	0.28
not specified		3 (10.0%)	6 (30.0%)	56 (31.8%)	**65 (28.8%)**	1.81
total		**30 (100%)**	**20 (100%)**	**176 (100%)**	**226 (100%)**	**6.3**

Focus on skeletal anomalies

Table 2: Cases of craniosynostosis reported to CARIS and WPSU, showing type of craniosynostosis and region of maternal residence in Wales

Type of craniosynostosis	Region of Wales			
	South East	Mid & West	North	Total
brachycephaly	24 (28.9%)	25 (26%)	14 (29.8%)	63 (27.9%)
scaphocephaly	23 (27.7%)	18 (18.8%)	8 (17.0%)	49 (21.7%)
trigonocephaly	5 (6.0%)	22 (22.9%)	6 (12.8%)	33 (14.6%)
lambdoid	1 (1.2%)	4 (4.2%)	0	5 (2.2%)
turricephaly	0	1 (1.0%)	0	1 (0.4%)
multiple types	6 (7.2%)	2 (2.1%)	2 (4.3%)	10 (4.4%)
not specified	24 (28.9%)	24 (25.0%)	17 (36.2%)	65 (28.8%)
Total	**83 (100%)**	**96 (100%)**	**47 (100%)**	**226 (100%)**

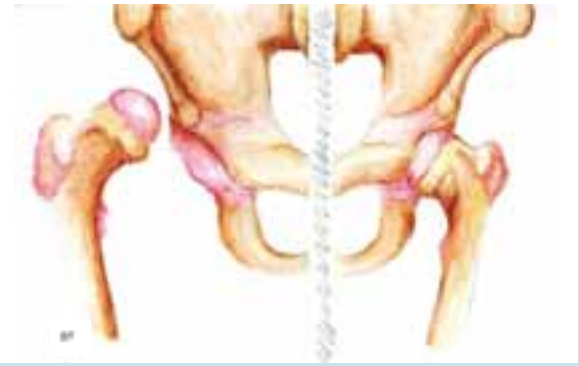
Developmental Dysplasia of Hip

Developmental dysplasia of the hip (DDH) was previously known as congenital dislocation of the hip (CDH). It is an abnormality in the hip joint that is usually present from birth.

The hip is a ball and socket joint. The ball is the head of the femur which fits into close contact with the socket, which is the acetabulum of the pelvis. In DDH, the normal anatomy of the hip joint does not develop,with an abnormality either in the shape of the head of the femur, the shape of the acetabulum, or the supporting structures around them. This prevents the normal close contact between the head of the femur. If mild, this results in subluxation of the hip. Dislocation occurs when the condition is so severe that there is no contact between the head of femur and acetabulum (figure 4).

DDH is usually present from birth and is more common in girls. When DDH is diagnosed and treated early in a young baby, the outcome is usually excellent. If treatment is delayed, the treatment is more complex and less successful.

About 2% of babies have some evidence of hip instability at birth, however by three months of age, only 1 to 2 per thousand have dislocated hips. Girls are more likely to be affected than boys, it is more common with increasing birth rank and the left hip is more often affected than the right.



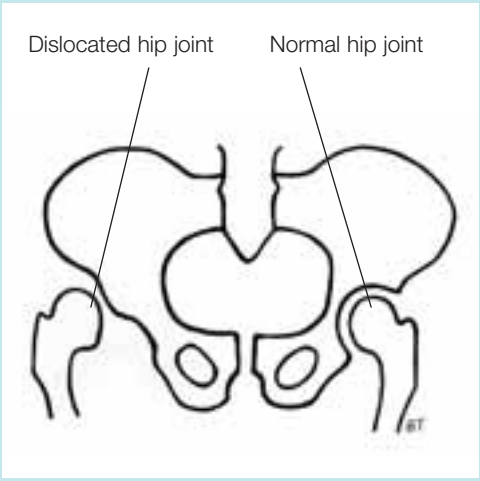


Figure 4: dislocated hip joint

Neonatal detection and treatment

Neonatal detection aims to reduce the number of late presentations of DDH. Unfortunately developmental dysplasia can occur in those who are noted to have a normal examination at birth[11].

Procedures to detect developmental dislocation of the hips are included in the physical examination of the newborn in Wales. Ultrasound assessment of the hips is done in a normal neonate if there are any risk factors including:

- breech presentation at delivery
- talipes or spinal abnormality
- family history of congenital dislocation of the hips

All of these procedures have limitations and diagnosis of this condition can be difficult.

Treatment aims to achieve a stable reduction of the dislocation and facilitate satisfactory further development of the hip. Options include:

- Pavlik hip harness or Von Rosen splint in a neonate
- Traction in an infant
- Open reduction +/- osteotomy or acetabuloplasty in an older child

Rates for surgery vary from 0.4 – 0.8 per 1,000 births depending on the centre.

Manual procedures to detect developmental dislocation of hips in neonates[11]

Hips are flexed to 90 degrees and instability detected by:

- Reduction of dislocation by abduction and forward pressure (Ortolani's test)
- Dislocation of hip by adduction and backward pressure (Barlow's test)

Developmental dislocation of the hip in Wales

In Wales from 1998 to 2008, 774 cases of developmental dysplasia were reported to CARIS. This gives an overall prevalence of 21.5 /10,000 live births or 2 cases per thousand live births. The ratio of male: female cases is 1:4. Of the total cases 298 were reported as having full dislocation (8.3 per 10,000 live births).These figures are in keeping with data published elsewhere.

11 Vane et al, Diagnosis and Management of Neonatal Hip Instability, J Paediatr Orthop vol 25, 3, 2005

Focus on skeletal anomalies

Limb abnormalities

Minor limb anomalies are common and can be associated with more severe defects and syndromes.

The most critical period of limb development is from 24-36 days after fertilisation (figure 5). This has been the conclusion from the thalidomide experience from 1957 to 1962 where the drug was given for morning sickness. Exposure of a pregnancy before day 33 to a powerful teratogen such as thalidomide may cause absence of limbs and hands. From day 34 to day 36, exposure can affect the digits causing absence or hypoplasia.

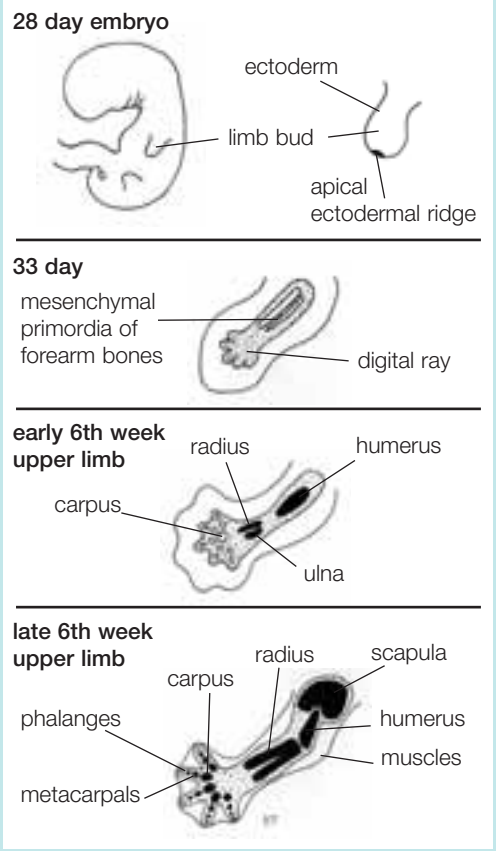


Figure 5: development of upper limb

Fingers and Toes

Adactyly – Absence of fingers and toes
Oligodactyly – Partial loss of fingers
Brachydactyly – Abnormally short fingers
Clinodactlyly – Inturning of the finger
Polydactyly – Extra digits (figure 6)
Pre axial – Extra digit on radial/tibial side
Post axial – Extra digit on ulnar/fibular side

Hands and Feet

Acheiria – Absence of hands (figure 7)
Acheiropody – Absence of hands and feet
Amelia – Absence of an extremity
Acromelia – Shortening of the hands/feet
Talipes – Club foot
Equinus – Extension of the foot
Apodia – Absence of the foot

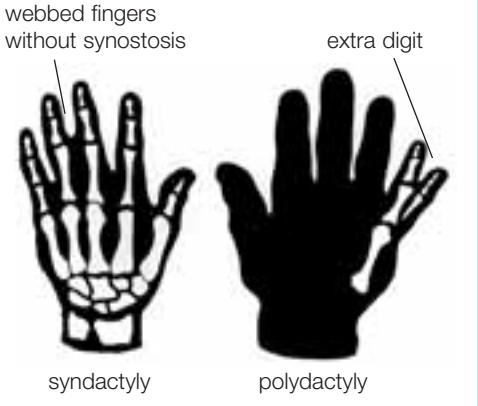


Figure 6

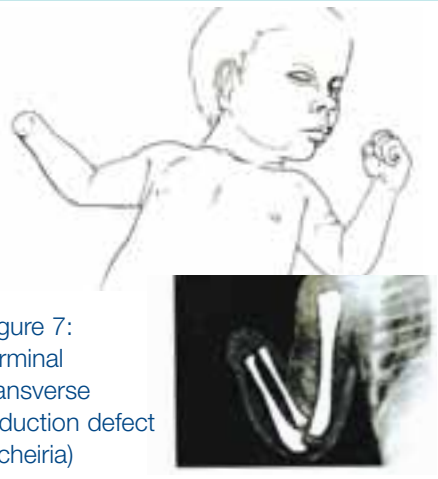


Figure 7: terminal transverse reduction defect (acheiria)

Arms and Legs

Camptomelia – Bent limb

Hemimelia – Absence of the distal portion of limb

Mesomelia – Shortening of the middle segment of limbs

Micromelia – Shortening of all the long bones

Phocomelia – Middle segment deficiency with normal proximal and distal segments

Limb deformities in Wales

Polydactyly and syndactyly are two of the most common limb deformities (figure 6).

- There were 455 cases of polydactyly reported in 1998 to 2008 (12.7 per 10,000 total births). The hands were affected about 2½ times more frequently than the feet.
- There were 339 reported cases of syndactyly (9.4 per 10,000 total births). Here, the toes were more commonly affected than the fingers. Skin webbing was more than twice as common as bony fusion.

Limb reduction anomalies

- 273 upper limb reduction defects were reported to CARIS, giving a prevalence of 7.6 per 10,000 total births. This includes six cases of amelia (0.2 per 10,000 total births and 13 cases of lobster claw (0.4 / 10,000 total births) (figure 8).
- 146 lower limb defects were also reported (4.1 per 10,000 total births). These included 6 cases of amelia (0.2 per 10,000 total births) and 4 cases of cleft foot (0.1 per 10,000 total births).

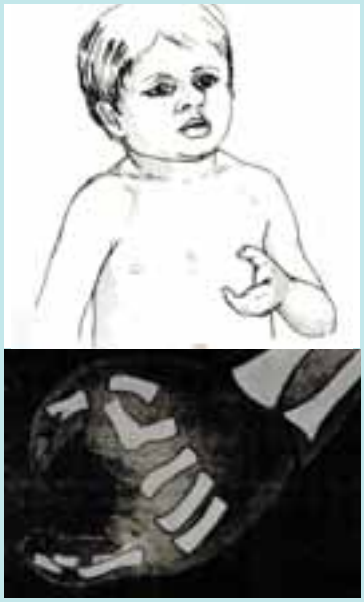


Figure 8: sketch and X-ray showing a lobster claw hand

Congenital Talipes Equinovarus[12]

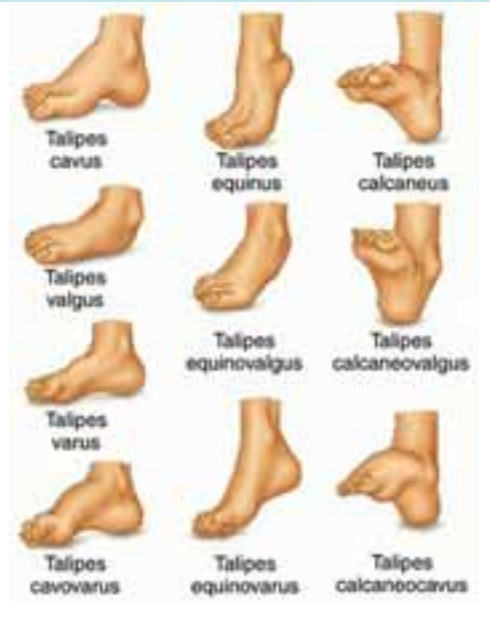
Congenital talipes equinovarus (club foot) is one of the more common congenital abnormalities affecting the lower limb occurring in about 1 in 1,000 births. It is twice as common in boys and those with a first degree relative affected are at significantly increased risk.

12 Congenital talipes equinovarus Siapkara and Duncan 2007 Journal of Bone and Joint Surgery 2007; 89-B:995-1000

Focus on skeletal anomalies

What is it?

The foot is adducted (bent inwards) and plantar inverted (toes pointing upwards) so that the sole of the foot points medially (inwards). Recent work has shown significant differences in limb length and girth width suggesting that CTEV may be part of a generalized disorder of development of the limb.



Positional talipes can be distinguished from CTEV if the deformity can be corrected by moving the limb passively.

Why does it happen?

Most studies suggest a genetic component with increasing rates seen in monozygotic twins. Other work has investigated seasonal variation with a suggestion of an intrauterine enterovirus infection, though this has not been confirmed.

Antenatal issues

Talipes can be diagnosed in the first trimester but is usually found later. Finding a view of the leg continuous with the foot in sagittal section on ultrasound is suggestive as this view is not possible in the normal fetus (figure 9).

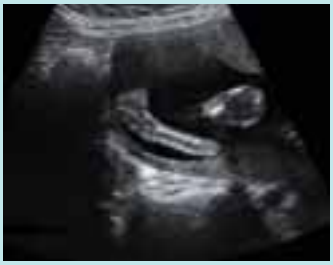


Figure 9: ultrasound scan showing talipes

In about 20% of cases, talipes is associated with other congenital abnormalities including spina bifida and can be a marker of chromosomal abnormalities or genetic syndromes. Associated anomalies seem to be more frequent with bilateral rather than unilateral talipes.

If other abnormalities are found on ultrasound then a karyotype is usually offered.

Management

Over the last 10 years the management of CTEV has changed with development of the Ponseti regime reducing the need for surgery.

Ponseti regime

This involves serial casting of the affected limb, changing the casts as frequently as every 5 days. Once the foot is corrected an abduction foot orthosis must be worn full time for 12 weeks, and then at night and nap time, up to the age of four years. The next step is to divide the Achilles tendon and transfer the tibialis anterior tendon. Results have been good and in one study only 6% needed further surgery.

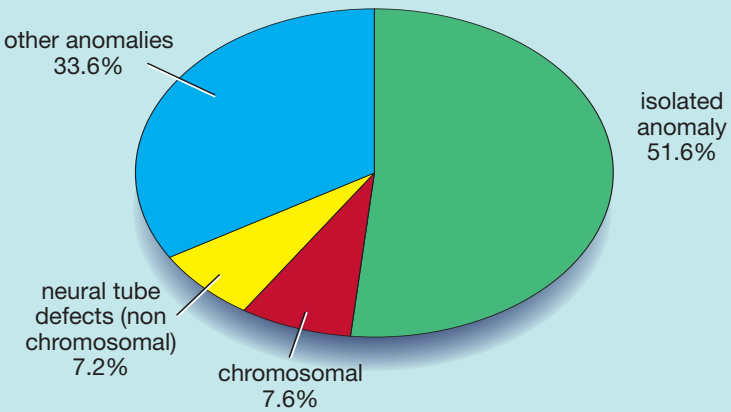
Surgery

Most centres reserve surgery for recurrent or resistant deformities. Usually this involves division of the fibrous knot which includes tissues deep to the peroneal tendons.

Talipes in Wales

CARIS has received reports of 816 cases of talipes (gross rate of 22.7 / 10,000 total births). Of these, 601 were liveborn (liveborn rate of 16.7 / 10,000 or 1 in 625 live births). Just over half of these occurred as isolated findings whilst about 40% were associated with other anomalies including neural tube defects (figure 10). These figures are higher than would be expected from the literature. Great care is taken by CARIS to try and exclude positional talipes, however it is possible that some over-reporting of this condition has occurred.

Figure 10: talipes cases 1998-2008 by type



Sirenomelia

The sirens in Homer's Odyssey had mermaid like lower extremities and this has given the name to the condition which is characterized by fusion of the legs.

Sirenomelia occurs when an abnormal single umbilical artery causes diversion of blood from the lower body with resulting fusion of the lower limbs and associated lower body abnormalities. These defects occur before the 23rd day of embryological development. Cases may be live born but the condition is usually ultimately fatal.

Fusion of lower limbs can result in:

- single tibia and femur with absent feet, or
- two each of femur, tibia and fibula with a single foot, or
- fused legs with two feet

Focus on skeletal anomalies

Associated abnormalities can include:

- renal agenesis
- absence of the bladder
- absence of sacrum and vertebral defects
- imperforate anus and absence of the rectum
- absence of external and internal genitalia

A single umbilical artery is a relatively common finding but development of sirenomelia is rare. The condition is more common in male fetuses (2.7 to 1) and in one of monozygotic twins. It has been suggested that a recent cluster of sirenomelia in Cali, Colombia, has been linked to the toxic waste of a landfill site contaminating the town's water supply[13].

The condition is self evident at birth or on antenatal ultrasound where appearances include:

- single or fused lower limb
- spine appears shortened
- absence of sacral curve
- renal agenesis
- single umbilical artery and possibly oligohydramnios

The prevalence of sirenomalia is given as 1 in 60,000 to 1 in 100,000 total births. In eleven years of reporting in Wales, twelve cases have been identified, giving an overall prevalence of 1 in 29,952 total births. This figure appears considerably higher than expected and has been reported to the International Clearing House for Birth Defects. However, numbers are small and just a few cases can make a big difference to reported rates.

Of the Welsh cases:

- 9 cases (75%) were detected antenatally. The others were fetal losses before the fetal anomaly scan.
- 2 cases were detected on dating scan (12-14 weeks) and the other 7 cases were detected at the anomaly scan between 16 and 23 weeks gestation.
- 8 cases ended in termination of pregnancy and 3 were spontaneous fetal losses between 14 and 17 weeks gestation. The remaining case was liveborn as part of a twin pregnancy but died the same day.
- there is no excess of male cases

Caudal Regression

Caudal regression syndrome is a rare disorder characterised by abnormal development of the lower spinal tract before the 23rd day of embryological development. This defect can be mistaken for sirenomelia and once was thought to be part of the same spectrum. Nowadays they are believed to be separate entities. The exact cause of caudal regression is unknown but shows a strong association with maternal diabetes. The outcome is generally poor and survivors may need extensive urological or orthopaedic treatment.

A wide range of abnormalities may occur including

- incomplete development of the sacrum and lumbar vertebrae
- disruption of the distal spinal cord causing neurological impairment
- limited growth of legs caused by lack of movement
- incontinence due to neurological loss

Associated anomalies include:

- renal agenesis
- imperforate anus

13 Clusters of sirenomelia in South America : Orioli et al, Birth Defects Res A Clin Mol Teratol 2009; 85:112-8

- cleft lip and palate
- microcephaly
- meningomyelocele

Diagnosis is usually by antenatal ultrasound, where typical findings include:

- spine appears shortened
- normal sacral curve lost
- lower limbs may be hypoplastic
- bladder may be large
- two umbilical arteries and normal liquor volume

Published prevalence rates are 1in 40,000 to 1 in 100,000 births. In Wales for the 11 years 1998-2008 there have been three cases, giving a gross prevalence of 1 in 119,810 total births. Maternal diabetes has not been reported in any of these cases. Two cases ended in termination and the other case was a live birth.

Achondroplasia

Achondroplasia is a genetic disorder of bone growth in which cartilage is not converted to bone at the growth plates, particularly of the long bones. It is the most common cause of the resulting characteristic appearance of abnormally short stature with disproportionally short limbs. The head is also characteristically shaped with the base of the skull poorly formed (from cartilage) whilst the vault forms normally (from membranes). Adult mean height is 132cm in males and 123cm in females. The condition is inherited as an autosomal dominant condition but 80% of cases are due to new genetic mutations.

The outlook for people with achondroplasia is generally good, with normal chances of intelligence, lifespan and fertility and no increased risk of osteoarthritis. Apart from any difficulties associated with extreme short stature, complications may include:

- hydrocephalus due to lack of space in the posterior fossa
- intervertebral disc degeneration or herniation
- 5-10% lifetime risk for spinal cord compression due to narrow vertebral arches

Treatment with growth hormone to improve adult height has been proposed but remains controversial as it can cause increased disproportion.

The prevalence of achondroplasia is estimated to range from about 1 in 10,000 births in Latin America to about 1 in 77,000 in Denmark. An average figure worldwide is approximately 1 in 25,000 births.

In Wales, 15 cases of achondroplasia have been reported to CARIS for 1998 – 2008. This gives a gross prevalence of 0.4 per 10,000 or about 1 in 24,000 total births.

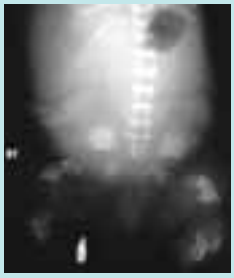


Figure 11: X-ray showing bulbous short femurs

Clinical features of achondroplasia

Recognisable at birth

Shortening and bowing of limbs

Bone ends are bulbous (see figure 11)

Feet and hands are short and broad

Head appears large

Frontal bossing, small face, depressed nasal bridge, prominent jaw

Mildly hypotonic with slow early motor progress

NHS fetal anomaly screening programme: relevance to Wales

Dr Colin Davies, Consultant Radiologist, Royal Glamorgan Hospital

Screening for fetal anomalies by an ultrasound scan has been in place since the 1970s and evolved on an ad hoc basis in most maternity units in both England and Wales. Originally based in specialised hospitals, increasing availability of technology and experience has meant that by 2002, most units provided some form of anomaly screening.

Anomaly scan

In England in 2002 the National Screening Committee commissioned a survey of antenatal screening services and as a result, the Fetal Anomaly Ultrasound Screening Programme was implemented. As part of this, the Fetal Anomaly Subgroup (FASG) was set up to establish national standards and a new menu for the 18 – 20 week anomaly scan. Much of the latter work was based on the existing RCOG 2000 Guidance.

These existing standards were scrutinised one by one and the rationale for their requirement was examined and their purpose validated. The intention was to make the scan more focused on conditions that were significant, because they were fatal, associated with morbidity or required immediate post-natal support.

The RCOG document suggested for example that a basic scan should not routinely include cardiac outflow tracts but did consider it important to clearly identify all three bones in all limbs. The FASG considered this carefully and concluded that time would be better spent focusing on cardiac abnormalities rather than a non lethal isolated limb problem. This is because a cardiac problem may require immediate post-natal support which could only be provided if antenatal detection had happened. The time saved by not having to confirm three bones in all limbs would therefore be better spent on cardiac outflow tract screening.

This rationale was applied to each element of the basic scan and the new template has now been created. The 18 – 20 week anomaly scan base menu is an integral part of a National Standards for England document that has been produced by the NHS Fetal Anomaly Screening Programme, due for publication in January 2010 and implementation from April 2010. All areas of this significant document have been consulted on widely within the service. Although aspects of the base menu have been found to be controversial during the consultation process, the rationale which has underpinned the whole of the review process has convinced the most hardened critics of the validity of the proposed changes.

This set of national standards applies to England alone. Within Wales, Antenatal Screening Wales has recently been consulting on its own set of standards, policies and protocols which in spirit and detail are not a great deal different from the English standards. In Wales we have previously used the RCOG 2000 guidance as our standard base menu and it therefore seems logical that following appropriate consultation, we will implement the new base menu guidance and incorporate it into our own national standards.

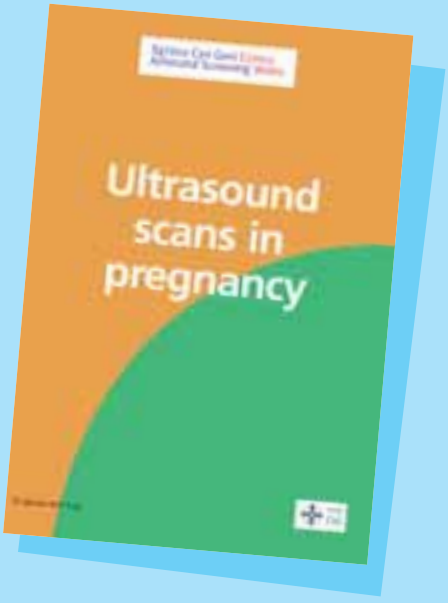
Soft markers

The FASG was also asked to review the contentious "soft marker" issue. Following much consultation and a multi-professional open discussion meeting in London, consensus has been reached which concurs with the decision taken by professionals within Wales in 2004. In fact the impressive data provided by CARIS and the Welsh Cytogenetic Service on detection rates since 2004 and presented at the London meeting was an important factor in acceptance of the proposed changes. The new guidance from England is virtually identical to that originally proposed by Antenatal Screening Wales in 2004 and specifically advises moving from the term "soft marker". The terms "normal variant" or "abnormality" are preferred i.e. echogenic cardiac focus is a normal variant and echogenic bowel is an abnormality. Conditions classed as abnormalities include thickened nuchal fold, ventriculomegaly and renal pelvic dilatation and these should be considered for further assessment. Once again this mirrors the advice already provided in Wales in 2004 and is a reflection of the proactive approach and high standards of antenatal screening provided by professionals in Wales, supported and guided by Antenatal Screening Wales.

Dr Colin Davies

Ultrasound Advisor to Antenatal Screening Wales

FASG member



CARIS champions

Hospital/Area	CARIS Lead in Paediatrics	CARIS Lead in Obstetrics	CARIS Coordinators
Bronglais	John Williams	Angela Hamon	Jo Mylum
Neath Port Talbot/ Princess of Wales	Katherine Creese	Sushama Hemmadi	Elaine Griffiths & Diane Evans
Neville Hall	Tom Williams	Delyth Rich	Tim Watkins
Powys	Chris Vulliamy	(not applicable)	Val Hester & Sue Tudor (Welshpool) Carole Stanley (Newtown)
Prince Charles	David Deekollu	Jonathan Rogers	Kindry Dennett
Royal Glamorgan	Jay Natarajan	Jonathan Pembridge	Nicola Ralph
Royal Gwent / Caerphilly Miners	Vera Antao	Anju Kumar	Tim Watkins
Singleton	Geraint Morris	Marsham Moselhi	Helen Jenkins / Val Vye
UHW / Llandough	Jenny Calvert	(awaiting confirmation)	Danielle Richards
West Wales General	(awaiting confirmation)	Roopam Goel	Anya Evans
Withybush	Devasettihalli Appana	Chris Overton	Julie York
Wrexham	Paveen Jauhai	Bid Kumar	Sue Yorwerth
Ysbyty Glan Clwyd	Ian Barnard	Maggie Armstrong	Jenny Butters
Ysbyty Gwynedd	Mair Parry	Mohammed Galal	Jackie Stockton & Sian Pugh-Davies